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Long-term effects of weight-reducing diets in people with hypertension (Review)

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[Intervention Review]

Long-term effects of weight-reducing diets in people with hypertension

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ABSTRACT

Background

All major guidelines for antihypertensive therapy recommend weight loss. Dietary interventions that aim to reduce body weight might therefore be a useful intervention to reduce blood pressure and adverse cardiovascular events associated with hypertension.

Objectives

Primary objectives

To assess the long-term effects of weight-reducing diets in people with hypertension on all-cause mortality, cardiovascular morbidity, and adverse events (including total serious adverse events, withdrawal due to adverse events, and total non-serious adverse events).

Secondary objectives

To assess the long-term effects of weight-reducing diets in people with hypertension on change from baseline in systolic blood pressure, change from baseline in diastolic blood pressure, and body weight reduction.

Search methods

For this updated review, the Cochrane Hypertension Information Specialist searched the following databases for randomised controlled trials up to April 2020: the Cochrane Hypertension Specialised Register, CENTRAL (2020, Issue 3), Ovid MEDLINE, Ovid Embase, and ClinicalTrials.gov. We also contacted authors of relevant papers about further published and unpublished work. The searches had no language restrictions.

Selection criteria

We included randomised controlled trials (RCTs) of at least 24 weeks' duration that compared weight-reducing dietary interventions to no dietary intervention in adults with primary hypertension.

Data collection and analysis

Two review authors independently assessed risks of bias and extracted data. Where appropriate and in the absence of significant heterogeneity between studies ($P > 0.1$), we pooled studies using a fixed-effect meta-analysis. In case of moderate or larger heterogeneity as measured by Higgins I^2, we used a random-effects model.

Main results

This second review update did not reveal any new trials, so the number of included trials remains the same: eight RCTs involving a total of 2100 participants with high blood pressure and a mean age of 45 to 66 years. Mean treatment duration was 6 to 36 months. We judged the

risks of bias as unclear or high for all but two trials. No study included mortality as a predefined outcome. One RCT evaluated the effects of dietary weight loss on a combined endpoint consisting of the necessity of reinstating antihypertensive therapy and severe cardiovascular complications. In this RCT, weight-reducing diet lowered the endpoint compared to no diet: hazard ratio 0.70 (95% confidence interval (CI) 0.57 to 0.87). None of the trials evaluated adverse events as designated in our protocol. The certainty of the evidence was low for a blood pressure reduction in participants assigned to weight-loss diets as compared to controls: systolic blood pressure: mean difference (MD) −4.5 mm Hg (95% CI −7.2 to −1.8 mm Hg) (3 studies, 731 participants), and diastolic blood pressure: MD −3.2 mm Hg (95% CI −4.8 to −1.5 mm Hg) (3 studies, 731 participants). We judged the certainty of the evidence to be high for weight reduction in dietary weight loss groups as compared to controls: MD −4.0 kg (95% CI −4.8 to −3.2) (5 trials, 880 participants). Two trials used withdrawal of antihypertensive medication as their primary outcome. Even though we did not consider this a relevant outcome for our review, the results of these RCTs strengthen the finding of a reduction of blood pressure by dietary weight-loss interventions.

Authors' conclusions

In this second update, the conclusions remain unchanged, as we found no new trials. In people with primary hypertension, weight-loss diets reduced body weight and blood pressure, but the magnitude of the effects are uncertain due to the small number of participants and studies included in the analyses. Whether weight loss reduces mortality and morbidity is unknown. No useful information on adverse effects was reported in the relevant trials.

PLAIN LANGUAGE SUMMARY

Do weight-loss diets affect blood pressure, and reduce the effects of high blood pressure (hypertension)?

What is high blood pressure (hypertension)?

Blood pressure is a measure of the force that your heart uses to pump blood around your body. It is usually given as two figures: the pressure when your heart pushes blood out (systolic pressure), and the pressure when your heart rests between beats (diastolic pressure). Blood pressure is considered to be high when systolic pressure is over 140 and/or diastolic pressure is over 90, often written as '140 over 90' and measured in millimetres of mercury (mm Hg). The risk of developing high blood pressure increases as you get older.

High blood pressure is one of the main causes of early death and disability around the world. It can increase people's risk of developing serious long-term health problems, such as heart attack or stroke. Lowering blood pressure in people with hypertension reduces the number of people who develop diseases of the heart and blood vessels (cardiovascular disease), which leads to fewer deaths and cardiovascular problems.

Weight and high blood pressure

High blood pressure is often related to unhealthy lifestyle habits, such as smoking, drinking too much alcohol, being overweight and not exercising enough. All treatment guidelines recommend keeping to a healthy weight and losing weight when needed. Some people choose to lose weight by following a diet, for example, by eating less fat, or by limiting the number of calories they eat.

Why we did this Cochrane Review

We wanted to find out if following a diet to lose weight has long-lasting effects on blood pressure, and whether it could reduce the unwanted effects of high blood pressure on people's health.

What did we do?

We searched for studies that compared the effects of following a weight-loss diet with not following a diet, in people with high blood pressure. We were interested in the effects of the diet on blood pressure and body weight. We also wanted to know how many people experienced any unwanted effects, how many people developed cardiovascular disease, and how many people died.

We looked for randomised controlled studies, in which the treatments people received were decided at random. This type of study usually gives the most reliable evidence about the effects of a treatment.

We assessed the reliability of the evidence we found. We considered factors such as: how the studies were conducted, how many people they involved, and whether their findings were consistent across studies.

Search date: we included evidence published up to April 2020.

What we found

We found eight studies in 2100 people with high blood pressure (average age 45 to 66 years). The studies were conducted in the USA (4 studies) and Europe (4 studies), and lasted 6 months to 36 months.

None of the studies reported useful information about any unwanted effects of following a weight-loss diet.

What are the results of our review?

A weight-loss diet probably enabled people to lose weight (5 studies, 888 people) and may have lowered their blood pressure (3 studies; 731 people), compared with people who did not follow a diet.

We did not find enough evidence about whether following a diet affected the number of people who died or developed cardiovascular disease. Three studies reported that no-one died during the study; only one study looked at how many people developed a cardiovascular disease.

How reliable are these results?

We are moderately confident that people with high blood pressure lose weight after following a weight-loss diet; however, these results might change if more evidence becomes available. We are less confident about whether a weight-loss diet lowers blood pressure, because these results are based on a small number of studies; this result is likely to change if more evidence becomes available.

Key messages

Although people with high blood pressure lost weight and had lower blood pressure after following a weight-loss diet, compared with people who did not follow the diet, we did not find enough reliable evidence to be certain about this result. We are uncertain whether following a weight-loss diet could reduce cardiovascular disease because we did not find enough studies that looked at this.

SUMMARY OF FINDINGS

Summary of findings 1. Weight-reducing diets versus no weight-reducing diets for adults with essential hypertension

Weight-reducing diets compared to no weight-reducing diets for adults with essential hypertension

Patient or population: Men and non-pregnant women ≥ 18 years old with essential hypertension

Intervention: Weight-reducing diets

Comparison: No weight-reducing diets

Outcomes	Effect estimate (95% CI)	No of Participants (studies)	Certainty of the evidence (GRADE)	Comments
Total mortality	0 versus 0	845 (3 studies)	⊕⊖⊖⊖ **very low** [a,b,c]	No death occurred in 3 of the included RCT
Cardiovascular morbidity Combined endpoint: necessity of reinstating antihypertensive therapy and severe cardiovascular complications Follow-up: 30 months	**HR 0.70** (0.57 to 0.87)	294 (1 study)	⊕⊖⊖⊖ **very low** [a,d,e]	Combined outcome includes events of very different severity
Adverse events	-	-	-	No useable results reported
Changes in systolic blood pressure [mm Hg] from baseline to end of study	**MD −4.49** (−7.20 to −1.78)	731 (3 studies)	⊕⊕⊖⊖ **low** [a,d]	-
Changes in diastolic blood pressure [mm Hg] from baseline to end of study	**MD −3.19** (−4.83 to −1.54)	731 (3 studies)	⊕⊕⊖⊖ **low** [a,d]	-
Changes in body weight [kg] from baseline to end of study	**MD −3.98** (−4.79 to −3.17)	880 (5 studies)	⊕⊕⊕⊖ **moderate** [a]	-

CI: confidence interval; **HR:** hazard ratio; **MD:** mean difference

GRADE Working Group grades of evidence
High certainty: Further research is very unlikely to change our confidence in the estimate of effect.
Moderate certainty: Further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.
Low certainty: 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 certainty: We are very uncertain about the estimate.

[a]High risk of bias in available randomised controlled trials.
[b]Low number of studies.
[c]No predefined outcome.
[d]Wide confidence intervals.
[e]Only 1 randomised controlled trial.

BACKGROUND

Description of the condition

Hypertension is a chronic non-communicable disease associated with an increased risk of cardiovascular mortality and morbidity. High blood pressure is one of the leading causes of premature death and disability worldwide. In 2015, 7.8 million deaths or 14% of total deaths were estimated to be related to systolic blood pressure (SBP) at or above 140 mmHg globally (Forouzanfar 2017). Lowering blood pressure levels in people with hypertension has been shown to be an effective means of reducing cardiovascular morbidity and mortality (Brunström 2018; Ettehad 2016; Thomopoulos 2014).

Epidemiological investigations have consistently revealed a positive correlation between excess body weight and the risk of high blood pressure (Lelong 2019; Nguyen 2019; WHO 2020; Zhao 2017). Several published systematic reviews of randomised controlled trials (RCTs) also support this assumption, and show that weight-loss interventions are well-established strategies to lower blood pressure in people with hypertension (Akonobi 2019; Aucott 2005; Dickinson 2006; Gay 2016; Horvath 2008; Stelmach-Mardas 2016). Furthermore, high body weight and hypertension independently contribute to cardiovascular diseases (GBD 2017). However, the observation that certain variables (for example, excess body weight, high blood pressure) are quantitatively related to more cardiovascular events does not necessarily mean that lowering these variables will automatically reduce the number of cardiovascular events. This may be due to the fact that the variable in question (for example, overweight) has no impact on aetiological pathways or that the damage to the cardiovascular system is already established and is only poorly or no longer reversible. It could also be the case that the treatment is effective and does lower cardiovascular events by reducing the risk factor, but at the same time increases cardiovascular or other risks through a different mechanism. An RCT is required to prove the effectiveness of an intervention, for which, ideally, a protocol was published prospectively. Many interventions that have been recommended on the basis of associations found in epidemiological studies eventually failed to show any beneficial effect, and sometimes even did harm in subsequent RCTs, for example a large dietary-intervention study of 8.1 years duration in 48,835 obese postmenopausal women (40% having hypertension) resulted in only a modest reduction in diastolic blood pressure and no significant reduction in any cardiovascular outcomes (Allison 2016; Howard 2006).

Nevertheless, major hypertension guidelines underline the effect of lifestyle modification as a first-step intervention to be considered in people with hypertension (ACC-AHA 2017; ESH-ESC 2018; Hypertension Canada 2018; NICE 2019). Weight reduction and weight loss maintenance are mandatory lifestyle changes. Body weight may be reduced by non-pharmacological, pharmacological, or invasive interventions. A Cochrane Review of pharmacological interventions for weight reduction in adults with essential hypertension showed that participants under therapy with orlistat or phentermine/topiramate could reduce their weight and blood pressure levels to a statistically significantly greater degree than participants in the placebo group (Siebenhofer 2016). In case of ineffectiveness of drug treatment, device-based therapies may be considered, principally targeting the treatment of resistant hypertension (ESH-ESC 2018).

The aim of this systematic review is to evaluate the potential beneficial and harmful long-term effects for people with hypertension who intend to reduce their body weight with non-pharmacological dietary interventions.

Description of the intervention

This review covers dietary interventions (with a duration of at least 24 weeks) that aim to reduce body weight (for example, dietary counselling, caloric restrictions, reduction in fat intake). We did not include other interventions such as dietary interventions with no primary intention of weight reduction, increase of physical activity or other non-drug approaches such as stress-reduction techniques.

How the intervention might work

Observational studies of non-pharmacological dietary measures in people with hypertension have suggested a positive association between body weight and blood pressure. One might therefore hypothesise that a dietary intervention with the aim of reducing body weight would reduce blood pressure and adverse cardiovascular events in people with hypertension.

Why it is important to do this review

For overweight people with established hypertension, it is commonly recommended that blood pressure should first be managed by non-pharmacological interventions, including weight reduction (ACC-AHA 2017; ESH-ESC 2018; Hypertension Canada 2018; NICE 2019). Since dietary interventions might support the efforts of people to reduce body weight, it is important for the physician to be informed about the efficacy and potential harms of diets before recommending them.

Other reviews and meta-analyses have shown that non-pharmacological weight-reducing interventions lead to a reduction in blood pressure (Akonobi 2019; Horvath 2008 IQWiG 2006). However, empirical data on the long-term effects of those interventions to lower the risk of mortality or cardiovascular morbidity are sparse.

This systematic review is the second update of the previously-published Cochrane Review (Siebenhofer 2010; Siebenhofer 2011; Semlitsch 2016).

OBJECTIVES

Primary objectives

To assess the long-term effects of weight-reducing diets in people with hypertension on all-cause mortality, cardiovascular morbidity, and adverse events (including total serious adverse events, withdrawal due to adverse events, and total non-serious adverse events).

Secondary objectives

To assess the long-term effects of weight-reducing diets in people with hypertension on change from baseline in systolic blood pressure, change from baseline in diastolic blood pressure, and body weight reduction.

METHODS

Criteria for considering studies for this review

Types of studies

We included RCTs of at least 24 weeks' duration that compared weight-reducing dietary interventions to no dietary intervention in adults with primary hypertension. Any additional pharmacological or non-pharmacological co-intervention must have been administered to all randomised participants and must not have been significantly different for the treatment and control groups at baseline or during the trial.

For example, we did not include a randomised trial with exercise plus diet versus no treatment. A trial in which all randomised participants exercised, and the only difference was a weight-reducing diet versus no treatment or placebo would have met the inclusion criteria.

Types of participants

We included men and non-pregnant women aged 18 years or older with essential hypertension (defined as baseline systolic blood pressure of at least 140 mm Hg or baseline diastolic blood pressure of at least 90 mm Hg, or both, or people on antihypertensive treatment).

Types of interventions

Dietary intervention with the intention to reduce body weight in comparison with no dietary intervention to reduce body weight.

Types of outcome measures

We included the following outcomes:

Primary outcomes

- total mortality
- cardiovascular morbidity
- adverse events (including total serious adverse events, withdrawal due to adverse events, and total non-serious adverse events)

Secondary outcomes

- change from baseline in systolic blood pressure
- change from baseline in diastolic blood pressure
- change in body weight

Search methods for identification of studies

Electronic searches

The Cochrane Hypertension Information Specialist searched the following databases, without language, publication year or publication status restrictions:

- the Cochrane Hypertension Specialised Register via the Cochrane Register of Studies (CRS-Web) (searched 14 April 2020);
- the Cochrane Central Register of Controlled Trials (CENTRAL 2020, Issue 3) via the Cochrane Register of Studies (CRS-Web) (searched 3 April 2020);
- MEDLINE Ovid (from 1946 onwards), MEDLINE Ovid Epub Ahead of Print, and MEDLINE Ovid In-Process & Other Non-Indexed Citations (searched 3 April 2020);
- Embase Ovid (from 1974 onwards) (searched 3 April 2020);
- ClinicalTrials.gov (www.clinicaltrials.gov) (searched 3 April 2020);
- World Health Organization International Clinical Trials Registry Platform (apps.who.int/trialsearch) (searched 6 July 2018). It was not possible to run an updated search on the ICTRP website due to the COVID-19 pandemic.

The Information Specialist modelled subject strategies for databases on the search strategy designed for MEDLINE. Where appropriate, they were combined with subject strategy adaptations of the sensitivity- and precision-maximising search strategy designed by Cochrane for identifying randomised controlled (as described in the *Cochrane Handbook for Systematic Reviews of Interventions* Version 6, Chapter 4 (Lefebvre 2019)). We present search strategies for major databases in Appendix 1.

Searching other resources

- The Cochrane Hypertension Information Specialist searched the Hypertension Specialised Register segment (which includes searches of MEDLINE, Embase, and Epistemonikos for systematic reviews) to retrieve existing reviews relevant to this systematic review, so that we could scan their reference lists for additional trials. The Specialised Register also includes searches for controlled trials in the Allied and Complementary Medicine Database (AMED), CAB Abstracts & Global Health, CINAHL, ProQuest Dissertations & Theses and Web of Science.
- We checked the bibliographies of included studies and any relevant systematic reviews identified for further references to relevant trials.
- Where necessary, we contacted authors of key papers and abstracts to request additional information about their trials.

Data collection and analysis

Selection of studies

Two review authors independently screened the title and abstract of each reference identified by the search and applied the inclusion criteria. We retrieved potentially relevant studies in full and again two review authors independently decided whether these studies met the inclusion criteria. In case of disagreement, we also obtained the full article, which the two review authors inspected independently. A third review author resolved disagreements. If a resolution of the disagreement was not possible, we added the article to those 'awaiting assessment' and contacted the authors of the study for clarification. We re-assessed the articles after receiving the authors' replies.

Data extraction and management

Two review authors independently extracted data from each included study using a standardised data extraction form. We resolved differences in data extraction by consensus, referring back to the original article. If necessary, we sought information from the authors of the primary studies. We extracted, checked, and recorded the following data.

- General information, including the sponsor of the trial (specified, known, or unknown) and country of publication.

- All characteristics of the trial, participants, interventions, and outcome measures were summarised as reported in the publication.
    - Characteristics of the trial comprised the study design, duration of the trial, method of randomisation, allocation concealment, blinding (participants, people administering treatment, outcome assessors) and testing of blinding. We reported the characteristics of randomised participants at baseline and checked the similarity of groups at baseline.
    - Characteristics of participants are summarised in the Characteristics of included studies table and comprise the number of participants in each group, how the participants were selected (random), exclusion criteria used, and general characteristics (e.g. age, gender, nationality, ethnicity).
    - Relevant information about duration of the intervention, length of follow-up (in months), and types of dietary weight-reducing interventions.
    - Data on outcome measures, including total mortality, cardiovascular morbidity (including stroke, myocardial infarction, sudden death, heart failure, etc.), total serious adverse events, withdrawals due to adverse events, total non-serious adverse events, mean change from baseline in systolic and diastolic blood pressure, as well as change in body weight.

Assessment of risk of bias in included studies

Two review authors independently assessed trials meeting the inclusion criteria to evaluate methodological quality. We resolved any differences in opinion by discussion with a third review author. We assessed all trials meeting the inclusion criteria using the 'Risk of bias' assessment tool under the categories of adequate sequence generation, allocation concealment, blinding, incomplete outcome data, selective reporting, and other potential biases (Higgins 2019).

We carefully evaluated important numerical data such as screened, eligible, and randomised participants, as well as intention-to-treat (ITT) and per-protocol (PP) populations. We investigated attrition rates, for example dropouts, losses to follow-up, and withdrawals. We critically appraised issues of missing data, ITT, and PP, and compared them to specifications for primary outcome parameters and power calculation.

Measures of treatment effect

We used the risk ratio (RR) with a 95% confidence interval (CI) for dichotomous variables such as total mortality, cardiovascular morbidity, total withdrawals, and withdrawals due to adverse events. We calculated the mean difference (MD) for the mean change in systolic as well as diastolic blood pressure and body weight between the groups. If the standard deviation of the mean change was not explicitly given in the study, we calculated it from confidence intervals and the standard error of the mean, or estimated it from P values.

The position of the participant during blood pressure measurement may affect the blood pressure-lowering effect. When measurements were reported for more than one position, the order of preference was: 1) sitting; 2) standing; and 3) supine (Musini 2009).

Unit of analysis issues

We intended to consider the level at which randomisation occurred, such as cross-over trials, cluster-randomised trials and multiple observations for the same outcome. If more than one comparison from the same trial was eligible for inclusion in the same meta-analysis, we either combined groups to create a single pair-wise comparison or appropriately reduced the sample size so that the same participants did not contribute more than once (splitting the 'shared' group into two or more groups). While the latter approach offers some solution to adjusting the precision of the comparison, it does not account for correlation arising because the same set of participants was included in multiple comparisons (Deeks 2019).

Dealing with missing data

If necessary, we contacted authors of trials reporting incomplete information to provide the missing information.

Assessment of heterogeneity

We assessed heterogeneity using Higgins I^2 (Higgins 2003).

Assessment of reporting biases

We tested publication bias and small-study effects in general using the funnel plot or other corrective analytical methods, depending on the number of clinical trials included in the systematic review.

Data synthesis

We summarised data statistically if they were available, sufficiently similar, and of adequate quality. We performed data synthesis and analyses using the Cochrane Review Manager 5 software (Review Manager 5). We performed statistical analysis according to the statistical guidelines referenced in the *Cochrane Handbook for Systematic Reviews of Interventions* (Deeks 2019). We used a fixed-effect model for the meta-analyses. In case of moderate or larger heterogeneity as measured by Higgins I^2, we used a random-effects model.

Subgroup analysis and investigation of heterogeneity

We performed subgroup analyses where appropriate. Heterogeneity among participants could be related to, for example, sex, age, body mass index, concomitant diseases, ethnicity, blood pressure at baseline, blood pressure goals, concomitant antihypertensive therapy, and socioeconomic status. In the case of substantial heterogeneity (I^2 greater than 50%), we had planned to perform sensitivity or subgroup analyses for the following items: study quality, PP versus ITT analyses, sex, age, body mass index, concomitant diseases, ethnicity, blood pressure at baseline, blood pressure goals, concomitant antihypertensive therapy, and socioeconomic status.

Sensitivity analysis

We tested the robustness of our results where appropriate, using several sensitivity analyses (for example study quality or PP versus ITT analyses, studies with large dropout rates and losses to follow-up).

Summary of findings and assessment of the certainty of the evidence

We used the GRADE approach to assess the certainty of the evidence (Guyatt 2011). The main results of the study, including a

summary of the data, the magnitude of the effect and the overall certainty of the evidence, are presented in Summary of findings 1.

We included all primary and secondary outcomes in Summary of findings 1, listed according to priority:

- Total mortality
- Cardiovascular morbidity
- Adverse events
- Change in systolic blood pressure
- Change in diastolic blood pressure
- Change in body weight

RESULTS

Description of studies

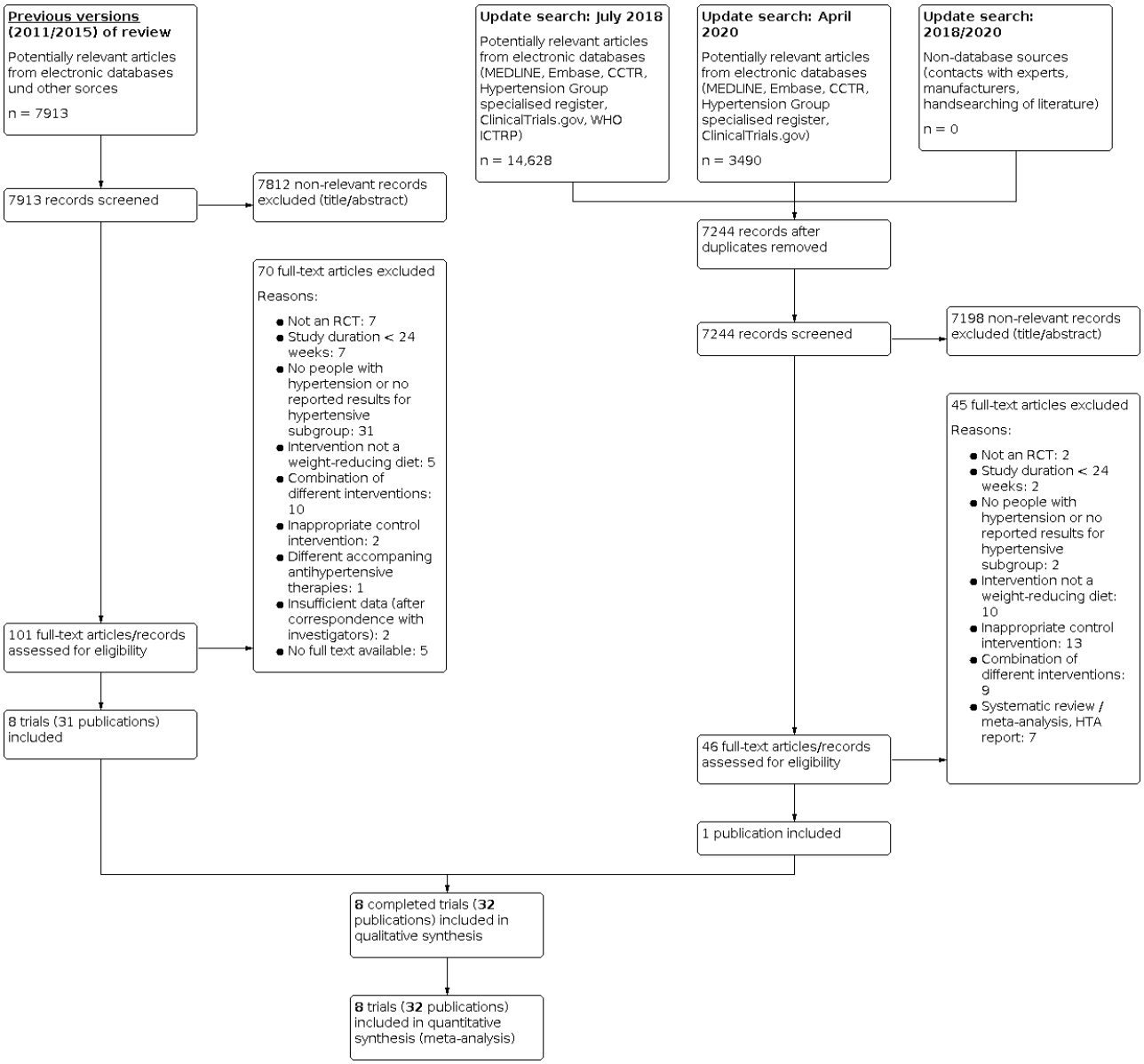
See: Characteristics of included studies; Characteristics of excluded studies.

Results of the search

Our update searches of the electronic databases in 2018 and 2020 yielded 14,628 and 3490 records, respectively. After de-duplication. 7244 records remained.

Of these 7244 publications, we excluded 7198 by consensus as not relevant to the question under study on the basis of their titles or abstracts, leaving 46 articles for further examination. After screening the full texts of these publications, we found only one publication that met the inclusion criteria. This article refers to a trial already included in the previous version of the review. We found no additional relevant trial for this review update. Finally, incorporating the additional publication to the 31 publications on eight trials from the previous version of the review, in this review update we include eight completed trials (32 articles/records) (see Figure 1 for details of the PRISMA statement (PRISMA 2009)).

Figure 1. Flow diagram.



Included studies

We have provided details of the characteristics of the included trials in the Characteristics of included studies table and in Table 1; Table 2; Table 3. The following gives a brief overview of the comparisons between dietary interventions with an intention to reduce body weight and no dietary interventions to reduce body weight.

All eight included trials had a parallel and open design (Cohen 1991; Croft 1986; DISH 1985; Jalkanen 1991; ODES 1995; Ruvolo 1994; TAIM 1992; TONE 1998), and three of them had a factorial design (ODES 1995; TAIM 1992; TONE 1998). Four studies were performed as single-centre trials (Cohen 1991; Croft 1986; ODES 1995; Ruvolo 1994), and three did not mention any industry sponsoring (Cohen 1991; Jalkanen 1991; Ruvolo 1994).

Participants and duration

The included trials involved a total of 2100 hypertensive participants with a mean age of 45 to 66 years, a baseline systolic blood pressure of 128 to 178 mm Hg, and a baseline diastolic blood pressure of 72 to 107 mm Hg. Mean treatment duration was 6 to 36 months (see Table 2; Table 3).

Interventions

In all trials, participants received either a dietary intervention with the aim of reducing body weight or no dietary intervention to reduce body weight.

Outcomes

Primary outcomes

Only one trial included the occurrence of clinical cardiovascular disease complications during follow-up as a predefined outcome

(TONE 1998). Three trials reported mortality rates during the study period (ODES 1995; Ruvolo 1994; TONE 1998). Two studies reported adverse events (DISH 1985; TONE 1998).

Secondary outcomes

Except for three trials (Cohen 1991; DISH 1985; TONE 1998), all included trials described the mean change in systolic and diastolic blood pressure. All but two trials (ODES 1995; TONE 1998) described mean change in body weight.

Excluded studies

The main reason for exclusion was a lack of sufficient results for the hypertensive subgroup in trials including normotensive as well as hypertensive participants. We excluded some studies because they were not randomised controlled trials, did not include participants with essential hypertension, did not aim for weight reduction or examined a combined intervention, provided an inappropriate control intervention or different accompanying therapies, had a duration of intervention less than 24 weeks, or full text was not available. We excluded two studies after personal communication (Curzio 1989; Haynes 1984). Both studies were performed in the 1980s, and electronic records or hard copies or both were no longer available to further clarify whether the studies were suitable for inclusion in our review. We have provided reasons for excluding each trial in the Characteristics of excluded studies table.

Risk of bias in included studies

Our judgements of the risks of bias for all included trials are shown in the 'Risk of bias' summary figures (Figure 2; Figure 3). For details, see the 'Risk of bias' tables in Characteristics of included studies. The following gives a brief overview.

Figure 2. Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

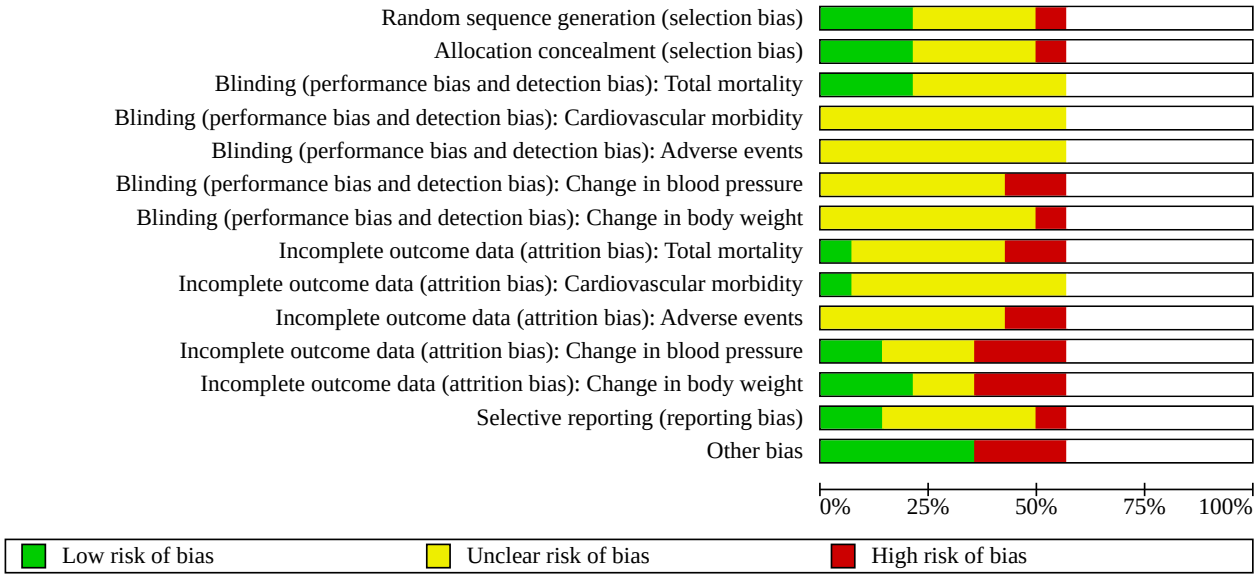
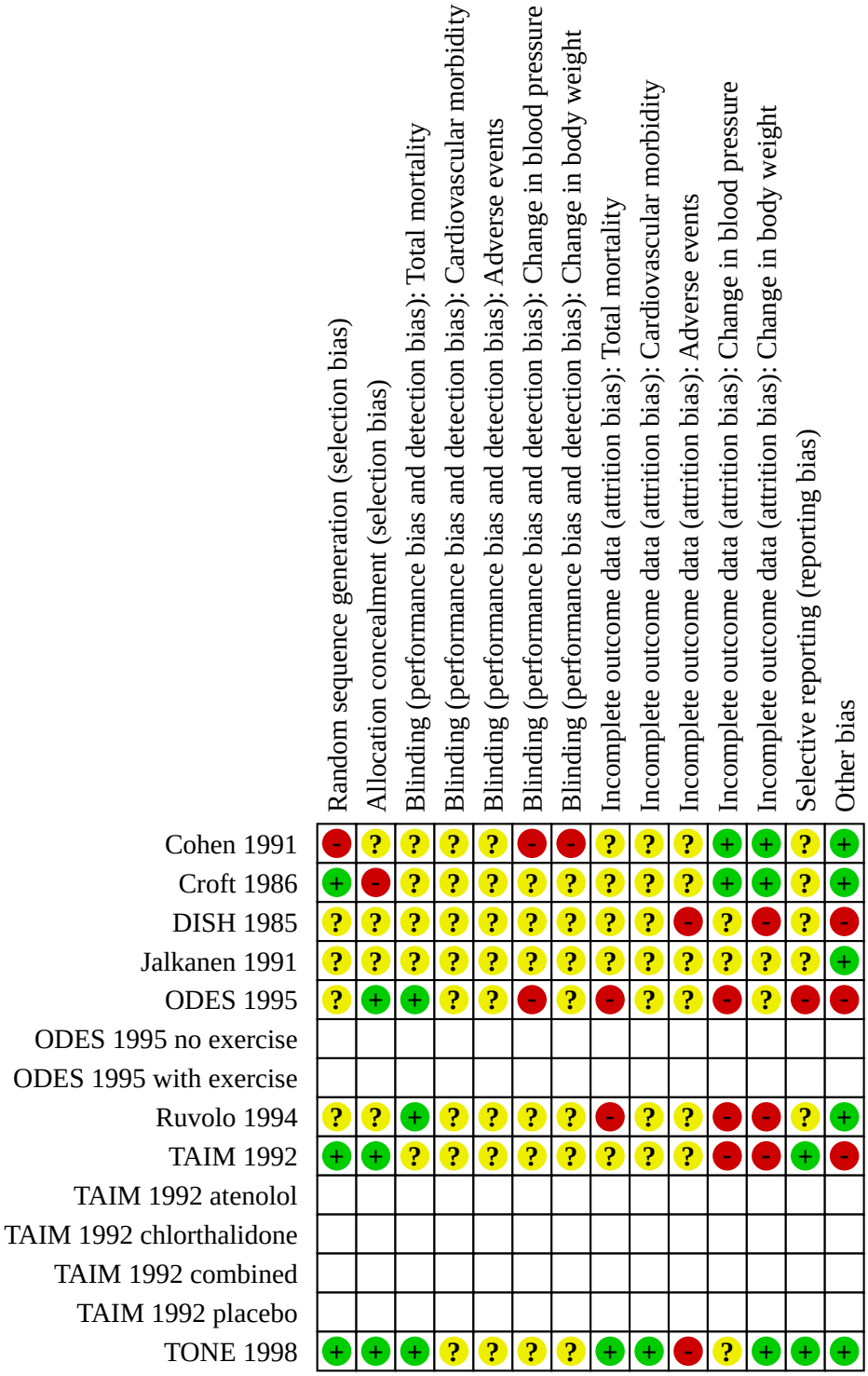


Figure 3. Risk of bias summary: review authors' judgements about each risk of bias item for each included study.



Allocation

Only two trials reported the method of randomisation (TAIM 1992; TONE 1998), and both of them had a factorial design. Only two trials described the method of concealment (ODES 1995; TAIM 1992). Cohen 1991 was a cluster-randomised trial in family practices, but without providing any information on allocation. In addition, the trial featured stratified randomisation of investigators instead of participants, with very small cluster size.

Blinding

All included trials had an open design in terms of participants and study personnel. In one trial (TONE 1998), an independent committee masked to intervention assignment evaluated the endpoints. In TAIM 1992, blood pressure endpoint assessment was blinded in only one out of three clinical centres due to logistical and budgetary considerations.

Incomplete outcome data

In Cohen 1991, the description of the outcome data was complete because there were no losses to follow-up. In DISH 1985, no withdrawals were reported for the endpoint of successful withdrawal from antihypertensive medication, but between 13% and 23% of values were missing for body weight at follow-up. In Jalkanen 1991 and Ruvolo 1994, only one to two participants were missing, but no reason for withdrawal was given. In TAIM 1992 and ODES 1995, study withdrawals were only reported for the whole study population, and no intention-to-treat analysis was performed. In TONE 1998, numbers of and reasons for withdrawals were missing, but 96% to 99% of participants were included in the follow-up analysis.

Selective reporting

There was a risk of selective reporting bias in one trial in which post hoc analyses of blood pressure were calculated, and results were not reported for all predefined outcomes (ODES 1995).

Other potential sources of bias

We could identify other potential sources of bias in three trials (DISH 1985; ODES 1995; TAIM 1992). In DISH 1985, participants were randomised before consent was obtained, and in two studies (ODES 1995; TAIM 1992) treatment in the intervention group seemed to be more intensive. For further details, please see the 'Risk of bias' tables and Figure 2 and Figure 3.

Effects of interventions

See: **Summary of findings 1** Weight-reducing diets versus no weight-reducing diets for adults with essential hypertension

See: Summary of findings 1

Primary outcomes

Mortality

None of the included trials was designed to evaluate the effects of weight-loss diet versus no diet on mortality. Three trials (ODES 1995; Ruvolo 1994; TONE 1998) reported that no participant died during the follow-up periods.

Cardiovascular morbidity

Only one trial evaluated the effects of dietary weight-loss intervention versus no dietary intervention, with a combined endpoint including cardiovascular complications (TONE 1998). After 30 months, the hazard ratio for participants in the dietary group to reach the combined endpoint, consisting of the necessity of reinstating antihypertensive therapy and severe cardiovascular complications, was 0.70 (95% confidence interval (CI) 0.57 to 0.87) compared with participants in the usual-care group. Altogether, there were 145 cardiovascular events during the study period, with 21 events (14.3%) in the weight-loss group, 23 events (15.6%) in the weight loss + sodium reduction group, 57 events (16.7%) in the usual-care group, and 44 events (12.9%) in the sodium-reduction group, respectively. There was no statistically significant difference between weight loss and no weight loss (P = 0.35).

Adverse events

None of the included trials evaluated the endpoint of adverse events as described in our protocol (including total serious adverse events, withdrawal due to adverse events, and total non-serious adverse events).

TONE 1998 classified adverse events by type (primary cardiovascular events) and time of occurrence (before, during, or after attempted antihypertensive drug withdrawals). However, no usable results were reported for the overweight subgroups with and without dietary interventions. DISH 1985 reported adverse events as withdrawals due to the need to resume antihypertensive medication; this was the case in 40.5% of participants in the intervention group and 64.7% of participants in the control group (P = 0.0015).

Secondary outcomes

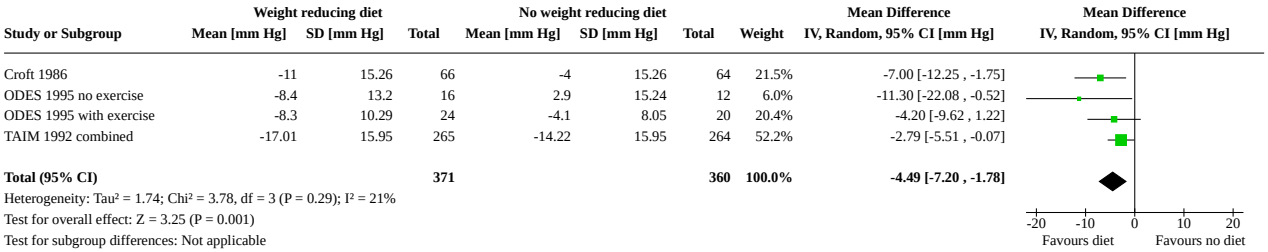
For details on secondary outcome data, see Table 4, Table 5, and Table 6. Due to between-study variability, we have presented results from random-effects models in the following analyses.

Changes in systolic blood pressure

Five trials investigating the effects of dietary versus no dietary intervention could not be included in the meta-analysis for systolic blood pressure. In two trials (DISH 1985; TONE 1998), successful withdrawal from antihypertensives was the primary outcome. In another trial (Cohen 1991), only the mean blood pressure change was reported, and in the trials Jalkanen 1991 and Ruvolo 1994, estimators for variance and P values for the change in systolic blood pressure were missing. Therefore, only three trials remained for analysis (731 participants).

In the case of TAIM 1992, the overall standard deviation (SD) presented for the combined analyses could be used for the meta-analysis. There was a significant reduction in systolic blood pressure, with a mean difference (MD) of −4.49 mm Hg (95% CI −7.20 to −1.78) in favour of dietary intervention. The test for heterogeneity gave a P value of 0.29, and Higgins I^2 indicated only low heterogeneity between studies (I^2 = 21%) (see Analysis 1.1; Figure 4). Differences in study quality could not explain heterogeneity. We could deduce no plausible explanation for heterogeneity from differences in study design, study duration, sample sizes, interventions, or characteristics of the included participants.

Figure 4. Forest plot of comparison: 1 Weight-reducing diet versus no weight-reducing diet, outcome: 1.1 Change in systolic blood pressure from baseline to endpoint [mm Hg].

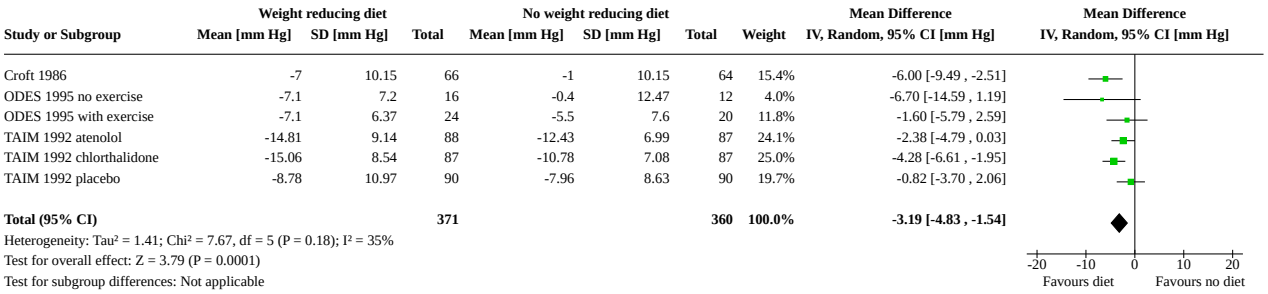


Changes in diastolic blood pressure

Five trials investigating the effects of dietary versus no dietary intervention could not be included in the meta-analysis for diastolic blood pressure. In two trials (DISH 1985; TONE 1998), successful withdrawal from antihypertensives was the primary outcome. In Cohen 1991, only the mean blood pressure change was reported, and Jalkanen 1991 and Ruvolo 1994 do not include an estimator for variance and P values for the change in diastolic blood pressure. Therefore, only three trials remained for analysis (731 participants).

In the case of TAIM 1992, the SDs presented for the subgroup (atenolol, chlorthalidone, placebo) analyses could be used for the meta-analysis. There was a significant reduction in diastolic blood pressure, with a MD of −3.19 mm Hg (95% CI −4.83 to −1.54) in favour of dietary intervention. The test for heterogeneity gave a P value of 0.18 (I^2 = 35%) (see Analysis 1.2; Figure 5). Differences in study quality could not explain heterogeneity. We could deduce no plausible explanation for heterogeneity from differences in study design, study duration, sample sizes, interventions, or characteristics of included participants.

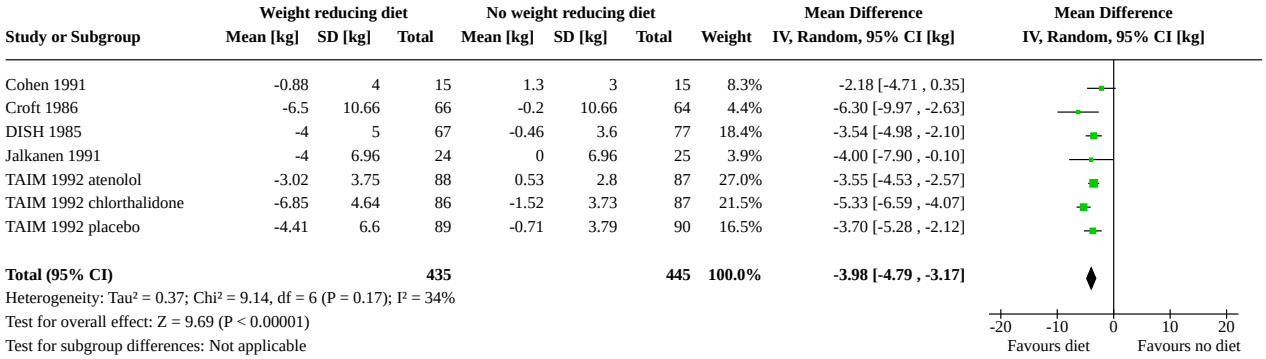
Figure 5. Forest plot of comparison: 1 Weight-reducing diet versus no weight-reducing diet, outcome: 1.2 Change in diastolic blood pressure from baseline to endpoint [mm Hg].



Body weight

Only three trials investigating the effects of dietary versus no dietary intervention could not be included in the meta-analysis for body weight. In two trials (ODES 1995; TONE 1998), no values for changes in body weight were presented, and in Ruvolo 1994 an estimator for variance and P values for the change in body weight was missing. Five trials (880 participants) therefore remained for analysis. In TAIM 1992, we could use the SDs presented for the subgroup (atenolol, chlorthalidone, and placebo) analyses. Dietary intervention was found to lower body weight significantly more effectively, with a MD of −3.98 kg (95% CI −4.79 to −3.17) in favour of dietary intervention. The test for heterogeneity gave a P value of 0.17 (I^2 = 34%) (see Analysis 1.3; Figure 6). Differences in study quality could not explain heterogeneity. We could deduce no plausible explanation for heterogeneity from differences in study design, study duration, sample sizes, interventions, or characteristics of included participants.

Figure 6. Forest plot of comparison: 1 Weight-reducing diet versus no weight-reducing diet, outcome: 1.3 Change in body weight from baseline to endpoint [kg].



Subgroup analyses

Not performed due to lack of data.

Sensitivity analyses

Not performed due to lack of data.

Publication and small-study bias

A clear interpretation of the funnel plot was not possible, which we mainly attributed to the relatively small number of included studies.

DISCUSSION

Summary of main results

This updated systematic review attempted to determine the long-term effects of weight loss through dietary interventions on patient-relevant endpoints, namely death, cardiovascular complications, and adverse events, in the antihypertensive therapy of people with essential hypertension. However, we found no currently-available randomised controlled trials designed to answer this question. We identified no new trials as a result of the update, yielding eight relevant trials that intended to reduce body weight (for example dietary counselling, caloric restrictions, reduction in fat intake) versus no dietary interventions. Of the eight included trials, we judged only two as having minor deficiencies of study quality (TAIM 1992; TONE 1998), while the other six studies have major deficiencies. Only one trial reported on cardiovascular complications, as part of a combined primary outcome consisting of the necessity of reinstating antihypertensive therapy and severe cardiovascular complications, and was in favour of the dietary-intervention group (TONE 1998). No valuable information on adverse effects was reported in any publications on the relevant trials. The meta-analyses showed that participants under dietary therapy could reduce their systolic and diastolic blood pressure and body weight levels statistically significantly more than participants in the control groups.

Two trials did not aim for blood pressure reduction, but used successful withdrawal of antihypertensive medication as a primary outcome (DISH 1985; TONE 1998). In DISH 1985, about 35% of the participants in the control group and about 60% in the intervention group remained without antihypertensive medication after 56 weeks. In TONE 1998, 93% of the participants in the weight-loss group and 87% in the control group could stop antihypertensive treatment. In the salt-lowered groups, 93% of both the dietary weight-loss intervention and the usual-care group could successfully be taken off medication. Even though successful withdrawal of antihypertensive treatment was not included as a chosen outcome in our review, it further underscores the success of dietary weight-loss interventions for reducing blood pressure.

In conclusion, in people with essential hypertension, therapy with dietary interventions to reduce body weight resulted in reductions in blood pressure and body weight. A reduction in body weight of approximately 4 kg was necessary to achieve a reduction of approximately 4.5 mm Hg systolic blood pressure and approximately 3.2 mm Hg diastolic blood pressure. However, the fact that only some of the studies could be included in the analyses weakens our conclusion. None of the studies provided data to answer the question of whether weight reduction can lower the risk of mortality or other patient-relevant endpoints.

Overall completeness and applicability of evidence

For this update we searched four electronic databases and the clinical trials registry (ClinicalTrials.gov) until April 2020, and the WHO clinical trials registry ICTRP until July 2018. We also searched the reference lists of included trials and relevant systematic reviews and meta-analyses. We assessed the quality of each study and summarised the results. The results of this review can therefore be taken to be complete and applicable. For full information, please see details in the relevant sections.

While the results of this review show that dietary interventions may be helpful in the antihypertensive therapy of overweight people with hypertension, major questions still remain. One point raised by Brian Haynes, a co-author we contacted for further clarification on whether his paper was relevant for inclusion in the review, was whether any effect on blood pressure-lowering persists when the participant's period of active weight loss ends. His clinical impression is that when weight loss stops (even if the weight loss is maintained?), the blood pressure goes back up (Haynes 2010 [pers comm]). However, there is still a lack of evidence about the long-term effects of weight loss on hypertension, as we could identify no long-term follow-up trials for our review. Indirect evidence from this assumption can be derived from the Swedish Obese Subject Study (Sjöström 2004), where participants successfully reduced their body weight by means of bariatric surgery. This study showed

that the postsurgical blood pressure reduction was still present two years after surgery, but increased again to baseline values after 10 years, despite continued weight loss. Secondly, it can be asked whether people with higher or lower blood pressure or higher or lower body weight at baseline might benefit in a different way from dietary intervention aiming to reduce body weight. It can, however, be assumed that the potential benefit on blood pressure might be greater in people with moderate-to-severe hypertension than in people with mild hypertension; in any case, we could find no correlation from the included studies. However, since the initial version of this review in 2011, no RCTs investigating the effect of weight-reducing diets in people with hypertension with a follow-up of at least six months were published,

Quality of the evidence

Of the eight trials included in our analyses, we judged only two as having minor deficiencies of quality (TAIM 1992; TONE 1998). All other trials have to be judged as having major deficiencies. The beneficial effects shown therefore reflect some degree of uncertainty. We have provided full details in the 'Risk of bias' tables in Characteristics of included studies.

Potential biases in the review process

A major limitation of this review is that, due to the lack of information in the included trials, we could draw no conclusions on the effects of the different dietary weight-loss interventions on patient-relevant long-term outcomes.

The results for the change in blood pressure outcomes could also be considered uncertain, as we included data from only three trials in the analyses. These results were mainly based on the TAIM 1992 study, which we judged to have a low risk of bias and contributed more than 70% of all participants to the meta-analyses. In addition, two of the trials that did not report results on blood pressure showed a reduction of antihypertensive medication as an indirect measure of blood pressure, which supports the findings of our meta-analyses. Furthermore, inclusion of the remaining studies from which data on blood pressure were available but were insufficient would probably not have changed the results, because these trials were all small and rated at high risk of bias.

The findings on body weight may also be regarded as uncertain, as results from only five trials were available for the analysis. Again, the TAIM 1992 trial had the highest weight in the analysis. These results are supported by results from the ODES 1995 study, which did not report on body weight, but found body mass index to be reduced to a greater extent among participants in the intervention groups.

Agreements and disagreements with other studies or reviews

There are only a few published systematic reviews on the long-term effects of weight-reducing diets in people with hypertension. One systematic review, *Effects of weight loss in overweight/obese individuals and long-term hypertension outcomes* (Aucott 2005), reached the same conclusion, i.e. that only short-term trials were available. The authors also warned "that extrapolation of short-term blood pressure changes with weight loss to the longer term is potentially misleading. The weight/hypertension relationship is complex and needs well-conducted studies with long-term follow-up to examine the effects of weight loss on hypertension outcomes". In addition, we were involved in the preparation of the scientific report on the evaluation of the benefits and harms of non-drug treatment strategies in people with essential hypertension (IQWiG 2006), and published a paper on this topic in 2008 (Horvath 2008). Since our last search for dietary interventions performed in February/March 2015 (Semlitsch 2016), we could identify no additional trials addressing our research question. We can therefore say with confidence that our findings are in agreement with other published reviews and studies in this field.

Some recent systematic reviews investigated the effect of weight-reducing diets on blood pressure in people with or without hypertension. Gay 2016 reported significant reductions in systolic and diastolic blood pressure with low-calorie diets after at least six months of follow-up in a mixed population of people with normal or raised blood pressure. A second review investigating the effect of commercial weight-loss programmes on cardiovascular risk factors in overweight or obese people with mostly normal blood pressure at baseline showed inconsistent results on blood pressure after six and 12 months of follow-up (Metha 2016).

AUTHORS' CONCLUSIONS

Implications for practice

Although trials on dietary interventions in people with elevated blood pressure demonstrated statistically significant decreases in weight loss and blood pressure, these findings are subject to a high risk of selective reporting bias. Furthermore, the available randomised controlled trial evidence provided no data on the effect of dietary interventions on mortality or morbidity, and none of the included trials reported valuable information on adverse events.

Implications for research

Long-term trials are needed, assessing the effect of dietary interventions to reduce body weight on mortality, morbidity, and adverse events in people with elevated blood pressure. Long-term follow-up data are also needed to determine the long-term effects of weight-reducing diets on blood pressure.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Cohen 1991

Study characteristics

Methods	Design: parallel, cluster-randomised Date: not stated

Cohen 1991 *(Continued)*

	Duration: 12 months Number of study centres: 1 Setting: model family practice unit (Pittsburgh), USA
Participants	Who participated: 30 hypertensive and obese people stratified by residents (residents, not participants, were randomised to intervention or control group) Main inclusion criteria: age 20 to 75 years; BMI ≥ 28 kg/m^2 (men); ≥ 27 kg/m^2 (women); SBP ≥ 140 mm Hg, DBP ≥ 90 mm Hg in 2 or more readings Main exclusion criteria: not described in detail Subgroup analyses: weight losers vs weight gainer
Interventions	Dietary intervention: physicians (n = 10) were taught by a behavioural psychologist; the goal of the dietary advice was to reduce the caloric content of the diet without radically changing the participant's lifestyle; monthly participant consultations and reviewing diet history sheet; the suggested diets were not specifically intended to be salt-reducing (N = 15) No dietary intervention: physicians (n = 8) received no special instructions or materials; the participants continued to be treated with their usual care (N = 15) Additional treatment: -
Outcomes	Primary outcomes: 1. Mortality: - 2. Cardiovascular morbidity: - 3. Adverse events: - Secondary outcomes: 1. Changes in systolic blood pressure [mm Hg]: - 2. Changes in diastolic blood pressure [mm Hg]: - 3. Changes in body weight [kg]: *Definition*: body weight change from baseline to 6 months, from baseline to 12 months, and from 6 months to 12 months Additional outcome measured in the trial: 1. Mean arterial blood pressure change in mm Hg 2. Change in number of antihypertensive medications 3. Number of visits
Study details	Length of follow-up: 12 months Trial terminated before regular end (for benefit / because of adverse events): No Trial ID: -
Publication details	Language of publication: English Funding: - Publication status: Full-text journal publication
Study aim	Quote from publication: "...to determine whether this was an effective milieu for the treatment of hypertension by weight reduction using a low-technology low-cost approach and involving only the physician as the therapeutic medium."
Notes	-
Risk of bias	

Cohen 1991 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Comment: No details on sequence generation are provided; stratified randomisation of investigators instead of participants with very small cluster size Quote: "The residents were stratified by residency year and randomly assigned to either control or experimental groups. ... The experimental or control status of a patient was determined by the status of the physician, and great care was taken to avoid contamination."
Allocation concealment (selection bias)	Unclear risk	Comment: Method of concealment is not described
Blinding (performance bias and detection bias) Total mortality	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Adverse events	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Change in blood pressure	High risk	Comment: Since the physicians assigned to the experimental group were taught about the weight-reducing programme, knowledge of the allocation intervention was not prevented during study
Blinding (performance bias and detection bias) Change in body weight	High risk	Comment: Since the physicians assigned to the experimental group were taught about the weight-reducing programme, knowledge of the allocation intervention was not prevented during study
Incomplete outcome data (attrition bias) Total mortality	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Adverse events	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Change in blood pressure	Low risk	Comment: no withdrawals; all participants were analysed
Incomplete outcome data (attrition bias) Change in body weight	Low risk	Comment: No withdrawals; all participants were analysed
Selective reporting (reporting bias)	Unclear risk	Comment: No study protocol available; no primary and secondary outcomes were defined in the publication
Other bias	Low risk	Comment: Non detected

Croft 1986

Study characteristics	
Methods	Design: parallel, randomised Date: not stated Duration: 6 months Number of study centres: 1 Setting: outpatient clinic (1 urban group practice), UK
Participants	Who participated: 176 newly-diagnosed hypertensive and obese people Main inclusion criteria: age between 35 and 60 years; BMI > 25 kg/m^2; SBP > 140 mm Hg or DBP > 90 mm Hg, or both, in 3 measurements Main exclusion criteria: SBP > 200 mm Hg; DBP > 114 mm Hg; previous antihypertensive medication; myocardial infarction or stroke within the previous 3 months; concurrent serious disease, conditions requiring diets, or medication likely to influence weight or blood pressure Subgroup analyses: none
Interventions	Dietary intervention: active dietary advice for weight reduction by 2 experienced dietitians emphasising the importance of weight reduction for blood pressure control (N = 87) No dietary intervention: visits at general practitioners, no active dietary advice; if participants indicated that they intended to lose weight, they were not discouraged but were given no specific advice or diet sheets (N = 89) Additional treatment: advice about modest restriction of salt use and reduction of excessive alcohol intake
Outcomes	Primary outcomes: 1. Mortality: - 2. Cardiovascular morbidity: - 3. Adverse events: - Secondary outcomes: 1. Changes in systolic blood pressure [mm Hg]: *Definition*: DBP change from baseline to endpoint visit 2. Changes in diastolic blood pressure [mm Hg]: *Definition*: DBP change from baseline to endpoint visit 3. Changes in body weight [kg]: *Definition*: body weight change from baseline to endpoint visit Additional outcomes measured in the study: 1. Start of antihypertensive medication
Study details	Length of follow-up: 6 months Trial terminated before regular end (for benefit / because of adverse events): No Trial ID: -
Publication details	Language of publication: English Funding: West Midlands Regional Research Committee; UK Publication status: Full-text journal publication
Study aim	Quote from publication: "...to examine the effect of weight reduction on blood pressure in newly diagnosed obese hypertensive patients and to investigate whether weight reduction is more successful in hypertensive dieters than in normotensive dieters."

Croft 1986 *(Continued)*

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: No details on sequence generation are provided, but according to IQWIG report adequate (IQWiG 2006)
Allocation concealment (selection bias)	High risk	Comment: Method of concealment is not described; not adequate according to IQWiG report (IQWiG 2006)
Blinding (performance bias and detection bias) Total mortality	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Adverse events	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Change in blood pressure	Unclear risk	Comment: No information on blinding
Blinding (performance bias and detection bias) Change in body weight	Unclear risk	Comment: No information on blinding
Incomplete outcome data (attrition bias) Total mortality	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Adverse events	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Change in blood pressure	Low risk	Quote: "... The data was submitted to an 'intention to treat' analysis which included all entrants and assumed that no further change in weight or blood pressure occurred for drop-outs after the last occasion on which they attended." Comment: Withdrawals: and reasons/descriptions (dietary intervention vs no dietary intervention): no reasons/descriptions reported: 17 vs 3
Incomplete outcome data (attrition bias) Change in body weight	Low risk	Quote: "... The data was submitted to an 'intention to treat' analysis which included all entrants and assumed that no further change in weight or blood pressure occurred for drop-outs after the last occasion on which they attended."

Croft 1986 *(Continued)*

		Comment: Withdrawals: and reasons/descriptions (dietary intervention vs no dietary intervention): no reasons/descriptions reported: 17 vs 3
Selective reporting (reporting bias)	Unclear risk	Comment: No study protocol available; no primary and secondary outcomes were defined
Other bias	Low risk	Comment: None detected

DISH 1985

Study characteristics	
Methods	Design: parallel, randomised, open Date: not stated Duration: 13 months (56 weeks) Number of study centres: 4 Setting: outpatient clinic, USA
Participants	Who participated: 584 people who were previously enrolled in the HDFP treated with antihypertensive drugs and who had sufficiently controlled hypertension. The dietary change on the return of hypertension after withdrawal of prolonged antihypertensive therapy (dish) included 7 treatment arms; the results of 2 of those arms met the inclusion criteria for this review (hypertensive and obese patients with either dietary intervention or not) Main inclusion criteria: HDFP participants; DBP ≥ 95 mm hg on first screening, confirmed by second screening with DBP ≥ 90 mm hg; patients had received antihypertensive medication for at least 5 years; eligible participants had to be "controlled"; hypertensive persons defined by: 1. no SBP > 180 mm Hg during previous year 2. average DBP < 95 mm Hg during previous year 3. average of last 2 DBP ≤ 90 mm Hg and neither > 95 mm Hg Main exclusion criteria: history of congestive heart failure; myocardial infarction; stroke or transient ischaemic attacks; creatinine level ≥ 2.5 mg/dl; ß-blocker therapy for angina; glucocorticoid therapy for indefinite period Subgroup analyses: results from participants with mild and severe hypertension (not clear whether subgroups were predefined or post hoc)
Interventions	Dietary intervention: according to revised "metropolitan life insurance" standards; intervention consisted of 8 initial weekly group sessions followed by monthly sessions plus individual consultation as needed (weight loss component of the trial: N = 87) No dietary intervention: no recommendations (weight loss component of the trial: N = 89) Additional treatment: discontinuation of antihypertensive treatment using a step-down withdrawal programme; bi-weekly consultations for BP measurement for 16 weeks followed by monthly consultations; no change in salt uptake
Outcomes	Primary outcomes: 1. Mortality: - 2. Cardiovascular morbidity: - 3. Adverse events: *Definition*: withdrawal due to the need to restart antihypertensive medication Secondary outcomes: 1. Changes in systolic blood pressure [mm Hg]: - 2. Changes in diastolic blood pressure [mm Hg]: - 3. Changes in body weight [kg]:

DISH 1985 *(Continued)*

	Definition: body weight change from baseline to endpoint visit Additional outcomes measured in the study: 1. Number of participants without antihypertensive medication 2. Change in sodium excretion
Study details	Length of follow-up: 13 months (56 weeks) Trial terminated before regular end (for benefit / because of adverse events): No Trial ID: -
Publication details	Language of publication: English Funding: grant from National Heart, Lung and Blood Institute; drugs were supplied by the following companies: Ayerst Laboratories, New York; Merck Sharp & Dohme, West Point, PA; Ciba-Geigy Corp, Summit, NJ; Boehringer Ingelheim Ltd., Ridgefield, CT; USV Pharmaceutical Corp, Tuckahoe, NY; G.D. Searle & Co, Chicago Publication status: Full-text journal publication
Study aim	Quote from publication: "... to determine whether long-term aggressive antihypertensive therapy can be withdrawn in selected patients without relapse and if the substitution of dietary modification will reduce the recidivism rate."
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: No details on sequence generation are provided
Allocation concealment (selection bias)	Unclear risk	Comment: Method of concealment is not described
Blinding (performance bias and detection bias) Total mortality	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Adverse events	Unclear risk	Comment: Open design; participants and investigators not blinded; no information on blinding for outcome assessors
Blinding (performance bias and detection bias) Change in blood pressure	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Change in body weight	Unclear risk	Comment: Open design; participants and investigators not blinded; no information on blinding for outcome assessors
Incomplete outcome data (attrition bias)	Unclear risk	Comment: Outcome not reported

DISH 1985 *(Continued)*
Total mortality

Incomplete outcome data (attrition bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Adverse events	High risk	Comment: Only withdrawals due to the need to resume antihypertensive medication were reported; no other adverse events were reported
Incomplete outcome data (attrition bias) Change in blood pressure	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Change in body weight	High risk	Comment: Withdrawals: and reasons/descriptions (dietary intervention vs no dietary intervention): concerning the endpoint success of withdrawal from antihypertensive medication: 0 vs 0; concerning body weight at week 56: 20 vs 12; although there were no losses to follow-up in the relevant subgroups for success of discontinuing antihypertensive treatment, for 13% respectively 23% participants weight at week 56 is not reported
Selective reporting (reporting bias)	Unclear risk	Comment: No study protocol available; no primary and secondary outcomes were defined in the publications
Other bias	High risk	Comment: 1. Randomisation before consent of participants (possible selection bias) 2. Different body weight at baseline 3. Participants were in previous trial for 5 years (selected population may not be representative)

Jalkanen 1991

Study characteristics	
Methods	Design: parallel, randomised Date: not stated Duration: 12 months Number of study centres: 2 Setting: outpatient clinic (2 hypertension clinics), Finland
Participants	Who participated: 50 overweight people with hypertensions (selected from files) Main inclusion criteria: age 35 to 59 years; BMI 27 to 34 kg/m^2; DBP ≥ 95 mm Hg Main exclusion criteria: - Subgroup analyses: none
Interventions	Dietary intervention: individually-planned energy-restricted diet of 1000 to 1500 kcal a day, weekly (after 6 months every 3 weeks); sessions including discussions and lessons on behavioural modification, choice of food, physical exercise, and medical aspects of overweight and weight reduction; 1½ hour duration; total number of lectures about 40 hours; the participants received leaflets on the reduction of salt and fat consumption and on the increase of physical activity; lectures by different medical experts; nutritionists interview; laboratory tests (N = 25)

Jalkanen 1991 *(Continued)*

	No dietary intervention: visits every 3 months; no personal counselling; nutritionists interview; laboratory tests (N = 25) Additional treatment: participants' doctors were asked to keep the dosage of antihypertensive drugs at the initial level
Outcomes	Primary outcomes: 1. Mortality: - 2. Cardiovascular morbidity: - 3. Adverse events: - Secondary outcomes: 1. Changes in systolic blood pressure [mm Hg]: *Definition*: SBP change from baseline to endpoint visit 2. Changes in diastolic blood pressure [mm Hg]: *Definition*: DBP change from baseline to endpoint visit 3. Changes in body weight [kg]: *Definition:* body weight change from baseline to endpoint visit Additional outcomes measured in the study: 1. Change in lipid parameters 2. Change in potassium and sodium excretions 3. Change in dietary factors (fats and protein)
Study details	Length of follow-up: 12 months Trial terminated before regular end (for benefit / because of adverse events): No Trial ID: -
Publication details	Language of publication: English Funding: - Publication status: Full-text journal publication
Study aim	Quote from publication: "...to test a comprehensive but practical intervention program aimed for general use in the non-pharmacological treatment of cardiovascular risk factors, especially overweight, hypertension and high serum lipids, in a primary health care setting."
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: No details on sequence generation are provided
Allocation concealment (selection bias)	Unclear risk	Comment: Method of concealment is not described
Blinding (performance bias and detection bias) Total mortality	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported

Jalkanen 1991 *(Continued)*

Blinding (performance bias and detection bias) Adverse events	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Change in blood pressure	Unclear risk	Comment: Open design; participants and investigators not blinded; no information on blinding for outcome assessors
Blinding (performance bias and detection bias) Change in body weight	Unclear risk	Comment: Open design; participants and investigators not blinded; no information on blinding for outcome assessors
Incomplete outcome data (attrition bias) Total mortality	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Adverse events	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Change in blood pressure	Unclear risk	Comment: ITT analysis unclear; Withdrawals: and reasons/descriptions (dietary intervention vs no dietary intervention): 1 (4%) vs 0; no reasons for withdrawals reported; No information on dealing with missing data
Incomplete outcome data (attrition bias) Change in body weight	Unclear risk	Comment: ITT analysis unclear; Withdrawals: and reasons/descriptions (dietary intervention vs no dietary intervention): 1 (4%) vs 0; no reasons for withdrawals reported; No information on dealing with missing data
Selective reporting (reporting bias)	Unclear risk	Comment: No study protocol available; no primary and secondary outcomes were defined in the publication
Other bias	Low risk	Comment: None detected

ODES 1995

Study characteristics	
Methods	Design: parallel, 2 x 2 factorial, randomised, open Date: not stated Duration: 12 months Number of study centres: unclear (probably 1, because all eligible participants were screened at the Ullevaal Hospital, Oslo) Setting: outpatient clinic, Norway
Participants	Who participated: 219 men and women ≥ 40 years old from screening programme for cardiovascular risk factors in Oslo (Norway) since 1981; participants were post hoc divided in tertiles according to DBP (tertile 1 DBP > 91 mm Hg, tertile 2 DBP 84 to 91 mm Hg, tertile 3 DBP < 84 mm Hg); only subgroups of tertile 1 (DBP > 91 mm Hg) will be reported in this review Main inclusion criteria: all criteria had to be fulfilled simultaneously (based on the screening performed 1 to 10 years before baseline examination): age 41 to 50 years + physical inactivity as measured by

ODES 1995 *(Continued)*

	questionnaire (exercising at most once a week) + BMI > 24 kg/m^2 + DBP 86 to 99 mm Hg + total serum cholesterol 5.20 to 7.74 mmol/l + HDL cholesterol < 1.20 mmol/l, fasting serum triglycerides > 1.4 mmol/l Main exclusion criteria: overt cardiovascular disease, diabetes, treatment with antihypertensive drugs or acetylsalicylic acid, lipid-lowering diet Subgroup analyses: none
Interventions	**No-exercise group**: Dietary intervention: individual dietary counselling for each participant together with participant's spouse; main emphasis was a low-calorie diet and a substantial increase in the intake of fish and fish products, an increase in the consumption of vegetables and fibre-rich products of complex carbohydrates, and a reduction in intake of sugar and saturated fat; target body weight reduction was agreed upon, usually 0.5 to 1 kg monthly according to Anderssen 1995 and 0.5 to 2 kg according to the design paper Urdal 1993; hypertensive participants were also advised to reduce salt intake Follow-up of dietary habits took place at months 3 and 9 (N = 122; hypertensive subgroup: N = not stated) No dietary intervention: no dietary counselling, no change in lifestyle (N = 97; hypertensive subgroup: N = not stated) **Exercise group**: Dietary intervention + exercise: individual counselling as mentioned above as well as additional supervised aerobic exercise programme consisting of circuit training and jogging for 1 hour 3 times a week No dietary intervention + exercise: no dietary counselling but same exercise programme as mentioned above Additional treatment: all participants were advised against smoking
Outcomes	Primary outcomes: 1. Mortality: - 2. Cardiovascular morbidity: - 3. Adverse events: - Secondary outcomes: 1. Changes in systolic blood pressure [mm Hg]: *Definition:* SBP change from baseline to endpoint visit 2. Changes in diastolic blood pressure [mm Hg]: *Definition:* DBP change from baseline to endpoint visit 3. Changes in body weight [kg]: *Definition:* changes in BMI from baseline to endpoint visit Additional outcomes measured in the study: 1. effect on haemostatic variables (primary study endpoint)
Study details	Length of follow-up: 12 months Trial terminated before regular end (for benefit / because of adverse events): No Trial ID: -
Publication details	Language of publication: English Funding: supported by grant from the Research Council of Norway, the Norwegian Council of Cardiovascular Diseases, and the insurance company Vital Friskvern Publication status: Full-text journal publication
Study aim	Quote from publication: "...to test whether dietary changes, exercise, or the combination affects the haemostatic system."

ODES 1995 *(Continued)*

Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Quote: "Each participant has a 25% chance of being allocated to each of the four treatment groups. The list is not blocked in any way, but randomization is stratified by sex." Comment: No details on sequence generation are provided
Allocation concealment (selection bias)	Low risk	Quote: "A sealed envelope is opened, revealing the randomization number and the name of the group to which the participant has been allocated." No information about numbered or opaque envelopes
Blinding (performance bias and detection bias) Total mortality	Low risk	Quote: "Unmasked, but blinded objective blood analyse Comment: Participants, investigators and outcome assessors not blinded
Blinding (performance bias and detection bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Adverse events	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Change in blood pressure	High risk	Quote: "Unmasked, but blinded objective blood analyses" Comment: Participants, investigators and outcome assessors not blinded
Blinding (performance bias and detection bias) Change in body weight	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Total mortality	High risk	Comment: No ITT analysis; withdrawals not reported for the hypertensive subgroup (tertile 1); withdrawals for the whole study population of normo- and hypertensives: *No-exercise subgroup* (dietary intervention vs no dietary intervention): 3 vs 0 *Exercise subgroup* (dietary intervention vs no dietary intervention): 2 vs 5 reasons for dropouts: • refused to participate: 5 • injury due to trial-associated exercise: 1 • carcinoma: 2 • exercise-unrelated herniated vertebral disk: 1 • cardiac event: 1
Incomplete outcome data (attrition bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias)	Unclear risk	Comment: Outcome not reported

ODES 1995 *(Continued)*
Adverse events

Incomplete outcome data (attrition bias) Change in blood pressure	High risk	Comment: No ITT analysis, although it was initially planned; withdrawals not reported for the hypertensive subgroup (tertile 1); withdrawals for the whole study population of normo- and hypertensives: *No-exercise subgroup* (dietary intervention vs no dietary intervention): 3 vs 0 *Exercise subgroup* (dietary intervention vs no dietary intervention): 2 vs 5 reasons for dropouts: • refused to participate: 5 • injury due to trial-associated exercise: 1 • carcinoma: 2 • exercise-unrelated herniated vertebral disk: 1 • cardiac event: 1
Incomplete outcome data (attrition bias) Change in body weight	Unclear risk	Comment: Outcome not reported
Selective reporting (reporting bias)	High risk	Comment: Post hoc analyses of blood pressure; not all predefined outcomes are reported for each tertile (e.g. quality of life)
Other bias	High risk	Comment: 1. Multiple testing was done without adjustment (e.g. Bonferroni correction) 2. Hypertensive participants in dietary-intervention group advised to reduce salt intake (intervention bias) 3. Tertile 3 was defined as DBP < 84 mm Hg, whereas inclusion criteria was DBP > 86 mm Hg. In total, 68 participants (31%) were analysed in tertile 3

ODES 1995 no exercise

Study characteristics	
Methods	see ODES 1995
Participants	
Interventions	
Outcomes	
Study details	
Publication details	
Study aim	
Notes	

ODES 1995 with exercise

Study characteristics	
Methods	see ODES 1995
Participants	
Interventions	
Outcomes	
Study details	
Publication details	
Study aim	
Notes	

Ruvolo 1994

Study characteristics	
Methods	Design: parallel, randomised Date: not stated Duration: 6 months Number of study centres: 1 Setting: outpatient clinic, Italy
Participants	Who participated: 32 overweight hypertensive patients on 10 mg amlodipine daily Main inclusion criteria: BMI > 30 kg/m^2, DBP > 100 mm Hg Main exclusion criteria: heart failure, coronary artery disease, diabetes mellitus Subgroup analyses: -
Interventions	Dietary intervention: weight-reducing diet, no restriction on salt uptake (N = 16) No dietary intervention: no counselling (N = 16) Additional treatment: amlodipine 10 mg
Outcomes	Primary outcomes: 1. Mortality: - 2. Cardiovascular morbidity: - 3. Adverse events: reported: - Secondary outcomes: 1. Changes in systolic blood pressure [mm Hg]: *Definition:* SBP change from baseline to endpoint visit 2. Changes in diastolic blood pressure [mm Hg]: *Definition:* DBP change from baseline to endpoint visit 3. Changes in body weight [kg]: *Definition:* body weight change from baseline to endpoint visit Additional outcomes measured in the study: 1. Change in left ventricular dimensions

Ruvolo 1994 *(Continued)*

	2. Change in heart rate
Study details	Length of follow-up: 6 months Trial terminated before regular end (for benefit / because of adverse events): No Trial ID: -
Publication details	Language of publication: Italian Funding: - Publication status: Full-text journal publication
Study aim	Quote from publication: "Scopo di questo studio è valutare se l´impostazione di un regime dietetico ipocalorico possa determinare modificazioni significative a carico del ventricolo sinistro in pazienti obesi ed ipertesi trattati con amlodipina."
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Comment: No details on sequence generation are provided
Allocation concealment (selection bias)	Unclear risk	Comment: Method of concealment is not described
Blinding (performance bias and detection bias) Total mortality	Low risk	Comment: Participants not blinded; no information on blinding for investigators or outcome assessors
Blinding (performance bias and detection bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Adverse events	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Change in blood pressure	Unclear risk	Comment: Participants not blinded; no information on blinding for investigators or outcome assessors
Blinding (performance bias and detection bias) Change in body weight	Unclear risk	Comment: Participants not blinded; no information on blinding for investigators or outcome assessors
Incomplete outcome data (attrition bias) Total mortality	High risk	Comment: ITT analysis unclear; withdrawals (dietary intervention vs no dietary intervention): 2 (13%) vs. 0; reasons for withdrawal not reported
Incomplete outcome data (attrition bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported

Ruvolo 1994 *(Continued)*

Incomplete outcome data (attrition bias) Adverse events	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Change in blood pressure	High risk	Comment: ITT analysis unclear; withdrawals (dietary intervention vs no dietary intervention): 2 (13%) vs. 0
Incomplete outcome data (attrition bias) Change in body weight	High risk	Comment: ITT analysis unclear; withdrawals (dietary intervention vs no dietary intervention): 2 (13%) vs. 0
Selective reporting (reporting bias)	Unclear risk	Comment: No study protocol provided; no primary and secondary outcomes were defined in the publication
Other bias	Low risk	Comment: None detected

TAIM 1992

Study characteristics	
Methods	Design: 3x3 factorial, randomised, open Date: 1985 - 1993 Duration: 6 months (phase I) Number of study centres: 3 Setting: outpatient clinic at 3 university hospitals (Bronx (New York), Birmingham (Alabama), Jackson (Mississippi)), USA
Participants	Who participated:878 obese hypertensive patients The trial consisted of 2 phases. Phase I was performed in a 3 x 3 factorial design with follow-up of 6 months. Phase II was performed in a 2 x 2 factorial design (usual care vs weight-reducing diet). Since dropout in usual-care group was 29% to 36% for phase II, only phase I will be analysed Main inclusion criteria: age 21 to 65 years; 110% to 116% of ideal body weight; sitting DBP (preliminary screened: treated ≤ 100 mm Hg, untreated 90 to 104 mm Hg; first clinic visit: 90 to 100 mm Hg; second clinic visit: < 115 mm Hg); no antihypertensive medication or discontinuation of current medication for at least 2 weeks before baseline BP measurement Main exclusion criteria: myocardial infarction within 1 year before study entry; medical history of stroke, bronchial asthma, insulin-dependent diabetes mellitus, or allergy to thiazides or ß-blockers; other major diseases (e.g. kidney disease, liver disease, or cancer); baseline creatinine ≥ 2 mg/dl; pregnancy; scheduled surgery Subgroup analyses: none
Interventions	Dietary intervention: weight-reducing diet (standard programme of diet counselling and nutrition education with the goal of a reduction of 10% of baseline weight or 4.54 kg, whichever was greater); 10 weekly group sessions within the first 6 months, subsequently individual or group counselling sessions with a nutritionist at least every 6 weeks, after 12 months dietary counselling on a quarterly basis (weight loss component of the trial: N = 291) No dietary intervention: no diet and nutritional counselling or education (weight loss component of the trial: N = 296) Additional treatment: pharmacological antihypertensive treatment according to subgroup allocation (placebo or diuretic or ß-blocker); medication was stepped up if BP reached predefined escape levels; regular monthly clinic visits for the first 6 months, every 3 months thereafter

TAIM 1992 *(Continued)*

Outcomes	Primary outcomes: 1. Mortality: - 2. Cardiovascular morbidity: - 3. Adverse events: - Secondary outcomes: 1. Changes in systolic blood pressure [mm Hg]: *Definition:* SBP change from baseline to endpoint visit 2. Changes in diastolic blood pressure [mm Hg]: *Definition:* DBP change from baseline to endpoint visit 3. Changes in body weight [kg]: *Definition:* body weight change from baseline to endpoint visit Additional outcomes measured in the study: 1. Change in sodium excretion 2. Change in potassium excretion 3. Quality of life (life satisfaction scale) 4. Symptoms and mental function (symptom checklist) 5. Expected side effects due to use of ß-blocker (physical complaint inventory)
Study details	Length of follow-up: 6 months (phase I) Trial terminated before regular end (for benefit / because of adverse events): No Trial ID: -
Publication details	Language of publication: English Funding: National Heart, Lung and Blood Institute Publication status: Full-text journal publication
Study aim	Quote from publication: "...to assess the 6-month effectiveness of weight loss and low sodium/high potassium diets, alone or in combination with diuretics or ß-blockers, in lowering diastolic blood pressure in persons with mild hypertension."
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Comment: No details on sequence generation are provided in publications, but according to IQWIG report adequate (IQWiG 2006)
Allocation concealment (selection bias)	Low risk	Comment: Method of concealment is not described in publications, but according to IQWIG report adequate (IQWiG 2006)
Blinding (performance bias and detection bias) Total mortality	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Adverse events	Unclear risk	Comment: Outcome not reported

TAIM 1992 *(Continued)*

Blinding (performance bias and detection bias) Change in blood pressure	Unclear risk	Comment: Participants, study personnel were not blinded, but data collection staff was masked to intervention assignment
Blinding (performance bias and detection bias) Change in body weight	Unclear risk	Comment: Participants, study personnel were not blinded, but data collection staff was masked to intervention assignment
Incomplete outcome data (attrition bias) Total mortality	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Cardiovascular morbidity	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Adverse events	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Change in blood pressure	High risk	Comment: No ITT analyses; withdrawals ranged from 1% to 12% in the study groups
Incomplete outcome data (attrition bias) Change in body weight	High risk	Comment: No ITT analyses; withdrawals ranged from 1% to 12% in the study groups
Selective reporting (reporting bias)	Low risk	Comment: Outcomes are reported as prespecified
Other bias	High risk	Comment: 1. Step-up medication: 20% (placebo/usual diet) vs 10% (placebo/weight-reducing diets); it is unclear how many participants required an additional open-label antihypertensive treatment; indication for step-up therapy is presented inconsistently between study-related publications 2. Number of randomised participants (878) is below calculated sample size (918), although 1940 participants were eligible

TAIM 1992 atenolol

Study characteristics	
Methods	see TAIM 1992
Participants	
Interventions	
Outcomes	
Study details	
Publication details	

TAIM 1992 atenolol *(Continued)*

Study aim	
Notes	

TAIM 1992 chlorthalidone

Study characteristics	
Methods	see TAIM 1992
Participants	
Interventions	
Outcomes	
Study details	
Publication details	
Study aim	
Notes	

TAIM 1992 combined

Study characteristics	
Methods	see TAIM 1992
Participants	
Interventions	
Outcomes	
Study details	
Publication details	
Study aim	
Notes	

TAIM 1992 placebo

Study characteristics	
Methods	see TAIM 1992

TAIM 1992 placebo *(Continued)*

Participants	
Interventions	
Outcomes	
Study details	
Publication details	
Study aim	
Notes	

TONE 1998

Study characteristics	
Methods	Design: parallel, 2 x 2 factorial, randomised, blinded endpoint evaluation Date: August 1992 - December 1995 Duration: 15 to 36 months Number of study centres: 4 Setting:outpatient clinic, USA
Participants	Who participated: 975 elderly, overweight and non-overweight, people with hypertension; participants were assigned to active intervention: sodium reduction (S^+), or weight loss (only overweight participants), or sodium reduction (S^+) and weight loss (only overweight participants) vs usual care Main inclusion criteria: age 60 to 80 years; BMI ≥ 27.8 kg/m^2 (men), BMI ≥ 27.3 kg/m^2 (women); SBP < 145 mm Hg and DBP < 85 mm Hg while taking 1 antihypertensive medication or 2 antihypertensive medications if 1 can be stopped during screening phase (combination of 1 diuretic and 1 non-diuretic drug are considered as 1 drug) Main exclusion criteria: heart attack or stroke within preceding 6 months; angina; congestive heart failure; insulin-dependent diabetes mellitus; BMI > 33 kg/m^2 (men), BMI > 37 kg/m^2 (women); unexplained or involuntary weight loss of 4.5 kg or greater during previous year; hypercreatinaemia; hyperkalaemia; hyperglycaemia; anaemia Subgroup analyses: age, gender, ethnicity
Interventions	Dietary intervention: achieving and maintaining a weight loss of 4.5 kg or greater; structured programmes with dietary advice provided to participants mainly in small groups to change their eating behaviours and to motivate participants to achieve and maintain their desired reductions; participants were required to increase amount of physical activity, but no detailed information was provided (weight loss component of the trial: N = 294) No dietary intervention: no study-related counselling (weight loss component of the trial: N = 294) Additional treatment: Salt restriction (S^+): achieving and maintaining a 24-hour dietary sodium intake of 80 mmol or less (as measured by 24-hour urine collection)
Outcomes	Primary outcomes: 1. Mortality: reported 2. Cardiovascular morbidity: reported 3. Adverse events:

TONE 1998 *(Continued)*

	Definition: presumed adverse events were assessed using a standardised approach that included questioning of participants, family members, and physicians and a review of physicians' records with blinded evaluation Secondary outcomes: 1. Changes in systolic blood pressure [mm Hg]: - 2. Changes in diastolic blood pressure [mm Hg]: - 3. Changes in body weight [kg]: reported for the combined groups only (both intervention (IG-S^+ and IG-S^-) vs both control (CG-S^+ and CG-S^-) groups) Additional outcomes measured in the study: 1. Primary study endpoint: failure of antihypertensive drug withdrawal due to: a. occurrence of high blood pressure measured at 1 or more follow-up visits according predefined values b. restart of treatment with antihypertensive medication due to other reasons or based on the decision of the treating doctors or study participants c. occurrence of clinical cardiovascular disease complications during follow-up 2. Weight reduction
Study details	Length of follow-up: 15 to 36 months Trial terminated before regular end (for benefit / because of adverse events): No Trial ID: -
Publication details	Language of publication: English Funding: National Heart, Lung and Blood Institute and National Institute on Aging grants Publication status: Full-text journal publication
Study aim	Quote from publication: "...to determine the feasibility, efficacy, and safety of sodium reduction and weight loss in older persons with hypertension."
Notes	-

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Quote: "using a computer program ... stratified by clinic and weight status ... blocking of variable length"
Allocation concealment (selection bias)	Low risk	Comment: Method of concealment is not described in publication, but according to IQWIG report supposable adequate (IQWiG 2006)
Blinding (performance bias and detection bias) Total mortality	Low risk	Comment: Participants, study personnel were not blinded, but an independent committee masked to intervention assignment evaluated the endpoints
Blinding (performance bias and detection bias) Cardiovascular morbidity	Unclear risk	Comment: Participants, study personnel were not blinded, but an independent committee masked to intervention assignment evaluated the endpoints
Blinding (performance bias and detection bias) Adverse events	Unclear risk	Comment: Participants, study personnel were not blinded, but an independent committee masked to intervention assignment evaluated the endpoints

TONE 1998 *(Continued)*

Blinding (performance bias and detection bias) Change in blood pressure	Unclear risk	Comment: Outcome not reported
Blinding (performance bias and detection bias) Change in body weight	Unclear risk	Comment: Participants, study personnel were not blinded, but an independent committee masked to intervention assignment evaluated the endpoints
Incomplete outcome data (attrition bias) Total mortality	Low risk	Comment: Numbers of withdrawals and reasons are missing, but 96% to 99% of participants were included at follow-up analysis
Incomplete outcome data (attrition bias) Cardiovascular morbidity	Low risk	Comment: Numbers of withdrawals and reasons are missing, but 96% to 99% of participants were included at follow-up analysis
Incomplete outcome data (attrition bias) Adverse events	High risk	Comment: No usable results were reported
Incomplete outcome data (attrition bias) Change in blood pressure	Unclear risk	Comment: Outcome not reported
Incomplete outcome data (attrition bias) Change in body weight	Low risk	Comment: Numbers of withdrawals and reasons are missing, but 96% to 99% of participants were included at follow-up analysis
Selective reporting (reporting bias)	Low risk	Comment: Outcomes are reported as prespecified
Other bias	Low risk	Comment: None detected

BMI: body mass index
BP: blood pressure
DBP: diastolic blood pressure
HDFP: Hypertension Detection an Follow-up Program
HDL: high-density lipoprotein
LOCF: last observation carried forward analysis
SBP: systolic blood pressure

Characteristics of excluded studies *[ordered by study ID]*

Study	Reason for exclusion
(no authors listed) 1993	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Abou-Raya 2014	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
ACTRN12610000049077	The study is not a randomised controlled trial
Allison 2016	The intervention in this study is not a weight-reducing diet
Andersen 1985	The intervention in this study is not a weight-reducing diet

Study	Reason for exclusion
Andrews 2011	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Angelico 2009	Full text of this study is not available
Appel 2006	The intervention in this study is not a weight-reducing diet
Ard 2005	The study is not a randomised controlled trial
Ard 2017	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Balas-Nakash 2014	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Banos 2015	The study includes a combination of different interventions
Bao 1999	Full text of this study is not available
Bartels 1974	The duration of the intervention is less than 24 weeks
Bazian 2004	The study includes a combination of different interventions
Bennett 2018	The study includes a combination of different interventions
Bouchonville 2014	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Cakir 2006	The study includes a combination of different interventions
Cambien 1986	Full text of this study is not available
Camhi 2010	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Chen 2009	The intervention in this study is not a weight-reducing diet
Childress 2008	Full text of this study is not available
Chirinos 2016	The study includes a combination of different interventions
Christensen 2013	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Coppell 2010	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Curzio 1989	No electronic records and/or hard copies available, therefore insufficient data for inclusion (personal communication)
Cutler 1997	The study includes a combination of different interventions
De Mello 2008	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup

Study	Reason for exclusion
Diaz 2014	The study does not include participants with essential hypertension
Di Mauro 1998	The control intervention in the study is inappropriate
Ebell 2013	The study is not a randomised controlled trial
Fagerberg 1989	The study includes different accompanying therapies
Gilliam 2012	The study is not a randomised controlled trial
Gillum 1983	The duration of the intervention is less than 24 weeks
Hall 2003	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Han 2017	The control intervention in the study is inappropriate
Haynes 1984	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Hayward 2010	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
He 2000	The study does not include participants with essential hypertension
Heinberg 2000	The study includes a combination of different interventions
Heshka 2003	The study is not a randomised controlled trial
Heyden 1974	The study includes a combination of different interventions
Hsieh 2009	The study is not a randomised controlled trial
Hua 2017	The study includes a combination of different interventions
Hyden 1973	The study includes a combination of different interventions
IRCT2015062422905N1	The control intervention in the study is inappropriate
Jones 1999	In this study the control group also includes a weight-reducing dietary intervention
Kanke 2015	The control intervention in the study is inappropriate
Karoff 1985	The duration of the intervention is less than 24 weeks
Karvetti 1992	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Katzel 1995	The study does not include participants with essential hypertension
Kawamura 1993	The duration of the intervention is less than 24 weeks
Kittiskulnam 2014	The study does not include participants with essential hypertension

Study	Reason for exclusion
Kolehmainen 2008	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Koopman 1990	The intervention in this study is not a weight-reducing diet
Korhonen 2003	Full text of this study is not available
Larson-Meyer 2010	The study does not include participants with essential hypertension
Lindgarde 2001	The intervention in this study is not a weight-reducing diet
Mason 2013	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Masuo 2012	The study includes a combination of different interventions
McCarron 2000	The duration of the intervention is less than 24 weeks
Melchart 2015	The study includes a combination of different interventions
Metz 2000	In this study the control group also includes a weight-reducing dietary intervention
Moore 2013	The control intervention in the study is inappropriate
NCT00142649	The control intervention in the study is inappropriate
NCT00661817	The intervention in this study is not a weight-reducing diet
NCT00783315	The control intervention in the study is inappropriate
NCT01724645	The duration of the intervention is less than 24 weeks
NCT02136264	The control intervention in the study is inappropriate
NCT02445833	The study is not a randomised controlled trial
NCT02454127	The control intervention in the study is inappropriate
NCT03288142	The intervention in this study is not a weight-reducing diet
Neuhouser 2012	The intervention in this study is not a weight-reducing diet
Noble 1971	The duration of the intervention is less than 24 weeks
Oshakbayev 2016	The study includes a combination of different interventions
Poppitt 2002	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Prentice 2017	The intervention in this study is not a weight-reducing diet
Pritchard 2002	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Reisin 1978	The duration of the intervention is less than 24 weeks

Study	Reason for exclusion
Rissanen 1985	The study is not a randomised controlled trial
Rosas 2015	The study includes a combination of different interventions
Salas-Salvado 2008	The intervention in this study is not a weight-reducing diet
Salinardi 2012	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Samaha 2003	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Schwab 2008	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Sedjo 2016	The study includes a combination of different interventions
Stamler 1985	The study includes a combination of different interventions
Tate 2011	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Trepanowski 2014	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Tunyan 2007	The study includes a combination of different interventions
Tuomilehto 2009	The study does not include participants with essential hypertension
Ueki 2016	The intervention in this study is not a weight-reducing diet
UMIN000002967	The control intervention in the study is inappropriate
UMIN000006582	The duration of the intervention is less than 24 weeks
UMIN000029395	The control intervention in the study is inappropriate
Vissers 2010	The study does not include participants with essential hypertension
Weil 2016	The control intervention in the study is inappropriate
Weiss 2016	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
WHO Europ.Coll.Grp. 1974	The study is not a randomised controlled trial
Wright 2017	The intervention in this study is not a weight-reducing diet
Yamada 2013	The study includes normotensive and hypertensive participants but reports no or insufficient results for the hypertensive subgroup
Zotova 2015	The control intervention in the study is inappropriate

DATA AND ANALYSES

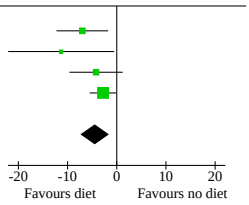
Comparison 1. Weight-reducing diet versus no weight-reducing diet

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1.1 Change in systolic blood pressure from baseline to endpoint	4	731	Mean Difference (IV, Random, 95% CI)	-4.49 [-7.20, -1.78]
1.2 Change in diastolic blood pressure from baseline to endpoint	6	731	Mean Difference (IV, Random, 95% CI)	-3.19 [-4.83, -1.54]
1.3 Change in body weight from baseline to endpoint	7	880	Mean Difference (IV, Random, 95% CI)	-3.98 [-4.79, -3.17]

Analysis 1.1. Comparison 1: Weight-reducing diet versus no weight-reducing diet, Outcome 1: Change in systolic blood pressure from baseline to endpoint

Study or Subgroup	Weight reducing diet Mean [mm Hg]	SD [mm Hg]	Total	No weight reducing diet Mean [mm Hg]	SD [mm Hg]	Total	Weight	Mean Difference IV, Random, 95% CI [mm Hg]
Croft 1986	-11	15.26	66	-4	15.26	64	21.5%	-7.00 [-12.25 , -1.75]
ODES 1995 no exercise	-8.4	13.2	16	2.9	15.24	12	6.0%	-11.30 [-22.08 , -0.52]
ODES 1995 with exercise	-8.3	10.29	24	-4.1	8.05	20	20.4%	-4.20 [-9.62 , 1.22]
TAIM 1992 combined	-17.01	15.95	265	-14.22	15.95	264	52.2%	-2.79 [-5.51 , -0.07]
Total (95% CI)			**371**			**360**	**100.0%**	**-4.49 [-7.20 , -1.78]**

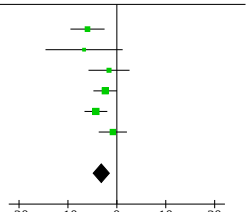
Heterogeneity: Tau² = 1.74; Chi² = 3.78, df = 3 (P = 0.29); I² = 21%
Test for overall effect: Z = 3.25 (P = 0.001)
Test for subgroup differences: Not applicable



Analysis 1.2. Comparison 1: Weight-reducing diet versus no weight-reducing diet, Outcome 2: Change in diastolic blood pressure from baseline to endpoint

Study or Subgroup	Weight reducing diet Mean [mm Hg]	SD [mm Hg]	Total	No weight reducing diet Mean [mm Hg]	SD [mm Hg]	Total	Weight	Mean Difference IV, Random, 95% CI [mm Hg]
Croft 1986	-7	10.15	66	-1	10.15	64	15.4%	-6.00 [-9.49 , -2.51]
ODES 1995 no exercise	-7.1	7.2	16	-0.4	12.47	12	4.0%	-6.70 [-14.59 , 1.19]
ODES 1995 with exercise	-7.1	6.37	24	-5.5	7.6	20	11.8%	-1.60 [-5.79 , 2.59]
TAIM 1992 atenolol	-14.81	9.14	88	-12.43	6.99	87	24.1%	-2.38 [-4.79 , 0.03]
TAIM 1992 chlorthalidone	-15.06	8.54	87	-10.78	7.08	87	25.0%	-4.28 [-6.61 , -1.95]
TAIM 1992 placebo	-8.78	10.97	90	-7.96	8.63	90	19.7%	-0.82 [-3.70 , 2.06]
Total (95% CI)			**371**			**360**	**100.0%**	**-3.19 [-4.83 , -1.54]**

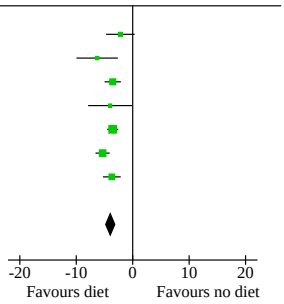
Heterogeneity: Tau² = 1.41; Chi² = 7.67, df = 5 (P = 0.18); I² = 35%
Test for overall effect: Z = 3.79 (P = 0.0001)
Test for subgroup differences: Not applicable



Analysis 1.3. Comparison 1: Weight-reducing diet versus no weight-reducing diet, Outcome 3: Change in body weight from baseline to endpoint

Study or Subgroup	Weight reducing diet Mean [kg]	SD [kg]	Total	No weight reducing diet Mean [kg]	SD [kg]	Total	Weight	Mean Difference IV, Random, 95% CI [kg]
Cohen 1991	-0.88	4	15	1.3	3	15	8.3%	-2.18 [-4.71 , 0.35]
Croft 1986	-6.5	10.66	66	-0.2	10.66	64	4.4%	-6.30 [-9.97 , -2.63]
DISH 1985	-4	5	67	-0.46	3.6	77	18.4%	-3.54 [-4.98 , -2.10]
Jalkanen 1991	-4	6.96	24	0	6.96	25	3.9%	-4.00 [-7.90 , -0.10]
TAIM 1992 atenolol	-3.02	3.75	88	0.53	2.8	87	27.0%	-3.55 [-4.53 , -2.57]
TAIM 1992 chlorthalidone	-6.85	4.64	86	-1.52	3.73	87	21.5%	-5.33 [-6.59 , -4.07]
TAIM 1992 placebo	-4.41	6.6	89	-0.71	3.79	90	16.5%	-3.70 [-5.28 , -2.12]
Total (95% CI)			**435**			**445**	**100.0%**	**-3.98 [-4.79 , -3.17]**

Heterogeneity: Tau² = 0.37; Chi² = 9.14, df = 6 (P = 0.17); I² = 34%
Test for overall effect: Z = 9.69 (P < 0.00001)
Test for subgroup differences: Not applicable



ADDITIONAL TABLES

Table 1. Overview of trial populations

Trial	Intervention(s) and comparator(s)	Description of power and sample size calculation	Screened/ eligible (N)	Randomised (N)	Safety (N)	ITT (N)	Finishing trial (N)	Randomised finishing trial (%)	Follow-up (extended follow-up)
Cohen 1991	diet	n.r.	67	15	n.r.	15	15	100	12 months
	no diet			15	n.r.	15	15	100	
Croft 1986	diet	no power calculation was performed	n.r.	66	n.r.	66	49	74	6 months
	no diet		n.r.	64	n.r.	64	61	95	
DISH 1985	diet	n.r.	584[a]	87	n.r.	n.r.	67	77	13 months (56 weeks)
	no diet			89	n.r.	n.r.	77	87	
Jalkanen 1991	diet	n.r.	25	25	n.r.	n.r.	24	96	12 months
	no diet		25	25	n.r.	n.r.	25	100	
ODES 1995	diet	The planned sample size is 220 randomised participants. Ten per cent are expected to drop out, leaving about 200 participants to complete the 1-year trial. The power will then be 80% for the detection of a standardized difference in response of 0.80 between two of the four randomised groups at the 5% two-sided significance level.	660[b]	55 (n.r.)[c]	n.r.	n.r.	52 (16)[c]	95 (n.r.)	12 months
	no diet			43 (n.r.)[c]	n.r.	n.r.	43 (12)[c]	100 (n.r.)	
	diet + physical activity			67 (n.r.)[c]	n.r.	n.r.	65 (24)[c]	97 (n.r.)	
	no diet + physical activity			54 (n.r.)[c]	n.r.	n.r.	49 (20)[c]	91 (n.r.)	
Ruvolo 1994	diet	n.r.	n.r.	16	n.r.	n.r.	14	88	6 months
	no diet			16	n.r.	n.r.	16	100	
TAIM 1992	diet + placebo	The sample size of about 195 within each drug group (587 total) for the weight loss component had 80% power to detect the following differences with a two-sided α = 0.05: (1) placebo/usual failure rate of 90% vs placebo/weight	878[b]	100[d]	n.r.	n.r.	89[d]	89	6 months (phase I)
	no diet + placebo			100[d]	n.r.	n.r.	90[d]	90	

Table 1. Overview of trial populations *(Continued)*

	diet + atenolol	loss failure rate of 60%, and (2) active drug/usual diet failure rate of 40% vs active drug/weight loss diet rate of 20%. These sample sizes also allowed for a 20% dropout rate by the end of the study.		96[d]	n.r.	n.r.	88[d]	92	
	no diet + atenolol			99[d]	n.r.	n.r.	87[d]	89	
	diet + chlorthalidone			95[d]	n.r.	n.r.	86[d]	91	
	no diet + chlorthalidone			97[d]	n.r.	n.r.	87[d]	90	
TONE 1998	diet without salt restriction	The study is designed to provide greater than 80% statistical power for detecting a 30% reduction in the rate of return to antihypertensive medication associated with the weight loss intervention and a 25% reduction in the rate of return to antihypertensive medication associated with the reduced Na intervention.	995[b]	147[d]	147[d]	147[d]	n.r.	96 to 99	15 to 36 months
	no diet without salt restriction			147[d]	147[d]	147[d]	n.r.		
	diet + salt restriction			147[d]	147[d]	147[d]	n.r.		
	no diet + salt restriction			144[d]	144[d]	144[d]	n.r.		

[a]Participants in all seven study groups.
[b]All participants.
[c]All participants (hypertensive subgroup).
[d]Weight loss component of the trial.

Table 2. Baseline characteristics (I)

Trial	Intervention(s) and comparator(s)	Description of participants	Nationality	Setting	Ethnic groups (%)	Duration of disease (mean years (SD))	Antihypertensive treatment (%)
Cohen 1991	diet	hypertensive and obese patients stratified by residents (residents not patients were randomised to intervention or control group)	USA	model family practice unit (Pittsburgh)	-	-	(number of medications: 1.6)

Table 2. Baseline characteristics (I) *(Continued)*

	no diet				-	-	(number of medications: 1.2)
Croft 1986	diet	newly diagnosed hypertensive and obese patients	Great Britain	outpatient clinic (1 urban group practice)	-	newly-diagnosed patients	0
	no diet				-		0
DISH 1985	diet	people who were previously enrolled in the HDFP treated with antihypertensive drugs and who had sufficiently controlled hypertension. The dietary change on the return of hypertension after withdrawal of prolonged antihypertensive therapy (DISH) included 7 treatment arms; the results of 2 of those arms met the inclusion criteria for this review (hypertensive and obese patients with either dietary intervention or not)	USA	outpatient clinic	Black (62)	at least 5 years	100
	no diet				Black (70)		100
Jalkanen 1991	diet	overweight hypertensive patients (selected from files)	Finland	outpatient clinic (2 hypertension clinics in Finland)	-	-	50
	no diet				-	-	50
ODES 1995	diet	men and women ≥ 40 years old from screening programme for cardiovascular risk factors in Oslo (Norway) since 1981; participants were post-hoc divided in tertiles according to DBP (tertile 1 DBP > 91 mm Hg, tertile 2 DBP 84 to 91 mm Hg, tertile 3 DBP < 84 mm Hg); only subgroups of tertile 1 (DBP > 91 mm Hg) will be reported here	Norwegian	outpatient clinic	-	-	0
	no diet				-	-	0
	diet + physical activity				-	-	0
	no diet + physical activity				-	-	0
Ruvolo 1994	diet	overweight hypertensive patients on 10 mg amlodipine daily	Italian	outpatient clinic	-	-	100 with amlodipine 10 mg
	no diet				-	-	100 with amlodipine 10 mg

Table 2. Baseline characteristics (I) *(Continued)*

TAIM 1992	diet + placebo	obese hypertensive patients	USA	outpatient clinic at 3 university hospitals (Bronx (New York), Birmingham (Alabama), Jackson (Mississippi))	White (67) Black (33)	-	0
	no diet + placebo				White (65) Black (35)	-	0
	diet + atenolol				White (67) Black (33)	-	100
	no diet + atenolol				White (67) Black (33)	-	100
	diet + chlorthalidone				White (67) Black (33)	-	100
	no diet + chlorthalidone				White (67) Black (33)	-	100
TONE 1998	diet without salt restriction	elderly, obese, and hypertensive patients; participants were assigned to active intervention: sodium reduction (S+), or weight loss, or sodium reduction (S+) and weight loss vs usual care	USA	outpatient clinic	White (73) African American (26)	11.3 (9.2)	100
	no diet without salt restriction				White (68) African American (32)	11.6 (8.0)	100
	diet + salt restriction				White (76) African American (24)	11.9 (9.5)	100
	no diet + salt restriction				White (70) African American (30)	11.9 (9.3)	100

Table 3. Baseline characteristics (II)

Trial	Intervention(s) and comparator(s)	Age (mean years (SD))	Sex (female %)	BMI (mean kg/m² (SD))	Body weight (mean kg (SD))	Sitting systolic blood pressure (mean mmHg (SD))	Sitting diastolic blood pressure (mean mmHg (SD))	Comorbid conditions (%)
Cohen 1991	diet	59	73	34.2	91.8	-	-	obesity (100)
	no diet	59.7	73	34	91.7	-	-	obesity (100)
Croft 1986	diet	-	56	-	86.7 (3.8)	161 (3.5)	98 (2.2)	obesity (100)
	no diet	-	39	-	82.2 (2.6)	161 (3.5)	96 (1.9)	obesity (100)
DISH 1985	diet	56.1	68	-	86 (17.3)	127.6	80.9	obesity (100)
	no diet	57.2	64	-	89.8 (17.8)	127.6	79.6	obesity (100)
Jalkanen 1991	diet	-	-	-	86 (14)	152 (17)	101 (8)	-
	no diet	-	-	-	80 (11)	155 (14)	102 (7)	-
ODES 1995	diet	-	-	29.9 (0.7)	-	144.5 (4.5)	97.3 (1.3)	-
	no diet	-	-	30 (1.3)	-	137.5 (2.5)	95.6 (1.1)	-
	diet + physical activity	-	-	29.6 (0.9)	-	142.8 (2.4)	97 (0.9)	-
	no diet + physical activity	-	-	29.5 (0.8)	-	139.5 (2.0)	96.4 (1.1)	-
Ruvolo 1994	diet	-	-	34 (4)	98 (8)	178 (8)	107 (5)	obesity
	no diet	-	-	34 (3)	97 (8)	176 (8)	106 (5)	obesity
TAIM 1992	diet + placebo	48.6	41	-	90	142.1	93.9	Smokers (14) Alcohol use (≥ 1 drink/week) (35)
	no diet + placebo	46.8	59	-	86	143.5	92.7	Smokers (15)

Table 3. Baseline characteristics (II) *(Continued)*

								Alcohol use (≥ 1 drink/week) (37)
	diet + atenolol	48	48	-	86	143.6	94.1	Smokers (13.5) Alcohol use (≥ 1 drink/week) (36.5)
	no diet + atenolol	47.5	36	-	89	140.5	92.7	Smokers (20.2) Alcohol use (≥ 1 drink/week) (44.4)
	diet + chlorthalidone	47.4	51	-	87	138	91.6	Smokers (17.9) Alcohol use (≥ 1 drink/week) (38.9)
	no diet + chlorthalidone	48.8	40	-	89	141.9	92.4	Smokers (13.4) Alcohol use (≥ 1 drink/week) (42.3)
TONE 1998	diet without salt restriction	66 (5)	51	31 (2.3)	87 (10)	130 (9)	72 (8)	Smokers (3) Alcohol use (≥ 1 drink/week) (35)
	no diet without salt restriction	66 (4)	59	31.3 (2.3)	86 (10)	128 (10)	72 (7)	Smokers (5) Alcohol use (≥ 1 drink/week) (32)
	diet + salt restriction	66 (4)	44	31.2 (2)	86 (10)	129 (9)	72 (7)	Smokers (7) Alcohol use (≥ 1 drink/week) (43)
	no diet + salt restriction	66 (4)	56	31.2 (2.5)	88 (11)	129 (9)	72 (8)	Smokers (5) Alcohol use (≥ 1 drink/week) (36)

Table 4. Body weight

Trial	Body weight [kg][a]					
	Intervention(s) and comparator(s)	Baseline	6 months	12 months	> 12 months	Change (baseline to end-point)
Cohen 1991	diet	92[b]	n. r.	n. r.	-[c]	−0.9 (4.0)
	no diet	92[b]	n. r.	n. r.	-[c]	+1.3 (3.0); P < 0.1
Croft 1986	diet	87 (4)	80 (4)	-[c]	-[c]	−6.5[b]
	no diet	82 (3)	82 (3)	-[c]	-[c]	−0.2[b]; P < 0.001
DISH 1985	diet	86 (17)	n. r.	n. r.	-[c]	−4.0 (5.0)
	no diet	90 (18)	n. r.	n. r.	-[c]	−0.5 (3.6); P < 0.05[e]
Jalkanen 1991	diet	86 (14)	n. r.	82 (13)	-[c]	−4.0[d]
	no diet	80 (11)	n. r.	80 (11)	-[c]	0.0[d]; P < 0.05
ODES 1995[f]	-	n. r.	n. r.	n. r.	n. r.	n. r.
Ruvolo 1994	diet	98 (8)	84 (9)	-[c]	-[c]	−14[b,g]
	no diet	97 (8)	95 (8)	-[c]	-[c]	−2[b,g]; P = n. r.
TAIM 1992	diet + placebo	90[b]	n. r.	n. r.	n. r.[h]	−4.4 (0.7)[j]
	no diet + placebo	86[b]	n. r.	n. r.	n. r.[h]	−0.7 (0.4)[j]; P = n. r.
	diet + atenolol	86[b]	n. r.	n. r.	n. r.[h]	−3.0 (0.4)[j]
	no diet + atenolol	89[b]	n. r.	n. r.	n. r.[h]	+0.5 (0.3)[j]; P = n. r.
	diet + chlorthalidone	87[b]	n. r.	n. r.	n. r.[h]	−6.9 (0.5)[j]
	no diet + chlorthalidone	89[b]	n. r.	n. r.	n. r.[h]	−1.5 (0.4)[j]; P = n. r.
TONE 1998	diet without salt restriction	87 (10)	n. r.	n. r.	n. r.	n. r.[k]
	no diet without salt restriction	86 (10)	n. r.	n. r.	n. r.	n. r.[k]
	diet + salt restriction	86 (10)	n. r.	n. r.	n. r.	n. r.[k]
	no diet + salt restriction	88 (11)	n. r.	n. r.	n. r.	n. r.[k]

[a]Mean (standard deviation), unless otherwise indicated.
[b]Data on variance missing.
[c]Observation period ≤ 12 months.
[d]Numbers calculated from the tables of publications. A mean weight reduction of 5 kg is stated in the text section.
[e]Information on body weight was available for 77% of participants in the intervention group and 87% of participants in the control group.

[f]Not mentioned for the hypertensive subgroup.
[g]Calculated from table 1 in Ruvolo 1994.
[h]Only change in body weight reported for 24 months; since no other outcomes were reported for this time, and change in body weight is not a primary endpoint of this report, data were not extracted.
[j]Standard error.
[k]Weight reduction of 3.9 vs 0.9 kg (P < 0.001) in overweight participants of both intervention groups together (with and without salt restriction) vs control group.
[n. r.]: not reported.

Table 5. Systolic blood pressure

Trial	Systolic blood pressure [mm Hg][a]					
	Intervention(s) and comparator(s)	Baseline	6 months	12 months	> 12 months	Change (baseline-to endpoint)
Cohen 1991	diet	n. r.[b]	n. r.	n. r.	-[c]	n. r.[b]
	no diet	n. r.[b]	n. r.	n. r.	-[c]	n. r.[b]
Croft 1986	diet	161 (4)	150 (4)	-[c]	-[c]	−11.0[d]
	no diet	161 (4)	157 (4)	-[c]	-[c]	−4.0[d]; P < 0.01
DISH 1985	-	-[e]	-[e]	-[e]	-[e]	-[e]
Jalkanen 1991	diet	152 (17)	n. r.	144 (20)	-[c]	−8.0[d]
	no diet	155 (14)	n. r.	140 (16)	-[c]	−15.0[d]; P = n. r.
ODES 1995	diet	145 (5)[f]	n. r.	n. r.	-[c]	−8.4 (3.3)[f]
	no diet	138 (3)[f]	n. r.	n. r.	-[c]	2.9 (4.4)[f]; P < 0.05
	diet + physical activity	143 (2)[f]	n. r.	n. r.	-[c]	−8.3 (2.1)[f]
	no diet + physical activity	140 (2)[f]	n. r.	n. r.	-[c]	−4.1 (1.8)[f]; P = n. r.
Ruvolo 1994	diet	178 (8)	145 (6)	-[c]	-[c]	−33[d,g]
	no diet	176 (8)	144 (6)	-[c]	-[c]	−32[d,g]; P = n. r.
TAIM 1992	diet + placebo	143[d]	n. r.[h]	n. r.	n. r.	−11.5[d]
	no diet + placebo	145[d]	n. r.[h]	n. r.	n. r.	−10.3[d]; P = n. r.
	diet + atenolol	143[d]	n. r.[h]	n. r.	n. r.	−18.1[d]
	no diet + atenolol	143[d]	n. r.[h]	n. r.	n. r.	−15.1[d]; P = n. r.
	diet + chlorthalidone	141[d]	n. r.[h]	n. r.	n. r.	−21.7[d]
	no diet + chlorthalidone	142[d]	n. r.[h]	n. r.	n. r.	−17.4[d]; P = n. r.
TONE 1998	-	-[e]	-[e]	-[e]	-[e]	-[e]

[a]Mean (SD), unless otherwise indicated.
[b]Only the mean arterial blood pressure is reported (at baseline: IG and CG 106 mm Hg each; change from baseline to endpoint: IG +3.0 (SD 14.2) mm Hg and CG -0.7 (SD 11.3) mm Hg).
[c]Observation period ≤ 12 months.
[d]Data on variance missing.
[e]Purpose of the study was not the change in blood pressure, but the number of participants without any antihypertensive drug requirements at the end of the study after successful withdrawal of antihypertensives.
[f]Standard error.
[g]Calculated from table 1 in Ruvolo 1994.
[h]Only changes from baseline are reported, no absolute values.
[n. r.]: not reported. [SD]: standard deviation.

Table 6. Diastolic blood pressure

Study	Diastolic blood pressure [mm Hg][a]					
	Intervention(s) and comparator(s)	Baseline	6 months	12 months	> 12 months	Change (baseline to endpoint)
Cohen 1991	diet	n. r.[b]	n. r.	n. r.	-[c]	n. r.[b]
	no diet	n. r.[b]	n. r.	n. r.	-[c]	n. r.[b]
Croft 1986	diet	98 (2)	91 (2)	-[c]	-[c]	−7.0[d]
	no diet	96 (2)	95 (2)	-[c]	-[c]	−1.0[d]; P < 0.001
DISH 1985	-	-[e]	-[e]	-[e]	-[e]	-[e]
Jalkanen 1991	diet	101 (8)	n. r.	90 (10)	-[c]	−11.0[d]
	no diet	102 (7)	n. r.	91 (7)	-[c]	−11.0[d]; P = n. r.
ODES 1995	diet	97 (1)[f]	n. r.	n. r.	-[c]	−7.1 (1.8)[f]
	no diet	96 (1)[f]	n. r.	n. r.	-[c]	−0.4 (3.6)[f]; ns
	diet + physical activity	97 (1)[f]	n. r.	n. r.	-[c]	−7.1 (1.3)[f]
	no diet + physical activity	96 (1)[f]	n. r.	n. r.	-[c]	−5.5 (1.7)[f]; P = n. r.
Ruvolo 1994	diet	107 (5)	84 (4)	-[c]	-[c]	−23[d,g]
	no diet	106 (5)	85 (5)	-[c]	-[c]	−21[d,g]; P = n. r.
TAIM 1992	diet	n. r.	n. r.[h]	n. r.	n. r.	−12.8 (10.0)
	no diet	n. r.	n. r.[h]		n. r.	−10.4 (7.8); P = 0.001
TONE 1998	-	-[e]	-[e]	-[e]	-[e]	-[e]

[a]Mean (SD), unless otherwise indicated.
[b]Only the mean arterial blood pressure is reported (at baseline: IG and CG 106 mm Hg each; change from baseline to endpoint: IG +3.0 (SD 14.2) mm Hg and CG −0.7 (SD 11.3) mm Hg).

[c]Observation period ≤ 12 months.
[d]Data on variance missing.
[e]Purpose of the study was not the change in blood pressure, but the number of participants without any antihypertensive drug requirements at the end of the study after successful withdrawal of antihypertensives.
[f]Standard error.
[g]Calculated from table 1 in Ruvolo 1994.
[h]Only changes from baseline are reported, no absolute values.
[n. r.]: not reported. [ns]: not significant. [SD]: standard deviation.

APPENDICES

Appendix 1. Search strategies

Database: Ovid MEDLINE(R) and Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Daily and Versions(R) <1946 to April 02, 2020>
Search Date: 3 April 2020
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1 nutrition therapy/
2 diet therapy/
3 ((aliment$ or diet$ or nutrition) adj2 (chang$ or counsel$ or dash or health? or intervention? or overweight? or pattern? or program$ or therap$ or treatment? or weight?)).ti,kf.
4 ((aliment$ or diet$ or nutrition) adj3 (chang$ or counsel$ or dash or health? or intervention? or overweight? or pattern? or program$ or therap$ or treatment? or weight?)).ab.
5 ((bodyweight? or calor$ or overweight? or weight?) adj2 (chang$ or control$ or lose or losing or loss or manag$ or reduc$)).ti,ab,kf.
6 or/1-5
7 hypertension/
8 essential hypertension/
9 blood pressure/
10 (antihypertens$ or hypertens$).ti,ab,kf,ot.
11 ((chang$ or elevat$ or high or rais$ or reduc$) adj4 blood pressur$).ti,ab,kf,ot.
12 ((chang$ or elevat$ or high or rais$ or reduc$) adj4 (arterial pressur$ or bloodpressur$$ or bp)).ti,ab,kf,ot.

13 or/7-12
14 randomized controlled trial.pt.
15 pragmatic clinical trial.pt.
16 controlled clinical trial.pt.
17 randomized.ab.
18 placebo.ab.
19 clinical trials as topic/

20 randomly.ab.
21 trial.ti.
22 or/14-21
23 animals/ not (humans/ and animals/)
24 22 not 23
25 6 and 13 and 24

Database: Cochrane Hypertension Specialised Register via Cochrane Register of Studies (CRS-Web)
Search Date: 14 April 2020

#1 MESH DESCRIPTOR Nutrition Therapy AND INSEGMENT
#2 MESH DESCRIPTOR Diet Therapy AND INSEGMENT
#3 (chang* OR elevat* OR high OR rais* OR reduc*) NEAR3 (arterial pressur* OR blood pressur* OR bloodpressur* OR bp):TI,AB AND INSEGMENT
#4 (#6 OR #7 OR #8 OR #9 OR #10) AND INSEGMENT
#5 RCT:DE AND INSEGMENT
#6 Review:ODE AND INSEGMENT
#7 (#12 OR #13) AND INSEGMENT
#8 #5 AND #11 AND #14 AND INSEGMENT

#9 ((aliment* OR diet* OR nutrition) NEAR2 (chang* OR counsel* OR dash OR health* OR intervention* OR overweight* OR pattern* or program* OR therap* OR treatment* OR weight*)) AND INSEGMENT
#10 (bodyweight* OR calor* OR overweight* OR weight*) AND (chang* OR control* OR lose OR losing OR loss OR manag* OR reduc*):TI AND INSEGMENT
#11 (#1 OR #2 OR #3 OR #4) AND INSEGMENT
#12 MESH DESCRIPTOR Hypertension AND INSEGMENT
#13 MESH DESCRIPTOR Essential Hypertension AND INSEGMENT
#14 MESH DESCRIPTOR Blood Pressure AND INSEGMENT
#15 (antihypertens* OR hypertens*) AND INSEGMENT
#16 ((aliment* OR diet* OR nutrition) NEAR2 (chang* OR counsel* OR dash OR health* OR intervention* OR overweight* OR pattern* or program* OR therap* OR treatment* OR weight*)) AND INSEGMENT
#17 (bodyweight* OR calor* OR overweight* OR weight*) AND (chang* OR control* OR lose OR losing OR loss OR manag* OR reduc*):TI AND INSEGMENT
#18 (#1 OR #2 OR #3 OR #4) AND INSEGMENT
#19 MESH DESCRIPTOR Hypertension AND INSEGMENT
#20 (chang* OR elevat* OR high OR rais* OR reduc*) NEAR3 (arterial pressur* OR blood pressur* OR bloodpressur* OR bp):TI,AB AND INSEGMENT
#21 MESH DESCRIPTOR Essential Hypertension AND INSEGMENT
#22 (#6 OR #7 OR #8 OR #9 OR #10) AND INSEGMENT
#23 MESH DESCRIPTOR Blood Pressure AND INSEGMENT
#24 RCT:DE AND INSEGMENT
#25 Review:ODE AND INSEGMENT
#26 (#12 OR #13) AND INSEGMENT
#27 #5 AND #11 AND #14 AND INSEGMENT
#28 (antihypertens* OR hypertens*) AND INSEGMENT
#29 (chang* OR elevat* OR high OR rais* OR reduc*) NEAR3 (arterial pressur* OR blood pressur* OR bloodpressur* OR bp):TI,AB AND INSEGMENT
#30 (#6 OR #7 OR #8 OR #9 OR #10) AND INSEGMENT
#31 RCT:DE AND INSEGMENT
#32 Review:ODE AND INSEGMENT
#33 (#12 OR #13) AND INSEGMENT
#34 #5 AND #11 AND #14 AND INSEGMENT

Database: Cochrane Central Register of Controlled Trials (Issue 3, 2020) via the Cochrane Register of Studies (CRS-Web)
Search Date: 3 April 2020

#1 MESH DESCRIPTOR Nutrition Therapy AND CENTRAL:TARGET
#2 MESH DESCRIPTOR Diet Therapy AND CENTRAL:TARGET
#3 ((aliment* OR diet* OR nutrition) NEAR2 (chang* OR counsel* OR dash OR health* OR intervention* OR overweight* OR pattern* OR program* OR therap* OR treatment* OR weight*)) AND CENTRAL:TARGET
#4 (bodyweight* OR calor* OR overweight* OR weight*) AND (chang* OR control* OR lose OR losing OR loss OR manag* OR reduc*):TI AND CENTRAL:TARGET
#5 (#1 OR #2 OR #3 OR #4) AND CENTRAL:TARGET
#6 MESH DESCRIPTOR Hypertension AND CENTRAL:TARGET
#7 MESH DESCRIPTOR Essential Hypertension AND CENTRAL:TARGET
#8 (antihypertens* OR hypertens*):TI,AB AND CENTRAL:TARGET
#9 (chang* OR elevat* OR high OR rais* OR reduc*) NEAR3 (arterial pressur* OR blood pressur* OR bloodpressur* OR bp):TI,AB AND CENTRAL:TARGET
#10 (#6 OR #7 OR #8 OR #9) AND CENTRAL:TARGET
#11 #5 AND #10 AND CENTRAL:TARGET

Database: Embase <1974 to 2020 April 02>
Search Date: 3 April 2020

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1 exp *diet therapy/
2 ((aliment$ or diet$ or nutrition) adj2 (chang$ or counsel$ or dash or health? or intervention? or overweight? or pattern? or program$ or therap$ or treatment? or weight?)).ti.
3 ((aliment$ or diet$ or nutrition) adj3 (chang$ or counsel$ or dash or health? or intervention? or overweight? or pattern? or program$ or therap$ or treatment? or weight?)).ab.
4 ((bodyweight? or calor$ or overweight? or weight?) adj2 (chang$ or control$ or lose or losing or loss or manag$ or reduc$)).tw.
5 or/1-4
6 exp hypertension/

7 (antihypertens$ or hypertens$).ti,ab,ot.
8 exp *blood pressure/
9 ((chang$ or elevat$ or high or rais$ or reduc$) adj3 (arterial pressur$ or bloodpressur$ or bp)).ti,ab,ot.
10 ((chang$ or elevat$ or high or rais$ or reduc$) adj3 blood pressur$).ti,ab,ot.
11 or/6-10
12 randomized controlled trial/
13 crossover procedure/
14 double-blind procedure/
15 (randomi?ed or randomly).tw.
16 (crossover$ or cross-over$).tw.
17 placebo.ab.
18 (doubl$ adj blind$).tw.
19 assign$.ab.
20 allocat$.ab.
21 or/12-20
22 (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.)
23 21 not 22
24 5 and 11 and 23

Database: ClinicalTrials.gov
Search Date: 3 April 2020

Condition or disease: Hypertension
Other terms: randomized AND (bodyweight OR overweight OR weight)
Study type: Interventional Studies (Clinical Trials)
Intervention/treatment: (diet OR weight loss OR weight reduc*)

Database: WHO International Clinical Trials Registry Platform (ICTRP)
Search Date: 6 July 2018

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hypertens* and diet* and bodyweight
hypertens* and diet* and overweight
hypertens* and diet* and weight
hypertens* and weight loss
hypertens* and weight reduc*

WHAT'S NEW

Date	Event	Description
11 May 2020	New search has been performed	We updated the search for new studies in April 2020. We identified no new studies that met the inclusion criteria for this review.
11 May 2020	New citation required but conclusions have not changed	Update published with changed authors, update search, conclusion unchanged.

HISTORY

Protocol first published: Issue 1, 2010
Review first published: Issue 9, 2011

Date	Event	Description
2 February 2016	New search has been performed	We updated the search for new studies in February 2015. We identified no new studies that met the inclusion criteria of this review. We have added a 'Summary of findings' table.
2 February 2016	New citation required but conclusions have not changed	Update published with changed authors, updated search, conclusions not changed.

CONTRIBUTIONS OF AUTHORS

Thomas Semlitsch: selection of studies, quality assessment of trials, data extraction, development of review updates, corresponding author.

Cornelia Krenn: selection of studies, development of review update.

Klaus Jeitler: protocol development, searching for trials for the initial version of the review, quality assessment of trials, data extraction.

Andrea Berghold: statistical analysis, development of final review.

Karl Horvath: protocol development, quality assessment of trials, data extraction, development of final review.

Andrea Siebenhofer: protocol development, quality assessment of trials, selection of studies, data extraction, development of final review and review update.

DECLARATIONS OF INTEREST

Andrea Siebenhofer, Klaus Jeitler, and Karl Horvath were involved in the preparation of a report on the evaluation of the benefits and harms of non-drug treatment strategies in people with essential hypertension: weight reduction for IQWiG, (German Institute for Quality and Efficiency in Health Care (iqwig.de/)).

Andrea Berghold: No known conflicts of interest.

Thomas Semlitsch: No known conflicts of interest.

Cornelia Krenn: No known conflicts of interest.

SOURCES OF SUPPORT

Internal sources

- Medical University of Graz, Austria

  Salary, office space, computer support, library resources
- Institute of General Practice, Goethe University Frankfurt, Germany

  Salary

External sources

- No sources of support supplied

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

Three new authors (Thomas Semlitsch, Christoph Pachler, and Reinhard Strametz) joined the team of review authors for the 2011 version of this review and provided substantive intellectual contributions that justify their inclusion as authors.

Nicole Pignitter changed her name to Nicole Posch due to marriage, and her new name was used in the 2016 update of this review.

Four authors (Andreas Waltering, Lars Hemkens, Christoph Pachler, and Reinhard Strametz) did not contribute to the 2016 update of this review and were removed from the list of authors.

Stephanie Poggenburg joined the team of authors for the 2016 update of this review and provided substantive intellectual contributions that justify her inclusion as author.

Two authors (Nicole Posch and Stephanie Poggenburg) did not contribute to the 2020 update of this review and were removed from the list of authors.

Cornelia Krenn joined the team of authors for the 2020 update of this review and provided substantive intellectual contributions that justify her inclusion as author.

INDEX TERMS

Medical Subject Headings (MeSH)

Antihypertensive Agents [therapeutic use]; Bias; Blood Pressure; Cardiovascular Diseases [prevention & control]; Diet, Reducing [*adverse effects]; Hypertension [*diet therapy] [drug therapy] [mortality]; Randomized Controlled Trials as Topic; Weight Loss

MeSH check words

Aged; Humans; Middle Aged