

# Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomised trials

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EDITORIAL by Strazzullo  
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## STUDY QUESTION

Does a longer term modest reduction in salt intake have a significant effect on blood pressure, hormones, and lipids?

## SUMMARY ANSWER

A modest reduction in salt intake for four or more weeks causes significant and, from a population viewpoint, important falls in blood pressure in both hypertensive and normotensive individuals, irrespective of sex and ethnic group. There were small physiological increases in plasma renin activity, aldosterone, and noradrenaline and no significant change in lipid concentrations.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Salt reduction can lower blood pressure and thereby reduces cardiovascular risk. A recent meta-analysis of randomised trials implied that salt reduction had adverse effects on hormones and lipids, which might mitigate any benefit that occurs with the reduction in blood pressure. That meta-analysis included a large number of trials with a big change in salt intake for only a few days. The current meta-analysis shows that a longer term modest reduction in salt intake lowers blood pressure without adverse effects on lipids and hormones. Furthermore, there is a dose-response relation between the reduction in salt intake and the fall in systolic blood pressure. Reductions in salt intake to the recommended level of 5-6 g/day will have a major effect on blood pressure, and a further reduction to 3 g/day will have a greater effect.

## Selection criteria for studies

We included randomised trials with a modest reduction in salt intake and duration of at least four weeks. The trials were identified from Medline, Embase, Cochrane Hypertension Group Specialised Register, Cochrane Central Register of Controlled Trials, and reference lists of relevant articles.

## Primary outcomes

Blood pressure, hormones, and lipids.

## Main results and role of chance

34 trials (3230 participants) were included. For an average reduction of 4.4 g/day in salt intake as measured by 24 hour urinary sodium, meta-analysis showed that the mean change in blood pressure was -4.18 mm Hg (95% confidence interval -5.18 to -3.18) for systolic blood pressure and -2.06 mm Hg (-2.67 to -1.45) for diastolic blood pressure. There was a significant association between the reduction in 24 hour urinary sodium and the decrease in systolic blood pressure. After adjustment for age, ethnic group, and blood pressure status, a 100 mmol reduction in 24 hour urinary sodium (6 g/day salt) predicted a fall in systolic blood pressure of 5.8 mm Hg (2.5 to 9.2, P=0.001). Meta-analysis by subgroup showed a significant decrease in blood pressure in both hypertensive and normotensive people, irrespective of sex and ethnic group. There was a small physiological increase in plasma renin activity (0.26 ng/mL/h, 95% confidence interval 0.17 to 0.36), aldosterone (73.20 pmol/L, 44.92 to 101.48), and noradrenaline (norepinephrine) (187 pmol/L, 39 to 336). There was no significant change in adrenaline (epinephrine) (37 pmol/L, -1 to 74), total cholesterol (0.05 mmol/L, -0.02 to 0.11), low density lipoprotein cholesterol (0.05 mmol/L, -0.01 to 0.12), high density lipoprotein cholesterol (-0.02 mmol/L, -0.06 to 0.01), or triglycerides (0.04 mmol/L, -0.02 to 0.09).

## Bias, confounding, and other reasons for caution

Despite inclusion of trials with duration of one month or longer, the median duration of salt reduction in our meta-analysis was only four weeks. It is unlikely that salt reduction has exerted its maximum effect by a few weeks. Additionally, the small effects on plasma renin activity, aldosterone, and noradrenaline could attenuate over time.

## Study funding/potential competing interests

FH is a member of Consensus Action on Salt and Health (CASH) and World Action on Salt and Health (WASH). GM is board member of World Hypertension League (WHL), chairman of Blood Pressure Association (BPA), chairman of CASH, and chairman of WASH. CASH and WASH are non-profit charitable organisations, and FH and GM do not receive any financial support from CASH or WASH.

Change in blood pressure and 24 hour urinary sodium from usual to reduced salt intake in hypertensive and normotensive individuals			
Outcome	No of trials	No of participants	Mean effect size (95% CI)
<b>Hypertensive people</b>			
Systolic blood pressure (mm Hg)	21	966	-5.39 (-6.62 to -4.15)
Diastolic blood pressure (mm Hg)	22	990	-2.82 (-3.54 to -2.11)
24 hour urinary sodium (mmol)	22	990	-75.29 (-81.76 to -68.83)
<b>Normotensive people</b>			
Systolic blood pressure (mm Hg)	12	2240	-2.42 (-3.56 to -1.29)
Diastolic blood pressure (mm Hg)	12	2240	-1.00 (-1.85 to -0.15)
24 hour urinary sodium (mmol)	12	2240	-75.38 (-89.90 to -60.86)

# Effect of lower sodium intake on health: systematic review and meta-analyses

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● EDITORIAL by Strazzullo  
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## STUDY QUESTION

What are the effects of decreased sodium intake on blood pressure, mortality, and morbidity from cardiovascular diseases and incidence of adverse effects in apparently healthy adults and children without acute illness?

## SUMMARY ANSWER

High quality evidence in 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. Low and very low quality evidence suggest that lower sodium intake is associated with reduced risk of all stroke, fatal stroke, and fatal coronary heart disease in adults.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Raised blood pressure is the main risk factor for mortality globally and sodium intake is associated with blood pressure and related cardiovascular diseases. This paper found that lower sodium intake reduces blood pressure in adults and children, is associated with a reduced risk of stroke and fatal coronary heart disease in adults, and has no adverse effect on blood lipids, catecholamine levels, or renal function.

## Selection criteria for studies

We conducted a systematic search of the Cochrane Central Register of Controlled Trials, Medline, Embase, WHO International Clinical Trials Registry Platform, LILACS, and the reference lists of reviews for randomised controlled trials and prospective cohort studies investigating sodium intake in adults and children without acute illness.

## Primary outcomes

The primary outcomes were blood pressure, renal function, blood lipids, and catecholamine levels in adults and

children; and all cause mortality, cardiovascular disease, stroke, and coronary heart disease in adults.

## Main results and role of chance

A reduction in sodium intake significantly reduced systolic blood pressure by 3.39 mm Hg (95% confidence interval 2.46 to 4.31 mm Hg) and diastolic blood pressure by 1.54 mm Hg (0.98 to 2.11 mm Hg) in adults. Decreased sodium intake had no significant adverse effect on blood lipids, catecholamine levels, or renal function in adults ( $P>0.05$ ). This evidence was high quality. 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 incidence (risk ratio 1.24, 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). This evidence was low and very low quality. In children, moderate quality evidence showed that lower sodium intake reduced systolic blood pressure by 0.84 mm Hg (0.25 to 1.43 mm Hg) and diastolic blood pressure by 0.87 mm Hg (0.14 to 1.60 mm Hg).

## Bias, confounding, and other reasons for caution

The  $\chi^2$  test for heterogeneity from the meta-analyses of blood pressure in adults suggested considerable heterogeneity ( $P<0.001$ ). However, the test may not be meaningful because heterogeneity across a large number of studies, as found in this review, is inevitable. The forest plot and the  $I^2$  test also suggested some degree of heterogeneity; however, there was no considerable variation in results or inconsistency in the direction of the effect across studies.

## Study funding/potential competing interests

This study was funded by World Health Organization funds, Kidney Evaluation Association Japan, and the governments of Japan and Republic of Korea.

Summary of select results of the effect of reduced sodium intake on health outcomes in non-acutely ill adults and children					
Outcomes	Study design	Effect (95% CI)*	No of participants (No of studies)	Quality of evidence (GRADE)	Comments
Stroke (all incident events, adults)	Cohort	RR 1.24 (1.08 to 1.43)	72 878 (10)	Very low	Data from cohort studies begin with GRADE of low; downgraded owing to inconsistency
Stroke (incident fatal events, adults)	Cohort	RR 1.63 (1.27 to 2.10)	48 645 (3)	Low	Data not downgraded
Coronary heart disease (incident fatal events, adults)	Cohort	RR 1.32 (1.13 to 1.53)	30 670 (3)	Low	Data not downgraded
Resting systolic blood pressure (adults)	Randomised controlled trials	MD 3.39 lower† (4.31 to 2.46 lower)	6736 (36)	High	Evidence suggests a dose-response with greater benefit to blood pressure as sodium intake decreases
Resting systolic blood pressure (children and young people)	Controlled trials	MD 0.84 lower† (1.43 to 0.25 lower)	1384 (9)	Moderate	Two studies with four comparisons were not randomised; downgraded owing to high risk of bias

RR=risk ratio; MD=mean difference.  
\*Risk ratios >1 calculated from cohort studies signify increased risk with increased sodium intake.  
†MD lower signifies a reduced blood pressure groups consuming less sodium (intervention) relative to control.

# Effect of increased potassium intake on cardiovascular risk factors and disease: systematic review and meta-analyses

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## STUDY QUESTION

What are the effects of increased potassium intake on blood pressure, mortality and morbidity from cardiovascular diseases, and incidence of adverse effects in apparently healthy adults and children without acute illness or impaired renal handling of potassium?

## SUMMARY ANSWER

High quality evidence shows that increased potassium intake reduces blood pressure in adults with hypertension and has no adverse effect on blood lipid concentrations, catecholamine concentrations, or renal function; higher potassium intake is also associated with a 24% reduced risk of stroke (moderate and low quality evidence); evidence in children is sparse but also suggests a benefit on blood pressure with higher potassium intake.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Low potassium intake has been associated with high blood pressure and risk of some cardiovascular diseases, but the evidence is not entirely consistent. This review provides the most comprehensive and up to date synthesis of literature on potassium intake and health outcomes and concludes that increased potassium intake is beneficial for reducing blood pressure and risk of stroke.

## Selection criteria for studies

We systematically searched the Cochrane Central Register of Controlled Trials, Medline, Embase, the World Health Organization International Clinical Trials Registry Platform, the Latin American and Caribbean Health Science Literature Database, and the reference lists of previous reviews for randomised controlled trials and prospective cohort studies investigating potassium intake in apparently healthy adults and children without acute illness or renal impairment that might compromise handling of potassium.

## Primary outcome(s)

The primary outcomes, as prioritised by the WHO Nutrition Expert Advisory Group, were blood pressure, blood lipid concentrations, catecholamine concentrations, and renal function in adults and children and all cause mortality, cardiovascular disease, stroke, and coronary heart disease in adults.

## Main results and role of chance

Twenty two randomised controlled trials (including 1606 participants) reporting blood pressure, blood lipids, catecholamine concentrations, or renal function and 11 cohort studies (127 038 participants) reporting all cause mortality, cardiovascular disease, stroke, or coronary heart disease contributed to the meta-analyses in adults. Increased potassium intake reduced systolic blood pressure by 3.49

## Estimates of effect of increased potassium on selected health outcomes in adults and children

Outcome	Effect estimate (95% CI)
Blood pressure (mean difference in mm Hg)*:	
Systolic (adults)	-3.49 (-5.15 to -1.82)
Diastolic (adults)	-1.96 (-3.06 to -0.86)
Systolic (children)	-0.28 (-1.05 to 0.49)
Disease endpoints in adults (risk ratio)†:	
Stroke	0.76 (0.66 to 0.89)
Cardiovascular disease	0.88 (0.70 to 1.11)
Coronary heart disease	0.96 (0.78 to 1.19)

\*Negative value for mean difference indicates greater reduction in blood pressure in intervention (higher potassium) relative to control (lower potassium).

†Risk ratio from cohort studies <1 indicates reduced risk with higher potassium intake.

(95% confidence interval 1.82 to 5.15) mm Hg and diastolic blood pressure by 1.96 (0.86 to 3.06) mm Hg in adults with hypertension but not in those without hypertension. Increased potassium intake had no significant adverse effect on blood lipid concentrations, catecholamine concentrations, or renal function in adults. Potassium intake was statistically significantly inversely associated with risk of incident stroke (risk ratio 0.76, 0.66 to 0.89). Associations between potassium intake and incident cardiovascular disease or coronary heart disease were not statistically significant. Three controlled trials and one cohort study in children suggested that increased potassium intake reduced systolic blood pressure by a non-significant 0.28 (-0.49 to 1.05) mm Hg.

## Bias, confounding, and other reasons for caution

The evidence for increased potassium reducing blood pressure in adults was of high or moderate quality according to the GRADE methodology. The evidence of no effect of increased potassium on blood lipid concentrations, catecholamine concentrations, or renal function was of high quality. The direct evidence for a protective effect of higher potassium intake on incident stroke was low because cohort studies began on the GRADE ranking as low quality, but the evidence was not downgraded for any reason. Recognising the limitations of any biomarker, we considered the change in systolic blood pressure as a proxy indicator and thus indirect evidence of the effect of sodium intake on risk of cardiovascular disease, stroke, and coronary heart disease. We downgraded this evidence for indirectness (use of a proxy indicator). The quality of evidence in children was low because of a high risk of bias and imprecision.

## Study funding/potential competing interests

Support was provided by WHO, the International Kidney Evaluation Association Japan, and the governments of Japan and Republic of Korea.

# Population-wide weight loss and regain in relation to diabetes burden and cardiovascular mortality in Cuba 1980-2010: repeated cross sectional surveys and ecological comparison of secular trends

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A video abstract about this study is available with the full online version of the paper

## STUDY QUESTION

Did the pattern of population-wide weight loss and regain in Cuba during and after the economic crisis of the 1990s result in changes in the burden of diabetes and cardiovascular disease?

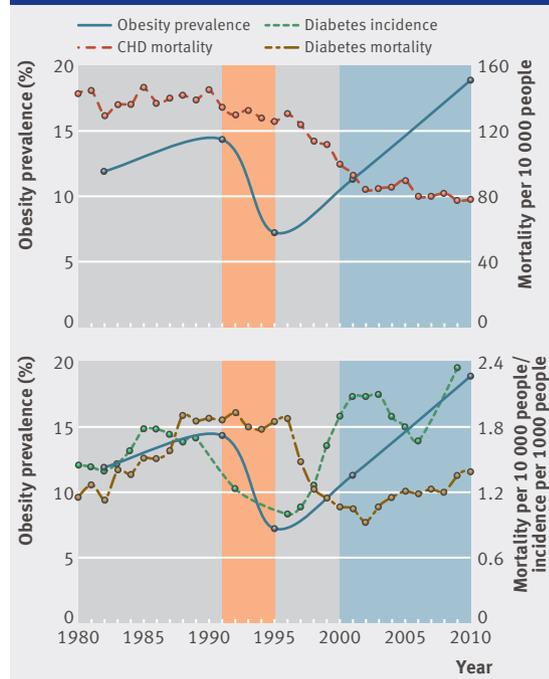
## SUMMARY ANSWER

The 1990s economic crisis in Cuba resulted in an average weight loss of 5.5 kg in the population, accompanied by rapid and substantial declines in the rates of diabetes and heart disease; as the economy recovered, obesity and diabetes rates rebounded promptly and diabetes mortality increased, while the decline in cardiovascular disease slowed.

## WHAT IS KNOWN AND WHAT THIS PAPER ADDS

Abrupt reductions in diabetes and cardiovascular death have been observed during food shortages in economically developed societies—primarily during the second world war—although no population-wide information was available on trends in weight, physical activity, or diabetes incidence and prevalence. Population-wide weight loss and regain in Cuba was found to be associated with improvements and declines in health burden, respectively.

## Patterns of obesity, diabetes, and mortality in Cuba 1980-2010



## Participants and setting

Mortality data were available for the entire Cuban population from 1980 to 2010.

## Design, size, and duration

Using repeated sample surveys in Cuba in 1980-2010, we examined trends in the prevalence of obesity and physical activity and the incidence and prevalence in diabetes. We compared these data with concurrent trends in mortality from diabetes and cardiovascular disease.

## Main results and the role of chance

Diabetes mortality fell by 50% in the five year interval near the end of the economic crisis, when the average weight loss in the population reached 5.5 kg. A rebound in weight drove prevalence of overweight and obesity up to pre-crisis levels (rising from 33.5% at the lowest point in 1995 to 52.9% in 2010). The population-wide gain in weight was immediately followed by an increase in diabetes prevalence and incidence of 116% and 140%, respectively. Six years into the weight rebound phase, diabetes mortality increased by 49% (from 9.3 deaths per 10 000 people in 2002 to 13.9 per 10 000 in 2010). We also observed a deceleration in the rate of decline in mortality from coronary heart disease (CHD). The magnitude of the observed trends and the absence of evidence indicating a shift in the assignment of cause of death rule out the possibility of a chance association.

## Bias, confounding, and other reasons for caution

Many lifestyle aspects changed in Cuba during the study period. Total calories available and nutrient composition in food changed considerably, and the requirement for active transport increased. Therefore, it is difficult to assign relative importance to these factors individually. More precise information was available on weight, and moderate weight loss was virtually universal, thus although the outcome is probably the result of a joint effect, inferences about a causal role for obesity are more robust.

## Generalisability to other populations

The social structure in Cuba, which rationed food equally and maintained the medical and public health system well, make it unlikely that an identical experience would be observed in other societies. However, the relevant association between changes in population-wide body weight and rates of diabetes and cardiovascular disease are almost certainly generalisable.

## Study funding/potential competing interests

No funding was used to support this research, and we declare no competing interests.