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Conflicting Evidence on Health Effects Associated with Salt Reduction Calls for a Redesign of the Salt Dietary Guidelines☆

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ABSTRACT

Ninety-five percent of the World's populations have a mean salt intake between 6 and 12 g, which is much lower than the tolerated daily level of up to 55 g/d. In spite of this, the recommended upper level by many health institutions is as low as 5.8 g/day. When reviewing the evidence for an upper level of 5.8 g/day, it becomes apparent that neither the supporting studies selected by the health institutions, nor randomized controlled trials and prospective observational studies disregarded by the health institutions, document that a salt intake below this 5.8 g, has beneficial health effects. Although there is an association between salt intake and blood pressure, both in randomized controlled trials and in observational studies, this association is weak, especially in non-obese individuals with normal blood pressure. Furthermore a salt intake below 5.8 g is associated with the activation of the renin-angiotensin-aldosteron system, an increase in plasma lipids and increased mortality. A redesign of the salt dietary guidelines, therefore, seems to be needed.

Contents

Abbreviations: AHA, American Heart Association; BMI, body mass index; BP, blood pressure; CDC, Centers for Disease Control and Prevention; CVD, cardiovascular disease; DASH, the Dietary Approaches to Stop Hypertension; FDA, Food and Drug Association; g/d, gram per day (24 h); HF, heart failure; HTN, hypertension; IOM, Institute of Medicine; Na, sodium (natrium); NAM, National Academy of Medicine; NHLBI, National Heart, Lung and Blood Institute; NIH, National Institute of Health; RAAS, renin-aldosterone-angiotensin system; RCTs, randomized controlled trials; SR, salt reduction; WASH, World Action on Salt and Health; WHO, World Health Organization.

☆ Statement of conflict of interest: see page 25.

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Introduction

Ninety-five percent of the World's populations have a mean salt intake between 6 and 12 g/d,[1] the minimum required amount being about 0.5 g/d.[2] Salt intake of up to about 55 g/d has been recorded.[3] Randomized controlled trials (RCTs) of salt intake in the interval 0.5–40 g/d have not reported deficiency or toxic symptoms.[4] Intoxication has been described after rapid intake of about 50 g or more over a few minutes.[5] Salt is essential for life, as it contributes to the action potentials and membrane potentials of cells and maintains extracellular volume and blood pressure (BP).[6] Centers in the brain regulate body salt, together with the renin-aldosterone-angiotensin system (RAAS) and the kidneys.[6,7]

Still, many health institutions agree that salt is as toxic as tobacco and, therefore, consider salt to be a target for prevention.[8,9] This position is based on a belief that salt not only maintains BP, but increases BP as a linear function of the ingested amount, leading to increased mortality.[8] In recent years a significant number of RCTs and population studies have questioned the harmful effects of salt.[4,10] Many health institutions disagree and still support interventions to reduce salt intake in the general population to below 5.8 g[8,9,11] in parallel with attempts to reject the outcomes of studies showing harmful effects of low salt intake.[12] Representatives from the American Heart Association (AHA) reviewed the methodological quality of 26 population studies to analyze whether methodological issues accounted for the lack of beneficial effects of low salt intake. They concluded that these studies, due to methodological issues, were not suited to form the basis for salt guidelines, which should instead be based on "the robust body of evidence linking Na with elevated blood pressure and the few existing general population trials of the effects of Na reduction on cardiovascular disease (CVD)".[12] However, as indicated in a meta-analysis of RCTs[4] this evidence may not be as robust as previously claimed.[12] We therefore find it pertinent to present a collective critical review of the quality of the key health evidence for salt reduction (SR) promoted by the health institutions in the context of the existing evidence from RCTs and prospective population studies.

Methods

We included RCTs and population studies as well as studies based on RCTs and population studies (meta-analyses and modeling studies) initiated or economically supported by the following health institutions and organizations, which give high priority to salt reduction: Centers for Disease Control and Prevention (CDC), National Institute of Health (NIH), National Heart, Lung and Blood Institute (NHLBI), Institute of Medicine (IOM, now National Academy of Medicine (NAM)), American Heart Association (AHA), Food and Drug Association (FDA), World Health Organization (WHO), and World Action on Salt and Health (WASH). The study identification was in part based on our previous systematic searches of RCTs[4] and population studies,[10] and reference lists from reports, studies and position papers published by the mentioned institutions.

Salt: effect on BP

IOM (now NAM) report on dietary salt reference intake

The upper limit for salt intake of 5.8 g recommended by health institutions originates from an IOM report,[8] which states, "most relevant to determining an upper level are the three trials in which the lowest level of dietary sodium intake was close to the adequate intake (Johnson et al., 2001; MacGregor et al., 1989; Sacks et al., 2001)." "In view of the results from these three trials, the lowest-observed adverse-effect level for dietary sodium is set at 2.3 g/day (5.8 g salt/day)." These 3 studies,[13-15] which randomized individuals to 3–4 different doses of salt (dose-response analyses), all showed a significant proportional increase in BP with increased salt intake both below and above a salt intake of 5.8 g, thus justifying the conclusion that salt intake should be below 5.8 g. Fig. 1 shows all known dose-response studies published at the time of the IOM evaluation. The 3 studies[13-15] considered by IOM were all studies of older individuals with hypertension (HTN) and those with the steepest dose-response relationships. The HTN study with the lowest dose-response relationship[16] and four normotensive studies without dose-response relationships (Fig. 1)[16,17] were not included in the evaluation. This selective inclusion was further emphasized by the fact that high BP and age biased the three selected studies.

The first study included older individuals with very high BP.[13] Members of the WASH group performed the second study.[14] This group has published 10 studies in individuals with HTN showing a mean effect of SR on systolic BP(SBP) of about 10 mm Hg, which is twice that reported in all other RCTs of HTN (4.85 mm Hg) (Table 1). This indicates a systematic bias, which only partly depends on the high baseline BP of the included populations. The chair of the 2005 IOM committee[7] was co-author of the third study.[15] This study, the Dietary Approaches to Stop Hypertension (DASH) study, is the most highlighted of the studies used to justify SR.

The Dietary Approaches to Stop Hypertension (DASH) studies[15,18]

In the first DASH study[18] 3 diets were compared, a control diet depleted in potassium, calcium and magnesium to the 25% percentile of the population in order "to ensure a marked contrast to the ideal dietary patterns". The ideal diet was rich in potassium, calcium, magnesium, carbohydrate, protein and fiber and low in fat. The third diet was in between these two diets. At the time of the design of this study it was well known that potassium intake was inversely associated with BP.[19,20] Thus the BP-reducing effect of the potassium rich fruit supplemented DASH diet, identified in this study, may in part be ascribed to the designed potassium depletion in the control group.

The experiences from the first DASH trial[18] were carried forward to the subsequent DASH sodium trial,[15] in which the intermediate diet was eliminated and the participants were randomized to the ideal and

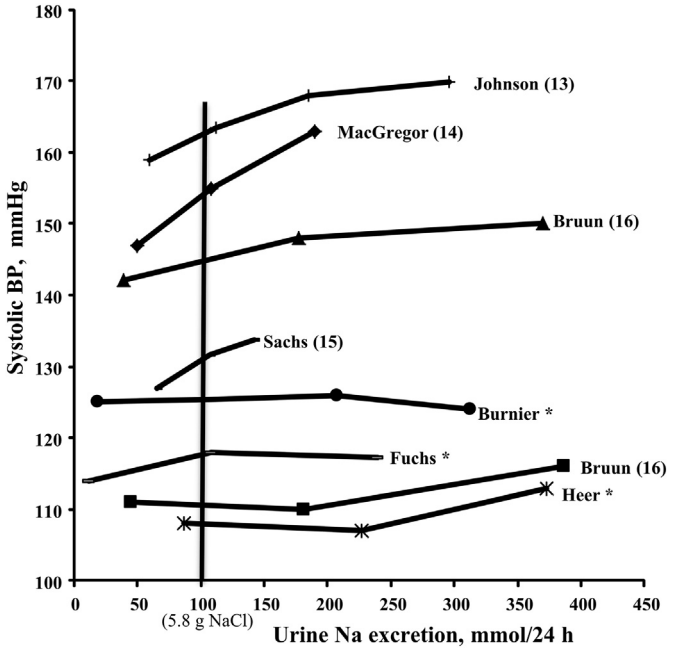

Fig. 1. Individual study systolic BP response to increasing changes in sodium urinary excretion (as a measure of sodium intake) in otherwise healthy normotensive and hypertensive individuals. Institute of Medicine[7] used studies 13, 14 and 15 to estimate the 5.8 g upper limit for salt intake *Burnier: J Hypertens 2000; 18:1657-64; *Fuchs: BJMBR 1987;20:25-34; *Heer: AJPRP 2000; 27: 278:F585-95.

Table 1
The effect of sodium reduction on systolic and diastolic blood pressure (SBP/DBP) in studies performed by researchers from the World Action on Salt and Health group.

Reference	Mean age (years)	Baseline SBP/DBP (mm Hg)	Duration, (days)	Sodium reduction (mmol)	Effect SBP/DBP (mm Hg)
1) Lancet 1982;i:351	49	156/98	28	76	−10/−5
2) BMJ 1987;294: 531	52	150/97	30	100	−13/−9
3) J Hypertens 1988;6:613	52	157/101	5	97	−9/−5.6
4) Lancet 1989;II:1244	57	163/100	30	141	−16/−9
5) Hypertension 1991;17:798	54	147/91	30	91	−9/−3
6) J Hypertens 1994;12:809	49	144/100	5	296	−11.6/−5
7) J Hum Hypertens1996;10:523	46	151/96	7	293	−15.2/−3.7
8) Lancet 1997;350:850	67	162/90	30	81	−7.2/−3.2
9) Hypertension 2005;46:308	63	156/100	28	78	−8/−3
10) Hypertension 2009;54:482	50	147/91	42	55	−5/−3
Mean effect of study 1–10, SBP					−10.21 [−12.75, −7.67]
Mean effect of study 1–10, DBP					−4.30 [−5.68, −2.92]
Mean effect of all hypertensive studies except study 1–10, SBP[a]					−4.85 [−5.80, −3.91]
Mean effect of all hypertensive studies except study 1–10, DBP[a]					−2.67 [−3.27, −2.07]

[a] Data obtained from the data file of reference 23.

control diets, respectively, and in addition crossed over to three different salt intake diets. SR reduced SBP by 6.7 mm Hg in the potassium depleted control diet and by 3 mm Hg in the ideal diet. A meta-analysis of five studies identified among 176 salt-reduction studies,[4] which in addition to allocation to a reduced salt diet also allocated participants to a combination of sodium reduction and potassium supplementation, shows a significant BP difference between a low sodium/low potassium diet versus a low sodium/high potassium diet (Fig. 2). This difference corresponds to the differences observed in the DASH sodium trial, indicating that the planned potassium depletion in the control group amplifies the BP reduction induced by salt reduction. Furthermore, the mean age, body mass index (BMI) and baseline BP of the included participants were significantly higher than the average American population. This general bias is reflected in a supplementary publication of the DASH trial, which shows that in younger individuals between 21 and 42 years, representing more than 50% of the American population, the supplied low-sodium/high potassium diet has no effect on SBP compared with the depleted low-sodium/low potassium diet.[21] Due to the design, interpretation and use of the DASH-sodium trial, it is a major limitation that the data from this government-funded trial are not publically available.[22]

WASH and WHO versus Cochrane: meta-analyses of the effect of reduced dietary salt intake on BP

Cochrane has published two salt-reduction reviews by two different author groups measuring exactly the same outcomes[4,23]; the justification being that the original review[4] investigates acute effects of SR, whereas the more recent review from 2004 by members of the WASH group[23] investigates longer-term effects. However, in 2004 there was no scientific justification for this distinction and a later review of longitudinal RCTs showed no differences in the effect of SR on BP between week 1 and week 6.[17] The WHO review[24,25] includes almost the same studies as the WASH review. Table 2 compares the original Cochrane review, the WASH review and the WHO review. In general there were no differences between the BP effects verifying that the distinction between acute and long-term studies is not justified. The marginally higher effect in the analysis of normotensive studies in the WASH review was due to the effect of the DASH study and 3 studies, which included both normotensive individuals and those with HTN (Table 3). After exclusion of these 4 studies the 8 remaining studies showed an effect, which was almost identical with the Cochrane review and the WHO review (Table 2).

CDC/FDA evidence for relation between reduced dietary salt intake and BP

Recently, the CDC and FDA released a proposal for voluntary guidelines to encourage food companies to steadily reduce sodium in processed and restaurant foods.[11,26] The argument was "strong evidence, including a recent analysis of more than 100 randomized clinical trials, that sodium reduction reduces blood pressure in adults." However, this analysis[27] was based on 65% HTN studies and 35% normotensive studies. The meta-regression line with a slope of 3.8 mm Hg per 100 mmol sodium (2.3 g sodium) was forced through zero and was primarily based on data adopted from the original Cochrane review.[4] The appropriate function with a constant reveals that the slope is only 2.27 mm Hg/100 mmol (Fig. 3). The authors applied the no-constant linearity from the mixed meta-regression analysis to both the HTN and the

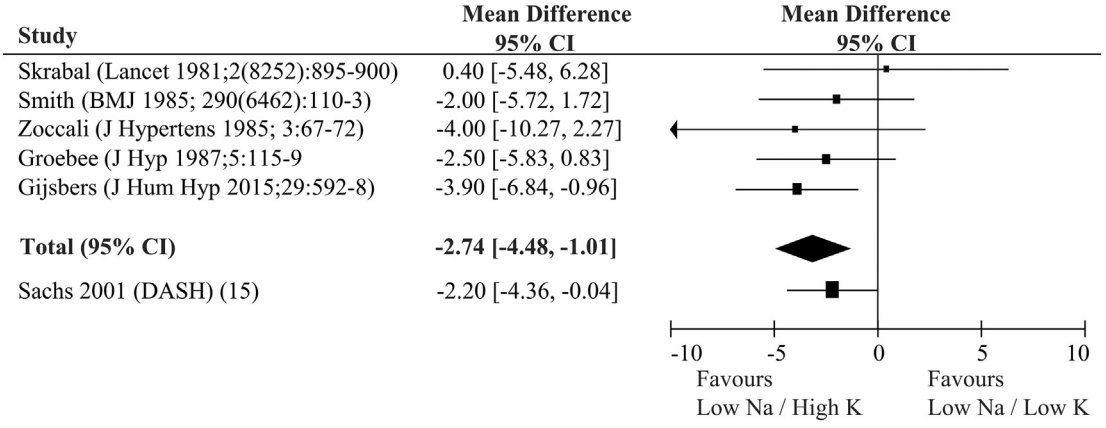

Fig. 2. Meta-analysis of the effect of low sodium/high potassium diet vs. low sodium/low potassium diet on systolic blood pressure and the effect of low sodium ideal diet (high potassium) vs. low sodium control diet (low potassium) in the DASH study.[15]

Table 2
Comparison of original Cochrane review (2003–2017), WASH group Cochrane review (2004–2013) and WHO review (2013): blood pressure.

	Graudal et al. 2003/2011 (original) Cochrane 2017 (4)		MacGregor et al. 2004 (WASH) Cochrane 2013 (23)		Aburto et al. WHO 2013 (25)	
	Hypertension	Normal BP	Hypertension	Normal BP	Hypertension	Normal BP#
N (n)	86 (6001)	90(8833)	22 (990)	12(2240)	24 (2273)	7 (3067)
Median Age (range), years	51.6	29	50	50	–	–
Median SBP/DBP, mm Hg	151/93	119/71	148/93	127/77	–	–
Median duration, weeks	4	1	5	4	4	4
Usual sodium, mean, mmol	183	199	162	153	–	–
Low sodium, mean, mmol	80	45	87	78	–	–
Sodium reduction, mean, mmol	103	154	75	75	–	–
Effect SBP/DBP	−5.51/−2.88	−1.09−/0.03	−5.39/−2.82	−2.42/−1	−4.06/−2.26	−1.38/−0.58
Effect SBP/DBP (subgroup) (N,n)		−1.31/−0.36 (59, 7125)[a]		−1.63/−0.43 (8, 2113)[b]		−1.38/−0.58 (7, 3067)

N: Number of studies; n: number of participants;
5 borderline studies were not included in the analysis.
[a] Studies with duration of at least 7 days.
[b] DASH study and studies of mixed hypertensive/normotensive individuals excluded.

normotensive individual studies and standardized the systolic BP effect to 2.3 g (100 mmol). In contrast, a separate meta-regression analysis of the normotensive studies shows that neither the assumption of linearity nor the cut point of zero is valid for the normotensive studies (Fig. 3). Thus the CDC and FDA assumed dose-response relationship is not valid for the 75% of the population with a normal BP.

CDC/NHLBI analysis of association between salt intake and BP in NHANES 2014

In the main article this recent analysis shows an association between sodium intake and BP, which is stronger than found in previous population studies (4.58/2.25 mm Hg/1 g Na).[28] However, according to eTable 2 in their supplement, this effect was mainly due to the adipose 50% of the population with a BMI above 30. In the group of participants with a BMI less than 30 the systolic BP effect was only 1.8 mm Hg/1 g Na. This is similar to the effect found in the worldwide Prospective Urban Rural Epidemiology (PURE) study (2.1 mm Hg/1 g Na), in which the study population had a mean BMI of 26.[29]

Salt: effect on hormones and lipids

WASH and WHO versus Cochrane: meta-analyses of the effect of reduced dietary salt intake on hormones and lipids

The effect of salt-reduction on renin, aldosterone, noradrenalin, adrenalin, cholesterol and triglyceride has been analyzed in the three previously mentioned meta-analyses.[4,23,25] The results are presented in Table 4. The original Cochrane review[4] reduces salt-intake to a mean level below 5.0 g in accordance with the recommendations, whereas the two small analyses of studies of at least 4 weeks duration[23,25] reduce salt intake down to, but not below, a mean level of 5.0 g corresponding to the WHO recommendations, which are to reduce salt below 5.0 g/d.[24] Thus, the level of salt intake, rather than the duration of the exposure, determines the occurrence of side effects. This has been verified in Yanomamo Indians on low-salt intake, who have persistently elevated levels of renin and aldosterone in the blood[2]; and in a cross-sectional study of individuals with normal BP and hypertension.[7] RAAS is activated by salt reduction in healthy and sick individuals, but McCarron suggested that in patients with heart failure (HF) and renal disease, whose RAAS is activated by a compromised renal perfusion, the activated RAAS might dictate a neural-driven increase in salt intake in an attempt to increase renal perfusion and suppress plasma renin activity and angiotensin II and its pathologic impact on the heart and vasculature.[30] Under these circumstances a high salt intake was suggested not to be causative, but more likely a compensatory response mechanism, serving as a natural RAAS inhibitor.[30] That interpretation is consistent with recent studies of patients with HF and renal disease showing that a low salt diet was not associated with reduced morbidity or mortality.[31,32]

Salt: effect on health outcomes

RCTs relating salt intake to health outcomes

RCTs measuring health effects have been performed in individuals with HTN and pre-HTN overweight individuals, but not in healthy

Table 3
Studies of participants with normal BP included in WASH Cochrane meta-analysis, 2013[23]

Reference	Baseline SBP/DBP mm Hg	Sodium intake, mmol High/low	SBP effect mm Hg	DBP effect mm Hg
Puska, Lancet 1983;I:1-5.	132/82	192/77	−1.5 (3.32)	−2.1 (2.03)
Watt, BMJ 1985;291:1525-8	113/65	130/68	(HH) −1.4 (0.74)	1.2 (0.93)
			(LL) −0.5 (0.82)	1.4 (0.9)
Mascioli, Hypertension 1991;17(S1):I21-6	131/84	179/109	−3.6 (0.9)	−2.3 (0.8)
TOHP I, JAMA 1992;267:1213-20	125/83	144/100	−1.7 (0.59)	−0.9 (0.42)
Cobiac, J Hypertens 1992;10:87-92	134/78	148/79	−1.7 (2.14)	0.8 (1.01)
Ruppert, Hypertens 1993;11:743-9	113/72	200/82	1.7 (2.39)	1 (1.64)
Nestel, Hypertens 1993;11:1387-94	129/77	157/106	(F) −6 (4.9)	−2 (3.31
			(M) −2(3.43)	−1 (2.65)
Schorr, J Hypertens 1996;14:131-5*	132/72 D12h**: 140/84	166/105	−7.2 (4.9)	−2.9 (2.61)
Cappucio, Lancet 1997;350:850-4*	149/84	167/91	−8.2 (3.07)	−3.9 (1.65)
TOHP II, Arch Intern Med 1997;157:657-67	128/86	178/135	−1.2 (0.5)	−0.7 (0.4)
DASH, NEJM 2001;344:3-10*	129/84	141/64	−5.3 (0.77)	−2.6 (0.5)
Melander, J Hypertens 2007;25:619-27*	136/78 D12h**: 141/90	140/51	−4.6 (2.1)	−2.8 (1.03)

*Excluded in sensitivity analysis; **12 h BP during daytime; HH: Parents high BP; LL: Parents low BP; F: Female; M: Male.

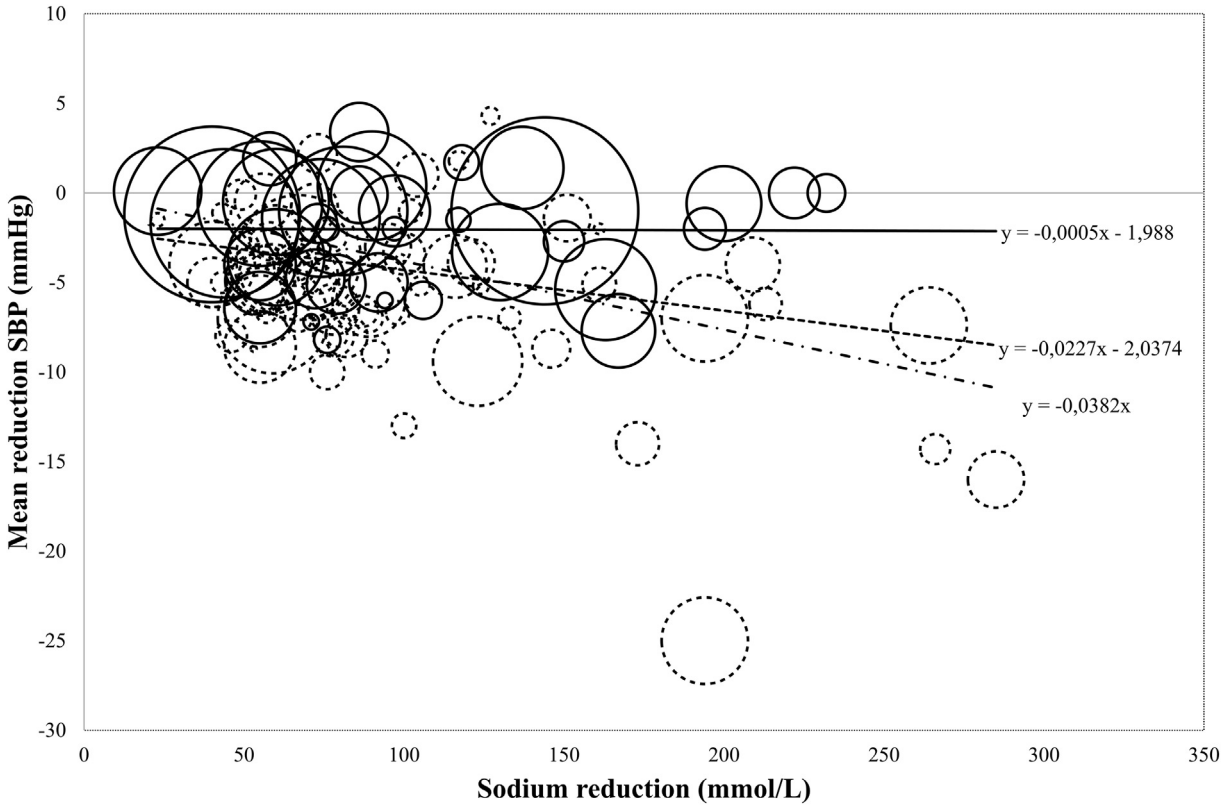

Fig. 3. Sodium reduction versus mean reduction of systolic blood pressure (MRSBP). Univariable analysis: Each circle shows the MRSBP outcome of one study comparing a reduced sodium intake versus a usual sodium intake (closed circles: Normotensive studies; stippled circles: Hypertensive studies). The size of the circle corresponds to its inverse variance weight of the MRSBP. Regression lines are shown for all studies with recommended method including a constant ($y = -0.0227\times-2.0374$), the no-constant method ($y = -0.0382\times$) and for normotensive studies only ($y = -0.0005\times-1.988$).

individuals. Collectively they showed a non-significant 24% reduction in CVD events in the low-salt group (data incompletely recorded) and no difference in all-cause mortality (data completely recorded).[33] The mean salt intake in the low-salt groups was 5.8 g or higher. Thus there are no RCTs to show health effects of salt-intake below 5.8 g.

Modeling studies relating salt intake to health outcomes

Modeling studies establish a dose-response relationship between salt intake and BP, which indirectly is used to translate salt reduction to reduction in mortality by means of data from observational studies linking BP to mortality. One modeling study[34] used the linear regression analysis based on data from the WASH meta-analysis (Table 3), data from the DASH study[15] (Fig. 1) and data from one of the WASH group studies[14] (Fig. 1) (study no. 4 in Table 1) to construct the dose-response analysis. Another study[27] used the data from the above described meta-regression analysis of 103 RCTs of which 65% were HTN. None of the modeling studies included side-effect data in the models, although side-effect data were available in the meta-analyses from which the BP data were adopted. These models predicted thousands to millions of saved lives by dietary salt reduction in contrast to real data from cohort studies, which indicate that low salt intake is associated with increased mortality.

Cohort studies relating salt intake to health outcomes

Evidence from WHO is based on a meta-analysis from 2009,[35] which was updated in 2013.[25] In the 2009 analysis the relative risk of higher versus lower salt intake was investigated by comparing the event rate in the two categories with a difference in average salt intake closest to 5.8 g/day. In the updated analysis[25] the overall effect estimate was generated comparing the risk of each outcome in the lowest salt intake group with the highest salt intake group. A third analysis used similar methods.[36] In several of the population studies the salt intake in the lowest salt group was within the usual range of salt intake (6–12 g). Thus, none of these three analyses provided data on the separate

Table 4
Comparison of original Cochrane review (2003–2017), WASH group Cochrane review (2004–2013) and WHO review (2013): hormones and lipids.

	Graudal et al. 2003/2011 (original) Cochrane 2017 (4)	MacGregor et al. 2004 (WASH) Cochrane 2013 (25)	Aburto et al. WHO 2013 (27)
N studies	16–88	4–14	4–11
Low sodium, mmol (Hy/No)	80/45	87/78	87/78
Effect renin SMD, (p)	1.22 (0.00001)	0.26 (0.00001)	–
Effect aldosterone pg/ml (p)	98 (0.00001)	73 (0.00001)	–
Effect noradrenaline pg/ml, (p)	64 (0.00001)	32 (0.01)	8.23 (NS)
Effect adrenalin pg/ml, (p)	8 (0.03)	6.7 (0.06)	6.90 (NS)
Effect cholesterol mg/ml, (p)	5.6 (0.0005)	1.9 (NS)	0.02 (NS)
Effect triglyceride mg/ml, (p)	7 (0.0006)	3.5 (NS)	0.04 (NS)

Hy Hypertensive; No: Normotensive.

significance of a low salt intake below 5.8 g. This was done in an IOM report, which concluded that outcomes of population studies were insufficient to show whether low salt intake below 5.8 g had beneficial or harmful health effects.[37] The first essential meta-analysis to investigate the separate effect of low salt intake indicated a U-shaped relationship between salt intake and mortality, especially in study samples representative for the general population adjusted for multiple effect modifiers.[10] Previously, several individual population studies had identified this U-shape.[31,38–40] Lately, the U-shape was again confirmed in a meta-analysis of four recent studies.[41] A separate analysis of individuals with HTN based on individual participant data confirmed the U-shape, but in individuals with normal BP only the low salt intake was associated with increased mortality, whereas a high salt intake up to 30 g per day was not.[41] Table 5 summarizes the results from the meta-analyses. All analyses agree that high salt intake above the mean usual intake is associated with increased mortality in populations of individuals with and without HTN. The latest of the analyses indicate that this effect only applies to those with HTN. Furthermore the analyses, which separately investigated low salt intake, agreed that low salt intake was associated with increased mortality.[10,41]

AHA advisory on cohort studies relating salt intake to health outcomes

Representatives of AHA reviewed a series of limitations in the population studies, which had the potential to alter the direction of the association between salt intake and health outcomes.[12] Potential for systematic error, for instance in the estimation of salt intake, was identified in most of the 26 reviewed population studies and specific systematic error was identified in 6. However, in order to reverse the direction of the health outcome the systematic error should misclassify specific groups and such systematic errors were not specifically identified. Random error due to single estimation of the salt intake was also potentially present in most studies. Multiple measurements could reduce this error and increase the precision of the estimation of the salt intake,[42] which should strengthen the direction of the outcome, but not reverse the outcome, as verified in two recent studies.[32,43] One study based on multiple 24-h sodium excretions did not find a significantly increased (or reduced) rate of CVD[44] or all-cause mortality[45] in the low salt group. The authors explained this contrast to the meta-analyses[10,41] as being due to the multiple salt intake estimates used in these analyses.[44,45] However, as it is less likely that multiple measurements reverse the direction of the outcome, the use of less precise food frequency questionnaires or spot urines to measure the sodium intake would probably have yielded similar results. A more reasonable explanation for the lack of U-shape may be that the investigated individuals suffered from overweight and pre-hypertension or that few individuals with few events were on a low salt diet, limiting the power to detect associations in the interval below 5.8 g.

The possibility that sick individuals eat less salt could also explain increased mortality associated with low salt intake (reverse causality).[12] We have not seen this hypothetical phenomenon verified in any study. Conversely, the recently published analysis of NHANES 2014 shows that individuals with HTN, diabetes mellitus, CVD and chronic kidney disease have salt intakes similar to healthy individuals. This study also showed that individuals reporting to have intentionally decreased their salt intake had the same salt intake as those reporting to have unchanged salt intake.[46] Besides, most of the population studies reported in the meta-analyses[10,41] adjusted for confounders including diseases. Finally, both of the large meta-analyses[10,41] and the largest of the population studies[40] showed that elimination of sick study populations and sick individuals strengthened the association between low-salt intake and mortality.

Table 5
Meta-analyses of population studies: relative risk (RR) for all-cause mortality (ACM), cardiovascular disease event (CVD) or stroke.

		RR (low salt versus usual salt)			RR (high salt versus usual/low salt)		
Reference	Populations	ACM	CVD	Stroke	ACM	CVD	Stroke
Strazzulo[35]	All (RPS + IPS)	–	–	–	–	1.14	1.23[a]
WHO[25]	All (RPS + IPS)	–	–	–	1.06	1.12	1.24[a]
Poggio[36]	All (RPS + IPS)	–	–	–	–	1.12[a]	–
Graudal[10]	All (RPS + IPS)	1.10[a]	1.10[a]	0.96	1.16[a]	1.12[a]	1.18[a]
Graudal[10]	RPS	1.16[*]	1.07	0.95	1.04	1.07	1.21[a]
Mente[41]	Normal BP	1.39[a]	1.28[a]	–	1.00	0.90	–
Mente[41]	Hypertesion	1.39[a]	1.35[a]	–	1.39[a]	1.26[a]	–

RPS: Representative population samples; IPS: Ill population samples.
[a] Statistically significant.

Conclusions

Various biases are prominent in studies supporting salt reduction, such as selective evaluation of mainly salt sensitive HTN study populations[8,27,34] (Table 1) or salt sensitive overweight study populations,[15,28,44,45] or intentional definition of study inclusion criteria to increase salt sensitivity of the group of participants being studied, such as high baseline BP, overweight and reduction of potassium to subnormal levels in the control diet,[15,44,45] and denial of potential low-salt side-effects.[25,27,34–36] The extraordinary associations of salt with BP and health outcomes in these studies disappear in subgroup analyses adjusting for these biases. This selective prioritization in the choice and methods of evidence to support dietary guidelines, such as Dietary Guidelines of America (DGA)[9] has been criticized previously.[47–50] Although the latter[50] mainly deals with fat and carbohydrate recommendations, it does emphasize the paradox that DGA says that it "concurs" with the IOM report, which states that the evidence is "inconsistent and insufficient to conclude that lowering sodium intakes below 2300 mg/day will have any effect on cardiovascular risk or overall mortality"[37] and yet DGA recommends that sodium intake "should be less than 2300 mg/day".[9] Recently, this distrust in the process for the establishment of DGA has been supported in the conclusion of a National Academy of Medicine report: "Collectively, these findings and conclusions compromise the integrity of the DGA and limit its ability to develop a full body of evidence on a continuous basis over time. The process to update the DGA should be comprehensively redesigned to allow it to adapt to changes in needs, evidence, and strategic priorities".[51] Temporarily, these concerns have had no impact. DGA and other health institutions maintain the idea that the majority of the World's populations have a too high salt intake. This idea should be evaluated in the context that this "high" salt intake (6–12 g) is in the low end of the tolerable interval (0.5–55 g), just above the level associated with side effects and increased mortality. A redesign of the salt DGA seems to be needed.

Conflict of interest

None.

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