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

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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. 1.25 million deaths worldwide). It is effective in both genders, any age, ethnic group, and in high-, medium- and low-income countries. Population salt reduction programmes are both feasible and effective (preventive imperative). Salt reduction programmes are cost-saving in all settings (high-, middle- and low-income countries) (economic imperative). Public health policies are powerful, rapid, equitable and cost-saving (political imperative). The important shift in 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. A key component of the denial strategy is misinformation (with 'pseudo' controversies). In general, poor science has been used to create uncertainty and to support inaction. This paper summarizes the evidence in favour of a global salt reduction strategy and analyses the peddling of well-worn myths behind the false controversies.

Keywords: blood pressure, cardiovascular disease, kidney disease, salt intake, stroke

INTRODUCTION

Since 1985 the World Health Organization (WHO) has been recommending a reduction in population salt intake to an average of 5 g 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 5 g per day. A significant step towards global policy action was the 2011 United Nations high-level meeting on non-communicable diseases, 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 5 g 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 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 about 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 from 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 and body weight. These facts have been proven over and over again and summarized in repeated systematic reviews and meta-analyses of small and large clinical trials in people with and without high BP.

Figure 1 shows the collective estimates of all meta-analyses published to date on the effect of salt reduction on BP in adults [15–24]. The meta-analyses differ in the time of the analysis, hence in the studies available there are differences in the inclusion criteria (short-term studies of <4 weeks versus longer-term studies of >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, 20–22]. 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, 23, 24]. In conclusion, the results of these analyses, despite different interpretations at the time of their publication, all agree on the following: (i) salt intake is one of the major determinants of BP in populations and individuals; (ii) a reduction in salt intake causes a dose-dependent reduction in BP; and (iii) 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 [25, 26].

Salt and cardiovascular outcomes

High BP contributes to strokes and heart attacks and a reduction in BP is associated with their reduction. The effect is

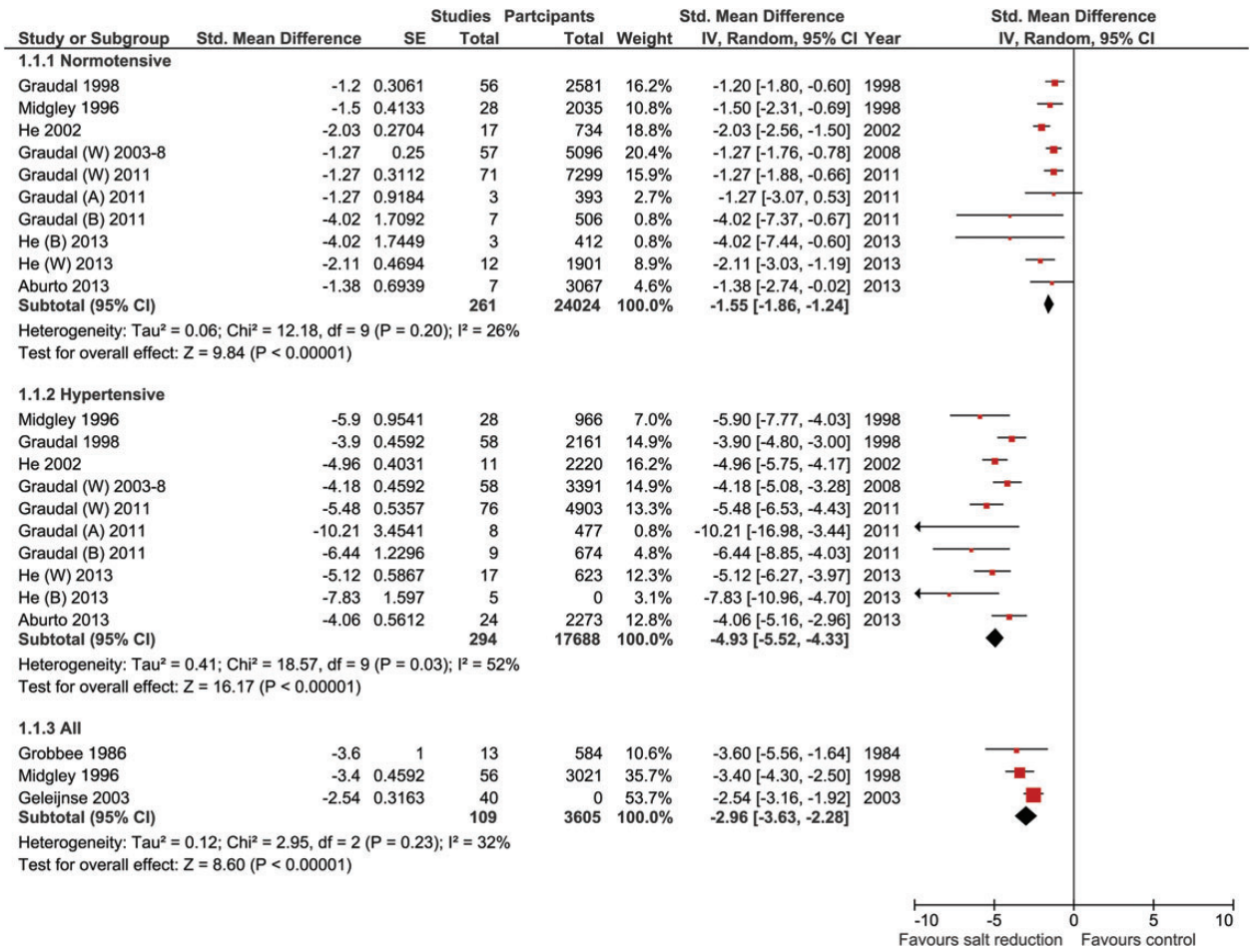

FIGURE 1: Forest-plot summarizing the results of published meta-analyses of randomized clinical trials of the effects of salt reduction on systolic blood pressure. Results are reported as standard mean difference and 95% confidence intervals (CIs) (re-drawn from Cappuccio and Capewell [14]). IV, inverse variance; W, White; B, Black; A, Asian.

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 [24, 27]. This is supported by a meta-analysis of the few randomized clinical trials available to date that have measured fatal and non-fatal outcomes [28]. 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 all trials' will never be conducted but, nevertheless, we should not refrain from implementing public health policies based on the available evidence so far [29]. 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, and dietary intake of fibre, fruit and vegetables 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 of these issues has been published by the American Heart Association [30].

Table 1 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 a true 'cause–effect' relationship,

Table 1. Methodological issues in the assessment of prospective observational studies of salt consumption and cardiovascular outcomes (re-drawn from Cobb *et al.* [30])

Domain 1	Errors with the greatest potential to alter the direction of association (with examples)	
	Systematic error in sodium assessment	Dong (2010), Stolarz-Skrzypek (2011), Alderman (1995, 1998), Cohen (2006, 2008), Gardener (2012) and Arcand (2011)
	• *Lower risk*: 24 h urine collections not part of routine clinical practice, no quality assurance, not excluding incomplete collections	
	• *Higher risk*: other 24 h urine collections, all dietary assessments, spot and overnight urine collections	
	Reverse causality	Dong (2010), Arcand (2011), Son (2011), McCausland (2012), Gardener (2012), O'Donnell (2011), Thomas (2011), Ekinci (2011) and Lennie (2011)
	• *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 (e.g.: heart failure, kidney disease, diabetes); removal of sick participants from analysis changes direction of association	
Domain 2	Errors with some potential to alter the direction of association (with examples)	
	Potential for residual confounding	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) and Cook (2009)
	• *Incomplete adjustment*: not including 2 or more of age, sex, race, SES, cholesterol, BMI or weight, smoking, diabetes; if diet-based, total calories; if 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	
Domain 3	Errors with the potential to lead to a false null result (with examples)	
	Random error in sodium assessment	Nagata (2004), Tuomilehto (2001), Cook (2009), Dong (2010), Arcand (2011), Alderman (1995), Son (2011), Ekinci (2011) and Yang (2011)
	• *Lower risk*: more than four 24 h urine assessments on average; FFQs	
	• *Intermediate risk*: between 2 and 4 24 h urine collections, or corrections for regression dilution bias; dietary reports	
	• *Higher risk*: urine collection <24 h or single 24 h urine collection; single dietary recall or 1-day food record	
	Insufficient power	
	• Less than 80% power to detect a 10% reduction in relative risk for every standard deviation in sodium intake	
	Studies using same data with divergent results	
	• *NHANES I studies*: same age group, same follow-up—inverse versus positive association	Alderman (1998), He (1999), Cohen (2008), Yang (2011)
	• *NHANES III studies*: different age groups, different follow-up—inverse versus positive association	

Reference list in Supplementary data, Appendix. SES, socioeconomic status; BMI, body mass index; FFQ, food frequency questionnaire.

and they must be interpreted in the context of other available evidence [31], including the limited but consistent evidence from randomized clinical trials on CVD outcomes [28].

Cost-effectiveness

Many studies have shown that a population reduction in salt intake is cost-saving for the health care system [14]. These conclusions have been reached with the use of different methodologies and using different assumptions. For example, in the USA, a reduction of 3 g of salt consumption per day would result in an estimated annual gain of 194 000 to 392 000 quality-adjusted life-years and estimated savings of $10 billion to $24 billion in health care costs, representing a $6 to $12 return on investment for each dollar spent on the regulatory programme [32]. If sustained over 10 years even more modest reductions in salt intake would be more cost-effective than using anti-hypertensive drugs in patients with hypertension [33]. Significant reductions in salt intake can only be achieved through reductions in the salt content of processed foods. Food reformulation can be either voluntary or mandatory. However, in Australia it has been shown that government legislation on salt limits in processed foods would yield health benefits up to 20 times greater than that achievable with voluntary approaches [34]. Cost savings are also estimated 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

Large multi-national commercial corporations primarily concerned with the profits deriving from maintaining high population salt intake and less with the health of the population have long been engaged in obstructive campaigns and activities against public health actions. They comprise mainly the food and beverage industry. Their strategies include mass media campaigns, biasing research findings, co-opting policy makers and health professionals, lobbying politicians and public officials, and encouraging voters to oppose public health regulation [12, 35, 36]. An important aspect of their strategy is misinformation through 'pseudo' controversies [37] and the publicizing of stale myths [13]. In general, poor science, using flawed methods [38], fabricated data [39] and robustly refuted results [40–42], has been manipulated to create uncertainty. In particular, the assertion that low salt intake may 'cause' heart disease has been recently disproved by US, Dutch and global studies using valid and appropriate methods [43].

WHO GAINS FROM THE CONTROVERSY?

Why is the food and beverage industry opposed to a reduction in salt intake? Salt is cheap.

In 2009, out of 27 million tons of salt sold in the United States only 1.5 million tons were of food-grade salt (<6%). The revenue, however, was about 16% (US$320 million out of a total revenue of US$2 billion). The use of salt in food manufacturing, nevertheless, generates substantial profits for the food and beverage industry (combined annual revenue of more than US$422 billion in 2012). A high salt intake generates profit by: (i) creating demand for salty foods through the desensitization of the taste buds; (ii) increasing the weight of meat products before packaging by injecting them with sodium salt bound to stabilizers; (iii) making cheap, unpalatable food edible at no extra cost; and (iv) causing thirst and high beverages consumption. High salt intake increases the consumption of high-calorie sugar-containing drinks, particularly in children, and alcohol intake. An implementation of recommended salt reduction targets would result in an average reduction in fluid consumption of ~350 mL per person per day [44], equivalent to a reduction of at least 2.3 sugar-sweetened soft drinks per week per child [45]. These effects would result in huge health and financial gains for governments, but 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. 1.25 million deaths worldwide). It is effective in both genders, any age, ethnic group, and high-, medium- and low-income countries. Population salt reduction programmes are both feasible and effective (preventive imperative). Salt reduction programmes are cost-saving in all settings (high-, middle- and low-income countries) (economic imperative). Public health policies are powerful, rapid, equitable and cost-saving (political imperative).

SUPPLEMENTARY DATA

Supplementary data are available online at http://ndt.oxfordjournals.org.

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CONFLICTS OF INTERESTS STATEMENT

None declared.

(See related articles by Graudal. Con: Reducing salt intake at the population level: is it really a public health priority? *Nephrol Dial Transplant* 2016; 31: 1398–1403; Zoccali and Mallamaci. Moderator's view: Salt, cardiovascular risk, observational research and recommendations for clinical practice. *Nephrol Dial Transplant* 2016; 31: 1405–1408)

REFERENCES

1. Sasaki N. The salt factor in apoplexy and hypertension: epidemiological studies in Japan. In: Yamori Y (ed). *Prophylactic Approach to Hypertensive Diseases*. New York: Raven Press, 1979, 467–474
2. Karppanen H, Mervaala E. Sodium intake and hypertension. *Prog Cardiovasc Dis* 2006; 49: 59–75
3. World Health Organization. *Reducing salt intake in populations. Report of a WHO Forum and Technical Meeting*. Geneva: World Health Organization, 2007, 1–60
4. World Health Organization. *Guideline: sodium intake for adults and children*. Geneva: World Health Organization, 2012, 1–46
5. *Proceedings of the first global ministerial conference on healthy lifestyle and non-communicable disease control*; 28–29 April 2011; Moscow. http://www.who.int/nmh/events/moscow_ncds_2011/conference_documents/en/ (29 June 2016, date last accessed)
6. *Sixty-sixth World Health Assembly follow-up to the political declaration of the high-level meeting of the General Assembly on the Prevention and Control of Non-communicable Diseases*. 25 May 2013. http://www.who.int/mediacentre/events/2013/wha66/en/ (29 June 2016, date last accessed)
7. Cappuccio FP, Capewell S, Lincoln P *et al.* Policy options to reduce population salt intake. *Br Med J* 2011; 343: 402–405
8. Swales JD. Salt saga continued. *Br Med J* 1988; 297: 307–308
9. Godlee F. The food industry fights for salt. *Br Med J* 1996; 312: 1239
10. Taube G. The (political) science of salt. *Science* 1998; 281: 898–907
11. Neal B, Land MA, Woodward M. An update on the salt wars—genuine controversy, poor science, or vested interest? *Curr Hypertens Rep* 2013; 15: 687–693
12. Brownell KD, Warner KE. The perils of ignoring history: Big Tobacco played dirty and millions died. How similar is Big Food? *Milbank Q* 2009; 87: 259–294
13. Cappuccio FP, Capewell S, He FJ *et al.* Salt: the dying echoes of the food industry. *Am J Hypertens* 2014; 27: 279–281
14. Cappuccio FP, Capewell S. Facts, issues and controversies in salt reduction for the prevention of cardiovascular disease. *Funct Food Rev* 2015; 7: 41–61
15. Grobbee DE, Hofman A. Does sodium restriction lower blood pressure? *Br Med J* 1986; 293: 27–29
16. Midgley JP, Matthew AG, Greenwood CMT *et al.* Effect of reduced dietary sodium on blood pressure. A meta-analysis of randomized controlled trials. *JAMA* 1996; 275: 1590–1597
17. Graudal NA, Galloe AM, Garred P. Effects of sodium restriction on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride. A meta-analysis. *JAMA* 1998; 279: 1383–1391
18. He FJ, MacGregor GA. Effect of modest salt reduction on blood pressure: a meta-analysis of randomized trials. Implications for public health. *J Hum Hypertens* 2002; 16: 761–770
19. Geleijnse JM, Kok FJ, Grobbee DE. Blood pressure response to changes in sodium and potassium intake: a metaregression analysis of randomized trials. *J Hum Hypertens* 2003; 17: 471–480
20. Graudal NA, Hubeck-Graudal T, Jurgens G. Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride. *Cochrane Database Syst Rev* 2011; 11: CD004022
21. Graudal NA, Hubeck-Graudal T, Jurgens G. Effects of low-sodium diet vs. high-sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterol, and triglyceride (Cochrane Review). *Am J Hypertens* 2012; 25: 1–15
22. Jurgens G, Graudal NA. Effects of low sodium diet versus high sodium diet on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride. *Cochrane Database Syst Rev* 2004; 1: CD004022
23. He FJ, Li J, MacGregor GA. Effect of longer term modest salt reduction on blood pressure: Cochrane systematic review and meta-analysis of randomized trials. *Br Med J* 2013; 346: f1325
24. Aburto NJ, Ziolkovska A, Hooper L *et al.* Effect of lower sodium intake on health: systematic review and meta-analyses. *Br Med J* 2013; 346: f1326
25. He FJ, MacGregor GA. Importance of salt in determining blood pressure in children: meta-analysis of controlled trials. *Hypertension* 2006; 48: 861–869
26. He FJ, Marrero NM, MacGregor GA. Salt and blood pressure in children and adolescents. *J Hum Hypertens* 2008; 22: 4–11
27. Strazzullo P, D'Elia L, Kandala NB *et al.* Salt intake, stroke, and cardiovascular disease: meta-analysis of prospective studies. *Br Med J* 2009; 339: b4567
28. He FJ, MacGregor GA. Salt reduction lowers cardiovascular risk: meta-analysis of outcome trials. *Lancet* 2011; 378: 380–382
29. Strazzullo P. Benefit assessment of dietary salt reduction: while the doctors study, should more people die? *J Hypertens* 2011; 29: 829–831
30. Cobb LK, Anderson CA, Elliot P *et al.* Methodological issues in cohort studies that relate sodium intake to cardiovascular disease outcomes: a science advisory from the American Heart Association. *Circulation* 2014; 129: 1173–1186
31. Whelton PK. Sodium, blood pressure, and cardiovascular disease: a compelling scientific case for improving the health of the public. *Circulation* 2014; 129: 1085–1087
32. Bibbins-Domingo K, Chertow GM, Coxson PG *et al.* Projected effect of dietary salt reductions on future cardiovascular disease. *N Engl J Med* 2010; 362: 590–599
33. Murray CJ, Lauer JA, Hutubessy RC *et al.* Effectiveness and costs of interventions to lower systolic blood pressure and cholesterol: a global and regional analysis on reduction of cardiovascular-disease risk. *Lancet* 2003; 361: 717–725
34. Cobiac LJ, Vos T, Veerman JL. Cost-effectiveness of interventions to reduce dietary salt intake. *Heart* 2010; 96: 1920–1925
35. Moodie R, Stuckler D, Monteiro C *et al.* Profits and pandemics: prevention of harmful effects of tobacco, alcohol, and ultraprocessed food and drink industries. *Lancet* 2013; 381: 670–679
36. Stuckler D, Nestle M. Big food, food systems, and global health. *PLoS Med* 2012; 9: e1001242
37. Campbell NR, Cappuccio FP, Tobe SW. Unnecessary controversy regarding dietary sodium: a lot about a little. *Can J Cardiol* 2011; 27: 404–406
38. Taylor RS, Ashton KE, Moxham T *et al.* Reduced dietary salt for the prevention of cardiovascular disease: a meta-analysis of randomized controlled trials (Cochrane Review). *Am J Hypertens* 2011; 24: 843–853
39. DiNicolantonio JJ, Di PP, Taylor RS *et al.* Low sodium versus normal sodium diets in systolic heart failure: systematic review and meta-analysis. *Heart* 2013. doi: 10.1136/heartjnl-2012-302337, Retraction notice. *Heart* 2013; published online March 12. doi:10.1136/heartjnl-2012-302337
40. Graudal N, Jurgens G, Baslund B *et al.* Compared with usual sodium intake, low- and excessive-sodium diets are associated with increased mortality: a meta-analysis. *Am J Hypertens* 2014; 27: 1929–1937
41. Kalogeropoulos AP, Georgiopoulou VV, Murphy RA *et al.* Dietary sodium content, mortality, and risk for cardiovascular events in older adults. The Health, Ageing, and Body Composition (Health ABC) Study. *JAMA Intern Med* 2015; 175: 410–419
42. Graudal N, Hubeck-Graudal T, Jurgens G *et al.* The significance of duration and amount of sodium reduction intervention in normotensive and hypertensive individuals: a meta-analysis. *Adv Nutr* 2015; 6: 169–177
43. Whelton PK, Appel LJ. Sodium and cardiovascular disease: what the data show. *Am J Hypertens* 2014; 27: 1143–1145
44. He FJ, Markandu ND, Sagnella GA *et al.* Effect of salt intake on renal excretion of water in humans. *Hypertension* 2001; 38: 317–320
45. He FJ, Marrero NM, MacGregor GA. Salt intake is related to soft drink consumption in children and adolescents: a link to obesity? *Hypertension* 2008; 51: 629–634