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SYSTEMATIC REVIEW IN CARDIOLOGY

A systematic review of Randomized Controlled Trials about some non-pharmacological interventions for treatment of hypertension: Physical exercise, sodium restriction, weight and alcohol use reduction

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Abstract

Introduction: Aim of this study was to systematically review available evidence to analyse how effective are some non-pharmacological interventions such as physical exercise, sodium restriction, weight reduction and alcohol reduction in the management of hypertension and to study which of them produce the greatest reduction in blood pressure.

Method: A systematic literature search was carried out on Pubmed, Medline, EBSCO and EMBASE, by using several key terms and following the PRISMA statement. Original papers and randomized clinical trials, published in English between 1988 and 2010 and regarding

hypertensive individuals as participants were included. The narrative synthesis system of analysis was used and the Revman 5.0 software was used to carry out heterogeneity analysis.

Results: A total of 51 RCT on salt restriction (*n* = 11, 22%), weight loss (*n* = 6, 12%), alcohol reduction (*n* = 7, 14%), physical exercise (*n* = 15, 29%), or a combination of these intervention modalities (*n* = 12, 23%) were included in our review. 94% of them reported a significant improvement on blood pressure following these interventions, whereas 6% of them reported a statistically non-significant improvement. None of the papers reported a post-intervention deterioration. Salt restriction was found to give the greatest reduction in blood pressure. However, significant heterogeneity exists among the results of the papers reviewed in our study.

Discussion and Conclusions: Our findings confirm that physical exercise, sodium restriction, weight and alcohol use reduction are four non-pharmacological interventions effective in the control of hypertension. As they involve lifestyle modification, policy interventions for primary prevention are recommended in this area.

Riassunto

Introduzione: L'obiettivo di questo studio è stato quello di sottoporre a revisione sistematica l'evidenza disponibile relativa all'efficacia di alcuni interventi non farmacologici per il trattamento dell'ipertensione arteriosa (esercizio fisico, dieta iposodica, calo ponderale e riduzione del consumo alcolico) e di stabilire quale di essi produca la maggiore riduzione dei livelli di pressione arteriosa.

Metodi: Una ricerca sistematica di letteratura è stata effettuata su Pubmed, Medline, EBSCO ed EMBASE, attraverso l'uso di parole chiave e seguendo il Prisma Statement. I lavori di ricerca originali ed i trial climici randomizzati (RCT), pubblicati in inglese tra il 1988 ed il 2010 con individui ipertesi come partecipanti, sono stati inclusi. E' stato adottato un sistema di analisi per la sintesi narrativa ed il software Revman 5.0 software è stato usato per condurre l'analisi di eterogeneità.

Risultati: Un totale di 51 RCT su restrizione sodica (*n* = 11, 22%), calo ponderale (*n* = 6, 12%), riduzione del consumo alcolico (*n* = 7, 14%), esercizio fisico (*n* = 15, 29%), o una combinazione di queste modalità di intervento (*n* = 12, 23%) sono stati inclusi nella nostra revisione. Il 94% di essi ha riportato un miglioramento significativo della pressione arteriosa seguendo questi interventi, mentre il 6% degli studi non ha evidenziato alcun miglioramento statisticamente significativo. Nessuno di essi ha evidenziato un peggioramento dopo l'intervento. La restrizione sodica è stato il tipo di intervento che ha determinato la maggiore riduzione dei livelli di pressione arteriosa. Tuttavia, esiste una significativa eterogeneità tra i risultati dei lavori revisionati nel nostro studio.

Discussione e Conclusioni: I nostri risultati confermano che l'esercizio fisico, la restrizione sodica, il calo ponderale e la riduzione del consumo alcolico sono quattro terapie non farmacologiche efficaci nel controllo dell'ipertensione arteriosa. Dal momento che essi implicano un cambiamento nello stile di vita, interventi pubblici di prevenzione primaria sono raccomandati in questo settore.

KEY WORDS: Our systematic review showed that some non-pharmacological interventions such as physical exercise, weight reduction, alcohol use reduction and, especially sodium restriction are essential in the management of hypertension. Therefore, policy interventions for lifestyle modifications are recommended in this area.

Competing interests: none declared

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INTRODUCTION

Globally, hypertension is now amongst the most prevalent medical conditions and forms one of the most important modifiable risk factors for cardiovascular diseases and mortality [1]. This disease is common, asymptomatic, readily detectable, and usually easily treatable. However, it often leads to lethal complication if left untreated [2]. The definition of hypertension has been evolving over the years, more recently, hypertension has been defined as 'the presence of sustained blood pressure of 140/90mmHg or above in an individual or the use of antihypertensive medication by an individual' [3]. High blood pressure has now been noted to be a trait as opposed to a specific disease and represents a quantitative rather than a qualitative deviation from normal, and therefore any definition of hypertension is arbitrary [4]. However, a useful and practical definition for hypertension is the level of blood pressure at which the benefits of treatment outweighs the costs and hazards; this level as evidence has shown to be so far 140/90mmHg [5].

Hypertension in the uncomplicated state is generally asymptomatic with symptoms like headache and dizziness, which is non-specific occurring only in a few individuals [6]. While being asymptomatic for many years in an affected individual, hypertension if left untreated or uncontrolled can lead to life-threatening complications including end-organ damage [7]. Indeed, the World Health Organisation estimates that about 62% of all cerebrovascular disease cases and 49% of ischaemic heart disease cases are attributable to hypertension [8].

The goal of treatment of hypertension is to prevent the long-term morbidity and mortality; the method and aggressiveness of treatment depends on several factors including presence of co-morbidities that often require tighter blood pressure control [9]. The reduction of blood pressure in hypertension has been noted to be associated with about 40% decrease in the risk of stroke and about 15% decrease in the risk of myocardial infarction [10].

Hypertension can be managed by non-pharmacological alone or as compliment to pharmacological interventions [11]. Non-pharmacological interventions can include weight reduction, dietary approach, physical activity (exercise), alcohol reduction, smoking cessation, stress management, sodium restriction. However, the interventions for which extensive studies have been carried out on their effectiveness in the treatment of hypertension include weight reduction, sodium restriction, exercise and alcohol use reduction [12]. These are those interventions whose efficacy in the treatment of hypertension is to be reviewed in this study.

The burden of disease

The prevalence of hypertension was placed at 26.4% of the world adult population with a prediction of increase of 60% by 2025 [1]. According to World Health Organisation [13], cardiovascular diseases, of which hypertension is the major risk factor, are responsible for one-third of global deaths and cardiovascular disease now is a leading and increasing contributor to the global burden of disease. Hypertension causes one in every 8 deaths making it the third leading cause of mortality in the world with about four million people dying annually as a direct result of hypertension [14]. Lawes et al [15] reports that hypertension is responsible for 7.6 million premature deaths worldwide, consisting about 13.5% of the global total and 92 million disability-adjusted life years (DALY's), which consists 6% of the world's total. Hypertension carries a huge economic burden on the already overstressed economies of the world particularly in the developing countries [16]. In the UK, in 2001 it cost the National Health Service about 840 million pounds, which form over 15% of total annual cost of all primary care drugs, to treat hypertension [17].

Background

Non-pharmacological therapy provides expanded options for blood pressure control in the treatment of hypertension. Interests in pharmacological interventions in hypertension management dates back to several decades and a large number of clinical trials have been carried out on a varied number of them including exercise, sodium restriction, alcohol reduction and weight reduction [18]. The Joint National Committee (JNC) on Detection, Evaluation and Treatment of High Blood Pressure (1988) in advising that the benefits of drug agents in the reduction of blood pressure should be balanced against the potential for long-term adverse effects by these drugs, recommended weight reduction, alcohol reduction and sodium restriction as non-pharmacological modalities to be incorporated in hypertension treatment programme [19]. Since 1988, exercise or physical activity was included among the JNC recommended non-pharmacological measures in hypertension treatment [20]. These recommendations notwithstanding, studies are still going on to analyse efficacy of these interventions.

Weight loss induced by caloric restriction lowers arterial blood pressure at all levels particularly in overweight patients and has beneficial effects in other diseases like diabetes [19]. The Framingham study reported reduction in blood pressure to be among the several factors associated with weight reduction [21], adding to the observation that blood pressure rarely increases with age in populations in which body weight does not increase with age [22]. A Cochrane Library review reported that an average weight loss in the range of 4-8% of body weight corresponds to a fall of 3 mmHg systolic blood pressure [23]. Several biological mechanisms may explain the link between overweight and blood pressure, but the most prominent is the over-reactivity of the renin angiotensin-aldosterone system. It has been shown that the circulating levels of renin activity and aldosterone are higher in obese than in non-obese and overactivity of this system is lowered by a reduction in body weight [24].

The quantity of sodium in the diet is another important determinant of blood pressure level and this association is discrete and progressive with no apparent threshold, hence restricting sodium intake is one important non-pharmacological intervention in treating hypertension [25]. In hypertension, the intake of salt by an individual shows a linear relationship with blood pressure level and decreased sodium ingestion to less than 100 mmol per day, potentially enhances blood pressure control in hypertensive individuals [26]. In a meta-analysis conducted on randomized controlled trials [27], Geleinjnse et al have demonstrated an average reduction in blood pressure levels of over 2.5 mmHg. Sodium restriction is believed to lower blood pressure by inducing volume contraction within the circulatory system [28].

Reduction in alcohol consumption is an important non-pharmacological measure in the treatment of hypertension among alcohol drinkers [8]. Alcohol has been demonstrated to exert a significant pressor effect on blood pressure even in small quantities [29]. Meta-analysis of randomised controlled trials by Xin et al [30] observed that decrease in intake of alcohol was linked to a

significant 3.3 mmHg decrease in systolic blood pressure and 2 mmHg decrease in diastolic blood pressure. Several pathogenic pathways have been proposed in the biological mechanism of alcohol effect on blood pressure with the increase in catecholamine excretion being among the most prominent [31].

Engaging in regular aerobic exercise is an essential component of the non-pharmacological therapy for treatment of hypertension [12]. Increase in aerobic physical activities such as brisk walking, jogging, swimming or cycling has been shown to reduce blood pressure significantly in hypertensive individuals. This reduction has been demonstrated to be independent of concomitant weight loss [32]. Meta-analysis of randomized controlled trials by Whelton et al [32] showed that performing aerobic exercises caused a net reduction in blood pressure of 3.8 mmHg systolic and 2.6 mmHg diastolic pressure compared to non-exercising control group. It is recommended that people engage exercise for a minimum of 30 minutes on at least 3 days per week to ensure sustained blood pressure control in hypertension [33]. The mechanism of exercise-induced reduction in blood pressure is unclear but may be associated with a decrease in peripheral vascular resistance and an increase in cardiac output [34].

These four modalities are becoming widely recommended strategies in the non-pharmacological control of blood pressure in hypertension, however there are still grey areas as to their effectiveness and which among them is most effective [35]. Indeed, few long-term studies on the effectiveness of these non-drug therapies have been carried out [36] and the efficacy of these interventions are still being evaluated, as it is especially necessary to ensure that offering these interventions to patients does not amount to disservice [37].

This review aimed to evaluate available evidence pertaining to the effectiveness of some selected non-pharmacological interventions in the management of hypertension, assessing which of them produces the greatest reduction in blood pressure. The evaluation of the efficacy of these interventions is expected to contribute to the existing body of knowledge by generating research-based information and recommendations in the control of the rising global burden of hypertension.

METHODOLOGY

Research design

The Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) statement was followed in this review. Systematic literature review was chosen as this study design may offer the best platform for an adequate analysis of non-pharmacological interventions in hypertension, thus providing evidence-based support for their implementation by stakeholders

and policymakers. This review was limited to some of the existing non-pharmacological treatments of hypertension, which are covered by extensive studies in scientific literature [18].

The study objective

The aim of this systematic literature review was to assess the available evidence regarding the effectiveness of some non-pharmacological interventions in the control of hypertension among adult hypertensive patients aged 18 years and older to investigate which of these interventions produce the greatest reduction in blood pressure.

Research questions

1. How effective are non-pharmacological interventions (physical exercise, sodium restriction, weight reduction and alcohol reduction) in the management of hypertension?
2. Which of the above non-pharmacological interventions produces the greatest reduction in blood pressure?

Outcome variables

Primary outcome measures:

- Effects of physical exercise on blood pressure
- Effects of weight reduction on blood pressure
- Effects of alcohol use reduction on blood pressure
- Effects of sodium restriction on blood pressure

Secondary outcome measure:

- Level of reduction of blood pressure produced by each of these interventions.

Inclusion criteria

- Studies which used hypertensive individuals as participants;
- Original studies including Randomized controlled trials (RCT), which reported on effects of the listed non-pharmacological interventions on blood pressure either alone or in their combinations;
- Studies in which participants were aged 18 years and older;
- Studies published in English language;

- Studies published between 1988 and 2010.

Exclusion criteria

- Papers different than reports of primary research;
- Studies different than original research and RCT;
- Studies including individuals under 18 years;
- Studies including individuals that were not affected by hypertension;
- Studies published in languages other than the English language;
- Studies published before 1988 and after 2010.

Sources of information

- EMBASE
- Medline
- EBSCO
- Pubmed

Search strategies

An extensive search for Randomized Controlled Trials, in order to inform the units of analysis for this work was done on the Pubmed, Medline, EMBASE, EBSCO electronic databases. The NHS library (Health Information Resources) available from its website at link www.library.nhs.uk., was used to access and search the Medline and Embase electronic databases simultaneously, while Pubmed and EBSCO were searched separately. The search duration for this study lasted from June through to July 2010. The search strategy used was developed using the Cochrane Review search strategy [38]. Details of the steps taken during the search as they were carried out are presented below.

The key terms for the search process were extracted from the JNC VII guidelines for the treatment of hypertension and include the words ‘Hypertension’, ‘non-pharmacological

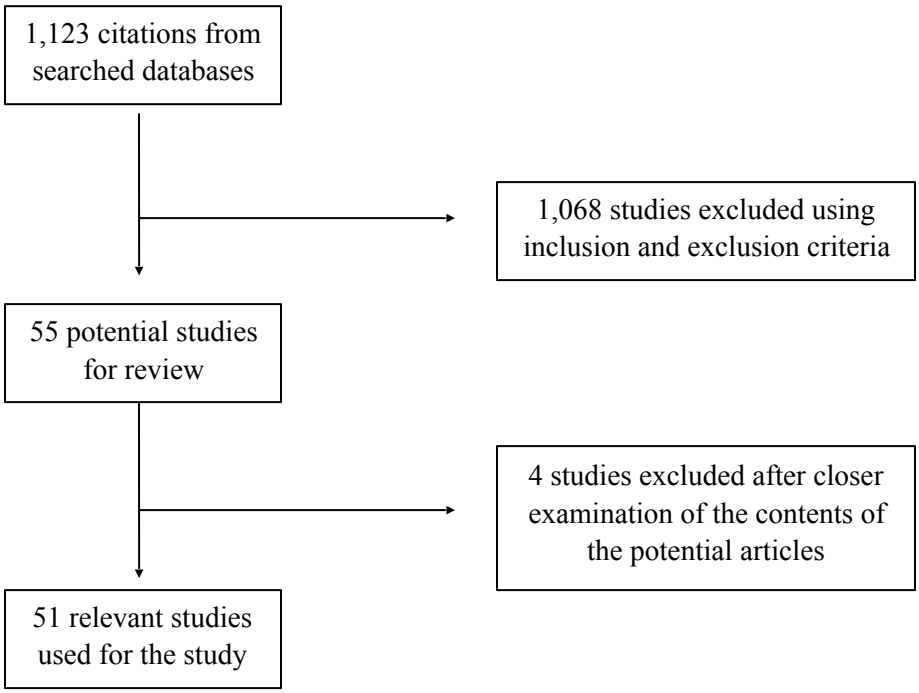
intervention', 'exercise', 'alcohol consumption', 'sodium restricted diet' and 'weight reduction'. Synonyms for these key words were identified and expanded using MESH-database to include: 'lifestyle modification', 'exercise therapy', 'alcohol drinking', 'salt reduction', 'sodium reduction', and 'weight loss'. Individual searches were done using the various key words and the synonyms both as 'subject headings' and as 'text words'. A search was also done on the key word 'effective'. The results obtained from these rigorous searches were combined using the Boolean operators 'AND/OR', while linking the searches to studies coded as Randomised Controlled Trial on the databases. Other limits applied to the searches included age (18 and above), English language, and publication year of 1988-2010. The Medline/Embase search using the NHS Library website yielded 683 studies. Separate searches of the databases were done on the key terms as follows; 'hypertension' yielded 22,6059 studies, 'exercise' yielded 139,754 studies, 'exercise therapy' gave 20,149 studies, 'alcohol consumption' gave 21,145 citations, 'alcohol drinking' yielded 41,662, 'sodium restricted diet' 5,105 studies, 'weight reduction' gave 5,360 studies, while 'effective' gave 90,531 studies. These obtained results were combined using the Boolean operators 'OR/AND' to yield 2,093 citations. The application of the limits such as Randomised Controlled Trials, adult aged 18 and above, English language and year of publication 1988-2010 yielded the 683 studies from this search strategy.

The year 1988 was chosen for the study because it was the year in which JNC [20] first included all the modalities of intervention being assessed in this review among their recommended non-pharmacological intervention in hypertension treatment.

This extensive and systematic search yielded a total of 1,123 papers, 683 studies from Medline/ EMBASE, 107 studies from EBSCO, and 333 from Pubmed. An in-depth review of the 1,123 potential review articles with the application of the pre-stated inclusion and exclusion criteria decreased the number of studies to a total of 55. Explosion of search terms used for this search were confirmed not to have raised the number of relevant papers when pilot searches were carried out with the explosion option.

Four studies were excluded after a closer examination of the contents of the selected search papers, because two articles were on hypertensive diabetes, another was a repetition of already selected article in a different title, while the other one compared individual and group counselling treatment on dietary salt restrictions.

Flow chart of the summary search conducted



Data extraction

The selected articles that formed the units of analysis for this review were further scrutinized to extract the relevant information required. In order to form a systematic approach and comprehensive representation in the evaluation of the data extracted from the various articles, a data extraction template created using Microsoft Excel was used to obtain required information from the units of analysis with the headings as shown below:

- Name of the authors, and title of the study
- Date of publication and name of journal
- Study setting and location
- Study design
- Randomisation
- Blinding
- Sample size

- Duration of study
- Intervention examined and the control
- Sample basic characteristics
- Outcome variable(s) and their values
- Duration of follow-up if any
- Statistical analysis
- Attrition and possible effect on outcome
- Authors interpretation of results
- Conclusion and any additional relevant information

Data analysis and role of authors

The narrative synthesis system of analysis was used for this study. This method of analysis was chosen due to variations existing among the sub-groups of research papers used in this review [39]. It followed the guideline named 'Guidance on the conduct of narrative synthesis in systematic reviews' by Popay et al [40]. The first author of this review carried out the search, data extraction, analysis and reporting of findings and discussion. The second author supervised the process and approved the final manuscript for publication. Both authors were in agreement to be accountable for the contents of the work.

Heterogeneity analysis

The Revman 5.0 software was used to carry out heterogeneity analysis and a forest plot was used to generate pictorial representation including the consistency or variation in the results extracted from the studies and show their degree of comparability. Clinical heterogeneity of the studies was examined and statistical heterogeneity analysis was carried out at subgroup level on the different modalities of intervention using the sample population, mean differences and standard deviations.

The groups were as follows:

- Weight control *versus* control group;
- Salt restriction *versus* control group;
- Physical exercise *versus* control group;

- Alcohol use reduction *versus* control group.

The degree of heterogeneity in these groups of intervention was assessed through the I^2 test, the Chi square test and the degree of freedom. The I^2 test value of 50% was considered as the threshold in this study, as adopted by the Cochrane collaboration [38]. An I^2 test value of above 50% was considered as high heterogeneity level and random effect model, being less sensitive, was used for analysis. While the more sensitive fixed effect model was used for analysis for the I^2 test value of less than 50%, which is of low heterogeneity [41], final judgments of presence of heterogeneity was made after considering the statistical significance as $P < 0.05$ value.

Sensitivity analysis

The presence of publication bias in this review was checked by carrying out a sensitivity analysis on the units of our research. Funnel plot was generated using similar data used in the heterogeneity analysis. The four reserved papers excluded from this study were collected and analysed with their data used together with the data from the included papers on a funnel plot, and their effect on the funnel plot observed. The funnel plot generated before and after adding excluded papers was assessed for symmetry or asymmetry to identify any bias. This tested the robustness of this review and assessed the criteria used in the selection of the units of analysis.

Quality assessment

The quality assessment of the articles used for this review was done using the criteria elaborated in the 'extending the Consolidated Standards of Reporting Trials (CONSORT) statement to Randomised Trials of Non-pharmacologic Treatment' by Boutron et al [42]. The CONSORT check list and scoring criteria used are as showed in Table 1.

Table 1. Quality Assessment Scoring System.

No	Check List Item	Score	Scoring System
1	Identification as RCT in Abstract	10	Present = 10, Absent = 0
2	Intervention and comparator in Abstract	10	All = 10, Some = 5, None = 0
3	Inclusion and exclusion criteria	10	All = 10, Either = 5, None = 0
4	Randomisation method explanation	10	Present = 10, Absent = 0
5	Intervention and Comparator details	10	Both = 10, Either = 5, None = 0
6	Participants' Flow Chart	10	Present = 10, Absent = 0
7	Baseline Characteristics	10	All = 10, Either = 5, None = 0

8	Number of participants starting study groups	10	All = 10, Either = 5, None = 0
9	Number of participants completing study	10	All = 10, Either = 5, None = 0
10	Limitation of study	10	Present = 10, Absent = 0

For the purpose of this analysis, points scored by individual articles were pooled into five bands; A, B, C, D, and E with the following interpretation:

A = 70 - 100 (High quality)

B = 60 < 70 (Good quality)

C = 50 < 60 (Moderate quality)

D = 40 < 50 (Fair quality)

E = 0 < 40 (Poor quality)

RESULTS

Availability of information

A total of 55 studies from the 1,123 citations obtained from the searches of peer reviewed articles, initially qualified for inclusion in this review. Four papers were excluded bringing the total articles used for this study to 51. Two of the 4 excluded articles carried out their work on diabetic hypertensive individuals, while one of the articles compared group counseling and individual counseling treatment of salt restricted diet. The fourth article was a duplicate of an already selected paper for the review on a different title. The excluded articles, however, were used afterly in the sensitivity analysis.

Findings

Out of the 51 reviewed papers in this work, 15 studies (29%) tested the effect of exercise on blood pressure control, 11 studies (22%) were on effect of sodium restriction, 7 studies (14%) were on effect of alcohol reduction and 6 studies (12%) tested the effect of weight reduction, while 12 (23%) studies were on effects of combinations of these interventions. They all were randomized controlled trials. The data from the units of analysis of this review showed that majority of the papers reported a statistically significant improvement in the blood pressure control for various interventions as measured by post intervention change in blood pressure level

of the participants. However, studies by Cooper et al (study 13) demonstrating effect of physical exercise, Little et al (study 20) showing the effect of diet, and William et al (study 24) looking at the effect of alcohol on the effects of blood pressure, reported a statistically non-significant improvement in blood pressure in their work and none of these reviewed papers reported a post-intervention increase in blood pressure.

Effects of physical exercise

15 studies (studies 2, 3, 10, 13, 17, 25, 30, 31, 32, 39, 41, 42, 43, 44 and 48) analysed the effect of physical exercise intervention on the control of blood pressure among adult hypertensive patients. Various forms of physical exercise were used in different studies including brisk walking by Kerrie et al (study 2), Seals et al (study 30), Douglas and Reiling (study 32) and Rodriguez et al (study 41); shadow boxing by Tsai et al (study 42); dancing by Xue et al (study 39) and cycling by Kinoshita et al (study 25) and Amigo et al (study 44), while Martin et al (study 17) combined brisk walking, jogging and cycling. 2 separate studies carried out by Martin et al (study 17) and Amigo et al (study 44) compared exercise intervention with placebo in the form of calisthenics and stretching, while the rest of the studies compared exercise to usual activity or no exercise. Most of the studies that used physical exercise as intervention (93%) reported a significant improvement in the blood pressure control with greatest decrease in blood pressure level occurring in the study carried out by Tsai et al (study 42), where 44 participants performed shadow boxing resulting in 10.9% decrease in blood pressure ($P < 0.001$). The least significant decrease in blood pressure was noted in the study carried out by Stewart et al (study 10), where resistance training was compared to usual physical activity reporting a non-significant decrease in blood pressure ($P < 0.31$).

Effects of sodium restriction

11 studies (studies 4, 8, 9, 12, 20, 22, 26, 36, 37, 45 and 51) were carried out about the effect of sodium restriction on the blood pressure control of participants. Studies by Meland et al (study 8) and Swift et al (study 37) used salt capsules in comparison with placebo capsules, while the rest of the studies on sodium restriction intervention used low sodium diet in comparison with usual salt intake of the participants. A study by Kojuri and Rahimi (study 9) observed ‘no added’ salt as the intervention and no-intervention as control.

Most of the studies on salt restriction (91%) reported a significant improvement in the blood pressure control of the participants with the greatest decrease in the blood pressure observed in a study conducted by Pimenta et al (study 22), in which 12 participants had low salt diet resulting in 15.8% reduction in blood pressure ($P < 0.0008$). The least significant decrease in blood pressure was observed in a study by Meland et al (study 8), where 23 participants who received

low sodium salt capsules were compared to those that received placebo capsules ($P = 0.02$). In a study carried out by Little et al (study 20), participants receiving low salt diet were compared to those with usual daily salt intake reporting a non-significant reduction of blood pressure among the intervention participants ($P = 0.07$).

Effects of alcohol use reduction

7 studies (study 1, 15, 23, 24, 29, 33 and 50) reported effect of alcohol reduction on the control of blood pressure among the participants. Williams et al (study 24) used cognitive alcohol reduction programme in their study, Maheswaran et al (study 29) used alcohol reduction advice, while Thierry et al (study 1), Ueshima et al (study 15), Baros et al (study 23), Kawano et al (study 33) and Stewart et al (study 50) used direct reduction in alcohol drinking as interventions to achieve-alcohol intake reduction in their studies.

Most of the papers on alcohol intervention (85%) reported a significant reduction in blood pressure among the intervention group subjects with the largest decrease reported in the study by Thierry et al (study 1) with 6% reduction in blood pressure ($P < 0.05$). The least significant decrease was reported in Kawano's et al (study 33) study with 0.5% blood pressure reduction. Williams's et al (24) study in which intervention participants were exposed to cognitive alcohol reduction programme compared to those exposed to usual alcohol intake reported a non-significant decrease in blood pressure among intervention participants ($P = 0.74$).

Effects of weight reductions

6 studies (studies 5, 14, 35, 47, 49 and 46) reported on the effect of weight reduction on the control of blood pressure in hypertension. Stevens et al (study 5) and Hinderliter et al (study 46) employed the behavioral weight management programme to achieve weight reduction in the intervention groups. Bao et al (study 14) and Nowson et al (study 49) used weight reduction diet; Geleinjnse et al (study 36) used the 1,000 calorie per day rice diet, while He et al (study 47) used group educational sessions in achieving their weight reduction intervention.

All the studies on weight reduction reported a significant reduction in blood pressure among the intervention participants with the largest reduction reported in a study by Bao et al (study 14), in which participants exposed to weight reduction diet had 5.4% decrease in blood pressure ($P < 0.01$). The least significant reduction in blood pressure amounting to 2% decrease was noted in the study conducted by Stevens et al (study 5).

Effects of combination of various modalities

12 studies (studies 6, 7, 11, 16, 18, 19, 21, 27, 28, 34, 38 and 40) reported on the effects of various combinations of the four modalities of non-pharmacological interventions with or

without drugs on the control of blood pressure in hypertension. Blumenthal et al (study 18) and Smith et al (study 34) compared individuals exposed to a combination of physical exercise and weight reduction to those exposed to no-intervention as control, reporting a significant (P <0.001) 5.1% and 2.1% reduction in blood pressure, among the intervention participants. Kastarinen et al (study 21) compared participants under intervention group that comprised a combination of all the four modalities of non-pharmacological treatment of hypertension to participants exposed to usual care as control. This study reported a 4.2% decrease in blood pressure among the intervention participants, which was statistically significant ($P = 0.003$) compared to the usual care group.

Neaton et al (study 6) compared participants treated with non-pharmacological interventions (exercise, sodium restriction, weight reduction and alcohol use reduction) in combination with drug treatment to individuals exposed to the same non-pharmacological interventions alone, reporting a significant reduction in blood pressure equal to 11.3% decrease among the intervention (non-pharmacological and drugs) group participants compared to the control (non-pharmacological alone) participants ($P < 0.001$). Langford et al (study 16) compared the combination of weight reduction and drug treatment as intervention to drug treatment alone as control and reported a 6.9% decrease in blood pressure among the intervention participants. This reduction was significant ($P < 0.001$). Berglund et al (study 7) compared individuals on drug treatment as intervention group to participants exposed to a combination of non-pharmacological modalities (weight reduction, sodium restriction and alcohol use reduction) that served as control. This research reported a 9.7% decrease in blood pressure among the intervention group participants ($P = 0.0003$).

Interventions producing greatest reduction in blood pressure

Kastarinen et al (study 21) utilised low salt diet as intervention and reported the greatest post-intervention decrease in blood pressure of 22.7 mmHg, amounting to a 15.8% decrease. The greatest reduction in blood pressure due to the exercise modality was reported in a study conducted by Tsai et al (study 42), where a post-intervention reduction of 15.6 mmHg, amounting to a 10.9% decrease, was reported. Among the reviewed papers, which reported on the effect of weight reduction on blood pressure, Nowson et al (study 49) showed the greatest post-intervention reduction of 7.6 mmHg, corresponding to a reduction as 5.4%. The greatest post-intervention decrease in blood pressure by alcohol intervention was in the study by Thierry et al (study 1), which reported a reduction of 13.8 mmHg, amounting to a 6 % decrease.

Comparison: Effects of different intervention modalities

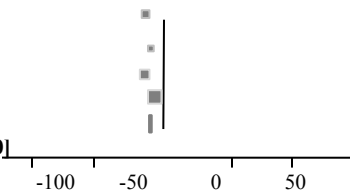
Outcome: Change in mean blood pressure

Table 1. Comparisons of different interventions effect on systolic blood pressure in hypertensive people.

	Experimental			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Alcohol reduction	-5.72	8.66	1000	2.34	7.62	1061	23.2%	-8.06[-8.77,-7.35]	
Exercise	-9.47	6.42	394	-2.15	6.97	327	11.9%	-7.32 [-8.31, -6.33]	
Salt restriction	-9.24	8	1174	1.67	7.85	1119	27.4%	-10.91 [-11.56, -10.26]	
Weight reduction	-5.68	5.47	772	1.02	5.55	743	37.5%	-6.70 [-7.26, -6.14]	
Total (95% CI)			**3340**			**3250**	**100%**	**-8.24 [-8.58, -7.90]**	

Heterogeneity: Chi ² = 98.21, df = 3 (P<0.00001); I² = 97%

Test for overall effect: Z = 47.54 (P<0.00001)



The plot of the blood pressure reduction effects of these various intervention modalities shows sodium restriction exerting the greatest reduction effect among the interventions. However, extreme caution is advised in adopting the representation of this plot as significant heterogeneity exists among the results of the papers reviewed in our study.

Heterogeneity analysis

Physical exercise

Clinical heterogeneity

In the exercise intervention subgroup, the papers reviewed in this work showed some clinical heterogeneity. Heterogeneity was found in the forms of exercise utilized in the studies, the demographic properties of the participants, number of participants used and the duration of study. Studies by Kerrie et al (study 2), Seals et al (study 30), Douglas and Reiling (study 32) and Rodriguez et al (study 41) used brisk walking as the form of exercise intervention, while Kinoshita et al (study 25) and Amigo et al (study 44) used cycling. Tsai et al (study 42) and Xue et al (study 39) used shadow boxing and dancing respectively, while Martin et al (study 17) used a combination of brisk walking, cycling and jogging.

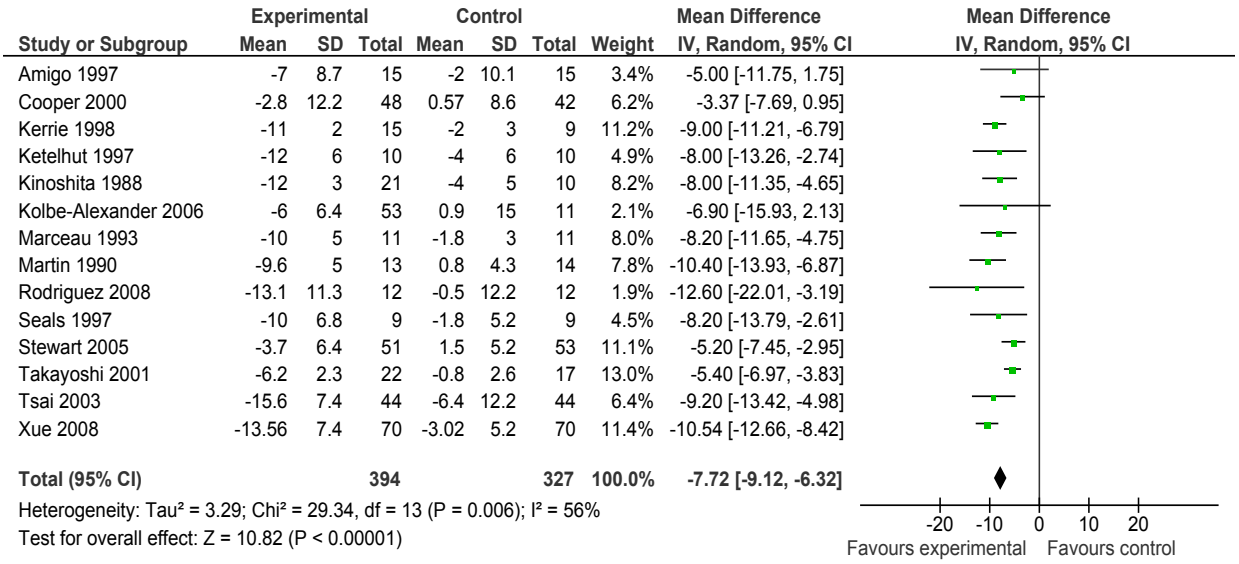
Also, there was a variation in the number of individuals participating in the various studies. The number of participants varied from as low as 9 in the study carried out by Marceau et al (study 31) to a high number of 140 participants by Miller et al (study 40). The study duration also varied greatly ranging from 5 weeks (Miller et al, study 40) to 18 months in the study conducted by Amigo et al (study 44). The variations in the study parameters enumerated above indicated high level of clinical heterogeneity.

Statistical heterogeneity

Comparison: Exercise Intervention vs. No exercise

Outcome: Change in mean blood pressure

Table 2. Effect of physical exercise intervention on blood pressure in hypertensive adults.



From the plot, it can be seen that most of the results of the papers used for this review do not overlap indicating presence of heterogeneity. The I^2 is 56% and above the 50% adopted for this study pointing to high heterogeneity among the papers, hence the random effect model. The level of statistical heterogeneity among the studies is shown to be statistically significant by the p-value of 0.006. The existence of both clinical and significant statistical heterogeneity among the papers on exercise intervention made it inappropriate to perform meta-analysis of the studies.

Salt restriction

Clinical heterogeneity

The papers used in this review that report on effect of salt restriction exhibit a certain degree of clinical heterogeneity. Various methods were used to achieve salt restriction in the intervention subjects including salt capsules by Meland et al (study 8) and Swift et al (study 37), 'no –added salt' study carried out by Kojuri and Rahimi (study 9) and low salt diet conducted by Appel et al (study 4), Sacks et al (study 12), Kastarinen et al (21), Pimenta et al (study 22), He et al (study

26), Geleinjnse et al (study 36), Weir et al (study 45) and Resnick et al (study 51). Variation also exists in the control variable as studies by Meland et al (study 8), He et al (study 26) and Swift et al (study 37) who used placebo capsules, while Appel et al (study 4), Kojuri and Rahimi (study 9), Sacks et al (study 12) and Geleinjnse et al (study 36) used usual salt diet. The number of participants also showed heterogeneity varying from 12 participants in the study conducted by Baros et al (study 23) to 613 participants used by Appel et al (study 4). The duration of trials also showed variation. It varied from 30 days in the study carried out by Cooper et al (study 13) to 18 months in the study carried out by Appel et al (study 4). The above findings indicate a certain level of clinical heterogeneity among the papers reporting on the effect of salt restriction on blood pressure.

Statistical heterogeneity

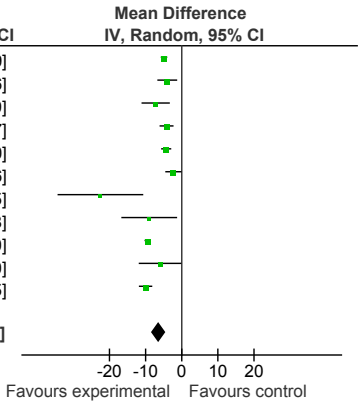
Comparison: Salt Restriction vs. Control

Outcome: Change in mean blood pressure

Table 3. Effect of Salt Restriction on blood pressure in hypertensive adults.

	Experimental			Control				Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI
Geleijnse 1994	-6.5	1.8	49	-1.6	1.8	51	12.0%	-4.90 [-5.61, -4.19]
He 2009	-4.8	12	187	-0.8	13	187	10.1%	-4.00 [-6.54, -1.46]
Kojuri 2007	-12.1	9.2	60	-4.9	6.6	20	8.5%	-7.20 [-10.91, -3.49]
Lawrence 2001	-4.6	11.3	317	-0.4	10.5	296	11.1%	-4.20 [-5.93, -2.47]
Little 1990	-6.4	2.7	36	-2.1	2.8	45	11.6%	-4.30 [-5.50, -3.10]
Meland 2009	-2	3	23	0.3	4	23	10.8%	-2.30 [-4.34, -0.26]
Pimenta 2009	-22.7	14	12	-0.2	15.1	12	2.3%	-22.50 [-34.15, -10.85]
Resnick 1994	-11	6	10	-2	10	9	4.4%	-9.00 [-16.52, -1.48]
Sacks 2001	-11.5	4.6	208	-2.1	2.3	204	12.0%	-9.40 [-10.10, -8.70]
Swift 2005	-8	13	40	-2	13	40	6.0%	-6.00 [-11.70, -0.30]
Weir 1998	-12	10.5	232	-2	7.3	232	11.2%	-10.00 [-11.65, -8.35]
Total (95% CI)			**1174**			**1119**	**100.0%**	**-6.34 [-8.30, -4.38]**

Heterogeneity: Tau² = 8.19; Chi² = 150.31, df = 10 (P < 0.00001); I² = 93%
Test for overall effect: Z = 6.34 (P < 0.00001)



The plot shows that results of the study 22 by Pimenta et al, with largest confidence interval and least weighting, does not overlap with most of the other studies; other results themselves showing no overlap and indicating heterogeneity among the studies. The I^2 value of 93% in the analysis is much above the 50% threshold set for this study reflecting high heterogeneity. Random effect model is hence also adopted here. The p-value for the forest plot is less than 0.00001, indicating significant statistical heterogeneity.

It is evident from the above information that there exist some clinical heterogeneity and significant statistical heterogeneity among the studies on effect of salt restriction on blood

pressure in this review. Hence, it was inappropriate to pool the results for purposes of meta-analysis.

Alcohol use reduction

Clinical heterogeneity

The papers analysed in this review that reported on the effect of alcohol reduction on blood pressure in hypertension showed some level of heterogeneity. Studies conducted by Thierry et al (study 1), Ueshima et al (study 15), Baros et al (study 23), Kawano et al (study 33) and Stewart et al (study 50) used reduced alcohol drinking in intervention groups, while Seals et al (study 30) used alcohol reduction advice and Kinoshita et al (study 25) used cognitive alcohol use reduction programme as interventions. Also varying was the number of participants in the studies, which ranged significantly from 34 participants in the study conducted by Kawano et al (study 33) to 1,383 participants enrolled in the study by Stewart et al (study 50). The duration of study also showed heterogeneity and ranged from 6 weeks by Ueshima et al (study 15) to 2 years by Thierry et al (study 1) and Cushman et al (study 24).

As demonstrated above, clinical heterogeneity exists among the reports of papers used to review the effect of alcohol reduction on blood pressure.

Statistical heterogeneity

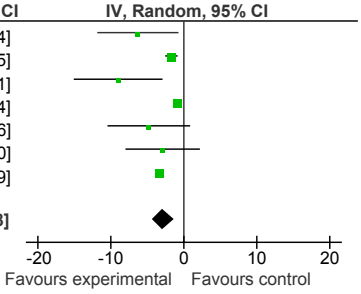
Comparison: Alcohol reduction Vs Control

Outcome: Change in mean blood pressure

Table 4. Effect of alcohol reduction on blood pressure in hypertensive adults.

	Experimental			Control				Mean Difference	Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Random, 95% CI	IV, Random, 95% CI
Baros 2008	-13.8	17.4	67	-7.5	14.2	62	6.1%	-6.30 [-11.76, -0.84]	
Cushman 1998	-3.6	1.5	27	-1.9	1.3	27	24.5%	-1.70 [-2.45, -0.95]	
Kawano 1998	-10	18	46	-1	13	74	5.3%	-9.00 [-14.99, -3.01]	
Maheswaran 1992	-5.5	2.1	138	-4.7	1.7	128	25.5%	-0.80 [-1.26, -0.34]	
Stewart 2008	-5.2	8	21	-0.4	10	20	5.9%	-4.80 [-10.36, 0.76]	
Thierry 1995	-3	11	34	-0.1	10	34	7.0%	-2.90 [-7.90, 2.10]	
Ueshima 1993	-4.1	2.6	667	-0.8	3.2	716	25.8%	-3.30 [-3.61, -2.99]	
Total (95% CI)			**1000**			**1061**	**100.0%**	**-2.81 [-4.35, -1.28]**	

Heterogeneity: Tau² = 2.37; Chi² = 90.55, df = 6 (P < 0.00001); I² = 93%
Test for overall effect: Z = 3.59 (P = 0.0003)



From the above plot, it can be seen that the results of the various studies are different lying on different planes and showing no overlap. Study 33 by Kawano et al, with the lowest weight and largest confidence interval lying further apart. This shows heterogeneity. The I^2 value of 93%

which is above the adopted threshold of 50% also points to high heterogeneity. The statistical heterogeneity noted among the studies on alcohol reduction is statistically significant as reflected by the p-value of less than 0.00001.

The presence of clinical and statistical heterogeneity observed among these studies on effect of alcohol reduction made it improper to pool the results from these papers.

Weight reduction

Clinical heterogeneity

The papers that were used to review the effect of weight reduction in this systematic review showed some level of clinical heterogeneity. Methods used to achieve weight reduction in the intervention groups varied, as studies carried out by Stevens et al (study 5) and Hinderliter et al (study 46) used behavioral weight management programme and studies carried out by Bao et al (study 14), Ard et al (study 35) and Nowson et al (study 49) used weight reduction meals, while He et al (study 47) used group educational sessions. The number of participants in the studies also varied and ranged from 32 participants in the study conducted by Bao et al (study 14) to 1,191 participants in the study carried out by Stevens et al (study 5). Heterogeneity was also observed in the duration of trial. It varied from 8 weeks in the study by Ard et al (study 35), to 36 months by Steven et al (study 5).

The above observation showed that clinical heterogeneity existed among the papers used for the review of effect of weight reduction on blood pressure in patients affected by hypertension.

Statistical heterogeneity

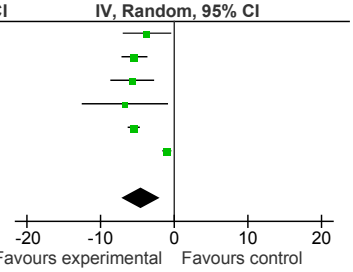
Comparison: Weight reduction Vs Control

Outcome: Change in mean blood pressure

Table 5. Effect of weight reduction on blood pressure in hypertensive adults.

	Experimental			Control				Mean Difference	Mean Difference
Study or Subgroup	**Mean**	**SD**	**Total**	**Mean**	**SD**	**Total**	**Weight**	**IV, Random, 95% CI**	**IV, Random, 95% CI**
Ard 2000	-4.3	8.7	44	-0.6	6.4	44	15.4%	-3.70 [-6.89, -0.51]	
Bao 1998	-7.2	2.4	16	-1.8	2.4	16	18.6%	-5.40 [-7.06, -3.74]	
He 2000	-6.9	6.4	53	-1.2	7.6	42	16.1%	-5.70 [-8.57, -2.83]	
Hinderliter 2002	-6.8	11	36	-0.1	10	19	10.0%	-6.70 [-12.46, -0.94]	
Nowson 2005	-7.6	1.5	27	-2.1	1.2	27	19.9%	-5.50 [-6.22, -4.78]	
Stevens 2001	-1.3	2.8	596	-0.3	5.7	595	20.0%	-1.00 [-1.51, -0.49]	
Total (95% CI)			**772**			**743**	**100.0%**	**-4.45 [-7.01, -1.90]**	

Heterogeneity: Tau² = 8.43; Chi² = 116.49, df = 5 (P < 0.00001); I² = 96%
Test for overall effect: Z = 3.41 (P = 0.0006)



From the plot, the results of the studies reviewed do not overlap, indicating presence of heterogeneity. Steven et al (study 5) shows the highest deviation. The I^2 value of the plot studies is 96% and together with the significant p-value of less than 0.00001 demonstrate high heterogeneity among these studies. The pooling of data from these studies was therefore inappropriate.

Sensitivity Analysis

The sensitivity analysis for the checking of the presence of publication bias in this work was carried out by comparing the funnel plot generated by some of the papers used in this review and that generated when the excluded papers of the study were added to some of those reviewed. The excluded papers were analysed and data extracted from them for the purpose of the funnel plot.

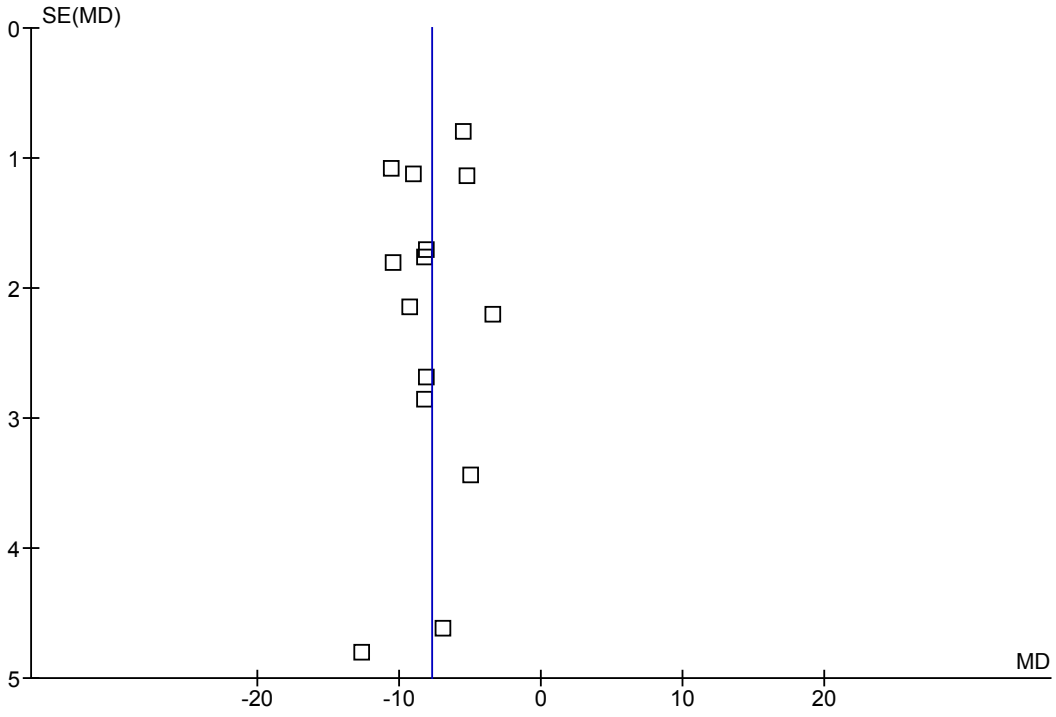


Figure 1. Funnel Plot of some of the included studies.

The funnel plot above exhibits relative symmetry with no obvious skewing to either side of the line of mean effect. There are 2 studies with large standard error, signifying low precision and are located at the lower region of the plot.

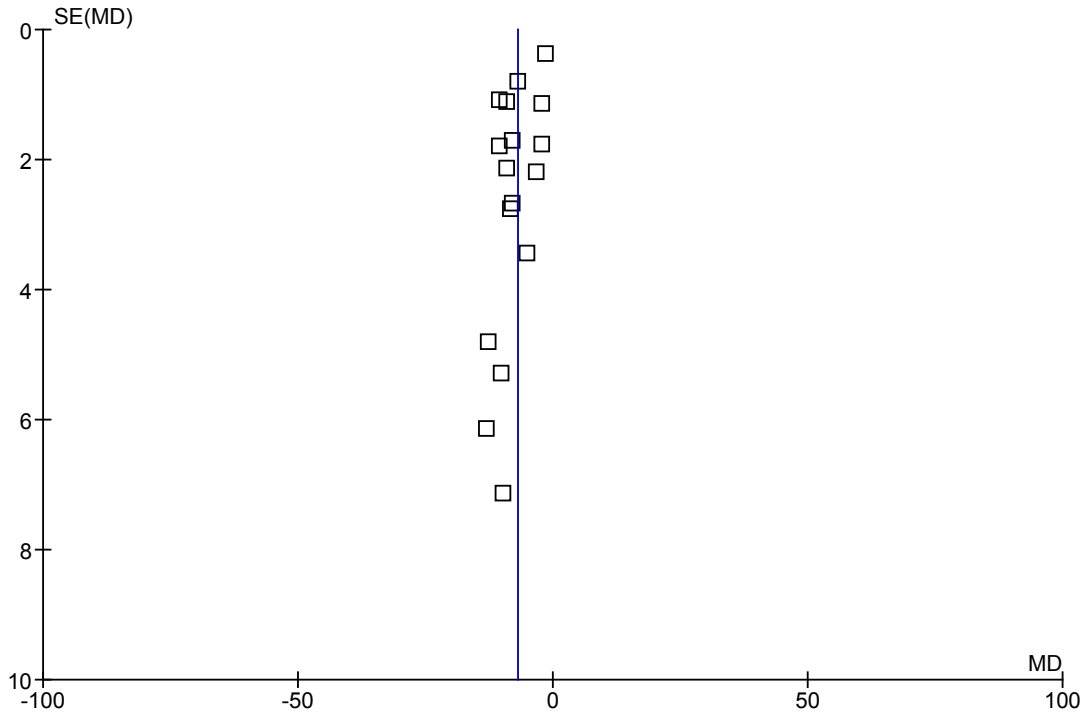


Figure 2. Funnel Plot of some included and excluded studies.

The funnel plot above with the excluded studies added showed some clustering around the line of mean effect tending to affect relatively the symmetry observed for the included studies. The relative summary observed in this plot indicates some publication bias in this study.

Quality assessment

The units of analysis used in this work were subjected to quality appraisal and graded appropriately using the criteria described in the methods and material section. The quality assessment (QA) showed that 64% of the units of analysis (33 studies) were of high quality on the strength of available evidence. 25% of the studies (13 studies) had QA grade of B (very good), while 6% (3 studies) had QA grade of C (good). 2 of the papers used in the review had QA grade of D and none of the papers fell below band D. All the papers reviewed reported the baseline characteristics of participants, which helped assess the effectiveness of their randomisation process. Overall, the units of analysis used in this study can be said to be of good strength as over 85% of the papers had QA grade that ranged from fair to high quality.

Table 6. Quality assessment of the studies included in the review (n = 51).

Study	First Author	Identification as RCT in Abstract	Intervention and comparator in Abstract	Inclusion and exclusion criteria	Randomisation method explanation	Intervention & Comparator details	Participants' Flow Chart	Baseline Characteristics	Participants entering study groups	Number of participants completing study	Limitation of study	Total score	Grade
1	Thierry	10	5	10	0	5	0	10	10	10	10	70	A
2	Kerrie	0	10	5	0	10	0	10	10	10	0	55	C
3	Takayoshi	10	10	10	10	10	0	10	10	10	0	80	A
4	Appel	10	10	10	0	10	0	10	10	10	10	80	A
5	Stevens	10	5	10	10	5	0	10	10	10	10	80	A
6	Neaton	10	5	10	10	10	0	10	10	10	10	85	A
7	Berglund	10	10	10	10	10	0	10	10	10	10	90	A
8	Meland	10	10	10	10	10	0	10	10	10	0	80	A
9	Kojuri	10	0	0	0	10	0	10	10	0	10	50	C
10	Stewart	10	10	10	0	10	10	10	10	10	10	90	A
11	Appel	10	10	10	10	10	10	10	10	10	0	90	A
12	Sacks	10	10	10	0	10	0	10	10	10	0	70	A
13	Cooper	10	10	5	10	10	10	10	10	10	0	85	A
14	Bao	10	5	10	0	10	0	10	10	10	0	65	B
15	Ueshima	10	10	10	0	10	0	10	10	0	10	70	A
16	Langford	10	10	10	10	10	0	10	10	10	0	80	A
17	Martin	10	10	5	0	10	0	10	10	10	10	75	A
18	Blumenthal	10	10	10	0	10	10	10	10	10	10	90	A
19	Whelton	10	10	10	0	10	10	10	10	10	0	80	A
20	Little	0	0	0	10	10	0	10	10	10	10	60	B
21	Kastarine	10	0	10	10	10	10	10	10	10	10	90	A
22	Pimenta	10	10	0	0	0	0	10	10	10	10	60	B
23	Baros	10	0	10	0	0	0	10	10	10	10	60	B
24	Williams	10	10	10	10	5	0	10	10	10	0	75	A
25	Kinoshita	0	10	0	0	5	0	10	10	10	0	45	D
26	He	10	10	10	10	5	0	10	10	10	0	75	A
27	Svetkey	10	10	0	0	10	10	10	10	10	0	70	A
28	Saptharishi	10	10	0	0	10	0	10	10	10	10	70	A

29	Maheshwaran	10	10	10	0	10	0	10	10	10	10	80	A
30	Seals	0	10	5	10	10	0	10	10	10	0	65	B
31	Marceau	0	10	0	0	10	0	10	10	10	0	50	C
32	Douglas	10	10	10	0	10	0	10	10	10	0	70	A
33	Kawano	10	10	5	0	10	0	10	10	10	0	65	B
34	Smith	0	10	5	10	10	0	0	10	10	10	65	B
35	Ard	10	10	0	10	10	10	10	10	10	10	90	A
36	Geleijnse	10	10	5	10	0	0	10	10	10	0	75	A
37	Swift	10	10	10	0	10	0	10	10	10	0	60	B
38	Malini	10	10	5	0	10	0	10	10	10	10	75	A
39	Xue	10	10	10	10	10	10	10	10	10	10	100	A
40	Miller	10	10	10	10	10	10	10	10	10	10	100	A
41	Rodriguez	0	10	10	0	10	0	10	10	10	0	60	B
42	Tsai	10	5	5	0	10	0	10	10	10	10	70	A
43	Ketelhut	0	0	5	0	10	0	10	10	10	0	45	D
44	Amigo	10	10	5	0	10	0	10	10	10	0	65	B
45	Weir	10	10	5	0	10	10	10	10	10	0	75	A
46	Hinderliter	10	10	5	0	10	0	10	10	10	0	65	B
47	He	10	10	10	0	0	0	10	10	10	0	60	B
48	Kolbe-Alexander	0	10	10	0	10	0	10	10	10	10	70	A
49	Nowson	10	10	10	10	10	0	10	10	10	0	80	A
50	Stewart	0	10	10	0	10	0	10	10	10	0	60	B
51	Resnick	0	10	10	0	10	0	10	10	10	10	70	A

DISCUSSION

This study reviewed a total of 51 randomized controlled trials that reported on effect of exercise, salt restriction, weight reduction, alcohol reduction or their various combinations as modalities in the non-pharmacological management of hypertension; 94% (48 studies) reported significant improvement in the control of blood pressure by these interventions, while 6% (3 studies) reported a statistically non-significant post-intervention improvement. None of the papers reviewed reported post-intervention increase in blood pressure level. Discussion of our findings was based on type of intervention.

Effectiveness of physical exercise in the control of blood pressure in patients affected by hypertension

In this review, 15 RCT reported on the effect of exercise on blood pressure control; all of the clinical trials included a total of 1,678 individuals, 93% of the papers reported a significant improvement in blood pressure control, while 7% reported a non-significant improvement. The improvement in blood pressure control through exercise intervention could be attributed to the reduction of the sympathetic nerve activity and increase in body levels of nitric oxide, noticed in individuals after exercise. Both reductions in sympathetic nerve activity and high levels of nitric oxide cause dilatation of peripheral vasculature and reduction in blood pressure [43]. Seals et al (study 30), Douglas and Reiling (study 32) and Rodriguez et al (study 41) used brisk walking as exercise intervention, which produced a significant post-intervention decrease in blood pressure. However, a study by Cooper et al (study 13), which also used brisk walking as exercise intervention produced a statistically non-significant post-intervention decrease in blood pressure. The result may be due to shorter duration of intervention (6 weeks) in the study as Costa (2002) [18] observed in meta-analysis that brisk walking resulted in a significant reduction in blood pressure only when the duration of intervention lasted 8 weeks and above. Hamer [43] also noted that it was the additive acute effect of bouts of exercise that brought about the blood pressure reduction effect of exercise.

Amigo et al (study 44) and Martin et al (study 17) with quality assessment score of 65 and 75, respectively compared aerobic exercise in the form of cycling as used in the study by Weir et al (study 45) and a combination of cycling, jogging and walking as performed in the study by Blumenthal et al (study 18) to calisthenics as placebo and reported a significant post-intervention decrease in blood pressure in aerobic exercise group. This result contradicts the findings of systematic review by Bhatt et al [44], that the reduction in blood pressure resulting from exercise is independent of the type of exercise that is carried out.

Effectiveness of sodium restriction in the control of blood pressure in patients affected by hypertension

A total of 11 studies that reported on effect of sodium restriction on blood pressure control were reviewed in the study, with the reviewed trials including a total of 2,154 participants. 90% of them reported a significant post-intervention improvement in blood pressure control, while 10% reported a statistically non-significant improvement. Post-intervention reduction in blood pressure observed with sodium restriction is believed to result from increase in arterial compliance caused by decreased sodium intake [45]. This is in addition to the decrease in vascular fluid retention observed in participants sodium restricted diet [6]. Studies carried out by Appel et al (study 4), Sacks et al (study 12), Geleinjnse et al (study 36), Weir et al (study 45) and Resnick et al (study 51) utilised low salt diet as their intervention and compared it to usual salt diet as control. All of them reported a significant improvement in the post-intervention blood pressure. However, the study by Kastarinen et al (study 21), which also utilised low salt diet

compared to participants' usual salt intake reported a non-significant improvement in the post-intervention blood pressure. This result may be due to the fact that urinary sodium excretion was not used to assess intervention participants' sodium intake as it was used in other studies. Feng et al [46] observed in a meta-analysis that urinary sodium excretion remains the only reliable criteria to assess level of sodium intake and general body sodium content, which in turn correlates with sodium restriction impact on blood pressure. Urinary sodium excretion of less than 77 mmol per day was noted as the threshold at which a significant effect on blood pressure is to be expected [47]. Intervention participants in the study carried out by Kastarinen et al (study 21) may not have reached this threshold in their sodium restriction.

Effectiveness of alcohol use reduction in the control of blood pressure in hypertension

7 studies that reported on the effect of alcohol use reduction were reviewed in this study. There was a total of 2,127 participants in the trials reviewed. 85% of the papers reported a significant post-intervention improvement in blood pressure control, while 15% reported a statistically non-significant improvement. Alcohol was noted to exert a pressor effect on the blood vessels by increasing circulating catecholamine levels. Improvement in blood pressure control observed after reduction in alcohol intake can be considered as to result from the decrease of these effects exerted by alcohol on the blood vessels [48]. The study by Maheswaran et al (study 29) had a quality assessment score of 80 grade A, utilised alcohol use reduction advise as intervention, compared to no-advice as control and reported 3.5% reduction in post-intervention blood pressure, which was significant ($P < 0.05$). The result of this study correlated with findings of a meta-analysis by Bertholet et al [49], in which 5,639 individuals were included, where advice to reduce alcohol consumption was noted to be effective in the control blood pressure among hypertensive patients. The UK NICE guidelines on hypertension treatment recommends that medical practitioners make advice to reduce alcohol consumption as an important part of their encounter with every hypertensive patient taking alcohol [50].

Study by Cushman et al (study 24) with quality assessment score of 75 grade A, utilised cognitive alcohol reduction programme as intervention and reported a statistically non-significant improvement in post-intervention blood pressure ($P = 0.74$). The result of this study may be explained by the fact that the programme was non-specific and resulted in average decrease of alcohol consumption of less than 14 drinks units per week. A meta-analysis by Mann et al [51] observed that alcohol reduction of less than 7 drinks per week needs to be maintained to achieve a significant reduction of blood pressure.

Effectiveness of weight reduction in the control of blood pressure in hypertension

The present study reviewed 6 RCT that reported on the effect of weight reduction on blood pressure among hypertensive adults. The studies included a total of 1,471 individuals. All the articles reviewed reported a significant post-intervention improvement on blood pressure. The reduction of blood pressure observed on a body weight basis was believed to result from the effects of the renin-aldosterone system and the sympathetic nervous system [52]. Studies conducted by Bao et al (study 14), Ard et al (study 35) and Nowson et al (study 49) utilised weight reduction diet in their intervention and compared it to usual calorie diet as controls. They reported a significant post-intervention reduction in blood pressure. All the three studies controlled for cofounders like physical activity. They were shown to be sufficiently well correlated with a meta-analysis carried out by Aucott et al [53], which observed that blood pressure reduction derived from weight reduction can be said to be independent of physical activity and result from low-calorie-diet induced weight reduction. The study conducted by He et al (study 47), with quality assessment score of 60 grade B, utilised group educational sessions as intervention compared to no-intervention group as control and reported 4% reduction blood pressure, which was significant ($P < 0.001$). This correlates with the findings of the review by Neter et al [54] and the recommendation by the British Hypertension Society [55], that education on low calories intake should be offered to hypertensive patients by health professionals as way of achieving weight loss and better control of blood pressure.

Effectiveness of combination of various modalities of non-pharmacological interventions in the control of blood pressure in hypertension

A total of 12 RCT in this review reported on the effect of combinations of various non-pharmacological modalities with or without drugs on blood pressure control among adult hypertensive. All the studies included a total of 5,226 individuals. All the 12 studies reviewed reported a post-intervention improvement in blood pressure. The study 6 by Neaton et al (1993) with a quality assessment score of 85 grade A, compared the 4 non-pharmacological interventions treated in our review in combination with drugs, to the same non-pharmacological interventions alone as control and reported a significant post-intervention reduction in blood pressure ($P < 0.001$), while the study by Langford (study 16) compared a combination of weight reduction and drug treatment to drug treatment alone as control and also reported a significant post-intervention reduction in blood pressure. The results of these studies correlated with the findings of the review by Beilin et al [56], which observed an additive effect of combination of drug and non-drug treatment of hypertension compared to either interventions used alone. This was in agreement with the recommendations by NICE (National Institute for Health and Care Excellence) [50] that health care professionals should offer combination of drug and non-pharmacological treatment to hypertensive individuals to enable them to benefit from the additive effects of these modalities.

The study conducted by Kastarine et al (study 22) with a quality assessment score of 90, grade A, compared a combination of all the four intervention to no-intervention as control and reported a significant post-intervention reduction in blood pressure of 4.2 %. This finding correlated with the findings of Collins et al (1990), who in their systematic review observed that maximal effects of blood pressure reduction are achieved with use of higher number of modalities of non-pharmacological interventions.

Intervention producing the great reduction in blood pressure

The pooled effect of the results of post-intervention reduction in mean systolic blood pressure from the papers reviewed, reporting on the effect of the various non-pharmacological interventions used alone, showed that a sodium restriction demonstrated the greatest reduction in blood pressure. This finding contradicts the conclusions by Ebrahim and Smith [57], who in a systematic review observed that weight reduction produced the greatest reduction in blood pressure when compared to salt restriction and physical exercise. This may be explained by the variation in the number of papers reviewed under each intervention modality. This difference emphasises that the results of this pooled effect is only for the purpose of comparison of these various interventions in this study and should be adopted with caution. The level of heterogeneity detected among the studies used in this study also makes this precaution very necessary.

CONCLUSION

The available evidence evaluated in this systematic review demonstrate that the non-pharmacological interventions such as sodium restriction, alcohol use reduction, weight reduction and exercise are effective in the control of blood pressure in patients affected by hypertension. The findings reported by majority of the reviewed RCT supported effectiveness of these interventions. Among the four non-pharmacological interventions reviewed in this systematic review, salt restriction was demonstrated to produce the greatest reduction in blood pressure among hypertensive adults.

Study limitations and recommendations for further research

This systematic literature review relied extensively on the results reported in the RCT published from 1988 to 2010. Although authors of this study used a quality assessment score, the limited number of papers reviewed makes it difficult to generalize our findings. Also, the variable number of papers covering each intervention modality, impacts on findings regarding the intervention that produces the greatest reduction.

Despite these limitations, this study may provide a body of evidence that demonstrates the effectiveness of the selected non-pharmacological interventions in the treatment of hypertension. However, the majority of the papers used for this study reported on studies that were of short duration, and there is a paucity of data on the long-term efficacy of these interventions. Therefore, further research needs to be conducted to ascertain long-term effects of these non-pharmacological interventions. Most of the non-pharmacological intervention modalities involved behavioral modification. The process of learning new behavior and dropping off old ones especially in adulthood is known to be with some challenges. This raises some concern about the level of compliance to these non-pharmacological interventions. Also, further investigations need to be carried out to ascertain other beneficial effects of these non-pharmacological in the overall reduction of risk of cardiovascular diseases and beneficial effects in combination with other types of non-pharmacological interventions such as smoking cessation. Besides the impact on blood pressure values, smoking is a powerful cardiovascular risk factor and quitting smoking is probably the single most effective lifestyle measure for the prevention of cardiovascular risk diseases [58].

Table 7. Findings about effects and other information of interventions described by studies included in this review (n = 51).

Study Number	Authors	Year	Type of non-pharmacological study and Journal name	Intervention	Control	Outcome (mean SBP Change, in mmHg)	P-value
1	Lang T et al.	1995	Improving hypertension control among excessive alcohol drinkers: a randomized controlled trial in France. Journal of Epidemiology and Community & community health, 49: 610-616	Alcohol reduction	No intervention	I = -13.8 C = -7.5	<0.05
2	Kerrie L et al.	2001	Increasing daily walking lowers blood pressure in postmenopausal women. Medicine & Science in Sports Exercise., 33(11) pp. 1825-1831	Physical exercise (brisk walking)	No exercise	I = -11 C =-2	<0.005
3	Takayoshi O et al.	2001	Effects of exercise training on home blood pressure values in older adults: a randomized controlled trial. Journal of Hypertension 19(6): 1045-1052	Physical exercise	No exercise	I = -6.2 C =-0.8	= 0.003
4	Lawrence J et al.	2001	Effects of reduced Sodium Intake on Hypertension Control in Older individuals. Archives of Internal Medicine, 161:685-693	Reduced sodium	Usual diet	I = -4.6 C =-0.4	<0.001

5	Stevens V et al.	2001	Long Term Weight Loss and Changes in Blood Pressure: results of the Trials of Hypertension Prevention, Phase II. Annals of Internal Medicine, 134:1-11	Weight reduction	Usual care	I = -1.3 C =-0.3	<0.01
6	Neaton J et al.	1993	Treatment of Mild Hypertension Study. JAMA, 270:713-724	Drug and non-pharmacological treatment	Non-pharmacological treatment alone	I = -15.9 C =-9.1	<0.001
7	Berglund A et al.	1989	Antihypertensive effect of diet compared with drug treatment in obese men with mild hypertension. British Medical Journal 299:480-485	Drug treatment	weight reduction -sodium restriction -alcohol reduction	I = -15 C =-4	= 0.0003
8	Meland E et al.	2009	Salt restriction among hypertensive patients: Modest blood pressure effect and no adverse effects. Scandinavian Journal of Primary Health Care, 27: 97-103	Sodium reduction	Placebo	I = -2 C =0.3	= 0.02
9	Kojuri J et al.	2007	Effect of “no added salt diet” on blood pressure control and 24-hour urinary sodium excretion in mild to moderate hypertension. BMC Cardiovascular Disorders, 7:34	“No added salt”	No intervention	I = -12.1 C =-4.9	= 0.001
10	Kerry J et al.	2005	Effect of Exercise on Blood Pressure in Older Persons A Randomised Controlled Trial. Archives of Internal Medicine, 165: 756-762	Physical exercise	Usual physical activity	I = -3.7 C =-1.5	<0.001
11	Lawrence J et al.	2003	Effects of comprehensive lifestyle modification on blood pressure control main results of the premier clinical trial. JAMA, 289(16): 2083-2093	-Weight reduction -Sodium restriction -Alcohol reduction -Physical exercise	No intervention	I = -12.5 C =-7.8	<0.001
12	Sacks F et al.	2001	Effects on blood pressure of reduced dietary sodium and the dietary approaches to stop hypertension (dash) diet. New England Journal of Medicine, 344(1): 3-10	Low salt diet	Usual diet	I = -11.5 C =-2.1	= 0.01
13	Cooper A et al.	2000	What is the magnitude of blood pressure response to a programme of moderate intensity exercise? Randomised controlled trial among sedentary adults with unmedicated hypertension. British Journal of General Practice, 50, 958-962	Physical exercise	Usual physical activity	I = -2.8 C =0.57	= 0.31
14	Bao D et al	1998	Effects of dietary fish and weight reduction on Ambulatory blood pressure in overweight hypertensives. Hypertension, 32:710-717	Weight reduction	No intervention	I = -7.2 C =-1.8	<0.01

15	Ueshima H et al.	1993	Effect of reduced alcohol consumption on blood pressure in untreated hypertensive men. Hypertension, 21: 248 – 252	Alcohol reduction	Usual alcohol intake	I = -4.1 C =-0.8	<0.05
16	Langford H et al.	1991	Effect of drug and diet treatment of mild hypertension on diastolic blood pressure. Hypertension 17: 210-217	-Weight reduction -Sodium restriction -Drugs	Drugs alone	I = -10.0 C =-7.8	<0.001
17	Martin J et al.	1990	Controlled trial of aerobic exercise in hypertension. Circulation, 81:1560-1567	Physical exercise	Placebo	I = -9.6 C =0.8	= 0.02
18	Blumenthal J et al.	2000	Exercise and weight loss reduce blood pressure in men and women with mild hypertension. Archives of Internal Medicine, 160: 1947-1958	-Physical exercise -Weight reduction	No intervention	I = -7.4 C =-0.9	<0.001
19	Whelton P et al.	1998	Sodium reduction and weight loss in the treatment of hypertension in older persons a randomized control trial of non-pharmacological interventions in the elderly. Journal of American Medical Association, 279 (11): 839 – 846	-Sodium reduction -Weight reduction	Usual	I = -5.3 C =-0.8	<0.001
20	Little P et al.	1990	A controlled trial of a low sodium, low fat, high fibre diet in treated hypertensive patients: the efficacy of multiple dietary intervention. Postgraduate Medical Journal, 66: 616-621	Sodium restriction	Usual diet	I = -6.4 C =-2.1	<0.07
21	Kastarinen M et al.	2002	Non-pharmacological treatment of hypertension in primary health care: a 2 year open randomized controlled trial of lifestyle intervention against hypertension in eastern Finland. Journal of Hypertension 20: 2505 – 2512	-Weight reduction -Sodium restriction -Physical exercise -Alcohol reduction	Usual care	I = -6.2 C =-2.2	= 0.003
22	Pimenta E et al.	2009	Effects of dietary sodium reduction on blood pressure in subjects with resistant hypertension: results from a randomized trial. Hypertension, 54(3): 475-481	Low salt diet	Normal salt diet	I = -22.7 C =-0.2	<0.0008
23	Baros A. et al.	2008	Alcohol consumption, % CDT, GGT and blood pressure change during alcohol treatment. Alcohol & Alcoholism 43(2): 192-197	No alcohol	Usual alcohol intake	I = -10.0 C =-1.0	= 0.003
24	William C et al.	1998	Prevention and treatment of hypertension study (PATHS): effects of an alcohol treatment program on blood pressure. Archives of Internal Medicine, 158: 1197 – 1207	Cognitive alcohol reduction programme	Usual alcohol intake	I = -5.5 C =-4.7	= 0.74
25	Kinoshita A et al.	1998	What type of hypertensives respond better to mild exercise therapy? Journal of Hypertension 6(4): s631-s63	Physical exercise	No exercise	I = -12 C =-4	<0.05

26	He F et al.	2009	Effect of modest salt reduction on blood pressure, urinary albumin and pulse wave velocity in white, black and Asian mild hypertensives. Hypertension 54: 482-488	Low salt diet	Placebo	I = -4.8 C =-0.8	<0.001
27	Svetky L et al.	2009	Hypertension improvement project randomised trial of quality improvement for physicians and lifestyle modification for patients. Hypertension 54: 1226-1233	-Weight reduction -Sodium restriction -Physical exercise -Alcohol reduction	Usual care	I = -7.1 C =-2.7	= 0.01
28	Sapatharishi L et al.	2009	Community based randomised controlled trial of non-pharmacological interventions in prevention and control of hypertension among young adults. Indian Journal of Community Medicine, 34(4): 329-334	-Physical exercise -Sodium restriction	No intervention	I = -5.3 C =-0.2	<0.05
29	Maheswaran R et al.	1992	Effectiveness of advice to reduce alcohol consumption in hypertensive patients. Hypertension 19: 79-84	Alcohol reduction	Usual alcohol consumption	I = -5.2 C =-0.4	<0.05
30	Seals R et al.	1997	Effect of regular exercise on elevated blood pressure in post menopausal women. American Journal of Cardiology 80: 49-55	Physical exercise	No exercise	I = -10.0 C =-1.8	<0.001
31	Marceau M et al.	1993	Effects of different training intensities on 24 hour blood pressure in hypertensive subjects. Circulation 88: 2803-2811	Physical exercise	No exercise	I = -10.0 C =-1.8	<0.05
32	Douglas R et al.	1991	Effects of regular exercise on 24 hour arterial pressure in older hypertensive humans. Hypertension 18: 583-592	Physical exercise	No intervention	I = -10.0 C =-3.0	<0.05
33	Kawano Y et al.	1998	Effects of alcohol restriction on 24 hour ambulatory blood pressure in Japanese men with hypertension. American Journal of Medicine 105:307-311	Alcohol reduction	Usual alcohol intake	I = -3.1 C =-0.1	<0.05
34	Smith P et al.	2007	Effects of exercise and weight loss on depressive symptoms among men and women with hypertension. Journal Psychosum Res 63(5): 463-469	-Physical exercise -Weight reduction	Waiting List	I = -3.1 C =0.0	<0.001
35	Ard J et al.	2000	Culturally sensitive weight loss programme produces significant reduction in weight, blood pressure and cholesterol in 8 weeks. Journal of National Medical Association 92: 515-523	Weight reduction	No intervention	I = -4.3 C =0.6	<0.01
36	Geleijnse J et al.	1994	Reduction in blood pressure with a low sodium, high potassium, high magnesium salt in older subjects with mild to moderate hypertension. British Medical Journal 309:436-40	Sodium restriction	Usual salt intake	I = -7.0 C =-1.6	<0.001

37	Swift P et al.	2005	Modest salt reduction reduces blood pressure and urine protein excretion in black hypertensives: a randomised control trial. Hypertension 46: 308-312	Reduced salt intake	Usual salt intake	I = -8.0 C =-2.0	<0.01
38	Parker M et al.	1990	Two-way factorial study of alcohol and salt restriction in treated hypertensive men. Hypertension 16: 398-406	-Alcohol reduction -Sodium restriction	No intervention	I = -4.7 C =-0.4	<0.001
39	Xue F et al.	2008	A randomised trial of a 5 week, manual based, self management programme for hypertension delivered in a cardiac patient club in Shanghai. BMC Cardiovascular Disorders 8: 10	Physical exercise	No exercise	I = 13.56 C =-3.02	<0.001
40	Miller E et al.	2002	Results of the diet, exercise and weight loss intervention trial. Hypertension 40: 612-618	-Weight reduction -Physical exercise -Sodium restriction	No intervention	I = -9.5 C =-1.1	<0.001
41	Rodriguez D et al.	2008	Efficiency of 2 sessions of jogging per week for the reduction of blood pressure in previously sedentary elderly hypertensive women. Fitness & Performance Journal 7(3): 169-74	Physical exercise	No intervention	I = -13.1 C =-0.5	=0.001
42	Tsai J et al.	2003	The beneficial effects of tai chi chuan on blood pressure and lipid profile and anxiety status in a randomised controlled trial. The Journal of Alternative and Complementary Medicine 9(5): 747-754	Physical exercise	No intervention	I = -15.6 C =-6.4	<0.001
43	Ketelhut R et al.	1997	Efficacy and position of endurance training as a non-drug therapy in the treatment of arterial hypertension. Journal of Human Hypertension 11: 651-655	Physical exercise	No exercise	I = -12.0 C =-4.0	<0.001
44	Amigo L et al.	1997	Comparison of physical exercise and muscle relaxation training in the treatment of mild hypertension. Stress Medicine 13: 59-65	Physical exercise	Placebo	I = -7.0 C =-2.0	<0.02
45	Weir M et al.	1988	Influence of race and dietary salt on the antihypertensive efficacy of an angiotensin-converting enzyme inhibitor or a calcium channel antagonist in salt-sensitive hypertensives. Hypertension 31:1088-1096	Sodium restriction	Usual salt intake	I = -12.0 C =-2.0	<0.05
46	Hinderliter A et al.	2002	Reduction of ventricular hypertrophy after exercise and weight loss in overweight patients with mild hypertension. Archives of Internal Medicine 162: 1333-1339	Weight reduction	Waiting list	I = -6.8 C = -0.1	<0.001
47	He J et al.	2000	Long term effects of weight loss and dietary sodium reduction on incidence of hypertension. Hypertension 35: 544-549	Weight reduction	No intervention	I = -6.9 C =-1.2	<0.001

48	Kolbe-Alexander T et al.	2006	Effectiveness of community based low intensity exercise programme for older adults. The Journal of Nutrition Health & Ageing 10(1): 21-29	Physical exercise	No intervention	I = -6.0 C =0.9	= 0.001
49	Nowson C et al.	2005	Blood pressure change with weight loss is affected by diet type in men. American Journal of Clinical Nutrition 81: 983-9	Weight reduction	Usual salt diet	I = -7.6 C =-2.1	<0.05
50	Stewart S et al.	2008	Blood pressure reduction during treatment for alcohol dependence: results from the Combining Medications and Behavioural interventions for Alcoholism. Addiction 103:1622-1628	Alcohol reduction	Usual alcohol intake	I = -4.1 C =-0.8	= 0.005
51	Resnick L et al.	1994	Intracellular ionic consequences of dietary salt loading in essential hypertension. Journal of Clinical Investigation 94: 1269-1276	Low salt diet	Usual salt intake	I = -11.0 C =-2.0	<0.05

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