The Science Behind Sodium Reduction
Key Scientific Abstracts Highlighting the Importance of Sodium Reduction

Aburto NJ, Ziolkovska A, Hooper L, et al. Effect of lower sodium intake on health: systematic review and meta-analyses. BMJ 2013;346:f1326.

OBJECTIVE:
To assess the effect of decreased sodium intake on blood pressure, related cardiovascular diseases, and potential adverse effects such as changes in blood lipids, catecholamine levels, and renal function.

DESIGN:
Systematic review and meta-analysis.

DATA SOURCES:
Cochrane Central Register of Controlled Trials, Medline, Embase, WHO International Clinical Trials Registry Platform, the Latin American and Caribbean health science literature database, and the reference lists of previous reviews.

STUDY SELECTION:
Randomised controlled trials and prospective cohort studies in non-acutely ill adults and children assessing the relations between sodium intake and blood pressure, renal function, blood lipids, and catecholamine levels, and in non-acutely ill adults all cause mortality, cardiovascular disease, stroke, and coronary heart disease.

STUDY APPRAISAL AND SYNTHESIS:
Potential studies were screened independently and in duplicate and study characteristics and outcomes extracted. When possible we conducted a meta-analysis to estimate the effect of lower sodium intake using the inverse variance method and a random effects model. We present results as mean differences or risk ratios, with 95% confidence intervals.

RESULTS:
We included 14 cohort studies and five randomised controlled trials reporting all cause mortality, cardiovascular disease, stroke, or coronary heart disease; and 37 randomised controlled trials measuring blood pressure, renal function, blood lipids, and catecholamine levels in adults. Nine controlled trials and one cohort study in children reporting on blood pressure were also included. In adults a reduction in sodium intake significantly reduced resting systolic blood pressure by 3.39 mm Hg (95% confidence interval 2.46 to 4.31) and resting diastolic blood pressure by 1.54 mm Hg (0.98 to 2.11). When sodium intake was <2 g/day versus ≥ 2 g/day, systolic blood pressure was reduced by 3.47 mm Hg (0.76 to 6.18) and diastolic blood pressure by 1.81 mm Hg (0.54 to 3.08). Decreased sodium intake had no significant adverse effect on blood lipids, catecholamine levels, or renal function in adults (P>0.05). There were insufficient randomised controlled trials to assess the effects of reduced sodium intake on mortality and morbidity. The associations in cohort studies between sodium intake and all cause mortality, incident fatal and non-fatal cardiovascular disease, and coronary heart disease were non-significant (P>0.05). Increased sodium intake was associated with an increased risk of stroke (risk ratio 1.24, 95% confidence interval 1.08 to 1.43), stroke mortality (1.63, 1.27 to 2.10), and coronary heart disease mortality (1.32, 1.13 to 1.53). In children, a reduction in sodium intake significantly reduced systolic blood pressure by 0.84 mm Hg (0.25 to 1.43) and diastolic blood pressure by 0.87 mm Hg (0.14 to 1.60).

CONCLUSIONS:
High quality evidence in non-acutely ill adults shows that reduced sodium intake reduces blood pressure and has no adverse effect on blood lipids, catecholamine levels, or renal function, and moderate quality evidence in children shows that a reduction in sodium intake reduces blood pressure. Lower sodium intake is also associated with a reduced risk of stroke and fatal coronary heart disease in adults. The totality of evidence suggests that most people will likely benefit from reducing sodium intake.

Adler AJ, Taylor F, Martin N, Gottlieb S, Taylor RS, Ebrahim S. Reduced dietary salt for the prevention of cardiovascular disease. Cochrane Database of Systematic Reviews 2014, Issue 12. Art. No.: CD009217. DOI: 10.1002/14651858.CD009217.pub3.

BACKGROUND:
This is an update of a Cochrane review that was first published in 2011 of the effects of reducing dietary salt intake, through advice to reduce salt intake or low-sodium salt substitution, on mortality and cardiovascular events.

OBJECTIVES:
1. To assess the long-term effects of advice and salt substitution, aimed at reducing dietary salt, on mortality and cardiovascular morbidity.2. To investigate whether a reduction in blood pressure is an explanatory factor in the effect of such dietary interventions on mortality and cardiovascular outcomes.

SEARCH METHODS:
We updated the searches of CENTRAL (2013, Issue 4), MEDLINE (OVID, 1946 to April week 3 2013), EMBASE (OVID, 1947 to 30 April 2013) and CINAHL (EBSCO, inception to 1 April 2013) and last ran these on 1 May 2013. We also checked the references of included studies and reviews. We applied no language restrictions.

SELECTION CRITERIA:
Trials fulfilled the following criteria: (1) randomised, with follow-up of at least six months, (2) the intervention was reduced dietary salt (through advice to reduce salt intake or low-sodium salt substitution), (3) participants were adults and (4) mortality or cardiovascular morbidity data were available. Two review authors independently assessed whether studies met these criteria.

DATA COLLECTION AND ANALYSIS:
A single author extracted data and assessed study validity, and a second author checked this. We contacted trial authors where possible to obtain missing information. We extracted events and calculated risk ratios (RRs) and 95% confidence intervals (CIs).

MAIN RESULTS:
Eight studies met the inclusion criteria: three in normotensives (n = 3518) and five in hypertensives or mixed populations of normo- and hypertensives (n = 3766). End of trial follow-up ranged from six to 36 months and the longest observational follow-up (after trial end) was 12.7 years.The risk ratios (RR) for all-cause mortality in normotensives were imprecise and showed no evidence of reduction (end of trial RR 0.67, 95% confidence interval (CI) 0.40 to 1.12, 60 deaths; longest follow-up RR 0.90, 95% CI 0.58 to 1.40, 79 deaths n=3518) or in hypertensives (end of trial RR 1.00, 95% CI 0.86 to 1.15, 565 deaths; longest follow-up RR 0.99, 95% CI 0.87 to 1.14, 674 deaths n=3085). There was weak evidence of benefit for cardiovascular mortality (hypertensives: end of trial RR 0.67, 95% CI 0.45 to 1.01, 106 events n=2656) and for cardiovascular events (hypertensives: end of trial RR 0.76, 95% CI 0.57 to 1.01,

194 events, four studies, n = 3397; normotensives: at longest follow-up RR 0.71, 95% CI 0.42 to 1.20, 200 events; hypertensives: RR 0.77, 95% CI 0.57 to 1.02, 192 events; pooled analysis of six trials RR 0.77, 95% CI 0.63 to 0.95, n = 5912). These findings were driven by one trial among retirement home residents that reduced salt intake in the kitchens of the homes, thereby not requiring individual behaviour change.Advice to reduce salt showed small reductions in systolic blood pressure (mean difference (MD) -1.15 mmHg, 95% CI -2.32 to 0.02 n=2079) and diastolic blood pressure (MD -0.80 mmHg, 95% CI -1.37 to -0.23 n=2079) in normotensives and greater reductions in systolic blood pressure in hypertensives (MD -4.14 mmHg, 95% CI -5.84 to -2.43 n=675), but no difference in diastolic blood pressure (MD -3.74 mmHg, 95% CI -8.41 to 0.93 n=675).Overall many of the trials failed to report sufficient detail to assess their potential risk of bias. Health-related quality of life was assessed in one trial in normotensives, which reported significant improvements in well-being but no data were presented.

AUTHORS' CONCLUSIONS:
Despite collating more event data than previous systematic reviews of randomised controlled trials, there is insufficient power to confirm clinically important effects of dietary advice and salt substitution on cardiovascular mortality in normotensive or hypertensive populations. Our estimates of the clinical benefits from advice to reduce dietary salt are imprecise, but are larger than would be predicted from the small blood pressure reductions achieved. Further well-powered studies would be needed to obtain more precise estimates. Our findings do not support individual dietary advice as a means of restricting salt intake. It is possible that alternative strategies that do not require individual behaviour change may be effective and merit further trials.

Bibbins-Domingo K, Chertow GM, Coxson PG, et al. Projected effect of dietary salt reductions on future cardiovascular disease. N Engl J Med 2010;362:590-9.

BACKGROUND:
The U.S. diet is high in salt, with the majority coming from processed foods. Reducing dietary salt is a potentially important target for the improvement of public health.

METHODS:
We used the Coronary Heart Disease (CHD) Policy Model to quantify the benefits of potentially achievable, population-wide reductions in dietary salt of up to 3 g per day (1200 mg of sodium per day). We estimated the rates and costs of cardiovascular disease in subgroups defined by age, sex, and race; compared the effects of salt reduction with those of other interventions intended to reduce the risk of cardiovascular disease; and determined the cost-effectiveness of salt reduction as compared with the treatment of hypertension with medications.

RESULTS:
Reducing dietary salt by 3 g per day is projected to reduce the annual number of new cases of CHD by 60,000 to 120,000, stroke by 32,000 to 66,000, and myocardial infarction by 54,000 to 99,000 and to reduce the annual number of deaths from any cause by 44,000 to 92,000. All segments of the population would benefit, with blacks benefiting proportionately more, women benefiting particularly from stroke reduction, older adults from reductions in CHD events, and younger adults from lower mortality rates. The cardiovascular benefits of reduced salt intake are on par with the benefits of population-wide reductions in tobacco use, obesity, and cholesterol levels. A regulatory intervention designed to achieve a reduction in salt intake of 3 g per day would save 194,000 to 392,000 quality-adjusted life-years and $10 billion to $24 billion in health care costs annually. Such an intervention would be cost-saving even

if only a modest reduction of 1 g per day were achieved gradually between 2010 and 2019 and would be more cost-effective than using medications to lower blood pressure in all persons with hypertension.
CONCLUSIONS:
Modest reductions in dietary salt could substantially reduce cardiovascular events and medical costs and should be a public health target.

Cook NR, Appel LJ, Whelton PK. Lower levels of sodium intake and reduced cardiovascular risk. Circulation 2014;129:981-9.

BACKGROUND:
Recent studies have raised the possibility of adverse effects of low sodium, particularly <2300 mg/d, on cardiovascular disease; however, these paradoxical findings might have resulted from suboptimal measurement of sodium and potential biases related to indication or reverse causation.

METHODS AND RESULTS:
Phases 1 and 2 of the Trials of Hypertension Prevention (TOHP) collected multiple 24-hour urine specimens among prehypertensive individuals. During extended post-trial surveillance, 193 cardiovascular events or cardiovascular disease deaths occurred among 2275 participants not in a sodium reduction intervention with 10 (TOHP II) or 15 (TOHP I) years of post-trial follow-up. Median sodium excretion was 3630 mg/d, with 1.4% of the participants having intake <1500 mg/d and 10% <2300 mg/d, consistent with national levels. Compared with those with sodium excretion of 3600 to <4800 mg/d, risk for those with sodium <2300 mg/d was 32% lower after multivariable adjustment (hazard ratio, 0.68; 95% confidence interval, 0.34-1.37; P for trend=0.13). There was a linear 17% increase in risk per 1000 mg/d increase in sodium (P=0.05). Spline curves supported a linear association of sodium with cardiovascular events, which continued to decrease from 3600 to 2300 and 1500 mg/d, although the data were sparse at the lowest levels. Controlling for creatinine levels had little effect on these results.

CONCLUSIONS:
Results from the TOHP studies, which overcome the major methodological challenges of prior studies, are consistent with overall health benefits of reducing sodium intake to the 1500 to 2300 mg/d range in the majority of the population, in agreement with current dietary guidelines.

Cook NR, Cutler JA, Obarzanek E, Buring JE, Rexrode KM, Kumanyika SK. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). BMJ 2007;334:885–8.

OBJECTIVE:
To examine the effects of reduction in dietary sodium intake on cardiovascular events using data from two completed randomised trials, TOHP I and TOHP II.

DESIGN:
Long term follow-up assessed 10-15 years after the original trial.

SETTING:
10 clinic sites in 1987-90 (TOHP I) and nine sites in 1990-5 (TOHP II). Central follow-up conducted by post and phone.

PARTICIPANTS:
Adults aged 30-54 years with prehypertension.

INTERVENTION:
Dietary sodium reduction, including comprehensive education and counselling on reducing intake, for 18 months (TOHP I) or 36-48 months (TOHP II).

MAIN OUTCOME MEASURE:
Cardiovascular disease (myocardial infarction, stroke, coronary revascularisation, or cardiovascular death).

RESULTS:
744 participants in TOHP I and 2382 in TOHP II were randomised to a sodium reduction intervention or control. Net sodium reductions in the intervention groups were 44 mmol/24 h and 33 mmol/24 h, respectively. Vital status was obtained for all participants and follow-up information on morbidity was obtained from 2415 (77%), with 200 reporting a cardiovascular event. Risk of a cardiovascular event was 25% lower among those in the intervention group (relative risk 0.75, 95% confidence interval 0.57 to 0.99, P=0.04), adjusted for trial, clinic, age, race, and sex, and 30% lower after further adjustment for baseline sodium excretion and weight (0.70, 0.53 to 0.94), with similar results in each trial. In secondary analyses, 67 participants died (0.80, 0.51 to 1.26, P=0.34).

CONCLUSION:
Sodium reduction, previously shown to lower blood pressure, may also reduce long term risk of cardiovascular events.

Coxson PG, Cook NR, Joffres M, et al. Mortality benefits from US population wide reduction in sodium consumption: projections from 3 modeling approaches. Hypertension 2013;61:564-70.

Computer simulations have been used to estimate the mortality benefits from population-wide reductions in dietary sodium, although comparisons of these estimates have not been rigorously evaluated. We used 3 different approaches to model the effect of sodium reduction in the US population over the next 10 years, incorporating evidence for direct effects on cardiovascular disease mortality (method 1), indirect effects mediated by blood pressure changes as observed in randomized controlled trials of antihypertension medications (method 2), or epidemiological studies (method 3).The 3 different modeling approaches were used to model the same scenarios: scenario A, gradual uniform reduction totaling 40% over 10 years; scenario B, instantaneous 40% reduction in sodium consumption sustained for 10 years to achieve a population-wide mean of 2200 mg/d; and scenario C, instantaneous reduction to 1500 mg sodium per day sustained for 10 years. All 3 methods consistently show a substantial health benefit for reductions in dietary sodium under each of the 3 scenarios tested. A gradual reduction in dietary sodium over the next decade (scenario A) as might be achieved with a range of proposed public health interventions would yield considerable health benefits over the next decade, with mean effects across the 3 models ranging from 280 000 to 500 000 deaths averted. Projections of instantaneous reductions illustrate the maximum benefits that could be achieved (0.7-1.2 million deaths averted in 10 years). Under 3 different modeling assumptions, the projected health benefits from reductions in dietary sodium are substantial.

Elliott P, Stamler J, Nichols R, Dyer AR, Stamler R, Kesteloot H, Marmot M. INTERSALT revisited: Further analyses of 24 hour sodium excretion and blood pressure within and across populations. BMJ 1996;312:1249-53.

OBJECTIVES:
To assess further the relation in Intersalt of 24 hour urinary sodium to blood pressure of individuals and populations, and the difference in blood pressure from young adulthood into middle age.

DESIGN:
Standardised cross sectional study within and across populations.

SETTING:
52 population samples in 32 countries.
SUBJECTS:
10,074 men and women aged 20-59.

MAIN OUTCOME MEASURES:
Association of sodium and blood pressure from within population and cross population multiple linear regression analyses with multivariate correction for regression dilution bias. Relation of sample median daily urinary sodium excretion to difference in blood pressure with age.

RESULTS:
In within population analyses (n = 10,074), individual 24 hour urinary sodium excretion higher by 100 mmol (for example, 170 v 70 mmol) was associated with systolic/diastolic blood pressure higher on average by 3/0 to 6/3 mm Hg (with and without body mass in analyses). Associations were larger at ages 40-59. In cross population analyses (n = 52), sample median 24 hour sodium excretion higher by 100 mmol was associated with median systolic/diastolic pressure higher on average by 5-7/2-4 mm Hg, and estimated mean difference in systolic/diastolic pressure at age 55 compared with age 25 greater by 10-11/6 mm Hg.

CONCLUSIONS:
The strong, positive association of urinary sodium with systolic pressure of individuals concurs with Intersalt cross population findings and results of other studies. Higher urinary sodium is also associated with substantially greater differences in blood pressure in middle age compared with young adulthood. These results support recommendations for reduction of high salt intake in populations for prevention and control of adverse blood pressure levels.

Emdin CA, Rahimi K, Neal B, Callender T, Perkovic V, Patel A. Blood Pressure Lowering in Type 2 Diabetes. A Systematic Review and Meta-analysis. JAMA. 2015;313(6):603-615.

IMPORTANCE:
Lowering blood pressure (BP) is widely used to reduce vascular risk in individuals with diabetes.

OBJECTIVE:
To determine the associations between BP-lowering treatment and vascular disease in type 2 diabetes.

DATA SOURCES AND STUDY SELECTION:
We searched MEDLINE for large-scale randomized controlled trials of BP-lowering treatment including patients with diabetes, published between January 1966 and October 2014.

DATA EXTRACTION AND SYNTHESIS:
Two reviewers independently extracted study characteristics and vascular outcome data. Estimates were stratified by baseline BP and achieved BP, and pooled using fixed-effects meta-analysis.

MAIN OUTCOMES AND MEASURES:
All-cause mortality, cardiovascular events, coronary heart disease events, stroke, heart failure, retinopathy, new or worsening albuminuria, and renal failure.

RESULTS:
Forty trials judged to be of low risk of bias (100,354 participants) were included. Each 10-mm Hg lower systolic BP was associated with a significantly lower risk of mortality (relative risk [RR], 0.87; 95% CI, 0.78-0.96); absolute risk reduction (ARR) in events per 1000 patient-years (3.16; 95% CI, 0.90-5.22), cardiovascular events (RR, 0.89 [95% CI, 0.83-0.95]; ARR, 3.90 [95% CI, 1.57-6.06]), coronary heart disease (RR, 0.88 [95% CI, 0.80-0.98]; ARR, 1.81 [95% CI, 0.35-3.11]), stroke (RR, 0.73 [95% CI, 0.64-0.83]; ARR, 4.06 [95% CI, 2.53-5.40]), albuminuria (RR, 0.83 [95% CI, 0.79-0.87]; ARR, 9.33 [95% CI, 7.13-11.37]), and retinopathy (RR, 0.87 [95% CI, 0.76-0.99]; ARR, 2.23 [95% CI, 0.15-4.04]). When trials were stratified by mean baseline systolic BP at greater than or less than 140 mm Hg, RRs for outcomes other than stroke, retinopathy, and renal failure were lower in studies with greater baseline systolic BP (P interaction <0.1). The associations between BP-lowering treatments and outcomes were not significantly different, irrespective of drug class, except for stroke and heart failure. Estimates were similar when all trials, regardless of risk of bias, were included.

CONCLUSIONS AND RELEVANCE:
Among patients with type 2 diabetes, BP lowering was associated with improved mortality and other clinical outcomes with lower RRs observed among those with baseline BP of 140 mm Hg and greater. These findings support the use of medications for BP lowering in these patients.

Ettehad D, Emdin CA, Kiran A, et al. Blood pressure lowering for prevention of cardiovascular disease and death: a systematic review and meta-analysis. Lancet 2016; 387: 957–67.

BACKGROUND:
The benefits of blood pressure lowering treatment for prevention of cardiovascular disease are well established. However, the extent to which these effects differ by baseline blood pressure, presence of comorbidities, or drug class is less clear. We therefore performed a systematic review and meta-analysis to clarify these differences.

METHOD:
For this systematic review and meta-analysis, we searched MEDLINE for large-scale blood pressure lowering trials, published between Jan 1, 1966, and July 7, 2015, and we searched the medical literature to identify trials up to Nov 9, 2015. All randomised controlled trials of blood pressure lowering treatment were eligible for inclusion if they included a minimum of 1000 patient-years of follow-up in each study arm. No trials were excluded because of presence of baseline comorbidities, and trials of antihypertensive drugs for indications other than hypertension were eligible. We extracted summary-

level data about study characteristics and the outcomes of major cardiovascular disease events, coronary heart disease, stroke, heart failure, renal failure, and all-cause mortality. We used inverse variance weighted fixed-effects meta-analyses to pool the estimates.

RESULTS:
We identified 123 studies with 613,815 participants for the tabular meta-analysis. Meta-regression analyses showed relative risk reductions proportional to the magnitude of the blood pressure reductions achieved. Every 10 mm Hg reduction in systolic blood pressure significantly reduced the risk of major cardiovascular disease events (relative risk [RR] 0·80, 95% CI 0·77-0·83), coronary heart disease (0·83, 0·78-0·88), stroke (0·73, 0·68-0·77), and heart failure (0·72, 0·67-0·78), which, in the populations studied, led to a significant 13% reduction in all-cause mortality (0·87, 0·84-0·91). However, the effect on renal failure was not significant (0·95, 0·84-1·07). Similar proportional risk reductions (per 10 mm Hg lower systolic blood pressure) were noted in trials with higher mean baseline systolic blood pressure and trials with lower mean baseline systolic blood pressure (all ptrend>0·05). There was no clear evidence that proportional risk reductions in major cardiovascular disease differed by baseline disease history, except for diabetes and chronic kidney disease, for which smaller, but significant, risk reductions were detected. β blockers were inferior to other drugs for the prevention of major cardiovascular disease events, stroke, and renal failure. Calcium channel blockers were superior to other drugs for the prevention of stroke. For the prevention of heart failure, calcium channel blockers were inferior and diuretics were superior to other drug classes. Risk of bias was judged to be low for 113 trials and unclear for 10 trials. Heterogeneity for outcomes was low to moderate; the I(2) statistic for heterogeneity for major cardiovascular disease events was 41%, for coronary heart disease 25%, for stroke 26%, for heart failure 37%, for renal failure 28%, and for all-cause mortality 35%.

INTERPRETATION:
Blood pressure lowering significantly reduces vascular risk across various baseline blood pressure levels and comorbidities. Our results provide strong support for lowering blood pressure to systolic blood pressures less than 130 mm Hg and providing blood pressure lowering treatment to individuals with a history of cardiovascular disease, coronary heart disease, stroke, diabetes, heart failure, and chronic kidney disease.

FUNDING:
National Institute for Health Research and Oxford Martin School.

Farquhar WB, Edwards DG, Jurkovitz CT, Weintraub WS. Dietary sodium and health. More than just blood pressure. J Am Coll Cardiol 2015;65(10):1042-50.

Sodium is essential for cellular homeostasis and physiological function. Excess dietary sodium has been linked to elevations in blood pressure (BP). Salt sensitivity of BP varies widely, but certain subgroups tend to be more salt sensitive. The mechanisms underlying sodium-induced increases in BP are not completely understood but may involve alterations in renal function, fluid volume, fluid-regulatory hormones, the vasculature, cardiac function, and the autonomic nervous system. Recent pre-clinical and clinical data support that even in the absence of an increase in BP, excess dietary sodium can adversely affect target organs, including the blood vessels, heart, kidneys, and brain. In this review, the investigators review these issues and the epidemiological research relating dietary sodium to BP and cardiovascular health outcomes, addressing recent controversies. They also provide information and strategies for reducing dietary sodium.

He FJ, Li J,MacGregor GA. Effect of longer-term modest salt reduction on blood pressure. Cochrane Database of Systematic Reviews 2013, Issue 4. Art. No.: CD004937. DOI: 10.1002/14651858.CD004937.pub2.

BACKGROUND:
A reduction in salt intake lowers blood pressure (BP) and, thereby, reduces cardiovascular risk. A recent meta-analysis by Graudal implied that salt reduction had adverse effects on hormones and lipids which might mitigate any benefit that occurs with BP reduction. However, Graudal's meta-analysis included a large number of very short-term trials with a large change in salt intake, and such studies are irrelevant to the public health recommendations for a longer-term modest reduction in salt intake. We have updated our Cochrane meta-analysis.

OBJECTIVES:
To assess (1) the effect of a longer-term modest reduction in salt intake (i.e. of public health relevance) on BP and whether there was a dose-response relationship; (2) the effect on BP by sex and ethnic group; (3) the effect on plasma renin activity, aldosterone, noradrenaline, adrenaline, cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglycerides.

SEARCH METHODS:
We searched MEDLINE, EMBASE, Cochrane Hypertension Group Specialised Register, Cochrane Central Register of Controlled Trials, and reference list of relevant articles.

SELECTION CRITERIA:
We included randomised trials with a modest reduction in salt intake and duration of at least 4 weeks.

DATA COLLECTION AND ANALYSIS:
Data were extracted independently by two reviewers. Random effects meta-analyses, subgroup analyses and meta-regression were performed.

MAIN RESULTS:
Thirty-four trials (3230 participants) were included. Meta-analysis showed that the mean change in urinary sodium (reduced salt vs usual salt) was -75 mmol/24-h (equivalent to a reduction of 4.4 g/d salt), the mean change in BP was -4.18 mmHg (95% CI: -5.18 to -3.18, I (2)=75%) for systolic and -2.06 mmHg (95% CI: -2.67 to -1.45, I (2)=68%) for diastolic BP. Meta-regression showed that age, ethnic group, BP status (hypertensive or normotensive) and the change in 24-h urinary sodium were all significantly associated with the fall in systolic BP, explaining 68% of the variance between studies. A 100 mmol reduction in 24 hour urinary sodium (6 g/day salt) was associated with a fall in systolic BP of 5.8 mmHg (95%CI: 2.5 to 9.2, P=0.001) after adjusting for age, ethnic group and BP status. For diastolic BP, age, ethnic group, BP status and the change in 24-h urinary sodium explained 41% of the variance between studies. Meta-analysis by subgroup showed that, in hypertensives, the mean effect was -5.39 mmHg (95% CI: -6.62 to -4.15, I (2)=61%) for systolic and -2.82 mmHg (95% CI: -3.54 to -2.11, I (2)=52%) for diastolic BP. In normotensives, the mean effect was -2.42 mmHg (95% CI: -3.56 to -1.29, I (2)=66%) for systolic and -1.00 mmHg (95% CI: -1.85 to -0.15, I (2)=66%) for diastolic BP. Further subgroup analysis showed that the decrease in systolic BP was significant in both whites and blacks, men and women. Meta-analysis of hormone and lipid data showed that the mean effect was 0.26 ng/ml/hr (95% CI: 0.17 to 0.36, I (2)=70%) for plasma renin activity, 73.20 pmol/l (95% CI: 44.92 to 101.48, I (2)=62%) for aldosterone, 31.67 pg/ml (95% CI: 6.57 to 56.77, I (2)=5%) for noradrenaline, 6.70 pg/ml (95% CI: -0.25 to 13.64, I (2)=12%) for adrenaline, 0.05 mmol/l (95% CI: -0.02 to 0.11, I

(2)=0%) for cholesterol, 0.05 mmol/l (95% CI: -0.01 to 0.12, I (2)=0%) for LDL, -0.02 mmol/l (95% CI: -0.06 to 0.01, I (2)=16%) for HDL, and 0.04 mmol/l (95% CI: -0.02 to 0.09, I (2)=0%) for triglycerides.

AUTHORS' CONCLUSIONS:
A modest reduction in salt intake for 4 or more weeks causes significant and, from a population viewpoint, important falls in BP in both hypertensive and normotensive individuals, irrespective of sex and ethnic group. With salt reduction, there is a small physiological increase in plasma renin activity, aldosterone and noradrenaline. There is no significant change in lipid levels. These results provide further strong support for a reduction in population salt intake. This will likely lower population BP and, thereby, reduce cardiovascular disease. Additionally, our analysis demonstrates a significant association between the reduction in 24-h urinary sodium and the fall in systolic BP, indicating the greater the reduction in salt intake, the greater the fall in systolic BP. The current recommendations to reduce salt intake from 9-12 to 5-6 g/d will have a major effect on BP, but are not ideal. A further reduction to 3 g/d will have a greater effect and should become the long term target for population salt intake.

He FJ, MacGregor GA. Salt reduction lowers cardiovascular risk: meta-analysis of outcome trials. The Lancet 2011; 378 (July 30):380-1. PMID: 21803192

No Abstract Available.

He FJ, Pombo-Rodrigues S, MacGregor GA. Salt reduction in England from 2003 to 2011: its relationship to blood pressure, stroke, and ischaemic heart disease mortality. BMJ Open 2014;4: e004549.

OBJECTIVES:
To determine the relationship between the reduction in salt intake that occurred in England, and blood pressure (BP), as well as mortality from stroke and ischaemic heart disease (IHD).

DESIGN:
Analysis of the data from the Health Survey for England.

SETTING AND PARTICIPANTS:
England, 2003 N=9183, 2006 N=8762, 2008 N=8974 and 2011 N=4753, aged ≥16 years.

OUTCOMES:
BP, stroke and IHD mortality.

RESULTS:
From 2003 to 2011, there was a decrease in mortality from stroke by 42% (p<0.001) and IHD by 40% (p<0.001). In parallel, there was a fall in BP of 3.0±0.33/1.4±0.20 mm Hg (p<0.001/p<0.001), a decrease of 0.4±0.02 mmol/L (p<0.001) in cholesterol, a reduction in smoking prevalence from 19% to 14% (p<0.001), an increase in fruit and vegetable consumption (0.2±0.05 portion/day, p<0.001) and an increase in body mass index (BMI; 0.5±0.09 kg/m(2), p<0.001). Salt intake, as measured by 24 h urinary sodium, decreased by 1.4 g/day (p<0.01). It is likely that all of these factors (with the exception of BMI), along with improvements in the treatments of BP, cholesterol and cardiovascular disease, contributed to the falls in stroke and IHD mortality. In individuals who were not on antihypertensive medication, there was a fall in BP of 2.7±0.34/1.1±0.23 mm Hg (p<0.001/p<0.001) after adjusting for age, sex, ethnic group, education, household income, alcohol consumption, fruit and vegetable intake

and BMI. Although salt intake was not measured in these participants, the fact that the average salt intake in a random sample of the population fell by 15% during the same period suggests that the falls in BP would be largely attributable to the reduction in salt intake rather than antihypertensive medications.

CONCLUSIONS:
The reduction in salt intake is likely to be an important contributor to the falls in BP from 2003 to 2011 in England. As a result, it would have contributed substantially to the decreases in stroke and IHD mortality.

Johnson C, Raj TS, Trudeau L, et al. The science of salt: a systematic review of clinical salt studies 2013 to 2014. J Clin Hypertens (Greenwich) 2015;17:401–11.

The authors provided a systematic review of the clinical and population health impact of increased dietary salt intake during 1 year. Randomized controlled trials or cohort studies or meta-analyses on the effect of sodium intake were examined from Medline searches between June 2013 to May 2014. Quality indicators were used to select studies that were relevant to clinical and public health. A total of 213 studies were reviewed, of which 11 (n=186,357) were eligible. These studies confirmed a causal relationship between increasing dietary salt and increased blood pressure and an association between several adverse health outcomes and increased dietary salt. A new association between salt intake and renal cell cancer was published. No study that met inclusion criteria found harm from lowering dietary salt. The findings of this systematic review are consistent with previous data relating increased dietary salt to increased blood pressure and adverse health outcomes.

Karppanen H, Mervaala E. Sodium intake and hypertension. Prog Cardiovasc Dis 2006;49:59-75. Review.

In current diets, the level of sodium is very high, whereas that of potassium, calcium, and magnesium is low compared with the level in diets composed of unprocessed, natural foods. We present the biologic rationale and scientific evidence that show that the current salt intake levels largely explain the high prevalence of hypertension. Comprehensive reduction of salt intake, both alone and particularly in combination with increases in intakes of potassium, calcium, and magnesium, is able to lower average blood pressure levels substantially. During the past 30 years, the one-third decrease in the average salt intake has been accompanied by a more than 10-mm Hg fall in the population average of both systolic and diastolic blood pressure, and a 75% to 80% decrease in both stroke and coronary heart disease mortality in Finland. There is no evidence of any harmful effects of salt reduction. Salt-reduction recommendations alone have a very small, if any, population impact. In the United States, for example, the per capita use of salt increased by approximately 55% from the mid-1980s to the late 1990s. We deal with factors that contribute toward increasing salt intakes and present examples of the methods that have contributed to the successful salt reduction in Finland.

Macgregor GA, Sagnella GA, Markandu ND, Singer DRG, Cappuccio FP. Double-blind study of three sodium intakes and long-term effects of sodium restriction in essential hypertension. Lancet 1989;2(8674):1244-7.

20 patients with mild hypertension (average supine blood pressure without treatment, 164/101 mm Hg) reduced their salt intake to 50 mmol (3 g) per day for a month. They then entered a 3 month double-blind randomised crossover study of three levels of sodium intake: 200, 100, and 50 mmol per day.

Blood pressure was significantly reduced on the middle and lowest sodium intakes. The average fall in blood pressure from the highest to the lowest sodium intake was 16/9 mm Hg. Patients continued to restrict their sodium intake for a further year. In 16 of the 20 patients blood pressure remained well controlled with salt restriction alone. Supine blood pressure at 1 year was 142/87 (SE 3/2) mm Hg with a 24 h urinary sodium excretion of 54 (7) mmol. These results show a progressive blood pressure fall as salt intake is reduced and that, in many patients with mild essential hypertension, blood pressure can be controlled without the need for drug therapy.

McMahon EJ, Campbell KL, Bauer JD, Mudge DW. Altered dietary salt intake for people with chronic kidney disease. Cochrane Database of Systematic Reviews 2015, Issue 2. Art. No.: CD010070. doi: 10.1002/14651858.CD010070.pub2.

BACKGROUND:
Salt intake shows great promise as a modifiable risk factor for reducing heart disease incidence and delaying kidney function decline in people with chronic kidney disease (CKD). However, a clear consensus of the benefits of reducing salt in people with CKD is lacking.

OBJECTIVES:
This review evaluated the benefits and harms of altering dietary salt intake in people with CKD.
SEARCH METHODS:
We searched the Cochrane Renal Group's Specialised Register to 13 January 2015 through contact with the Trials' Search Co-ordinator using search terms relevant to this review.

SELECTION CRITERIA:
We included randomised controlled trials (RCTs) that compared two or more levels of salt intake in people with any stage of CKD.

DATA COLLECTION AND ANALYSIS:
Two authors independently assessed studies for eligibility and conducted risk of bias evaluation. Results were expressed as risk ratios (RR) and their 95% confidence intervals (CI) for dichotomous outcomes, and mean difference (MD) and 95% CI for continuous outcomes. Mean effect sizes were calculated using the random-effects models.

MAIN RESULTS:
We included eight studies (24 reports, 258 participants). Because duration of the included studies was too short (1 to 26 weeks) to test the effect of salt restriction on endpoints such as mortality, cardiovascular events or CKD progression, changes in salt intake on blood pressure and other secondary risk factors were applied. Three studies were parallel RCTs and five were cross-over studies. Selection bias was low in five studies and unclear in three. Performance and detection biases were low in two studies and unclear in six. Attrition and reporting biases were low in four studies and unclear in four. One study had the potential for high carryover effect; three had high risk of bias from baseline characteristics (change of medication or diet) and two studies were industry funded. There was a significant reduction in 24 hour sodium excretion associated with low salt interventions (range 52 to 141 mmol) (8 studies, 258 participants: MD -105.86 mmol/d, 95% CI -119.20 to -92.51; I(2) = 51%). Reducing salt intake significantly reduced systolic blood pressure (8 studies, 258 participants: MD -8.75 mm Hg, 95% CI -11.33 to -6.16; I(2) = 0%) and diastolic blood pressure (8 studies, 258 participants: MD -3.70 mm Hg, 95% CI -5.09 to -2.30; I(2) = 0%). One study reported restricting salt intake reduced the risk of oedema by 56%. Salt restriction significantly increased plasma renin activity (2 studies, 71

participants: MD 1.08 ng/mL/h, 95% CI 0.51 to 1.65; I(2) = 0%) and serum aldosterone (2 studies, 71 participants: 6.20 ng/dL (95% CI 3.82 to 8.58; I(2) = 0%). Antihypertensive medication dosage was significantly reduced with a low salt diet (2 studies, 52 participants): RR 5.48, 95% CI 1.27 to 23.66; I(2) = 0%). There was no significant difference in eGFR (2 studies, 68 participants: MD -1.14 mL/min/1.73 m(2), 95% CI -4.38 to 2.11; I(2) = 0%), creatinine clearance (3 studies, 85 participants): MD -4.60 mL/min, 95% CI -11.78 to 2.57; I(2) = 0%), serum creatinine (5 studies, 151 participants: MD 5.14 µmol/L, 95% CI -8.98 to 19.26; I(2) = 59%) or body weight (5 studies, 139 participants: MD -1.46 kg; 95% CI -4.55 to 1.64; I(2) = 0%). There was no significant change in total cholesterol in relation to salt restriction (3 studies, 105 participants: MD -0.23 mmol/L, 95% CI -0.57 to 0.10; I(2) = 0%) or symptomatic hypotension (2 studies, 72 participants: RR 6.60, 95% CI 0.77 to 56.55; I(2) = 0%). Salt restriction significantly reduced urinary protein excretion in all studies that reported proteinuria as an outcome, however data could not be meta-analysed.

AUTHORS' CONCLUSIONS:
We found a critical evidence gap in long-term effects of salt restriction in people with CKD that meant we were unable to determine the direct effects of sodium restriction on primary endpoints such as mortality and progression to end-stage kidney disease (ESKD). We found that salt reduction in people with CKD reduced blood pressure considerably and consistently reduced proteinuria. If such reductions could be maintained long-term, this effect may translate to clinically significant reductions in ESKD incidence and cardiovascular events. Research into the long-term effects of sodium-restricted diet for people with CKD is warranted, as is investigation into adherence to a low salt diet.

Mills KT, Chen J, Appel LJ, Kusek JW, Alper A, Delafontaine P, et al, for the Chronic Renal Insufficiency Cohort (CRIC) Study Investigators. Sodium Excretion and the Risk of Cardiovascular Disease in Patients with Chronic Kidney Disease. JAMA 2016; 315(20):2200-2210.

IMPORTANCE:
Patients with chronic kidney disease (CKD) are at an increased risk of cardiovascular disease (CVD) compared with the general population. Prior studies have produced contradictory results on the association of dietary sodium intake with risk of CVD, and this relationship has not been investigated in patients with CKD.

OBJECTIVE:
To evaluate the association between urinary sodium excretion and clinical CVD events among patients with CKD.

DESIGN, SETTING, AND PARTICIPANTS:
A prospective cohort study of patients with CKD from 7 locations in the United States enrolled in the Chronic Renal Insufficiency Cohort Study and followed up from May 2003 to March 2013.

EXPOSURES:
The cumulative mean of urinary sodium excretion from three 24-hour urinary measurements and calibrated to sex-specific mean 24-hour urinary creatinine excretion.

MAIN OUTCOMES AND MEASURES:
A composite of CVD events defined as congestive heart failure, stroke, or myocardial infarction. Events were reported every 6 months and confirmed by medical record adjudication.

RESULTS:
Among 3757 participants (mean age, 58 years; 45% women), 804 composite CVD events (575 heart failure, 305 myocardial infarction, and 148 stroke) occurred during a median 6.8 years of follow-up. From lowest (<2894 mg/24 hours) to highest (≥4548 mg/24 hours) quartile of calibrated sodium excretion, 174, 159, 198, and 273 composite CVD events occurred, and the cumulative incidence was 18.4%, 16.5%, 20.6%, and 29.8% at median follow-up. In addition, the cumulative incidence of CVD events in the highest quartile of calibrated sodium excretion compared with the lowest was 23.2% vs 13.3% for heart failure, 10.9% vs 7.8% for myocardial infarction, and 6.4% vs 2.7% for stroke at median follow-up. Hazard ratios of the highest quartile compared with the lowest quartile were 1.36 (95% CI, 1.09-1.70; P = .007) for composite CVD events, 1.34 (95% CI, 1.03-1.74; P = .03) for heart failure, and 1.81 (95% CI, 1.08-3.02; P = .02) for stroke after multivariable adjustment. Restricted cubic spline analyses of the association between sodium excretion and composite CVD provided no evidence of a nonlinear association (P = .11) and indicated a significant linear association (P < .001).

CONCLUSIONS AND RELEVANCE:
Among patients with CKD, higher urinary sodium excretion was associated with increased risk of CVD.

Mozaffarian, MD, Fahimi S, Sing GM, et al. Global sodium consumption and death from cardiovascular causes. NEJM 2014;371:624-34

BACKGROUND:
High sodium intake increases blood pressure, a risk factor for cardiovascular disease, but the effects of sodium intake on global cardiovascular mortality are uncertain.

METHODS:
We collected data from surveys on sodium intake as determined by urinary excretion and diet in persons from 66 countries (accounting for 74.1% of adults throughout the world), and we used these data to quantify the global consumption of sodium according to age, sex, and country. The effects of sodium on blood pressure, according to age, race, and the presence or absence of hypertension, were calculated from data in a new meta-analysis of 107 randomized interventions, and the effects of blood pressure on cardiovascular mortality, according to age, were calculated from a meta-analysis of cohorts. Cause-specific mortality was derived from the Global Burden of Disease Study 2010. Using comparative risk assessment, we estimated the cardiovascular effects of current sodium intake, as compared with a reference intake of 2.0 g of sodium per day, according to age, sex, and country.

RESULTS:
In 2010, the estimated mean level of global sodium consumption was 3.95 g per day, and regional mean levels ranged from 2.18 to 5.51 g per day. Globally, 1.65 million annual deaths from cardiovascular causes (95% uncertainty interval [confidence interval], 1.10 million to 2.22 million) were attributed to sodium intake above the reference level; 61.9% of these deaths occurred in men and 38.1% occurred in women. These deaths accounted for nearly 1 of every 10 deaths from cardiovascular causes (9.5%). Four of every 5 deaths (84.3%) occurred in low- and middle-income countries, and 2 of every 5 deaths (40.4%) were premature (before 70 years of age). The rate of death from cardiovascular causes associated with sodium intake above the reference level was highest in the country of Georgia and lowest in Kenya.

CONCLUSIONS:

In this modeling study, 1.65 million deaths from cardiovascular causes that occurred in 2010 were attributed to sodium consumption above a reference level of 2.0 g per day. (Funded by the Bill and Melinda Gates Foundation.).

Poggio R, Gutierrez L, Matta MG, et al. Daily sodium consumption and CVD mortality in the general population: systematic review and meta-analysis of prospective studies. Pub Health Nut 2014: 18(4): 695-704

OBJECTIVE:
The purpose of the present study was to determine whether elevated dietary Na intake could be associated with CVD mortality.

DESIGN:
We performed a systematic review and meta-analysis of prospective studies representing the general population. The adjusted relative risks and their 95 % confidence intervals were pooled by the inverse variance method using random-effects models. Heterogeneity, publication bias, subgroup and meta-regression analyses were performed. Settings MEDLINE (since 1973), Embase (since 1975), the Cochrane Library (since 1976), ISI Web of Science, Google Scholar (until September 2013) and secondary referencing were searched for inclusion in the study. Subject Eleven prospective studies with 229 785 participants and average follow-up period of 13.37 years (range 5.5-19 years).

RESULTS:
Higher Na intake was significantly associated with higher CVD mortality (relative risk=1.12; 95 % CI 1.06, 1.19). In the sensitivity analysis, the exclusion of studies with important relative weights did not significantly affect the results (relative risk=1.08; 95 % CI 1.01, 1.15). The meta-regression analysis showed that for every increase of 10 mmol/d in Na intake, CVD mortality increased significantly by 1 % (P=0.016). Age, hypertensive status and length of follow-up were also associated with increased CVD mortality.

CONCLUSIONS:
Higher Na intake was associated with higher CVD mortality in the general population; this result suggests a reduction in Na intake to prevent CVD mortality from any cause.

Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. DASH – Sodium Collaborative Research Group. NEJM 2001;344:3-10.

BACKGROUND:
The effect of dietary composition on blood pressure is a subject of public health importance. We studied the effect of different levels of dietary sodium, in conjunction with the Dietary Approaches to Stop Hypertension (DASH) diet, which is rich in vegetables, fruits, and low-fat dairy products, in persons with and in those without hypertension.

METHODS:
A total of 412 participants were 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 high, intermediate, and low levels of sodium for 30 consecutive days each, in random order.

RESULTS:
Reducing the sodium intake from the high to the intermediate level reduced the systolic blood pressure by 2.1 mm Hg (P<0.001) during the control diet and by 1.3 mm Hg (P=0.03) during the DASH diet. Reducing the sodium intake from the intermediate to the low level caused additional reductions of 4.6 mm Hg during the control diet (P<0.001) and 1.7 mm Hg during the DASH diet (P<0.01). The effects of sodium were observed in participants with and in those without hypertension, blacks and those of other races, and women and men. The DASH diet was associated with a significantly lower systolic blood pressure at each sodium level; and the difference was greater with high sodium levels than with low ones. As compared with the control diet with a high sodium level, the DASH diet with a low sodium level led to a mean systolic blood pressure that was 7.1 mm Hg lower in participants without hypertension, and 11.5 mm Hg lower in participants with hypertension.

CONCLUSIONS:
The reduction of sodium intake to levels below the current recommendation of 100 mmol per day and the DASH diet both lower blood pressure substantially, with greater effects in combination than singly. Long-term health benefits will depend on the ability of people to make long-lasting dietary changes and the increased availability of lower-sodium foods.

Singh GM, Danaei G, Farzadfar F et al. The Age-Specific Quantitative Effects of Metabolic Risk Factors on Cardiovascular Diseases and Diabetes: A Pooled Analysis. PLoS ONE 2013:8(7): e65174. doi:10.1371/journal.pone.0065174

BACKGROUND:
The effects of systolic blood pressure (SBP), serum total cholesterol (TC), fasting plasma glucose (FPG), and body mass index (BMI) on the risk of cardiovascular diseases (CVD) have been established in epidemiological studies, but consistent estimates of effect sizes by age and sex are not available.

METHODS:
We reviewed large cohort pooling projects, evaluating effects of baseline or usual exposure to metabolic risks on ischemic heart disease (IHD), hypertensive heart disease (HHD), stroke, diabetes, and, as relevant selected other CVDs, after adjusting for important confounders. We pooled all data to estimate relative risks (RRs) for each risk factor and examined effect modification by age or other factors, using random effects models.

RESULTS:
Across all risk factors, an average of 123 cohorts provided data on 1.4 million individuals and 52,000 CVD events. Each metabolic risk factor was robustly related to CVD. At the baseline age of 55-64 years, the RR for 10 mmHg higher SBP was largest for HHD (2.16; 95% CI 2.09-2.24), followed by effects on both stroke subtypes (1.66; 1.39-1.98 for hemorrhagic stroke and 1.63; 1.57-1.69 for ischemic stroke). In the same age group, RRs for 1 mmol/L higher TC were 1.44 (1.29-1.61) for IHD and 1.20 (1.15-1.25) for ischemic stroke. The RRs for 5 kg/m(2) higher BMI for ages 55-64 ranged from 2.32 (2.04-2.63) for diabetes, to 1.44 (1.40-1.48) for IHD. For 1 mmol/L higher FPG, RRs in this age group were 1.18 (1.08-1.29) for IHD and 1.14 (1.01-1.29) for total stroke. For all risk factors, proportional effects declined with age, were generally consistent by sex, and differed by region in only a few age groups for certain risk factor-disease pairs.

CONCLUSION:
Our results provide robust, comparable and precise estimates of the effects of major metabolic risk factors on CVD and diabetes by age group.

Suckling RJ, He FJ, MacGregor GA. Altered dietary salt intake for preventing and treating diabetic kidney disease. Cochrane Database of Systematic Reviews 2010, Issue 12. Art. No.: CD006763. doi10.1002/14651858.CD006763.pub2.

BACKGROUND:
There is strong evidence that our current consumption of salt is a major factor for increased blood pressure (BP) and a modest reduction in salt intake lowers BP whether BP levels are normal or raised. Tight control of BP in diabetics lowers the risk of strokes, heart attacks and heart failure and slows the progression of diabetic kidney disease (DKD). Currently there is no consensus in restricting salt intake in diabetic patients.

OBJECTIVES:
To evaluate the effect of altered salt intake on BP and markers of cardiovascular disease and DKD.

SEARCH STRATEGY:
In January 2010, we searched the Cochrane Renal Group's Specialised Register, CENTRAL (in The Cochrane Library), MEDLINE (from 1966) and EMBASE (from 1980) to identify appropriate articles.

SELECTION CRITERIA:
We included all randomised controlled trials of salt reduction in individuals with type 1 and type 2 diabetes.

DATA COLLECTION AND ANALYSIS:
Two authors independently assessed studies and resolved differences by discussion with a third independent author. We calculated mean effect sizes using both the fixed-effect and random-effects models.

MAIN RESULTS:
Thirteen studies (254 individuals) met our inclusion criteria. These included 75 individuals with type 1 diabetes and 158 individuals with type 2 diabetes. The median reduction in urinary sodium was 203 mmol/24 h (11.9 g/day) in type 1 diabetes and 125 mmol/24 h (7.3 g/day) in type 2 diabetes. The median duration of salt restriction was one week in both type 1 and type 2 diabetes. BP was reduced in both type 1 and type 2 diabetes. In type 1 diabetes (56 individuals), salt restriction reduced BP by -7.11/-3.13 mm Hg (systolic/diastolic); 95% CI: systolic BP (SBP) -9.13 to -5.10; diastolic BP (DBP) -4.28 to -1.98). In type 2 diabetes (56 individuals), salt restriction reduced BP by -6.90/-2.87 mm Hg (95% CI: SBP -9.84 to -3.95; DBP -4.39 to -1.35). There was a greater reduction in BP in normotensive patients, possibly due to a larger decrease in salt intake in this group.

AUTHORS' CONCLUSIONS:
Although the studies are not extensive, this meta-analysis shows a large fall in BP with salt restriction, similar to that of single drug therapy. All diabetics should consider reducing salt intake at least to less than 5-6 g/day in keeping with current recommendations for the general population and may consider lowering salt intake to lower levels, although further studies are needed.

Patel SM, Cobb P, Saydah S, Zhang X, de Jesus JM, Cogswell ME. Dietary sodium reduction does not affect circulating glucose concentrations in fasting children or adults: Findings from a systematic review and meta-analysis. J Nutr 2015;145:505–13.

BACKGROUND:
Although evidence shows that reduced sodium intake lowers blood pressure, some studies suggest that sodium reduction may adversely affect insulin resistance and glucose tolerance.

OBJECTIVES:
The objectives were to assess the effects of sodium reduction on glucose tolerance, evaluate strengths and weaknesses of the relevant scientific literature, and provide direction for future research.

METHODS:
We searched The Cochrane Library, MEDLINE, EMBASE, CINAHL, and Web of Science through August 2014. Both randomized and nonrandomized intervention trials were included in our meta-analyses. The effects of sodium reduction on glucose tolerance were evaluated in 37 articles, but because of a lack of comparable data, 8 trials were excluded from the meta-analyses.

RESULTS:
Participants were 10-79 y old, either primarily healthy or with hypertension. In meta-analyses of 20 randomized, crossover trials (n = 504 participants) and 9 nonrandomized crossover trials (n = 337), circulating glucose concentrations of fasting participants were not affected by reduction in sodium intake. In contrast, in meta-analyses of 19 of the 20 randomized, crossover trials (n = 494), fasting insulin concentrations were 9.53 pmol/L higher (95% CI: 5.04, 14.02 pmol/L higher) with sodium reduction. In 9 nonrandomized trials (n = 337), fasting insulin did not differ with reduced sodium intake. Results differed little when the analyses were restricted to studies with a low risk of bias and duration of ≥7 d.

CONCLUSIONS:
This meta-analysis revealed no evidence that, in trials with a short intervention and large reductions in sodium, circulating glucose concentrations differed between groups. Recommendations for future studies include extending intervention durations, ensuring comparability of groups at baseline through randomization, and assessing sodium intakes relevant to population sodium reduction. In addition, analyses on other metabolic variables were limited because of the number of trials reporting these outcomes and lack of consistency across measures, suggesting a need for comparable measures of glucose tolerance across studies.

Udagawa K, Miyoshi M, Yoshiike N. Mid-term evaluation of "Health Japan 21": focus area for the nutrition and diet. Asia Pac J Clin Nutr 2008;17(Suppl 2):445-52

This paper provides a review of the mid-term evaluation of "Health Japan 21" and dis-cusses the status of progress towards the goals of items within the "Nutrition and diet" area. Among 14 items investigated, an improving trend was observed in eight items, though there was no improvement in five items. Whilst the percentage of obese individuals significantly increased during the 25 years from 1976 to 1999, secular trend showed that it has become unchanged since 2000, when "Health Japan 21" was enacted, regardless of gender and age. Another favorable finding was a decreasing trend of salt intake especially in the age group of 50-59 years. Besides, the analyses of the proportion of the persons "who

have interest in dietary improvement" among the ones "who believe there are problems in their diet" showed that an increased awareness of inappropriate diet and also in the motivation to improve it, especially among males aged 50-59 years. On the other hand, some items showed worsening trend; e.g. decrease in vegetable intake, decrease of persons who are aware of their own optimal weight and practice weight control. Thus, the progress within Health Japan 21 was assessed as not necessarily satisfactory. In order to ensure the progress of "Health Japan 21" towards 2010, it is now crucial to effectively incorporate "Japanese Food Guide Spinning Top" and a new strategy of non-communicable diseases prevention focusing on the control of metabolic syndrome, which will be launched in April 2008, into the national health promotion program.

Vliet BNV, Montani J-P. The time course of salt-induced hypertension, and why it matters. Int J Obesity 2008;32:535-47.

The epidemiology of salt-induced hypertension has been explored in detail in animal studies, in some cases involving exposures to excess dietary salt for much of the animal's lifespan. The results of these studies demonstrate the presence of two distinct time courses of the blood pressure response to a high salt intake: an acute (rapid) blood pressure response occurring over days to weeks, and a slow and progressive blood pressure response that develops over extremely long periods of time, amounting to a significant fraction of the lifespan in normal individuals. The acute form of salt sensitivity is well known in humans, having often been demonstrated as a fall in blood pressure during the period of salt restriction. The slow and progressive form of salt sensitivity has been demonstrated directly in rats and chimpanzees and is also evident in analyses of human cross-population data as a salt dependency of age-associated changes of blood pressure. This slow and progressive component of salt-induced hypertension may be attributable, at least in part, to a progressive rise in the acute salt sensitivity of blood pressure during sustained exposure to high salt. However, a progressively irreversible or 'self sustaining' component of salt-induced hypertension has also been demonstrated in rat studies. This irreversible component has not been completely characterized, but its presence raises the possibility that blood pressure responses to salt restriction may not fully reveal the contribution of salt to blood pressure or the epidemiology of hypertension. These various components of salt sensitivity (acute vs slow, reversible vs irreversible) should be considered in any comprehensive explanation of the effects of salt on blood pressure and especially in experimental studies of the genetic and physiological mechanisms underlying salt-induced hypertension.

Whelton PK, Appel LJ, Espeland MA, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). JAMA 1998;279:839–46.

CONTEXT:
Nonpharmacologic interventions are frequently recommended for treatment of hypertension in the elderly, but there is a paucity of evidence from randomized controlled trials in support of this recommendation.

OBJECTIVE:
To determine whether weight loss or reduced sodium intake is effective in the treatment of older persons with hypertension.

DESIGN:
Randomized controlled trial.

PARTICIPANTS:
A total of 975 [corrected] men and women aged 60 to 80 years with systolic blood pressure lower than 145 mm Hg and diastolic blood pressure lower than 85 mm Hg while receiving treatment with a single antihypertensive medication.

SETTING:
Four academic health centers.

INTERVENTION:
The 585 obese participants were randomized to reduced sodium intake, weight loss, both, or usual care, and the 390 nonobese participants were randomized to reduced sodium intake or usual care. Withdrawal of antihypertensive medication was attempted after 3 months of intervention.

MAIN OUTCOME MEASURE:
Diagnosis of high blood pressure at 1 or more follow-up visits, or treatment with antihypertensive medication, or a cardiovascular event during follow-up (range, 15-36 months; median, 29 months).

RESULTS:
The combined outcome measure was less frequent among those assigned vs not assigned to reduced sodium intake (relative hazard ratio, 0.69; 95% confidence interval [CI], 0.59-0.81; P<.001) and, in obese participants, among those assigned vs not assigned to weight loss (relative hazard ratio, 0.70; 95% CI, 0.57-0.87; P<.001). Relative to usual care, hazard ratios among the obese participants were 0.60 (95% CI, 0.45-0.80; P<.001) for reduced sodium intake alone, 0.64 (95% CI, 0.49-0.85; P=.002) for weight loss alone, and 0.47 (95% CI, 0.35-0.64; P<.001) for reduced sodium intake and weight loss combined. The frequency of cardiovascular events during follow-up was similar in each of the 6 treatment groups.

CONCLUSION:
Reduced sodium intake and weight loss constitute a feasible, effective, and safe nonpharmacologic therapy of hypertension in older persons.