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Dietary Salt Intake and Cardiovascular Disease: Summarizing the Evidence

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ABSTRACT

We present a narrative review of the literature linking dietary salt intake with cardiovascular health outcomes in humans and list the tools and strategies to reduce salt intake at the population level. There is a strong agreement among experts that dietary salt intake should be reduced, targeting average population levels less than 5 g per day. The main aim of this reduction is a decline in cardiovascular morbidity and mortality. Experimental data clearly show that reducing salt intake lowers blood pressure. Considering that high blood pressure is a major cardiovascular risk factor, this provides indirect evidence that salt reduction should improve cardiovascular health.[1] There is also recent direct evidence that reducing salt intake reduces the incidence of cardiovascular disease. Direct evidence linking reduction in salt intake with decreased overall and cardiovascular mortality is more limited and disputed and the data for stroke are inconsistent. Thus, there is a debate on the quality and nature of the available evidence, particularly on the magnitude of the benefit provided by the achievable reduction in salt intake. Yet, there are no known deleterious consequences of the proposed reduction in salt intake. Several countries have adopted policies aiming at reducing salt intake in the general population. The relevant tools and strategies are directed to both the food industry and the consumers. At the industry level, the most efficient measure is legislation on the salt content of selected foods, an approach much more (cost) effective than voluntary reductions. None of the interventions aiming at reducing salt intake has been rigorously evaluated. In view of recurrent controversies, any intervention in this field should be accompanied by an appropriate monitoring and evaluation program.

Keywords: Salt, mortality, cardiovascular disease, sodium

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INTRODUCTION

The purpose of this narrative review is to summarize the existing literature linking dietary salt intake* with cardiovascular health outcomes in humans, taking into account the level of evidence in a context of recurrent controversies (Table 1). This review does not cover studies performed in hospital settings with patients. A further purpose is to list the possible tools and strategies to reduce salt intake at the global level.

Table 1

Cardiovascular health outcomes that have been associated with high dietary salt intake in humans

Health outcome	Direction	Strength of the evidence
High blood pressure and Hypertension	↑	+++
Cardiovascular disease events	↑	+++
Cardiovascular mortality	↑	+
Overall mortality	↑	(+)
Stroke	↑	(+)
Left-ventricular hypertrophy	↑	(+)

+++ strong evidence (experimental data in form of multiple randomized controlled trials), ++ convincing evidence (other experimental data with consistent results), + moderate evidence (limited experimental data), (+) some evidence (observational data).

The World Health Organisation (WHO) recommends an average population salt intake of less than 5 g per day.[2] Following technical meetings on July 1-2, 2010 in London and in October 2012 in Canada, the WHO published a report entitled "Creating an enabling environment for population-based salt reduction strategies".[3] Several countries have adopted policies aiming at reducing dietary salt intake in the general population, such as Finland, France, UK, Japan, Australia and New Zealand.[4]

* Salt stands here for Sodium chloride (NaCl). Prevention campaigns discussed in this paper are related only to sodium.

Yet, the rationale for lowering dietary salt intake at the population level is still being debated in the scientific literature, which has been ongoing for many years now.[5] The controversy has been revived by recent publications, notably a prospective study showing that low baseline urinary sodium excretion was associated with higher cardiovascular mortality.[6] However, the observational nature of this study limits the strength of this evidence.

Salt intake influences cardiovascular morbidity and mortality mainly because of its positive association with blood pressure[7] (Table 2). Hypertension (high blood pressure) is a major modifiable cardiovascular risk factor that affects one in four adults worldwide and is responsible for a high burden of disease in high-, middle- and low-income countries. A systematic Cochrane review by Taylor, et al. on the effects of randomized controlled trials of at least six months duration showed that reducing dietary salt intake led to a non-significant decrease in cardiovascular morbidity and mortality. Taylor, et al. concluded that "there is still insufficient power to exclude clinically important effects of reduced dietary salt on mortality or cardiovascular morbidity in normotensive or hypertensive populations."[7] A re-analysis including six trials (but excluding the heart failure trial) showed that reduced dietary salt intake was associated with non-significant reductions in all-cause mortality (4% to 10%) and cardiovascular mortality (31%) and a significant reduction in cardiovascular events (20%).[8] Even when looking at the same set of data, experts appear to reach different conclusions.[7,8] This probably reflects the fact that available data are insufficient to produce undisputable conclusions. Two population-based interventional studies at the level of two cities have been performed: a Portuguese study provides evidence that a population strategy to reduce salt intake was able to lower blood pressure[9] and a Belgian study found no effect of such intervention.[10] Here again results are inconclusive.

By contrast, recent public health reports highlighted that reduction in dietary salt intake at the population level is one of the most cost-effective public health strategies worldwide.[11,12]

The purpose of this narrative review is to summarize the existing literature linking dietary salt intake with cardiovascular health outcomes in humans, taking into account the level of evidence in a context of recurrent controversies. A further purpose is to list the possible tools and strategies to reduce the salt intake at the global level.

PHYSIOLOGICAL NEEDS IN SALT INTAKE

A minimum daily sodium intake is necessary for essential physiological functions. The recommended minimal daily sodium intake is 550 mg/day, which corresponds to 1.5 g of salt (NaCl) per day. It is estimated that adolescents and adults need a minimum amount of 500 mg of sodium and 850 mg of chloride per day, which corresponds to 1.3 g of salt per day. The levels of dietary salt intake currently consumed in most countries worldwide are much higher and well above physiological needs.[13]

DIETARY SALT INTAKE AND BLOOD PRESSURE: A SHORT HISTORICAL PERSPECTIVE

As early as the beginning of the 20th century, Ambard and Beaujard recognized the role of dietary salt restriction in lowering blood pressure in humans.[14] In the 1920s, Allen demonstrated the effectiveness of salt restriction in the treatment of hypertension and suggested that salt restriction at the population level would reduce cardiovascular morbidity and mortality.[15] In the 1940s, Kempner found that a rice-fruit diet very low in salt was able to lower blood pressure in severely hypertensive patients.[16] In the 1960s, Dahl was the first to report a positive association between dietary salt intake and the prevalence of hypertension across populations.[17] In the 1970s, Froment. et al. conducted an ecologic study (based on published data) that analysed urinary sodium excretion and blood pressure across 28 populations: higher blood pressure and steeper age-related blood pressure were positively associated with urinary sodium excretion, a proxy for dietary salt intake.[18] In the 1980s, the INTERSALT study showed that populations with low dietary salt intakes (i.e., less than 3 g/24h or 1.1 g of sodium/24h) experience a lower blood pressure increase with age and that the increase in systolic blood pressure with age was positively associated to dietary salt intake.[19] This likely reflects the association of aging with increased blood pressure sensitivity to salt. In the 1990s, an overview of data collected for 47,000 non-African subjects from 24 communities confirmed the positive association between blood pressure and urinary sodium excretion across and within populations, and the strengthening of this association with age.[1,20] In the 2000s, in the INTERMAP study, the blood pressure difference between Northern and Southern China, was found to be partly due to dietary salt intake.[21]

Table 2

Meta-analyses of blood pressure change in response to reduced dietary sodium intake in randomized controlled trials.

Study	Sample size		Na reduction (mmol/24h)		Blood pressure reduction [mm Hg] Systolic (SE or 95%CI) Diastolic (SE or 95%CI)		Notes
	NT	HT	NT	HT	NT	HT	
Cutler, et al. 1991[81]	760	873	76		1.7 (1.0) 1.0 (0.7)	4.9 (1.3) 2.6 (0.8)	21/23 studies with duration > 4 weeks
Midgley, et al. 1996[82]	2374	1131	125	95	1.0 (0.51-1.56) 0.1 (0.32-0.51)	3.7 (2.35-5.05) 0.9 (0.13-1.85)	BP decrease for a 100 mmol reduction in Na intake
Cutler, et al. 1997[83]	1689	1043	76	77	1.90 (0.72) 1.09 (0.48)	4.83 (1.04) 2.45 (0.68)	
Graudal, et al. 1998[84]	2581	2161	160	118	1.2 (0.6-1.8) 0.26 (-0.3-0.9)	3.9 (3.0-4.8) 1.9 (1.3-2.5)	Median duration (NT): 8 days Median duration (HT): 4 weeks
He and MacGregor, 2002[85]	2220	734	74	78	2.03 (0.27) 0.97 (0.21)	4.96 (0.40) 2.73 (0.24)	Trials with duration > 4 weeks
He and MacGregor, 2004[86]	2220	802	74	78	2.03 (1.50-2.56) 0.99 (0.57-1.40)	5.06 (4.31-5.81) 2.70 (2.24-3.16)	Trials with duration > 4 weeks
He and MacGregor, 2007[87]	966		42%		1.17 (0.56-1.78) 1.29 (0.65-1.94)		Children aged < 18 years Median duration : 4 weeks
Taylor, et al. 2011[7]	2079	675			1.1 (-0.11-2.34) 0.80 (-0.23-1.37)	4.14 (-2.43-5.84) 2.00 (-0.70-4.70)	Only includes trials with data on cardiovascular morbidity and on mortality.

DBP = diastolic blood pressure; SBP = systolic blood pressure; NT = normotensive persons; HT = hypertensive persons.

In the past 30 years, a large number of randomized controlled trials have analyzed the effect of reducing salt intake on blood pressure. Table 2 summarises the results of meta-analyses of these randomized controlled trails. Most trials explored the effect of short-term salt reduction (usually a few weeks). Sodium reductions of 70 to 100 mmol (i.e., 4.1 to 5.9 g of salt) significantly reduce systolic/diastolic blood pressure in hypertensive (i.e., about 3-5/1-2 mm Hg, respectively) and in normotensive people (i.e., about 1-2/0-1 mm Hg, respectively). Such small reductions are expected, if sustained and applied to the general population, to lead to a substantial reduction in cardiovascular events.

DIETARY SALT INTAKE AND BLOOD PRESSURE: THE MECHANISMS

It is now widely recognized that an alteration in sodium handling by the kidney plays a crucial role in the pathogenesis of all forms of hypertension, although recent findings suggest that new molecular mechanisms in the skin could play an important role as well.[22] Considerable debate exists with respect to the precise mechanisms that lead to primary hypertension and to blood pressure sensitivity to salt. By describing the relationship between systemic blood pressure and sodium balance, Guyton has demonstrated the key role of water and sodium excretion by the kidneys in the long-term regulation of blood pressure.[23-25] Kimura and Brenner[26] separated forms of secondary hypertension into sodium-sensitive and sodium-resistant. More recently, Johnson and colleagues[27,28] have hypothesised that, over time, hypertension may shift from an initially salt-resistant to a subsequent salt-sensitive type upon the accumulation of subtle renal injury. Johnson and colleagues proposed a unifying pathway for the pathogenesis of hypertension (and salt-sensitive hypertension) that combines many of the previously formulated hypotheses[29]: salt-sensitivity likely results from an imbalance between vasoconstrictors (renin-angiotensin-aldosteron system and the sympathetic nervous system) and vasodilators (nitric oxide and the kallikrein-kinin system), in parallel with substances and mechanisms leading to progressive renal glomerular and/or tubular injuries. Additional observations that strengthen the view that sodium plays a key role in blood pressure control are that (i) almost all rare monogenic forms of hypertension are salt sensitive[30] and (ii) all blood pressure candidate genes identified so far are either directly or indirectly associated with renal sodium handling in humans.[31]

Table 3

Observational longitudinal studies on the association between dietary sodium intake and all-cause mortality

Study	Country, sex, [age]	N (n events)	Follow-up (years)	Na intake (mmol/24h)	Result: HR [95%CI]
Tunstall-Pedoe, et al. 1997[37]	UK, M/F, [40-59]	11,629 (M: 383; F: 208)	7.6	M: 200; F: 150[a]	**Per 1 unit increase in quintiles of Na intakes:** M: 0.92 [0.84-1.00]; F: 0.97 [0.86-1.10]
Alderman, et al. 1998[88]	US, M/F, [25-75]	11,346 (3,923)	About 20	M: 109; F: 74[b]	**From lowest to highest quartiles of Na intakes:** 23.18 to 19.01 per 1000 person-years; p<0.0001 **From lowest to highest quartiles of Na/calorie intakes:** 20.27 to 21.71 per 1000 person-years, p=0.14
He, et al. 1999[89]	US, M/F, [25-74]	Overweight: 2,688 (810) Normal weight: 6,797 (1676)	19.0	Overweight: 83[b] Normal weight: 92[b]	**Per 100 mmol/24h increase in Na intake:** Overweight: 1.32 [1.16-1.50] Normal weight: 0.98 [0.88-1.09]
Tuomilehto, et al. 2001[38]	Finland, M/F, [25-64]	2,436 (M: 136; F: 44)	About 10	M: 216; F:162[a]	**Per 100 mmol/24h increase in Na intake:** M: 1.30 [1.06-1.59]; F: 0.91 [0.56-1.47]
Cohen, et al. 2006[90]	US, M/F, [30-74]	7,154 (1343)	13.7	118[b]	**Per 43 mmol/24h increase in Na intake:** 0.93 [0.87-1.00], P=0.06

Table 3 contd.

Study	Country, sex, [age]	N (n events)	Follow-up (years)	Na intake (mmol/24h)	Result: HR [95%CI]
Geleijnse, et al. 2007[35]	Netherlands, M/F, [≥55]	Case-cohort, 1448 controls (795 death cases)	5.0	Controls: 117[a,c] Cases: 107[a,c]	**RR per SD increase in urine Na (~70 mmol/24h):** 1.12 [0.86-1.46] in subjects free of CVD and HT 0.95 [0.81-1.12] in all subjects Overweight : 1.19 [0.86-1.66] in free of CVD and HT **RR per SD increase in urine Na/K ratio:** 1.13 [0.93-1.36] in subjects free of CVD and HT 1.01 [0.91-1.12] in all subjects Overweight: 1.19 [1.02-1.39] in free of CVD and HT
Cohen, et al. 2008[91]	US, M/F, [≥30]	8,699 (1150)	8.7	139[b]	**HR for first compared to fourth quartile of Na intake:** 1.30 [0.94-1.80], p=0.11
Taylor, et al. 2011[7]	DNA, M/F, [39-66]	NT: 3518 (60) HT: 2058 (513)	1.5-3		**RR:** 0.67 [0.40-1.12] **RR:** 0.97 [0.83-1.13]

Methods used to assess salt intake: [a] from 24 hour urine collection; [b] from single 24 h dietary recall; [c] estimated from overnight urine collection.
CVD = cardiovascular disease; DNA = does not apply; HR = hazard ratio; HT = hypertension; RR = relative risk = SD, standard deviation.

DIETARY SALT INTAKE AND OVERALL MORTALITY

The Trials of Hypertension Prevention (TOHP), phase I (n=744) and II (n=2382) provide the first experimental evidence that link interventions aiming at reducing dietary sodium to all-cause mortality in humans.[32] TOHP I and II interventions included persons with pre-hypertension (defined as a mean diastolic blood pressure of 80-89 mm Hg without antihypertensive medication) and lasted for 18 and 26-48 months, respectively, with subsequent observational follow-up for cardiovascular outcomes for about 15 and ten years, respectively.[32] At the end of the interventions, net sodium reductions were 44 mmol/24h and 33 mmol/24h in TOHP I and II, respectively.[32] Participants in the sodium reduction arm experienced a non-significant 20 percent lower all-cause mortality as compared to persons in the control group (hazard ratio: 0.80; 95%CI: 0.51-1.26).[20] As only 67 deaths occurred during follow-up, power to detect a small reduction in mortality was low.[32] In a randomized controlled trial conducted in Taiwan among 1981 Veterans (mean age: 75 years), the group assigned to potassium-enriched salt had a non-significant ten percent lower all-cause mortality (age-adjusted hazard ratio: 0.90; 95%CI: 0.79-1.06) after a median follow-up of 2.6 years compared to the controlled group assigned to regular salt.[33] A recent systematic Cochrane review by Taylor, et al.[7] on the effects of randomized controlled trials of at least six months duration (that included the two TOHP trials and three other trials) showed that reducing dietary salt intake led to a non-significant decrease in cardiovascular mortality. The risk ratio for all-cause mortality of reduced salt intake was 0.67 (0.40-1.12) in 3,818 normotensive participants (60 deaths) and 0.97 (0.83-1.13) in 2,058 hypertensive participants (513 deaths).[7]

A few prospective observational studies analyzed the association of dietary sodium intake and all-cause mortality[34-38] (Table 3). In the study by Tuomilehto, et al.,[38] high dietary sodium intake was positively associated with 32 percent increased all-cause mortality in men. The association with all-cause mortality was only observed in overweight men.[38] Two other studies found some evidence of such a relationship in overweight individuals only.[35,36] In the Scottish Heart Health Study, there was no evidence of an association between dietary sodium intake and all-cause mortality,[37] but the analyses were only adjusted for age.

In the National Health and Nutrition Examination Survey (NHANES I) Epidemiologic Follow-up Study, there was an inverse association between urinary sodium excretion and all-cause mortality.[34] By contrast, a direct association between sodium/calorie ratio was observed with all-cause mortality.[34] This study however suffers from important methodological flaws.[39]

Additional data are required to better delineate the specific contributions of sodium, potassium, magnesium and calcium intakes. The data published so far do not provide a clear and definitive answer, but suggest that the benefit of dietary sodium reduction on overall mortality is likely modest but may be larger in overweight persons.[35,36,38] These results are important considering that blood pressure and cholesterol explain about 45 percent of the increased risk of coronary heart disease observed in overweight and obesity.[40]

DIETARY SALT INTAKE AND CARDIOVASCULAR DISEASE

In a randomized controlled trial conducted in Taiwan among 1,981 Veterans (mean age: 75 years), the group assigned to potassium-enriched salt had 41 percent lower cardiovascular mortality (age-adjusted hazard ratio: 0.59; 95%CI: 0.37-0.95) after a median follow-up of 2.6 years compared to the controlled group assigned to regular salt.[33]

Data from the TOHP I (n=744) and TOHP II (n=2382) trials represent the first experimental evidence to link interventions aiming at reducing dietary sodium and cardiovascular disease incidence in humans.[32] Participants in the sodium reduction arm experienced a significant 30 percent lower incidence of cardiovascular disease (defined as myocardial infarction, stroke, coronary artery bypass graft, percutaneous transluminal coronary angioplasty or death with a cardiovascular cause) as compared to participants in the control group (hazard ratio: 0.70; 95%CI: 0.53-0.94).[32] In the above-mentioned Cochrane meta-analysis of randomized controlled trials of reduced salt intake of at least six months duration, Taylor, at al.[7] found non-significant relative risk reductions for cardiovascular disease events of 0.71 (95%CI: 0.42-1.20) in normotensive and 0.84 (95%CI: 0.57-1.23) in hypertensive participants. He and McGregor[8] re-analysed the data after pooling normotensive and hypertensive participants and found salt reduction to be associated with a significant 20 percent reduction in the risk of cardiovascular disease events (relative risk: 0.80; 0.64-0.99).

A few prospective observational studies analyzed the association of dietary sodium intake and cardiovascular disease mortality[34-38] (Table 4). Results are inconsistent as two studies[36,38] found a positive association between dietary sodium intake and cardiovascular mortality, in particular in overweight subjects, whereas other studies found no such association.[34,35] In the Scottish Heart Health Study, a positive association between dietary sodium intake and coronary deaths was found in women, but not in men.[37] In the NHANES I Epidemiologic Follow-up Study, a negative association

Table 4

Observational longitudinal studies on the association between dietary sodium intake and cardiovascular mortality

Study	Country, sex, [age]	N (n events)	Follow-up (years)	Na intake (mmol/24h)	Result: HR [95%CI]
Tunstall-Pedoe, et al. 1997[37]	UK, M/F, [40-59]	11,629 (M: 159; F: 47)	7.6	M: 200; F: 150[a]	**Per 1 unit increase in quintiles of Na intakes:** M: 0.98 [0.86-1.13]; W: 1.14 [0.87-1.49]
Alderman, et al. 1998[88]	US, M/F, [25-75]	11,346 (3,923)	About 20	M: 109; F: 74[b]	**From lowest to highest quartiles of Na intakes:** 11.80 to 9.60 per 1000 person-years; p<0·0019 **From lowest to highest quartiles of Na/calorie intakes:** 9.73 to 11.35 per 1000 person-years, p=0.017
He, et al. 1999[89]	US, M/F, [25-74]	Overweight: 2,688 (329) Normal weight: 6,797 (566)	19.0	Overweight: 83[b] Normal weight: 92[b]	**Per 100 mmol/24h increase in Na intake:** Overweight: 1.45 [1.20-1.75] Normal weight: 1.00 [0.84-1.19]
Tuomilehto, et al. 2001[38]	Finland, M/F, [25-64]	2,436 (M: 72; F: 15)	About 10	M: 216; F:162[a]	**Per 100 mmol/24h increase in Na intake:** M: 1.38 [1.04-1.82]; W: 1.43 [0.73-2.78]
Geleijnse, et al. 2007[35]	Netherlands, M/F, [≥55]	Case-cohort, 1448 controls (217 CVD death cases)	5.0	Controls: 117[a,c] Cases: 99[a,c]	**RR per SD increase in urinary Na (~70 mmol/24h):** 0.83 [0.47-1.44] in subjects free of CVD and HT 0.77 [0.60-1.01] in all subjects **RR per SD increase in urinary Na/K ratio:** 0.91 [0.65-1.27] in free of CVD and HT 0.92 [0.80-1.07] in all subjects

Methods used to assess salt intake: [a] from 24 hour urine collection; [b] from single 24 h dietary recall; [c] estimated from overnight urine collection.
CVD= cardiovascular disease; HR= hazard ratio; HT = hypertension; RR = relative risk; SD = standard deviation.

was found between dietary salt intake and cardiovascular mortality, but the association was positive when using sodium/calorie ratio.[34] However, as stated earlier, this latter study suffers from important methodological flaws.[39] Further data are needed to clarify this issue. Strazzullo, et al., conducted a meta-analysis which found a significant positive association of higher compared to lower salt intake with incident cardiovascular disease (relative risk: 1.17; 95%CI: 1.02;1.32).[41]

In the New York City Worksite Blood Pressure Study conducted among 2,937 treated hypertensive patients, increased dietary salt intake, assessed using 24-hour urine collection, was associated with decreased incidence of myocardial infarction (relative risk: 0.68; 95%CI: 0.46-0.91 for a 66 mmol/24h reduction in urinary sodium excretion).[42] A limitation of this study is that participants were advised to avoid high sodium food for five days before the 24-hour urine collection.[42]

DIETARY SALT INTAKE AND STROKE

There is no experimental data linking dietary salt intake to stroke.

With respect to observational studies, several cohorts analyzed the association of dietary sodium intake with the risk of stroke (Table 5).[36,38,43-46] The data gathered so far are inconsistent, as some studies found a positive association between dietary sodium intake and stroke incidence,[36,45] whereas others did not[35,38,43,44,46] Two studies[35,38] estimated dietary sodium intake using 24-hour urine collection, the others used either a 24-hour recall or a food frequency questionnaire at baseline. The study by Tuomilehto, et al.[38] found a non-significant positive association between 24-hour urinary sodium excretion and stroke incidence ((hazard ratio: 1.23; 95%CI: 0.94-1.62) or a 100 mmol/24h increase in dietary sodium intake, without adjustment for SBP), but as few events occurred (n=84), this study may have been underpowered to analyze this specific relationship. Strazzullo, et al., conducted a meta-analysis which found a significant positive association of higher compared to lower salt intake with stroke (relative risk: 1.23; 95%CI: 1.06-1.43).[41]

Ecologic data support a direct association between high sodium intake and stroke mortality,[47-49] the latter being considered as a major marker of hypertension prevalence.

Table 5

Observational longitudinal studies on the association between dietary sodium intake and stroke

Study	Country, sex, [age]	N (n events)	Follow-up (years)	Na intake (mmol/24h)	Result: HR [95%CI]
Kagan, et al. 1985[43]	Japan, M, [45-68]	7,895 (238)	10.0	~ 100[b]	No association between Na intake and incidence of stroke
Ascherio, et al. 1998[46]	US, M/F, [40-75]	43,738 (328)	8.0	Single FFQ	No association between Na intake and incidence of stroke
He, et al. 1999[89]	US, M/F, [25-74]	Overweight: 2,688 (250) Normal weight: 6,797 (430)	19.0	Overweight: 83[b] Normal weight: 92[b]	**Per 100 mmol/24h increase in Na intake:** Overweight incidence: 1.32 [1.07-1.64]; mortality: 1.89 [1.31-2.74] Normal weight incidence: 0.98 [0.83-1.16]; mortality: 0.90 [0.63-1.28]
Tuomilehto, et al. 2001[38]	Finland, M/F, [25-64]	2,436 (84)	About 10	M: 216; F:162[a]	**Per 100 mmol/24h increase in Na intake:** Incidence: 1.23 [0.94-1.62] (non-BP adjusted) Incidence: 1.13 [0.84-1.51] (BP adjusted)
Nagata, et al. 2004[45]	Japan, M/F, [≥35]	29,079 (269)	7.0	M: 236; F: 217[c]	**HR in highest vs. lowest tertile of Na intake:** Incidence: M: 2.33 [1.23-4.45]; W: 1.70 [0.96-3.02]
Geleijnse, et al. 2007[35]	Netherlands, M/F, [≥55]	Case-cohort, 1448 controls (181 stroke cases)	5.0	Controls: 117[a,d] Cases: 115[a,d]	**RR per SD increase in urinary Na (~70 mmol):** Incidence: 1.08 [0.80-1.46]
Larsson, et al. 2008[44]	Finland, M, [50-69] Smokers only.	26,556 (3,365)	13.6	~ 200[c]	**HR in highest vs. lowest quintile of Na intake:** Cerebral infarction inc: 1.04 [0.92-1.18] Intracerebral hemorrhage inc: 1.28 [0.93-1.75] Subarachnoid hemorrhage inc: 0.84 [0.54-1.30]

Methods used to assess salt intake: [a] from 24 hour urine collection; [b] from single 24 h dietary recall; [c] food frequency questionnaire; [d] estimated from overnight urine collection. CVD = cardiovascular disease; FFQ = food frequency questionnaire; HR = hazard ratio; HT = hypertension; inc, incidence; RR = relative risk; SD = standard deviation.

DIETARY SALT INTAKE AND LEFT-VENTRICULARHYPER-TROPHY

Left-ventricular hypertrophy is a target organ damage associated with increased cardiovascular morbidity and mortality.[50-52] Sodium consumption has been linked to the presence of left ventricular hypertrophy in adults,[53] in children and adolescents.[54] Some evidence suggests that reducing dietary sodium intake results in regression of left ventricular hypertrophy, independently of blood pressure level.[55,56]

CURRENT RECOMMENDATIONS IN VIEW OF THE EXISTING CONTROVERSY

Despite the ongoing controversy, we consider that recommendations to lower dietary salt intake in the general population are justified because of: (1) the strong link between salt intake and blood pressure, with stronger effect in older people and in hypertensive patients in a context of population ageing; (2) the existence of some experimental evidence that modest reduction in salt intake is beneficial in the absence of experimental evidence that it is harmful; (3) the need to put more emphasis on cost-effective preventive measures in a world in which most people (and countries) cannot afford expensive medicine and treatment.

TOOLS AND STRATEGIES TO REDUCE DIETARY SALT INTAKE

The average salt intake in most populations considerably exceeds the recommended values. Although the direct association between excessive salt intake and overall or cardiovascular deaths is still a matter of discussion, the benefit of salt reduction via reduced blood pressure and cardiovascular events is likely and several countries have started to implement population-based strategies to reduce salt intake.[4] Such decisions took into account the fact that the probability of doing harm is low or non-existent, that high salt intake is also likely associated with diseases other than cardiovascular disease (such as stomach cancer,[57,58] obesity[59] and osteoporosis[60]) and that this strategy is considered as one of the most cost-effective public health strategies worldwide.[11,12,61]

Salt reduction should be conducted at both the industry and the consumer levels. At the industry level, the most efficient measure is legislation restricting the salt content of selected foods. This approach has

been suggested to be ten to twenty times more (cost) effective than voluntary reductions in United States[11] and in Australian modelling studies.[62] If legislation on specific foods is to be produced, previous knowledge of the main sources of dietary salt intake is needed.

Regulation of food marketing, with restrictions on the content, volume and timing of advertisements or the inclusion of messages on healthy diet (as it currently occurs in France) is another possibility,[63] although its effect might vary according to the educational or economical level of the target population.[64] The voluntary engagement of some food manufacturers in health-promoting marketing initiatives is remarkable, but its public health impact remains to be assessed.[65] Agreements with the food and catering industry towards voluntary reductions of the salt content of selected food items could be achieved,[66] although, in some countries, the commitments obtained were rather permissive and allowed food companies to circumvent the stated intents.[67]

A tax on salty foods has also been proposed, although the food industry can partly compensate the resulting increased cost by decreased production costs or profit margins, which may have an adverse effect regarding the consumption of other foods.[68]

A better strategy is a targeted food tax combined with an appropriate subsidy on healthy foods such as fruits and vegetables.[69] Improved food labelling could also help, namely regarding salt and not sodium content, as most consumers are unable to convert sodium into salt values.[70] The reduction in salt content should be made progressively and in the long term, so that consumers are unaware of the changes. Finally, all these changes should also take into account possible limitations of salt reduction in food processing.[71]

At the consumer level, information campaigns should be initiated and maintained, as they can effectively change dietary behaviour.[72,73] Although public relations and community-based educational activities might achieve the same effect as a paid advertising campaign, the effect of the latter rapidly vanishes once the campaign ends.[73] Further, the costs of a paid advertising campaign might be very small compared to the financing of (non-healthy) food advertising (USD $26 billion per year in the US,[74] CHF 331 million in Switzerland[75]). It will also be diluted in the large number of (unhealthy) food advertisements present either on television[76] or on print media.[77] Hence, the use of a paid advertising campaign might not be very cost-effective.

Nutrition education at school is another possibility, but its effect on behaviour appears to be limited.[78] An interesting alternative would be the

use of tailored computer interventions as suggested elsewhere,[79] but their cost might be too high and their impact at the population has not been adequately assessed.

Finally, a study conducted in France[80] showed that, regarding food and vegetable consumption, the costs per life-year saved are lower for information campaign (EUR €3,000), followed by Value-Added Tax (VAT) reduction (EUR €99,000) and food stamp policy (EUR €403,000). However, the information campaign would save fewer life-years than VAT reduction. The food stamp policy could reduce health inequalities between low-income consumers and others, whereas the opposite effect would occur for the other scenarios.

CONCLUSIONS

There is a strong agreement among experts that average population dietary salt intake should be reduced, targeting the levels recommended by WHO, namely, less than 5 g per day. With the exception of the historical examples of Finland and Japan, there is no recent data from countries that have implanted population-based strategies to lower dietary salt intake such as the United Kingdom to give a signal that they are going from 10 g/day to 5 g/day.

The main aim of this reduction is to affect a substantial decline in cardiovascular morbidity and mortality. A careful analysis of the available literature shows however that the epidemiological evidence is still incomplete and that the size of the benefit of such a reduction is still debated. The best evidence is indirect and rests on the observation that reducing salt intake lowers blood pressure. There is also recent direct evidence that reducing salt intake reduces the incidence of cardiovascular disease. While there is some experimental evidence that reducing salt intake could benefit people, there is no experimental evidence that modest reduction in dietary salt intake would harm people.

The controversy mainly rests on observational longitudinal data mostly based on a single baseline estimation of dietary salt intake in the presence of substantial inter-individual variability in salt intake. Several countries have therefore adopted public health policies aiming at reducing salt intake in the general population. The relevant tools and strategies are directed to both the food industry and the consumers. At the industry level, the most efficient measure is legislation on the salt content of selected foods, an approach more (cost) effective than voluntary reductions. At the consumer level, information campaigns, nutrition education at school and tailored

computer interventions are possible, but costly and with likely limited impact. None of the interventions aiming at reducing salt intake has been rigorously evaluated. Thus, any intervention in this field should be accompanied by an appropriate monitoring and evaluation program conducted in the population, gathering data and producing information on the reduction in salt intake, the impact on blood pressure and, finally, on the level of cardiovascular morbidity and mortality.

Acronyms List:
NHANES = National Health and Nutrition Examination Survey
TOHP = Trials of Hypertension Prevention
VAT = Value-Added Tax

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