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

Pro position

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Abbreviations: BP: blood pressure; CVD: cardiovascular disease; NCDs: non-communicable diseases; WHO: World Health Organization

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Abstract

A reduction in salt intake reduces blood pressure, stroke and other cardiovascular events, including chronic kidney disease, by as much as 23% (i.e. 1.25M deaths worldwide). It is effective in both genders, any age, ethnic group, high, medium and low-income countries. Population salt reduction programmes are both feasible and effective *(preventive imperative)*. Salt reduction programmess are cost-saving in all settings (high-, middle- and low-income countries) *(economic imperative)*. Public health policies are powerful, rapid, equitable, cost-saving *(political imperative)*. The important shift in the public health has not occurred without obstinate opposition from organizations concerned primarily with the profits deriving from population high salt intake and less with public health benefits. Key components of the denial strategy are misinformation (with ‘‘pseudo’’ controversies). In general, poor science has been used to create uncertainty and to support inaction. This paper summarises the evidence in favour of a global salt reduction strategy and analyses the peddling of well-worn myths behind the false controversies.

Abstract Words: 158

Introduction

Since 1985 the World Health Organization (WHO) has been recommending a reduction in population salt intake to an average of 5g per day from a country customary consumption. However, no action plan was ever put in place globally, although noticeable implementations in Japan[1] and Finland[2] led to dramatic reductions in cardiovascular disease (CVD) and stroke rates associated with substantial reductions in population salt intake. Over the following 20 years both scientific evidence and public health initiatives have led to renewed recommendations from the WHO in 2007[3] and 2012[4] not to exceed a population average salt intake of 5g per day. A significant step toward global policy action was the 2011 United Nations high-level meeting on non-communicable diseases (NCDs), which set a target for population salt reduction as a priority to reduce premature CVD mortality by 2025[5]. Revised WHO guidelines now recommend a 30% reduction of salt intake by 2025 and a final maximum target of 5g per day[4]. The latter target was then adopted by the 66th World Health Assembly through its resolution in 2013[6]. A number of policy options for the implementation of national programmes globally are now available[7] and population salt reduction is underway in many countries worldwide[8].

"Salt debate"

In parallel with these actions, a *'salt debate'* has filled the pages of health magazines and newspapers for years. From John Swales' original scepticism in 1988[9] to the Godlee's sharp call to reality in 1996[10], the debate has transcended the scientific arena into public opinion and media campaigns with increasingly passionate tones[11]. The controversy has been particularly heated since the translation of the results of scientific studies into public health and policy actions[7] and the *'salt debate'* has become for some a *'salt war'*[12]. The progression of this debate into a war resembles past and present debates (let us think at John Snow and the cholera epidemic of the 19th century, the long-lasting denial of the harm of tobacco smoking of the 20th century, the global warming and climate change debate of the 21st century), when the translation of science into practice clashes with vested interests[12-14].

The evidence

Salt and blood pressure

The scientific facts are: salt is causally related to blood pressure (BP), the higher the salt intake, the higher the BP, an effect seen since birth[14]. A small and sustained reduction in salt intake (up to 50% of what we eat now) causes a fall in BP in almost everyone across the whole range of BP, although individuals will respond more or less, depending on factors like age, ethnicity, initial levels of BP, body weight. These facts have been proven over and over again and summarised in repeated systematic reviews and meta-analyses of small and large clinical trials in people with and without high BP.

[INSERT FIGURE HERE)

*The **Figure*** shows the collective estimates of all meta-analyses published to date on the effect of salt reduction on BP in adults[15-25]. The meta-analyses differ for the time of the analysis, hence the number of overall studies available, the inclusion criteria (short-term studies of less than 4 weeks versus longer-term studies of more than 4 weeks), the proportion of normotensive and hypertensive participants, the study designs (cross-over, parallel group, blinded, and unblinded), and the proportion of relevant subgroups (by gender, age, and ethnic group). Despite differences between studies, the range of pooled weighted estimates of effect are all in favour of salt reduction. Furthermore their 95% confidence intervals are compatible with each other, indicating consistency, with differences between them likely due to random variation. Furthermore, when using very 'short-term salt restriction' trials with very large changes in salt intake (unlikely to be comparable to 'longer-term more moderate salt reduction' ones) it has been argued that changes in metabolic and hormone variables may occur[17, 20-23]. These changes are due to rapid and transient activation of sympathetic adrenergic activity and haemoconcentration, not detected in longer-term and moderate salt reduction trials[18, 24-25]. In conclusion, the results of these analyses, despite different interpretations at the time of their publication, all agree on the following: (1) salt intake is one of the major determinants of BP in populations and individuals; (2) a reduction in salt intake causes a

dose-dependent reduction in BP; and (3) the effect is seen in both sexes, in people of all ages and ethnic groups, and with all starting BPs. Similar results have been described in children[26-27].

Salt and cardiovascular outcomes

High BP contributes to strokes and heart attacks and a reduction in blood pressure is associated with their reduction. The effect is related to the size of the fall in BP. It is therefore conceivable that a moderate reduction in salt intake in a population would help reduce stroke and heart attacks through a reduction in BP. The collective evidence from systematic reviews of prospective longitudinal studies indicates that a lower salt intake is associated with a lower incidence of fatal and non-fatal cardiovascular events, in particular stroke[25,28]. This is supported by a meta-analysis of the few randomised clinical trials available to date which have measured fatal and non-fatal outcomes[29]. However, to prove that a reduction of salt intake in populations over an extended period of time reduces the rate of strokes and heart attacks a randomized double-blind placebo-controlled clinical trial would be needed. It has been argued that such a 'mother of trials' will never be conducted but, nevertheless, we should not refrain from implementing public health policies based on the available evidence so far[30]. Never was a randomized clinical trial of tobacco smoking and lung cancer carried out in humans to *'prove'* that smoking causes lung cancer and that we should eventually ban tobacco. Furthermore, an assessment of the bulk of evidence underlying population action of salt reduction dwarfs the evidence that today supports accepted policies on weight reduction, physical inactivity, dietary intake of fibre, fruit and vegetable for the prevention of both cancer and CVD. A recent controversy has been fuelled by a series of reports of analyses of prospective observational studies suggesting that lower salt intake might be associated with increased risk of CVD events, in particular coronary events and heart failure. These studies have been the object of intense scrutiny due to numerous methodological issues present in observational studies that would introduce fatal biases (errors) in the results and, hence, erroneous conclusions. A comprehensive account on these issues has been published by the American Heart Association[31].

[INSERT TABLE HERE]

The **Table** provides a simple schematic summary of these methodological issues determining contrasting results. In brief, the risk of errors pertains the domains of systematic errors in the assessment of salt intake, the presence of 'reverse causality' bias, the presence of residual confounding, random errors and insufficient statistical power. Moreover, prospective observational studies do not imply true 'cause-effect' relationship, and they must be interpreted in the context of other available evidence[32], including the limited but consistent evidence from randomised clinical trials on CVD outomes[29].

Cost-effectiveness

Albeit applying different methods and models of assessment in different health care systems and under different assumptions, several studies have invariably demonstrated that a reduction in salt intake is cost-saving for the health care system (see[14] for review). In the United States, a salt reduction of 3g per day would result in an estimated annual gain of 194,000 to 392,000 QALYs and estimated savings of $10 billion to $24 billion (US) in health care costs. That represents $6 to $12 (US) return on investment for each dollar spent on the regulatory program[33]. Even a more modest reduction of 1g per day achieved gradually over 10 years would be more cost-effective than using medications to lower BP in all patients with hypertension[34]. These economic savings would be achieved with either voluntary or mandatory reductions in the salt content of processed foods. However, health benefits would be up to 20 times greater with government legislation on salt limits in processed foods[35]. Cost savings are also estimated for a 15% reduction in salt intake in low- and middle-income countries, which would avert 13.8 million deaths over 10 years at an initial cost of less than $0.40 (US) per person per year. In conclusion, population salt reduction is an effective and cost-saving public health measure.

The myths

The important shift in the public health debate from 'whether' salt reduces the risk to 'how' to best lower salt intake to reduce CVD has not occurred without obstinate opposition from organizations concerned primarily with the profits deriving from population high salt intake and less with public health benefits. The food and beverage

industry has been particularly obstructive regarding public health actions, either directly or through its public relations organizations. Its strategies have included mass media campaigns, biasing research findings, co-opting policy makers and health professionals, lobbying politicians and public officials, encouraging voters to oppose public health regulation[12,36-37]. Key components of this denial strategy are misinformation (with ''pseudo'' controversies)[38] and the peddling of numerous rather well-worn myths[13]. In general, poor science has been used to create uncertainty and to support inaction. Clear examples are given by recent debates generated by publications using flawed methodologies[39] (see **Table**) and subsequently retracted data[40] robustly rebutted by the scientific community but sadly still used to support the controversy[41-43]. In particular, the claim that low salt intake may 'cause' coronary death has been proven not to be true, as shown by US, Dutch, and global studies using valid and appropriate methods[44]. Finally, reiterated myths have been disseminated to consumers and lay audience to create doubts[13-14].

Who gains from the controversy?

Why is the food and beverage industry so opposed to an approximate one third global reduction in salt intake? Salt is a cheap commodity everywhere. In 2009, more than 27 million tons of salt were sold in the United States for a revenue of US$2 billion; only 1.5 million tons of food-grade salt fetched more than US$320 million. Notwithstanding these figures, the use of salt in food manufacturing generates substantial profits for the food and beverage industry. The world's 10 largest food and non-alcoholic beverage companies—feeding an estimated global population of several hundred million in more than 200 countries daily — generated a combined annual revenue of more than US$422 billion in 2012. A high salt intake contributes to the profit through several mechanisms: (i) it will generate a demand for salty foods through a slow process of desensitization of the taste buds; (ii) since sodium salts are hygroscopic, absorbing and binding water, the practice of injecting meat products with sodium salt bound to stabilizers increases the weight of meat products before packaging so that the water trapped in the meat is sold at the price of meat; (iii) salt makes cheap, unpalatable food edible at no extra cost; (iv) it causes thirst and an increase in the use of mineral waters, soft drinks and often alcoholic beverages. The high use of sugar-containing drinks would contribute to the epidemic of

obesity, particularly in children, and high salt intake might encourage an increase in alcohol intake. A reduction in salt intake as recommended by the WHO would result in an average reduction in fluid consumption of approximately 350 mL per day per person[45]. In children, this would also lead to a reduction of at least 2.3 sugar-sweetened soft drinks per week per child[46]. Although this would result in large beneficial effects to the health of the population and financial gains for governments, it would be a multibillion-dollar loss to the industry from reduced sales of bottled water, soft drinks and alcoholic beverages.

Conclusions

A reduction in salt intake reduces BP, stroke and other cardiovascular events by as much as 23% (i.e. 1.25M deaths worldwide). It is effective in both genders, any age, ethnic group, high, medium and low-income countries. Population salt reduction programmes are both feasible and effective *(preventive imperative)*. Salt reduction programmess are cost-saving in all settings (high-, middle- and low-income countries) *(economic imperative)*. Public health policies are powerful, rapid, equitable, cost-saving *(political imperative)*.

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Conflicts of interests

None to declare

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Figure. Forest-plot summarising the results of published meta-analyses of randomized clinical trials of the effects of salt reduction on systolic blood pressure. Results are reported as SMD and 95% C.I.s. (re-drawn from Reference 14)

Table. Methodological issues in the assessment of prospective observational studies of salt consumption and cardiovascular outcomes (re-drawn from Reference 31) Reference list in Appendix 1.

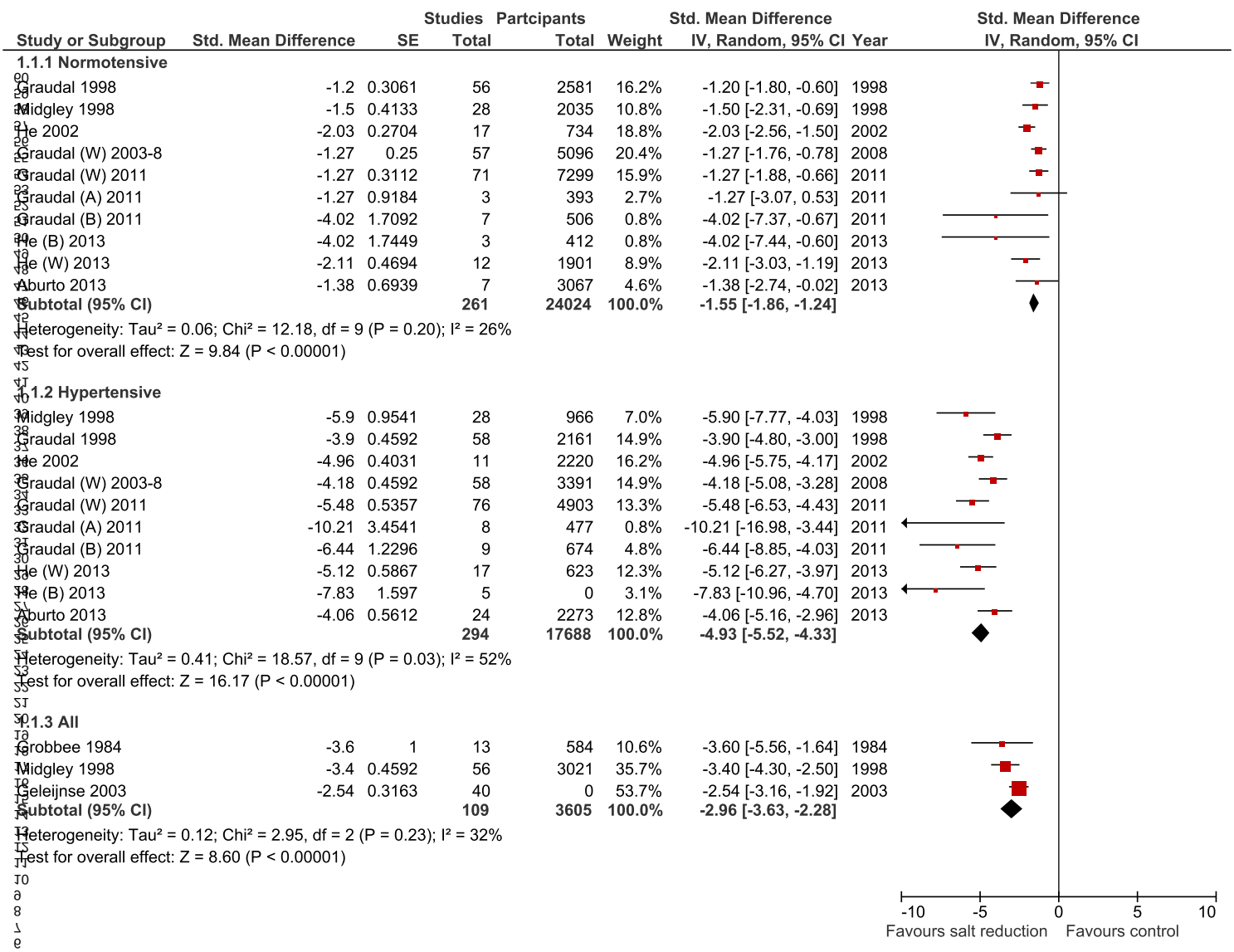
Studies Partcipants Std. Mean Difference Std. Mean Difference
Study or Subgroup Std. Mean Difference SE Total Total Weight IV, Random, 95% CI Year IV, Random, 95% CI
1.1.1 Normotensive
Graudal 1998 -1.2 0.3061 56 2581 16.2% -1.20 [-1.80, -0.60] 1998
Midgley 1998 -1.5 0.4133 28 2035 10.8% -1.50 [-2.31, -0.69] 1998
He 2002 -2.03 0.2704 17 734 18.8% -2.03 [-2.56, -1.50] 2002
Graudal (W) 2003-8 -1.27 0.25 57 5096 20.4% -1.27 [-1.76, -0.78] 2008
Graudal (W) 2011 -1.27 0.3112 71 7299 15.9% -1.27 [-1.88, -0.66] 2011
Graudal (A) 2011 -1.27 0.9184 3 393 2.7% -1.27 [-3.07, 0.53] 2011
Graudal (B) 2011 -4.02 1.7092 7 506 0.8% -4.02 [-7.37, -0.67] 2011
He (B) 2013 -4.02 1.7449 3 412 0.8% -4.02 [-7.44, -0.60] 2013
He (W) 2013 -2.11 0.4694 12 1901 8.9% -2.11 [-3.03, -1.19] 2013
Aburto 2013 -1.38 0.6939 7 3067 4.6% -1.38 [-2.74, -0.02] 2013
Subtotal (95% CI) 261 24024 100.0% -1.55 [-1.86, -1.24]
Heterogeneity: Tau² = 0.06; Chi² = 12.18, df = 9 (P = 0.20); I² = 26%
Test for overall effect: Z = 9.84 (P < 0.00001)
1.1.2 Hypertensive
Midgley 1998 -5.9 0.9541 28 966 7.0% -5.90 [-7.77, -4.03] 1998
Graudal 1998 -3.9 0.4592 58 2161 14.9% -3.90 [-4.80, -3.00] 1998
He 2002 -4.96 0.4031 11 2220 16.2% -4.96 [-5.75, -4.17] 2002
Graudal (W) 2003-8 -4.18 0.4592 58 3391 14.9% -4.18 [-5.08, -3.28] 2008
Graudal (W) 2011 -5.48 0.5357 76 4903 13.3% -5.48 [-6.53, -4.43] 2011
Graudal (A) 2011 -10.21 3.4541 8 477 0.8% -10.21 [-16.98, -3.44] 2011
Graudal (B) 2011 -6.44 1.2296 9 674 4.8% -6.44 [-8.85, -4.03] 2011
He (W) 2013 -5.12 0.5867 17 623 12.3% -5.12 [-6.27, -3.97] 2013
He (B) 2013 -7.83 1.597 5 0 3.1% -7.83 [-10.96, -4.70] 2013
Aburto 2013 -4.06 0.5612 24 2273 12.8% -4.06 [-5.16, -2.96] 2013
Subtotal (95% CI) 294 17688 100.0% -4.93 [-5.52, -4.33]
Heterogeneity: Tau² = 0.41; Chi² = 18.57, df = 9 (P = 0.03); I² = 52%
Test for overall effect: Z = 16.17 (P < 0.00001)
1.1.3 All
Grobbee 1984 -3.6 1 13 584 10.6% -3.60 [-5.56, -1.64] 1984
Midgley 1998 -3.4 0.4592 56 3021 35.7% -3.40 [-4.30, -2.50] 1998
Geleijnse 2003 -2.54 0.3163 40 0 53.7% -2.54 [-3.16, -1.92] 2003
Subtotal (95% CI) 109 3605 100.0% -2.96 [-3.63, -2.28]
Heterogeneity: Tau² = 0.12; Chi² = 2.95, df = 2 (P = 0.23); I² = 32%
Test for overall effect: Z = 8.60 (P < 0.00001)
-10 -5 0 5 10
Favours salt reduction Favours control

Table. Methodological issues in the assessment of prospective observational studies of salt consumption and cardiovascular outcomes.

Domain 1	Errors with the greatest potential to alter the direction of association (with examples)	
	Systematic error in sodium assessment • *Lower risk*: 24h urine collections not part of routine clinical practice, no quality assurance, not excluding incomplete collections. • *Higher risk*: other 24h urine collections, all dietary assessments, spot and overnight urine collections.	Dong 2010; Stolarz-Skrzypek 2011; Alderman 1995; 1998; Cohen 2006; 2008; Gardener 2012; Arcand 2011
	Reverse causality • *Lower risk*: participants recruited from general population and pre-existing CVD excluded • *Intermediate risk*: sick populations not excluded or included despite stated otherwise; presence of CVD risk factors; specific sick populations • *Higher risk*: specific sick populations (eg: heart failure, kidney disease, diabetes); removal of sick participants from analysis changes direction of association	Dong 2010; Arcand 2011; Son 2011; McCausland 2012; Gardener 2012; O'Donnell 2011; Thomas 2011; Ekinci 2011; Lennie 2011
Domain 2	**Errors with some potential to alter the direction of association (with examples)**	
	Potential for residual confounding • *Incomplete adjustment*: not including 2 or more of age, sex, race, SES, cholesterol, BMI or weight, smoking, diabetes; if diet-based, total calories; in urine-based weight, BMI or creatinine excretion • *Imbalance across sodium intake levels*: age difference across sodium groups >5 years; sex or race distribution across sodium groups >20% • *Inadequate follow*-up: low level of follow-up (<80%) or of uncertain quality for outcome assessment	Alderman 1995; 1998; Takachi 2010; Tunstall-Pedoe 1997; Tuomilehto 2001; Stolarz-Skrzypek 2011; Dong 2010; Arcand 2011; McCausland 2012; Son 2011; Thomas 2011; Ekinci 2011; Nagata 2004; Umesawa 2008; Cook 2009
Domain 3	**Errors with the potential to lead to a false null result (with examples)**	
	Random error in sodium assessment • *Lower risk*: more than four 24h urine assessments on average; FFQs • *Intermediate risk*: between 22-4 24h urine collections, or corrections for regression dilution bias; dietary reports • *Higher risk*: urine collection <24h or single 24h urine collection; single dietary recall or 1-dat food record Insufficient power • Less than 80% power to detect a 10% reduction in relative risk for every standard deviation in sodium intake	Nagata 2004; Tuomilehto 2001; Cook 2009; Dong 2010; Arcand 2011; Alderman 1995; Son 2011; Ekinci 2011; Yang 2011
	Studies using same data with divergent results	
	• *NHANES I studies*: same age group, same follow-up – inverse vs positive association • *NHANES III studies*: different age groups, different follow-up – inverse vs positive association	Alderman 1998; He 1999 Cohen 2008; Yang 2011