Expert testimony on salt and cardiovascular disease

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1. Introduction

1.1 Raised blood pressure (BP) is the first cause of death and disability in adults worldwide [1]. It is responsible for up to 62% of strokes and 49% of coronary heart disease (CHD) [2].

1.2 The absolute risks of CVD associated with the levels of BP increases with age [3]. Whilst the relative risk is greater in younger age groups, the absolute risk (also referred to as attributable risk) is much greater in older age groups, because CVD becomes more common as we grow older.

1.3 There is a graded relationship between BP and CVD, beginning at ~115/75 mmHg [3]. Randomised clinical trials of intervention with drugs that lower BP have reduced CVD outcomes over 5 years by approximately the amount predicted from observational studies, supporting causality [4].

1.4 Although the risk of CVD increases progressively with increasing BP, the greatest number of CVD deaths attributable to BP occurs in the upper half of the usual BP (that is at around 130/80 mmHg). This is because there are so many individuals having BP around this level in the population [5].

1.5 Individuals with a BP within these levels would not currently be treated with drugs [6]. Therefore, a population-based approach through non-pharmacological measures (for example diet and life-style) is the only feasible option. Achieving at a small downward shift in the distribution of BP in the whole population, will achieve a surprisingly large CVD reduction.

2 Evidence relating salt to BP

2.1 Definitions

2.1.1 For the purpose of this report, the word salt is used to refer to sodium chloride intake.

2.1.2 Publications refer to sodium intake as either mass or millimolar amounts of sodium, or mass of sodium chloride (salt). (1g sodium chloride = 17.1 millimolar amounts of sodium or 393.4 mg of sodium).

2.1.3 For UK residents, over three quarters of dietary salt intake is concealed in processed food, rather than being added at the table or during cooking. The term limitation of dietary salt intake implies the reduction of total sodium intake from all dietary sources including, for example, additives such as monosodium glutamate and preservatives.

2.2 Interventions in individuals: evidence from randomised controlled clinical trials

2.2.1 Animal, human genetics, epidemiological and migration studies, population-based intervention studies and randomised controlled clinical trials consistently demonstrate a close direct relationship between levels of salt intake and levels of BP [7-9].

2.2.2 The BP-lowering effect of a reduction in salt intake is effective in men and women, in all ethnic groups, in all age groups, in both normotensive and hypertensive individuals [10]. It is additive to the effect of anti-hypertensive medications [11] and other non-pharmacological treatments for BP [12-13].

2.2.3 Numerous meta-analyses of randomised controlled salt reduction clinical trials in adults with and without hypertension [14-20] and children [21] have been published. These meta-analyses included trials of at least one month duration. The estimates of effects were consistent with significant reductions in BP following a reduction in salt intake.

2.2.4 The most recent meta-analysis [20] included 17 trials in hypertensives (n=734 individuals) and 11 trials in normotensives (n=2,220). The median reduction in 24h urinary sodium excretion was 78 mmol (equivalent to 4.6 g of salt/day) in hypertensives and 74 mmol in normotensives. The pooled estimates of BP fall were 5.0/2.7 mmHg in hypertensives and 2.0/1.0 mmHg in normotensives. Weighted linear regression analyses showed a dose response: a reduction of 100 mmol/day (6 g of salt) in salt intake predicted a significant fall in BP of 7.1/3.9 mmHg in hypertensives and 3.6/1.7 mmHg in normotensives.

2.2.5 Dose-response effects have also been demonstrated in two randomised controlled clinical trials, [12,22]. In individuals with normal BP not qualifying in the UK for drug therapy [22] the DASH-Sodium feeding trial, studied three levels of salt intake (8, 6 and 4 g of salt/day) on two different diets. From High to Low salt diet BP fell by 6.7/3.5 mmHg whilst on the usual American l diet and by 3.0/1.6 mmHg whilst on the already healthy DASH diet rich in fruits, vegetables and low-fat dairy products.

2.2.6 One meta-analysis [21] included 10 trials (n=966) in children and adolescents younger than 18 years. Salt intake was reduced by an average of 42% for a median duration of 4 weeks (range 2 weeks to 3 years). The pooled estimates of BP fall were 1.2/1.3 mmHg.

2.2.7 In three trials of infants (n=551), with a median duration of 20 weeks (range 8 weeks to 6 months) [21] salt intake was reduced by an average of 54% . The mean systolic BP fall was 2.5 mmHg.

2.3 Population-based intervention studies: the evidence

2.3.1 Several population-based intervention studies on the effect of a reduction in salt intake on BP have been carried out [23-27].

2.3.2 The most successful intervention study is the one conducted in two similar villages in Portugal [23], which achieved a difference of approximately 50% in salt intake between the two villages. After 2 years' intervention, there was a difference of 13/6 mm Hg in BP between the two villages.

2.3.3 A recent randomized community-based intervention trial was carried out in 550 individuals in two rural villages in north-eastern Japan. The study demonstrated that dietary counselling for 1 year reduced salt intake by 2.3 g/day as measured by 24h urinary sodium and this was associated with a decrease of 3.1 mmHg in systolic BP [27].

2.3.4 Two studies [25-26] did not achieve a change in salt intake and the BP did not change.

3. Evidence relating salt intake to CVD

3.1 There is limited controlled intervention trial over a long term to establish with an experimental design that a modest reduction in salt intake prevents cardiovascular outcomes [28], Useful evidence comes from population-based longitudinal prospective studies, natural experiments and predictions from population BP effects.

3.2 Population-based longitudinal prospective studies

3.2.1 We performed an extensive systematic review [29]. Seventeen papers were identified [28, 30-45]. Thirteen studies provided 19 cohort samples [28, 30-31,34,36,38-45]. They included 177,836 male and female participants, aged 25 to 79 years. Follow-up ranged 3.5 to 19 years. There were 5,346 strokes and 5,246 total CVD events. Salt intake was assessed by 24h dietary recall (n=4), FFQ (n=4), 24h urine excretion (n=4) and questionnaire (n=1). Higher salt intake was associated with greater risk of stroke (RR: 1.23; 95% CI 1.06 to 1.43; P=0.007) and CVD (1.14; 0.99 to 1.34; P=0.07). There was significant heterogeneity. For CVD the exclusion of a single outlier resulted in a revised pooled estimate of 1.17 (1.02 to 1.34; P=0.02).

3.3 Natural experiments

3.3.1 *Japan.* In the late 1950s stroke deaths were among the highest in the world, Certain regions, particularly the north, had very high salt consumption. The numbers of strokes in different parts of Japan were directly related to the amount of salt consumed. The Japanese Government therefore initiated a campaign to reduce salt intake which fell over the following decade from 13.5 to 12.1 g/day. (in the north from 18 to 14 g/day). There was a parallel fall in BP in adults and children, and an 80% reduction in stroke mortality [46]. Falls occurred despite large increases in population fat intake, cigarette smoking, alcohol consumption and body mass index.

3.3.2 *Finland.* Since the 1970s, Finland aimed to reduce salt intake in the whole population [47-48] with (a) collaboration with the food industry to develop reduced-salt food products and (b) raising the general awareness among consumers. Over 30 years, salt intake has reduced by one-third. Both systolic

and diastolic BP fell over 10 mmHg. Both stroke and CHD mortality decreased 75–80% with an increase of 5–6 years in life expectancy [48].

3.4 Predictions from population BP effects

3.4.1 In 2001 the estimated salt intake in the UK (from 24h urine collection in a representative population sample) was 9.5 g/day. In 2008 the estimate is 8.6 g/day [49].

3.4.2 In England & Wales the government target is set at 6 g/day by 2012. The US DASH target is 4g/day.

3.4.3 As a conservative estimate a reduction of 3 g/d in salt intake would result in a fall in BP of 2.5/1.4 mmHg [50]. This would reduce strokes by 12% (systolic), 14% (diastolic) and CHD by 9% - 10% [51].

3.4.4 In the United Kingdom, the total number of stroke deaths is 60,666 per year, and the total number of CHD deaths is 124,037 per year [52].A reduction of 3 g/d in salt intake would therefore prevent ~7,300 to 8,300 stroke deaths and 10,600 to 12,400 CHD deaths per year totalling some 20,000 fewer CVD deaths annually. The effects on stroke and CHD would be expected to almost double if salt intake were reduced by 6 g/d and triple with a 9 g/d reduction.

3.4.5 In normotensives, salt reductions would also have large effects on stroke and CHD. A 3 g/day reduction in salt intake would reduce strokes by approximately 9% and CHD by 6% .

3.4.6 Not all CVD is fatal. It can be estimated that the benefit of salt reduction on non-fatal CVD disease and disability would be greater.

3.4.7 There is no evidence of harmful effects of a modest reduction in salt intake.

4. Cost-effectiveness

4.1 Several economic studies have assessed the health effects and financial cost of reducing population salt intake [53-58]. All of these analyses have demonstrated that a reduction in salt intake is very cost-effective.

4.2 In a Norwegian population [53] the interventions consisted of: population-wide targeted information campaigns, decreases in salt content of processed foods, labelling changes, enforced taxation/subsidization of foods with high/low salt content. The baseline hypothesis was that the intervention would produce a 50% reduction in the daily salt consumption. A Markov model estimated health outcomes and economic parameters over 25 years. The results showed an overall mortality reduction of 1–2%, an increase in the average life expectancy and a 5% reduction in the number of people requiring treatment for raised BP. Modelling of the economic outcomes suggested that the intervention would result in a net saving of US$ 270 million over 25 years.

4.3 Another study [54] compared the cost-effectiveness of reducing population salt intake with a range of interventions for lowering BP or cholesterol. The 17 interventions targeting salt reduction comprised legislation or voluntary agreements to ensure appropriate labelling changes and stepwise decreases in the salt content of processed foods. The WHO-CHOICE project was used to estimate cost–effectiveness in 14 sub-regions defined by geographic proximity and basic epidemiology. Health benefits were estimated employing a multistage modelling tool (four health states) that allows a trace of what would happen in a given population over 100 years, with and without each intervention. The results indicated that measures to decrease salt intake, such as labelling changes and strategies to change manufactured products, are potentially very cost effective. Legislation was more cost effective than voluntary agreements and could both necessary [59] and acceptable (60). In particular, non-personal health interventions, including government action to stimulate a reduction in the salt content of processed foods, were cost-effective ways to limit CVD and could avert over 21 million DALYs (disability-adjusted life years) per year worldwide.

4.4 One trial examined the effects of potassium-enriched salt (containing almost two thirds less sodium chloride) on CVD mortality and medical expenditures in elderly veterans [55]. In veteran retirement homes 1,981 veterans (mean age 75 yrs) attending five kitchens were randomised to potassium-enriched salt (experimental group) or regular salt (control group) for ~31 mo.. The incidence of CVD-related deaths was decreased to 13.1 per 1,000 persons (27 deaths in 2,057 person-years)

compared with the experimental and control groups and 20.5 per 1,000 (66 deaths in 3,218 person-years) respectively. A 41% reduction in CVD mortality (age-adjusted hazard ratio: 0.59; 95% CI: 0.37, 0.95) was observed in the experimental group. Persons in the experimental group lived 0.3–0.9 years longer and spent significantly less (~US $426/y) in inpatient care for CVD than did the control group.

4.5 A study in Canada [57] estimated that a reduction of 4.6 g/day in salt intake would decrease hypertension prevalence by 30% and almost double the control rate of hypertension. This would save approximately $430 million per year from drugs, physician visits and laboratory testing directly related to hypertension.

4.6 A more recent study examined strategies to reduce salt intake and control tobacco use in 23 low- and middle income countries which account for 80% of chronic disease burden in the developing world [58]. The 15% modest reduction in salt intake could be achieved by a voluntary reduction in the salt content of processed foods and condiments by manufacturers, plus a sustained mass media campaign aimed to encourage dietary change within households and communities. A 15% reduction in mean population salt intake over a decade could avert 8.5 million cardiovascular deaths. Implementing such salt reduction programmes was estimated to cost US$0.09 per person per year.

4.7 A 3g/day reduction in salt intake in the UK (e.g. from 9 to 6 g/day) would avert ~20,200 deaths per year, this would equate to 170,000 QALYs being gained and an annual saving of £ 5.1 bn [61].

4.8 In conclusion, the cost–effects are consistent for population-wide reductions in dietary salt consumption. The evidence strongly supports the more widespread introduction of national programmes to reduce dietary salt consumption. However, few planners and policy makers are aware of these data. The currently limited impact of the cost–effectiveness data can be addressed by the development of national estimates, the presentation of the results in formats more easily comprehensible to policymakers, and the incorporation of cost–effectiveness data into coherent national programmes seeking to change dietary salt policy..

5. Perceived barriers and myths

5.1 Myth 1. Consumer taste preference, i.e. people prefer saltier products and if the salt content was lowered it would lead to consumer rejection.

5.1.1 However, as salt intake falls, the salt taste receptors in the mouth become more sensitive to lower concentrations of salt within a couple of months [62]. Lower concentrations of salt then taste as salty as the earlier higher concentrations.

5.1.2 Furthermore, once salt intake is reduced, people prefer food with less salt [63].

5.1.3 Consumer experience in the UK confirms that where salt has been reduced in major brand products with a gradual and sustained method, there has been no reduction in sales and no complaints about taste.

5.2 Myth 2. Consistency of food technology, e.g. meat burgers require salt to extend shelf life as well as helping the product to bind together; bread requires salt to aid the manufacturing process in large-scale plant bakeries, to retain acceptable flavour, structure and for crust development.

5.2.1 However, UK experience indicates that in the early stages of a salt reduction programme it is possible to take 5-15% of the salt out of a product without unacceptable change in flavour.

5.3 Myth 3. Food Safety, e.g. salt reduction in some food categories may reduce shelf-life and alter their microbiological features

5.3.1 However, many microbiological modelling tools can be used to predict the safety and shelf-life of food and hence help the industry (e.g. www.combase.cc/default.html)

5.4 Profits versus public health

5.4.1 Salt makes unpalatable food made at low cost.

5.4.2 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 [47].

5.4.3 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 [47, 64-65].

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