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3 1 **Reducing salt intake at population level: is it really a public health priority?**

4
5 2 **Pro position**

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7 3
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13 7
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15 9
16 10 **Word count:** 2012

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21 15 **Appendix:** 1

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23 17
24 18 **Key words:** blood pressure; cardiovascular disease; stroke; kidney disease; salt intake;
25 19 policy

26 20
27 21 **Abbreviations:** BP: blood pressure; CVD: cardiovascular disease; NCDs: non-
28 22 communicable diseases; WHO: World Health Organization

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1
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3 33 **Abstract**
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5 34 A reduction in salt intake reduces blood pressure, stroke and other cardiovascular events,
6 35 including chronic kidney disease, by as much as 23% (i.e. 1.25M deaths worldwide). It is
7 36 effective in both genders, any age, ethnic group, high, medium and low-income
8 37 countries. Population salt reduction programmes are both feasible and effective
9 38 (*preventive imperative*). Salt reduction programmes are cost-saving in all settings (high-,
10 39 middle- and low-income countries) (*economic imperative*). Public health policies are
11 40 powerful, rapid, equitable, cost-saving (*political imperative*). The important shift in the
12 41 public health has not occurred without obstinate opposition from organizations
13 42 concerned primarily with the profits deriving from population high salt intake and less
14 43 with public health benefits. Key components of the denial strategy are misinformation
15 44 (with “pseudo” controversies). In general, poor science has been used to create
16 45 uncertainty and to support inaction. This paper summarises the evidence in favour of a
17 46 global salt reduction strategy and analyses the peddling of well-worn myths behind the
18 47 false controversies.
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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 Japan¹ and Finland² 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 2007³ and 2012⁴ 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 2025⁵. Revised WHO guidelines now recommend a 30% reduction of salt intake by 2025 and a final maximum target of 5g per day⁴. The latter target was then adopted by the 66th World Health Assembly through its resolution in 2013⁶. A number of policy options for the implementation of national programmes globally are now available⁷ and population salt reduction is underway in many countries worldwide⁸.

“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 1988⁹ to the Godlee’s sharp call to reality in 1996¹⁰, the debate has transcended the scientific arena into public opinion and media campaigns with increasingly passionate tones¹¹. The controversy has been particularly heated since the translation of the results of scientific studies into public health and policy actions⁷ 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 interests¹²⁻¹⁴.

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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 birth¹⁴. 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 adults¹⁵⁻²⁵. 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

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3 114 dose-dependent reduction in BP; and (3) the effect is seen in both sexes, in people of all
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5 115 ages and ethnic groups, and with all starting BPs. Similar results have been described in
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7 116 children²⁶⁻²⁷.

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10 118 *Salt and cardiovascular outcomes*

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12 119 High BP contributes to strokes and heart attacks and a reduction in blood pressure is
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14 120 associated with their reduction. The effect is related to the size of the fall in BP. It is
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16 121 therefore conceivable that a moderate reduction in salt intake in a population would help
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18 122 reduce stroke and heart attacks through a reduction in BP. The collective evidence from
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20 123 systematic reviews of prospective longitudinal studies indicates that a lower salt intake is
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22 124 associated with a lower incidence of fatal and non-fatal cardiovascular events, in
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24 125 particular stroke^{25,28}. This is supported by a meta-analysis of the few randomised clinical
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26 126 trials available to date which have measured fatal and non-fatal outcomes²⁹. However, to
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28 127 prove that a reduction of salt intake in populations over an extended period of time
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30 128 reduces the rate of strokes and heart attacks a randomized double-blind placebo-
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32 129 controlled clinical trial would be needed. It has been argued that such a 'mother of trials'
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34 130 will never be conducted but, nevertheless, we should not refrain from implementing
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36 131 public health policies based on the available evidence so far³⁰. Never was a randomized
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38 132 clinical trial of tobacco smoking and lung cancer carried out in humans to 'prove' that
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40 133 smoking causes lung cancer and that we should eventually ban tobacco. Furthermore, an
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42 134 assessment of the bulk of evidence underlying population action of salt reduction dwarfs
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44 135 the evidence that today supports accepted policies on weight reduction, physical
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46 136 inactivity, dietary intake of fibre, fruit and vegetable for the prevention of both cancer
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48 137 and CVD. A recent controversy has been fuelled by a series of reports of analyses of
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50 138 prospective observational studies suggesting that lower salt intake might be associated
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52 139 with increased risk of CVD events, in particular coronary events and heart failure. These
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54 140 studies have been the object of intense scrutiny due to numerous methodological issues
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56 141 present in observational studies that would introduce fatal biases (errors) in the results
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58 142 and, hence, erroneous conclusions. A comprehensive account on these issues has been
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60 143 published by the American Heart Association³¹.

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145 **[INSERT TABLE HERE]**

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5 147 The **Table** provides a simple schematic summary of these methodological issues
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7 148 determining contrasting results. In brief, the risk of errors pertains the domains of
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9 149 systematic errors in the assessment of salt intake, the presence of ‘reverse causality’
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11 150 bias, the presence of residual confounding, random errors and insufficient statistical
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13 151 power. Moreover, prospective observational studies do not imply true ‘cause-effect’
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15 152 relationship, and they must be interpreted in the context of other available evidence³²,
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17 153 including the limited but consistent evidence from randomised clinical trials on CVD
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19 154 outcomes²⁹.

20 21 156 *Cost-effectiveness*

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23 157 Albeit applying different methods and models of assessment in different health care
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25 158 systems and under different assumptions, several studies have invariably demonstrated
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27 159 that a reduction in salt intake is cost-saving for the health care system (see¹⁴ for review).
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29 160 In the United States, a salt reduction of 3g per day would result in an estimated annual
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31 161 gain of 194,000 to 392,000 QALYs and estimated savings of \$10 billion to \$24 billion (US)
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33 162 in health care costs. That represents \$6 to \$12 (US) return on investment for each dollar
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35 163 spent on the regulatory program³³. Even a more modest reduction of 1g per day achieved
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37 164 gradually over 10 years would be more cost-effective than using medications to lower BP
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39 165 in all patients with hypertension³⁴. These economic savings would be achieved with
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41 166 either voluntary or mandatory reductions in the salt content of processed foods.
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43 167 However, health benefits would be up to 20 times greater with government legislation
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45 168 on salt limits in processed foods³⁵. Cost savings are also estimated for a 15% reduction in
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47 169 salt intake in low- and middle-income countries, which would avert 13.8 million deaths
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49 170 over 10 years at an initial cost of less than \$0.40 (US) per person per year. In conclusion,
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51 171 population salt reduction is an effective and cost-saving public health measure.

52 53 172 54 55 173 **The myths**

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57 174 The important shift in the public health debate from ‘whether’ salt reduces the risk to
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59 175 ‘how’ to best lower salt intake to reduce CVD has not occurred without obstinate
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176 opposition from organizations concerned primarily with the profits deriving from
177 population high salt intake and less with public health benefits. The food and beverage

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3 178 industry has been particularly obstructive regarding public health actions, either directly
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5 179 or through its public relations organizations. Its strategies have included mass media
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7 180 campaigns, biasing research findings, co-opting policy makers and health professionals,
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9 181 lobbying politicians and public officials, encouraging voters to oppose public health
10 182 regulation^{12,36-37}. Key components of this denial strategy are misinformation (with
11 183 “pseudo” controversies)³⁸ and the peddling of numerous rather well-worn myths¹³. In
12 184 general, poor science has been used to create uncertainty and to support inaction. Clear
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14 185 examples are given by recent debates generated by publications using flawed
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16 186 methodologies³⁹ (see **Table**) and subsequently retracted data⁴⁰ robustly rebutted by the
17 187 scientific community but sadly still used to support the controversy⁴¹⁻⁴³. In particular, the
18 188 claim that low salt intake may ‘cause’ coronary death has been proven not to be true, as
19 189 shown by US, Dutch, and global studies using valid and appropriate methods⁴⁴. Finally,
20 190 reiterated myths have been disseminated to consumers and lay audience to create
21 191 doubts¹³⁻¹⁴.

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23 193 **Who gains from the controversy?**

24 194 Why is the food and beverage industry so opposed to an approximate one third global
25 195 reduction in salt intake? Salt is a cheap commodity everywhere. In 2009, more than 27
26 196 million tons of salt were sold in the United States for a revenue of US\$2 billion; only 1.5
27 197 million tons of food-grade salt fetched more than US\$320 million. Notwithstanding these
28 198 figures, the use of salt in food manufacturing generates substantial profits for the food
29 199 and beverage industry. The world’s 10 largest food and non-alcoholic beverage
30 200 companies—feeding an estimated global population of several hundred million in more
31 201 than 200 countries daily — generated a combined annual revenue of more than US\$422
32 202 billion in 2012. A high salt intake contributes to the profit through several mechanisms:
33 203 (i) it will generate a demand for salty foods through a slow process of desensitization of
34 204 the taste buds; (ii) since sodium salts are hygroscopic, absorbing and binding water, the
35 205 practice of injecting meat products with sodium salt bound to stabilizers increases the
36 206 weight of meat products before packaging so that the water trapped in the meat is sold
37 207 at the price of meat; (iii) salt makes cheap, unpalatable food edible at no extra cost; (iv) it
38 208 causes thirst and an increase in the use of mineral waters, soft drinks and often alcoholic
39 209 beverages. The high use of sugar-containing drinks would contribute to the epidemic of
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3 210 obesity, particularly in children, and high salt intake might encourage an increase in
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5 211 alcohol intake. A reduction in salt intake as recommended by the WHO would result in an
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7 212 average reduction in fluid consumption of approximately 350 mL per day per person⁴⁵. In
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9 213 children, this would also lead to a reduction of at least 2.3 sugar-sweetened soft drinks
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11 214 per week per child⁴⁶. Although this would result in large beneficial effects to the health of
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13 215 the population and financial gains for governments, it would be a multibillion-dollar loss
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15 216 to the industry from reduced sales of bottled water, soft drinks and alcoholic beverages.
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218 **Conclusions**

19 219 A reduction in salt intake reduces BP, stroke and other cardiovascular events by as much
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21 220 as 23% (i.e. 1.25M deaths worldwide). It is effective in both genders, any age, ethnic
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23 221 group, high, medium and low-income countries. Population salt reduction programmes
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25 222 are both feasible and effective (*preventive imperative*). Salt reduction programmes are
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27 223 cost-saving in all settings (high-, middle- and low-income countries) (*economic*
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29 224 *imperative*). Public health policies are powerful, rapid, equitable, cost-saving (*political*
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31 225 *imperative*).
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34 227 **Acknowledgments**

35 228 This work has been conducted under the remit of the terms of reference of the World
36
37 229 Health Organization Collaborating Centre for Nutrition at the University of Warwick.
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40 231 **Conflicts of interests**

41 232 None to declare
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23 353 **Figure.** Forest-plot summarising the results of published meta-analyses of randomized
24 354 clinical trials of the effects of salt reduction on systolic blood pressure. Results are reported
25 355 as SMD and 95% C.I.s. (re-drawn from Reference 14)
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30 357 **Table.** Methodological issues in the assessment of prospective observational studies of salt
31 358 consumption and cardiovascular outcomes (re-drawn from Reference 31) Reference list in
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33 359 Appendix 1.
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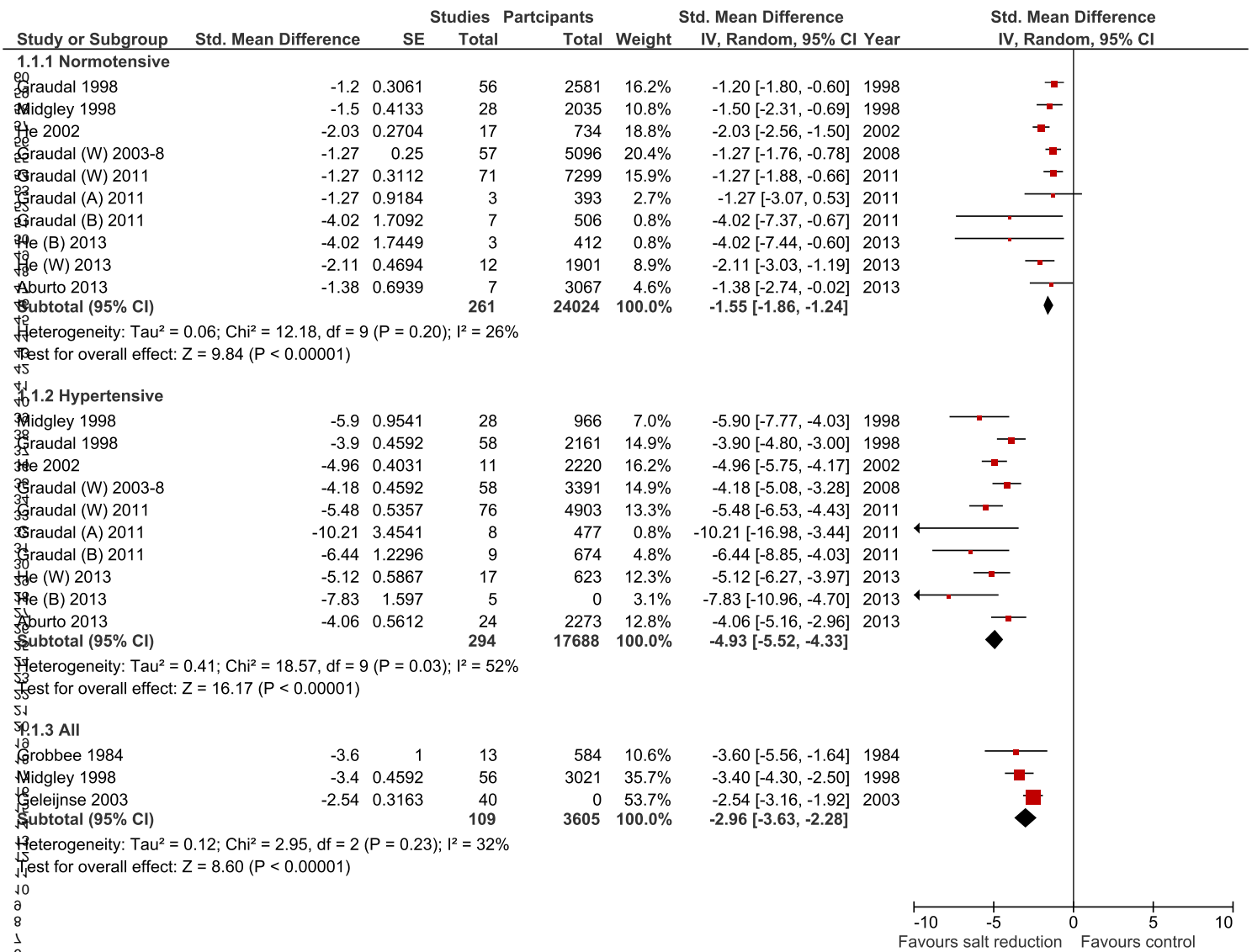


Table. Methodological issues in the assessment of prospective observational studies of salt consumption and cardiovascular outcomes.

Domain 1	Errors with the greatest potential to alter the direction of association (with examples)	
	Systematic error in sodium assessment <ul style="list-style-type: none"> • <i>Lower risk</i>: 24h urine collections not part of routine clinical practice, no quality assurance, not excluding incomplete collections. • <i>Higher risk</i>: 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 <ul style="list-style-type: none"> • <i>Lower risk</i>: participants recruited from general population and pre-existing CVD excluded • <i>Intermediate risk</i>: sick populations not excluded or included despite stated otherwise; presence of CVD risk factors; specific sick populations • <i>Higher risk</i>: 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 <ul style="list-style-type: none"> • <i>Incomplete adjustment</i>: 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 • <i>Imbalance across sodium intake levels</i>: age difference across sodium groups >5 years; sex or race distribution across sodium groups >20% • <i>Inadequate follow-up</i>: 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 <ul style="list-style-type: none"> • <i>Lower risk</i>: more than four 24h urine assessments on average; FFQs • <i>Intermediate risk</i>: between 2-4 24h urine collections, or corrections for regression dilution bias; dietary reports • <i>Higher risk</i>: urine collection <24h or single 24h urine collection; single dietary recall or 1-dat food record Insufficient power <ul style="list-style-type: none"> • 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	
	<ul style="list-style-type: none"> • <i>NHANES I studies</i>: same age group, same follow-up – inverse vs positive association • <i>NHANES III studies</i>: different age groups, different follow-up – inverse vs positive association 	Alderman 1998; He 1999 Cohen 2008; Yang 2011