Systematic review of long term effects of advice to reduce dietary salt in adults

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Abstract

Objective To assess the long term effects of advice to restrict dietary sodium in adults with and without hypertension.

Design Systematic review and meta-analysis of randomised controlled trials.

Data sources Cochrane library, Medline, Embase, and bibliographies.

Study selection Unconfounded randomised trials that aimed to reduce sodium intake in healthy adults over at least 6 months. Inclusion decisions, validity and data extraction were duplicated. Random effects meta-analysis, subgrouping, sensitivity analysis, and meta-regression were performed.

Outcomes Mortality, cardiovascular events, blood pressure, urinary sodium excretion, quality of life, and use of antihypertensive drugs.

Results Three trials in normotensive people (n=2326), five trials in those with untreated hypertension (n=387), and three trials in people being treated for hypertension (n=801) were included, with follow up from six months to seven years. The large high quality (and therefore most informative) studies used intensive behavioural interventions. Deaths and cardiovascular events were inconsistently defined and reported. There were 17 deaths, equally distributed between intervention and control groups. Systolic and diastolic blood pressures were reduced (systolic by 1.1 mm Hg, 95% confidence interval 1.8 to 0.4 mm Hg; diastolic by 0.6 mm Hg, 1.5 to −0.3 mm Hg) at 13 to 60 months, as was urinary 24 hour sodium excretion (by 35.5 mmol/24 hours, 47.2 to 23.9). Degree of reduction in sodium intake and change in blood pressure were not related.

Conclusions Intensive interventions, unsuited to primary care or population prevention programmes, provide only small reductions in blood pressure and sodium excretion, and effects on deaths and cardiovascular events are unclear. Advice to reduce sodium intake may help people on antihypertensive drugs to stop their medication while maintaining good blood pressure control.

Introduction

Several systematic reviews have reported that restricting sodium intake in people with hypertension reduces their blood pressure.[1–5] However, most of the trials in these systematic reviews were short term and did not allow for complete adjustment of blood pressure to altered sodium intake or reduced motivation for following dietary restrictions over time. Also, some trials increased sodium intake in one arm and compared this with a reduced sodium intake in the other arm and so did not estimate likely effects of cutting down on sodium in a normal diet.[6 7] No review on long term outcomes has been carried out since 1998,[7] although large relevant trials have been published.

The value of lowering blood pressure depends on its effects on cardiovascular events and deaths. The published systematic reviews on the effect of salt restriction on blood pressure and other risk factors have disagreed about the size of blood pressure changes[8] and the effects on cardiovascular events and deaths. We assessed, in people with and without hypertension, the efficacy of advice to reduce dietary sodium intake over at least six months on mortality, cardiovascular events, blood pressure, urinary sodium excretion, quality of life, and use of antihypertensive medications.

Methods

A previous large scale search for dietary trials and cardiovascular disease covered the Cochrane library, Medline, Embase, CAB abstracts, CVRCT registry, and SIGLE to May 1998 plus bibliographies of collected papers and reviews.[9] We carried out a further search, seeking trials on sodium restriction and blood pressure in Medline, Embase, and the Cochrane library (to July 2000). We checked bibliographies of systematic reviews and included trials; the searches were not limited by language.

We included trials in which randomisation was adequate, there was a usual or control diet group, the intervention aimed to reduce sodium intake, the intervention was not multifactorial, the participants were not children, acutely ill, pregnant, or institutionalised, follow up was at least 26 weeks, and data on any of the review outcomes were available.

For this review our primary outcomes were mortality and cardiovascular events, blood pressure, and urinary sodium excretion. We also collected data on quality of life and use of antihypertensive medication.

Two authors (LH and CB) assessed inclusion and validity and carried out data extraction independently in duplicate. Any differences were resolved by

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discussion and, when necessary, by a third reviewer (SE). For assessment of quality we collected data on randomisation procedure, allocation concealment, blinding of participants, providers of care, outcome assessors, and losses to follow up.[10]

For urinary sodium excretion and blood pressure we collected data on mean (SD) change from baseline for intervention and control groups at intermediate (latest data point from 6 to 12 months), late (13 to 60 months), and very late (after 60 months) follow up. Four trials provided baseline and follow up values, with SD or SE, but no SD for the change from baseline.[11–14] We used three studies in which data were provided at baseline and follow up and mean differences given[15–17] to calculate values for the correlations between baseline and follow up (for the control and experimental groups for systolic and diastolic blood pressure values but not for urinary sodium excretion).[18] We used a conservative estimate (lowest correlation) to compute the SD of mean changes for four studies without this data. Correlations varied from −5.79 to 0.56.

In factorial trials of calorie and sodium reduction we used only data from the sodium reduction and control groups because, of three such factorial trials,[17 19 20] two showed definite[17] or probable[19] interaction effects. In one trial data on urinary sodium excretion were not available for sodium reduction groups alone but event and medication data were available and were used in analyses.[20] Calorie reduction and calories plus sodium reduction arms were included in a sensitivity analysis.

We attempted to contact authors of all included trials for further information on trial characteristics, quality, and outcomes (including number and type of cardiovascular events, deaths, quality of life assessments, urinary sodium excretion, intake of other nutrients, blood pressure, and weight) as well as information on further published or unpublished trials.

Two trials were cluster randomised. In one small trial 19 general practitioners were randomised to deliver simple advice on low salt diets or no such advice to 77 patients.[13] Patient numbers in the intervention and control groups were reduced to an effective sample size as described by Hauck,[21] assuming the intraclass correlation (appropriate for nonfamilial clusters such as randomised practice units) to be 0.5.[22] The other cluster randomised trial individually randomised "index" men and women and then included members of their families in the trial.[23] We used only the "index" participants in our meta-analysis.

We checked the meta-analyses (weighted mean differences, random effects model, on Cochrane Collaboration Review Manager 4.1 software) for heterogeneity by visual inspection and by Cochran's test. We used sensitivity analysis to assess the robustness of the results to exclusion of the data with estimated SDs, or use of the largest correlations to estimate these SDs, exclusion of trials with unknown or inadequate allocation concealment, and addition of weight reduction arms.[10 24] We used the STATA metareg command[25] for random effects meta-regression.[26] We did not use funnel plots to investigate the presence of publication bias because the number of trials in each group was too small.

We used subgrouping of trials and meta-regression to examine the effects on blood pressure of length of follow up on sodium excretion and blood pressure, initial systolic blood pressure, presence or absence of hypertension, age, and change in sodium excretion.

Results

Study characteristics

Figure 1 shows details of exclusion and inclusion of studies. Table 1 shows the characteristics of the 11 trials included.

We included three trials in people without hypertension (n=2326),[16 17 19] five in people with untreated hypertension (n=387),[11 13 15 23 27] and three in people with treated hypertension (n=801),[12 14 20] with follow up from six months to seven years. The people without hypertension were healthy (predominantly white men, mean age 40 years) with high normal blood pressure. The people with untreated hypertension were aged 16 to 64 years, while those with treated hypertension were aged 55 to 67 years. In trials on people with hypertension, sex and ethnic characteristics were generally poorly documented. All the trials in people without hypertension, but only one trial in people with treated hypertension,[20] used a comprehensive behavioural change programme, whereas the others used varying types of advice or leaflets.

The quality of the trials, as judged by concealment of allocation, seemed higher in the trials in people without hypertension. Other aspects of quality that we assessed included blinding of outcome assessment and losses to follow up (table 1). There were different methods of dealing with missing data associated with losses to follow up. Most trials attempted to blind outcome assessors.

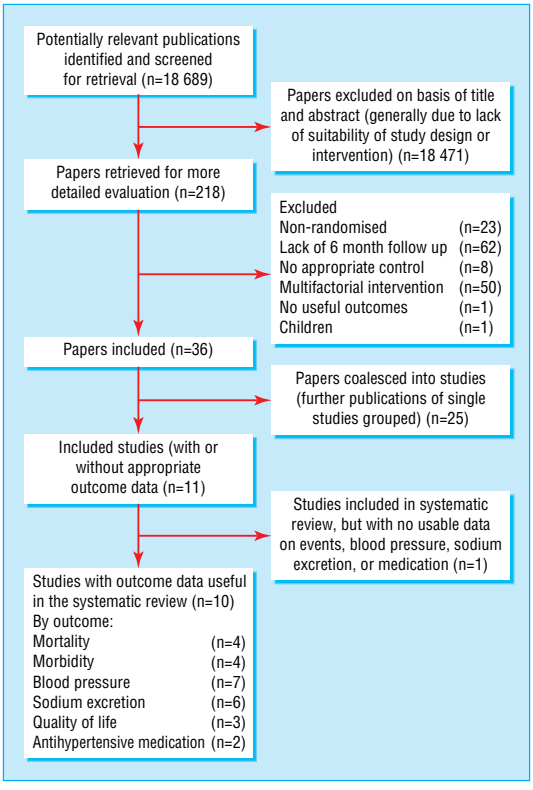

Fig 1 Flow diagram of systematic review (QUOROM statement flow diagram)

Table 1 Characteristics of trials of sodium restriction included in meta-analysis

Trial name	Participants	Intervention	Control	Outcomes	Quality
People without hypertension					
HPT 1990 (USA)[19]	Mean age 39 years, 62% men, 84% white, DBP 78-89 mm Hg, not on AHTM	196 assigned to dietary and behavioural change programme; 174 followed up at 6 months, 175 at 36 months; target USE ⩽70	196 assigned to no dietary counselling; 191 followed up at 6 months, 178 at 36 months	BP and USE at 0, 6, 36 months, % on antihypertensive drugs	Allocation adequately concealed; participants not blinded; outcome assessors blinded; participants with no follow up excluded; others given reading from last visit (or treated BP if higher)
TOHP phase I 1992 (USA)16	Mean age 43 years, 71% male, 77% white, DBP 80 to 89 mm Hg, not on AHTM	327 assigned to group nutrition and behavioural counselling programme; 301 followed up at 12 months, 304 at 18 months; target USE 80	417 assigned to no intervention; 392 analysed at 12 months, 395 at 18 months	BP and USE at 0, 6, 12, 18 months	Allocation adequately concealed; participants not blinded; outcome assessors blinded; participants with no follow up reading taken as zero change, others given reading from last visit
TOHP phase II 1997 (USA)[17]	Mean age 44 years, 67% male, 81% white, DBP 83 to 89 mm Hg, SBP ⩽140 mm Hg, not on AHTM	594 assigned to dietary and behavioural change programme, intensive early on, contact maintained later; 529 followed up at 6 months, 515 at 36 months; target USE 70	596 assigned to no active intervention; 538 analysed at 6 months, 514 at 36 months	BP and USE at 0, 6, 18, 36 months (42 or 48 months sometimes)	Allocation adequately concealed participants not blinded outcome assessors blinded; participants with no follow up reading given random value from range of results, others given reading from last visit
People with untreated hypertension					
Morgan 1978 (Australia)[15 28]	>50 years, all men, DBP 95-109 mm Hg, no AHTM	34 for BP (35 for mortality) assigned to instruction to reduce their dietary sodium chloride intake; 26 followed up at 24 months (all followed for mortality); target sodium intake 70-100 mmol/24 hours	33 for BP (42 for mortality) assigned to no dietary treatment; 21 followed up at 24 months (all followed for mortality)	BP and USE at 0, 6, 12, 18, 24 months	Concealment of allocation unclear; participants not blinded; outcome assessors blinded; participants with no follow up excluded, reading at last visit used for remainder
Costa 1981 (Italy)[11]	Age range 16-31 years, "untreated borderline hypertension"	21 assigned to receive low salt diet; 20 followed up; target 3 g NaCl/day	20 advised on diet with unrestricted salt; 21 [sic] followed up	BP and intralymphocytic sodium at 0 and 12 months	Concealment of allocation unclear; participants not blinded; unclear if outcome assessors blinded; adjustment for losses not specified
Thaler 1982 (New Zealand)[23]	Mean age 41 years, 48% male, index subjects: SBP 137-180 mm Hg, 21% on AHTM (family members also included)	80 (38 index + 42 family) assigned to salt restriction programme for whole family; 69 followed up at 8 months; USE target not stated	84 (39 index + 45 family) asked to eat usual diet, 67 followed up at 8 months	USE at 0 and 8 months	Concealment of allocation unclear; participants not blinded; unclear if outcome assessors blinded; losses excluded
Silman 1983 (UK)[27]	Aged 50 to 64, DBP 95-104 mm Hg	12 assigned to general health education group package with spouses plus taught about low salt diet; 10 followed up at 12 months; USE target 100	16 assigned to general health education group package only; 15 followed up at 12 months	BP and USE at 0, 1, 2, 3, 6, 12 months	Concealment of allocation unclear; participants not blinded; unclear if outcome assessors blinded; losses excluded; baseline readings for "excluded" compared with those for "included"
Alli 1992 (Italy)13	Mean age 48 years, 42% men, BMI<30, DBP 90-104 mm Hg, not on AHTM	40 assigned (by GP randomisation) to receive low sodium dietary advice; 26 followed up at 12 months; USE target ⩽80	37 assigned (by GP randomisation) to maintain usual diet; 30 followed up at 12 months	BP and USE at 1, 3, 6, 9, 12 months	Allocation inadequately concealed (cluster randomisation by GP); participants not blinded; assessors not blinded; losses excluded
People with treated hypertension					
Morgan 1987 (Australia)[14]	Mean age 61 years, all men, DBP <85 mm Hg on AHTM (>100 uncontrolled)	10 assigned to low sodium diet; 10 followed up at 9 months; target sodium intake 50-75 mmol/24 hours	10 assigned to maintained normal diet; 10 followed up at 9 months	Necessity to restart AHTM after withdrawal, USE at 0 and 9 months	Concealment of allocation unclear; participants not blinded; outcome assessors blinded; last BP reading before reinstatement was used; all had at least one follow up
Arroll 1995 (New Zealand)[12]	Mean age 55 years, 52% men, on AHTM (DBP >70 to 105 mm Hg or SBP >155 to 180 mm Hg)	51 asked to reduce use of high salt foods, salt added at table and in cooking; 44 followed up at 6 months; USE targets not stated	49 assigned to no intervention; 43 followed up at 6 months	BP and AHTM levels after withdrawal of AHTM at 0 and 6 months, USE at 6 months	Concealment of allocation unclear; participants not blinded; outcome assessors blinded; losses excluded from BP measurement, no adjustment made for those who decreased or stopped medication
TONE 1998 (USA)[20]	Mean age 67 years, 49% men, 76% white, on AHTM, DBP <85 mm Hg, SBP <145 mm Hg	340 assigned to group plus individual nutrition and behavioural counselling programme; 310 followed up at 30 months; USE target <80	341 assigned to no counselling; 314 followed up at 30 months	Combined BP, use of AHTM, and cardiovascular events. USE at 0, 9, 18, 30 months	Allocation adequately concealed; participants not blinded; outcome assessors blinded; used survival analysis with censoring to project proportions free of end points

AHTM=antihypertensive medication, SBP=systolic blood pressure, DBP=diastolic blood pressure, USE = urinary sodium excretion, in mmol/ 24 hours, GP=general practitioner.

Mortality and cardiovascular events

Mortality and cardiovascular events were inconsistently reported. No differences in periods of admission to hospital were seen between intervention groups in the hypertension prevention trial (no further data were provided).[19] Morgan et al reported that three participants in the control group and two participants on low sodium diets were treated for cardiac failure, with four cardiovascular deaths in the low sodium group and two in the control group.[15 28] The trial of non-pharmacological interventions in elderly people recorded a wide range of cardiovascular events: 57 in control participants and 44 in those on low sodium diets (relative risk 0.77, 95% confidence interval 0.41 to 1.14).[20 29] However, only nine of these events were due to stroke or myocardial infarction. Overall, the trials

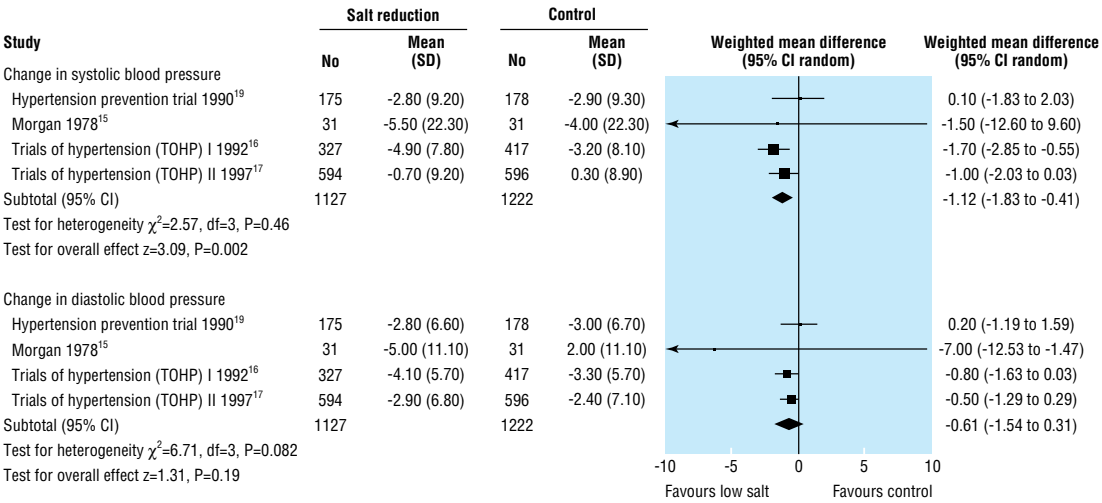

Fig 2 Change in systolic and diastolic blood pressure achieved in trials of 13 to 60 months (mm Hg)

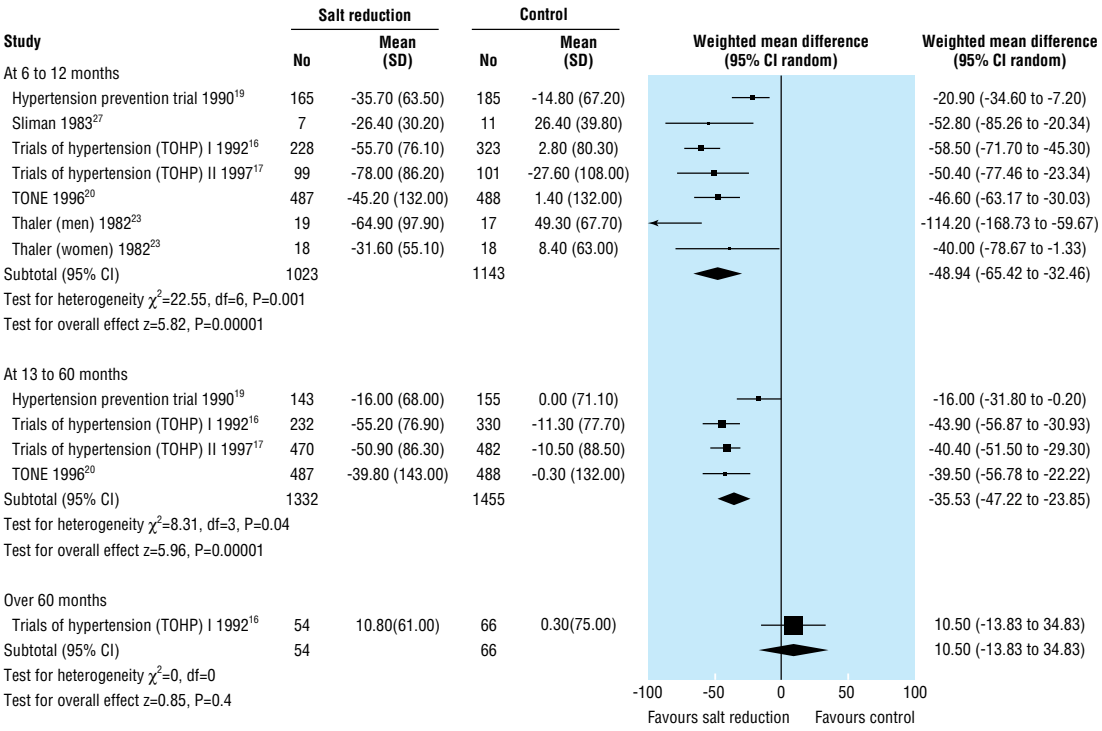

Fig 3 Change in urinary sodium achieved in trials of 6 to 12 months, 13 to 60 months, and >60 months (mmol Na/24 hours)

reported few deaths: nine in control groups and eight in low sodium groups.

Blood pressure

Table 2 shows changes in blood pressure and urinary sodium excretion for each trial, and table 3 shows pooled changes at intermediate and late assessments (fig 2). Reductions in systolic and diastolic blood pressure were apparent at both intermediate (2.5 mm Hg, 3.8 to 1.2; 1.2 mm Hg, 1.8 to 0.7, respectively) and late follow up (1.1 mm Hg, 1.8 to 0.4; 0.6 mm Hg, 1.5 to −0.3). When we carried out sensitivity analyses excluding low quality trials, which included all trials on people with untreated hypertension, the statistical heterogeneity that had been apparent for systolic blood pressure at intermediate follow up and diastolic blood pressure at late follow up was no longer apparent. As these trials were small the effect on pooled estimates of change in blood pressure was minor. Sensitivity analyses including all arms of the factorial trials,[17 19] suggest that inclusion of weight reduction arms reduces the effect on blood pressure. Meta-regression of change in blood pressure up to 12 months that used all trials with relevant data showed

Table 2 Results of trials included in meta-analysis. Figures are mean (SD) for blood pressure (mm Hg) and urinary sodium excreted in 24 hours (mmol) for control and interventions groups

Trial name	Initial mean systolic BP	Change in systolic BP at latest point to 12 months	Change in systolic BP at latest point after 12 months	Initial mean diastolic BP	Change in diastolic BP at latest point to 12 months	Change in diastolic BP at latest point after 12 months	Initial urinary sodium	Change in urinary sodium at latest point to 12 months	Change in urinary sodium at latest point after 12 months
People without hypertension									
HPT 1990									
Control	123.9	–2.1 (8.3)* at 6 months	–2.9 (9.3)* at 36 months	83.0	–3.0 (6.9)* at 6 months	–3.0 (6.7)* at 36 months	164.9†	–14.8 (67.2)† at 6 months	0.0 (71.1)† at 36 months
Intervention	124.0	–3.8 (7.9)* at 6 months	–2.8 (9.2)* at 36 months	82.6	–3.4 (6.6)* at 6 months	–2.8 (6.6)* at 36 months	162.6†	–35.7 (63.5)† at 6 months	–16.0 (68.0)† at 36 months
TOHP phase I 1992									
Control	125.1 (8.1)	–3.9 (7.4) at 12 months	–3.16 (8.1) at 18 months	83.9 (2.8)	–3.4 (5.7) at 12 months	–3.3 (5.7) at 18 months	156.4 (60.5)	2.8 (80.3) at 6 months	–11.3 (77.7) at 18 months
Intervention	124.8 (8.5)	–5.8 (7.5) at 12 months	–4.9 (7.8) at 18 months	83.7 (2.7)	–4.4 (5.4) at 12 months	–4.1 (5.7) at 18 months	154.6 (59.9)	–55.7 (76.1) at 6 months	–55.2 (76.9) at 18 months
TOHP phase II 1997									
Control	127.3 (6.4)	–2.2 (8.1) at 6 months	0.3 (8.9) at 36 months	85.8 (1.9)	–2.8 (6.1) at 6 months	–2.4 (7.1) at 36 months	188.0 (80.9)	–27.6 (108.0) at 6 months	–10.5 (88.5) at 36 months
Intervention	127.7 (6.6)	–5.1 (8.6) at 6 months	–0.7 (9.2) at 36 months	86.1 (1.9)	–4.4 (6.7) at 6 months	-2.9 (6.8) at 36 months	186.1 (80.7)	–78.0 (86.2) at 6 months	–50.9 (86.3) at 36 months
People with untreated hypertension									
Morgan 1978									
Control	165 (16.7)	–3 (22.3) at 12 months	–4 (22.3) at 24 months	97 (8.6)	1 (11.1)	2 (11.1) at 24 months	191 (35)	Not given	–11 at 24 months
Intervention	160 (22.3)	–3 (22.3) at 12 months	–5.5 (22.3) at 24 months	97 (8.7)	-3 (11.1)	–5 (11.1) at 24 months	195 (55.0)		–38 at 24 months
Costa 1981									
Control	143.4 (13)	4.3 (18.8)‡ at 12 months		84.1 (7)	–0.2 (32.6)‡ at 12 months		Not given		Not given
Intervention	143.3 (15)	–14.0 (18.5)‡ at 12 months		84.2 (9)	–6.1 (31.7)‡ at 12 months				
Thaler 1982, index men									
Control	139 (12)	3.4 (17.4)§ at 12 months		90 (12)	0.8 (9.2)§ at 12 months		159.5 (72.5)	49.3 (67.7) at 12 months	
Intervention	137 (14)	–5.0 (8.3)§ at 12 months		86 (9)	0.6 (9.2)§ at 12 months		178.1 (76.5)	–64.9 (97.9) at 12 months	
Thaler, index women									
Control	148 (25)	1.1 (14.4)§ at 12 months		83 (12)	2.8 (8.5)§ at 12 months		120.1 (41.5)	8.4 (63.0) at 12 months	
Intervention	145 (18)	–11.1 (24.2)§ at 12 months		86 (11)	–6.8 (11.9)§ at 12 months		118.0 (39.9)	–31.6 (55.1) at 12 months	
Silman 1983									
Control	160.5	–20.0 (24.0) at 12 months		98.3	–11.4 (10.5) at 12 months		146.5	26.4 (39.8) at 12 months	
Intervention	165.3	–28.7 (26.6) at 12 months		98.8	–17.7 (11.4) at 12 months		150.8	–26.4 (30.2) at 12 months	
Alli 1992									
Control	148.3 (10.6)	–0.3 (16.4)‡ at 12 months		97.2 (3.8)	–2.7 (16.6)‡ at 12 months		177.3 (61.7)	–4.2¶ at 12 months	
Intervention	150.8 (8.7)	–6.6 (13.6)‡ at 12 months		97.0 (3.1)	–6.4 (18.5)‡ at 12 months		177.3 (61.0)	8.6¶ at 12 months	
People with treated hypertension									
Morgan 1987									
Control	143 (15.8)	35 (25.7)‡§ at 9 months		81 (6.3)	17 (28.7)‡§		163 (50.6)	–8	
Intervention	143 (15.8)	12 (21.5)‡§ at 9 months		83 (6.3)	7 (22.2)‡§		168 (37.9)	–93	
Arroll 1995									
Control	145.3 (15.7)	–6.2 (21.0)‡§ at 6 months		94.0 (9.8)	–4.8 (36.1)‡§ at 6 months		Not given	Not given	
Intervention	145.4 (15.9)	–9.1 (21.7)‡§ at 6 months		86.4 (9.9)	–1.7 (34.9)‡§ at 6 months				
TONE 1998									
Control	128 (9)			71 (7)			146.2	1.4 (132)** at 9 months	–0.3 (132)** at 30 months
Intervention	129 (9)			72 (7)			145.3	–45.2 (132)** at 9 months	–39.8 (143)** at 30 months

*Change data adjusted for baseline differences in composition of treatment groups on 12 covariates
†8 hour overnight urine samples collected, means (SD) adjusted to 24 hour data (×3.8).
‡SD calculated as explained in methods.
§Levels of antihypertensive medications altered in some participants through study so data not used in meta-analyses.
¶Data measured off graph, so estimated.
**Data include urinary sodium data for those in weight loss group (added into control, total n=488) and weight loss plus sodium reduction group (added into intervention, total n=487) as this information was not available for separate intervention groups.

Table 3 Results of meta-analysis, subgrouping, and sensitivity analysis

Type of analysis	No of studies	Weighted mean difference (95% CI)	P value for heterogeneity
Sodium excretion (mmol Na/24 hours)			
Overall analysis (at 6 to 12 months)	6	−48.9 (−65.4 to −32.5)	0.001
Sensitivity analysis:			
Allocation concealment	4	−43.6 (−62.6 to −24.6)	0.001
Including weight arms	6	−44.3 (−58.4 to −30.2)	<0.001
Overall analysis (at 13 to 60 months)	4	−35.5 (−47.2 to −23.9)	0.04
Sensitivity analysis:			
Allocation concealment	4	−35.5 (−47.2 to −23.9)	0.04
Including weight arms	4	−33.3 (−42.0 to −24.6)	0.05
Overall analysis (at >60 months)	1	10.5 (−13.8 to 34.8)	
Systolic blood pressure (mm Hg)			
Overall analysis (at 6 to 12 months)	7	−2.5 (−3.8 to −1.2)	0.08
Sensitivity analysis:			
Drop calculated SD	5	−2.3 (−3.0 to −1.7)	0.57
Smallest calculated SD	7	−3.1 (−4.8 to −1.3)	0.01
Allocation concealment	3	−2.3 (−3.1 to −1.6)	0.31
Including weight arms	7	−1.6 (−3.0 to −0.2)	<0.001
Subgroups:			
No hypertension	3	−2.3 (−3.1 to −1.6)	0.31
Untreated hypertension	4	−8.0 (−15.8 to −0.2)	0.15
Overall analysis (at 13 to 60 months)	4	−1.1 (−1.8 to −0.4)	0.46
Sensitivity analysis:			
Allocation concealment	3	−1.1 (−1.9 to −0.3)	0.28
Including weight arms	4	−0.5 (−1.4 to 0.4)	0.10
Subgroups:			
No hypertension	3	−1.1 (−1.9 to −0.3)	0.28
Untreated hypertension	1	−1.5 (−12.6 to 9.6)	
Overall analysis (at >60 months)	1	−3.8 (−7.9 to 0.3)	
Diastolic blood pressure (mm Hg)			
Overall analysis (at 6 to 12 months)	7	−1.2 (−1.8 to −0.7)	0.51
Sensitivity analysis:			
Drop calculated SD	5	−1.2 (−1.8 to −0.6)	0.31
Smallest calculated SD	7	−1.3 (−2.1 to −0.6)	0.25
Allocation concealment	3	−1.2 (−1.8 to −0.6)	0.28
Including weight arms	7	−0.7 (−1.5 to 0.1)	0.05
Subgroups:			
No hypertension	3	−1.2 (−1.8 to −0.6)	0.28
Untreated hypertension	4	−4.5 (−8.7 to −0.4)	0.97
Overall analysis (at 13 to 60 months)	4	−0.6 (−1.5 to 0.3)	0.08
Sensitivity analysis:			
Allocation concealment	3	−0.5 (−1.1 to 0.0)	0.48
Including weight arms	4	−0.3 (−1.0 to 0.4)	0.06
Subgroups:			
No hypertension	3	−0.5 (−1.1 to 0.0)	0.48
Untreated hypertension	1	−7.0 (−12.5 to −1.5)	
Overall analysis (at >60 months)	1	−2.2 (−4.8 to 0.4)	
Dropouts			
Overall analysis in low sodium *v* control groups (latest follow up)	10	RR=1.04 (0.86 to 1.25)	0.55

RR=relative risk.

no relation with change in urinary sodium excretion, baseline systolic blood pressure, or age (table 4).

Urinary sodium excretion

We found reductions in urinary 24 hour sodium excretion at both intermediate (48.9 mmol/24 hours, 65.4 to 32.5) and late follow up (35.5 mmol/24 hours, 47.2 to 23.9) (fig 3). We identified significant heterogeneity in both analyses that was not explained by trial quality. One trial in people without hypertension found that at seven years sodium excretion in a small subset of the original sample was similar in intervention and control groups.[30]

Quality of life

Information on quality of life was patchy, with no common outcome measures. The hypertension prevention trial asked participants whether they were having problems with their diets.[31] Of those in the low sodium group, 69% reported problems such as inconvenience and difficulty with adherence when eating out at some time during the three years of the trial, and problems were reported at 42% of clinic visits.

The trials of hypertension prevention, phase I (TOHP I), reported psychological wellbeing scores, which improved significantly in participants in the low sodium groups at 18 months compared with the non-intervention control group.[32] Thaler et al reported that participants did not find it difficult to stop adding salt at table, but many found cutting down on salt in cooking harder.[23] Most found their low salt bread (salt cut from 2.1% to 1.0% dry weight) and salt-free butter acceptable. Only 13% of participants reported their salt restricted diet as unpleasant or worse. Overall dropout rates, a possible marker of quality of life on trial, were similar (relative risk 1.04; 0.86 to 1.25) in low sodium and control groups.

Antihypertensive medications used

Low salt diets seemed to allow people with hypertension to stop taking medication. In one small trial that compared 10 men in each group, six on low sodium diets had not restarted antihypertensive drugs at six months compared with only one in the control group (relative risk 0.44; 0.20 to 0.98).[14] In a larger study of 975 participants, primary end points (a combination of high blood pressure at any visit, restarting antihypertensive medication, or any clinical cardiovascular disease) were less common in the low sodium group (relative risk 0.83, 0.75 to 0.92).[20]

Discussion

Eleven long term randomised controlled trials of dietary salt reduction (including 3491 participants) provided few data on mortality (17 deaths in total), cardiovascular events, or quality of life but did show significant falls in systolic blood pressure (1.1 mm Hg, 1.8 to 0.4) and urinary sodium excretion (35.5 mmol/24 hours, 47.2 to 23.9) at 13 to 60 months after initial advice. Falls in diastolic blood pressure were smaller and were consistent with no effect (0.6 mm Hg, 1.5 to −0.3). A low salt diet may help people on

Table 4 Meta-regression: effects of mean baseline systolic blood pressure, change in sodium excretion, mean age of participants on systolic blood pressure at 6 to 12 months

	Trials in people with and without hypertension			Trials in people without hypertension		
Explanatory variable	**Slope coefficient (95% CI)**	**Constant**	**No of trials**	**Slope coefficient (95% CI)**	**Constant**	**No of trials**
Mean baseline systolic blood pressure	−0.173 (−0.356 to 0.010)	19.5	7	−0.362 (−0.826 to 0.102)	43.3	3
Mean change in urinary sodium excretion at 6-12 months	0.013 (−0.049 to 0.075)	−1.68	4	0.013 (−0.057 to 0.084)	−1.63	3
Mean age of participants at baseline	0.118 (−0.188 to 0.424)	−7.46	7	−0.213 (−0.630 to 0.203)	6.81	3

antihypertensive drugs to stop their medication without loss of blood pressure control.

Limitations and strengths of review

Health promotion interventions involve several stages before any health outcome is seen. Firstly, the advice must result in changed behaviour (cutting down on salt in food) and, secondly, that behaviour must result in an improved health outcome (reduced cardiovascular illness, increased life expectancy). A major limitation of this review is that we were not able to assess the overall effect of advice to reduce dietary sodium on mortality or morbidity as too few events occurred. Instead we assessed several intermediate outcomes including urinary sodium excretion and blood pressure.

The observed sodium reduction of about a quarter of usual intake in US and UK populations may be an overestimate.[33] Almost half the participants in one trial ate differently on food record days, eating less food and substituting simpler foods and also eating less salt.[34] The completeness of urine samples is not known and it has been suggested that less salty foods were eaten on collection days in the trial of Thaler et al[23] (O Simpson, personal communication, 2001).

While both urinary sodium excretion and blood pressure fell, the salt reduction may not have caused the fall in blood pressure. Alterations in diet aimed at reducing salt intake may systematically affect other dietary components (such as alcohol, potassium, or energy intake) that themselves alter blood pressure. This might explain why we found no relation between the degree of reduction in sodium excretion and change in blood pressure. However, the number of

Table 5 Characteristics of systematic reviews on salt and blood pressure

Trial	Inclusion criteria (population, intervention, outcome, design)	Only randomised data included?	Normotensive or hypertensive	Median (range) duration of trials	No of trials (No of participants)	Fall in sodium excretion (mmol/24 hours)*	Pooled mean difference* (95% CI) (mm Hg)		Quality assessment and other detail
							Systolic BP	Diastolic BP	
Graudal 1998[4]	Mean age >15 years; low sodium or high sodium diet, no confounding; urinary sodium excretion measured, systolic, diastolic or mean BP reported	Yes, random allocation, parallel or crossover	Normotensive	8 (4-1100) days	56 (2581)	160	−1.2 (−0.6 to −1.8)	−0.26 (0.3 to −0.9)	Subgrouping by open/single blind or double blind method did not affect results. Statistical heterogeneity noted
			Hypertensive	28 (4-365) days	58 (2161)	118	−3.9 (−3.0 to −4.8)	−1.9 (−1.3 to −2.5)	
Midgley 1996[2]	Not on antihypertensive drugs; dietary sodium intervention; diastolic and systolic BP measurement, urinary sodium excretion; English language, full length journal articles	Yes, randomised controlled trials (crossover or parallel design)	Normotensive	14 (4-1095) days	28 (2374)	125 (95 to 156)	−1.6 (−2.41 to −0.89)	−0.5 (−1.18 to 0.11)	Significant heterogeneity seen, reduced but not eliminated when studies subgrouped according to quality characteristics. Evidence of publication bias provided
			Hypertensive	29 (4-730) days	28 (1131)	95 (71 to 119)	−5.9 (−7.77 to −4.12)	−3.8 (−4.78 to −2.9)	
Law 1991[1]†	Not on antihypertensive drugs; dietary sodium restriction, not confounded; 24 hour urine collection, systolic and/or diastolic BP	No	Normotensive	1.5 (0.7 to 16) weeks	15 (?)	Not stated	Not stated	Not stated	Quality not assessed. Individual trial data compared with pooled observational data, rather than pooled together
			Hypertensive	5 (0.7 to 104) weeks	63 (?)	Not stated	Not stated	Not stated	
Cutler 1997[3]	Adult; sodium goals 28-273 mmol/24 hours, no confounding allowed; lab-based measure of sodium intake, systolic and/or diastolic BP measured	Yes, randomised controlled trials (crossover or parallel design), published only	Normotensive	1 (0.5 to 36) months	12 (1689)	Median ~90 (range 16 to 210)	−1.5 (−2.1 to −1.0)	−0.8 (−1.3 to −0.3)	Subgrouping by double blind or not had no significant effect on overall outcome. Regression analyses used for publication bias failed to reject null hypothesis
			Hypertensive	2 (1-24) months	22 (1043)	Median ~71 (range 27 to 171)	−3.8 (−4.9 to −2.8)	−2.1 (−2.8 to −1.5)	
Alam 1999[5]	Aged >50 years; changes in dietary NaCl; blood pressure	Yes, published English-language randomised controlled trials, crossover or parallel	Normotensive (2 trials) or with essential hypertension (9 trials)	14 (9-104) weeks	11 (485)	Median 80 (range 23 to 260)	−5.6 (−6.9 to −4.3)	−3.5 (−4.4 to −2.6)	Score tended to be high (average score >70%)
Ebrahim and Davey Smith 1998[7]	Adult; dietary sodium reduction *v* control; diastolic and systolic BP measurement, urinary sodium excretion	Yes, randomised controlled trials of at least 6 months duration	Normotensive	Not stated	2 (1095)	Not stated	−1.3 (−2.7 to 0.1)	−0.8 (−1.8 to 0.2)	Quality not assessed
			Hypertensive	Not stated	6 (466)	Not stated	−2.9 (−5.8 to 0.0)	−2.1 (−4.0 to −0.1)	
This review, 6-12 months	Adult; sodium reduced diet *v* usual diet; urinary sodium excretion, systolic and/or diastolic BP measurements taken 6 to 12 months or more than 13 to 60 months after intervention	Yes, parallel randomised controlled trials	Normotensive	6 (6 to 12) months	3 (2326)	43 (16 to 70)	−2.3 (−3.1 to −1.6)	−1.2 (−1.8 to −0.6)	Sensitivity analysis (removing trials where allocation concealment is poor or unclear) had no effect on direction or significance of results
			Hypertensive	12 (12 to 12) months	4 (223)	48 (33 to 63)	−8.0 (−15.7 to −0.3)	−4.3 (−7.1 to −1.6)	
This review, 13-60 months			Normotensive	36 (18 to 36) months	3 (2326)	34 (19 to 50)	−1.1 (−1.9 to −0.3)	−0.5 (−1.1 to 0.0)	
			Hypertensive	24 months	1 (77)	40 (22 to 57)	−1.5 (−12.6 to 9.6)	−7.0 (−12.5 to −1.5)	

*Weighted mean (95% CI) unless stated otherwise. Weighting for all pooled data by inverse variance.
†Review estimates that in people aged 50-59 reduction in 50 mmol Na/24 hours would lead to reduction of 5 mm Hg in systolic and 2.5 mmHg in diastolic blood pressure in people without hypertension and reduction of 7 mm Hg and 3.5 mm Hg, respectively, in people with hypertension.

trials is small and relating a mean change in blood pressure to a mean change in urinary sodium is statistically weak. In previous meta-analyses an association was seen in some cases but not others (table 5). Data on individual participants are required to take this issue further.

Despite the importance of answering the question of the long term effects of dietary salt restriction, most of the many randomised controlled trials published have been of short duration and can show only that salt restriction is capable of reducing blood pressure but provide no useful information for primary care practice. As randomised controlled trials are available, we have not included population surveys, cohorts, or animal trials that are unable to estimate the unconfounded effects of salt restriction in human populations and are difficult to interpret.[35]

Is it realistic to ask people to alter their salt intake long term? Advice to reduce dietary salt is common in primary care and is a central part of the guidelines produced by the British Hypertension Society.[36] Despite a great deal of ongoing encouragement and support used in the trials included in this review, it seems that salt reduction attenuates over time. In routine primary care the intervention is likely to be less intense and therefore of more limited impact.

Comparison with previous studies

It is unclear what effects a low sodium diet has on cardiovascular events and mortality. Lowering sodium intake may have adverse effects on vascular endothelium through stimulation of the renin-angiotensin system[37] and on serum total and low density lipoprotein cholesterol concentrations.[4] In cohort studies, lower salt intake in people with hypertension has been associated with higher levels of cardiovascular disease[38] and in general populations with greater all cause mortality.[39 40] However, among obese people lower salt intake may be associated with a reduced risk of cardiovascular events.[41 42] These apparently contradictory findings may be explained by confounding or by differential sensitivity to salt intake but make it less clear that salt restriction is without hazards.

We expected that short duration trials would achieve larger reductions in blood pressure that would attenuate over time. As shown in table 5, short term trials of median length of eight days showed a greater reduction in urinary sodium excretion but a similar fall in systolic blood pressure to the findings from long term trials of median length 36 months in this review. The recent dietary approaches to stop hypertension (DASH) trial showed that over a 30 day period with intensive measures, which included provision of all food, systolic blood pressure can fall substantially (by 6.7 mm Hg, 5.4 to 8.0 mm Hg),[43] but this finding is of little relevance to the issue of achieving long term reductions in blood pressure by practical means in primary care.

Implications

Long term maintenance of low sodium intake is difficult, even with a great deal of support, advice, and encouragement. A policy of reduction in salt intake for the entire population through cutting salt concentrations in processed foods,[44] as recently announced by the UK chief medical officer,[45] can achieve small reductions in blood pressure across the whole population for sustained periods of time. Individual reduction of risk would be small, but across a whole population the effects may be substantial.[46 47]

However, raised blood pressure is only one risk factor for cardiovascular disease and overall clinical benefits (or harms) of a low sodium diet are unclear. Revisiting all participants of the large trials in people without hypertension some years later to assess long term effects of low sodium dietary advice on mortality and cardiovascular morbidity would be a cost effective and relatively rapid way to assess the clinical effectiveness of advice to reduce sodium intake. There is strong justification for a large scale, long term randomised controlled trial to explore the cost effectiveness of such advice if it is to remain a part of the strategy for prevention and treatment of hypertension.

What is already known on this topic

Restricting sodium intake in people with hypertension reduces blood pressure

Long term effects (on blood pressure, mortality, and morbidity) of reduced salt intake in people with and without hypertension are unclear

What this study adds

Few deaths and cardiovascular events have been reported in salt reduction trials

Meta-analysis shows that blood pressure was reduced (systolic by 1.1 mm Hg, diastolic by 0.6 mm Hg) at 13 to 60 months, with a reduction in sodium excretion of almost a quarter (35.5 mmol/24 hours)

The interventions used were highly intensive and unsuited to primary care or population prevention programmes

Lower salt intake may help people on antihypertensive drugs to stop their medication while maintaining good control of blood pressure, but there are doubts about effects of sodium reduction on overall health

Conclusions

On present evidence intensive interventions, unsuited to primary care or population prevention programmes, produce uncertain effects on mortality and cardiovascular events and only small reductions in blood pressure. However, advice to reduce sodium intake in the diet may help some people on antihypertensive drugs to stop their medication while maintaining good control of blood pressure.

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independently searched, decided on trial inclusion or exclusion, extracted data, and assessed study quality. LH, CB, and SE performed and duplicated the statistical analyses. SE and GDS were primary advisers, guiding and interpreting the review. LH is the guarantor.

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