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Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride (Review)

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[Intervention Review]

Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride

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ABSTRACT

Background

In spite of more than 100 years of investigations the question of whether a reduced sodium intake improves health is still unsolved.

Objectives

To estimate the effects of low sodium intake versus high sodium intake on systolic and diastolic blood pressure (SBP and DBP), plasma or serum levels of renin, aldosterone, catecholamines, cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglycerides.

Search methods

The Cochrane Hypertension Information Specialist searched the following databases for randomized controlled trials up to March 2016: the Cochrane Hypertension Specialised Register, the Cochrane Central Register of Controlled Trials (CENTRAL) (2016, Issue 3), MEDLINE (from 1946), Embase (from 1974), the World Health Organization International Clinical Trials Registry Platform, and ClinicalTrials.gov. We also searched the reference lists of relevant articles.

Selection criteria

Studies randomising persons to low-sodium and high-sodium diets were included if they evaluated at least one of the above outcome parameters.

Data collection and analysis

Two review authors independently collected data, which were analysed with Review Manager 5.3.

Main results

A total of 185 studies were included. The average sodium intake was reduced from 201 mmol/day (corresponding to high usual level) to 66 mmol/day (corresponding to the recommended level).

The effect of sodium reduction on blood pressure (BP) was as follows: white people with normotension: SBP: mean difference (MD) -1.09 mmHg (95% confidence interval (CI): -1.63 to -0.56; P = 0.0001); 89 studies, 8569 participants; DBP: + 0.03 mmHg (MD 95% CI: -0.37 to 0.43; P = 0.89); 90 studies, 8833 participants. *High-quality evidence.*

Black people with normotension: SBP: MD -4.02 mmHg (95% CI:-7.37 to -0.68; P = 0.002); seven studies, 506 participants; DBP: MD -2.01 mmHg (95% CI:-4.37 to 0.35; P = 0.09); seven studies, 506 participants. *Moderate-quality evidence.*

Asian people with normotension: SBP: MD -0.72 mmHg (95% CI: -3.86 to 2.41; P = 0.65); DBP: MD -1.63 mmHg (95% CI:-3.35 to 0.08; P =0.06); three studies, 393 participants. *Moderate-quality evidence.*

White people with hypertension: SBP: MD -5.51 mmHg (95% CI: -6.45 to -4.57; P < 0.00001); 84 studies, 5925 participants; DBP: MD -2.88 mmHg (95% CI: -3.44 to -2.32; P < 0.00001); 85 studies, 6001 participants. *High-quality evidence.*

Black people with hypertension: SBP MD -6.64 mmHg (95% CI:-9.00 to -4.27; P = 0.00001); eight studies, 619 participants; DBP -2.91 mmHg (95% CI:-4.52, -1.30; P = 0.0004); eight studies, 619 participants. *Moderate-quality evidence.*

Asian people with hypertension: SBP: MD -7.75 mmHg (95% CI:-11,44 to -4.07; P < 0.0001) nine studies, 501 participants; DBP: MD -2.68 mmHg (95% CI: -4.21 to -1.15; P = 0.0006). *Moderate-quality evidence.*

In plasma or serum, there was a significant increase in renin (P < 0.00001), aldosterone (P < 0.00001), noradrenaline (P < 0.00001), adrenaline (P < 0.03), cholesterol (P < 0.0005) and triglyceride (P < 0.0006) with low sodium intake as compared with high sodium intake. All effects were stable in 125 study populations with a sodium intake below 250 mmol/day and a sodium reduction intervention of at least one week.

Authors' conclusions

Sodium reduction from an average high usual sodium intake level (201 mmol/day) to an average level of 66 mmol/day, which is below the recommended upper level of 100 mmol/day (5.8 g salt), resulted in a decrease in SBP/DBP of 1/0 mmHg in white participants with normotension and a decrease in SBP/DBP of 5.5/2.9 mmHg in white participants with hypertension. A few studies showed that these effects in black and Asian populations were greater. The effects on hormones and lipids were similar in people with normotension and hypertension. Renin increased 1.60 ng/mL/hour (55%); aldosterone increased 97.81 pg/mL (127%); adrenalin increased 7.55 pg/mL (14%); noradrenalin increased 63.56 pg/mL: (27%); cholesterol increased 5.59 mg/dL (2.9%); triglyceride increased 7.04 mg/dL (6.3%).

PLAIN LANGUAGE SUMMARY

The effect of a low salt diet on blood pressure and some hormones and lipids in people with normal and elevated blood pressure

Review question

Studies in which participants were distributed by chance into groups with high and low salt intake were analysed to investigate the effect of reduced salt intake on blood pressure (BP) and potential side effects of sodium reduction on some hormones and lipids.

Background

As a reduction in salt intake decreases blood pressure (BP) in individuals with elevated BP, we are commonly advised to cut down on salt. However, the effect of salt reduction on BP in people with a normal BP has been questioned. Furthermore, several studies have shown that salt reduction activates the salt conserving hormonal system (renin and aldosterone), the stress hormones (adrenalin and noradrenalin) and increases fatty substances (cholesterol and triglyceride) in the blood.

Search date

The present evidence is current to April 2016.

Study characteristics

One hundred and eighty-five intervention studies of 12,210 individuals lasting four to 1100 days were included, which evaluated at least one of the effect measures. Participants were healthy or had elevated blood pressure. Longitudinal studies have shown that the effect of reduced salt intake on BP is stable after at maximum seven days and population studies have shown that very few people eat more than 14.5 g salt per day. Therefore, we also perfomed subgroup sub-analyses of 125 studies with a duration of at least seven days and a salt intake of maximum 14.5 g.

Study funding sources

Forty-four studies did not mention support. One hundred and twenty-two studies were supported by public foundations. Twelve studies were supported by the pharmaceutical industry and one study by an electronic company. Six studies were supported by food industry organisations.

Key results

The mean dietary sodium intake was reduced from 11.5 g per day to 3.8 g per day. The reduction in SBP/DBP in people with normotension was about 1/0 mmHg, and in people with hypertension about 5.5/2.9 mmHg. In contrast, the effect on hormones and lipids were similar

in people with normotension and hypertension. Renin increased 1.60 ng/mL/hour (55%); aldosterone increased 97.81 pg/mL (127%); adrenalin increased 7.55 pg/mL (14%); noradrenalin increased 63.56 pg/mL (27%); cholesterol increased 5.59 mg/dL (2.9%); triglyceride increased 7.04 mg/dL (6.3%).

Quality of evidence

Only randomised controlled trials were included and the basic grade of evidence was therefore considered to be high, although the grade of evidence was downgraded in some of the smaller analyses. In general, the description of the randomisation procedure was insufficient, introducing a bias which could exaggerate the effects, but many of the studies were published in a period where it was not customary to report such descriptions. The majority of studies were open, but the outcomes of these did not differ from the outcomes of the double-blind studies. Almost all individual studies of participants with normal blood pressure (BP) show no significant effect of sodium reduction on BP, whereas a large number of studies in people with hypertension did show significant effect of sodium reduction on BP. Thus, there was a high grade of consistency between the outcomes of the individual studies and the outcomes of the meta-analyses. Sensitivity analyses of studies lasting at least one week (the time of maximal efficacy) confirmed the primary analyses. Finally, the impact of commercial interests on the outcomes was negligible.

SUMMARY OF FINDINGS

Summary of findings for the main comparison.

Low sodium intake compared with high sodium intake for blood pressure

Patient or population: White population with normal or elevated blood pressure, but otherwise healthy

Settings: Hospitals units in Europe and North America

Intervention: Low sodium intake

Comparison: High sodium intake

Outcomes	Relative effect (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
White population, normotensive, SBP mmHg	-1.09 (-1.63 to -0.56)	8569 (89)	⊕⊕⊕⊕ **high**	
White population, normotensive, DBP mmHg	0.03 (-0.37 to 0.43)	8833 (90)	⊕⊕⊕⊕ **high**	
White population, hypertensive, SBP mmHg	-5.51 (-6.45 to -4.57)	5925 (84)	⊕⊕⊕⊕ **high**	
White population, hypertensive, DBP mmHg	-2.88 (-3.44 to -2.32)	6001 (85)	⊕⊕⊕⊕ **high**	

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

DBP: diastolic blood pressure; **SBP:** systolic blood pressure

Summary of findings 2.

Low sodium intake compared with high sodium intake for blood pressure

Patient or population: Black population with normal or elevated blood pressure, but otherwise healthy

Settings: Hospital units in North America, UK and Africa

Intervention: Low sodium intake

Comparison: High sodium intake

Outcomes	Mean difference (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Black population, normotensive, SBP mmHg	-4.02 (-7.37 to -0.68)	506 (7)	⊕⊕⊕⊖ **moderate**[1]	
Black population, normotensive, DBP mmHg	-2.01 (-4.37 to 0.35)	506 (7)	⊕⊕⊕⊖ **moderate**[1]	
Black population, hypertensive, SBP mmHg	-6.64 (-9.00 to -4.27)	619 (8)	⊕⊕⊕⊖ **moderate**[1]	
Black population, hypertensive, DBP mmHg	-2.91 (-4.52 to -1.30)	619 (8)	⊕⊕⊕⊖ **moderate**[1]	

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

DBP: diastolic blood pressure; **SBP:** systolic blood pressure

1. Downgraded due to the wide confidence intervals

Summary of findings 3.

Low sodium intake compared with high sodium intake for blood pressure

Patient or population: Asian population with normal or elevated blood pressure, but otherwise healthy

Settings: Hospital units in Japan and China

Intervention: Low sodium intake

Comparison: High sodium intake

Outcomes	Mean difference (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Asian population, normotensive, SBP mmHg	-0.72 (-3.86 to 2.41)	393 (3)	⊕⊕⊕⊖ **moderate**[1]	
Asian population, normotensive, DBP	-1.63 (-3.35 to 0.08)	393 (3)	⊕⊕⊕⊖ **moderate**[1]	

mmHg			
Asian population, hypertensive, SBP mmHg	-7.75 (-11.44 to -4.07)	501 (8)	⊕⊕⊕⊖ **moderate**[1]
Asian population, hypertensive, DBP mmHg	-2.68 (-4.21 to -1.15)	501 (8)	⊕⊕⊕⊖ **moderate**[1]

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

DBP: diastolic blood pressure; **SBP:** systolic blood pressure

1. Downgraded due to the wide confidence intervals

Summary of findings 4.

Low sodium intake compared with high sodium intake for hormones

Patient or population: Participants with normal or elevated blood pressure, but otherwise healthy

Settings: Hospital units

Intervention: Low sodium intake

Comparison: High sodium intake

Outcomes	Mean difference (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Renin SMD	1.22 (1.07 to 1.37) *N*: 1.44 (1.24 to 1.65)* *H*: 0.91 (0.71 to 1.10)*	5498 (88)	⊕⊕⊕⊕ **high**	
Aldosterone pg/mL	97.81 (82.56 to 113.05) *N*: 115.83 (91.74 to 139.91)* *H*: 73.02 (55.94 to 90.09)*	4884 (65)	⊕⊕⊕⊕ **high**	
Noradrenaline pg/mL	63.56 (42.66 to 84.46) *N*: 66.50 (41.72 to 91.29)* *H*: 57.36 (14.10 to 100.61)*	1736 (36)	⊕⊕⊕⊕ **high**	
Adrenaline	7.55 (0.85 to 14.26)	662 (16)	⊕⊕⊕⊖ **moderate**[1]	

pg/mL	*N*:4.45 (3.43 to 12.33)* *H*:13.45 (1.25 to 25.66)*

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

Very low quality: We are very uncertain about the estimate.

SMD: standardised mean difference

N*: Study populations with mean SBP < 140 mmHg
H*:Study populations with mean SBP > 140 mmHg
1. Downgraded due to the wide confidence interval

Summary of findings 5.

Low sodium intake compared with high sodium intake for lipids

Patient or population: Participants with normal or elevated blood pressure, but otherwise healthy

Settings: Hospital units

Intervention: Low sodium intake

Comparison: High sodium intake

Outcomes	Mean difference (95% CI)	No of Participants (studies)	Quality of the evidence (GRADE)	Comments
Cholesterol mg/dL	5.64 (2.46, 8.82) *N*:7.46 (3.65, 11.28)* *H*:2.55 (-2.69, 7.80)*	1800 (27)	⊕⊕⊕⊖ **moderate[1]**	
Trigyceride mg/dL	7.04 (3.04, 11.05) *N*: 6.88 (1.18, 12.59)* *H*: 7.19 (1.57, 12.81)*	1390 (19)	⊕⊕⊕⊖ **moderate[1]**	
High-density lipoprotein (HDL) mg/dL	-0.29 (-1.66, 1.08)	1442 (19)	⊕⊕⊕⊖ **moderate[1]**	
Low-density lipoprotein (LDL) mg/dL	3.12 (-0.41, 6.64)	1358 (17)	⊕⊕⊕⊖ **moderate[1]**	

GRADE Working Group grades of evidence
High quality: Further research is very unlikely to change our confidence in the estimate of effect.

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

Downgraded due to the wide confidence intervals.

BACKGROUND

Description of the condition

Some health institutions (WHO 2012), and dietary recommendations (ADG 2015), assume that reduction in salt intake from "high" to "low" levels is associated with reduction in systolic and diastolic blood pressure (SBP and DBP), which might result in a decrease in mortality. However, the definitions of “high”, “normal” and “low” sodium intake are unclear. The present usual sodium intake indicates that an intake in the interval 109 mmol/day to 209 mmol/day (McCarron 2013; Powles 2013, Table 1) would be “normal”, a high sodium intake would be above 209 mmol/day and a low sodium intake would be below 109 mmol/day, but according to the health institutions a “normal” sodium intake is below 100 mmol/day (ADG 2015), or below 87 mmol/day (WHO 2012), and a sodium intake above 100 mmol/day is “high”, whereas a “low” sodium intake is not defined. The confusion is strengthened by the use of different terms to describe salt (salt (sodium chloride) and sodium) and different units for salt/sodium intake (mg/day or mmol/day). To reduce the confusion we have shown the different definitions and units for salt and sodium intake in Table 1. In the present review, which represents a third update of the first meta-analysis that includes an analysis of hormones and lipids in addition to blood pressure (Graudal 1998), updated in 2003 (Jürgens 2003) and 2011 (Graudal 2011), we use the term "sodium" and the unit "mmol".

Blood pressure is associated with mortality (Collins 1990).The hypothesis that a reduced sodium intake (sodium reduction) will reduce blood pressure (BP) and subsequently reduce morbidity and mortality was raised in 1904 on the basis of individual patient cases (Ambard 1904). Subsequently in 1907, these results were opposed (Löwenstein 1907). The clinical and physiological effects of salt published in studies during the first half of the 20th century were reviewed in 1949 (Chapman 1949). Consequently, scientific studies have been performed for almost 70 years before modern standard scientific randomised controlled trials (RCTs) (1000 Parijs 1973) and observational studies (Kagan 1985) were performed in humans. However, these scientific studies are interpreted differently (Taubes 1998, Graudal 2005, Bayer 2012). While health institutions (ADG 2015, WHO 2012) support sodium reduction below 100 mmol/day sceptics have claimed that this recommended upper limit (UL) for sodium intake is based on a biased selection of evidence (Folkow 2011), and is inconsistent with Institute of Medicine’s definition of an adequate nutrient intake, which is “the approximate intake found in apparently healthy populations" (IOM 2006; Heaney 2013). For sodium "the approximate intake in apparently healthy populations" is between 90 mmol/day and 248 mmol/day (Table 1).

The present Cochrane review is based on a meta-analysis published in 1998 (Graudal 1998). In 1998, the usual sodium intake was known in some populations, but it was not well-defined worldwide until recently (Table 1). The present upper level of 100 mmol/day was defined in 2005 (IOM 2005). Furthermore, the significance of the duration of sodium reduction was not established. In 1998, we therefore included all available randomised studies, irrespective of sodium intake and duration of intervention, assuming that the average values of multiple studies would be relevant for the general population. We separated study populations in a group of populations with normal BP to investigate the potential effect of sodium reduction in the general population and in a group of hypertensive populations to investigate the potential effect of sodium reduction as a treatment for hypertensive individuals. In a cross-sectional multiple regression analysis including many covariates we found that the duration of the sodium reduction intervention had no impact on the effect of sodium reduction on BP (Graudal 1998). In addition to this cross-sectional meta-regression analysis, a recent meta-analysis of longitudinal studies measuring the BP-effect of sodium reduction several times during the observation period showed that there was no difference in SBP effect or DBP effect between week one and week six, thus estimating the time point for maximal efficacy to be at maximum at one week (Graudal 2015). These results are shown in Table 2. In the Graudal 1998 analysis, the average sodium intake in the non-reduced group was 203 mmol/day and in the reduced group it was 62 mmol/day. In the two following updates of the review, the corresponding sodium reductions were from 205 mmol/day to 64 mmol/day (Jürgens 2003) and from 202 mmol/day to 67 mmol/day (Graudal 2011). We now know (McCarron 2013; Powles 2013) that this reduction corresponds to a reduction from a high usual level to the present recommended levels (defined in 2005 (IOM 2005) and in 2012 (WHO 2012) i.e. the present review is relevant in the context of evaluating the consequences of the present recommendations to reduce sodium intake to a level below 100 mmol/day.

Description of the intervention

As in the previous meta-analyses, RCTs are included, which allocate participants to two diets with a different content of salt (sodium chloride) or to either salt tablets or placebo tablets. The compliance in the RCTs is ensured by measurement of sodium excretion in the urine, which is accepted to be a reliable surrogate for the measuring of sodium intake. The sodium content of the “high” and “low” sodium diets were not defined according to the recommendations or the usual sodium intake, but just to describe the relative content of the two randomised study populations.

How the intervention might work

Extracellular fluid volume (ECFV) is determined by the balance between sodium intake and renal excretion of sodium. A steady state exists whereby sodium intake equals output, while ECFV is expanded during salt loads and shrunken during salt restriction (Palmer 2008). Thus, the idea behind sodium reduction is to shrink ECFV in order to decrease BP. The precondition for this idea is that the smaller ECFV associated with the decrease in BP has no counteracting effects on health outcomes that could outweigh the BP-effect.

Why it is important to do this review

A verification of the hypothetical sodium-BP relationship would support continuous attempts to lower sodium intake in order to reduce mortality. In this context it is important to define the correct UL for a healthy sodium intake, which would have a significant impact on the strategy to lower sodium intake. For instance if 100 mmol/day is the correct UL, more than 95% of the World’s populations should reduce sodium intake, but if the UL is 250 mmol/day, only about 5% should reduce sodium intake. In the latter case, a strategy to lower sodium intake in the general population would not be necessary, which would save significant efforts and costs. The same would be the case if the sodium-BP relationship could be denied, as indicated by many RCTs of participants with normal BP (Graudal 2011). Worst case scenario

is that sodium reduction could lead to side effects, which might trump the potential BP effect and result in increased mortality, as indicated by longitudinal observational studies (Alderman 2010, Pfister 2014, O'Donnell 2014, Graudal 2014; Mente 2016). Consequently, it is important to investigate the effect of sodium reduction not only on BP, but also on potential surrogate markers for clinical side effects.

OBJECTIVES

The purpose of the present review was to estimate the influence of low- versus high-dietary sodium intake on systolic blood pressure (SBP) and diastolic blood pressure (DBP), and blood concentrations of renin, aldosterone, catecholamines, cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL) and triglyceride to contribute to the evaluation of the possible suitability of sodium reduction as a prophylaxis initiative and treatment of hypertension.

METHODS

Criteria for considering studies for this review

Types of studies

Randomised controlled trials (RCTs) allocating participants to diets with different sodium contents, the lowest defined as “low” and the highest defined as “high”, and in which the sodium intake was estimated by the 24-hour urinary sodium excretion (either measured on the basis of a 24-hour urine collection, or estimated from a sample of at least eight hours).

Types of participants

Persons with normal or elevated blood pressure irrespective of race and age were included. Studies systematically investigating unhealthy patients with other diseases than elevated blood pressure, for instance diabetes or heart failure, were excluded.

Types of interventions

The intervention was a change in sodium intake, the study populations randomly being divided into a group eating a “low” sodium diet or a "high" sodium diet. As "low" and "high" were not specifically defined in relation to the usual intake or the definitions of the health institutions (Table 1), both diets could contain any amount of sodium, the assumption being that in most studies a "low" sodium diet would contain sodium within the low range (< 100 mmol)/day or usual range (100 mmol to 250 mmol/day) and the “high” sodium diet would contain sodium within the usual range (100 mmol to 250 mmol/day) or above the usual range (≥ 250 mmol/day). Confounding was not allowed, i.e. studies treating persons with a concomitant intervention such as an antihypertensive medication, potassium supplementation or weight reduction were only included if the concomitant intervention was identical during the low and the high-sodium diet.

Types of outcome measures

Outcome measures were effects on SBP, DBP, renin, aldosterone, adrenaline, noradrenaline, triglyceride, cholesterol, LDL and HDL. In studies reporting BP only as mean arterial pressure (MAP), SBP was estimated from SBP = 1.3 MAP + 1.4, and DBP was estimated from DBP = 0.83 MAP – 0.7 (Tozawa 2002). Separate meta-analyses were performed for each outcome measure. Concerning blood pressure, participants were stratified according to ethnicity (Whites, Blacks and Asians) and according to level of blood pressure (hypertension or normotension). Hypertension was defined as SBP ≥ 140 mmHg and/or DBP ≥ 90 mmHg. Study populations in which participants were treated with antihypertensive treatment were defined as hypertensive irrespective of baseline BP. In studies that investigated different ethnicities and different BP levels, the first priority was to separate these subgroups. If separate data were not given, the study data would be analysed according to the biggest subgroup. Concerning all other outcome variables, no stratifications were performed.

Primary outcomes

All outcomes were considered primary outcomes.

Secondary outcomes

None.

Search methods for identification of studies

Electronic searches

The Cochrane Hypertension Information Specialist conducted systematic searches in the following databases for randomised controlled trials without language, publication year or publication status restrictions:

- the Cochrane Hypertension Specialised Register via the Cochrane Register of Studies (searched 7 March 2016);
- the Cochrane Central Register of Controlled Trials (CENTRAL; 2016, Issue 3) via the Cochrane Register of Studies Online (CRSO) (searched 7 March 2016);
- MEDLINE Ovid (from 1946 onwards), and MEDLINE Ovid In-Process & Other Non-Indexed Citations (searched 7 March 2016);
- Embase Ovid (searched 7 March 2016);
- ClinicalTrials.gov (www.clinicaltrials.gov) searched 7 March 2016).

The Hypertension Group Specialised Register includes controlled trials from searches of CAB Abstracts & Global Health, CINAHL, Cochrane Central Register of Controlled Trials, Embase, MEDLINE, ProQuest Dissertations & Theses, PsycINFO, Web of Science and the WHO International Clinical Trials Registry Platform (ICTRP).

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 5.1.0, Box 6.4.d. (Handbook 2011)). Search strategies for major databases are provided in Appendix 1.

Searching other resources

- The Cochrane Hypertension Information Specialist searched the Hypertension Specialised Register segment (which includes searches of MEDLINE for systematic reviews) to retrieve existing systematic reviews relevant to this systematic review, so that we could scan their reference lists for additional trials.
- 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.

Searches carried out for previous versions of this review

Trial search: Parijs and colleagues published the first RCT of the effect of sodium reduction on BP in 1973 (1000 Parijs 1973). In our first meta-analysis (Graudal 1998), a literature search in MEDLINE (1966-through December 1997) was performed using the following combinations of search terms: 1) salt or sodium, 2) restriction or dietary, 3) blood pressure or hypertension, 4) randomized or random. We combined 1, 2, 3 and 4 and found 291 references. Of these, 76 randomised trials from 60 references met the inclusion criteria. From the reference lists of these articles and from four previous meta-analyses (Grobbee 1986, Law 1991, Cutler 1991, Midgley 1996), an additional 23 references reporting on 39 trials were identified, resulting in a total of 83 references.

Similar searches were made for hormones and lipids changing the third search term (blood pressure or hypertension) with the hormone or lipid term resulting in additional five sub-studies dealing with hormones and lipids (Jula-Karanko 1992, Jula-Mäki 1992 1026 Koolen 1984(2), 1104 Overlack 1993, Ruppert 1994). Of these 88 references, three dealing exclusively with diabetes patients were excluded in the 2003 update (Dodson 1989, Mühlhauser 1996, Miller 1997).

In January 2002, a repeated search was performed through December 2001, revealing an additional 12 references, of which one was excluded because it only included patients with diabetes (Imanishi 2001). Accordingly, the 2004 updated review included a total of 96 references.

In December 2009, a literature search for the 2011 update was performed from 1950 through December 2009. This search revealed a total of 511 references in Ovid MEDLINE, 282 in Ovid EMBASE and 1428 in Cochrane CENTRAL. Headlines and abstracts were read and 44 articles from MEDLINE (26 included), eight from Embase (one included) and 129 from CENTRAL (45 included) were retrieved as full-text papers for further review. A total of 72 new references investigating at least one of the effect variables met the inclusion criteria for this review. The search was not limited to English language studies. Two studies in Italian were identified and included. During the present revision, we discovered that in a few of the previously included studies, some subgroup data were published in two papers. To avoid duplication due to including subgroup data from several papers, we included them from the main paper only. As a result, three previously included references were excluded (Steegers 1991, Ruppert 1991, Ruppert 1994). The most recent search was performed on July 21, 2011, revealing 293 additional references. After screening of titles and abstracts, four full-text papers were retrieved, of which two contained data to be included. Consequently a total of 167 studies were supposed to be included in the 2011 updated version of this systematic review. However, in connection with the present update, a recount revealed a counting error, as the number of references in reality was 166.

Data collection and analysis

Selection of studies

See Search methods for identification of studies.

Review author NG performed the study selection for the 1998 version (Graudal 1998) and the 2003 version (Jürgens 2003). Review authors NG and GJ independently performed the supplementary study selection for the 2011 version (Graudal 2011. NG and THG independently performed the supplementary study selection for the current 2016 version. Discrepancies were resolved by agreement.

Data extraction and management

Two authors independently recorded the following data from each trial:

1. the sample size (N);
2. the mean age of participants;
3. the fraction of females, males; Whites, Blacks and Asians;
4. the duration of the intervention;
5. the sodium reduction measured as the difference between 24-hour urinary sodium excretion during low-sodium and high-sodium diets and standard deviation (SD);
6. SBP (SD) and DBP (SD) before and after intervention;
7. difference between changes in SBP and DBP obtained during low-sodium and high-sodium diets and the SD of these differences;
8. for cross-over studies, when possible, the overall effect estimate and standard error (SE);
9. levels of hormones and lipids in the blood and their standard deviations during low-sodium and high-sodium diets. Concerning lipids, cholesterol units of mmol/L were transformed to mg/dL by means of the factor 38.6 and triglyceride units of mmol/L were transformed to mg/dL by means of the factor 88.4. Other renin units than ng/mL/hour were when possible transformed to ng/mL/hour, and units of aldosterone, noradrenalin and adrenalin other than pg/mL were transformed to pg/mL by means of the molecular weights.

If there were discrepancies between review authors they looked at the data together and came to an agreement.

Assessment of risk of bias in included studies

This was performed using the Cochrane 'Risk of bias' tool, including recording of allocation, blinding, incomplete outcome data and selective reporting. Subgroup analyses of the primary analysis of SBP were performed for contrasting sources of bias appearing from the 'Risk of bias' analysis.

Measures of treatment effect

This was defined as the mean difference (MD) between the changes from baseline to end of treatment during low- and high-sodium diets. When units within an analysis were different the standardised mean difference (SMD) was used.

Unit of analysis issues

Blood pressure (BP)

Combined analyses were performed including both parallel and cross-over studies. The generic inverse variance data type was used to analyse the effect in order to ensure that the weight of the cross-over studies was not underestimated compared with the parallel studies. For parallel studies, the SE was calculated in the usual way as follows: SE (diff) = sqrt $SE_1^{\ 2} + SE_2^{\ 2}$. For cross-over studies the

given SE (difference) was used. A linear regression equation linking the given SE to the calculated SE (sqrt $SE_1^2 + SE_2^2$) was calculated by means of the studies which reported both SE (difference) and SE on BP during both intervention periods. This equation was used to transform all calculated SEs to estimated "true" SEs (difference) in cross-over studies that did not report SE (difference). In this way, it was ensured that cross-over studies were attributed proper weight compared with the parallel studies. There were not enough studies to calculate separate equations for Black and Asian populations and therefore the equations calculated in the white populations were used to transform these SEs when necessary.

Hormones and lipids

The very few parallel studies were excluded and the large fraction of cross-over studies were analysed separately. As the large majority of cross-over studies reported separate data for each intervention period instead of overall estimates of effect, the continuous data type was used in the separate analyses of the cross-over studies.

Dealing with missing data

If the SD was not reported it was calculated from a given SE, 95% confidence interval (CI), P value or t value, estimated from a figure or imputed from the formula SD (change) = sq root (SD1sq + SD2sq), SD1 is SD on blood pressure before intervention and SD2 is SD on blood pressure after intervention.

Assessment of heterogeneity

A Chi^2 test included in the forest plot was used to assess whether observed differences in results are compatible with chance alone. A low P value (or a large Chi^2 statistic relative to its degree of freedom) provides evidence of heterogeneity of intervention effects (variation in effect estimates beyond chance).

Assessment of reporting biases

Funnel plots were assessed for asymmetry. Selective reporting of SBP and DBP was recorded

Data synthesis

Individual study subgroup data defined before randomisation based on ethnicity and state of hypertension were included in the meta-analysis as subgroups, whereas sodium sensitivity subgroups, which were defined by the authors of the individual studies after they had analysed the data, were combined by the present authors and subsequently the combined data were included in the meta-analyses.

The mean difference (MD) was calculated for outcome measures with identical units in the included studies (BP without transformation of data (all measured as mmHg), adrenaline, aldosterone, noradrenalin and lipids, after transformation). The standardised mean difference (SMD) was calculated for outcome measures with different units (renin), but a separate calculation of MD for the majority of renin studies with identical unit (ng/mL/hour) was also performed. With the MD method, the difference in effect between two treatments is divided by the SD of the measurements. By that transformation, the effect measures become dimensionless and the outcomes from trials, which have used different units, can consequently be combined. As we accumulated data from a series of studies that had been performed by researchers operating independently, and as the goal of the analysis was to extrapolate to other populations, we used a random-effects model in our primary analysis to estimate the summary measure as the mean of a distribution of effects.

Level of significance: In case of multiple independent comparisons, it is important to avoid coincidental significance. Ten meta-analyses were performed. However, the SBP and DBP comparisons are not independent of each other and BP depends on renin and aldosterone as well as catecholamines. Concerning lipids, these are mutually dependent, whereas the dependency on BP and hormones is not obvious. Consequently, the 10 meta-analyses could be sub-classified into a group of meta-analyses of mutually dependent BP and hormones and an independent group of meta-analyses of mutually dependent lipid fractions. Consequently, the level of significance was reduced by means of the formula 1-0.95 x 1/N = 1-0.95 x 1/2 = 0.025, (N = number of independent investigations = 2).

Subgroup analysis and investigation of heterogeneity

Since the previous version of this review, we now have reasonable evidence to determine the time of maximal efficacy to be one week (Table 2). Therfore, there is a risk that studies lasting for less than one week may underestimate the effect of sodium reduction. Furthermore, evidence has appeared to indicate that all of the world's populations have a mean sodium intake below 250 mmol/day (Table 1), and as dose-response studies have indicated that sodium reductions from very high levels have bigger effects than reductions from usual levels (Graudal 2015), such studies may contribute to overestimate the effect. We therefore performed a subgroup analysis intending to eliminate these potential biases on SBP and DBP (stratified according to normal BP or hypertension) and renin, aldosterone, noradrenalin, adrenalin, cholesterol triglyceride, HDL and LDL by exclusion of studies with a duration of less than seven days and sodium intake above 250 mmol/day.

Sources of bias: subgroup analyses were performed for contrasting sources of bias appearing from the 'Risk of bias' analysis.

Sensitivity analysis

Sensitivity analyses were performed excluding studies giving rise to asymmetry in the funnel plots.

RESULTS

Description of studies

Results of the search

During this 2016 update, we identified two studies with duplicate data, which were subsequently excluded (Jula-Karanko 1992;Jula-Mäki 1992), as all data could be extracted from a later paper (1110 Jula 1994).

In September 2014, a literature search for the present update was performed as described in "Search methods for identification of studies". The de-duplicated results from the searches revealed 626 articles. On the basis of titles, 549 were excluded. Seventy-seven abstracts were read and 27 full-text articles obtained, of which, nine fulfilled the inclusion criteria. In a supplementary search in April 15 2015, an additional 102 references were identified. Six articles were obtained, of which three fulfilled the inclusion criteria.The last updated search was performed on 7 March 2016. The de-

duplicated results from the searches revealed 994 articles. During the primary screening, 687 were excluded and on the basis of titles and abstracts, a further 236 articles were eliminated. Seventy-one abstracts were read in detail and 29 full-text articles obtained, of which, seven fulfilled the inclusion criteria. Additionally, two articles were identified from a reference list of a review article. A WHO International Clinical Trials Registry Platform search using the search term “diet and sodium” revealed 141 trials, but none were included.

A total of 185 references (164 from the 2011 review plus 9 + 3 + 9 new references) were thus included in the present updated 2016 version.

Included studies

See Characteristics of included studies.

One hundred and eighty-five references were included in the review. Eight included only data on hormones and lipids, whereas 177 included BP data, as well as hormone and lipid data in a significant number of these. The total number of study populations with BP outcomes included in the primary analysis was 206. The median of the mean ages was 44 years (range: 12 to 73), which is a little higher than the median age of most populations (typically 35 years) and the mean sodium intake in the high-sodium group was 201 mmol/day (SD: 69) and in the low-sodium group was 66 mmol/day (SD: 47), corresponding to a mean sodium reduction of 135 mmol/day.The median of the mean ages of the study's 125 white populations included in the subgroup analysis (duration of at least seven days, a sodium intake of less than 250 mmol/day) was 45.4 years (range: 13 to 73) the mean sodium intake in the high-sodium group was 177 mmol/day (SD: 35) and in the low-sodium group was 68 mmol/day (SD: 36), corresponding to a mean sodium reduction of 109 mmol/day. The mean BP in the normotensive study populations was 119/71 mmHg, which is close to the population mean of the USA population (119/71 mmHg) (Wright 2011), and a little higher than the mean of the normotensive fraction of the USA population (115/70 mmHg) (Wright 2011). The mean BP in the untreated hypertensive study populations was 151/93 mmHg and in the treated hypertensive study populations was 144/88 mmHg, both of which are higher than corresponding pressures in the USA population (146/84 mmHg and 131/72 mmHg) (Wright 2011).

In 83 studies including 7729 participants, there was information of the baseline 24-hour sodium excretion, not influenced by diets. This was 159 mmol/24-hour (range: 90-274 mmol) (10-90 percentiles: 123-194 mmol).

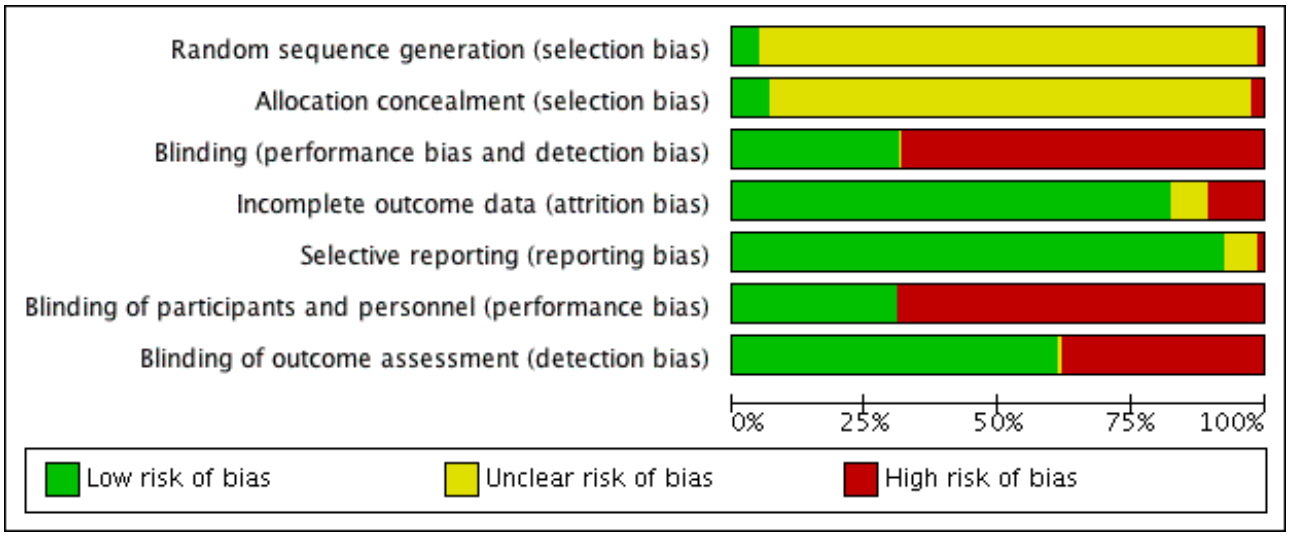
Excluded studies

See Characteristics of excluded studies.

Risk of bias in included studies

See Characteristics of included studies and Figure 1

Figure 1. 'Risk of bias' graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.



The obligatory trial quality criterion was randomisation. Double-blind, single-blind or open studies with a parallel or a cross-over design were accepted. A study was defined as single-blind if an investigator measured BP without knowledge of the diet or by a computerised manometer, and as open if precautions to decrease observer bias were not mentioned.

We found two important contrasts: general blinding and blinding of outcome detection (Figure 1). We performed subgroup analyses of BP in both normotensive and hypertensive white populations, but not in the black and Asian populations due to the small numbers of trials. We did not perform subgroup analyses on the biochemical outcomes (hormones and lipids) as they are supposed to be performed blindly in 100% of cases.

Allocation

Only 14 studies (1034 Watt 1985; 1078 Egan 1991; 1081 TOHP I 1992; 1107 MacFadyen 1994;1135 TOHP II 1997; 1136 van Buul 1997;1142 Knuist 1998; 1195 Jessani 2008; 1197 Dickinson 2009; 1198 He 2009; 1206 Graffe 2012; 1208 Todd 2012; 1217 Markota 2015; 1225 Gijsbers 2015), either partly or sufficiently explained the allocation

sequence generation and concealment. Consequently, there is a general significant risk that allocation was not unbiased.

Blinding

Fifty-six studies were reported to be double-blind and in 115 studies, the risk of detection bias was estimated to be low (Figure 1). Separate analyses were performed on studies with low and high risks of general blinding and outcome detection.

Incomplete outcome data

Based on the information given in the individual articles, incomplete outcome data generally was a small problem (Figure 1). However, only a few studies showed flow charts of the fate of the participants. Therefore, this bias may be significant.

Selective reporting

Based on the information given in the individual articles, reporting bias was small (Figure 1). However, as protocols did not exist for the vast majority of studies, this evaluation may be imprecise.

Other potential sources of bias

The effect of an intervention on BP may depend on factors such as baseline BP and ethnicity. Therefore, a biased distribution of such factors in the included study populations compared with the general population may bias the effect of the intervention found in the meta-analysis to be different from the potential effect in the general population. We therefore performed separate analyses for hypertensive and normotensive individuals and for different ethnicities.

Effects of interventions

See: **Summary of findings for the main comparison**; **Summary of findings 2**; **Summary of findings 3**; **Summary of findings 4**; **Summary of findings 5**

See Data and analyses.

Blood pressure in white participants

See Summary of findings for the main comparison

In the meta-analyses of trials of white participants with normal blood pressure (BP), the mean difference (MD) was a change in systolic blood pressure (SBP) of -1.09 mmHg (95% CI: -1.63 to -0.56) (P = 0.0001) (89 trials, 8569 trials) (Analysis 1.1; Figure 2), and in diastolic blood pressure (DBP) of + 0.03 mmHg (95% CI: -0.37 to 0.43) (P = 0.89) (90 trials, (8833 participants) (Analysis 1.2; Figure 3) (*high-quality evidence)*.

Figure 2. Forest plot of comparison: 1 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in whites, outcome: 1.2 Whites, normotensive, SBP.

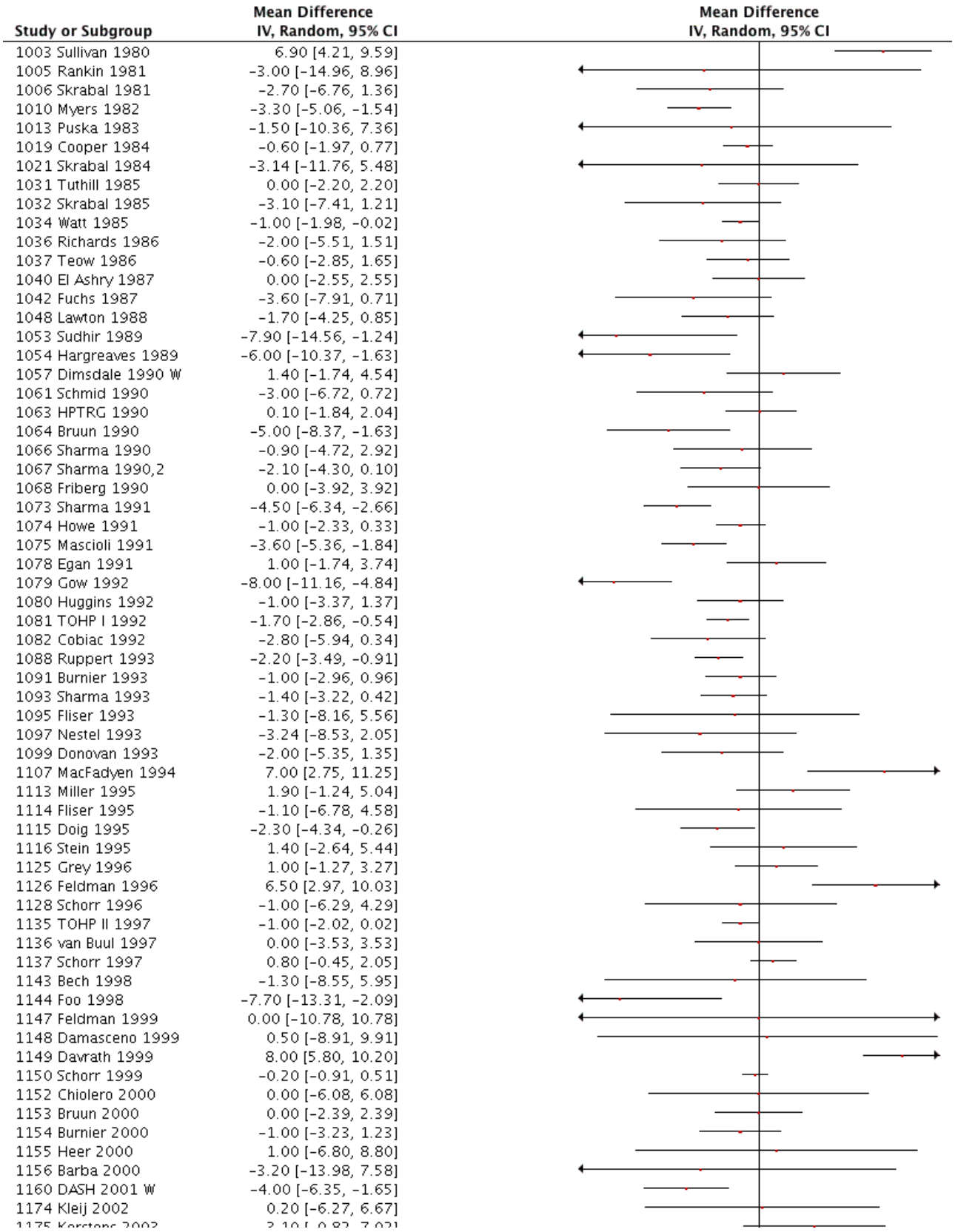


Figure 2. (Continued)

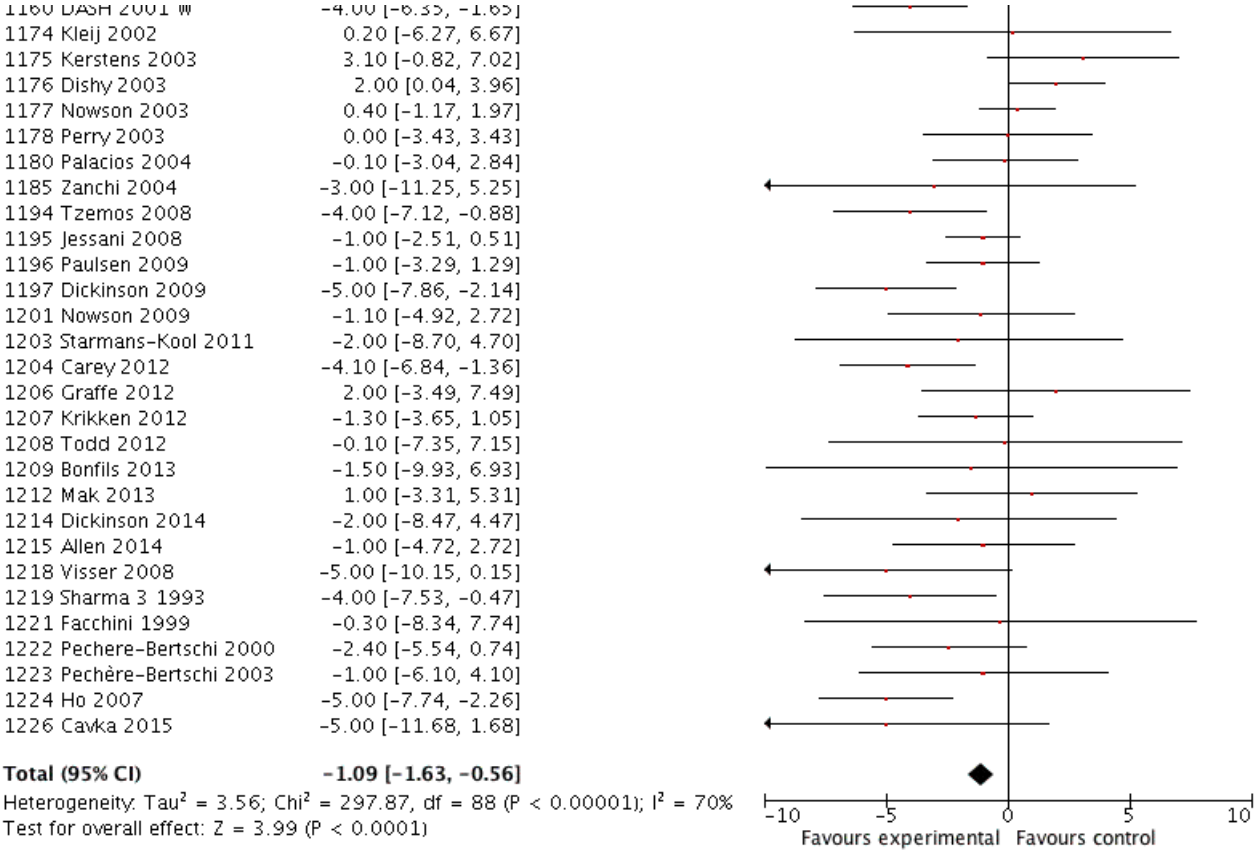


Figure 3. Forest plot of comparison: 1 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in whites, outcome: 1.2 Whites, normotensive, DBP.

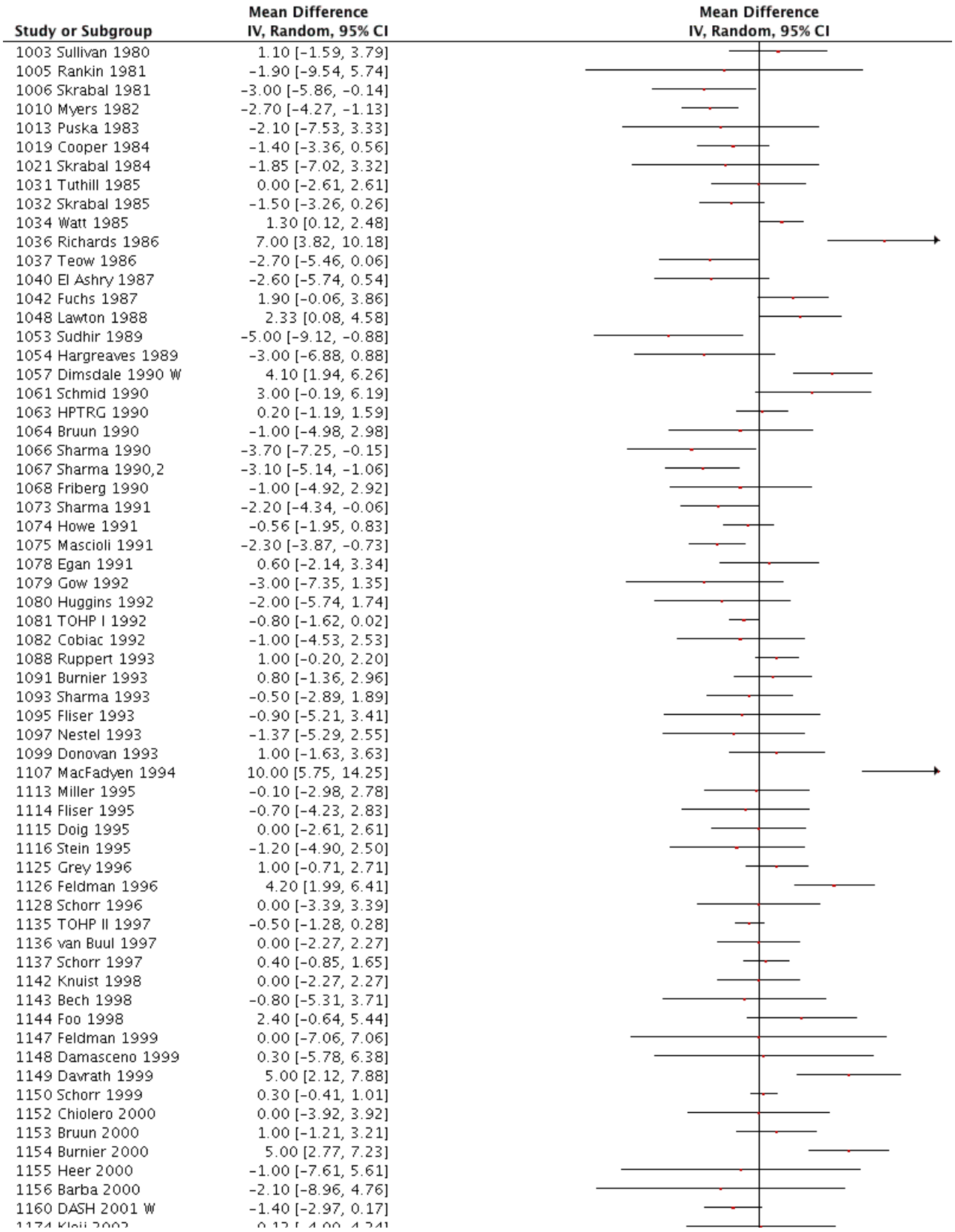
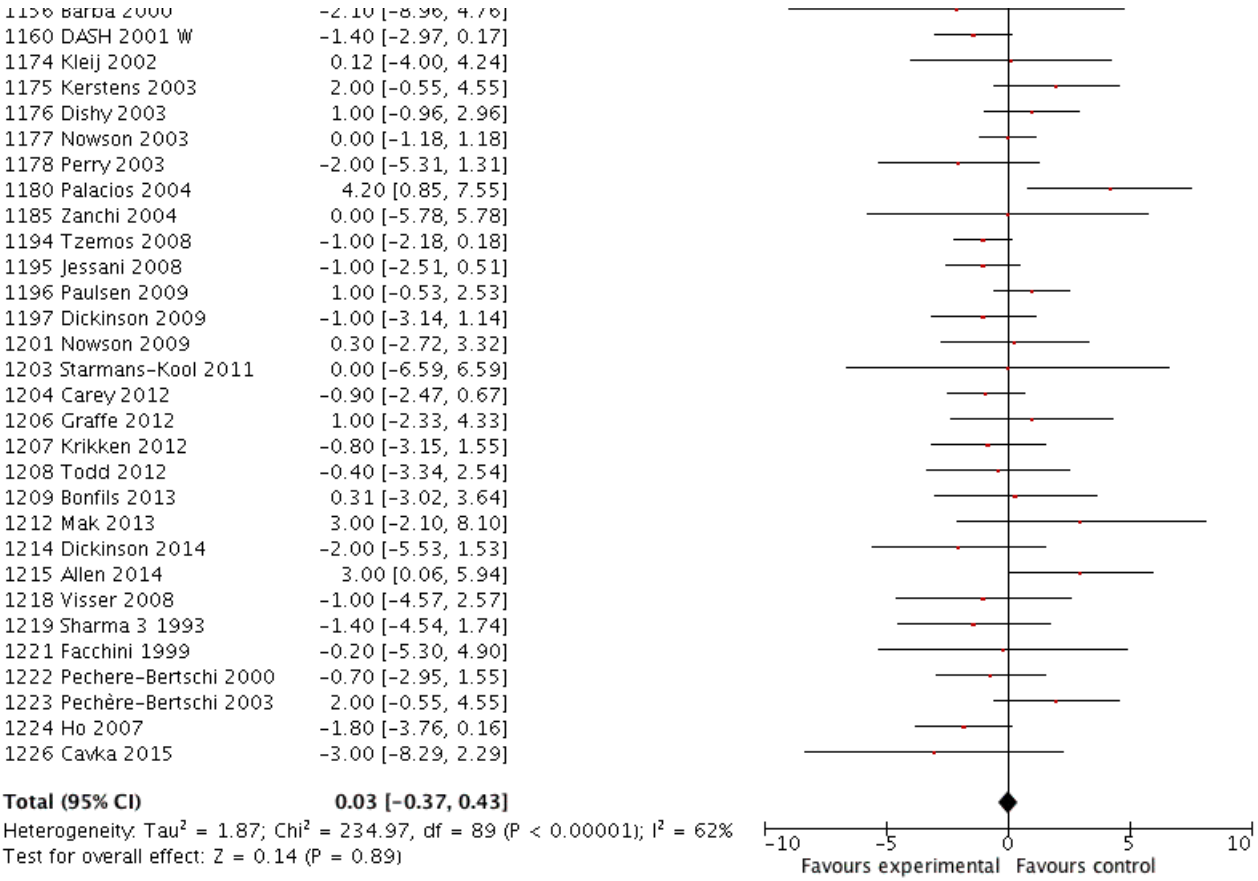


Figure 3. (Continued)



In subgroup meta-analyses of trials with a duration of at least one week and a sodium intake of a maximal 250 mmol/day, the MD showed a decrease in SBP of -1.31 mmHg (-1.83 to -0.80) (P = 0.00001) (59 trials, 7125 participants) (Analysis 4.1) and in DBP of -0.36 mmHg (95% CI: -0.79, 0.07) (P = 0.10) (61 trials) (Analysis 4.2). A further elimination of five studies, which, although the mean BP was normal, did include individuals with hypertension, reduced the SBP/DBP effect to -1.08/-0.24 mmHg.

In the trials of white people with elevated BP, MD showed a decrease in SBP of -5.51 mmHg (95% CI: -6.45 to -4.57) (P < 0.00001) (84 trials, 5925 participants) (Analysis 1.3), and in DBP of -2.88 mmHg (95% CI: -3.44 to -2.32) (P < 0.00001) (85 trials, 6001 participants) (Analysis 1.4) (*high-quality evidence*).

In subgroup meta-analyses of trials with a duration of at least one week and a sodium intake of a maximal 250 mmol/day, MD showed a decrease in SBP of -5.02 mmHg (-6.00 to -4.05) (P < 0.00001) (63 trials) (Analysis 4.3) and in DBP of -2.78 mmHg (95% CI: -3.42 to -2.14) (P < 0.00001) (64 trials) (Analysis 4.4).

Blood pressure in black participants

See Summary of findings 2

In the meta-analyses of seven trials involving 506 black participants with normal BP, MD showed a decrease in SBP of -4.02 mmHg (95% CI:-7.37 to -0.68) (P = 0.02) (Analysis 2.1) and in DBP of -2.01 mmHg (95% CI:-4.37, 0.35) (P = 0.09) (Analysis 2.2) (*moderate-quality evidence*).

In the meta-analyses of eight trials of 619 black participants with elevated BP, MD showed a decrease in SBP of -6.64 mmHg (95% CI:-9.00, -4.27)

(P = 0.00001) (Analysis 2.3) and in DBP of -2.91 mmHg (95% CI:-4.52, -1.30) (P = 0.0004) (Analysis 2.4) (*moderate-quality evidence*).

Blood pressure in Asian participants

See Summary of findings 3

In the meta-analyses of three trials involving 393 Asian participants with normal BP, MD showed a decrease in SBP of -0.72 mmHg (95% CI: -3.86, 2.41) (P = 0.65) (Analysis 3.1) and in DBP of -1.63 mmHg (95% CI:-3.35 to 0.08) (P= 0.06) (Analysis 3.2) (*moderate-quality evidence*).

In the meta-analyses of nine trials involving 501 Asian participants with elevated BP, MD showed a decrease in SBP of of -7.75 mmHg (95% CI:-11.44, -4.07) (P < 0.0001) (Analysis 3.3) and in DBP of -2.68 mmHg (95% CI: -4.21 to -1.15)(P = 0.0006) (Analysis 3.4) (*moderate-quality evidence*).

Renin

See Summary of findings 4

Two parallel trials were excluded (1110 Jula 1994; 1155 Heer 2000).

In the remaining 82 cross-over trials (5498 participants) of measurement of renin (including 88 comparisons reported in the Data & analyses), the standardised mean difference (SMD) of sodium reduction was 1.22 standardized units (95% CI: 1.07 to 1.37) (Z= 15.68, P < 0.00001) (Analysis 5.1) (*high-quality evidence*). In 73 comparisons, which all had the same unit (ng/mL/hour), either directly or after transformation, the MD was 1.60 ng/mL/hour (95% CI: 1.40 to 1.79) (Z= 16.04, P < 0.00001).

In comparisons with a duration of at least seven days and a sodium intake of less than 250 mmol/day (44 trials, 3470 participants), the SMD was 1.05 standardized units (95% CI: 0.85 to 1.24), (Z= 10.35, P < 0.00001) (Analysis 6.1) In 39 comparisons using ng/mL/hour as the unit, the corresponding MD was 1.30 ng/mL/hour (95% CI: 1.06 to 1.53), (Z= 10.65, P < 0.00001). The effect in normotensive participants was significantly higher than in hypertensive participants (Summary of findings 4).

Aldosterone

See Summary of findings 4

Three parallel trials were excluded (1110 Jula 1994; 1111 Howe 1994; 1155 Heer 2000).

In the remaining 65 cross-over trials (4884 participants) of measurement of aldosterone, MD was 97.81 pg/mL (95% CI: 82.56 to 113.05) (Z = 12.58, P < 0.00001) (Figure 4, Analysis 5.2) (*high-quality evidence*). In comparisons with duration of at least one week and sodium intake of less than 250 mmol/day (34 trials, 3128 participants), MD was 95.59 pg/mL (95% CI: 74.12 to 117.05), P = 0.00001 (Analysis 6.2).The effect in normotensive participants was significantly higher than in hypertensive participants (Summary of findings 4).

Figure 4. Forest plot of comparison: 5 Effect of salt reduction on hormones, outcome: 5.2 Aldosterone (pg/mL).

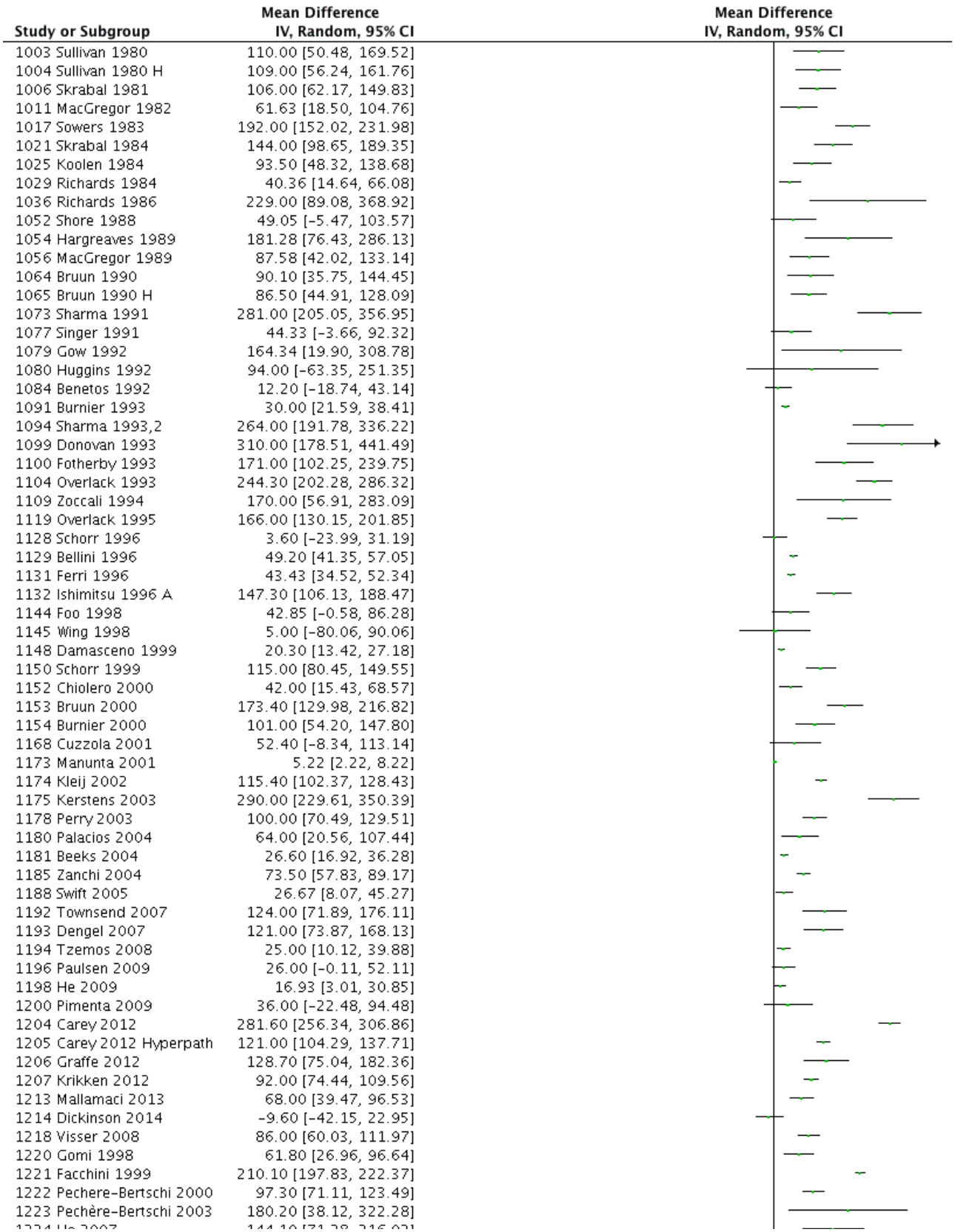
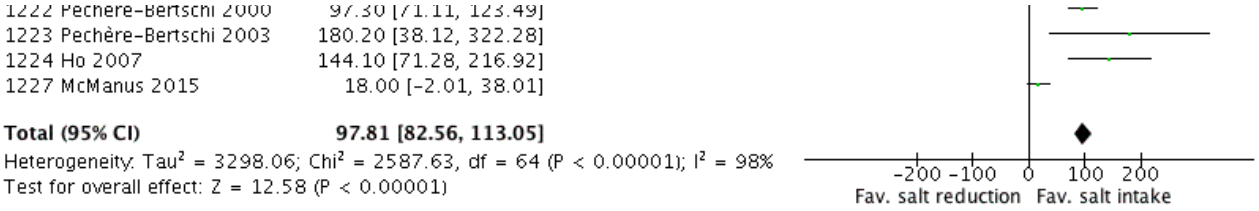


Figure 4. (Continued)



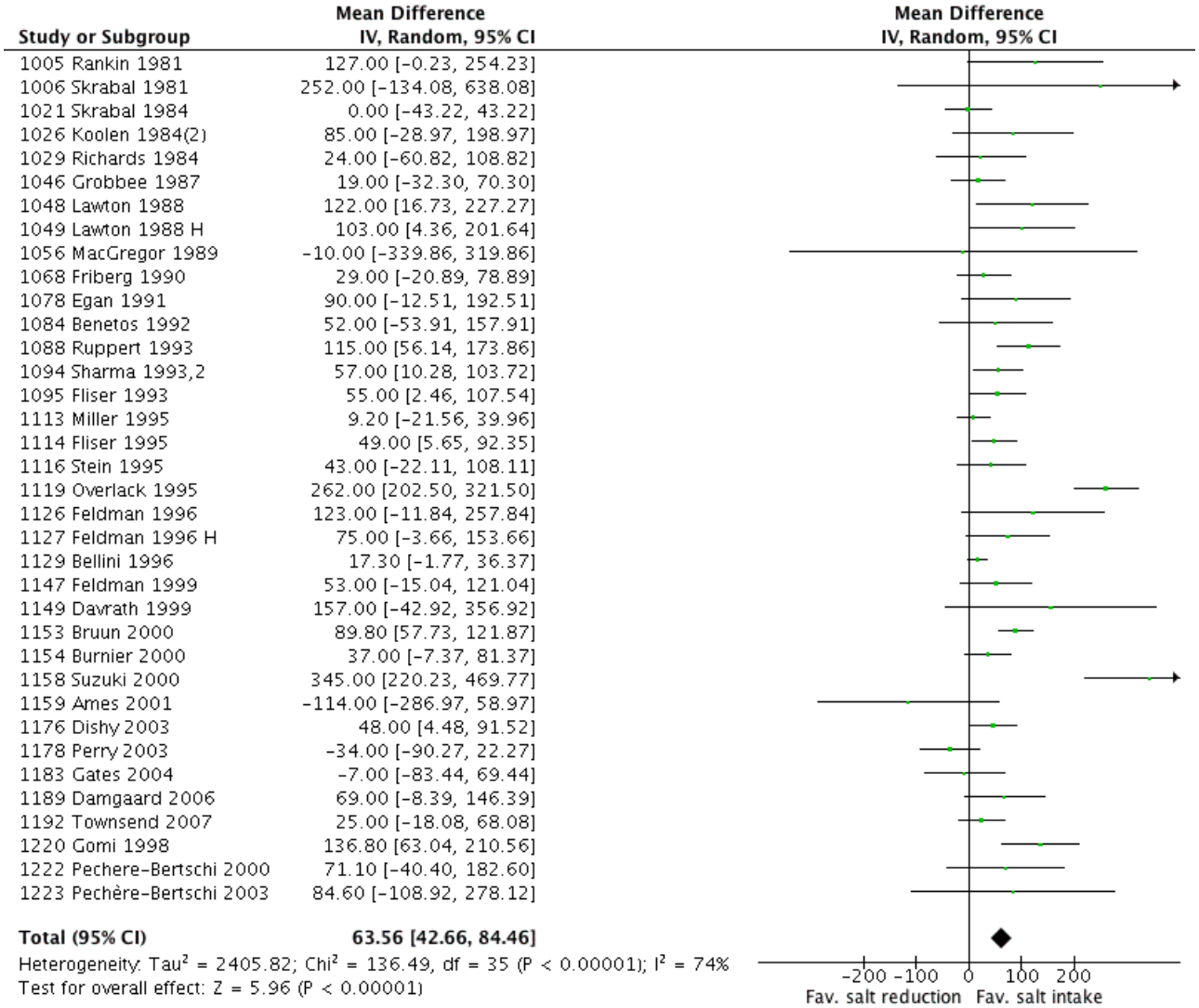
Noradrenaline

See Summary of findings 4

One parallel trial was excluded (1110 Jula 1994).

In the remaining 34 cross-over trials (1736 participants) of measurement of noradrenaline (including 36 comparisons reported in the Data & analyses), MD was 63.56 pg/mL (95% CI: 42.66 to 84.46), (z = 5.96, P = 0.00001) (Figure 5, Analysis 5.3) (*high-quality evidence*). In comparisons with duration of at least one week and a sodium intake of less than 250 mmol/day (23 studies, 964 participants) MD was 48.66 pg/mL (95% CI: 28.88 to 68.44), P = 0.00001 (Analysis 6.3). There was no difference between normotensive participants and hypertensive participants (Summary of findings 4).

Figure 5. Forest plot of comparison: 5 Effect of salt reduction on hormones, outcome: 5.3 Noradrenaline (pg/mL).



Adrenaline

See Summary of findings 4

One parallel trial was excluded (1110 Jula 1994).

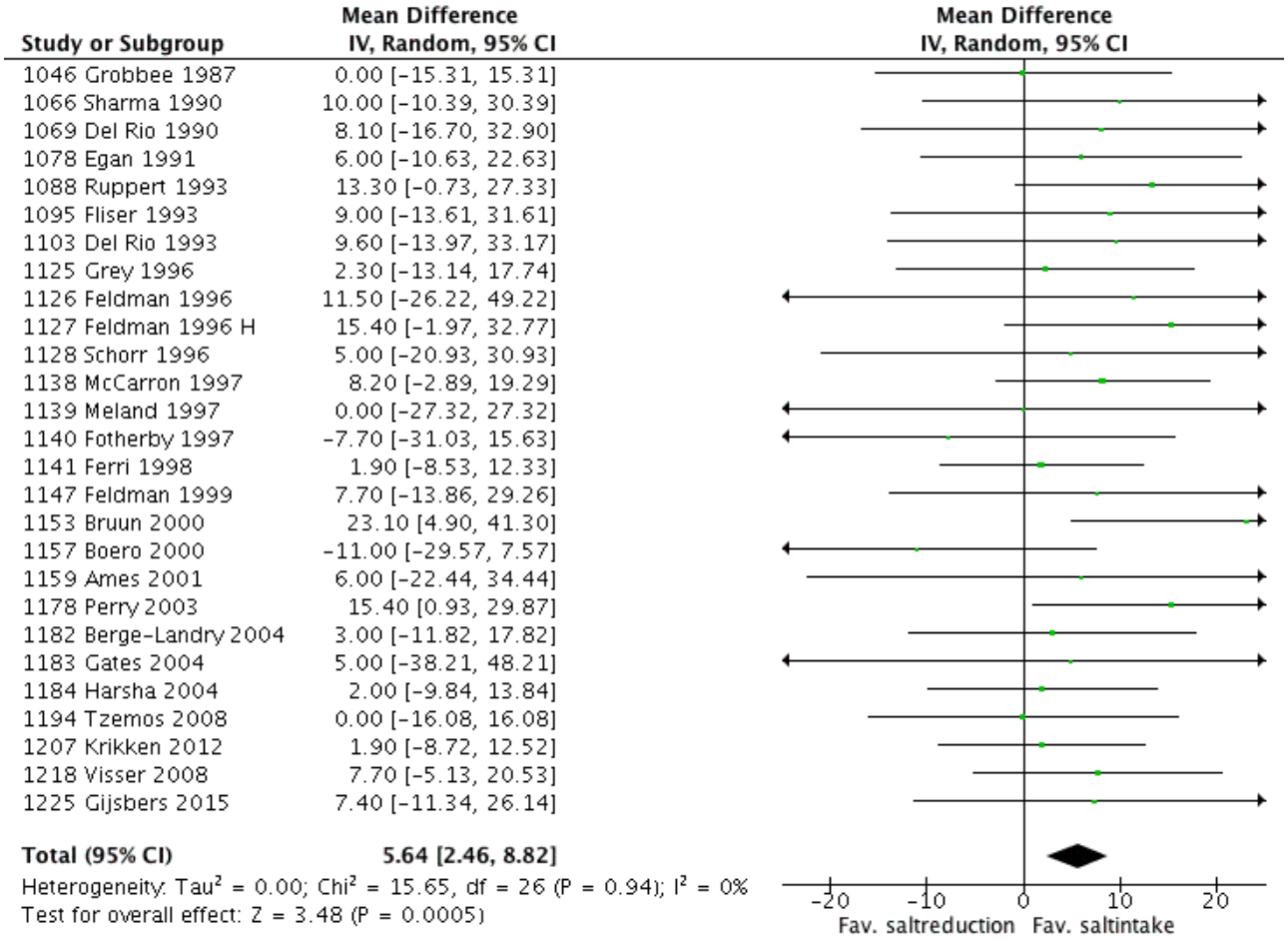
In the remaining 15 cross-over trials (662 participants) of measurement of adrenaline (including 16 comparisons reported in the Data & analyses), MD was 7.55 pg/mL (95% CI: 0.85 to 14.26), (z = 2.21, P = 0.03) (Analysis 5.4) (*moderate-quality evidence*). In comparisons with duration of at least one week and sodium intake of less than 250 mmol/day (12 studies, 486 participants) MD was 7.79 pg/mL (95% CI: 0.31 to 15.28), P = 0.04 (Analysis 6.4). There was no difference between normotensive participants and hypertensive participants (Summary of findings 4).

Cholesterol

See Summary of findings 5

Three parallel trials were excluded (1015 Bulpitt 1984; 1085 Sciarrone 1992; 1199 Meland 2009). In the remaining 26 cross-over trials (1800 participants) of measurement of cholesterol (including 27 comparisons reported in the Data & analyses), MD showed an increase of 5.64 mg/dL (95% CI: 2.46 to 8.82), P = 0.0005 (Figure 6, Analysis 7.1) (*moderate-quality evidence*). In comparisons with duration of at least one week and sodium intake of less than 250 mmol/day (20 trials, 1180 participants) MD was 4.88 mg/dL (95% CI: 1.19 to 8.56), P = 0.01 (Analysis 8.1). The effect in normotensive participants was significantly higher than in hypertensive participants (Summary of findings 5)

Figure 6. Forest plot of comparison: 6 Effect of salt reduction on lipids, outcome: 6.1 Cholesterol.



Triglyceride

See Summary of findings 5

Two parallel trials were excluded (1085 Sciarrone 1992; 1199 Meland 2009) .

In the remaining 19 cross-over trials (1390 participants) of measurement of triglyceride, MD showed an increase of 7.04 mg/dL (95% CI: 3.04 to 11.05), P = 0.0006 (Analysis 7.2) (*moderate-quality evidence*). In comparisons with duration of at least one week and sodium intake of less than 250 mmol/day (12 trials, 770 participants) the effect was 6.92 (mg/dL [95% CI: 1.82 to 12.02), P = 0.008 (Analysis 8.2). There was no difference between normotensive participants and hypertensive participants (Summary of findings 5)

High-density lipoprotein (HDL)

See Summary of findings 5

Two parallel trials were excluded (1085 Sciarrone 1992; 1199 Meland 2009).

In the remaining 19 cross-over trials (1442 participants) of measurement of HDL, there was no effect of sodium reduction on serum HDL: MD: -0.29 mg/dL (95% CI: -1.66 to 1.08) P = 0.68 (Analysis 7.3) (*moderate-quality evidence*). This result did not change in comparisons with duration of at least one week and sodium intake of less than 250 mmol/day (-0.67 mg/dL (-2.18 to 0.83), P = 0.38 (14 trials, 948 participants)) (Analysis 8.3).

Low-density lipoprotein (LDL)

See Summary of findings 5

One parallel trial was excluded (1085 Sciarrone 1992).

In the remaining 17 cross-over trials (1358 participants) of measurement of LDL, MD showed a non-significant increase of 3.12 mgdL (95% CI: -0.41, to, 6.64), P = 0.08 (Analysis 7.4). In comparisons with duration of at least one week and sodium intake of less than 250 mmol/day (12 trials, 864 participants), MD was 3.63 mgdL (95% CI: -0.44 to 7.69), P = 0.08 (Analysis 8.4).

Bias analyses

Bias analysis: Comparing low bias risk versus high bias risk of general blinding and blinding of outcome detection for SBP-outcomes in white people with normotension and hypertension showed no important differences. See Data and analyses: 9 Bias analyses.

Additional subgroup analyses

Hormones and lipids

Inclusion of the few parallel studies did not change any of the results (data not shown).

Sensitivity analyses

The funnel plots of all analyses were investigated. For each funnel plot, all studies giving rise to asymmetry were eliminated. The resulting effect was compared with the original analysis. All these analyses showed only marginal effects without significance (not shown).

DISCUSSION

Summary of main results

The effect of sodium reduction from an average high usual intake (201 mmol/day) to the recommended level (66 mmol/day) was small in study populations with normal blood pressure (BP) (-1.09/+0.03 mmHg) corresponding to a mean arterial pressure effect of only -0.3 mmHg . In hypertensive study populations the effect was (-5.51/-2.88 mmHg). In a subgroup analysis intending to eliminate the potential bias of a very short intervention duration (< seven days) and very high sodium intake (> 250 mmol/day), the decrease in BP in study populations with a normal BP (-1.31/-0.36 mmHg) and hypertension (-5.02/-2.78 mmHg) was also small. The effect of sodium reduction on hormones and on lipids showed statistically significant increases in renin, aldosterone, noradrenalin, cholesterol and triglyceride in the primary analysis, as well as in the subgroup analysis, whereas the increase in adrenalin was borderline significant (P < 0.03). The increase in cholesterol in the low-salt group seemed mainly to be due to an increase in low-density lipoprotein (LDL), which was borderline significant. The slight decrease in high-density lipoprotein (HDL) in the low-salt group was not significant.

The analysis of black populations showed that the effect of sodium reduction in black people with normotension corresponded to the one found in black people with hypertension. This was in contrast to the analyses of white and Asian populations in whom the effect was smaller in those who were normotensive than in those who were hypertensive. However, compared with previous analyses (Graudal 1998; Jürgens 2003), the diverging results within the black populations and between the black and white populations are smaller. In a recent detailed analysis, we found that a significant fraction of the differences between the three ethnicity groups could be ascribed to differences in baseline BP, age, and amount of sodium reduction. Furthermore there was no difference in BP outcome between ethnicity groups investigated in the same study (Graudal 2015b) indicating that the differences found in the present meta-analysis mainly may be due to confounders rather than ethnical differences.

Overall completeness and applicability of evidence

In the primary analysis, population samples from the whole BP distribution of the populations were included. In this analysis, the intake of sodium in the “high” sodium group was in the interval 100 mmol/day to 795 mmol/day in 205 comparisons (99%), and below 100 mmol/day in one comparison, the mean level being 201 mmol/day. The intake of sodium in the low-sodium group was below 100 mmol/day in 168 comparisons (82%) and above 100 mmol/day in 38 comparisons, the mean level being 66 mmol/day. In the subgroup analysis, the intake of sodium in the “high” sodium group was in the interval 109 mmol/day to 248 mmol/day in 143 comparisons (99%), and below 100 mmol/day in one comparison, the mean level being 167 mmol/day. The intake of sodium in the low-sodium group was below 100 mmol/day in 114 comparisons (80%) and above 100 mmol/day in 30 comparisons, the mean level being 60 mmol/day. Consequently, this meta-analysis in general compares the effects of a dietary sodium intake, which is lower than usual and in accordance with the recommendations to reduce sodium below 100 mmol/day with a sodium intake, which is within the present world-wide usual range of sodium intake, the level in the primary analysis being in the high end of the usual intake and the level in the subgroup analysis being close to the world mean of 159 mmol/day (Table 1). The mean and the range of the baseline 24-hour sodium excretion of the included populations before diet manipulation (159 mmol/24 hours (10 to 90 percentile: 123 to 194)) were almost identical with the usual range of sodium intake in the world's populations (McCarron 2013; Powles 2013). Thus, the present review shows the consequences of the recommendations of the health institutions, which is to reduce the usual sodium intake of the world's populations (90 mmol/day to 250 mmol/day) to a level below 87 mmol/day to 100 mmol/day.

Quality of the evidence

The study populations included in the present meta-analysis were in general very heterogeneous with large variations in baseline BP, age, sodium intake and degree of sodium reduction. The analyses of BP and hormones were generally very heterogeneous. Especially, the I^2 values for renin and aldosterone were very high, but as renin and aldosterone rise sharply with sodium reduction below 2.3 g sodium, but only moderately above 2.3 g sodium (Brunner 1972; Graudal 1998), the extreme heterogeneity of the

outcomes of these variables is not surprising. In spite of the clinical heterogeneity, no heterogeneity was detected in the meta-analyses of lipid outcomes implying that these outcomes are robust. The number of studies included in the BP analyses (n = 206) is substantial as is the number of participants (more than 6000). This should allow robust conclusions. The fundamental quality criterion was randomisation, but a weakness is that very few of the studies described the sequence generation and the random allocation procedures leaving a substantial bias risk of insufficient randomisation, which could not be explored in a meaningful way due to the lack of contrasts between the number of studies with low and high risk of these biases (Figure 1). Another weakness was that a large number of studies were not double-blind. However, concerning this source of bias, there were no obvious trends towards different effects in the low-risk blinded groups compared with the high-risk open groups (Analysis 9.1; Analysis 9.2; Analysis 9.3; Analysis 9.4; Analysis 9.5; Analysis 9.6; Analysis 9.7; Analysis 9.8).

Potential biases in the review process

The present review is the largest of the many existing meta-analyses on sodium reduction, and other meta-analyses have not identified studies, which were not identified by our search. Our analysis is the largest partly because our selection criteria were less restrict. Therefore, a fraction of the included studies had an experimental character investigating a sodium intake far beyond the sodium intake in the general population for only four to six days, which may not be relevant for the general population on long-term sodium reduction. The fact that the subgroup analysis eliminating the potential short-term intervention bias and very high sodium intake bias showed similar results as the primary analysis indicates that the inclusion of extreme studies had a minor impact on the mean of the outcome effects. Other meta-analyses have extracted almost identical data in the individual studies indicating that our data extraction is unbiased. Finally, elimination of studies giving rise to asymmetry in the funnel plots did not change the results indicating a low risk of publication bias.

Agreements and disagreements with other studies or reviews

The scientific evidence behind the sodium reduction recommendations is a series of studies and meta-analyses, which are biased by high baseline blood pressure, high age and overweight (Graudal (3) 2016). The most prominent of these studies (DASH 2001), was additionally biased by a control group diet, which was designed to contain only half of the normal amount of potassium. Despite these studies are irrelevant as evidence for pubic health recommendations, the Food and Drug Administration (FDA) has released draft proposed voluntary guideline to encourage companies to steadily reduce sodium in processed foods (Frieden TR 2016), the main argument being a dose-response meta-regression analysis of mixed normotensive and hypertensive study populations, which was biased because it included mainly studies with high blood pressure and inappropriately forced the dose-response relationship through zero and thereby further doubled the postulated effect. In contrast, previous meta-analyses of randomised controlled trials (RCTs) have shown similar results of sodium reduction on BP. In 1986, Grobbee and Hofman combined 13 studies of persons with normal and elevated BP in a meta-analysis and found a significant hypotensive effect of reduced sodium intake on SBP of -3.6 mmHg and a non-significant effect on DBP of -2.0 mmHg (Grobbee 1986). In 1991, a second meta-analysis of 24 RCTs showed an effect of -4.0/-2.5 mmHg for persons with elevated BP and -1.0/-0.2 for persons with normal BP (Cutler 1991). This was verified in an update from 1997 (Cutler 1997). In 1996, a meta-analysis of 53 RCTs showed an effect of -3.7/-0.9 mmHg in persons with elevated BP and -1.0/-0.1 in persons with normal BP (Midgley 1996). In an analysis of eight RCTs lasting for at least six months, the effect was -2.9/-2.1 mmHg for persons with elevated BP and -1.3/- 0.8 mmHg for persons with normal BP (Ebrahim 1998). These results were confirmed in an update (Hooper 2002). All these similar results confirm that selection of RCTs based on magnitude of sodium difference or duration of the intervention does not significantly change the overall effect size estimate. These meta-analyses indicate that major disagreements about this effect size no longer seem to exist. However, there is still significant disagreement regarding the relevance of the effect size and the relevance of potential side effects (Taubes 1998).

The effect of sodium reduction on BP in hypertensive and normotensive study populations in the present review matches the effects found in most of these previous reviews, although the effect of sodium reduction on BP in normotensives is marginally lower than in the meta-analysis, which supports the WHO recommendations (Aburto 2013). In hypertensive study populations, there was no differences between the WHO review and our review. In normotensive study populations, the difference was small, the BP effect in the WHO review being -1.38/-0.58 mmHg and in ours being -1.09/0.03 (-1.31/-0.36 in the subgroup analysis).This study differed from ours as it only included studies lasting at least four weeks. However, as duration has no impact on the BP effect (Table 2), a more reliable explanation for the difference between the WHO review and our review is that the study populations with normal BP in the WHO review generally have a high baseline BP in the upper 50% percentile of the population.

According to WHO, the small effect in normotensive study populations is sufficient to recommend sodium reduction for the whole population, the assumption being that the association between BP and mortality is consistent. This, however, may not be the case. For instance, beta-blockers reduce BP in hypertensive individuals, but not mortality (Wiysonge 2012), and a recent meta-analysis of patients with diabetes showed that antihypertensive treatment reduces the risk of mortality and cardiovascular morbidity in diabetes patients with SBP higher than 140 mm Hg, but if SBP is less than140 mm Hg further treatment is associated with an increased risk of cardiovascular death, with no observed benefit (Brunström 2016). Such studies indicate that it is not possible to extend the general association of BP with mortality (Collins 1990) to the effect of a BP-reducing intervention on mortality. The reason for this inconsistency may be side effects of the intervention. However, while short duration has been suggested to underestimate the BP effect, it has concomitantly been suggested to overestimate possible adverse effects on hormones and lipids. This idea that the duration of the intervention tends to underestimate some physiological outcomes and overestimate others has not been documented, but still has been used to disregard side effects shown in studies lasting less than four weeks. Very few studies lasting more than for weeks have investigated side effects, and further more these studies do not reduce sodium to the recommended level, but to levels above 87 mmol/day, and therefore the side effects in these few studies may not be fully disclosed. In contrast, the present analysis shows that the adverse effects on hormones

and lipids are significant, when the sodium intake is lowered from a high usual sodium intake to a level in accordance with the recommendations of the health institutions. In addition, we have just shown that sodium reduction results in an increase in heart rate of 2.4% (Graudal (2) 2016). This may be an important side effect as resting heart rate is directly associated with mortality (Ho 2014; Jensen 2012). The assumption that at least some of these effects may be persistent and not just temporary has been indicated in observational studies. Yanomamo Indians, who persistently ingest very small amounts of sodium, have a three times higher level of renin in the blood and a 10 times higher excretion of aldosterone in the urine than normal controls (Oliver 1975). Furthermore, renin and aldosterone rise slowly as long as the intake is above 100 mmol/day, but exponentially, when sodium intake is reduced to levels below 100 mmol/day (Brunner 1972). Thus, the present meta-analysis provides a possible explanation for the small effect of reduced sodium intake on blood pressure: compensatory activation of the renin-aldosterone system is proportional to the degree of sodium reduction. Furthermore, the increases in noradrenaline and adrenaline may contribute to this counter-regulation (Warren 1980) and contribute to an increase in heart rate.

The very small effect of sodium reduction on BP in healthy individuals shown in the present review and other reviews including the WHO review, the risk of significant side effects shown in this review, and the possibility that an intervention to reduce BP may not reduce mortality (Wiysonge 2012), and even may increase mortality in some population groups with a normal BP (Brunström 2016) indicate that the BP-effect is not sufficient as a basis for recommendations in the general population, but should be verified in studies directly relating sodium intake with morbidity and mortality. Unfortunately, RCTs of the effect of sodium reduction below 100 mmol/day on mortality in healthy individuals do not exist (Graudal (1) 2016). A recently updated meta-analysis of eight RCTs with follow-up data on morbidity and mortality found a non-significant trend versus reduced cardiovascular (CV) morbidity, but could not demonstrate reduced all-cause mortality in the low-sodium group (Adler 2014). These trials were performed in overweight pre-hypertensive or hypertensive individuals and the sodium reduction was not below 100 mmol/day, but down to 100 mmol/day.

The sodium-mortality relationship has also been estimated by means of 27 observational studies (Alderman 2010; Mente 2016; O'Donnell 2014; Pfister 2014), which directly asses the relationship between sodium intake in the individual and mortality. Most of these studies were evaluated in an IOM report (IOM 2013). This IOM report did not confirm the 100 mmol/day upper level for sodium intake, which was defined in a previous IOM report (IOM 2005), but concluded that "Science was insufficient and inadequate to establish whether reducing sodium intake below 2300 mg/d (100 mmol) either decreases or increases CVD risk in the general population". A later meta-analysis of these population studies found that a sodium intake below 114 mmol/day was associated with increased mortality, as was a sodium intake above 214 mmol/day (Graudal 2014). Increased mortality with high sodium intake has also been shown in another meta-analysis, which, however, did not investigate the effect of a low sodium intake (Strazzulo 2009). This U-shaped relation between sodium intake and mortality has been identified in several individual population studies (O'Donnell 2011; O'Donnell 2014; Pfister 2014; Thomas 2011). The health institutions, however, generally do not accept this evidence from the observational studies (Gunn 2013; Whelton 2012; WHO 2012). In a recent paper, which discusses methodological issues of observational studies, representatives of the American Heart Association state that the association of low sodium intake with increased mortality observed in observational studies may reflect that sick people have a low sodium intake (reverse causality: sick people with a high mortality have a low sodium intake, it is not the low sodium intake, which increases the mortality) (Cobb 2014). This hypothesis is not directly supported by the observational studies, as the outcomes generally are adjusted for confounders such as cardiovascular and renal diseases and diabetes and show that the mortality associated with a low sodium intake is higher in healthy populations than in populations including sick individuals (Graudal 2014; O'Donnell 2014). Table 3 shows a meta-analysis of the risk of all-cause mortality in Study populations within the usual sodium intake range versus a low sodium intake below 114 mmol/day (Graudal 2014) or below 130 mmol/day (O'Donnell 2014). The analysis is confined to include samples of individuals representative of the general populations and all individual study analyses are adjusted for multiple confounders such as cardiovascular disease, hypertension and diabetes. To further reduce the risk of reverse causality, the most healthy subgroup was included in the analysis, when results were given for subgroups, The possibility of reverse causality can never be completely excluded, but as a minimum there is no indication in population studies that sodium intake below 100 mmol/day has beneficial health effects in healthy individuals. In the NHANES I and III studies this was demonstrated by independent groups (Alderman 1998; Cohen 2008; He 1999; Yang 2011).

The BP effect of reduced sodium intake has been related to age. Freedman and Petitti analysed data from Intersalt (Intersalt 1988) and found the paradox that along with the significant association between increase in blood pressure with age and the salt excretion in urine, there was an inverse relationship between estimated BP and salt excretion in urine at age 20. Freedman stated that unless you preferred to conclude that salt should be eaten in high doses by youngsters and in reduced amounts by the elderly, the findings were probably due to uncontrolled confounding, not to variation in salt intake (Freedman 2001). Furthermore, it is now clear that the BP of different age cohorts in a cross-sectional study like Intersalt is not representative of each other, verified by a study showing that recent birth cohorts attained lower BP than did earlier birth cohorts in the period 1887 to 1994 (Goff 2001). According to this study, based on data from more than 50,000 persons, it can be estimated that the median BP is about 15 mmHg lower in a 50-year old person from a recent birth cohort compared with a 50-year old from a birth cohort from the late 19th century. Consequently, there has been a dramatic fall in BP during the 20th century. In this context, the possible mean arterial pressure effect of sodium reduction of -0.3 mmHg in normotensive persons seems negligible. Finally, it has been difficult to maintain a significant sodium reduction in longer-term studies, which should be taken into consideration, when recommending sodium reduction. One reason for this could be that the sodium intake is regulated by neuro-physiological and hormonal mechanisms (Geerling 2008), and therefore difficult to diverge from.

The hypothetical consequences of the present findings are that people with normotension would have no benefit from sodium reduction, but may suffer from harms, because sodium reduction has a negligible effect on BP, but results in significant side effects.

People with hypertension may benefit due to the effect on BP, but may also suffer from harms due to the side effects. This is exactly what was found in the most recent meta-analysis of four population studies (133,000 individuals) in which the authors had access to individual participant data (Mente 2016). The conclusion was "Compared with moderate sodium intake, high sodium intake is associated with an increased risk of cardiovascular events and death in hypertensive populations (no association in normotensive population), while the association of low sodium intake with increased risk of cardiovascular events and death is observed in those with or without hypertension. These data suggest that lowering sodium intake is best targeted at populations with hypertension who consume high sodium diets", a conclusion, which matches perfectly with the results of the present meta-analysis.

AUTHORS' CONCLUSIONS

Implications for practice

The present meta-analysis shows that a low- versus high-sodium diet in white people with normal blood pressure (BP) decreases BP less than 1%. A significant concomitant increase in plasma renin, plasma aldosterone, plasma noradrenalin, and to a lesser degree of plasma adrenaline may contribute to the small effect of sodium reduction on BP. Furthermore, sodium reduction resulted in a significant increase in plasma cholesterol and plasma triglyceride, which expressed in percentage, was numerically larger than the decrease in BP. Due to the relatively small effects and due to the antagonistic nature of the effects (decrease in BP, increase in hormones and lipids), these results do not support that sodium reduction may have net beneficial effects in a population of white people with normal BP.

In white people with elevated BP, sodium reduction decreases BP by about 3.5%, indicating that sodium reduction may be used as a supplementary treatment for hypertension. In Asian and black people the effect of sodium reduction was a little larger than in white people, but at present too few studies have been carried out to conclude different from that above.

Implications for research

The data suggesting that black and Asian populations are more sensitive to sodium reduction than white people requires further studies. In future studies of mixed populations, it is important that the effects on white, black and Asian populations are reported separately. Population studies have shown a U-shaped association between sodium intake and mortality indicating that the beneficial effect of sodium reduction on BP outweigh the harmful effect on hormones and lipids at sodium intake above the usual sodium intake, but that the harms of sodium reduction outweigh the benefits at sodium intake below the usual sodium intake. Long-term randomised controlled trials (RCTs) with mortality and morbidity outcomes would be desirable to confirm or reject these findings. However, such studies may not be practicable. After 185 RCTs and 27 population studies without an obvious signal in favour of sodium reduction below 100 mmol/day, another position could be to accept that the present usual sodium intake may be the optimal intake for the general population.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

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

1000 Parijs 1973

Methods	Op CO
Participants	N 17 (22) Hyp Age 41
Interventions	SR 98 Dur 28
Outcomes	SBP DBP
Notes	LoFo: 5 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement

1000 Parijs 1973 *(Continued)*

Random sequence generation (selection bias)	High risk	Each patient received a number
Allocation concealment (selection bias)	High risk	Those with uneven numbers were instructed to take a low-sodium diet during the first period and a high-sodium diet during the second period and vice versa for those with even numbers
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	High risk	Immediate attrition: 5 participants. 17 completed regular sodium period, 15 completed low sodium period. The outcome measurement was based on the 15 participants, who completed both periods. Total attrition 7 participants, i.e. there was no difference in attrition between the two treatment periods, but the total attrition was significant (32%).
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1001 Mark 1975

Methods	Op CO
Participants	N 6 Hyp Age 28
Interventions	SR 305 Dur 10
Outcomes	SBP DBP Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information

1001 Mark 1975 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1002 Morgan 1978

Methods	SB P
Participants	N 62, M/F:62/0 Hyp Age 60
Interventions	SR 23 Dur 90
Outcomes	SBP DBP
Notes	LoFO: 3 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study

1002 Morgan 1978 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 3/62
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1003 Sullivan 1980

Methods	S CO
Participants	N 27 Norm Age 29
Interventions	SR 146 Dur 4
Outcomes	SBP DBP Aldo Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	High risk	Only the 10 first participants received the high and low salt diets in random order until it was established that the order of administration did not appear to make a difference in the results
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0

1003 Sullivan 1980 *(Continued)*

Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Measurements were mad by 2 observers who were not aware of the participant's dietary state

1004 Sullivan 1980 H

Methods	Op CO
Participants	N 19 Hyp Age27
Interventions	SR153 Dur4
Outcomes	SBP DBP Aldo Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	High risk	Only the 10 first participants received the high- and low-salt diets in random order until it was established that the order of administration did not appear to make a difference in the results
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias)	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1004 Sullivan 1980 H *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Measurements were mad by 2 observers who were not aware of the participant 's dietary state

1005 Rankin 1981

Methods	Op CO
Participants	N 8 (M/F:8/0) Normotension Age 30
Interventions	SR 776 (796-20) Dur 6
Outcomes	MAP, NE
Notes	LoFo: 0

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1006 Skrabal 1981

Methods	Op CO
Participants	N 20 Norm Age 23
Interventions	SR 150 Dur 14
Outcomes	SBP DBP Aldo Renin NA A
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1007 Morgan 1981

Methods	SB P
Participants	N 12

1007 Morgan 1981 *(Continued)*

	Hyp Age 38
Interventions	SR 67 Dur 56
Outcomes	DBP
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	High risk	SBP effect not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1009 Ambrosioni 1982

Methods	SB CO
Participants	N 25 Hyp Age 23
Interventions	SR 60 Dur 42
Outcomes	SBP DBP
Notes	LoFo:1

1009 Ambrosioni 1982 *(Continued)*

	IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 1
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1010 Myers 1982

Methods	Op CO
Participants	N 136 Norm Age 39
Interventions	SR 130 Dur 14
Outcomes	SBP DBP
Notes	Included 182 LoFo: 46 IT: yes (results not shown, but reported to be "similar")

Risk of bias

Bias	Authors' judgement	Support for judgement

1010 Myers 1982 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow-up 46/182
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1011 MacGregor 1982

Methods	DB CO
Participants	N19 Hyp Age 49
Interventions	SR 76 Dur 28
Outcomes	SBP DBP Aldo Renin
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information

1011 MacGregor 1982 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	Double-blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double-blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double-blind study

1012 Beard 1982

Methods	Op P
Participants	N90 Hyp Age48
Interventions	SR124 Dur 84
Outcomes	SBP DBP
Notes	Included 113 LoFo:23 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias)	High risk	Lost to follow up LS: 11/56; US: 12/57

1012 Beard 1982 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1013 Puska 1983

Methods	SB P
Participants	N38 Norm Age40
Interventions	SR90 Dur72
Outcomes	SBP DBP
Notes	LoFo: 4 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Lost to follow up normotensive, LS: 2/19; US: 0/19; Lost to follow up hypertensive, LS: 2/15; US: 0/19
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias)	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1013 Puska 1983 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Low risk	outcome detection blinded

1015 Bulpitt 1984

Methods	Op P
Participants	N 65 (M/F29/36)(B/W/A.0/65/0) Hypertension Age 54.6
Interventions	SR 59 (161-102) Dur 90
Outcomes	SBP, DBP, Chol
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	The low sodium group received dietary advice, the reference group did not
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1016 Silman 1983

Methods	Op P
Participants	N28 Hyp Age55
Interventions	SR 63 Dur 90
Outcomes	SBP DBP
Notes	LoFo: 7 IT: No Weighted average of BP effects obtained ar 1,2,3,6 and 12 months.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up LS: 0/12; US: 7/16
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1017 Sowers 1983

Methods	Op CO
Participants	N 9 (M/F:9/0) Normotension Age 23

1017 Sowers 1983 *(Continued)*

Interventions	SR 154 (196-42) Dur 5
Outcomes	renin, Aldo
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up LS 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1018 Watt 1983

Methods	DB CO
Participants	N18 Hyp Age52
Interventions	SR 56 Dur 28
Outcomes	SBP DBP Renin
Notes	Included 20 LoFo:2

1018 Watt 1983 *(Continued)*

	IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information
Selective reporting (reporting bias)	Low risk	Lost to follow up 2/20
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1019 Cooper 1984

Methods	SB CO
Participants	N59 Norm Age16
Interventions	SR55 Dur 24
Outcomes	SBP DBP
Notes	Included 124(1984+1984b) LoFo: 11 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement

1019 Cooper 1984 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up: 11/24
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1021 Skrabal 1984

Methods	Op CO
Participants	N30 Norm Age23
Interventions	SR137 Dur14
Outcomes	SBP DBP Aldo Renin NA A
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information

1021 Skrabal 1984 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1023 Gillies 1984

Methods	Op CO
Participants	N 24 (M/F:14/10)(B/W/A.0/24/0) Hypertension Age 56.7
Interventions	SR 77 (169-92) Dur 42
Outcomes	SBP, DBP
Notes	LoFo:4. 24 of 28 completed the study. IT:No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias)	Low risk	Lost to follow up: 4/28

1023 Gillies 1984 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1024 Erwteman 1984

Methods	S BP
Participants	N94 (22 blacks) Hyp Age46
Interventions	SR58 Dur28
Outcomes	SBP DBP
Notes	Included 107 LoFo: 13 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 13/107. " No apparent relation between treatment and discontinuing the trial"
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1024 Erwteman 1984 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1025 Koolen 1984

Methods	Op CO
Participants	N20 Hyp Age41
Interventions	SR213 Dur14
Outcomes	SBP DBP Aldo Renin NA
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1025 Koolen 1984 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1026 Koolen 1984(2)

Methods	S CO
Participants	N25 Caucasians Hyp Age41
Interventions	SR 208 Dur 14
Outcomes	NA
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1027 Fagerberg 1984

Methods	Op

1027 Fagerberg 1984 *(Continued)*

	P
Participants	N30 Hyp Age51
Interventions	SR99 Dur63
Outcomes	SBP DBP
Notes	Included 34 LoFo: 4 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Lost to follow up 4/34. Group association unclear
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1028 Maxwell 1984

Methods	Op P
Participants	N30 Hyp Age 46
Interventions	SR161

1028 Maxwell 1984 *(Continued)*

	Dur 84
Outcomes	SBP DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1029 Richards 1984

Methods	SB CO
Participants	N12 Hyp Age36
Interventions	SR100 Dur28
Outcomes	SBP DBP Aldo Renin NA
Notes	Included 16

1029 Richards 1984 *(Continued)*

	LoFo: 4 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 4/16
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1030 Resnick 1985

Methods	Op CO
Participants	N12 Hyp Age
Interventions	SR190 Dur5
Outcomes	SBP DBP Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement

1030 Resnick 1985 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1031 Tuthill 1985

Methods	DB P
Participants	N 191 (M/F:0/191) Normotension Age 17
Interventions	SR 14 (600 mg) Dur 56
Outcomes	SBP, DBP
Notes	LoFo: 13. 191 of 204 completed the study. IT: No

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study

1031 Tuthill 1985 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 13/204. Group association unclear
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1032 Skrabal 1985

Methods	SB CO
Participants	N34 Norm Age23
Interventions	SR144 Dur14
Outcomes	SBP DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1032 Skrabal 1985 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1034 Watt 1985

Methods	DB CO
Participants	N31 Norm Age23
Interventions	SR60 Dur28
Outcomes	SBP DBP
Notes	Included 75 (1985+1985b) LoFo: 9 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Low risk	The statistician randomised and labelled the containers of the tablets without calling on the research team
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 9/75
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias)	Low risk	Double blind study

1034 Watt 1985 *(Continued)*

All outcomes	

1036 Richards 1986

Methods	SB CO
Participants	N 8 males Norm Age36
Interventions	SR181 Dur4
Outcomes	SBP DBP Aldo Renin
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1037 Teow 1986

Methods	Op

1037 Teow 1986 *(Continued)*

	CO
Participants	N9 Norm Age25
Interventions	SR 200 Dur 14
Outcomes	SBP DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1038 Logan 1986

Methods	Op P
Participants	N86 Hyp Age47
Interventions	SR43 Dur180

1038 Logan 1986 *(Continued)*

Outcomes	SBP DBP
Notes	LoFo: ?

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Insufficient information
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1039 ANHMRCDS 1986

Methods	SB P
Participants	N100 Hyp Age53
Interventions	SR70 Dur 84
Outcomes	SBP DBP
Notes	Included 107 LoFo:19 IT: No

Risk of bias

1039 ANHMRCDS 1986 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up LS: 10/52; US: 9/55
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1040 El Ashry 1987

Methods	SB CO
Participants	N13 Norm Age24
Interventions	SR222 Dur14
Outcomes	SBP DBP Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information

1040 El Ashry 1987 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1042 Fuchs 1987

Methods	Op CO
Participants	N6 Norm Age20
Interventions	SR99 Dur9
Outcomes	SBP DBP
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0

1042 Fuchs 1987 *(Continued)*

Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1044 Morgan 1987

Methods	SB P
Participants	N20 Hyp Age58
Interventions	SR57 Dur60
Outcomes	SBP DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1044 Morgan 1987 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1045 Kurtz 1987

Methods	DB CO
Participants	N5 Hyp Age58
Interventions	SR217 Dur7
Outcomes	SBP DBP
Notes	Included 7 LoFo: 2 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 2/7
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1046 Grobbee 1987

Methods	DB CO
Participants	N40 Hyp Age24
Interventions	SR72 (129-57) Dur42
Outcomes	SBP DBP Renin NA A Chol
Notes	Included 42 LoFo: 2 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 2/42
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1047 MacGregor 1987

Methods	DB CO

1047 MacGregor 1987 *(Continued)*

Participants	N15 Hyp Age52
Interventions	SR100 Dur30
Outcomes	SBP DBP
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1048 Lawton 1988

Methods	Op CO
Participants	N13 Norm Age24
Interventions	SR313 Dur6
Outcomes	SBP DBP

1048 Lawton 1988 *(Continued)*

	Renin NA
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1049 Lawton 1988 H

Methods	Op CO
Participants	N9 Hyp Age25
Interventions	SR328 Dur6
Outcomes	SBP DBP Renin NA
Notes	LoFo: 0

Risk of bias

1049 Lawton 1988 H *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1050 Morgan 1988

Methods	SB CO
Participants	N16 Hyp Age63
Interventions	SR50 Dur14
Outcomes	SBP DBP Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information

1050 Morgan 1988 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	outcome detection blinded

1051 Morgan 1988,2

Methods	DB CO
Participants	N 8 Hypertension Age 63
Interventions	SR 67 (135-68) Dur 14
Outcomes	SBP, DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0

1051 Morgan 1988,2 *(Continued)*

Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1052 Shore 1988

Methods	SB CO
Participants	N6 Hyp Age
Interventions	SR 97 Dur5
Outcomes	SBP DBP Aldo Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias)	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1052 Shore 1988 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Low risk	outcome detection blinded

1053 Sudhir 1989

Methods	Op CO
Participants	N 6 (M/F:6/0)(B/W/A.0/6/0) Normotension Age 35
Interventions	SR 134 (163-29) Dur 12
Outcomes	SBP, DBP, renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1054 Hargreaves 1989

Methods	DB CO
Participants	N8 Norm Age23
Interventions	SR106 Dur14
Outcomes	SBP DBP Aldo Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1055 ANHMRCDS 1989

Methods	Op P
Participants	N103 Hyp Age58

1055 ANHMRCDS 1989 *(Continued)*

Interventions	SR63 Dur 48
Outcomes	SBP DBP
Notes	Included 111 LoFo:8 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up LS: 4/54; US: 4/57
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1056 MacGregor 1989

Methods	DB CO
Participants	N20 Hyp Age57
Interventions	SR150 Dur30
Outcomes	SBP DBP Aldo Renin

1056 MacGregor 1989 *(Continued)*

	NA
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1057 Dimsdale 1990 W

Methods	Op CO
Participants	N19 (White) Norm Age34
Interventions	SR183 Dur5
Outcomes	SBP DBP Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement

1057 Dimsdale 1990 W *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1058 Dimsdale 1990 WH

Methods	Op CO
Participants	N17 (White) Hyp Age34
Interventions	SR 198 Dur 5
Outcomes	SBP DBP Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias)	High risk	Open study

1058 Dimsdale 1990 WH *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1059 Dimsdale 1990 B

Methods	Op CO
Participants	N23 (Black) Norm Age34
Interventions	SR178 Dur5
Outcomes	SBP DBP Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1059 Dimsdale 1990 B *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1060 Dimsdale 1990 BH

Methods	Op CO
Participants	N16 (Black) Hyp Age34
Interventions	SR178 Dur5
Outcomes	SBP DBP Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias)	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1060 Dimsdale 1990 BH *(Continued)*

All outcomes

1061 Schmid 1990

Methods	SB CO
Participants	N9 Norm Age32
Interventions	SR190 Dur7
Outcomes	SBP DBP
Notes	Allocation: random numbers LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1062 Schmid 1990 H

Methods	SB

1062 Schmid 1990 H *(Continued)*

	CO
Participants	N9 Hyp Age36
Interventions	SR Dur
Outcomes	SBP DBP
Notes	Allocation: random numbers LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information: "with the help of random numbers"
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1063 HPTRG 1990

Methods	SB P
Participants	N 579 Norm Age40
Interventions	SR23 Dur 1100

1063 HPTRG 1990 *(Continued)*

Outcomes	SBP DBP
Notes	Included 634 LoFo: 65 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up LS: 30/312; US: 35/322
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1064 Bruun 1990

Methods	Op CO
Participants	N10 Norm Age46
Interventions	SR341 Dur4
Outcomes	SBP DBP Aldo Renin
Notes	LoFo: 0

1064 Bruun 1990 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1065 Bruun 1990 H

Methods	Op CO
Participants	N12 Hyp Age47
Interventions	SR331 Dur4
Outcomes	SBP DBP Aldo Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information

1065 Bruun 1990 H *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1066 Sharma 1990

Methods	SB CO
Participants	N15 Norm Age24
Interventions	SR192 (210.7-18.7) Dur 7
Outcomes	SBP DBP Chol HDL LDL TG
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias)	High risk	Open study

1066 Sharma 1990 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1067 Sharma 1990,2

Methods	SB CO
Participants	N 40 (M/F:40/0)(B/W/A.0/40/0) Normotension Age 25
Interventions	SR 214 (239-25) Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 5. 40 of 45 completed the study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1067 Sharma 1990,2 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1068 Friberg 1990

Methods	Op CO
Participants	N10 Norm Age33
Interventions	SR117 Dur 13
Outcomes	SBP DBP Renin NA
Notes	LoFo:4 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 4/10
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1068 Friberg 1990 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1069 Del Rio 1990

Methods	DB CO
Participants	N 15 (B/W/A 0/15/0) Hypertension, Age 49
Interventions	SR 100 (190-90) Dur 14
Outcomes	SBP, DBP, chol, trig
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1070 Parker 1990

Methods	DB P

1070 Parker 1990 *(Continued)*

Participants	N31 Hyp Age50
Interventions	SR73 Dur28
Outcomes	SBP DBP
Notes	1990 + 1990 b Included 63 LoFo: 4 before randomization IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0 after randomization
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1072 Mtabaji 1990

Methods	Op P
Participants	N30 (Black) Norm Age
Interventions	SR272 Dur7

1072 Mtabaji 1990 *(Continued)*

Outcomes	SBP (MBP +1/3MBP) DBP (MBP-1/3MBP)
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1073 Sharma 1991

Methods	SB CO
Participants	N23 Norm Age25
Interventions	SR 246 Dur6
Outcomes	SBP DBP Aldo
Notes	1991 + 1991b included 25 LoFo. 2 IT: No

1073 Sharma 1991 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 2/23
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1074 Howe 1991

Methods	Op CO
Participants	N 100 (M/F:52/48)(B/W/A.0/100/0) Normotension Age 13
Interventions	SR 81 (179-98) Dur 28
Outcomes	SBP, DBP
Notes	LoFo:10. 90 of 100 completed the study. IT:No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information

1074 Howe 1991 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 10/100
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1075 Mascioli 1991

Methods	DB CO
Participants	N 48 (M/F:38/10) Norm Age52
Interventions	SR70 Dur28
Outcomes	SBP DBP
Notes	included 50 LoFo. 2 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias)	Low risk	Lost to follow up 2/50

1075 Mascioli 1991 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1076 Carney 1991

Methods	DB CO
Participants	N11 Hyp Age54
Interventions	SR102 Dur 42
Outcomes	SBP DBP Renin
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias)	Low risk	Double blind study

1076 Carney 1991 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1077 Singer 1991

Methods	DB CO	
Participants	N21(6 blacks) Hyp Age54	
Interventions	SR91 Dur30	
Outcomes	SBP DBP Aldo Renin	
Notes	LoFo: 0	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1078 Egan 1991

Methods	DB CO
Participants	N27 Hyp Age39
Interventions	SR194 (214-21) Dur7
Outcomes	SBP (MBP+1/3MBP) DBP (MBP-1/3MBP) Renin NA l Chol LDL
Notes	Eandomisation schedule LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Low risk	
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0/27
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1079 Gow 1992

Methods	Op

1079 Gow 1992 *(Continued)*

	CO
Participants	N 9 Norm Age not given
Interventions	SR 94 (111-17) Dur7
Outcomes	SBP DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1080 Huggins 1992

Methods	DB CO
Participants	N 9 (M/F:7/2)(B/W/A.0/9/0) Normotension Age 25
Interventions	SR 97 (170-73) Dur 14

1080 Huggins 1992 *(Continued)*

Outcomes	SBP, DBP, renin, aldo
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1081 TOHP I 1992

Methods	SB P
Participants	N744 (131 blacks) Norm Age43
Interventions	SR 47 Dur 550
Outcomes	SBP DBP
Notes	LoFo: 0 IT: yes

Risk of bias

Bias	Authors' judgement	Support for judgement

1081 TOHP I 1992 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Low risk	Randomization assignments were received from the coordinating center by telephone or sealed opaque envelopes were used to convey the treatment assignment.
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1082 Cobiac 1992

Methods	DB P
Participants	N52 Norm Age66
Interventions	SR75 Dur28
Outcomes	SBP DBP
Notes	Included 114(1992+1992b) LoFo: 7 before randomization, 1 after IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information

1082 Cobiac 1992 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 1/107
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1084 Benetos 1992

Methods	DB CO
Participants	N20 Hyp Age42
Interventions	SR78 Dur 28
Outcomes	SBP DBP Aldo Renin NA A
Notes	Included 22 LoFo: 2 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias)	Low risk	Double blind study

1084 Benetos 1992 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 2/22
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1085 Sciarrone 1992

Methods	DB P
Participants	N91 Hyp Age54
Interventions	SR82 Dur 56
Outcomes	SBP DBP Chol HDL LDL TG
Notes	95 included LoFO: 4 IT: No Lipid values were estimated on the basis of initial values(table 2) and changes (figure 4)

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study

1085 Sciarrone 1992 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 4/95. Group association unclear
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1088 Ruppert 1993

Methods	SB CO
Participants	N30 Norm Age46 salt sensitive
Interventions	SR270 Dur7
Outcomes	SBP DBP Aldo Renin NA
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0

1088 Ruppert 1993 *(Continued)*

Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1091 Burnier 1993

Methods	Op CO
Participants	N16 Norm Age29
Interventions	SR186 Dur6
Outcomes	SBP DBP Aldo Renin
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias)	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1091 Burnier 1993 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1093 Sharma 1993

Methods	SB CO	
Participants	N16 Norm Age24	
Interventions	SR 224 Dur7	
Outcomes	SBP DBP	
Notes	LoFo: 0	

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1094 Sharma 1993,2

Methods	Op CO
Participants	N 15 (M/F:15/0)(B/W/A.0/15/0) Normotension Age 25
Interventions	SR 198 (219-21) Dur 6
Outcomes	Renin, aldo, NE
Notes	LoFo: 5. 15 of 20 completed the study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Randomisation according to a Latin-Square design
Blinding (performance bias and detection bias) All outcomes	High risk	Open
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 5/20
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1095 Fliser 1993

Methods	SB CO
Participants	N8 Norm Age25 +Doxazosin
Interventions	SR190 (211-21)

1095 Fliser 1993 *(Continued)*

	Dur8
Outcomes	SBP (MBP+1/3MBP) DBP (MBP-1/3MBP) NA Chol HDL LDL TG
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1097 Nestel 1993

Methods	DB P
Participants	N36 Norm Age66
Interventions	SR56 Dur42
Outcomes	SBP DBP

1097 Nestel 1993 *(Continued)*

Notes	Included 70 (1993+1993b) LoFo: 4 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 4/70. Group association unclear
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1099 Donovan 1993

Methods	SB CO
Participants	N8 Norm Age36
Interventions	SR152 Dur5
Outcomes	SBP DBP Aldo Renin
Notes	LoFo. 0

Risk of bias

1099 Donovan 1993 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1100 Fotherby 1993

Methods	DB CO
Participants	N17 Hyp Age73
Interventions	SR79 Dur 35
Outcomes	SBP DBP Aldo Renin
Notes	Included 18 LoFo. 1 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information

1100 Fotherby 1993 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 1/18
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1101 Redon-Mas 1993

Methods	Op P
Participants	N418 Hyp Age55
Interventions	SR104 Dur28
Outcomes	SBP DBP
Notes	574 included LoFo: 156 IT: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study

1101 Redon-Mas 1993 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up LS: 57/287; US: 99/287
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1102 Ruilope 1993

Methods	DB P
Participants	N19 Hyp Age
Interventions	SR69 Dur21
Outcomes	SBP DBP
Notes	LoFo. 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1102 Ruilope 1993 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1103 Del Rio 1993

Methods	DB CO
Participants	N30 Hyp Age49
Interventions	SR151 (198-47) Dur 14
Outcomes	SBP DBP Renin Chol HDL TG
Notes	Included 47 LoFo. 17 IT: no

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 17/47
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias)	Low risk	Double blind study

1103 Del Rio 1993 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1104 Overlack 1993

Methods	SB CO
Participants	N30 salt sensitive Norm Age46
Interventions	SR270 Dur7
Outcomes	Aldo Renin NA
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1107 MacFadyen 1994

Methods	DB CO
Participants	N 12 (M/F:12/0)(B/W/A.0/12/0) Normotension Age 24
Interventions	SR 40 (165-115) Dur 4
Outcomes	SBP, DBP, renin
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Low risk	Independently prepared schedule by Department of Pharmacy
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1108 Buckley 1994

Methods	SB CO
Participants	N12 (3 blacks) Hyp Age49
Interventions	SR 296

1108 Buckley 1994 *(Continued)*

	Dur 5
Outcomes	SBP DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1109 Zoccali 1994

Methods	SB CO
Participants	N 15 Hyp Age 45
Interventions	SR 163 Dur 7
Outcomes	SBP DBP Aldo Renin
Notes	LoFo: 0

1109 Zoccali 1994 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1110 Jula 1994

Methods	Op P
Participants	N76 Hyp Age44
Interventions	SR57 Dur365
Outcomes	SBP DBP Aldo Renin NA A
Notes	Included 91 LoFo: 15 IT: No

Risk of bias

1110 Jula 1994 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1111 Howe 1994

Methods	DB P
Participants	N 56 (M/F:31/25)(B/W/A.0/56/0) Hypertension Age 55
Interventions	SR 80 (158-78) Dur 42
Outcomes	SBP, DBP, aldo
Notes	LoFo:5. 56 of 61 completed the study. IT:No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias)	Low risk	Double blind study

1111 Howe 1994 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 5/61. Group association unclear
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1112 Iwaoka 1994

Methods	Op CO
Participants	N 31 (M/F:17/14)(B/W/A.0/0/31) Hypertension Age 48
Interventions	SR 266 (298-32) Dur 7
Outcomes	SBP, DBP
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1112 Iwaoka 1994 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1113 Miller 1995

Methods	DB CO
Participants	N 36 (M/F:36/0)(B/W/A.0/36/0) Normotension Age 23
Interventions	SR 58 (191-133) Dur 14
Outcomes	SBP, DBP, NE
Notes	LoFo: 4. 36 of 40 completed the study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 4/40
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1114 Fliser 1995

Methods	Op CO
Participants	N 14 (M/F:14/0)(B/W/A.0/14/0) Normotension Age 26
Interventions	SR 180 (203-23) Dur 7
Outcomes	MAP, renin, NE
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1115 Doig 1995

Methods	DB CO
Participants	N 81(M/F 81/0 (B/W/A 0/81/0) Normotension, Age 25
Interventions	SR 112 (130-18)

1115 Doig 1995 *(Continued)*

	Dur 4
Outcomes	SBP, DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1116 Stein 1995

Methods	Op CO
Participants	N 7 (M/F:7/0)(B/W/A.0/7/0) Normotension Age 33.7
Interventions	SR 183 (201-18) Dur 5
Outcomes	SBP, DBP, renin, NE
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement

1116 Stein 1995 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1117 Arrol 1995

Methods	Op P
Participants	N 181 (M/F:95/86)(B/W/A.0/181/0) Hypertension Age 55
Interventions	SR 16 (122-106) Dur 182
Outcomes	SBP, DBP
Notes	LoFo: 27. 181 of 208 completed study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study

1117 Arrol 1995 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 27/208. group association unclear
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1118 Draaijer 1995

Methods	Op CO
Participants	N 10 (M/F:10/0)(B/W/A.0/10/0) Hypertension Age 41
Interventions	SR 131 (283-24) Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias)	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1118 Draaijer 1995 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1119 Overlack 1995

Methods	DB CO
Participants	N11 Hyp Age61
Interventions	SR240 Dur7
Outcomes	SBP (MBP+1/3MBP) DBP (MBP-1/3MBP) Aldo Renin NA
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1122 Dubbert 1995

Methods	P SB
Participants	N 122 (B/W/A.67/55/0) Hypertension Age 62
Interventions	SR 45 (187-142) Dur 90
Outcomes	SBP, DBP
Notes	LoFo: 36. 122 of 158 completed the study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	random number table, randomisation procedure stratified by race
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up LS:24/106; US: 12/52
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1124 Weir 1995

Methods	SB CO
Participants	N11 (8 black) Hyp Age60 sodium sensitive

1124 Weir 1995 *(Continued)*

Interventions	SR146 Dur14
Outcomes	SBP DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1125 Grey 1996

Methods	DB CO
Participants	N34 Norm Age23
Interventions	SR133 (185-52) Dur7
Outcomes	SBP DBP Chol HDL LDL

1125 Grey 1996 *(Continued)*

	TG
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1126 Feldman 1996

Methods	DB CO
Participants	N5 Norm Age27
Interventions	SR176 Dur7
Outcomes	SBP (MBP+1/3MBP) DBP (MBP-1/3MBP) NA A Chol
Notes	LoFo: 0

Risk of bias

1126 Feldman 1996 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1127 Feldman 1996 H

Methods	DB CO
Participants	N8 Hyp Age27
Interventions	SR178 Dur7
Outcomes	SBP (MBP+1/3MBP) DBP (MBP-1/3MBP) NA A Chol
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information

1127 Feldman 1996 H *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1128 Schorr 1996

Methods	DB CO
Participants	N16 Norm Age 64
Interventions	SR 74 (175.2-104.8) Dur28
Outcomes	SBP DBP Aldo Renin Chol HDL LDL TG
Notes	Included 21 LoFo: 5 IT: 0

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information

1128 Schorr 1996 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 5/21
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1129 Bellini 1996

Methods	DB CO
Participants	N 43 (M/F:43/0)(B/W/A.0/43/0) Hypertension Age 46
Interventions	SR 121 (233-112) Dur 14
Outcomes	SBP, DBP, renin, aldo, NE
Notes	LoFo: 12. 43 of 55 completed study. IT: No

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias)	High risk	Lost to follow up 12/55

1129 Bellini 1996 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1130 Inoue 1996

Methods	DB CO
Participants	N 14 (M/F:8/6)(B/W/A.4/7/3) Hypertension Age 46
Interventions	SR 293 (329-36) Dur 7
Outcomes	SBP, DBP
Notes	LoFo:0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study

1130 Inoue 1996 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1131 Ferri 1996

Methods	DB CO
Participants	N61 Hyp Age47
Interventions	SR264 Dur14
Outcomes	SBP DBP Aldo Renin
Notes	79 were included. 65 were randomised. LoFo: 4 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 4/65
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1132 Ishimitsu 1996 A

Methods	Op CO
Participants	N HT: 23 (M/F:11/12) NT 7 (M/F:3/4)(B/W/A.0/0/30) Hypertension and normotension Age 54
Interventions	SR 194 (217-23) Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1133 Ishimitsu 1996 AH

Methods	Op CO
Participants	N HT: 23 (M/F:11/12) NT 7 (M/F:3/4)(B/W/A.0/0/30) Hypertension and normotension Age 54
Interventions	SR 194 (217-23)

1133 Ishimitsu 1996 AH *(Continued)*

	Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1134 Cappuccio 1997

Methods	DB CO
Participants	N47 Hyp Age67
Interventions	SR83 Dur 30
Outcomes	SBP DBP
Notes	Included 52 randomised 48 LoFo: 1 IT: No

1134 Cappuccio 1997 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 1
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1135 TOHP II 1997

Methods	SB P
Participants	N1190 (203 blacks) High norm Age 42
Interventions	SR40 Dur 1100
Outcomes	SBP DBP
Notes	LoFo:161 IT: yes

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information

1135 TOHP II 1997 *(Continued)*

Allocation concealment (selection bias)	Low risk	Randomization was performed by telephone contact with the TOHP coordinating center or by opening a sealed opaque envelope
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up LS: 79/596; US: 82/594
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1136 van Buul 1997

Methods	Op CO
Participants	N 232 (M/F:0/232)(B/W/A.0/232/0) Normotension Age 28
Interventions	SR 65 (140-75(week 28)) Dur 196
Outcomes	SBP, DBP
Notes	LoFo: 28. 242 of 270 completed the study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Low risk	Randomisation by a closed envelope system
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias)	Low risk	Lost to follow up 28/270

1136 van Buul 1997 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1137 Schorr 1997

Methods	SB CO
Participants	N27 Norm Age25 sodium sensitive
Interventions	SR208 Dur7
Outcomes	SBP (MBP+1/3MBP) DBP (MBP-1/3MBP)
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias)	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study

1137 Schorr 1997 *(Continued)*
All outcomes

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1138 McCarron 1997

Methods	DB CO
Participants	N99 (24 blacks) Hyp Age52
Interventions	SR 55.4 (175.9-120.5) Dur28
Outcomes	SBP DBP Chol HDL LDL TG
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1139 Meland 1997

Methods	DB CO
Participants	N 16 (M/F:13/3)(B/W/A.0/16/0) Hypertension Age 50
Interventions	SR 66 (191-125) Dur 56
Outcomes	SBP, DBP, chol, HDL
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1140 Fotherby 1997

Methods	DB CO
Participants	N 17 (M/F:4/13)(B/W/A.0/17/0) Hypertension Age 73
Interventions	SR 79 (174-95)

1140 Fotherby 1997 *(Continued)*

	Dur 35
Outcomes	Chol, HDL, LDL, Trig
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1141 Ferri 1998

Methods	DB CO
Participants	N, HT: 39; NT 8 (B/W/A.0/47/0) Hypertension and normotension Age 45
Interventions	SR 170 (200-30) Dur 14
Outcomes	Chol, HDL, LDL, trig
Notes	30/76 were eliminated/lost before randomization. 39 of 46 randomised hypertensives + 8 controls completed the study.

Risk of bias

1141 Ferri 1998 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	Lost to follow up 7/46 HT
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1142 Knuist 1998

Methods	Op P
Participants	N 361 (80% Caucasian) Pregnant women, Normotension Age 27.5
Interventions	SR 40 (124-84) Dur 35 (mean duration)
Outcomes	DBP
Notes	LoFo: 67. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Low risk	Block randomisation. Treatment allocation in opaque sealed envelopes.
Blinding (performance bias and detection bias)	High risk	Open study

1142 Knuist 1998 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up LS: 35/184; US: 32/177
Selective reporting (reporting bias)	High risk	SBP effect not reported
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1143 Bech 1998

Methods	Op CO
Participants	N 12 (M/F:6/6)(B/W/A.0/12/0) Normotension Age 23.8
Interventions	SR 235 (273-38) Dur 5
Outcomes	MAP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Unclear risk	Insufficient information

1143 Bech 1998 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1144 Foo 1998

Methods	DB CO
Participants	N 18, (8 males, 10 females) Normotensive Mean age 51
Interventions	SR 149 (227-78) Dur 6
Outcomes	SBP DBP Renin Aldosterone
Notes	LoFo: 0 SDs estimated on the basis of p-values

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study

1144 Foo 1998 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1145 Wing 1998

Methods	DB CO
Participants	N17 Hyp Age61
Interventions	SR59 Dur42
Outcomes	SBP DBP
Notes	39 included 19 randomised LoFo: 2 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 2/19
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1146 Herlitz 1998

Methods	DB CO
Participants	N 6 (M/F 6/0)(B/W/A 0/6/0) treated hypertension (from150/106 to 124/82) Age 46
Interventions	SR 98 (325-227) Dur 6
Outcomes	SBP DBP Renin
Notes	Included 8 LoFO: 2 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 2/8
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1147 Feldman 1999

Methods	Op CO
Participants	N 8 (M/F:8/0)(B/W/A.0/8/0) Normotension

1147 Feldman 1999 *(Continued)*

	Age 33
Interventions	SR 159 (207-48) Dur 7
Outcomes	SBP, DBP, chol, NE
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1148 Damasceno 1999

Methods	DB CO
Participants	N 39 (19HT and 20NT) (M/F:19/20)(B/W/A 39/0/0) Hypertension and normotension Age HT 43; NT 38
Interventions	SR HT: 81 (114-33); NT: 180 (210-30) Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 0

1148 Damasceno 1999 *(Continued)*

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1149 Davrath 1999

Methods	SB CO
Participants	N 8 Norm Age 25
Interventions	SR 95 Dur 5
Outcomes	SBP DBP Renin NA A
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement

1149 Davrath 1999 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1150 Schorr 1999

Methods	SB CO
Participants	N 187 (M/F:187/0)(B/W/A.0/187/0) Normotension Age 25
Interventions	SR 206 (225-19) Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 13. 187 of 200 completed study. IT: No.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study

1150 Schorr 1999 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 13/200
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1151 Uzu 1999

Methods	SB CO
Participants	N70 (Japanese) Hyp Age50
Interventions	SR173 (204-31) Dur7
Outcomes	SBP DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1151 Uzu 1999 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1152 Chiolero 2000

Methods	Op CO
Participants	N Hyp: 38 (M/F:21/17); Norm: 12 (M/F:6/6) (B/W/A.0/50/0) Hypertension and normotension Age 43 and 40
Interventions	SR 183 (255-72) and 201 (265-64) Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 5. 38 of 43 and 12 of 12 completed study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 5/43 (Hyp) and 0/12 (Norm)
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1153 Bruun 2000

Methods	Op CO
Participants	N 42 (M/F:34/8)(B/W/A.0/42/0) Normotension Age 26
Interventions	SR 237 (273-36) Dur 4
Outcomes	SBP, DBP, renin, aldo, NE, E, chol, HDL, LDL, Trig
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1154 Burnier 2000

Methods	Op CO
Participants	N 15 (M/F:15/0)(B/W/A.0/15/0) Hypertension and normotension Age 22.7
Interventions	SR 131 (144-13)

1154 Burnier 2000 *(Continued)*

	Dur 7
Outcomes	SBP, DBP, renin, aldo, NE, E
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1155 Heer 2000

Methods	Op CO
Participants	N 32 (M/F:32/0)(B/W/A.0/32/0) Normotension Age 25
Interventions	SR139 (226-87) Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement

1155 Heer 2000 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1156 Barba 2000

Methods	DB CO
Participants	N 7 (M/F:7/0)(B/W/A.0/7/0) Normotension Age 32
Interventions	SR 154 (177-23) Dur 7
Outcomes	MAP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study

1156 Barba 2000 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1157 Boero 2000

Methods	Op CO
Participants	N 13 (M/F:10/3)(B/W/A.0/13/0) Hypertension Age 51
Interventions	SR 209 (270-61) Dur 14
Outcomes	SBP, DBP, Chol, HDL, LDL, Trig,
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias)	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study

1157 Boero 2000 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information

1158 Suzuki 2000

Methods	Op CO	
Participants	N 20 (M/F:9/11)(B/W/A.0/0/20) Hypertension Age 59	
Interventions	SR 116 (167-51) Dur 7	
Outcomes	nocturnal MAP, NE and E	
Notes	LoFo:0	

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1159 Ames 2001

Methods	SB CO
Participants	13 (M/F: 6/7) Hyp Age 60
Interventions	SR 133 (265-132) Dur 28
Outcomes	SBP DBP NA A TG: Chol: HDL: LDL:
Notes	21 patients included 8 diabetes patients excluded LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Single blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1160 DASH 2001 W

Methods	DB

1160 DASH 2001 W *(Continued)*

	CO
Participants	N54 Norm Non-black Age 48
Interventions	SR55 Dur30
Outcomes	SBP DBP not mentioned, see DASH 2
Notes	LoFo: 5% IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 5%
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The personnel involved in the collection of the outcome data were unaware of participants diet assignment

1161 DASH 2001 WH

Methods	DB CO
Participants	N37 Hyp Non-black Age 48

1161 DASH 2001 WH *(Continued)*

Interventions	SR 55 Dur 30
Outcomes	SBP DBP not mentioned, see DASH 2b
Notes	LoFo: 5% IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 5%
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The personnel involved in the collection of the outcome data were unaware of participants diet assignment

1162 DASH 2001 B

Methods	DB CO
Participants	N68 Norm Black Age 48
Interventions	SR55 Dur30
Outcomes	SBP DBP not mentioned, see DASH 2c
Notes	LoFo: 5%

1162 DASH 2001 B *(Continued)*

	IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 5%
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The personnel involved in the collection of the outcome data were unaware of participants diet assignment

1163 DASH 2001 BH

Methods	DB CO
Participants	N46 Hyp Black Age 48
Interventions	SR 55 Dur 30
Outcomes	SBP DBP not mentioned, see DASH 2d
Notes	LoFo: 5% IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement

1163 DASH 2001 BH *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 5%
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	The personnel involved in the collection of the outcome data were unaware of participants diet assignment

1168 Cuzzola 2001

Methods	DB CO
Participants	N 19 Hyp Age 47
Interventions	SR 161 Dur: 14
Outcomes	SBP DBP Aldo Renin
Notes	Data available in patients in upper tertile of sodium excretion (19 of 55 patients)

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information

1168 Cuzzola 2001 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	High risk	Data available in patients in upper tertile of sodium excretion (19 of 55 patients)
Selective reporting (reporting bias)	High risk	Only BP data for the upper sodium reduction tertile was reported
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1169 Seals 2001

Methods	Op P
Participants	N 35 (M/F:0/35)(B/W/A.0/34/1) Hypertension Age 64
Interventions	SR 46 (132-86) Dur 90
Outcomes	SBP, DBP, Chol, HDL, LDL, Trig
Notes	LoFo: 4. 35 of 39 completed the study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up LS: 1/18; US: 3/21

1169 Seals 2001 *(Continued)*

Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1170 TONE 2001 W

Methods	SB P
Participants	N 471 (non-blacks) Hyp Age 66
Interventions	SR 40 DUR: 105
Outcomes	SBP DBP
Notes	2001 + 2001b included 681 (LS: 340; US: 341) Attended last visit: LS 310; US: 314 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 57/681. Group association unclear
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1170 TONE 2001 W *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1171 TONE 2001 B

Methods	SB P
Participants	N 142 (blacks) Hyp Age 66
Interventions	SR 40 DUR: 105
Outcomes	SBP DBP
Notes	2001 + 2001b included 681 (LS: 340; US: 341) Attended last visit: LS 310; US: 314 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 57/681. Group association unclear
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1171 TONE 2001 B *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1172 Johnson 2001

Methods	DB CO
Participants	N 40 Hypertension Age 69
Interventions	SR 73 (185-112) Dur 14
Outcomes	SBP, DBP
Notes	LoFo:6; 40 of 46 completed the study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Sequenced treatments in Latin square design
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 6/46
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1173 Manunta 2001

Methods	SB

1173 Manunta 2001 *(Continued)*

	CO
Participants	N20 (M/F: 16/4) Hyp Age 48
Interventions	SR 110 Dur 14
Outcomes	Renin Aldosteron
Notes	138 included in acute study. 20 with SR> 100 mmol included in 14 day study. LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1174 Kleij 2002

Methods	Op CO
Participants	N 27 (M/F:20/7)(B/W/A.0/27/0) Norm Age 24.8
Interventions	SR 186 (236-50) Dur 7

1174 Kleij 2002 *(Continued)*

Outcomes	MAP Ren, Aldo
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1175 Kerstens 2003

Methods	Op CO
Participants	N 28 (M/F:21/7)(B/W/A.0/28/0) Norm Age 24
Interventions	SR 202 (248-42) Dur 7
Outcomes	MAP Ren, Aldo
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement

1175 Kerstens 2003 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1176 Dishy 2003

Methods	Op CO
Participants	N 25 (2 blacks, 23 whites) Norm Mean age 34 (18-50)
Interventions	SR 300 (321-21) Dur 6
Outcomes	SBP DBP Renin A
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias)	High risk	Open study

1176 Dishy 2003 *(Continued)*
All outcomes

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1177 Nowson 2003

Methods	Op CO
Participants	N 108 (M/F:44/64/20 dropouts)(B/W/A.0/108/0) normotension Age 47
Interventions	SR 90 (140-50) Dur 28
Outcomes	SBP, DBP, renin
Notes	LoFo: 20. 108 completed study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 20/128
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1177 Nowson 2003 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1178 Perry 2003

Methods	Op CO
Participants	N 15 (M/F:15/0)(B/W/A.0/15/0) Normotension Age 26
Interventions	SR 105 (175-70) Dur 5
Outcomes	SBP, DBP, renin, aldo, NE, Chol, trig
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1179 Nakamura 2003 A

Methods	DB P
Participants	N 65 (M/F:41/24)(B/W/A.0/0/65) Hypertension and normotension Age 46.6
Interventions	SR 20 (1.4g) Dur 42
Outcomes	SBP, DBP,
Notes	LoFo 1

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up LS: 1/33; US: 0/32
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1180 Palacios 2004

Methods	Op CO
Participants	N 40 (M/F:0/23/17 dropouts) (B/W/A.15/8/0) Normotension Age 13
Interventions	SR 86 (120-34)

1180 Palacios 2004 *(Continued)*

	Dur 21
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 17. 23 completed study

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 17/40
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1181 Beeks 2004

Methods	OP CO
Participants	N 117 (M/F:67/50)(B/W/A.0/117/0) Hyp Age 54
Interventions	SR 99 (171-72) Dur 7
Outcomes	SBP DBP Aldo
Notes	LoFo: 0

Risk of bias

1181 Beeks 2004 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1182 Berge-Landry 2004

Methods	Op CO
Participants	N 48 (M/F:38/10)(B/W/A.12/34/2) Hyp Age 51
Interventions	SR 285 (309-24) Dur 28
Outcomes	SBP DBP Cho Trig
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information

1182 Berge-Landry 2004 *(Continued)*

Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1183 Gates 2004

Methods	DB CO
Participants	N 12 (M/F:6/6)(B/W/A.0/12/0) Hyper Age 64
Interventions	SR 95 (155-60) Dur 28
Outcomes	SBP DBP Chol, HDL, LDL, Trig, Renin, NE, E
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0

1183 Gates 2004 *(Continued)*

Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1184 Harsha 2004

Methods	DB CO
Participants	N 193 (M/F:89/104)(B/W/A.57/136/0) Mixed Hyper/Norm Age 49
Interventions	SR 77 (141-64) Dur 30
Outcomes	Chol, HDL, LDL, Trig, Renin, NE, E
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias)	Low risk	Double blind study

1184 Harsha 2004 *(Continued)*

All outcomes

1185 Zanchi 2004

Methods	DB CO
Participants	N 10 (M/F:10/0)(B/W/A.0/10/0) Normotension Age 25
Interventions	SR 250 (270-20) Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1186 Forrester 2005 N

Methods	Op CO
Participants	58 Nigerians (M/F: 34/24)

1186 Forrester 2005 N *(Continued)*

	Norm (114.6/72.9) Mean age 46.6 (25-55)
Interventions	SR 72.2 Dur 21
Outcomes	SBP DBP
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Block randomisation
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1187 Forrester 2005 J

Methods	Op CO
Participants	56 Jamaicans (M/F: 34/22) Norm (125.9/76.3) Mean age 40.8 (25-55)
Interventions	SR 78.8 Dur 21
Outcomes	SBP DBP

1187 Forrester 2005 J *(Continued)*

Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Block randomisation
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1188 Swift 2005

Methods	DB CO
Participants	N 40 (M/F:17/23)(B/W/A 40/0/0) Hypertension Age 50
Interventions	SR 78 (167-89) Dur 28
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 7. 40 of 47 completed study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information

1188 Swift 2005 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 7/47
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1189 Damgaard 2006

Methods	Op CO
Participants	N 14 (M/F:14/0)(B/W/A.0/14/0) Norm Age 57
Interventions	SR 129 (188-59) Dur 7
Outcomes	SBP DBP NE and E
Notes	LoFo: 2 excluded because of side effects

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study

1189 Damgaard 2006 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 2/14
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1190 Takahashi 2006

Methods	Op CO
Participants	N 448 (M/F:145/303)(B/W/A.0/0/448) Hypertension (107) and normotension (341) Age 56.4
Interventions	SR 38 (237-199) Dur 365
Outcomes	SBP, DBP
Notes	LoFo: 102. 448 of 550 completed study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomisation: computer generated random number
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 102/550
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias)	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1190 Takahashi 2006 *(Continued)*

All outcomes		
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1191 Melander 2007

Methods	DB CO
Participants	N 39 (M/F: 20/19) Mixed hypertensive and normotensive (144/90.6) Age 53
Interventions	SR 89 (140-51) Dur 28
Outcomes	SBP DBP renin
Notes	LoFo: 7. 39 completed. IT: No Diet + salt capsules/placebo

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 7/46
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1192 Townsend 2007

Methods	Op CO
Participants	N 20 (M/F:12/8)(B/W/A.10/9/1) Norm Age 30
Interventions	SR 171 (194-23) Dur 6
Outcomes	SBP DBP Aldo Renin
Notes	Randomized 21. LoFo: 3 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Prespecified randomised blocked table
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 3/21
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1193 Dengel 2007

Methods	DB CO
Participants	N 28, 10 males, 18 females, 5 blacks, 23 whites

1193 Dengel 2007 *(Continued)*

	Hypertension Mean age 63
Interventions	SR 155 (191-36) Dur 8
Outcomes	SBP -10 DBP -4 Renin 1.64 ng/s Aldo 334.2
Notes	LoFo: 0 Blood pressure effects estimated from figure 1. The effects of two genotype groups were added to one group and calculated as simple means.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1194 Tzemos 2008

Methods	DB CO
Participants	N 16 (M/F:16/0)(B/W/A.0/16/0) Normotension Age 27
Interventions	SR 149 (225-76) Dur 5

1194 Tzemos 2008 *(Continued)*

Outcomes	SBP, DBP, renin, aldo, chol, HDL, LDL, Trig,
Notes	LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1195 Jessani 2008

Methods	Op CO
Participants	N 184 (M/F:87/97)(B/W/A.0/184/0) Normotension Age 50
Interventions	SR 81 (138-57) Dur 7
Outcomes	SBP, DBP
Notes	LoFo:16; 184 of 200 completed the study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement

1195 Jessani 2008 *(Continued)*

Random sequence generation (selection bias)	Low risk	Randomisation by computer generated numbers
Allocation concealment (selection bias)	Low risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 16/200
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1196 Paulsen 2009

Methods	DB CO
Participants	N 22 (M/F:12/10)(B/W/A.0/22/0) Normotension Age 47
Interventions	SR 47 (357-310) Dur 4
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 5. 22 of 27 completed study. IT: No.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study

1196 Paulsen 2009 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 5/27
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1197 Dickinson 2009

Methods	Op CO
Participants	N 29 (M/F: 7/22) Normotension (116/73) Mean age 63
Interventions	SR 92 (156-64) Dur 14
Outcomes	SBP DBP
Notes	32 included. LoFo: 3 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	computer generated
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 3/32
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1197 Dickinson 2009 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1198 He 2009

Methods	DB CO
Participants	Whites: 77; Blacks: 75; Asians: 35 Hypertension (Baseline BP 147/91) Mean Age 50
Interventions	SR 55 (165-110) Dur 42
Outcomes	SBP DBP Renin Aldosterone
Notes	LoFO: W/B/A: 6/6/6 IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated, ethnic stratification
Allocation concealment (selection bias)	Low risk	Tablets supplied by independent company
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 18/187
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias)	Low risk	Double blind study

1198 He 2009 *(Continued)*
All outcomes

1199 Meland 2009

Methods	Op P
Participants	N 46 (M/F:34/12)(B/W/A.0/46/0) Hypertension Age 56
Interventions	SR 43 (126-83) Dur 56
Outcomes	SBP, DBP, Aldo, Chol, Trig
Notes	LoFo: 0. 71 tested, 46 included.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0/46
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1200 Pimenta 2009

Methods	Op CO

1200 Pimenta 2009 *(Continued)*

Participants	N 12 (M/F:4/8)(B/W/A.6/6) Hypertension Age 55.5
Interventions	SR 206 (252-46) Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	LoFo: 1. 12 of 13 completed study. IT: No

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 1/13
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1201 Nowson 2009

Methods	Op P
Participants	N 111 women 59 normotensives and 35 hypertensives completed Mean age 59
Interventions	SR 42 (108-66) Dur 98
Outcomes	SBP DBP

1201 Nowson 2009 *(Continued)*

Notes	LoFo: 16 IT: No. Two different diets were compared and there was other differences between the diets than sodium intake. These differences were assumed not to influence blood pressure.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information. Randomisation stratified by BMI
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up LS: 7/53; US: 9/58
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1202 Weir 2010

Methods	CO, SB
Participants	N 132 (M/F: 73/59, W/B/A: 115/15/2) Hypertension Mean age: 51.5
Interventions	SR 123 (208-85) 28 days
Outcomes	SBP DBP
Notes	LoFo 17

Risk of bias

Bias	Authors' judgement	Support for judgement

1202 Weir 2010 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Single blind
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 17/132
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1203 Starmans-Kool 2011

Methods	CO DB
Participants	10 males Normotension Mean age 32
Interventions	SR 97 (191-94) 14 days
Outcomes	SBP DBP
Notes	LoFo 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information

1203 Starmans-Kool 2011 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1204 Carey 2012

Methods	Op CO
Participants	N 185 (M/F:72/113)(B/W/A.0/183/0) Norm Age 47
Interventions	SR 204 (188-59) Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	No report of excluded participants. LoFo of those reported 0.

Risk of bias

Bias	**Authors' judgement**	**Support for judgement**
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias)	Unclear risk	No report of screening of participants. LoFo of those reported 0.

1204 Carey 2012 *(Continued)*
All outcomes

Selective reporting (reporting bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1205 Carey 2012 Hyperpath

Methods	Op CO
Participants	N 211 (M/F:129/82)(B/W/A.Mixed) Hypertension Age 49.2
Interventions	SR 211 Dur 7
Outcomes	SBP, DBP, renin, aldo
Notes	No report of excluded participants. LoFo of those reported 0.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No report of excluded participants. LoFo of those reported 0.
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1205 Carey 2012 Hyperpath *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1206 Graffe 2012

Methods	DB CO
Participants	N 21 (M/F:10/11)(B/W/A.0/11/0) Norm Age 26
Interventions	SR 172 Dur 4
Outcomes	SBP, DBP, renin, aldo
Notes	Included 25 LoFo: 4

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	A computer-generated randomization list was drawn up by an independent colleague.
Allocation concealment (selection bias)	Low risk	A copy of the list was given to the hospital kitchen, and the original was kept in a sealed envelope at the department. The code was revealed when the study was finished.
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow-up 4/25
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1207 Krikken 2012

Methods	Op, CO
Participants	N 65 (M/F:65/0)(B/W/A.0/65/0)
Interventions	SR 192 Dur 7
Outcomes	SBP, DBP, Ren, Aldo, Chol, HDL, LDL
Notes	No report of excluded participants. LoFo of those reported 0.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No report of excluded participants. LoFo of those reported 0.
Selective reporting (reporting bias)	Unclear risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1208 Todd 2012

Methods	SB, Co
Participants	N 23 (M/F:5/18)(B/W/A.0/23/0) Normotension Age 43.7
Interventions	SR 140 Dur 28

1208 Todd 2012 *(Continued)*

Outcomes	SBP, DBP
Notes	28 screened, 25 included, 23 randomized. LoFo. 4

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization was carried out by a third party using http:// www.randomization.com to generate the randomization sequence for the tomato juice interventions.
Allocation concealment (selection bias)	Low risk	The sequence was given to the Dunedin hospital pharmacy, where a study dedicated pharmacist added the allocated amount of salt to the tomato juice.
Blinding (performance bias and detection bias) All outcomes	Low risk	Single blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 4/23
Selective reporting (reporting bias)	Unclear risk	No distinct selective reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	The investigators remained blind to the randomization sequence throughout the study. Participants were initially blind to the randomization sequence, but once they began each phase of the intervention they were aware of the presence or absence of added salt. They were asked not to tell the investigator which tomato juice they had received.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1209 Bonfils 2013

Methods	Op, CO
Participants	12 obese with treated hypertension, N 12 (M/F:5/7)(B/W/A.0/12/0), Age 43 12 obese with normal BP, N 12 (M/F:5/7)(B/W/A.0/12/0), Age 39 12 non-obese controls with normal BP, N 12 (M/F:5/7)(B/W/A.0/12/0), Age 39
Interventions	SR 131 Dur 5
Outcomes	SBP, DBP
Notes	LoFo no information

Risk of bias

1209 Bonfils 2013 *(Continued)*

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Simple randomization, that is tossing a coin to decide whether patients should have low-salt diet followed by high-salt diet or vice versa.
Allocation concealment (selection bias)	High risk	The primary investigator assigned participants to the interventions according to the randomization sequence. The patients were not blinded for treatment assignment.
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No report of excluded participants. LoFo of those reported 0.
Selective reporting (reporting bias)	Unclear risk	No distinct reporting bias
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1212 Mak 2013

Methods	Op, CO
Participants	N 13 (M/F:12/1)(B/W/A.0/13/0) Normotension Age 24
Interventions	SR: 190 Dur: 7
Outcomes	SBP, DBP
Notes	No report of excluded participants. LoFo of those reported 0.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information

1212 Mak 2013 *(Continued)*

Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No report of excluded participants. Lost to follow up of those reported 0.
Selective reporting (reporting bias)	Unclear risk	Insufficient information
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Insufficient information

1213 Mallamaci 2013

Methods	Op, CO
Participants	N 32 (M/F:23/9)(B/W/A.0/32/0) Hypertension Age 48
Interventions	SR 165 Dur 14
Outcomes	SBP, DBP, renin, aldo
Notes	32 of 102 screened were randomized. LoFo: 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias)	Low risk	Lost to follow up 0/32

1213 Mallamaci 2013 *(Continued)*

All outcomes		
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1214 Dickinson 2014

Methods	SB, CO
Participants	N 25 (M/F:/)(B/W/A.0/25/0) Normotension Age 35.1
Interventions	SR 42 Dur 42
Outcomes	SBP, DBP, renin, aldo,
Notes	Screened 87, Randomized 50, allocated to diet 34, received diet 25

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	Unclear risk	Single blind
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 9/34
Selective reporting (reporting bias)	Unclear risk	No distinct selective reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.

1214 Dickinson 2014 *(Continued)*

Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1215 Allen 2014

Methods	Op, CO
Participants	N 70 (M/F:26/44)(B/W/A.0/70/0) Normotension Age 24
Interventions	SR 83 Dur 5
Outcomes	SBP, DBP
Notes	No report of excluded participants. LoFo of those reported 0.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No report of excluded participants. lost to follow up of those reported 0/70.
Selective reporting (reporting bias)	Unclear risk	No distinct selective reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1216 Barros 2015

Methods	Op,

1216 Barros 2015 *(Continued)*

	P
Participants	N 35 (M/F:12/24) (B/W/A. ? Brazilians) Hypertension Age 55.5
Interventions	SR: 48 Dur: 28
Outcomes	SBP, DBP
Notes	38 of 56 screened were randomized. LoFo 3

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Participants were randomized "according to the order of visit"
Allocation concealment (selection bias)	High risk	"Participants received plastic bags containing the daily amount of salt." "Participants were not aware of the type of salt they were receiving" (but the researcher was.
Blinding (performance bias and detection bias) All outcomes	High risk	Single blind (participant)
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up LS: 3/19; US: 0/19
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1217 Markota 2015

Methods	Op, P
Participants	N 150 (M/F:77/73) (B/W/A. 0/150/0) Hypertension Age 59.4
Interventions	SR: 28 Dur: 60

1217 Markota 2015 *(Continued)*

Outcomes	SBP, DBP
Notes	150 of 171 fulfilling inclusion criteria were randomized. LoFo 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Low risk	instructions in sealed envelopes
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0/150
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1218 Visser 2008

Methods	Op, CO
Participants	N 34 (M/F:34/0)(B/W/A.0/34/0) Normotension Age 26.5
Interventions	SR 181 Dur 7
Outcomes	SBP, DBP, renin, aldo, cholesterol
Notes	No report of excluded participants. Lost to follow up of those reported 0.

Risk of bias

Bias	Authors' judgement	Support for judgement

1218 Visser 2008 *(Continued)*

Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	No report of excluded participants. Lost to follow up of those reported 0.
Selective reporting (reporting bias)	Unclear risk	No distinct selective reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	High risk	Open study: Detection bias due to knowledge of the allocated interventions by outcome assessors

1219 Sharma 3 1993

Methods	SB, CO
Participants	N 18 (M/F:18/0)(B/W/A.0/18/0) Normotension Age 24
Interventions	SR 218 Dur 7
Outcomes	SBP, DBP
Notes	No report of excluded participants. Lost to follow up 0.

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias)	High risk	Open study

1219 Sharma 3 1993 *(Continued)*

All outcomes		
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0/18
Selective reporting (reporting bias)	Low risk	No distinct selective reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1220 Gomi 1998

Methods	Op, CO
Participants	N 12 (M/F:8/4)(B/W/A.0/0/12) Hypertension Age 51.8
Interventions	SR 70 Dur 7
Outcomes	SBP, DBP, renin, aldosterone, noradrenalin
Notes	LoFo 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0.
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1220 Gomi 1998 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1221 Facchini 1999

Methods	Op, CO
Participants	N 19 (M/F:17/2)(B/W/A.0/19/0) Normotension Age 43
Interventions	SR 168.7 Dur 5
Outcomes	SBP, DBP, renin, aldosterone
Notes	LoFo 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1222 Pechere-Bertschi 2000

Methods	Op, CO
Participants	N 35 (M/F:0/35)(B/W/A.0/35/0) Normotension Age 28.9
Interventions	SR 177.8 Dur 7
Outcomes	SBP, DBP, renin, aldosterone, noradrenalin
Notes	LoFo 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0/35
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1223 Pechère-Bertschi 2003

Methods	Op, CO
Participants	N 27 (M/F:0/27)(B/W/A.0/27/0) Normotension

1223 Pechère-Bertschi 2003 *(Continued)*

	Age 26
Interventions	SR 192.8 Dur 7
Outcomes	SBP, DBP, renin, aldosterone, noradrenalin, adrenalin
Notes	LoFo 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0/27
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1224 Ho 2007

Methods	Op, CO
Participants	N 25 (M/F:8/17)(B/W/A.0/25/0) Normotension Age 48.8
Interventions	SR 206.9 Dur 14
Outcomes	SBP, DBP, renin, aldosterone

1224 Ho 2007 *(Continued)*

Notes	101 screened, 44 included, LoFo 19

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	High risk	Lost to follow up 19/44
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1225 Gijsbers 2015

Methods	DB, CO
Participants	N 36 (M/F:24/12)(B/W/A.0/36/0) Hypertension Age 65.8
Interventions	SR 206.9 Dur 28
Outcomes	SBP, DBP, cholesterol, triglyceride, HDL, LDL
Notes	83 screened, 37 randomized, lost to follow up 1

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	computer-generated table

1225 Gijsbers 2015 *(Continued)*

Allocation concealment (selection bias)	Low risk	independent person
Blinding (performance bias and detection bias) All outcomes	Low risk	Double blind study
Incomplete outcome data (attrition bias) All outcomes	Low risk	lost to follow up 1/37
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Double blind study
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Double blind study

1226 Cavka 2015

Methods	SB, P
Participants	N 54 (M/F:0/54)(B/W/A.0/54/0) Normotension Age 20
Interventions	SR 149.4 Dur 7
Outcomes	SBP, DBP, renin, aldosterone
Notes	LoFo 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Single blind

1226 Cavka 2015 *(Continued)*

Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up LS: 0/24; US: 0/30
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting
Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

1227 McManus 2015

Methods	Op, CO
Participants	N 60 (M/F:27/33)(B/W/A.0/60/0) Normotension Age 50.1
Interventions	SR 102.7 Dur 5
Outcomes	Aldosterone
Notes	LoFo 0

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Insufficient information
Allocation concealment (selection bias)	Unclear risk	Insufficient information
Blinding (performance bias and detection bias) All outcomes	High risk	Open study
Incomplete outcome data (attrition bias) All outcomes	Low risk	Lost to follow up 0/60
Selective reporting (reporting bias)	Low risk	No distinct selective outcome reporting

1227 McManus 2015 *(Continued)*

Blinding of participants and personnel (performance bias) All outcomes	High risk	Open study: Performance bias due to knowledge of the allocated interventions by participants and personnel during the study.
Blinding of outcome assessment (detection bias) All outcomes	Low risk	Outcome detection blinded

A: adrenaline; **Age**: mean age of persons in trial; **Chol:** cholesterol; **CO:** cross-over; **DB:** double blind; **DBP:** net change of diastolic blood pressure, mmHg; **Dur:** duration of intervention, days; **HDL:** high-density lipoprotein; **Hyp:** hypertensive; **LDL:** low-density lipoprotein; **TG:** triglyceride; **LoFo:** number lost to follow-up; **IT:** "intention-to-treat" of those lost to follow-up; **N:** number of persons in trial; **NA:** noradrenaline; **Norm:** normotensive; **Op:** open; **P:** parallel; **SB:** single-blind; **SBP:** net change of systolic blood pressure, mmHg; **SR:** sodium reduction, mmol/24hours

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

Study	Reason for exclusion
Anderson 1990	No data on urine sodium excretion
Dodson 1989	Includes only patients with diabetes mellitus
Imanishi 2001	Includes only patients with diabetes mellitus
Jula-Karanko 1992	Duplicate: all data could be extracted from a later paper (1110 Jula 1994)
Jula-Mäki 1992	Duplicate: all data could be extracted from a later paper (1110 Jula 1994)
Miller 1997	Includes only patients with diabetes mellitus
Mühlhauser 1996	Includes only patients with diabetes mellitus
Palmer 1989	No data on urine sodium excretion
Parfrey 1981	Withdrawal of paper by the authors due to erroneous form
Ruppert 1991	Sub-study of 1088 Ruppert 1993
Ruppert 1994	Sub-study of 1088 Ruppert 1993
Steegers 1991	Sub-study of 1136 van Buul 1997

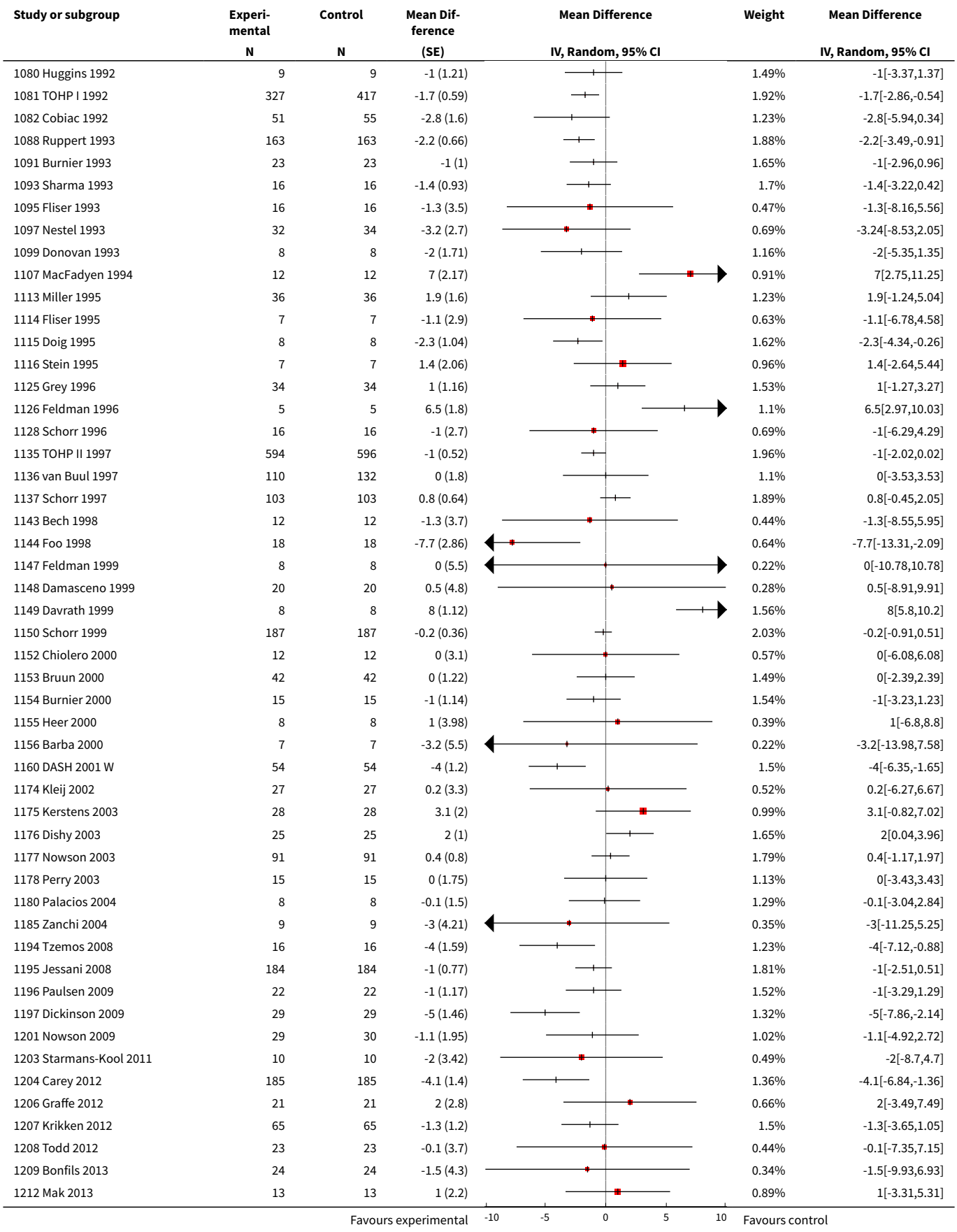
DATA AND ANALYSES

Comparison 1. Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Whites

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 White population, normotensive, SBP	89	8569	Mean Difference (Random, 95% CI)	-1.09 [-1.63, -0.56]
2 White population, normotensive, DBP	90	8833	Mean Difference (Random, 95% CI)	0.03 [-0.37, 0.43]
3 White population, hypertensive, SBP	84	5925	Mean Difference (Random, 95% CI)	-5.51 [-6.45, -4.57]
4 White population, hypertensive, DBP	85	6001	Mean Difference (Random, 95% CI)	-2.88 [-3.44, -2.32]

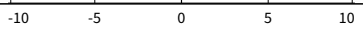
Analysis 1.1. Comparison 1 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Whites, Outcome 1 White population, normotensive, SBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1003 Sullivan 1980	27	27	6.9 (1.37)		1.38%	6.9[4.21,9.59]
1005 Rankin 1981	8	8	-3 (6.1)		0.18%	-3[-14.96,8.96]
1006 Skrabal 1981	20	20	-2.7 (2.07)		0.96%	-2.7[-6.76,1.36]
1010 Myers 1982	136	136	-3.3 (0.9)		1.72%	-3.3[-5.06,-1.54]
1013 Puska 1983	19	19	-1.5 (4.52)		0.31%	-1.5[-10.36,7.36]
1019 Cooper 1984	113	113	-0.6 (0.7)		1.85%	-0.6[-1.97,0.77]
1021 Skrabal 1984	52	52	-3.1 (4.4)		0.33%	-3.14[-11.76,5.48]
1031 Tuthill 1985	65	126	0 (1.12)		1.56%	0[-2.2,2.2]
1032 Skrabal 1985	62	62	-3.1 (2.2)		0.89%	-3.1[-7.41,1.21]
1034 Watt 1985	66	66	-1 (0.5)		1.97%	-1[-1.98,-0.02]
1036 Richards 1986	8	8	-2 (1.79)		1.11%	-2[-5.51,1.51]
1037 Teow 1986	9	9	-0.6 (1.15)		1.54%	-0.6[-2.85,1.65]
1040 El Ashry 1987	26	26	0 (1.3)		1.43%	0[-2.55,2.55]
1042 Fuchs 1987	17	17	-3.6 (2.2)		0.89%	-3.6[-7.91,0.71]
1048 Lawton 1988	22	22	-1.7 (1.3)		1.43%	-1.7[-4.25,0.85]
1053 Sudhir 1989	6	6	-7.9 (3.4)		0.5%	-7.9[-14.56,-1.24]
1054 Hargreaves 1989	8	8	-6 (2.23)		0.88%	-6[-10.37,-1.63]
1057 Dimsdale 1990 W	19	19	1.4 (1.6)		1.23%	1.4[-1.74,4.54]
1061 Schmid 1990	9	9	-3 (1.9)		1.05%	-3[-6.72,0.72]
1063 HPTRG 1990	174	177	0.1 (0.99)		1.65%	0.1[-1.84,2.04]
1064 Bruun 1990	10	10	-5 (1.72)		1.15%	-5[-8.37,-1.63]
1066 Sharma 1990	15	15	-0.9 (1.95)		1.02%	-0.9[-4.72,2.92]
1067 Sharma 1990,2	40	40	-2.1 (1.12)		1.56%	-2.1[-4.3,0.1]
1068 Friberg 1990	10	10	0 (2)		0.99%	0[-3.92,3.92]
1073 Sharma 1991	23	23	-4.5 (0.94)		1.69%	-4.5[-6.34,-2.66]
1074 Howe 1991	90	90	-1 (0.68)		1.87%	-1[-2.33,0.33]
1075 Mascioli 1991	48	48	-3.6 (0.9)		1.72%	-3.6[-5.36,-1.84]
1078 Egan 1991	9	9	1 (1.4)		1.36%	1[-1.74,3.74]
1079 Gow 1992	9	9	-8 (1.61)		1.22%	-8[-11.16,-4.84]



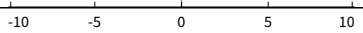
Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1080 Huggins 1992	9	9	-1 (1.21)		1.49%	-1[-3.37,1.37]
1081 TOHP I 1992	327	417	-1.7 (0.59)		1.92%	-1.7[-2.86,-0.54]
1082 Cobiac 1992	51	55	-2.8 (1.6)		1.23%	-2.8[-5.94,0.34]
1088 Ruppert 1993	163	163	-2.2 (0.66)		1.88%	-2.2[-3.49,-0.91]
1091 Burnier 1993	23	23	-1 (1)		1.65%	-1[-2.96,0.96]
1093 Sharma 1993	16	16	-1.4 (0.93)		1.7%	-1.4[-3.22,0.42]
1095 Fliser 1993	16	16	-1.3 (3.5)		0.47%	-1.3[-8.16,5.56]
1097 Nestel 1993	32	34	-3.2 (2.7)		0.69%	-3.24[-8.53,2.05]
1099 Donovan 1993	8	8	-2 (1.71)		1.16%	-2[-5.35,1.35]
1107 MacFadyen 1994	12	12	7 (2.17)		0.91%	7[2.75,11.25]
1113 Miller 1995	36	36	1.9 (1.6)		1.23%	1.9[-1.24,5.04]
1114 Fliser 1995	7	7	-1.1 (2.9)		0.63%	-1.1[-6.78,4.58]
1115 Doig 1995	8	8	-2.3 (1.04)		1.62%	-2.3[-4.34,-0.26]
1116 Stein 1995	7	7	1.4 (2.06)		0.96%	1.4[-2.64,5.44]
1125 Grey 1996	34	34	1 (1.16)		1.53%	1[-1.27,3.27]
1126 Feldman 1996	5	5	6.5 (1.8)		1.1%	6.5[2.97,10.03]
1128 Schorr 1996	16	16	-1 (2.7)		0.69%	-1[-6.29,4.29]
1135 TOHP II 1997	594	596	-1 (0.52)		1.96%	-1[-2.02,0.02]
1136 van Buul 1997	110	132	0 (1.8)		1.1%	0[-3.53,3.53]
1137 Schorr 1997	103	103	0.8 (0.64)		1.89%	0.8[-0.45,2.05]
1143 Bech 1998	12	12	-1.3 (3.7)		0.44%	-1.3[-8.55,5.95]
1144 Foo 1998	18	18	-7.7 (2.86)		0.64%	-7.7[-13.31,-2.09]
1147 Feldman 1999	8	8	0 (5.5)		0.22%	0[-10.78,10.78]
1148 Damasceno 1999	20	20	0.5 (4.8)		0.28%	0.5[-8.91,9.91]
1149 Davrath 1999	8	8	8 (1.12)		1.56%	8[5.8,10.2]
1150 Schorr 1999	187	187	-0.2 (0.36)		2.03%	-0.2[-0.91,0.51]
1152 Chiolero 2000	12	12	0 (3.1)		0.57%	0[-6.08,6.08]
1153 Bruun 2000	42	42	0 (1.22)		1.49%	0[-2.39,2.39]
1154 Burnier 2000	15	15	-1 (1.14)		1.54%	-1[-3.23,1.23]
1155 Heer 2000	8	8	1 (3.98)		0.39%	1[-6.8,8.8]
1156 Barba 2000	7	7	-3.2 (5.5)		0.22%	-3.2[-13.98,7.58]
1160 DASH 2001 W	54	54	-4 (1.2)		1.5%	-4[-6.35,-1.65]
1174 Kleij 2002	27	27	0.2 (3.3)		0.52%	0.2[-6.27,6.67]
1175 Kerstens 2003	28	28	3.1 (2)		0.99%	3.1[-0.82,7.02]
1176 Dishy 2003	25	25	2 (1)		1.65%	2[0.04,3.96]
1177 Nowson 2003	91	91	0.4 (0.8)		1.79%	0.4[-1.17,1.97]
1178 Perry 2003	15	15	0 (1.75)		1.13%	0[-3.43,3.43]
1180 Palacios 2004	8	8	-0.1 (1.5)		1.29%	-0.1[-3.04,2.84]
1185 Zanchi 2004	9	9	-3 (4.21)		0.35%	-3[-11.25,5.25]
1194 Tzemos 2008	16	16	-4 (1.59)		1.23%	-4[-7.12,-0.88]
1195 Jessani 2008	184	184	-1 (0.77)		1.81%	-1[-2.51,0.51]
1196 Paulsen 2009	22	22	-1 (1.17)		1.52%	-1[-3.29,1.29]
1197 Dickinson 2009	29	29	-5 (1.46)		1.32%	-5[-7.86,-2.14]
1201 Nowson 2009	29	30	-1.1 (1.95)		1.02%	-1.1[-4.92,2.72]
1203 Starmans-Kool 2011	10	10	-2 (3.42)		0.49%	-2[-8.7,4.7]
1204 Carey 2012	185	185	-4.1 (1.4)		1.36%	-4.1[-6.84,-1.36]
1206 Graffe 2012	21	21	2 (2.8)		0.66%	2[-3.49,7.49]
1207 Krikken 2012	65	65	-1.3 (1.2)		1.5%	-1.3[-3.65,1.05]
1208 Todd 2012	23	23	-0.1 (3.7)		0.44%	-0.1[-7.35,7.15]
1209 Bonfils 2013	24	24	-1.5 (4.3)		0.34%	-1.5[-9.93,6.93]
1212 Mak 2013	13	13	1 (2.2)		0.89%	1[-3.31,5.31]

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1214 Dickinson 2014	25	25	-2 (3.3)		0.52%	-2[-8.47,4.47]
1215 Allen 2014	70	70	-1 (1.9)		1.05%	-1[-4.72,2.72]
1218 Visser 2008	34	34	-5 (2.63)		0.72%	-5[-10.15,0.15]
1219 Sharma 3 1993	18	18	-4 (1.8)		1.1%	-4[-7.53,-0.47]
1221 Facchini 1999	19	19	-0.3 (4.1)		0.37%	-0.3[-8.34,7.74]
1222 Pechere-Bertschi 2000	35	35	-2.4 (1.6)		1.23%	-2.4[-5.54,0.74]
1223 Pechère-Bertschi 2003	27	27	-1 (2.6)		0.73%	-1[-6.1,4.1]
1224 Ho 2007	25	25	-5 (1.4)		1.36%	-5[-7.74,-2.26]
1226 Cavka 2015	30	24	-5 (3.41)		0.49%	-5[-11.68,1.68]
Total (95% CI)					**100%**	**-1.09[-1.63,-0.56]**
Heterogeneity: Tau²=3.56; Chi²=297.87, df=88(P<0.0001); I²=70.46%						
Test for overall effect: Z=3.99(P<0.0001)						



Analysis 1.2. Comparison 1 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Whites, Outcome 2 White population, normotensive, DBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1003 Sullivan 1980	27	27	1.1 (1.37)		1.13%	1.1[-1.59,3.79]
1005 Rankin 1981	8	8	-1.9 (3.9)		0.25%	-1.9[-9.54,5.74]
1006 Skrabal 1981	20	20	-3 (1.46)		1.06%	-3[-5.86,-0.14]
1010 Myers 1982	136	136	-2.7 (0.8)		1.69%	-2.7[-4.27,-1.13]
1013 Puska 1983	19	19	-2.1 (2.77)		0.44%	-2.1[-7.53,3.33]
1019 Cooper 1984	113	113	-1.4 (1)		1.48%	-1.4[-3.36,0.56]
1021 Skrabal 1984	52	52	-1.8 (2.64)		0.48%	-1.85[-7.02,3.32]
1031 Tuthill 1985	65	126	0 (1.33)		1.17%	0[-2.61,2.61]
1032 Skrabal 1985	62	62	-1.5 (0.9)		1.59%	-1.5[-3.26,0.26]
1034 Watt 1985	66	66	1.3 (0.6)		1.91%	1.3[0.12,2.48]
1036 Richards 1986	8	8	7 (1.62)		0.94%	7[3.82,10.18]
1037 Teow 1986	9	9	-2.7 (1.41)		1.1%	-2.7[-5.46,0.06]
1040 El Ashry 1987	26	26	-2.6 (1.6)		0.96%	-2.6[-5.74,0.54]
1042 Fuchs 1987	17	17	1.9 (1)		1.48%	1.9[-0.06,3.86]
1048 Lawton 1988	22	22	2.3 (1.15)		1.33%	2.33[0.08,4.58]
1053 Sudhir 1989	6	6	-5 (2.1)		0.68%	-5[-9.12,-0.88]
1054 Hargreaves 1989	8	8	-3 (1.98)		0.73%	-3[-6.88,0.88]
1057 Dimsdale 1990 W	19	19	4.1 (1.1)		1.38%	4.1[1.94,6.26]
1061 Schmid 1990	9	9	3 (1.63)		0.94%	3[-0.19,6.19]
1063 HPTRG 1990	174	177	0.2 (0.71)		1.79%	0.2[-1.19,1.59]
1064 Bruun 1990	10	10	-1 (2.03)		0.71%	-1[-4.98,2.98]
1066 Sharma 1990	0	0	-3.7 (1.81)		0.82%	-3.7[-7.25,-0.15]
1067 Sharma 1990,2	40	40	-3.1 (1.04)		1.44%	-3.1[-5.14,-1.06]
1068 Friberg 1990	10	10	-1 (2)		0.72%	-1[-4.92,2.92]
1073 Sharma 1991	23	23	-2.2 (1.09)		1.39%	-2.2[-4.34,-0.06]
1074 Howe 1991	90	90	-0.6 (0.71)		1.79%	-0.56[-1.95,0.83]
1075 Mascioli 1991	48	48	-2.3 (0.8)		1.69%	-2.3[-3.87,-0.73]
1078 Egan 1991	9	9	0.6 (1.4)		1.11%	0.6[-2.14,3.34]



Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1079 Gow 1992	9	9	-3 (2.22)		0.62%	-3[-7.35,1.35]
1080 Huggins 1992	9	9	-2 (1.91)		0.77%	-2[-5.74,1.74]
1081 TOHP I 1992	327	417	-0.8 (0.42)		2.08%	-0.8[-1.62,0.02]
1082 Cobiac 1992	51	55	-1 (1.8)		0.83%	-1[-4.53,2.53]
1088 Ruppert 1993	163	163	1 (0.61)		1.9%	1[-0.2,2.2]
1091 Burnier 1993	23	23	0.8 (1.1)		1.38%	0.8[-1.36,2.96]
1093 Sharma 1993	16	16	-0.5 (1.22)		1.26%	-0.5[-2.89,1.89]
1095 Fliser 1993	16	16	-0.9 (2.2)		0.63%	-0.9[-5.21,3.41]
1097 Nestel 1993	32	34	-1.4 (2)		0.72%	-1.37[-5.29,2.55]
1099 Donovan 1993	8	8	1 (1.34)		1.16%	1[-1.63,3.63]
1107 MacFadyen 1994	12	12	10 (2.17)		0.65%	10[5.75,14.25]
1113 Miller 1995	36	36	-0.1 (1.47)		1.05%	-0.1[-2.98,2.78]
1114 Fliser 1995	7	7	-0.7 (1.8)		0.83%	-0.7[-4.23,2.83]
1115 Doig 1995	8	8	0 (1.33)		1.17%	0[-2.61,2.61]
1116 Stein 1995	7	7	-1.2 (1.89)		0.78%	-1.2[-4.9,2.5]
1125 Grey 1996	34	34	1 (0.87)		1.62%	1[-0.71,2.71]
1126 Feldman 1996	5	5	4.2 (1.13)		1.35%	4.2[1.99,6.41]
1128 Schorr 1996	16	16	0 (1.73)		0.87%	0[-3.39,3.39]
1135 TOHP II 1997	594	596	-0.5 (0.4)		2.09%	-0.5[-1.28,0.28]
1136 van Buul 1997	110	132	0 (1.16)		1.32%	0[-2.27,2.27]
1137 Schorr 1997	103	103	0.4 (0.64)		1.86%	0.4[-0.85,1.65]
1142 Knuist 1998	149	145	0 (1.16)		1.32%	0[-2.27,2.27]
1143 Bech 1998	12	12	-0.8 (2.3)		0.59%	-0.8[-5.31,3.71]
1144 Foo 1998	18	18	2.4 (1.55)		0.99%	2.4[-0.64,5.44]
1147 Feldman 1999	8	8	0 (3.6)		0.29%	0[-7.06,7.06]
1148 Damasceno 1999	20	20	0.3 (3.1)		0.37%	0.3[-5.78,6.38]
1149 Davrath 1999	8	8	5 (1.47)		1.05%	5[2.12,7.88]
1150 Schorr 1999	187	187	0.3 (0.36)		2.13%	0.3[-0.41,1.01]
1152 Chiolero 2000	12	12	0 (2)		0.72%	0[-3.92,3.92]
1153 Bruun 2000	42	42	1 (1.13)		1.35%	1[-1.21,3.21]
1154 Burnier 2000	15	15	5 (1.14)		1.34%	5[2.77,7.23]
1155 Heer 2000	8	8	-1 (3.37)		0.32%	-1[-7.61,5.61]
1156 Barba 2000	7	7	-2.1 (3.5)		0.3%	-2.1[-8.96,4.76]
1160 DASH 2001 W	54	54	-1.4 (0.8)		1.69%	-1.4[-2.97,0.17]
1174 Kleij 2002	27	27	0.1 (2.1)		0.68%	0.12[-4,4.24]
1175 Kerstens 2003	28	28	2 (1.3)		1.19%	2[-0.55,4.55]
1176 Dishy 2003	25	25	1 (1)		1.48%	1[-0.96,2.96]
1177 Nowson 2003	91	91	0 (0.6)		1.91%	0[-1.18,1.18]
1178 Perry 2003	15	15	-2 (1.69)		0.9%	-2[-5.31,1.31]
1180 Palacios 2004	8	8	4.2 (1.71)		0.89%	4.2[0.85,7.55]
1185 Zanchi 2004	9	9	0 (2.95)		0.4%	0[-5.78,5.78]
1194 Tzemos 2008	16	16	-1 (0.6)		1.91%	-1[-2.18,0.18]
1195 Jessani 2008	184	184	-1 (0.77)		1.73%	-1[-2.51,0.51]
1196 Paulsen 2009	22	22	1 (0.78)		1.71%	1[-0.53,2.53]
1197 Dickinson 2009	29	29	-1 (1.09)		1.39%	-1[-3.14,1.14]
1201 Nowson 2009	29	30	0.3 (1.54)		1%	0.3[-2.72,3.32]
1203 Starmans-Kool 2011	10	10	0 (3.36)		0.32%	0[-6.59,6.59]
1204 Carey 2012	185	185	-0.9 (0.8)		1.69%	-0.9[-2.47,0.67]
1206 Graffe 2012	21	21	1 (1.7)		0.89%	1[-2.33,4.33]
1207 Krikken 2012	65	65	-0.8 (1.2)		1.28%	-0.8[-3.15,1.55]
1208 Todd 2012	23	23	-0.4 (1.5)		1.03%	-0.4[-3.34,2.54]

Favours experimental -10 -5 0 5 10 Favours control

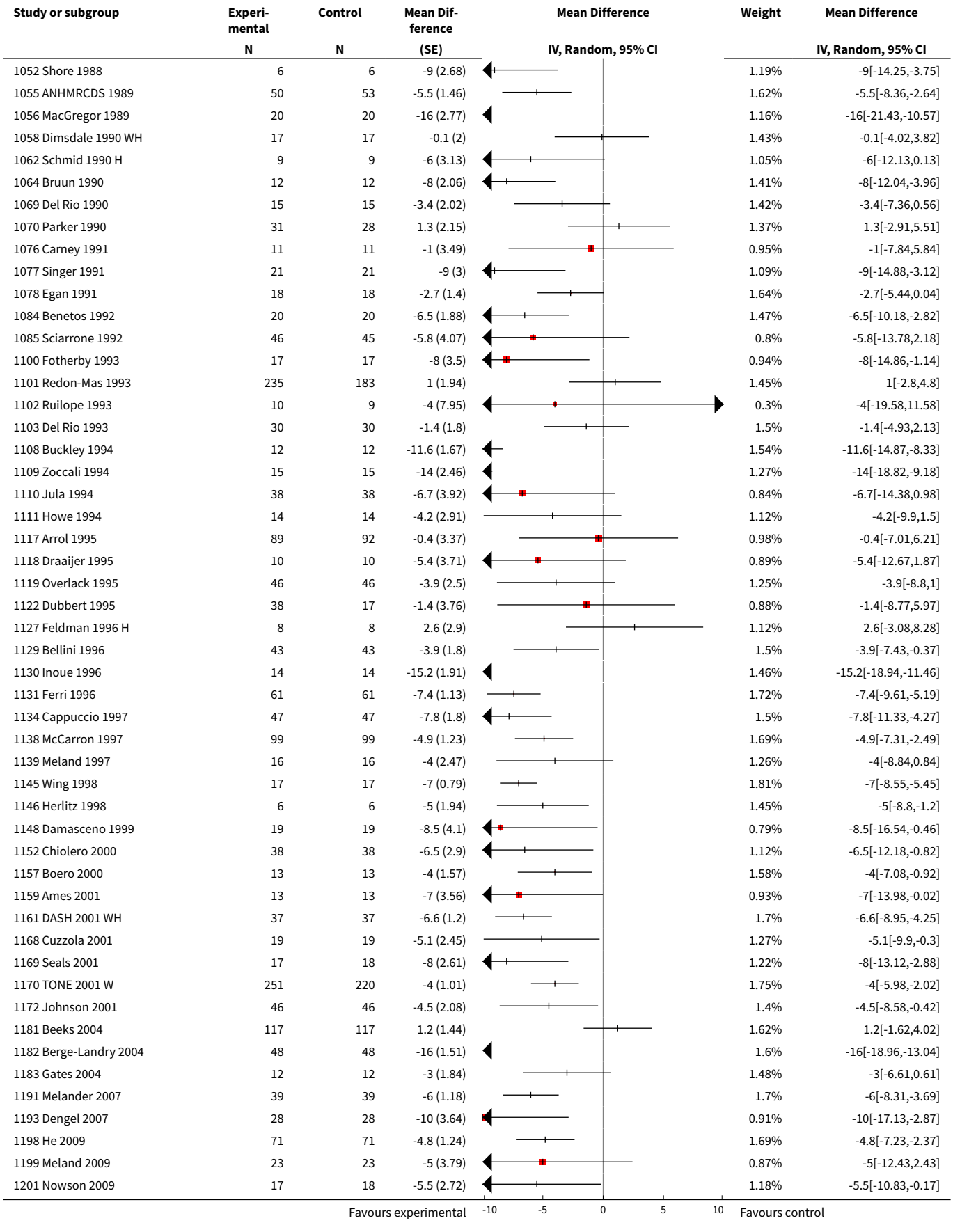
Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1209 Bonfils 2013	24	24	0.3 (1.7)		0.89%	0.31[-3.02,3.64]
1212 Mak 2013	13	13	3 (2.6)		0.49%	3[-2.1,8.1]
1214 Dickinson 2014	25	25	-2 (1.8)		0.83%	-2[-5.53,1.53]
1215 Allen 2014	70	70	3 (1.5)		1.03%	3[0.06,5.94]
1218 Visser 2008	34	34	-1 (1.82)		0.82%	-1[-4.57,2.57]
1219 Sharma 3 1993	18	18	-1.4 (1.6)		0.96%	-1.4[-4.54,1.74]
1221 Facchini 1999	19	19	-0.2 (2.6)		0.49%	-0.2[-5.3,4.9]
1222 Pechere-Bertschi 2000	35	35	-0.7 (1.15)		1.33%	-0.7[-2.95,1.55]
1223 Pechère-Bertschi 2003	27	27	2 (1.3)		1.19%	2[-0.55,4.55]
1224 Ho 2007	25	25	-1.8 (1)		1.48%	-1.8[-3.76,0.16]
1226 Cavka 2015	30	24	-3 (2.7)		0.46%	-3[-8.29,2.29]
Total (95% CI)					**100%**	**0.03[-0.37,0.43]**
Heterogeneity: Tau²=1.87; Chi²=234.97, df=89(P<0.0001); I²=62.12%						
Test for overall effect: Z=0.14(P=0.89)						

Favours experimental -10 -5 0 5 10 Favours control

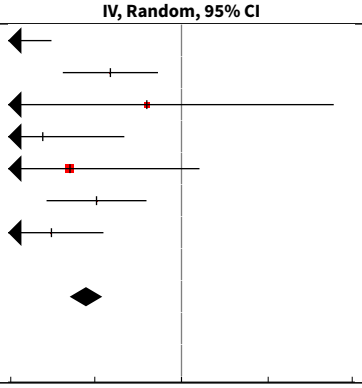
Analysis 1.3. Comparison 1 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Whites, Outcome 3 White population, hypertensive, SBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1000 Parijs 1973	15	17	-6.7 (9.75)		0.21%	-6.7[-25.81,12.41]
1001 Mark 1975	6	6	-13.1 (1.71)		1.53%	-13.1[-16.45,-9.75]
1002 Morgan 1978	31	31	-1.5 (5.55)		0.54%	-1.5[-12.38,9.38]
1003 Sullivan 1980	19	19	1.2 (1.93)		1.45%	1.2[-2.58,4.98]
1009 Ambrosioni 1982	25	25	-2.2 (1.57)		1.58%	-2.2[-5.28,0.88]
1011 MacGregor 1982	19	19	-10 (2.76)		1.17%	-10[-15.41,-4.59]
1012 Beard 1982	45	45	-5.2 (4.85)		0.64%	-5.2[-14.71,4.31]
1013 Puska 1983	15	19	1.8 (5.57)		0.53%	1.8[-9.12,12.72]
1015 Bulpitt 1984	32	33	-4.2 (6.28)		0.45%	-4.2[-16.51,8.11]
1016 Silman 1983	12	16	3.5 (11.39)		0.16%	3.5[-18.82,25.82]
1018 Watt 1983	18	18	-0.5 (1.5)		1.6%	-0.5[-3.44,2.44]
1023 Gillies 1984	24	24	-2.4 (2.51)		1.25%	-2.4[-7.32,2.52]
1024 Erwteman 1984	44	50	-2.7 (4.01)		0.82%	-2.7[-10.56,5.16]
1025 Koolen 1984	20	20	-6.2 (2.54)		1.24%	-6.2[-11.18,-1.22]
1027 Fagerberg 1984	15	15	-3.7 (7.14)		0.36%	-3.7[-17.69,10.29]
1028 Maxwell 1984	18	12	-2 (6.72)		0.4%	-2[-15.17,11.17]
1029 Richards 1984	12	12	-4 (2.79)		1.16%	-4[-9.47,1.47]
1030 Resnick 1985	12	12	-3 (1.5)		1.6%	-3[-5.94,-0.06]
1038 Logan 1986	43	43	-1.1 (4.18)		0.78%	-1.1[-9.29,7.09]
1039 ANHMRCDS 1986	48	52	-4.8 (3.92)		0.84%	-4.8[-12.48,2.88]
1044 Morgan 1987	10	10	-6 (8.95)		0.25%	-6[-23.54,11.54]
1045 Kurtz 1987	5	5	-16 (2)		1.43%	-16[-19.92,-12.08]
1046 Grobbee 1987	40	40	-0.8 (1.51)		1.6%	-0.8[-3.76,2.16]
1047 MacGregor 1987	15	15	-13 (3.29)		1%	-13[-19.45,-6.55]
1050 Morgan 1988	16	16	-3 (2.74)		1.17%	-3[-8.37,2.37]
1051 Morgan 1988,2	8	8	-7 (3)		1.09%	-7[-12.88,-1.12]

Favours experimental -10 -5 0 5 10 Favours control

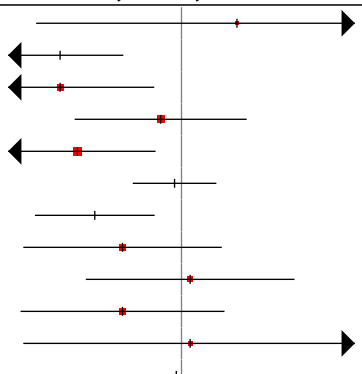


Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1202 Weir 2010	132	132	-9.4 (0.97)		1.76%	-9.4[-11.3,-7.5]
1204 Carey 2012	185	185	-4.1 (1.4)		1.64%	-4.1[-6.84,-1.36]
1209 Bonfils 2013	12	12	-2 (5.5)		0.54%	-2[-12.78,8.78]
1213 Mallamaci 2013	32	32	-8 (2.4)		1.29%	-8[-12.7,-3.3]
1216 Barros 2015	19	16	-6.4 (3.81)		0.86%	-6.43[-13.9,1.04]
1217 Markota 2015	76	74	-4.9 (1.47)		1.61%	-4.9[-7.78,-2.02]
1225 Gijsbers 2015	36	36	-7.5 (1.53)		1.59%	-7.5[-10.5,-4.5]
Total (95% CI)					**100%**	**-5.51[-6.45,-4.57]**
Heterogeneity: Tau²=12.07; Chi²=335.8, df=83(P<0.0001); I²=75.28%						
Test for overall effect: Z=11.5(P<0.0001)						



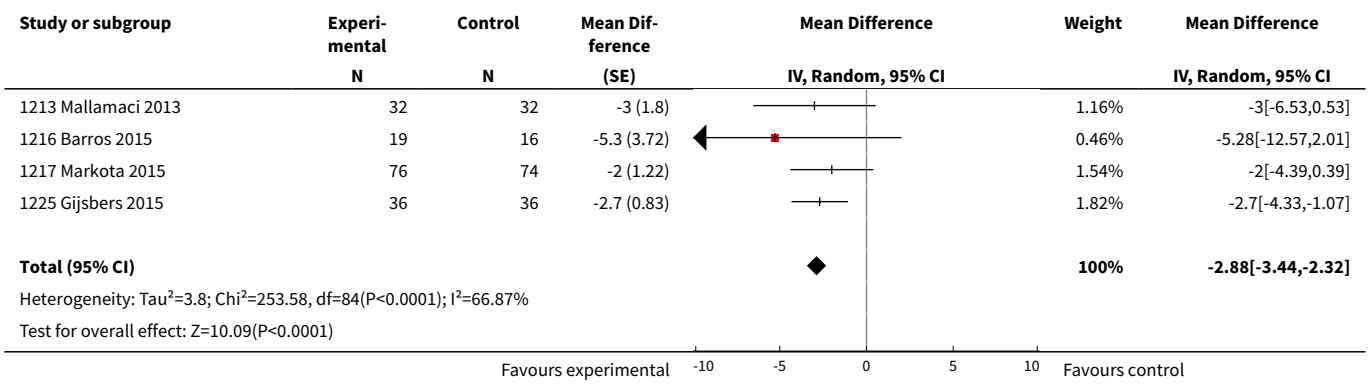
Analysis 1.4. Comparison 1 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Whites, Outcome 4 White population, hypertensive, DBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1000 Parijs 1973	15	17	3.2 (5.91)		0.21%	3.2[-8.38,14.78]
1001 Mark 1975	6	6	-7 (1.86)		1.12%	-7[-10.65,-3.35]
1002 Morgan 1978	31	31	-7 (2.77)		0.71%	-7[-12.43,-1.57]
1003 Sullivan 1980	19	19	-1.2 (2.53)		0.8%	-1.2[-6.16,3.76]
1007 Morgan 1981	12	12	-6 (2.3)		0.9%	-6[-10.51,-1.49]
1009 Ambrosioni 1982	25	25	-0.4 (1.23)		1.53%	-0.4[-2.81,2.01]
1011 MacGregor 1982	19	19	-5 (1.76)		1.18%	-5[-8.45,-1.55]
1012 Beard 1982	45	45	-3.4 (2.92)		0.66%	-3.4[-9.12,2.32]
1013 Puska 1983	15	19	0.5 (3.07)		0.62%	0.5[-5.52,6.52]
1015 Bulpitt 1984	32	33	-3.4 (3)		0.64%	-3.4[-9.28,2.48]
1016 Silman 1983	12	16	0.5 (4.91)		0.29%	0.5[-9.12,10.12]
1018 Watt 1983	18	18	-0.3 (0.8)		1.84%	-0.3[-1.87,1.27]
1023 Gillies 1984	24	24	-2.6 (2.21)		0.94%	-2.6[-6.93,1.73]
1024 Erwteman 1984	44	50	-2.5 (2.46)		0.83%	-2.5[-7.32,2.32]
1025 Koolen 1984	20	20	-4.9 (1.64)		1.26%	-4.9[-8.11,-1.69]
1027 Fagerberg 1984	15	15	-3.1 (4.06)		0.4%	-3.1[-11.06,4.86]
1028 Maxwell 1984	18	12	2 (3.84)		0.44%	2[-5.53,9.53]
1029 Richards 1984	12	12	-3 (2.26)		0.92%	-3[-7.43,1.43]
1030 Resnick 1985	12	12	-1 (1.38)		1.43%	-1[-3.7,1.7]
1038 Logan 1986	43	43	0 (2.34)		0.88%	0[-4.59,4.59]
1039 ANHMRCDS 1986	48	52	-4.2 (1.88)		1.11%	-4.2[-7.88,-0.52]
1044 Morgan 1987	10	10	-4 (4.3)		0.37%	-4[-12.43,4.43]
1045 Kurtz 1987	5	5	-8 (2)		1.05%	-8[-11.92,-4.08]
1046 Grobbee 1987	40	40	-0.8 (1.44)		1.39%	-0.8[-3.62,2.02]
1047 MacGregor 1987	15	15	-9 (3.05)		0.62%	-9[-14.98,-3.02]
1050 Morgan 1988	16	16	-4 (2.19)		0.95%	-4[-8.29,0.29]
1051 Morgan 1988,2	8	8	-6 (3)		0.64%	-6[-11.88,-0.12]
1052 Shore 1988	6	6	-5.6 (3.01)		0.63%	-5.6[-11.5,0.3]
1055 ANHMRCDS 1989	50	53	-2.8 (0.84)		1.81%	-2.8[-4.45,-1.15]
1056 MacGregor 1989	20	20	-9 (1.79)		1.16%	-9[-12.51,-5.49]



Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1058 Dimsdale 1990 WH	17	17	0.8 (2)		1.05%	0.8[-3.12,4.72]
1062 Schmid 1990 H	9	9	-1.9 (2.06)		1.01%	-1.9[-5.94,2.14]
1064 Bruun 1990	12	12	-4 (2.03)		1.03%	-4[-7.98,-0.02]
1069 Del Rio 1990	15	15	-1.1 (1.78)		1.17%	-1.1[-4.59,2.39]
1070 Parker 1990	31	28	0.6 (0.9)		1.77%	0.6[-1.16,2.36]
1076 Carney 1991	11	11	1 (2.96)		0.65%	1[-4.8,6.8]
1077 Singer 1991	21	21	-3 (2)		1.05%	-3[-6.92,0.92]
1078 Egan 1991	18	18	-1.7 (1.4)		1.41%	-1.7[-4.44,1.04]
1084 Benetos 1992	20	20	-3.7 (1.28)		1.5%	-3.7[-6.21,-1.19]
1085 Sciarrone 1992	46	45	-0.4 (2.28)		0.91%	-0.4[-4.87,4.07]
1100 Fotherby 1993	17	17	1 (2)		1.05%	1[-2.92,4.92]
1101 Redon-Mas 1993	235	183	1.9 (0.94)		1.74%	1.9[0.06,3.74]
1102 Ruilope 1993	10	9	-4 (2.69)		0.74%	-4[-9.27,1.27]
1103 Del Rio 1993	30	30	-0.5 (1.25)		1.52%	-0.5[-2.95,1.95]
1108 Buckley 1994	12	12	-5.8 (1.88)		1.11%	-5.8[-9.48,-2.12]
1109 Zoccali 1994	15	15	-8 (1.4)		1.41%	-8[-10.74,-5.26]
1110 Jula 1994	38	38	-3.8 (1.73)		1.2%	-3.8[-7.19,-0.41]
1111 Howe 1994	14	14	-1.5 (1.94)		1.08%	-1.5[-5.3,2.3]
1117 Arrol 1995	92	89	-1.2 (2.11)		0.99%	-1.2[-5.34,2.94]
1118 Draaijer 1995	10	10	0.8 (2.5)		0.81%	0.8[-4.1,5.7]
1119 Overlack 1995	46	46	-2.5 (1.6)		1.28%	-2.5[-5.64,0.64]
1122 Dubbert 1995	38	17	-0.5 (1.67)		1.24%	-0.5[-3.77,2.77]
1127 Feldman 1996 H	8	8	1.6 (1.8)		1.16%	1.6[-1.93,5.13]
1129 Bellini 1996	43	43	-4.9 (0.72)		1.89%	-4.9[-6.31,-3.49]
1130 Inoue 1996	14	14	-3.7 (1.66)		1.24%	-3.7[-6.95,-0.45]
1131 Ferri 1996	61	61	-3.5 (0.74)		1.87%	-3.5[-4.95,-2.05]
1134 Cappuccio 1997	47	47	-3.3 (1)		1.7%	-3.3[-5.26,-1.34]
1138 McCarron 1997	99	99	-2.9 (0.81)		1.83%	-2.9[-4.49,-1.31]
1139 Meland 1997	16	16	-3 (1.36)		1.44%	-3[-5.67,-0.33]
1145 Wing 1998	17	17	-4 (1.15)		1.59%	-4[-6.25,-1.75]
1146 Herlitz 1998	6	6	-3 (1.54)		1.32%	-3[-6.02,0.02]
1148 Damasceno 1999	19	19	-5.4 (2.6)		0.77%	-5.4[-10.5,-0.3]
1152 Chiolero 2000	38	38	-4.2 (1.8)		1.16%	-4.2[-7.73,-0.67]
1157 Boero 2000	13	13	-3 (1.31)		1.48%	-3[-5.57,-0.43]
1159 Ames 2001	13	13	-2 (2.38)		0.86%	-2[-6.66,2.66]
1161 DASH 2001 WH	37	37	-2.7 (0.8)		1.84%	-2.7[-4.27,-1.13]
1168 Cuzzola 2001	19	19	0.1 (1.55)		1.31%	0.1[-2.94,3.14]
1169 Seals 2001	17	18	-2 (1.66)		1.24%	-2[-5.25,1.25]
1170 TONE 2001 W	251	220	-1.6 (0.69)		1.91%	-1.6[-2.95,-0.25]
1172 Johnson 2001	46	46	-0.6 (1.46)		1.37%	-0.6[-3.46,2.26]
1181 Beeks 2004	117	117	-1.8 (0.78)		1.85%	-1.8[-3.33,-0.27]
1182 Berge-Landry 2004	48	48	-8 (1.04)		1.67%	-8[-10.04,-5.96]
1183 Gates 2004	12	12	-1.2 (1.46)		1.37%	-1.2[-4.06,1.66]
1191 Melander 2007	39	39	-2.3 (0.86)		1.79%	-2.3[-3.99,-0.61]
1193 Dengel 2007	28	28	-4 (3.59)		0.49%	-4[-11.04,3.04]
1198 He 2009	71	71	-2.2 (0.66)		1.92%	-2.2[-3.49,-0.91]
1199 Meland 2009	23	23	-5 (1.38)		1.43%	-5[-7.7,-2.3]
1201 Nowson 2009	17	18	-3.6 (1.59)		1.29%	-3.6[-6.72,-0.48]
1202 Weir 2010	132	132	-5.7 (0.66)		1.92%	-5.7[-6.99,-4.41]
1204 Carey 2012	211	211	-9.3 (1.1)		1.63%	-9.3[-11.46,-7.14]
1209 Bonfils 2013	12	12	-1 (2.9)		0.67%	-1[-6.68,4.68]

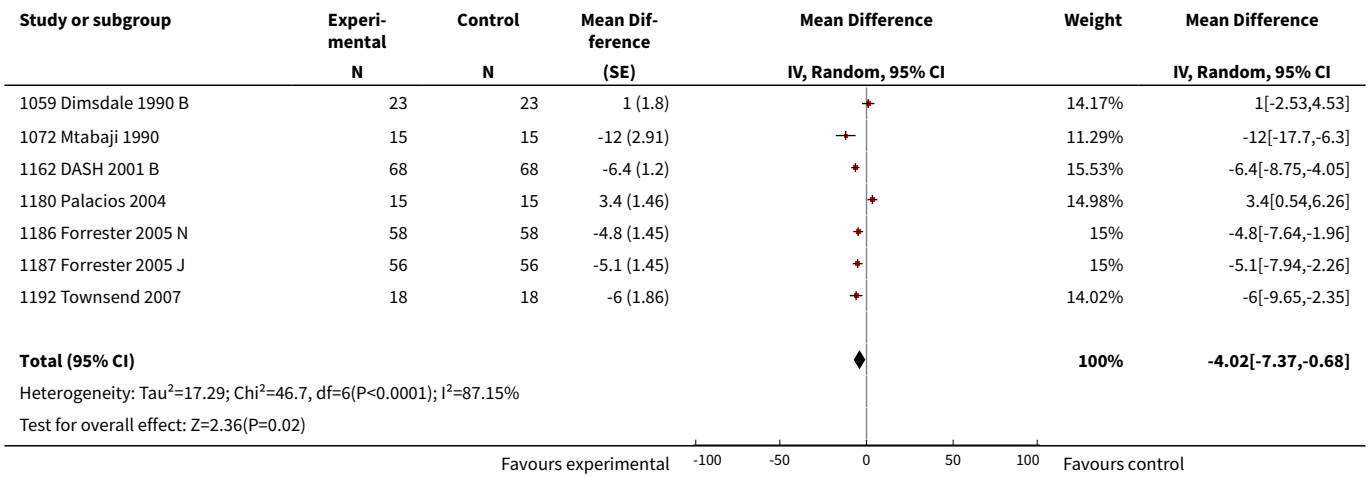
Favours experimental -10 -5 0 5 10 Favours control



Comparison 2. Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Blacks

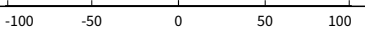
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Black population, normotensive, SBP	7	506	Mean Difference (Random, 95% CI)	-4.02 [-7.37, -0.68]
2 Black population, normotensive, DBP	7	506	Mean Difference (Random, 95% CI)	-2.01 [-4.37, 0.35]
3 Black population, hypertensive, SBP	8	619	Mean Difference (Random, 95% CI)	-6.64 [-9.00, -4.27]
4 Black population, hypertensive, DBP	8	619	Mean Difference (Random, 95% CI)	-2.91 [-4.52, -1.30]

Analysis 2.1. Comparison 2 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Blacks, Outcome 1 Black population, normotensive, SBP.



Analysis 2.2. Comparison 2 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Blacks, Outcome 2 Black population, normotensive, DBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1059 Dimsdale 1990 B	23	23	4.3 (1.4)		15.15%	4.3[1.56,7.04]
1072 Mtabaji 1990	15	15	-6 (2.91)		9.02%	-6[-11.7,-0.3]
1162 DASH 2001 B	68	68	-3.9 (0.8)		17.58%	-3.95[-5.52,-2.38]
1180 Palacios 2004	15	15	-0.1 (1.94)		12.75%	-0.1[-3.9,3.7]
1186 Forrester 2005 N	58	58	-3.2 (1)		16.85%	-3.2[-5.16,-1.24]
1187 Forrester 2005 J	56	56	-2.2 (1.45)		14.93%	-2.2[-5.04,0.64]
1192 Townsend 2007	18	18	-4 (1.72)		13.72%	-4[-7.37,-0.63]
Total (95% CI)					**100%**	**-2.01[-4.37,0.35]**
Heterogeneity: Tau^2=7.6; Chi^2=31.12, df=6(P<0.0001); I^2=80.72%						
Test for overall effect: Z=1.67(P=0.09)						



Favours experimental — Favours control

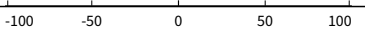
Analysis 2.3. Comparison 2 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Blacks, Outcome 3 Black population, hypertensive, SBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1060 Dimsdale 1990 BH	16	16	-6 (2)		14.74%	-6[-9.92,-2.08]
1122 Dubbert 1995	43	24	-1.4 (3.76)		7.27%	-1.4[-8.77,5.97]
1124 Weir 1995	22	22	-2.8 (6.1)		3.38%	-2.76[-14.72,9.2]
1163 DASH 2001 BH	46	46	-8.6 (1.2)		19.9%	-8.6[-10.95,-6.25]
1171 TONE 2001 B	66	76	-4.9 (1.71)		16.54%	-4.9[-8.25,-1.55]
1188 Swift 2005	40	40	-8 (2.06)		14.38%	-8[-12.04,-3.96]
1198 He 2009	69	69	-4.8 (1.24)		19.63%	-4.8[-7.23,-2.37]
1200 Pimenta 2009	12	12	-22.7 (5.4)		4.16%	-22.7[-33.28,-12.12]
Total (95% CI)					**100%**	**-6.64[-9,-4.27]**
Heterogeneity: Tau^2=5.88; Chi^2=17.62, df=7(P=0.01); I^2=60.27%						
Test for overall effect: Z=5.5(P<0.0001)						

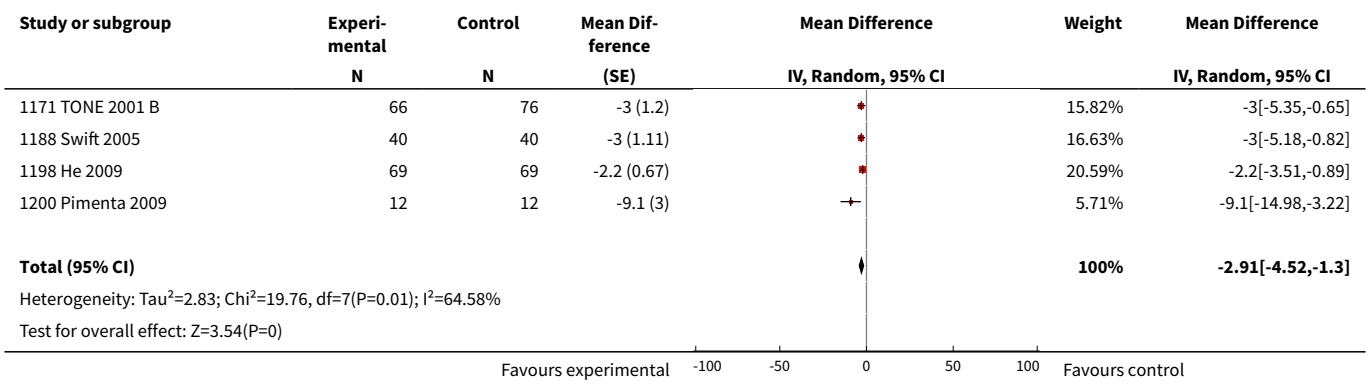
Favours experimental — Favours control

Analysis 2.4. Comparison 2 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Blacks, Outcome 4 Black population, hypertensive, DBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1060 Dimsdale 1990 BH	16	16	2 (2.5)		7.44%	2[-2.9,6.9]
1122 Dubbert 1995	43	24	-0.5 (1.67)		12.02%	-0.5[-3.77,2.77]
1124 Weir 1995	22	22	-1.2 (5.12)		2.33%	-1.2[-11.24,8.84]
1163 DASH 2001 BH	46	46	-5.2 (0.8)		19.46%	-5.25[-6.82,-3.68]



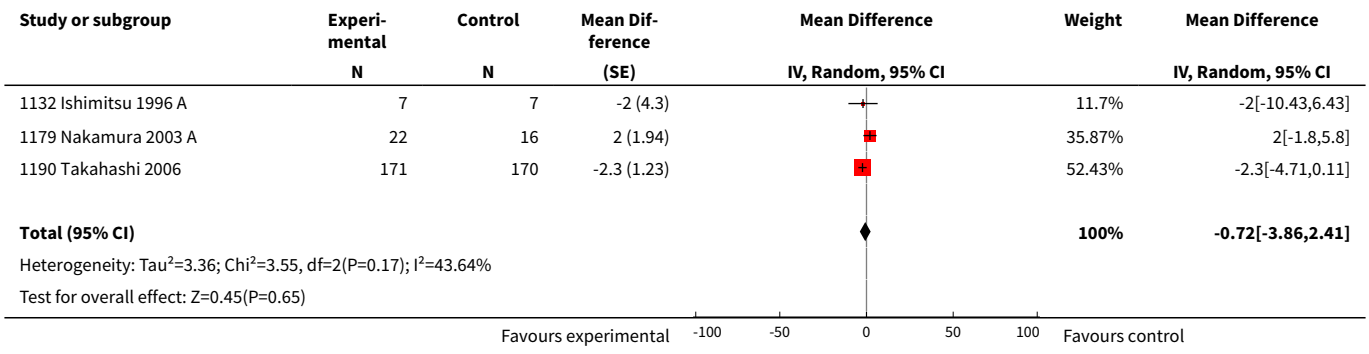
Favours experimental — Favours control



Comparison 3. Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Asians

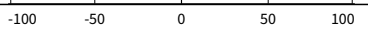
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Asians population normotensive, SBP	3	393	Mean Difference (Random, 95% CI)	-0.72 [-3.86, 2.41]
2 Asian population, normotensive, DBP	3	393	Mean Difference (Random, 95% CI)	-1.63 [-3.35, 0.08]
3 Asian population, hypertensive, SBP	8	501	Mean Difference (Random, 95% CI)	-7.75 [-11.44, -4.07]
4 Asian population, hypertensive, DBP	8	501	Mean Difference (Random, 95% CI)	-2.68 [-4.21, -1.15]

Analysis 3.1. Comparison 3 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Asians, Outcome 1 Asians population normotensive, SBP.



Analysis 3.2. Comparison 3 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Asians, Outcome 2 Asian population, normotensive, DBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1132 Ishimitsu 1996 A	7	7	-2 (3.6)		5.92%	-2[-9.06,5.06]
1179 Nakamura 2003 A	22	16	-5.5 (2.92)		9%	-5.5[-11.22,0.22]
1190 Takahashi 2006	171	170	-1.2 (0.95)		85.07%	-1.2[-3.06,0.66]
Total (95% CI)					**100%**	**-1.63[-3.35,0.08]**
Heterogeneity: Tau^2=0; Chi^2=1.97, df=2(P=0.37); I^2=0%						
Test for overall effect: Z=1.87(P=0.06)						

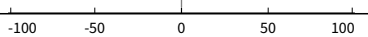


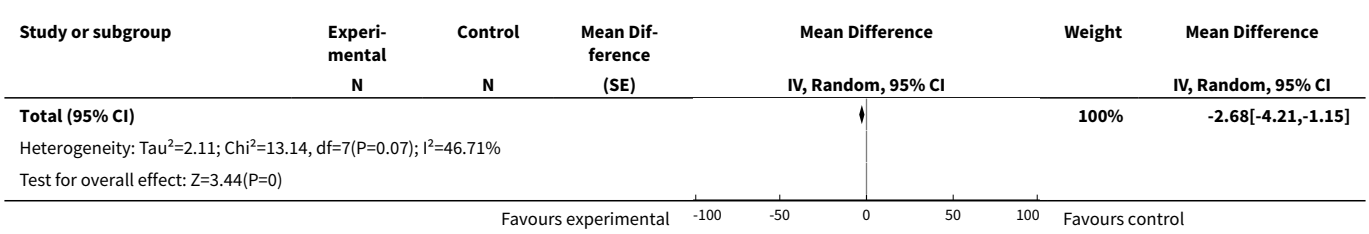
Analysis 3.3. Comparison 3 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Asians, Outcome 3 Asian population, hypertensive, SBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1112 Iwaoka 1994	31	31	-14.3 (2.73)		12.92%	-14.3[-19.65,-8.95]
1132 Ishimitsu 1996 A	23	23	-15.7 (6)		6.32%	-15.7[-27.46,-3.94]
1151 Uzu 1999	70	70	-14 (1.95)		14.91%	-14[-17.82,-10.18]
1158 Suzuki 2000	20	20	-4.1 (1.36)		16.25%	-4.1[-6.77,-1.43]
1179 Nakamura 2003 A	10	16	-5.8 (4.62)		8.57%	-5.8[-14.86,3.26]
1190 Takahashi 2006	53	54	-5.2 (2.38)		13.83%	-5.2[-9.86,-0.54]
1198 He 2009	28	28	-5.4 (1.93)		14.96%	-5.4[-9.18,-1.62]
1220 Gomi 1998	12	12	-1.1 (3)		12.23%	-1.1[-6.98,4.78]
Total (95% CI)					**100%**	**-7.75[-11.44,-4.07]**
Heterogeneity: Tau^2=19.89; Chi^2=31.88, df=7(P<0.0001); I^2=78.04%						
Test for overall effect: Z=4.12(P<0.0001)						

Analysis 3.4. Comparison 3 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Asians, Outcome 4 Asian population, hypertensive, DBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1112 Iwaoka 1994	31	31	-4.6 (1.38)		15.16%	-4.6[-7.3,-1.9]
1132 Ishimitsu 1996 A	23	23	-5.5 (3.2)		4.92%	-5.5[-11.77,0.77]
1151 Uzu 1999	70	70	-5 (1.26)		16.45%	-5[-7.47,-2.53]
1158 Suzuki 2000	20	20	-2.1 (1.42)		14.74%	-2.1[-4.88,0.68]
1179 Nakamura 2003 A	10	16	-5 (3.47)		4.3%	-5[-11.8,1.8]
1190 Takahashi 2006	53	54	0.1 (1.68)		12.33%	0.1[-3.19,3.39]
1198 He 2009	28	28	-2.2 (1.04)		19.06%	-2.2[-4.24,-0.16]
1220 Gomi 1998	12	12	0.3 (1.6)		13.03%	0.3[-2.84,3.44]

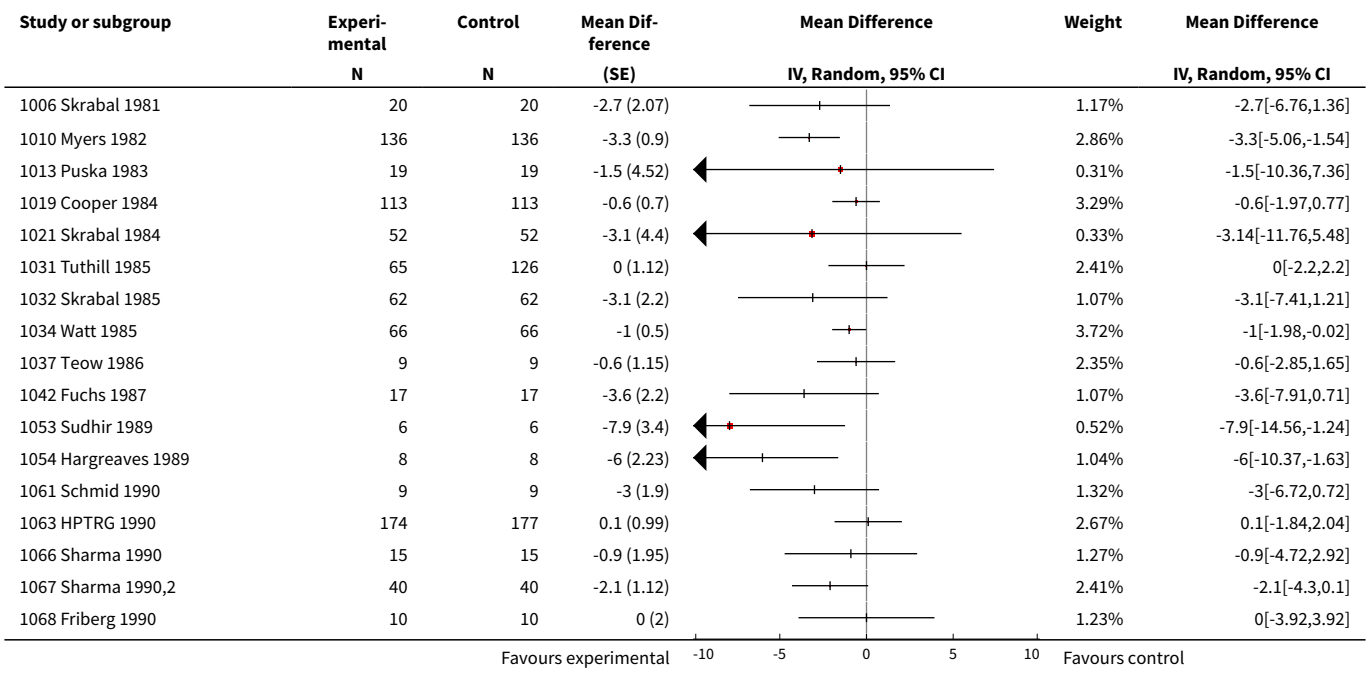


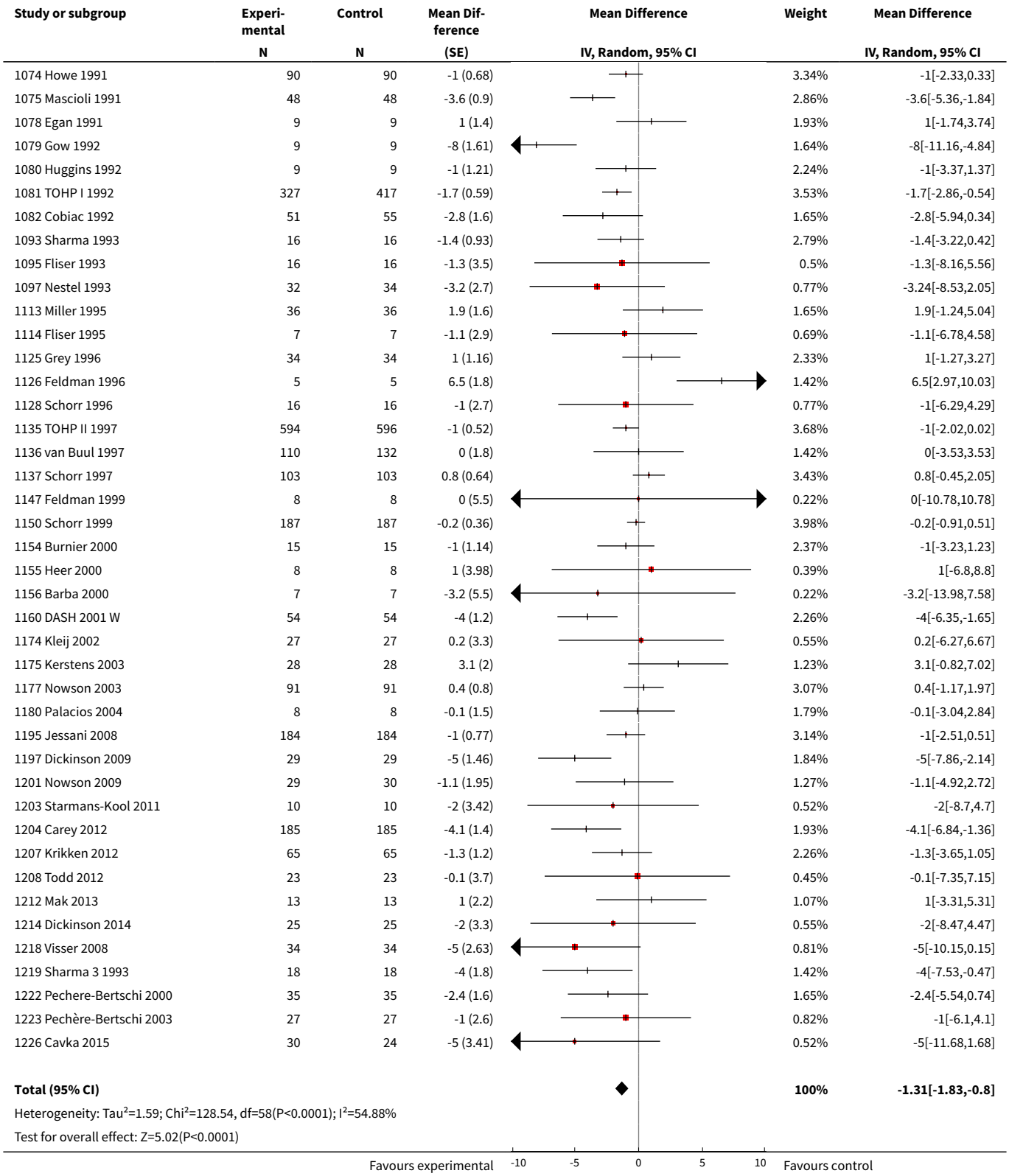


Comparison 4. Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Whites, subgroup analysis

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 White population, normotensive, SBP	59	7125	Mean Difference (Random, 95% CI)	-1.31 [-1.83, -0.80]
2 White population, normotensive, DBP	61		Mean Difference (Random, 95% CI)	-0.36 [-0.79, 0.07]
3 White population, hypertensive, SBP	63		Mean Difference (Random, 95% CI)	-5.02 [-4.00, -4.05]
4 White population, hypertensive, DBP	64		Mean Difference (Random, 95% CI)	-2.78 [-3.42, -2.14]

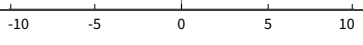
Analysis 4.1. Comparison 4 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Whites, subgroup analysis, Outcome 1 White population, normotensive, SBP.



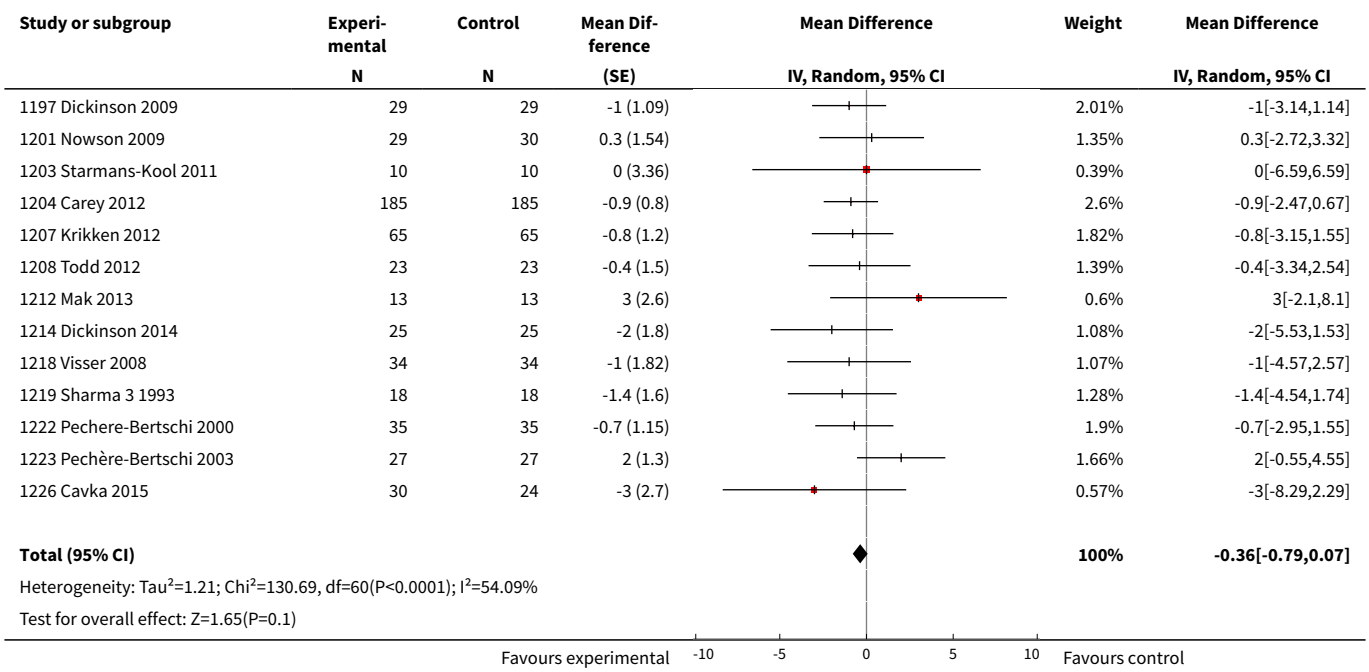


Analysis 4.2. Comparison 4 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Whites, subgroup analysis, Outcome 2 White population, normotensive, DBP.

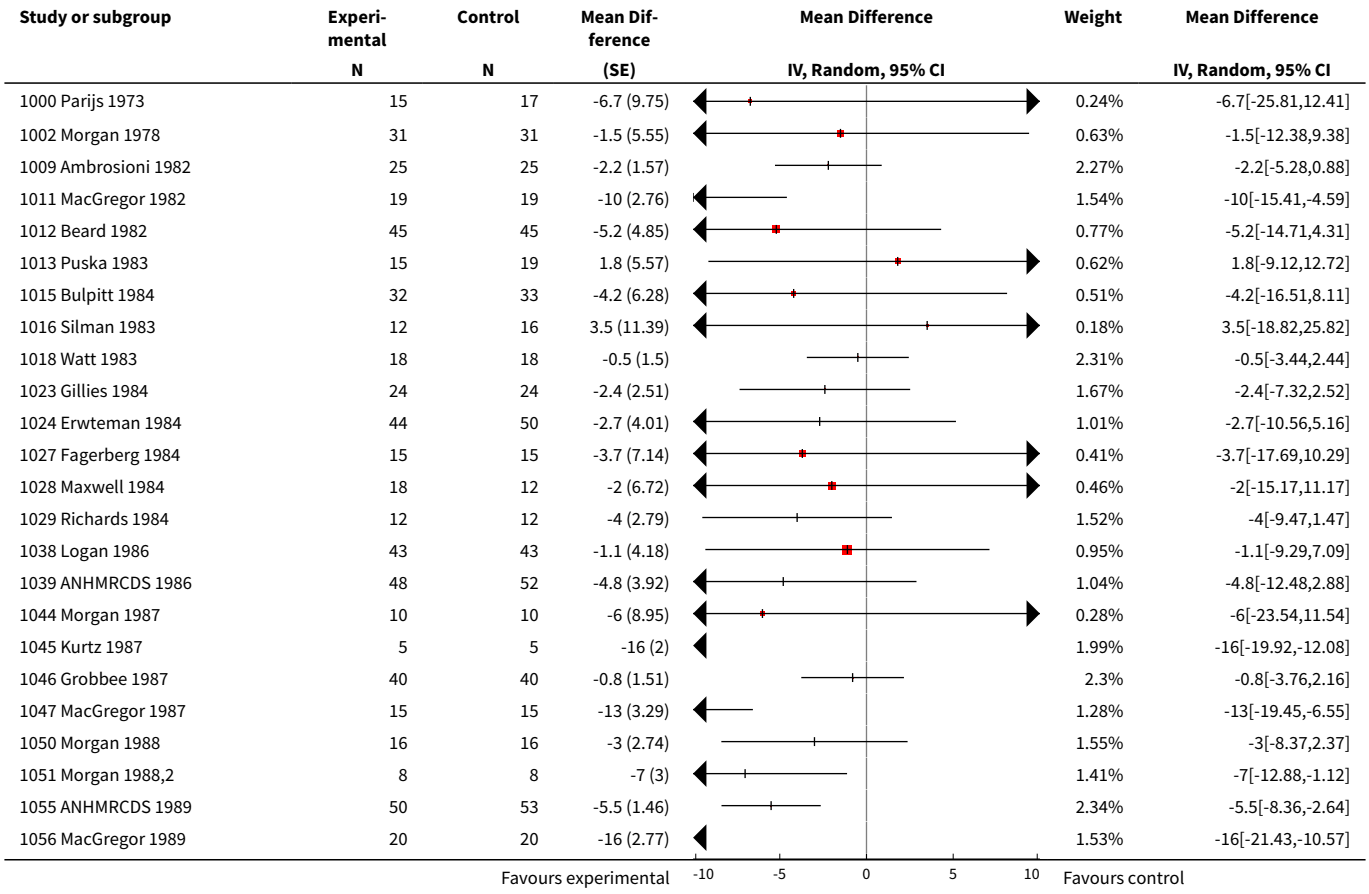
Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1006 Skrabal 1981	20	20	-3 (1.46)		1.44%	-3[-5.86,-0.14]
1010 Myers 1982	136	136	-2.7 (0.8)		2.6%	-2.7[-4.27,-1.13]
1013 Puska 1983	19	19	-2.1 (2.77)		0.54%	-2.1[-7.53,3.33]
1019 Cooper 1984	113	113	-1.4 (1)		2.18%	-1.4[-3.36,0.56]
1021 Skrabal 1984	52	52	-1.8 (2.64)		0.59%	-1.85[-7.02,3.32]
1031 Tuthill 1985	65	126	0 (1.33)		1.62%	0[-2.61,2.61]
1032 Skrabal 1985	62	62	-1.5 (0.9)		2.39%	-1.5[-3.26,0.26]
1034 Watt 1985	66	66	1.3 (0.6)		3.07%	1.3[0.12,2.48]
1037 Teow 1986	9	9	-2.7 (1.41)		1.51%	-2.7[-5.46,0.06]
1042 Fuchs 1987	17	17	1.9 (1)		2.18%	1.9[-0.06,3.86]
1053 Sudhir 1989	6	6	-5 (2.1)		0.86%	-5[-9.12,-0.88]
1054 Hargreaves 1989	8	8	-3 (1.98)		0.94%	-3[-6.88,0.88]
1061 Schmid 1990	9	9	3 (1.63)		1.25%	3[-0.19,6.19]
1063 HPTRG 1990	174	177	0.2 (0.71)		2.81%	0.2[-1.19,1.59]
1066 Sharma 1990	0	0	-3.7 (1.81)		1.07%	-3.7[-7.25,-0.15]
1067 Sharma 1990,2	40	40	-3.1 (1.04)		2.1%	-3.1[-5.14,-1.06]
1068 Friberg 1990	10	10	-1 (2)		0.92%	-1[-4.92,2.92]
1074 Howe 1991	90	90	-0.6 (0.71)		2.81%	-0.56[-1.95,0.83]
1075 Mascioli 1991	48	48	-2.3 (0.8)		2.6%	-2.3[-3.87,-0.73]
1078 Egan 1991	9	9	0.6 (1.4)		1.52%	0.6[-2.14,3.34]
1079 Gow 1992	9	9	-3 (2.22)		0.79%	-3[-7.35,1.35]
1080 Huggins 1992	9	9	-2 (1.91)		0.99%	-2[-5.74,1.74]
1081 TOHP I 1992	327	417	-0.8 (0.42)		3.48%	-0.8[-1.62,0.02]
1082 Cobiac 1992	51	55	-1 (1.8)		1.08%	-1[-4.53,2.53]
1093 Sharma 1993	16	16	-0.5 (1.22)		1.79%	-0.5[-2.89,1.89]
1095 Fliser 1993	16	16	-0.9 (2.2)		0.8%	-0.9[-5.21,3.41]
1097 Nestel 1993	32	34	-1.4 (2)		0.92%	-1.37[-5.29,2.55]
1113 Miller 1995	36	36	-0.1 (1.47)		1.43%	-0.1[-2.98,2.78]
1114 Fliser 1995	7	7	-0.7 (1.8)		1.08%	-0.7[-4.23,2.83]
1125 Grey 1996	34	34	1 (0.87)		2.45%	1[-0.71,2.71]
1126 Feldman 1996	5	5	4.2 (1.13)		1.94%	4.2[1.99,6.41]
1128 Schorr 1996	16	16	0 (1.73)		1.15%	0[-3.39,3.39]
1135 TOHP II 1997	594	596	-0.5 (0.4)		3.52%	-0.5[-1.28,0.28]
1136 van Buul 1997	110	132	0 (1.16)		1.89%	0[-2.27,2.27]
1137 Schorr 1997	103	103	0.4 (0.64)		2.98%	0.4[-0.85,1.65]
1142 Knuist 1998	149	145	0 (1.16)		1.89%	0[-2.27,2.27]
1147 Feldman 1999	8	8	0 (3.6)		0.34%	0[-7.06,7.06]
1150 Schorr 1999	187	187	0.3 (0.36)		3.6%	0.3[-0.41,1.01]
1154 Burnier 2000	15	15	5 (1.14)		1.92%	5[2.77,7.23]
1155 Heer 2000	8	8	-1 (3.37)		0.38%	-1[-7.61,5.61]
1156 Barba 2000	7	7	-2.1 (3.5)		0.36%	-2.1[-8.96,4.76]
1160 DASH 2001 W	54	54	-1.4 (0.8)		2.6%	-1.4[-2.97,0.17]
1174 Kleij 2002	27	27	0.1 (2.1)		0.86%	0.12[-4,4.24]
1175 Kerstens 2003	28	28	2 (1.3)		1.66%	2[-0.55,4.55]
1177 Nowson 2003	91	91	0 (0.6)		3.07%	0[-1.18,1.18]
1180 Palacios 2004	8	8	4.2 (1.71)		1.17%	4.2[0.85,7.55]
1185 Zanchi 2004	9	9	0 (2.95)		0.49%	0[-5.78,5.78]
1195 Jessani 2008	184	184	-1 (0.77)		2.67%	-1[-2.51,0.51]



Favours experimental | Favours control



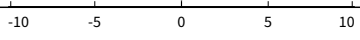
Analysis 4.3. Comparison 4 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Whites, subgroup analysis, Outcome 3 White population, hypertensive, SBP.



Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1062 Schmid 1990 H	9	9	-6 (3.13)		1.35%	-6[-12.13,0.13]
1069 Del Rio 1990	15	15	-3.4 (2.02)		1.97%	-3.4[-7.36,0.56]
1070 Parker 1990	31	28	1.3 (2.15)		1.89%	1.3[-2.91,5.51]
1077 Singer 1991	21	21	-9 (3)		1.41%	-9[-14.88,-3.12]
1078 Egan 1991	18	18	-2.7 (1.4)		2.38%	-2.7[-5.44,0.04]
1084 Benetos 1992	20	20	-6.5 (1.88)		2.06%	-6.5[-10.18,-2.82]
1085 Sciarrone 1992	46	45	-5.8 (4.07)		0.99%	-5.8[-13.78,2.18]
1100 Fotherby 1993	17	17	-8 (3.5)		1.19%	-8[-14.86,-1.14]
1101 Redon-Mas 1993	235	183	1 (1.94)		2.02%	1[-2.8,4.8]
1102 Ruilope 1993	10	9	-4 (7.95)		0.34%	-4[-19.58,11.58]
1103 Del Rio 1993	30	30	-1.4 (1.8)		2.11%	-1.4[-4.93,2.13]
1109 Zoccali 1994	15	15	-14 (2.46)		1.7%	-14[-18.82,-9.18]
1110 Jula 1994	38	38	-6.7 (3.92)		1.04%	-6.7[-14.38,0.98]
1111 Howe 1994	14	14	-4.2 (2.91)		1.46%	-4.2[-9.9,1.5]
1117 Arrol 1995	89	92	-0.4 (3.37)		1.25%	-0.4[-7.01,6.21]
1122 Dubbert 1995	38	17	-1.4 (3.76)		1.09%	-1.4[-8.77,5.97]
1127 Feldman 1996 H	8	8	2.6 (2.9)		1.46%	2.6[-3.08,8.28]
1129 Bellini 1996	43	43	-3.9 (1.8)		2.11%	-3.9[-7.43,-0.37]
1134 Cappuccio 1997	47	47	-7.8 (1.8)		2.11%	-7.8[-11.33,-4.27]
1138 McCarron 1997	99	99	-4.9 (1.23)		2.48%	-4.9[-7.31,-2.49]
1139 Meland 1997	16	16	-4 (2.47)		1.7%	-4[-8.84,0.84]
1145 Wing 1998	17	17	-7 (0.79)		2.73%	-7[-8.55,-5.45]
1161 DASH 2001 WH	37	37	-6.6 (1.2)		2.5%	-6.6[-8.95,-4.25]
1169 Seals 2001	17	18	-8 (2.61)		1.62%	-8[-13.12,-2.88]
1170 TONE 2001 W	251	220	-4 (1.01)		2.61%	-4[-5.98,-2.02]
1172 Johnson 2001	46	46	-4.5 (2.08)		1.93%	-4.5[-8.58,-0.42]
1181 Beeks 2004	117	117	1.2 (1.44)		2.35%	1.2[-1.62,4.02]
1183 Gates 2004	12	12	-3 (1.84)		2.09%	-3[-6.61,0.61]
1191 Melander 2007	39	39	-6 (1.18)		2.51%	-6[-8.31,-3.69]
1193 Dengel 2007	28	28	-10 (3.64)		1.14%	-10[-17.13,-2.87]
1198 He 2009	71	71	-4.8 (1.24)		2.48%	-4.8[-7.23,-2.37]
1199 Meland 2009	23	23	-5 (3.79)		1.08%	-5[-12.43,2.43]
1201 Nowson 2009	17	18	-5.5 (2.72)		1.56%	-5.5[-10.83,-0.17]
1202 Weir 2010	132	132	-9.4 (0.97)		2.63%	-9.4[-11.3,-7.5]
1204 Carey 2012	185	185	-4.1 (1.4)		2.38%	-4.1[-6.84,-1.36]
1213 Mallamaci 2013	32	32	-8 (2.4)		1.74%	-8[-12.7,-3.3]
1216 Barros 2015	19	16	-6.4 (3.81)		1.07%	-6.43[-13.9,1.04]
1217 Markota 2015	76	74	-4.9 (1.47)		2.33%	-4.9[-7.78,-2.02]
1225 Gijsbers 2015	36	36	-7.5 (1.53)		2.29%	-7.5[-10.5,-4.5]
Total (95% CI)					**100%**	**-5.02[-6,-4.05]**

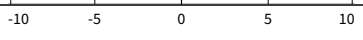
Heterogeneity: Tau^2=8.4; Chi^2=194.41, df=62(P<0.0001); I^2=68.11%

Test for overall effect: Z=10.12(P<0.0001)

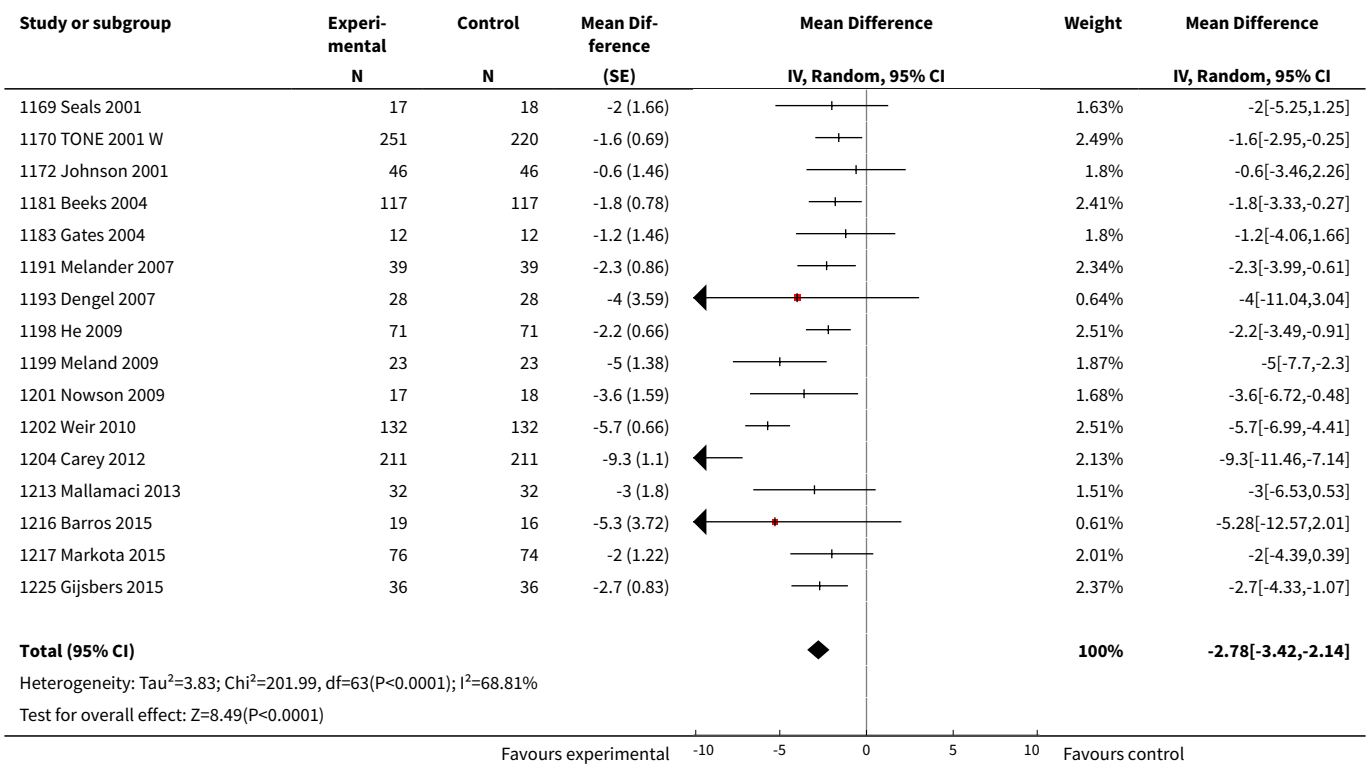


Analysis 4.4. Comparison 4 Effect of salt reduction on systolic blood pressure (SBP) and diastolic blood pressure (DBP) in Whites, subgroup analysis, Outcome 4 White population, hypertensive, DBP.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Random, 95% CI	Weight	Mean Difference IV, Random, 95% CI
1000 Parijs 1973	15	17	3.2 (5.91)		0.28%	3.2[-8.38,14.78]
1002 Morgan 1978	31	31	-7 (2.77)		0.93%	-7[-12.43,-1.57]
1007 Morgan 1981	12	12	-6 (2.3)		1.17%	-6[-10.51,-1.49]
1009 Ambrosioni 1982	25	25	-0.4 (1.23)		2%	-0.4[-2.81,2.01]
1011 MacGregor 1982	19	19	-5 (1.76)		1.55%	-5[-8.45,-1.55]
1012 Beard 1982	45	45	-3.4 (2.92)		0.87%	-3.4[-9.12,2.32]
1013 Puska 1983	15	19	0.5 (3.07)		0.81%	0.5[-5.52,6.52]
1015 Bulpitt 1984	32	33	-3.4 (3)		0.83%	-3.4[-9.28,2.48]
1016 Silman 1983	12	16	0.5 (4.91)		0.38%	0.5[-9.12,10.12]
1018 Watt 1983	18	18	-0.3 (0.8)		2.4%	-0.3[-1.87,1.27]
1023 Gillies 1984	24	24	-2.6 (2.21)		1.23%	-2.6[-6.93,1.73]
1024 Erwteman 1984	44	50	-2.5 (2.46)		1.08%	-2.5[-7.32,2.32]
1027 Fagerberg 1984	15	15	-3.1 (4.06)		0.53%	-3.1[-11.06,4.86]
1028 Maxwell 1984	18	12	2 (3.84)		0.58%	2[-5.53,9.53]
1029 Richards 1984	12	12	-3 (2.26)		1.2%	-3[-7.43,1.43]
1038 Logan 1986	43	43	0 (2.34)		1.15%	0[-4.59,4.59]
1039 ANHMRCDS 1986	48	52	-4.2 (1.88)		1.45%	-4.2[-7.88,-0.52]
1044 Morgan 1987	10	10	-4 (4.3)		0.48%	-4[-12.43,4.43]
1045 Kurtz 1987	5	5	-8 (2)		1.37%	-8[-11.92,-4.08]
1046 Grobbee 1987	40	40	-0.8 (1.44)		1.81%	-0.8[-3.62,2.02]
1047 MacGregor 1987	15	15	-9 (3.05)		0.82%	-9[-14.98,-3.02]
1050 Morgan 1988	16	16	-4 (2.19)		1.24%	-4[-8.29,0.29]
1051 Morgan 1988,2	8	8	-6 (3)		0.83%	-6[-11.88,-0.12]
1055 ANHMRCDS 1989	50	53	-2.8 (0.84)		2.36%	-2.8[-4.45,-1.15]
1056 MacGregor 1989	20	20	-9 (1.79)		1.52%	-9[-12.51,-5.49]
1062 Schmid 1990 H	9	9	-1.9 (2.06)		1.33%	-1.9[-5.94,2.14]
1069 Del Rio 1990	15	15	-1.1 (1.78)		1.53%	-1.1[-4.59,2.39]
1070 Parker 1990	31	28	0.6 (0.9)		2.31%	0.6[-1.16,2.36]
1077 Singer 1991	21	21	-3 (2)		1.37%	-3[-6.92,0.92]
1078 Egan 1991	18	18	-1.7 (1.4)		1.85%	-1.7[-4.44,1.04]
1084 Benetos 1992	20	20	-3.7 (1.28)		1.96%	-3.7[-6.21,-1.19]
1085 Sciarrone 1992	46	45	-0.4 (2.28)		1.19%	-0.4[-4.87,4.07]
1100 Fotherby 1993	17	17	1 (2)		1.37%	1[-2.92,4.92]
1101 Redon-Mas 1993	235	183	1.9 (0.94)		2.27%	1.9[0.06,3.74]
1102 Ruilope 1993	10	9	-4 (2.69)		0.97%	-4[-9.27,1.27]
1103 Del Rio 1993	30	30	-0.5 (1.25)		1.99%	-0.5[-2.95,1.95]
1109 Zoccali 1994	15	15	-8 (1.4)		1.85%	-8[-10.74,-5.26]
1110 Jula 1994	38	38	-3.8 (1.73)		1.57%	-3.8[-7.19,-0.41]
1111 Howe 1994	14	14	-1.5 (1.94)		1.41%	-1.5[-5.3,2.3]
1117 Arrol 1995	92	89	-1.2 (2.11)		1.29%	-1.2[-5.34,2.94]
1122 Dubbert 1995	38	17	-0.5 (1.67)		1.62%	-0.5[-3.77,2.77]
1127 Feldman 1996 H	8	8	1.6 (1.8)		1.51%	1.6[-1.93,5.13]
1129 Bellini 1996	43	43	-4.9 (0.72)		2.46%	-4.9[-6.31,-3.49]
1134 Cappuccio 1997	47	47	-3.3 (1)		2.22%	-3.3[-5.26,-1.34]
1138 McCarron 1997	99	99	-2.9 (0.81)		2.39%	-2.9[-4.49,-1.31]
1139 Meland 1997	16	16	-3 (1.36)		1.89%	-3[-5.67,-0.33]
1145 Wing 1998	17	17	-4 (1.15)		2.08%	-4[-6.25,-1.75]
1161 DASH 2001 WH	37	37	-2.7 (0.8)		2.4%	-2.7[-4.27,-1.13]



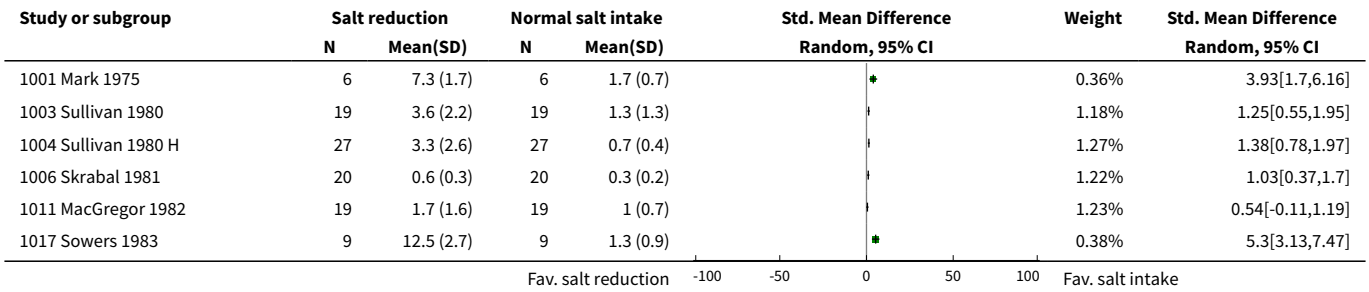
Favours experimental | Favours control



Comparison 5. Effect of salt reduction on hormones

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Renin (ng/mL/hour)	88	5498	Std. Mean Difference (IV, Random, 95% CI)	1.22 [1.07, 1.37]
2 Aldosterone (pg/mL)	65	4884	Mean Difference (IV, Random, 95% CI)	97.81 [82.56, 113.05]
3 Noradrenaline (pg/mL)	36	1736	Mean Difference (IV, Random, 95% CI)	63.56 [42.66, 84.46]
4 Adrenaline (pg/mL)	16	662	Mean Difference (IV, Random, 95% CI)	7.55 [0.85, 14.26]

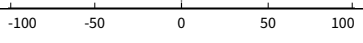
Analysis 5.1. Comparison 5 Effect of salt reduction on hormones, Outcome 1 Renin (ng/mL/hour).



Study or subgroup	Salt reduction		Normal salt intake		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
1018 Watt 1983	18	2.9 (3)	18	1.3 (3)		1.21%	0.54[-0.13,1.2]
1021 Skrabal 1984	52	0.8 (0.4)	52	0.3 (0.2)		1.4%	1.51[1.07,1.95]
1025 Koolen 1984	20	3.2 (1.3)	20	1.9 (0.9)		1.21%	1.12[0.45,1.79]
1029 Richards 1984	12	2.1 (1.5)	12	1.7 (1.1)		1.1%	0.3[-0.51,1.1]
1030 Resnick 1985	12	6 (5.2)	12	1.8 (2)		1.05%	1.03[0.17,1.9]
1036 Richards 1986	8	130 (56.6)	8	18 (17)		0.67%	2.54[1.13,3.94]
1040 El Ashry 1987	26	7 (6)	26	2.2 (1.8)		1.28%	1.07[0.49,1.65]
1046 Grobbee 1987	40	17 (8.9)	40	14.5 (8.2)		1.4%	0.29[-0.15,0.73]
1048 Lawton 1988	9	3.5 (1.8)	9	0.5 (0.4)		0.78%	2.2[0.97,3.43]
1049 Lawton 1988 H	13	3.2 (1.1)	13	0.3 (0.1)		0.72%	3.66[2.33,4.98]
1050 Morgan 1988	16	1.4 (1.3)	16	0.8 (1.1)		1.18%	0.47[-0.23,1.18]
1052 Shore 1988	6	1 (0.8)	6	0.4 (0.2)		0.78%	0.99[-0.24,2.22]
1053 Sudhir 1989	6	1 (0.2)	6	0.7 (0.2)		0.71%	1.47[0.13,2.81]
1054 Hargreaves 1989	8	3.4 (0.7)	8	1.9 (0.7)		0.78%	1.85[0.62,3.08]
1056 MacGregor 1989	20	2.3 (1.8)	20	1.4 (1.3)		1.24%	0.56[-0.08,1.19]
1057 Dimsdale 1990 W	16	10.2 (6.8)	16	1.8 (2)		1.09%	1.63[0.82,2.45]
1058 Dimsdale 1990 WH	19	6.9 (3.5)	19	3 (3.1)		1.19%	1.17[0.47,1.86]
1059 Dimsdale 1990 B	17	10.9 (7)	17	2.8 (2.5)		1.12%	1.5[0.73,2.28]
1060 Dimsdale 1990 BH	23	10.7 (5.8)	23	2.6 (2.9)		1.19%	1.75[1.06,2.44]
1064 Bruun 1990	12	37.5 (20.4)	12	10.4 (9)		0.98%	1.66[0.71,2.61]
1065 Bruun 1990 H	10	70.8 (29.1)	10	20.8 (12.7)		0.83%	2.13[0.99,3.28]
1068 Friberg 1990	10	0.7 (0.3)	10	0.5 (0.3)		0.98%	1.07[0.12,2.02]
1076 Carney 1991	11	3.9 (3.3)	11	1.6 (2)		1.04%	0.81[-0.07,1.68]
1077 Singer 1991	21	4.2 (3.1)	21	2.8 (2.4)		1.26%	0.48[-0.14,1.09]
1078 Egan 1991	27	3.4 (2)	27	1.4 (1)		1.28%	1.25[0.67,1.84]
1079 Gow 1992	9	1.9 (0.8)	9	0.7 (0.4)		0.81%	1.99[0.81,3.17]
1080 Huggins 1992	9	8.6 (1.8)	9	6.1 (3.3)		0.95%	0.9[-0.09,1.88]
1084 Benetos 1992	20	26.5 (13)	20	24.9 (16.1)		1.25%	0.11[-0.51,0.73]
1088 Ruppert 1993	163	8.2 (5.1)	163	1.2 (0.8)		1.51%	1.91[1.65,2.18]
1091 Burnier 1993	23	0.9 (0.4)	23	0.4 (0.2)		1.23%	1.4[0.75,2.05]
1094 Sharma 1993,2	15	5.9 (4)	15	1.7 (1.6)		1.1%	1.34[0.54,2.14]
1099 Donovan 1993	8	6 (2.6)	8	1.5 (0.6)		0.71%	2.3[0.96,3.65]
1100 Fotherby 1993	17	1.2 (0.8)	17	0.9 (0.6)		1.2%	0.51[-0.18,1.19]
1103 Del Rio 1993	30	3.1 (1.7)	30	1.3 (0.7)		1.3%	1.36[0.8,1.93]
1109 Zoccali 1994	15	5.3 (3.5)	15	2.5 (2.7)		1.14%	0.87[0.12,1.63]
1114 Fliser 1995	7	1.2 (0.5)	7	0.3 (0.1)		0.64%	2.34[0.87,3.8]
1116 Stein 1995	7	4 (2.4)	7	1 (0.3)		0.76%	1.62[0.36,2.88]
1118 Draaijer 1995	10	3.8 (1.9)	10	0.5 (0.4)		0.81%	2.27[1.1,3.45]
1119 Overlack 1995	45	2.1 (1.1)	45	0.2 (0.2)		1.31%	2.38[1.84,2.93]
1128 Schorr 1996	16	0.9 (1.5)	16	0.7 (0.9)		1.19%	0.18[-0.51,0.88]
1129 Bellini 1996	53	2.5 (0.7)	53	1.6 (0.5)		1.4%	1.55[1.11,1.98]
1131 Ferri 1996	61	2.2 (0.8)	61	0.9 (0.5)		1.4%	1.89[1.47,2.32]
1132 Ishimitsu 1996 A	30	2.6 (2.2)	30	0.4 (0.4)		1.29%	1.41[0.84,1.98]
1144 Foo 1998	18	20.1 (7.6)	18	11.4 (8)		1.18%	1.09[0.38,1.8]
1145 Wing 1998	17	4.1 (4.1)	17	3.3 (3.3)		1.21%	0.21[-0.46,0.88]
1146 Herlitz 1998	6	19.6 (37.7)	6	1.7 (0.7)		0.82%	0.62[-0.55,1.79]
1148 Damasceno 1999	39	2.8 (5.6)	39	1.1 (3.5)		1.39%	0.35[-0.1,0.8]
1149 Davrath 1999	8	1.7 (2.3)	8	0.9 (2.3)		0.95%	0.31[-0.68,1.3]
1150 Schorr 1999	187	3 (2.6)	187	0.7 (0.9)		1.53%	1.22[1,1.44]
1152 Chiolero 2000	38	0.8 (0.7)	38	0.4 (0.4)		1.38%	0.62[0.16,1.08]
1153 Bruun 2000	42	57 (28)	42	19 (13)		1.35%	1.72[1.22,2.23]
1154 Burnier 2000	15	1.8 (1.4)	15	0.6 (0.4)		1.11%	1.17[0.38,1.95]

Fav. salt reduction -100 -50 0 50 100 Fav. salt intake

Study or subgroup	Salt reduction N	Salt reduction Mean(SD)	Normal salt intake N	Normal salt intake Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1168 Cuzzola 2001	19	3.7 (2.6)	19	2.9 (2.2)		1.23%	0.36[-0.28,1]
1173 Manunta 2001	20	4 (2.3)	20	2.8 (2.3)		1.24%	0.51[-0.12,1.14]
1174 Kleij 2002	27	0.8 (0.2)	27	0.3 (0.1)		1.1%	3.06[2.26,3.86]
1175 Kerstens 2003	28	1.5 (1.3)	28	0.5 (0.4)		1.3%	1.13[0.57,1.7]
1176 Dishy 2003	25	3 (2.5)	25	1 (1)		1.27%	1.03[0.44,1.63]
1177 Nowson 2003	85	2 (2.4)	85	1.4 (1.6)		1.49%	0.29[-0.01,0.59]
1178 Perry 2003	15	25 (10.4)	15	13.4 (7.3)		1.11%	1.25[0.46,2.05]
1180 Palacios 2004	23	1 (1)	23	0.6 (0.6)		1.28%	0.48[-0.11,1.06]
1183 Gates 2004	12	0.7 (0.3)	12	0.4 (0.2)		1.05%	1.01[0.15,1.87]
1185 Zanchi 2004	10	1 (0.4)	10	0.3 (0.2)		0.89%	1.73[0.67,2.8]
1188 Swift 2005	40	0.2 (0.2)	40	0.1 (0.1)		1.38%	0.78[0.32,1.23]
1191 Melander 2007	39	32.4 (18.4)	39	17.4 (11.2)		1.37%	0.98[0.5,1.45]
1192 Townsend 2007	18	33 (21)	18	16 (8.8)		1.18%	1.03[0.33,1.73]
1193 Dengel 2007	28	1.9 (0.8)	28	0.3 (0.9)		1.23%	1.96[1.31,2.6]
1194 Tzemos 2008	16	0.6 (0.1)	16	0.4 (0.1)		1.05%	1.95[1.09,2.81]
1196 Paulsen 2009	22	6 (3)	22	5 (3.5)		1.27%	0.3[-0.29,0.9]
1198 He 2009	169	0.2 (0.3)	169	0.1 (0.2)		1.53%	0.43[0.22,0.65]
1200 Pimenta 2009	12	2.7 (11.3)	12	0.6 (0.5)		1.1%	0.25[-0.55,1.06]
1204 Carey 2012	185	5.8 (3.6)	185	0.5 (0.3)		1.51%	2.08[1.82,2.33]
1205 Carey 2012 Hyperpath	221	2.7 (2.9)	221	0.6 (0.7)		1.54%	1.01[0.81,1.21]
1206 Graffe 2012	21	26.4 (33)	21	7.7 (4.6)		1.24%	0.78[0.15,1.41]
1207 Krikken 2012	65	5.7 (3)	65	2.1 (1.3)		1.43%	1.53[1.13,1.92]
1213 Mallamaci 2013	32	2.5 (3.2)	32	0.9 (0.5)		1.35%	0.7[0.2,1.21]
1214 Dickinson 2014	25	14.7 (9.7)	25	14.7 (7.4)		1.31%	0[-0.55,0.55]
1218 Visser 2008	34	6.2 (2.7)	34	2.8 (1.4)		1.31%	1.57[1.03,2.12]
1220 Gomi 1998	12	1.9 (1)	12	0.8 (0.5)		1.03%	1.26[0.37,2.15]
1221 Facchini 1999	19	2.8 (0.4)	19	0.4 (0.1)		0.42%	8.11[6.08,10.14]
1222 Pechere-Bertschi 2000	35	0.9 (0.7)	35	0.2 (0.2)		1.33%	1.41[0.88,1.93]
1223 Pechère-Bertschi 2003	27	2.8 (1.6)	27	1 (0.5)		1.26%	1.53[0.91,2.14]
1224 Ho 2007	25	24 (10)	25	7 (5)		1.18%	2.12[1.41,2.82]
Total ***	**2749**		**2749**			**100%**	**1.22[1.07,1.37]**
Heterogeneity: Tau²=0.38; Chi²=499.82, df=87(P<0.0001); I²=82.59%							
Test for overall effect: Z=15.68(P<0.0001)							



Analysis 5.2. Comparison 5 Effect of salt reduction on hormones, Outcome 2 Aldosterone (pg/mL).

Study or subgroup	Salt reduction N	Salt reduction Mean(SD)	Normal salt intake N	Normal salt intake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1003 Sullivan 1980	27	167 (145)	27	57 (62.4)		1.43%	110[50.48,169.52]
1004 Sullivan 1980 H	19	164 (113.3)	19	55 (30.5)		1.5%	109[56.24,161.76]
1006 Skrabal 1981	21	159 (82)	21	53 (61.4)		1.59%	106[62.17,149.83]
1011 MacGregor 1982	19	140.6 (81.7)	19	78.9 (50.3)		1.6%	61.63[18.5,104.76]
1017 Sowers 1983	9	237 (60)	9	45 (12)		1.63%	192[152.02,231.98]
1021 Skrabal 1984	52	228 (162)	52	84 (40)		1.58%	144[98.65,189.35]
1025 Koolen 1984	20	194.2 (80.5)	20	100.7 (64.4)		1.58%	93.5[48.32,138.68]
1029 Richards 1984	12	148.1 (27.5)	12	107.8 (36.2)		1.74%	40.36[14.64,66.08]
1036 Richards 1986	8	300 (198)	8	71 (39.6)		0.72%	229[89.08,368.92]

Study or subgroup	Salt reduction N	Salt reduction Mean(SD)	Normal salt intake N	Normal salt intake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1052 Shore 1988	6	149.3 (58)	6	100.3 (35.8)		1.49%	49.05[-5.47,103.57]
1054 Hargreaves 1989	8	281.1 (146.8)	8	99.8 (36.7)		0.98%	181.28[76.43,286.13]
1056 MacGregor 1989	20	195 (90.3)	20	107.4 (51.6)		1.58%	87.58[42.02,133.14]
1064 Bruun 1990	10	129.7 (86.5)	10	39.6 (14.4)		1.49%	90.1[35.75,144.45]
1065 Bruun 1990 H	12	108.1 (72.1)	12	21.6 (14.4)		1.61%	86.5[44.91,128.09]
1073 Sharma 1991	23	353 (146)	23	72 (115)		1.26%	281[205.05,356.95]
1077 Singer 1991	21	214.8 (82.6)	21	170.5 (76)		1.55%	44.33[-3.66,92.32]
1079 Gow 1992	9	270.7 (206.5)	9	106.3 (78.9)		0.69%	164.34[19.9,308.78]
1080 Huggins 1992	9	317 (186)	9	223 (153)		0.62%	94[-63.35,251.35]
1084 Benetos 1992	20	96.9 (63.5)	20	84.7 (30.9)		1.71%	12.2[-18.74,43.14]
1091 Burnier 1993	23	65.2 (19.2)	23	35.2 (7.4)		1.82%	30[21.59,38.41]
1094 Sharma 1993,2	15	326 (141)	15	62 (22)		1.3%	264[191.78,336.22]
1099 Donovan 1993	8	380 (169.7)	8	70 (84.9)		0.78%	310[178.51,441.49]
1100 Fotherby 1993	17	228 (114)	17	57 (89)		1.34%	171[102.25,239.75]
1104 Overlack 1993	163	295 (142)	163	50.7 (234)		1.61%	244.3[202.28,286.32]
1109 Zoccali 1994	15	330 (201.4)	15	160 (96.8)		0.91%	170[56.91,283.09]
1119 Overlack 1995	45	235 (116)	45	69 (40)		1.67%	166[130.15,201.85]
1128 Schorr 1996	16	64.9 (43.3)	16	61.3 (36)		1.73%	3.6[-23.99,31.19]
1129 Bellini 1996	53	159.5 (14.3)	53	110.3 (25.4)		1.83%	49.2[41.35,57.05]
1131 Ferri 1996	61	129.9 (23.6)	61	86.4 (26.5)		1.82%	43.43[34.52,52.34]
1132 Ishimitsu 1996 A	30	211 (108)	30	63.7 (39.7)		1.62%	147.3[106.13,188.47]
1144 Foo 1998	18	118.5 (79.3)	18	75.6 (50.5)		1.6%	42.85[-0.58,86.28]
1145 Wing 1998	17	129 (129)	17	124 (124)		1.17%	5[-80.06,90.06]
1148 Damasceno 1999	39	27.8 (21)	39	7.5 (6.3)		1.83%	20.3[13.42,27.18]
1150 Schorr 1999	187	275 (222)	187	160 (94)		1.68%	115[80.45,149.55]
1152 Chiolero 2000	38	102 (74)	38	60 (38.8)		1.74%	42[15.43,68.57]
1153 Bruun 2000	42	226 (141)	42	52.6 (27)		1.6%	173.4[129.98,216.82]
1154 Burnier 2000	15	157 (89.1)	15	56 (24.8)		1.56%	101[54.2,147.8]
1168 Cuzzola 2001	19	211.3 (110)	19	158.9 (78.4)		1.42%	52.4[-8.34,113.14]
1173 Manunta 2001	20	17.3 (4.8)	20	12.1 (4.8)		1.83%	5.22[2.22,8.22]
1174 Kleij 2002	27	174 (33)	27	58.6 (10.2)		1.81%	115.4[102.37,128.43]
1175 Kerstens 2003	28	437 (152)	28	147 (59)		1.42%	290[229.61,350.39]
1178 Perry 2003	15	160 (50)	15	60 (30)		1.72%	100[70.49,129.51]
1180 Palacios 2004	23	100 (100)	23	36 (36)		1.6%	64[20.56,107.44]
1181 Beeks 2004	117	77.1 (45.9)	117	50.5 (27.3)		1.82%	26.6[16.92,36.28]
1185 Zanchi 2004	10	128.2 (20.5)	10	54.7 (14.8)		1.8%	73.5[57.83,89.17]
1188 Swift 2005	40	124.3 (50.2)	40	97.7 (32.9)		1.79%	26.67[8.07,45.27]
1192 Townsend 2007	18	159 (109)	18	35 (29)		1.51%	124[71.89,176.11]
1193 Dengel 2007	28	189 (117)	28	68 (50)		1.56%	121[73.87,168.13]
1194 Tzemos 2008	16	58 (29)	16	33 (9)		1.8%	25[10.12,39.88]
1196 Paulsen 2009	22	234 (40)	22	208 (48)		1.74%	26[-0.11,52.11]
1198 He 2009	169	148.5 (67.4)	169	131.6 (63.1)		1.81%	16.93[3.01,30.85]
1200 Pimenta 2009	12	144 (91)	12	108 (49)		1.44%	36[-22.48,94.48]
1204 Carey 2012	185	319 (172.3)	185	37.4 (32.4)		1.75%	281.6[256.34,306.86]
1205 Carey 2012 Hyperpath	211	176 (118)	211	55 (37.7)		1.79%	121[104.29,137.71]
1206 Graffe 2012	21	209.8 (122)	21	81.1 (29.3)		1.49%	128.7[75.04,182.36]
1207 Krikken 2012	65	132 (68)	65	40 (24.4)		1.79%	92[74.44,109.56]
1213 Mallamaci 2013	32	117 (75.6)	32	49 (32.6)		1.72%	68[39.47,96.53]
1214 Dickinson 2014	25	100 (52.3)	25	109.6 (64.5)		1.69%	-9.6[-42.15,22.95]
1218 Visser 2008	34	130 (73.3)	34	44 (24.4)		1.74%	86[60.03,111.97]

Fav. salt reduction -400 -200 0 200 400 Fav. salt intake

Study or subgroup	Salt reduction N	Salt reduction Mean(SD)	Normal salt intake N	Normal salt intake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1220 Gomi 1998	12	130 (55.3)	12	68.2 (27.1)		1.67%	61.8[26.96,96.64]
1221 Facchini 1999	19	243.3 (27)	19	33.2 (4)		1.81%	210.1[197.83,222.37]
1222 Pechere-Bertschi 2000	35	147.8 (72.1)	35	50.5 (32.4)		1.74%	97.3[71.11,123.49]
1223 Pechère-Bertschi 2003	27	216.2 (374.8)	27	36 (37.5)		0.71%	180.2[38.12,322.28]
1224 Ho 2007	25	216.2 (180.2)	25	72.1 (45.1)		1.29%	144.1[71.28,216.92]
1227 McManus 2015	60	43.2 (57.7)	60	25.2 (54.1)		1.78%	18[-2.01,38.01]
Total * **	**2442**		**2442**			**100%**	**97.81[82.56,113.05]**

Heterogeneity: Tau²=3298.06; Chi²=2587.63, df=64(P<0.0001); I²=97.53%

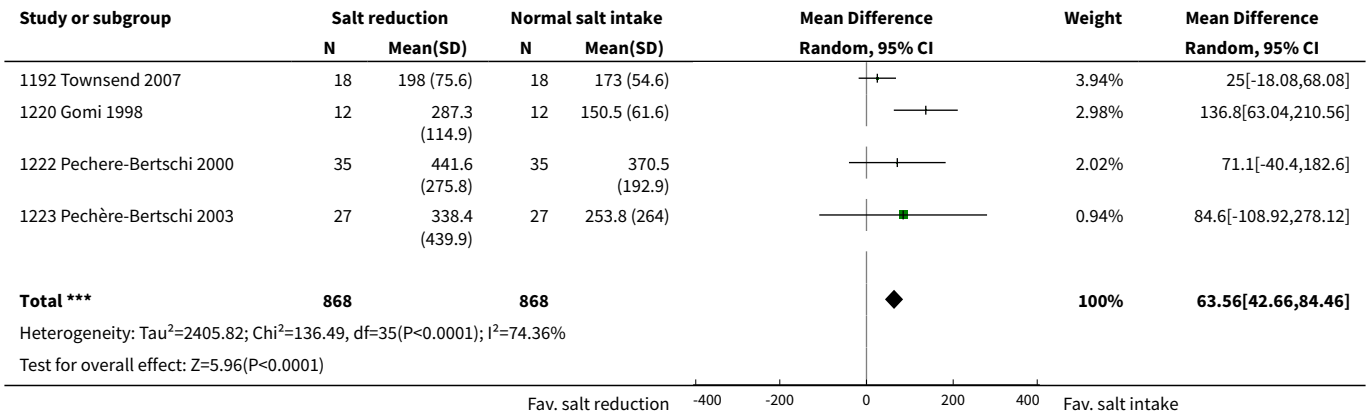
Test for overall effect: Z=12.58(P<0.0001)

Fav. salt reduction -400 -200 0 200 400 Fav. salt intake

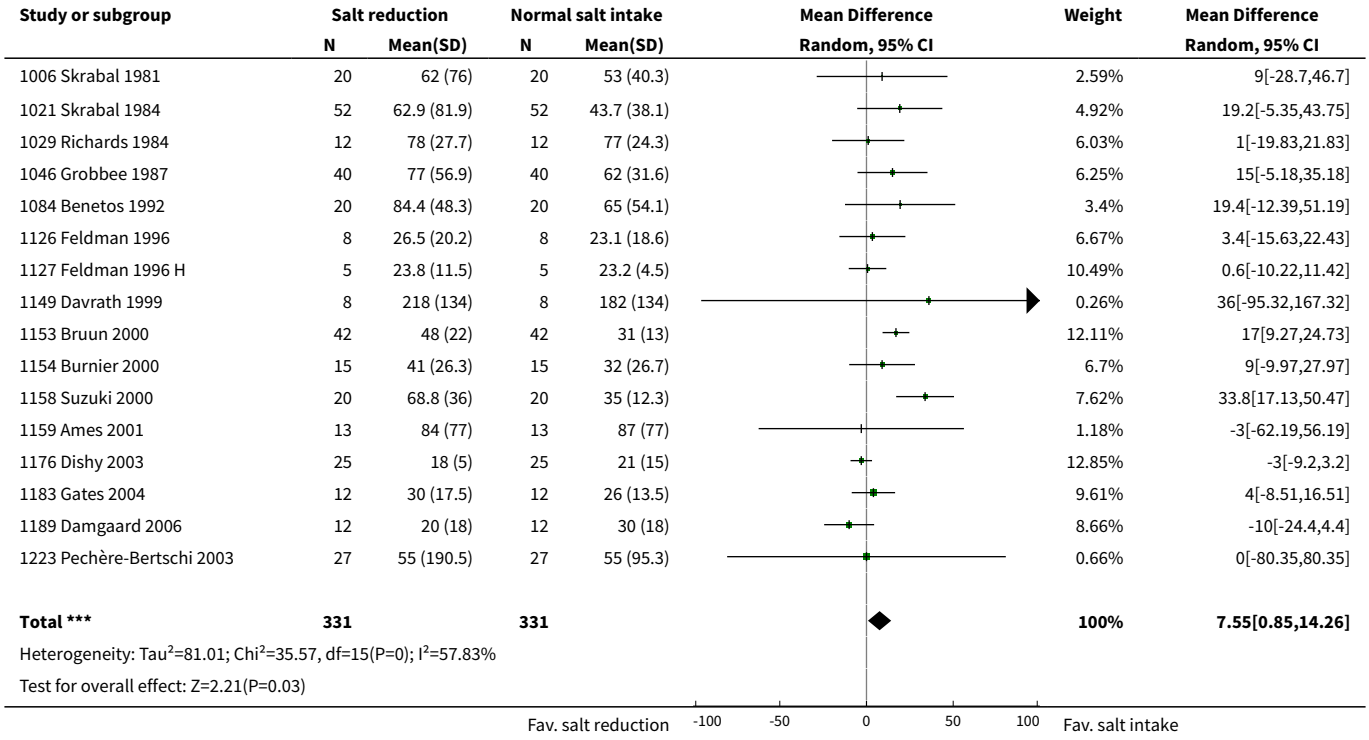
Analysis 5.3. Comparison 5 Effect of salt reduction on hormones, Outcome 3 Noradrenaline (pg/mL).

Study or subgroup	Salt reduction N	Salt reduction Mean(SD)	Normal salt intake N	Normal salt intake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1005 Rankin 1981	8	234 (178)	8	107 (45)		1.72%	127[-0.23,254.23]
1006 Skrabal 1981	20	605 (811)	20	353 (344)		0.28%	252[-134.08,638.08]
1021 Skrabal 1984	52	254 (93)	52	254 (129)		3.93%	0[-43.22,43.22]
1026 Koolen 1984(2)	20	452 (165)	20	367 (201)		1.96%	85[-28.97,198.97]
1029 Richards 1984	12	429 (114.3)	12	405 (97)		2.66%	24[-60.82,108.82]
1046 Grobbee 1987	40	239 (120.2)	40	220 (113.8)		3.68%	19[-32.3,70.3]
1048 Lawton 1988	9	305 (141)	9	183 (78)		2.15%	122[16.73,227.27]
1049 Lawton 1988 H	13	351 (137)	13	248 (119)		2.3%	103[4.36,201.64]
1056 MacGregor 1989	20	576 (536.7)	20	586 (527.7)		0.37%	-10[-339.86,319.86]
1068 Friberg 1990	10	262 (56.9)	10	233 (56.9)		3.72%	29[-20.89,78.89]
1078 Egan 1991	27	284 (255)	27	194 (94)		2.21%	90[-12.51,192.51]
1084 Benetos 1992	20	300 (152.1)	20	248 (187.8)		2.14%	52[-53.91,157.91]
1088 Ruppert 1993	163	419 (314)	163	304 (220)		3.44%	115[56.14,173.86]
1094 Sharma 1993,2	15	252 (82)	15	195 (42.4)		3.82%	57[10.28,103.72]
1095 Fliser 1993	16	227 (101)	16	172 (36)		3.64%	55[2.46,107.54]
1113 Miller 1995	36	221.6 (63)	36	212.4 (70)		4.29%	9.2[-21.56,39.96]
1114 Fliser 1995	7	178 (49)	7	129 (32)		3.93%	49[5.65,92.35]
1116 Stein 1995	7	213 (62.4)	7	170 (61.9)		3.24%	43[-22.11,108.11]
1119 Overlack 1995	45	686 (160)	45	424 (126)		3.42%	262[202.5,321.5]
1126 Feldman 1996	8	320 (172)	8	197 (91)		1.59%	123[-11.84,257.84]
1127 Feldman 1996 H	5	155 (87)	5	80 (22)		2.83%	75[-3.66,153.66]
1129 Bellini 1996	53	237.8 (52.2)	53	220.5 (47.9)		4.55%	17.3[-1.77,36.37]
1147 Feldman 1999	8	195 (82)	8	142 (54)		3.15%	53[-15.04,121.04]
1149 Davrath 1999	8	493 (204)	8	336 (204)		0.89%	157[-42.92,356.92]
1153 Bruun 2000	42	224.5 (86.3)	42	134.7 (61.6)		4.25%	89.8[57.73,121.87]
1154 Burnier 2000	15	186 (62)	15	149 (62)		3.9%	37[-7.37,81.37]
1158 Suzuki 2000	20	707 (260)	20	362 (116)		1.76%	345[220.23,469.77]
1159 Ames 2001	13	665 (225)	13	779 (225)		1.12%	-114[-286.97,58.97]
1176 Dishy 2003	25	174 (65)	25	126 (90)		3.92%	48[4.48,91.52]
1178 Perry 2003	15	237 (74)	15	271 (83)		3.52%	-34[-90.27,22.27]
1183 Gates 2004	12	290 (80.5)	12	297 (108.5)		2.9%	-7[-83.44,69.44]
1189 Damgaard 2006	12	254 (90)	12	185 (103)		2.87%	69[-8.39,146.39]

Fav. salt reduction -400 -200 0 200 400 Fav. salt intake



Analysis 5.4. Comparison 5 Effect of salt reduction on hormones, Outcome 4 Adrenaline (pg/mL).



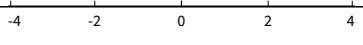
Comparison 6. Effect of salt reduction on hormones, subgroup analysis

Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Renin (ng/mL/hour)	44	3470	Std. Mean Difference (IV, Random, 95% CI)	1.05 [0.85, 1.24]
2 Aldosterone (pg/mL)	34	3128	Mean Difference (IV, Random, 95% CI)	95.59 [74.12, 117.05]

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
3 Noradrenaline (pg/mL)	23	964	Mean Difference (IV, Random, 95% CI)	48.66 [28.88, 68.44]
4 Adrenaline (pg/mL)	12	486	Mean Difference (IV, Random, 95% CI)	7.79 [0.31, 15.28]

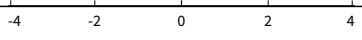
Analysis 6.1. Comparison 6 Effect of salt reduction on hormones, subgroup analysis, Outcome 1 Renin (ng/mL/hour).

Study or subgroup	Salt reduction		Normal salt intake		Std. Mean Difference	Weight	Std. Mean Difference
	N	Mean(SD)	N	Mean(SD)	Random, 95% CI		Random, 95% CI
1006 Skrabal 1981	20	0.6 (0.3)	20	0.3 (0.2)		2.3%	1.03[0.37,1.7]
1011 MacGregor 1982	19	1.7 (1.6)	19	1 (0.7)		2.33%	0.54[-0.11,1.19]
1017 Sowers 1983	9	12.5 (2.7)	9	1.3 (0.9)		0.66%	5.3[3.13,7.47]
1018 Watt 1983	18	2.9 (3)	18	1.3 (3)		2.3%	0.54[-0.13,1.2]
1021 Skrabal 1984	52	0.8 (0.4)	52	0.3 (0.2)		2.7%	1.51[1.07,1.95]
1029 Richards 1984	12	2.1 (1.5)	12	1.7 (1.1)		2.05%	0.3[-0.51,1.1]
1046 Grobbee 1987	40	17 (8.9)	40	14.5 (8.2)		2.69%	0.29[-0.15,0.73]
1050 Morgan 1988	16	1.4 (1.3)	16	0.8 (1.1)		2.23%	0.47[-0.23,1.18]
1053 Sudhir 1989	6	1 (0.2)	6	0.7 (0.2)		1.28%	1.47[0.13,2.81]
1054 Hargreaves 1989	8	3.4 (0.7)	8	1.9 (0.7)		1.42%	1.85[0.62,3.08]
1056 MacGregor 1989	20	2.3 (1.8)	20	1.4 (1.3)		2.36%	0.56[-0.08,1.19]
1068 Friberg 1990	10	0.7 (0.3)	10	0.5 (0.3)		1.81%	1.07[0.12,2.02]
1077 Singer 1991	21	4.2 (3.1)	21	2.8 (2.4)		2.39%	0.48[-0.14,1.09]
1078 Egan 1991	27	3.4 (2)	27	1.4 (1)		2.44%	1.25[0.67,1.84]
1079 Gow 1992	9	1.9 (0.8)	9	0.7 (0.4)		1.47%	1.99[0.81,3.17]
1080 Huggins 1992	9	8.6 (1.8)	9	6.1 (3.3)		1.76%	0.9[-0.09,1.88]
1084 Benetos 1992	20	26.5 (13)	20	24.9 (16.1)		2.38%	0.11[-0.51,0.73]
1100 Fotherby 1993	17	1.2 (0.8)	17	0.9 (0.6)		2.26%	0.51[-0.18,1.19]
1103 Del Rio 1993	30	3.1 (1.7)	30	1.3 (0.7)		2.48%	1.36[0.8,1.93]
1109 Zoccali 1994	15	5.3 (3.5)	15	2.5 (2.7)		2.14%	0.87[0.12,1.63]
1114 Fliser 1995	7	1.2 (0.5)	7	0.3 (0.1)		1.15%	2.34[0.87,3.8]
1128 Schorr 1996	16	0.9 (1.5)	16	0.7 (0.9)		2.25%	0.18[-0.51,0.88]
1129 Bellini 1996	53	2.5 (0.7)	53	1.6 (0.5)		2.7%	1.55[1.11,1.98]
1144 Foo 1998	18	20.1 (7.6)	18	11.4 (8)		2.23%	1.09[0.38,1.8]
1145 Wing 1998	17	4.1 (4.1)	17	3.3 (3.3)		2.28%	0.21[-0.46,0.88]
1150 Schorr 1999	187	3 (2.6)	187	0.7 (0.9)		2.99%	1.22[1,1.44]
1154 Burnier 2000	15	1.8 (1.4)	15	0.6 (0.4)		2.09%	1.17[0.38,1.95]
1173 Manunta 2001	20	4 (2.3)	20	2.8 (2.3)		2.36%	0.51[-0.12,1.14]
1174 Kleij 2002	27	0.8 (0.2)	27	0.3 (0.1)		2.06%	3.06[2.26,3.86]
1175 Kerstens 2003	28	1.5 (1.3)	28	0.5 (0.4)		2.47%	1.13[0.57,1.7]
1177 Nowson 2003	85	2 (2.4)	85	1.4 (1.6)		2.9%	0.29[-0.01,0.59]
1183 Gates 2004	12	0.7 (0.3)	12	0.4 (0.2)		1.96%	1.01[0.15,1.87]
1191 Melander 2007	39	32.4 (18.4)	39	17.4 (11.2)		2.64%	0.98[0.5,1.45]
1193 Dengel 2007	28	1.9 (0.8)	28	0.3 (0.9)		2.33%	1.96[1.31,2.6]
1198 He 2009	169	0.2 (0.3)	169	0.1 (0.2)		2.99%	0.43[0.22,0.65]
1204 Carey 2012	185	5.8 (3.6)	185	0.5 (0.3)		2.95%	2.08[1.82,2.33]
1205 Carey 2012 Hyperpath	221	2.7 (2.9)	221	0.6 (0.7)		3.01%	1.01[0.81,1.21]
1207 Krikken 2012	65	5.7 (3)	65	2.1 (1.3)		2.77%	1.53[1.13,1.92]



Fav. salt reduction — Fav. salt intake

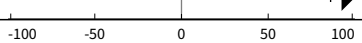
Study or subgroup	Salt reduction N	Salt reduction Mean(SD)	Normal salt intake N	Normal salt intake Mean(SD)	Std. Mean Difference Random, 95% CI	Weight	Std. Mean Difference Random, 95% CI
1213 Mallamaci 2013	32	2.5 (3.2)	32	0.9 (0.5)		2.58%	0.7[0.2,1.21]
1214 Dickinson 2014	25	14.7 (9.7)	25	14.7 (7.4)		2.5%	0[-0.55,0.55]
1218 Visser 2008	34	6.2 (2.7)	34	2.8 (1.4)		2.51%	1.57[1.03,2.12]
1220 Gomi 1998	12	1.9 (1)	12	0.8 (0.5)		1.91%	1.26[0.37,2.15]
1222 Pechere-Bertschi 2000	35	0.9 (0.7)	35	0.2 (0.2)		2.55%	1.41[0.88,1.93]
1223 Pechère-Bertschi 2003	27	2.8 (1.6)	27	1 (0.5)		2.4%	1.53[0.91,2.14]
Total ***	**1735**		**1735**			**100%**	**1.05[0.85,1.24]**
Heterogeneity: Tau²=0.33; Chi²=268.66, df=43(P<0.0001); I²=83.99%							
Test for overall effect: Z=10.36(P<0.0001)							



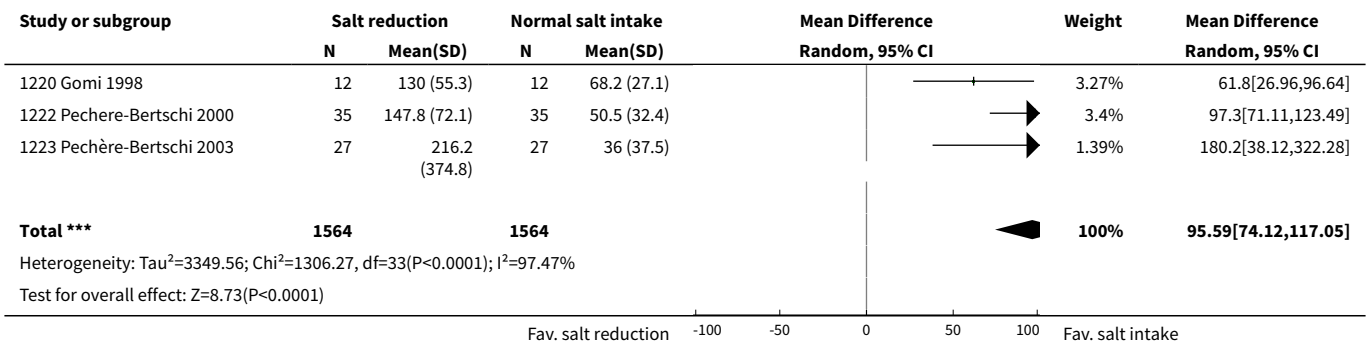
Fav. salt reduction — Fav. salt intake

Analysis 6.2. Comparison 6 Effect of salt reduction on hormones, subgroup analysis, Outcome 2 Aldosterone (pg/mL).

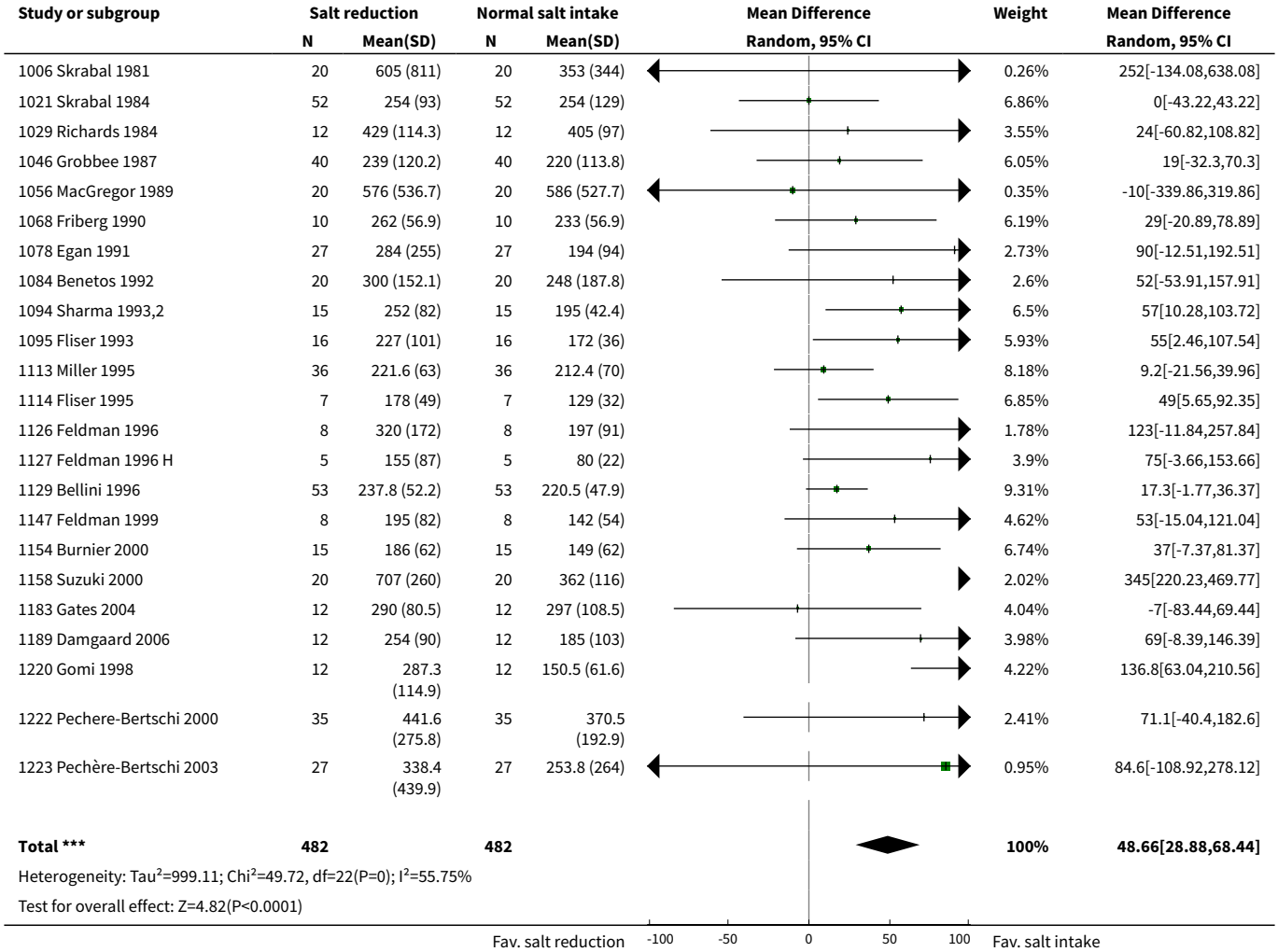
Study or subgroup	Salt reduction N	Salt reduction Mean(SD)	Normal salt intake N	Normal salt intake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1006 Skrabal 1981	21	159 (82)	21	53 (61.4)		3.12%	106[62.17,149.83]
1011 MacGregor 1982	19	140.6 (81.7)	19	78.9 (50.3)		3.13%	61.63[18.5,104.76]
1021 Skrabal 1984	52	228 (162)	52	84 (40)		3.09%	144[98.65,189.35]
1029 Richards 1984	12	148.1 (27.5)	12	107.8 (36.2)		3.41%	40.36[14.64,66.08]
1054 Hargreaves 1989	8	281.1 (146.8)	8	99.8 (36.7)		1.93%	181.28[76.43,286.13]
1056 MacGregor 1989	20	195 (90.3)	20	107.4 (51.6)		3.08%	87.58[42.02,133.14]
1077 Singer 1991	21	214.8 (82.6)	21	170.5 (76)		3.04%	44.33[-3.66,92.32]
1079 Gow 1992	9	270.7 (206.5)	9	106.3 (78.9)		1.37%	164.34[19.9,308.78]
1080 Huggins 1992	9	317 (186)	9	223 (153)		1.22%	94[-63.35,251.35]
1084 Benetos 1992	20	96.9 (63.5)	20	84.7 (30.9)		3.33%	12.2[-18.74,43.14]
1099 Donovan 1993	8	380 (169.7)	8	70 (84.9)		1.53%	310[178.51,441.49]
1100 Fotherby 1993	17	228 (114)	17	57 (89)		2.62%	171[102.25,239.75]
1109 Zoccali 1994	15	330 (201.4)	15	160 (96.8)		1.8%	170[56.91,283.09]
1128 Schorr 1996	16	64.9 (43.3)	16	61.3 (36)		3.38%	3.6[-23.99,31.19]
1129 Bellini 1996	53	159.5 (14.3)	53	110.3 (25.4)		3.56%	49.2[41.35,57.05]
1132 Ishimitsu 1996 A	30	211 (108)	30	63.7 (39.7)		3.16%	147.3[106.13,188.47]
1145 Wing 1998	17	129 (129)	17	124 (124)		2.29%	5[-80.06,90.06]
1150 Schorr 1999	187	275 (222)	187	160 (94)		3.28%	115[80.45,149.55]
1154 Burnier 2000	15	157 (89.1)	15	56 (24.8)		3.06%	101[54.2,147.8]
1173 Manunta 2001	20	17.3 (4.8)	20	12.1 (4.8)		3.58%	5.22[2.22,8.22]
1174 Kleij 2002	27	174 (33)	27	58.6 (10.2)		3.53%	115.4[102.37,128.43]
1175 Kerstens 2003	28	437 (152)	28	147 (59)		2.79%	290[229.61,350.39]
1181 Beeks 2004	117	77.1 (45.9)	117	50.5 (27.3)		3.56%	26.6[16.92,36.28]
1193 Dengel 2007	28	189 (117)	28	68 (50)		3.05%	121[73.87,168.13]
1198 He 2009	169	148.5 (67.4)	169	131.6 (63.1)		3.53%	16.93[3.01,30.85]
1204 Carey 2012	185	319 (172.3)	185	37.4 (32.4)		3.41%	281.6[256.34,306.86]
1205 Carey 2012 Hyperpath	211	176 (118)	211	55 (37.7)		3.51%	121[104.29,137.71]
1207 Krikken 2012	65	132 (68)	65	40 (24.4)		3.5%	92[74.44,109.56]
1213 Mallamaci 2013	32	117 (75.6)	32	49 (32.6)		3.37%	68[39.47,96.53]
1214 Dickinson 2014	25	100 (52.3)	25	109.6 (64.5)		3.31%	-9.6[-42.15,22.95]
1218 Visser 2008	34	130 (73.3)	34	44 (24.4)		3.4%	86[60.03,111.97]



Fav. salt reduction — Fav. salt intake

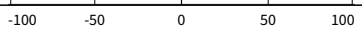


Analysis 6.3. Comparison 6 Effect of salt reduction on hormones, subgroup analysis, Outcome 3 Noradrenaline (pg/mL).



Analysis 6.4. Comparison 6 Effect of salt reduction on hormones, subgroup analysis, Outcome 4 Adrenaline (pg/mL).

Study or subgroup	Salt reduction N	Salt reduction Mean(SD)	Normal salt intake N	Normal salt intake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1006 Skrabal 1981	20	62 (76)	20	53 (40.3)		3.33%	9[-28.7,46.7]
1021 Skrabal 1984	52	62.9 (81.9)	52	43.7 (38.1)		6.48%	19.2[-5.35,43.75]
1029 Richards 1984	12	78 (27.7)	12	77 (24.3)		8.05%	1[-19.83,21.83]
1046 Grobbee 1987	40	77 (56.9)	40	62 (31.6)		8.38%	15[-5.18,35.18]
1084 Benetos 1992	20	84.4 (48.3)	20	65 (54.1)		4.4%	19.4[-12.39,51.19]
1126 Feldman 1996	8	26.5 (20.2)	8	23.1 (18.6)		8.98%	3.4[-15.63,22.43]
1127 Feldman 1996 H	5	23.8 (11.5)	5	23.2 (4.5)		14.79%	0.6[-10.22,11.42]
1154 Burnier 2000	15	41 (26.3)	15	32 (26.7)		9.02%	9[-9.97,27.97]
1158 Suzuki 2000	20	68.8 (36)	20	35 (12.3)		10.38%	33.8[17.13,50.47]
1183 Gates 2004	12	30 (17.5)	12	26 (13.5)		13.4%	4[-8.51,16.51]
1189 Damgaard 2006	12	20 (18)	12	30 (18)		11.94%	-10[-24.4,4.4]
1223 Pechère-Bertschi 2003	27	55 (190.5)	27	55 (95.3)		0.83%	0[-80.35,80.35]
Total ***	**243**		**243**			**100%**	**7.79[0.31,15.28]**
Heterogeneity: Tau^2=68.14; Chi^2=19.45, df=11(P=0.05); I^2=43.45%							
Test for overall effect: Z=2.04(P=0.04)							

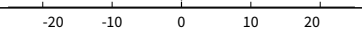


Comparison 7. Effect of salt reduction on lipids

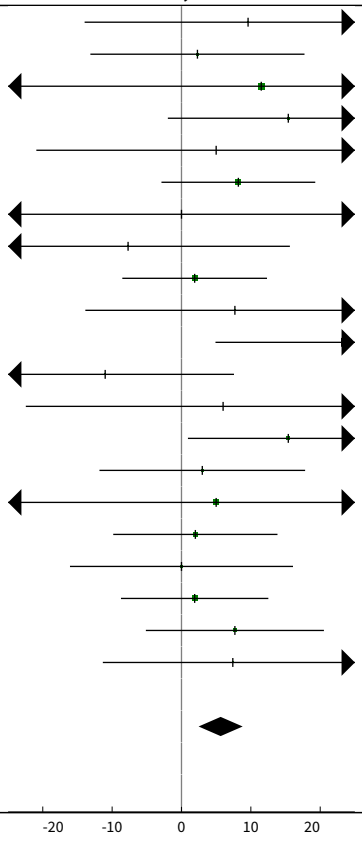
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Cholesterol (mg/dL)	27	1800	Mean Difference (IV, Random, 95% CI)	5.64 [2.46, 8.82]
2 Trigyceride (mg/dL)	19	1390	Mean Difference (IV, Random, 95% CI)	7.04 [3.04, 11.05]
3 High density lipoprotein, HDL (mg/dL)	19	1442	Mean Difference (IV, Random, 95% CI)	-0.29 [-1.66, 1.08]
4 Low density lipoprotein, LDL (mg/dL)	17	1358	Mean Difference (IV, Fixed, 95% CI)	3.12 [-0.41, 6.64]

Analysis 7.1. Comparison 7 Effect of salt reduction on lipids, Outcome 1 Cholesterol (mg/dL).

Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1046 Grobbee 1987	40	184 (31.6)	40	184 (38)		4.31%	0[-15.31,15.31]
1066 Sharma 1990	15	174 (30)	15	164 (26.9)		2.43%	10[-10.39,30.39]
1069 Del Rio 1990	15	229.7 (32.7)	15	221.6 (36.5)		1.64%	8.1[-16.7,32.9]
1078 Egan 1991	27	175 (31.2)	27	169 (31.2)		3.65%	6[-10.63,22.63]
1088 Ruppert 1993	163	221.1 (68)	163	207.8 (61.1)		5.13%	13.3[-0.73,27.33]
1095 Fliser 1993	8	154 (24)	8	145 (22.1)		1.98%	9[-13.61,31.61]

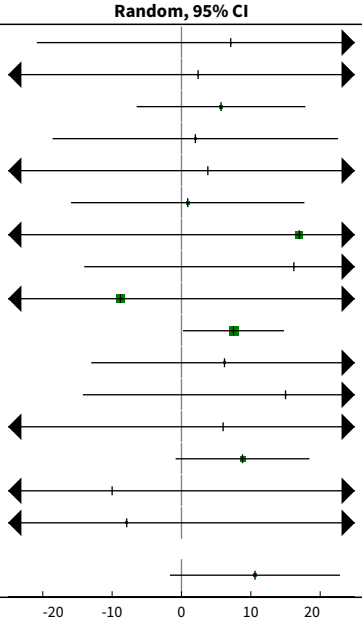


Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1103 Del Rio 1993	30	223.6 (47.7)	30	214 (45.5)		1.82%	9.6[-13.97,33.17]
1125 Grey 1996	34	162.5 (31.3)	34	160.2 (33.6)		4.24%	2.3[-13.14,17.74]
1126 Feldman 1996	8	184.8 (43.5)	8	173.3 (32.7)		0.71%	11.5[-26.22,49.22]
1127 Feldman 1996 H	5	165.6 (17.7)	5	150.2 (8.9)		3.35%	15.4[-1.97,32.77]
1128 Schorr 1996	16	233 (33.2)	16	228 (41.2)		1.5%	5[-20.93,30.93]
1138 McCarron 1997	99	223.6 (39.8)	99	215.4 (39.8)		8.22%	8.2[-2.89,19.29]
1139 Meland 1997	16	220 (46.4)	16	220 (30.9)		1.36%	0[-27.32,27.32]
1140 Fotherby 1997	17	196.9 (34.7)	17	204.6 (34.7)		1.86%	-7.7[-31.03,15.63]
1141 Ferri 1998	39	198.8 (23.5)	39	196.9 (23.5)		9.29%	1.9[-8.53,12.33]
1147 Feldman 1999	8	193 (22)	8	185.3 (22)		2.18%	7.7[-13.86,29.26]
1153 Bruun 2000	42	200.7 (42.5)	42	177.6 (42.6)		3.05%	23.1[4.9,41.3]
1157 Boero 2000	13	201 (24.5)	13	212 (23.8)		2.93%	-11[-29.57,7.57]
1159 Ames 2001	13	222 (37)	13	216 (37)		1.25%	6[-22.44,34.44]
1178 Perry 2003	15	150.5 (18.5)	15	135.1 (21.8)		4.83%	15.4[0.93,29.87]
1182 Berge-Landry 2004	48	231 (39)	48	228 (35)		4.6%	3[-11.82,17.82]
1183 Gates 2004	12	196.5 (54)	12	191.5 (54)		0.54%	5[-38.21,48.21]
1184 Harsha 2004	66	208.1 (34.7)	66	206.1 (34.7)		7.21%	2[-9.84,13.84]
1194 Tzemos 2008	16	154.4 (23.2)	16	154.4 (23.2)		3.91%	0[-16.08,16.08]
1207 Krikken 2012	65	156.3 (30.9)	65	154.4 (30.9)		8.96%	1.9[-8.72,12.52]
1218 Visser 2008	34	173.7 (27)	34	166 (27)		6.14%	7.7[-5.13,20.53]
1225 Gijsbers 2015	36	218.5 (41.7)	36	211.1 (39.4)		2.88%	7.4[-11.34,26.14]
Total ***	**900**		**900**			**100%**	**5.64[2.46,8.82]**
Heterogeneity: Tau^2=0; Chi^2=15.65, df=26(P=0.94); I^2=0%							
Test for overall effect: Z=3.48(P=0)							

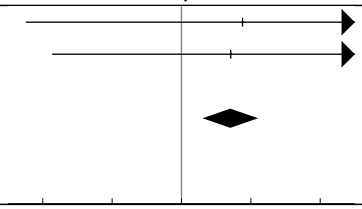


Analysis 7.2. Comparison 7 Effect of salt reduction on lipids, Outcome 2 Trigyceride (mg/dL).

Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1066 Sharma 1990	15	91.1 (35.4)	15	84 (42.4)		2.05%	7.1[-20.85,35.05]
1069 Del Rio 1990	15	102.7 (46.2)	15	100.3 (39.9)		1.68%	2.4[-28.49,33.29]
1088 Ruppert 1993	163	83.1 (57.4)	163	77.4 (54.6)		10.85%	5.7[-6.46,17.86]
1095 Fliser 1993	8	75 (21)	8	73 (21)		3.79%	2[-18.58,22.58]
1103 Del Rio 1993	30	120 (67)	30	116.2 (65)		1.44%	3.8[-29.6,37.2]
1125 Grey 1996	34	83.1 (35.4)	34	82.2 (35.4)		5.67%	0.9[-15.93,17.73]
1128 Schorr 1996	16	129 (84)	16	112 (38)		0.79%	17[-28.17,62.17]
1138 McCarron 1997	99	167.6 (122)	99	151.4 (93)		1.76%	16.2[-14.02,46.42]
1140 Fotherby 1997	17	123.8 (61.9)	17	132.6 (61.9)		0.93%	-8.8[-50.41,32.81]
1141 Ferri 1998	39	108.3 (19.9)	39	100.8 (11.9)		30.3%	7.5[0.22,14.78]
1153 Bruun 2000	42	90.2 (53.9)	42	84 (33.6)		4.35%	6.2[-13.01,25.41]
1157 Boero 2000	13	99 (37.5)	13	84 (38.5)		1.88%	15[-14.22,44.22]
1159 Ames 2001	13	135 (49)	13	129 (49)		1.13%	6[-31.67,43.67]
1178 Perry 2003	15	70.7 (15.5)	15	61.9 (11.1)		17.24%	8.8[-0.85,18.45]
1182 Berge-Landry 2004	48	167 (85)	48	177 (93)		1.26%	-10[-45.64,25.64]
1183 Gates 2004	12	112.3 (92.8)	12	120.2 (154.7)		0.15%	-7.9[-109.97,94.17]
1184 Harsha 2004	64	114 (35.4)	64	103.4 (35.4)		10.67%	10.6[-1.67,22.87]

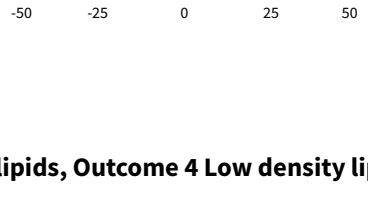


Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1194 Tzemos 2008	16	132.6 (53)	16	123.8 (35.4)		1.65%	8.8[-22.43,40.03]
1225 Gijsbers 2015	36	131.7 (55.7)	36	124.6 (55.7)		2.42%	7.1[-18.63,32.83]
Total ***	**695**		**695**			**100%**	**7.04[3.04,11.05]**
Heterogeneity: Tau²=0; Chi²=3.74, df=18(P=1); I²=0%							
Test for overall effect: Z=3.45(P=0)							



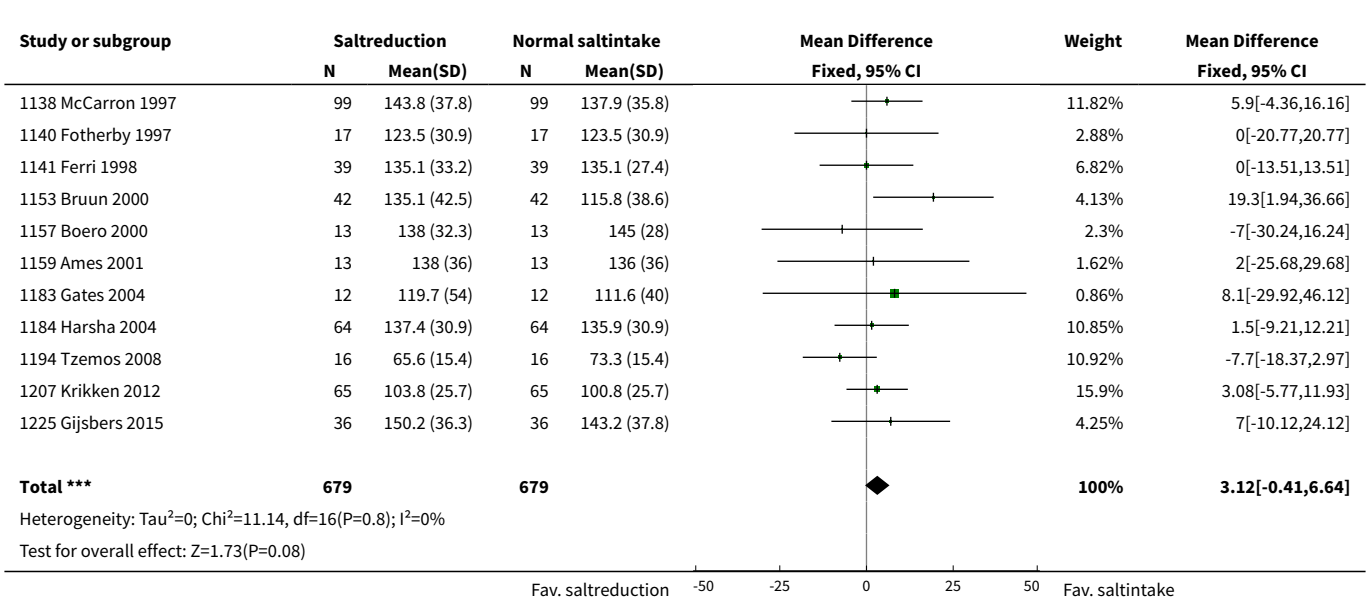
Analysis 7.3. Comparison 7 Effect of salt reduction on lipids, Outcome 3 High density lipoprotein, HDL (mg/dL).

Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1066 Sharma 1990	15	32.7 (9)	15	34.3 (5.9)		6.33%	-1.6[-7.05,3.85]
1088 Ruppert 1993	163	59.1 (29.9)	163	55.7 (23.4)		5.53%	3.4[-2.43,9.23]
1095 Fliser 1993	8	51 (15)	8	53 (13.9)		0.94%	-2[-16.15,12.15]
1103 Del Rio 1993	30	45.2 (11)	30	48 (10.3)		6.45%	-2.8[-8.2,2.6]
1125 Grey 1996	34	42.7 (8.7)	34	41.6 (6.8)		13.63%	1.1[-2.61,4.81]
1128 Schorr 1996	16	36 (9.2)	16	33 (8)		5.26%	3[-2.97,8.97]
1138 McCarron 1997	99	49.2 (14.1)	99	49.1 (13.8)		12.38%	0.1[-3.79,3.99]
1139 Meland 1997	16	42.5 (15.4)	16	46.3 (15.4)		1.65%	-3.8[-14.47,6.87]
1140 Fotherby 1997	17	42.5 (23.2)	17	50.2 (11.6)		1.23%	-7.7[-20.03,4.63]
1141 Ferri 1998	39	53.7 (20.5)	39	53.1 (18.5)		2.5%	0.6[-8.07,9.27]
1153 Bruun 2000	42	48.3 (15.4)	42	44.4 (11.6)		5.52%	3.9[-1.93,9.73]
1157 Boero 2000	13	43 (11)	13	45 (10.5)		2.75%	-2[-10.27,6.27]
1159 Ames 2001	13	62 (19)	13	59 (19)		0.88%	3[-11.61,17.61]
1183 Gates 2004	12	53.7 (27)	12	55.6 (40.5)		0.25%	-1.9[-29.44,25.64]
1184 Harsha 2004	64	47.9 (13.1)	64	48.6 (13.1)		9.11%	-0.7[-5.24,3.84]
1194 Tzemos 2008	16	42.5 (11.6)	16	46.3 (11.6)		2.91%	-3.8[-11.84,4.24]
1199 Meland 2009	23	48.3 (26.2)	23	50.2 (26.2)		0.82%	-1.9[-17.04,13.24]
1207 Krikken 2012	65	48.3 (9.7)	65	50.2 (9.7)		17.06%	-1.93[-5.25,1.39]
1225 Gijsbers 2015	36	57.1 (13.1)	36	57.5 (13.9)		4.82%	-0.4[-6.64,5.84]
Total ***	**721**		**721**			**100%**	**-0.29[-1.66,1.08]**
Heterogeneity: Tau²=0; Chi²=10.34, df=18(P=0.92); I²=0%							
Test for overall effect: Z=0.42(P=0.68)							



Analysis 7.4. Comparison 7 Effect of salt reduction on lipids, Outcome 4 Low density lipoprotein, LDL (mg/dL).

Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1066 Sharma 1990	15	120.3 (30)	15	110.1 (24.6)		3.23%	10.2[-9.43,29.83]
1078 Egan 1991	27	113.4 (28.6)	27	108.6 (25.5)		5.97%	4.8[-9.64,19.24]
1088 Ruppert 1993	163	148.8 (67.6)	163	139.1 (67.6)		5.78%	9.7[-4.98,24.38]
1095 Fliser 1993	8	94 (16.1)	8	86 (19)		4.19%	8[-9.24,25.24]
1125 Grey 1996	34	101 (29)	34	102.8 (31.3)		6.05%	-1.8[-16.14,12.54]
1128 Schorr 1996	16	172 (32)	16	165 (33.2)		2.44%	7[-15.59,29.59]

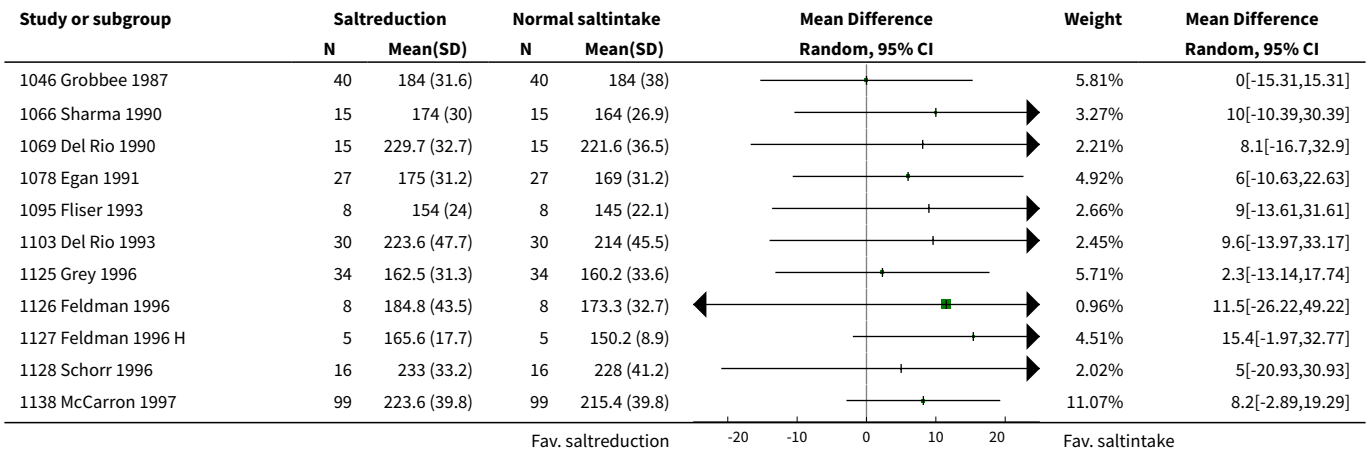


Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1138 McCarron 1997	99	143.8 (37.8)	99	137.9 (35.8)		11.82%	5.9[-4.36,16.16]
1140 Fotherby 1997	17	123.5 (30.9)	17	123.5 (30.9)		2.88%	0[-20.77,20.77]
1141 Ferri 1998	39	135.1 (33.2)	39	135.1 (27.4)		6.82%	0[-13.51,13.51]
1153 Bruun 2000	42	135.1 (42.5)	42	115.8 (38.6)		4.13%	19.3[1.94,36.66]
1157 Boero 2000	13	138 (32.3)	13	145 (28)		2.3%	-7[-30.24,16.24]
1159 Ames 2001	13	138 (36)	13	136 (36)		1.62%	2[-25.68,29.68]
1183 Gates 2004	12	119.7 (54)	12	111.6 (40)		0.86%	8.1[-29.92,46.12]
1184 Harsha 2004	64	137.4 (30.9)	64	135.9 (30.9)		10.85%	1.5[-9.21,12.21]
1194 Tzemos 2008	16	65.6 (15.4)	16	73.3 (15.4)		10.92%	-7.7[-18.37,2.97]
1207 Krikken 2012	65	103.8 (25.7)	65	100.8 (25.7)		15.9%	3.08[-5.77,11.93]
1225 Gijsbers 2015	36	150.2 (36.3)	36	143.2 (37.8)		4.25%	7[-10.12,24.12]
Total * **	**679**		**679**			**100%**	**3.12[-0.41,6.64]**
Heterogeneity: Tau²=0; Chi²=11.14, df=16(P=0.8); I²=0%							
Test for overall effect: Z=1.73(P=0.08)							

Comparison 8. Effect of salt reduction on lipids, subgroup analysis

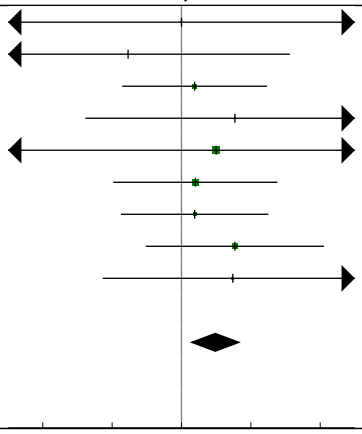
Outcome or subgroup title	No. of studies	No. of partici-pants	Statistical method	Effect size
1 Cholesterol (mg/dL)	20	1180	Mean Difference (IV, Random, 95% CI)	4.88 [1.19, 8.56]
2 Trigyceride (mg/dL)	12	770	Mean Difference (IV, Fixed, 95% CI)	6.92 [1.82, 12.02]
3 High density lipoprotein, HDL (mg/dL)	14	948	Mean Difference (IV, Fixed, 95% CI)	-0.67 [-2.18, 0.83]
4 Low density lipoprotein, LDL (mg/dL)	12	864	Mean Difference (IV, Fixed, 95% CI)	3.63 [-0.44, 7.69]

Analysis 8.1. Comparison 8 Effect of salt reduction on lipids, subgroup analysis, Outcome 1 Cholesterol (mg/dL).



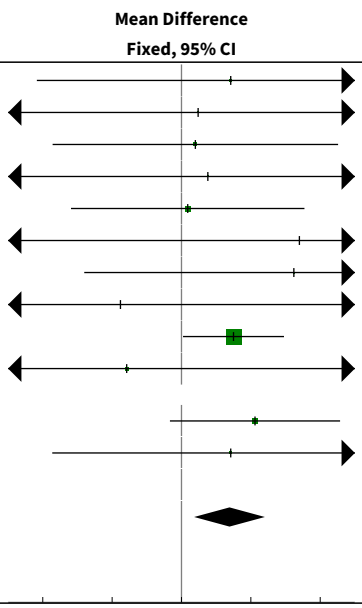
Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1046 Grobbee 1987	40	184 (31.6)	40	184 (38)		5.81%	0[-15.31,15.31]
1066 Sharma 1990	15	174 (30)	15	164 (26.9)		3.27%	10[-10.39,30.39]
1069 Del Rio 1990	15	229.7 (32.7)	15	221.6 (36.5)		2.21%	8.1[-16.7,32.9]
1078 Egan 1991	27	175 (31.2)	27	169 (31.2)		4.92%	6[-10.63,22.63]
1095 Fliser 1993	8	154 (24)	8	145 (22.1)		2.66%	9[-13.61,31.61]
1103 Del Rio 1993	30	223.6 (47.7)	30	214 (45.5)		2.45%	9.6[-13.97,33.17]
1125 Grey 1996	34	162.5 (31.3)	34	160.2 (33.6)		5.71%	2.3[-13.14,17.74]
1126 Feldman 1996	8	184.8 (43.5)	8	173.3 (32.7)		0.96%	11.5[-26.22,49.22]
1127 Feldman 1996 H	5	165.6 (17.7)	5	150.2 (8.9)		4.51%	15.4[-1.97,32.77]
1128 Schorr 1996	16	233 (33.2)	16	228 (41.2)		2.02%	5[-20.93,30.93]
1138 McCarron 1997	99	223.6 (39.8)	99	215.4 (39.8)		11.07%	8.2[-2.89,19.29]

Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Random, 95% CI	Weight	Mean Difference Random, 95% CI
1139 Meland 1997	16	220 (46.4)	16	220 (30.9)		1.82%	0[-27.32,27.32]
1140 Fotherby 1997	17	196.9 (34.7)	17	204.6 (34.7)		2.5%	-7.7[-31.03,15.63]
1141 Ferri 1998	39	198.8 (23.5)	39	196.9 (23.5)		12.51%	1.9[-8.53,12.33]
1147 Feldman 1999	8	193 (22)	8	185.3 (22)		2.93%	7.7[-13.86,29.26]
1183 Gates 2004	12	196.5 (54)	12	191.5 (54)		0.73%	5[-38.21,48.21]
1184 Harsha 2004	66	208.1 (34.7)	66	206.1 (34.7)		9.71%	2[-9.84,13.84]
1207 Krikken 2012	65	156.3 (30.9)	65	154.4 (30.9)		12.06%	1.9[-8.72,12.52]
1218 Visser 2008	34	173.7 (27)	34	166 (27)		8.26%	7.7[-5.13,20.53]
1225 Gijsbers 2015	36	218.5 (41.7)	36	211.1 (39.4)		3.88%	7.4[-11.34,26.14]
Total * **	**590**		**590**			**100%**	**4.88[1.19,8.56]**
Heterogeneity: Tau²=0; Chi²=5.38, df=19(P=1); I²=0%							
Test for overall effect: Z=2.59(P=0.01)							



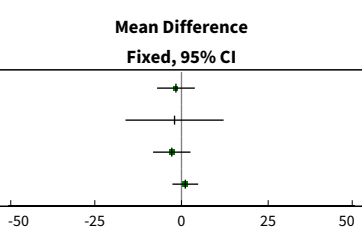
Analysis 8.2. Comparison 8 Effect of salt reduction on lipids, subgroup analysis, Outcome 2 Trigyceride (mg/dL).

Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1066 Sharma 1990	15	91.1 (35.4)	15	84 (42.4)		3.33%	7.1[-20.85,35.05]
1069 Del Rio 1990	15	102.7 (46.2)	15	100.3 (39.9)		2.73%	2.4[-28.49,33.29]
1095 Fliser 1993	8	75 (21)	8	73 (21)		6.15%	2[-18.58,22.58]
1103 Del Rio 1993	30	120 (67)	30	116.2 (65)		2.33%	3.8[-29.6,37.2]
1125 Grey 1996	34	83.1 (35.4)	34	82.2 (35.4)		9.19%	0.9[-15.93,17.73]
1128 Schorr 1996	16	129 (84)	16	112 (38)		1.28%	17[-28.17,62.17]
1138 McCarron 1997	99	167.6 (122)	99	151.4 (93)		2.85%	16.2[-14.02,46.42]
1140 Fotherby 1997	17	123.8 (61.9)	17	132.6 (61.9)		1.5%	-8.8[-50.41,32.81]
1141 Ferri 1998	39	108.3 (19.9)	39	100.8 (11.9)		49.16%	7.5[0.22,14.78]
1183 Gates 2004	12	112.3 (92.8)	12	120.2 (154.7)		0.25%	-7.9[-109.97,94.17]
1184 Harsha 2004	64	114 (35.4)	64	103.4 (35.4)		17.3%	10.6[-1.67,22.87]
1225 Gijsbers 2015	36	131.7 (55.7)	36	124.6 (55.7)		3.93%	7.1[-18.63,32.83]
Total * **	**385**		**385**			**100%**	**6.92[1.82,12.02]**
Heterogeneity: Tau²=0; Chi²=2.38, df=11(P=1); I²=0%							
Test for overall effect: Z=2.66(P=0.01)							

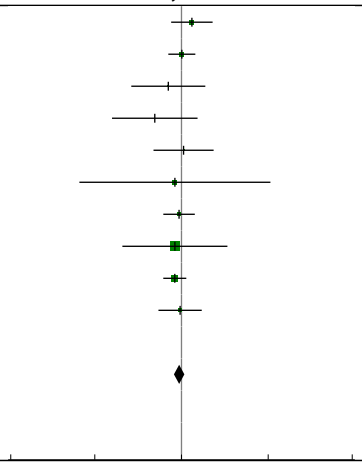


Analysis 8.3. Comparison 8 Effect of salt reduction on lipids, subgroup analysis, Outcome 3 High density lipoprotein, HDL (mg/dL).

Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1066 Sharma 1990	15	32.7 (9)	15	34.3 (5.9)		7.68%	-1.6[-7.05,3.85]
1095 Fliser 1993	8	51 (15)	8	53 (13.9)		1.14%	-2[-16.15,12.15]
1103 Del Rio 1993	30	45.2 (11)	30	48 (10.3)		7.83%	-2.8[-8.2,2.6]
1125 Grey 1996	34	42.7 (8.7)	34	41.6 (6.8)		16.53%	1.1[-2.61,4.81]

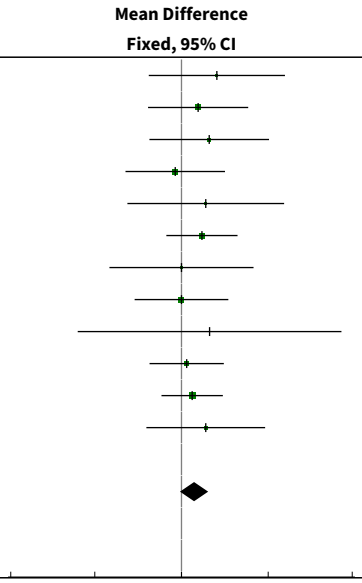


Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1128 Schorr 1996	16	36 (9.2)	16	33 (8)		6.38%	3[-2.97,8.97]
1138 McCarron 1997	99	49.2 (14.1)	99	49.1 (13.8)		15.02%	0.1[-3.79,3.99]
1139 Meland 1997	16	42.5 (15.4)	16	46.3 (15.4)		2%	-3.8[-14.47,6.87]
1140 Fotherby 1997	17	42.5 (23.2)	17	50.2 (11.6)		1.5%	-7.7[-20.03,4.63]
1141 Ferri 1998	39	53.7 (20.5)	39	53.1 (18.5)		3.03%	0.6[-8.07,9.27]
1183 Gates 2004	12	53.7 (27)	12	55.6 (40.5)		0.3%	-1.9[-29.44,25.64]
1184 Harsha 2004	64	47.9 (13.1)	64	48.6 (13.1)		11.06%	-0.7[-5.24,3.84]
1199 Meland 2009	23	48.3 (26.2)	23	50.2 (26.2)		0.99%	-1.9[-17.04,13.24]
1207 Krikken 2012	65	48.3 (9.7)	65	50.2 (9.7)		20.69%	-1.93[-5.25,1.39]
1225 Gijsbers 2015	36	57.1 (13.1)	36	57.5 (13.9)		5.85%	-0.4[-6.64,5.84]
Total * **	**474**		**474**			**100%**	**-0.67[-2.18,0.83]**
Heterogeneity: Tau^2=0; Chi^2=5.47, df=13(P=0.96); I^2=0%							
Test for overall effect: Z=0.88(P=0.38)							



Analysis 8.4. Comparison 8 Effect of salt reduction on lipids, subgroup analysis, Outcome 4 Low density lipoprotein, LDL (mg/dL).

Study or subgroup	Saltreduction N	Saltreduction Mean(SD)	Normal saltintake N	Normal saltintake Mean(SD)	Mean Difference Fixed, 95% CI	Weight	Mean Difference Fixed, 95% CI
1066 Sharma 1990	15	120.3 (30)	15	110.1 (24.6)		4.29%	10.2[-9.43,29.83]
1078 Egan 1991	27	113.4 (28.6)	27	108.6 (25.5)		7.93%	4.8[-9.64,19.24]
1095 Fliser 1993	8	94 (16.1)	8	86 (19)		5.56%	8[-9.24,25.24]
1125 Grey 1996	34	101 (29)	34	102.8 (31.3)		8.04%	-1.8[-16.14,12.54]
1128 Schorr 1996	16	172 (32)	16	165 (33.2)		3.24%	7[-15.59,29.59]
1138 McCarron 1997	99	143.8 (37.8)	99	137.9 (35.8)		15.71%	5.9[-4.36,16.16]
1140 Fotherby 1997	17	123.5 (30.9)	17	123.5 (30.9)		3.83%	0[-20.77,20.77]
1141 Ferri 1998	39	135.1 (33.2)	39	135.1 (27.4)		9.06%	0[-13.51,13.51]
1183 Gates 2004	12	119.7 (54)	12	111.6 (40)		1.14%	8.1[-29.92,46.12]
1184 Harsha 2004	64	137.4 (30.9)	64	135.9 (30.9)		14.43%	1.5[-9.21,12.21]
1207 Krikken 2012	65	103.8 (25.7)	65	100.8 (25.7)		21.13%	3.08[-5.77,11.93]
1225 Gijsbers 2015	36	150.2 (36.3)	36	143.2 (37.8)		5.64%	7[-10.12,24.12]
Total * **	**432**		**432**			**100%**	**3.63[-0.44,7.69]**
Heterogeneity: Tau^2=0; Chi^2=2.29, df=11(P=1); I^2=0%							
Test for overall effect: Z=1.75(P=0.08)							



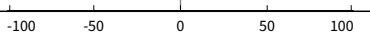
Comparison 9. Bias analyses

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 White population, normotensive, SBP blinding-high	66	7100	Mean Difference (Fixed, 95% CI)	-0.91 [-1.19, -0.63]

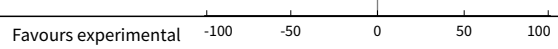
Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
2 White population, normotensive, SBP blinding-low	24	1193	Mean Difference (Fixed, 95% CI)	-1.05 [-1.61, -0.50]
3 White population, normotensive, SBP outcome-assesed-high	36	2771	Mean Difference (Fixed, 95% CI)	-1.12 [-1.60, -0.65]
4 White population, normotensive, SBP outcome-assesed-low	56	5768	Mean Difference (Fixed, 95% CI)	-0.89 [-1.18, -0.60]
5 White population, hypertensive, SBP blinding-high	45	3814	Mean Difference (Fixed, 95% CI)	-6.03 [-6.64, -5.41]
6 White population, hypertensive, SBP blinding-low	36	1911	Mean Difference (Fixed, 95% CI)	-5.78 [-6.39, -5.17]
7 White population, hypertensive, SBP outcome-assesed-high	27	2470	Mean Difference (Fixed, 95% CI)	-6.07 [-6.95, -5.19]
8 White population, hypertensive, SBP outcome-assesed-low	55	3433	Mean Difference (Fixed, 95% CI)	-5.71 [-6.23, -5.19]

Analysis 9.1. Comparison 9 Bias analyses, Outcome 1 White population, normotensive, SBP blinding-high.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1003 Sullivan 1980	27	27	6.9 (1.37)		1.1%	6.9[4.21,9.59]
1005 Rankin 1981	8	8	-3 (6.1)		0.06%	-3[-14.96,8.96]
1006 Skrabal 1981	20	20	-2.7 (2.07)		0.48%	-2.7[-6.76,1.36]
1010 Myers 1982	136	136	-3.3 (0.9)		2.55%	-3.3[-5.06,-1.54]
1013 Puska 1983	19	19	-1.5 (4.52)		0.1%	-1.5[-10.36,7.36]
1019 Cooper 1984	113	113	-0.6 (0.7)		4.22%	-0.6[-1.97,0.77]
1021 Skrabal 1984	52	52	-3.1 (4.4)		0.11%	-3.14[-11.76,5.48]
1032 Skrabal 1985	34	34	-3.1 (2.2)		0.43%	-3.1[-7.41,1.21]
1036 Richards 1986	8	8	-2 (1.79)		0.65%	-2[-5.51,1.51]
1037 Teow 1986	9	9	-0.6 (1.15)		1.56%	-0.6[-2.85,1.65]
1040 El Ashry 1987	26	26	0 (1.3)		1.22%	0[-2.55,2.55]
1042 Fuchs 1987	17	17	-3.6 (2.2)		0.43%	-3.6[-7.91,0.71]
1048 Lawton 1988	13	13	-2 (1.56)		0.85%	-2[-5.06,1.06]
1053 Sudhir 1989	6	6	-7.9 (3.4)		0.18%	-7.9[-14.56,-1.24]
1057 Dimsdale 1990 W	19	19	1.4 (1.6)		0.81%	1.4[-1.74,4.54]
1061 Schmid 1990	9	9	-3 (1.9)		0.57%	-3[-6.72,0.72]
1063 HPTRG 1990	174	177	0.1 (0.99)		2.11%	0.1[-1.84,2.04]
1064 Bruun 1990	10	10	-5 (1.72)		0.7%	-5[-8.37,-1.63]
1066 Sharma 1990	15	15	-0.9 (1.95)		0.54%	-0.9[-4.72,2.92]
1067 Sharma 1990,2	40	40	-2.1 (1.12)		1.65%	-2.1[-4.3,0.1]
1068 Friberg 1990	10	10	0 (2)		0.52%	0[-3.92,3.92]
1073 Sharma 1991	23	23	-4.5 (0.94)		2.34%	-4.5[-6.34,-2.66]
1074 Howe 1991	90	90	-1 (0.68)		4.47%	-1[-2.33,0.33]

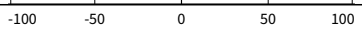


Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1079 Gow 1992	9	9	-8 (1.61)		0.8%	-8[-11.16,-4.84]
1081 TOHP I 1992	327	417	-1.7 (0.59)		5.94%	-1.7[-2.86,-0.54]
1088 Ruppert 1993	163	163	-2.2 (0.66)		4.75%	-2.2[-3.49,-0.91]
1091 Burnier 1993	23	23	-1 (1)		2.07%	-1[-2.96,0.96]
1093 Sharma 1993	16	16	-1.4 (0.93)		2.39%	-1.4[-3.22,0.42]
1095 Fliser 1993	0	0	0 (0)			Not estimable
1099 Donovan 1993	8	8	-2 (1.71)		0.71%	-2[-5.35,1.35]
1114 Fliser 1995	7	7	-1.1 (2.9)		0.25%	-1.1[-6.78,4.58]
1116 Stein 1995	7	7	1.4 (2.06)		0.49%	1.4[-2.64,5.44]
1135 TOHP II 1997	594	596	-1 (0.52)		7.65%	-1[-2.02,0.02]
1136 van Buul 1997	110	132	0 (1.8)		0.64%	0[-3.53,3.53]
1137 Schorr 1997	103	103	0.8 (0.64)		5.05%	0.8[-0.45,2.05]
1142 Knuist 1998	0	0	0 (0)			Not estimable
1143 Bech 1998	12	12	-1.3 (3.7)		0.15%	-1.3[-8.55,5.95]
1147 Feldman 1999	0	0	0 (0)			Not estimable
1149 Davrath 1999	8	8	8 (1.12)		1.65%	8[5.8,10.2]
1150 Schorr 1999	187	187	-0.2 (0.36)		15.96%	-0.2[-0.91,0.51]
1152 Chiolero 2000	12	12	0 (3.1)		0.22%	0[-6.08,6.08]
1153 Bruun 2000	42	42	0 (1.22)		1.39%	0[-2.39,2.39]
1154 Burnier 2000	15	15	-1 (1.14)		1.59%	-1[-3.23,1.23]
1155 Heer 2000	8	8	1 (3.98)		0.13%	1[-6.8,8.8]
1160 DASH 2001 W	54	54	-4 (1.2)		1.44%	-4[-6.35,-1.65]
1174 Kleij 2002	27	27	0.2 (3.3)		0.19%	0.2[-6.27,6.67]
1175 Kerstens 2003	28	28	3.1 (2)		0.52%	3.1[-0.82,7.02]
1176 Dishy 2003	25	25	2 (1)		2.07%	2[0.04,3.96]
1177 Nowson 2003	91	91	0.4 (0.8)		3.23%	0.4[-1.17,1.97]
1178 Perry 2003	15	15	0 (1.75)		0.68%	0[-3.43,3.43]
1180 Palacios 2004	8	8	-0.1 (1.5)		0.92%	-0.1[-3.04,2.84]
1189 Damgaard 2006	12	12	0 (4.7)		0.09%	0[-9.21,9.21]
1195 Jessani 2008	184	184	-1 (0.77)		3.49%	-1[-2.51,0.51]
1197 Dickinson 2009	29	29	-5 (1.46)		0.97%	-5[-7.86,-2.14]
1201 Nowson 2009	29	30	-1.1 (1.95)		0.54%	-1.1[-4.92,2.72]
1204 Carey 2012	185	185	-4.1 (1.4)		1.06%	-4.1[-6.84,-1.36]
1207 Krikken 2012	65	65	-1.3 (1.2)		1.44%	-1.3[-3.65,1.05]
1209 Bonfils 2013	12	12	-2 (6.1)		0.06%	-2[-13.96,9.96]
1212 Mak 2013	13	13	1 (2.2)		0.43%	1[-3.31,5.31]
1218 Visser 2008	34	34	-5 (2.63)		0.3%	-5[-10.15,0.15]
1219 Sharma 3 1993	18	18	-4 (1.8)		0.64%	-4[-7.53,-0.47]
1221 Facchini 1999	19	19	-0.3 (4.1)		0.12%	-0.3[-8.34,7.74]
1222 Pechere-Bertschi 2000	35	35	-2.4 (1.6)		0.81%	-2.4[-5.54,0.74]
1223 Pechère-Bertschi 2003	27	27	-1 (2.6)		0.31%	-1[-6.1,4.1]
1224 Ho 2007	25	25	-5 (1.4)		1.06%	-5[-7.74,-2.26]
1226 Cavka 2015	30	24	-5 (3.41)		0.18%	-5[-11.68,1.68]
Total (95% CI)					**100%**	**-0.91[-1.19,-0.63]**
Heterogeneity: Tau^2=0; Chi^2=230.1, df=62(P<0.0001); I^2=73.05%						
Test for overall effect: Z=6.33(P<0.0001)						



Analysis 9.2. Comparison 9 Bias analyses, Outcome 2 White population, normotensive, SBP blinding-low.

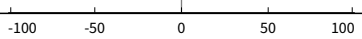
Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1031 Tuthill 1985	65	126	0 (1.12)		6.39%	0[-2.2,2.2]
1034 Watt 1985	66	66	-1 (0.5)		32.08%	-1[-1.98,-0.02]
1054 Hargreaves 1989	8	8	-6 (2.23)		1.61%	-6[-10.37,-1.63]
1075 Mascioli 1991	48	48	-3.6 (0.9)		9.9%	-3.6[-5.36,-1.84]
1078 Egan 1991	9	9	1 (1.4)		4.09%	1[-1.74,3.74]
1080 Huggins 1992	9	9	-1 (1.21)		5.48%	-1[-3.37,1.37]
1082 Cobiac 1992	51	55	-2.8 (1.6)		3.13%	-2.8[-5.94,0.34]
1097 Nestel 1993	32	34	-3.2 (2.7)		1.1%	-3.24[-8.53,2.05]
1107 MacFadyen 1994	12	12	7 (2.17)		1.7%	7[2.75,11.25]
1113 Miller 1995	36	36	1.9 (1.6)		3.13%	1.9[-1.24,5.04]
1115 Doig 1995	8	8	-2.3 (1.04)		7.42%	-2.3[-4.34,-0.26]
1125 Grey 1996	34	34	1 (1.16)		5.96%	1[-1.27,3.27]
1126 Feldman 1996	5	5	6.5 (1.8)		2.48%	6.5[2.97,10.03]
1128 Schorr 1996	16	16	-1 (2.7)		1.1%	-1[-6.29,4.29]
1134 Cappuccio 1997	18	18	-8.1 (2.77)		1.05%	-8.1[-13.53,-2.67]
1144 Foo 1998	18	18	-7.7 (2.86)		0.98%	-7.7[-13.31,-2.09]
1148 Damasceno 1999	20	20	0.5 (4.8)		0.35%	0.5[-8.91,9.91]
1156 Barba 2000	7	7	-3.2 (5.5)		0.27%	-3.2[-13.98,7.58]
1185 Zanchi 2004	9	9	-3 (4.21)		0.45%	-3[-11.25,5.25]
1194 Tzemos 2008	16	16	-4 (1.59)		3.17%	-4[-7.12,-0.88]
1196 Paulsen 2009	22	22	-1 (1.17)		5.86%	-1[-3.29,1.29]
1203 Starmans-Kool 2011	10	10	-2 (3.42)		0.69%	-2[-8.7,4.7]
1206 Graffe 2012	21	21	2 (2.8)		1.02%	2[-3.49,7.49]
1208 Todd 2012	23	23	-0.1 (3.7)		0.59%	-0.1[-7.35,7.15]
Total (95% CI)					**100%**	**-1.05[-1.61,-0.5]**
Heterogeneity: Tau^2=0; Chi^2=74.3, df=23(P<0.0001); I^2=69.04%						
Test for overall effect: Z=3.72(P=0)						



Favours experimental — Favours control

Analysis 9.3. Comparison 9 Bias analyses, Outcome 3 White population, normotensive, SBP outcome-assesed-high.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1005 Rankin 1981	8	8	-3 (6.1)		0.16%	-3[-14.96,8.96]
1006 Skrabal 1981	20	20	-2.7 (2.07)		1.38%	-2.7[-6.76,1.36]
1010 Myers 1982	136	136	-3.3 (0.9)		7.31%	-3.3[-5.06,-1.54]
1021 Skrabal 1984	52	52	-3.1 (4.4)		0.31%	-3.14[-11.76,5.48]
1037 Teow 1986	9	9	-0.6 (1.15)		4.48%	-0.6[-2.85,1.65]
1042 Fuchs 1987	17	17	-3.6 (2.2)		1.22%	-3.6[-7.91,0.71]
1048 Lawton 1988	13	13	-2 (1.56)		2.43%	-2[-5.06,1.06]
1057 Dimsdale 1990 W	19	19	1.4 (1.6)		2.31%	1.4[-1.74,4.54]
1064 Bruun 1990	10	10	-5 (1.72)		2%	-5[-8.37,-1.63]
1068 Friberg 1990	10	10	0 (2)		1.48%	0[-3.92,3.92]
1074 Howe 1991	90	90	-1 (0.68)		12.8%	-1[-2.33,0.33]
1079 Gow 1992	9	9	-8 (1.61)		2.28%	-8[-11.16,-4.84]



Favours experimental — Favours control

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1091 Burnier 1993	23	23	-1 (1)		5.92%	-1[-2.96,0.96]
1114 Fliser 1995	7	7	-1.1 (2.9)		0.7%	-1.1[-6.78,4.58]
1116 Stein 1995	7	7	1.4 (2.06)		1.39%	1.4[-2.64,5.44]
1136 van Buul 1997	110	132	0 (1.8)		1.83%	0[-3.53,3.53]
1142 Knuist 1998	0	0	0 (0)			Not estimable
1143 Bech 1998	12	12	-1.3 (3.7)		0.43%	-1.3[-8.55,5.95]
1147 Feldman 1999	8	8	0 (5.5)		0.2%	0[-10.78,10.78]
1152 Chiolero 2000	12	12	0 (3.1)		0.62%	0[-6.08,6.08]
1153 Bruun 2000	42	42	0 (1.22)		3.98%	0[-2.39,2.39]
1154 Burnier 2000	15	15	-1 (1.14)		4.55%	-1[-3.23,1.23]
1155 Heer 2000	8	8	1 (3.98)		0.37%	1[-6.8,8.8]
1174 Kleij 2002	27	27	0.2 (3.3)		0.54%	0.2[-6.27,6.67]
1175 Kerstens 2003	28	28	3.1 (2)		1.48%	3.1[-0.82,7.02]
1176 Dishy 2003	25	25	2 (1)		5.92%	2[0.04,3.96]
1177 Nowson 2003	91	91	0.4 (0.8)		9.25%	0.4[-1.17,1.97]
1178 Perry 2003	15	15	0 (1.75)		1.93%	0[-3.43,3.43]
1180 Palacios 2004	8	8	-0.1 (1.5)		2.63%	-0.1[-3.04,2.84]
1189 Damgaard 2006	12	12	0 (4.7)		0.27%	0[-9.21,9.21]
1195 Jessani 2008	184	184	-1 (0.77)		9.98%	-1[-2.51,0.51]
1197 Dickinson 2009	29	29	-5 (1.46)		2.78%	-5[-7.86,-2.14]
1201 Nowson 2009	29	30	-1.1 (1.95)		1.56%	-1.1[-4.92,2.72]
1204 Carey 2012	185	185	-4.1 (1.4)		3.02%	-4.1[-6.84,-1.36]
1215 Allen 2014	70	70	-1 (1.9)		1.64%	-1[-4.72,2.72]
1218 Visser 2008	34	34	-5 (2.63)		0.86%	-5[-10.15,0.15]
Total (95% CI)					**100%**	**-1.12[-1.6,-0.65]**
Heterogeneity: Tau²=0; Chi²=70.62, df=34(P=0); I²=51.85%						
Test for overall effect: Z=4.62(P<0.0001)						

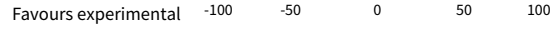
Favours experimental -100 -50 0 50 100 Favours control

Analysis 9.4. Comparison 9 Bias analyses, Outcome 4 White population, normotensive, SBP outcome-assesed-low.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1003 Sullivan 1980	27	27	6.9 (1.37)		1.19%	6.9[4.21,9.59]
1013 Puska 1983	19	19	-1.5 (4.52)		0.11%	-1.5[-10.36,7.36]
1019 Cooper 1984	113	113	-0.6 (0.7)		4.57%	-0.6[-1.97,0.77]
1031 Tuthill 1985	65	126	0 (1.12)		1.79%	0[-2.2,2.2]
1032 Skrabal 1985	34	34	-3.1 (2.2)		0.46%	-3.1[-7.41,1.21]
1034 Watt 1985	66	66	-1 (0.5)		8.96%	-1[-1.98,-0.02]
1036 Richards 1986	8	8	-2 (1.79)		0.7%	-2[-5.51,1.51]
1040 El Ashry 1987	26	26	0 (1.3)		1.33%	0[-2.55,2.55]
1054 Hargreaves 1989	8	8	-6 (2.23)		0.45%	-6[-10.37,-1.63]
1061 Schmid 1990	9	9	-3 (1.9)		0.62%	-3[-6.72,0.72]
1063 HPTRG 1990	174	177	0.1 (0.99)		2.29%	0.1[-1.84,2.04]
1064 Bruun 1990	10	10	-5 (1.72)		0.76%	-5[-8.37,-1.63]
1066 Sharma 1990	15	15	-0.9 (1.95)		0.59%	-0.9[-4.72,2.92]
1067 Sharma 1990,2	40	40	-2.1 (1.12)		1.79%	-2.1[-4.3,0.1]

Favours experimental -100 -50 0 50 100 Favours control

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1073 Sharma 1991	23	23	-4.5 (0.94)		2.53%	-4.5[-6.34,-2.66]
1075 Mascioli 1991	48	48	-3.6 (0.9)		2.77%	-3.6[-5.36,-1.84]
1078 Egan 1991	9	9	1 (1.4)		1.14%	1[-1.74,3.74]
1080 Huggins 1992	9	9	-1 (1.21)		1.53%	-1[-3.37,1.37]
1081 TOHP I 1992	327	417	-1.7 (0.59)		6.43%	-1.7[-2.86,-0.54]
1082 Cobiac 1992	51	55	-2.8 (1.6)		0.87%	-2.8[-5.94,0.34]
1088 Ruppert 1993	163	163	-2.2 (0.66)		5.14%	-2.2[-3.49,-0.91]
1093 Sharma 1993	16	16	-1.4 (0.93)		2.59%	-1.4[-3.22,0.42]
1095 Fliser 1993	16	16	-1.3 (3.5)		0.18%	-1.3[-8.16,5.56]
1097 Nestel 1993	32	34	-3.2 (2.7)		0.31%	-3.24[-8.53,2.05]
1099 Donovan 1993	8	8	-2 (1.71)		0.77%	-2[-5.35,1.35]
1107 MacFadyen 1994	12	12	7 (2.17)		0.48%	7[2.75,11.25]
1113 Miller 1995	36	36	1.9 (1.6)		0.87%	1.9[-1.24,5.04]
1115 Doig 1995	8	8	-2.3 (1.04)		2.07%	-2.3[-4.34,-0.26]
1125 Grey 1996	34	34	1 (1.16)		1.66%	1[-1.27,3.27]
1126 Feldman 1996	5	5	6.5 (1.8)		0.69%	6.5[2.97,10.03]
1128 Schorr 1996	16	16	-1 (2.7)		0.31%	-1[-6.29,4.29]
1134 Cappuccio 1997	18	18	-8.1 (2.77)		0.29%	-8.1[-13.53,-2.67]
1135 TOHP II 1997	594	596	-1 (0.52)		8.28%	-1[-2.02,0.02]
1137 Schorr 1997	103	103	0.8 (0.64)		5.47%	0.8[-0.45,2.05]
1144 Foo 1998	18	18	-7.7 (2.86)		0.27%	-7.7[-13.31,-2.09]
1148 Damasceno 1999	20	20	0.5 (4.8)		0.1%	0.5[-8.91,9.91]
1149 Davrath 1999	8	8	8 (1.12)		1.79%	8[5.8,10.2]
1150 Schorr 1999	187	187	-0.2 (0.36)		17.28%	-0.2[-0.91,0.51]
1156 Barba 2000	7	7	-3.2 (5.5)		0.07%	-3.2[-13.98,7.58]
1160 DASH 2001 W	54	54	-4 (1.2)		1.56%	-4[-6.35,-1.65]
1185 Zanchi 2004	9	9	-3 (4.21)		0.13%	-3[-11.25,5.25]
1194 Tzemos 2008	16	16	-4 (1.59)		0.89%	-4[-7.12,-0.88]
1196 Paulsen 2009	22	22	-1 (1.17)		1.64%	-1[-3.29,1.29]
1203 Starmans-Kool 2011	10	10	-2 (3.42)		0.19%	-2[-8.7,4.7]
1206 Graffe 2012	21	21	2 (2.8)		0.29%	2[-3.49,7.49]
1207 Krikken 2012	65	65	-1.3 (1.2)		1.56%	-1.3[-3.65,1.05]
1208 Todd 2012	23	23	-0.1 (3.7)		0.16%	-0.1[-7.35,7.15]
1209 Bonfils 2013	12	12	-2 (6.1)		0.06%	-2[-13.96,9.96]
1212 Mak 2013	13	13	1 (2.2)		0.46%	1[-3.31,5.31]
1214 Dickinson 2014	25	25	-2 (3.3)		0.21%	-2[-8.47,4.47]
1219 Sharma 3 1993	18	18	-4 (1.8)		0.69%	-4[-7.53,-0.47]
1221 Facchini 1999	19	19	-0.3 (4.1)		0.13%	-0.3[-8.34,7.74]
1222 Pechere-Bertschi 2000	35	35	-2.4 (1.6)		0.87%	-2.4[-5.54,0.74]
1223 Pechère-Bertschi 2003	27	27	-1 (2.6)		0.33%	-1[-6.1,4.1]
1224 Ho 2007	25	25	-5 (1.4)		1.14%	-5[-7.74,-2.26]
1226 Cavka 2015	30	24	-5 (3.41)		0.19%	-5[-11.68,1.68]
Total (95% CI)					**100%**	**-0.89[-1.18,-0.6]**
Heterogeneity: Tau²=0; Chi²=234.81, df=55(P<0.0001); I²=76.58%						
Test for overall effect: Z=5.95(P<0.0001)						

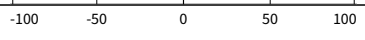


Analysis 9.5. Comparison 9 Bias analyses, Outcome 5 White population, hypertensive, SBP blinding-high.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1000 Parijs 1973	15	17	-6.7 (9.75)		0.1%	-6.7[-25.81,12.41]
1001 Mark 1975	6	6	-13.1 (1.71)		3.35%	-13.1[-16.45,-9.75]
1002 Morgan 1978	31	31	-1.5 (5.55)		0.32%	-1.5[-12.38,9.38]
1003 Sullivan 1980	19	19	1.2 (1.93)		2.63%	1.2[-2.58,4.98]
1009 Ambrosioni 1982	25	25	-2.2 (1.57)		3.97%	-2.2[-5.28,0.88]
1012 Beard 1982	45	45	-5.2 (4.85)		0.42%	-5.2[-14.71,4.31]
1013 Puska 1983	15	19	1.8 (5.57)		0.32%	1.8[-9.12,12.72]
1016 Silman 1983	12	16	3.5 (11.39)		0.08%	3.5[-18.82,25.82]
1023 Gillies 1984	24	24	-2.4 (2.51)		1.55%	-2.4[-7.32,2.52]
1024 Erwteman 1984	44	50	-2.7 (4.01)		0.61%	-2.7[-10.56,5.16]
1025 Koolen 1984	20	20	-6.2 (2.54)		1.52%	-6.2[-11.18,-1.22]
1027 Fagerberg 1984	15	15	-3.7 (7.14)		0.19%	-3.7[-17.69,10.29]
1028 Maxwell 1984	18	12	-2 (6.72)		0.22%	-2[-15.17,11.17]
1029 Richards 1984	12	12	-4 (2.79)		1.26%	-4[-9.47,1.47]
1030 Resnick 1985	12	12	-3 (1.5)		4.35%	-3[-5.94,-0.06]
1038 Logan 1986	43	43	-1.1 (4.18)		0.56%	-1.1[-9.29,7.09]
1039 ANHMRCDS 1986	48	52	-4.8 (3.92)		0.64%	-4.8[-12.48,2.88]
1044 Morgan 1987	10	10	-6 (8.95)		0.12%	-6[-23.54,11.54]
1050 Morgan 1988	16	16	-3 (2.74)		1.3%	-3[-8.37,2.37]
1052 Shore 1988	6	6	-9 (2.68)		1.36%	-9[-14.25,-3.75]
1055 ANHMRCDS 1989	50	53	-5.5 (1.46)		4.59%	-5.5[-8.36,-2.64]
1058 Dimsdale 1990 WH	17	17	-0.1 (2)		2.45%	-0.1[-4.02,3.82]
1062 Schmid 1990 H	9	9	-6 (3.13)		1%	-6[-12.13,0.13]
1064 Bruun 1990	12	12	-8 (2.06)		2.31%	-8[-12.04,-3.96]
1101 Redon-Mas 1993	235	183	1 (1.94)		2.6%	1[-2.8,4.8]
1108 Buckley 1994	12	12	-11.6 (1.67)		3.51%	-11.6[-14.87,-8.33]
1109 Zoccali 1994	15	15	-14 (2.46)		1.62%	-14[-18.82,-9.18]
1110 Jula 1994	38	38	-6.7 (3.92)		0.64%	-6.7[-14.38,0.98]
1117 Arrol 1995	89	92	-0.4 (3.37)		0.86%	-0.4[-7.01,6.21]
1118 Draaijer 1995	10	10	-5.4 (3.71)		0.71%	-5.4[-12.67,1.87]
1152 Chiolero 2000	12	12	0 (3.1)		1.02%	0[-6.08,6.08]
1157 Boero 2000	13	13	-4 (1.57)		3.97%	-4[-7.08,-0.92]
1161 DASH 2001 WH	37	37	-6.6 (1.2)		6.8%	-6.6[-8.95,-4.25]
1169 Seals 2001	17	18	-8 (2.61)		1.44%	-8[-13.12,-2.88]
1170 TONE 2001 W	251	220	-4 (1.01)		9.6%	-4[-5.98,-2.02]
1181 Beeks 2004	117	117	1.2 (1.44)		4.72%	1.2[-1.62,4.02]
1182 Berge-Landry 2004	48	48	-16 (1.51)		4.29%	-16[-18.96,-13.04]
1199 Meland 2009	23	23	-5 (3.79)		0.68%	-5[-12.43,2.43]
1201 Nowson 2009	17	18	-5.5 (2.72)		1.32%	-5.5[-10.83,-0.17]
1202 Weir 2010	132	132	-9.4 (0.97)		10.4%	-9.4[-11.3,-7.5]
1205 Carey 2012 Hyperpath	211	211	-16 (1.7)		3.39%	-16[-19.33,-12.67]
1209 Bonfils 2013	12	12	-2 (5.5)		0.32%	-2[-12.78,8.78]
1213 Mallamaci 2013	32	32	-8 (2.4)		1.7%	-8[-12.7,-3.3]
1216 Barros 2015	19	16	-6.4 (3.81)		0.67%	-6.43[-13.9,1.04]
1217 Markota 2015	76	74	-4.9 (1.47)		4.53%	-4.9[-7.78,-2.02]
Total (95% CI)					**100%**	**-6.03[-6.64,-5.41]**

Heterogeneity: Tau^2=0; Chi^2=227.18, df=44(P<0.0001); I^2=80.63%

Test for overall effect: Z=19.27(P<0.0001)



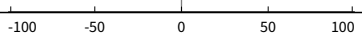
Favours experimental — Favours control

Analysis 9.6. Comparison 9 Bias analyses, Outcome 6 White population, hypertensive, SBP blinding-low.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1011 MacGregor 1982	19	19	-10 (2.76)		1.27%	-10[-15.41,-4.59]
1018 Watt 1983	18	18	-0.5 (1.5)		4.31%	-0.5[-3.44,2.44]
1045 Kurtz 1987	5	5	-16 (2)		2.42%	-16[-19.92,-12.08]
1046 Grobbee 1987	40	40	-0.8 (1.51)		4.25%	-0.8[-3.76,2.16]
1047 MacGregor 1987	15	15	-13 (3.29)		0.9%	-13[-19.45,-6.55]
1051 Morgan 1988,2	8	8	-7 (3)		1.08%	-7[-12.88,-1.12]
1056 MacGregor 1989	20	20	-16 (2.77)		1.26%	-16[-21.43,-10.57]
1069 Del Rio 1990	15	15	-3.4 (2.02)		2.37%	-3.4[-7.36,0.56]
1070 Parker 1990	31	28	1.3 (2.15)		2.1%	1.3[-2.91,5.51]
1076 Carney 1991	11	11	-1 (3.49)		0.8%	-1[-7.84,5.84]
1077 Singer 1991	21	21	-9 (3)		1.08%	-9[-14.88,-3.12]
1084 Benetos 1992	20	20	-6.5 (1.88)		2.74%	-6.5[-10.18,-2.82]
1085 Sciarrone 1992	46	45	-5.8 (4.07)		0.59%	-5.8[-13.78,2.18]
1100 Fotherby 1993	17	17	-8 (3.5)		0.79%	-8[-14.86,-1.14]
1102 Ruilope 1993	10	9	-4 (7.95)		0.15%	-4[-19.58,11.58]
1103 Del Rio 1993	30	30	-1.4 (1.8)		2.99%	-1.4[-4.93,2.13]
1111 Howe 1994	14	14	-4.2 (2.91)		1.14%	-4.2[-9.9,1.5]
1119 Overlack 1995	46	46	-3.9 (2.5)		1.55%	-3.9[-8.8,1]
1127 Feldman 1996 H	8	0	2.6 (2.9)		1.15%	2.62[-3.06,8.3]
1129 Bellini 1996	43	43	-3.9 (1.8)		2.99%	-3.9[-7.43,-0.37]
1130 Inoue 1996	14	14	-15.2 (1.91)		2.66%	-15.2[-18.94,-11.46]
1131 Ferri 1996	61	61	-7.4 (1.13)		7.59%	-7.4[-9.61,-5.19]
1134 Cappuccio 1997	29	29	-6.6 (2.51)		1.54%	-6.6[-11.52,-1.68]
1138 McCarron 1997	99	99	-4.9 (1.23)		6.41%	-4.9[-7.31,-2.49]
1139 Meland 1997	16	16	-4 (2.47)		1.59%	-4[-8.84,0.84]
1145 Wing 1998	17	17	-7 (0.79)		15.53%	-7[-8.55,-5.45]
1146 Herlitz 1998	6	6	-5 (1.94)		2.57%	-5[-8.8,-1.2]
1148 Damasceno 1999	19	19	-8.5 (4.1)		0.58%	-8.5[-16.54,-0.46]
1159 Ames 2001	13	13	-7 (3.56)		0.76%	-7[-13.98,-0.02]
1168 Cuzzola 2001	19	19	-5.1 (2.45)		1.61%	-5.1[-9.9,-0.3]
1172 Johnson 2001	46	46	-4.5 (2.08)		2.24%	-4.5[-8.58,-0.42]
1183 Gates 2004	12	12	-3 (1.84)		2.86%	-3[-6.61,0.61]
1191 Melander 2007	39	39	-6 (1.18)		6.96%	-6[-8.31,-3.69]
1193 Dengel 2007	28	28	-10 (3.64)		0.73%	-10[-17.13,-2.87]
1198 He 2009	71	71	-4.8 (1.24)		6.3%	-4.8[-7.23,-2.37]
1225 Gijsbers 2015	36	36	-7.5 (1.53)		4.14%	-7.5[-10.5,-4.5]
Total (95% CI)					**100%**	**-5.78[-6.39,-5.17]**

Heterogeneity: $Tau^2=0$; $Chi^2=139.06$, df=35(P<0.0001); $I^2=74.83\%$

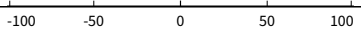
Test for overall effect: Z=18.56(P<0.0001)



Favours experimental — Favours control

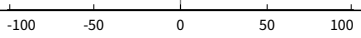
Analysis 9.7. Comparison 9 Bias analyses, Outcome 7 White population, hypertensive, SBP outcome-assesed-high.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1000 Parijs 1973	15	17	-6.7 (9.75)		0.21%	-6.7[-25.81,12.41]
1001 Mark 1975	6	6	-13.1 (1.71)		6.96%	-13.1[-16.45,-9.75]
1012 Beard 1982	45	45	-5.2 (4.9)		0.85%	-5.2[-14.8,4.4]
1015 Bulpitt 1984	32	33	-4.2 (6.28)		0.52%	-4.2[-16.51,8.11]
1016 Silman 1983	12	16	3.5 (11.39)		0.16%	3.5[-18.82,25.82]
1023 Gillies 1984	24	24	-2.4 (2.51)		3.23%	-2.4[-7.32,2.52]
1025 Koolen 1984	20	20	-6.2 (2.54)		3.16%	-6.2[-11.18,-1.22]
1027 Fagerberg 1984	15	15	-3.7 (7.14)		0.4%	-3.7[-17.69,10.29]
1028 Maxwell 1984	18	12	-2 (6.72)		0.45%	-2[-15.17,11.17]
1030 Resnick 1985	12	12	-3 (1.5)		9.05%	-3[-5.94,-0.06]
1038 Logan 1986	43	43	-1.1 (4.18)		1.17%	-1.1[-9.29,7.09]
1055 ANHMRCDS 1989	50	53	-5.5 (1.46)		9.55%	-5.5[-8.36,-2.64]
1058 Dimsdale 1990 WH	17	17	-0.1 (2)		5.09%	-0.1[-4.02,3.82]
1065 Bruun 1990 H	12	12	-8 (2.6)		3.01%	-8[-13.1,-2.9]
1101 Redon-Mas 1993	235	183	1 (1.94)		5.41%	1[-2.8,4.8]
1110 Jula 1994	38	38	-6.7 (3.92)		1.32%	-6.7[-14.38,0.98]
1117 Arrol 1995	89	92	-0.4 (3.37)		1.79%	-0.4[-7.01,6.21]
1118 Draaijer 1995	10	10	-5.4 (3.71)		1.48%	-5.4[-12.67,1.87]
1152 Chiolero 2000	38	38	-6.5 (2.9)		2.42%	-6.5[-12.18,-0.82]
1169 Seals 2001	17	18	-8 (2.61)		2.99%	-8[-13.12,-2.88]
1181 Beeks 2004	117	117	1.2 (1.44)		9.82%	1.2[-1.62,4.02]
1182 Berge-Landry 2004	48	48	-16 (1.51)		8.93%	-16[-18.96,-13.04]
1199 Meland 2009	23	23	-5 (3.79)		1.42%	-5[-12.43,2.43]
1201 Nowson 2009	17	18	-5.5 (2.72)		2.75%	-5.5[-10.83,-0.17]
1205 Carey 2012 Hyperpath	211	211	-16 (1.7)		7.04%	-16[-19.33,-12.67]
1216 Barros 2015	19	16	-6.4 (3.81)		1.4%	-6.43[-13.9,1.04]
1217 Markota 2015	76	74	-4.9 (1.47)		9.42%	-4.9[-7.78,-2.02]
Total (95% CI)					**100%**	**-6.07[-6.95,-5.19]**
Heterogeneity: Tau²=0; Chi²=155.92, df=26(P<0.0001); I²=83.33%						
Test for overall effect: Z=13.45(P<0.0001)						



Analysis 9.8. Comparison 9 Bias analyses, Outcome 8 White population, hypertensive, SBP outcome-assesed-low.

Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1002 Morgan 1978	31	31	-1.5 (5.55)		0.23%	-1.5[-12.38,9.38]
1003 Sullivan 1980	19	19	1.2 (1.93)		1.87%	1.2[-2.58,4.98]
1009 Ambrosioni 1982	25	25	-2.2 (1.57)		2.83%	-2.2[-5.28,0.88]
1011 MacGregor 1982	19	19	-10 (2.76)		0.92%	-10[-15.41,-4.59]
1013 Puska 1983	15	19	1.8 (5.57)		0.23%	1.8[-9.12,12.72]
1018 Watt 1983	18	18	-0.5 (1.5)		3.1%	-0.5[-3.44,2.44]
1024 Erwteman 1984	44	50	-2.7 (4.01)		0.43%	-2.7[-10.56,5.16]
1029 Richards 1984	12	12	-4 (2.79)		0.9%	-4[-9.47,1.47]
1039 ANHMRCDS 1986	48	52	-4.8 (3.92)		0.45%	-4.8[-12.48,2.88]



Study or subgroup	Experimental N	Control N	Mean Difference (SE)	Mean Difference IV, Fixed, 95% CI	Weight	Mean Difference IV, Fixed, 95% CI
1044 Morgan 1987	10	10	-6 (8.95)		0.09%	-6[-23.54,11.54]
1045 Kurtz 1987	5	5	-16 (2)		1.75%	-16[-19.92,-12.08]
1046 Grobbee 1987	40	40	-0.8 (1.51)		3.06%	-0.8[-3.76,2.16]
1047 MacGregor 1987	15	15	-13 (3.29)		0.65%	-13[-19.45,-6.55]
1050 Morgan 1988	16	16	-3 (2.74)		0.93%	-3[-8.37,2.37]
1051 Morgan 1988,2	8	8	-7 (3)		0.78%	-7[-12.88,-1.12]
1052 Shore 1988	6	6	-9 (2.68)		0.97%	-9[-14.25,-3.75]
1056 MacGregor 1989	20	20	-16 (2.77)		0.91%	-16[-21.43,-10.57]
1062 Schmid 1990 H	9	9	-6 (3.13)		0.71%	-6[-12.13,0.13]
1069 Del Rio 1990	15	15	-3.4 (2.02)		1.71%	-3.4[-7.36,0.56]
1070 Parker 1990	31	28	1.3 (2.15)		1.51%	1.3[-2.91,5.51]
1076 Carney 1991	11	11	-1 (3.49)		0.57%	-1[-7.84,5.84]
1077 Singer 1991	21	21	-9 (3)		0.78%	-9[-14.88,-3.12]
1084 Benetos 1992	20	20	-6.5 (1.88)		1.98%	-6.5[-10.18,-2.82]
1085 Sciarrone 1992	46	45	-5.8 (4.07)		0.42%	-5.8[-13.78,2.18]
1100 Fotherby 1993	17	17	-8 (3.5)		0.57%	-8[-14.86,-1.14]
1102 Ruilope 1993	10	9	-4 (7.95)		0.11%	-4[-19.58,11.58]
1103 Del Rio 1993	30	30	-1.4 (1.8)		2.16%	-1.4[-4.93,2.13]
1108 Buckley 1994	12	12	-11.6 (1.67)		2.5%	-11.6[-14.87,-8.33]
1109 Zoccali 1994	15	15	-14 (2.46)		1.15%	-14[-18.82,-9.18]
1111 Howe 1994	14	14	-4.2 (2.91)		0.82%	-4.2[-9.9,1.5]
1119 Overlack 1995	46	46	-3.9 (2.5)		1.12%	-3.9[-8.8,1]
1122 Dubbert 1995	38	17	-1.4 (3.76)		0.49%	-1.4[-8.77,5.97]
1129 Bellini 1996	43	43	-3.9 (1.8)		2.16%	-3.9[-7.43,-0.37]
1130 Inoue 1996	14	14	-15.2 (1.91)		1.91%	-15.2[-18.94,-11.46]
1131 Ferri 1996	61	61	-7.4 (1.13)		5.47%	-7.4[-9.61,-5.19]
1134 Cappuccio 1997	29	29	-6.6 (2.51)		1.11%	-6.6[-11.52,-1.68]
1138 McCarron 1997	99	99	-4.9 (1.23)		4.62%	-4.9[-7.31,-2.49]
1139 Meland 1997	16	16	-4 (2.47)		1.14%	-4[-8.84,0.84]
1145 Wing 1998	17	17	-7 (0.79)		11.19%	-7[-8.55,-5.45]
1146 Herlitz 1998	6	6	-5 (1.94)		1.86%	-5[-8.8,-1.2]
1148 Damasceno 1999	19	19	-8.5 (4.1)		0.42%	-8.5[-16.54,-0.46]
1159 Ames 2001	13	13	-7 (3.56)		0.55%	-7[-13.98,-0.02]
1161 DASH 2001 WH	37	37	-6.6 (1.2)		4.85%	-6.6[-8.95,-4.25]
1168 Cuzzola 2001	19	19	-5.1 (2.45)		1.16%	-5.1[-9.9,-0.3]
1170 TONE 2001 W	251	220	-4 (1.01)		6.85%	-4[-5.98,-2.02]
1172 Johnson 2001	46	46	-4.5 (2.08)		1.61%	-4.5[-8.58,-0.42]
1173 Manunta 2001	20	20	-5.2 (2)		1.75%	-5.2[-9.12,-1.28]
1183 Gates 2004	12	12	-3 (1.84)		2.06%	-3[-6.61,0.61]
1191 Melander 2007	39	39	-6 (1.18)		5.02%	-6[-8.31,-3.69]
1193 Dengel 2007	28	28	-10 (3.64)		0.53%	-10[-17.13,-2.87]
1198 He 2009	71	71	-4.8 (1.24)		4.54%	-4.8[-7.23,-2.37]
1202 Weir 2010	132	132	-9.4 (9.7)		0.07%	-9.4[-28.41,9.61]
1209 Bonfils 2013	12	12	-2 (5.5)		0.23%	-2[-12.78,8.78]
1213 Mallamaci 2013	32	32	-8 (2.4)		1.21%	-8[-12.7,-3.3]
1225 Gijsbers 2015	36	36	-7.5 (1.53)		2.98%	-7.5[-10.5,-4.5]
Total (95% CI)					**100%**	**-5.71[-6.23,-5.19]**

Heterogeneity: Tau²=0; Chi²=184.65, df=54(P<0.0001); I²=70.76%

Test for overall effect: Z=21.6(P<0.0001)

Favours experimental -100 -50 0 50 100 Favours control

ADDITIONAL TABLES

Table 1. Sodium intake

Reference	Recommended upper level*	World, lower range*	World, lower 2.5%*	World, mean*	World, Upper 97.5%*	World, upper range*
ADG 2015	100 (2300) (5800)					
WHO 2012	87 (2000) (5046)					
McCarron 2013		90 (2070) (5220)	109 (2500) (6320)	159 (3660) (9220)	209 (4810) (12120)	248 (5700) (14400)
Powles 2013		95 (2200) (5510)		172 (3950) (10000)		240 (5520) (13920)

1. number: mmol; 2. number: mg sodium; 3. number: mg sodium chloride

Table 2. Differences in BP effects of reduced sodium intake at different time points in longitudinal studies

Comparison	References	SBP diff. (95% CI)	P	DBP diff. (95% CI)	P
Week 1 vs.2	1070 Parker 1990;1180 Palacios 2004;1183 Gates 2004;1188 Swift 2005	-0.18 (-3.03 to 2.67)	0.90	0.12 (-2.53 to 2.77)	0.93
Week 1 vs.4	1070 Parker 1990;1088 Ruppert 1993;1128 Schorr 1996;1180 Palacios 2004;1183 Gates 2004;1186 Forrester 2005 N	-0.50 (-3.20 to 2.20)	0.72	0.35 (-2.02 to 2.72)	0.77
Week 2 vs.4	1011 MacGregor 1982;1039 ANHMRCDS 1986;1055 ANHMRCDS 1989;1070 Parker 1990;1075 Mascioli 1991;1082 Cobiac 1992 1097 Nestel 1993;1100 Fotherby 1993;1080 Huggins 1992;1183 Gates 2004;1186 Forrester 2005 N;1201 Nowson 2009	-0.10 (-1.88 to 1.68)	0.91	-0.20 (-1.12 to 0.72)	0.67
Week 2 vs.6	1039 ANHMRCDS 1986;1055 ANHMRCDS 1989;1085 Sciarrone 1992;1097 Nestel 1993;1201 Nowson 2009	-0.50 (-2.66 to 1.66)	0.65	-0.42 (-1.69 to 0.85)	0.52
Week 4 vs.6	1039 ANHMRCDS 1986;1055 ANHMRCDS 1989;1085 Sciarrone 1992;1097 Nestel 1993;1201 Nowson 2009	0.39 (-1.77 to 2.55)	0.72	-0.22 (-1.50 to 1.06)	0.74

Data from Graudal 2015

Table 3. Association of low sodium intake with mortality in prospective observational studies

Study	Multiple adjust-ment*	Exclusion	N (LS)	N (US)	RR/OR (95% CI)
Alderman 1998 (NHANES I)	Yes	None	2837	8509	0.88 (0.80, to, 0.97)
He 1999 (NHANES I)	Yes	Overweight (BMI > 27.3)	1699	5098	0.98 (0.88 to 1.09)
Tuomilehto 2001	Yes	Males**	634	311	0.91 (0.56 to 1.48)
Cohen 2006 (NHANES II)	Yes	None	3711	3443	0.78 (0.67 to 0.91)
Gelijnse 2007	Yes	CVD and HT	392	392	1.12 (0.86 to 1.46)
Cohen 2008 (NHANES III)	Yes	None	2175	4350	0.83 (0.73 to 0.94)
Yang 2011 (NHANES III)	Yes	Overweight (BMI > 25)	3067	6133	0.93 (0.73 to 1.18)
Stolarz-Skrzypek 2011	Yes	None	1250	1220	0.82 (0.62 to 1.08)
Gardener 2012	Yes	None	1138	961	0.89 (0.74 to 1.07)
Pfister 2014 (Norfolk)	Yes	0-2 year events	3070	9249	0.92 (0.82 to 1.02)
O'Donnell 2014 (PURE)	Yes	CVD, Cancer, DM, smokers	6162	38643	0.62 (0.54 to 0.71)]
Total (95% CI)#			21369	67078	0.84 (0.76 to 0.93)
Total (95% CI)##			21123	65450	0.87 (0.76 to 0.98)

Only studies, which were representative for the general population and which adjusted for confounders were included.
If subgroup results were given, the results of the most healthy subgroup was used in the analysis to reduce the possibility of reverse causation
#With primary NHANES analyses (Alderman 1998, Cohen 2008)
With NHANES re-analyses (He 1999, Yang 2011)
* Studies were generally adjusted for at least sex, age and CVD risk factors
** In the male group a low salt intake group could not be identified, as the salt intake in the lowest salt intake quartile was up to 159 mmol.
BMI: body mass index; **CVD:** cardiovascular disease; **DM:** diabetes mellitus; **HT:** hypertension

APPENDICES

Appendix 1. Search strategies

Database: Ovid MEDLINE(R) 1946 to Present with Daily Update
Search Date: 7 March 2016

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1 sodium chloride, dietary/ (5340)
2 sodium, dietary/ (7840)
3 sodium/ (101026)
4 (sodium or salt).tw. (346998)
5 or/1-4 (400932)

6 diet, sodium-restricted/ (5815)
7 ((salt or sodium) adj5 (chang$ or curb$ or diet$ or free or intake or limit$ or load$ or low$ or minimi$ or reduc$ or restrict$ or supplement $)).tw. (50878)
8 or/6-7 (53160)
9 hypertension/ (207011)
10 hypertens$.tw. (322915)
11 exp blood pressure/ (260732)
12 (blood pressure or bloodpressure or bp).tw. (317168)
13 or/9-12 (707443)
14 renin/ (27614)
15 renin.tw. (43610)
16 aldosterone/ (22706)
17 aldosterone.tw. (28823)
18 exp catecholamines/ (242929)
19 (catecholamine$ or sympathin$ or dopamine$ or hydroxytyramine$ or dihydroxyphenethylamine or intropin or epinephrine or adrenaline or epitrate or vaponefrin or medihaler-epi or micronefrin or micronephrine or racepinephrine or epifrin or lyophrin or norepinephrin$ or noradrenaline or levarterenol or levonorepinephrine or levophed or arterenol or levonor or orciprenaline or metaproterenol or alupent or metaprel or alotec or astmopent).tw. (246296)
20 exp cholesterol/ (142389)
21 (cholesterol$ or epicholesterol$ or azacosterol$ or diazacholesterol$ or hydroxycholesterol$ or 19-iodocholesterol$ or iodocholesterol $ or ketocholesterol$ or oxocholesterol$ or lipid$ or glyceride$ or triglyceride$ or glycolipid$ or lipoprotein$ or ldl or hdl).tw. (533921)
22 or/14-21 (953557)
23 randomized controlled trial.pt. (407656)
24 controlled clinical trial.pt. (90132)
25 randomized.ab. (304936)
26 placebo.ab. (155515)
27 clinical trials as topic/ (175120)
28 randomly.ab. (215798)
29 trial.ti. (132445)
30 or/23-29 (931053)
31 animals/ not (humans/ and animals/) (4161827)
32 30 not 31 (852135)
33 5 and 8 and (13 or 22) and 32 (1933)
34 remove duplicates from 33 (1925)

****

Database: Cochrane Central Register of Controlled Trials <2016, Issue 3> via Cochrane Register of Studies Online
Search Date: 7 March 2016

#1 MESH DESCRIPTOR Sodium Chloride, Dietary 211
#2 MESH DESCRIPTOR Sodium, Dietary 328
#3 MESH DESCRIPTOR Sodium 1917
#4 (salt or sodium):TI,AB 18678
#5 #1 OR #2 OR #3 OR #4 19256
#6 MESH DESCRIPTOR Diet, Sodium-Restricted 518
#7 (salt or sodium) near5 (chang* or curb* or diet* or free or intake or limit* or load* or low* or minimi* or reduc* or restrict* or supplement*) 3206
#8 #6 OR #7 3206
#9 MESH DESCRIPTOR Hypertension 13753
#10 (antihypertens* or hypertens*):TI,AB 32980
#11 MESH DESCRIPTOR Blood Pressure EXPLODE ALL TREES 24184
#12 (blood pressure or bloodpressure or bp) 55509
#13 #9 OR #10 OR #11 OR #12 71017
#14 renin 4518
#15 aldosterone 3221
#16 MESH DESCRIPTOR Catecholamines EXPLODE ALL TREES 8599
#17 (catecholamine* or sympathin* or dopamine* or hydroxytyramine* or dihydroxyphenethylamine or intropin or epinephrine or adrenaline or epitrate or vaponefrin or medihaler-epi or micronefrin or micronephrine or racepinephrine or epifrin or lyophrin or norepinephrin* or noradrenaline or levarterenol or levonorepinephrine or levophed or arterenol or levonor or orciprenaline or metaproterenol or alupent or metaprel or alotec or astmopent) 16533
#18 MESH DESCRIPTOR Cholesterol EXPLODE ALL TREES 8755

#19 (cholesterol* or epicholesterol* or azacosterol* or diazacholesterol* or hydroxycholesterol* or 19-iodocholesterol* or iodocholesterol* or ketocholesterol* or oxocholesterol* or lipid* or glyceride* or triglyceride* or glycolipid* or lipoprotein* or ldl or hdl) 37244
#20 #14 OR #15 OR #16 OR #17 OR #18 OR #19 59594
#21 #5 AND #8 AND #13 OR #20 1820

****

Database: Embase <1980 to 2016 March 04>
Search Date: 7 March 2016
---
1 sodium chloride, dietary/ (7530)
2 sodium, dietary/ (6109)
3 sodium/ (91427)
4 (sodium or salt).tw. (424462)
5 or/1-4 (472096)
6 diet, sodium-restricted/ (8257)
7 ((salt or sodium) adj5 (chang$ or curb$ or diet$ or free or intake or limit$ or load$ or low$ or minimi$ or reduc$ or restrict$ or supplement $)).tw. (61099)
8 or/6-7 (64792)
9 exp hypertension/ (545880)
10 hypertens$.tw. (476727)
11 exp blood pressure/ (434877)
12 (blood pressure or bloodpressure or bp).tw. (428835)
13 or/9-12 (1125448)
14 renin/ (25693)
15 renin.tw. (51567)
16 aldosterone/ (30390)
17 aldosterone.tw. (34355)
18 exp catecholamine/ (324747)
19 (catecholamine$ or sympathin$ or dopamine$ or hydroxytyramine$ or dihydroxyphenethylamine or intropin or epinephrine or adrenaline or epitrate or vaponefrin or medihaler-epi or micronefrin or micronephrine or racepinephrine or epifrin or lyophrin or norepinephrin$ or noradrenaline or levarterenol or levonorepinephrine or levophed or arterenol or levonor or orciprenaline or metaproterenol or alupent or metaprel or alotec or astmopent).tw. (288546)
20 exp cholesterol/ (239050)
21 (cholesterol$ or epicholesterol$ or azacosterol$ or diazacholesterol$ or hydroxycholesterol$ or 19-iodocholesterol$ or iodocholesterol $ or ketocholesterol$ or oxocholesterol$ or lipid$ or glyceride$ or triglyceride$ or glycolipid$ or lipoprotein$ or ldl or hdl).tw. (688622)
22 or/14-21 (1238526)
23 randomized controlled trial/ (394072)
24 crossover procedure/ (46238)
25 double-blind procedure/ (126561)
26 (randomi?ed or randomly).tw. (845561)
27 (crossover$ or cross-over$).tw. (78158)
28 placebo.ab. (219858)
29 (doubl$ adj blind$).tw. (159441)
30 assign$.ab. (271379)
31 allocat$.ab. (97448)
32 or/23-31 (1264495)
33 (exp animal/ or animal.hw. or nonhuman/) not (exp human/ or human cell/ or (human or humans).ti.) (5457724)
34 32 not 33 (1101675)
35 5 and 8 and (13 or 22) and 34 (2193)
36 remove duplicates from 35 (2167)

****

Database: Hypertension Group Specialised Register via Cochrane Register of Studies
Search Date: 7 March 2016

#1 ((salt or sodium):TI)
#2 ((chang* or curb* or diet* or free or intake or limit* or load* or low* or minimi* or reduc* or restrict* or supplement*))
#3 RCT:DE
#4 (Meta-Analysis OR Review):MISC2
#5 #1 AND (#2) AND ((#3 OR #4)) (708)

****

Database: ClinicalTrials.gov
Search Date: 7 March 2016

Search terms: (salt OR sodium) AND randomized
Study type: Interventional Studies
Interventions: diet
Outcome Measures: blood pressure (113)

****

Medline In-Process: 98

Total: 1925 + 1820 + 2167 + 708 + 113 + 98 = 6831

After de-duplication: 3269

WHAT'S NEW

Date	Event	Description
4 January 2017	New citation required but conclusions have not changed	updated version of the review with up-to-date search and methodology
4 January 2017	New search has been performed	1. Twenty-one new references were included. One erroneously double-counted and two previously included duplicate references were excluded. 2. Separate analyses of mean blood pressure (MBP) in white participants were excluded. Instead MBP effects were transformed to SBP and DBP effects by means of regression analyses and included in the SBP and DBP analyses. 3. Previous subgroup analyses of studies with a duration of at least four weeks (BP), two to four weeks (hormones and lipids) and lipid studies with sodium reduction to moderate levels were eliminated. 4. Instead, a subgroup analysis of studies lasting at least seven days and with a sodium intake of maximum 250 mmol/day in the high sodium group was performed on all outcomes. 5. The text of the review includes new subheadings available in Rev Man.

HISTORY

Protocol first published: Issue 1, 2003
Review first published: Issue 1, 2003

Date	Event	Description
17 November 2002	New search has been performed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Graudal NA: Study design and definition of selection criteria; Data collection and analysis; Formulation of manuscript

Hubeck-Graudal T: Data collection and analysis; Revision of manuscript.

Jürgens G: Data collection and analysis; Revision of manuscript.

DECLARATIONS OF INTEREST

None.
All authors are employed at public institutions. None of the authors has any connection with or receives funds from the food and salt industries or has commercial interests that might bear on this article.

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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

This review was invited on the basis of the first published version in JAMA in 1998 and therefore a formal protocol was not performed.

The purpose and the methods of the present update are essentially identical with the 1998 JAMA version and the previous Cochrane versions.

INDEX TERMS

Medical Subject Headings (MeSH)

*Diet, Sodium-Restricted; African Continental Ancestry Group; Aldosterone [blood]; Asian Continental Ancestry Group; Blood Pressure [*drug effects] [radiation effects]; Catecholamines [blood]; Cholesterol [blood]; Epinephrine [blood]; European Continental Ancestry Group; Hypertension [*diet therapy] [ethnology]; Norepinephrine [blood]; Randomized Controlled Trials as Topic; Recommended Dietary Allowances; Renin [blood]; Sodium Chloride, Dietary [*pharmacology]; Triglycerides [blood]

MeSH check words

Humans