

# Facts, Issues, and Controversies in Salt Reduction for the Prevention of Cardiovascular Disease

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Current salt consumption in human societies is now much greater than needed for survival. Furthermore, high salt intake substantially increases blood pressure (BP) in both animals and humans. Conversely, a reduction in salt intake causes a dose-dependent reduction in BP in men and women of all ages and ethnic groups and in patients already on medication. The risk of strokes and heart attacks rises with increasing BP but can be decreased by antihypertensive drugs. However, the majority of cardiovascular disease (CVD) events occur in the numerous individuals with “normal” BP levels below the “clinically hypertensive” level which might trigger drug therapy. Nonpharmacological prevention is therefore the only option to reduce the majority of such events. Reductions in population salt intake consistently reduce the number of subsequent CVD events (with additional benefits for the heart, kidneys, stomach, and skeleton). Indeed, this is one of the most important public health measures for reducing the global CVD burden. The most successful policies involve comprehensive which ideally include population monitoring, health education, and reformulation to reduce the salt content concealed in processed foods (which represent over 75% of daily salt intake). Such population-wide salt reduction policies are generally powerful, rapid, equitable, and cost saving. Inevitably, the food and beverage industries, which profit from marketing salt, will try to oppose such policies. However, public health has triumphed in those countries prepared to consider the necessary levers: regulation, legislation, and even taxation. A comprehensive reformulation strategy for processed foods can provide an effective first step.

**Key words:** Cardiovascular prevention, public health policy, salt (sodium) intake

## Salt Intake in the Development of Humankind: Evolutionary Observations

The consumption of salt began to rise between 5,000 and 10,000 years ago. The earliest use of salt is reported to have taken place on Lake Yuncheng in northern China around 6000 BC.<sup>1</sup> All known human societies, even the most primitive, consume per capita more salt than they physiologically require. Salt has been referred to as the “primordial addiction.”<sup>2</sup> It is important to consider our intakes of salt in the light of our evolutionary history,

as discordance between our modern-day diet and the traditional hunter-gatherer diet under which our genome was selected may provide insight into the fundamental mechanisms of chronic disease pathogenesis.<sup>3–5</sup> The Neolithic revolution, approximately 10,000 years ago, saw a move away from traditional hunter-gatherer practices and the introduction of human settlement, agriculture, and animal husbandry.<sup>6</sup> These practices mark the beginning of a period of profound change to the composition of the human diet and to the availability of various foods, finally culminating in today’s modern diet.<sup>4</sup> These changes have occurred over an evolutionarily minute timescale and are in conflict with our genetically determined biochemistry, which has evolved over a protracted length of time.<sup>5</sup> For reasons not fully understood, the initial rise in human salt consumption paralleled the advent of agriculture and the decline of meat consumption of hunter-gatherer societies.<sup>7</sup> Salt became a necessity of life and the first international commodity of trade, giving it great symbolic importance and economic value, representing one of the earliest industries and the first state monopoly.<sup>1</sup> Primitive methods of salt production were not simple; salt was a relative (but bulky) luxury, posing distribution challenges. Salt use

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became a way to affirm “social distance”<sup>8</sup> because of its unique properties of enhancing flavors and fulfilling hedonic rewards.<sup>9</sup> This mechanism was later understood to be an acquired characteristic of salt taste bud regulation.<sup>10</sup> Probably the most important factor leading to an increase in human salt consumption was the discovery that putting meat and other foods into concentrated salt solutions could preserve them. Until modern times, salt provided the principal way of preserving food and protecting it against decay.<sup>1</sup> With the advent of electricity and refrigeration, particularly in the developed world, the need for salt as a preservative has rapidly diminished. However, the human consumption of salt has not declined and has increased in some instances,<sup>11</sup> significantly contributing to the development of chronic diseases.

### Salt Intake and Blood Pressure

The concept of an association of high salt intake with high blood pressure (BP) was first attributed to *The Yellow Emperor’s Classic of Internal Medicine* (by Huang Ti Nei Ching Su Wen, 2698–2598 BC). In the early 20th century, Ambard and Beaujard<sup>12</sup> described the clinical association between levels of salt intake and levels of BP in humans, later clarified by Kempner in 1948<sup>13</sup> with salt-free rice-diet experiments.

#### Animal Experiments

Since 1948, these effects have been studied in detail in numerous experimental rat models, like Dahl and colleagues salt-sensitive rats,<sup>14</sup> Aoki and colleagues spontaneously hypertensive and stroke-prone hypertensive rats,<sup>15</sup> and Bianchi’s Milan strain of rats.<sup>16</sup> In all cases, a clear dose-dependent effect was described between the levels of salt intake and the levels of BP and cardiovascular complications. Chimpanzees, the species phylogenetically closest to humans, were studied by Denton and colleagues in two landmark experiments.<sup>17,18</sup> In the first, a colony of 26 free-living chimpanzees in Gabon were studied while on their low-salt high-potassium diet and were then fed a high-salt diet for 6 months. Their diet was then reversed to the usual diet. During these periods, both BP and urinary sodium and potassium were measured. The results showed unequivocally for the first time that increasing salt intake caused a large rise of BP, which was reversed upon a return to a low-salt diet. The study was repeated with 110 chimpanzees housed in Bastrop, Texas, that were randomized to receiving either a diet with 250 mmol of sodium (~14.5 g of salt) per day or a diet with half that amount of sodium per day (~7.3 g of salt)

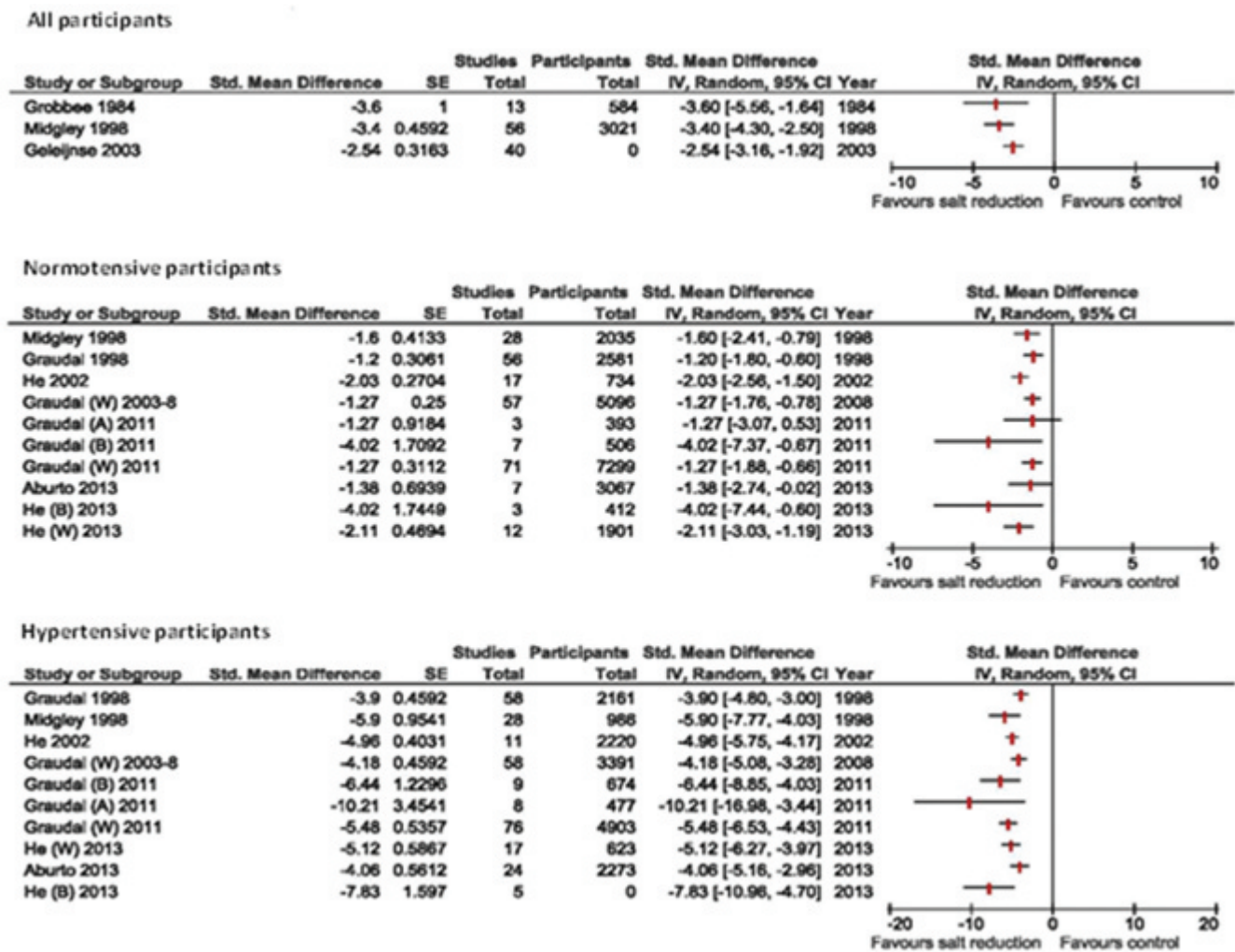
for 2 years. At the end of the study, the group that ate half the amount of salt (a 7 g difference from the other group) had a 6/4 mm Hg–lower systolic and diastolic BP when compared to the other group. This study confirmed the significant effect of salt reduction within human dietary limits and the sustained effect over 2 years.

### Salt and Blood Pressure in Humans

Epidemiological and migration studies, natural experiments, population-based intervention studies, and randomized controlled clinical trials all provide evidence of a direct link between salt intake and BP.<sup>19</sup> The results of the Intersalt Cooperative Study well summarizes an association between salt intake and BP and a steep relationship between salt intake and the rise in BP observed with age.<sup>20</sup> Numerous randomized clinical trials have been performed over the last 40 years. They have been repeatedly and systematically reviewed and meta-analyzed since 1984.<sup>21–31</sup> Figure 1 shows the collective estimates of all meta-analyses published to date on the effect of salt reduction on BP in adults. The meta-analyses differ for the time of the analysis, hence the number of overall studies available, 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). In light of these differences between studies, the range of pooled weighted estimates of effect ranged from –10.2 to –1.2 mm Hg for systolic BP and from –4.08 to –0.05 mm Hg for diastolic BP, respectively, in favor of salt reduction. More important, the 95% confidence intervals of all the pooled estimates were compatible with each other, indicating consistency, with differences between them likely being due to random variation. 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.<sup>32,33</sup>

#### “Salt Sensitivity”

A moderate reduction in salt intake reduces BP in most but not all individuals. The effect on BP varies largely from person to person.<sup>34</sup> Salt sensitivity has a variety of determinants, including race and ethnicity,<sup>35</sup> age,<sup>36</sup> body mass



**Figure 1.** Forest plots summarizing the results of published meta-analyses of randomized controlled trials of the effects of salt reduction on systolic blood pressure. Results report weighted mean effects and 95% confidence intervals. IV = inverse variance; Std = standard.

index,<sup>37–39</sup> and diet quality, as well as associated disease states (eg, hypertension, diabetes, and renal dysfunction). It is partially under genetic control, as these individuals, whether considered “normotensive” or “hypertensive,” tend to have a positive family history of hypertension.<sup>40</sup> The BP response to a moderate change in salt intake is normally distributed.<sup>41</sup> Many experimental models have been used for the past 40 years to attempt an individual characterization of so-called salt sensitivity. These methods have included BP responses to (1) acute and large changes in salt intake, with or without diuretic-induced volume depletion and (2) moderate changes in salt intake over days in normotensive volunteers,<sup>42</sup> patients, or general population.<sup>43</sup> They also included response of the renin-angiotensin-aldosterone system<sup>43–45</sup> and the clearance of endogenous lithium, a noninvasive method for assessing

segmental renal tubular sodium handling<sup>45</sup> and considered a proxy for salt sensitivity.<sup>46,47</sup>

Measures of salt sensitivity are associated with more severe cardiovascular risk factor profiles,<sup>39,48–50</sup> and they are negative prognostic indicators.<sup>39,49</sup> Although less easy to detect, salt sensitivity is present also in normotensive people. In a small clinical study with a long-term follow-up, normotensive salt-sensitive individuals had a cumulative mortality as high as that of hypertensive patients.<sup>51</sup>

#### *Interaction with Drug Therapy*

Hypertension control remains suboptimal in many countries despite recent improvements. Most people require more than one drug to control their high BP to target,<sup>52</sup> and resistant hypertension is now becoming a

reason for concern.<sup>53</sup> One of the main causes of resistant hypertension is a high salt intake, and one therapeutic way to potentiate drug-induced fall in BP is to accompany drug therapy with moderate salt reduction.<sup>54</sup> In fact, a moderate reduction in salt intake is effective in lowering BP on its own, but it is also additive to pharmacological therapy and can be as effective as a low-dose thiazide diuretic.<sup>55</sup> The degree of renal protection seen with sodium reduction, however, is not seen with the use of diuretics.<sup>56</sup> A reduction in sodium intake reduces sodium delivery to the distal tubule by increasing proximal tubular sodium reabsorption,<sup>45,47</sup> whereas diuretics will not. Increased sodium delivery to the distal tubule (especially in the outer medulla, the site most vulnerable to ischemic injury) would explain why high sodium intake is harmful to the kidney even when associated with the use of diuretics.<sup>56</sup> Finally, the BP-lowering effect of dietary salt reduction would be more pronounced when associated with drug classes that block the renin-angiotensin-aldosterone system (such as angiotensin-converting enzyme inhibitors, angiotensin receptor blockers, renin inhibitors, antialdosterone compounds, and beta blockers).

### Blood Pressure and Cardiovascular Disease

Blood pressure is responsible for approximately 50% of deaths from coronary heart disease (CHD) and more than 60% of deaths from stroke—the two leading causes of preventable death, morbidity, and disability in the world.<sup>57,58</sup> The risk of these cardiovascular diseases (CVDs) increases progressively with increasing BP, and there is a graded relationship between BP and CVD, down to or even below 115/75 mm Hg.<sup>59</sup> When high BP (140/90 mm Hg or higher) is lowered with drugs, there is a reduction in both CHD and stroke events of the magnitude consistent with observational studies.<sup>60</sup> However, the majority of CVD events attributable to BP occur at around 130/80 mm Hg or less because there are so many more individuals in the population who have this “normal” BP.<sup>61</sup> Since we would not treat with drugs the majority of individuals with a BP of 130/80 mm Hg,<sup>62</sup> a population-based approach through nonpharmacological measures (ie, diet and lifestyle) is the only feasible option. Achieving a small downward shift in the distribution of BP in the whole population would achieve a surprisingly large reduction in CVD (ie, a 2.5% decrease in mortality rates for every 1 mm Hg decrease in systolic BP).

### Salt Intake and Cardiovascular Disease

Natural experiments of salt reduction programs in Japan and Finland over the last 40 years have suggested a

substantial benefit of these programs in contributing to a reduction in population BP and hence the incidence of stroke and CHD.<sup>63,64</sup> There are almost no long-term randomized trials of salt reduction and cardiovascular (CV) outcomes. This is due to ethical considerations, methodological challenges regarding compliance over time, extended duration, large sample size, and difficulty in securing financial support.<sup>65</sup> Therefore, observational prospective cohort studies with many years of follow-up and assessments of exposure (salt intake) and outcomes (heart attacks and strokes) remain the next best option. A meta-analysis of these studies suggests that a 5 g higher salt intake is associated with a 17% greater risk of total CVD and, crucially, a 23% greater risk of stroke.<sup>66</sup> However, the nature of these studies does not establish causality. The risk of methodological problems in cohort studies that relate sodium intake to cardiovascular disease outcomes is high. Systematic as well as random errors in sodium assessment, the potential for residual confounding, the likelihood of reverse causality, and crucially, the selection of high-risk and sick older patients on multiple drug therapy can all lead to biased conclusions.<sup>67–71</sup> These problems are seen in some cohort studies that suggest an increased risk of CHD at lower levels of salt intake. How do we know then whether the higher salt intake is the “direct” cause of the higher risk of stroke? Many years ago, Sir Austin Bradford Hill indicated a number of criteria that an observational epidemiological study should fulfil in order to support the concept of causality.<sup>72</sup> These criteria, for example, were used to suggest the causal link between cigarette smoking and lung cancer, for which no clinical trials were available. Many of these criteria in support of causality apply to the association between salt intake and CVD. The association between higher salt intake and stroke is moderately strong; pooled adjusted relative risks range between 1.10 and 1.30.<sup>31,66</sup> There is a dose-response relationship between the level of salt intake and the risk of stroke.<sup>66</sup> The association with outcomes is consistent across different countries. High salt intake precedes the development of outcomes in prospective studies. One study, phases I and II of the Trials of Hypertension Prevention (TOHP), provides to date the only evidence of a randomized trial of salt reduction on outcomes.<sup>73–77</sup> Compared to a control group, a reduction of 25 to 30% in salt consumption in the intervention group caused a fall in BP at 18 and 36 months and a reduction in CV events. Ten to 15 years later, the BP and the CV mortality were still lower in participants who had originally been randomized to the intervention group (TOHP, phases I and II). Finally, a recent meta-analysis of randomized clinical trials of salt reduction in which vital

outcomes were also recorded during follow-ups ranging from 7 months to 11.5 years indicates a statistically significant 20% reduction in total CV outcomes (relative risk [RR] = 0.80 [95% CI, 0.64–0.99]).<sup>78</sup>

### Other Effects of Dietary Salt Reduction

High salt intake is an independent predictor of left ventricular mass, and a reduction in salt intake causes a regression of left ventricular hypertrophy.<sup>79</sup> High salt intake causes an increase in renal blood flow and glomerular filtration rate, and a reduction in salt intake appears to normalize the hyperfiltration seen in normotensive individuals more sensitive to the effect of salt.<sup>43</sup> A high salt intake increases urinary calcium losses; this in turn causes increased levels of parathyroid hormone, 1,25-dihydroxyvitamin D, serum osteocalcin (a marker of bone formation), urinary cyclic adenosine monophosphate, and urinary hydroxyproline (a marker of bone resorption).<sup>80,81</sup> If substantial calcium losses are sustained over many decades, increased excretion of calcium in the urine may result in an increased risk of urinary tract stones,<sup>82–86</sup> and the increased movement of calcium from bone may result in higher rates of bone mineral loss, thereby increasing the risk of osteoporosis, particularly in menopausal women.<sup>87–89</sup> A reduction in salt intake is therefore an effective strategy for reducing hypercalciuria in hypertensive patients as well as those who form kidney stones<sup>84,90</sup> and is a useful long-term preventive strategy to help reduce the risk of bone mineral density loss and osteoporosis in later life.<sup>80,87–89</sup> In a recent meta-analysis of prospective studies, dietary salt intake was directly associated with the risk of gastric cancer, with progressively increasing risk across consumption levels.<sup>91</sup> In the pooled analysis, “high” and “moderately high” salt intake versus “low” salt intake were all associated with an increased risk of gastric cancer (RR = 1.68 [95% CI, 1.17–2.41] and 1.41 [95% CI, 1.03–1.93], respectively). High salt intake induces thirst and an increased fluid intake that is then retained in the intravascular compartment, causing an increase in total blood volume. Both the heart and the kidney are the main organs that compensate for these changes through hormonal responses (renin-angiotensin-aldosterone axis and atrial natriuretic peptide), increased systolic ejection, and increased blood flow and renal clearances. Dysregulation of these systems may lead to fluid retention that can be aggravated by high salt intake and ameliorated or cured by a reduction in salt intake. Congestive heart failure may be triggered by high salt intake; “rebound” sodium and fluid retention following

diuretic withdrawal can be minimized or avoided by low salt intake prior to withdrawal.<sup>92</sup> Finally, there is evidence to suggest a direct effect of high salt intake, independent of its BP effect, on endothelial cell signaling, oxidative stress, and the progression of kidney disease.<sup>93,94</sup>

### Population-Wide Salt Reduction for Prevention of Cardiovascular Disease

#### Development of Public Health and Policy Recommendations

The importance of a population reduction in salt intake for the prevention and control of high BP and of CVD had been recognized since the 1970s with successful national and regional programs in Japan<sup>63</sup> and Finland.<sup>64</sup> In 1985, the World Health Organization (WHO) issued recommendations to member states for a reduction in salt intake down to an average of 5 g per day. However, no action plans were put in place. In the meantime, Finland implemented a national program successfully pursued over more than 20 years. Salt intake fell from 13.0 g to 10.0 g per day in men and from 10.5 g to 7.6 g per day in women.<sup>95</sup> At the same time, there was a 20% reduction in BP,<sup>96</sup> even though body mass index increased. These reductions were associated with a substantial decline in both CHD (55% in men and 68% in women)<sup>97</sup> and stroke mortality (66% in men and 60% in women).<sup>95</sup> These benefits were clear even after adjustment for the concomitant decreases in total and LDL cholesterol.<sup>95</sup> Indeed, two thirds of the falls in CVD mortality in all Western countries (mainly falls in BP reflecting dietary salt reduction and reduced smoking rates and total cholesterol levels) have been attributed to improvements in risk factors.<sup>64,96–98</sup> Since the 1980s, both scientific evidence and public health initiatives reflecting a decreased intake of salt have accumulated, leading in 2007<sup>99</sup> and 2012<sup>100</sup> to renewed recommendations from the WHO not to exceed a population average salt intake of 5 g per day. These recommendations are now followed by numerous countries worldwide<sup>101</sup> (Table 1). The most recent significant step toward global policy action was the 2011 United Nations high-level meeting on noncommunicable diseases, which set a target for population salt reduction as a priority to reduce premature mortality by 2025.<sup>102,103</sup> The revised WHO guidelines now recommend a 30% reduction of salt intake by 2025 and a final maximum target of 5 g per day.<sup>100</sup> The latter target was then adopted by the 66th World Health Assembly through its resolution in 2013.<sup>104</sup> At present, salt intake exceeds the recommended level in almost all

**Table 1.** The Narrative History of Salt Reduction Policies: Four Decades of Setbacks and Successes

Year	Event	Reach	Source
1970s	National programs of salt reduction for the prevention of stroke mortality	Japan	
1970s	Regional (North Karelia) and National programs of salt reduction to reduce CVD mortality	Finland	
1985	The WHO publishes global recommendations for a reduction in dietary salt intake below 5 g per day	Global	
1988	INTERSALT publishes its first scientific paper describing levels of salt intake worldwide and indicating a strong association between levels of salt intake, levels of BP and the rise in BP with age	Global	BMJ 1988;297:319–28
1991	Landmark scientific papers reviewing the global evidence of the direct link between levels of salt intake and levels of BP	Global	BMJ 1991;302: 611–5, 815–8, 819–24
	The Committee On Medical Aspects (COMA) of Food Policy publishes a report which sets Reference Nutrient Intakes for salt at no more than 4 g per day	UK	Dietary reference values for food, energy and nutrients for the United Kingdom
1994	COMA publishes a report which recommended that salt intake should be reduced gradually from 9 to 6 g per day. However, the Chief Medical Officer (CMO) for England does not accept the recommendations.	UK	Nutritional aspects of cardiovascular disease
1996	Consensus Action on Salt & Health (CASH) is set up to endorse the COMA recommendations. It comprises 22 expert scientific members	UK	
2001	The CMO for England gives his support to a national salt target of no more than 6 g per day	UK	CMO Annual Report
2002	The Food Standard Agency (FSA) commits to a nationwide salt reduction initiative to reduce salt intake to 6 g per day	UK	“Sid the slug,” “Check the label;” “Is your food full of it?” National Campaigns
	The WHO publishes a report establishing that high BP alone is responsible for 50% of cases of CVD worldwide and that the salt intake of industrialised countries is very high, with more than 75% of salt coming from processed foods	Global	Preventing risk and promoting a healthy lifestyle
2003	The Scientific Advisory Committee on Nutrition (SACN) publishes a report recommending a reduction in salt intake to less than 6 g per day in adults. It also provides recommendations for children under the age of 11	UK	Salt and Health Report
	Landmark scientific paper indicates that salt intake should be reduced to 3 g per day to achieve the greatest possible benefits.	Global	Hypertension 2003;42:1093–9
2004	Salt reduction is included in the WHO Global strategy on diet, physical activity and health	Global	Global Strategy on Diet, Physical Activity and Health
2005	World Action on Salt & Health (WASH) is set up to support salt reduction initiatives worldwide. It comprises more than 400 expert members in five continents.	Global	
2006	The FSA sets voluntary salt reduction targets for the food industry	UK	
2007	The WHO publishes recommendations on the reduction in salt intake to less than 5 g per day to prevent CVD.	Global	Reducing salt intake in populations
	The European Salt Action Network (ESAN) is set up under the auspices of the WHO and chaired by the FSA	Europe	
	The American Heart Association publishes a report calling for a major reduction in the salt content of processed and restaurant food.	USA	Arch Intern Med 2007;167:1460–8
	Landmark scientific paper indicating the cost-effectiveness of a population strategy of salt reduction for the prevention of CVD globally	Global	Lancet 2008;370:2044–53
2008	Population average salt intake falls by 10%, from 9.5 to 8.6 g per day.	UK	
	The FSA sets new voluntary salt reduction targets	UK	
	The Mayor of New York City announces his plan to cut salt levels in processed foods by 20% over 5 years.	USA	

Table 1. Continued

Year	Event	Reach	Source
2009	Landmark scientific paper indicates that a 5 g per day reduction in habitual population salt intake is associated with a 23% reduction in the rates of stroke and a 17% reduction in the rates of total CVD.	Global	BMJ 2009;339:b4567
	The Pan-American Health Organization (PAHO) sets up the PAHO/WHO Regional Expert Group for Cardiovascular Disease Prevention through Population-wide Dietary Salt Reduction	Americas	
	The Ministry of Health of Italy launches a national salt reduction campaign and establishes salt reduction targets for bread. It also funds the first national survey of salt intake (MINISAL-GIRCSI).	Italy	“Guadagnare salute,” “O” sale mio,” “Più sale, meno sale,” “MINISAL.”
2010	Landmark scientific paper indicates the public health benefits of population salt reduction and the medical cost reduction associated with it.	USA	NEJM 2010;362:590–9
	The Institute of Medicine (IOM) of the National Academies recommends strategies for a population salt reduction	USA	Strategies to reduce sodium intake in the United States
	The Government of Canada publishes a national strategy for a population reduction in salt intake	Canada	Sodium reduction strategy for Canada
	The National Institute for Health & Clinical Excellence (NICE) publishes recommendations for the prevention of CVD, with population salt reduction as first goal.	UK	PHG 25: Prevention of cardiovascular disease
	The FSA publishes key catering and manufacturer commitments to salt reduction.	UK	
	The WHO convenes a global meeting in the UK to create an enabling environment for salt reduction strategies.	Global	Creating an enabling environment for population-based salt reduction strategies
	The WHO convenes a global meeting in Canada to establish strategies for monitoring and surveillance.	Global	Strategies to monitor and evaluate population sodium consumption and sources of sodium in the diet
2011	66 <sup>th</sup> World Health Assembly includes a 30% reduction in salt intake in the “25 by 25” initiative seeking to reduce preventable mortality globally by one quarter by 2025.	Global	
	Population average salt intake falls further from 8.6 g per day (in 2008) to 8.1 g per day, for a total reduction since the campaign started of 1.4 g per day (approx. 15%)	UK	
	The Public Health Responsibility Deal outlines health commitments by the food industry. They include salt reduction based on targets set in 2012.	UK	
2012	The WHO publishes update guidelines for the reduction of salt intake.	Global	Sodium intake for adults and children
	The Government of South Africa first to legislate on wide reformulation of food for salt content.	S Africa	
2013	The Parliament of Argentina approves the “Law on salt.” It sets baseline maximum levels of sodium content for different food groups and indicates progressive decreases over time. The law also establishes sanctions for breaches.	Argentina	
	Evidence of socioeconomic inequalities in salt consumption in Britain.	UK	BMJ Open 2013;3:e002246
2014	Socioeconomic inequalities in salt consumption in Britain persist despite successful population reduction	UK	BMJ Open 2014;4:e005683
	Agreement between the Ministry of Health of Brazil and the Brazilian Association of Food Industry (ABIA) succeeded in removing ~1.3 tons of salt from buns, loaf bread and noodles and instant pasta achieving 94 to 100% of the set targets.	Brazil	

Table 1. Continued

Year	Event	Reach	Source
	Landmark study estimates that 1.65 million deaths from cardiovascular causes can be attributed to sodium consumption > 2.0 g per day, globally.	Global	NEJM 2014;371:624–34

BP = Blood Pressure; CVD = Cardiovascular Disease; INTERSALT = International Study of Sodium, Potassium, and Blood Pressure; WHO = World Health Organization.

countries in the world, with small differences by age and sex.<sup>101,105</sup>

### Three-Pronged Approach and Policy Options to Reduce Salt Intake in Entire Populations

The issue is no longer “whether” reducing salt intake is of public benefit but rather “how” best to achieve a steady, significant, and sustained reduction in salt consumption. What are the options available to governments, health organizations, individuals, and stakeholders? Which policies are best suited for local needs? How effective are they, and how do we monitor success?

An effective program to reduce population salt intake is based on three fundamental pillars: communication, reformulation, and monitoring<sup>106–108</sup> (Figure 2). These

three pillars will cover a variety of complementary and mutually reinforcing approaches, including health promotion and awareness campaigns, collaboration with industry to progress voluntary or regulatory reformulation programs, the use of salt substitutes in households and in food manufacturing, and crucially, the monitoring of salt content in food and population salt consumption.<sup>109–111</sup> A successful example is the salt reduction campaign in the United Kingdom, achieving a 15% (1.4 g per day) reduction in salt intake over 7 years.<sup>111–116</sup> The UK Food Standard Agency pursued a sustained program to facilitate progressive reformulation by industry. Although the program was officially “voluntary,” successive health ministers had clearly signaled their readiness to legislate if necessary.<sup>111</sup>

In cases in which the majority of the population salt intake comes from processed food and the catering sector,

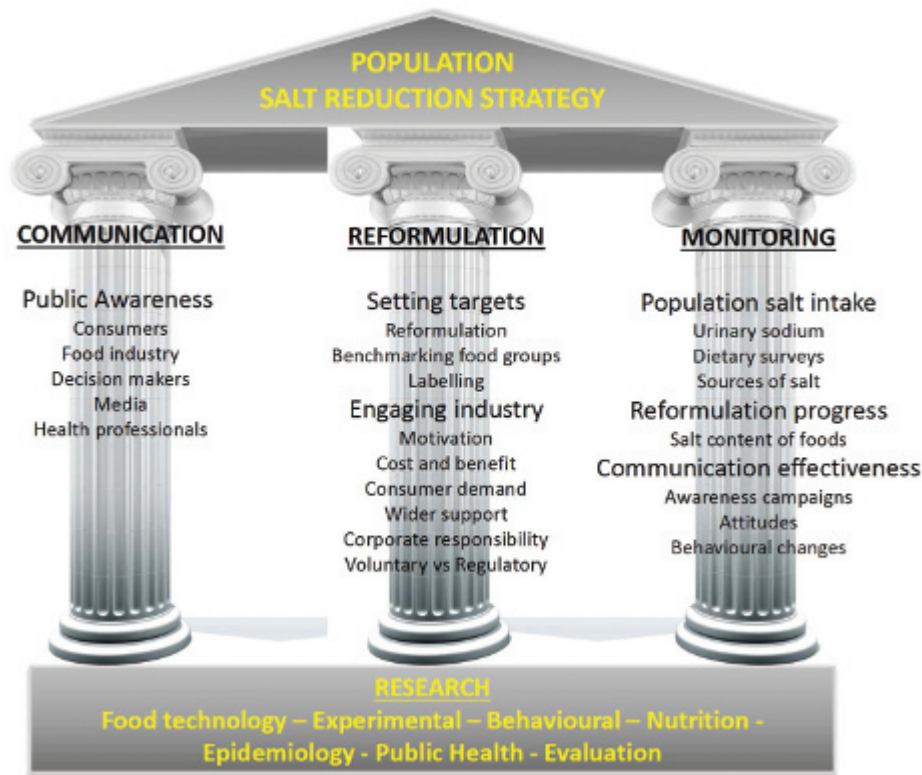


Figure 2. Three-pronged strategy for successful salt reduction.



voluntary collaboration with the industry, reinforced by a regulatory framework, is advocated.<sup>106,117–119</sup> A good self-regulatory voluntary system has benefits in that it saves government resources and is less confrontational, more flexible, and speedier than government regulation.<sup>120</sup> Self-regulation tends to be less effective than legislation<sup>120</sup> and hence is often less cost-effective.<sup>121</sup> Indeed, there is consistent evidence that the addition of a regulatory framework is more effective<sup>122</sup> and cost-effective than the voluntary approach alone.<sup>121,123–126</sup> Successful examples of these approaches can be seen in Finland<sup>64</sup> and more recently in the New York City initiative.<sup>127</sup> Where salt is mainly added to food at household levels, as in some parts of rural Africa,<sup>128,129</sup> health promotion and education may still be an option.<sup>128</sup> Finally, salt-substitution policies are being tested in China, where it might provide an alternative for that country<sup>130</sup> because the majority of salt intake there, unlike most westernized countries, derives from salt added to food through salted condiments and during food preparation at home.<sup>131</sup>

These policy interventions are currently being tested or implemented worldwide through national (eg, UK, Italy, Canada, USA, Australia) and international (European Salt Action Network, WHO Global Initiative, Pan-American Health Organization Programme) initiatives. The latter has led to high-level agreements by the governments of many countries (Mexico, Argentina, Chile, Costa Rica, and Brazil) to implement national programs for population dietary salt reduction for the prevention of CVD.<sup>132</sup>

### Evaluation and Quantitative Comparison of Contrasting Policy Approaches through Modeling

Taking Argentina as an example, policies adopted in that country may reduce salt intake by about 0.8 g per day.<sup>133</sup> According to the CHD Policy Model, this should translate into a systolic BP reduction of between 0.9 and 1.8 mm Hg. This could in turn avert approximately 20,000 deaths, 13,000 myocardial infarcts, and 10,000 strokes over the next decade. Similar results come from a variety of different modeling methodologies applied to diverse populations (Table 2). Many are based on the effect sizes from the meta-analysis by Strazzullo et al.<sup>66</sup> In the UK population, a reduction of 3 g per day in salt intake could result in approximately 6,600 fewer CVD deaths per year, according to O’Flaherty and colleagues,<sup>134</sup> or, according to a more conservative approach used by Barton and colleagues,<sup>135</sup> some 4,450 fewer CV deaths and 30,000

fewer CV events per annum, along with total 95,000 life-years gained, 130,000 quality-adjusted life-years (QALYs), and overall financial savings of approximately £350 million per decade. Further supportive evidence comes from empirical data. These consistently demonstrate that with diet-based population-wide risk factor reductions, substantial declines in event rates can happen very rapidly (ie, in years rather than decades).<sup>136,137</sup>

When different policy approaches are compared, an effectiveness hierarchy becomes apparent (Figure 3). Thus, individually based approaches such as advice or social marketing are relatively weak, whereas more “upstream” population-wide policy approaches generally achieve much larger reductions in salt intake. The exemplars are the comprehensive programs in Finland and Japan, followed more recently by the United Kingdom.

### Cost-Effectiveness

The application of policies to reduce salt intake across an entire population is an effective and cost-saving public health measure. Several studies have assessed the health effects and the health care–related costs of reducing population salt intake. Albeit applying different methods and models of assessment in different health care systems and under different assumptions, their results have invariably demonstrated that a reduction in salt intake is cost saving for the health care system.<sup>118,121,123–126,135,138–147</sup> (see Table 2). For example, in the United States, a salt reduction of 3 g 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.<sup>123</sup> Even a modest reduction of 1 g per day achieved gradually over 10 years would be more cost-effective than using medications to lower BP in all patients with hypertension.<sup>143</sup> 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.<sup>121</sup> Similarly, in Argentina, population salt reduction would be one of the most cost-effective approaches to preventing noncommunicable disease.<sup>126</sup> 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.<sup>124</sup> However, these models do not include (1) costs to industry when food is reformulated and (2) savings and social benefits unrelated

**Table 2.** Global Overview of Salt Reduction Policies and Estimated Benefits

Author (Year)	Country	Method of Intervention	Policy Goal	Effectiveness	Cost Savings
Selmer (2000)	Norway	Simulation modeling Information campaigns and development of new industry food products with less salt	Reduction in salt consumption	52,293 life-years saved*	\$117m (US) saving over 25 years*
Murray (2003)	WHO (Choice) Global	(1) Voluntary agreement with industry AmrB EurA SearD (2) Legislation AmrB EurA SearD	Reduction in salt consumption	DALYs averted per year: 300,000 700,000 500,000 600,000 1,300,000 1,000,000	Cost per DALY (total per year) Int \$ 24 (7.2m) Int \$ 44 (30.8m) Int \$ 37 (18.5m) Int \$ 13 (7.8m) Int \$ 23 (29.9m) Int \$ 19 (19m)
Chang (2006)	Taiwan	RCT–potassium-enriched salt	Reduction in sodium chloride consumption	Increased survival	\$426 (US) saved per year
Kristiansen (2006)	Denmark	Contingent evaluation through computer- assisted personal interviewing	Willingness to pay for a population salt reduction		Cost: \$148m (US) Willingness to pay: \$468m (US)
Joffres (2007)	Canada	Modeling 1,840 mg/d sodium reduction in hypertensives	Reduction in salt intake in hypertensives	Reduced physician, laboratory, and drug costs	\$430m (CAD) per year
Asaria (2007)	WHO Global	Simulation modeling	15% salt reduction LMIC HIC	8.5m deaths averted over 10 years	Cost per person per year < \$0.40 (US) \$0.50–1.00 (US)
Palar (2009)	USA	Simulation modeling 2,300 mg/d population sodium reduction	Population reduction in salt intake	312,000 QALYs gained per year Reduced health care costs	\$ 32b (US) saving per year \$18b (US) saving
Dall (2009a:b)	USA	Simulation modeling 400 mg/d sodium reduction in untreated hypertensives	Reduction in salt intake in untreated hypertensives		\$2.3b (US) saving per year
Rubinstein (2009)	Argentina	Cooperation between governments, consumer associations, and bakery chambers to reduce salt in bread	Less salt in bread	719 DALYs gained per year	\$151 (ARS) per DALY
Smith-Spangler (2010)	USA	(1) Government collaboration with food manufacturers to voluntarily cut sodium in processed foods (2) Sodium tax	Food reformulation with less salt Increase in salt cost for industrial use by 40% expected to reduce consumption	2,060,790 QALYs gained over lifetime 1,313,304 QALYs gained over lifetime	\$32.1b (US) saving over lifetime \$22.4b (US) saving over lifetime

Table 2. Continued

Author (Year)	Country	Method of Intervention	Policy Goal	Effectiveness	Cost Savings
Bibbins-Domingo (2010)	USA	Simulation modeling	Salt reduction 1 g/d 3 g/d	QALYs gained per year 75,000 to 120,000 220,000 to 350,000	Cost saving <sup>†</sup> \$10–24b (US) saving per year <sup>‡</sup>
Cobiac (2010)	Australia	(1) Incentives for voluntary changes by food manufacturers (2) Legislation and enforcement	Food reformulation with less salt	5300 DALYs gained 110,000 DALYs gained	Cost saving Cost saving
Barton (2011)	England & Wales	Generic spreadsheet model after consultation with stakeholders (part of NICE process)	Population reduction in salt intake of 3 g/d following legislation	Cases prevented: 32.2/1,000/10 yr Deaths prevented: 4.43/1,000/10 yr Life-years gained: 96/1,000/10 yr QALY gained: 131/1,000/10 yr	Total savings: £347m/10 yr Annual savings: £40m/yr
Gase (2011)	Los Angeles County, CA, USA	Adaptation of HIA methods to mathematically simulated salt reduction through food-procurement policy to reduce salt consumption	Reduction in salt consumption of 233 mg sodium per day in LA County	5% decrease in hypertension prevalence	Health care savings: \$630,000 (US)/yr in LA County
Martikainen (2011)	Finland	Markov Model simulation with dynamic population structure (2010–2030 [ie, 20 yr])	Population salt reduction by 1.0 g/d	QALY gained (20 years): 26,142	Cost saving (including reduced productivity loss): €146.5m in 20 years

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AmrB = Latin American with low adult child mortality; ARS = Argentinian Dollars; b = billion; DALY = disability-adjusted life-years; EurA = Europe with very low adult and child mortality; HIA = Health Impact Assessment; HIC = high income countries; Int = international; LA = Los Angeles; LMIC = low- and middle-income country; m = million; NICE = National Institute of Health and Clinical Excellence; QALY = quality-adjusted life-years; RCT = randomized controlled trial; SearD = Southeast Asia with high rates of adult and child mortality; WHO = World Health Organization.

\*Discounted over 25 years.

<sup>†</sup>Cost saved per dollar spent: \$15.4 (US).

<sup>‡</sup>Cost saved per dollar spent: \$26.1 (US).

to health care that arise from reductions of morbidity, disability, and death.

### Inequalities

The Marmot Review<sup>148</sup> has recently reviewed the evidence that social inequalities are important determinants of ill health in the British population, highlighting the social gradient in health inequalities whereby people of poorer background not only die sooner but spend more of their lives with disabilities. Health inequalities arise from a complex interaction of many factors, all affected by

economic and social status. One of these factors is poor diet and nutrition.

Both hypertension and CVD are more prevalent in socioeconomically deprived parts of the population. These groups are more likely to depend of cheaper, unhealthy processed food diets that are high in salt. Furthermore, among disadvantaged occupational and ethnic groups in the United Kingdom, knowledge of government guidance was lower and voluntary table salt use and total salt intake were higher.<sup>115</sup> Salt intake can thus be 5 to 10% higher in socioeconomically deprived groups.<sup>149</sup> In England and Wales, despite a national salt intake reduction of

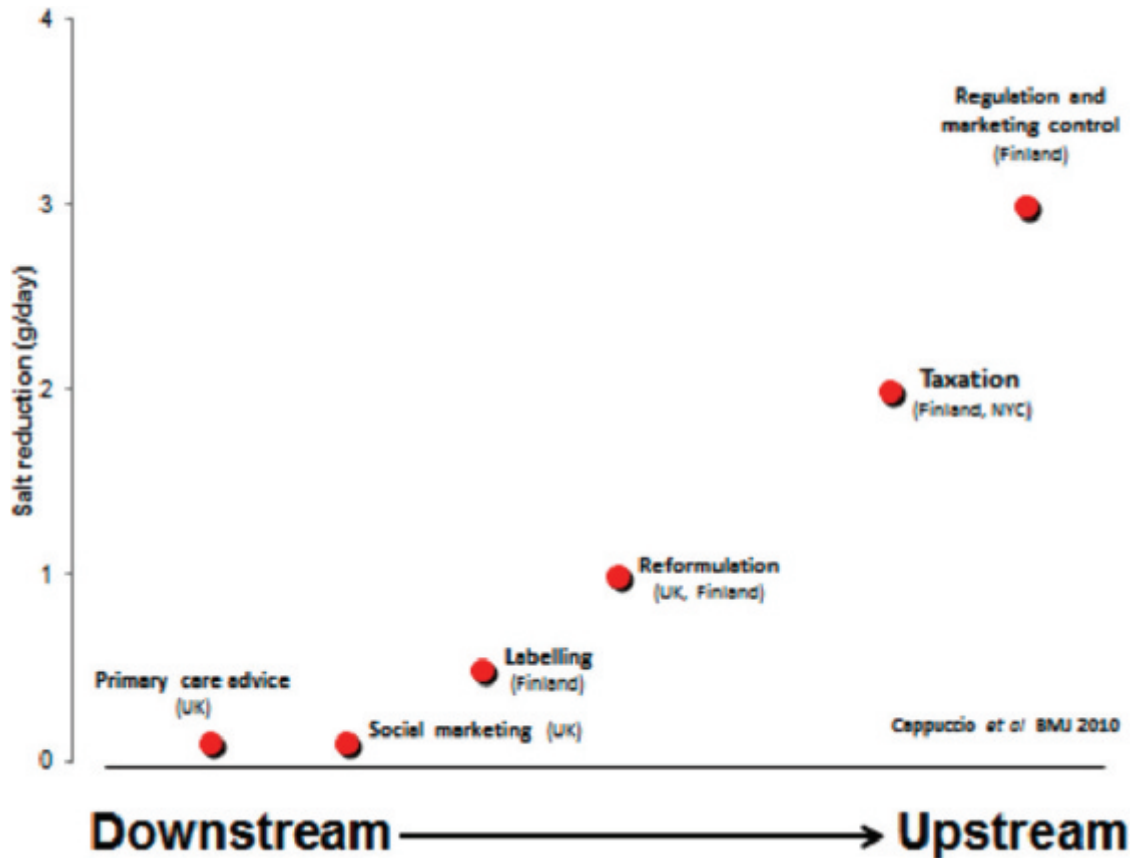


Figure 3. Comparison of different policy approaches to salt reduction: the effectiveness hierarchy.

approximately 1.4 g per day, the socioeconomic difference has remained.<sup>150</sup>

The Marmot Review Group's recent report<sup>148</sup> subsequently emphasized that health inequalities are preventable through policies aiming at reducing health inequalities, because they are usually "structural."<sup>151</sup> Furthermore, risk of chronic disease (eg, hypertension) associated with low parental social status can be decreased by subsequent improvement in social status.<sup>152</sup>

### Salt Reduction in Low- and Middle-Income Countries

A reduction in dietary salt intake is also feasible in low- and middle-income countries (LMICs), as it is possible to decrease salt content in low-cost foods while maintaining some familiar meals.<sup>153</sup> Thus, modest reductions in salt intake could substantially reduce CVD throughout India without affecting the current effectiveness of local iodization programs, due to low intake of iodized salt.<sup>154</sup>

The authors recently compared three policy approaches in four Middle Eastern countries: a health promotion campaign, the labeling of food packaging, and the

mandatory reformulation of salt content in processed food. In all four countries, most policies were cost saving compared with the baseline. The combination of all three policies (reducing salt consumption by about 30%) could achieve cost savings of approximately \$6 million in Palestine, \$39 million in Syria, \$235 million in Tunisia, and \$1,300 million in Turkey per decade, plus the gain of approximately 2,700 life-years, 6,450 life-years, 31,000 life-years, and 380,000 life-years, respectively.<sup>155</sup> However, in spite of the declaration by the UN World Health Assembly, there is still a disconnection between the burden of noncommunicable disease and national policy responses, particularly in LMICs.<sup>156</sup> Furthermore, a gradient across measures of inequalities is present for the degree of implementation of current salt reduction policies in Western countries.<sup>157</sup>

### Role of the Food Industry

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

**Table 3.** The Salt Myths: Some of the Tactics Used by the Food and Salt Industries to Sabotage Science and Resist Regulation

<i>Myth</i>	<i>Fact</i>
Our body needs salt	The body efficiently conserves salt. It is very difficult to eat too little salt as salt is already in most foods we eat every day. People in some remote areas of the world or in rural areas of developing countries still survive on a fraction of the amount of salt eaten in the Western world. There is no evidence of harmful effects of a modest reduction in salt intake.
The current salt intake is a physiologically set normal range in adult humans	During several million years of evolution mankind has survived on very little salt in the diet (less than 0.25 g of salt per day). Even in modern times, this very low intake is still seen in the Yanomano and Xingu Indians living in the humid and hot environment of the Amazon jungle. They eat less than 1,200 mg of sodium (3 g of salt) per day, their BP does not rise with age and stroke events are rare. Meanwhile in industrialised populations, the high sodium intake, typically 3,600 to 4,800 mg of sodium (9 to 12 g of salt) per day is very recent phenomenon in evolutionary terms. In these groups, BP rises steadily with age, followed by stroke and CHD.
The “normal” salt intake is between 7.0 and 12.5 g per day	The range of dietary salt reported by some as “normal” is only the “usual” range in industrialized westernized countries. It is <u>not</u> a physiological normal. The physiological level compatible with life is seen when access to dietary salt is limited, as in parts of the Amazon. Furthermore, this excessive sodium intake is not a matter of personal choice. Only 15–20% of sodium in our diets comes from that added to food by consumers.
Salt intake in the US has not changed during the past 50 years	NHANES data suggests an increase in salt intake in the US over the past 35 years. NHANES used 24 h dietary recall that does not quantify the amount of discretionary salt. Therefore the results indicate an increase in salt intake from processed food. If 24 h urinary sodium (biomarker for salt intake) has not changed during the past 50 years, then there would have been a reduction in the amount of salt discretionarily added to food by individuals.
Public policy cannot modify salt intake	The short term experience in the UK (15% or 1.4 g salt per day population reduction achieved in 7 years) and longer term experience in Finland and Japan (about 3 g salt per day population reduction achieved over two decades) demonstrate that public health policy can lead to substantial reductions in population salt intake. This is paralleled by significant reductions in population BP and in stroke rates, with ensuing cost savings. These salt reductions have very little to do with changing individual behavior, but mainly reflect a healthier environment: the reformulation of industrially-produced and distributed food with lower sodium content. The vast majority of individuals in most developed countries have little choice over how much salt they are eating because of the global distribution of processed food. Secondly, the health benefits of salt reduction are greater if mandatory regulations for food reformulation are introduced.
We need salt in hot climates or when we exercise because we sweat a lot	We only lose a small amount of salt through sweat. We are adaptable. The less salt we eat, the lower the salt content of our sweat. Thus in hot climates, it is important to drink plenty of water to avoid dehydration. But we do not need to eat more salt.
Consumer taste preferences make change impossible	As salt intake falls, the salt taste receptors in the mouth become more sensitive to lower concentrations of salt within a couple of months. Furthermore, consumer experience in the UK confirms that where salt has been gradually reduced in major brand products, there has been no reduction in sales and no complaints about taste. Furthermore, once salt intake is reduced, people prefer food with less salt.
Only old people need to worry about how much salt they eat	Eating too much salt raises BP at any age, starting at birth and affecting children of all ages.
Traditional highly salted foods do not seem to harm the Portuguese	Average salt intake in Portugal is high, approximately 15 g per day. However, BP is higher in Portugal than in neighboring countries and their stroke rates have been traditionally amongst the highest in Europe. This has improved recently, after Portugal had started to reduce population salt intake.
Only people with hypertension need to reduce their salt intake	A reduction in salt intake reduces BP in both normotensive and hypertensive individuals. It is even more important that people “without” hypertension reduce their salt intake, because the population-wide number of cardiovascular events that can be attributed to their level of BP is high, but their BP does not make them eligible for drug therapy.

Table 3. Continued

<i>Myth</i>	<i>Fact</i>
A reduction in salt intake below 7.0 g per day activates the renin-angiotensin system	There is no evidence for choosing 7.0 g of salt per day as a cut-off point. When salt intake is reduced, the activation of the renin-angiotensin system is a normal physiological response, similar to that which happens with diuretic treatment. Outcome trials have demonstrated clear benefits of diuretics on CVD outcomes. Additionally, with a longer-term modest reduction in salt intake, there is only a very small increase in plasma renin activity, and this is true in any ethnic group.
Salt intakes below 7.0 g per day could be potentially harmful	This claim is based on either flawed or unreliable evidence, as extensively argued in recent years. On the contrary, there is much evidence that a modest reduction in salt intake has many beneficial effects on health and is one of the most cost-effective ways to reduce CVD in the population.
Rock salt, sea salt or other posh salts are better than table salt	All these salts contain sodium chloride, whether in grains, crystals, flakes or with different color appearance.
Food technology cannot change, eg, “bread requires salt to aid the manufacturing process in large-scale plant bakeries, to retain acceptable flavor, structure and for crust development”	The very successful UK Food Standards Agency salt reduction program clearly demonstrates that it is possible to take 5–15% of the salt out of a product without noticeable changes in flavor. Finland and Japan have done better still.
Food Safety prevents change, eg, “salt reduction in some food categories may reduce shelf-life and alter their microbiological features” and “meat burgers require salt to extend shelf-life as well as helping the product to bind together”	Salt is seldom used as a preservative in the 21st century. Furthermore, many microbiological modeling tools can be used to help the industry predict the safety and shelf-life of food.
Profits take priority over public health	Increasing the salt concentration in meat products in conjunction with other water binding chemicals increases the amount of water that can be bound as a gel into the meat. The weight of the product can be increased by up to 20% with water at no cost. Profits are correspondingly increased, health is decreased. Crucially, salt is a major determinant of thirst. Any reduction in salt intake will reduce fluid consumption with a subsequent reduction in soft drink and mineral water sales. This would benefit current childhood obesity problems, but is correspondingly seen as a threat by the soft drinks industry.

BP = Blood Pressure; CHD = Coronary Heart Disease; NHANES = National Health And Nutrition Examination Survey.

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.<sup>158,159</sup> These tactics, which are similar to those used in the past by the tobacco industry, are applied by the food industry to any campaign for reductions in salt, saturated and trans fats, refined sugar, and calorie-dense foods, and for the regulation of food reformulation to prevent current epidemics of chronic diseases.<sup>120,160</sup> Key components of this denial strategy are misinformation (with “pseudo” controversies)<sup>67</sup> and the peddling of numerous rather well-worn myths.<sup>161</sup> 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<sup>162–166</sup> and subsequently retracted data<sup>167</sup> robustly rebutted by the scientific community<sup>67–69,167–170</sup> but sadly still used to support the controversy.<sup>171</sup> In particular, the claim that low salt intake may “cause” CHD<sup>162,164,172–175</sup> has been proven to be not true, as shown by US, Dutch, and global studies using valid and appropriate methods.<sup>176–178</sup> Finally, reiterated myths have been disseminated to consumers and lay audience to create doubts.<sup>161</sup> Table 3 lists some of these myths and the answers to them.

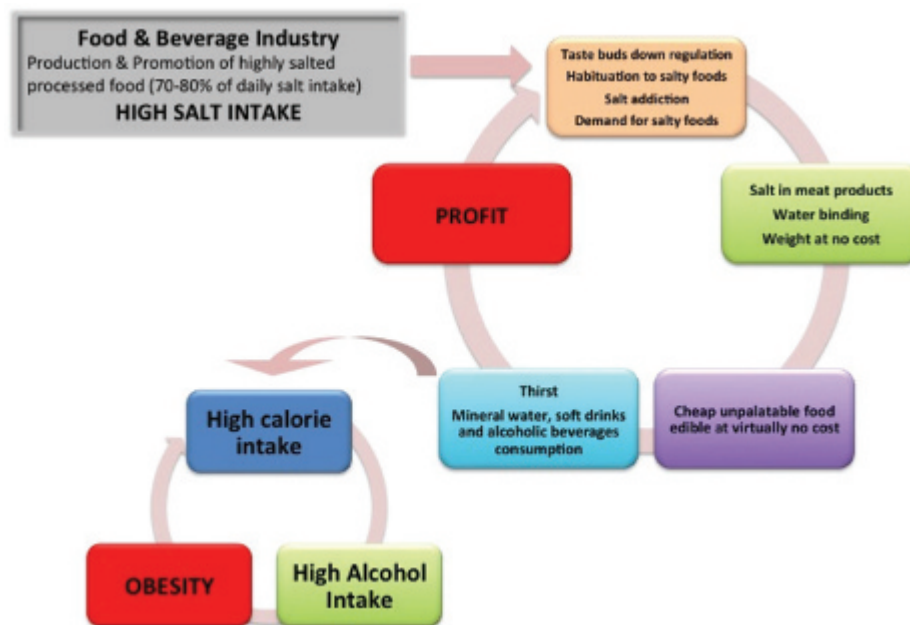
Why is the food and beverage industry so opposed to an approximate one third global reduction in salt intake? Salt is a cheap commodity in the modern world, even in

LMICs. In 2009, more than 27 million tons of salt were sold in the United States for a revenue of \$2 billion (US); only 1.5 million tons of food-grade salt fetched more than \$320 million (US).<sup>179–182</sup> 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 nonalcoholic beverage companies—daily feeding an estimated global population of several hundred million in more than 200 countries—generated a combined annual revenue of more than \$422 billion (US) in 2012.<sup>180</sup> How does a high salt intake in populations contribute to this profit? Figure 4 gives a schematic indication of the “cycle of profit” associated with high salt intake. A high salt intake will generate a demand for salty foods through a slow process of desensitization of the taste buds. A high salt diet down-regulates taste buds, allowing habituation, required for higher salt concentrations to provide the “saltiness” reward, a condition of “salt addiction.” Sodium salts are often hygroscopic, absorbing and binding water. Industrialized meat production has for years used the practice of injecting meat products with sodium salt bound to stabilizers, consequently increasing the weight of meat products before packaging. The proportion of water trapped in the meat is then sold at the price of meat. Salt makes cheap, unpalatable food edible at no extra cost. Finally, high salt intake causes thirst and an increase in the use of mineral waters and soft drinks and often the use of alcoholic beverages. The use of

sugar-containing drinks would contribute to the epidemic of obesity, particularly in children,<sup>184</sup> and it might encourage an increase in alcohol intake. It is therefore no surprise to see that a large proportion of the snack industry is indeed owned or associated with the large beverage corporations. Studies have clearly shown that 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.<sup>185</sup> In children, this would also lead to a reduction of at least 2.3 sugar-sweetened soft drinks per week per child.<sup>186</sup> Although this would result in large beneficial effects to the health of the population<sup>184</sup> and financial gains for governments, it would represent a multibillion-dollar loss to the industry from reduced sales of bottled water and soft drinks.

## Conclusions

Human salt consumption has increased to levels that are at least 10 times greater than needed, contributing to the secular epidemic of CVD through its effect on BP. The WHO, the World Health Assembly, and many countries around the world have all independently appraised the scientific evidence of the health benefits and cost savings associated with the implementation of a population-wide moderate reduction in sodium intake (30% by 2025) and have agreed on global targets. Reducing dietary sodium will save tens of thousands of lives every year. Future



**Figure 4.** How adding salt is lucrative to the food and beverage industries but harmful to health.

governments and civil society will be increasingly unwilling to accept the burden of eminently avoidable disease. A gradual decrease in the sodium concealed in food products offers perhaps the easiest change for the general population and the greatest potential for success. The responsibility of food manufacturers in contributing to the epidemic of CVD must be acknowledged. The industry can voluntarily contribute to disease prevention through effective food reformulation, or risk being subjected to state-led market interventions and mandatory actions.

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