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Con: Reducing salt intake at the population level: is it really a public health priority?

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ABSTRACT

Scientific evidence to support the recommended salt intake of < 5.8 g/day is virtually non-existingent. There are no randomized controlled trials (RCTs) to investigate the effect of salt reduction (SR) below 5.8 g on health outcomes. The effect of SR on blood pressure (BP) reaches maximal efficacy at 1 week. RCTs in healthy individuals lasting at least 1 week show that the effect of SR on BP is <1 mmHg, but that SR has significant side effects, including increases in renin, aldosterone, noradrenalin, adrenalin, cholesterol and triglyceride. Still, disregarding confounders and side effects, health authorities use BP effects obtained in studies of pre-hypertensive and hypertensive patients to recommend SR in the healthy population and use these biased BP effects in statistical models indirectly to project millions of saved lives. These fantasy projections are in contrast to real data from prospective observational population studies directly associating salt intake with mortality, which show that salt intake <5.8 g/day is associated with an increased mortality of ∼15%. The population studies also show that a very high salt intake >12.2 g is associated with increased mortality. However, since <5% of populations consume such high amounts of salt, SR at the population level should not be a public health priority. Consequently, this policy should be abolished, not because any attempt to implement it has failed, and not because it costs taxpayers and food consumers unnecessary billions of dollars, but because—if implemented—it might kill people instead of saving them.

Keywords: blood pressure, cardiovascular, clinical trial, epidemiology, meta-analysis

INTRODUCTION

A 2013 Institute of Medicine (IOM) report [1] concluded that there is not sufficient data to conclude that individuals benefit from salt intake lower than the present usual intake, which in 95% of the world's population is 6.6–12.2 g (2620–4830 mg sodium) (114–210 mmol) [2], a conclusion confirmed by observational studies [3–5]. Still, many health organizations recommend a radical reduction in salt intake to a level <5.8 g (2300 mg sodium). However, this public health priority is flawed [6, 7].

THE POLICY TO REDUCE SALT INTAKE HAS ITS ORIGIN IN IDEOLOGY

The ideological salt–BP conflict was initiated in 1904, summarized in 1949 [8, 9] and ran for 70 years before the first randomized controlled trial (RCT) in 1973 [10] and an observational study in 1985 [11] were performed in humans.

THE MYTH OF THE FOOD INDUSTRY CONSPIRACY

According to advocates for salt reduction (SR), the food industries, by adding salt to pre-prepared food, undermine the health of their customers. The devoted advocates claim that sceptics are under the influence of the food industry and compare sceptics with tobacco lobbyists [12]. However, the salt-reduction-leads-to-blood-pressure-reduction idea is not that brilliant and does call for an independent critique, verified by observational studies and RCTs and two large meta-analyses relating salt to mortality, BP and side effects [5, 13], which all are independent of commercial interests. Finally, public health institutions and the food industry nowadays cooperate to promote the production of low-salt foods [14], indicating a new reciprocity between previous opponents, which creates an unanswered question of potential risk: what are the health consequences of the methods or substances used to substitute salt.

SALT IS THE ONLY EXISTING NUTRIENT DEEMED TO BE UNHEALTHY WITHIN THE USUAL INTAKE RANGE

IOM's definition of adequate nutrient intake (AI) is 'the approximate intake found in apparently healthy populations' [15]. For salt, this intake is 6.6–12.2 g [2]. Conflicting with its own definition, however, IOM defined the AI for salt to be 3.3–3.8 g [15]. The World Health Organization (WHO), the US Centers for Disease Control and Prevention (CDC), the American Heart Association (AHA) and the British National Institute for Health and Clinical Excellence (NICE) have adopted this position and defined an upper limit for a healthy salt intake to be 5.8 g, i.e. radically below the established salt intake in healthy populations.

SALT INTAKE IS DEEMED 'NORMAL' AT LEVELS CONSUMED BY VIRTUALLY NO ONE

According to these health institutions, the 2.5% of the world's populations that meet their recommendations has a normal salt intake, whereas the other 7 billion people have a high intake. This idea is based on the evolutionary discordance hypothesis according to which modern man genetically is identical with his Palaeolithic ancestors, who are claimed to be genetically predisposed to a low-salt diet [16]. However, during the 2.5 million year Palaeolithic period, many diet patterns have been identified [17]. Furthermore, the fact that humans are equipped with a neuro-endocrine system [18] and kidneys, which handle enormous variations in salt intake, indicates that humans are not genetically designed to one specific salt diet.

SALT-CONSERVING HORMONES INCREASE EXPONENTIALLY AT LOW SALT INTAKE

Renin and aldosterone levels are low within the usual salt intake range, but increase exponentially below 5.8 g [19], verified to be a persistent effect in Brazilian Indians on a chronic low-salt diet [20]. The latter finding supports that humans are not genetically determined to a low-salt diet. A meta-analysis of 14 studies, which reduced salt to levels in the vicinity of 5.8 g, found small effects of SR on renin and aldosterone [21]. However, a meta-analysis of 53 studies, which included many studies reducing salt below 5.8 g, showed a significant proportional effect of SR on renin and aldosterone [22].

STRESS HORMONES INCREASE SIGNIFICANTLY AT SALT INTAKE LEVELS <5.8 G

Several studies have shown significant increases in adrenalin and noradrenalin, confirmed in a meta-analysis of 33 studies reducing usual salt intake to <5.8 g [13]. However, this was not observed in a meta-analysis of six studies reducing salt to a level in the vicinity of 5.8 g [21].

THE MYTH OF THE AUTHORITY OF HEALTH INSTITUTIONS I: NATIONAL HEART LUNG AND BLOOD INSTITUTE–SPONSORED STUDIES ARE BIASED TO EXAGGERATE THE EFFECT OF SR ON BLOOD PRESSURE

The advocate's unconditional acceptance of the SR position of public health institutions and reference to these institutions as 'authorities' is circular, because the advocates and the public health institutions all belong to the same network, who distribute funding, perform trials and, on behalf of governments, make decisions. The biased procedures in this closed, authoritarian network have nothing to do with science. Table 1 shows the effect of RCTs sponsored by the National Heart, Lung and Blood Institute (NHLBI) [23–26]. The characteristics of the typical overweight study populations show higher baseline BP and mean age every time a new study appears and an increase in the number of African American participants. In the Dietary Approaches to Stop Hypertension (DASH)-sodium trial [26], the potassium content in the control diet was only half that in the average American diet. Low potassium intake is well known to increase sodium sensitivity [27], and therefore the DASH-sodium trial was designed with at least five confounding variables favouring SR: high baseline BP, low potassium intake, older age, high BMI and high percentage of African American participants. In accordance with these concerns, the DASH-sodium researchers went through litigation to avoid publishing the individual participant data [28], contributing to the notion that these data may include 'controversial' information. The fact that studies biased in favour of salt sensitivity show only small effects (Table 1) [23–26] indicates that SR would have minimal effects on BP in the general population. This is emphasized by a supplementary publication of the DASH trial [29] that—in a disregarded subanalysis—shows that in individuals

Table 1. The effect of SR on BP in studies sponsored by the NHLBI

Study	Reference	Potassium[a]	Age[b]	Baseline BP[c]	BMI[d]	African American, %	Duration, months	SR, mmol	Effect BP, mmHg
HPT 1990	*Arch Intern Med* 1990; 150: 153	2562	39	124.3/82.7	29	16	36	17	+0.1/+0.2
TOHP I 1992	*JAMA* 1992; 267: 1213	2423	42.6	125.1/83.9	29.5	15	6	44	−1.7/−0.9
TOHP II 1997	*Arch Intern Med* 1997; 157: 657	2574	44.2	127.7/86.1	31	18	36	42	−2.9/−1.6
DASH 2001 DASH diet	*N Engl J Med* 2001; 344: 3	3159	47	134/86	29	57	1	77	−3.0/−1.6
DASH 2001 control diet	*N Engl J Med* 2001; 344: 3	1638	49	135/86	30	56	1	77	−6.7/−3.5

[a]Mean potassium intake of American population: 2640 mg.
[b]Median age of American population: 37 years.
[c]Median baseline BP of American population: 119/71 mmHg.
[d]Mean BMI of American population (>20 years): 28.

between 21 and 41 years of age there is no significant effect of a low-sodium/high-potassium diet on BP. As the median age of the American population is 37 years, this indicates that SR has no effect on BP in >50% of Americans. Finally, the much shorter duration of the last study [26] (1 month) probably reflects a deliberate strategy change, as the previous studies [23–25] (duration 6–36 months) revealed that significant SR is difficult to implement for a longer period. To conclude, these trials do not reflect the authority of a public institution, but rather a bias intended to sustain a questionable policy.

THE MYTH OF THE AUTHORITY OF HEALTH INSTITUTIONS II: UNBIASED ANALYSES OF THE TRIALS OF HYPERTENSION PREVENTION SHOW NO EFFECT OF SR ON MORBIDITY AND MORTALITY

In 2007, data from the Trials of Hypertension Prevention (TOHP) studies [24, 25], randomizing participants to low-salt and usual-salt diets, were analysed with cardiovascular disease (CVD) events (available in 77% of the participants) and all-cause mortality (ACM) (available in 100% of the participants) as outcomes according to the randomized groups (intention-to-treat) and in a supplementary analysis after adjustment for seven confounders [30]. In the adjusted analysis, the CVD outcome was lower in the low-salt group ($P = 0.018$), but not ACM ($P = 0.34$). There was no difference in CVD ($P = 0.19$) or ACM ($P = 0.58$) in the intention-to-treat analysis. In 2009, a reanalysis was published, but participants on salt restriction were excluded, transforming the study from an RCT to an observational study associating quartiles of salt intake on the basis of 24-h urine excretions with CVD, but not with ACM [31]. The primary analysis showed no significant association between salt intake and CVD events ($P = 0.38$). A borderline significant inverse association was found between potassium and CVD events ($P = 0.08$). Consequently, the identified association between the sodium:potassium ratio and CVD events ($P = 0.04$) was driven by potassium and not by sodium. In 2014, a third elaboration of the TOHP studies was performed [32]. The authors investigated four sodium intake intervals divided by the values 2300, 3600 and 4800 mg, now including potassium excretion as a covariate in the primary analysis, which, however, still did not show a significant association between sodium excretion and CVD outcomes ($P = 0.13$). They also constructed a spline plot, which just reached statistical significance for 'linearity' ($P = 0.044$). However, due to several biases, the value of this analysis is limited: (i) as outcome events were only recorded in 77% of the patients, ∼57 events were not accounted for; (ii) the outcome in the low-salt group was based on only 17 events; (iii) the removal of just 2 of 74 events from the reference group to the 17 events in the lowest salt group would change the 'continuously descending straight line' to a U-shaped curve; (iv) after so many efforts to reach a significant P-value, a statistical correction for multiple comparisons would have been appropriate; (v) the authors did not respond to several challenges concerning the design of the study [33], but stated that the analyses were pre-specified, a statement that is invalid, as such pre-specifications have never been published; (vi) the omission not to analyze the most reliable outcome, ACM, which was recorded in 100% of the participants, is inappropriate; and (vii) the data were obtained in obese borderline hypertensive persons and therefore these results, even if they were correct, are not suitable for public policymaking.

THE MYTH OF THE AUTHORITY OF HEALTH INSTITUTIONS III: TRIALS BY 'WORLD ACTION ON SALT AND HEALTH' ARE BIASED BY HYPERTENSION AND AGE

The World Action on Salt and Health (WASH) group has performed 10 trials of the effects of salt restriction on BP. They are all biased by older age and high baseline BP and show an effect that is twice that of comparable trials [34]. Therefore, they do not reflect reliable authority, but a specific knowledge of how to identify a significant effect of SR on BP and a biased use of this effect: investigate older individuals with high BP and apply the effect to healthy individuals.

THE ASSUMED BP EFFECT OF SR IN HEALTHY INDIVIDUALS IS VIRTUALLY NON-EXISTENT

About 50% of RCTs investigating the effect of SR on BP have been performed in participants with BP in the upper 25th percentile of the population. This has contributed to the general impression of a significant association between salt intake and BP. However, just as antihypertensive treatments are not indicated for healthy individuals, an effect of SR on BP in hypertensive individuals does not justify a general SR policy, verified by the fact that in 64 RCTs with a duration of at least 7 days, a salt intake of maximally 15 g (250 mmol) and BP <131/78 mmHg, corresponding to the limit for the upper 25th percentile of the BP distribution in the American population, the effect of 6 g (108 mmol) SR on BP is 1/0.4 mmHg (unpublished data from Graudal *et al.* [13]). In another meta-analysis, the effect in persons with normal BP was claimed to be 2/1 mmHg [21]. The authors of this analysis included only studies lasting at least 4 weeks, because of a claim that the effect of SR depended on the duration. However, a recent meta-analysis of longitudinal studies measuring the BP effect of SR several times during the observation period showed that there was no difference in systolic BP (SBP) effect or diastolic BP (DBP) effect between weeks 1 and 6, thus defining the time point for maximal efficacy to be 1 week [35]. The restricted inclusion criteria of the alternative review [21] resulted in the inclusion of study populations that, all except two, had baseline BP within the upper 50th percentile of the American population, and therefore this meta-analysis is not suitable for public policymaking. The missing link between salt and BP in >50% of a population is verified by the previously mentioned disregarded outcome of the DASH study, which showed no effect of SR on BP in individuals <41 years of age [29].

NO RCTs INVESTIGATE THE EFFECT OF SR BELOW 5.8 G ON HEALTH OUTCOMES

A recently updated meta-analysis of eight RCTs with follow-up data on morbidity and mortality found a non-significant trend versus reduced CVD morbidity, but could not demonstrate reduced ACM in the low-salt group [36]. The reported 24-h sodium intakes in the low-salt group in these eight studies varied between 2300 mg (5.8 g salt) and 3800 mg (9.6 g salt).

THERE ARE NO RCT INVESTIGATING THE EFFECT OF SR ON HEALTH OUTCOMES IN HEALTHY INDIVIDUALS

A pooled analysis of the above-mentioned eight trials [36] shows a marginally significant increase in CVD outcomes, but still no difference in the most reliable outcome, ACM. As the trials were not performed in healthy individuals, but in older, overweight pre-hypertensive or hypertensive individuals, the results are not suitable for public policymaking, although the identical ACM risk in the low and usual salt intake groups of study populations with a theoretical increased risk of CVD indicates that SR is not beneficial.

PROJECTED EFFECTS ON MORTALITY BASED ON RCTS ARE MISLEADING

Modelling studies use data from RCTs and meta-analyses to establish a dose–response relationship between salt intake and BP. By means of data from observational studies, which link BP to mortality, this dose–response relationship is used to translate SR to a reduction in mortality. However, most of the RCTs in the dose–response analyses include participants with a high baseline BP and older age, resulting in overestimation of the dose–response relationship, which is further amplified by forcing the dose–response relationship through zero to increase the slope of the relationship. Potential side effects are consistently ignored in these models. The latest example of a modelling study to use this biased technique [37] adopted our Cochrane data [13] to design the dose–response relationship. Although the authors knew that the very same studies, which showed a BP effect, also showed an increase in renin, aldosterone, adrenalin, noradrenalin, cholesterol and triglyceride, the authors ignored these data. The amplification of the BP effect and the accompanying disregard of side effects explain why modelled outcomes are not in accordance with the outcomes of observational studies based on real data.

RCTS SHOW THAT SR BELOW 5.8 g LEADS TO INCREASES IN CHOLESTEROL AND TRIGLYCERIDE

A meta-analysis of eight studies showed no effect of SR within the usual salt intake range on serum cholesterol and serum triglyceride [21]. In a meta-analysis of 24 studies, which reduced salt intake below 5.8 g, there was a significant increase in both serum cholesterol and serum triglyceride, and these increases were independent of the baseline BP [13].

OBSERVATIONAL STUDIES SHOW THAT SALT INTAKE BELOW 5.8 g IS ASSOCIATED WITH INCREASED MORTALITY

The main objections against observational studies are (i) that the methods to measure salt intake are inaccurate and (ii) the risk of reverse causality due to the possibility that unhealthy individuals eat less salt. However, in the Prospective Urban Rural Epidemiology (PURE) study of >100 000 participants worldwide [4], the authors documented a direct relationship

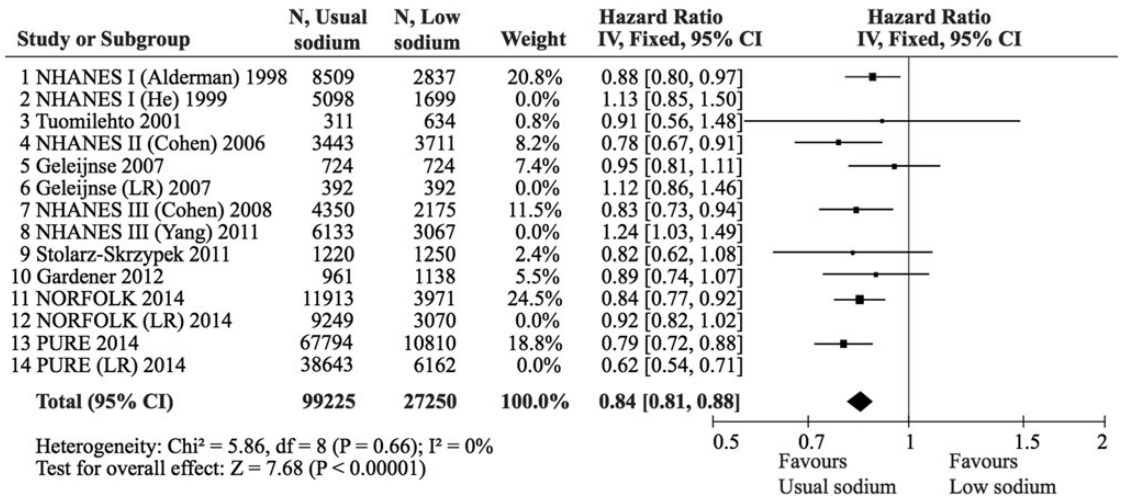

FIGURE 1: All-cause mortality (ACM), usual sodium versus low sodium. Results from nine population-representative observational studies adjusted for multiple confounders. Exchanging the first analyses of the NHANES studies (1, 7) with the reanalyses (2, 8): HR = 0.87 [0.82, 0.91], P < 0.00001. Further exchanging primary analyses (5, 11, 13) with analyses of low-risk populations (6, 12, 14): HR = 0.86 [0.81, 0.92], P < 0.00001. LR, low risk (reproduced with permission, *American Journal of Hypertension*).[41]

between salt intake and BP, which was stronger in participants with hypertension than in participants with normal BP [38]. These results are similar to those identified in RCTs [13, 22]. The study also demonstrated that at the low end, sodium intake was inversely associated with mortality, while at the high end, it was directly associated with mortality [4]. If the 'inaccurate' salt intake measurements are sufficient to identify this well-known BP pattern [38], there is no reason to assume that they are insufficient to identify mortality outcomes [4].

The U-shaped association observed in the PURE study was also found in a contemporary independent analysis [3]. Furthermore, the mortality risk associated with lowsalt intake increased when sick participants were eliminated from the analyses, indicating that reverse causality was not a problem [4]. A similar finding was seen in a meta-analysis of 25 observational studies, which showed that the association between lowsalt intake and mortality was greater when only studies of healthy populations adjusted for multiple confounders were included in the meta-analysis [5]. Figure 1 shows an updated version of this analysis. These findings indicate that lowsalt intake is not a confounder, but a distinct risk factor for increased mortality.

CONCLUSION

A PubMed search using 'dietary salt or dietary sodium' as a searchterm reveals ∼27 000 hits with a variety of outcomes. Therefore, a review of evidence can be biased to support any view. Opposing views are frequently occurring in the salt conflict, which is well characterized by a quote by Brooks, who stated, 'authors can be pictured as intellectual partisans of their own opinions, scouring the literature for justification' [39]. Scoured literature was used to define the present adequate intake of salt by a 2005 IOM committee in conflict with IOM's general definition of an adequate intake of a nutrient [40]. The advocates mask scouring as 'selection of quality', where 'quality' in reality is nothing but a euphemism for the 'right' outcome. The fact is that scoured RCTs [23–26, 30], meta-analyses [21] and modelled projection studies [37] supporting the idea of SR below 5.8 g are biased by multiple confounders and therefore not suitable for public policymaking, which should be based on complete systematic reviews.

The link between salt intake and BP is minimal in individuals with a normal BP eating salt within the present usual intake range. In contrast, the potential side effects of SR on salt-conserving hormones, stress hormones and lipids are independent of the baseline BP and will affect the majority of the population. This exposure to classic CVD risk factors with an intervention that will have no or at best a minimal effect on BP seems imprudent. In accordance with this finding, prospective observational studies linking individual salt intake with mortality show that low intake below 5.8 g is associated with increased mortality, as is very high intake above 12.2 g. However, since <5% of populations consume such high amounts of salt, reducing salt intake at the population level should not be a public health priority.

CONFLICT OF INTEREST STATEMENT

Some opinions, arguments and statements used in this opinion paper have been published in other articles, but the present presentation approach has not been published previously in whole or part. None declared.

(See related articles by Cappuccio. Pro: Reducing salt intake at population level: is it really a public health priority? *Nephrol Dial Transplant* 2016; 31: 1392–1396; Zoccali and Mallamaci. Moderator's view: Salt, cardiovascular risk, observational research and recommendations for clinical practice. *Nephrol Dial Transplant* 2016; 31: 1405–1408)

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Opponent's comments

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Dr Graudal's hostile and scare-mongering article is full of inaccuracies, selected arguments and false statements. He considers the 2013 Institute of Medicine (IOM) report, the remit of which was limited [1], dismissing the positions of the previous IOM report, the World Health Organization, the US Centers for Disease Control and Prevention, the American Heart Association, the British National Institute for Health and Clinical Excellence and many other national health organizations statements that informed the 2011 United Nations resolution and the 2013 World Health Assembly deliberation that the population salt reduction strategy is the second most effective strategy for the prevention of cardiovascular disease (CVD) globally. The presence of a food industry conspiracy biasing research and co-opting unscrupulous opinion leaders to divert attention from salt with surreptitious new theories has been extensively documented over the years [2]. In contrast, the alleged conspiracy of global health organizations in producing a sound piece of public health advice is another fabrication to divert attention again.

Sodium chloride (salt) is not a nutrient. At the current levels added to food, salt is a toxic chemical. Dr Graudal confuses the concepts of *usual/habitual* and *adequate/normal*. If we all smoked, smoking would be normal. If we were to define obesity today, we would have to raise the cut-off points for obesity in many countries. A body mass index of 30 kg/m^2 would not indicate obesity because most people in the population weigh that much. If we were to define the adequate levels of physical activity, we should accept that the normality would be not exercising at all. So it is for salt intake! The *usual/habitual* levels are not *adequate/normal* levels.

Dr Graudal continues to pursue two surreptitious arguments: (i) that the effect of salt reduction on blood pressure (BP) is non-existent and (ii) that salt reduction increases hormones that could be dangerous. His first argument is answered in Figure 1. For the second, he only quotes his meta-analyses including short-term acute studies of salt deprivation. I have already addressed the flaw of his argument and shown that