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Abbreviations and acronyms

CHD	coronary heart disease
CI	confidence interval
CVD	cardiovascular disease
DASH	Dietary Approaches to Stop Hypertension
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HDL	high-density lipoprotein
HIV	human immunodeficiency virus
ICTRP	International Clinical Trials Registry Platform
IQR	interquartile range
ITT	intention-to-treat
LILACS	Latin American and Caribbean Health Science Literature Database
LDL	low-density lipoprotein
NCD	noncommunicable disease
PRISMA	preferred reporting items for systematic reviews and meta-analyses
RCT	randomized controlled trial
SD	standard deviation
VLDL	very low-density lipoprotein
WHO	World Health Organization

Symbols

>	greater than
<	less than
≥	equal to or greater than
≤	equal to or less than

1 Introduction

1.1 Background

Noncommunicable diseases (NCDs) are the leading cause of mortality and morbidity globally (*1*). The major NCDs currently account for approximately 60% of all deaths and 43% of disease burden globally, and these levels are expected to continue to rise (*2, 3*). In 2008, cardiovascular disease (CVD) accounted for 17 million deaths, 48% of all deaths from NCDs. CVD accounts for as much mortality as infectious disease, nutritional deficiency, and maternal and perinatal conditions combined (*2*).

Sodium has been of interest in public health nutrition for decades, mainly because of its association with hypertension and CVDs, especially coronary heart disease (CHD) and stroke. High blood pressure is a major risk factor for both stroke and CHD. Overall, the evidence suggests that, for most individuals, the higher their sodium consumption, the higher their blood pressure (*4*). Increasing blood pressure may be the primary mechanism by which increased sodium intake affects CVD, stroke and CHD. High blood pressure accounts for 62% of strokes and 49% of CHD. Additionally, diets that are high in sodium may have independent but additive harmful effects on left ventricular hypertrophy, progression of renal disease, and risk of CVD and stroke. It has been estimated that a reduction in dietary intake of sodium of 50 mmol/day would reduce the number of people needing antihypertensive therapy by 50%, the number of deaths from strokes by 22% and the number of deaths from CHD by 16% (*5*). High sodium intake also presents a challenge for excretion by the kidneys, which is another potential mechanism for affecting blood pressure and risk of NCD. Increased sodium intake may lead to increased urinary protein excretion and may thus increase the rate of deterioration of renal function (*5, 6*).

1.2 Need for this review

To date, expert groups have recommended to the World Health Organization (WHO) appropriate levels for sodium consumption in two publications:

- the WHO Study Group report: Diet, nutrition and the prevention of chronic diseases (7);
- the report of the joint WHO/Food and Agriculture Organization of the United Nations (FAO) Expert Consultation: *Diet, nutrition and the prevention of chronic disease* (*5*).

Also, recommendations have been published in the context of CVD prevention:

- in adults who have experienced a coronary event, in *Prevention of recurrent heart attacks and strokes in low and middle income populations: evidence-based recommendations for policy makers and health professionals* (8);
- in adults at risk for CVD in *Prevention of cardiovascular disease: guidelines for assessment and management of cardiovascular risk* (*9*).

The current WHO recommendation for adults is to reduce the consumption of sodium to < 2 g or < 90 mmol (< 5 g salt) per day (*5*). This value was deemed appropriate and was

adopted as the recommendation on sodium consumption to prevent CVD (*9*). A plethora of evidence means that the scientific community is in broad agreement that decreasing salt intake can decrease blood pressure and risk of CVD in most individuals (*4*). Nonetheless, a Cochrane Review on longer term effects of salt reduction published in 2004 concluded that further benefits in blood pressure in individuals with or without hypertension can occur with a reduction of sodium intake to as low as 50 mmol/day (i.e. 3 g salt/day), indicating that it may be necessary to adjust the recommended level (*10*). Other normative agencies around the globe have published recommendations on sodium intake that suggest certain subgroups of the population may require differing recommendations for sodium consumption. For example, the Institute of Medicine produced an evidence-based report on sodium consumption (*11*) that informed the 2005 United States Dietary Guidelines and the Canadian Dietary Guidelines. Although the recommended upper limit for sodium consumption was 100 mmol (2.3 g), it was recognized that lower levels of intake could be beneficial. Also, the Institute of Medicine, and the countries of Australia and New Zealand recommend a lower consumption level for subgroups of the population, such as hypertensive adults. WHO does not currently have a recommendation for specific groups based on ethnicity, age or other risk factors. The 2007 recommendations that related to CVD outcomes did explore separate recommendations based on a combined risk of CVD that included the variables of age and hypertension status (*9*). These recommendations concluded that the recommendation to consume < 90 mmol sodium/day (i.e. < 5 g salt/day) was appropriate for all groups, regardless of current risk of CVD (*9*).

In light of these recent publications and the ever increasing importance of NCDs globally, WHO undertook this review. The WHO Nutrition Guidance Expert Advisory Group made use of this document when generating WHO guidelines on sodium intake.

1.3 Objectives

The overall objective of the review was to assess the effect of reduced sodium intake compared with usual sodium intake on blood pressure, renal function, blood lipids and other adverse outcomes in adults.

Specific objectives were to assess whether there is any effect on blood pressure, renal function, blood lipids and other adverse outcomes in adults of:

- consuming less sodium compared with consuming more sodium;
- reducing sodium intake by 1/3 or more compared with reducing sodium intake by < 1/3;
- consuming sodium at a level of < 2 g/day compared with consuming ≥ 2 g/day;
- consuming sodium at a level of < 1.2 g/day compared with consuming > 1.2 g/day, and compared with consuming 1.2–2 g/day.

2 Methods

2.1 Criteria for considering studies for this review

Study type

We included in the review randomized controlled trials (RCTs) of both individual and cluster randomization design.

Participants

Studies considered for inclusion were those involving adults (≥ 16 years of age) of either gender, from the general population (free living) or specific groups (e.g. refugee populations). We considered studies in apparently healthy populations who may have been at risk of, or have had, hypertension; were known to have hypertension; or were known to have normal blood pressure. We also considered studies in people with chronic conditions such as overweight or obesity, diabetes or chronic nephrolithiasis (a chronic form of kidney stones). We excluded studies targeting those who were acutely ill or infected with human immunodeficiency virus(HIV).

Outcome measures

The primary outcome measures were:

- blood pressure;
- renal function;
- adverse effects including increased total cholesterol, low-density lipoprotein (LDL) cholesterol, or triglycerides; decreased high-density lipoprotein (HDL) cholesterol; increased adrenaline or noradrenaline; and any other adverse effects reported by study authors.

Secondary outcomes were all other outcomes reported by the original study authors.

Types of interventions

We were interested in comparisons of reduced sodium intake achieved through any means with a usual or higher sodium intake. The comparisons might also include other co-interventions such as physical activity, provided that the co-intervention was identical in the intervention and control groups. Studies that had lifestyle or dietary intervention arms (which resulted in lower sodium intake in one arm) were included, provided the only difference between the study arms was a targeted intervention that resulted in reduced sodium intake.

We also included studies in which all participants received some medical treatment (e.g. diuretics or beta blockers), and in which one study arm had reduced sodium intake and one had usual sodium intake, provided the only difference between the intervention and the control was the level of sodium intake.

2.2 Identification of studies

We searched for studies in two phases. In the first phase, we searched for high-quality systematic reviews on reduced sodium consumption that included the outcomes of interest. If the inclusion criteria for an identified review were similar or equivalent to those of the current review, we used the reference list from that review as a list of potential studies, and completed the list by searching the literature published subsequent to the search date used in that review. In some cases, we contacted the original authors of the systematic review to request their data, so that we could explore the data in such a way as to answer our objectives.

In the second phase, we undertook a complete search for data published since the date of the search performed in the identified systematic reviews (see *Electronic databases* and *Other resources*, below).

Electronic databases

We searched the following electronic databases:

- The Cochrane Central Register of Controlled Trials (24 August 2011);
- MEDLINE (PubMed searched on 6 July 2011 for all outcomes other than renal, which was searched for on 23 August 2011);
- EMBASE (searched on 2 August 2011);
- WHO International Clinical Trials Registry Platform (ICTRP, 23 August 2011);
- The Latin American and Caribbean Health Science Literature Database (LILACS, 6 August 2011).

The detailed strategy used for the electronic search is given in **Annex 1**.

Other resources

We also searched for further trials on the WHO web site[1] and in the reference lists of identified papers. For assistance in identifying ongoing or unpublished studies, we contacted the WHO Department of Nutrition for Health and Development and other international partners, such as academic and research institutions with a known interest in this field.

[1] www.who.int/nutrition

2.3 Data collection and analysis

2.3.1 Selection of studies

Identified references were independently assessed for potential relevance by two reviewers. The title, abstract and keywords of every record retrieved were scanned independently by the two authors, to determine which studies required further assessment.

A full article was retrieved when the information given in the title, abstract and keywords suggested that the study:

- included an intervention that planned to or achieved a reduced sodium intake (however, for inclusion in the review, a difference of > 40 mmol/day must have been achieved);
- had a prospective design and a control group;
- did not target patients who were acutely ill or infected with HIV;
- had a duration of at least 1 month (4 weeks);
- reported an outcome of interest.

We also retrieved the full article when it was unclear from scanning the title and abstract whether a study met the above criteria.

Differences in opinion were resolved by discussion and consensus. The two review authors independently assessed all the potentially eligible studies for inclusion according to the above prespecified inclusion criteria. Where studies were published only as abstracts, or contained little information on methods, we attempted to contact the authors to obtain further details of study design and results.

Where differences in opinion existed, they were resolved by consulting a third party and reaching consensus. If it was not possible to resolve differences of opinion, the reference was added to those “awaiting assessment”, and authors were contacted for clarification. An adapted preferred reporting items for systematic reviews and meta-analyses (PRISMA) flowchart of study selection was generated (**Figure 3.1**) (*12*).

2.3.2 Data extraction and management

For studies that fulfilled inclusion criteria, the two authors independently abstracted relevant population and intervention characteristics using standard data extraction templates (**Annex 2**), with any disagreements resolved by discussion and consensus. Any relevant missing information on the study was sought from the authors of the original reference. The data extraction form included the following items:

- *General information* – published or unpublished, title, authors, reference or source, contact address, country, language of publication, year of publication, duplicate publications, sponsor and setting.
- *Trial characteristics* – design, duration of follow-up, method of randomization, allocation concealment and blinding (patients, people administering treatment and outcome assessors).

- *Interventions* – placebo included, interventions (dose, route and timing), comparison interventions (dose, route and timing) and co-medications.
- *Participants* – sampling (random or convenience), exclusion criteria, total number and number in comparison groups, sex, age, baseline characteristics, diagnostic criteria, similarity of groups at baseline (including any comorbidities), assessment of compliance, withdrawals or losses to follow-up (reasons or description), subgroups, status of blood pressure and status of medication to control blood pressure.
- *Outcomes* – outcomes specified above, any other outcomes assessed, other events, length of follow-up and quality of reporting of outcomes.
- *Results* – for outcomes specified above and including a measure of variation, and, if necessary, converted to measures of effect specified below.
- *Objective* – stated objective of the study.

Duplicate publications

In the case of duplicate publications and companion references of a primary study, we tried to maximize yield of information by simultaneously evaluating all available data.

2.3.3 Assessment of risk of bias in included studies

Data were entered into Review Manager software (RevMan 2008) and checked for accuracy by a second author. In cases of disagreement, a third party was consulted and a judgement was made based on consensus. We assessed risk of bias using the broad categories recommended in the *Cochrane handbook for systematic reviews of interventions* (*13*).

Randomization (checking for possible selection bias)

For each included study, we described the method used to generate the randomization sequence in sufficient detail to allow an assessment of whether it should produce comparable groups. Methods of randomization were categorized as one of the following:

- *adequate* – trials in which any truly random process was used (e.g. random number table or computer random number generator);
- *inadequate* – trials in which any non-random process was used (e.g. odd or even date of birth; hospital or clinic record number);
- unclear.

Allocation concealment (checking for possible selection bias)

For each included study, we described the method used to conceal the allocation sequence in sufficient detail to determine whether intervention allocation could have been foreseen in advance of or during recruitment, or changed after assignment. Methods were categorized as:

- *adequate* – for example, telephone or central randomization, consecutively numbered sealed opaque envelopes;

- *inadequate* – for example, open allocation, unsealed or non-opaque envelopes, alternation, date of birth;
- unclear.

Blinding (checking for possible performance bias)

For each included study, we described the methods used, if any, to blind study participants and personnel from knowledge of which intervention a participant received. We judged studies to be at low risk of bias if they were blinded, or if we judged that the lack of blinding was unlikely to have affected the results. We assessed blinding separately for different outcomes or classes of outcomes. Methods were categorized as: *adequate*, *inadequate* or *unclear* for:

- participants
- personnel
- outcome assessors.

Incomplete outcome data (checking for possible attrition bias through withdrawals, drop-outs, protocol deviations)

For each included study, and for each outcome or class of outcomes, we described the completeness of data, including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported; the numbers included in the analysis at each stage (compared with the total number of randomized participants); reasons for attrition or exclusion where reported; and whether missing data were balanced across groups or were related to outcomes. Methods were categorized as:

- *adequate* – trials in which few drop-outs or losses to follow-up were noted and an intention-to-treat (ITT) analysis was possible;
- *inadequate* – trials in which the rate of exclusion was at least 20%, or there were wide differences in exclusions between groups, whether or not ITT was used;
- unclear.

Selective reporting bias

For each included study, we described how we investigated the possibility of selective outcome reporting bias and what we found. Methods were categorized as:

- *adequate* – trials in which it was clear whether all of the prespecified outcomes and all expected outcomes of interest to the review had been reported;
- *inadequate* – trials in which not all prespecified outcomes had been reported, one or more reported primary outcomes were not prespecified, outcomes of interest were reported incompletely and so could not be used, or results of a key outcome that would have been expected to have been reported were not reported;
- unclear.

Other sources of bias

For each included study, we described any important concerns we had about other possible sources of bias, such as similarity of the groups at baseline. We assessed whether each study was free of other problems that could put it at risk of bias, recording answers as *yes*, *no* or *unclear*.

2.3.4 Measures of treatment effect

Continuous variables were expressed as mean differences with 95% confidence intervals (CI).

2.3.5 Missing data

We obtained relevant missing data from authors, where feasible, and carefully evaluated important numerical data (e.g. screened versus randomized patients and whether the analysis included ITT). We also investigated attrition rates (e.g. drop-outs, losses to follow-up and withdrawals), and critically appraised issues of missing data.

2.3.6 Data synthesis

Data were summarized statistically if they were available, sufficiently similar and of sufficient quality. Statistical analyses were performed according to the statistical guidelines referenced in the *Cochrane handbook for systematic reviews of interventions* (*13*). Overall results were calculated based on the random-effects model. Where data were reported in forms that could not easily be converted into standard measures, data were summarized in a narrative format, and different comparisons were analysed separately.

Assessment of heterogeneity

We identified heterogeneity by visual inspection of the forest plots, and by using a standard Chi-squared test and a significance level of $\alpha = 0.1$, in view of the low power of this test. We specifically examined heterogeneity with the I^2 statistic, quantifying inconsistency across studies to assess the impact of heterogeneity on the meta-analysis (*14, 15*), where a I^2 statistic ≥ 75% indicates a considerable level of inconsistency. Where heterogeneity was found, we attempted to determine the potential causes by examining individual study and subgroup characteristics.

2.3.7 Subgroup analysis

We conducted both overall and subgroup analyses for each outcome, to explore effect-size differences between groups by:

- gender (male, versus female, versus heterogeneous group);
- hypertensive status (all participants with hypertension, versus all participants without hypertension, versus heterogeneous or unspecified status);
- achieved absolute sodium intake level in intervention group (achieved < 2 g/day versus ≥ 2 g/day);
- achieved absolute sodium intake level in intervention group (achieved < 1.2 g/day versus ≥ 1.2 g/day);

- achieved relative sodium intake level in intervention group (achieved 1/3 (33%) or greater reduction relative to control versus achieved < 1/3 reduction relative to control);
- status of medication use to control blood pressure (all participants taking medication, versus no participants taking medication, versus heterogeneous or unspecified medication status);
- duration (< 3 months versus 3–6 months versus > 6 months);
- study design (parallel versus crossover);
- type of blood pressure device used (automatic versus manual);
- method for measuring blood pressure (supine office versus seated office versus standing office versus combination office versus supine home versus seated home versus standing home versus combination home).

2.3.8 Sensitivity analysis

We carried out a sensitivity analysis to examine the effects of removing studies at high risk of bias from the analysis. We considered a study to be of high risk of bias if it was graded as inadequate in both the randomization and allocation concealment, and in either blinding or loss to follow-up. Other studies were considered to be at low risk of bias.

We also carried out a sensitivity analysis to examine the effect of comorbidities on outcomes by removing studies where all participants had chronic conditions such as overweight, obesity, diabetes and impaired glucose tolerance.

2.3.9 Quality of the body of evidence

We used funnel plots to assess the potential existence of small study bias (*16, 17*). A "risk of bias summary" (**Annex 4**) and "risk of bias graph" (**Annex 5**) were generated. GRADEProfiler software (version 3.6) was used to assess the quality of the body of evidence according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) methodology outlined in *GRADE: an emerging consensus on rating quality of evidence and strength of recommendations* (*18*).

3 Results

3.1 Results of the search

3.1.1 Phase 1: Search for recent, high-quality systematic reviews

The search for recent, high-quality systematic reviews resulted in the identification of three systematic reviews (*10, 19, 20*). Two were reviews of the effects of reduced sodium on blood pressure, plasma renin activity, aldosterone, noradrenaline and blood lipids in adults (*10, 20*). The inclusion criteria for those reviews were broader than those being used in the current review; therefore, the reference lists from those reviews were used to identify studies to be included in the current systematic review. The third was a review of the effects of reduced sodium intake on hypertension, and risk of pre-eclampsia and eclampsia in pregnant women (*19*). Because that review was only 2 years old, it was used as part of the body of evidence on the effects of reduced sodium in pregnant women.

3.1.2 Phase 2: Search for randomized controlled trials

Flow through screening, inclusion and exclusion

The process of selection of studies is shown in **Figure 3.1**. The search for RCTs in electronic databases resulted in 9802 references (published manuscripts and unpublished study reports). A further 31 studies for potential inclusion were identified by scanning the reference lists of relevant high-quality systematic reviews and of included studies. Five additional potential studies were identified through direct communication with study authors. Thus, a total of 9838 studies were considered for possible inclusion in the systematic review.

We excluded 9426 references on the basis of the titles because of their obvious lack of relevance to this review. Screening of abstracts excluded another 209 references that did not meet basic criteria for inclusion. A further 118 references were duplications, leaving a total of 85 unique studies that were fully reviewed for possible inclusion in the review. After reviewing the methods sections, we excluded a further 41 references, leaving 44 for inclusion in the review. Of these, six did not contribute to the review: five because they are awaiting classification and one because it is ongoing. Additional information is being requested from the authors for one included reference; until such time as that information is retrieved, the study also cannot contribute to the meta-analyses. Hence, 38 references were included in the review, with 37 of these contributing data to the meta-analyses.

3.2 Retrieval of missing data

The following authors were contacted and generously provided additional information regarding their studies: Gary Nicholls (*21*), Eivind Meland (*22*), Frank Sacks, Lawrence Appel, Bill Volmeer, Gayle Meltesen (*23*), Jennifer Keogh (*24*), Loris Borghi (*25-27*), Rob Walker (*28*), Susan Sciarrone (*29*), Ingrid Muhlhauser (*30*), Matthew Weir (*31*), Pauline Swift (*32, 33*), Peter Howe (*34, 35*) and John Chalmers (*36, 37*).

3.3 Included studies

3.3.1 Settings

All included studies were published in English. Three studies were undertaken in Sweden (*38-40*), seven in Australia (*29, 34-37, 41, 42*)), one in France (*43*), 11 in the United Kingdom of Great Britain and Northern Ireland (UK) (*33, 44-53*), six in the United States of America (USA) (*23, 54-58*), three in the Netherlands (*59-62*) two in Norway (*22, 63*), two in Germany (*30, 64*), one in Belgium (*65*), one in Finland (*60*) and one in New Zealand (*21*). The ongoing study is being undertaken in Italy (*25*). Notably absent were studies undertaken in lower and middle income countries, or in the regions of Africa, Asia or Latin America.

3.3.2 Design

Details of the characteristics of the included studies are shown in Section 3.8.1 (*Characteristics of included studies*).

All studies reporting blood pressure, adverse effects and renal outcomes in adults were RCTs. Fourteen studies had a parallel design (*22, 29, 30, 34, 35, 37-39, 41, 47, 56, 57, 60, 62*), 21 had a crossover design (*21, 23, 33, 40, 43-46, 48-51, 53-55, 58, 59, 61, 63-65*) and two had both a parallel design phase and a crossover design phase (*25, 36, 52*).

The study duration ranged from 4 weeks (*23, 30, 33, 34, 40, 43-45, 48, 49, 53, 55, 58, 64, 65*) to 36 months (*57*). Of the 38 studies, 31 had a duration of < 3 months (*6, 21-23, 29, 30, 33-36, 38-41, 43-46, 49, 51, 53-55, 58-61, 63-66*). One study had a parallel phase of 3 months followed by a 1-month crossover phase (*52*). One study reported results after 1, 2, 3, 6 and 12 months of intervention (*47*).

Five studies were undertaken in individuals without hypertension (*40, 41, 56, 57, 64*), 24 in individuals with hypertension (*21, 22, 29, 33, 35-39, 43, 45, 47-52, 54, 55, 58, 61-63, 65*) and eight in a heterogeneous group of individuals with and without hypertension (*23, 30, 34, 44, 46, 53, 59, 60*), of which one study reported results separately for the participants with and without hypertension (*53*).

No studies were conducted in women only, or reported results for women separately from men. Two studies were conducted in men only (*38, 39*), and 35 in a mixed population of men and women (*21-23, 29, 30, 33-37, 40, 41, 43-65*).

3.3.3 Participants

The number of participants in the studies ranged from 16 (*21, 30, 63*) to 2382 (*57*). In total, there were 5508 participants: 4145 in studies of parallel design and 1363 in studies of crossover design. At baseline of the studies, there were 1478 participants with hypertension, 3263 without hypertension and 767 with undisclosed hypertensive status.

3.3.4 Interventions

All studies were intended to compare health outcomes between a group of participants consuming higher or usual sodium intake and a group consuming reduced sodium. The intervention in 12 studies was dietary advice or education on how to achieve a reduced

sodium diet (*21, 37, 39, 47, 52, 56-60, 62, 65*); one study supplied participants with food of a known sodium level (*23*). Most studies, 24, had a run-in period where all participants achieved a reduced sodium intake via some combination of dietary advice, education, counselling, or provision of key foods (e.g. butter and bread) with reduced sodium content, followed by participants receiving either sodium tablets or placebo tablets identical in appearance to sodium tablets (*22, 29, 30, 33-36, 38, 40, 41, 43-46, 48-51, 53-55, 61, 63, 64*). Compliance with intervention and control was monitored in all studies using 24-hour urinary sodium excretion.

Twenty-seven studies contributed one comparison between a reduced sodium group and a corresponding control group (*21, 22, 30, 33, 36, 38-41, 43, 45-56, 58, 60, 61, 63, 64*). Eight studies contributed two comparisons between two reduced sodium groups and two corresponding control groups (*23, 29, 34, 35, 37, 44, 57, 65*), one study contributed three comparisons (*59*), and a further study contributed four comparisons (*62*). Overall, the 37 studies contributed 50 comparisons between a reduced sodium group and a corresponding control group for the generation of the overall estimate of effect of sodium intake on blood pressure and other outcomes. There were also two studies with one control group and two reduced sodium groups of differing levels of sodium intake (*49, 62*). These two studies contributed one additional comparison each for the subgroup analyses based on achieved sodium intake in the intervention group at follow-up. These two studies also allowed for a direct comparison of varying levels of sodium intake and the effect on these health outcomes.

The achieved sodium intake in the reduced sodium group at follow-up was < 1.2 g/day in four comparisons from three studies (*29, 40, 49*). Twenty-two comparisons had an achieved sodium intake in the reduced sodium group of ≥ 1.2 g/day but < 2 g/day (*22, 34, 35, 37, 43, 44, 48, 54, 58, 60-62, 64*). Twenty-three comparisons had an achieved sodium intake in the reduced sodium group of ≥ 2.0 g/day but < 3 g/day (*21, 30, 33, 38, 39, 41, 45-47, 49-51, 53, 55, 56, 59, 63, 65*). Four comparisons had an achieved sodium intake in the reduced sodium group of ≥ 3 g/day (*52, 57, 65*). In seven comparisons, the relative decrease in the reduced sodium group compared with control was < 1/3 (*23, 47, 52, 55, 65*). In 22 comparisons, the relative decrease in the reduced sodium group compared with the control group was ≥ 1/3 but < 1/2 (50%) (*22, 29, 33, 34, 36, 37, 41, 43, 45, 53, 62*). In 21 comparisons, the relative decrease in the reduced sodium group compared with the control group was ≥ 1/2 (*21, 23, 30, 33, 34, 37-41, 45-52, 54, 56, 57, 60, 63, 64*).

In 27 studies, the participants were not taking any medication to control blood pressure (*21, 23, 30, 33, 34, 36-41, 43, 45-54, 56, 57, 60, 63, 64*). In four studies, the status of consumption of medication to control blood pressure was unknown or unspecified (*22, 29, 44, 61*). In six studies there were comparisons between a control and reduced sodium group; in addition, all participants were given diuretics (*59, 62, 65*), beta blockers (*62*), a combination of diuretics and beta blockers (*62*), angiotensin-converting enzyme inhibitors (*35*), angiotensin II antagonists (*59*), direct renin inhibitors (*58*), or calcium-channel blockers (*55*). In three of these studies there was also a comparison of control and reduced sodium diet without medication (*59, 62, 65*).

3.3.5 Outcome measures

Resting blood pressure (systolic and diastolic)

Thirty-six studies (*21-23, 29, 30, 33-41, 43-53, 55-65*) contributed a total of 49 comparisons to the combined analysis of resting blood pressure. Seventeen studies measured resting blood pressure with an automatic device (*21, 29, 30, 33-37, 41, 43, 48-50, 53, 59, 60, 64*), and 19 measured blood pressure with a manual device (*22, 23, 30, 38-40, 44, 45, 47, 51, 52, 55-58, 61-63, 65*). Fifteen studies measured supine blood pressure in the office (*21, 29, 33, 38-40, 43, 48, 49, 51-53, 61, 62, 65*), 18 measured seated blood pressure in the office (*22, 23, 34-37, 41, 44, 45, 50, 55-60, 63, 64*), eight measured standing blood pressure in the office (*21, 48, 49, 51-53, 62, 65*), and one used the average of a combination of measures of blood pressure taken in the office (*30*). One study measured resting blood pressure at home as the average of a combination of measurement methods (*30*).

Ambulatory blood pressure (systolic and diastolic)

Six studies measured ambulatory blood pressure (*33, 40, 46, 50, 51, 58*). All six measured 24-hour ambulatory blood pressure, and five also reported day and night ambulatory blood pressure (*33, 40, 46, 50, 51*). Ambulatory blood pressure was always measured with an automatic device.

Blood lipids

Eleven studies reported quantitatively the total serum or plasma cholesterol (*22, 23, 29, 30, 51, 53-55, 59, 63, 64*). Nine studies reported quantitative results for HDL cholesterol (*22, 23, 29, 30, 51, 54, 55, 63, 64*). Seven studies reported quantitative results for LDL cholesterol (*22, 23, 29, 51, 54, 55, 64*) and eight for total triglycerides (*22, 23, 29, 51, 53-55, 64*). Another four studies reported qualitatively the change in blood lipids without providing numerical data (*35-37, 62*).

Catecholamine levels

One study reported urinary adrenaline (*38*), and two reported results on urinary noradrenaline (*38, 39*). Four studies reported results on plasma adrenaline (*21, 43, 54, 61*), and seven reported results on plasma noradrenaline (*21, 38, 43, 49, 54, 61, 64*).

Renal function

Renal function was measured by various indicators in 13 studies. Two studies reported urinary protein excretion (*33, 59*), three reported urinary albumin excretion (*46, 50, 51*), two reported protein:creatinine ratio (*33, 59*), one reported albumin:creatinine ratio (*46*) and two reported creatinine clearance (*51, 59*). Eleven studies reported results for serum or plasma creatinine (*37, 40, 48-52, 59, 61-63*). One study reported glomerular filtration rate (*40*).

Other adverse effects

Three studies reported the incidence of minor adverse effects such as headache, stomach cramps and oedema (*51, 55, 58*).

3.4 Excluded studies

Reasons for exclusion of the 41 excluded studies are given in **Table 3.77**, below.

Reasons for exclusion were as follows: 11 studies were not RCTs (*24, 26, 31, 67-74*); 11 had differences between intervention and control other than level of sodium intake (*25, 27, 39, 75-82*); 10 were of a duration of < 1 month (*83-92*); seven had no measure of 24-hour urinary sodium excretion for measure of compliance (*28, 93-98*); one did not include outcomes of interest (*99*); and one had an intervention that did not achieve at least a 40 mmol difference in sodium intake relative to control (*100*).

3.5 Effects of interventions

The effects of reduced sodium in pregnant women were reported in the systematic review by Duley and colleagues (*19*). The review included only two studies, and they showed no significant effect of reduced sodium on prevalence of hypertension in pregnant women; however, only five women in the reduced and usual sodium groups developed hypertension. The sparseness of event data made it impossible to determine whether reduced sodium had any effect on the development of hypertension. There was no quantitative measure of the continuous variable of blood pressure. Importantly, no adverse effects on mother or infant were detected with a reduced sodium diet.

The meta-analyses in the current systematic review showed the effects of reduced sodium versus control in adults on blood pressure, blood lipids, catecholamine levels and renal function. The findings are summarized in the effect estimate tables (**Tables 3.78–3.88**) and in **Figures 3.2–3.27**; the summary of findings of indicators of renal function that could not be combined in the meta-analysis are found in **Table 3.89**.

3.5.1 Resting blood pressure

Indirect comparisons

The meta-analysis of change in systolic blood pressure is shown in **Figure 3.2** and **Table 3.78**. Systolic blood pressure was reduced by reduced sodium intake relative to usual sodium intake by 3.39 mmHg (95%CI: 2.46, 4.31). The reduction in systolic blood pressure was greater in studies specifically targeting individuals with hypertension (4.06 mmHg, 95%CI: 2.96, 5.15) than in studies targeting individuals without hypertension (1.38 mmHg, 95%CI: 0.02, 2.74). In the eight studies of heterogeneous populations that included individuals with or without hypertension, the reduction in systolic blood pressure was not statistically different from either the group of individuals with hypertension or the group without hypertension, but was significantly different from zero (3.41 mmHg, 95%CI: 1.69, 5.13) (**Figure 3.3**).

Systolic blood pressure was reduced to a greater degree when usual sodium intake was reduced by ≥ 1/3 (3.79 mmHg, 95%CI: 2.75, 4.82) compared with a reduction in intake of < 1/3 (1.45 mmHg, 95%CI: 0.60, 2.29). There was no statistically significant difference in the reduction in systolic blood pressure when the reduction in sodium intake achieved was to an intake of < 2 g/day (3.39 mmHg, 95%CI: 2.09, 4.69) compared with an achieved reduction to an intake of ≥ 2 g/day (2.68 mmHg, 95%CI: 1.70, 3.66), or when the achieved reduction was

to an intake of < 1.2 g/day (6.39 mmHg, 95%CI: 3.25, 9.53) compared with an intake of > 1.2 g/day (3.23 mmHg, 95%CI: 2,28, 4.17). (**Figures 3.4–3.6**).

A reduction in systolic blood pressure was detected in studies of < 3 months' duration (4.07 mmHg, 95%CI: 3.02, 5.12) and 3–6 months' duration (1.91 mmHg, 95%CI: 0.23, 3.60). In the three studies of > 6 months' duration, the reduction was not statistically significant (0.88 mmHg, 95%CI: –0.23, 2.00) (**Figure 3.7**).

The reduction in systolic blood pressure with reduced sodium intake was not affected by the type of blood pressure device used (automatic 4.04 mmHg, 95%CI: 2.97, 5.10 versus manual 2.93 mmHg, 95%CI: 1.71, 4.15). Nor was it affected by the method of blood pressure measurement used (supine office 4.69 mmHg, 95%CI: 3.06, 6.33 versus seated office 2.91 mmHg, 95%CI: 1.82, 3.99 versus standing office 4.44 mmHg, 95%CI: 1.96, 6.92) (**Figures 3.8–3.10**).

The reduction in systolic blood pressure with reduced sodium intake was detected in individuals not taking medication to control blood pressure (3.66 mmHg, 95%CI: 2.47, 4.85), taking medication to control blood pressure (4.55 mmHg, 95%CI: 2.51, 6.59) and with undetermined status of consumption of medication to control blood pressure (1.67 mmHg, 95%CI: 0.34, 3.01) (**Figure 3.11**).

Study design did not significantly affect the reduction in systolic blood pressure with reduction in sodium intake (parallel design 2.47 mmHg, 95%CI: 1.43, 3.51 versus crossover design 4.04 mmHg, 95%CI: 2.81, 5.27) (**Figure 3.12**).

The meta-analysis of change in diastolic blood pressure is shown in **Figure 3.13** and **Table 3.79**. Diastolic blood pressure was reduced by reduced sodium intake relative to usual sodium intake by 1.54 mmHg (95%CI: 0.98, 2.11).

The results for the subgroup analyses were similar to those for systolic blood pressure. The reduction in diastolic blood pressure was statistically significant in studies specifically targeting individuals with hypertension (2.26 mmHg, 95%CI: 1.50, 3.02), but did not reach statistical significance in studies targeting individuals without hypertension (0.62 mmHg, 95%CI: –0.08, 1.31) or targeting heterogeneous groups of individuals with or without hypertension (1.04 mmHg, 95%CI: –0.05, 2.13).

Diastolic blood pressure was significantly reduced when the reduction in sodium intake was ≥ 1/3 of usual sodium intake (1.70 mmHg, 95%CI: 1.02, 2.34), and when it was < 1/3 of usual sodium intake (0.74 mmHg, 95%CI: 0.19, 1.28). There was no statistically significant difference in the reduction in diastolic blood pressure when the reduction in sodium intake achieved was to an intake of < 2 g/day (1.54 mmHg, 95%CI: 0.63, 2.46) relative to an achieved reduction of an intake of ≥ 2 g/day (1.21 mmHg, 95%CI: 0.70, 1.72). The reduction in diastolic blood pressure was not statistically significant in the four studies with an achieved reduction was to an intake of < 1.2 g/day (2.47 mmHg, 95%CI: –0.92, 5.86), but was statistically significant in the 35 studies with an achieved reduction was to an intake of ≥ 1.2 g/day (1.58 mmHg, 95%CI: 0.99, 2.17).

A reduction in diastolic blood pressure was detected in studies of < 3 months' duration (1.67 mmHg, 95%CI: 1.02, 2.33) and of 3–6 months' duration (1.33 mmHg, 95%CI: 0.15, 2.50). There were only three studies with a duration of > 6 months, and the reduction in diastolic blood pressure in these studies was not statistically significant (0.45 mmHg, 95%CI: –0.34, 1.25).

The reduction in diastolic blood pressure with reduced sodium intake was not affected by the type of blood pressure device used (automatic 1.75 mmHg, 95%CI: 0.95, 2.54 versus manual 1.40 mmHg, 95%CI: 0.62, 2.18). Nor was it affected by the method of blood pressure measurement used (supine office 2.03 mmHg, 95%CI: 1.03, 3.03 versus seated office 1.38 mmHg, 95%CI: 0.68, 2.07 versus standing office 1.86 mmHg, 95%CI: 0.38, 3.34).

The reduction in diastolic blood pressure with reduced sodium intake was detected in individuals not taking medication to control blood pressure (1.70 mmHg, 95%CI: 1.04, 2.37) and in those taking medication to control blood pressure (2.05 mmHg, 95%CI: 0.91, 3.19). The reduction in diastolic blood pressure was not statistically significant in studies that included individuals with undetermined status of consumption of medication to control blood pressure (0.45 mmHg, 95%CI: –1.03, 1.93).

The study design did not significantly affect the reduction in diastolic blood pressure with reduction in sodium intake (parallel design 1.33 mmHg, 95%CI: 0.62, 2.04 versus crossover design 1.70 mmHg, 95%CI: 0.97, 2.43).

Direct comparisons

In the two studies that randomized participants to reduced sodium, very reduced sodium or control (*23, 49*), a total of three comparisons contributed to the meta-analysis directly comparing the effect of differing levels of sodium intake on blood pressure. The results of the meta-analyses are shown in **Figures 3.14** and **3. 15**, and in **Table 3.80**. The two comparisons of sodium intake levels in the Dietary Approaches to Stop Hypertension study (SodiumDASH) each had one intervention group that reduced sodium intake by > 1/3 of control and a group that reduced sodium intake by < 1/3 of control. This meta-analysis detected a significant decrease in systolic blood pressure of 3.14 mmHg (95%CI: 0.30, 5.98) and diastolic blood pressure of 1.70 mmHg (95%CI: 0.33, 3.07) in the group that achieved a > 1/3 relative reduction in sodium intake compared with the group that achieved a < 1/3 relative reduction in sodium intake.

There were three comparisons in which one intervention arm achieved a sodium intake of < 2 g/day and another intervention arm achieved a sodium intake of > 2 g/day. The meta-analysis detected a significant decrease in systolic blood pressure of 3.47 mmHg (95%CI: 0.76, 6.18) and diastolic blood pressure of 1.81 mmHg (95%CI: 0.54, 3.08) in the arm that achieved an absolute intake of < 2 g/day compared with the arm that achieved an absolute intake of > 2 g/day. There was only one comparison in which an intervention arm achieved a sodium intake of < 1.2 g/day and another achieved a sodium intake of > 1.2 g/day (*49*). The reduction in the arm that achieved < 1.2 g/day was not statistically significant for systolic blood pressure (8.00 mmHg, 95%CI: –1.73, 17.73) or diastolic blood pressure (4.00 mmHg, 95%CI: –1.58, 9.58) relative to the reduction in the arm that achieved ≥ 1.2 g/day.

3.5.2 Ambulatory blood pressure

Ambulatory systolic blood pressure (**Figure 3.16** and **Table 3.81**) was significantly reduced by reduced sodium intake relative to usual sodium intake (5.51 mmHg, 95%CI: 3.16, 7.87). The reduction was greater, but not statistically significantly so, when only studies targeting individuals with hypertension were included (6.53 mmHg, 95%CI: 3.22, 9.84). A single study targeted only individuals without hypertension and another targeted a heterogeneous population of individuals with or without hypertension. The achieved intake in the reduced sodium group did not significantly affect the reduction in systolic blood pressure (reduction to an intake of < 2 g/day 7.78 mmHg, 95%CI: 3.74, 11.81 versus reduction to an intake of ≥ 2 g/day 3.85 mmHg, 95%CI: 2.53, 5.17). Only one study had an achieved relative sodium intake in the intervention group of < 1/3 of control, and only one study had an achieved absolute intake of < 1.2 g/day; thus, comparisons of these intake levels to other achieved intake levels were difficult to interpret.

Ambulatory systolic blood pressure was significantly reduced by reduced sodium intake when 24-hour ambulatory blood pressure was measured (5.51 mmHg, 95%CI: 3.16, 7.78), as well as daytime pressure (3.85 mmHg, 95%CI: 2.57, 5.14) and night-time pressure (4.16 mmHg, 95%CI: 2.63, 5.70). All studies reporting ambulatory systolic blood pressure were of a duration of < 3 months and had a crossover study design.

Ambulatory diastolic blood pressure (**Figure 3.17** and **Table 3.82**) was significantly reduced by reduced sodium intake relative to usual sodium intake (2.94 mmHg, 95%CI: 1.51, 4.36). The reduction was not statistically significantly different when only studies targeting individuals with hypertension were included (3.50 mmHg, 95%CI: 1.27, 5.73). The achieved intake in the reduced sodium group did not significantly affect the reduction in diastolic blood pressure (reduction to an intake of < 2 g/day 4.39 mmHg, 95%CI: 1.47, 7.31 versus reduction to an intake of ≥ 2 g/day 2.00 mmHg, 95%CI: 0.86, 3.14).

Ambulatory diastolic blood pressure was significantly reduced by reduced sodium intake when 24-hour ambulatory pressure was measured (2.94 mmHg, 95%CI: 1.51, 4.36), as well as daytime pressure (2.06 mmHg, 95%CI: 0.92, 3.20) and night-time pressure (2.44 mmHg, 95%CI: 1.26, 3.62).

All studies reporting ambulatory diastolic blood pressure were of a duration of < 3 months and had a crossover study design.

3.5.3 Blood lipids

Total cholesterol

Total cholesterol was quantified in 11 studies with 2339 total participants. Reduced sodium intake relative to usual sodium intake had no effect on total cholesterol (0.02 mmol/L, 95%CI: –0.03, 0.07) (**Figure 3.18** and **Table 3.83**). The result was not affected by the hypertensive status of the participants (hypertensive 0.01 mmol/L, 95%CI: –0.16, 0.17 versus heterogeneous 0.02 mmol/L, 95%CI: –0.03, 0.08). Only one study that targeted individuals without hypertension reported results on total cholesterol. The results were not affected by the relative reduction in sodium intake (< 1/3 of control –0.01 mmol/L, 95%CI: –0.08, 0.05

versus ≥ 1/3 of control 0.01 mmol/L, 95%CI: –0.04, 0.07), or the absolute reduction in achieved intake (< 2 g/day 0.02 mmol/L, 95%CI: –0.03, 0.08 versus ≥ 2 g/day –0.02 mmol/L, 95%CI: –0.08, 0.03 or < 1.2 g/day –0.06 mmol/L, 95%CI: –0.33, 0.22 versus ≥ 1.2 g/day 0.02 mmol/L, 95%CI: –0.03, 0.08).

All studies quantifying total cholesterol were of a duration of < 3 months. The results did not differ by medication status (taking medication to control blood pressure 0.06 mmol/L, 95%CI: –0.23, 0.34 versus not taking medication to control blood pressure 0.03 mmol/L, 95%CI: –0.03, 0.08). The results also did not differ by study design (parallel design –0.12 mmol/L, 95%CI: –0.35, 0.12 versus crossover design 0.03 mmol/L, 95%CI: –0.03, 0.08).

Four other studies measured total cholesterol and reported qualitatively that there was no relative change in total cholesterol concentration in the reduced sodium and control groups (*35-37, 62*).

HDL cholesterol

HDL cholesterol was quantified in nine studies with a total of 2047 participants. Reduced sodium intake relative to usual sodium intake reduced HDL cholesterol concentration by 0.01 mmol/L, with borderline statistical significance (95%CI: 0.00, 0.03) (**Figure 3.19** and **Table 3.84**). The result was similar when only the studies targeting individuals with hypertension were included in the analysis (0.06 mmol/L, 95%CI: 0.00, 0.12). In the two studies targeting a heterogeneous population, the reduction was not statistically significant (0.01 mmol/L, 95%CI: –0.01, 0.02). Only one study targeted individuals without hypertension. HDL cholesterol concentration was reduced by 0.01 mmol/L, with borderline significance (95%CI: 0.00, 0.03) when the achieved intake was a decrease of ≥ 1/3 of the usual intake. There was no change in HDL cholesterol when the achieved intake was < 1/3 usual intake (0.00 mmol/L, 95%CI: –0.02, 0.01). There was no significant reduction in HDL cholesterol when the achieved intake was < 2 g/day (0.01 mmol/L, 95%CI: –0.01, 0.03) or ≥ 2 g/day (0.01 mmol/L, 95%CI: –0.01, 0.02). In the two studies that achieved a reduction of sodium intake of < 1.2 g/day, a significant reduction in HDL cholesterol concentration of 0.10 mmol/L (95%CI: 0.01, 0.19) was detected. In the seven studies that achieved an intake of ≥ 1.2 g/day, the reduction was not significant (0.01 mmol/L, 95%CI: –0.01, 0.02).

All studies that quantified HDL cholesterol had a duration of < 3 months. The reduction in HDL concentration was not significant in the studies in which the population was not taking medication to control blood pressure (0.01 mmol/L, 95%CI: –0.01, 0.02). No studies were found that involved populations taking medication to control blood pressure. In the two studies in which the population was heterogeneous or had unspecified medication status, the reduction in HDL cholesterol concentration was 0.09 mmol/L (95%CI: 0.01, 0.17).

The reduction in HDL cholesterol concentration was statistically significant in the three studies with a parallel design (0.09 mmol/L, 95%CI: 0.01, 0.17), but not in the six with a crossover design (0.01 mmol/L, 95%CI: –0.01, 0.02).

One study measured HDL cholesterol and reported qualitatively that there was no relative change in HDL concentration in the reduced sodium and control groups (*62*).

LDL cholesterol

Six studies, with a total of 1909 participants, reported results of LDL cholesterol concentration. A reduction in sodium intake did not affect LDL cholesterol (0.03 mmol/L, 95%CI: –0.02, 0.08) (**Figure 3.20** and **Table 3.85**). This result was not affected by blood pressure status, achieved sodium intake (relative or absolute), duration, medication status or study design.

Total triglycerides

Eight studies with a total of 2049 participants quantified results of total triglyceride concentration. A reduction in sodium intake did not affect total triglyceride concentration (0.04 mmol/L, 95%CI: –0.01, 0.09) (**Figure 3.21** and **Table 3.86**). In the two studies targeting a heterogeneous population or unspecified population in terms of hypertensive status, the increase in triglyceride concentration was 0.05 mmol/L, which had borderline statistical significance (95%CI: 0.00, 0.11). In the four studies targeting individuals with hypertension, there was a decrease in triglyceride concentration of 0.05 mmol/L, which did not reach statistical significance (95%CI: –0.19, 0.29). Only one study that targeted individuals without hypertension reported on triglyceride concentration. Triglyceride concentration was not affected by achieved sodium intake (relative or absolute), duration or medication status. One study measured triglyceride concentration and reported qualitatively that there was no relative change in triglycerides concentration in the reduced sodium and control groups (*35*).

3.5.4 Catecholamine levels

The only study that reported urinary adrenaline concentration had 18 participants; it detected no effect of reduced sodium on urinary adrenaline (–13.10 pg/mL, 95%CI: –29.24, 3.04). The two studies that reported urinary noradrenaline concentration had 53 participants and detected no effect of reduced sodium intake on urinary noradrenaline (17.13 pg/mL, 95%CI: –34.06, 68.33).

The four studies that reported plasma adrenaline had 168 participants; they detected no effect of reduced sodium on plasma adrenaline (6.90 pg/mL, 95%CI: –2.17, 15.96) (**Figure 3.22** and **Table 3.87**). Seven studies, with a total of 265 participants, reported plasma noradrenaline. There was no effect of reduced sodium on plasma noradrenaline concentration (8.23 pg/mL, 95%CI: –27.84, 44.29) (**Figure 3.23** and **Table 3.87**). This result was not affected by hypertensive status or achieved sodium intake. No other comparisons were possible.

3.5.5 Renal function

Urinary protein excretion and protein:creatinine ratio were measured in four comparisons in two studies (*33, 59*) (**Figures 3.24** and **3.25**, and **Table 3.88)**; however, the two studies used different methods of measurement and could not be combined in a meta-analysis. The combined effect of the three comparisons of the Vogt study was a decrease in urinary protein excretion of 76.61 ng/mL filtrate, which was not statistically significant (95%CI: –0.97, 154.20). The comparison from the Swift study reported a decrease in urinary protein excretion of 75 mg/24 hours (standard deviation [SD] 30 mg/24 hours), with reduced sodium intake relative to control (93 mg/24 hours; SD 48), which was statistically significant

(*P* = 0.008). The combined effect of the three comparisons of the Vogt study on protein:creatinine ratio was a statistically significant decrease of 0.40 mg protein/mmol creatinine (95%CI: 0.07, 0.73). The protein:creatinine ratio in the Swift study was significantly reduced (*P* = 0.032) by 0.9 mg protein/mmol creatinine in the reduced sodium relative to the control group.

Because urinary albumin excretion is skewed, the median and interquartile ranges (IQRs) from the three studies reporting that outcome were reported but not meta-analysed (*46, 50, 51*). The summary of the findings are shown in **Table 3.84**. The Fotherby study reported no change in urinary albumin excretion between the reduced sodium group (median 9 mg/24 hour, IQR 3–21) and control (median 9 mg/24 hour, IQR 4–33). He and colleagues reported a significant decrease in urinary albumin excretion (*P* < 0.001) in the reduced sodium group (median 9.1 mg/24 hour, IQR 6.6–14.0) versus control (median 10.2 mg/24 hour, IQR 6.8–18.9). The Suckling study reported a non-significant (*P* = 0.185) decrease in urinary albumin with consumption of reduced sodium (median 4.2 mg/24 hour, IQR 2.8–8.2) intake relative to control (median 4.7 mg/24 hour, IQR 3.2–12.1). The Suckling study also reported a significant reduction in albumin:creatinine ratio (*P*= 0.014) for the reduced sodium group (median 0.64 mg/24 hour, IQR 0.3–1.1) relative to control (median 0.73 mg/24 hour, IQR 0.5–1.5). The He study reported a reduced albumin:creatinine ratio (*P* < 0.001) in the reduced sodium group (median 0.66 mg/24 hour, IQR 0.44–1.22) compared with control (median 0.81 mg/24 hour, IQR 0.47–1.43).

The meta-analysis of the four comparisons in the two studies (*51, 59*) that measured creatinine clearance found a non-significant decrease of 7.67 mL/min (95%CI: –0.83, 16.17) in the reduced sodium compared with the control group (**Figure 3.26**).

Ten studies measured serum or plasma creatinine levels. Of those, five quantified the results in seven comparisons (*40, 50, 51, 59, 61*). There was no significant effect on creatinine level between reduced sodium and control (1.68 μmol/L, 95%CI: –0.65, 4.00) (**Figure 3.27**). Three studies (*49, 55, 66*) reported no difference in serum creatinine level between reduced sodium and control, but did not quantify results. Two studies measured serum creatinine but did not report results (*37, 62*).

One study measured glomerular filtration rate and reported no statistically significant difference between reduced sodium (99 mL/min per 1.73 m^2, SD 21) and control (104 mL/min per 1.73m^2, SD 25) groups (*40*).

3.5.6 Other adverse effects

Three studies reported the incidence of minor adverse effects such as headache, stomach cramps and oedema (*51, 55, 58*). The Fotherby study noted that all participants completed the study with no adverse effects reported during any treatment phase. The McCarron study noted that participants complained of side-effects such as oedema and headache with equal frequency in the reduced sodium treatment and control groups. The Weir study reported that adverse effects such as dizziness, fatigue, headache and diarrhoea were reported by 25.4% of participants in the low-sodium diet group and 24.2% in the control group.

3.6 Sensitivity analysis

No sensitivity analysis based on high risk of bias was undertaken because no studies were determined to be at high risk of bias. Removal of studies in individuals with comorbidities such as overweight (*38*), obesity (*39*), diabetes (*30, 52*), either diabetes or impaired glucose tolerance (*46*), or proteinuria (*59*) had little effect on the results of the meta-analyses of blood pressure or adverse effects (data not shown). Additionally, in running the analyses, only the studies expressly conducted with samples of individuals with hypertension were included, and there was little change in the results (data not shown).

3.7 Quality of the body of evidence

The funnel plots generated for each of the main outcomes gave no indication of publication bias (**Annex 3**). The risk of bias summary (**Annex 4**) and risk of bias graph (**Annex 5**) suggest that the entire body of evidence was not at risk of serious problems due to bias. Although several studies reported that personnel were not blinded, most reported that participants were blinded. Blinding of outcome assessors was reported in 17 studies but not in the other 19. Outcome assessors were reported as not blinded in only two studies. There was no bias due to selective reporting or incomplete outcome, with most studies reporting low risk of bias. Few studies reported on random sequence generation or allocation concealment; therefore, 29 and 28 studies respectively were categorized as at unclear risk of bias in these regards. No studies were considered at high risk of bias through a combination of high risk in sequence generation and allocation concealment, and either blinding or loss to follow-up.

The GRADE evidence profiles for each of the review's specific objectives contain the assessment of the quality of evidence for all indicators of blood pressure, blood lipids, renal function, and catecholamine levels (**Annex 6**). The evidence for decreased sodium reducing blood pressure was of high or moderate quality. The evidence for no effect on renal function, blood lipids and catecholamine levels was of high quality.

High-quality evidence indicated that decreasing sodium intake by > 1/3 of the control intake reduced blood pressure more than decreasing sodium intake by ≤ 1/3 of the control intake, and that there was no differential effect on total cholesterol. However, the evidence was from only one study with two comparisons for the blood pressure outcome, and from two studies with three comparisons for total cholesterol.

High-quality evidence showed that decreasing sodium intake to an absolute intake of < 2 g/day had a greater effect on reducing blood pressure than reducing sodium to an absolute intake of ≥ 2 g/day, and showed no differential effect on total cholesterol, HDL cholesterol, LDL cholesterol or noradrenaline. However, the evidence was from two studies with three comparisons for blood pressure, and from only one study for the other outcomes.

There was moderate-quality evidence from only one study with one comparison that an absolute intake of < 1.2 g sodium/day had a greater effect on reducing blood pressure than reducing sodium to an absolute intake of ≥ 1.2 g/day. This single study also provided high-quality evidence that there was no differential effect on noradrenaline.

3.8 Tables

3.8.1 Characteristics of included studies

Table 3.1 Andersson 1984

Methods	Parallel study design of reduced sodium, fat and carbohydrate diet and participants randomized to sodium tablets or not; conducted in Sweden
Participants	23 adults with hypertension not taking medication to control blood pressure and all 20–40% overweight
Interventions	Group 1 – reduced sodium, fat and carbohydrate diet plus sodium tablets (control) Group 2 – reduced sodium, fat and carbohydrate diet (reduced sodium)
Outcomes	Resting blood pressure Left ventricular hypertrophy Haemodynamic indicators Urinary noradrenaline Plasma noradrenaline Cardiac output Mean arterial pressure
Notes	1) Sodium reduction achieved: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 2.5 months (9–11 weeks) 5) Sex – male 6) Blood pressure method – manual 7) Blood pressure method – supine office

References: (*38, 101*)

Table 3.2 Risk of bias table Andersson 1984

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	High risk	Providers and participants were not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessor was blinded
Incomplete outcome data (attrition bias)	Low risk	< 5% loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.3 ANHMRC 1989

Methods	Parallel design study followed by a crossover design study of reduced sodium diet and randomized to receive sodium tablets or placebo tablet; conducted in Australia
Participants	111 men and women with diastolic blood pressure 90–100 mmHg not taking medication to control blood pressure
Interventions	Group 1 – reduced sodium in diet through counselling plus 80 mmol sodium/day in sodium chloride tablets and thus no change in sodium intake (control) Group 2 – reduced sodium in diet through counselling plus placebo tablets and thus reduced sodium intake (achieved 90 mmol/day average)
Outcomes	Resting blood pressure Plasma cholesterol Urinary creatinine excretion
Notes	1) Sodium reduction achieved: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 2 months 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – seated office

References: (*36, 102, 103*)

Table 3.4 Risk of bias table ANHMRC 1989

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Unclear risk	Providers were blinded but the blinding of participants was unclear and unlikely
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Parallel study had low loss to follow-up; however, the crossover study had high loss to follow-up
Selective reporting (reporting bias)	Low risk	Results stated that plasma cholesterol and gamma glutamyl transferase did not change from baseline to follow-up between groups, but change not quantified

Table 3.5 Benetos 1992

Methods	Crossover design study of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets; conducted in France
Participants	20 adults with mild to moderate hypertension not taking medication to control blood pressure
Interventions	Group 1 – reduced sodium diet plus 60 mmol sodium in tablets/day (control) Group 2 – reduced sodium diet plus lactose (placebo) tablets/day (reduced sodium)
Outcomes	Resting blood pressure Plasma adrenaline Plasma noradrenaline Plasma renin activity Plasma aldosterone
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – supine office

Reference: (*43*)

Table 3.6 Risk of bias table Benetos 1992

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Participants and providers were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up < 10% (only two participants)
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.7 Cappuccio 1997

Methods	Crossover design study of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets; conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	48 adults over the age of 60 both with or without hypertension not taking medication to control blood pressure
Interventions	Group 1 – reduced sodium diet plus 120 mmol/day in sodium tablets (control) Group 2 – reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Serum cholesterol Serum triglyceride Fasting glucose
Notes	1) Sodium reduction achieved: > 1/3 of control/both > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – both 4) Duration of follow-up – 1 month (4 weeks) 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – supine office and standing office

Reference: (*53*)

Table 3.8 Risk of bias table Cappuccio 1997

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random-generated numbers handled by author not involved in the clinical assessment
Allocation concealment (selection bias)	Low risk	Handled by someone not involved in the clinical assessment
Blinding of participants and personnel (performance bias)	Low risk	Participants and providers were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported at 2% (only one participant)
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.9 Chalmers 1986

Methods	Parallel study design with participants randomized to control diet, high potassium diet, reduced sodium diet, and high potassium/reduced sodium diet; conducted in Australia
Participants	212 adults with hypertension not receiving medication to control blood pressure
Interventions	Group 1 – Control diet through counselling and education Group 2 – High potassium diet through counselling and education Group 3 – Reduced sodium diet through counselling and education Group 4 – High potassium/reduced sodium diet through counselling and education
Outcomes	Resting blood pressure Urinary electrolytes Urinary creatinine excretion Serum potassium Serum creatinine Serum cholesterol* Serum gamma glutamyl transferase* * Stated that pre-diet cholesterol and gamma glutamyl transferase were similar between groups and did not change over course of study
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 3 months 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – seated office Second phase of study included provision of supplements to same participants but results not used in this review

Reference: (*37*)

Table 3.10 Risk of bias table Chalmers 1986

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	High risk	Participants and providers were not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up 5.7%
Selective reporting (reporting bias)	Unclear risk	Stated that pre-diet cholesterol and gamma glutamyl transferase were similar between groups and did not change over course of study, but values not quantified; results of serum creatinine not reported

Table 3.11 Cobiac 1992

Methods	Parallel study design of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets in addition to either fish oil or sunflower oil; conducted in Australia
Participants	114 apparently healthy individuals 60–80 years of age not being medically treated for hypertension
Interventions	Group 1 – reduced sodium diet plus fish oil and 80 mmol sodium/day (fish control) Group 2 – reduced sodium diet plus fish oil and placebo (fish reduced sodium) Group 3 – reduced sodium diet plus sunflower oil and 80 mmol sodium/day (sun control) Group 4 – reduced sodium diet plus sunflower oil and placebo (sun reduced sodium)
Outcomes	Resting blood pressure
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – both 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – seated office

Reference: (*34*)

Table 3.12 Risk of bias table Cobiac 1992

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization schedule
Allocation concealment (selection bias)	Low risk	Concealed by dispensing in masked, individually coded containers
Blinding of participants and personnel (performance bias)	Low risk	Participants and providers were blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors blinded
Incomplete outcome data (attrition bias)	Unclear risk	Loss to follow-up reported at 7% but not clear from which group
Selective reporting (reporting bias)	Low risk	All stated outcomes reported

Table 3.13 Sodium DASH 2001

Methods	Crossover design, feeding study and participants randomly assigned to eat either a control diet typical of intake in the United States of America or the Sodium DASH diet; within the assigned diet, participants ate foods with control (150 mmol sodium/day target), low (100 mmol sodium/day target), and very low (50 mmol sodium/day target) levels of sodium; conducted in the United States of America
Participants	412 adults with and without hypertension not taking medication to control blood pressure.
Interventions	Group 1 – Sodium DASH diet with sodium target 150 mmol/day (Sodium DASH control) Group 2 – Sodium DASH diet with sodium target 100 mmol/day (Sodium DASH low sodium) Group 3 – Sodium DASH diet with sodium target 50 mmol/day (Sodium DASH very low sodium) Group 4 – Normal diet with sodium target 150 mmol/day (control) Group 5 – Normal diet with sodium target 100 mmol/day (low sodium) Group 6 – Normal diet with sodium target 50 mmol/day (very low sodium)
Outcomes	Resting blood pressure Urinary urea nitrogen excretion Urinary creatinine excretion Serum total cholesterol Serum LDL cholesterol Serum HDL cholesterol Serum total triglycerides Serum total cholesterol:HDL ratio
Notes	1) Sodium reduction achieved: Reduced sodium: < 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention Very reduced sodium: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – both 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – seated office

DASH, Dietary Approaches to Stop Hypertension; HDL, high-density lipoprotein; LDL, low-density lipoprotein

References: (*23, 104*)

Table 3.14 Risk of bias table Sodium DASH

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generated
Allocation concealment (selection bias)	Low risk	Allocation occurred at central location
Blinding of participants and personnel (performance bias)	High risk	Participants and providers were not blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up 5.3%
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.15 Dodson 1989

Methods	Parallel design study where participants were randomized to a reduced sodium diet or a "usual sodium" diet followed by a crossover design study of reduced sodium diet where participants were randomized to receive sodium tablets or placebo tablets; conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	34 adults with hypertension and diabetes, some of whom were taking medication and some of whom were not
Interventions	Parallel design phase: Group 1 – normal diet (control) Group 2 – reduced sodium diet (reduced sodium) Crossover design phase: Group 3 – reduced sodium diet plus sodium tablets 80 mmol/day (control crossover) Group 4 – reduced sodium diet plus placebo tablets (reduced sodium crossover)
Outcomes	Resting blood pressure Serum urea Patients in whom normal blood pressure was achieved
Notes	1) Sodium reduction achieved Parallel design phase: < 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention Crossover design phase: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult – (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 3 months (parallel)/1 month(crossover) 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – supine office and standing office

Reference: (*52*)

Table 3.16 Risk of bias table Dodson 1989

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	High risk	Participants and providers were not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	< 5% loss to follow-up in the parallel phase but > 20% in the crossover phase
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.17 Erwteman 1984

Methods	Parallel study design where participants were randomized to reduced sodium or usual sodium diet; participants were also randomized to drug treatment group (beta-blocker, diuretic, or combination of beta-blocker and diuretic) and then crossover to other drug treatments
Participants	107 adults with hypertension (20–70 years) who did not have diabetes
Interventions	No medication: • Group 1 – normal sodium diet plus no drug therapy (control) • Group 2 – reduced sodium diet plus no drug therapy (reduced sodium) Beta-blocker • Group 3 – normal sodium diet plus beta-blocker (control-B) • Group 4 – reduced sodium diet plus beta-blocker (reduced sodium-B) Diuretic • Group 5 – normal sodium diet plus diuretic (control-D) • Group 6 – reduced sodium diet plus diuretic (reduced sodium-D) Beta-blocker and diuretic: • Group 7 – normal sodium diet plus combination beta-blocker and diuretic (control-C) • Group 8 – reduced sodium diet plus combination beta-blocker and diuretic (reduced sodium-C)
Outcomes	Resting blood pressure Plasma glucose Plasma creatinine Plasma cholesterol Plasma HDL cholesterol Plasma uric acid Adverse effects
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 6 months (24 weeks) 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – supine office and standing office

HDL, high-density lipoprotein
Reference: (*62*)

Table 3.18 Risk of bias table Erwteman 1984

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	High risk	Participants and providers were not blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias)	Unclear risk	Loss to follow-up reported as 12% but not clear from which groups
Selective reporting (reporting bias)	Unclear risk	Reported no relative change in cholesterol, high-density lipoprotein and glucose without quantifying results

Table 3.19 Fagerberg 1984

Methods	Parallel study design of nutrition education; conducted in Sweden
Participants	34 adult men with hypertension and obesity without secondary forms of hypertension not taking medication to control blood pressure
Interventions	Group 1 – dietary advice for reduced calorie, fat and carbohydrate diet (control) Group 2 – dietary advice for reduced calorie, fat and carbohydrate diet plus reduced sodium diet (reduced sodium)
Outcomes	Resting blood pressure Intra-arterial blood pressure Heart rate Urinary noradrenaline (24 hour)
Notes	1) Sodium reduction achieved: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 2.5 months (9–12 weeks) 5) Sex – male 6) Blood pressure method – manual 7) Blood pressure method – supine office

Reference: (*39*)

Table 3.20 Risk of bias table Fagerberg 1984

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	High risk	Participants and personnel not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessor blinded
Incomplete outcome data (attrition bias)	Unclear risk	Loss to follow-up of 12% but not clear from which group
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.21 Fotherby 1993

Methods	Crossover design study of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets. Conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	18 adults with hypertension not taking medication for the hypertension
Interventions	Group 1 – reduced sodium diet plus 80 mmol/day of sodium tablets (control) Group 2 – reduced sodium diet plus equivalent placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Ambulatory blood pressure Urinary creatinine excretion Urinary electrolytes Urinary sodium: creatinine ratio Urinary potassium:creatinine ratio Urine volume Plasma aldosterone Plasma renin activity Heart rate Serum cholesterol Serum HDL cholesterol Serum LDL cholesterol Serum triglyceride Urinary albumin excretion Serum calcium Serum creatinine Serum uric acid Serum parathyroid hormone Adverse effects
Notes	1) Sodium reduction achieved: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1.25 months 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic (ambulatory)/manual (office) 7) Blood pressure method – supine office and standing office and ambulatory 24-hour/ambulatory day/ambulatory night

HDL, high-density lipoprotein; LDL, low-density lipoprotein
References: (*51, 105*)

Table 3.22 Risk of bias table Fotherby 1993

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Participants and providers were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	One participant (5.6%) lost to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.23 Gates 2004

Methods	Crossover design study of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets; conducted in the United States of America
Participants	24 adults with hypertension over 50 years of age not taking medication to control blood pressure
Interventions	Group 1 – Reduced dietary intake of sodium plus sodium tablets prescribed to reach baseline sodium intake values (control) Group 2 – Reduced dietary intake of sodium plus placebo (reduced sodium)
Outcomes	Resting blood pressure Carotid artery compliance Carotid artery stiffness Adrenaline (assumed plasma) Noradrenaline (assumed plasma) Triglyceride (assumed plasma) Cholesterol (assumed plasma) HDL cholesterol (assumed plasma) LDL cholesterol (assumed plasma) VLDL cholesterol (assumed plasma) Serum glucose Serum insulin
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention < 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – supine office

HDL, high-density lipoprotein; LDL, low-density lipoprotein; VLDL, very low-density lipoprotein
Reference: (*54*)

Table 3.24 Risk of bias table Gates 2004

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Participants and providers were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessor was blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported as 0%
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.25 Grobbee 1987

Methods	Crossover study design of reduced sodium diet with participants randomly assigned to sodium tablets or placebo tablets (or potassium tablets); conducted in the Netherlands
Participants	40 adults with hypertension (18–28 years old) who may or may not have been medically treated for hypertension
Interventions	Group 1 – reduced sodium diet plus 90 mmol sodium/day tablets (control) Group 2 – reduced sodium diet plus placebo tablets (reduced sodium) Group 3 – reduced sodium diet plus potassium tablets (results not included in this review)
Outcomes	Resting blood pressure Pulse rate Cardiac output Cardiac index Urinary creatinine Plasma noradrenaline Plasma adrenaline Plasma renin Serum creatinine Serum cholesterol Serum uric acid
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1.5 months 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – supine office

Reference: (*61*)

Table 3.26 Risk of bias table Grobbee 1987

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Participants and providers blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported as 0%
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.27 He 2009

Methods	Crossover study design of reduced sodium diet and participants randomized to sodium tablets or placebo tablets; conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	185 adults with hypertension with no history of medical treatment for elevated blood pressure
Interventions	Group 1 – reduced sodium diet plus 90 mmol sodium in tablets/day (control) Group 2 – reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Ambulatory blood pressure Pulse rate Pulse wave velocity Plasma renin activity Plasma creatinine Plasma aldosterone Urinary creatinine excretion Urinary calcium excretion Urinary albumin excretion
Notes	1) Sodium reduction achieved: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1.5 months 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic (resting and ambulatory) 7) Blood pressure method – seated office and ambulatory 24-hour/ambulatory day/ambulatory night

References: (*50, 106, 107*)

Table 3.28 Risk of bias table He 2009

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated random number conducted by external company
Allocation concealment (selection bias)	Low risk	External company conducted allocation of treatment or placebo
Blinding of participants and personnel (performance bias)	Low risk	Participants and providers blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessor blinded
Incomplete outcome data (attrition bias)	Low risk	< 10% loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.29 Howe 1994

Methods	Parallel study design of reduced sodium diet and participants randomized to sodium tablets or placebo tablets in addition to either olive oil tablets or fish oil tablets; conducted in Australia
Participants	61 adults with hypertension who were being medically treated with angiotensin-converting enzyme inhibitors
Interventions	Group 1 – reduced sodium diet plus olive oil and 80 mmol sodium in tablets/day (olive control) Group 2 – reduced sodium diet plus olive oil and placebo tablets/day (olive reduced sodium) Group 3 – reduced sodium diet plus fish oil and 80 mmol sodium in tablets/day (fish control) Group 4 – reduced sodium diet plus fish oil and placebo tablets/day (fish reduced sodium)
Outcomes	Resting blood pressure Plasma total cholesterol Plasma triglycerides Serum thromboxanes Plasma aldosterone Urinary creatinine
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1.5 months 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – seated office

Reference: (*35*)

Table 3.30 Risk of bias table Howe 1994

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated randomization schedule
Allocation concealment (selection bias)	Low risk	Concealed by dispensing in masked, individually coded containers
Blinding of participants and personnel (performance bias)	Low risk	Participants and personnel blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessor blinded
Incomplete outcome data (attrition bias)	Unclear risk	8% loss to follow-up but not clear from which group
Selective reporting (reporting bias)	Low risk	Noted there was no change in cholesterol or triglycerides but did not quantify the results

Table 3.31 MacGregor 1982

Methods	Crossover study design of reduced sodium diet and participants randomized to sodium tablets or placebo tablets; any one individual took the same number of tablets each day, but between individuals the amount varied from 70 to 120 mmol sodium per day; conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	19 adults with hypertension not taking medical treatment for hypertension
Interventions	Group 1 – reduced sodium diet plus sodium tablets to restore baseline sodium intake (control) Group 2 – reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Pulse rate Urinary creatinine excretion Plasma urea Plasma creatinine Plasma renin activity Plasma aldosterone
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – supine office and standing office

Reference: (*66*)

Table 3.32 Risk of bias table MacGregor 1982

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Providers and participants were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported as 0%
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.33 MacGregor 1989

Methods	Crossover study design of reduced sodium diet and participants randomized to 160 mmol sodium in tablets, 70 mmol sodium in tablets or placebo in tablets; conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	20 adults with hypertension not taking medication to control blood pressure
Interventions	Group 1 – reduced sodium diet plus 160 mmol sodium in tablets/day (control) Group 2 – reduced sodium diet plus 70 mmol sodium + nine placebo tablets/day (reduced sodium) Group 3 – reduced sodium diet plus 16 placebo tablets/day (very reduced sodium)
Outcomes	Resting blood pressure Pulse rate Urinary creatinine excretion Plasma urea Plasma creatinine Plasma noradrenaline Plasma renin activity Plasma aldosterone
Notes	1) Sodium reduction achieved Reduced sodium: > 1/3 of control; > 2 g/day in intervention; > 1.2 g/day in intervention Very reduced sodium: > 1/3 of control; < 2 g/day in intervention; < 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – supine office and standing office

Reference: (*49*)

Table 3.34 Risk of bias table MacGregor 1989

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Providers and participants were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported as 0%
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.35 McCarron 1997

Methods	Crossover study design of reduced sodium diet and participants randomly assigned sodium tablets or placebo tablets; conducted in the United States of America
Participants	99 adults with hypertension given isradipine (calcium-channel blocker) to reduce blood pressure
Interventions	Group 1 – reduced sodium diet plus sodium tablets 100 mmol/day (control) Group 2 – reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Plasma total cholesterol Plasma HDL cholesterol Plasma LDL cholesterol Plasma triglycerides Total cholesterol:HDL ratio Blood urea nitrogen Urinary creatinine Plasma albumin Adverse effects (e.g. headache, oedema, etc.)
Notes	1) Sodium reduction achieved: < 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1 month (4 weeks) 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – seated office

HDL, high-density lipoprotein; LDL, low-density lipoprotein
Reference: (*55*)

Table 3.36 Risk of bias table McCarron 1997

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated sequence
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Participants and personnel were blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	2% loss to follow-up
Selective reporting (reporting bias)	Low risk	Authors stated that participants reported adverse events with equal frequency during both reduced sodium and control phases of the trial; it was reported that mean values for blood urea nitrogen, creatinine, plasma albumin, and the lipoprotein profile were unchanged

Table 3.37 Meland 1997

Methods	Crossover study design of reduced sodium diet and participants randomized to sodium tablets or placebo tablets; conducted in Norway
Participants	16 adults with hypertension not receiving medication for hypertension
Interventions	Group 1 – reduced sodium diet plus 50 mmol/day sodium tablets (control) Group 2 – reduced sodium diet plus placebo (reduced sodium)
Outcomes	Resting blood pressure Urinary creatinine excretion Plasma creatinine Serum total cholesterol Serum HDL cholesterol Serum glucose Serum insulin C-peptide Serum insulin
Notes	1) Sodium reduction achieved: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 2 months 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – seated office

HDL, high-density lipoprotein
Reference: (*63*)

Table 3.38 Risk of bias table Meland 1997

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Providers and participants were blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported as 0%
Selective reporting (reporting bias)	Low risk	All primary outcomes reported

Table 3.39 Meland 2009

Methods	Parallel study design of reduced sodium diet and participants randomized to sodium tablets or placebo tablets; conducted in Norway
Participants	46 adults with hypertension possibly taking medication to control blood pressure
Interventions	Group 1 – reduced sodium diet plus 50 mmol sodium in tablets/day (control) Group 2 – reduced sodium diet plus placebo tablets/day (reduced sodium)
Outcomes	Resting blood pressure Serum aldosterone Fasting serum insulin C-peptide Fasting serum glucose Serum total cholesterol Serum HDL cholesterol Serum total triglycerides
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 2 months 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – seated office

HDL, high-density lipoprotein
Reference: (*22*)

Table 3.40 Risk of bias table Meland 2009

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Providers and participants were blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded.
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported as 0%.
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.41 Melander 2007

Methods	Crossover study design of reduced sodium diet and participants randomized to sodium tablets or placebo tablets; conducted in Sweden
Participants	46 adults without hypertension without history of hypertension, diabetes or kidney disease or taking medication for those conditions
Interventions	Group 1 – reduced sodium diet plus 100 mmol/day sodium tablets (control) Group 2 – reduced sodium diet plus placebo (reduced sodium)
Outcomes	Resting blood pressure Ambulatory blood pressure Urinary creatinine excretion Glomerular filtration rate Serum creatinine Serum electrolytes Plasma renin activity Plasma aldosterone.
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention < 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – normotensive 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic (ambulatory)/manual (office) 7) Blood pressure method – supine office and ambulatory 24-hour/ambulatory day/ambulatory night

Reference: (*40*)

Table 3.42 Risk of bias table Melander 2007

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Providers and participants were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	High risk	> 15% loss to follow-up and unclear from which intervention phase
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.43 Morgan 1981

Methods	Crossover design study of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets; conducted in Australia
Participants	48 adults with hypertension 28–50 years of age, some of whom were taking medication to control hypertension
Interventions	Group 1 – reduced sodium diet plus 50 mmol/day sodium tablets (control) Group 2 – reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting diastolic blood pressures Urinary urea concentration Urinary creatinine concentration
Notes	1) Sodium reduction achieved: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 2 months 5) Sex – male/female/both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – supine office

Reference: (*42*)

Table 3.44 Risk of bias table Morgan 1981

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	High risk	Participants and providers were not blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias)	Unclear risk	No report of amount loss to follow-up
Selective reporting (reporting bias)	High risk	Systolic blood pressure not reported

Table 3.45 Muhlhauser 1996

Methods	Parallel design study of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets; conducted in Germany
Participants	16 adults with hypertension with insulin-dependent diabetes mellitus not taking medication to control blood pressure
Interventions	Group 1 – reduced sodium diet plus 100 mmol/day sodium tablets (control) Group 2 – reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Glycated haemoglobin (HbA1C) C Insulin dosage Serum cholesterol Serum HDL cholesterol Proteinuria Urinary creatinine clearance Glomerular filtration rate Renal plasma flow Filtration fraction Renal vascular resistance Plasma aldosterone Plasma total renin activity Plasma angiotensin-converting enzyme Plasma angiotensin II Atrial natriuretic peptide Plasma adrenaline Plasma noradrenaline
Notes	1) Sodium reduction achieved: > 1/3 of control/both > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – both 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic (home)/manual (office) 7) Blood pressure method – combination office/combination home

HDL, high-density lipoprotein
Reference: (*30*)

Table 3.46 Risk of bias table Muhlhauser 1996

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generation of sequence
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Participants and providers were blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported as 0%
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.47 Nestel 1993

Methods	Parallel study design of reduced sodium diet and participants randomized to sodium tablets or placebo tablets and either safflower oil or DGLA
Participants	66 adults without hypertension (60–79 years) not taking medication to control blood pressure
Interventions	Group 1 – reduced sodium diet plus sodium tablets and DGLA or safflower oil (control) Group 2 – reduced sodium diet plus placebo tablets and DGLA or safflower oil (reduced sodium)
Outcomes	Resting blood pressure Plasma total cholesterol Plasma HDL cholesterol Plasma triglycerides Plasma fatty acid profile
Notes	1) Sodium reduction achieved: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – normotensive 4) Duration of follow-up – 1.5 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – seated office

DGLA, dihomogammalinolenic acid; HDL, high-density lipoprotein
Reference: (*41*)

Table 3.48 Risk of bias table Nestel 1993

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Providers and participants were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported as 0%
Selective reporting (reporting bias)	High risk	Cholesterol, HDL cholesterol, and triglycerides not reported

HDL, high-density lipoprotein

Table 3.49 Parijs 1973

Methods	Crossover study design with four intervention periods: during two intervention periods, participants consumed a normal sodium diet and during two intervention periods, participants consumed a reduced sodium diet; during each type of diet consumption, there was one period with placebo consumption and one period with diuretic consumption; conducted in Belgium
Participants	22 adults with hypertension
Interventions	Group 1 – normal sodium diet plus placebo tablets/day (control-placebo) Group 2 – reduced sodium diet plus placebo tablets/day (reduced sodium-placebo) Group 3 – normal sodium diet plus diuretic in tablets/day (control-diuretic) Group 4 – reduced sodium diet plus diuretic in tablets/day (reduced sodium-diuretic)
Outcomes	Resting blood pressure Serum electrolytes Serum uric acid Urinary creatinine excretion Uric acid clearance
Notes	1) Sodium reduction achieved No medication phase: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention Diuretic phase: < 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – supine office and standing office

Reference: (*65*)

Table 3.50 Risk of bias table Parijs 1973

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Intervention group decided by odd or even number; manner in which numbers were generated and given to participants not clear
Allocation concealment (selection bias)	High risk	Allocation was based on odd/even number already known by trialist
Blinding of participants and personnel (performance bias)	High risk	Personnel and participants not blinded to diet treatment
Blinding of outcome assessment (detection bias)	High risk	Outcomes assessors not blinded to diet treatment
Incomplete outcome data (attrition bias)	High risk	Loss to follow-up > 20% in all groups
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.51 Puska 1983

Methods	Parallel study design with randomization to usual diet, reduced sodium diet, or low fat diet; conducted in Finland
Participants	72 adults (in control and reduced sodium groups, 114 total) with no major health problems and not taking medication for hypertension (couples were the unit of randomization)
Interventions	Group 1 – maintain "normal" diet (control) Group 2 – reduced sodium diet achieved through counselling and provision of "key" low salt options (reduced sodium) Group 3 – low fat diet achieved through counselling and provision of "key" low fat options (low fat) (results not included in this review)
Outcomes	Resting blood pressure
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – both 4) Duration of follow-up – 1.5 months 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – seated office

Reference: (*60*)

Table 3.52 Risk of bias table Puska 1983

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	High risk	Providers and participants were not blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors blinded
Incomplete outcome data (attrition bias)	Low risk	< 10% loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.53 Richards 1984

Methods	Crossover study design with dietary manipulation to have usual sodium intake, reduced sodium intake, or increased potassium intake; conducted in New Zealand
Participants	16 adults with hypertension not taking medication for hypertension
Interventions	Group 1 – control diet with sodium target of 180 mmol/day + 60 mmol potassium/day (control) Group 2 – reduced sodium diet with sodium target of 80 mmol/day + 60 mmol potassium/day (reduced sodium) Group 3 – high potassium diet with sodium target of 180 mmol/day and 200 mmol potassium/day (high potassium – results not included in this review)
Outcomes	Resting blood pressure Plasma renin activity Plasma noradrenaline Plasma adrenaline Plasma aldosterone Plasma angiotensin II Mean intra-arterial pressure Plasma electrolytes
Notes	1) Sodium reduction achieved*: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1–1.5 months 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – supine office and standing office * Values estimated based on figure provided in manuscript

Reference:(*21*)

Table 3.54 Risk of bias table Richards 1984

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	High risk	Providers and participants were not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	High risk	25% loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.55 Ruppert 1993

Methods	Crossover study design with participants provided diets of 85 mmol sodium and randomized to sodium tablets or placebo tablets; conducted in Germany
Participants	25 adults without hypertension not taking medication to reduce blood pressure
Interventions	Group 1 – diet of 85 mmol sodium plus 115 mmol sodium/day in tablet (control) Group 2 – diet of 85 mmol sodium plus placebo in tablet (reduced sodium)
Outcomes	Resting blood pressure Mean arterial pressure Heart rate Plasma renin activity Plasma noradrenaline Serum total cholesterol Serum LDL cholesterol Serum HDL cholesterol Serum triglycerides Serum total protein
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – normotensive 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – seated office

HDL, high-density lipoprotein; LDL, low-density lipoprotein
Reference: (*64*)

Table 3.56 Risk of bias table Ruppert 1993

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Providers and participants were blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported as 0%
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.57 Sciarrone 1992

Methods	Parallel study design of reduced sodium diet with either low fat/high fibre or normal intake (2 × 2 factorial trial) and participants randomly assigned sodium tablets or placebo tablets; conducted in Australia
Participants	95 adults with hypertension 20–69 years old, some of whom were taking medication for hypertension
Interventions	Reduced sodium/low fat diet Group 1 – low-sodium/low-fat diet plus 100 mmol/day sodium tablets (control low fat) Group 2 – low-sodium/low-fat diet plus placebo tablets (low sodium low fat) Reduced sodium/normal fat diet Group 3 – low-sodium/normal-fat diet plus 100 mmol/day sodium tablets (control) Group 4 – low-sodium/normal-fat diet plus placebo tablets (low sodium)
Outcomes	Resting blood pressure Urinary creatinine Serum urea Serum creatinine Serum glucose Serum uric acid Serum protein Serum albumin Serum gamma glutamyl transferase Serum alkaline phosphatase Plasma total cholesterol Plasma triglyceride Plasma HDL cholesterol Plasma LDL cholesterol Plasma renin activity
Notes	1) Sodium reduction achieved Low fat reduced sodium versus low fat: > 1/3 of control < 2 g/day in intervention < 1.2 g/day in intervention Norm fat/reduced sodium versus norm fat: > 1/3 of control < 2 g/day in intervention < 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 2 months 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – supine office

HDL, high-density lipoprotein; LDL, low-density lipoprotein
Reference:(*29*)

Table 3.58 Risk of bias table Sciarrone 1992

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Participants and personnel blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	< 5% loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.59 Silman 1983

Methods	Parallel study design with participants randomized to reduced sodium dietary education to reduce sodium intake or to control healthy lifestyle education; conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	28 adults with hypertension who were not taking medication for blood pressure
Interventions	Group 1 – healthy lifestyle education (control) Group 2 – education to reach reduced sodium diet plus healthy lifestyle education (reduced sodium)
Outcomes	Resting blood pressure
Notes	1) Sodium intake achieved 1 month: < 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 3 months: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 6 months: < 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 12 months: < 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1 month, 2 months, 3 months, 6 months, 12 months 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – not reported

Reference: (*47*)

Table 3.60 Risk of bias table Silman 1983

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	High risk	Providers and participants were not blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	10% loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.61 Suckling 2010

Methods	Crossover design study of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets; conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	26 individuals with type 2 diabetes and 20 with impaired glucose tolerance, all with untreated normal or mild hypertension
Interventions	Group 1 – reduced sodium diet plus unclear amount per day of sodium tablets (control) Group 2 – reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Ambulatory blood pressure Urinary albumin excretion Urinary albumin:creatinine ratio
Notes	1) Sodium reduction achieved: < 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – both 4) Duration of follow-up – 1.5 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic (ambulatory) 7) Blood pressure method – ambulatory 24 hr/ambulatory day/ambulatory night * Publication was conference abstract and details on type of device used for resting blood pressure and position of patient during measurement were unclear; also, risk of bias cannot be assessed from abstract

Reference: (*46*)

Table 3.62 Risk of bias table Suckling 2010

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Not sufficient data to make judgement
Allocation concealment (selection bias)	Unclear risk	Not sufficient data to make judgement
Blinding of participants and personnel (performance bias)	Unclear risk	Not sufficient data to make judgement
Blinding of outcome assessment (detection bias)	Unclear risk	Not sufficient data to make judgement
Incomplete outcome data (attrition bias)	Unclear risk	Not sufficient data to make judgement
Selective reporting (reporting bias)	Unclear risk	Not sufficient data to make judgement

Table 3.63 Swift 2005

Methods	Crossover study design of reduced sodium diet; participants randomized to sodium tablets or placebo tablets; conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	46 black adults with hypertension not taking medication to control blood pressure
Interventions	Group 1 – reduced sodium diet plus 120 mmol sodium in tablets (control) Group 2 – reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Ambulatory blood pressure (24-hour, day, night) Plasma renin activity Plasma aldosterone Atrial natriuretic peptide Total urinary protein excretion Urinary creatinine excretion
Notes	1) Sodium reduction achieved: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic (ambulatory and office) 7) Blood pressure method – supine office and ambulatory 24-hour/ambulatory day/ambulatory night

Reference: (*33*)

Table 3.64 Risk of bias table Swift 2005

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer generation of randomization sequence
Allocation concealment (selection bias)	Low risk	Allocation conducted by pharmacy
Blinding of participants and personnel (performance bias)	Low risk	Providers and participants were blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	13% loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.65 TOHP 1992

Methods	Parallel study design of participants randomly assigned to weight reduction, sodium reduction, stress management or control; conducted in the United States of America
Participants	744 (in control and reduced sodium groups) adults without hypertension, not taking antihypertensive medications
Interventions	Group 1 – no intervention (control) Group 2 – educational campaign to reduce sodium intake (reduced sodium)
Outcomes	Resting blood pressure Number of hypertensive events
Notes	1) Sodium reduction achieved: < 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – normotensive 4) Duration of follow-up – 18 months 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – seated office

References: (*56, 108*)

Table 3.66 Risk of bias table TOHP 1992

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Low risk	Concealment of allocation at a central location
Blinding of participants and personnel (performance bias)	High risk	Providers and participants were not blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	< 5% loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.67 TOHP 1997

Methods	Parallel design study with an intervention implemented in a 2X2 factorial design which included control, reduced sodium, weight loss, and reduced sodium/weight loss groups; conducted in the United States of America
Participants	2382 adults without hypertension not taking medication to control blood pressure
Interventions	Group 1 – no intervention (control) Group 2 – educational campaign to reduce sodium intake(reduced sodium) Group 3 – educational campaign to reduce weight (weight loss) Group 4 – educational campaign to reduce weight and sodium intake(reduced sodium/weight loss)
Outcomes	Resting blood pressure Incidence of hypertension
Notes	1) Sodium reduction achieved: < 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – normotensive 4) Duration of follow-up – 36 months 5) Sex -both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – seated office

References: (*57, 109-111*)

Table 3.68 Risk of bias table TOHP 1997

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Low risk	Concealment of allocation at a central location
Blinding of participants and personnel (performance bias)	High risk	Providers and participants were not blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	< 5% loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.69 Vogt 2008

Methods	Crossover design study with participants randomized to reduced sodium or high sodium diet and additionally placebo, angiotensin II antagonist (losartan) or losartan and HCT; conducted in the Netherlands
Participants	34 adults without hypertension (18–70 years old) or diabetes
Interventions	Group 1 – high sodium diet (about 200 mmol/day) (control) Group 2 – low-sodium diet (about 50 mmol/day) (low sodium) Group 3 – high sodium diet (about 200 mmol/day) + losartan therapy (control-L) Group 4 – low-sodium diet (about 50 mmol/day) + losartan therapy (low sodium-L) Group 5 – high sodium diet (about 200 mmol/day) + losartan+ HCT therapy (control-LHCT) Group 6 – low-sodium diet (about 50 mmol/day) + losartan+ HCT therapy (low sodium-LHCT)
Outcomes	Resting blood pressure Urinary creatinine Urinary urea excretion Urinary protein excretion Protein:creatinine ratio Mean arterial pressure Serum creatinine Serum urea Total cholesterol Total serum protein Serum albumin Serum uric acid Plasma aldosterone Plasma renin Aldosterone:renin ratio
Notes	1) Sodium reduction achieved Placebo: > 1/3 of control > 2 g/day in inter > 1.2 g/day in inter Losartan: > 1/3 of control > 2 g/day in inter > 1.2 g/day in inter Losartan + HCT: > 1/3 of control > 2 g/day in inter > 1.2 g/day in inter 2) Age – adult (≥ 15 years) 3) Group – not specified 4) Duration of follow-up – 1.5 months 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic 7) Blood pressure method – seated office

HCT, hydrochlorothiazide; inter, intervention
Reference: (*59*)

Table 3.70 Risk of bias table Vogt 2008

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Computer-generated sequence by pharmacist
Allocation concealment (selection bias)	Low risk	Allocation completed by external pharmacist
Blinding of participants and personnel (performance bias)	High risk	Providers and participants were not blinded
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded until data analysis
Incomplete outcome data (attrition bias)	Low risk	< 5% loss to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.71 Watt 1983

Methods	Crossover study design of reduced sodium diet; participants randomized to sodium tablets or placebo tablets; conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	20 adults with hypertension not taking medication to control blood pressure
Interventions	Group 1 – reduced sodium diet plus 80 mmol sodium in tablets/day (control) Group 2 – reduced sodium diet plus 8 placebo tablets/day (reduced sodium)
Outcomes	Resting blood pressure Arterial pressure Plasma renin activity
Notes	1) Sodium reduction achieved: > 1/3 of control > 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – seated office

Reference: (*45*)

Table 3.72 Risk of bias table Watt 1983

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Providers and participants were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Two participants (10%) lost to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported

Table 3.73 Watt 1985

Methods	Crossover study design of reduced sodium diet; participants randomized to sodium tablets or placebo tablets; conducted in the United Kingdom of Great Britain and Northern Ireland
Participants	75 adults with unspecified hypertensive status and unspecified status of medication to control blood pressure
Interventions	Group 1 – reduced sodium diet plus 80 mmol sodium in tablets/day (control) Group 2 – reduced sodium diet plus 8 placebo tablets/day (reduced sodium)
Outcomes	Resting blood pressure Plasma renin activity
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – not specified 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – manual 7) Blood pressure method – seated office

Reference: (*44*)

Table 3.74 Risk of bias table Watt 1985

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	Unclear risk	No description of method of concealment of allocation
Blinding of participants and personnel (performance bias)	Low risk	Providers and participants were blinded
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Unclear risk	Unclear reasons for loss to follow-up or distribution of those lost
Selective reporting (reporting bias)	Unclear risk	All outcomes reported

Table 3.75 Weir 2010

Methods	Crossover study design with participants assigned to low or usual sodium diets; conducted in the United States of America
Participants	132 adults with hypertension, 18–60 years of age, all provided direct renin inhibitor, aliskiren
Interventions	Group 1 – usual sodium diet plus aliskiren (control) Group 2 – reduced sodium diet plus aliskiren (reduced sodium)
Outcomes	Resting blood pressure 24-hour ambulatory blood pressure Plasma renin activity Plasma aldosterone Urinary creatinine excretion Adverse events
Notes	1) Sodium reduction achieved: > 1/3 of control < 2 g/day in intervention > 1.2 g/day in intervention 2) Age – adult (≥ 15 years) 3) Group – hypertensive 4) Duration of follow-up – 1 month 5) Sex – both (heterogeneous) 6) Blood pressure method – automatic(ambulatory)/manual (office) 7) Blood pressure method – seated office and ambulatory 24 hour

Reference: (*58*)

Table 3.76 Risk of bias table Weir 2010

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	No description of method of sequence generation
Allocation concealment (selection bias)	High risk	No concealment of allocation used
Blinding of participants and personnel (performance bias)	High risk	Providers and participants were not blinded
Blinding of outcome assessment (detection bias)	High risk	Outcome assessors were not blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up equal in diet groups and < 15% total
Selective reporting (reporting bias)	Unclear risk	All outcomes reported

3.8.2 Excluded studies

Table 3.77 Reasons for exclusion of excluded studies

Study ID	Reason for exclusion
Ames 1991 (*67*)	Not an RCT
Appel 2006 (*75*)	Sodium intake level not only difference between intervention and control
Berglund 1976 (*68*)	Not an RCT
Borghi 2002 (*112*)	Sodium intake level not only difference between intervention and control
Burgess 1988 (*83*)	Duration < 4 weeks
Campese 1982 (*84*)	Duration < 4 weeks
Cappuccio 2006 (*100*)	Did not achieve ≥ 40 mmol difference in sodium intake between groups
Charlton 2008 (*76*)	Sodium intake level not only difference between intervention and control
CSSSCG 2007 (*77*)	Sodium intake level not only difference between control and intervention
Dengel 1996 (*31*)	Not an RCT
Fagerberg 1985b (*101*)	Sodium intake level not only difference between intervention and control
Forrester 2010 (*99*)	Did not report on outcomes of interest
Friberg 1990 (*85*)	Duration < 4 weeks
He 2003 (*113*)	Not an RCT
He 2005 (*70*)	Not an RCT
Ito 1989 (*86*)	Duration < 4 weeks
Jessani 2007 (*87*)	Duration < 4 weeks
Keogh ICTRP (*24*)	Not an RCT
Kimura 1985 (*88*)	Duration < 4 weeks
Kojuri 2007 (*71*)	Not an RCT
Mahajan 2010 (*93*)	Did not measure 24-hour urinary sodium excretion to quantify sodium intake
Makela 2008 (*78*)	Sodium intake level not only difference between intervention and control
Mascioli 1991 (*94*)	Did not measure 24-hour urinary sodium excretion to quantify sodium intake
Meschi 2011 (*72*)	Not an RCT
Morikawa 2011 (*95*)	Did not measure 24-hour urinary sodium excretion to quantify sodium intake
Nouvenne 2009 (*26*)	Not an RCT
Nouvenne 2010 (*26*)	Sodium intake level not only difference between intervention and control
Parfrey 1981a (*74*)	No control group
Parfrey 1981b (*73*)	No control group
Rankin 1981 (*89*)	Duration < 4 weeks
Rayner 2012 (*79*)	Sodium intake level not only difference between intervention and control
Santos 2010 (*80*)	Sodium intake level not only difference between intervention and control
Saptharishi 2009 (*96*)	Did not measure 24-hour urinary sodium excretion to quantify sodium intake

Study ID	Reason for exclusion
Schorr 1996 (*81*)	Sodium intake level not only difference between intervention and control
Stein 1995 (*90*)	Duration < 4 weeks
Todd 2010 (*97*)	Did not measure 24-hour urinary sodium excretion to quantify sodium intake
Todd ICTRP (*28*)	Did not measure 24-hour urinary sodium excretion to quantify sodium intake
Warren 1980 (*91*)	Duration < 4 weeks
Wocial 1981 (*92*)	Duration < 4 weeks
Yamakoshi 2006 (*98*)	Did not measure 24-hour urinary sodium excretion to quantify sodium intake
Zhou 2009 (*82*)	Sodium intake level not only difference between intervention and control

RCT, randomised controlled trial

3.8.3 Effect estimate tables

Blood pressure

Table 3.78 Resting systolic blood pressure

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.1 Resting systolic BP (all)	36	6736	–3.39 [-4.31, -2.46]
1.2 Resting systolic BP (subgroups)	36		Subtotals only
1.2.1 Achieved relative sodium reduction (< 1/3 of control)	8	3995	–1.45 [–2.29, –0.60]
1.2.2 Achieved relative sodium reduction (≥ 1/3 of control)	30	3521	–3.79 [–4.82, –2.75]
1.2.3 Achieved sodium intake in intervention (< 2 g/day)	16	2415	–3.39 [–4.69, –2.09]
1.2.4 Achieved sodium intake in intervention (≥ 2 g/day)	22	5141	–2.68 [–3.66, –1.70]
1.2.5 Achieved sodium intake in intervention (< 1.2 g/day)	3	209	–6.39 [–9.53, –3.25]
1.2.6 Achieved sodium intake in intervention (≥ 1.2 g/day)	34	6567	–3.23 [–4.17, –2.28]
1.2.8 BP status (normal BP)	7	3133	–1.38 [-2.74, -0.02]
1.2.9 BP status (hypertension)	24	2273	–4.06 [–5.15, –2.96]
1.2.10 BP status (heterogeneous)	8	1490	–3.41 [–5.13, –1.69]
1.2.11 Duration (< 3 months)	31	3335	–4.07 [–5.12, –3.02]
1.2.12 Duration (3–6 months)	5	2817	–1.91 [–3.60, –0.23]
1.2.13 Duration (> 6 months)	3	2862	–0.88 [–2.00, 0.23]
1.2.15 Sex (male)	2	53	–9.10 [–16.63, –1.57]
1.2.16 Sex (heterogeneous)	34	6749	–3.34 [–4.25, –2.42]
1.2.17 Type of BP device (automatic)	17	1678	–4.04 [–5.10, –2.97]
1.2.18 Type of BP device (manual)	19	5048	–2.93 [–4.15, –1.71]
1.2.19 Type of BP measure (supine office)	15	1127	–4.69 [–6.33, –3.06]
1.2.20 Type of BP measure (seated office)	18	5542	–2.91 [–3.99, –1.82]
1.2.21 Type of BP measure (standing office)	8	705	–4.44 [–6.92, –1.96]
1.2.22 Type of BP measure (combo office)	1	16	–7.00 [–14.84, 0.84]
1.2.26 Type of BP measure (combo home)	1	16	–9.00 [–18.32, 0.32]
1.2.27 Hypertension medication status (not taking medication)	27	5456	–3.66 [–4.85, –2.47]
1.2.28 Hypertension medication status (taking medication)	6	927	–4.55 [–6.59, –2.51]
1.2.29 Hypertension medication status (heterogeneous or not specified)	6	419	–1.67 [–3.01, –0.34]

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.2.30 Study design (parallel)	16	4147	–2.47 [–3.51, –1.43]
1.2.31 Study design (crossover)	22	2849	–4.04 [–5.27, –2.81]

BP, blood pressure; CI, confidence interval

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Table 3.79 Resting diastolic blood pressure

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.3 Resting diastolic BP (all)	36	6736	–1.54 [–2.11, –0.98]
1.4 Resting diastolic BP (subgroups)	36		Subtotals only
1.4.1 Achieved relative sodium reduction (< 1/3 of control)	8	4001	–0.74 [–1.28, –0.19]
1.4.2 Achieved relative sodium reduction (≥ 1/3 of control)	30	3521	–1.68 [–2.34, –1.02]
1.4.3 Achieved sodium intake in intervention (< 2 g/day)	16	2415	–1.54 [–2.46, –0.63]
1.4.4 Achieved sodium intake in intervention (≥ 2 g/day)	22	5147	–1.21 [–1.72, –0.70]
1.4.5 Achieved sodium intake in intervention (< 1.2 g/day)	3	209	–2.47 [–5.86, 0.92]
1.4.6 Achieved sodium intake in intervention (≥ 1.2 g/day)	34	6480	–1.58 [–2.17, –0.99]
1.4.8 BP status (normotensive)	6	3067	–0.58 [–1.29, 0.014]
1.4.9 BP status (hypertensive)	24	2273	–2.26 [–3.02, –1.50]
1.4.10 BP status (heterogeneous)	8	1490	–1.04 [–2.13, 0.05]
1.4.11 Duration (< 3 months)	31	3351	–1.67 [–2.33, –1.02]
1.4.12 Duration (3–6 months)	5	2817	–1.33 [–2.50, –0.15]
1.4.13 Duration (> 6 months)	3	2862	–0.45 [–1.25, 0.34]
1.4.15 Sex (male)	2	53	–4.83 [–8.98, –0.68]
1.4.16 Sex (heterogeneous)	34	6749	–1.50 [–2.07, –0.94]
1.4.17 Type of BP device (automatic)	17	1678	–1.75 [–2.54, –0.95]
1.4.18 Type of BP device (manual)	19	5048	–1.40 [–2.18, –0.62]
1.4.19 Type of BP measure (supine office)	15	1127	–2.03 [–3.03, –1.03]
1.4.20 Type of BP measure (seated office)	18	5542	–1.38 [–2.07, –0.68]
1.4.21 Type of BP measure (standing office)	8	705	–1.86 [–3.34, –0.38]
1.4.22 Type of BP measure (combo office)	1	16	–1.00 [–6.00, 4.00]
1.4.26 Type of BP measure (combo home)	1	16	–1.00 [–5.44, 3.44]
1.4.27 Hypertension medication status (not taking	27	5456	–1.70 [–2.37, –1.04]

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
medication)			
1.4.28 Hypertension medication status (taking medication)	6	927	–2.05 [–3.19, –0.91]
1.4.29 Hypertension medication status (heterogeneous or not specified)	6	419	–0.45 [–1.93, 1.03]
1.4.30 Study design (parallel)	16	4147	–1.33 [–2.04, –0.62]
1.4.31 Study design (crossover)	22	2849	–1.70 [–2.43, –0.97]

BP, blood pressure; CI, confidence interval

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Table 3.80 Resting systolic and diastolic blood pressure: direct comparisons of varying levels of achieved intake

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
4.1 Resting systolic blood pressure	2		Subtotals only
4.1.1 Sodium reduced < 1/3 versus ≥ 1/3	1	780	–3.14 [–5.98, –0.30]
4.1.2 Sodium reduced to < 2 g/day versus ≥ 2 g/day	2	820	–3.47 [–6.18, –0.76]
4.1.3 Sodium reduced to < 1.2 g/day versus ≥ 1.2 g/day	1	40	–8.00 [–17.73, 1.73]
4.2 Resting diastolic blood pressure	2		Subtotals only
4.2.1 Sodium reduced to < 1/3 versus ≥ 1/3	1	780	–1.70 [–3.07, –0.33]
4.2.2 Sodium reduced to < 2 g/day versus ≥ 2 g/day	2	820	–1.81 [–3.08, –0.54]
4.2.3 Sodium reduced to < 1.2 g/day versus ≥ 1.2 g/day	1	40	–4.00 [–9.58, 1.58]

CI, confidence interval

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Table 3.81 Ambulatory systolic blood pressure

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.5 Ambulatory systolic BP (all)	6	850	–5.51 [–7.87, –3.16]
1.6 Ambulatory systolic BP (subgroups)	6		Subtotals only
1.6.1 Achieved relative sodium reduction (< 1/3 of control)	1	92	–3.30 [–5.07, –1.53]
1.6.2 Achieved relative sodium reduction (≥ 1/3 of control)	5	758	–6.28 [–9.00, –3.56]
1.6.3 Achieved sodium intake in intervention (< 2 g/day)	2	308	–7.78 [–11.81, –3.74]
1.6.4 Achieved sodium intake in intervention (≥ 2 g/day)	4	542	–3.85 [–5.17, –2.53]
1.6.5 Achieved sodium intake in intervention (< 1.2 g/day)	1	78	–5.00 [–10.29, 0.29]
1.6.6 Achieved sodium intake in intervention (≥ 1.2 g/day)	5	772	–5.61 [–8.29, –2.93]
1.6.8 BP status (normotensive)	1	78	–5.00 [–10.29, 0.29]
1.6.9 BP status (hypertensive)	4	680	–6.53 [–9.84, –3.22]
1.6.10 BP status (heterogeneous)	1	92	–3.30 [–5.07, –1.53]
1.6.17 Type of BP measure (24 hour)	6	850	–5.51 [–7.87, –3.16]
1.6.18 Type of BP measure (day)	5	620	–3.85 [–5.14, –2.57]
1.6.19 Type of BP measure (night)	5	620	–4.16 [–5.70, –2.63]
1.6.20 Hypertension medication status (not taking medication)	5	620	–3.92 [–5.20, –2.63]
1.6.21 Hypertension medication status (taking medication)	1	230	–9.30 [–12.01, –6.59]

BP, blood pressure, CI, confidence interval

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Table 3.82 Ambulatory diastolic blood pressure

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.7 Ambulatory diastolic blood pressure (all)	6	850	–2.94[–4.36, –1.51]
1.8 Ambulatory diastolic blood pressure (subgroups)	6		Subtotals only
1.8.1 Achieved relative sodium reduction (< 1/3 of control)	1	92	–1.80 [–3.37, –0.23]
1.8.2 Achieved relative sodium reduction (≥ 1/3 of control)	5	758	–3.36 [–5.07, –1.64]
1.8.3 Achieved sodium intake in intervention (< 2 g/day)	2	308	–4.39 [–7.31, –1.47]
1.8.4 Achieved sodium intake in intervention (≥ 2 g/day)	4	542	–2.00 [–3.14, –0.86]
1.8.5 Achieved sodium intake in intervention (< 1.2 g/day)	1	78	–2.70 [–5.72, 0.32]
1.8.6 Achieved sodium intake in intervention (≥ 1.2 g/day)	5	772	–3.00 [–4.72, –1.27]
1.8.8 BP status (normotensive)	1	78	–2.70 [–5.72, 0.32]
1.8.9 BP status (hypertensive)	4	680	–3.50 [–5.73, –1.27]
1.8.10 BP status (heterogeneous)	1	92	–1.80 [–3.37, –0.23]
1.8.17 Type of BP measure (24 hour)	6	850	–2.94 [–4.36, –1.51]
1.8.18 Type of BP measure (day)	5	620	–2.06 [–3.20, –0.92]
1.8.19 Type of BP measure (night)	5	620	–2.44 [–3.62, –1.26]
1.8.20 Hypertension medication status (not taking medication)	5	620	–2.09 [–3.15, –1.02]
1.8.21 Hypertension medication status (taking medication)	1	230	–5.70 [–7.87, –3.53]

BP, blood pressure, CI, confidence interval

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Blood lipids

Table 3.83 Total cholesterol

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.9 Total cholesterol (all)	11	2339	0.02 [–0.03, 0.07]
1.10 Total cholesterol (subgroups)	11		Subtotals only
1.10.1 Achieved relative sodium reduction (< 1/3 of control)	2	1754	–0.01 [–0.08, 0.05]
1.10.2 Achieved relative sodium reduction (≥ 1/3 of control)	10	2195	0.01 [–0.04, 0.07]
1.10.3 Achieved sodium intake in intervention (< 2 g/day)	5	1821	0.02 [–0.03, 0.08]
1.10.4 Achieved sodium intake in intervention (≥ 2 g/day)	7	2128	–0.02 [–0.08, 0.03]
1.10.5 Achieved sodium intake in intervention (< 1.2 g/day)	2	115	–0.06 [–0.33, 0.22]
1.10.6 Achieved sodium intake in intervention (≥ 1.2 g/day)	9	2274	0.02 [–0.03, 0.08]
1.10.8 BP status (normotensive)	1	100	0.00 [–0.46, 0.46]
1.10.9 BP status (hypertensive)	6	421	0.01 [–0.16, 0.17]
1.10.10 BP status (heterogeneous)	4	1868	0.02 [–0.03, 0.08]
1.10.17 Hypertension medication status (not taking medication)	8	1926	0.03 [–0.03, 0.08]
1.10.18 Hypertension medication status (taking medication)	2	326	0.06 [–0.23, 0.34]
1.10.19 Hypertension medication status (not specified)	2	137	–0.11 [–0.35, 0.13]
1.10.20 Study design (parallel)	3	153	–0.12 [–0.35, 0.12]
1.10.21 Study design (cross–over)	8	2236	0.03 [–0.03, 0.08]

BP, blood pressure, CI, confidence interval

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Table 3.84 HDL cholesterol

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.11 HDL cholesterol (all)	9	2031	–0.01 [–0.03, 0.00]
1.12 HDL cholesterol (subgroups)	9		Subtotals only
1.12.1 Achieved relative sodium reduction (< 1/3 of control)	2	1754	–0.00 [–0.02, 0.01]
1.12.2 Achieved relative sodium reduction (≥ 1/3 of control)	8	1903	–0.01 [–0.03, 0.00]
1.12.3 Achieved sodium intake in intervention (< 2 g/day)	5	1821	–0.01 [–0.03, 0.01]
1.12.4 Achieved sodium intake in intervention (≥ 2 g/day)	5	1836	–0.01 [–0.02, 0.01]
1.12.5 Achieved sodium intake in intervention (< 1.2 g/day)	2	115	–0.10 [–0.19, –0.01]
1.12.6 Achieved sodium intake in intervention (≥ 1.2 g/day)	7	1982	–0.01 [–0.02, 0.01]
1.12.8 BP status (normotensive)	1	100	–0.04 [–0.23, 0.15]
1.12.9 BP status (hypertensive)	6	421	–0.06 [–0.12, –0.00]
1.12.10 BP status (heterogeneous)	2	1576	–0.01 [–0.02, 0.01]
1.12.17 Hypertension medication status (not taking medication)	7	1960	–0.01 [–0.02, 0.01]
1.12.19 Hypertension medication status (not specified)	2	137	–0.09 [–0.17, –0.01]
1.12.20 Study design (parallel)	3	153	–0.09 [–0.17, –0.01]
1.12.21 Study design (cross–over)	6	1944	–0.01 [–0.02, 0.01]

BP, blood pressure, CI, confidence interval, HDL, high-density lipoprotein

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Table 3.85 LDL cholesterol

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.13 LDL cholesterol (all)	6	1909	0.03 [–0.02, 0.08]
1.14 LDL cholesterol (subgroups)	6		Subtotals only
1.14.1 Achieved relative sodium reduction (< 1/3 of control)	2	1710	–0.01 [–0.06, 0.04]
1.14.2 Achieved relative sodium reduction (≥ 1/3 of control)	5	1765	0.02 [–0.03, 0.07]
1.14.3 Achieved sodium intake in intervention (< 2 g/day)	4	1731	0.02 [–0.03, 0.07]
1.14.4 Achieved sodium intake in intervention (≥ 2 g/day)	3	1744	–0.01 [–0.06, 0.04]
1.14.5 Achieved sodium intake in intervention (< 1.2 g/day)	2	115	0.01 [–0.29, 0.31]
1.14.6 Achieved sodium intake in intervention (≥ 1.2 g/day)	4	1844	0.03 [–0.02, 0.08]
1.14.8 BP status (normotensive)	1	100	0.13 [–0.27, 0.54]
1.14.9 BP status (hypertensive)	4	343	0.08 [–0.11, 0.27]
1.14.10 BP status (heterogeneous)	1	1516	0.02 [–0.03, 0.07]
1.14.17 Hypertension medication status (not taking medication)	4	1674	0.02 [–0.03, 0.07]
1.14.18 Hypertension medication status (taking medication)	1	194	0.16 [–0.11, 0.43]
1.14.19 Hypertension medication status (not specified)	1	91	–0.01 [–0.32, 0.30]
1.14.20 Study design (parallel)	1	91	–0.01 [–0.32, 0.30]
1.14.21 Study design (cross–over)	5	1868	0.03 [–0.02, 0.08]

BP, blood pressure, CI, confidence interval, LDL, low-density lipoprotein

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Table 3.86 Triglycerides

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.15 Triglycerides (all)	8	2049	0.04 [–0.01, 0.09]
1.16 Triglycerides (subgroups)	7		Subtotals only
1.16.1 Achieved relative sodium reduction (< 1/3 of control)	2	1710	0.02 [–0.07, 0.10]
1.16.2 Achieved relative sodium reduction (≥ 1/3 of control)	6	1814	0.04 [–0.02, 0.09]
1.16.3 Achieved sodium intake in intervention (< 2 g/day)	4	1686	0.04 [–0.02, 0.09]
1.16.4 Achieved sodium intake in intervention (≥ 2 g/day)	4	1838	0.01 [–0.04, 0.07]
1.16.5 Achieved sodium intake in intervention (< 1.2 g/day)	1	24	–0.09 [–1.23, 1.05]
1.16.6 Achieved sodium intake in intervention (≥ 1.2 g/day)	6	1984	0.04 [–0.01, 0.09]
1.16.8 BP status (normotensive)	1	100	–0.06 [–0.26, 0.14]
1.16.9 BP status (hypertensive)	4	298	–0.05 [–0.29, 0.19]
1.16.10 BP status (heterogeneous)	2	1610	0.05 [–0.00, 0.11]
1.16.17 Hypertension medication status (not taking medication)	5	1768	0.04 [–0.01, 0.10]
1.16.18 Hypertension medication status (taking medication)	1	194	0.18 [–0.17, 0.53]
1.16.19 Hypertension medication status (not specified)	1	46	–0.30 [–0.70, 0.10]
1.16.20 Study design (parallel)	1	46	–0.30 [–0.70, 0.10]
1.16.21 Study design (cross–over)	6	1962	0.05 [–0.01, 0.10]

BP, blood pressure, CI, confidence interval

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Table 3.87 Catecholamine levels

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.17 Adrenaline (urinary) (all)	1	18	–13.10 [–29.24, 3.04]
1.19 Noradrenaline (urinary) (all)	2	53	17.13 [–34.06, 68.33]
1.21 Adrenaline (plasma) (all)	4	168	6.90 [–2.17, 15.96]
1.22 Adrenaline (plasma) (subgroups)	4		Subtotals only
1.22.3 Achieved sodium intake in intervention (< 2 g/day)	3	144	8.27 [–1.79, 18.33]
1.22.4 Achieved sodium intake in intervention (≥ 2 g/day)	1	24	1.00 [–19.87, 21.87]
1.22.5 Achieved sodium intake in intervention (< 1.2 g/day)	1	24	4.00 [–8.46, 16.46]
1.22.6 Achieved sodium intake in intervention (≥ 1.2 g/day)	3	144	10.15 [–3.05, 23.36]
1.22.17 Hypertension medication status (not taking medication)	3	88	4.87 [–5.27, 15.01]
1.22.19 Hypertension medication status (not specified)	1	80	15.00 [–5.26, 35.26]
1.23 Noradrenaline (plasma) (all)	7	265	8.23 [–27.84, 44.29]
1.24 Noradrenaline (plasma) (subgroups)	6		Subtotals only
1.24.3 Achieved sodium intake in intervention (< 2 g/day)	5	218	24.93 [–11.36, 61.21]
1.24.4 Achieved sodium intake in intervention (≥ 2 g/day)	2	48	28.58 [–53.41, 110.57]
1.24.5 Achieved sodium intake in intervention (< 1.2 g/day)	2	48	–7.15 [–80.83, 66.53]
1.24.6 Achieved sodium intake in intervention (≥ 1.2 g/day)	5	218	33.84 [–3.32, 71.00]
1.24.8 BP status (normotensive)	1	50	79.10 [–17.95, 176.15]
1.24.9 BP status (hypertensive)	5	192	18.77 [–16.75, 54.28]
1.24.17 Hypertension medication status (not taking medication)	5	162	30.94 [–12.96, 74.83]
1.24.19 Hypertension medication status (heterogenous or not specified)	1	80	19.00 [–32.29, 70.29]

BP, blood pressure, CI, confidence interval

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Table 3.88 Renal function (various indicators)

Outcome or subgroup[a]	Studies	Participants	Effect estimate [95% CI]
1.25 Urinary protein excretion (all)	1	198	–76.61 [–154.20, 0.97]
1.27 Protein:creatinine ratio (all)	1	198	0.40 [–0.73, –0.07]
1.28 Creatinine clearance (all)	2	232	–7.67 [–16.17, 0.83]
1.29 Serum creatinine (all)	5	728	1.68 [–0.65, 4.00]
1.30 Glomerular filtration rate (all)	1	78	–5.00 [–15.25, 5.25]

CI, confidence interval

[a] Statistical method used: mean difference (inverse variance, random effects model with 95%CI)

Table 3.89 Urinary albumin indicators

Outcome	Study ID	Reduced sodium			Higher sodium			*P*
		n	Median	IQR	n	Median	IQR	
Urinary albumin excretion								
	Fotherby 1993	17	9	3–21	17	9	4–33	> 0.05
	He 2009	169	9.1	6.6–14.0	169	10.2	6.8–18.9	0.001
	Suckling 2010	46	4.2	2.8–8.2	46	4.7	3.2–12.1	0.185
Albumin:creatinine ratio								
	He 2009	169	0.66	0.44–1.22	169	0.81	0.47–1.43	0.001
	Suckling 2010	46	0.64	0.3–1.1	46	0.73	0.5–1.5	0.014

IQR, interquartile range

3.9 Figures

Figure 3.1 Flow through screening, inclusion, exclusion

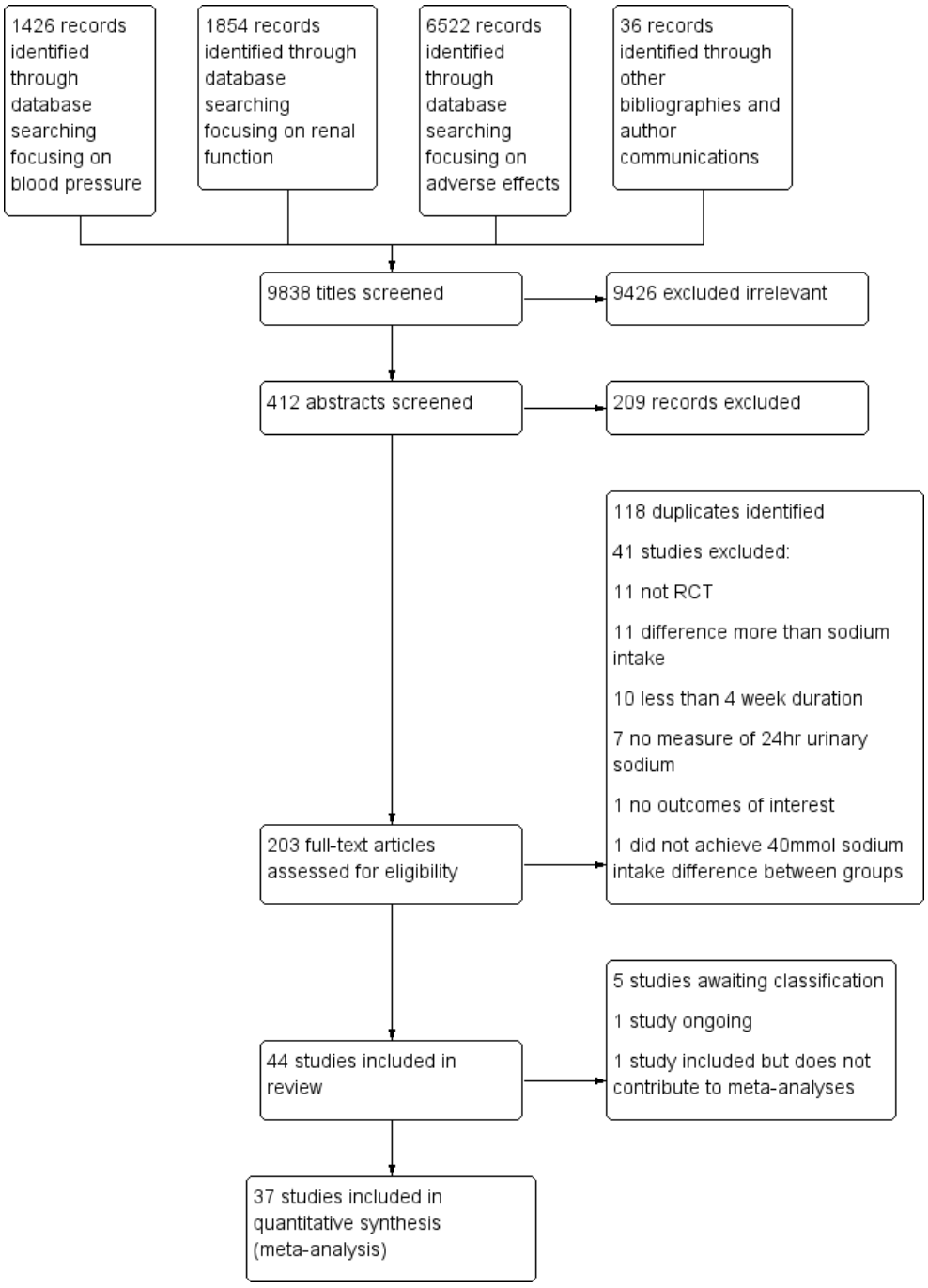


Figure 3.2 Resting systolic blood pressure: all adults

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
ANDERSSON 1984	138	15.5	10	146.4	14.8	13	0.5%	-8.40 [-20.93, 4.13]
ANHMRC 1989	149.1	13	50	152.2	14	53	2.0%	-3.10 [-8.31, 2.11]
BENETOS 1992	142.6	12	20	149.1	10	20	1.4%	-6.50 [-13.35, 0.35]
CAPPUCCIO 1997	155.9	21.6	47	163.2	20.6	47	1.0%	-7.30 [-15.83, 1.23]
CHALMERS 1986	-8.9	7.2	48	-3.8	7.4	52	3.5%	-5.10 [-7.96, -2.24]
CHALMERS 1986	-7.9	6.6	51	-7.7	7.9	49	3.5%	-0.20 [-3.06, 2.66]
COBIAC 1992	126.3	7.42	25	127.7	5.14	27	3.0%	-1.40 [-4.90, 2.10]
COBIAC 1992	127.8	5.05	26	132.5	5.99	28	3.5%	-4.70 [-7.65, -1.75]
DASH 2001	126	6.75	192	132.7	6.5	192	4.8%	-6.70 [-8.03, -5.37]
DASH 2001	123.8	6.6	198	126.8	6.6	198	4.8%	-3.00 [-4.30, -1.70]
DODSON 1989	160.5	22.5	17	167.6	11.5	17	0.5%	-7.10 [-19.11, 4.91]
ERWTEMAN 1984	128.5	16.3	44	134.6	15.9	50	1.5%	-6.10 [-12.63, 0.43]
ERWTEMAN 1984	128.1	15	44	126.8	11.6	50	1.9%	1.30 [-4.18, 6.78]
ERWTEMAN 1984	135.3	14.8	44	137	13.6	50	1.7%	-1.70 [-7.47, 4.07]
ERWTEMAN 1984	141	15.4	44	142.9	16.4	50	1.5%	-1.90 [-8.33, 4.53]
FAGERBERG 1984	138.8	13.17	15	148.3	13.17	15	0.8%	-9.50 [-18.93, -0.07]
FOTHERBY 1993	171	21	17	179	18	17	0.5%	-8.00 [-21.15, 5.15]
GROBBEE 1987	135.7	9	40	136.5	13	40	2.1%	-0.80 [-5.70, 4.10]
HE 2009	141	12	169	146	13	169	3.7%	-5.00 [-7.67, -2.33]
HOWE 1994	135	18.71	14	140	14.97	14	0.5%	-5.00 [-17.55, 7.55]
HOWE 1994	138	14.97	14	139	22.45	14	0.4%	-1.00 [-15.13, 13.13]
MACGREGOR 1982	144	18	19	154	18	19	0.6%	-10.00 [-21.45, 1.45]
MACGREGOR 1989	155	13	20	163	18	20	0.8%	-8.00 [-17.73, 1.73]
MCCARRON 1997	133.6	12.6	97	138.5	12.8	97	3.0%	-4.90 [-8.47, -1.33]
MELAND 1997	141	12.24	16	145	16.33	16	0.7%	-4.00 [-14.00, 6.00]
MELAND 2009	-5.001	9.52	23	-0.001	9.52	23	1.8%	-5.00 [-10.50, 0.50]
MELANDER 2007	125	12.4	39	132	14.7	39	1.6%	-7.00 [-13.04, -0.96]
MUHLHAUSER 1996	128	8	8	135	8	8	1.1%	-7.00 [-14.84, 0.84]
NESTEL 1993	123	10	32	128	14	34	1.7%	-5.00 [-10.84, 0.84]
PARIJS 1973	154.6	21.8	16	154	17.7	17	0.4%	0.60 [-13.00, 14.20]
PARIJS 1973	167.8	24.3	15	174.5	20.02	17	0.3%	-6.70 [-22.25, 8.85]
PUSKA 1983	137.2	16	34	136	13	38	1.4%	1.20 [-5.58, 7.98]
RICHARDS 1984	144.7	14	12	149.9	15	12	0.6%	-5.20 [-16.81, 6.41]
RUPPERT 1993	112	11	25	110.3	13	25	1.4%	1.70 [-4.98, 8.38]
SCIARRONE 1992	-9.3	9.8	27	-1.8	10.1	21	1.8%	-7.50 [-13.19, -1.81]
SCIARRONE 1992	-7.6	10.9	19	-3.3	6.5	24	1.8%	-4.30 [-9.85, 1.25]
SILMAN 1983	138.6	19.62	10	139.1	17.25	15	0.4%	-0.50 [-15.47, 14.47]
SUCKLING 2010	131.2	12.89	46	135.5	13.56	46	1.9%	-4.30 [-9.71, 1.11]
SWIFT 2005	151	13	40	159	13	40	1.8%	-8.00 [-13.70, -2.30]
TOHP 1992	-4.86	7.81	327	-3.16	8.11	417	4.9%	-1.70 [-2.85, -0.55]
TOHP 1997	-0.7	9	515	0.6	8.5	514	5.0%	-1.30 [-2.37, -0.23]
TOHP 1997	-0.5	9	537	-0.8	8.7	527	5.0%	0.30 [-0.76, 1.36]
VOGT 2008	121	11.49	33	125	17.23	33	1.3%	-4.00 [-11.07, 3.07]
VOGT 2008	128	17.23	33	135	17.23	33	1.0%	-7.00 [-15.31, 1.31]
VOGT 2008	137	17.23	33	143	22.98	33	0.8%	-6.00 [-15.80, 3.80]
WATT 1983	136	4.6	18	136.5	4.5	18	3.4%	-0.50 [-3.47, 2.47]
WATT 1985	112.2	3.1	35	113.6	3.1	35	4.7%	-1.40 [-2.85, 0.05]
WATT 1985	110.2	3.23	31	110.7	3.23	31	4.6%	-0.50 [-2.11, 1.11]
WEIR 2010	131.9	12.9	115	139.9	14.2	115	3.0%	-8.00 [-11.51, -4.49]
Total (95% CI)			**3304**			**3432**	**100.0%**	**-3.39 [-4.31, -2.46]**

Heterogeneity: Tau² = 4.17; Chi² = 135.80, df = 48 (P < 0.00001); I² = 65%
Test for overall effect: Z = 7.18 (P < 0.00001)

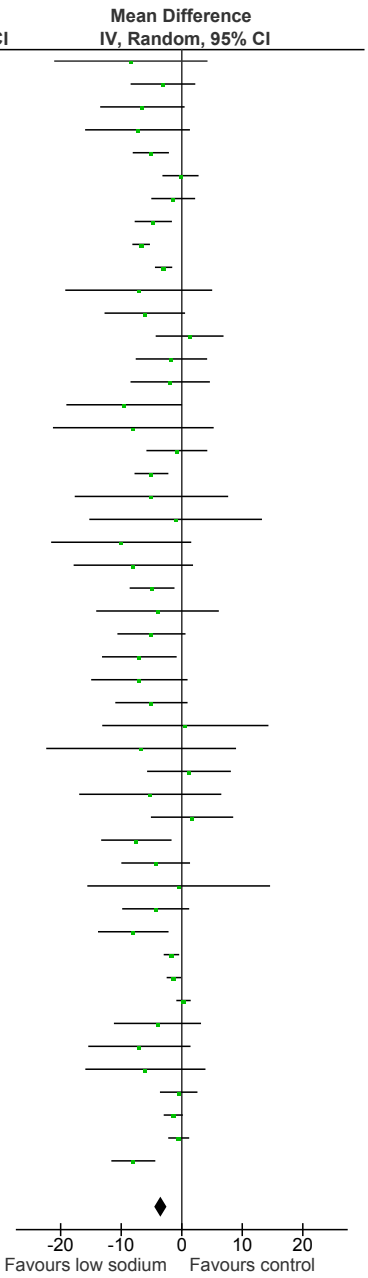


Figure 3.3 Resting systolic blood pressure: blood pressure subgroups

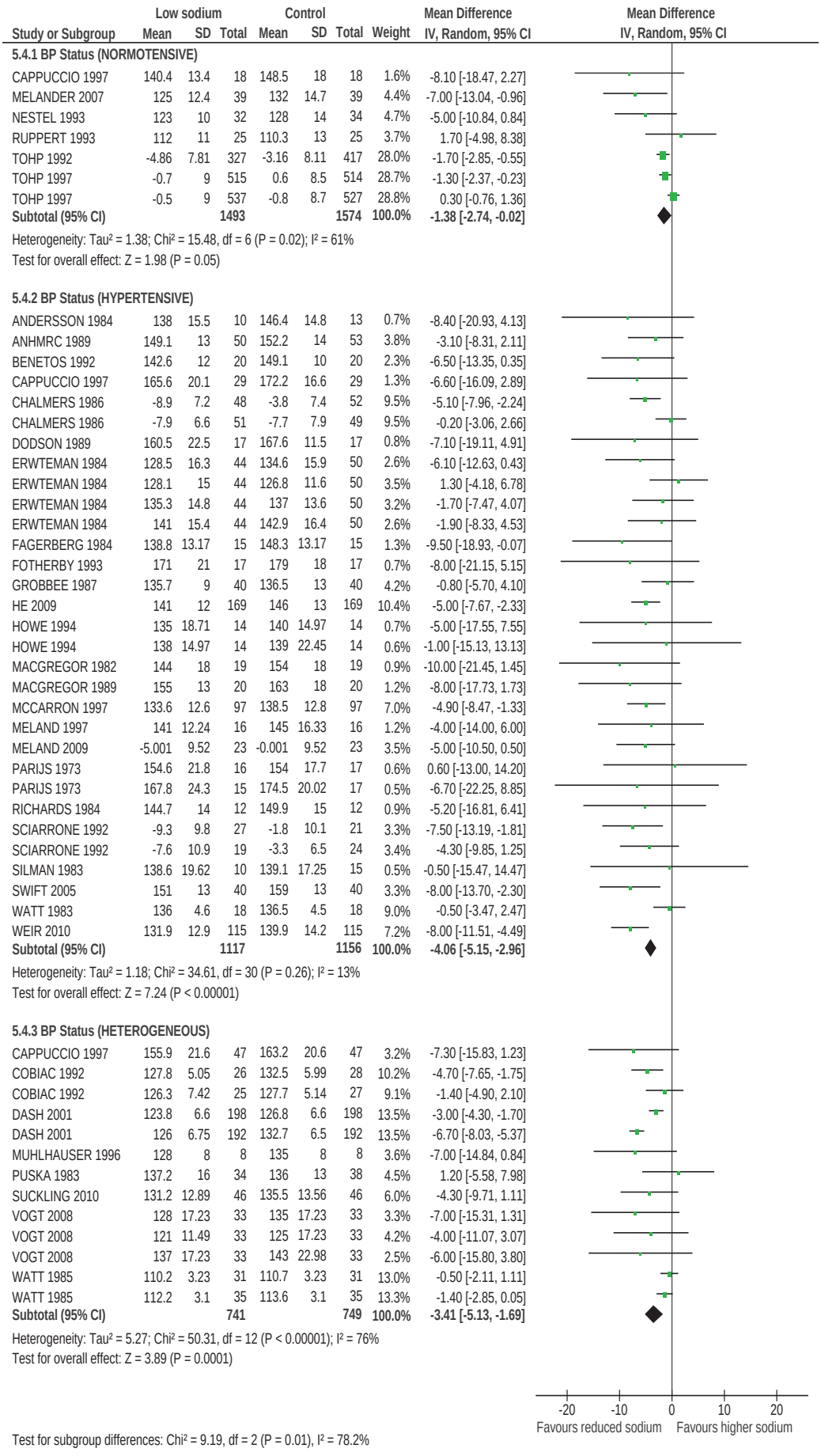
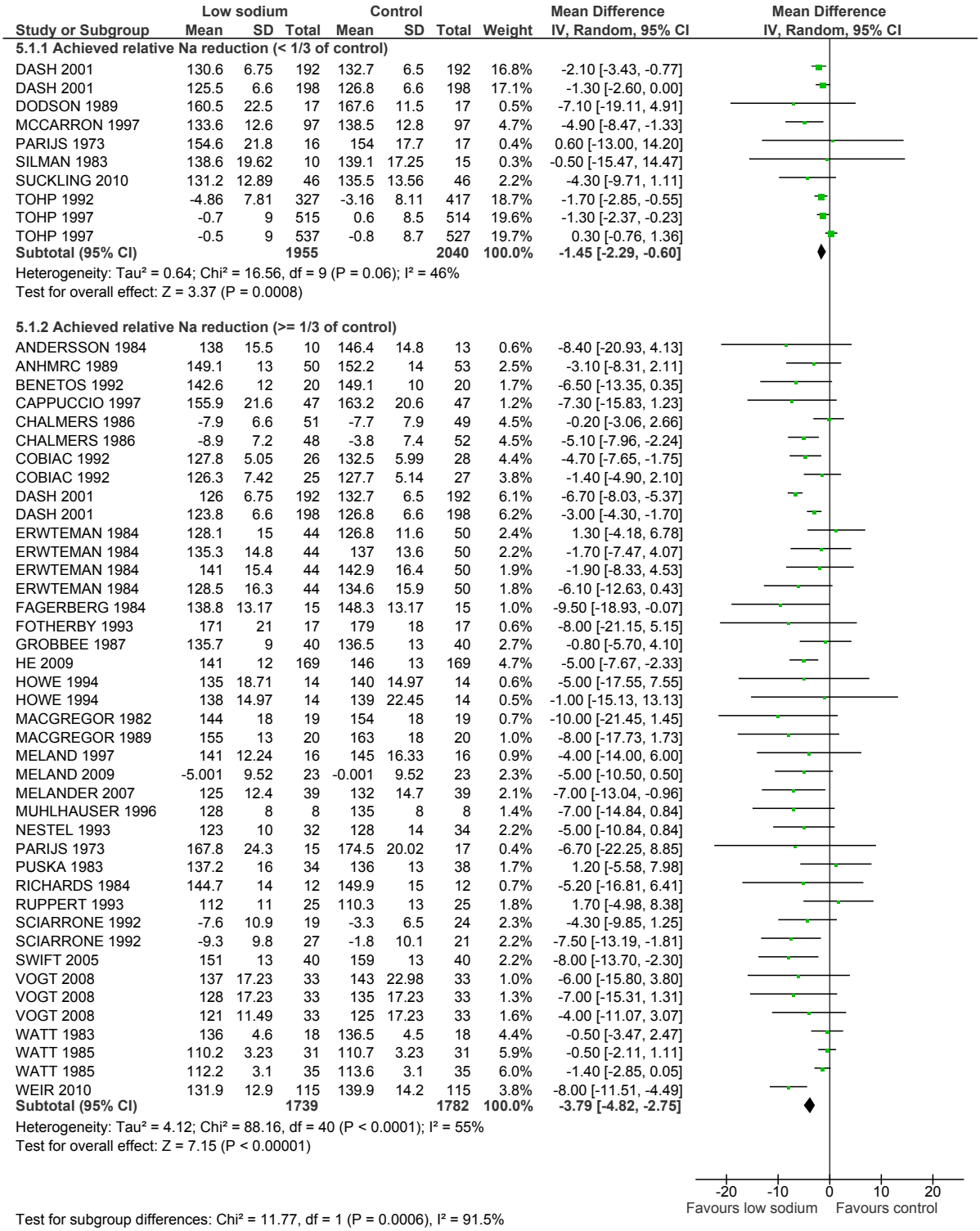


Figure 3.4 Resting systolic blood pressure: relative intake achieved subgroups (indirect comparison)



Test for subgroup differences: Chi² = 11.77, df = 1 (P = 0.0006), I² = 91.5%

Figure 3.5 Resting systolic blood pressure: absolute intake achieved subgroups (indirect comparison of < 2 g/day vs > 2 g/day)

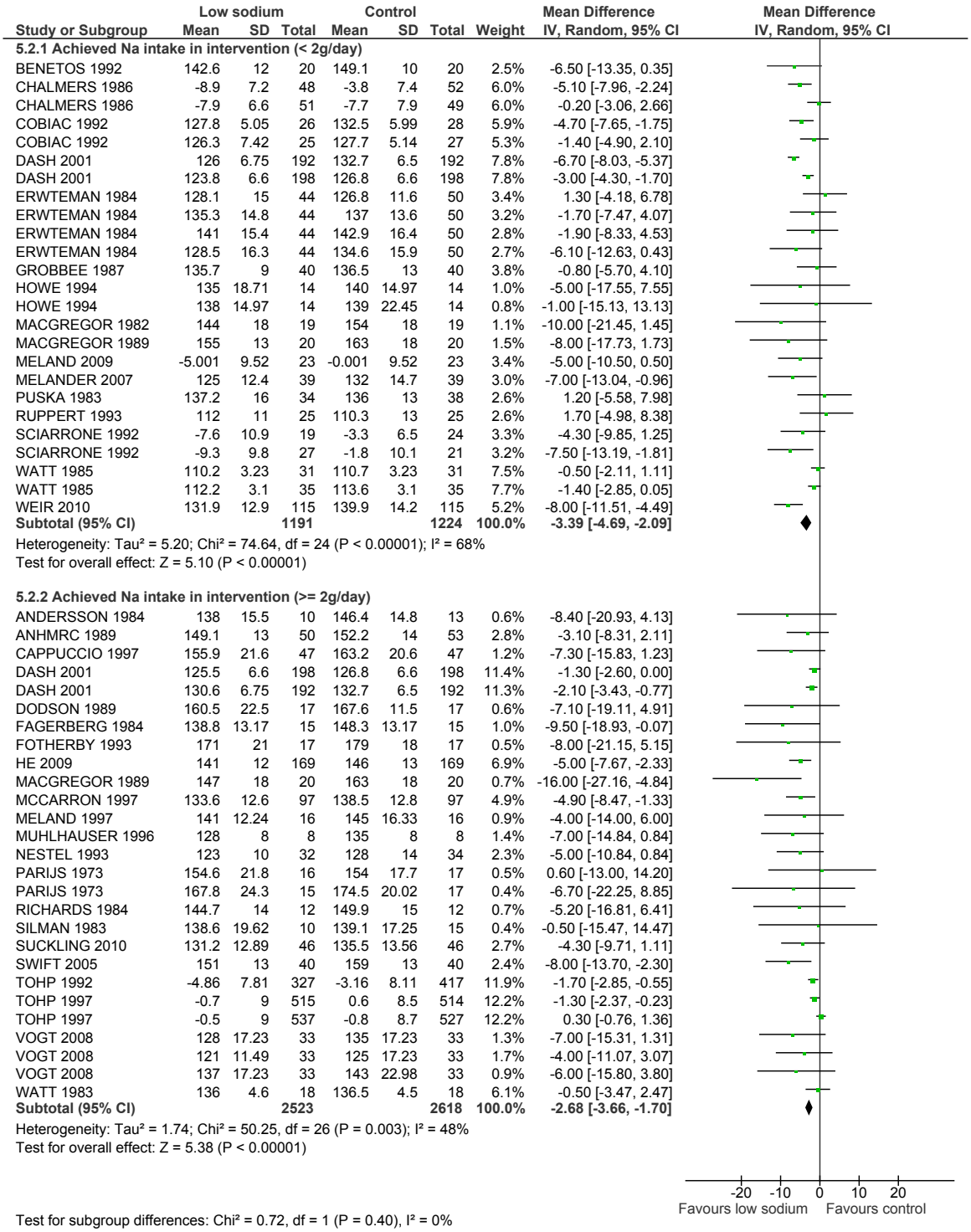


Figure 3.6 Resting systolic blood pressure: absolute intake achieved subgroups (indirect comparison of < 1.2 g/day vs > 1.2 g/day)

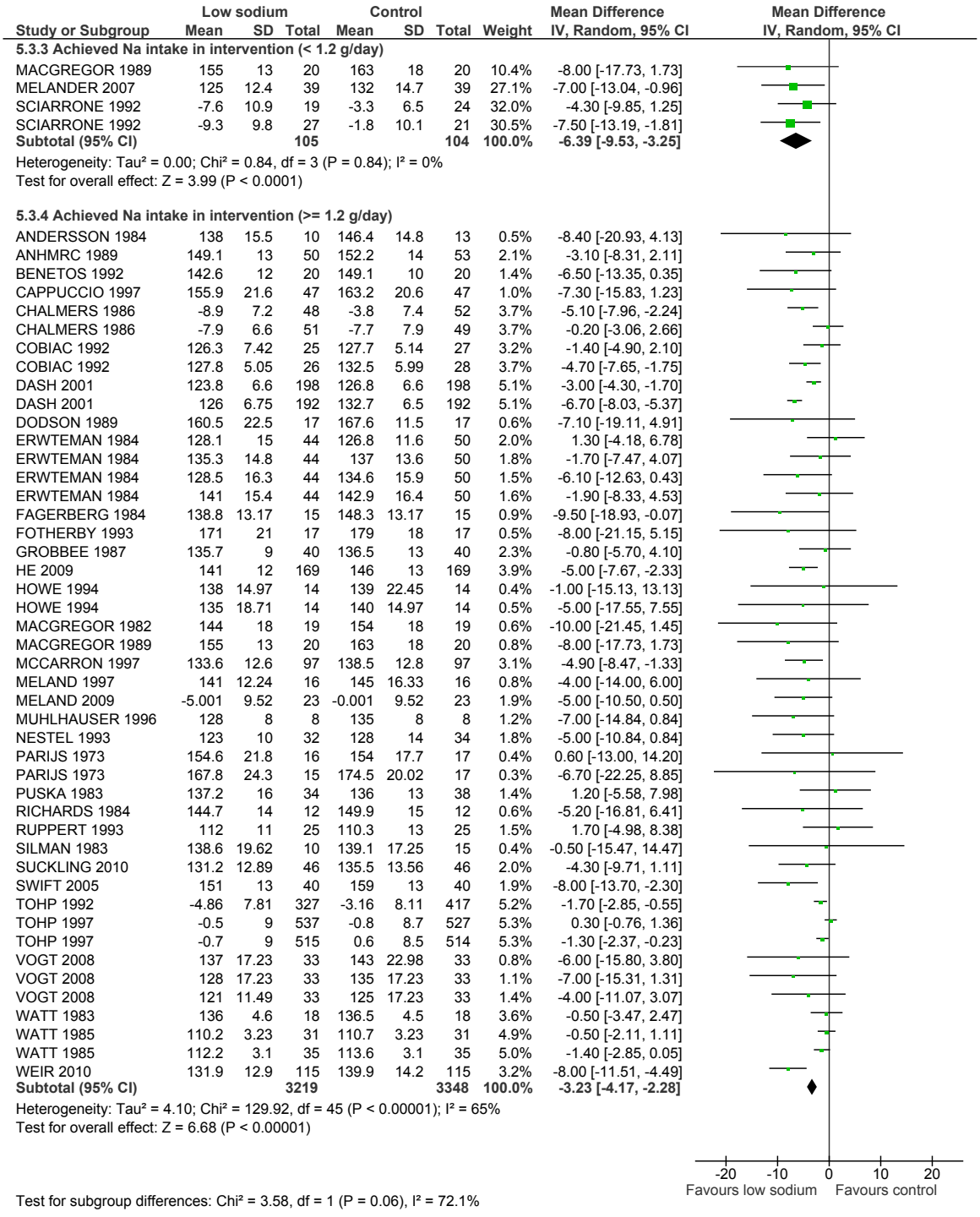


Figure 3.7 Resting systolic blood pressure: duration subgroups

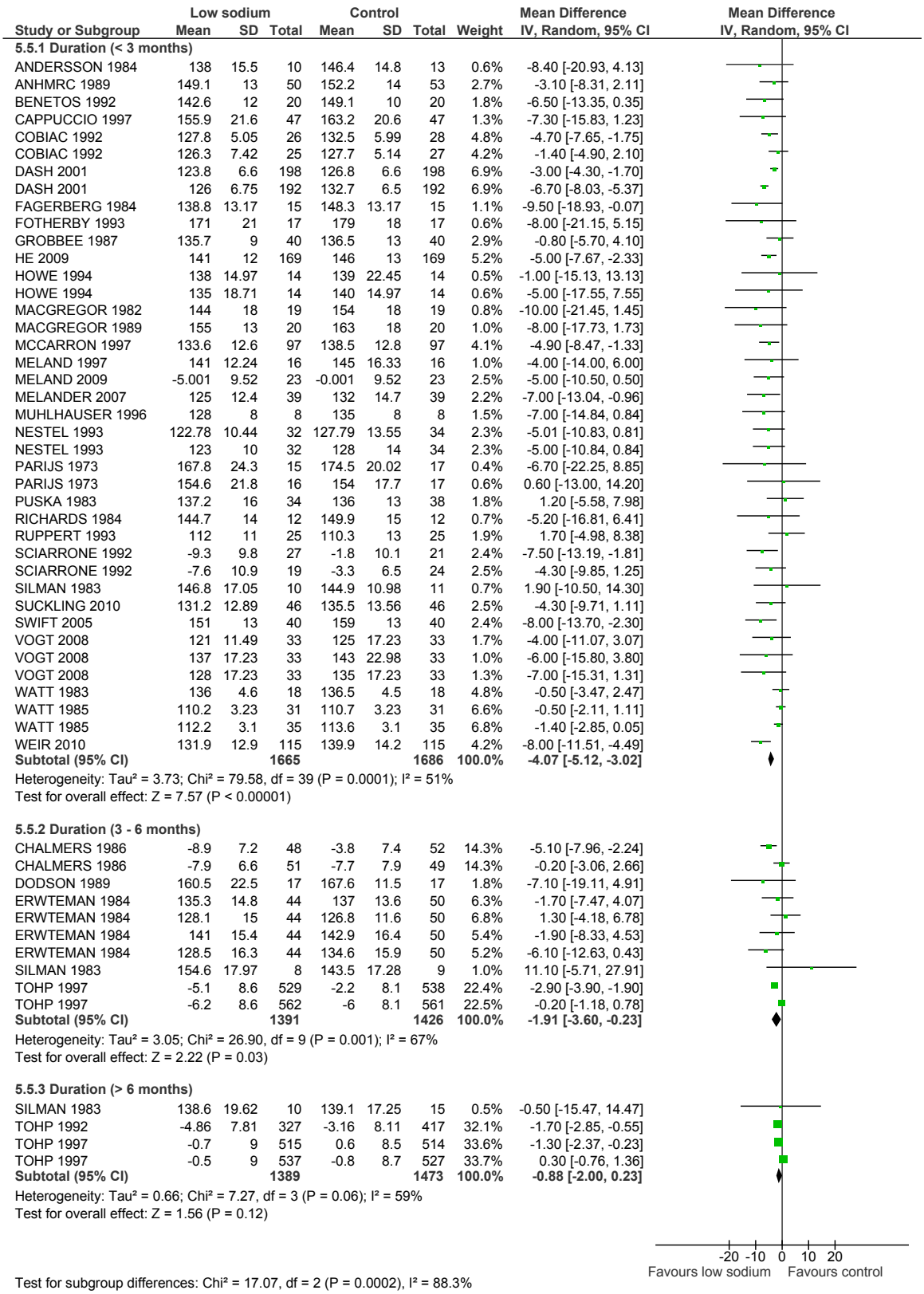


Figure 3.8 Resting systolic blood pressure: blood pressure device subgroups

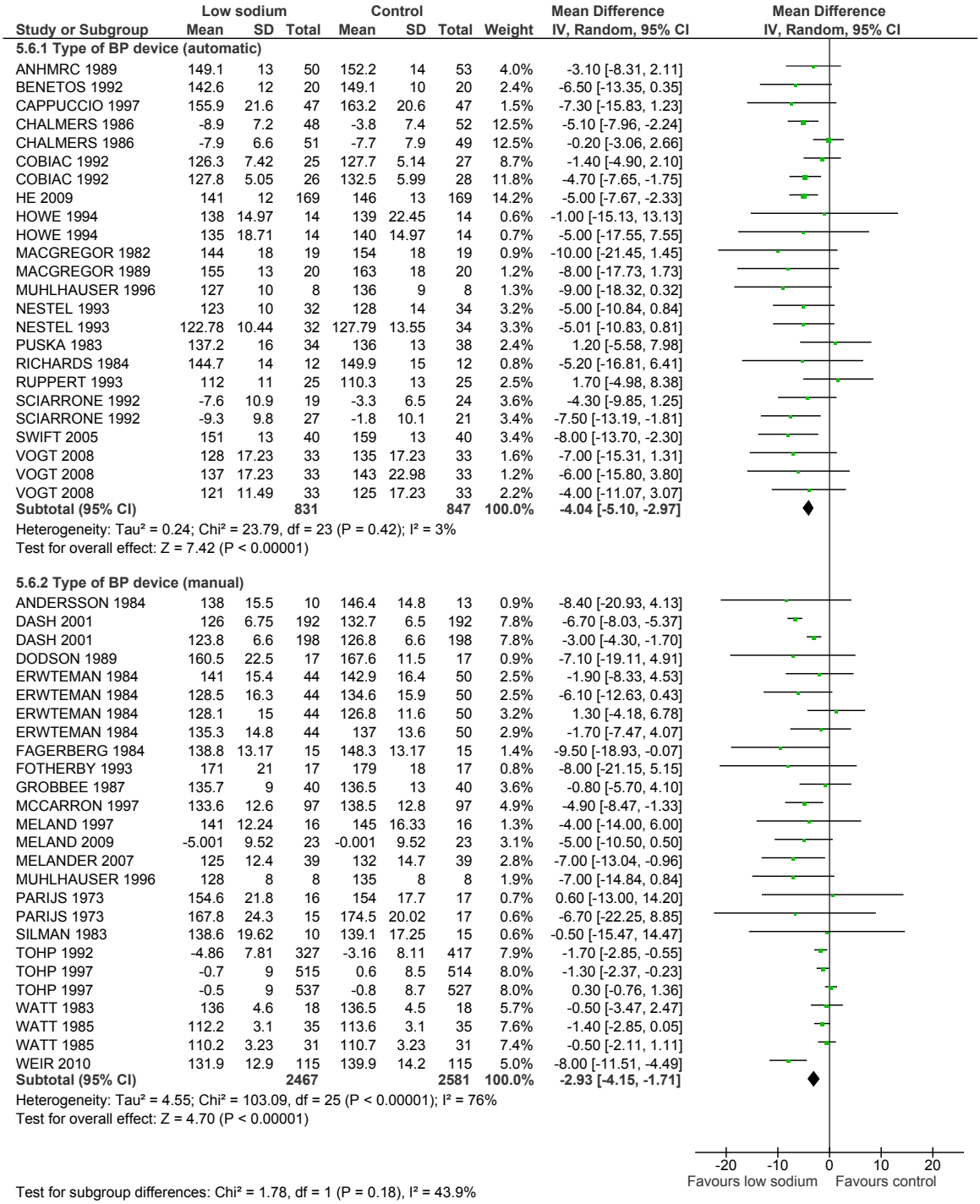
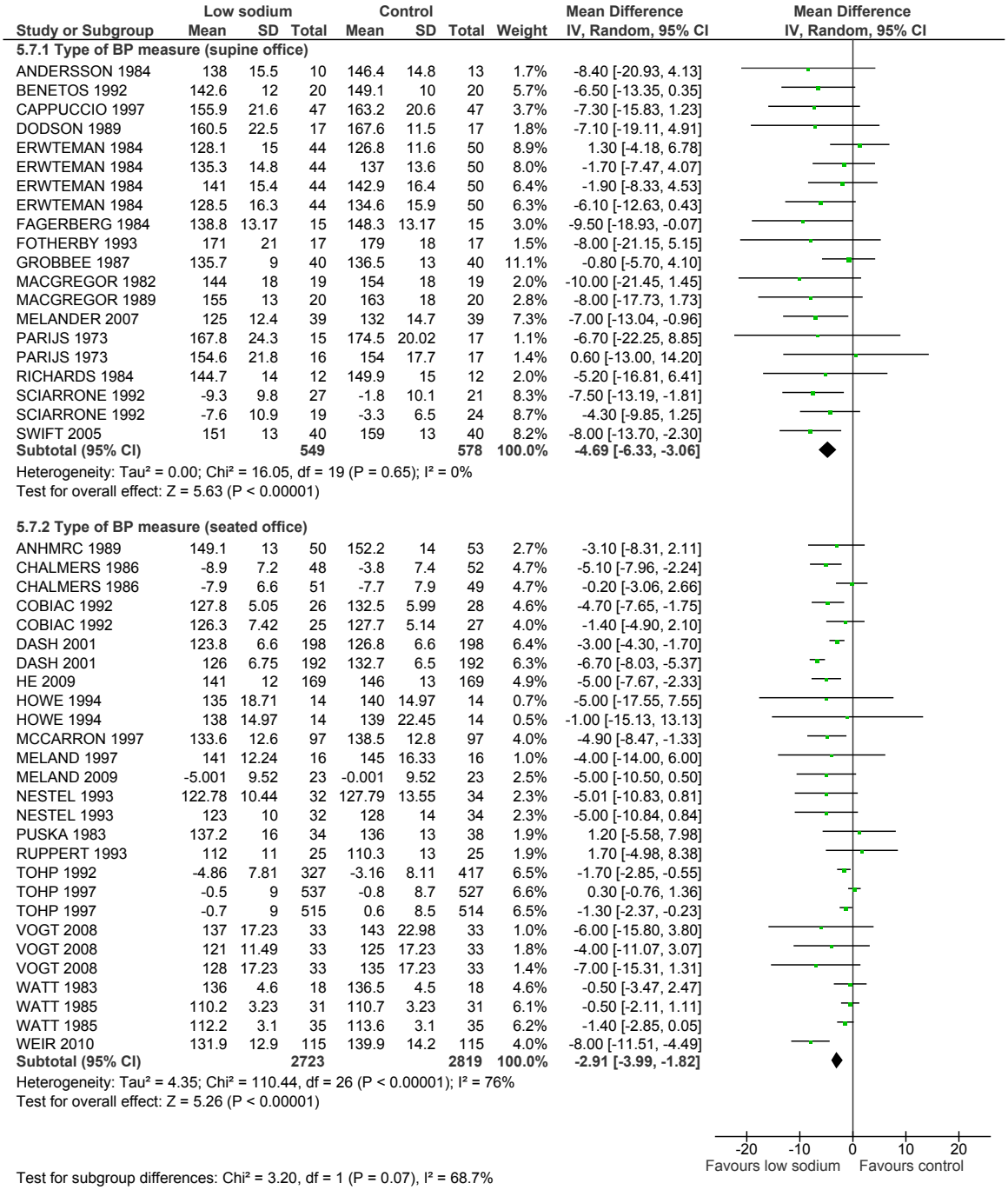
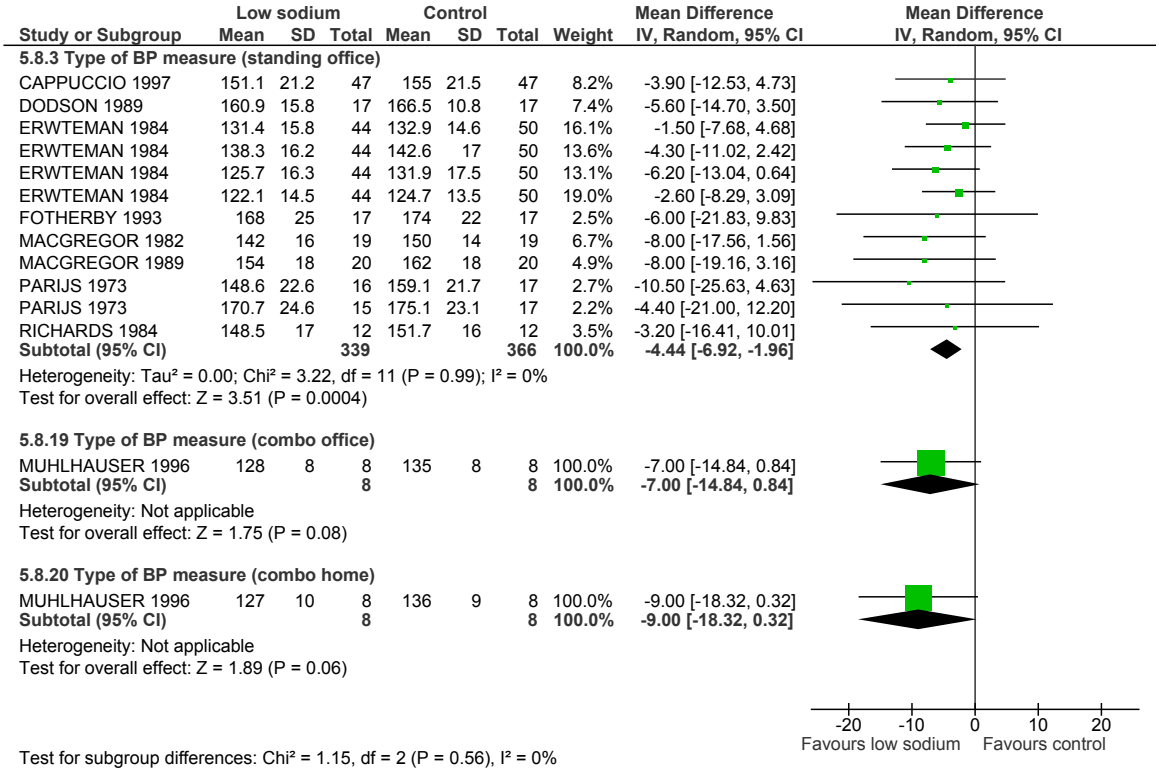


Figure 3.9 Resting systolic blood pressure: blood pressure measurement method subgroups



Test for subgroup differences: Chi² = 3.20, df = 1 (P = 0.07), I² = 68.7%

Figure 3.10 Resting systolic blood pressure: blood pressure measurement method subgroups (continued)



Test for subgroup differences: Chi² = 1.15, df = 2 (P = 0.56), I² = 0%

Figure 3.11 Resting systolic blood pressure: blood pressure medication subgroups

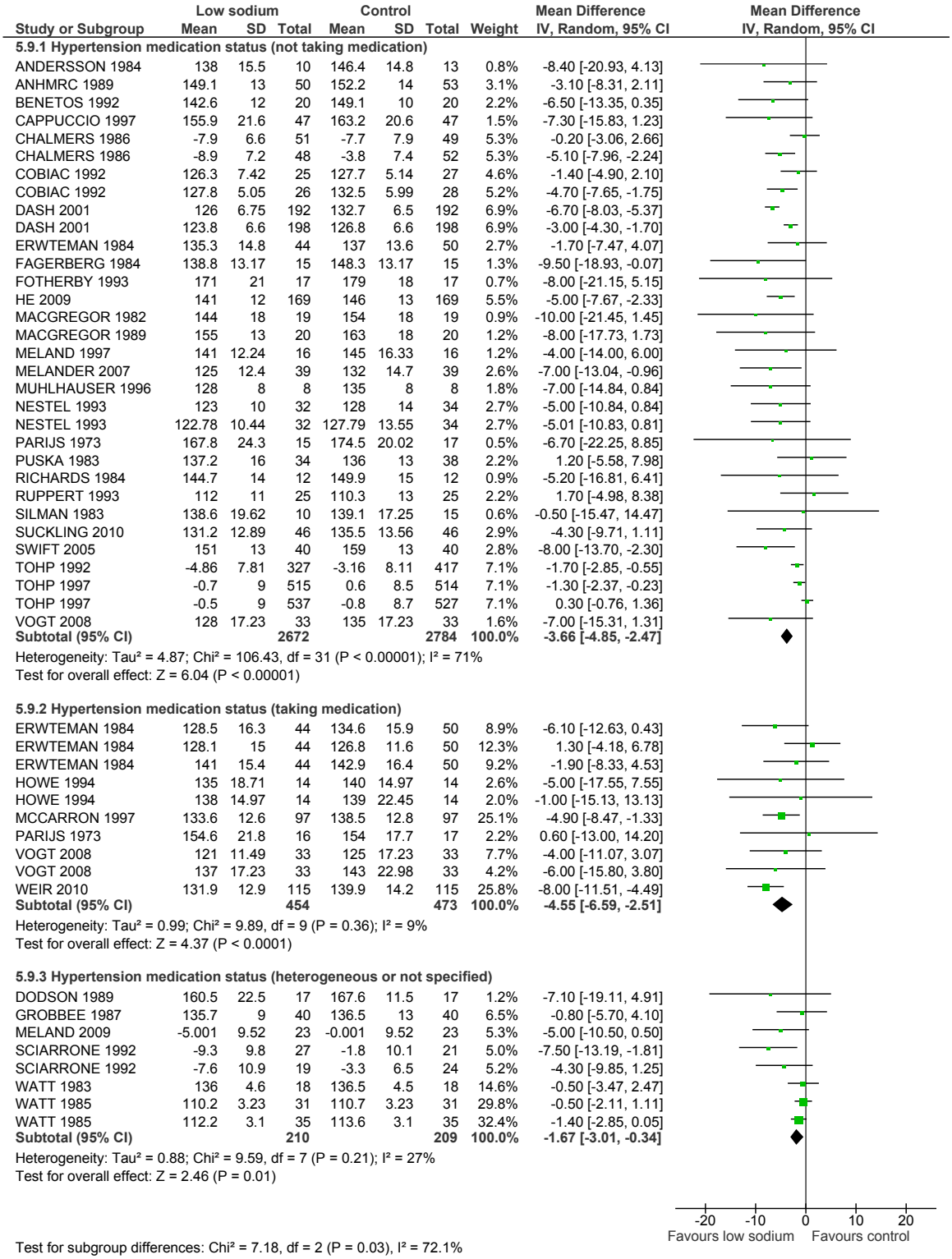


Figure 3.12 Resting systolic blood pressure: study design subgroups

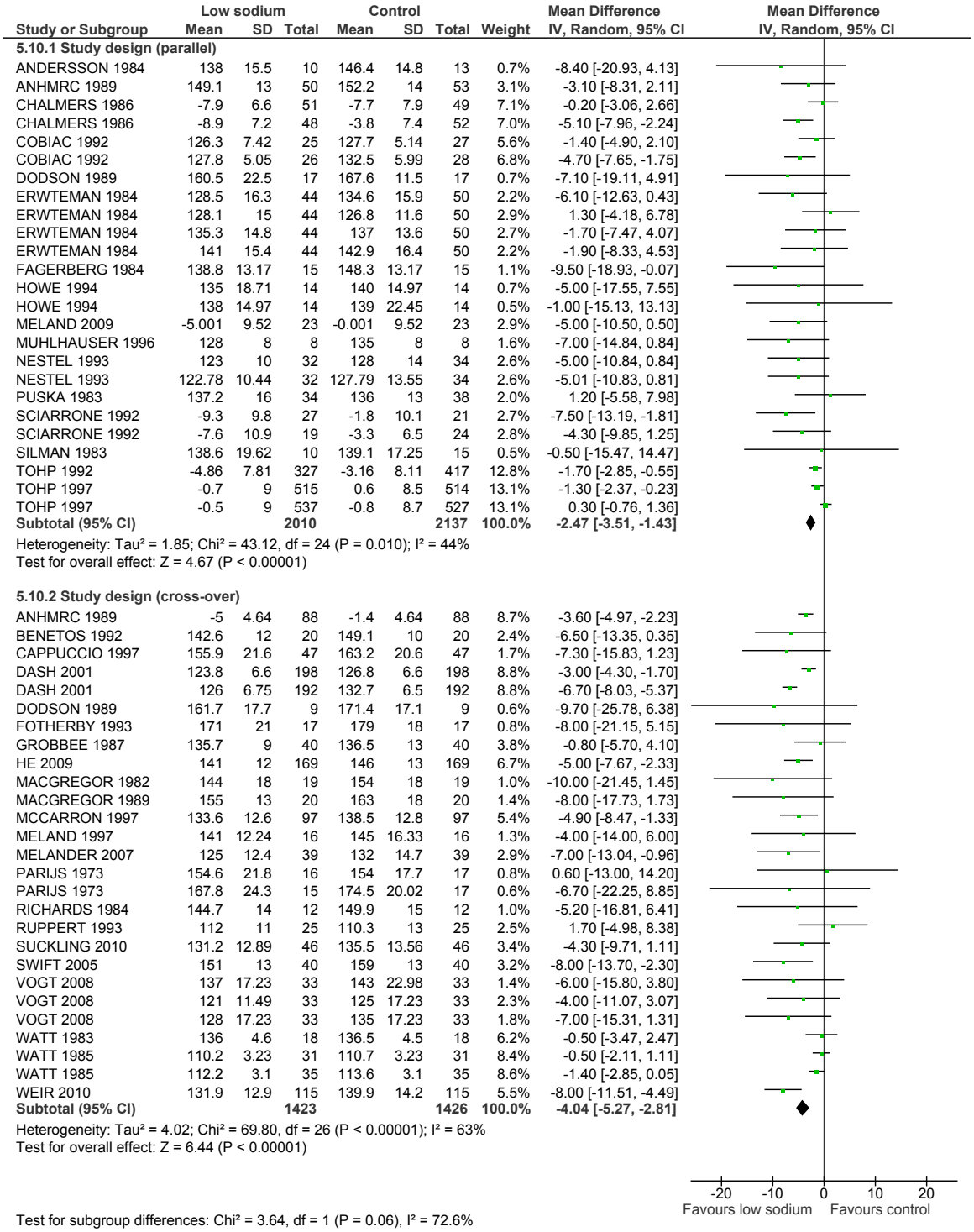


Figure 3.13 Resting diastolic blood pressure: all adults

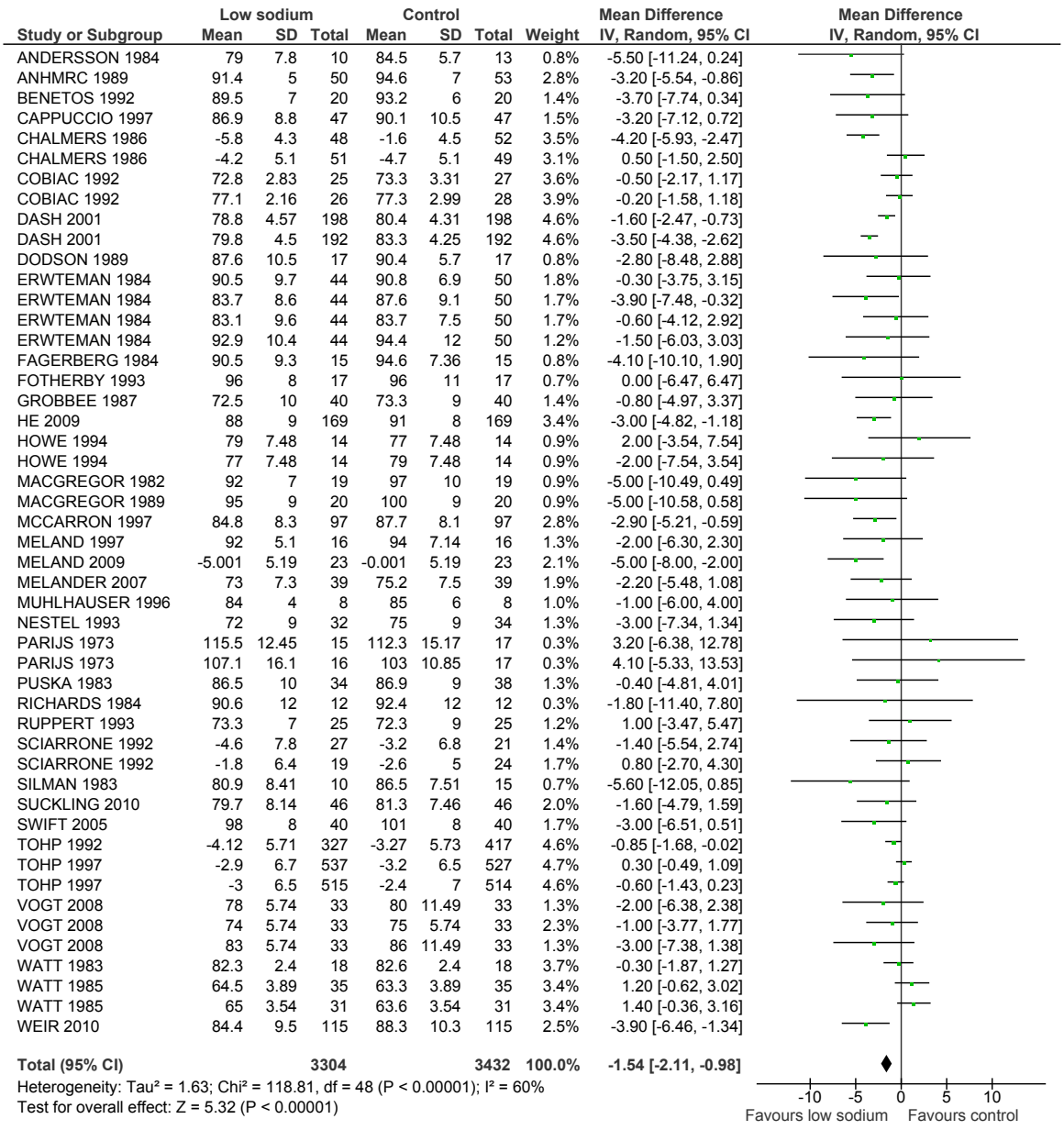
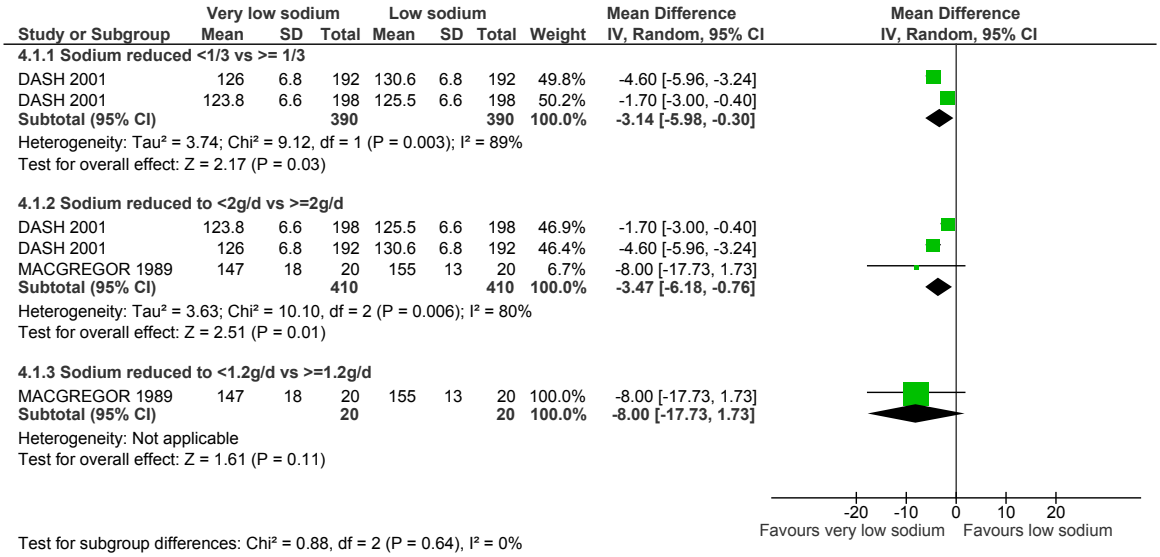
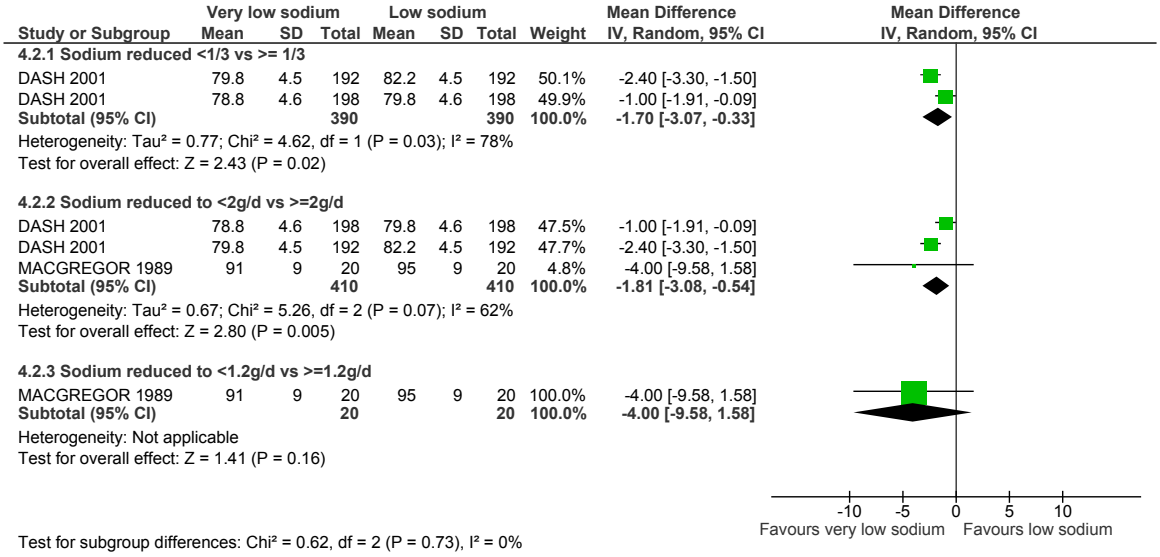


Figure 3.14 Resting systolic blood pressure: direct comparison of varying levels of sodium intake



Test for subgroup differences: Chi² = 0.88, df = 2 (P = 0.64), I² = 0%

Figure 3.15 Resting diastolic blood pressure: direct comparison of varying levels of sodium intake



Test for subgroup differences: Chi² = 0.62, df = 2 (P = 0.73), I² = 0%

Figure 3.16 Ambulatory systolic blood pressure: all

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
FOTHERBY 1993	145	15	16	150	16	16	4.1%	-5.00 [-15.75, 5.75]
HE 2009	137	11	169	141	10	169	23.6%	-4.00 [-6.24, -1.76]
MELANDER 2007	131	11.1	39	136	12.7	39	11.9%	-5.00 [-10.29, 0.29]
SUCKLING 2010	-3.31	4.32	46	-0.01	4.32	46	25.7%	-3.30 [-5.07, -1.53]
SWIFT 2005	139	11	40	146	11	40	13.3%	-7.00 [-11.82, -2.18]
WEIR 2010	124.2	10.4	115	133.5	10.6	115	21.4%	-9.30 [-12.01, -6.59]
Total (95% CI)			**425**			**425**	**100.0%**	**-5.51 [-7.87, -3.16]**

Heterogeneity: Tau² = 4.79; Chi² = 14.60, df = 5 (P = 0.01); I² = 66%
Test for overall effect: Z = 4.60 (P < 0.00001)

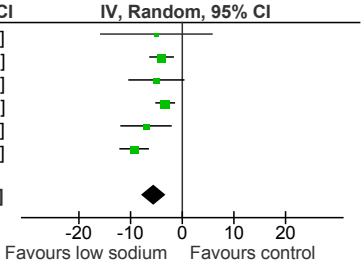


Figure 3.17 Ambulatory diastolic blood pressure: all

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
FOTHERBY 1993	85	13	16	87	12	16	2.5%	-2.00 [-10.67, 6.67]
HE 2009	84	9	169	86	9	169	23.4%	-2.00 [-3.92, -0.08]
MELANDER 2007	82.3	6.6	39	85	7	39	14.4%	-2.70 [-5.72, 0.32]
SUCKLING 2010	-1.81	3.84	46	-0.01	3.84	46	27.2%	-1.80 [-3.37, -0.23]
SWIFT 2005	91	7	40	94	9	40	11.6%	-3.00 [-6.53, 0.53]
WEIR 2010	78.4	8.2	115	84.1	8.6	115	20.9%	-5.70 [-7.87, -3.53]
Total (95% CI)			**425**			**425**	**100.0%**	**-2.94 [-4.36, -1.51]**

Heterogeneity: Tau² = 1.32; Chi² = 9.13, df = 5 (P = 0.10); I² = 45%
Test for overall effect: Z = 4.03 (P < 0.0001)

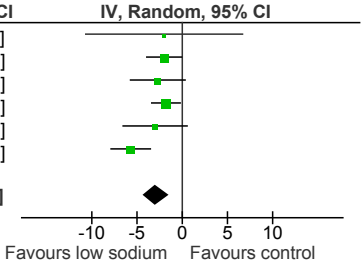


Figure 3.18 Total cholesterol

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
CAPPUCCIO 1997	6	1	47	5.9	1.1	47	1.5%	0.10 [-0.33, 0.53]
DASH 2001	0.008637	0.57	390	0.000001	0.57	390	43.4%	0.01 [-0.07, 0.09]
DASH 2001	0.04807	0.58	390	0.00001	0.58	390	41.9%	0.05 [-0.03, 0.13]
FOTHERBY 1993	5.1	0.9	17	5.3	0.9	17	0.8%	-0.20 [-0.81, 0.41]
GATES 2004	5.09	1.04	12	4.96	1.39	12	0.3%	0.13 [-0.85, 1.11]
MCCARRON 1997	5.78	1.04	97	5.57	1.02	97	3.3%	0.21 [-0.08, 0.50]
MELAND 1997	5.7	1.22	16	5.7	0.82	16	0.5%	0.00 [-0.72, 0.72]
MELAND 2009	-0.21	0.78	23	-0.01	0.78	23	1.4%	-0.20 [-0.65, 0.25]
MUHLHAUSER 1996	5.43	1.47	8	5.74	1.09	8	0.2%	-0.31 [-1.58, 0.96]
RUPPERT 1993	4.97	0.8	25	4.97	0.85	25	1.3%	0.00 [-0.46, 0.46]
SCIARRONE 1992	-0.6	0.7	27	-0.6	1.1	21	1.0%	0.00 [-0.54, 0.54]
SCIARRONE 1992	0.1	0.4	19	0.2	0.7	24	2.5%	-0.10 [-0.43, 0.23]
VOGT 2008	5.9	1.15	33	6.1	1.72	33	0.6%	-0.20 [-0.91, 0.51]
VOGT 2008	5.6	1.72	33	5.8	1.15	33	0.6%	-0.20 [-0.91, 0.51]
VOGT 2008	5.5	1.15	33	5.7	1.15	33	0.9%	-0.20 [-0.75, 0.35]
Total (95% CI)			**1170**			**1169**	**100.0%**	**0.02 [-0.03, 0.07]**

Heterogeneity: Tau² = 0.00; Chi² = 5.91, df = 14 (P = 0.97); I² = 0%
Test for overall effect: Z = 0.80 (P = 0.43)

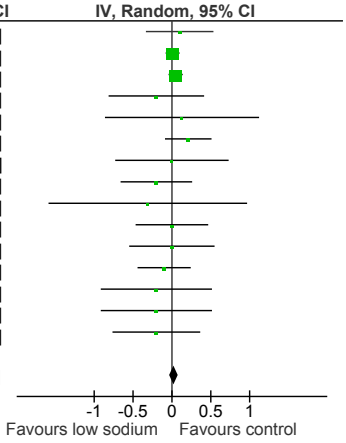


Figure 3.19 HDL cholesterol

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
DASH 2001	-0.01915	0.16	390	0.00001	0.16	390	46.5%	-0.02 [-0.04, 0.00]
DASH 2001	0.004784	0.16	390	0.000001	0.16	390	46.5%	0.00 [-0.02, 0.03]
FOTHERBY 1993	1.1	0.6	17	1.3	0.3	17	0.2%	-0.20 [-0.52, 0.12]
GATES 2004	1.39	0.69	12	1.44	1.04	12	0.0%	-0.05 [-0.76, 0.66]
MCCARRON 1997	1.27	0.37	97	1.27	0.36	97	2.2%	0.00 [-0.10, 0.10]
MELAND 1997	1.1	0.41	16	1.2	0.41	16	0.3%	-0.10 [-0.38, 0.18]
MELAND 2009	-0.051	0.35	23	-0.001	0.35	23	0.6%	-0.05 [-0.25, 0.15]
MUHLHAUSER 1996	1.42	0.47	8	1.42	0.36	8	0.1%	0.00 [-0.41, 0.41]
RUPPERT 1993	1.44	0.31	25	1.48	0.36	25	0.7%	-0.04 [-0.23, 0.15]
SCIARRONE 1992	0	0.2	19	0.1	0.3	24	1.0%	-0.10 [-0.25, 0.05]
SCIARRONE 1992	-0.2	0.2	27	-0.1	0.2	21	1.8%	-0.10 [-0.21, 0.01]
Total (95% CI)			**1024**			**1023**	**100.0%**	**-0.01 [-0.03, 0.00]**

Heterogeneity: Tau² = 0.00; Chi² = 8.12, df = 10 (P = 0.62); I² = 0%
Test for overall effect: Z = 1.39 (P = 0.16)

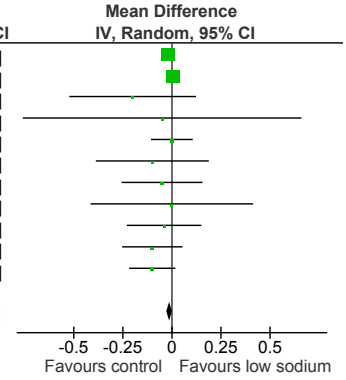


Figure 3.20 LDL cholesterol

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
DASH 2001	0.003527	0.5	379	0.000001	0.5	379	46.8%	0.00 [-0.07, 0.07]
DASH 2001	0.04113	0.51	379	0.00001	0.51	379	45.0%	0.04 [-0.03, 0.11]
FOTHERBY 1993	3.2	0.8	17	3.2	0.8	17	0.8%	0.00 [-0.54, 0.54]
GATES 2004	3.1	1.39	12	2.89	1.04	12	0.2%	0.21 [-0.77, 1.19]
MCCARRON 1997	3.72	0.98	97	3.56	0.94	97	3.2%	0.16 [-0.11, 0.43]
RUPPERT 1993	3.31	0.72	25	3.18	0.75	25	1.4%	0.13 [-0.28, 0.54]
SCIARRONE 1992	-0.4	0.7	27	-0.5	0.9	21	1.1%	0.10 [-0.37, 0.57]
SCIARRONE 1992	0.1	0.7	19	0.2	0.7	24	1.3%	-0.10 [-0.52, 0.32]
Total (95% CI)			**955**			**954**	**100.0%**	**0.03 [-0.02, 0.08]**

Heterogeneity: Tau² = 0.00; Chi² = 2.32, df = 7 (P = 0.94); I² = 0%
Test for overall effect: Z = 1.11 (P = 0.27)

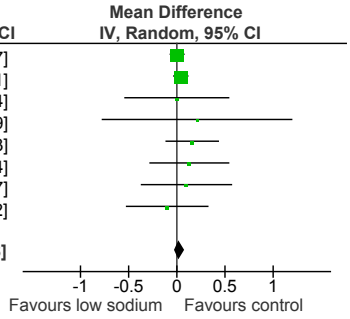


Figure 3.21 Triglycerides

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
CAPPUCCIO 1997	1.5	0.6	47	1.4	0.7	47	3.8%	0.10 [-0.16, 0.36]
DASH 2001	0.07238	0.57	379	0.00001	0.57	379	40.4%	0.07 [-0.01, 0.15]
DASH 2001	0.02945	0.56	379	0.00001	0.56	379	41.9%	0.03 [-0.05, 0.11]
FOTHERBY 1993	1.4	0.7	17	1.5	0.7	17	1.2%	-0.10 [-0.57, 0.37]
GATES 2004	1.27	1.04	12	1.36	1.73	12	0.2%	-0.09 [-1.23, 1.05]
MCCARRON 1997	1.89	1.38	97	1.71	1.05	97	2.2%	0.18 [-0.17, 0.53]
MELAND 2009	-0.31	0.69	23	-0.01	0.69	23	1.7%	-0.30 [-0.70, 0.10]
RUPPERT 1993	0.85	0.36	25	0.91	0.36	25	6.7%	-0.06 [-0.26, 0.14]
SCIARRONE 1992	0.1	1.3	27	-0.1	1	21	0.6%	0.20 [-0.45, 0.85]
SCIARRONE 1992	0	0.8	19	-0.2	0.7	24	1.3%	0.20 [-0.26, 0.66]
Total (95% CI)			**1025**			**1024**	**100.0%**	**0.04 [-0.01, 0.09]**

Heterogeneity: Tau² = 0.00; Chi² = 6.35, df = 9 (P = 0.70); I² = 0%
Test for overall effect: Z = 1.63 (P = 0.10)

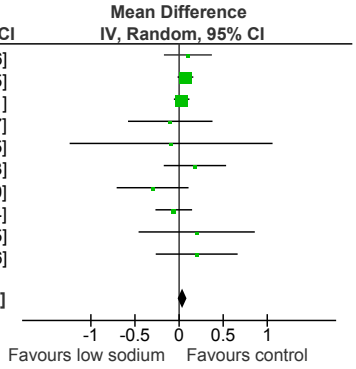


Figure 3.22 Plasma adrenaline

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
BENETOS 1992	84.4	48	20	65	54	20	8.2%	19.40 [-12.26, 51.06]
GATES 2004	30	17	12	26	14	12	52.9%	4.00 [-8.46, 16.46]
GROBBEE 1987	77	57	40	62	32	40	20.0%	15.00 [-5.26, 35.26]
RICHARDS 1984	78	28	12	77	24	12	18.9%	1.00 [-19.87, 21.87]
Total (95% CI)			**84**			**84**	**100.0%**	**6.90 [-2.17, 15.96]**

Heterogeneity: Tau² = 0.00; Chi² = 1.73, df = 3 (P = 0.63); I² = 0%
Test for overall effect: Z = 1.49 (P = 0.14)

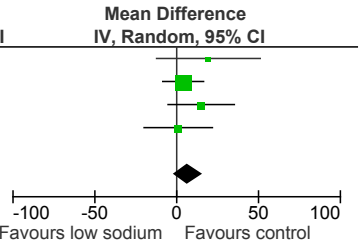


Figure 3.23 Plasma noradrenaline

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
ANDERSSON 1984	161	61	10	210	51	13	26.2%	-49.00 [-95.88, -2.12]
BENETOS 1992	300	152	20	248	188	20	9.3%	52.00 [-53.95, 157.95]
GATES 2004	290	80	12	297	107	12	15.4%	-7.00 [-82.59, 68.59]
GROBBEE 1987	239	120	40	220	114	40	24.1%	19.00 [-32.29, 70.29]
MACGREGOR 1989	683	409	12	586	409	12	1.2%	97.00 [-230.26, 424.26]
RICHARDS 1984	429	114	12	405	97	12	13.1%	24.00 [-60.69, 108.69]
RUPPERT 1993	501.2	180	25	422.1	170	25	10.7%	79.10 [-17.95, 176.15]
Total (95% CI)			**131**			**134**	**100.0%**	**8.23 [-27.84, 44.29]**

Heterogeneity: Tau² = 717.74; Chi² = 8.88, df = 6 (P = 0.18); I² = 32%
Test for overall effect: Z = 0.45 (P = 0.65)

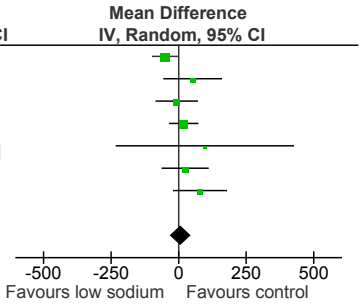


Figure 3.24 Urinary protein excretion

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
VOGT 2008	189	172.34	33	253	247.02	33	57.0%	-64.00 [-166.76, 38.76]
VOGT 2008	518	488.29	33	591	448.08	33	11.8%	-73.00 [-299.11, 153.11]
VOGT 2008	286	269.99	33	387	304.46	33	31.2%	-101.00 [-239.84, 37.84]
Total (95% CI)			**99**			**99**	**100.0%**	**-76.61 [-154.20, 0.97]**

Heterogeneity: Tau² = 0.00; Chi² = 0.18, df = 2 (P = 0.92); I² = 0%
Test for overall effect: Z = 1.94 (P = 0.05)

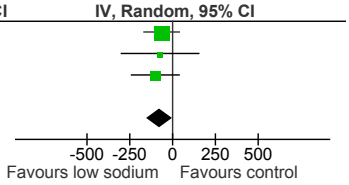


Figure 3.25 Protein:creatinine ratio

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
VOGT 2008	0.82	0.78	33	1.14	0.97	33	59.6%	-0.32 [-0.74, 0.10]
VOGT 2008	1.33	1.2	33	1.91	1.4	33	27.2%	-0.58 [-1.21, 0.05]
VOGT 2008	2.37	2.3	33	2.77	1.3	33	13.2%	-0.40 [-1.30, 0.50]
Total (95% CI)			**99**			**99**	**100.0%**	**-0.40 [-0.73, -0.07]**

Heterogeneity: Tau² = 0.00; Chi² = 0.45, df = 2 (P = 0.80); I² = 0%
Test for overall effect: Z = 2.40 (P = 0.02)

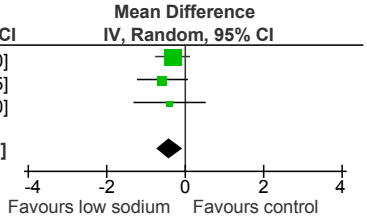


Figure 3.26 Creatinine clearance

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
FOTHERBY 1993	97	31	17	95	32	17	16.1%	2.00 [-19.18, 23.18]
VOGT 2008	75	28.72	33	86	34.47	33	30.9%	-11.00 [-26.31, 4.31]
VOGT 2008	82	34.47	33	89	28.72	33	30.9%	-7.00 [-22.31, 8.31]
VOGT 2008	83	40.21	33	94	34.47	33	22.1%	-11.00 [-29.07, 7.07]
Total (95% CI)			**116**			**116**	**100.0%**	**-7.67 [-16.17, 0.83]**

Heterogeneity: Tau² = 0.00; Chi² = 1.12, df = 3 (P = 0.77); I² = 0%
Test for overall effect: Z = 1.77 (P = 0.08)

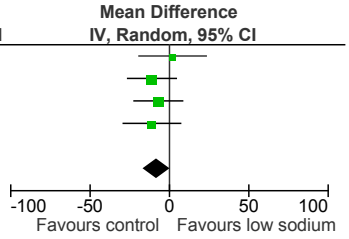
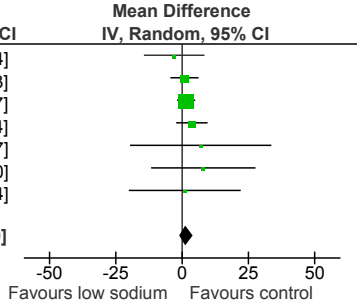


Figure 3.27 Serum creatinine

Study or Subgroup	Low sodium Mean	SD	Total	Control Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
FOTHERBY 1993	85	18	17	88	15	17	4.4%	-3.00 [-14.14, 8.14]
GROBBEE 1987	93.81	11.5	40	92.92	11.5	40	21.3%	0.89 [-4.15, 5.93]
HE 2009	83.8	15	169	82.3	14.7	169	53.9%	1.50 [-1.67, 4.67]
MELANDER 2007	84.1	12.6	39	80.4	12.8	39	17.0%	3.70 [-1.94, 9.34]
VOGT 2008	143	57.45	33	136	51.7	33	0.8%	7.00 [-19.37, 33.37]
VOGT 2008	129	40.21	33	121	40.21	33	1.4%	8.00 [-11.40, 27.40]
VOGT 2008	126	40.21	33	125	45.96	33	1.2%	1.00 [-19.84, 21.84]
Total (95% CI)			**364**			**364**	**100.0%**	**1.68 [-0.65, 4.00]**

Heterogeneity: Tau² = 0.00; Chi² = 1.85, df = 6 (P = 0.93); I² = 0%
Test for overall effect: Z = 1.41 (P = 0.16)



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Annex 1: Electronic search strategy

A1 Search strategy

Effect of reduced sodium intake on blood pressure, renal disease blood lipids, and other potential adverse effects

A1.1 Blood pressure

Identified Cochrane systematic review by He and MacGregor 2008:

- Use He and MacGregor reference list for potential studies
- Electronic search from 2005 to 2011

PubMed

- 1 January 2005 to 6 July 2011

(blood pressure[MeSH] OR hypertension[MeSH] OR blood pressure[tiab] OR hypertension[tiab]) AND (sodium[MeSH] OR salt[MeSH] OR sodium chloride[MeSH] OR sodium[tiab] OR salt[tiab] OR sodium chloride[tiab]) AND (diet[MeSH] OR dietary[MeSH] OR intake[MeSH] OR restriction[MeSH] or reduction[MeSH] OR diet[tiab] OR dietary[tiab] OR intake[tiab] OR restriction[tiab] or reduction[tiab]) AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (animals [mh] NOT humans [mh])

EMBASE

- 1 January 2005 to 2 August 2011

(1) sodium/blood pressure in adults

Step 1

'sodium chloride'/exp OR 'sodium'/exp OR salt:ti,ab OR sodium:ti,ab

Step 2

'diet'/exp OR 'electrolyte intake'/exp OR 'diet restriction'/exp or 'dietary':ti,ab OR 'diet':ti,ab OR intake:ti,ab OR restriction:ti,ab or restricted:ti,ab or restrictive:ti,ab or reduce:ti,ab or reduced;ti, ab OR reduction:ti,ab

Step 1 AND Step 2

Step 3

'randomized controlled trial'/exp OR 'controlled trial':ab,ti OR 'randomized':ab,ti AND 'randomised':ab,ti OR placebo:ab,ti OR 'drug therapy':ab,ti OR randomly:ab,ti OR trial:ab,ti OR groups:ab,ti

Step 4

(Step 1 AND Step 2 AND Step 3) AND [2005-2012]/py

Step 5

(Step 1 AND Step 2) AND [randomized controlled trial]/lim AND [2005-2012]/py

Step 6

(Step 4 OR Step 5) AND [animals]/lim

Step 7

(Step 4 OR Step 5) AND [animals]/lim AND [humans]/lim

Step 8

(Step 4 OR Step 5) NOT Step 6

Step 9

Step 8 OR Step 7

LILACS

- No date limit, run on 06 August 2011

(blood pressure OR hypertension) AND (sodium OR salt) AND (diet OR dietary OR intake OR restriction or reduction) AND (randomized controlled trial OR controlled clinical trial OR randomized OR placebo OR drug therapy OR randomly OR trial OR groups)

Cochrane central register of controlled trials

- 1 January 2005 to 24 August 2011

(blood pressure OR hypertension) AND (sodium OR salt) AND (diet OR dietary OR intake OR restriction or reduction) AND (randomized controlled trial OR controlled clinical trial OR randomized OR placebo OR drug therapy randomly OR trial OR groups)

WHO International Clinical Trials Registry Platform

- No date limit, run on 23 August 2011

(blood pressure AND sodium) OR (blood pressure AND salt) OR (hypertension AND sodium) OR (hypertension AND salt)

A1.2 Adverse effects

- No systematic reviews identified with similar or equivalent inclusion criteria
- Run electronic search for RCTs

PubMed

- No date limit, run 06 July 2011

(salt[MeSH] OR sodium[MeSH] OR salt[tiab] OR sodium[tiab]) AND (noradrenaline[MeSH] OR norepinephrine[MeSH] OR noradrenaline[tiab] OR norepinephrine[tiab] OR catecholamine[MeSH] OR catecholamine[tiab] OR cholesterol[MeSH] OR triglycerides[MeSH] OR low density lipoprotein[MeSH] OR high density lipoprotein[MeSH] OR LDL[tiab] OR HDL[tiab] OR cholesterol[tiab] OR triglyceride[tiab]) AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (animals [mh] NOT humans [mh])

EMBASE

- No date limit, run 02 August 2011

Step 1

'sodium chloride'/exp OR 'sodium'/exp OR salt:ti,ab OR sodium:ti,ab

Step 2

'noradrenalin'/exp OR 'adrenor':ab,ti OR 'alginodia':ab,ti OR 'arterenal':ab,ti OR 'arterenol':ab,ti OR 'baycain green':ab,ti OR 'd noradrenalin':ab,ti OR 'dextro noradrenalin':ab,ti OR 'dextro noradrenaline':ab,ti OR 'dl arterenol':ab,ti OR 'dl noradrenalin':ab,ti OR 'dl noradrenalin hydrochloride':ab,ti OR 'l alpha aminomethyl 3, 4 dihydroxybenzyl alcohol':ab,ti OR 'l noradrenalin':ab,ti OR 'l noradrenalin hydrochloride':ab,ti OR 'l noradrenaline':ab,ti OR 'l norepinephrine':ab,ti OR 'levarterenol':ab,ti OR 'levo noradrenalin':ab,ti OR 'levo noradrenaline':ab,ti OR 'levo norepinephrine':ab,ti OR 'levonor':ab,ti OR 'levophed':ab,ti OR 'neomelubrin':ab,ti OR 'neurogenic noradrenalin':ab,ti OR 'noradrec':ab,ti OR 'noradrenalin hydrochloride':ab,ti OR 'noradrenalin reduction':ab,ti

OR 'noradrenaline':ab,ti OR 'noradrine':ab,ti OR 'norepinephrin':ab,ti OR 'norepinephrine':ab,ti OR 'norepinephrine hydrochloride':ab,ti OR 'norexadrin':ab,ti OR 'revarterenol':ab,ti OR 'sympathin':ab,ti OR 'sympathin e':ab,ti OR 'catecholamine'/exp OR 'catechol amine; catecholamin':ab,ti OR 'catecholamines':ab,ti OR 'cathecholamine':ab,ti OR 'dextro pyrocatecholamine':ab,ti OR 'endogenous catecholamine':ab,ti OR 'pyrocatechinamine':ab,ti OR 'pyrocatecholamine':ab,ti OR 'hydroxy 5 cholestene':ab,ti OR '3beta hydroxy 5 cholestene':ab,ti OR '3beta hydroxycholest 5 ene':ab,ti OR '5 cholesten 3beta ol':ab,ti OR 'beta cholesterol':ab,ti OR 'cholest 5 en 3beta ol':ab,ti OR 'cholest 5 ene 3 ol':ab,ti OR 'cholesterin':ab,ti OR 'cholesterine':ab,ti OR 'cholesterol release':ab,ti OR 'dythol':ab,ti OR 'nsc 8798':ab,ti OR 'cholesterol'/exp OR 'riacylglycerol' OR 'acylglycerol, tri':ab,ti OR 'fatty acid triglyceride':ab,ti OR 'triacyl glyceride':ab,ti OR 'triglyceride':ab,ti OR 'triglycerides':ab,ti OR 'tryglyceride':ab,ti OR 'beta lipoprotein':ab,ti OR 'ldl':ab,ti OR 'lipoprotein, beta':ab,ti OR 'lipoprotein, low density':ab,ti OR 'lipoproteins, ldl' OR 'low density lipoprotein'/exp OR 'lpha 7 lipoprotein':ab,ti OR 'alpha lipoprotein':ab,ti OR 'hdl':ab,ti OR 'high density lipoprotein phospholipid':ab,ti OR 'lipoprotein, alpha':ab,ti OR 'lipoprotein, high density':ab,ti OR 'lipoproteins, hdl':ab,ti OR 'pre alpha lipoprotein':ab,ti OR 'very high density lipoprotein' OR 'high density lipoprotein'/exp AND ([cochrane review]/lim OR [controlled clinical trial]/lim OR [meta analysis]/lim OR [randomized controlled trial]/lim OR [systematic review]/lim)

Step 3

('noradrenalin'/exp OR 'adrenor':ab,ti OR 'alginodia':ab,ti OR 'arterenal':ab,ti OR 'arterenol':ab,ti OR 'baycain green':ab,ti OR 'd noradrenalin':ab,ti OR 'dextro noradrenalin':ab,ti OR 'dextro noradrenaline':ab,ti OR 'dl arterenol':ab,ti OR 'dl noradrenalin':ab,ti OR 'dl noradrenalin hydrochloride':ab,ti OR 'l alpha aminomethyl 3, 4 dihydroxybenzyl alcohol':ab,ti OR 'l noradrenalin':ab,ti OR 'l noradrenalin hydrochloride':ab,ti OR 'l noradrenaline':ab,ti OR 'l norepinephrine':ab,ti OR 'levarterenol':ab,ti OR 'levo noradrenalin':ab,ti OR 'levo noradrenaline':ab,ti OR 'levo norepinephrine':ab,ti OR 'levonor':ab,ti OR 'levophed':ab,ti OR 'neomelubrin':ab,ti OR 'neurogenic noradrenalin':ab,ti OR 'noradrec':ab,ti OR 'noradrenalin hydrochloride':ab,ti OR 'noradrenalin reduction':ab,ti OR 'noradrenaline':ab,ti OR 'noradrine':ab,ti OR 'norepinephrin':ab,ti OR 'norepinephrine':ab,ti OR 'norepinephrine hydrochloride':ab,ti OR 'norexadrin':ab,ti OR 'revarterenol':ab,ti OR 'sympathin':ab,ti OR 'sympathin e':ab,ti OR 'catecholamine'/exp OR 'catechol amine; catecholamin':ab,ti OR 'catecholamines':ab,ti OR 'cathecholamine':ab,ti OR 'dextro pyrocatecholamine':ab,ti OR 'endogenous catecholamine':ab,ti OR 'pyrocatechinamine':ab,ti OR 'pyrocatecholamine':ab,ti OR 'hydroxy 5 cholestene':ab,ti OR '3beta hydroxy 5 cholestene':ab,ti OR '3beta hydroxycholest 5 ene':ab,ti OR '5 cholesten 3beta ol':ab,ti OR 'beta cholesterol':ab,ti OR 'cholest 5 en 3beta ol':ab,ti OR 'cholest 5 ene 3 ol':ab,ti OR 'cholesterin':ab,ti OR 'cholesterine':ab,ti OR 'cholesterol release':ab,ti OR 'dythol':ab,ti OR 'nsc 8798':ab,ti OR 'cholesterol'/exp OR 'riacylglycerol' OR 'acylglycerol, tri':ab,ti OR 'fatty acid triglyceride':ab,ti OR 'triacyl glyceride':ab,ti OR 'triglyceride':ab,ti OR 'triglycerides':ab,ti OR 'tryglyceride':ab,ti OR 'beta lipoprotein':ab,ti OR 'ldl':ab,ti OR 'lipoprotein, beta':ab,ti OR 'lipoprotein, low density':ab,ti OR 'lipoproteins, ldl' OR 'low

density lipoprotein'/exp OR 'lpha 7 lipoprotein':ab,ti OR 'alpha lipoprotein':ab,ti OR 'hdl':ab,ti OR 'high density lipoprotein phospholipid':ab,ti OR 'lipoprotein, alpha':ab,ti OR 'lipoprotein, high density':ab,ti OR 'lipoproteins, hdl':ab,ti OR 'pre alpha lipoprotein':ab,ti OR 'very high density lipoprotein' OR 'high density lipoprotein'/exp) AND ('randomized controlled trial'/exp OR 'controlled trial':ab,ti OR 'randomized':ab,ti OR 'randomised':ab,ti OR placebo:ab,ti OR 'drug therapy':ab,ti OR randomly:ab,ti OR trial:ab,ti OR groups:ab,ti)

Step 4

'low density lipoprotein'/exp/dd_dt OR 'cholesterol'/exp/dd_dt OR 'noradrenalin'/exp/dd_dt OR 'high density lipoprotein'/exp/dd_dt

Step 5

Step 1 AND (Step 2 OR Step 3 OR Step 4)

Step 6

Step 5 AND [animals]/lim

Step 7

Step 5 AND [animals]/lim AND [humans]/lim

Step 8

Step 5 NOT Step 6

Step 9

Step 7 OR Step 8

LILACS

- No date limit, run on 06 August 2011

(salt OR sodium) AND (noradrenaline OR norepinephrine OR catecholamine OR cholesterol OR triglycerides OR low density lipoprotein OR high density lipoprotein OR LDL OR HDL)

Limit human

WHO International Clinical Trials Registry Platform

- No date limit, run on 23 August 2011

salt AND noradrenaline OR salt AND norepinephrine OR salt AND catecholamine OR salt AND cholesterol OR salt AND triglycerides OR salt AND low density lipoprotein OR salt AND high density lipoprotein OR salt AND LDL OR salt AND HDL OR sodium AND noradrenaline OR sodium AND norepinephrine OR sodium AND catecholamine OR sodium AND cholesterol OR sodium AND triglycerides OR sodium AND low density lipoprotein OR sodium AND high density lipoprotein OR sodium AND LDL OR sodium AND HDL

Cochrane Central Register of Controlled Trials

- No dates limit run on 24 August 2011

(salt OR sodium) AND (noradrenaline OR norepinephrine OR catecholamine OR cholesterol OR triglycerides OR low density lipoprotein OR high density lipoprotein OR LDL OR HDL) AND (randomized controlled trial OR controlled clinical trial OR randomized OR placebo OR drug therapy OR randomly OR trial OR groups)

A1.3 Renal function

- No systematic reviews identified with similar or equivalent inclusion criteria
- Run electronic search for RCTs

EMBASE

No date limit, run on 02 August 2011

Step 1

'sodium chloride'/exp OR 'sodium'/exp OR salt:ti,ab OR sodium:ti,ab

Step 2

('kidney diseases':ab,ti OR 'kidney disorder':ab,ti OR 'kidney pathology':ab,ti OR 'nephropathy':ab,ti OR 'perinephritis':ab,ti OR 'perirenal infection':ab,ti OR 'renal disease':ab,ti OR 'renal disorder':ab,ti OR 'unilateral kidney disease':ab,ti OR 'kidney disease'/exp OR renal:ab,ti OR analgesic AND nephropathy:ab,ti OR 'chronic kidney disease':ab,ti OR 'cystinuria':ab,ti OR 'diabetic nephropathy':ab,ti OR 'fabry disease':ab,ti OR 'gitelman syndrome':ab,ti OR 'glomerulopathy':ab,ti OR 'gordon syndrome':ab,ti OR 'hepatorenal syndrome':ab,ti OR 'hiv associated nephropathy':ab,ti OR 'immunoglobulin a nephropathy':ab,ti OR 'kidney amyloidosis':ab,ti OR 'kidney calcification':ab,ti OR 'kidney colic':ab,ti OR 'kidney cyst':ab,ti OR 'kidney dysfunction':ab,ti OR 'kidney failure':ab,ti OR 'kidney fibrosis':ab,ti OR 'kidney hemorrhage':ab,ti OR 'kidney hypertrophy':ab,ti OR 'kidney infarction':ab,ti OR 'kidney infection':ab,ti OR 'kidney injury':ab,ti OR 'kidney ischemia':ab,ti OR 'kidney malformation':ab,ti OR 'kidney necrosis':ab,ti OR 'kidney pain':ab,ti OR 'kidney papilla necrosis':ab,ti OR 'kidney polycystic disease':ab,ti OR 'kidney rupture':ab,ti OR 'kidney scar':ab,ti OR 'kidney tubule acidosis':ab,ti OR 'kidney tubule damage':ab,ti OR 'kidney tubule

disorder':ab,ti OR 'kidney tumor':ab,ti OR 'liddle syndrome':ab,ti OR 'lowe syndrome':ab,ti OR 'meckel syndrome':ab,ti OR 'medullary sponge kidney':ab,ti OR 'nephritis':ab,ti OR 'nephrogenic diabetes insipidus':ab,ti OR 'nephrolithiasis':ab,ti OR 'nephronophthisis':ab,ti OR 'nephrosis':ab,ti OR 'nephrotoxicity':ab,ti OR 'perirenal abscess':ab,ti OR 'prune belly syndrome':ab,ti OR 'pyelectasis':ab,ti OR 'reflux nephropathy':ab,ti OR 'renal diabetes':ab,ti OR 'renal graft dysfunction':ab,ti OR 'renovascular disease':ab,ti OR 'silent kidney':ab,ti OR 'uric acid nephropathy':ab,ti OR 'kidney disease'/exp) AND ([cochrane review]/lim OR [controlled clinical trial]/lim OR [meta analysis]/lim OR [randomized controlled trial]/lim OR [systematic review]/lim)

Step 3

('kidney diseases':ab,ti OR 'kidney disorder':ab,ti OR 'kidney pathology':ab,ti OR 'nephropathy':ab,ti OR 'perinephritis':ab,ti OR 'perirenal infection':ab,ti OR 'renal disease':ab,ti OR 'renal disorder':ab,ti OR 'unilateral kidney disease':ab,ti OR 'kidney disease'/exp OR renal:ab,ti OR analgesic AND nephropathy:ab,ti OR 'chronic kidney disease':ab,ti OR 'cystinuria':ab,ti OR 'diabetic nephropathy':ab,ti OR 'fabry disease':ab,ti OR 'gitelman syndrome':ab,ti OR 'glomerulopathy':ab,ti OR 'gordon syndrome':ab,ti OR 'hepatorenal syndrome':ab,ti OR 'hiv associated nephropathy':ab,ti OR 'immunoglobulin a nephropathy':ab,ti OR 'kidney amyloidosis':ab,ti OR 'kidney calcification':ab,ti OR 'kidney colic':ab,ti OR 'kidney cyst':ab,ti OR 'kidney dysfunction':ab,ti OR 'kidney failure':ab,ti OR 'kidney fibrosis':ab,ti OR 'kidney hemorrhage':ab,ti OR 'kidney hypertrophy':ab,ti OR 'kidney infarction':ab,ti OR 'kidney infection':ab,ti OR 'kidney injury':ab,ti OR 'kidney ischemia':ab,ti OR 'kidney malformation':ab,ti OR 'kidney necrosis':ab,ti OR 'kidney pain':ab,ti OR 'kidney papilla necrosis':ab,ti OR 'kidney polycystic disease':ab,ti OR 'kidney rupture':ab,ti OR 'kidney scar':ab,ti OR 'kidney tubule acidosis':ab,ti OR 'kidney tubule damage':ab,ti OR 'kidney tubule disorder':ab,ti OR 'kidney tumor':ab,ti OR 'liddle syndrome':ab,ti OR 'lowe syndrome':ab,ti OR 'meckel syndrome':ab,ti OR 'medullary sponge kidney':ab,ti OR 'nephritis':ab,ti OR 'nephrogenic diabetes insipidus':ab,ti OR 'nephrolithiasis':ab,ti OR 'nephronophthisis':ab,ti OR 'nephrosis':ab,ti OR 'nephrotoxicity':ab,ti OR 'perirenal abscess':ab,ti OR 'prune belly syndrome':ab,ti OR 'pyelectasis':ab,ti OR 'reflux nephropathy':ab,ti OR 'renal diabetes':ab,ti OR 'renal graft dysfunction':ab,ti OR 'renovascular disease':ab,ti OR 'silent kidney':ab,ti OR 'uric acid nephropathy':ab,ti OR 'kidney disease'/exp) AND ('randomized controlled trial'/exp OR 'controlled trial':ab,ti OR 'randomized':ab,ti OR 'randomised':ab,ti OR placebo:ab,ti OR 'drug therapy':ab,ti OR randomly:ab,ti OR trial:ab,ti OR groups:ab,ti)

Step 4

'kidney disease'/exp/dm_dt

Step 5

Step 1 AND (Step 2 OR Step 3 OR Step 4)

Step 6

Step 5 AND [animals]/lim

Step 7

Step 5 AND [animals]/lim AND [humans]/lim

Step 8

Step 5 NOT Step 6

Step 9

Step 7 OR Step 8

LILACS

- No date limit, run on 06 August 2011

(salt OR sodium) AND (renal disease OR renal) AND (dietary OR diet OR diets OR restriction OR reduction OR reduce OR restrict)

Limit human

PubMed

- 01 March 2011 to 23 August 2011

(salt[MeSH] OR sodium[MeSH] OR salt[tiab] OR sodium[tiab]) AND (renal disease[MeSH] OR renal[tiab]) AND (dietary[MeSH] OR diet[MeSH] OR diets[MeSH] OR restriction[MeSH] OR reduction[MeSH] OR reduce[MeSH] OR restrict[MeSH]) AND (randomized controlled trial [pt] OR controlled clinical trial [pt] OR randomized [tiab] OR placebo [tiab] OR drug therapy [sh] OR randomly [tiab] OR trial [tiab] OR groups [tiab]) NOT (animals [mh] NOT humans [mh])

WHO International Clinical Trials Registry Platform

- No date limit, run on 23 August 2011

(salt AND renal disease) OR (sodium AND renal disease)

Cochrane Central Register of Controlled Trials

- No date limit, run on 24 August 2011

(salt OR sodium) AND (renal disease OR renal) AND (dietary OR diet OR diets OR restriction OR reduction OR reduce OR restrict)

Annex 2: Example extraction sheet

A2 Data extraction form

1. Participants

Study ID Date

Extractor (initials): Type of report:

Trial title

Authors:_____

Journal (vol:pages:date):_____

Language of report: Country:_____

Duplicate publication: YES/NO_____

Funding source:

Inclusion criteria (including sex, age, diagnostic criteria, co-morbidity)	Exclusion criteria (including sex, age, diagnostic criteria, co-morbidity)

Were intervention and control groups comparable at baseline?

Notes:

(Circle following attributes of study)

1) Sodium reduction achieved – < 1/3 of control/> 1/3 of control/both

– < 2 g/day in intervention/> 2 g/day in intervention

– < 1.2 g/day in intervention/> 1.2 g/day in intervention

– < 1.2 g/day in intervention/between 1.2 and 2 g/day in control or in other intervention arm

2) Age – adult (16 years or greater)/children (1–15 years)

3) Group – Normotensive/hypertensive/both/not specified

4) Duration of follow-up (in months) –

5) Sex – male/female/both (heterogeneous)

6) Type of blood pressure device – automatic/manual

7) Type of blood pressure measurement – supine office/seated office/standing office/combo office/ supine home/seated home/standing home/combo home/24-hour ambulatory/day ambulatory/night ambulatory

2. Methods

Objective as stated in manuscript:

Overview of methods (include detail on method of measurement of sodium intake, study site)

	Method
Method of randomization: a) Truly random? (computer generated, random numbers, coin toss, shuffle, etc.) A or b) Not stated or unclear? B or c) Quasi-randomized or systematic? (patient number, date of birth, alternate) C or d) Allocation not used? D	
Allocation concealment: a) Adequate? A or (central allocation at trials office or pharmacy, sequentially numbered or coded vials, other methods where the trialists allocating treatment could not be aware of the treatment) b) Unclear B or c) Inadequate? C or (allocation was alternate (by patient, day of the week, admission ward, etc.) or based on information, such as date of birth, already known to the trialists) d) Not used? D	
Blinding : Participant blinded – Yes No Unclear Provider blinded – Yes No Unclear Outcome assessor blinded – Yes No Unclear A – Adequate B – Unclear C – Inadequate	
Loss to follow-up: < 5% 5–9.9% 10–19.9% ≥ 20% Unclear A – Adequate B – Unclear C – Inadequate	

Participants	Group 1	Group 2	Group 3	Group 4	Total
Age (mean and SD)					
Sex					
N originally randomized					
Final samples					
% Loss to follow-up					

3. Interventions

Type of intervention

Group 1 –

Group 2 –

Group 3 –

Group 4 –

Comments:

Intervention/Control	Group 1	Group 2	Group 3	Group 4
Name				
Total duration				
Assessment of compliance				
Sodium intake achieved at follow-up				

Starting time of intervention:

Ending time of intervention:

4. Outcomes

Outcomes measured in the study

Adults all:

Adults normotensive:

Adults hypertensive:

Comparisons made in study:

Subgroup analyses in study:

Outcome – categorical	**Group 1**		**Group 2**		**Group 3**		**Group 4**	
	n	**(N)**	**n**	**(N)**	**n**	**(N)**	**n**	**(N)**
ADULTS – all								
Elevated systolic blood pressure								
Elevated diastolic blood pressure								
NPS								
ADULTS – normotensive								
Elevated systolic blood pressure								
Elevated diastolic blood pressure								
NPS								
ADULTS -hypertensive								
Elevated systolic blood pressure								
Elevated diastolic blood pressure								
NPS								

NPS, not previously specified

Outcome – continuous	Group 1		Group 2		Group 3		Group 4	
	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)	n	Mean (SD)
ADULTS – all								
Systolic blood pressure								
Diastolic blood pressure								
Adrenaline								
Noradrenaline								
Cholesterol								
Triglyceride								
HDL								
LDL								
NPS								
ADULTS – normotensive								
Systolic blood pressure								
Diastolic blood pressure								
Adrenaline								
Noradrenaline								
Cholesterol								
Triglyceride								
HDL								
LDL								
NPS								
ADULTS – hypertensive								
Systolic blood pressure								
Diastolic blood pressure								
Adrenaline								
Noradrenaline								
Cholesterol								
Triglyceride								
HDL								
LDL								
NPS								

NPS, not previously specified

Contact details

Name

Address (including e-mail)

Investigator contacted for more information YES/NO

Data Requested Obtained Available

General conclusions and information about process variables – costs, etc.

Exclusions after data extraction (check and amend eligibility form)

Reasons for exclusion: (Study design? Participants? Intervention? Other?)
Data entered into RevMan by: On (date) Data checked by: On (date)

Annex 3: Funnel plots

Figure A3.1 Resting systolic blood pressure

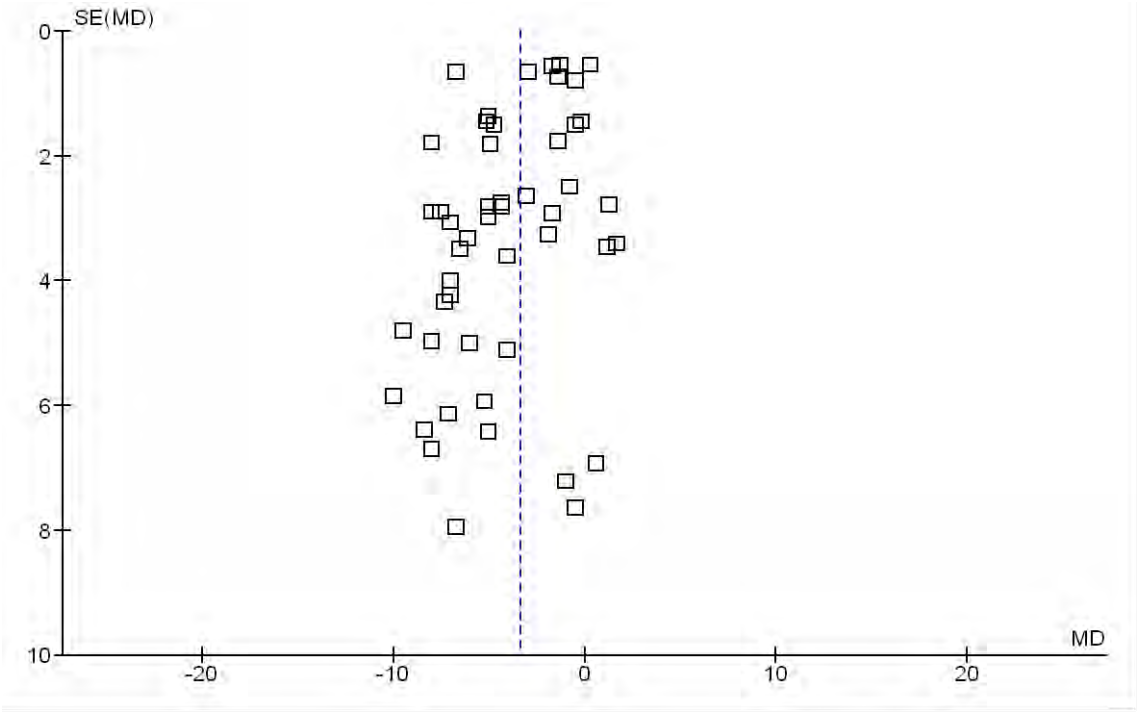


Figure A3.2 Resting diastolic blood pressure

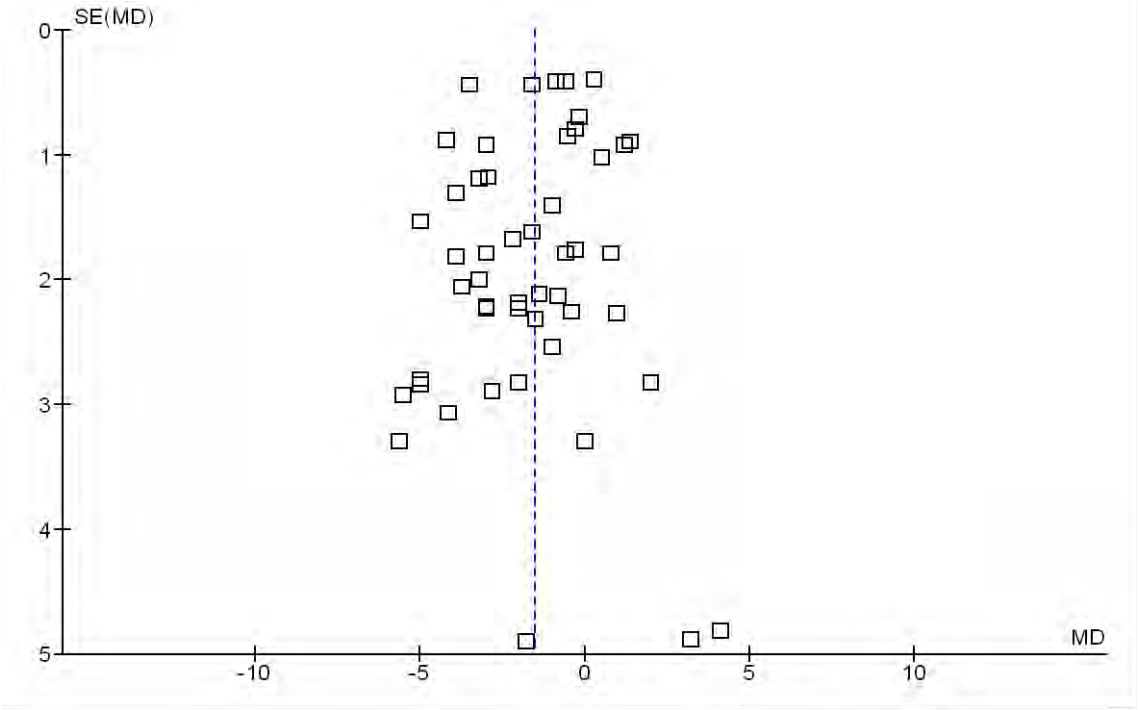


Figure A3.3 Total cholesterol level

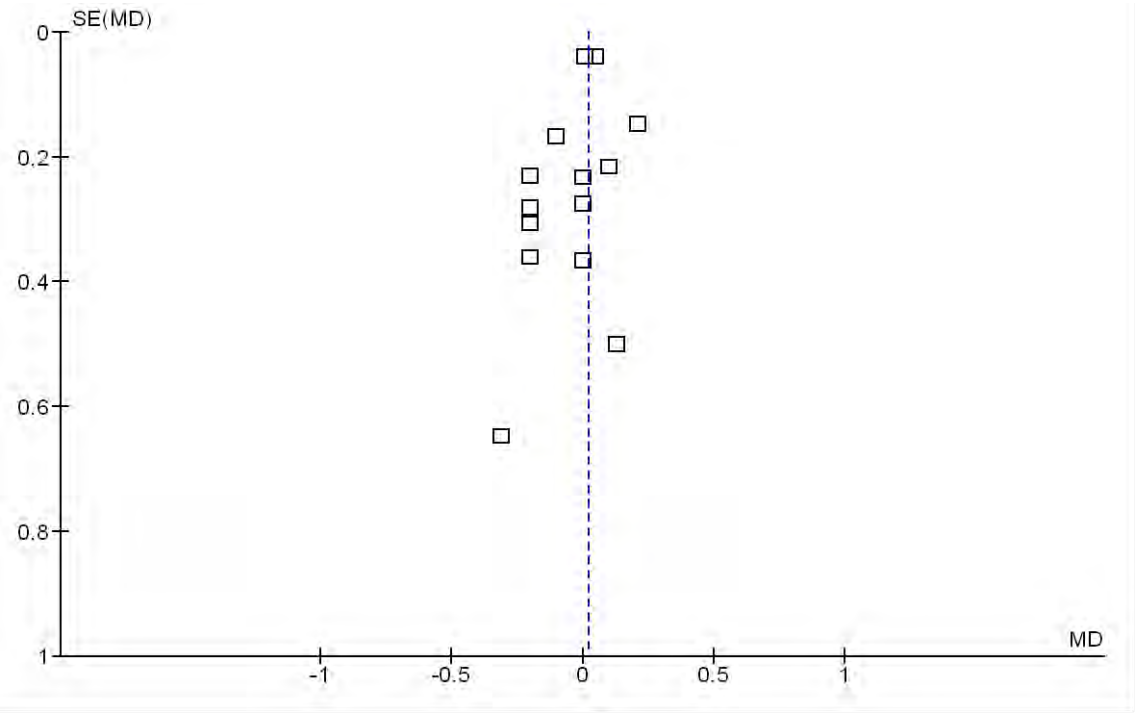


Figure A3.4 Plasma noradrenaline

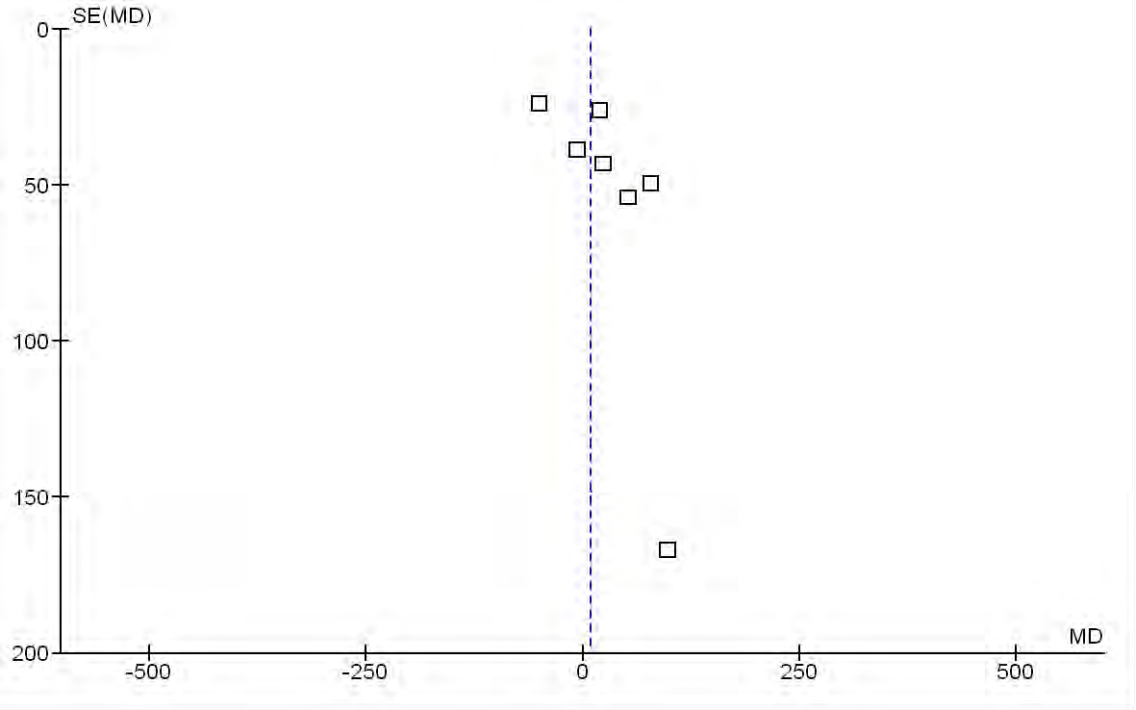
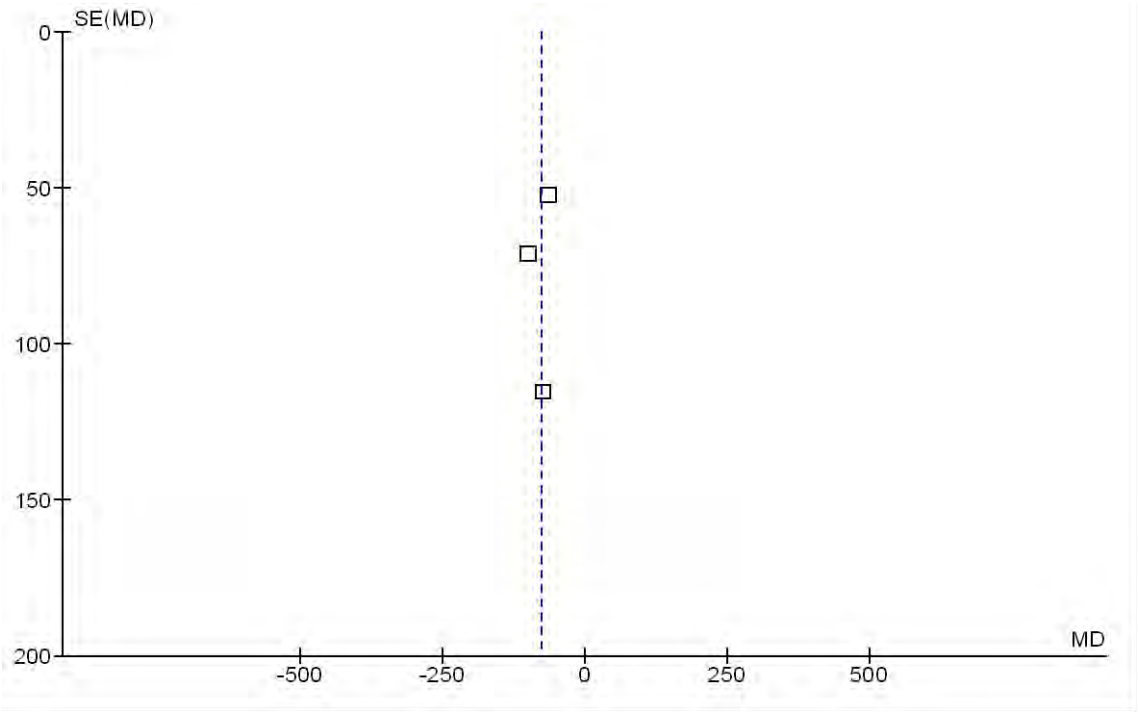
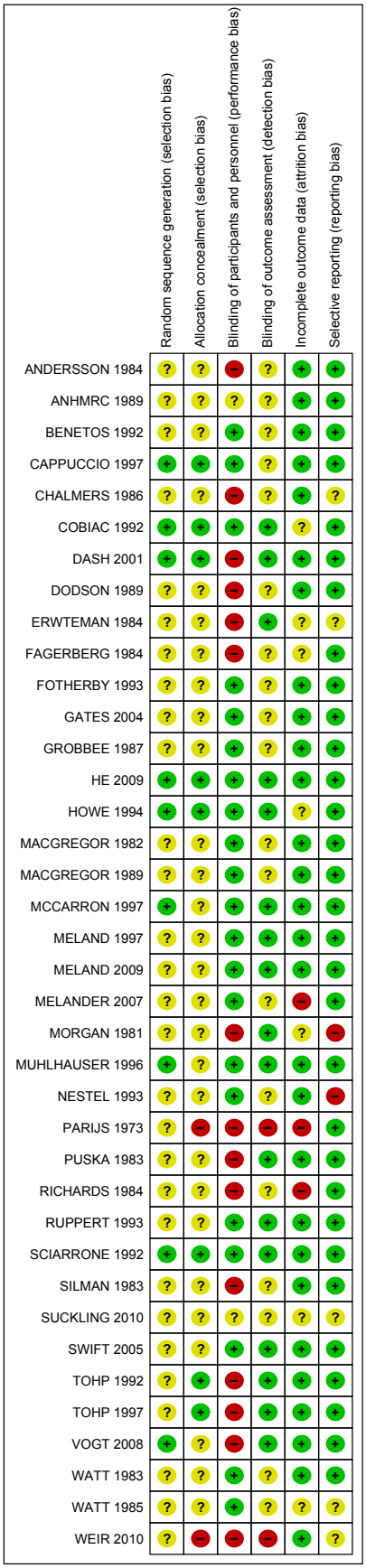


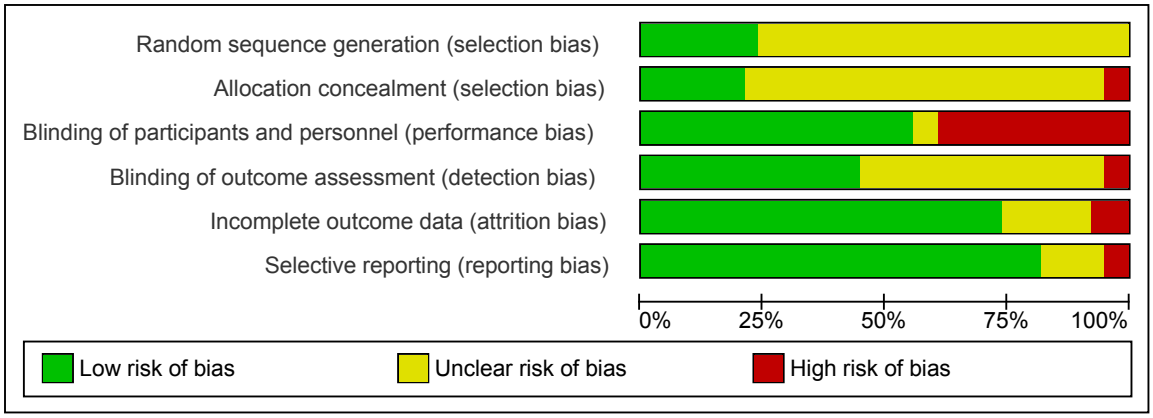
Figure A3.5 Urinary protein excretion



Annex 4: Risk of bias summary



Annex 5: Risk of bias graph



Annex 6: GRADE evidence profiles

Research question: What is the effect of decreased sodium intake relative to higher intake in adults (≥ 16 years)

Quality assessment							Participants		Effect		
No of studies/ comparisons	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	considerations	Decreased Sodium	Control	Absolute (95% CI)	Quality	Importance
Resting systolic blood pressure (follow-up 1 - 36 months; units mmHg; better indicated by lower values)											
36 / 49	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	3304	3432	MD 3.39 lower (4.31 to 2.46 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Resting diastolic blood pressure (follow-up 1 - 36 months; units mmHg; better indicated by lower values)											
36 / 49	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	3304	3432	MD 1.54 lower (2.11 to 0.98 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Ambulatory systolic blood pressure (follow-up 1 - 1.5 months; units mmHg; better indicated by lower values)											
6 / 6	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	425	425	MD 5.51 lower (7.87 to 3.16 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Ambulatory diastolic blood pressure (follow-up 1 - 1.5 months; units mmHg; better indicated by lower values)											
6 / 6	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	425	425	MD 2.94 lower (4.36 to 1.51 lower)	⊕⊕⊕⊕ HIGH	CRITICAL
Serum creatinine (follow-up 1 - 1.5 months; units µmol/L; better indicated by lower values)											
5 / 7	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	364	364	MD 1.68 higher (0.65 lower to 4 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Urinary protein excretion (follow-up 1.5 months; units ng/mL filtrate; Better indicated by lower values)											
1 / 3	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	99	99	MD 76.61 lower (154.2 lower to 0.97 higher)	⊕⊕⊕⊕ HIGH[2]	IMPORTANT
Protein:creatinine ratio (follow-up 1.5 months; units mg protein per mmol creatinine; Better indicated by lower values)											
1 / 3	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	99	99	MD 0.4 lower (0.73 to 0.07 lower)	⊕⊕⊕⊕ HIGH[2]	IMPORTANT
Creatinine clearance (follow-up 1.25 - 1.5 months; units ml/min; Better indicated by higher values)											
2 / 4	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	116	116	MD 7.67 lower (16.17 lower to 0.83 higher)	⊕⊕⊕⊕ HIGH[3]	IMPORTANT
Glomerular filtration rate (follow-up 1 months; units ml/min per 1.73m2; Better indicated by higher values)											
1 / 1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	39	39	MD 5 lower (15.25 lower to 5.25 higher)	⊕⊕⊕⊕ HIGH[4]	IMPORTANT
Total cholesterol (follow-up 1 - 2 months; units mmol/L ; better indicated by lower values)											
11 /15	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	1170	1169	MD 0.02 higher (0.03 lower to 0.07 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
HDL cholesterol (follow-up 1 - 2 months; units mmol/L; better indicated by higher values)											
9 / 11	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious imprecision[5]	none	1024	1023	MD 0.01 lower (0.03 lower to 0 higher)	⊕⊕⊕ MODERATE	IMPORTANT
LDL cholesterol (follow-up 1 - 2 months; units mmol/L; better indicated by lower values)											
6/ 8	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	955	954	MD 0.03 higher (0.02 lower to 0.08 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Triglycerides (follow-up 1 - 2 months; units mmol/L ; better indicated by lower values)											
8 / 10	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	1025	1024	MD 0.04 higher (0.01 lower to 0.09 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Adrenaline (plasma) (follow-up 1 - 1.5 months; units pg/mL; better indicated by lower values)											
4 / 4	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	84	84	MD 6.9 higher (2.17 lower to 15.96 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Noradrenaline (plasma) (follow-up 1 - 2.5 months; units pg/mL; better indicated by lower values)											
7 / 7	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	131	134	MD 8.23 higher (27.84 lower to 44.29 higher)	⊕⊕⊕⊕ HIGH	IMPORTANT
Adrenaline (urinary) (follow-up 2.5 months; units pg/mL; better indicated by lower values)											
1 / 1	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	8	10	MD 13.1 lower (29.24 lower to 3.04 higher)	⊕⊕⊕⊕ HIGH[4]	IMPORTANT
Noradrenaline (urinary) (follow-up 2.5 months; units pg/mL; better indicated by lower values)											
2 / 2	randomised trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[1]	none	25	28	MD 17.13 higher (34.06 lower to 68.33 higher)	⊕⊕⊕⊕ HIGH[6]	IMPORTANT

[1] 95%CI crosses zero and does not cross a threshold of relevant change and is therefore considered a precise estimate of no effect and not downgraded for imprecision.
[2] Only one study with three comparisons included in generation of estimate
[3] Only two studies with four comparisons included in generation of estimate
[4] Only one study included in generation of estimate
[5] Upper confidence limit is 0.00
[6] Only two studies with two comparisons included in generation of estimate

Research question: What is the effect of decreasing sodium intake by > 1/3 of control versus decreasing sodium intake by ≤ 1/3 of control in adults (≥ 16 years)?

Quality assessment							Participants		Effect		
No of studies/ comparisons	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Sodium decreased by > 1/3 control	Sodium decreased by <= 1/3 control	Absolute (95% CI)	Quality	Importance
Resting systolic blood pressure (follow-up 1 month; units mmHg; better indicated by lower values)											
1 / 2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	390	390	MD 3.14 lower (5.98 to 0.3 lower)	⊕⊕⊕⊕ HIGH[1]	CRITICAL
Resting diastolic blood pressure (follow-up 1 month; units mmHg; better indicated by lower values)											
1 / 2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	390	390	MD 1.70 lower (3.07 to 0.33 lower)	⊕⊕⊕⊕ HIGH[1]	CRITICAL
Ambulatory systolic blood pressure											
0 / 0	No direct evidence available										
Ambulatory diastolic blood pressure											
0 / 0	No direct evidence available										
Serum creatinine											
0 / 0	No direct evidence available										
Urinary protein excretion											
0 / 0	No direct evidence available										
Protein:creatinine ratio											
0 / 0	No direct evidence available										
Creatinine clearance											
0 / 0	No direct evidence available										
Glomerular filtration rate											
0 / 0	No direct evidence available										
Total cholesterol											
2 / 3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	877	877	MD 0.01 lower (0.08 lower to 0.05 higher)	⊕⊕⊕⊕ HIGH[3]	IMPORTANT
HDL cholesterol											
0 / 0	No direct evidence available										
LDL cholesterol											
0 / 0	No direct evidence available										
Triglycerides											
0 / 0	No direct evidence available										
Adrenaline (plasma)											
0 / 0	No direct evidence available										
Noradrenaline (plasma)											
0 / 0	No direct evidence available										
Adrenaline (urinary)											
0 / 0	No direct evidence available										
Noradrenaline (urinary)											
0 / 0	No direct evidence available										

[1] Only one study with two comparisons included in generation of estimate

[2] 95%CI crosses zero and does not cross a threshold of relevant change and is therefore considered a precise estimate of no effect and not downgraded for imprecision.

[3] Only two studies with three comparisons included in generation of estimate

Research question: What is the effect of decreased sodium to an absolute intake < 2 g/day versus decreased sodium to an absolute intake ≥ 2 g/day in adults (≥ 16 years)?

Quality assessment							Participants		Effect		
No of studies/ comparisons	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	considerations	intake < 2g/day	intake>= 2g/day	Absolute (95% CI)	Quality	Importance
Resting systolic blood pressure (follow-up 1 - 36 months; units mmHg; better indicated by lower values)											
2 / 3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	410	410	MD 3.47 lower (6.18 to 0.76 lower)	⊕⊕⊕⊕ HIGH[1]	CRITICAL
Resting diastolic blood pressure (follow-up 1 - 36 months; units mmHg; better indicated by lower values)											
2 / 3	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision	none	410	410	MD 1.81 lower (3.08 to 0.54 lower)	⊕⊕⊕⊕ HIGH[1]	CRITICAL
Ambulatory systolic blood pressure											
0 / 0	No direct evidence available										
Ambulatory diastolic blood pressure											
0 / 0	No direct evidence available										
Serum creatinine											
0 / 0	No direct evidence available										
Urinary protein excretion											
0 / 0	No direct evidence available										
Protein:creatinine ratio											
0 / 0	No direct evidence available										
Creatinine clearance											
0 / 0	No direct evidence available										
Glomerular filtration rate											
0 / 0	No direct evidence available										
Total cholesterol (follow-up 1 month; units mmol/L; better indicated by lower values)											
1 / 2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	390	390	MD 0.05 higher (0.06 lower to 0.17 higher)	⊕⊕⊕⊕ HIGH[3]	IMPORTANT
HDL cholesterol (follow-up 1 month; units mmol/L; better indicated by higher values)											
1 / 2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	390	390	MD 0.00 lower (0.02 lower to 0.02 higher)	⊕⊕⊕⊕ HIGH[3]	IMPORTANT
LDL cholesterol (follow-up 1 month; units mmol/L; better indicated by lower values)											
1 / 2	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	379	379	MD 0.04 higher (0.06 lower to 0.15 higher)	⊕⊕⊕⊕ HIGH[3]	IMPORTANT
Triglycerides											
0 / 0	No direct evidence available										
Adrenaline											
0 / 0	No direct evidence available										
Noradrenaline (plasma) (follow-up 1 month; units pg/mL; better indicated by lower values)											
1 / 1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[2]	none	12	12	MD 107 lower (437 lower to 223 higher)	⊕⊕⊕⊕ HIGH[4]	IMPORTANT
Adrenaline (urinary)											
0 / 0	No direct evidence available										
Noradrenaline (urinary)											
0 / 0	No direct evidence available										

[1] Only two studies with three comparisons included in generation of estimate

[2] 95%CI crosses zero and does not cross a threshold of relevant change and is therefore considered a precise estimate of no effect and not downgraded for imprecision.

[3] Only one study with two comparisons included in generation of estimate

[4] Only one study with one comparison included in generation of estimate

Research question: What is the effect of decreased sodium to absolute intake < 1.2 g/day versus decreased sodium to absolute intake ≥ 1.2 g/day in adults (≥ 16 years)?

Quality assessment							Participants		Effect		
No of studies/ comparisons	Design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Absolute intake < 1.2 g/day	Absolute intake >= 1.2g/day	Absolute (95% CI)	Quality	Importance
Resting systolic blood pressure (follow-up 1 month; units mmHg; better indicated by lower values)											
1 / 1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious imprecision[1]	none	20	20	MD 8.00 lower (17.73 lower to 1.73 higher)	⊕⊕⊕ MODERATE[2]	CRITICAL
Resting diastolic blood pressure (follow-up 1 month; units mmHg; better indicated by lower values)											
1 / 1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	serious imprecision[1]	none	20	20	MD 4.00 lower (9.58 lower to 1.58 higher)	⊕⊕⊕ MODERATE[2]	CRITICAL
Ambulatory systolic blood pressure											
0 / 0	No direct evidence available										
Ambulatory diastolic blood pressure											
0 / 0	No direct evidence available										
Serum creatinine											
0 / 0	No direct evidence available										
Urinary protein excretion											
0 / 0	No direct evidence available										
Protein:creatinine ratio											
0 / 0	No direct evidence available										
Creatinine clearance											
0 / 0	No direct evidence available										
Glomerular filtration rate											
0 / 0	No direct evidence available										
Total cholesterol											
0 / 0	No direct evidence available										
HDL cholesterol											
0 / 0	No direct evidence available										
LDL cholesterol											
0 / 0	No direct evidence available										
Triglycerides											
0 / 0	No direct evidence available										
Adrenaline											
0 / 0	No direct evidence available										
Noradrenaline (plasma) (follow-up 1 month; units pg/mL; better indicated by lower values)											
1 / 1	randomized trials	no serious risk of bias	no serious inconsistency	no serious indirectness	no serious imprecision[3]	none	12	12	MD 107 lower (437 lower to 223 higher)	⊕⊕⊕⊕ HIGH[2]	IMPORTANT
Adrenaline (urinary)											
0 / 0	No direct evidence available										
Noradrenaline (urinary)											
0 / 0	No direct evidence available										

[1] 95% CI crosses zero

[2] Only one study with one comparison included in generation of estimate

[3] 95%CI crosses zero and does not cross a threshold of relevant change and is therefore considered a precise estimate of no effect and not downgraded for imprecision.

Annex 7: Lists of tables and figures

Tables

Figures

Full list of references

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