Online Supporting Materials for manuscript entitled
Effect of lower sodium intake on health: systematic review and meta-analyses

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OSM 1: Electronic search strategy

A. Search Strategy for studies reporting blood pressure, blood lipids, catecholamine levels, and other potential adverse effects

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 and requested the data in order to 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 review.

Electronic databases

We searched the following electronic databases:

- The Cochrane Central Register of Controlled Trials;
- MEDLINE;
- EMBASE;
- WHO International Clinical Trials Registry Platform;
- The Latin American and Caribbean Health Science Literature Database.

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 For assistance in identifying ongoing or unpublished studies, we contacted the WHO Department of Nutrition for Health and Development and other international partners, such as academic and research institutions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.

Blood Pressure (Adults)
Identified Cochrane systematic review by He and MacGregor 2008.
1) Use He and McGregor reference list for potential studies
2) Electronic search from 2005-2011

a. PubMed
01 January 2005 to 06 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

[1] www.who.int/nutrition

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])

b.EMBASE
01 January 2005 to 02 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
c. *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)
d. Cochrane central register of controlled trials
Limit by Dates 01 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)
e. WHO International Clinical Trials Registry Platform (ICTRP)
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)

Blood Pressure (Children)

Identified systematic review of the literature published by the Dietary Guidelines for Americans Committee (DGAC) 2010

1) Use DGAC reference list for potential studies

2) Electronic search from 2009-2011

a. *PubMed*

01 January 2009 - 06 July 2011

("Hypertension"[Majr] OR "blood pressure"[Majr]) AND ("Sodium, Dietary"[Mesh] OR ("sodium, dietary"[MeSH Terms] OR "sodium"[MeSH Terms]) OR "sodium chloride"[mesh]) AND "humans"[Filter]

all child 0-18 yrs, January 1, 2009 to July 6, 2011

b. *EMBASE*

01 January 2009 - 02 August 2011

2) Blood Pressure (Children)

Step 1

'hypertension'/exp/mj OR 'blood pressure'/exp/mj

Step 2

'child'/exp OR 'children'/exp OR 'youth'/exp OR youth* OR newborn* OR 'newborn'/exp OR 'new born' OR 'childhood disease'/exp OR 'baby'/exp OR babies OR 'infant'/exp OR infant* OR childhood* OR toddler* OR kid OR kids OR 'young patient' OR boy* OR girl* OR 'young age' OR pediatr* OR paediatr* OR 'child death'/exp OR 'child health'/exp OR 'child care'/exp OR 'childhood mortality'/exp OR 'child hospitalization'/exp OR 'pediatric hospital'/exp OR child* AND [2009-2012]/py

Step 3

(Step 1 AND Step 2) AND [animals]/lim

Step 4

(Step 1 AND Step 2) AND [animals]/lim AND [humans]/lim

Step 5

(Step 1 AND Step 2) NOT Step 3

Step 4 OR Step 5

c. *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)

Limit Adolescent, Child, Preschool

d. WHO International Clinical Trials Registry Platform (ICTRP)

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)

e. *Cochrane Central Register of Controlled Trials*

01 January 2005 - 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)

Adverse Effects (Adults and Children)

1) No systematic reviews identified with similar or equivalent inclusion criteria.

2) Run electronic search for RCTs

a. 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])

b. *EMBASE*

No date limit run 02 August 2011

3) Adverse Effects (Adults and Children)

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

c. *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
d. WHO International Clinical Trials Registry Platform (ICTRP)
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
e. 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)

<u>Renal Function (Adults)</u>
1) No systematic reviews identified with similar or equivalent inclusion criteria.
2) Run electronic search for RCTs
a. *EMBASE*
No date limit run on 02 August 2011
4) Renal Function (Adults)
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

b. *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
c. 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])
d. WHO International Clinical Trials Registry Platform (ICTRP)
No date limit run on 23 August 2011
(salt AND renal disease) OR (sodium AND renal disease)
e. Cochrane Central Register of Controlled Trials
No dates 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)

B. Search for studies reporting all-cause mortality, cardiovascular disease, stroke, or coronary heart disease.

B.1. Search for systematic reviews and meta-analyses

We searched the PubMed database and The Cochrane Library in August 2011 for systematic reviews on sodium intake and CVD, stroke and CHD. We considered systematic reviews of RCTs and cohort studies. We also contacted authors of the systematic reviews to consult about any other published systematic reviews.

Electronic searches

Because recent, high-quality systematic reviews were found, we did not conduct a separate electronic search for studies on the effect of increased sodium on CVD morbidity and mortality.

Other resources

We searched for further trials on the WHO web site[2] 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. We also contacted the authors of the systematic reviews on this topic to identify any potentially relevant studies in the recent literature.

[2] www.who.int/nutrition

OSM 2: Study Characteristics

A. Adult RCTs included in the systematic review reporting blood pressure, renal function, blood lipids, or catecholamine levels

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 hypertensive adults not taking medical therapy to control blood pressure and all 20-40% overweight.
Interventions	Group1 -- reduced sodium, fat and CHO diet plus sodium tablets (control) Group2 -- reduced sodium, fat and CHO diet (reduced sodium)
Outcomes	Resting blood pressure LV hypertrophy Hemodynamic indicators Urinary noradrenaline Plasma noradrenaline Cardiac output Mean arterial pressure (MAP)
Notes	1) Sodium reduction achieved - **>1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **2.5 months** (**9-11 weeks)** 5) Sex - **male** 6) Blood pressure method - **manual** 7) Blood pressure method -**supine office**

Risk of bias table

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 if 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

ANHMRC 1989

Methods	**Parallel design study** followed by a **cross-over design** study of reduced sodium diet and randomized to receive sodium tablets or placebo tablets. Conducted in Australia
Participants	111 men and women with DBP 90- 100 not taking medical therapy to control blood pressure.
Interventions	Group1 -- reduced sodium in diet through counselling plus 80mmol sodium per day in sodium chloride tablets and thus no change in sodium intake (control) Group2 -- reduced sodium in diet through counselling plus placebo tablets and thus reduced sodium intake (achieved 90mmol/day average)
Outcomes	Resting blood pressure Plasma cholesterol Urinary creatinine excretion
Notes	1) Sodium reduction achieved - **>1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **2 months** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **seated office**

Risk of bias table

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 subjects was unclear and unlikely
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear if outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	Parallel study had low loss to follow-up, however, the cross-over study had high loss-to-follow up
Selective reporting (reporting bias)	Low risk	Results stated that plasma cholesterol and GGT did not change from baseline to follow-up between groups but change not quantified.

BENETOS 1992

Methods	**Cross-over design** study of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets. Conducted in France
Participants	20 mild to moderate hypertensive adults not taking medical therapy to control blood pressure
Interventions	Group1 -- reduced sodium diet plus 60 mmol sodium in tablets / day (control) Group2 -- 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** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **supine office**

Risk of bias table

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 if outcome assessors blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up <10% (only 2 participants)
Selective reporting (reporting bias)	Low risk	All outcomes reported.

CAPPUCCIO 1997

Methods	**Cross-over design** study of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets. Conducted in the UK.
Participants	48 adults over the age of 60 who were either normotensive or hypertensives not taking medical therapy to control blood pressure
Interventions	Group1 -- reduced sodium diet plus 120mmol / day in sodium tablets (control) Group2 -- 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 - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **both** 4) Duration of follow-up (in months) - **1 month (4 weeks)** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **supine office** and **standing office**

Risk of bias table

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 if outcome assessors were blinded.
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up reported at 2% (only 1 participant)
Selective reporting (reporting bias)	Low risk	All outcomes reported

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 hypertensive adults not receiving medical therapy to control blood pressure.
Interventions	Group1 -- Control diet through counselling and education Group2 -- High potassium diet through counselling and education Group3 -- Reduced sodium diet through counselling and education Group4 -- High potassium/reduced sodium diet through counselling and education
Outcomes	Resting blood pressure Urinary electrolytes Urinary creatinine excretion Serum K Serum creatinine Serum cholesterol* Serum gamma-glutamyl transferase* *** Stated that pre-diet cholesterol and GGT were similar between groups and did not change over course of study**
Notes	1) Sodium reduction achieved - **>1/3 of control** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **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.

Risk of bias table

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 if 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 GGT were similar between groups and did not change over course of study but values not quantified. Results of serum creatinine not reported.

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 60-80 year olds not being medically treated for hypertension
Interventions	Group1 -- reduced sodium diet plus fish oil and 80 mmol sodium / day (fish control) Group2 -- reduced sodium diet plus fish oil and placebo (fish reduced sodium) Group3 -- reduced sodium diet plus sunflower oil and 80 mmol Na / day (sun control) Group4 -- reduced sodium diet plus sunflower oil and placebo (sun reduced sodium)
Outcomes	Resting blood pressure
Notes	1) Sodium reduction achieved - **>1/3 of control** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **both** 4) Duration of follow-up (in months) - **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **seated office**

Risk of bias table

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

DASH 2001

Methods	**Cross-over design**, feeding study and participants randomly assigned to eat either a control diet typical of intake in the United States or the DASH diet. Within the assigned diet, participants ate foods with control (150 mmol Na/day target), low (100 mmol Na/day target), and very low (50 mmol Na/day target) levels of sodium. Conducted in the United States of America.
Participants	412 hypertensive or non-hypertensive adults not taking medical therapy to control blood pressure.
Interventions	Group 1 -- DASH diet with sodium target 150 mmol/day (DASH control) Group 2 -- DASH diet with sodium target 100 mmol/day (DASH low Na) Group 3 -- DASH diet with sodium target 50 mmol/day (DASH very low Na) Group 4 -- Normal diet with sodium target 150 mmol/day (control) Group 5 -- Normal diet with sodium target 100 mmol/day (low Na) Group 6 -- Normal diet with sodium target 50 mmol/day (very low Na)
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** - **>2g/d in intervention** - **>1.2 g/d in intervention** Very reduced sodium - **>1/3 of control** - **<2g / d in intervention** -**<1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **both** 4) Duration of follow-up (in months) - **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **seated office**

Risk of bias table

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

DODSON 1989

Methods	**Parallel design study** where participants were randomized to a reduced sodium diet or a "usual-sodium" diet followed by a **cross-over design** study of reduced sodium diet where participants were randomized to receive sodium tablets or placebo tablets. Conducted in the United Kingdom.
Participants	34 hypertensive, diabetic adults some of whom were taking medication and some of whom were not.
Interventions	**Parallel design phase** Group1 - normal diet (control) Group2 - reduced sodium diet (reduced sodium) **Cross-over design phase** Group 3 - reduced sodium diet plus sodium tablets (80mmol/day) (control cross over) Group 4 - reduced sodium diet plus placebo tablets (reduced sodium cross over)
Outcomes	Resting blood pressure Serum urea Patients in whom normal BP was achieved
Notes	1) Sodium reduction achieved Parallel Design phase - **<1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** Cross-over Design phase - **>1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) **Age- Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **3 months (parallel) / 1 month(cross-over)** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **supine office** and **standing office**

Risk of bias table

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 if outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	<5% loss to follow-up in the parallel phase but > 20% in the cross-over phase
Selective reporting (reporting bias)	Low risk	All outcomes reported

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 cross-over to other drug treatments.
Participants	107 adult hypertensive (20-70 years) not suffering diabetes.
Interventions	**No medication** Group1 -- normal sodium diet plus no drug therapy (control) Group2 -- reduced sodium diet plus no drug therapy (reduced sodium) **Beta-blocker** Group3 -- normal sodium diet plus beta-blocker (control-B) Group4 -- reduced sodium diet plus beta-blocker (reduced sodium-B) **Diuretic** Group5 -- normal sodium diet plus diuretic (control-D) Group6 -- reduced sodium diet plus diuretic (reduced sodium-D) **Beta-blocker and diuretic** Group5 -- normal sodium diet plus combination beta-blocker and diuretic (control-C) Group6 -- reduced sodium diet plus combination beta-blocker and diuretic (reduced sodium-C)
Outcomes	Resting blood pressure Plasma glucose Plasma creatinine Plasma cholesterol Plasma HDL Plasma urate Adverse effects
Notes	1) Sodium reduction achieved - **>1/3 of control** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **6 months (24 weeks)** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **supine office** and **standing office**

Risk of bias table

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, HDL and glucose without quantifying results.

FAGERBERG 1984

Methods	**Parallel study design** of nutrition education. Conducted in the Sweden.
Participants	34 obese hypertensive adult men without secondary forms of hypertension not taking medical therapy to control blood pressure.
Interventions	Group1 -- dietary advice for reduced calorie, fat and CHO diet (control) Group2 -- dietary advice for reduced calorie, fat and CHO 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** -**>2g/d in intervention** -**> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **2.5 months (9-12 weeks)** 5) Sex - **male** 6) Blood pressure method - **manual** 7) Blood pressure method -**supine office**

Risk of bias table

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 if outcome assessor blinded
Incomplete outcome data (attrition bias)	Unclear risk	12% loss to follow-up but not clear from which group.
Selective reporting (reporting bias)	Low risk	All outcomes reported

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.
Participants	18 hypertensive adults not taking medical therapy for the hypertension
Interventions	Group1 - reduced sodium diet plus 80mmol/d of sodium tablets (control) Group2 - reduced sodium diet plus equivalent placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Ambulatory blood pressure Ambulatory blood pressure Urinary creatinine excretion Urinary electrolytes Urinary Na: creatinine ratio Urinary K:creatinine ratio Urine volume Plasma aldosterone Plasma Renin Activity Heart rate Serum cholesterol Serum HDL Serum LDL Serum triglyceride Urinary albumin excretion Serum calcium Serum creatinine Serum urate Serum Parathyroid hormone Adverse effects
Notes	1) Sodium reduction achieved - **>1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater**) 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **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 hr** / **ambulatory day** / **ambulatory night**

Risk of bias table

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 if outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	1 participant (5.6%) lost to follow-up
Selective reporting (reporting bias)	Low risk	All outcomes reported.

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 hypertensive adults over 50 years of age not taking medical therapy to control blood pressure.
Interventions	Group1 -- Reduced dietary intake of Na plus Na tablets prescribed to reach baseline Na intake values (control) Group2 -- Reduced dietary intake of Na 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 (assumed plasma) LDL (assumed plasma) VLDL (assumed plasma) Serum glucose Serum insulin
Notes	1) Sodium reduction achieved - **>1/3 of control** - **< 2g / d in intervention** - **<1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **supine office**

Risk of bias table

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 if 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

GELEIJNSE 1990

Methods	**Cohort** study in children comparing tertiles of sodium intake over seven year follow-up and change in blood pressure during that time. Conducted in the Netherlands.
Participants	233 children 5-17 years of age in final analysis
Interventions	No intervention
Outcomes	Change in resting blood pressure over time
Notes	1) **Not applicable** 2) Age- **children (1-14 yrs)** 3) Group - **not specified** 4) Duration of follow-up (in months) - **84 months (7 years)** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - / **manual** 7) Blood pressure method - **seated office**

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	High risk	Not random
Selection of participants (selection bias)	Low risk	Participants were randomly drawn from population survey
Allocation concealment (selection bias)	Unclear risk	Not applicable
Blinding of participants and personnel (performance bias)	Unclear risk	Not applicable
Blinding of outcome assessment (detection bias)	Low risk	Outcome assessors were blinded to tertile of sodium intake of participants
Incomplete outcome data (attrition bias)	High risk	The loss to follow-up was very high (>50%) and selection of final sample not explained clearly.
Selective reporting (reporting bias)	Low risk	All outcomes reported.
Defining Exposure (confounding)	Low risk	Sodium intake was estimated from overnight urinary sodium excretion taken on multiple occasions
Other confounding	Unclear risk	No other potential confounders were controlled for

GROBBEE 1987

Methods	**Cross-over 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 hypertensive young adults (18-28 years) who may or may not have been medically treated for hypertension.
Interventions	Group1 -- reduced sodium diet plus 90 mmol sodium / day tablets (control) Group2 -- reduced sodium diet plus placebo tablets (reduced sodium) Group3 -- 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** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **1.5 months** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **supine office**

Risk of bias table

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 if 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

HE 2009

Methods	**Cross-over study design** of reduced sodium diet and participants randomized to sodium tablets or placebo tablets. Conducted in the United Kingdom.
Participants	185 hypertensive adults with no history of medical treatment for elevated blood pressure.
Interventions	Group1 -- reduced sodium diet plus 90mmol sodium in tablets / day (control) Group2 -- reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Ambulatory blood pressure Pulse rate Pulse wave velocity Plasma renin activity Plase creatinine Plasma Aldosterone Urinary creatinine excretion Urinary calcium excretion Urinary albumin excretion
Notes	1) Sodium reduction achieved - **>1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **1.5 months** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic (resting and ambulatory)** 7) Blood pressure method - **seated office** and **ambulatory 24 hr** / **ambulatory day** / **ambulatory night**

Risk of bias table

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

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 hypertensive adults who were being medically treated with ACE inhibitors
Interventions	Group1 -- reduced sodium diet plus olive oil and 80 mmol Na in tablets / day (olive control) Group2 -- reduced sodium diet plus olive oil and placebo tablets / day (olive reduced sodium) Group3 -- reduced sodium diet plus fish oil and 80 mmol sodium in tablets / day (fish control) Group4 -- 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** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **1.5 months** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **seated office**

Risk of bias table

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.

MACGREGOR 1982

Methods	**Cross-over 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.
Participants	19 hypertensive adults not taking medical treatment for hypertension.
Interventions	Group1 -- reduced sodium diet plus sodium tablets to restore baseline sodium intake (control) Group2 -- 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** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **supine office** and **standing office**

Risk of bias table

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 if 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

MACGREGOR 1989

Methods	**Cross-over 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.
Participants	20 hypertensives adults not taking medical therapy to control blood pressure
Interventions	Group1 -- reduced sodium diet plus 160 mmol sodium in tablets / day (control) Group2 -- reduced sodium diet plus 70mmol sodium + 9 placebo tablets / day (reduced sodium) Group3 -- 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** - **>2g/d in intervention** - **> 1.2 g/d in intervention** very reduced sodium - **>1/3 of control** - **< 2g / d in intervention** - **<1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **supine office** and **standing office**

Risk of bias table

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 if 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

MCCARRON 1997

Methods	**Cross-over study design** of reduced sodium diet and participants randomly assigned sodium tablets or placebo tablets. Conducted in the United States of America.
Participants	99 hypertensive adults given isradipine (calcium channel blocker) to reduce blood pressure.

Interventions	Group1 -- reduced sodium diet plus sodium tablets 100mmol/day (control) Group2 -- 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 (BUN) Urinary creatinine Plasma albumin Adverse effects (e.g. head ache, edema, etc.)
Notes	1) Sodium reduction achieved - **<1/3 of control** -**>2g/d in intervention** -**> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **1 month (4 weeks)** 5) Sex - **both (heterogeneous)** 6) Blood pressure method -**manual** 7) Blood pressure method -**seated office**

Risk of bias table

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 subjects 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.

MELAND 1997

Methods	**Cross-over study design** of reduced sodium diet and participants randomized to sodium tablets or placebo tablets. Conducted in Norway.
Participants	16 hypertensive adults not receiving medical therapy for hypertension.
Interventions	Group1 -- reduced sodium diet plus 50 mmol/day sodium tablets (control) Group2 -- reduced sodium diet plus placebo (reduced sodium)
Outcomes	Resting blood pressure Urinary creatinine excretion Plasma creatinine Serum total cholesterol Serum HDL Serum glucose Serum insulin C-peptide Serum insulin
Notes	1) Sodium reduction achieved - **>1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **2 months** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **seated office**

Risk of bias table

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

MELAND 2009

Methods	**Parallel study design** of reduced sodium diet and participants randomized to sodium tablets or placebo tablets. Conducted in Norway.
Participants	46 hypertensive adults possibly taking medical therapy to control blood pressure.
Interventions	Group1 -- reduced sodium diet plus 50 mmol sodium in tablets / day (control) Group2 -- 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** - **< 2g / d in intervention** **- > 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater**) 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **2 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method **manual** 7) Blood pressure method **seated office**

Risk of bias table

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

MELANDER 2007

Methods	**Cross-over study design** of reduced sodium diet and participants randomized to sodium tablets or placebo tablets. Conducted in Sweden.
Participants	46 normotensive adults without history of hypertension, diabetes or kidney disease or taking medication for those conditions.
Interventions	Group1 -- reduced sodium diet plus 100 mmol/day sodium tablets (control) Group2 -- 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** - **< 2g / d in intervention** - **<1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **Normotensive** 4) Duration of follow-up (in months) – **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic (ambulatory)** / **manual (office)** 7) Blood pressure method - **supine office** and **ambulatory 24 hr / ambulatory day / ambulatory night**

Risk of bias table

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 if 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.

MORGAN 1981

Methods	**Crossover design study** of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets. Conducted in the Australia.
Participants	48 hypertensive adults 28 - 50 years of age some of whom were taking medical therapy to control hypertension.
Interventions	Group1 -- reduced sodium diet plus 50 mmol/day sodium tablets (control) Group2 -- 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** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **2 months** 5) Sex - male / female / **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **supine office**

Risk of bias table

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

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 hypertensive adults with IDDM not taking medical therapy to control blood pressure.
Interventions	Group1 -- reduced sodium diet plus 100mmol/day Na tablets (control) Group2 -- reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting blood pressure HbAc Insulin dosage Serum cholesterol Serum HDL Proteinuria, Urinary creatinine-clearance Glomerular filtration rate (GFR) Renal plasma flow Filtration fraction Renal vascular resistance Plasma aldosterone Plasma total rennin activity, Plasma angiotensin converting enzyme Plasma antiotensin II Atrial natriuretic peptide Plasma adrenaline Plasma noradrenaline
Notes	1) Sodium reduction achieved - **>1/3 of control / both** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **both** 4) Duration of follow-up (in months) - **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic (home)** / **manual (office)** 7) Blood pressure method - **combination office** / **combination home**

Risk of bias table

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

NESTEL 1993

Methods	**Parallel study design** of reduced sodium diet and participants randomized to sodium tablets or placebo tablets and either safflower oil or dihomogammalinolenic acid (DGLA).
Participants	66 normotensive older adults (60-79 years) not taking medical therapy to control blood pressure.
Interventions	Group1 -- reduced sodium diet plus sodium tablets and DGLA or safflower oil (control) Group2 -- reduced sodium diet plus placebo tablets and DGLA or safflower oil (reduced sodium)
Outcomes	Resting blood pressure Plasma total cholesterol Plasma HDL Plasma triglycerides Plasma fatty acid profile
Notes	1) Sodium reduction achieved - **>1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **Normotensive** 4) Duration of follow-up (in months) - **1.5 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **seated office**

Risk of bias table

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 if 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, and triglycerides not reported

PARIJS 1973

Methods	**Cross-over 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 hypertensive adults.
Interventions	Group1 -- normal sodium diet plus placebo tablets / day (control-placebo) Group2 -- reduced sodium diet plus placebo tablets / day (reduced sodium-placebo) Group3 -- normal sodium diet plus diuretic in tablets / day (control-diuretic) Group4 -- 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** - **>2g/d in intervention** - **> 1.2 g/d in intervention** Diuretic phase - **<1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater**) 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **supine office** and **standing office**

Risk of bias table

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Unclear risk	Intervention group decided by odd or even number. Manner that 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	Los to follow-up > 20% in all groups
Selective reporting (reporting bias)	Low risk	All outcomes reported

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 medical therapy for hypertension. (couples were the unit of randomization)
Interventions	Group1 -- maintain "normal" diet (control) Group2 -- reduced sodium diet achieved through counselling and provision of "key" low salt options (reduced sodium) Group3 -- 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** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **both** 4) Duration of follow-up (in months) – **1.5 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **seated office**

Risk of bias table

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

RICHARDS 1984

Methods	**Cross-over study design** with dietary manipulation to have usual sodium intake, reduced sodium intake, or increased potassium intake. Conducted in New Zealand.
Participants	16 hypertensive adults not taking medical therapy for hypertension.
Interventions	Group1 -- control diet with sodium target of 180 mmol/day + 60mmol K/day (control) Group2 -- reduced sodium diet with sodium target of 80 mmol /day + 60mmol K/day (reduced sodium) Group 3 -- high potassium diet with sodium target of 180 mmol/day and 200 mmol K / day (high potassium - results not included in this review)
Outcomes	Resting blood pressure Plasma rennin 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** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **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

Risk of bias table

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 if 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

RUPPERT 1993

Methods	**Cross-over study design** with participants provided diets of 85mmol sodium and randomized to sodium tablets or placebo tablets. Conducted in Germany
Participants	25 non-hypertensive adults not taking medical therapy to reduce blood pressure.
Interventions	Group1 -- diet of 85 mmol sodium plus 115 mmol sodium/day in tablet (control) Group2 -- 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 Serum HDL Serum triglycerides Serum total protein
Notes	1) Sodium reduction achieved - **>1/3 of control** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **Normotensive** 4) Duration of follow-up (in months) – **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **seated office**

Risk of bias table

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

SCIARRONE 1992

Methods	**Parallel study design** of reduced sodium diet with either low-fat/high fibre or normal intake (2X2 factorial trial) and participants randomly assigned sodium tablets or placebo tablets. Conducted in Australia.
Participants	95 hypertensive adults between 20-69 years old some of whom were taking medical therapy for hypertension.
Interventions	**Reduced sodium/Low Fat Diet** Group1 -- low Na/low fat diet plus 100mmol/d Na tablets (control low fat) Group2 -- low Na/low fat diet plus placebo tablets (low Na low fat) **Reduced sodium/Normal Fat Diet** Group3 -- low Na/normal fat diet plus 100mmol/d Na tablets (control) Group4 -- low Na/normal fat diet plus placebo tablets (low Na)
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 Plasma LDL Plasma renin activity
Notes	1) Sodium reduction achieved Low fat / reduced sodium vs low fat - **>1/3 of control** -**< 2g / d in intervention** -**<1.2 g/d in intervention** - Norm fat / reduced sodium vs norm fat - **>1/3 of control** - **< 2g / d in intervention** **<1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater**) 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **2 months** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **supine office**

Risk of bias table

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

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.
Participants	28 adults with hypertension who were not taking medical therapy for blood pressure.
Interventions	Group1 -- healthy lifestyle education (control) Group2 -- education to reach reduced sodium diet plus healthy lifestyle education (reduced sodium)
Outcomes	Resting blood pressure
Notes	**1) Sodium intake achieved** **1 months** - **<1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** **3 months** - **>1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** **6 months** - **<1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** **12 months** - **<1/3 of control** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **1month/2months/3months/6months/12 months** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **not reported**

Risk of bias table

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 if 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

SUCKLING 2010

Methods	**Cross-over design study** of reduced sodium diet and participants randomized to receive sodium tablets or placebo tablets. Conducted in the United Kingdom.
Participants	26 Type II diabetics and 20 individuals with impaired glucose tolerance all with untreated normal or mild hypertension.
Interventions	Group1 -- reduced sodium diet plus unclear amount /day of sodium tablets (control) Group2 -- 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** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **both** 4) Duration of follow-up (in months) - **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 BP and position of patient during measurement are unclear. Also, risk of bias cannot be assessed from abstract

Risk of bias table

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

SWIFT 2005

Methods	**Cross-over study design** of reduced sodium diet and participants randomized to sodium tablets or placebo tablets. Conducted in the United Kingdom
Participants	46 hypertensive blacks not taking medical therapy to control blood pressure.
Interventions	Group1 -- reduced sodium diet plus 120mmol sodium in tablets (control) Group2 -- reduced sodium diet plus placebo tablets (reduced sodium)
Outcomes	Resting blood pressure Ambulatory blood pressure (24hr, 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** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic (ambulatory and office)** 7) Blood pressure method - **supine office** and **ambulatory 24 hr / ambulatory day / ambulatory night**

Risk of bias table

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

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) non-hypertensive adults not taking antihypertensive medications.
Interventions	Group1 -- no intervention (control) Group2 -- 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** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **Normotensive** 4) Duration of follow-up (in months) - **18 months** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **seated office**

Risk of bias table

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

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 non-hypertensive adults not taking medical therapy to control blood pressure.
Interventions	Group1 -- no intervention (control) Group2 -- educational campaign to reduce sodium intake(reduced sodium) Group3 -- educational campaign to reduce weight (weight loss) Group4 -- 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** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **Normotensive** 4) Duration of follow-up (in months) - **36 months** 5) Sex -**both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **seated office**

Risk of bias table

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.

VOGT 2008

Methods	**Cross-over design study** with participants randomized to reduced sodium or high sodium diet and additionally placebo, angiotensin II antagoinst (losartan) or losartan and hydrochlorothiazide (HCT). Conducted in the Netherlands.
Participants	34 hypertensive adults (18-70 years) without diabetes.
Interventions	Group1 -- high Na diet (~200mmol/d) (control) Group2 -- low Na diet (~50 mmol/d) (low Na) Group3 -- high Na diet (~200mmol/d) + losartan therapy (control-L) Group4 -- low Na diet (~50 mmol/d) + losartan therapy (low Na -L) Group5 -- high Na diet (~200mmol/d) + losartan+ HCT therapy (control-LHCT) Group6 -- low Na diet (~50 mmol/d) + losartan+ HCT therapy (low Na -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** - **>2g/d in inter.** - **> 1.2 g/d in inter** Losartan - **>1/3 of control** - **>2g/d in inter** - **> 1.2 g/d in inter** Losartan +HCT - **>1/3 of control** - **>2g/d in inter** - **>1.2 g/d in inter** 2) Age- **Adult (15 yrs or greater)** 3) Group - **not specified** 4) Duration of follow-up (in months) - **1.5 months** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic** 7) Blood pressure method - **seated office**

Risk of bias table

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.

WATT 1983

Methods	**Cross-over study design** of reduced sodium diet and participants randomized to sodium tablets or placebo tablets. Conducted in the United Kingdom.
Participants	20 hypertensive adults not taking medical therapy to control blood pressure.
Interventions	Group1 -- reduced sodium diet plus 80 mmol sodium in tablets / day (control) Group2 -- 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** - **>2g/d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) - **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **seated office**

Risk of bias table

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 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 if outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	2 participants (10%) lost to follow-up.
Selective reporting (reporting bias)	Low risk	All outcomes reported

WATT 1985

Methods	**Cross-over study design** of reduced sodium diet and participants randomized to sodium tablets or placebo tablets. Conducted in the United Kingdom.
Participants	75 adults with unspecified hypertensive status and unspecified status of medical therapy to control blood pressure..
Interventions	Group1 -- reduced sodium diet plus 80 mmol sodium in tablets / day (control) Group2 -- 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** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **not specified** 4) Duration of follow-up (in months) - **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **manual** 7) Blood pressure method - **seated office**

Risk of bias table

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 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 if outcome assessors were blinded
Incomplete outcome data (attrition bias)	Unclear risk	Unclear reasons for loss-to-follow or distribution of those lost.
Selective reporting (reporting bias)	Unclear risk	All outcomes reported

WEIR 2010

Methods	**Cross-over study design** with participants assigned to low or usual sodium diets. Conducted in the United States of America
Participants	132 hypertensive adults, 18 to 60 years of age all provided direct renin inhibitor, Aliskiren.
Interventions	Group1 -- usual sodium diet plus Aliskiren (control) Group2 -- 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** - **< 2g / d in intervention** - **> 1.2 g/d in intervention** 2) Age- **Adult (15 yrs or greater)** 3) Group - **hypertensive** 4) Duration of follow-up (in months) – **1 month** 5) Sex - **both (heterogeneous)** 6) Blood pressure method - **automatic(ambulatory)** / **manual (office)** 7) Blood pressure method - **seated office** and **ambulatory 24 hr**

Risk of bias table

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

B. Adult Cohort studies included in the systematic review reporting all-cause mortality, cardiovascular disease, stroke, or coronary heart disease

Alderman 1995

Methods	Cohort study conducted in the USA; data taken from a union-sponsored hypertensive treatment programme
Participants	2937 mildly and moderately hypertensive adults; worksite-based cohort; participants given antihypertensive medical therapy as part of the programme
Interventions	Participants had a measurement of sodium intake and were divided into sex-specific quartiles of sodium intake and incidence of CVD outcomes compared among quartiles Men: Quartile 1–2.1 g Na/day Quartile 2–2.5 g Na/day Quartile 3–3.5 g Na/day Quartile 4–4.0 g Na/day Women: Quartile 1–1.5 g Na/day Quartile 2–1.9 g Na/day Quartile 3–2.7 g Na/day Quartile 4–3.2 g Na/day
Outcomes	Stroke Myocardial infarction Outcome results reported for men and women separately
Notes	Follow-up time: 3.8 year average Sodium measured through 24-hour urinary sodium excretion Yearly follow-up Morbid and mortal events assessed through review of hospital charts and death certificates; in some rare cases, data confirmed through physicians outside the programme, family members or friends, or through union records Models were unadjusted Models did not adjust for blood pressure

Na, sodium

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Unclear risk	Participants were volunteers with high blood pressure to participate in a union-sponsored systematic hypertension treatment programme
Blinding of participants and personnel (performance bias)	Low risk	Personnel were blinded
Blinding of outcome assessment (detection bias)	Low risk	Blinding of outcome assessors
Incomplete outcome data (attrition bias)	Low risk	Reported that there was no loss to follow-up
Selective reporting (reporting bias)	Low risk	The reasons for not reporting some of the prespecified outcomes were explained
Defining exposure (confounding)	Low risk	24-hour urinary sodium excretion
Other confounding	Unclear risk	Models were only adjusted for race and age; therefore, other potential important confounders may have influenced results

Cohen 2006

Methods	Cohort study conducted in the USA; used data from NHANES II
Participants	7154 men and women 30–74 years old
Interventions	Measured diet and risk factors at baseline and followed for 13.7 years (mean): Lower half – 1.6 g Na/day Upper half – 3.7 g Na/day
Outcomes	Death from cardiovascular disease All-cause mortality Death from coronary heart disease Death from stroke (cerebrovascular disease)
Notes	Follow-up: 13.7 years (mean) Sodium intake measured using one 24-hour dietary recall Excluded individuals with self-reported history of heart disease or stroke, taking low-salt diet for medical reasons, those who died during ≤6 month initial follow-up, and those with the highest or lowest 1% reported intake of sodium or calories Fully-adjusted models adjusted for age, sex, race, smoking, alcohol, antihypertension treatment, SBP, BMI, education, physical activity, potassium intake, history of diabetes, serum cholesterol, calories Models adjusted for SBP Less adjusted models (not adjusted for blood pressure) were not presented.

BMI, body mass index; NHANES, National Health and Nutrition Examination Survey; SBP, systolic blood pressure

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Unclear risk	Baseline examination part of USA (NHANES) II (1976–1980); exclusion of self-reported history of heart disease or stroke
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Low risk	Outcome was mortality
Incomplete outcome data (attrition bias)	Unclear risk	Mortality statistics taken from National Death Index and Social Security Administration Death Master File and all those not reported as deceased assumed to be alive; emigration not taken into account.
Selective reporting (reporting bias)	Low risk	Prespecified outcomes reported
Defining exposure (confounding)	High risk	Sodium measured through one 24-hour dietary recall
Other confounding	Low risk	Models tested for significance of other common risk factors

Cohen 2008

Methods	Cohort study conducted in the USA; used data from NHANES III
Participants	8699 male and female adults >30 years of age
Interventions	Measured diet and risk factors at baseline and followed for 8.7 years (mean): Quartile 1 – 2.1 g Na/day Quartile 2 – 2.5 g Na/day Quartile 3 – 3.5 g Na/day Quartile 4 – 4.1 g Na/day
Outcomes	Death from cardiovascular disease All-cause mortality
Notes	Follow-up 8.7 years (mean) Sodium intake measured using one 24-hour dietary recall. 13,065 adults over 30 years of age participated in the NHANES III study; analysis excluded individuals with self-reported history of congestive heart failure, heart attack or stroke, taking low-salt diet for medical reasons, those who died during ≤6 month initial follow-up, and those with the high or low sodium or calories Fully-adjusted models adjusted for age, sex, race, potassium intake, added salt, BMI, education, smoking, hypertension treatment, SBP, cholesterol, diabetes, cancer, physical activity, alcohol Models adjusted for systolic blood pressure Less adjusted models adjusted for age, sex, race, calories.

BMI, body mass index; NHANES, National Health and Nutrition Examination Survey; SBP, systolic blood pressure

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Unclear risk	Baseline examination part of NHANES III (1988–1994); exclusion of self-reported history of heart disease or stroke and consumption of low salt for health reasons
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Low risk	Outcome was mortality
Incomplete outcome data (attrition bias)	Unclear risk	Mortality statistics taken from National Death Index and Social Security Administration Death Master File and all those not reported as deceased assumed to be alive; emigration not taken into account
Selective reporting (reporting bias)	Low risk	Prespecified outcomes reported
Defining exposure (confounding)	High risk	Sodium measured through 1–24 hour dietary recall
Other confounding	Low risk	Models tested for significance of other common risk factors

NHANES, National Health and Nutrition Examination Survey

Cook 2007

Methods	Cohort study conducted in the USA
Participants	2415 (at baseline) men and women 30–54 years of age Cook I = 327 and Cook II = 417
Interventions	Cook I = randomized to low sodium or control diet and in Cook II randomized to low sodium, low sodium and weight control, weight control only or control; intervention was 18 months in Cook I and 36 months in Cook II Subsequently all participants followed-up for a time of 10–15 years post conclusion of the interventions Cook I: low sodium – 2.29 g Na/day higher sodium – 3.34 g Na/day Cook II: low sodium – 3.23 g Na/day higher sodium – 4.02 g Na/day
Outcomes	Myocardial infarction Stroke Coronary revascularisation Cardiovascular death
Notes	Follow-up: 10–15 years Sodium intake measured using 24-hour urinary sodium excretion Fully-adjusted models adjusted for age, race, sex, weight loss, baseline weight, sodium excretion Models did not adjust for blood pressures

Na, sodium

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Low risk	Participants previously participated in RCT and selected from clinics
Blinding of participants and personnel (performance bias)	Unclear risk	Blinded during RCT; unclear whether personnel blinded during follow-up study
Blinding of outcome assessment (detection bias)	Unclear risk	Unclear whether outcome assessors blinded during follow-up study
Incomplete outcome data (attrition bias)	Low risk	> 70% response rate after 10–15 follow-up
Selective reporting (reporting bias)	Low risk	Prespecified outcomes reported
Defining exposure (confounding)	Low risk	24-hour urinary sodium excretion
Other confounding	Unclear risk	Controlled for some common confounders but not all.

RCT, randomized controlled trial

Ekinci 2011

Methods	Cohort study conducted in Australia
Participants	638 patients with type 2 diabetes, mean age 64 years, 85% had hypertension (defined by the use of antihypertensive and/or blood pressure >140/90)
Interventions	Baseline measurement of sodium intake and population divided into tertiles and outcomes compared between tertiles: Low tertile – <150 mmol/day Middle tertile – 150–208 mmol/day High tertile – >208 mmol/day
Outcomes	All-cause mortality Cardiovascular mortality
Notes	Follow-up: 11 years Sodium intake measured using 24-hour urinary sodium excretion Fully-adjusted models adjusted for sex, pre-existing CVD, eGFR, atrial fibrillation, urinary albumin excretion rate, SBP, diabetes duration Models adjusted for SBP Less adjusted models (not adjusted for blood pressure) were not presented.

CVD, cardiovascular disease; GFR, glomerular filtration rate; SBP, systolic blood pressure

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Low risk	638 patients attending a single diabetes clinic
Blinding of participants and personnel (performance bias)	Unclear risk	No blinding described
Blinding of outcome assessment (detection bias)	Unclear risk	No blinding described
Incomplete outcome data (attrition bias)	Low risk	Low loss to follow-up (<3%)
Selective reporting (reporting bias)	Low risk	Prespecified outcomes reported
Defining exposure (confounding)	Low risk	24-hour urinary sodium excretion
Other confounding	Low risk	Controlled for other common risk factors

Geleijnse CCDS2007

Methods	Cohort study (case-cohort analysis) conducted in the Netherlands
Participants	1448 adult men and women, mean age 69.2, blood pressure status not specified, heterogeneous blood pressure medication population
Interventions	Analysis of sodium in the diet and also analysed K intake in diet and results presented as risk per 1 SD change in intake (69 mmol or 1.9 g/day)
Outcomes	Relative risk of incident MI Incident stroke CVD mortality All-cause mortality
Notes	Follow-up: 5.5 years Sodium measured by overnight urinary sodium excretion. Computerized information system used by general practitioners used to quantify incident events; research physicians verified all information on incident events using records and hospital discharge letters Fully-adjusted models adjusted for age, sex, sodium intake, BMI, smoking, diabetes, use of diuretics, education, calories, alcohol, calcium, saturated fat, potassium intake Models did not adjust for blood pressure

BMI, body mass index; CVD, cardiovascular disease, MI, myocardial infarction; SD, standard deviation

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Low risk	Participants selected from Rotterdam Study; controls were randomly selected from individuals who did not have an incident event during the follow-up period
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No description of blinding of outcome assessor
Incomplete outcome data (attrition bias)	Low risk	Reported no loss to follow-up and selected a random sample of individuals without an incident event as the control group
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Defining exposure (confounding)	Low risk	Exposure to sodium via urinary excretion
Other confounding	Low risk	Models controlled for other common risk factors

He 1999

Methods	Cohort study undertaken in the USA; follow-up epidemiological study on the NHANES I
Participants	9485 adults 25–74 years of age during NHANES survey of 1971–75
Interventions	Assessment of sodium intake as well as overweight and other demographic and physiological indicators were measured at baseline and follow-up measures in 1982, 1984, 1986, 1987, and 1992: Quartile 1 – 1.4 Na g/day Quartile 2 – 1.7 Na g/day Quartile 3 – 2.3 Na g/day Quartile 4 – 2.6 Na g/day
Outcomes	Incident CVD Death from CVD Incident stroke Death from stroke Incident coronary heart disease Death from coronary heart disease Outcomes reported for overweight and non-overweight participants separately.
Notes	Follow-up: 11–22 years Sodium intake measured by one 24 hour dietary recall Participants followed up directly Death certificate required to confirm mortality and incident events required documentation for verification Excluded those without exposure data, self-reported history of heart attack, heart failure, or stroke at baseline or were using a low-salt diet at baseline (n from low-salt diet =337) Fully-adjusted models adjusted for age, sex, race, SBP. serum cholesterol level, diabetes, BMI, diuretic use, physical activity, education, smoking, alcohol, calories Models adjusted for SBP Less adjusted models adjusted for age, sex, race

BMI, body mass index; NHANES, National Health and Nutrition Examination Survey; SBP, systolic blood pressure

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Unclear risk	Selection from NHANES would be low risk selection through multistage complex random sampling; however, excluded those without exposure data, self-reported history of heart attack, heart failure, or stroke at baseline or using a low-salt diet at baseline (n=337)
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	Not clear whether outcome assessors were blinded
Incomplete outcome data (attrition bias)	Low risk	4% loss to follow-up
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Defining exposure (confounding)	High risk	One 24-hour dietary recall
Other confounding	Low risk	Models controlled for other common risk factors

NHANES, National Health and Nutrition Examination Survey

Kagan 1985

Methods	Cohort study conducted in the state of Hawaii, USA
Participants	7088 men of Japanese ancestry living in Hawaii, USA, aged 45–68 years; all participants were free of stroke at baseline and individuals with previous CHD or cancer, or those who reported that their previous day's dietary intake was atypical, were excluded
Interventions	Baseline measurement of sodium intake and population divided into quintiles and outcomes compared between quintiles: Quintile 1 – 1.8 g Na/day Quintile 2 – 2.1 g Na/day Quintile 3 – 2.7 g Na/day Quintile 4 – 3.5 g Na/day Quintile 5 – 3.9 g Na/day
Outcomes	Stroke Stroke subtype Death by stroke
Notes	Follow-up: 10 years Sodium intake measured through 24 hour dietary recall Men follow-up directly and surveillance of hospital discharges and death certificates were used data collection of outcomes Fully-adjusted models adjusted for age Models did not adjust for blood pressure

CHD, coronary heart disease; Na, sodium; USA, United States of America

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Unclear risk	Selection of participants not clearly described
Blinding of participants and personnel (performance bias)	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias)	Unclear risk	Blinding not described
Incomplete outcome data (attrition bias)	Unclear risk	Loss to follow-up not reported
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Defining exposure (confounding)	High risk	One 24-hour dietary recall, which did not include use of salt or soy sauce at the table
Other confounding	High risk	Models controlled for age only

Larsson CCDS2008

Methods	Cohort study conducted in Finland
Participants	26556 adult men, age range 50–69 at baseline, BP status not specified, not specified whether taking BP medication; all were smokers at baseline and were excluded if they had a history of cancer or other serious disease; received anticoagulant therapy; used vitamin E, A or beta-carotene supplements; self-reported having suffered stroke; or had incomplete dietary data; all participants had originally been in an RCT of smokers to assess the effect of alpha-tocopherol or beta-carotene on risk of development of lung cancer
Interventions	Intervention: analysis of Na and K intake in diet: Quintile 1 -- 97.5mmol/day (K) and 3.92 g/Na Quintile 2 -- 152.1mmol/day (K) and 5.86 g/Na
Outcomes	All stroke (fatal and non-fatal) Stroke subtypes according to quintiles of Mg, K and Na intake
Notes	Follow-up: 13.6 years on average Sodium intake measured through FFQ validated through food records End-ponts were ascertained through record linkage with the National Hospital Discharge Register and the National Register of Causes of Death Sex – men only Fully-adjusted models adjusted for age, smoking, BMI, SBP, DBP, serum total cholesterol, HDL cholesterol, diabetes, history of CHD, physical activities, alcohol, calories Models adjusted for SBP and DBP Less adjusted models adjusted for age, supplementation group

BMI, body mass index; BP, blood pressure; CHD, coronary heart disease; DBP, diastolic blood pressure; FFQ, Food Frequency Questionnaire; HDL, high-density lipoprotein; K, potassium; Mg, magnesium; Na, sodium; RCT, randomized controlled trial; SBP, systolic blood pressure

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	High risk	Participants had originally agreed to participate in study on effect of alpha-tocopherol or beta-carotene on risk of development of lung cancer; all were smokers at baseline
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Unclear risk	No description of blinding of outcome assessor
Incomplete outcome data (attrition bias)	Unclear risk	End points were based on record linkage with the National Hospital Discharge Register and National Register of Causes of Death. Emigration not accounted for and if record not found participant considered without outcome
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Defining exposure (confounding)	Unclear risk	Exposure to Na via FFQ validated through comparison with food records
Other confounding	Low risk	Models controlled for other common risk factors

FFQ, food frequency questionnaire; Na, sodium

Nagata 2004

Methods	Cohort study conducted in Japan
Participants	13,355 men and 15724 women in Takayama City, Gifu Japan ≥35 years of age
Interventions	Usual diet including sodium intake was assessed using FFQs Men: Low tertile – 4.1 g/day Middle tertile – 5.2 g/day High tertile – 6.6 g/day Women: Low tertile – 3.8 g/day Middle tertile – 4.8 g/day High tertile – 6.0 g/day
Outcomes	Death from stroke Death from ischemic stroke Death from intracerebral hemorrhage
Notes	Follow-up: 7 years FFQ used to measure sodium intake Data presented separately for women and men End-points ascertained through mandatory death registration Fully-adjusted models adjusted for age, marital status, education, BMI, smoking, alcohol, exercise, hypertension, diabetes, intake of protein, total energy, potassium and vitamin E intake Models did not control for blood pressure but did control for history of hypertension at baseline.

BMI, body mass index; FFQ, food frequency questionnaire

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Low risk	All participants of city 35 years and older were eligible and participation rate at baseline was >85%
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Low risk	Mortality was outcome
Incomplete outcome data (attrition bias)	Low risk	<5% loss to follow-up through emigration
Selective reporting (reporting bias)	Low risk	Death registration required by law and all prespecified outcomes reported
Defining exposure (confounding)	Unclear risk	1-year recall FFQ used, which was validated against 3-day diet records, 4-day diet recalls and 12-day diet records over 1 year
Other confounding	Low risk	Models controlled for other common risk factors

FFQ, food frequency questionnaire

O'Donnell 2011

Methods	Cohort study conducted in 40 countries.
Participants	28880 participants aged ≥55 years from 733 centres from 40 countries with established CVD or high-risk diabetes mellitus; patients were ineligible if they had heart failure, low ejection fraction, significant valvular disease, serum creatinine >3.0 mg/dL, renal artery stenosis, nephrotic range proteinuria, or blood pressure higher than 160/100 mmHg
Interventions	Baseline measurement of sodium intake and population divided into seven subgroups and outcomes compared between subgroups Subgroup 1 – <2 g/day Subgroup 2 – 2–2.99 g/day Subgroup 3 – 3–3.99 g/day Subgroup 4 – 4–5.99 g/day Subgroup 5 – 6–6.99 g/day Subgroup 6 – 7–8 g/day Subgroup 7 – >8 g/day
Outcomes	All-cause mortality Death from CVD Death from non-CVD Incident MI Incident congestive heart failure Incident stroke
Notes	Median follow-up: 56 months (25–75 percentiles, 53–60 months) 24-hour sodium and potassium urinary excretion was estimated from a fasting morning urine samples Fully-adjusted models are unadjusted Models did not adjust for blood pressure

CVD, cardiovascular disease; MI, myocardial infarction

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Low risk	Participants from other trials from 733 centres from 40 countries with established CVD or high-risk diabetes mellitus who provided a baseline urine sample; two cohorts were combined because both trials recruited participants from the same sites, time period, using the same eligibility criteria., and used the same methods to capture baseline clinical data and outcome measures
Blinding of participants and personnel (performance bias)	Unclear risk	No description of blinding of participants and personnel
Blinding of outcome assessment (detection bias)	Unclear risk	No description of blinding of outcome assessor
Incomplete outcome data (attrition bias)	Low risk	Low loss to follow-up reported (0.2%)
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Defining exposure (confounding)	Low risk	24-hour sodium urinary excretion was estimated from a fasting morning urine samples
Other confounding	High risk	Models are unadjusted

Stolarz-Skrzypek 2011

Methods	Cohort study conducted in Belgium and other European countries
Participants	3681 participants without CVD from a Flemish cohort (Flemish Study on Environment, Genes, and Health Outcomes) and a cohort across Europe (European Project on Genes in Hypertension)
Interventions	Baseline measurement of sodium intake and the population was divided into tertiles and outcomes compared between tertiles Low tertile – 50–126 mmol/day for women and 50–158 mmol/day for men Middle tertile – 127–177 mmol/day for women and 159–221 mmol/day for men High tertile – 178–400 mmol/day for women and 222–400 mmol/day for men
Outcomes	All-cause mortality Death from CVD Death from non-CVD Incident CVD Incident CHD Incident stroke
Notes	Median follow-up: 7.9years Sodium intake measured by 24-hour urinary sodium concentration Fully-adjusted models adjusted for study population, sex and baseline variables: age, body mass index, systolic blood pressure, 24-hour urinary potassium excretion, antihypertensive drug treatment, smoking and drinking alcohol, diabetes, total cholesterol, and educational attainment Models controlled for blood pressure Less adjusted models, which adjusted for all covariates other than blood pressure or antihypertensive treatment, also available

CVD, cardiovascular disease

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Low risk	Participants without cardiovascular disease selected from large Flemish and European cohorts
Blinding of participants and personnel (performance bias)	Unclear risk	No description of blinding of participants and personnel
Blinding of outcome assessment (detection bias)	Unclear risk	No description of blinding of outcome assessor
Incomplete outcome data (attrition bias)	Low risk	Reported zero loss to follow-up
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Defining exposure (confounding)	Low risk	24-hour urinary sodium excretion
Other confounding	Low risk	Models controlled for other common risk factors

Tunstall-Pedoe 1997

Methods	Cohort study conducted in Scotland
Participants	11629 men and women 40– 59 years of age randomly selected from 25 districts of Scotland
Interventions	Baseline measurement of sodium intake and population divided into quintiles and outcomes compared between quintiles; K also measured Quintile 1 – 1.8 g Na/day Quintile 2 – 2.1 g Na/day Quintile 3 – 2.7 g Na/day Quintile 4 – 3.5 g Na/day Quintile 5 – 3.9 g Na/day
Outcomes	Myocardial infarction (non-fatal) Coronary artery surgery Death from coronary disease (the sum of which was considered all coronary heart disease) All-cause mortality
Notes	Follow-up: 7.6 years Sodium intake measured through 24-hour urinary sodium excretion Outcomes measured through death certificates and hospital/clinician records Fully-adjusted models adjusted for age. Models did not adjust for blood pressure

K, potassium; Na, sodium

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Low risk	Random select of clinics then patients of clinics. Selection from the Scottish Heart Health Study
Blinding of participants and personnel (performance bias)	Low risk	Personnel not aware of urinary sodium while conducting other measurements
Blinding of outcome assessment (detection bias)	Low risk	Mortality was outcome and morbidity measured through hospital and clinician records
Incomplete outcome data (attrition bias)	Unclear risk	Loss to follow-up limited to emigration but amount of loss to follow-up unclear
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Defining exposure (confounding)	Low risk	24-hour urinary sodium excretion
Other confounding	High risk	Models only controlled for age

Tuomilehto 2001

Methods	Cohort study conducted in Finland
Participants	1173 men and 1263 women 25–64 years of age; excluded from CHD analysis if had an acute coronary event (n= 34) before baseline and excluded from stroke analysis if had an acute cerebrovascular event (n=16) before baseline, but each type of patient could be included in the analysis for the other event Men: Quartile 1 – 3.7 Na g/day Quartile 2 – 4.2 Na g/day Quartile 3 – 5.4 Na g/day Quartile 4 – 6.0 Na g/day Women: Quartile 1 – 2.7 Na g/day Quartile 2 – 3.1 Na g/day Quartile 3 – 4.0 Na g/day Quartile 4 – 4.5 Na g/day
Interventions	Measured sodium and other dietary exposures and other CVD risk factors at baseline
Outcomes	Incident coronary event Incident stroke event Death from coronary heart disease Death from cardiovascular disease All-cause mortality
Notes	Follow-up: 8–13 years Sodium intake measured via 24-hour urinary sodium excretion End-points were measured through Statistics Finland (mortality) and national hospital discharge registers (morbidity) Fully-adjusted models adjusted for age, study year, smoking, serum total, HDL cholesterol, SBP, BMI Models adjusted for blood pressure Less adjusted models adjusted for age, study year

BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; HDL, high-density lipoprotein; Na, sodium; SBP, systolic blood pressure

Risk of bias table

Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Low risk	Randomly selection sample of men and women from two eastern provinces of Finland
Blinding of participants and personnel (performance bias)	High risk	No blinding
Blinding of outcome assessment (detection bias)	Low risk	Mortality and morbidity measured through national registry systems
Incomplete outcome data (attrition bias)	Low risk	Participants followed through health registry system
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Defining exposure (confounding)	Low risk	24-hour urinary sodium
Other confounding	Low risk	Models controlled for other common risk factors

Umesawa CCDS2008

Methods	Cohort study conducted in Japan; sample derived from 45 communities across Japan
Participants	58730 (23119 men and 35611 women) adult men and women, age range 40–79 years, blood pressure status was not specified, not specified whether taking blood pressure medication
Interventions	Na and K intake in diet measured and quintiles compared on outcomes: Quintile 1 (35mmol)K – 1.15 g Na Quintile 2 (44mmol)K – 1.68 g Na Quintile 3 (51mmol)K – 2.07 g Na Quintile 4 (58mmol)K – 2.51 g Na Quintile 5 (68mmol)K – 3.11 g Na
Outcomes	Mortality from stroke Mortality from CHD Mortality total CVD
Notes	Follow-up: 12.7 year (average) Sodium intake measured through FFQ End points measured by death certificate Fully-adjusted models adjusted for age, sex, BMI, smoking, alcohol, history of hypertension, diabetes, menopause and hormone replacement therapy (women), sports activities, walking time, education, perceived mental stress, calcium intake Models did not control for BP but did control for history of hypertension

BMI, body mass index; CHD, coronary heart disease; CVD, cardiovascular disease; FFQ, food frequency questionnaire; Na, sodium

Risk of bias table

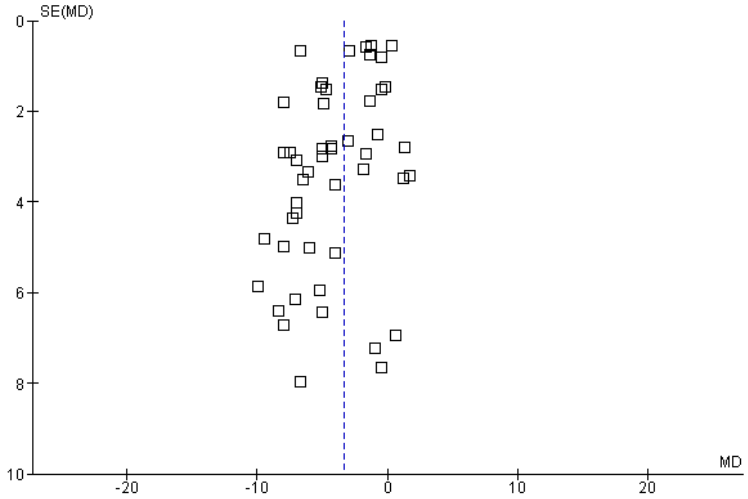
Bias	Authors' judgement	Support for judgement
Selection of participants (selection bias)	Low risk	Selection from Japanese Collaborative Cohort Study
Blinding of participants and personnel (performance bias)	Unclear risk	Blinding not described
Blinding of outcome assessment (detection bias)	Low risk	Specifically noted that those assessing death certificates were blinded
Incomplete outcome data (attrition bias)	Low risk	Loss to follow-up <5%
Selective reporting (reporting bias)	Low risk	All prespecified outcomes reported
Defining exposure (confounding)	Unclear risk	Exposure to sodium via dietary records
Other confounding	Low risk	Models controlled for other common risk factors

C. Children RCTs, non-RCTs and cohort studies included in the review reporting blood pressure

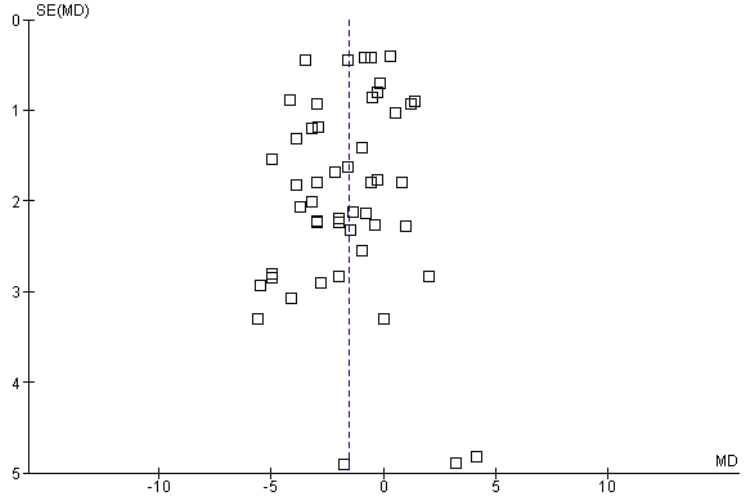
Study ID	Country	Study design	Duration	Methods of estimating sodium intake	Type of intervention	Outcome (systolic blood pressure, diastolic blood pressure) measurements
Controlled trials						
Calabrese 1985	USA	RCT (parallel)	12 weeks	Overnight urinary sodium and dietary assessment	Feeding (all water)	Were measured on a bi-weekly basis with the first screening the week before trial beginning
Ellison 1989	USA	Non-RCT (cross-over data used)	1 year	Dietary assessment	Feeding (daily at boarding school)	Each student measured his/her own blood pressure each week using an automatic device
Gillum 1981	USA	RCT (parallel)	1 year	24-hour urinary sodium and dietary assessment	Diet advice or education	Were determined at the first and one-year follow-up home visit
Howe 1985	Australia	Non-RCT (cross-over)	3 weeks	Overnight urinary sodium and dietary assessment	Diet advice or education	Were taken at baseline, three and six weeks
Howe 1991	Australia	RCT (crossover)	4 weeks	Overnight urinary sodium and dietary assessment	Diet advice or education	Were measured weekly
Miller 1988	USA	Non-RCT (parallel)	12 weeks	24-hour urinary sodium	Diet advice or education	Were measured weekly
Palacios 2004	USA	RCT (cross-over)	3 weeks	24-hour urinary sodium and dietary assessment	Feeding (all food)	Were measured every other day
Sinaiko 1993	USA	RCT (parallel)	3 years	24-hour urinary sodium	Diet advice or education	Were measured every 3 months
Trevisan 1981	USA	RCT (parallel)	24 days	24-hour urinary sodium and laboratory analysis of duplicate food samples	Feeding (lunch food daily)	Were measured on the first and the last day
Cohort studies						
Geleijnse 1990	the Netherlands	Cohort	7 years	24-hour urinary sodium	No intervention	Change in blood pressure over time

OSM 3: Funnel plots

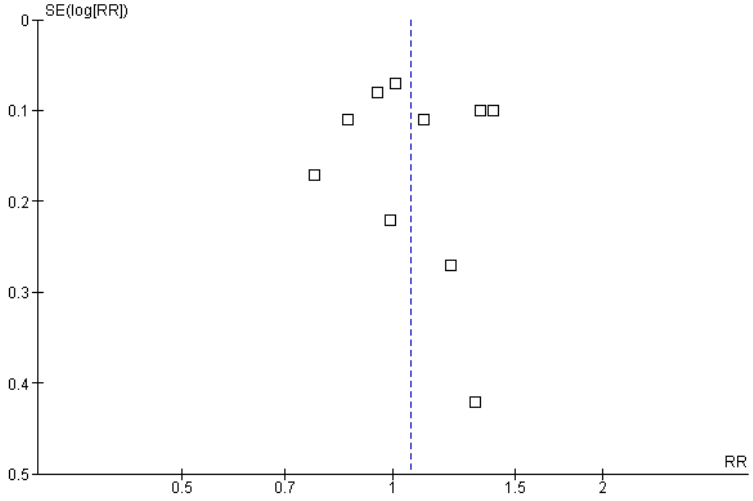
Funnel plot 1: Resting systolic blood pressure in adults



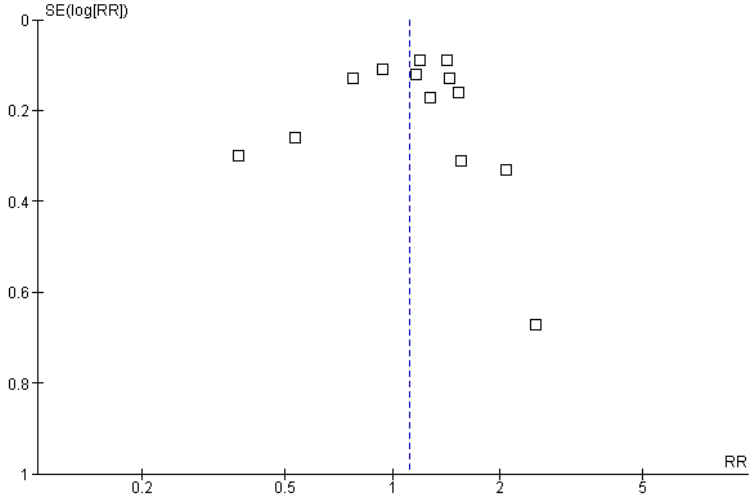
Funnel plot 2: Resting diastolic blood pressure in adults



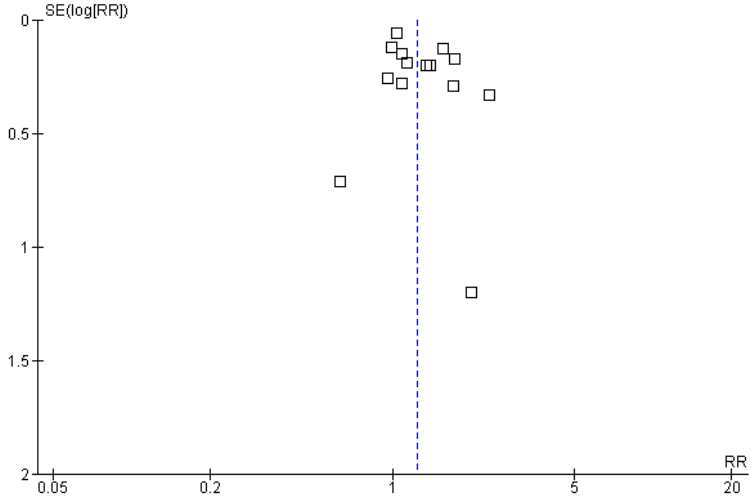
Funnel plot 3: All-cause mortality in adults



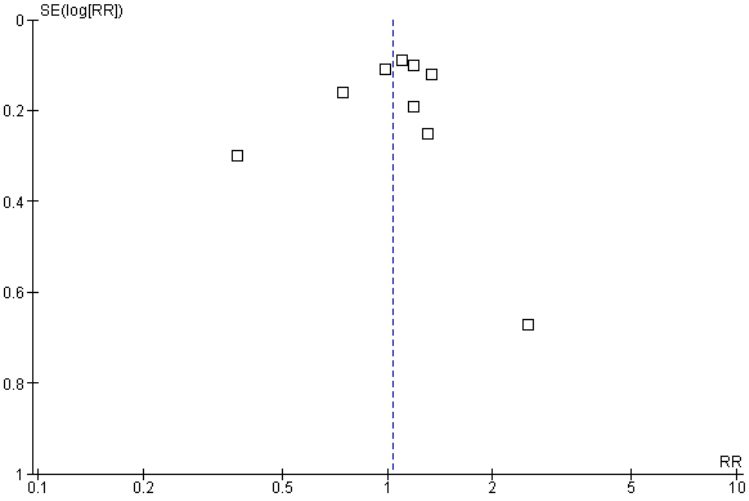
Funnel plot 4: Cardiovascular disease in adults



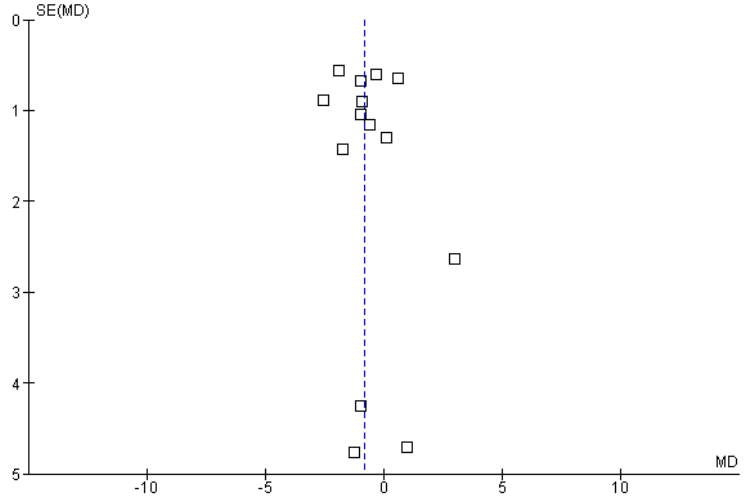
Funnel plot 5: Stroke in adults



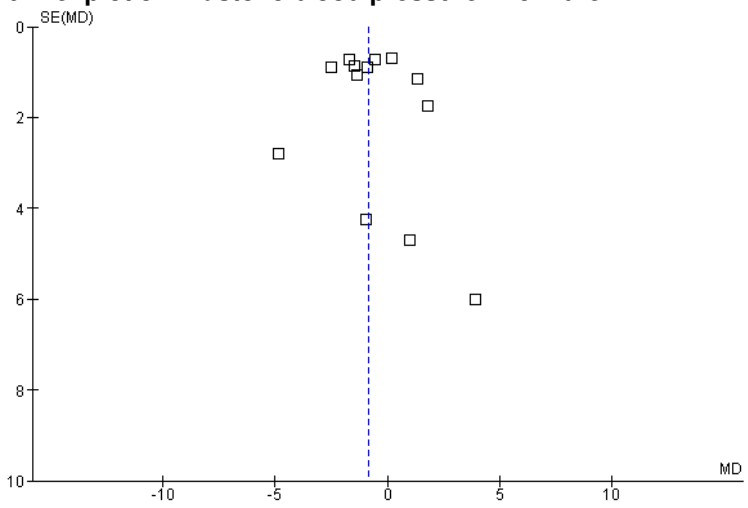
Funnel plot 6: Coronary heart disease in adults



Funnel plot 7: Systolic blood pressure in children

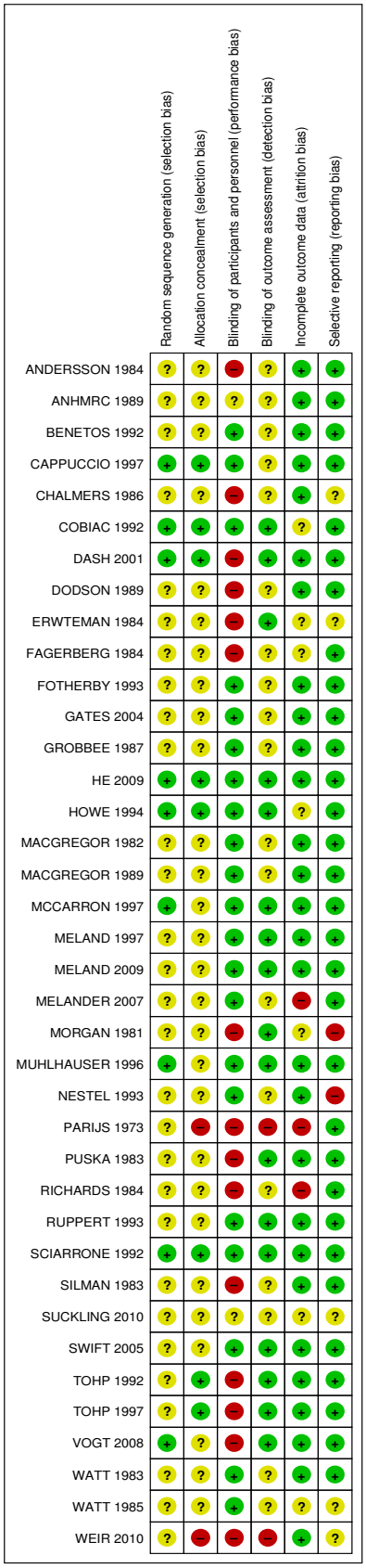


Funnel plot 8: Diastolic blood pressure in children

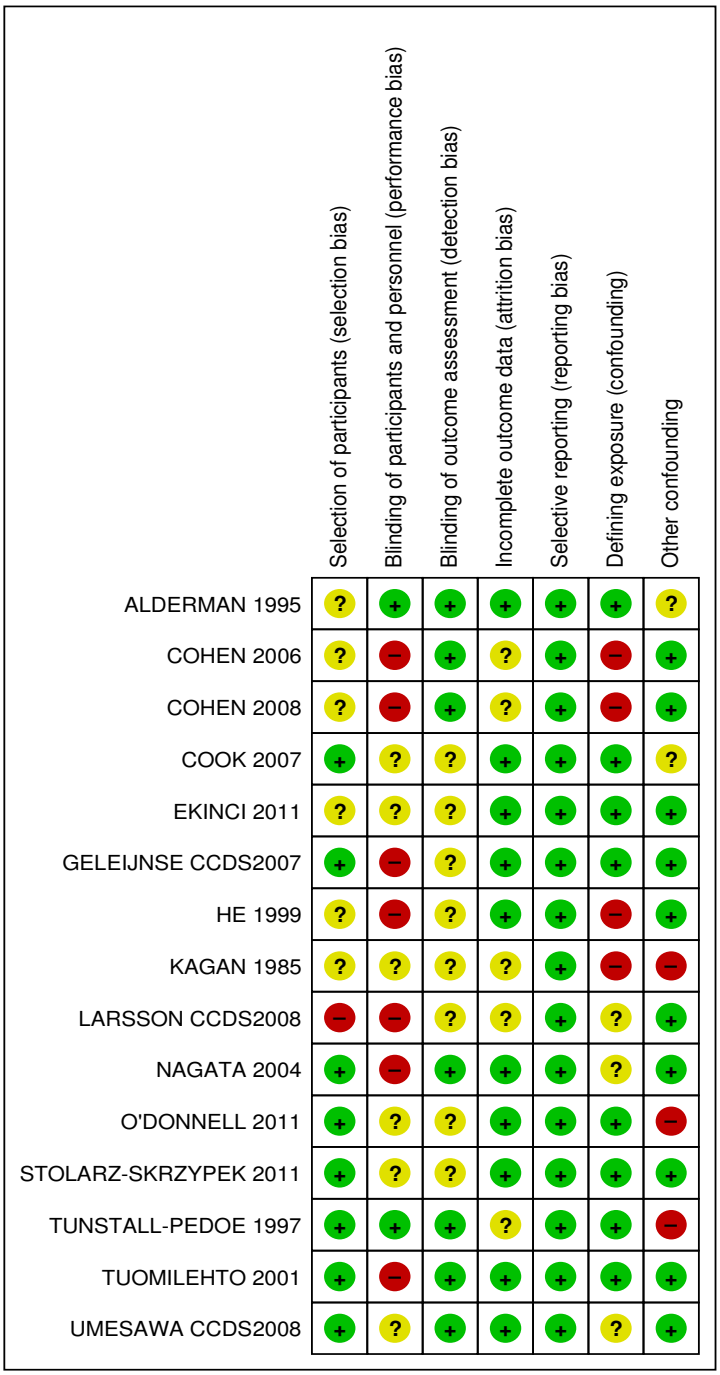


OSM 4: Risk of bias summary

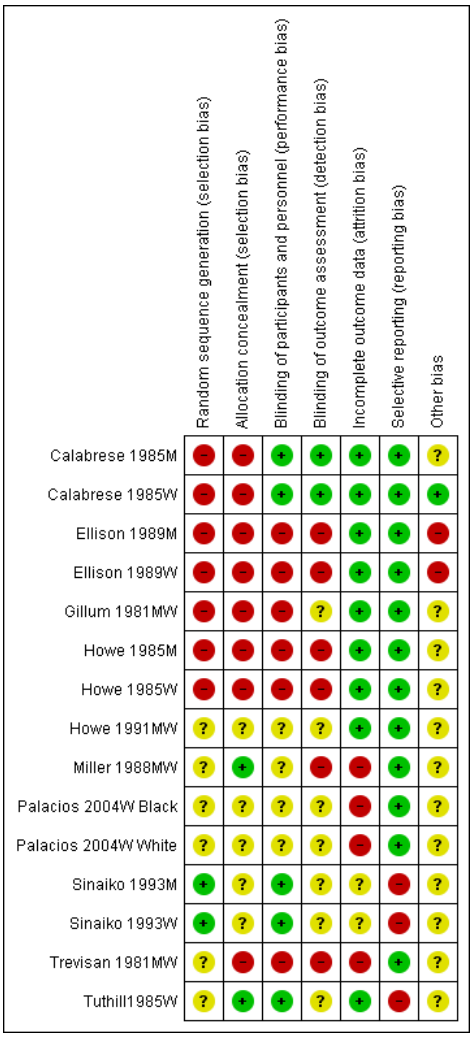
Risk of bias summary: RCTs reporting blood pressure, renal function, blood lipids, or catecholamine levels in adults



Risk of bias summary: Cohort studies reporting all-cause mortality, cardiovascular disease, stroke, or coronary heart disease in adults

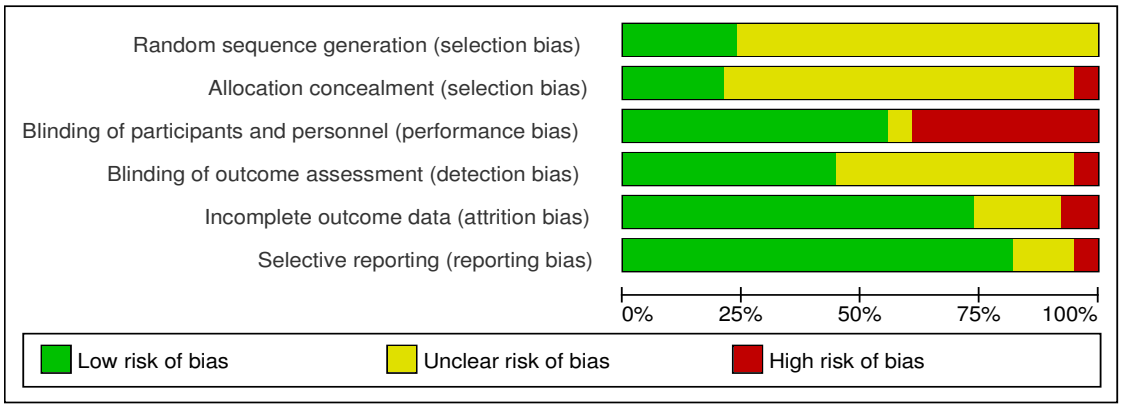


Risk of bias summary: Controlled-trials and one cohort study reporting blood pressure in children

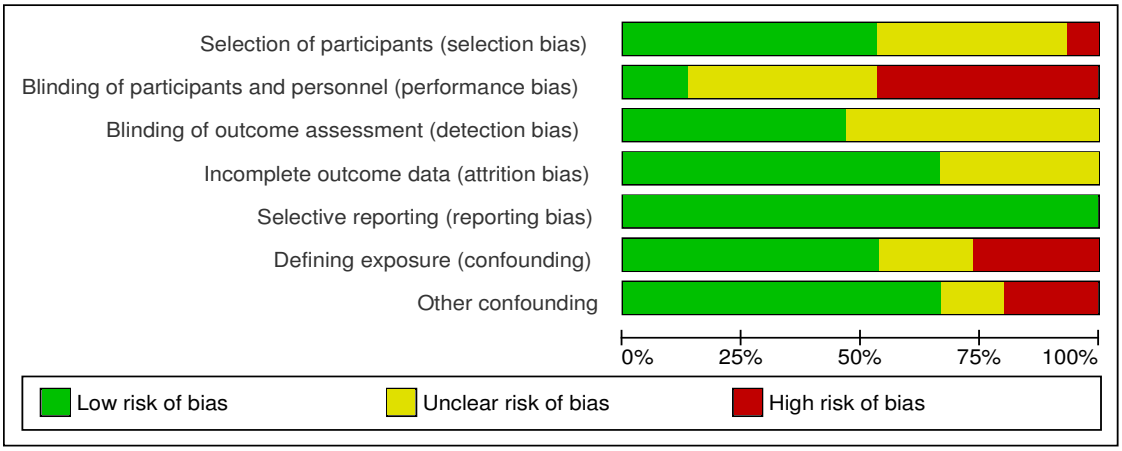


OSM 5: Risk of bias graph

Risk of bias graph: RCTs reporting blood pressure, renal function, blood lipids, or catecholamine levels in adults



Risk of bias graph: Cohort studies reporting all-cause mortality, cardiovascular disease, stroke, or coronary heart disease in adults



Risk of bias graph: Controlled-trials and one cohort study reporting blood pressure in children