Public health impact of salt reduction

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This research was conducted under the auspices of the Graduate School VLAG (Advanced studies in Food Technology, Agrobiotechnology, Nutrition and Health Sciences).

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Maria A.H. Hendriksen

Thesis

submitted in fulfilment of the requirements for the degree of doctor
at Wageningen University
by the authority of the Rector Magnificus
Prof. Dr A.P.J. Mol
in the presence of the
Thesis Committee appointed by the Academic Board
to be defended in public
on Monday 26 October 2015
at 1:30 p.m. in the Aula.

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Public health impact of salt reduction,
224 pages.

PhD thesis, Wageningen University, Wageningen, NL (2015)
With references, with summaries in Dutch and English

ISBN 978-94-6257-546-2

Abstract

The health and economic burden related to cardiovascular diseases is substantial and prevention of these diseases remains a challenge. There is convincing evidence that high salt intake affects blood pressure and the risk of cardiovascular diseases. As salt intake is far above the recommended maximum level of intake, salt reduction may help to reduce cardiovascular disease incidence. However, the effect of salt reduction initiatives on intake levels and long-term health is largely unknown. The main aim of the research described in this thesis is to assess salt intake and the potential health impact of salt reduction in the Netherlands and in Europe. This is addressed by estimating the potential effect of salt reduction strategies on salt intake, by monitoring the effect of the ongoing salt reduction initiatives in the Netherlands between 2006 and 2010 on daily salt intake and by projecting the expected long-term health benefits of salt reduction in the Netherlands and Europe.

Firstly, we used data from the Dutch National Food Consumption Survey 2007–2010 and the Dutch Food Composition Database 2010 to study the effect of two potential salt reduction scenarios on salt intake from processed foods. In the first scenario, sodium levels in processed foods were reduced towards their minimum feasible sodium level. In the second scenario, foods were substituted by a low-salt alternative within the same food category. This study demonstrated that daily salt intake from foods could be reduced below the recommended maximum intake of 6 g/d, provided these strategies are successfully implemented.

Secondly, the effect of the ongoing salt reduction initiatives in the Netherlands between 2006 and 2010 was evaluated. Dutch adults in two cross-sectional studies (n=317 in 2006 and n=342 in 2010) collected a single 24h urine sample. Despite the initiatives of the food industry to reduce sodium levels in processed foods, no statistically significant difference in daily salt intake was observed between 2006 (8.7 g/d) and 2010 (8.5 g/d).

Thirdly, the long-term health impact of salt reduction was assessed for the Netherlands using the RIVM Chronic Disease Model and for Europe using the Dynamic Model for Health Impact Assessment (DYNAMO-HIA). A two-step approach was used: the effect of salt reduction on blood pressure was estimated, which was subsequently translated into occurrence of cardiovascular diseases. Substantial changes in incident stroke (6.0%) and acute myocardial infarction (4.4%) can be expected in the Netherlands if sodium contents in processed foods were reduced to the minimum feasible level. The potential health impact of population-wide adherence to the salt intake guideline of the World Health Organization (maximum of 5 g/d)

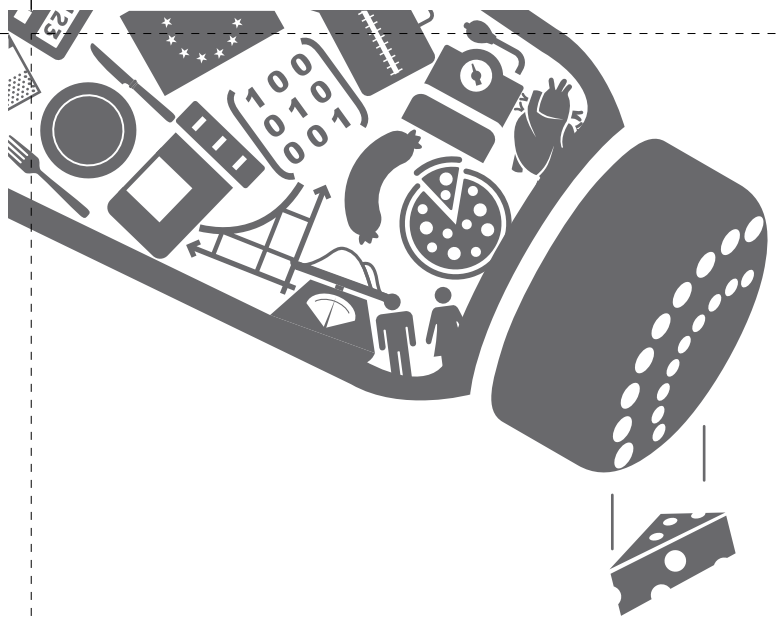
ranged for nine European countries between 10.1% in Finland to 23.1% in Poland for stroke, and between 6.6% in Finland to 15.5% in Poland for ischemic heart diseases.

Finally, a methodological comparison of seven population health models on salt reduction revealed that these models vary in underlying assumptions. We demonstrated that these differences in assumptions may substantially affect the health impact estimates.

In conclusion, technologically feasible salt reductions in processed foods or changes in dietary behaviour may, if implemented successfully, lead to a substantial lowering of daily salt intake, and thereby contribute to considerable health gain. Cross-country comparisons of health impact of salt reduction strategies might benefit from more transparency on the necessary assumptions in the various population health impact models for salt reduction used worldwide.

Voor mijn vader.

Contents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Chapter 1

General introduction

The burden of cardiovascular diseases

Non-communicable diseases (NCDs), such as cancer, diabetes and cardiovascular diseases (CVD) are the leading cause of death in adults and are the main contributors to health loss worldwide (1). In the Netherlands, CVD is the first cause of death in women and second cause of death in men, after cancer (2). Since the 1970s, mortality rates from cardiovascular diseases have decreased dramatically (3; 4). Coronary heart disease mortality decreased by almost 80% in men and women over the period 1980–2011 (4), while stroke mortality decreased by almost 65% (3). Developments in preventive medicine (e.g. anti-hypertensive medication or statins), new surgical techniques and improved health care system have partly contributed to this decline (3). Despite the decline in mortality, the burden of disease due to cardiovascular diseases increased and CVD contributed most to the total burden of disease in the Netherlands in 2014 (2). In 2014, 10% of the total burden of disease was due to coronary heart disease, followed by stroke (7%) (2).

Hypertension as a major risk factor for cardiovascular diseases

Hypertension is an important risk factor for cardiovascular diseases and is defined as a systolic blood pressure of ≥140 mmHg and/or diastolic blood pressure of ≥90 mmHg and/or use of antihypertensive medication (5). Elevated blood pressure levels accounted for 7% of the global Disability Adjusted Life Years (DALYs) in 2010 (6). Almost half of the Dutch population aged 35 to 70 years has hypertension (2) and the prevalence of hypertension increased over the past decades in the Netherlands (2).

Lifestyle factors, such as overweight, unhealthy dietary habits and low levels of physical activity are important determinants of hypertension; a low intake of alcohol and a high intake of fruit and vegetables, dietary fibre, nuts and low-fat dairy are factors that may reduce blood pressure levels (7).

Salt intake in relation to blood pressure and cardiovascular diseases

Excessive salt intake, in the form of sodium chloride, is a main risk factor for hypertension (e.g. (8; 9)). The INTERSALT study, a cross-sectional study conducted in 32 countries among 10,079 subjects aged 20–59 years, found a positive and independent linear relation between 24h urinary sodium excretion and systolic blood pressure (SBP) (10). Furthermore, a recent meta-analysis of randomized controlled trials in adults shows that salt reduction significantly

reduces SBP by 3.39 (95% CI 2.46–4.31) mmHg and diastolic blood pressure (DBP) by 1.54 (95% CI 0.98–2.11) mmHg (11). Hypertensive individuals (SBP -4.06 (95% CI 5.15–2.96) have higher responses to salt reduction compared to normotensive individuals (SBP -1.38 (95% CI -2.74–0.02) (11). Also in children, salt reduction reduces blood pressure (12).

Salt intake has been associated with an increased risk of cardiovascular disease. A meta-analysis of observational studies concluded in 2009 that high salt intake significantly increased the risk of stroke by 23% and the risk of total cardiovascular disease increased by 14% (13). In 2013, the American Institute of Medicine (IOM) wrote a comprehensive review of the available evidence from human studies, systematic reviews and meta-analysis published between 2003 and 2012 in the association between salt intake and cardiovascular diseases. They concluded that there was a positive association between high sodium intake and risk of cardiovascular disease incidence and mortality, and all-cause mortality (14). An important remark was that the reviewed studies were highly variable in methodological quality, especially with respect to the salt intake measurements. The American IOM concluded that an intake of 2,300 mg sodium per day (equals 5.1 g salt per day) is expected to reduce the risk of cardiovascular diseases outcomes in the general population. Later publications confirmed the findings of the IOM (15; 16).

Dietary guidelines for salt intake

Based on the adverse effects of salt intake, international and national institutes have established dietary guidelines for sodium intake. The World Health Organization (WHO) recommends a sodium intake of less than 2 g/d (= 5 g/d salt) (17). This recommendation is based on the evidence for sodium intake in relation to blood pressure and cardiovascular diseases and applies to all individuals. The Dutch Health Council recommends a maximum salt intake of 6 g/d (= 2.4 g sodium) (18). This recommendation is based on the evidence for the adverse effects of sodium intake on blood pressure, but also takes into account the feasibility of salt reduction given the current salt intake. At the time of the publication of the dietary recommendations in 2006, sodium intake in the Dutch population was not known. An estimation from an EPIC-calibration study, conducted between 1995 and 1997 among 190 individuals indicated a salt intake of almost 9.8 g/d (18).

Cardiovascular diseases contribute most to the burden of diseases worldwide, including in the Netherlands. An important risk factor for cardiovascular disease is hypertension. There is convincing evidence that salt intake is positively related to blood pressure. At the moment of the publication of the dietary guidelines in the Netherlands by the Dutch Health Council in 2006, the salt intake was not known, but likely above the recommended intake.

Public health benefits of salt reduction

Sodium in processed foods

Over 80% of the daily sodium intake in the Netherlands is added during food processing (19). Five to ten percent of the daily sodium intake comes from sodium naturally present in a variety of foods, such as milk, meat and shellfish, and 10 to 15% of the salt intake is added during cooking or at the table (**Figure 1.1**). Thus, if consumers limit or stop the use of discretionary salt, their intake will still be above the recommended maximum because of the current sodium content in processed foods.

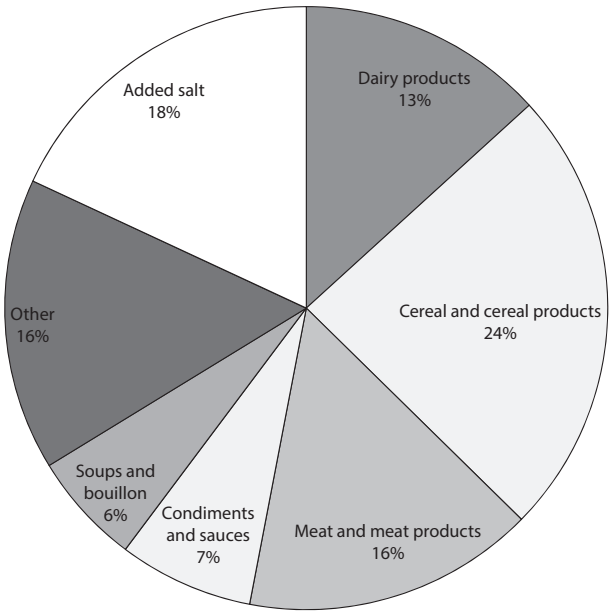

Figure 1.1 Sources of salt in the Netherlands. Adapted from (19).

Sodium chloride (=salt) has important functions in foods. First, sodium reduces water activity, thereby preventing microbial growth (20; 21). In certain foods, such as processed meats or cheese, added salt mainly functions as a preservative. Second, sodium contributes to the development of physical properties of foods that are beneficial for processing or developing final product qualities (22). In bread, for example, sodium has an effect on gluten development and regulation of fermentation (21; 23). Finally, salt is added to a large variety of foods (e.g. salty snacks or soups) to enhance flavour and/or to reduce the bitterness of foods (22). Similar processed foods have large variation in sodium levels, suggesting it is technically feasible to reduce sodium levels without compromising to taste (24).

The WHO and national governmental advisory groups, such as the Dutch Health Council, encourages the food industry to reduce the level of sodium in processed foods. The concept of sodium reduction in processed foods is considered an important and cost-effective strategy to lower the burden of cardiovascular disease (25). It will affect the entire population (population-based approach) and salt intake will reduce without modification of the habitual food intake. Furthermore, the consumer will get acquainted to the less salty taste when sodium levels in foods are gradually reduced (26; 27).

Policy measures for salt reduction

The development and implementation of salt reduction strategies is widespread; in 2014, 59 initiatives were identified worldwide (28). The WHO supports countries to implement salt reduction strategies and established a network in partnerships. In Europe, since 2008 27 countries are united in the European Salt Action Network where best practices on salt reduction are exchanged and discussed on policy level. Furthermore, they have developed a framework for salt reduction programmes with three main pillars: 1) food reformulation; 2) consumer awareness and education campaigns and 3) environmental changes. Also in 2008, the EU High Level Group on Diet, Physical Activity and Health developed a Framework for National Salt Initiative, which was approached and adopted by EU Member States (29). This framework aimed to support EU Member States to achieve the WHO target of salt intake. In addition, a common minimum European benchmark for a 16% salt reduction from baseline 2008 levels was established over a 4-year period, to be realized across all food products in EU Member States.

An overview of world-wide salt reduction initiatives demonstrates that the food industry is involved by commitment to voluntary targets, or mandatory limits on sodium levels in foods

have been set by the government (28). The targets are specified by food (group), taking into account the technological challenges related to sodium reduction for each food group (28). The focus is generally on foods that contribute most to salt intake, based on market share or consumption (30), as this will have the largest impact on daily salt intake.

Monitoring of the progress of the policy interventions is essential to evaluate the effectiveness of the salt reduction initiative. In the UK, for example, sodium levels of branded breakfast cereals were reduced by 49% and of cakes by 25% (31). Due to the efforts of the food industry and the awareness campaign the daily salt intake decreased from 9.5 g/d in 2000–2001 to 8.6 g/d in 2008 (31) and to 8.1 g/d in 2011 (32). This shows that substantial sodium reduction in processed foods is needed to achieve a relevant reduction in daily salt intake.

A negative consequence of sodium reduction in processed foods in the Netherlands might be the iodine supply in the population. In the Netherlands, the diet is iodine-deplete, leading to goitre in adults and to mental retardation in children if the mother is deplete during pregnancy (33; 34). Salt iodization is considered the primary strategy for eliminating iodine deficiency disorders (35). The WHO acknowledges that the recommendation of salt reduction should not conflict salt iodization. Monitoring of iodine intake is necessary to assess if iodine intake is affected by salt reduction (17).

Long-term health consequences of salt reduction

Lower population blood pressure achieved through salt reduction may lead to lower cardiovascular disease morbidity and mortality. The consequences of implementing salt reduction strategies can be forecasted by health impact assessments (HIA) models. HIA models combine information from different sources to assess how the effects of a policy intervention (here salt reduction) will develop over time. In a HIA the current situation (status quo) is compared with a hypothetical *what if* situation. For example, the question answered in a HIA is "How many disease cases are averted if salt intake is reduced to the recommended maximum intake compared with the current situation".

Models used to quantify the potential health impact differ in complexity (36). A potential impact fraction (PIF) is the proportional change in incidence (or mortality) as a function of change in exposure (37). A PIF estimation is relatively easy to perform, because it requires only information on the present level of exposure, expected change in exposure and present incidence or mortality of a certain disease. A limitation is that those estimations do not

take into account population dynamics or changes in risk factor states over time (38). More complex models can model populations that vary in age and/or gender structure, take into account changes of the population over time (dynamic models) and model risk factor states. Those models need additional parameters and require more assumptions.

In the past decade, several studies predicted the long-term health impact of salt reduction (e.g. (39; 40; 41; 42; 43; 44; 45)). In 2003, He and MacGregor predicted that a 3 g/d reduction in daily salt intake would reduce stroke mortality by 12% in the UK (39). Bibbins-Domingo *et al.* used the CHD policy model (markov-type model) to predict the health gain of a 3 g/d daily salt reduction in the US population over a period of 10 years and compared the results with other blood pressure lowering interventions (41). They predicted a reduction in stroke between 5.2% and 8.2% in the USA. The authors conclude that salt reduction was an effective intervention to reduce cardiovascular events and can save medical costs, also in comparison with population-wide interventions on tobacco use and obesity. Cobiac *et al.* evaluated interventions for salt reduction using a lifetable approach for the Australian population and concluded that an intervention of mandatory limits of sodium levels in processed foods could avert 18% of the total DALYs attributable to high salt intake in Australia (42).

As shown above, there is variation in the modelling approach and outcome in the estimation of the potential effect of salt reduction on morbidity and mortality. There is currently no consensus on the most appropriate model (46). A study by Coxson *et al.* simulated the effect of salt reduction using three different modelling approaches (47). The authors demonstrated that for a 3-gram lower salt intake a total of 280,000 deaths could be averted in the USA based on an indirect modelling approach (modelling salt reduction on morbidity and mortality through blood pressure), but this number almost doubled (500,000 deaths) when a direct modelling approach was used. Thus, alignment of methods to assess health impact of salt reduction may be necessary for policy makers in order to understand the potential effect of salt reduction.

The majority of daily salt intake comes from processed foods. Reducing sodium levels in processed foods and changing dietary behaviour is essential to reduce daily salt intake. Ultimately, reducing daily salt intake will contribute to lower blood pressure levels and subsequently to fewer cardiovascular disease events. The magnitude of the impact of measures to reduce salt on daily salt intake and on long-term health is not known for the Dutch situation and for Europe.

Outline of this thesis

This thesis follows the outline of **Figure 1.2**. The main focus of this thesis is on health benefits of salt reduction in the Netherlands and Europe. The first aim is to assess the potential impact of salt reduction strategies on salt intake in the Netherlands. The second aim is to monitor the salt intake in the Netherlands and evaluate the effect of an actual salt reduction initiative in the Netherlands. The third aim is to assess the long-term health benefit of salt reduction on population health in the Netherlands and in Europe.

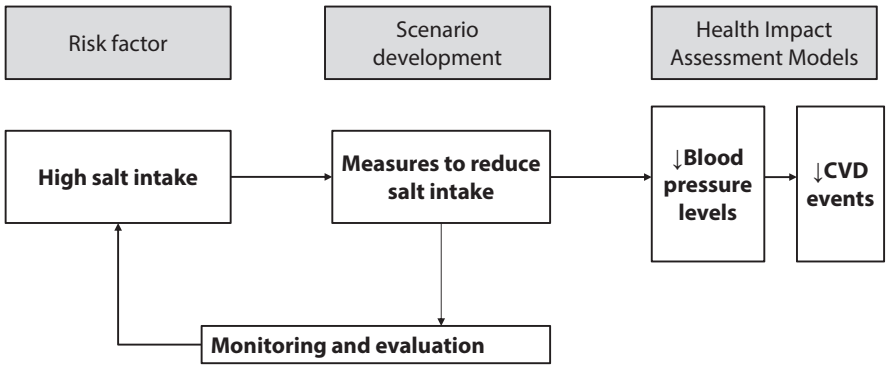

Figure 1.2 Outline of research in this thesis.

Potential impact of salt reduction in the Netherlands on salt intake

To address the first aim of the study, two hypothetical measures to reduce daily salt intake were evaluated for the Netherlands in using scenario analysis. The potential effect of those scenarios on daily salt intake were assessed and described in **Chapter 2**. To address the second aim of the thesis, the actual implementation of a Dutch salt reduction strategy was evaluated. In 2006, the Task Force Salt Reduction was initiated by the Federation of the Dutch Food and Grocery Industry, in which the partners committed themselves to voluntary sodium reduction in the processed foods concerned by on average 12% in 2010. In 2010, the effect of the initial salt reduction strategy was evaluated. The National Institute for Public Health (RIVM) was requested by the Ministry of Public Health, Welfare and Sports to monitor the effect on daily salt intake in the Dutch population. The results of this evaluation by measuring sodium levels in 24h urine samples are described in **Chapter 3**.

In the Netherlands iodized salt is used in bread, and other bakery foods. Sodium reduction in foods may therefore interfere with the policy on salt iodization. A simulation study of Verkaik *et al.* suggested that sodium reduction in processed foods by 50% will reduce the iodine intake in the Dutch population from 264 µg/d in men and 204 µg/d in women to 201 µg/d in men and 162 µg/d in women, but intakes will still be adequate (48). However, daily iodine intake should be monitored to assess the effect of sodium reduction in processed foods on iodine intake. Therefore, the daily iodine intake in the Netherlands was also evaluated in **Chapter 3**, using 24h urinary iodine excretion levels.

Long-term health benefits of salt reduction

The long-term health benefits of salt reduction are not known for the Dutch situation. Therefore, a health impact assessment methodology to assess the effect of two salt reduction strategies on long-term health benefits in the Netherlands was developed and applied (**Chapter 4**). A comparison of salt reduction in the Netherlands and several European countries was made by developing a health impact assessment method for Europe (**Chapter 5**). Finally, in order to understand the variability in published outcomes of the health impact assessments of salt reduction, an analysis of characteristics and underlying features of the health impact assessment models for estimating the health gain of population-wide salt reduction was performed (**Chapter 6**).

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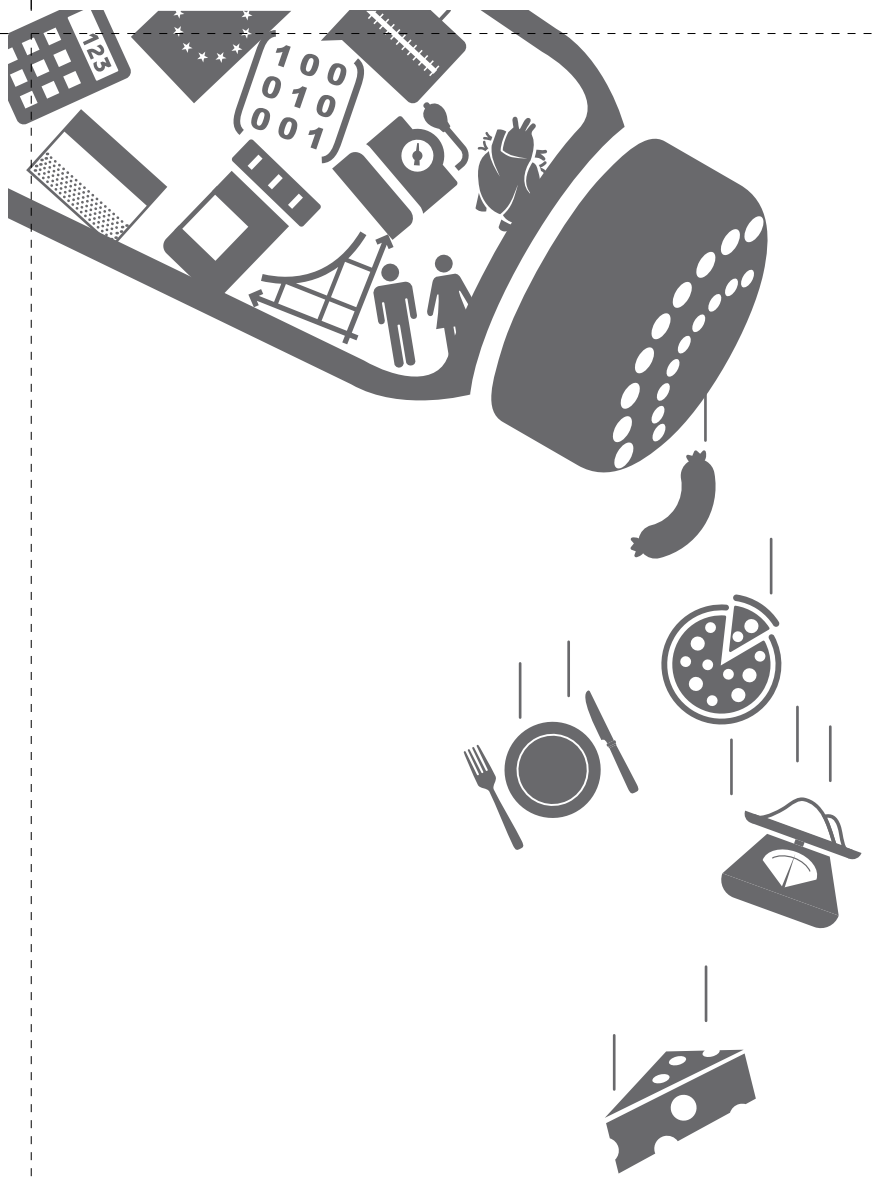
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Chapter 2

Nutritional impact of sodium reduction strategies on sodium intake from processed foods

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Published in the European Journal of Clinical Nutrition 2015. Epub ahead of print
Doi:10.1038/ejcn2015.15

Abstract

Background/objectives: Sodium intake in the Netherlands is substantially above the recommended intake of 2,400 mg/d. This study aimed to estimate the effect of two sodium reduction strategies; i.e. modification of composition of industrially processed foods towards the technological feasible minimum level or alteration of consumers' behaviour on sodium intake in the Netherlands.

Subjects/methods: Data from the Dutch National Food Consumption Survey (2007–2010) and the Food Composition Table (2011) were used to estimate current sodium intake. In a first scenario, levels in processed foods were reduced towards their technological feasible minimum level (sodium reduction in processed foods scenario). The minimum feasible levels were based on literature searches or expert judgment. In the second scenario, foods consumed were divided into similar food (sub)groups. Subsequently, foods were replaced by low-sodium alternatives (substitution of processed foods scenario). Sodium intake from foods was calculated based on the mean of two observation days for the current food consumption pattern and the scenarios.

Results: Sodium levels of processed foods could be reduced in most food groups by 50%, and this may reduce median sodium intake from foods by 38% (from 3,042 mg/d to 1,886 mg/d in adult men). Substitution of foods may reduce sodium intake by 47% (from 3,042 mg/d to 1,627 mg/d in adult men), due to many low-sodium alternatives within food groups.

Conclusions: In the Netherlands reduction of sodium intake by modification of food composition or by alteration of behaviour may substantially reduce the median sodium intake from foods below the recommended sodium intake.

Introduction

Almost half of the Dutch population has an elevated blood pressure (1) and has therefore an increased risk of developing cardiovascular diseases (2). Studies have shown a positive association between salt intake and blood pressure, and a reduction in daily sodium intake leads to a reduction in blood pressure levels (3). In the Netherlands sodium intake substantially exceeds the recommended intake of 2,400 mg/d. Median sodium intake in adults was estimated to be 3,400 mg/d (4).

Worldwide the prevention of cardiovascular diseases is considered an important action to reduce the burden of diseases. Reduction of the populations' sodium intake is mentioned among the five priority interventions by the WHO (5). In this context, many countries are committed to reduce the population sodium intake towards the recommended levels. Their sodium reduction strategies generally consist of two important components: reformulation of existing foods to achieve lower sodium content in foods and consumer awareness or behaviour change programs to increase the knowledge of the adverse effects of excessive sodium intake and discretionary sodium use by consumers (6).

Countries such as Finland and the United Kingdom have initiated sodium reduction strategies for many years. Consequently, the mean sodium intake in Finland over the period 1979–2002 decreased by more than 1,200 mg/d to 3,960 mg/d among men and to 3,040 mg/d among women (7). Sodium reduction in processed foods contributed substantially to this decrease in sodium intake, but also the consumer awareness of high sodium intake increased (8). The British government initiated a salt reduction program through a media campaign to increase public awareness of high salt intake and engaged stakeholders to develop realizable targets for sodium content in processed foods. These interventions decreased the mean sodium intake from 3,840 mg/d in 2001 to 3,240 mg/d in 2011 (9). Despite the initiatives, sodium intake in both countries is still above the recommended intake for a large group of the population.

In the Netherlands population salt intake reduction is also an important objective to improve dietary intake. Sodium reduction in processed foods is considered the crucial intervention, while less attention is given to lower the use of discretionary salt and to consumption of foods high in sodium. Monitoring sodium levels in processed foods shows that there is much variation in sodium levels within product groups (10) and also shows that food industry had not yet achieved its targets for sodium reduction in processed foods in the Netherlands

of 10% in 2010 (10). A new voluntary agreement on sodium reduction between the Dutch Ministry of Health, food industry and caterers include a stepwise reduction in sodium levels (11). Exploring the effects of both salt reduction strategies in the Netherlands will be essential in order to support salt reduction campaigns.

In the present study we estimate the impact on sodium intake of the Dutch population of two salt reduction strategies. The first strategy is to lower sodium in processed foods to its technologically feasible minimum level. The second strategy is to reduce sodium intake by intentionally choosing for low-sodium alternatives within certain food groups.

Methods

Food composition and food intake data

Sodium levels in foods were derived from the Dutch Food Composition Table (NEVO) published in 2011 (12). This table was updated for missing data and outdated sodium levels were re-evaluated and updated if needed.

Food consumption data were obtained from the Dutch National Food Consumption Survey 2007–2010 (DNFCS 2007–2010) (13). In short, this survey included a representative sample of the Dutch population aged 7 to 69 years and the dietary assessment was based on two non-consecutive 24h recalls. For children aged 7–15 years the two 24h recalls were carried out by means of face-to-face interviews during home visits with caregivers. Participants aged 16 years and older were interviewed unannounced by telephone. Each participant was interviewed twice with an interval of about 4 weeks. In total 3,819 subjects completed two 24h recalls (net response rate 69%).

Scenarios

We established two scenarios representing the two most important strategies to reduce sodium intake: (I) modification of composition of industrially processed foods and (II) alteration of consumers' behaviour. In the first scenario sodium levels in industrially processed foods were reduced towards their technologically feasible minimum levels (Sodium reduction scenario). In the second scenario, appealing to consumers' behaviour change, actually consumed foods were replaced by low-sodium alternatives (substitution scenario).

Sodium reduction in processed foods scenario

The Dutch Food Composition Table 2011 was used to identify processed foods that contained added sodium chloride (12). Foods were selected if the sum of the food consumed in the total study population was more than 500 mg sodium/d (N=338 processed foods) based on the DNFCS 2007–2010.

Food technologists performed an assessment of the minimum technological feasible levels of sodium in processed foods based on experience and review of scientific and technological literature. The following criteria were considered. (a) Sodium reduction should be technologically feasible within 5 years. Processing and formulation adaptations may be mandatory, but should be technologically feasible within this timeframe. If available, regular foods with reduced sodium content were identified as proof of feasibility. (b) The foods should still be microbiological safe. The boundaries of microbiological safety were assessed on water activity and specific food product composition. Reduction of refrigerated shelf life may be necessary in certain cases. (c) The products should be acceptable for consumers regarding taste and texture. The acceptability on taste was based on current knowledge on consumer acceptance of sodium-replacing ingredients and minerals. Furthermore, consumer taste preference adaptation to lower saltiness intensity was assumed as a result of gradual industry-wide implementation of sodium reduction (14; 15). The texture of the food should not be changed significantly to comply with consumer demands. In addition, we did not consider current legislative or economic hurdles restricting the reduction of sodium in processed foods. A summary of the results of technologically feasible sodium levels per food subcategory level are presented in Annex I.

The sodium levels of the selected foods were replaced with their minimal technological feasible level. In the Food Composition Database some foods are used to calculate the sodium levels of other foods, as generic food ("bread multigrain average"; N=261) or as food item part of a recipe calculation ("brownies"; N=77). If a sodium-reduced food was part of another food, then we recalculated the sodium level of these particular foods.

Substitution of processed foods scenario

Sodium reduction was simulated by substituting processed foods containing industrially added sodium by low-sodium alternatives within the same food group, as available in the Dutch Food Composition Table 2011. Foods belonging to the following food groups were included in this scenario: fruits and vegetables, legumes, potatoes, cereal and cereal products, dairy products, meat and meat products, fats, soups, condiments and sauces,

snacks, cakes and pies, (soft)drinks, sandwich filling, main meals, mixed salads, lunches and unclassified. No food products were substituted in the food groups fruit juices, water, coffee and tea, soft drinks and legumes, because these foods hardly contain any industrially added sodium. All processed foods reported to be consumed in DNFCS 2007–2010 were classified according to the use of a food. If foods within a food group differed substantially in terms of common use, a sub-classification was made in order to substitute all foods within a food group by an appropriate alternative. Within each food (sub)group, the food with the lowest sodium content was identified as the low-sodium alternative for the whole food (sub) group. Occasionally, the food product with the lowest sodium levels was not an appropriate substitute, because of undesirable levels of other components in this food or because it was a unique food. In such cases, it was decided not to use this food item as an alternative, but to select the food item second lowest in sodium levels.

Data analyses

We calculated for each individual food item the percentage change in sodium level based on the current and new sodium levels of processed foods. The median sodium reduction of all individual foods was considered the percentage reduction that could be achieved.

Sodium intake distribution (median, 25th percentile (P25) and 75th percentile (P75)) was calculated for the current food consumption pattern and for both scenarios by summing the sodium levels in foods per subject per observation day and dividing it by the number of observation days (i.e. 2). We estimated the sodium intake for each individual food category for the total study population and for consumers of those food categories. We did not consider discretionary sodium use, as the purpose of this study was focused on the sodium intake from (processed) foods.

Energy intake was calculated for the substitution scenario in order to examine whether the scenario based upon replacement of foods by low-sodium alternatives might result in different energy intakes.

Results

Sodium levels in foods

The Dutch National Food Composition Table contained in total 1599 individual food items that were consumed during the DNFCS 2007–2010, of which 45% (N=727) belonged to food groups that contributed most to sodium intake. The current sodium levels varied considerably between and within food (sub)groups (**Table 2.1**).

In the sodium reduction scenario the majority of the foods (N=630) we changed the sodium levels to their lowest technological feasible level (40% in margarines to 100% in soft cheeses, processed meats, savoury snacks, cakes, pastries and sauces (<10% fat)). In most food groups, the realized sodium reduction was 50%, but ranged from 36% in pastries to 70% in canned vegetables.

In the substitution scenario 44% of the foods could be replaced by 124 foods that were lowest in sodium. In all food groups, the majority of the foods could be replaced by a low-sodium alternative (75%–100%). In most food groups, the percentage reduction that can be obtained with a currently available low-sodium alternative is more than 75%. However, some foods in certain food groups had almost similar sodium levels compared to the currently available low-sodium alternatives (e.g. sauces <10% fat 17% reduction; soups 19% reduction) (**Table 2.1**).

Sodium intake by foods

The percentage of consumers per food groups differed substantially, ranging from 3% for meat substitutes to 99% for bread (**Table 2.2**). Bread had the highest contribution to sodium intake (651 mg/d) among the total population and among the consumers. In certain food groups the percentage of consumers was limited, but the contribution to sodium intake among consumers was relatively high. For example, only a quarter of the population consumes soups, but the median sodium intake from soups among consumers is 505 mg/d.

The potential of sodium reduction intake in the sodium reduction scenario ranged from 16% for pies to 67% for cream cheeses for consumers of these food categories. In the substitution scenario, the potential ranged from 15% for soups to 100% for fats.

Table 2.1 Sodium levels (mg/100g) of processed foods in present diet in sodium reduction in processed foods scenarios and in the substitution of processed foods scenario

Food (sub)group[a]	Foods contributing most to present sodium intake	Foods with lowest technologically feasible sodium levels			Foods with sodium reduction by substitution		
	Sodium level (mg/100g)	Number of foods with reduced sodium level	Sodium level (mg/100g)	Median reduction[b]	Number of foods with reduced sodium level	Sodium level (mg/100g)	Median reduction[b]
	Median (min-max)	N (%)	Median (min-max) [c]	%	N (%)	Median (min-max) [c]	%
Vegetables							
Canned vegetables (N=52)	242 (1.7–7158)	32 (62)	91 (9–2648)	70	50 (96)	25 (1.7–7158)	88
Dairy products							
Hard cheese (N=31)	770 (50–1032)	28 (90)	374 (78–501)	50	31 (100)	430 (50–450)	47
Soft cheese (N=22)	614 (86–1750)	22 (100)	298 (43–875)	50	22 (100)	86 (86–250)	74
Cream cheese (N=12)	1150 (60–1500)	11 (92)	520 (270–750)	50	12 (100)	250 (250–250)	78
Cereals and cereal products							
Bread (N=75)	470 (30–661)	73 (97)	245 (145–342)	50	75 (100)	290 (30–432)	37
Bread substitutes (N=24)	483 (5-800)	21 (88)	288 (2.5-400)	50	23 (96)	235 (5–235)	51
Breakfast cereals (N=32)	200 (0-650)	20 (63)	181 (10-325)	50	32 (100)	10 (0–10)	95
Meat and meat products							
Processed meat (N=61)	906 (246–1974)	61 (100)	400 (229–856)	59	61 (100)	704 (246–704)	23
Meat substitutes (N=24)	500 (6–815)	22 (92)	271 (45–408)	50	24 (100)	6 (6–6)	99
Fat							
Low-fat margarine (N=21)	20 (0–200)	11 (52)	130 (20–220)	50	21 (100)	0 (0–0)	100
Margarine (N=10)	16 (0–482)	4 (40)	91 (65–166)	50	10 (100)	0 (0–0)	100
Cooking fat (N=12)	390 (2.5–600)	5 (42)	200 (162–300)	50	9 (75)	2.5 (2.5–2.5)	99

Table 2.1 continues on next page

Table 2.1 ***Continued***

Food (sub)group[a]	Foods contributing most to present sodium intake	Foods with lowest technologically feasible sodium levels			Foods with sodium reduction by substitution		
	Sodium level (mg/100g)	Number of foods with reduced sodium level	Sodium level (mg/100g)	Median reduction[b]	Number of foods with reduced sodium level	Sodium level (mg/100g)	Median reduction[b]
	Median (min-max)	N (%)	Median (min-max) [c]	%	N (%)	Median (min-max) [c]	%
Snacks							
Savory snacks (N=23)	596 (123–776)	23 (100)	240 (47–394)	50	21 (91)	145 (97–145)	78
Chips (N=29)	660 (2–1333)	25 (86)	338 (100–667)	50	29 (100)	2 (2–2)	100
Cakes and pies							
Cakes (N=13)	388 (55–452)	13 (100)	150 (35–270)	46	13 (100)	55 (55–55)	86
Biscuits (N=83)	220 (12–550)	79 (95)	120 (7–297)	46	82 (99)	12 (12–124)	93
Pastry (N=14)	254 (180–457)	14 (100)	156 (97–247)	36	14 (100)	180 (180–180)	29
Pie (N=48)	159 (14–330)	42 (88)	125 (9–232)	47	46 (96)	14 (14–14)	90
Condiments and sauces							
Sauces <10% fat (N=16)	717 (61–1300)	15 (94)	350 (2–650)	52	12 (75)	434 (61–1300)	17
Sauces >10% fat (N=25)	672 (61–1075)	25 (100)	320 (3–1825)	50	23 (92)	330 (61–880)	59
Meal sauces -prepared (N=71)	268 (0.6–1366)	57 (80)	226 (12–683)	52	70 (99)	1.8 (1.8–790)	92
Soups, bouillon							
Soups (N=29)	337 (0–505)	27 (93)	171 (129–253)	50	29 (100)	272 (10–272)	19

Abbreviations: max, maximum; min, minimum.

[a] Food (sub)groups represent food groups that contribute most to sodium intake from processed foods. Other food groups were also assessed, but are not reported here.

[b] Percentage reduction is the median value of the percentage reduction that is obtained by the reduction of each individual food item.

[c] Median and range are foods that could have reduced sodium levels or could be substituted.

Table 2.2 Sodium intake from processed foods in present diet, in technological feasible scenario and in substitution scenario among consumers

		Current sodium intake	Sodium reduction in processed foods scenario		Substitution processed foods scenario	
	Consumers	Sodium intake (mg/d)[a]	Sodium intake (mg/d)[a]	Median reduction[b]	Sodium intake (mg/d)[a]	Median reduction[b]
	%	P50 (P25–P75)	P50 (P25–P75)	%	P50 (P25–P75)	%
Vegetables						
Canned vegetables	40	67 (24–139)	35 (13–65)	48	9 (3–21)	87
Dairy products						
Hard cheese	73	241 (142–393)	120 (65–193)	50	126 (75–207)	48
Soft cheese	18	69 (35–140)	35 (15–83)	49	25 (12–44)	64
Cream cheese	8	162 (108–270)	54 (27–88)	67	35 (23–53)	78
Cereals and cereal products						
Bread	99	651 (450–887)	332 (230–447)	49	370 (259–508)	43
Bread substitutes	33	48 (24–85)	23 (10–44)	52	24 (12–38)	50
Breakfast cereals	20	20 (6–71)	14 (6–38)	30	3 (2–4)	85
Meat and meat products						
Processed meat	75	173 (94–293)	66 (38–124)	62	112 (68–211)	35
Meat substitutes	3	197 (122–345)	138 (73–190)	30	3 (2–3)	98
Fat						
Low-fat margarine	57	17 (6–35)	9 (3–17)	47	0 (0–0)	100
Margarine	40	15 (5–31)	6 (2–12)	60	0 (0–0)	100
Cooking fat	46	8 (2–22)	4 (1–10)	50	0 (0–0)	100

Table 2.2 continues on next page

Table 2.2 ***Continued***

		Current sodium intake	Sodium reduction in processed foods scenario		Substitution processed foods scenario	
	Consumers	Sodium intake (mg/d)[a]	Sodium intake (mg/d)[a]	Median reduction[b]	Sodium intake (mg/d)[a]	Median reduction[b]
	%	P50 (P25–P75)	P50 (P25–P75)	%	P50 (P25–P75)	%
Snacks						
Savory snacks	20	235 (190–360)	193 (135–276)	18	51 (34–73)	78
Chips	41	147 (77–264)	85 (38–159)	42	1 (0–1)	99
Cakes and pies						
Cakes	12	65 (13–133)	30 (23–61)	54	11 (8–18)	83
Biscuits	66	55 (30–95)	30 (18–55)	45	3 (2–6)	95
Pastry	23	57 (29–77)	34 (16–45)	40	38 (16–54)	33
Pie	29	69 (33–122)	58 (27–87)	16	7 (5–10)	90
Condiments and sauces						
Sauces <10% fat	31	58 (30–113)	32 (16–63)	45	27 (13–59)	53
Sauces >10% fat	54	64 (28–118)	31 (12–61)	52	25 (9–58)	61
Meal sauces - prepared	52	93 (38–218)	59 (23–123)	37	15 (0–119)	84
Soups, bouillon						
Soups	27	505 (350–739)	283 (175–459)	44	429 (227–618)	15

[a] Mean of two observation days.
[b] Median reduction is the median value of the reduction in sodium intake of all participants in the DNFCS 2007–2010.

Table 2.3 Daily sodium and energy intake from processed foods in present diet, technologically feasible sodium reduction scenario and substitution scenario

	Current sodium intake		Sodium reduction in processed foods scenario			Substitution processed foods scenario		
	Sodium intake (mg/d) [a]	Energy intake (MJ/d)	Sodium intake (mg/d) [a]	Reduction in median sodium intake [b]	Energy intake (MJ/d)	Sodium intake (mg/d) [a]	Reduction in median sodium intake [b]	Energy intake (MJ/d)
	P50 (P25–P75)	P50 (P25–P75)	P50 (P25–P75)	%	P50 (P25–P75)	P50 (P25–P75)	%	P50 (P25–P75)
Boys 7–18y (N=856)	2,544 (2,000–3,214)	9.6 (8.0–11.4)	1,635 (1,295–2,071)	36	9.6 (8.0–11.4)	1,319 (1,008–1,678)	48	10.0 (8.5–12.1)
Girls 7–18y (N=857)	2,194 (1,778–2,632)	8.3 (7.2–9.5)	1,392 (1,153–1,693)	37	8.3 (7.2–9.5)	1,096 (882–1,392)	50	8.9 (7.5–10.1)
Men 19–69y (N=1,055)	3,042 (2,419–3,718)	10.7 (8.9–12.9)	1,886 (1,468–2,348)	38	10.7 (8.9–12.9)	1,627 (1,264–2,060)	47	11.4 (9.5–13.6)
Women 19–69y (N=10,51)	2,286 (1,806–2,877)	7.9 (6.6–9.6)	1,449 (1,138–1,779)	37	7.9 (6.6–9.6)	1,215 (934–1,542)	47	8.7 (7.3–10.4)

[a] Mean of two observation days.

[b] Percentage reduction between the median current sodium intake (P50) and the median sodium intake (P50) in the processed foods scenario and the substitution scenario.

Daily sodium intake

Median sodium intake from all foods was 3,042 mg/d in men aged 19–69y and 2,286 mg/d in women aged 19–69y in the current situation (**Table 2.3**). Children and adolescents had a sodium intake of 2,544 mg/d (boys) and 2,194 mg/d (girls). When sodium levels were reduced towards the lowest technological feasible levels, median sodium intake was reduced by 36% in boys, 37% in girls, 38% in men, and 37% in women. In the substitution scenario the sodium intake was reduced even further by 48% in boys, 50% in girls and 47% in both men and women.

The median energy intake increased by 700 kJ for adult men and 800 kJ for adult women in the substitution scenario, which is a 6% and 9% increase compared with the reference energy intake (P50 = 10.7 MJ for men and 7.9 MJ for women (**Table 2.3**)). In the sodium reduction scenario, no changes in energy intake are to be expected, as food consumption remains the same and only the sodium content is modulated.

Discussion

It was estimated that the level of sodium chloride in processed foods can be reduced by 50% in most food groups in the Netherlands. This simulation study shows that such reduction will lead to a 38% lower sodium intake compared with the current overall sodium intake from foods. In most food groups low-sodium alternatives are available and substituting processed foods by their low-sodium alternatives will result in a sodium intake reduction from foods of 47%. The potential for sodium intake reduction varies widely between food groups (15%–100%).

Data used in the present study reflects current Dutch food consumption patterns and composition of currently available foods together with up-to-date sodium levels. This detailed information enables us to distinguish several sources of sodium intake, and to examine the shift in sodium intake in hypothetical situations. However, we had to make some assumptions to estimate the impact on sodium intake reduction for both scenarios. In the substitution scenario, selection of appropriate low-sodium alternatives in pre-defined food groups may be arbitrary. Low-sodium alternatives may be rather extreme alternatives, although selected products are existing and commonly available. In addition, replacing all foods within a (sub) food group by a single low-sodium alternative is not likely to happen in real life. Food choices are influenced by many motives, like taste, price and habitual behaviour (16; 17; 18). Changing

consumer behaviour may intervene at different levels and is challenging. Therefore, the sodium intake reduction observed in the substitution processed foods scenario should be considered as the maximal change in salt intake that can be achieved by currently available foods.

We classified foods in various food (sub)groups, but even within those groups, foods may substantially differ in terms of use or composition. For example all breakfast cereals like cornflakes were replaced by muesli. Muesli is relatively slightly processed food and contains only cereals, nuts and dried fruit, without added salt. The selected low-sodium alternative muesli has a much lower sodium level than could ever be achieved by technological modifications of cornflakes. Therefore, the substitution processed foods scenario has much more potential in sodium reduction compared with technological modifications. To make the simulation as realistic as possible we have limited the alternatives to common food products which are comparable to the original foods in the (sub)group.

In the sodium reduction processed foods scenario, sodium reduction was based on what is expected to be the lowest feasible sodium level within five year. We considered the microbiological safety and technological aspects of sodium reduction in the assessment of the minimal technological feasible level. However, technological feasible adaptations like a shorter shelf-life, adjusted product formulation and processing conditions which can be realized by the food industry in the near future are needed. For example in cold cuts, sodium replacement level is estimated by replacing sodium salts by alternative minerals and the minimal sodium level is estimated by limits of sensory acceptability. Other industrial relevant factors like cost and yield were not considered. The technological feasible levels presented here are substantially higher than the voluntary levels of reduction in the current sodium reduction initiative in the Netherlands. In this , the food industry choose for a more stepwise approach (11). So, in more recent sodium reduction initiatives the food industry has increased its voluntary levels of salt reduction, although they are not yet close to the technologically feasible levels. The level of reduction may compromise taste perception, and an immediate reduction in sodium in processed foods may lead to rejection of the product. However, gradually adjustment of sodium levels over time will conceal changes in taste, as observed by a study where substantial sodium reduction of 52% did not lead to lower consumption of bread as compared with a control group (19).

We observed a large variation in sodium levels within food groups and within the current food consumption pattern. The availability of many low-sodium alternatives make alterations of food consumption patterns an essential strategy to reduce sodium intake. In certain food

groups, the narrow range in sodium levels indicates that sodium reduction of those foods will be essential compared to appealing to consumer behaviour. In food groups such as bread, sauces, soups and processed meats, sodium reduction seems inevitable, as there are hardly any low-sodium alternatives. In other food groups, such as cheese, technological challenges or regulations cause the narrow range of sodium levels. Furthermore, a link between sodium and fat content of foods is apparent. In particular in the (sub)groups meat, pastry and soups, the low sodium alternatives have a relative high fat content. This can also explain the higher energy intake as a negative side effect of this salt reduction strategy.

Sodium intake estimates in the present analyses are based on intake from foods and does not include the salt that is added during cooking at home, in restaurants and by caterers, or at the table. Consequently, estimates of total sodium intake will be higher than estimated intake from foods in the present study. Average discretionary salt use is estimated to be 800 mg/d in adults (20). In the current situation, median sodium intake from processed foods do already exceed the recommended intake of 2,400 mg sodium for boys and men (21), but is slightly lower for girls and women. However, median sodium intake including discretionary salt will exceed the recommendation. In both scenarios median salt intake from processed foods is below 2,400 mg sodium. In the sodium reduction scenario, additional discretionary salt use will not exceed the recommended intake in both men and women, but in the substitution scenario, median total salt intake will be close to the recommended intake in men. An important additional strategy will be to reduce the level of discretionary salt, not only at home, but also for meals that are eaten in restaurants or at caterers. These sectors are included in the present agreement of salt reduction as well (11). Monitoring their sodium use will be essential.

The advantage of sodium reduction in processed foods is that consumers do not have to modify their habitual dietary food pattern (22). Experiences from the UK show that sodium reductions in certain food groups of 20 to 30%, and in some other product groups even up to 70%, have been achieved over the period 2001–2011 (23). Unfortunately, sodium reduction did not take place in all food groups, and not all foods within a food group were sodium-reduced. As a consequence, these actions led to an overall sodium reduction in the UK of 15% over this ten-year period (9). Sodium intake remained above the recommended intake. In our best-case simulation, sodium levels should decrease by on average 50% in *all* processed foods to arrive at a sodium intake below the recommended intake. Comparison between the real-life intervention in the UK and our simulation study show that major efforts from the food industry are needed.

Excessive salt intake is an important risk factor for high blood pressure and subsequently for cardiovascular diseases. Reducing salt intake is considered an important strategy to reduce the burden of disease related to cardiovascular disease. Substantial changes in food intake by intentionally choosing low-salt alternatives may lead to a sodium intake reduction of 48%, and reducing sodium levels in processed foods towards their minimal technological feasible sodium levels may lower the sodium intake by 37%. The changes are substantial and may contribute to a median sodium intake from processed foods below the recommended intake.

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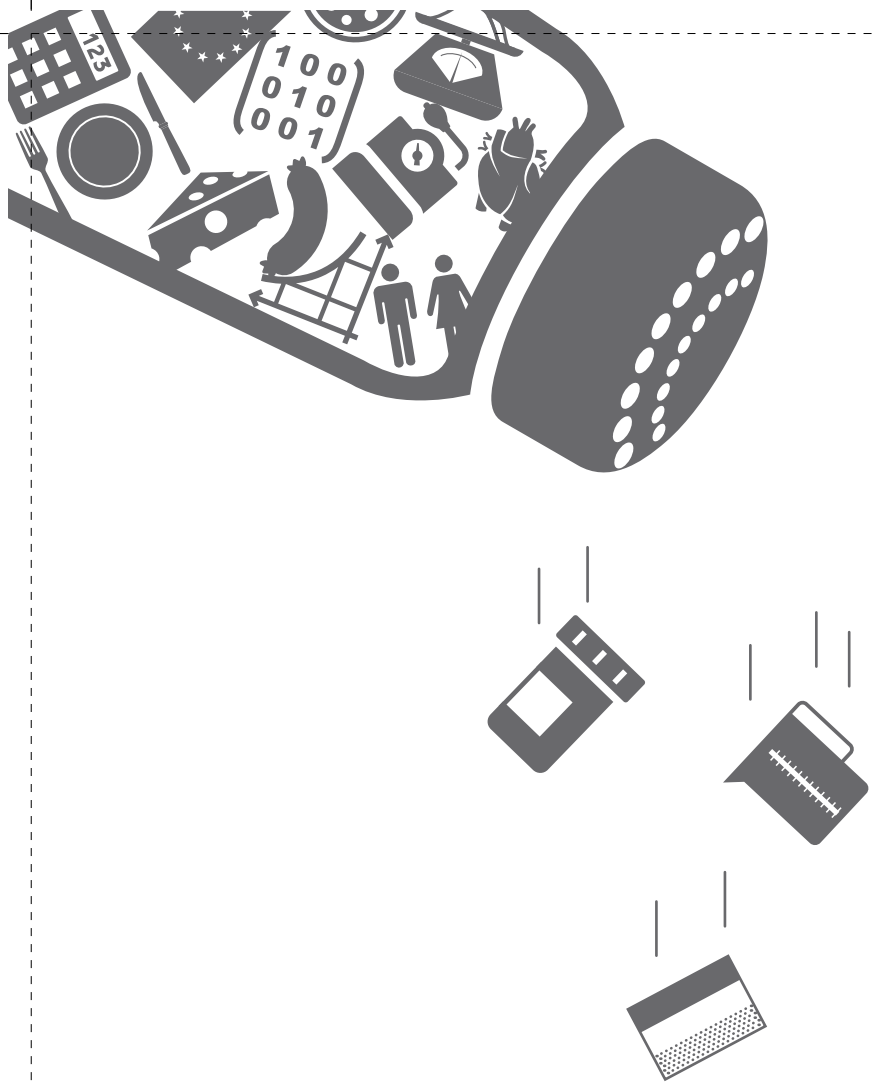

Chapter 3

Monitoring salt and iodine intakes in Dutch adults between 2006 and 2010 using 24h urinary sodium and iodine excretions

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Published in Public Health Nutrition, 2014 Jul;17(7): 1431-8
Doi 10.1017/s1368980013001481

Abstract

Objective: To monitor the effectiveness of salt reduction initiatives in processed foods and changes in Dutch iodine policy on sodium and iodine intake in Dutch adults between 2006 and 2010.

Design: Two cross-sectional studies, among adults living in Doetinchem, the Netherlands, conducted in 2006 and 2010 using identical protocols. Participants collected single 24h urine samples and completed two short questionnaires on food consumption and urine collection procedures. Daily intakes of salt, iodine, potassium and sodium-to-potassium ratio were estimated, based on the analysis of sodium, potassium and iodine excreted in urine.

Setting: Doetinchem, the Netherlands.

Subjects: Men and women aged 19 to 70 years were recruited through random sampling of the Doetinchem population, and among participants of the Doetinchem Cohort Study (2006: n=317, mean age 48.9y, 43% men; 2010 n=342, mean age 46.2y, 45% men).

Results: While median iodine intake was lower in 2010 (179 µg/d) compared to 2006 (257 µg/d; $p<0.0001$), no difference in median salt intake was observed (8.7 g/d in 2006 versus 8.5 g/d in 2010, $p=0.70$). In 2006, median potassium intake was 3.0 g/d against 3.2 g/d in 2010 ($p<0.01$). In this 4-year period, median sodium-to-potassium ratio improved from 2.4 in 2006 to 2.2 in 2010 ($p<0.001$).

Conclusions: Despite initiatives to lower salt in processed foods, dietary salt intake in this population remains well above the recommended intake of 6 grams per day. Iodine intake is still adequate, although a decline was observed between 2006 and 2010. This reduction is probably due to changes in iodine policy.

Introduction

High salt intake is considered an important contributor to the burden of cardiovascular diseases worldwide (1). A high salt intake is associated with hypertension, which in turn can increase the risk of cardiovascular disease (2; 3). Furthermore, a low potassium intake and especially a high sodium-to-potassium ratio have also been associated with higher blood pressure levels and increased incidence of cardiovascular disease (4).

Many countries have initiated salt reduction strategies in order to reduce the population's salt intake (5). In 2006 the Health Council of the Netherlands published Dutch guidelines for a healthy diet, advising a reduction in salt consumption to less than 6 grams per day (6). At that time little was known about Dutch salt intake, apart from a 24h sodium excretion study among 190 Dutch participants of the EPIC calibration study. This study, conducted between 1995 and 1997, observed a salt intake of 9.8 g/d (7). The Health Council of the Netherlands concluded that a reduction of salt intake towards the realisable target of 6 g/d could only be achieved if sodium levels in commercially prepared foods would be reduced. As a response, the Federation of the Dutch Food and Grocery Industry (FNLI) initiated a Taskforce Salt to reduce the level of sodium in processed foods. Their target in 2006 was to reduce sodium concentrations in certain categories of processed foods by 12% by 2010.

An insufficient iodine intake may result in hypothyroidism (8). The estimated average requirement for adults is 95 μg/d (9). Iodine levels naturally present in the Dutch diet are not adequate (10). Since 1999, iodised salt has been permitted in a restricted number of processed foods (bread and bread substitutes (70–85 mg I/kg salt), processed meat (20–30 mg I/kg salt) or table salt (30–40 mg I/kg salt)) to prevent iodine-deficiency disorder. In 2008, the iodine intake of the Dutch population was considered adequate (10). The Dutch iodine policy was evaluated in anticipation of changes in European food legislation. Simulations showed that the upper level of iodine intake could be exceeded if the number of food groups to which iodised salt was added was extended, using similar maximum levels of iodine fortification as in bread or bread substitutes, processed meat or table salt (11). In these simulations it was assumed that 50% of the processed foods would contain iodised salt. Additional analyses showed that the iodine content of iodised salt in bread and bread substitutes of maximal 65 mg I/kg salt, as well as maximal 25 mg I/kg salt in other processed foods of would be most optimal, and the iodine fortification policy was changed accordingly (12). Reduction of (iodised) salt in processed foods may also affect iodine intake. Subsequent monitoring of iodine intake is thus important in view of identifying potential iodine deficiencies (13).

Salt and iodine intake cannot be precisely quantified using food consumption survey data, as the amount of (iodised) discretionary salt is difficult to quantify. Moreover, limited information is available on the presence of iodised salt in Dutch processed foods. The preferred method to estimate salt and iodine intake is by 24h urine collections (14).

The aim of the present study was to evaluate the effectiveness of salt reduction efforts and changes in iodine policy in a Dutch population between 2006 and 2010 by monitoring salt and iodine intake using 24h urinary excretions of sodium and iodine.

Methods

Design and participants

In 2006 and 2010, monitoring surveys were carried out among adults aged 19–70 years in Doetinchem, a town in the eastern part of the Netherlands. In both surveys half of the study population were recruited from individuals (aged 35–70 years) participating in an ongoing long-term monitoring study on chronic disease risk factors (the Doetinchem Cohort Study (DCS)) and half of the participants were randomly drawn from the municipal register of Doetinchem (General Doetinchem Population Sample (GDPS)) (aged 19–45 years). As the DCS has aged, most participants were over 35 years at the time of sampling for the surveys. In order to cover the whole age range of interest (19–70 years) younger participants (19–45 years) were recruited from a random sample of the general population. Those participating in 2006 were not invited to take part in the 2010 survey in order to obtain independent samples. Pregnant women and people suffering from renal diseases were excluded from participation.

In 2006, a total number of 840 individuals were invited to participate (n=400 from DCS and n=440 from GDPS). Positive response rate was 68% among DCS participants and 19% among individuals from the GDPS. In total, 333 individuals completed the study in 2006 (n=251 (63%) from DCS and n=82 (19%) from GDPS). In 2010, 1,686 individuals were invited (n=334 from DCS and n=1,352 from GDPS, with positive response rates of 69% (n=229) and 15% (n=208) respectively). 61% (n=205) of DCS members and 11% (n=152) individuals from GDPS completed the study in 2010 (in total n=357 individuals).

This study was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving participants were approved by the Medical Ethics Committee of the University Medical Centre Utrecht. Written informed consent was obtained from all participants.

24h urine collections

Single 24h urine collection took place in November 2006 and 2010 using identical protocols and procedures. Samples were collected on specified days (weekdays and weekends). Detailed written and oral instructions were given on how to collect the 24h urine sample. Participants were asked to discard their first morning urine void, and then collect all urine in collection jars voided over the following 24 hours up and including the first morning urine void the next day. Participants recorded the time of start and finish of urine collection, as well as the completeness of the collection in a diary. Specimens were stored in a cool place (e.g. refrigerator or cellar) until delivery to the Municipal Health Service the following day, where specimens were processed and stored in 15 mL aliquots at -80°C. Upon collection of the jars research assistants verified the collection procedure and measured the volume of the 24h urine sample.

Questionnaires

A short self-reported, semi-structured questionnaire was administered to collect data on smoking status, educational level (in the 2010 survey only), use of medication and food supplements. Upon collection of the jars, research assistants verified any uncertainty or inconsistency of reported answers with participants. The use of discretionary salt (yes or no) in the week before collection was assessed, as well as whether or not this salt was iodised. Recorded dietary supplements were checked for iodine and sodium content in the Dutch Supplement Database (15). Participants were classified as having diabetes, suffering from thyroid disorders or taking diuretics, based on their medication use.

Laboratory analyses

In 2006 and 2010, urinary sodium and potassium concentration (mmol/L) was determined in each specimen by indirect potentiometry using the Synchron LX system (mean inter-assay CV 1.1% for sodium and 1.8% for potassium (2006) and 1.3% for potassium and 0.9% for sodium (2010)) (16). In 2006, urinary iodine concentration (nmol/L) was determined in a microtiterplate format using ammonium persulfate digestion (17) based on the Sandell-Kolthoff reaction (mean inter-assay CV of 6%) (18). In 2010, iodine concentration (nmol/L) was determined by ammonium persulfate digestion in a PCR system followed by the Sandell-Kolthoff reaction in a microtiterplate format (mean total assay CV of 16%). In 2010, the

lowest validated level was 45 μg/L, so samples with an iodine value below 45 μg/L (n=62) were set to 45 μg/L. In order to exclude extreme incomplete 24h urine samples, creatinine concentration (mmol/L) was measured by the Jaffé method using the Synchron LX system (mean inter-assay CV is 2.9% in 2006 and 1.8% in 2010) (19).

Estimation of 24h urinary excretion and intake

Multiplying the sodium, potassium and creatinine concentration levels (mmol/L) by the total volume of urine (L) resulted in the sodium, potassium and creatinine excretions in mmol/d. Excretion in g/d was calculated by multiplying the molar mass (sodium = 23 g/mol; potassium = 39 g/mol and creatinine = 113 g/mol) with the excretion in mmol/d divided by 1000. Sodium-to-potassium molar ratio was expressed by dividing the sodium concentration (mmol/L) by the potassium concentration (mmol/L). Iodine excretion over a 24h period (μg/d) was determined by multiplying the iodine concentration in nmol/L with the molar mass of iodine (126 g/mol) times 1000 and the total volume of the urine specimen (in L).

Intake of sodium, iodine and potassium was calculated by multiplying the excretion with the factor 100/95, 100/92 and 100/77 respectively, reflecting the estimated proportions of intake that are excreted via urine (20). Sodium intake was converted to salt intake by multiplication with factor 2.54.

Statistical analyses

Participants were excluded from statistical analyses for the following reasons: unknown urine volume (2006 n=2 and 2010 n=1), extreme incomplete urine collection (based on creatinine excretion ≤5.0 mmol/d, or ≤6.0 mmol/d together with a urine volume of <1L (21) (2006 n=10 and 2010 n=0) and missing or overcollection of more than one urine void (2006 n=4 and 2010 n=14). The final study population included 317 participants in 2006 and 342 participants in 2010.

The normality of the data was verified with the Kolmogorov-Smirnov test. The distributions of continuous variables were characterised by means ± SD for normally distributed data and by medians (P50), P25 and P75 (inter quartile range (IQR)), for non-normally distributed data. Differences in salt and iodine intake between 2006 and 2010 were assessed by the Mann-Whitney test, with significance set at $p<0.05$ (2-sided). Pearson correlation coefficients were calculated to examine the associations between salt intake and iodine or potassium intake,

and adjusted for 24h urine creatinine excretion and sex. All analyses were performed using SAS version 9.2 (SAS Institute INC, Cary, NC, USA).

Results

General characteristics

The participants in 2010 were slightly younger (46.2 (SD 14.5 y)) than in 2006 (48.9 (SD 14.0 y)) (p=0.02). The proportion of men, smokers, users of dietary supplements and participants taking medication was similar in both surveys (**Table 3.1**). In 2006, the proportion of participants who reported discretionary salt use was statistically significantly higher compared to 2010 (88% vs. 81% respectively, p=0.009) (**Table 3.1**).

Mean urinary volume collected over 24 hours was 2,292 ml in 2006 and 1,977 ml in 2010. Mean 24h urinary creatinine excretion was lower in 2006 compared with 2010 (10.3 mmol/d vs. 12.0 mmol/d, p<0.0001).

Sodium excretion and estimated sodium and salt intake

In 2006, median 24h urinary sodium excretion was almost similar to that in 2010; 141 mmol/d (IQR 109 to 179 mmol/d) and 139 mmol/d (IQR 107 to 178 mmol/d) respectively (p=0.75; **Table 3.2**). Median salt intake was estimated to be 8.7 g/d (IQR 6.7 to 11.0 g/d) in 2006 and 8.5 g/d (IQR 6.6 to 10.9 g/d) in 2010 (**Figure 3.1**).

In 2006 and 2010, the median sodium excretion from participants who reported using discretionary salt in the week before urine collection were almost similar to that of participants who did not use discretionary salt (P50 141 mmol/d vs 148 mmol/d in 2006 (p=0.79) and 139 mmol/d vs 137 mmol/d in 2010 (p=0.88)). Exclusion of participants taking diabetes medication (2006 (n=6), 2010 (n=8)) or diuretics (2006 (n=20), 2010 (n=24)) did not affect median sodium excretions (data not shown).

Median potassium intake increased from 3.0 g/d (IQR 2.4 to 2.7 g/d) in 2006 to 3.2 g/d (IQR 2.7 to 4.0 g/d) in 2010 (p=0.0005). Sodium-to-potassium ratio improved over this period (2.4 vs. 2.2, **Table 3.2**; p=0.0001). Potassium intake was weakly correlated with sodium intake (2006 r=0.19; 2010 r=0.21).

Table 3.1 General characteristics of the study population from Doetinchem, the Netherlands, in 2006 and 2010

	2006 (n=317)						2010 (n=342)								
	Overall		Men		Women		Overall			Men			Women		
	Mean or n	SD or %	Mean or n	SD or %	Mean or n	SD or %	Mean or n	SD or %	p-value*	Mean or n	SD or %	p-value	Mean or n	SD or %	p-value
Age (year)	48.9	14.0	51.2	13.7	47.1	14.2	46.2	14.5	0.02	47.0	14.8	0.02	45.6	14.2	
Sex	-	-	137	43	180	57	-	-	-	154	45	0.32	188	55	0.68
Educational level†									-			-			-
Low	-	-	-	-	-	-	62	18		36	23		26	14	
Middle	-	-	-	-	-	-	175	51		70	46		105	56	
High	-	-	-	-	-	-	99	29		46	30		53	28	
Other	-	-	-	-	-	-	5	1		2	1		3	2	
Smoking status									0.60			0.04			0.08
Current	59	19	25	18	34	19	52	15		28	18		24	13	
Occasional	15	5	6	4	9	5	16	5		11	7		5	3	
Former	121	38	62	45	59	33	129	38		46	30		83	44	
Non smoker	121	38	44	32	77	43	145	42		69	45		76	40	

Table 3.1 continues on next page

Table 3.1 ***Continued***

	2006 (n=317)						2010 (n=342)								
	Overall		Men		Women		Overall			Men			Women		
	Mean or n	SD or %	Mean or n	SD or %	Mean or n	SD	Mean or n	SD or %	p-value*	Mean or n	SD or %	p-value	Mean or n	SD or %	p-value
Use of dietary supplements															
Sodium-containing	14	4	3	2	11	6	4	1	0.01	2	1	0.56	2	1	0.01
Iodine-containing	61	19	18	13	43	24	51	15	0.14	23	15	0.66	28	15	0.03
Medication use															
Diabetes	6	2	4	3	2	1	8	2	0.69	3	2	0.58	5	3	0.28
Blood pressure (diuretics)	20	6	9	7	11	6	24	7	0.71	10	6	0.98	14	7	0.61
Disorders of thyroid gland	7	2	1	<1	6	3	9	3	0.72	0	0	0.28	9	5	0.48
Use of discretionary salt															
All users	280	88	121	88	159	88	277	81	0.009	116	75	0.04	161	86	0.44
Users who use iodised salt	212	76	96	79	116	73	206	74	0.71	79	68	0.05	127	79	0.22

Data for age expressed as mean and standard deviation; data for all other variables presented as number and percentage. * p-values are from comparable group in 2006; †Educational level was defined as low (primary school, lower vocational, low or intermediate general education), middle (intermediate vocational education and higher general education), high (higher vocational education and university) and other (not defined).

Table 3.2 Sodium, potassium and iodine excretions based on 24h urine collections in Doetinchem, the Netherlands in 2006 and 2010

	Overall						Men						Women					
	N	Mean	SD	P50	P25–P75	p-value*	N	Mean	SD	P50	P25–P75	p-value*	N	Mean	SD	P50	P25–P75	p-value*
Sodium excretion (mmol/d)																		
2006	317	148	55	141	109–179		137	164	55	160	117–206		180	136	51	128	101–159	
2010	342	148	58	139	107–178	0.75	154	174	63	163	126–212	0.24	188	128	43	122	96–154	0.11
Potassium excretion (mmol/d)																		
2006	317	62	23	59	47–74		137	70	26	69	54–82		180	57	18	55	43–66	
2010	342	68	23	64	53–79	0.0005	154	76	26	72	58–89	0.008	188	61	18	60	50–71	0.03
Sodium/potassium ratio																		
2006	317	2.5	0.9	2.4	1.9–3.1		137	2.5	0.9	2.3	1.9–3.0		180	2.5	0.9	2.5	1.9–3.1	
2010	342	2.3	0.9	2.2	1.7–2.7	<0.0001	154	2.4	0.9	2.3	1.9–2.8	0.14	188	2.2	0.9	2.1	1.6–2.5	<0.0001
Iodine excretion (µg/d)																		
2006	317	265	150	236	165–313		137	295	163	265	203–332		180	245	137	210	148–300	
2010	342	183	91	165	119–227	<0.0001	154	216	106	202	136–270	<0.0001	188	157	65	147	108–193	<0.0001

P50, 50th percentile (median); P25–P75, 25th–75th percentile (Interquartile range). * p-values are from comparable group in 2006.

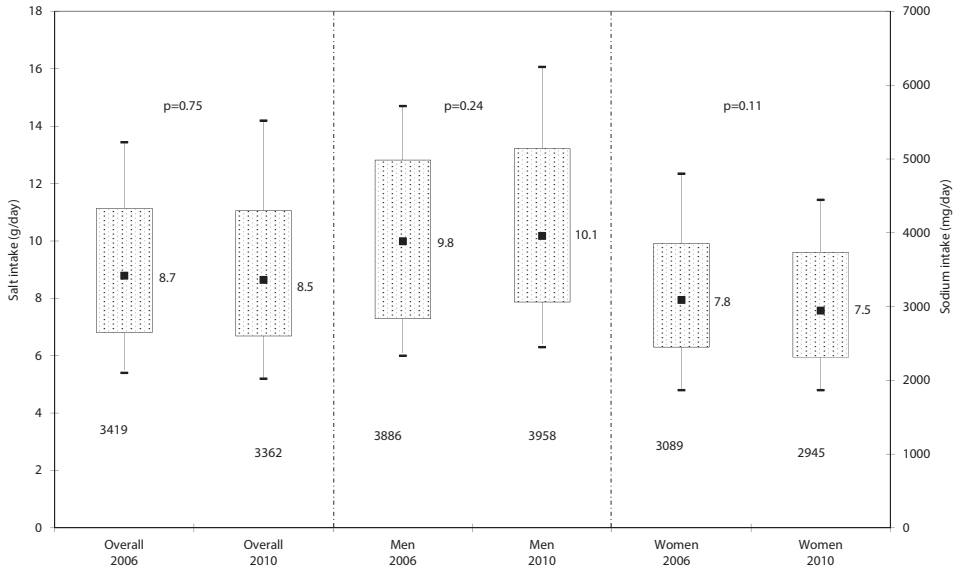

Figure 3.1 Sodium and salt intake distributions in 2006 and 2010 as estimated from 24 h urinary sodium excretions in Doetinchem, the Netherlands; overall and according to sex.
Box-and-whisker plots in which the bottom and top whiskers represent the 10th and 90th percentile (P10 and P90), respectively; the bottom and top of the box represent the 25th and 75th percentile (P25 and P75; interquartile range), respectively; and ■ represents the 50th percentile (P50; median). Numbers beneath each box are the median sodium intake.

Iodine excretion and estimated iodine intake

Median iodine excretion declined significantly from 2006 to 2010 (236 µg/d (IQR 165 to 313 µg/d) in 2006 and 165 µg/d (IQR 119 to 227 µg/d) in 2010, p<0.0001). These excretion levels correspond to estimated iodine intakes of 257 µg/d and 179 µg/d respectively (**Figure 3.2**). Iodine intake was weakly correlated with salt intake (2006 r=0.36; 2010 r=0.30).

In 2006, participants who reported using iodised discretionary salt showed a higher iodine excretion (P50 248 µg/d) than those who did not (P50 220 µg/d; p=0.01). In 2010, iodine excretion was not statistically different between users (P50 172 µg/d) and non-users of iodised discretionary salt (163 µg/d; p=0.45). Exclusion of participants taking thyroid medication (2006 (n=7), 2010 (n=9)) did not affect median iodine excretions.

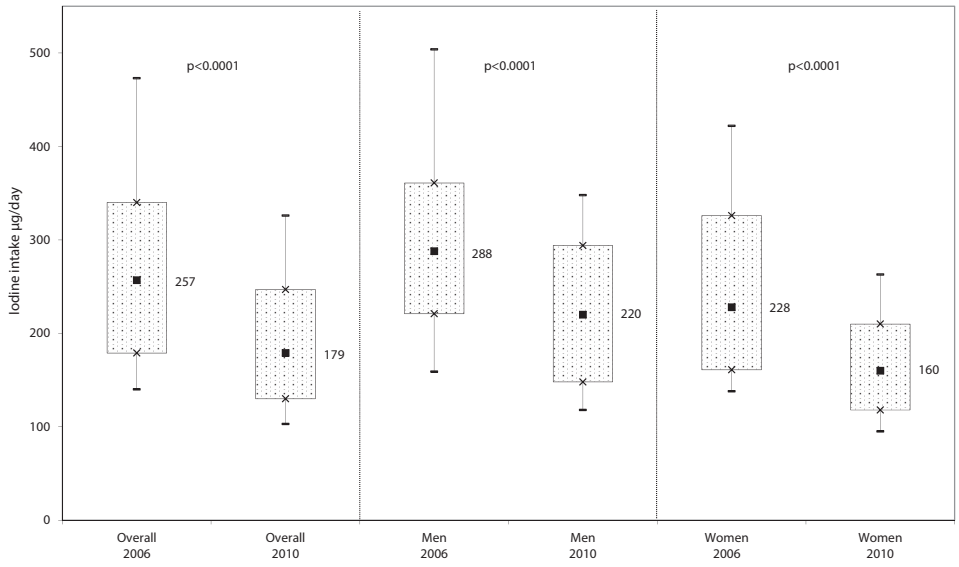

Figure 3.2 Iodine intake distribution in 2006 and 2010 as estimated from 24 h urinary sodium excretions in Doetinchem, the Netherlands; overall and according to sex.
Box-and-whisker plots in which the bottom and top whiskers represent the 10th and 90th percentile (P10 and P90), respectively; the bottom and top of the box represent the 25th and 75th percentile (P25 and P75; interquartile range), respectively; and ■ represents the 50th percentile (P50; median).

Discussion

This monitoring study conducted in 2006 and 2010 among two independent samples of adults living in Doetinchem, the Netherlands, shows that salt intake has not changed over this 4-year period (8.7 vs. 8.5 g/d) and still exceeds the recommended maximum intake of 6 grams per day. Sodium-to-potassium ratio improved over this period due to a higher potassium intake in 2010 compared with 2006. Iodine intake was significantly lower in 2010 compared with 2006, but may still be considered adequate as compared to the estimated average requirement of 95 µg/d (9).

In 2006, the Dutch food industry initiated sodium reduction in food on a voluntary basis. After four years, they reported a 10% sodium reduction in processed foods compared with 2006 (22). We did not observe a decline in salt intake over this period in this monitoring survey, suggesting that the actions of the Dutch food industry did not result in a significant reduction in salt intake at the population level. Power calculations showed that we had sufficient power to detect a difference of at least 8% in daily salt intake in the total population between 2006 and 2010. However, we observed a non-significant difference of only 2% in

total salt intake. This is in line with recent data from the Dutch Food Safety Authority. They monitored the sodium content in certain categories of processed foods in 2009, 2010 and 2011 and did not observe a reduction in sodium content (23). We were unable to detect any change in salt intake over this period. This may be explained by the fact that not all food producers have yet reduced sodium content in their processed foods, or not all industry associations have committed themselves to sodium reduction in processed foods. Sodium reduction may also be achieved by substituting sodium chloride by potassium chloride. Although we observed an increase in potassium intake we did not see a simultaneous decrease in sodium intake, suggesting that higher intakes of potassium in 2010 are likely to be explained by other factors, such as an increase in consumption of potassium-rich foods.

In the UK, reductions in sodium levels of up to 70% in certain processed foods led to a decrease in the average salt intake from 9.5 g/d in 2000–2001 to 8.6 g/d in 2008 (24) and to 8.1 g/d in 2011 (25). This shows that substantial sodium reduction in processed foods is needed if a relevant salt intake reduction is to be achieved.

The present monitoring study showed a substantial reduction in iodine intake from 2006 (257 µg/d) to 2010 (179 µg/d). This may be because iodised salt was not used in processed foods other than bread. A simulation study estimating the optimal fortification levels assumed that 50% of the processed foods would contain iodised salt. However, an inventory conducted in 2012 showed that very few foods other than bread contained iodised salt (26). While the maximum fortification level of iodised salt in bread was reduced, the use of iodised salt in processed foods was not extended. These results substantiate our conclusion that reduced iodine intake observed in the present study is likely due to the reduced iodine levels in bread and because of the limited use of iodised salt in processed foods. It could also be that the reported sodium reduction in bread has led to lower iodine intake, as bread is an important source of iodine. Therefore, monitoring the use of iodised salt in foods, as well as monitoring iodine intake, is important when evaluating the implementation of new iodine regulations, since further reductions of sodium levels in processed foods are foreseen (26).

Iodine fortification regulations differ across European countries. In the UK for example, iodine intake is ensured through iodine-rich artificial feed for cattle and the subsequent encouragement of milk consumption (27). Iodised salt is rarely available in the UK (28). In contrast, Denmark has a mandatory iodine fortification programme of bread salt and household salt where, after implementation of this programme in 2000, iodine excretion increased substantially from 94 µg/d in 1997–1998 to 145 µg/d in 2004–2005 (29). Obviously,

salt reduction strategies in different countries will influence iodine intake differently and monitoring of iodine intake should be considered when iodised salt is used in processed foods.

A strength of this study is that we used the preferred method to estimate the salt and iodine intakes on a population level. The current study design was adequate to examine trends in median salt and iodine intake, because intakes were assessed in two independent samples from the same source population. General characteristics of the two surveys were highly comparable. Furthermore, power calculations showed that the number of participants in both samples was sufficient to observe a 10% change in salt intake for men and women separately, and a difference of 8% for the total population.

A limitation of our study is that we did not have a reliable method to assess the completeness of 24h urine collections, by using PABA tablets (20). However, a recent study showed that in a population-based monitoring study estimates of potassium excretion were very similar regardless of whether or not a PABA check was taken into account (30). As an alternative strategy to control for incomplete urine collections, we excluded participants with extreme creatinine levels in combination with a low 24h urine volume for normal weight adults (21). However, the usefulness of creatinine as a check on the completeness of 24h urine collections has been widely debated (31; 32), particularly without information on body weight as in the present study. In order to identify incomplete 24h urine collections, particular attention was paid by trained researchers to start and end times of urine collections to identify over- or under collection.

Other limitations relate to the comparability of our findings to the general Dutch population. Participants were sampled from a single Dutch town and half of the study population was recruited from a large ongoing monitoring study. In addition, the high burden on study volunteers may affect the participation rate (14). Compared with the general population, participants in the study were more highly educated and were more likely to be non-smokers (33). Since these individuals since to have healthier dietary patterns, the salt and iodine intake that we report here may be underestimated compared with the general Dutch population.

Salt and iodine intake vary greatly on a day-to-day basis at the individual level (34). Therefore, using single 24h sodium and iodine excretion will result in a wider intake distribution compared with the true, usual intake and thus the prevalence of participants with extreme usual intakes will be overestimated based on a single 24h urine. In addition, this will reduce the power to determine a statistically significant difference between the median intakes of

both years. With respect to salt intake the prevalence of participants above the recommended maximum intake of 6 grams per day will be underestimated. It can be estimated that at least 84% of the participants in 2006 and at least 82% in 2010 had an intake above 6 grams per day. For iodine, a maximum of 2% in 2006 and 7% in 2010 had an intake below the estimated average requirement of 95 μg/d. Iodine deficiency is a particular concern for young children and pregnant women (8). The estimated average requirement for pregnant women is higher (160 μg/d) compared with the general population. In 2006 a maximum of 20% of the women of childbearing age (<45 years) had an iodine intake below 160 μg/d, while in 2010 this was a maximum of 50%. It may be necessary to monitor the iodine intake of pregnant women in the Netherlands.

Total salt intake has not changed over the period 2006 to 2010, whereas iodine intake has been significantly reduced, based on a monitoring study conducted in adults aged 19–70 years from a single Dutch town. In that same period the sodium-to-potassium ratio improved. Monitoring of actual salt and iodine intake in the population over time is needed to assess the effectiveness of sodium reduction initiatives or policy changes related to iodine fortification.

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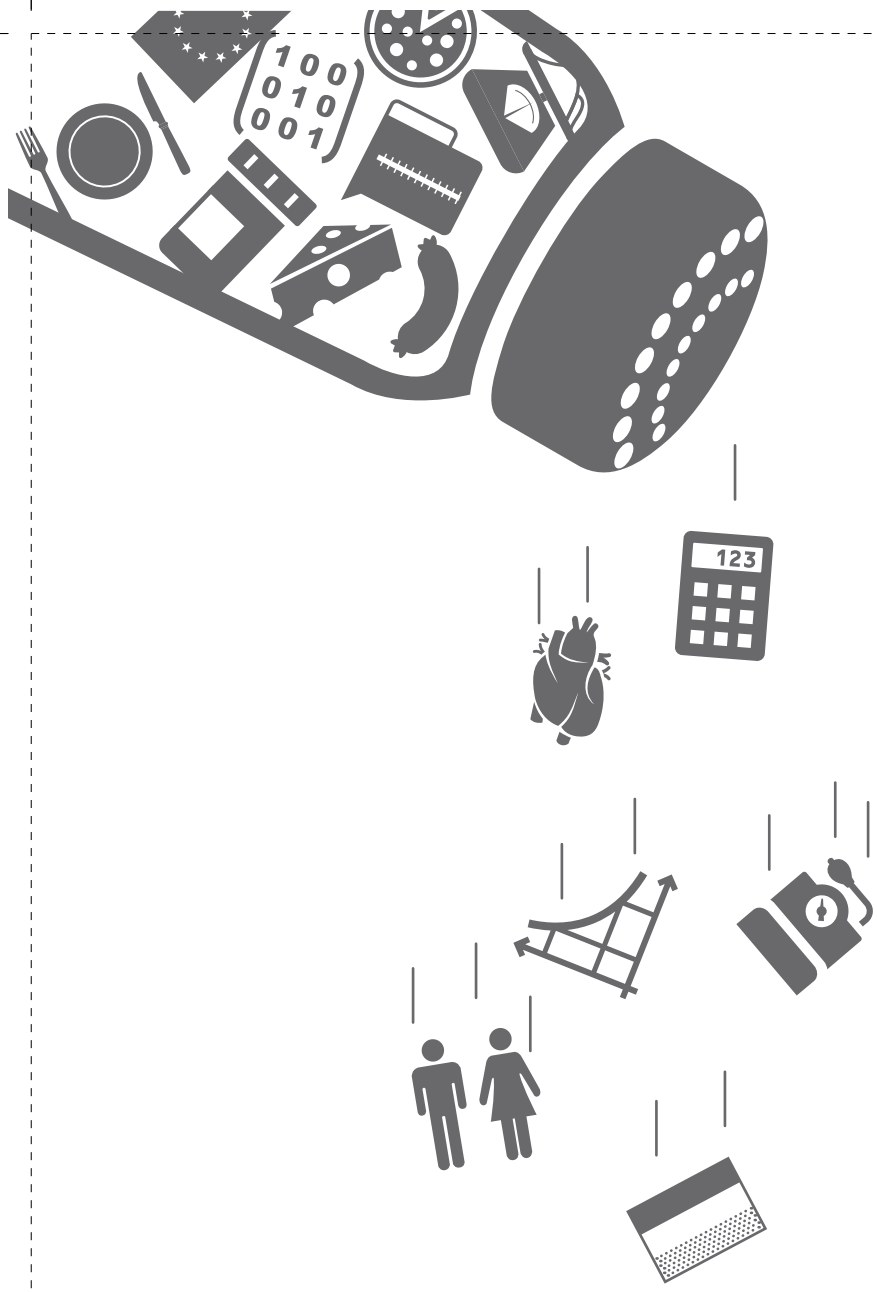
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Chapter 4

Potential impact of salt reduction in processed foods on health

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Published in American Journal of Clinical Nutrition, 2014 Mar;99(3): 446-53
Doi: 10.3945/ajcn.113.062018

Abstract

Background: Excessive salt intake has been associated with hypertension and increased cardiovascular disease morbidity and mortality. Reducing salt intake is considered an important public health strategy in the Netherlands.

Objective: Evaluation of the health benefits for the Dutch population of salt reduction strategies related to processed foods.

Design: Three salt reduction scenarios were developed: (a) substitution of high-salt foods by low-salt foods; (b) reducing sodium content in processed foods; (c) adherence to the recommended maximum of 6 gram per day. Health outcomes were obtained in two steps: after modelling salt intake into blood pressure levels, the Chronic Disease Model (CDM) was used to translate modelled blood pressures into incidences of cardiovascular diseases, disability-adjusted life years (DALY) and life expectancy. Health outcomes of the scenarios were compared to health outcomes obtained on current salt intake.

Results: In total 4.8% of acute myocardial infarction cases, 1.7% of congestive heart failure cases and 5.8% of stroke cases might be prevented if salt intake is according to the recommended maximum intake. The burden of disease might reduce by 56,400 DALYs and life expectancy might increase by 0.15 year for a 40-year old individual. Substitution of foods by comparable low-salt alternatives would lead to slightly higher salt intake reductions and thus in more health gain. The estimates for sodium reduction in processed foods would be slightly lower.

Conclusion: Substantial health benefits might be achieved when added salt is removed from processed foods, and when consumers choose more for low-salt food alternatives.

Introduction

Cardiovascular diseases (CVD) are the second main cause of mortality in the Netherlands (1). In 2007, approximately 40,000 people died from CVD (1). Although the absolute CVD mortality figure will decrease in the future, the number of years people will live with CVD is expected to increase. This was due to the decline in mortality rate from CVD since the 1970s (2).

Hypertension is a main risk factor for CVD (3). Higher sodium intakes have been shown to be associated with higher blood pressure levels (4; 5) and thus have been linked to CVD. Therefore, it is assumed that salt reduction will lead to lower blood pressure levels and consequently to lower incidences of CVD.

In the Netherlands more than 85% of the population exceed the recommended maximum intake of 6 grams per day (6). About 80% of the Dutch salt intake results from processed foods (6). Therefore, the Health Council of the Netherlands emphasized the need to reduce the amount of salt used in commercially manufactured foods as an important measure to reduce the salt intake (7).

Recently several studies have assessed the potential impact of salt reduction on population health (8; 9; 10; 11; 12). For example, Bibbins-Domingo et al. projected that an average of 3 gram salt reduction per individual would lead to substantial reduction in cardiovascular events (60,000 to 120,000 cases of coronary heart disease in the USA population) and direct medical costs ($10 billion to $24 billion) over a 10-year period (8). Several studies assessed the health effects in case current salt intakes would be reduced to levels recommended by World Health Organization or national authorities, but only a few examined the potential health effects of more specified salt reduction strategies. For example, Cobiac *et al.* compared the health effects of several salt reduction strategies, including those that are related to the current voluntary salt reductions by food manufacturers and to governmental legislation aiming for more moderate salt levels in foods (13). Cobiac *et al.* concluded that although voluntary salt reduction goals by the food industry may improve public health, more regulatory actions from the government are needed to achieve relevant improvements in population health.

In the present study, the expected health effects of two specified salt reduction strategies and of adherence to the recommended intake have been evaluated for the Dutch situation. One salt reduction strategy relates to nutritional behaviour and reflects the substitution of high salt products by comparable low-salt alternatives that are already commercially available.

The other strategy relates to the effect of salt reduction in processed foods and represents a major reduction in sodium levels in processed foods.

Methods

The simulated health outcomes of two different salt reduction scenarios and of the scenario reflecting the recommended maximum salt intake of 6 g/d for all individuals have been compared to the health outcomes obtained with the current salt intake.

Current salt intake

The current salt intake estimate was based upon the food consumption data from the Dutch National Food Consumption Survey 2007–2010 (DNFCS 2007–2010) (14). A representative sample of the population aged 6 to 69 years (N=3,819) was interviewed twice on non-consecutive days to report their 24h food intake of the previous day, including foods that were eaten out-of-home. Participants reported their discretionary salt use in additional questionnaires. Food consumption data were combined with sodium contents of foods in the Dutch National Food Composition Table 2011 (15). This version of the food composition table includes recent analyses on several foods (e.g. bread). The amount of discretionary salt was estimated using a probabilistic model (16; 17). Application of this model resulted in *usual* total salt intake distributions stratified by age and gender (See Annex II – paragraph 1). We assumed that salt intake of individuals older than 69 years would be equal to the salt intake of individuals aged 60 to 69 years. The estimated total salt intake was compared with 24h sodium excretions in the Netherlands (18), which demonstrated the validity of our 24h recall method.

Salt reduction strategies and resulting salt intake distributions

The first salt reduction strategy concerned food choice behaviour to adopt a healthier diet. In this scenario, foods with the lowest salt content substituted for foods with a higher salt level within the same food group. The sodium contents of processed foods were taken from the food composition table 2011 and were classified into food (sub)categories. Within each food (sub)category, the food item with the lowest sodium content was used to replace all the other foods within the same food category (all canned vegetables by freshly boiled equivalent).

The second strategy concerned salt reduction in processed foods. We virtually reduced the content of sodium in processed foods, taking into account that in some foods major sodium reductions are possible and in others hardly any. On average, we virtually reduced sodium contents in processed foods by 50%. This *salt reduction processed foods scenario* reflects major sodium reductions in processed foods. For the two salt reduction strategies, data from the DNFCS 2007–2010 and the specially prepared strategy-specific food composition tables were combined to calculate usual salt intakes (including estimated use of discretionary salt, as described before). In the third *recommended maximum intake scenario*, each individual from the DNFCS 2007–2010 with a usual salt intake above 6 g/day was set back to an intake of 6 g/day exactly (recommended maximum intake). We compared the reduction scenarios with the *current salt intake scenario*, in which salt intake distribution characterised by age and sex was the same as the current salt intake.

From salt intake distributions to systolic blood pressure distributions

Baseline age- and sex specific measured systolic blood pressure distributions of the Dutch population were taken from the Monitoring project on Chronic Disease Risk Factors (MORGEN) study (19) and the Rotterdam Study (20). The MORGEN cohort is a large monitoring study in the Netherlands and consists of a general population sample of men and women (n=22,654) aged 20–59 years from three Dutch towns (Amsterdam, Maastricht and Doetinchem). Systolic blood pressure distributions for subjects older than 55 years were taken from the Rotterdam Study. This cohort consists of 7,983 subjects aged 55 years and older from a suburb of Rotterdam. The measured blood pressure distributions in the general population were adjusted to usual blood pressure values using the variance of the measured values (See Annex II – paragraph 2.1).

The association between salt intake reduction and systolic blood pressure reduction was derived from a meta-analysis of He and MacGregor (4). This meta-analysis included intervention studies of 4 weeks or longer, with a range of salt reductions, and with no concomitant interventions (e.g. no use of antihypertensive medication). He and MacGregor have shown that the dose-response relation between salt intake and blood pressure is different between normo- and hypertensive subjects, i.e. the reduction in systolic blood pressure per gram of salt depends on initial blood pressure levels. They estimated that a 6g salt reduction leads to a 7.2 mmHg reduction among hypertensive subjects and 3.6 mmHg reduction among normotensive subjects. Based on the dose-response relation of this meta-analysis (4) and

based on the current Dutch salt intake and systolic blood pressure distribution, we derived the following dose-response relation between salt intake (SI) and systolic blood pressure (SBP):

$$SBP = c\, e^{\beta SI} - \alpha \qquad (4.1)$$

The regression coefficients α (-105) and β (0.03) were estimated using the data of the meta-analysis of He and MacGregor (4) (See Annex II – paragraph 2.2). The variation in blood pressure was affected by more factors than just salt intake (e.g. overweight). Therefore, we assumed that c was a random variable that is lognormal distributed which depends on sex and age. We estimated the mean and variance of c using usual salt intake and blood pressure data of the DNFCS 2007–2010 and MORGEN study and Rotterdam study, respectively.

We assumed that individuals, who take antihypertensive medications showed a similar response as individuals who did not take antihypertensive medications but were otherwise similar.

Using equation 4.1, the usual salt intake distributions of our scenarios were converted into usual systolic blood pressure distributions for each scenario. These usual blood pressure distributions were input parameters of RIVM-CDM (see below)

From blood pressure distributions to health outcomes

RIVM Chronic Disease Model

The effects of the change in blood pressure distributions on the incidence of diseases and mortality was calculated by the RIVM-CDM version 5.1. A detailed overview of the model has been published elsewhere (21) (See Annex II – paragraph 2.3). Briefly, the RIVM-CDM is a Markov-type multistate transition model. It simulates the life course of Dutch population cohorts in terms of changing risk factor classes and disease states. Time is modelled in discrete intervals of 1 year. In the present study, the health benefits of a closed cohort were simulated.

Model inputs

The input data consisted of initial distributions of the risk factors in classes and of diseases in disease states, transition rates between risk factor classes and disease states, relative risks and disability weights. All parameters were age and sex specific. Parameters values have been derived from statistical data representing the Dutch population. The usual systolic blood pressure distribution resulting from salt intake scenarios were divided into 4 classes (<120 mmHg, 120–139 mmHg, 140–159 mmHg and ≥160 mmHg) and were the main

model input. We simulated the age-related change in systolic blood pressure through 1-year transition probabilities that conserved the age-specific distribution of usual blood pressure over time (See Annex II – paragraph 2.4). Relative risks for the effect of usual blood pressure on acute myocardial infarction (AMI) and cerebrovascular accident (CVA) were derived from Lewington *et al.* (3) and were defined for unit changes of blood pressure. Relative risk value for congestive heart failure (CHF) was calculated by combining relative risk values presented in literature (See Annex II - paragraph 2.5). Mortality rates due to AMI, CVA and CHF were estimated using aggregated cross-sectional data on incidence and prevalence of current mortality from cardiovascular diseases (22).The risk of mortality from cardiovascular diseases was independent from systolic blood pressure or salt intake levels.

Model outputs

The incidence of cardiovascular diseases events (AMI, CHF and CVA) and all-cause mortality rates were model output variables. To assess the long-term effect of the salt reduction strategies, the fate of the adult population of ≥20 years has been simulated over a 20-year period. Output variables were the cumulative incidence of AMI, CHF and CVA and the cumulative all-cause mortality over this 20-year period.

The burden of disease of a particular scenario was calculated as the difference in disability-adjusted life years (DALYs) lived between that particular scenario and the *current salt intake* (See Annex II – paragraph 2.6). The disability weights are from the Dutch Disease Weights Study (23). Cumulative DALYs lived were calculated over lifetime for a cohort of 40-year old individuals. Finally, the effect of the salt reduction strategies on life expectancy was evaluated for 40-year old individuals by extending the simulation period until the last individual had died (24).

Uncertainty analysis

To test the sensitivity of the dose-response relationship between salt intake and blood pressure, alternative dose-response relationships parameters were estimated based on the lower and the upper bound of the dose-response relationship reported in He and MacGregor (4) for both normotensive and hypertensive subjects. The uncertainty interval for α was -92 to -109 and for β 0.2 to 0.3 (See Annex II – paragraph 2.7).

Results

Salt intake and blood pressure reductions

The median current salt intake of the Dutch population aged 20 years and older was 8.4 g/d and the age-standardized mean current systolic blood pressure 128.2 mmHg (**Table 4.1**). In the salt reduction processed foods scenario, the median salt intake would decrease by 28%, and blood pressure by 1.2%. The substitution processed foods scenario would result in a salt reduction of 35% and in a blood pressure reduction of 1.5%, whereas the recommended maximum intake scenario (6 g/d) required a median salt intake reduction of 29%, and would reduce the systolic blood pressure by 1.3% (**Table 4.1** and **Figure 4.1**).

Reduction in cardiovascular diseases and mortality from these diseases

When the salt intake in the Netherlands remained the same throughout the coming 20 years (current salt intake scenario), 667,600 cases of AMI, 902,900 cases of CHF and 896,500 cases of CVA were projected to occur (**Table 4.2**). If salt intake is reduced to the recommended maximum salt intake (6 g/d), an overall of 4.8% of cases of AMI, 1.7% of cases of CHF and 5.8% of cases of CVA might be prevented. Similar percentages were found in the salt reduction in processed foods scenario, and slightly higher reductions would be found on the substitution scenario, as shown in **Table 4.2**.

The reductions in disease incidences would not be stable throughout the 20-year period. **Figure 4.2** showed the annual estimates of the differences in incidences of AMI, CHF and CVA between the salt reduction scenarios and the current salt intake scenario. The difference in incidence of AMI, CHF and CVA might be more pronounced after the initial

Table 4.1 Current salt intake and systolic blood pressure (SBP) in the Netherlands and in the salt reduction scenarios

	Median salt intake (g/d)		Age-standardized mean SBP (mmHg)	
Current salt intake scenario	8.4		128.2	
Reduction	*in g/d*	*%*	*in mmHg*	*%*
Salt reduction processed foods scenario	-2.3	28	-1.5	1.2
Substitution processed foods scenario	-3.0	35	-1.9	1.5
Recommended maximum intake scenario	-2.5	29	-1.6	1.3

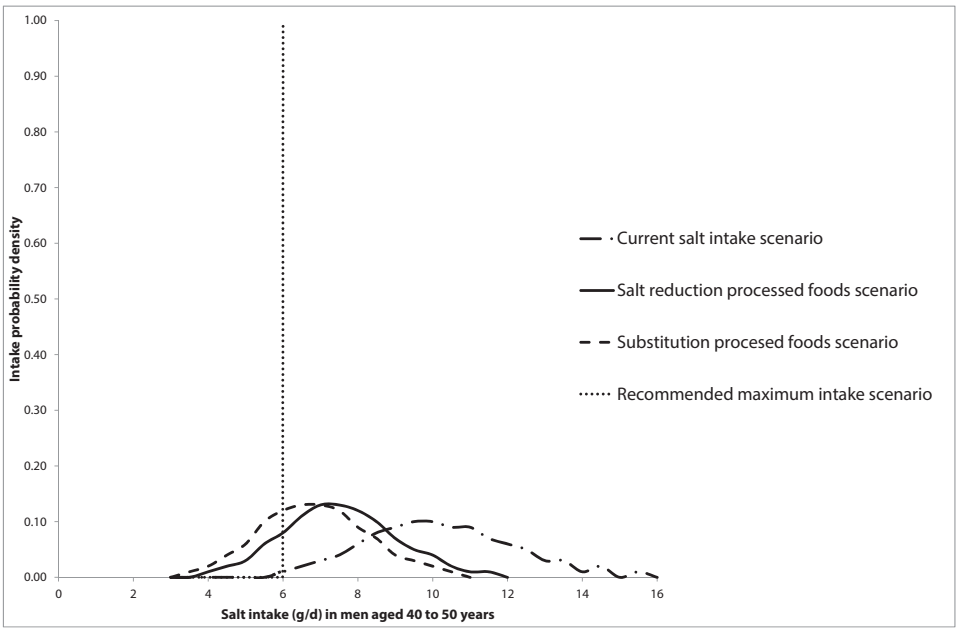

Figure 4.1 Distributions of salt intake in the current salt intake and in the three salt reduction initiatives, an example of 40 to 50 year old men (__ . __ Current salt intake; _ _ _ Substitution processed foods scenario; ___ Salt reduction processed foods scenario; … Recommended maximum intake scenario).

years of the implementation of the strategies, and in the hypothetical situation of 70 years of implementation, the incidence of all AMI, CVA and CHF would be similar in the reference scenario.

All-cause mortality might be reduced by 0.7% when salt intake was reduced to the recommended maximum salt intake (**Table 4.2**). The same percentage would be found for the salt reduction in processed foods scenario, and a slightly higher reduction would be found for the substitution processed foods scenario.

The reduction in mortality was also not stable throughout the 20-year period. **Figure 4.3** showed the annual estimates of the differences in all-cause mortality between the salt reduction scenarios and the current salt intake scenario. In the first 25 years of the implementation of the salt reduction scenarios and the scenario representing the recommended maximum intake, the mortality would be reduced. However, as this is a fixed cohort, eventually the total population died and after 25 years, all-cause mortality would increase until the total cohort has died.

Table 4.2 Projected cumulative disease incidence and mortality over 20 years for the Dutch population age ≥20 years

	Cumulative disease incidence						Cumulative all-cause mortality	
	AMI		CHF		CVA		Mortality	
	Cases (N)		Cases (N)		Cases (N)		Cases (N)	
Current salt intake scenario	667,600		902,900		896,500		3,423,000	
Salt reduction scenarios	*Cases averted*	*%*	*Cases averted*	*%*	*Cases averted*	*%*	*Cases delayed*	*%*
Salt reduction processed foods scenario	29,200 (20,800 to 37,600)[a]	4.4	16,600 (11,800 to 21,400)	1.8	53,400 (36,600 to 70,200)	6.0	25,150 (17,600 to 32,700)	0.7
Substitution processed foods scenario	35,500 (25,400 to 45,600)	5.3	20,000 (14,300 to 25,700)	2.2	64,300 (44,100 to 84,400)	7.2	30,400 (21,300 to 39,500)	0.9
Recommended maximum intake scenario	31,800 (22,500 to 41,100)	4.8	15,300 (10,800 to 19,900)	1.7	51,900 (34,900 to 68,900)	5.8	25,300 (17,500 to 33,200)	0.7

[a] Numbers between brackets represent the lower and upper bound of the sensitivity analyses.

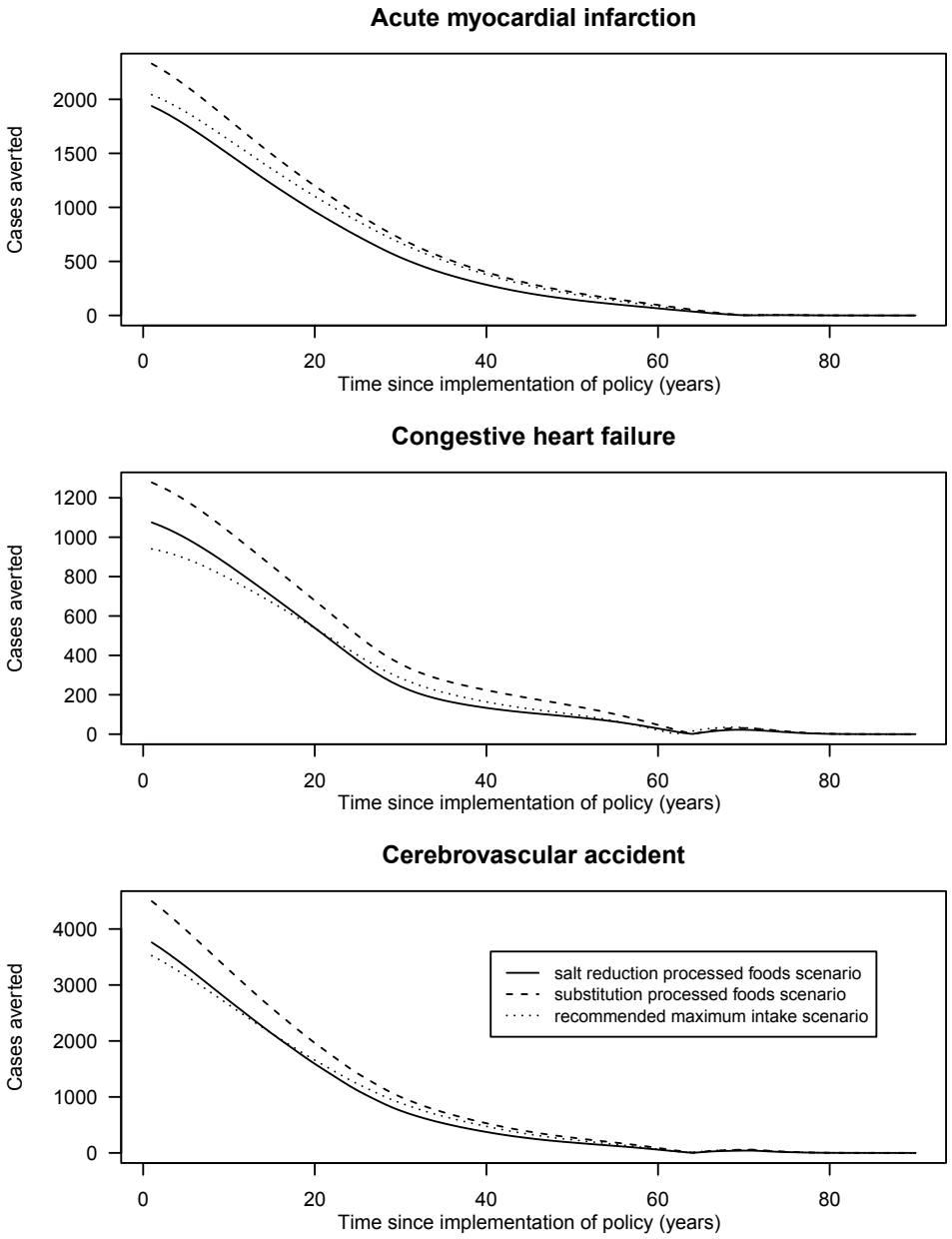

Figure 4.2 Projected annual estimates of the differences in AMI, CHF and CVA incidences of the salt reduction initiatives compared with current salt intakes for men and women (- - - Substitution processed foods scenario; ___ Salt reduction processed foods scenario; … Recommended maximum intake scenario).

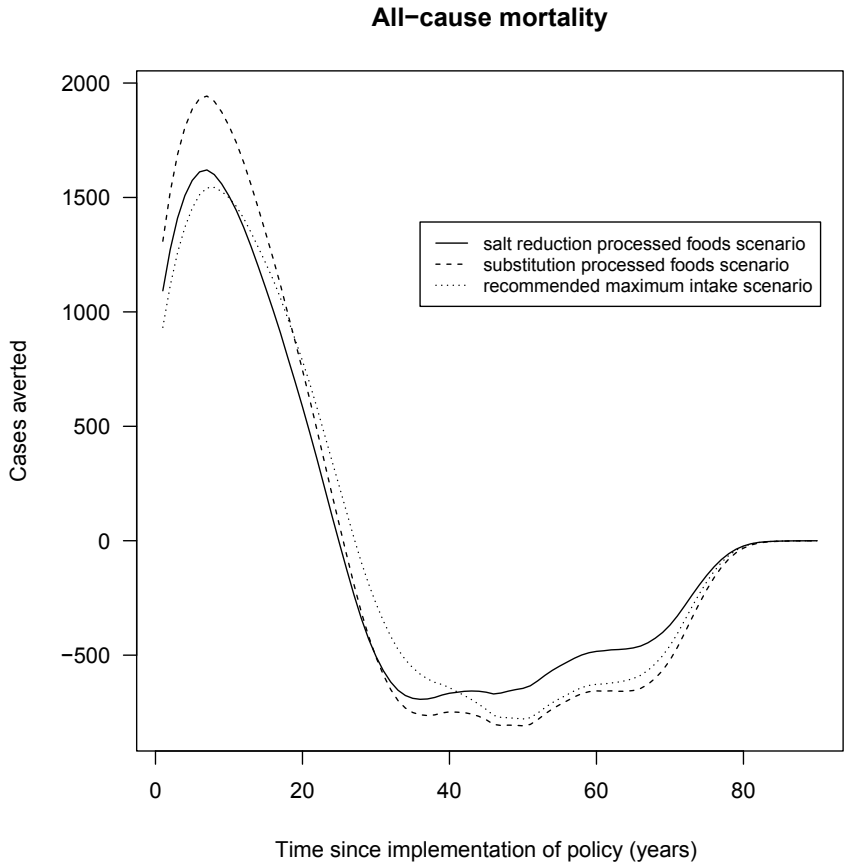

Figure 4.3 Projected annual estimates of the differences in all-cause mortality of the salt reduction initiatives compared with current salt intakes for men and women (- - - Substitution processed foods scenario; ___ Salt reduction processed foods scenario; … Recommended maximum intake scenario).

Health gain in DALYs and life expectancy

A 40-year old individual would increase the number of disability-adjusted life years lived by 0.5% (56,400 DALYs) if he would equal his salt intake to the recommended maximum intake for the rest of his life (**Table 4.3**). The reduced incidence in cardiovascular diseases and the decrease in mortality may prolong life expectancy. Life expectancy for a 40-year old individual would increase by 0.4% (0.15 years) in the recommended maximum intake scenario. Similar health gains were found for the salt reduction in processed foods scenario and for the substitution of processed foods scenario (**Table 4.3**).

Table 4.3 Projected cumulative disability-adjusted life years (DALY) and projected life expectancy (LE) for a cohort of Dutch 40-year old individuals over lifetime

	Cumulative DALYs		LE	
	DALYs[a]		Years	
Current salt intake scenario	10,611,000		41.23	
Salt reduction scenarios				
Gain compared to current salt intake	*DALYs change*	*%*	*Years gained*	*%*
Salt reduction processed foods scenario	-56,000 (-39,700 to -72,300)[b]	0.5	0.15 (0.11 to 0.19)	0.4
Substitution processed foods scenario	-67,900 (-48,300 to -87,600)	0.6	0.18 (0.13 to 0.23)	0.4
Recommended maximum intake scenario	-56,400 (-39,500 to -73,200)	0.5	0.15 (0.11 to 0.20)	0.4

[a] The DALYs are calculated as the difference in DALYs lived, between scenarios and the current salt intake scenario. Note that DALYs measure health loss. A negative DALY change reflects a health gain.
[b] Numbers between brackets represent the lower and upper bound of the sensitivity analyses.

Discussion

This study showed that if salt intake in the Dutch population would be reduced about 30%, systolic blood pressure would decrease by about 1.6 mmHg, and consequently, substantially less CVD and mortality would occur. If all people would keep to the maximum of 6 g/d, there would be 4.8% reduction in new cases of AMI. For CHF and CVA these reductions would be 1.7% and 5.8% and mortality rates would decrease by 0.7%.

An important strength of our study is that in preparing the salt reduction scenarios we relied upon a recent and extensive food consumption survey including individual food consumption patterns and foods eaten out of home and on a sodium-updated food composition table. In the scenarios the change in salt intake varied among individuals, as individuals with a high salt intake could reduce more than individuals with a low salt intake.

The results of our simulation study are limited by any uncertainty related to the data entered into the model. We did not have national representative blood pressure levels available of individuals older than 69 year and had to estimate the salt intake in older adults. We used blood pressure categories instead of continues blood pressure levels. In addition, future trends in determinants or treatment of blood pressure or CVD may impact the outcomes of our model but we did not take these (largely unknown) changes into account.

It has been suggested that there is no compelling evidence from randomized controlled trials that salt restriction will result in lower CVD events (25), but a re-analysis of this data showed a

significant risk reduction (26). An adverse effect of current salt intake levels on CVD through blood pressure was recently confirmed by the US Institute of Medicine after combining all available evidence from clinical outcome studies (27). In our two-step modelling approach, we therefore combined risk estimates from studies of salt intake to blood pressure and blood pressure to cardiovascular disease. The dose-response association between salt intake and blood pressure was based on a meta-analysis of randomized controlled trials lasting more than four weeks (4). We considered reductions obtained with such randomized controlled trails representative for sustained blood pressure reductions. Changes in age-related blood pressure due to successful salt reduction, however, were unknown and are therefore assumed unchanged. This may have caused on overestimation of the potential health gain in our study. We simulated a stronger impact of salt reduction in hypertensive than in normotensive individuals, although stronger estimates may also be valid for other subgroups (e.g. obese or individuals taking antihypertensive medications) (28; 29; 30). The partial sensitivity analysis showed that the variation in health gain depending on the dose-response association between salt intake and blood pressure only slightly affected our findings.

The risk estimates from blood pressure to CVD from a meta-analysis of long-term observational studies including more than one million adults (3) were regarded representative for the general population as opposed to estimates obtained from meta-analyses of randomized controlled trials (31). Apart from effects on CVD, salt reduction may lower the risk of other diseases, such as renal and gastric disease (32; 33). Our model was not designed for these diseases and therefore the overall potential impact of salt reduction may be underestimated.

Salt reduction to the recommended maximum intake of 6 g/d is challenging. This study modelled two maximal potential scenarios related either to reduce salt intake through behavioural change (substitution processed foods scenario) or through food reformulation (salt reduced processed foods scenario). Both approaches yielded roughly similar estimates and are close to the recommended maximum intake. It should be stressed that both scenarios may overestimate the actual salt intake reduction. Presumably not every individual can be persuaded to choose a diet with low-salt alternatives. Likewise, it would require major efforts by food industry to reduce sodium content in processed foods by 50%. In certain foods sodium can easily be reduced while in other foods sodium reduction will be more challenging. Thus, the health benefits of more realistic versions of our strategies will probably be lower than the projected effects in our study.

The present study shows that achieving the recommended maximum salt intake would reduce the incidence of cardiovascular diseases by roughly 4%, the all-cause mortality rate by 0.7% and would increase the life-expectancy by 0.15 years. The reduction in all-cause mortality is smaller than simulated by others (8; 12). There are some explanations for our estimates being somewhat more conservative for mortality. CVD mortality has strongly declined over the past 30 years in the Netherlands (1) and our model makes use of recent CVD mortality rates. Another explanation may be that our model includes competing risk and substitute morbidity and mortality: when risks of morbidity of cardiovascular diseases have been reduced, more individuals will suffer and die from other diseases. A third explanation may be that our model assumed no association between salt intake, blood pressure and mortality conditioning on CVD. So, with a reduced salt intake less people will develop cardiovascular disease but those who have it have the same probability of dying.

Recently, various studies have examined the effects of salt reduction on health (8; 9; 10; 11; 12; 13). The main conclusions from these studies are that salt reduction would lead to a substantial reduction in incidence of cardiovascular diseases and mortality. The reductions in cardiovascular disease morbidity in our study are in line with the estimations of the reported studies. However, differences between studies concerning the type of model used, salt-blood pressure response, age from which modelling starts and the duration of the modelling period, initial levels of usual salt intake and blood pressures all affect the outcomes of the simulation and make direct comparison difficult. Some of these studies evaluate the effects of a 3 gram salt reduction on health, leaving aside the question how to achieve the intended salt reduction (8; 10; 11). Others evaluate the effects of various population strategies to achieve salt reduction (12; 13). It would be worthwhile to consider the wider macroeconomic consequences of salt intake reduction, and considered the costs of our projected scenarios (34). However, these costs should be mapped out and was beyond the scope of the present study.

Various dietary and lifestyle factors affect CVD prevalence. Therefore, focus and policies on other dietary and lifestyle factors such as overweight, physical activity and smoking would also reduce the incidence of CVD and subsequently the burden of disease. In a recent Dutch study also using the RIVM-CDM changes in incidence of major diseases was simulated when the intake of various nutrients and food groups (fruits and vegetables, saturated and trans fatty acids and fish) were according to the dietary recommendations (35). Health gains due to saturated fatty acids intake according to the recommendations were similar to the results of salt reduction. However, the largest health effects can be obtained by increasing the fruit and vegetable and fish consumption to the recommended level (35).

To conclude, our study shows that substantial reductions in salt intake are needed in the Dutch population to reach the recommended maximum level of intake. Once achieved by food reformulation or by behavioural change, however, this might result in considerable and relevant health gain.

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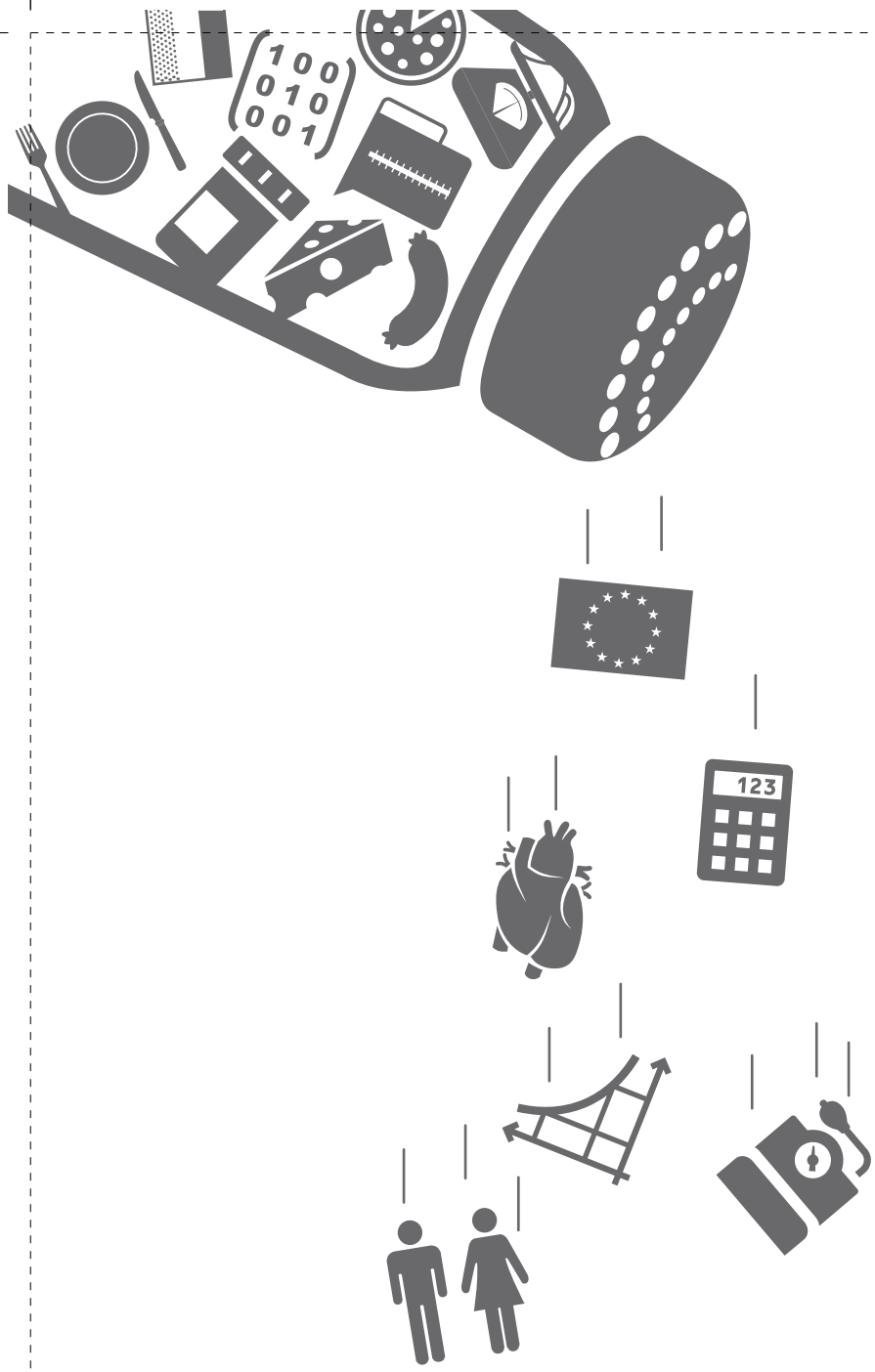
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Chapter 5

Health gain by salt reduction in Europe: a modeling study

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Published in PLoSOne, 2015 Mar 31;10(3)e0118873
Doi: 10.1371/journal.pone.0118873

Abstract

Excessive salt intake is associated with hypertension and cardiovascular diseases. Salt intake exceeds the World Health Organization population nutrition goal of 5 grams per day in the European region. We assessed the health impact of salt reduction in nine European countries (Finland, France, Ireland, Italy, Netherlands, Poland, Spain, Sweden and United Kingdom).

Through literature research we obtained current salt intake and systolic blood pressure levels of the nine countries. The population health modeling tool DYNAMO-HIA including country-specific disease data was used to predict the changes in prevalence of ischemic heart disease and stroke for each country estimating the effect of salt reduction through its effect on blood pressure levels. A 30% salt reduction would reduce the prevalence of stroke by 6.4% in Finland to 13.5% in Poland. Ischemic heart disease would be decreased by 4.1% in Finland to 8.9% in Poland. When salt intake is reduced to the WHO population nutrient goal, it would reduce the prevalence of stroke from 10.1% in Finland to 23.1% in Poland. Ischemic heart disease would decrease by 6.6% in Finland to 15.5% in Poland. The number of postponed deaths would be 102,100 (0.9%) in France, and 191,300 (2.3%) in Poland. A reduction of salt intake to 5 grams per day is expected to substantially reduce the burden of cardiovascular disease and mortality in several European countries.

Introduction

Hypertension is one of the leading causes of cardiovascular diseases in the European region and contributes substantially to the burden of non-communicable diseases (1). Prevention of hypertension and thus cardiovascular diseases is important to improve public health.

A major determinant of hypertension is excessive salt intake. There is convincing evidence that reducing salt intake will have a beneficial effect on blood pressure, thereby reducing the incidence of cardiovascular disease (2; 3). A population-wide salt reduction program is considered a cost-effective strategy (4) and to reduce the growing burden of disease related to hypertension and cardiovascular disease, the World health Organization (WHO) recommends reducing salt intake in the general population below 5 grams per day (5).

Currently, salt intake in the WHO European region largely exceeds this population nutrient goal (6). Therefore, several countries have developed operational salt reduction programs. The most effective salt reduction strategies seem to be those that combine product reformulation, consumer awareness and education, linked to appropriate monitoring mechanisms. Finland and the United Kingdom (UK) have been identified as good examples of successful salt reduction strategies (7). In those countries salt intake has decreased over the past years (8; 9), but in both countries salt intake is still above the population nutrient goal.

Earlier modelling studies concluded that salt reduction would lead to substantial reduction in cardiovascular diseases (10; 11; 12; 13). For example, Barton *et al*. projected a yearly reduction of 4450 cardiovascular deaths when salt intake was reduced by 3 grams per day in England and Wales (10). Unfortunately, such country projections do not allow for a direct comparison with other countries due to variation in population health modelling tools used and assumptions made.

Hence, we have quantified for nine European countries (Finland, France, Ireland, Italy, the Netherlands, Poland, Spain, Sweden and UK) the health effect of (a) a 30% reduction in current mean population salt intake, according to the WHO global strategy on non-communicable diseases, and the health effect of (b) achieving the WHO population nutrient goal of 5 grams per day using the same population health modelling tool DYNAMO-HIA and the same assumptions. We included countries that were included in the DYNAMO-HIA model, as well as participated in the European Salt Action Network, a network that promotes the harmonization of salt reduction programmes in EU countries. The health effects for ischemic heart disease (IHD) and stroke morbidity and total mortality were

examined. Additionally, we examined the robustness of the model in case of missing data and with differences in assumptions made.

Methods

Literature study on salt intake and blood pressure levels

We performed an extensive literature search (Scopus) to obtain national representative salt intake (sodium chloride) and blood pressure levels. Government websites of Ministries of Health, National Public Health Institutes or any other government institutes in Europe were additionally searched in order to identify data published in grey literature. We searched for studies in adult populations aged 18 to 90 years that were recently published (after 2000). Preferably data was stratified by sex and age and included a description of the distribution of salt intake and/or blood pressure levels in the population (e.g. by providing both mean and standard deviation (SD)). There were no exclusions based on report language.

Country data that were most recently published were preferred to older publications. In addition, data that was nationally representative was preferred to publications on regional or municipal salt intake or blood pressure. Salt intake based on 24h urine collections was preferred to data from dietary surveys as they may not include salt added during cooking and at table.

Imputation of missing salt intake or blood pressure data

In case of incomplete data, we contacted authors to obtain the missing data. When authors did not respond to our requests or when this data was not available, missing data was imputed as follows: we estimated the distribution of salt intake over age and gender from earlier published studies when no distribution of salt intake data was available (Poland). When sex-specific salt intake was not reported, we estimated this by applying the sex-specific salt intake ratio from studies that reported sex-specific salt intake to the overall salt intake (Poland). In those countries where age-specific salt intake was available (France, Italy, Netherlands, Sweden and UK), we could not observe a consistent trend of salt intake over age. Therefore, we assumed that salt intake was similar across all ages. For salt intake estimates that did not include an estimate of discretionary salt use (France, Ireland and Sweden), we assumed that 80% of total salt intake would come from the reported salt intake (14) and added an additional 20%.

Systolic blood pressure levels were mostly available by separate age categories. It was assumed that systolic blood pressure increased linearly over age and missing values for each age were predicted by fitting a regression line through the available systolic blood pressure levels over the crude age categories, taking the midpoint of each age category as fitting point. In addition, it was assumed that the blood pressure distribution was similar for the age categories.

Salt intake scenarios

Current salt intake distribution was categorized into nine different categories (<4 g/d, 4–6 g/d, 6–8 g/d, 8–10 g/d, 10–12 g/d, 12–14 g/d, 14–16 g/d, 16–18 g/d and >18 g/d). Individuals were distributed over these categories assuming that the sex-specific salt intake in the population followed a lognormal distribution (see paragraph 1 in Annex III).

We modelled the health gain hypothetically obtained when mean population salt intake was reduced by 30% by shifting the whole salt distribution by 30% down, and then re-categorizing the new salt intake distribution into the salt intake categories (see paragraph 1 in Annex III). We also assessed the potential health gain with the population nutrient goal of 5 grams per day. This was modelled by shifting all individuals from their current intake categories towards the intake category of 4–6 g/d. Individuals who were already in the <4 g/d or in the 4–6 g/d category remained in this category.

Modelling salt intake to blood pressure and cardiovascular disease

Salt intake categories were further subdivided into salt intake categories of 0.5 g/d. The prevalence of individuals within these subcategories was based again on the assumed log-normal distribution of salt intake in the population.

The dose-response relation between salt intake (x) and systolic blood pressure (SBP) (y) was derived from a meta-analyse of He and MacGregor (2), and transformed into a continuous, exponential association, resulting in a higher effect of salt reduction in hypertensive subjects as compared with normotensive subjects:

$$y = c \cdot \exp(\beta \cdot x) - \alpha \qquad (5.1)$$

where α equals -105, β equals 0.03 and c is a person specific (random) coefficient (log-normally distributed) (see paragraph 2 in Annex III).

Equation 5.1 was used to calculate the SBP distribution for each salt intake subcategory of 0.5 g/d (see paragraph 3 in Annex III). The mean and standard deviation of log(c) were chosen so that the mean and standard deviation of the resulting SBP distribution for each age and gender were equal to the SBP distribution in the population. As data on the SBP distributions in the population were based on single measurements, not taking short-term variation into account, we did not take the population standard deviation directly from the publications, but adjusted the standard deviation with a factor 0.6 to remove the within-subject variation from the population standard deviation. Relative risks between usual SBP on one hand and IHD and stroke on the other hand were derived from Lewington *et al.* (15). Using these relative risks, and equation 5.1, a relative risk within each salt intake subcategory was calculated for IHD or stroke. Next, the weighted mean RR within each salt intake category was calculated based on all RRs of the subcategories. This modelling step was repeated for each country and resulted in country-specific relative risks (see paragraph 4 in Annex III).

DYNAMO-HIA

Salt intake categories and the relative risks derived from the association between salt intake, systolic blood pressure and cardiovascular were incorporated in the DYNAMO-HIA model (version 1.2) and were used to estimate the effect of salt reduction on the prevalence of cardiovascular diseases (IHD or stroke) and through this on all-cause mortality. More detailed information on the methodology of DYNAMO-HIA is described elsewhere (16; 17). In short, DYNAMO-HIA is a dynamic, Markov-type model that uses actual population data and accounts for changing population compositions, risk factor prevalence and disease burden in several European countries. DYNAMO-HIA requires demographic data and epidemiological information on incidence, prevalence and disease-specific mortality for relevant diseases, by age and sex. As output, the model estimates summary measures of population health. In the model used in the present study, salt intake influences mortality only through its influence on the incidence of IHD and stroke (see paragraph 5 in Annex III).

We compared the current salt intake with the situation in which the total population has a mean salt reduction of 30% or if salt intake was 5 grams per day for all subjects. We assumed that each individual would maintain the same salt intake over the modelling period. Therefore, we specified zero-transition rates between the salt intake categories. We assessed the health impact over a 20-year period for the population aged ≥18 y. We present the results on the prevalence of IHD, stroke and all-cause mortality, life expectancy and disability-adjusted life expectancy.

Robustness of the model

We used Monte Carlo simulations to estimate uncertainties around the estimates of our model. We used the upper and lower bound of the effects of reduction on blood pressure based on the confidence intervals of He and MacGregor (2), and the upper and lower bound of the association between blood pressure and CVD as presented by Lewington (15). These intervals were assumed to have a normal probability distribution. The mean and 95% confidence intervals for 100 simulations were reported (see paragraph 6 in Annex III).

In addition, we examined whether our model was robust in case of missing values and of deviations from current assumptions used in estimating the impact of salt reduction towards 5 grams per day. In these analyses, we included countries with least missing values (Italy, Netherlands, Spain and UK), where we had age and sex specific salt intake available and where salt intake estimates were based on 24h urine collections. We examined whether the use of age-specific salt intake or blood pressure levels leads to different outcome estimates compared to using average salt intake or blood pressure.

Results

Current salt intake and systolic blood pressure levels and its reduction

Estimated salt intake ranged in men from 9.4 g/d in Finland to 13.3 g/d in Poland, respectively, and in women from 7.3 g/d in Finland to 10.0 g/d in Poland (**Table 5.1**). The systolic blood pressure was lowest in Sweden in both men and women (128.0 mmHg and 120.7 mmHg respectively) and highest in men in France (138.5 mmHg) and in women in Poland (133.9 mmHg). The projected salt reductions were highest in Poland in both men and women in both scenarios (**Table 5.1**), and lowest in Finland.

Prevalence reduction of IHD, stroke and mortality

Table 5.2 shows the reduction in the prevalence of individuals with stroke and IHD, expected after a 20-year period in the 30% intake reduction scenario as well as in the 5 gram/day scenario, compared with the current salt intake scenario. For a 30% reduction in salt intake the prevalence of stroke would be reduced by 6.4% (N=8,200; 95% CI 7,600–8,700) in Finland to 13.5% (N=106,100; 95% CI 102,300–109,900) in Poland. IHD would be reduced by 4.1% (N=13,700; 95% CI 12,700–14,600) in Finland to 8.9% in Poland (N=125,100; 95% CI 119,500–130,800).

Table 5.1 Current salt intake and salt intake in the salt reduction scenarios for the nine countries

Country	Year	Current salt intake (g/d)		30% salt reduction on population level (g/d)		Salt intake of 5 g/d for all individuals	
		Mean (SD)	Mean (SD)	Mean reduction	Mean reduction	Mean reduction	Mean reduction
		Men	Women	Men	Women	Men	Women
Finland	2002 (8)	9.4 (4.0)	7.3 (2.9)	-2.8	-2.2	-4.4	-2.3
France[a]	2006–2007 (35)	11.0 (2.8)	8.0 (2.0)	-3.3	-2.4	-6.0	-3.0
Ireland[a]	2008–2010 (36)	10.4 (2.4)	7.6 (1.8)	-3.1	-2.3	-5.4	-2.6
Italy	2008(37)	11.0 (4.0)	8.6 (3.3)	-3.3	-2.6	-6.0	-3.6
Netherlands	2010 (38)	10.9 (3.9)	7.8 (2.7)	-3.4	-2.3	-5.9	-2.8
Poland	2009 (39)	13.3 (4.0)	10.0 (3.1)	-4.0	-3.0	-8.3	-5.0
Spain	2009 (40)	11.5 (4.8)	8.4 (3.9)	-3.4	-2.5	-6.5	-3.4
Sweden[a]	2010–2011 (41)	11.4 (2.9)	8.7 (2.1)	-3.4	-2.6	-6.4	-3.7
UK	2008 (42)	9.7 (4.1)	7.7 (4.8)	-2.9	-2.3	-4.7	-2.7

[a] Salt intake is estimated based on salt intake from food records and includes an estimation of discretionary salt use of 20%.

Table 5.2 Projected disease prevalence and mortality reduction over 20 years for the population aged 18 to 95 years in nine European countries

	Stroke			Ischemic heart disease			Mortality		
Country	Current	Reduction	%	Current	Reduction	%	Current	Reduction	%
Finland	127,300			329,500			1,096,800		
30% salt reduction		8,200 (7,600–8,700)	6.4		13,700 (12,700–14,600)	4.1		8,500 (8,000–9,000)	0.8
5 grams per day		12,900 (12,100–13,600)	10.1		21,800 (20,400–23,300)	6.6		13,500 (12,800–14,200)	1.2
France	942,700			1,084,500			11,831,400		
30% salt reduction		101,700 (97,500–105,800)	10.8		84,400 (80,300–88,500)	7.8		66,500 (63,700–69,300)	0.6
5 grams per day		153,500 (147,300–159,700)	16.3		129,900 (123,600–136,100)	12.0		102,100 (97,800–106,300)	0.9
Ireland	72,900			176,000			641,800		
30% salt reduction		7,200 (6,900–7,500)	9.9		12,000 (11,400–12,600)	6.8		6,200 (5,900–8,600)	1.0
5 grams per day		10,200 (9,800–10,600)	14.0		17,500 (16,600–18,400)	10.0		9,000 (8,600–9,300)	1.4
Italy	1,395,200			1,956,500			12,776,800		
30% salt reduction		141,400 (135,500–147,300)	10.1		142,900 (135,500–150,00)	7.3		103,000 (98,600–107,500)	0.8
5 grams per day		222,900 (213,600–232,100)	16.0		228,300 (216,300–240,200)	11.7		163,300 (156,200–170,300)	1.3
Netherlands	303,200			700,000			3,117,100		
30% salt reduction		33,100 (31,600–34,700)	10.9		48,600 (45,700–51,500)	6.9		29,900 (28,400–31,400)	1.0
5 grams per day		50,000 (47,600–52,300)	16.5		75,600 (71,100–80,100)	10.8		46,100 (43,800–48,400)	1.5
Poland	788,900			1,408,600			8,345,900		
30% salt reduction		106,100 (102,300–109,900)	13.5		125,100 (119,500–130,800)	8.9		109,500 (105,200–113,700)	1.3
5 grams per day		181,900 (175,500–188,300)	23.1		218,900 (209,000–228,900)	15.5		191,300 (183,900–198,700)	2.3

Table 5.2 continues on next page

Table 5.2 ***Continued***

	Stroke			Ischemic heart disease			Mortality		
Country	Current	Reduction	%	Current	Reduction	%	Current	Reduction	%
Spain	782,700			1,023,700			8,585,500		
30% salt reduction		87,800 (84,000–91,600)	11.2		79,600 (75,200–83,900)	7.8		59,100 (56,400–61,700)	0.7
5 grams per day		143,200 (137,100–149,300)	18.3		131,500 (124,400–138,600)	12.8		97,400 (93,100–101,700)	1.1
Sweden	183,900			414,900			1,897,500		
30% salt reduction		17,800 (16,800–18,800)	9.7		26,500 (24,700–28,400)	6.4		14,400 (13,600–15,300)	0.8
5 grams per day		28,100 (26,600–29,700)	15.3		42,700 (39,700–45,700)	10.3		23,100 (21,700–24,400)	1.2
UK	1,336,400			2,612,300			12,416,400		
30% salt reduction		133,900 (127,500–140,200)	10.0		175,600 (165,600–185,500)	6.7		98,500 (93,600–103,400)	0.8
5 grams per day		202,400 (192,900–211,900)	15.1		268,100 (253,000–283,300)	10.3		149,400 (142,000–156,700)	1.2

Numbers reported are the mean (95% CI) for 100 simulations.

The reduction of salt intake to 5 grams per day would reduce the prevalence of stroke from 10.1% (N=12,900; 95% CI 12,100–13,600) in Finland to 23.1% (N=181,900; 95% CI 175,500–188,300) in Poland, and of IHD by 6.6% (N=21,800; 95% CI 20,400–23,300) in Finland to 15.5% (N=218,900; 95% CI 209,000–228,900) in Poland. **Table 5.2** also shows the number of deaths postponed due to salt reduction. Reduction in mortality due a reduction in CVD ranges from almost 102,100 (95% CI 97,800–106,300) (0.9%) in France to 191,300 (95% CI 183,900–198,700) (2.3%) in Poland.

Life expectancy and disability adjusted life expectancy

Life expectancy increases in all participating countries after reducing salt intake towards 5 g/d compared with the current salt intake. The life expectancy is increased by 0.2 years in 60 year old males from France, Italy, Spain, Sweden and UK and to 0.5 years in Poland (**Table 5.3**). In 60-year old women, the life expectancy gained is somewhat lower. The absolute gain is higher in younger individuals than in older individuals. The increase is disability-adjusted life expectancy is somewhat higher compared to life expectancy (**Table 5.3**).

Robustness of model in case of missing values and/or assumptions made (sensitivity analyses)

We observed a stronger reduction in the prevalence of stroke in the Netherlands and UK when we included average salt intake in our model as compared with age-specific salt intake (**Figure 5.1**), especially in the UK. This is because the average salt intake in the UK population was higher than the salt intake in the UK elderly, particularly the part of the population that will benefit most from salt reduction. If average blood pressure levels were included in the DYNAMO-HIA model the health impact estimates were lower as compared with age-specific salt intake and age-specific blood pressure levels in all countries.

Discussion

Using the dynamic population health modelling tool DYNAMO-HIA, we have been able to quantify the potential impact of a 30% salt reduction in the population and the effect of a reduction to 5 grams per day for all individuals on cardiovascular diseases and mortality in nine European countries. It is the first study that is able to compare the variation in cardiovascular diseases and mortality that could be averted due to salt reduction in nine

Table 5.3 Current life expectancy (LE) and disability-adjusted life expectancy (DALE) and its prolongation (in years and relative change (%)) for a 20-year old and 60-year old individual as a result of reducing dietary salt intake to 5 grams per day in the nine European countries over lifetime

		20-year old individual				60-year old individual			
		Men		Women		Men		Women	
		Current situation (yrs)	Gain in years (%)	Current situation (yrs)	Gain in years (%)	Current situation (yrs)	Gain in years (%)	Current situation (yrs)	Gain in years (%)
Finland	LE	56.7	0.5 (0.9)	63.4	0.0 (0)	20.9	0.3 (1.4)	25.4	0.0 (0)
	DALE	51.1	0.7 (1.4)	55.8	0.0 (0)	16.9	0.4 (2.4)	20.2	0.0 (0)
France	LE	57.8	0.3 (0.5)	64.7	0.1 (0.2)	21.8	0.2 (0.9)	26.8	0.0 (0)
	DALE	52.0	0.5 (1.0)	56.6	0.2 (0.4)	17.5	0.3 (1.7)	20.9	0.1 (0.5)
Ireland	LE	58.0	0.4 (0.7)	62.3	0.2 (0.3)	20.8	0.3 (1.4)	24.2	0.2 (0.8)
	DALE	52.5	0.6 (1.1)	55.5	0.2 (0.4)	16.9	0.4 (2.4)	19.4	0.2 (1.0)
Italy	LE	59.1	0.4 (0.7)	64.5	0.2 (0.3)	21.8	0.2 (0.9)	26.0	0.2 (0.8)
	DALE	53.5	0.6 (1.1)	56.9	0.4 (0.7)	17.6	0.4 (2.3)	20.6	0.3 (1.5)
Netherlands	LE	58.2	0.4 (0.7)	62.4	0.2 (0.3)	20.7	0.2 (1.0)	24.4	0.2 (0.8)
	DALE	52.5	0.6 (1.1)	54.8	0.2 (0.4)	16.7	0.4 (2.4)	19.1	0.2 (1.0)
Poland	LE	51.8	0.7 (1.4)	60.2	0.4 (0.7)	17.7	0.4 (2.3)	22.8	0.3 (1.3)
	DALE	45.7	0.9 (2.0)	51.6	0.5 (1.0)	13.7	0.5 (3.6)	17.2	0.4 (2.3)
Spain	LE	58.0	0.3 (0.5)	64.4	0.1 (0.2)	21.4	0.2 (0.9)	26.0	0.1 (0.4)
	DALE	52.4	0.6 (1.1)	57.0	0.3 (0.5)	17.2	0.4 (2.3)	20.5	0.2 (1.0)
Sweden	LE	59.3	0.3 (0.5)	63.4	0.1 (0.2)	21.8	0.2 (0.9)	25.1	0.1 (0.4)
	DALE	53.3	0.6 (1.1)	55.8	0.2 (0.4)	17.6	0.4 (2.3)	19.8	0.2 (1.0)
UK	LE	57.9	0.3 (0.5)	62.0	0.2 (0.3)	21.1	0.2 (0.9)	24.2	0.1 (0.4)
	DALE	51.9	0.5 (1.0)	54.4	0.3 (0.6)	16.9	0.3 (1.8)	19.0	0.2 (1.0)

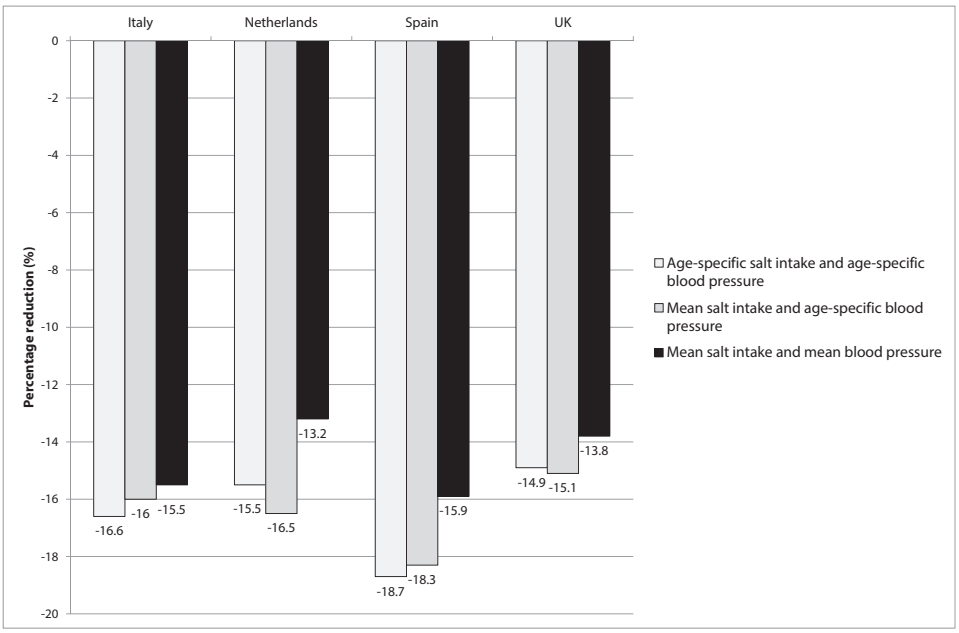

Figure 5.1 Percentage reduction in prevalence of stroke due to modification of input parameters salt intake and systolic blood pressure (for Italy, Netherlands, Spain and UK) when salt intake is reduced to 5 g/d.

European countries. A 30% salt reduction will already reduce the prevalence of stroke and IHD and will reduce the number of deaths in all nine European countries. Salt reduction to 5 grams per day will lead to further reductions in cardiovascular diseases and mortality.

The cardiovascular disease prevalence and averted cases of cardiovascular disease by salt reduction varied across the European countries; Poland would have more than twice as big a reduction in CVD than Finland, where salt intake has already been lowered substantially over the last few decades. In general, high salt intake is the main determinant of stronger reductions in cardiovascular diseases. Moreover, we observed that health benefits of salt reduction are mediated by systolic blood pressure. Countries with raised current blood pressure levels (e.g. Ireland) have more beneficial effects of salt reduction as compared with countries with lower current blood pressure (e.g. Netherlands) although salt intake is comparable between the Netherlands and Ireland. The calculations showed a relatively small reduction in all-cause mortality because the DYNAMO-HIA model assumes no direct association between salt intake and mortality, but only an indirect relation through the incidence of diseases. However, the all-cause reduction in mortality will be mainly due to the reduction in cardiovascular disease mortality. The increase in life expectancy

and disability-adjusted life is relatively higher in older individuals compared with younger individuals, because this intervention is more likely to postpone mortality in older adults than in younger adults.

This study shows that salt reduction below the population nutrient goal of 5 grams per day as recommended by WHO will have substantial benefits for public health across the WHO European Region. Although the salt intake levels vary across the countries, all intakes exceed the WHO population nutrient goal of 5 grams per day. Substantial reductions are needed to reach this goal (on average 47%), and the intermediate reduction of 30% is considered a more realistic target to be achieved in 2025 (18). Generally, processed foods are the main contributor to salt intake in West-European countries and major salt reduction can only be achieved if sodium levels of processed foods are significantly reduced.

In several European countries, voluntary sodium reductions have been implemented. In the UK, for example, the salt reduction program has been underway since 2003. Over this period, sodium levels in several processed foods decreased by 30 to 40%, and consumer awareness of high-salt products and use of discretionary salt increased (19; 20). The concurrent salt reduction in the population was 15% (from 9.5 g/d in 2001 to 8.1 g/d in 2011) (9), but the actual impact on blood pressure and cardiovascular disease is yet unknown. In Finland and the UK, the population-wide salt reduction co-incided with simultaneous reduction in blood pressure, but causality cannot be conclusively inferred from such an ecological association (21; 22). Only a restricted number of population-based interventions studies have been carried out that aimed to reduce the populations' salt intake and evaluate its effect on blood pressure levels. Some studies show that reduction in salt intake could not be achieved or maintained and that therefore no change in blood pressure levels could be observed (23; 24). Another study that did successfully decrease salt intake demonstrated a reduction in blood pressure in the population (25) was critized due to the inclusion of many hypertensive subjects which meant that the results could not be extrapolated to the general population (26). In the present study, we adapted the dose-response association between salt intake and blood pressure from a meta-analysis of He and MacGregor, which included intervention studies with duration of 4 weeks or more (2). However, the median duration of those interventions was 4 weeks and it can be questioned whether the effect observed in these studies will last over our 20 year simulation period.

Several modelling studies have concluded that sodium reduction in processed foods (mandatory or voluntary) is a very cost-effective measure, as the benefits in terms of cost

reduction would significantly outweigh the costs of the intervention (10; 12; 27; 28; 29). Cobiac *et al*. argues that programmes that stimulate the food industry to reduce the sodium levels in processed foods voluntarily may be recommended to improve public health, but it is anticipated that regulatory actions will be needed to achieve the maximal potential effect on public health (12), simply because this will result in lower salt intake levels.

This health modelling tool can be used to compare the health impacts of salt reduction scenarios between European countries and thus explore the variation in potential health impact. We took into account the variation in salt intake and blood pressure distributions in the nine countries and included country-specific demographic and cardiovascular disease prevalence data in the DYNAMO-HIA model. Moreover, we modelled an increased salt sensitivity for hypertensive individuals because of a convincing stronger dose-response association for hypertensive individuals compared with normotensive individuals reported in literature (2). However, modelling is always a simplification of reality and is limited by the model input parameters. We had to impute data if this was not available (estimation of discretionary salt, sex-specific or distribution of salt intake). Moreover, we imputed age-specific systolic blood pressure levels based on blood pressure levels that were presented according to crude age categories. We tested the robustness of our model to explore the sensitivity on the outcomes of the model when we modified the input parameter salt intake and blood pressure on the outcomes of the model. We observed that age-specific salt intake yielded quite similar results compared to mean salt intake, unless salt intake in older adults is considerable lower than the average salt intake, as observed in the UK. In contrast, one mean blood pressure estimate will substantially reduce the modelled health benefits of salt reduction, likely due to the increase in blood pressure at older age and the subsequent increase in incidence and prevalence of stroke and IHD (15). These robustness analyses show that our current strategy to impute missing data still provided acceptable estimate and that population mean salt intake can be used as a proxy for age-specific salt intake. Unfortunately, our model did not include other diseases that have been associated with high salt intake, such as congestive heart failure (30; 31; 32). In addition, we were not able to incorporate other effects related to salt reduction, such as kidney diseases, osteoporosis or gastric cancer (33; 34). Therefore, the projected effects are likely to be an underestimation of the overall effects that salt reduction can achieve.

In conclusion, this study shows that reducing salt intake to maximally 5 grams per day will substantially reduce the prevalence of cardiovascular diseases across nine European countries. Salt reduction will largely contribute to the reduction in burden of NCDs. Even

a 30% mean salt reduction is beneficial for public health, and may be a more realistic target to achieve by 2025.

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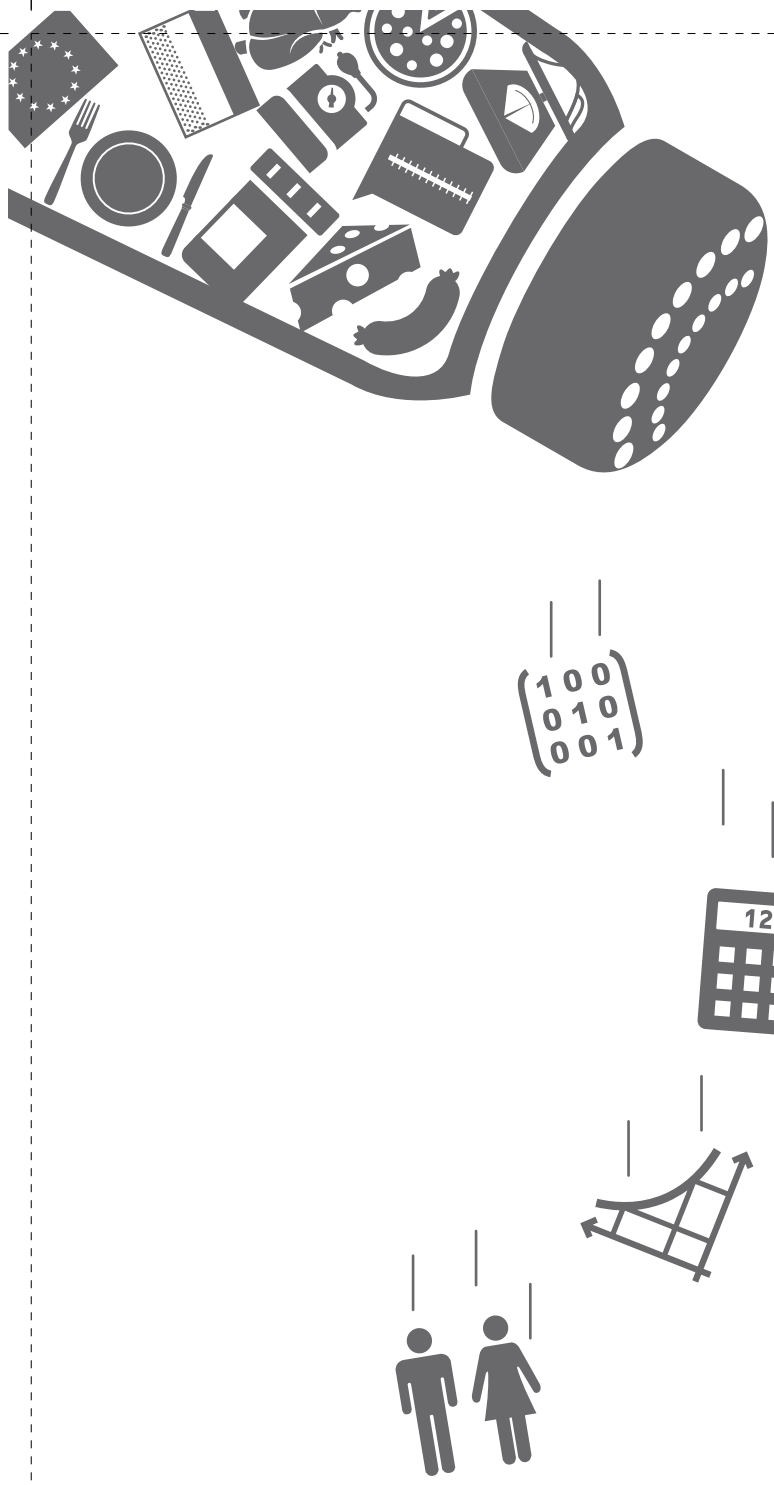
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Chapter 6

Sources of heterogeneity and its consequences in health impact assessments of salt reduction

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In preparation

Abstract

Introduction: The estimated impact of salt reduction on population health varies between studies, due to differences in models used and underlying assumptions. We examined whether specific parameters explain these differences in otherwise comparable population health models.

Methods: We selected seven population health models described in the literature that estimated the impact of salt reduction on blood pressure and subsequently on morbidity and mortality in western populations. We compared those HIA models based on four sets of key characteristics and their underlying assumptions and parameters. In an additional step, the parameters were varied one by one in a default approach (the DYNAMO-HIA model) to examine how they would influence the estimated health impact in the Dutch population. The simulated incidence of ischemic heart disease and stroke and life expectancy for each alternative simulation was compared with the default approach.

Results: We compared three dynamic HIA models and four static HIA models. Variation between the models related to the relative risks used for the salt to blood pressure and blood pressure to health association, to the shape of the dose-response relation between salt and blood pressure and to certain intrinsic HIA model structures. Modifying the effect sizes in the salt to health association resulted in the strongest change in health impact estimates (33% lower health impact estimate), whereas other changes had little influence on the estimated health impact. In all simulations, the health gain was substantial.

Conclusion: Differences in HIA model parameters may affect the health impact estimate. Therefore, transparency and clear description of the assumptions used is crucial.

Introduction

The World Health Organization (WHO) recently estimated that poor diet and physical inactivity account for 10% of global disability adjusted life years (DALYs) (1), with high salt intake being a major contributor (1). Such quantitative effects are estimated using mathematical models for forecasting future morbidity and mortality. Quantitative effects are often used to evaluate the long-term effects of a policy measure or intervention (2). Various models have been developed to forecast the long-term health impact of policy measures, but they may differ in approach (e.g. use of Population Attributable Fractions (PAFs), (multistate)life-tables or Markov-type models), and subsequently in underlying assumptions (e.g. 3; 4; 5; 6).

Substantial health gain can be expected from salt reduction. The WHO has set a target to reduce population salt intake by 30%, aiming at an average of 5 gram per day by 2025 (7). Sodium reduction in processed foods and raising awareness of consumers on salt reduction are the primary interventions to reduce the level of salt intake. For several countries, the expected health gain (e.g. averted morbidity or DALYs) related to salt reduction have been calculated (8; 9; 10; 11; 12). These studies used different approaches to quantify the health impact of salt reduction. Differences in modelling approaches can affect the number of diseases averted or the number of deaths postponed. To illustrate, Coxson *et al.* demonstrated that a 3-gram lower salt intake could avert 280,000 deaths in the USA using a dynamic-state transition model that estimated salt reduction on blood pressure and subsequently on mortality, but this number almost doubled (500,000 deaths) when a direct effect on mortality was estimated using relative risks from a post-hoc observational analysis of an RCT of sodium reduction (11). Even in otherwise comparable health impact assessment models, these estimates may also lead to heterogeneity in estimated health outcomes. For example, Scarborough *et al.* observed that applying the assumptions of the CHD policy model leads to a calculated 8 to 16% of CVD deaths being postponed, while a similar analysis using the DIETRON model suggested a postponement of 4 to 6% (13). Such heterogeneities may be due to variation in underlying assumptions on the salt intake to health effect association or due to intrinsic factors of the models. Therefore, insight in the underlying assumptions and model structures is essential to interpret and compare the outcomes of population health models.

The objective of the present study is to gain insight in how assumptions applied in different health impact assessment (HIA) models may result in heterogeneity in health impact

estimates. We first identified seven models used to calculate the health impact of salt reduction, and describe their differences. In a following step we used the population health modelling tool DYNAMO-HIA to estimate to what extent the variation in the modelling parameters used in these models affect the outcome of health impact estimates.

Methods

Selection of models

We searched PubMed for research papers that calculated the long-term health impact of salt reduction published until August 2013, using 'salt reduction', 'health impact assessment' and 'modelling study' as key words. We restricted our search to models that included projections over time, reported more estimates than just cost-effectiveness estimates, represented a real-life population and that were published in English. This search yielded five models: CHD policy model (11; 14); PRIME model (former DIETRON model) (13); Proportional MultiState Life-Table (PMSLT) (10); Global burden of disease (GBD) (1) and RIVM-CDM (15).

We also identified three additional salt reduction models that fulfilled the above mentioned criteria, but at the time of our search the results had not yet been published (IMPACT model (16), DYNAMO-HIA model (17) and UK Health Forum model. Since the UK Health Forum Model on salt reduction is not yet published, our present analyses concern seven models.

Identification of model characteristics

We identified four key characteristics of the models related to the aim of the study, the model used and the output obtained (see **Figure 6.1**). In our view the most relevant parameters of the four characteristics are clustered in seven boxes in **Figure 6.1**.

Parameter selection of characteristics for modelling exercise

We selected the DYNAMO-HIA model to calculate the effect of the modification of the parameters on the health impact estimates. A detailed description of the model can be found elsewhere (4; 17). We identified those parameters within sets of key characteristics that differed between the selected models. Subsequently, we evaluated which parameters could be modified in the DYNAMO-HIA approach. The ten selected parameters are marked

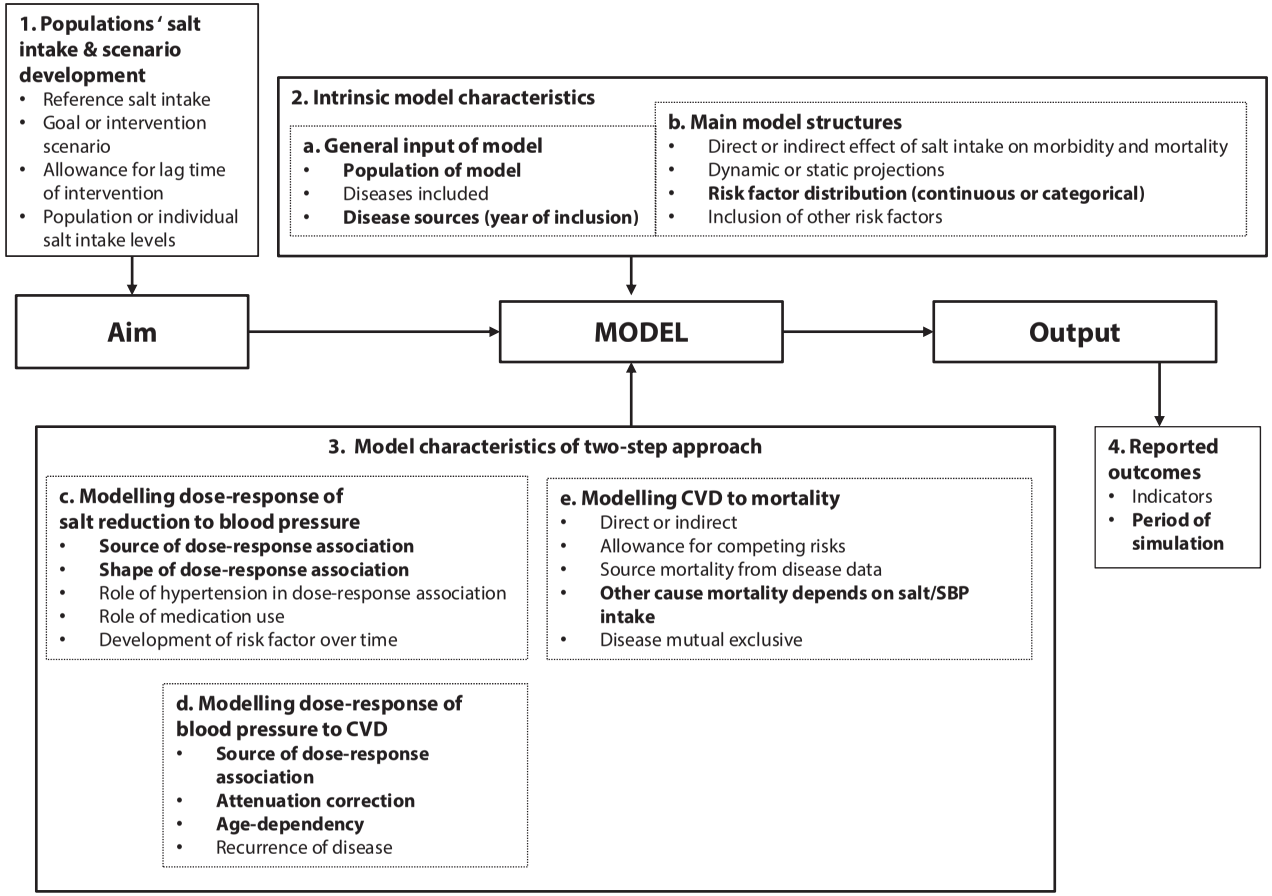

Figure 6.1 Four key characteristics and its underlying assumptions of the modelling approaches of salt reduction. The ten selected parameters are marked bold.

bold in **Figure 6.1**. There are also other parameters that differ between the selected models, but those parameters are too closely related to the modelling concept or could not be modulated in another modelling setting. For example, a model may provide either dynamic or static projections. Such a parameter could not be modified. Therefore such parameters are not included in the present analysis. We also did not model any parameters related to the characteristic "Population salt intake and scenario development".

Varying modifiable parameters using DYNAMO-HIA

The selected parameters were incorporated in the DYNAMO-HIA model one at a time. The shape and the source of the dose-response association for salt reduction to blood pressure were combined into a single parameter. We used DYNAMO-HIA version 2.07. In all situations, we simulated the health impact of a 3-gram salt reduction for the Dutch population. The default situation of the DYNAMO-HIA approach and the alternative simulations are presented in **Table 6.1**. The alternative simulations were each compared with the default situation. In an additional simulation we mirrored the CHD policy model approach (14) in DYNAMO-HIA, using the following model input 1) age range of the population from 35 to 80 years; 2) relative risks for the salt to SBP relation from a meta-analysis of randomized controlled trials; 3) change of mean blood pressure levels within categories; 4) relative risks for the BP to CVD relation from the Framingham Study and 5) 'other cause mortality' (that is, other causes than the modelled diseases IHD and stroke) depended on the current blood pressure levels. For each simulation, we report the effect on the incidence of stroke and ischemic heart disease (IHD). We also estimated the effect on the life expectancy for a 60-year old individual. An overview of relative risks used in the calculations is presented in Annex IV.

Results

Model characteristics and their parameters

Table 6.2 shows the parameters of the main model characteristics for all seven models. With respect to the population salt intake and scenario development, we observed that all models simulated a different salt reduction: estimating the effect of an intervention or a fixed target. In the scenarios, no lag time of the intervention was assumed, except for the CHD policy model, and a change in salt intake at population level was estimated, except for

Table 6.1 Overview of the assumptions within the DYNAMO-HIA approach (default situation) and its modifications in the alternative simulations

Characteristics	Default situation	Alternations compared to default situation
General input of model		
Population of model	>18 years	35–80 years
Disease sources	GP registries, 2001	GP registries and hospital registration from 2010
Main model structures		
Risk factor distribution	Categorical for salt intake (per 2 g salt), but continuous blood pressure distribution	Categorical for salt intake (per 2 g salt), and categorical for blood pressure (per 20 mmHg) • Shift of prevalence between categories (RIVM-CDM approach)[b] • Change of mean blood pressure within category (CHD policy approach)
Modelling dose-response of salt reduction to blood pressure		
Shape and source of dose-response association	He and MacGregor, 2004 (18) Exponential	Law *et al.*, 1991 (19) Linear
Modelling dose-response of blood pressure to CVD		
Source of dose-response association	Prospective Studies Collaboration, 2002, age-specific	Framingham Risk Estimates, unadjusted for age[b] (23)
Attenuation correction	Measured blood pressure adjusted for within-subject variation	Measured blood pressure
Age-dependent	Yes	No age-dependency using Framingham risk estimates
Modelling effect of CVD to mortality		
Other cause[a] of death mortality depends on salt intake/SBP	No	Yes
Reported outcomes		
Period of simulation	10 years	Extended to 20 years Extended to 50 years

[a] Other than stroke and IHD.
[b] In annex IV, tables 1–4, the variation in relative risks used in the salt intake categories and blood pressure categories for the default and alternative simulations is presented.

Table 6.2 Comparison of main model characteristics of the models that calculated health impact of salt intake reduction

Modelling approaches	CHD policy model (11; 14)	Proportional multistate life table (10)	RIVM-CDM (15)	PRIME Model (13)	IMPACT model (16)	Global burden of disease (25)	DYNAMO-HIA (17)
Population salt intake & scenario development							
Goal	1 g/d reduction; 2 g/d reduction; 3 g/d reduction	4 specific interventions	2 specific interventions and goal intake to 6 g/d	Goal: 6 g/d	2–20% intake reduction due to specific interventions	Theoretical minimum risk exposure	30% reduction Goal: 5 g/d
Lag times	Gradual reduction in sensitivity analyses	No	No	No	1 year after baseline	No	No
Salt intake levels	Population level & population shift	Population level & population shift	Individual level and individual shift	Population level & population shift	Population level	Population level	Population level and shift
General input data of model							
Population of model	35–80y	>30y	>20y	<75y	Total population	Total population	>18y
Diseases included	Cardiac arrest, MI, CHD and stroke	IHD, stroke	AMI, CVA, CHF	IHD, stroke	AMI, post AMI, HF, angina, post revascularisation	Stomach cancer, IHD, strokes, several other CVD, chronic kidney disease	IHD, stroke

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Table 6.2 ***Continued***

Modelling approaches	CHD policy model (11; 14)	Proportional multistate life table (10)	RIVM-CDM (15)	PRIME Model (13)	IMPACT model (16)	Global burden of disease (25)	DYNAMO-HIA (17)
Disease sources (year)	Prevalence: Survey Incidence: hospital register, MI registry (2000) from USA	Australian burden of disease (<2008 and trends to 2020)	Dutch GP and Hospital register (2007)	UK cause-specific mortality (2007)	Hospital statistics, MI audit project, GP-register from UK (1993–2010 and predicted to 2020)	DISMOD-MR (3) (2010)	Dutch GP registry (2003)
Main model structures							
Effect of salt on CVD/ other disease	Indirect	Indirect	Indirect	Indirect	Indirect	Indirect (SBP-CVD) and direct (stomach cancer)	Indirect
Projections	Dynamic	Dynamic	Dynamic	Static	Static	Static	Dynamic
Risk factor distribution	Categorical	Continuous	Continuous (salt) Categorical (SBP)	Continuous	Continuous	Continuous	Categorical (salt) and continuous (SBP)
Other risk factors	Yes, multiplicative	No	Not used (but optional)	Yes, multiplicative	No	No	No
Modelling dose-response of salt intake on blood pressure							
Source of dose-response association	He & MacGregor, 2004 (18) for low risk estimate and (20; 21) for high risk estimates	Law *et al.*, 1991 (19)	He & MacGregor, 2004 (18)	He & MacGregor, 2008 (26)	He & MacGregor, 2004 (18)	Own meta-analysis based on He and MacGregor 2008 and Graudal *et al.*, 2011 (27)	He & MacGregor, 2004 (18)

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Table 6.2 ***Continued***

Modelling approaches	CHD policy model (11; 14)	Proportional multistate life table (10)	RIVM-CDM (15)	PRIME Model (13)	IMPACT model (16)	Global burden of disease (25)	DYNAMO-HIA (17)
Shape	Linear	Linear	Exponential	Linear	Linear	Linear	Exponential
Role of hypertension	By hypertension; >65 years is hypertension	Depends on SBP level	Depends on SBP level	In normotensives only, age-dependent from DASH trial	By hypertension	By age	Depends on SBP level
Medication use	Medication is treated similar as hypertension	Ignored	Ignored	Ignored	Ignored	Ignored	Ignored
Development of risk factor over time	Unchanged	Unchanged	Unchanged	N/A	N/A	N/A	Unchanged
Modelling dose-response of blood pressure to CVD							
Source of dose-response association	Framingham risk scores (23)	Prospective Studies Collaboration (22)	Prospective Studies Collaboration and own meta-analysis (CHF) (22)	Prospective Studies Collaboration (22)	INTERHEART (24)	Prospective Studies Collaboration (22) for CVD	Prospective Studies Collaboration (22)

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Table 6.2 ***Continued***

Modelling approaches	CHD policy model (11; 14)	Proportional multistate life table (10)	RIVM-CDM (15)	PRIME Model (13)	IMPACT model (16)	Global burden of disease (25)	DYNAMO-HIA (17)
Attenuation correction	No	No	Yes	No	No	No	Yes
Age-dependent	No (age effect not significant)	Yes	Yes	Yes	Yes	Yes	Yes
Recurrence of disease	Ignored	Ignored	Ignored	Ignored	Ignored	Ignored	Ignored
Modelling effect of CVD to mortality							
Direct or indirect	Indirect (incl direct fatality)	Indirect	Indirect	Direct	Direct	Direct	Indirect
Competing risks	Yes	Yes	Yes	N/A	N/A	N/A	Yes
Source mortality from disease data	Framingham adjusted for trends in risk factors and calibrated to national cause of death data; specific data sources separating out over categories	Australian burden of disease	Record linkage of Dutch GP registry and hospital register	N/A	Median survival, estimated 2020 mortality	DISMOD-MR	GP registry

Table 6.2 continues on next page

Table 6.2 ***Continued***

Modelling approaches	CHD policy model (11; 14)	Proportional multistate life table (10)	RIVM-CDM (15)	PRIME Model (13)	IMPACT model (16)	Global burden of disease (25)	DYNAMO-HIA (17)
Mortality depends on salt intake/SBP before diseases	Yes	No	No	N/A	N/A	N/A	No
Mortality depends on salt intake/SBP after disease	No	No	No	N/A	N/A	N/A	No
Diseases mutual exclusive	Partly	No (independent)	No (independent)	N/A	Yes	One at the time	No (independent)
Reported outcomes							
Indicator	Incidence, all-cause mortality and QALYs	DALY, lifetime mortality and morbidity	LYG, DALY, incidence and mortality	Cause-specific mortality	LYG, DPP	DALY (YLL, YLD)	Prevalence, mortality and DALYs
Period of simulation	10y	Lifetime	20y	N/A	10y	N/A	20y

LYG: life years gained; DPP: deaths prevented or postponed; QALY: quality adjusted life years; DALY: disability adjusted life years; YLD: years lived with disease; YLL: years lived lost.

RIVM-CDM where individual shifts in salt intake were used. With respect to the general input data of the model, the age range of the population exposed to the intervention also differed. All models estimated the effect of salt reduction on CVD mediated by SBP. We observed that only GBD included diseases other than CVD. Obviously, prevalence and incidence data of the diseases were based on country-specific registries and databases. Concerning the main model structures, we identified four dynamic (CHD policy model, RIVM-CDM, DYNAMO-HIA and PMSLT) and three static models (PRIME, IMPACT and GBD). Salt intake and/or systolic blood pressure (SBP) were divided into categories in the CHD policy model, RIVM-CDM and DYNAMO-HIA, but were considered continuous in the other models. The effect of SBP changes over categories was approached differently between RIVM-CDM and the CHD policy model. In RIVM-CDM, the prevalence of the population within the SBP categories changed. In the CHD policy model the mean SBP shifted within the SBP categories.

Five HIA models derived the salt-blood pressure estimate from the same meta-analysis of randomized controlled trials (18) and one model from a meta-analysis of observational studies (19). The CHD policy approach used a lower estimate based on the meta-analysis of randomized controlled trials (18), and used a higher estimate based on data from clinical trials (20; 21). Models that used the parameters from He and MacGregor (18) fitted separate linear dose-response relations for normotensive and hypertensive subjects, or constructed an exponential dose-response relationship that depended on blood pressure. The association between blood pressure and cardiovascular diseases was derived in most models (RIVM-CDM, PMSLT, DYNAMO-HIA, PRIME and GBD) from the Prospective Studies Collaboration (22). RIVM-CDM and DYNAMO-HIA corrected the variance of the measured SBP levels of the population for the within-subject variability (attenuation correction). PMSLT, PRIME and GBD used only the population-average SBP levels and not its variance. The CHD policy model and the IMPACT model obtained the effect size of the SBP to CVD morbidity relationship from specific cohort studies, namely the Framingham Cohort Study and the INTERHEART Study (23; 24).

A combination of disease incidence and mortality and integrative measures (such as DALYs) are mostly reported as outcome measure. The period of simulation varies between 10 years (CHD policy model and IMPACT model) to lifetime (PMSLT).

Effect of the modifications of parameters on health impact

Table 6.3 shows the various estimates of the impact of a 3-gram salt reduction (using the DYNAMO-HIA model) for the population aged 18 years and older in the Netherlands applying nine different modelling assumptions. In the default situation, a 3 gram salt reduction resulted in a 10.5% reduction (N=30,800) in stroke incidence and a 7.9% reduction in IHD incidence (N=38,100). The gain in life expectancy was 0.16 for men and 0.14 for women (**Figure 6.2**).

The largest changes in health impact estimates were observed when different risk estimates for the relationship between salt intake and disease occurrence were used. In the simulation using risk estimates for the relation between blood pressure and diseases from the Framingham Cohort Study, the absolute numbers as well as the percentage reduction of the estimated disease incidence was considerably lower compared with the default situation (7.5% (N=22,000) reduction for stroke and 4.8% (N=23,400) for IHD; **Table 6.3**). This means a Δ33% decreased estimate for stroke and a Δ40% decreased estimated for IHD compared with the default situation. The health impact estimates increased if the linear association between salt intake and blood pressure taken from the study of Law *et al*. were incorporated

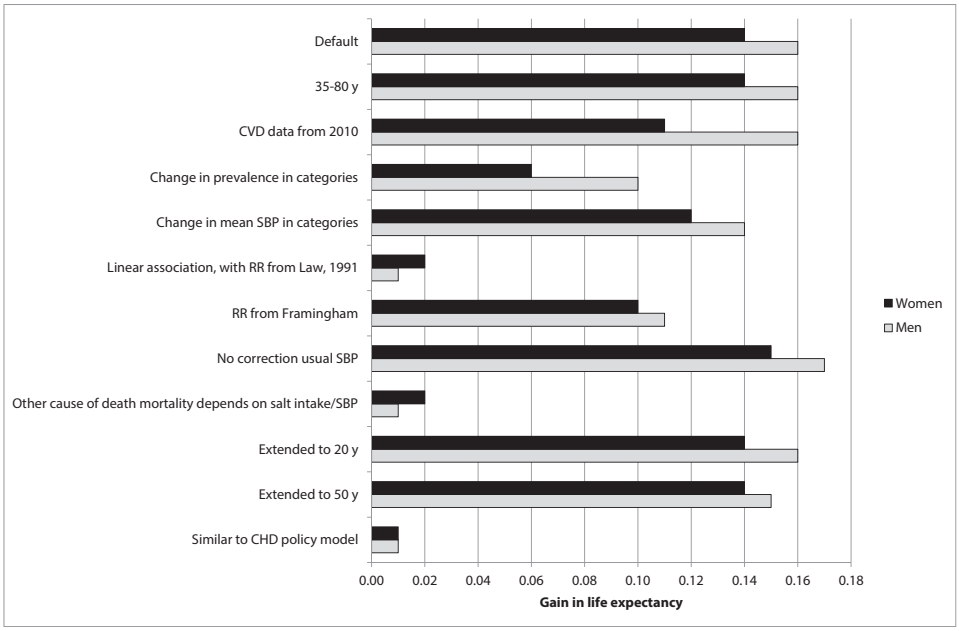

Figure 6.2 Gain in life expectancy for men and women aged 60 between 3 gram salt intake reduction and current salt intake in the various for the various simulations.

Table 6.3 Effect of eight modifiable features on the health impact estimate of a 3 gram salt reduction using the DYNAMO-HIA model

		CVA incidence				IHD incidence			
		Baseline	3 g/d salt intake reduction	Absolute difference	% reduction (% difference with default approach)	Baseline	3 g/d salt intake reduction	Absolute difference	% reduction (% difference with default approach)
	Default[a]	292,700	261,900	30,800	10.5	483,600	445,500	38,100	7.9
General input of the model									
Population of model	35–80 y	253,500	225,000	28,500	11.2 (+6%)	445,400	409,800	35,600	8.0 (1%)
Disease sources	CVD data from 2010	275,200	246,300	28,900	10.5 (0%)	528,000	487,000	41,000	7.8 (-1%)
Main model structures									
Risk factor distribution	Change in prevalence in categories	288,500	367,600	20,900	7.2 (-31%)	478,800	452,800	26,000	5.4 (-32%)
	Change in mean SBP in categories	290,800	261,300	29,500	10.1 (-4%)	482,000	444,400	37,600	7.8 (-1%)
Modelling effect of salt reduction in blood pressure									
Salt intake – SBP	Linear association, with RR from Law, 1991 (19)	293,400	256,200	37,300	12.7 (+19%)	483,700	437,400	46,300	9.6 (+22%)
Modelling effect of blood pressure on CVD									
SBP-CVD	RR from Framingham (23)	292,900	270,900	22,000	7.5 (-33%)	483,600	460,200	23,400	4.8 (-40%)
Attenuation correction	No correction usual SBP	292,700	258,400	34,300	11.7 (+11%)	483,600	442,600	41,000	8.5 (+8%)
Modelling effect of CVD on mortality									
Mortality also depends on SBP directly[b]	Other cause of death mortality depends on salt intake/SBP	292,700	261,400	31,300	10.7 (+2%)	483,600	444,600	39,000	8.1 (+3%)

Table 6.3 continues on next page

Table 6.3 ***Continued***

		CVA incidence				IHD incidence			
		Baseline	3 g/d salt intake reduction	Absolute difference	% reduction (% difference with default approach)	Baseline	3 g/d salt intake reduction	Absolute difference	% reduction (% difference with default approach)
Reported outcomes									
Period of simulation	Extended to 20y	652,400	586,400	66,000	10.1 (-4%)	1,066,700	986,500	80,200	7.5 (-5%)
	Extended to 50y	1,889,200	1,717,800	171,400	9.0 (-14%)	2,808,100	2,621,974	186,200	6.6 (-16%)
Combined approach									
	Similar to CHD policy model	252,900	233,300	16,900	7.8 (-26%)	445,200	422,900	22,300	5.0 (-37%)

[a] Default situation: 10-year period, population aged >18 years and older, correction for RDR. RR salt intake and SBP from He and MacGregor 2004 (exponential), RR SBP-CVD Lewington *et al*., 2002, measured SBP corrected with regression dilution ratio.

[b] The pathway from SBP to mortality in this model is both through the "indirect" effect of SBP increasing stroke and IHD incidence, and through a direct effect on mortality from other causes.

in the model (reduction of 12.5% (N=36,500) for stroke and 9.6% (N=46,300) for IHD). This means a Δ19% increased estimate for stroke and a Δ22% increased estimate for IHD compared to the default situation.

Other parameters that also may lead to substantial differences with the default situation are changing the prevalence of the population within the SBP categories as a consequence of salt reduction (Δ31% decreased estimate for stroke and Δ32% decreased estimate for IHD as compared to the default situation; see **Table 6.3**). Other parameters may lead to a small impact, such as no correction for usual blood pressure, or to no effect at all (e.g. calculations extended to 20y). The combined approach with modifications similar to the CHD policy model led to a stroke reduction of 7.8% and to an IHD reduction of 5.0%. This means a Δ26% decreased estimate for stroke and a Δ37% decreased estimate for IHD compared to the default situation.

Gain in life expectancy (**Figure 6.2**) followed a similar trend as the results in **Table 6.3**. However, a lower gain in life expectancy was observed for the linear association from Law *et al*. (19) and the CHD policy model approach.

Discussion

Our overview of selected HIA models of salt reduction showed that despite the many differences between the models there are also some similarities, for example that all studies examined the effect of salt intake on CVD as mediated by systolic blood pressure. Differences in assumptions between HIA models mainly concerned the effects sizes of the relationship between salt intake and systolic blood pressure, and between systolic blood pressure and disease occurrence, the shape of the dose-response association and certain intrinsic model structures, such as categorization of salt intake and/or blood pressure or dynamic versus static models. In the present study, we assessed to what extent model parameters may determine health impact estimates using a standard population health modelling approach (DYNAMO-HIA) for the Dutch situation. In the default situation, a 3 gram salt reduction reduced the incidence of CVA by 10.5% and the incidence of IHD by 7.9%. Substituting parameters relating to the association between salt intake and blood pressure and blood pressure to CVD changed the health impact estimates most substantially. Substituting the relative risks of blood pressure on CVD reduced the default estimate impact assessment by 33% for stroke and 40% for IHD. After this, using blood pressure in classes, and letting salt

intake change the proportion of the population in each class (reduction of HIA estimate by 27% for stroke and by 18% for IHD) appeared to have the most effect on the outcome estimate.

This is the first study that systematically compared various indirect and complex modelling approaches for salt reduction based on four predefined sets of key model characteristics and their underlying assumptions. Some limitations of the study need to be addressed. First, the models were compared based on predefined characteristics and parameters, while other differences have not been taken into account. Second, we selected the DYNAMO-HIA model to quantify the effect of salt on health and for the Dutch population only. The estimated differences in the alternative simulations may vary if this exercise is replicated in other models or in other populations. Finally, we only varied a limited set of parameters in DYNAMO-HIA model, and thus we cannot quantify the impact of remaining differences, such as the allowance of competing risks or the difference between static or dynamic models. The potential difference between dynamic and static models was not assessed, as it was considered an un-adjustable, intrinsic aspect of the population health models. We can only speculate how this difference will affect the health impact estimate. Dynamic models take changes due to selective mortality and ageing and competing risks into account. This will probably give a more accurate estimation of the future health gain. However, dynamic models also require additional data leading to increased uncertainties due to the increased data demands and to more complex model structures (2), leading to more uncertainty around the health impact estimate.

Health impact estimates changed when parameters were replaced by alternative parameters. Three assumptions seem to be most influential on the relative and absolute outcome of the health impact assessment: the sources of relative risks used in the blood pressure to health association, the dose-response between salt intake and blood pressure and the distribution of risk factors. Obviously, weaker effect sizes of salt on health, such as those from the Framingham Cohort Study compared to Prospective Studies Collaboration will lower the health impact estimate. We cannot distinguish whether the stronger health impact estimate as a result of the data from Law *et al*. was due to the shape of the dose-response association or due to the different effect size. Using categorical risk factor distributions seemed to reduce the sensitivity of the model to changes in salt intake. This is probably due to the fact that lowering salt intake will decrease blood pressure in all subjects, but only a few subjects will shift to a lower blood pressure category and thereby reduce the risk of developing CVD.

Uncertainty analyses show how the health impact estimate depends on the underlying assumptions and parameters within a single population health model and is therefore helpful to identify the range of the expected effect. However, uncertainty analyses are often only applied to a limited set of model parameters, for example the relative risks. The present study showed that also intrinsic model parameters contribute to the variation in the health impact estimates. Therefore, there is a clear need for transparency in HIA models, if necessary in a technical appendix, where transparency refers to the clear description of the model structures and (demographic) input data used.

Comparing the variation in outcomes from substituting a single parameter in a model was informative to identify the main assumptions that could contribute to the heterogeneity in the outcomes of published studies. In practice, HIA models vary in several underlying assumptions. Mirroring our approach to the approach used by the CHD policy model resulted in an impact estimate higher than the estimate of the CHD policy model (for example, CVA 7.8% for DYNAMO-HIA vs 5.2% of CHD policy model). Thus, by making approaches comparable we could not fully explain the variation between the models. Obviously, there will be some remaining differences, such as the difference in demographic data (such as country-specific incidence and prevalence of CVD). Therefore, a comparative study of the various models using similar input data (demographic as well as intervention scenario) could help to understand how the impact assessment differs between the various models, taking into account the mutual differences between the models.

Our results are in line with the modelling exercise performed by Coxson *et al.* (11) concluding that different modelling approaches lead to substantial health impact of salt reduction. The present study distinguishes itself from the methodology used by Coxson *et al.* as we applied different modelling strategies in a single population health modelling tool based on the differences observed in published modelling approaches. Especially differences in the strength of the dose-response association from salt to health seemed to contribute to heterogeneity of health impact estimates reported. Transparency of the models structures and (demographic) data used is essential to be able to interpret the outcomes of a health impact assessment.

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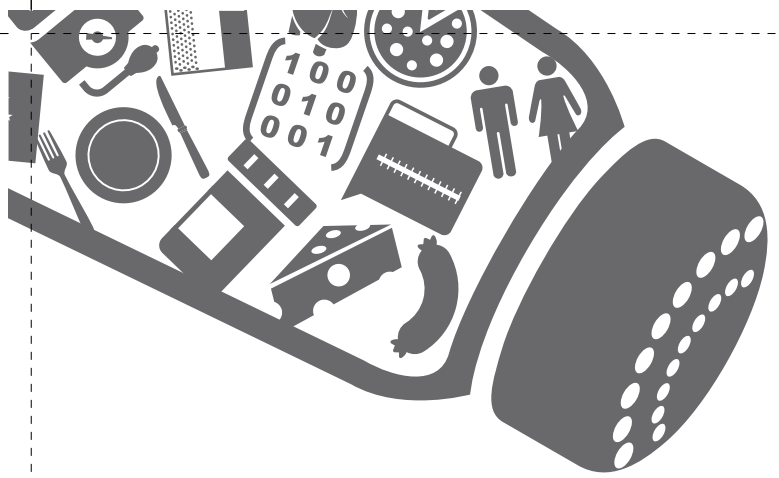
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Chapter 7

General discussion

The main aim of the research described in this thesis was to evaluate the health benefits of salt reduction at population level. The objectives were 1) to assess the impact of potential salt reduction strategies on salt intake in the Netherlands (**Chapter 2**), 2) to monitor the salt intake in the Netherlands and to evaluate the progress of the actual salt reduction initiatives in the Netherlands (**Chapter 3**) and 3) to assess the long-term health benefit of salt reduction on population health in the Netherlands and in Europe (**Chapter 4, 5 & 6**) (**Figure 7.1**). This last chapter includes for each objective a summary of the main findings, an overview of the methodological challenges and a discussion on the possible implications for public health.

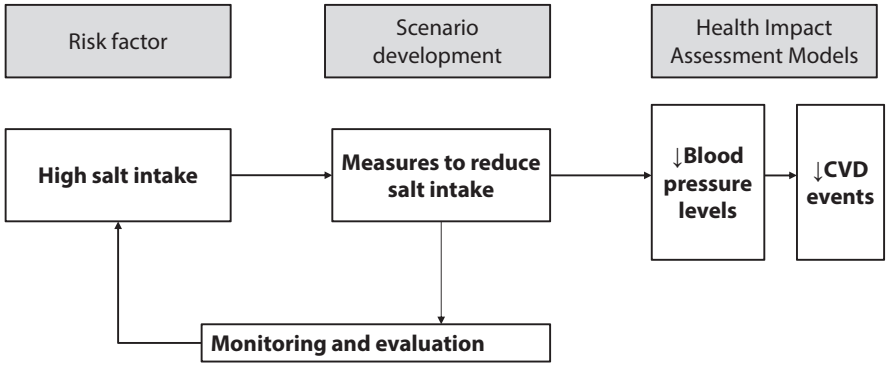

Figure 7.1 Overview of research described in this thesis.

Potential effect of sodium reduction initiatives on salt intake

We evaluated to what extent two salt reduction interventions, namely reducing sodium levels in processed foods or changing dietary behaviour, would reduce daily sodium intake in the Dutch population (**Chapter 2**). In order to do so, we created two scenarios in which the first scenario sodium levels in processed foods were reduced to their minimal technological feasible sodium level (in the current context) and in the second scenario foods were replaced by low-sodium alternatives. On average, sodium levels in processed foods could be reduced by 50%, leading to a reduction of 38% in daily salt intake. Within all food groups (such as bread, soups or cakes) low-sodium alternatives are already available on the market, reducing the daily sodium intake from processed foods and resulting in an estimated reduction of 47%. Both scenarios suggest that daily salt intake can be lowered substantially by choosing low-sodium alternatives or through a maximal sodium reduction in processed foods.

Methodological considerations

In **Chapter 2**, salt intake was assessed using data from the Dutch National Food Consumption Survey 2007–2010 (based on two independent 24h dietary recalls) combined with the Dutch Food Composition Database (NEVO) 2011 (1; 2). This method enabled us to identify the food sources of daily salt intake and to assess the potential effect of salt reduction in processed foods and the effect of choosing low-salt alternatives on changes in daily salt intake in a representative sample of the Dutch population. However, 24h dietary recalls may not be valid for estimating the absolute value of total daily salt intake, since the amount of discretionary salt cannot be accurately assessed. To overcome this issue, Verkaik-Kloosterman *et al*. developed a probabilistic model to estimate the amount of discretionary salt use (3; 4) based on data from food consumption surveys. This enabled us to estimate total daily salt intake using food consumption survey data (methodology was applied in **Chapter 4**). The generic Dutch food composition database NEVO was used as a reference database for the sodium levels of processed foods (2). However, this database may be limited in its usefulness to assess the potential of sodium reduction. Firstly, no distinction between salt naturally present in foods and added during food production can be made. Such information would be helpful to identify the potential minimal sodium levels in processed foods. Secondly, comparable foods are aggregated because of the generic character of the NEVO database. Generic foods (e.g. whole grain bread, average) may include various brands with a wide range of sodium levels (5). Since no distinction of the sodium levels between brands is made, it should be realized that the potential of sodium reduction or of choosing low-salt alternatives might be different for a generic food than for some individual brands. Thirdly, there may be some changes in sodium content of processed foods over time in the Netherlands. Therefore, it is crucial that the NEVO database is up-to-date. The NEVO database used in **Chapter 2** was not updated on a regular basis with respect to sodium levels. Since then, improvements have been made. Since 2012, the NEVO database has been updated annually focusing on foods that contribute most to salt, saturated fat and added sugar intake (5). Food manufacturers and food sectors supply compositional data on a voluntary basis, and analytical data are provided by the Dutch Foods and Consumer Safety Authority (6; 7; 8). These recent developments improve the usefulness of the Dutch food composition database in scenario analysis related to food reformulation.

Scenario analyses were applied to evaluate the potential effect on salt intake by effective food reformulation or by change in food choice (**Chapter 2**). Such scenario analyses are performed to predict future intakes after the implementation of a policy intervention (for

example on food reformulation or on fortification) (9; 10; 11). The estimated impact is only theoretical and offers the magnitude of an effect. Often, it is a simplification of reality. Still, a scenario must be valid in qualitative terms ('Will the intervention reduce salt intake?') and quantitative terms ('Is the estimated impact on salt intake plausible?'). The scenarios applied in **Chapter 2** are qualitatively valid since both interventions have the potential to reduce salt intake. The quantitative validity of both scenarios is challenging, since the assumptions used in **Chapter 2** are rather extreme. However, in future, technological advances may lead to lower sodium contents in processed foods than assessed in **Chapter 2**. Therefore, the outcome of the study should be interpreted as the maximal effect that could be obtained in the current context of high salt intake.

Evaluation of the assumptions used in scenario analysis is essential, especially if the outcomes are used to support policy makers in decision making. In that case one needs to ascertain whether the changes that take place are conform the assumptions that were made earlier in the scenario analyses. To illustrate, we give the following example. Policy makers reduced the fortification level of iodised salt based on the assumption that 50% of processed foods would contain iodized salt if the allowance to use iodised salt in processed foods would be extended (12). However, in practice, the actual use of iodized salt in the various food categories was probably much lower than anticipated with a consequent decline in iodine intake (13). This example highlights the importance of policy evaluation. In fact, women of childbearing age were identified as a potential group that might be at risk of iodine deficiency during pregnancy and lactation (**Chapter 3**).

Implications for public health

The advantage of sodium reduction in processed foods, as compared to behavioural interventions, is that the entire population is exposed to processed foods, including high-risk groups, such as persons with a low-socioeconomic status who are difficult to reach, or children (14). However, a prerequisite for success is commitment from the food industry to reduce the sodium levels in many foods over a wide range of food categories, including the foods that are more likely to be consumed by high-risk groups (15). In addition, sodium reduction should be implemented stepwise so that the reduction may take place relatively unnoticed, while the population will adapt to the less salty taste (16).

As a follow-up on the Dutch Task Force Salt Reduction active between 2006 and 2010, a new Agreement on Improvement of Product Composition: salt, saturated fat, sugar (calories) (in

Dutch: 'Akkoord Verbetering Productsamenstelling: zout, verzadigd vet, suiker (calorieën)') was signed in 2014 under the supervision of the Dutch Ministry of Health, Welfare and Sport (17). In this Agreement, several stakeholders involved in food production, catering and retail are represented. The stakeholders made voluntary commitments to reduce the sodium content of foods by setting benchmarks per food category. By 2020, daily salt intake should be at a maximum of 6 g/d. A scientific advisory committee evaluates the commitments on the feasibility and ambition and the commitments are approved as appropriate targets by a steering committee of representative stakeholders and the Ministry (17). Independent from the other food sectors, the bakery industry requested the government in 2008 to set mandatory maximum levels of sodium chloride in dry matter of flour, gradually reducing levels from 2.1% in 2008 to 1.8% by 2013 (18).

The implementation of the Agreement by evaluating the sodium levels in processed foods was and will be monitored by the Dutch National Institute for Public Health and the Environment in 2012 and 2014. Sodium levels in bread were reduced by 21% between 2011 and 2014 (5). Also in the food groups 'cheese', 'canned legumes' and 'canned vegetables' successful sodium reduction was achieved by 11%, 54% and 28% respectively. In the other food groups, no significant or no reduction was observed (5). There are some limitations in the current monitoring system of sodium levels in processed foods. Monitoring is mostly based on generic foods, while successful sodium reduction may have been achieved in certain individual brands. Furthermore, a small salt reduction in a food that has a large market share may have a more favourable impact on daily salt intake than a large reduction of a less frequently consumed food (19). As demonstrated in **Chapter 2**, sodium reduction in less frequently consumed foods is favourable for consumers of such foods, but hardly makes a difference on a population level. A database containing brand-specific information, including market share, would be useful, but a comprehensive database is not yet available in the Netherlands.

Despite all present efforts, the achieved reduction of sodium content in processed foods is still a long way from the technologically feasible minimal levels (**Chapter 2**). A question to be raised is how to achieve further sodium reduction in processed foods. Some may argue that regulation will be more effective than voluntary target levels to achieve relevant salt reduction (20). As an example, in the Netherlands, the significant reduction of sodium levels in bread was achieved after setting mandatory sodium content in bread. However, the feasibility of regulation may be limited, since a law lacks flexibility (15), as a law may need to be revised if the industry is to meet the targets laid down in the law. In some countries, such as South

Africa or Argentina, legislation on sodium content in processed foods was implemented a few years ago (15). Monitoring of the progress of these initiatives may demonstrate the feasibility and impact of mandatory sodium levels in processed foods.

The Dutch Agreement is based on the principle that the healthy choice should be the easy choice. In **Chapter 2** we demonstrated that it is already possible to consume less than 6 g/d given the current food supply, but a limitation of the current low-sodium alternatives means that they may be higher in saturated fat or added sugar. Front-of-package logos may be helpful to consumers in choosing foods that are low(er) in sodium, as well as in saturated fat and added sugar (21). Another favourable effect of front-of-package logos may be that they work as an incentive to the food industry to reduce the level of sodium in processed foods. For example, a study by Vyth *et al*. showed that sodium levels in processed foods were reduced in foods containing the front-of-package logo 'Choices' (22). Interventions to reduce total daily salt intake should also target the awareness on the use of discretionary salt. It is likely that a joint intervention of changes in dietary behaviour as well as sodium reduction in processed foods will be most effective. Monitoring the effect on daily salt intake is essential to monitor the progress of initiatives such as the Dutch on Agreement on Improvement of Product Composition: salt, saturated fat, sugar (calories).

Monitoring and evaluation of salt reduction

We monitored the effect of sodium reduction in processed foods and other salt reducing initiatives on daily salt intake over the period 2006 to 2010 in a sample of the Dutch population (**Chapter 3**). The industry-initiated Dutch Task Force Salt aimed to reduce the sodium levels in processed foods by 12% in several food groups between 2006 and 2010, but the efforts of the Task Force Salt did not result in a reduction in daily salt intake in 2010 (8.7 g/d in 2006 and 8.5 g/d in 2010). Due to changes in the iodine fortification policy, iodine intake did significantly decrease over the same period. However, the iodine intake could still be considered as adequate.

Methodological considerations

The 24h urinary sodium excretion we used (**Chapter 3**) is considered the gold standard to estimate daily salt intake (23), as it also includes discretionary salt intake. The validity of the estimate based on the 24h urine sample relates to the proper (i.e. complete) collection.

In our study (**Chapter 3**), there was limited information on the completeness of the 24h urine sample, namely self-reported missed voids and a fixed cut-off value for 24h creatinine excretion. A more reliable method to determine the completeness of the 24h urine samples could improve the accuracy of the daily salt intake estimate. For instance, the fixed cut-off values could be replaced by cut-off values based on body weight, as the creatinine levels are strongly associated with body weight (24; 25), or participants could also take *para*-aminobenzoic acid (PABA) tablets (25; 26). Applying the alternative methods to estimate the completeness of the urine samples will improve the validity of the daily salt intake estimate.

The people who participated in the 24h urine collection may differ from the general Dutch population in two ways. Firstly, collecting a complete 24h urine sample may be a large burden for the participants, resulting in low participation rates. Health-conscious individuals are more likely to participate leading to bias in the daily salt intake estimate for the general population (25). Secondly, the data was only collected in Doetinchem, a rural town in the eastern part of the Netherlands. Differences in dietary patterns between the Doetinchem population and an urban population may exist. For example, migrants were under-represented in our study. The salt intake estimates based on the urine samples could be compared with the estimations of salt intake from the DNFCS 2007–2010 using the probabilistic approach of Verkaik-Kloosterman *et al*. to estimate total salt intake (3; 4). The salt intake estimates for men and women were almost similar (**Chapter 3** and **Table 7.1**) (27). This finding suggests that the salt intake estimations from the 24h urine study may be an appropriate reflection of the daily salt intake of the Dutch population.

Salt intake estimates based on a single 24h urine sample do not take into account the large within-subject variation and may not represent long-term intake. Therefore, sodium intake estimated from a single 24h urine sample has a wider distribution than the true, habitual intake (28). A single 24h urine sample used to examine the adverse consequences of salt

Table 7.1 Daily salt intake estimates (in g/d) from the Dutch National Food Consumption Survey (DNFCS) 2007–2010 (N=3819), and based on 24h urine samples from Doetinchem in 2010 (N=342)

	Men			Women		
	19–30y	31–50y	51–70y	19–30y	31–50y	51–70y
DNFCS 2007–2010	10.1	10.1	9.3	7.5	7.5	7.3
	19–50y		51–70y	19–50y		51–70y
24h urine samples (2010)	10.3		10.0	7.5		7.3

intake has two implications. Firstly, the proportion of the population above the recommended maximum salt intake will be underestimated. Secondly, if an unadjusted distribution is used in a study on the association between salt intake and health, the estimate of salt intake on health is biased to the null values (29). This regression dilution may be corrected for, using the within-subject variation of salt intake (30). However, this requires a study with multiple 24h urine samples per person (28; 31). Obviously, this is impossible to implement in large study populations. Furthermore, the burden for the participants will increase, which may lead to lower participation rates and incomplete samples. It would be interesting to explore whether the methodology applied in food consumption surveys to estimate habitual salt intake can be estimated from two 24h urine samples. Two potential methodologies are possible: collecting a second 24h urine sample in a subset of subjects who participate in the monitoring survey using 24h urine samples, or obtaining the within-subject variation from another study and applying this to the urinary monitoring study.

Monitoring the daily salt intake in the Dutch population is essential to evaluate the progress of the Agreement on Food Reformulation. Therefore, in November 2015 daily salt intake will again be monitored by collecting new 24h urine samples in the population in Doetinchem. In addition, the potential adverse consequences of the intervention, such as the resulting iodine intake, will be monitored.

Long-term health impact of salt reduction in the Netherlands and Europe

We assessed the long-term health benefits of daily salt reduction on population health for the Netherlands and for Europe (**Chapters 4 and 5**). We assessed the health impact of salt reduction in the Netherlands using the RIVM Chronic Disease Model (**Chapter 4**) for the two salt reduction scenarios as described in **Chapter 2**. These scenarios related to the minimum feasible sodium levels in processed foods as well as on changes in dietary behaviour. In an additional scenario, we assessed the health gain when the salt intake was in accordance with the Dutch recommended maximum intake of 6 g/d. In **Chapter 5**, we assessed the health impact of salt reduction in nine European countries according to the targets set by the World Health Organization (30% reduction and ultimately to 5 g/d in 2025) using the DYNAMO-HIA model. In the modelling approaches of the studies described in **Chapter 4 and 5** the effect of salt reduction on cardiovascular disease was mediated by blood pressure reduction. In both studies, the impact of daily salt reduction on long-term health is

substantial over a 20 year period. In the Netherlands, sodium reduction in processed foods would reduce the incidence of stroke by 6.0% (4.1%–7.8%) and acute myocardial infarction (AMI) by 4.4% (3.1%–5.6%). Changes in dietary behaviour would reduce the incidence of stroke by 7.2% (4.9%–9.4%) and AMI by 5.3% (3.8%–6.8%). A reduced intake, according to the recommended maximum intake, averts 5.8% (3.9%–7.7%) of the cases of stroke and 4.8% (3.4%–6.2%) of the cases of AMI. Substantial health impacts were also observed in the selected nine European countries. A salt reduction of 30% will already reduce the prevalence of stroke ranging from 6.4% (6.0%–6.8%) in Finland to 13.5% (13.0%–13.9%) in Poland and the prevalence of Ischemic heart disease (IHD) ranging from 4.1% (3.9%–4.4%) in Finland to 8.9% (8.5%–9.3%) in Poland (**Chapter 5**). An intake of 5 g/d will lead to a 10.1% (9.5%–10.7%) reduction of prevalence of stroke in Finland and to 23.1% (22.2%–23.1%) in Poland and the prevalence of IHD will be reduced by 6.6% (6.2%–7.1%) in Finland and by 15.5% (14.8%–16.3%) in Poland.

In **Chapter 6**, seven different population health models used in the health impact assessment of salt reduction are compared according to four predefined characteristics and underlying assumptions. This comparison led to the conclusion that there is much variation in the underlying assumptions between the models. The extent to which variation in several of the underlying assumptions could affect the outcome of the population health models was assessed in alternative simulations using the default approach as described in **Chapter 5**. In all eight simulations, the health impact of a 3 gram salt reduction was substantial. However, the assumptions in the salt intake to blood pressure association and the size of the relative risks for the relation between blood pressure and cardiovascular disease could change the health impact for stroke by -33% and +19% respectively and for IHD by -40% and +22% respectively. Also the way blood pressure is included as a categorical instead of a continuous entity changed the health impact estimate for stroke by -31% and for IHD by 32%. This shows a clear need for transparency within and data documentation in health impact assessments in model calculations.

Methodological considerations

In **Chapter 4, 5 and 6** population health models were used to forecast the health impact of salt reduction in the Netherlands and in nine European countries. Population health models are a useful tool to quantify the long-term effects of an intervention in a rapid and cost-efficient way (32). However, the outcome is always a simplification of the reality and

depends on the evidence base on the effect of the risk factor on the health outcome, the validity of the population health model and the data included in the model (33). These aspects are discussed in the following paragraphs.

Evidence base on the effect of the risk factor. The causality of the associations built into population health models should be qualitatively and quantitatively plausible (34). The strength of the association between salt intake and cardiovascular disease is one of the main factors that determine the magnitude of the health impact estimates (**Chapter 6**). Therefore, the effect size of this relationship should accurately reflect the true effect of salt to health. The effect of salt reduction on blood pressure is demonstrated by several meta-analyses of randomized controlled trials (35; 36; 37). Subsequently, the association between blood pressure and cardiovascular disease is also well-established (38). Therefore, the health impact assessments executed for the Netherlands (**Chapter 4**) and for nine countries in Europe (**Chapter 5**) assumed the causal chain from salt intake to blood pressure and then to cardiovascular disease. The uncertainties related to the size of the effect of salt on blood pressure, as well as the size of the relative risks between blood pressure and cardiovascular disease were taken into account in sensitivity analyses. A potential limitation of our analysis is that we have only estimated the health impact on cardiovascular disease, while high salt intake could also influence other disease endpoints such as renal failure or gastric cancer (39; 40; 41; 42).

Validity of population health models. In population health models, three criteria exist to assess the validity of the model: formal validity, plausibility and predictive validity (34). *Formal validity* or verification relates to the degree to which valid methods have been applied correctly. In general, the DYNAMO-HIA model and the RIVM-CDM used in **Chapter 4, 5 and 6** are both multi-state Markov-type models with risk factor states taking into account the dynamics of the population over time. Both models have been reviewed extensively in scientific literature (43; 44; 45; 46; 47; 48). The *plausibility* relates to the understandability, applicability and plausibility of the theoretical framework. As previously discussed, the causal effect of salt to blood pressure to cardiovascular disease is sufficiently established. The *predictive validity* of the model is the validation of the model predictions to the true effects. Although this is considered to be essential, the predictive validation of RIVM-CDM and DYNAMO-HIA has not been established. Firstly, it is time-consuming to wait for many years to compare the outcome of the model with the actual effects observed. Secondly, in reality, many factors that are assumed stable in the model are not stable in reality (here, for example the survival rate is assumed to be stable, but might increase due to improvements in

the treatment of cardiovascular disease). Finally, a control group is lacking, so it is difficult to allocate the observed effects to the intervention. Some methods have been proposed to assess the predictive validity of the model (partial predictive validation by focusing on intermediary outcomes (in this thesis blood pressure) or historical data validation by using knowledge of initial conditions and outcomes in the past), but have not been applied in the research described in this thesis. Despite this limitation, the outcome of the health impact modelling can be used as a tool for decision making, as it indicates the effect of an intervention scenario and a status quo scenario under current conditions.

Data availability. Comprehensive exposure and health data needed to describe the health impact is not readily available. In the health impact assessment in nine European countries (**Chapter 5**), the salt intake and blood pressure data for four of the participating countries did not meet the initial inclusion criteria. Age- or gender-specific salt intake data was not reported and information on the distribution of salt intake was not available. In addition, blood pressure levels were only available in crude age ranges. Some data imputation and aggregation needed to be done to be able to assess the health impact. An analysis of the robustness of these assumptions showed that some assumptions had little effect on the health impact estimates (mean salt intake and age-specific blood pressure) while others had more substantial effects (mean blood pressure levels). This shows that one should carefully verify the effect of data imputations.

Data availability also applies to incidence, prevalence and excess mortality data needed in RIVM-CDM and DYNAMO-HIA. Earlier studies showed that this data may be inconsistent over the different disease information sources (44; 49). For example, the reported incidence of stroke based on hospital registries does not correspond to the observed prevalence of stroke that is reported by Statistics Netherlands. In RIVM-CDM and DYNAMO-HIA, DISMOD methodology was applied to retrieve consistent data on the incidence, prevalence and mortality data (50).

Our comparison between the published models used to estimate health impact of salt reduction (**Chapter 6**) provided insight into the complexity of the population health models and their underlying assumptions. Also the research described in this thesis illustrates that a direct comparison between the health impact estimates for the Netherlands is hardly possible. First of all, different salt reduction scenarios were applied and the underlying differences between RIVM-CDM and DYNAMO-HIA exist. But even a direct comparison of the papers using DYNAMO-HIA is not possible because of the different model versions

used (version 1.2 in **Chapter 5** and version 2.07 in **Chapter 6**). In version 1.2 we could only estimate the change in CVD *prevalence* while in version 2.07 we were able to estimate the impact on CVD *incidence*. These differences underline the need for clear documentation of the data included in the model and the version of the model used. Transparency in the modelling exercise will help scientists and policy makers to judge and interpret the outcomes of a health impact assessment.

Implications for public health

Population health modelling tools may support policy makers in deciding which policy intervention will be most effective, or even cost-effective. Our studies demonstrated that salt reduction can be important to improve the populations' health by reducing the burden of cardiovascular disease morbidity and mortality in the Netherlands as well as in Europe. However, an important question that can be raised is whether the salt reduction scenarios that are included in our population health models, as well as in the models published in literature, are practically feasible. For all possible interventions of salt reduction the prevention paradox applies: a small change in a risk factor at individual level will have a large effect at population level (51). However, to achieve a small change in blood pressure (e.g. 1.9 mmHg), salt intake must be reduced quite substantially by 3 g/d (**Chapter 4**). Several health impact calculations estimated the effect of a 3 gram salt reduction or adherence to the dietary guidelines, but do not specify how this reduction will be achieved. Compared with the achievements of the salt reduction initiatives on daily salt intake in 2010 in the Netherlands (**Chapter 3**) a 3-gram salt reduction or adherence to the recommended maximum intake seems very ambitious. Temme *et al.* performed a simplified calculation of the current nutritional impact of the Dutch Agreement on Food Reformulation on daily salt intake and estimated that total daily salt intake would be reduced by 5% (equals to 0.4 g/d of salt) (5). Such a small reduction would have little impact on blood pressure and ultimately on CVD. The UK salt reduction initiative of the FSA, implemented from 2003 until now is often referred to as a "best practice" of the salt reduction initiative. An evaluation of the project in 2012 summarized the achievements of the initiative between 2003 and 2010 (52). For example, the majority of the retailers met the targets in 2010, and between 2006 and 2008 the sodium level in cakes was reduced by 25% and in sweets and savoury biscuits by 44% and 25% respectively. In addition, the consumer awareness of undesired high salt intake, expressed as the percentage of adults who claimed to look at food labels, increased from 29% in 2004 to 50% in 2009. The daily salt intake reduced from 9.5 g/d in 2001 to 8.1 g/d in 2011 (1.4 g/d or 15%) (53). This

demonstrates that there is a substantial gap between the achievements of the salt reduction initiatives to date and the expected health effects of a 3 gram salt reduction scenario used in the population health models.

Sodium reduction in processed foods is recognized as a cost-effective strategy (54; 55; 56; 57). This can be explained by the fact that the costs of the implementation of the intervention are relatively low from a governmental perspective (e.g. costs for legislation or the monitoring of the intervention) and the gain in terms of reduced disease incidence are high (fewer hospital admissions). In the present research, we did not estimate the cost-effectiveness of the intervention, because the societal costs related to implementing the interventions are not yet clear and should be considered. The implementation of sodium reduction in processed foods may require substantial investment by the industry, such as higher costs of sodium substitutes, or costs related to research and development of salt alternatives (58). An estimation of the reformulation costs is complicated, and we consider this to be outside the scope of the present research. However, some have argued that the magnitude of the expected health impact, will mean the societal cost-benefit ratio will be in favour of salt reduction (59).

The health impact of salt reduction in the Netherlands (**Chapter 4**) and in nine European countries (**Chapter 5**) may be considered in the light of the impact of other (lifestyle) interventions or policy measures. Bibbins-Domingo *et al.* compared the effect of a 3-gram salt reduction with other public health (smoking cessation and weight loss) and clinical interventions (statin therapy for primary prevention and pharmacological treatment of hypertension) on cardiovascular disease mortality in the USA (60), and concluded that the benefits of salt reduction were similar to those interventions. The burden of disease of several lifestyle factors was assessed in the Public Health Status and Forecast 2014 of the RIVM. Smoking (13.1%), overweight (5.2%) and sedentary lifestyle (3.5%) were the most important contributors to the Dutch burden of disease, followed by a diet high in salt (1.9% - estimated using the approach developed in **Chapter 5**), a diet low in fruit (1.8%), fish (1.5%) or vegetables (0.5%) (61). On a global level, the Global Burden of Disease estimated that a diet low in fruit (4.2% of global DALYs) made the largest contribution to the attributable burden in 2010, followed by a diet high in salt (2.5% of global DALYs), low in nuts and seeds (2.1% of global DALYs) and low in vegetables (1.5%) (62). The three leading risk factors for global disease burden were estimated to be hypertension (7.0%), tobacco smoking (6.3%) and alcohol use (5.5%). A limitation of such a comparison is that the effects are considered to be independent from each other. In practice, those risk factors are interrelated and often

cluster in individuals (63; 64). It is likely that all assessments of each individual risk factor will overestimate the health impact of a dietary pattern or "lifestyle pattern". Future research should explore the health impact of such complex dietary and lifestyle patterns, for example the overall health impact of the 'Agreement on Improvement of Product Composition: salt, saturated fat, sugar (calories)'.

Finally, attention should be given to the promising results of two observations in Finland and the UK after the salt reduction strategies were implemented (65; 66). In Finland, a drop in blood pressure was observed over three decades simultaneously after the implementation of a nation-wide sodium reduction (66). In the UK, an analysis of two independent samples of participants from the Health Survey of England showed that the average systolic blood pressure levels decreased by 3 mmHg from 2003 to 2011 for the population not using anti-hypertensive medication, in the similar period of the UK salt reduction initiative (65). Because of the ecological nature of the observations, one cannot ascertain that the observed reduction on blood pressure levels can be attributed to the salt reduction. However, it does support the notion that salt reduction may be beneficial for public health.

International perspective

The salt intake levels that were needed for the health impact assessment of salt reduction in Europe (**Chapter 5**), as well as other inventories on salt intake in Europe (23; 67), showed that high salt intake is prominent in all countries and subsequently the potential health gain that can be achieved according to the targets of the WHO, is substantial. In certain countries, such as Poland, the potential effects of salt reduction seem to be extremely high (**Chapter 5**). However, in those countries, sustainable efforts to reduce salt intake will be needed in order to be successful. Coherence of policies between countries or EU-wide regulations will help to increase the effectiveness of the interventions, for example by its effect on the sodium levels of foods from all over Europe (59).

At the moment, food reformulation is one of the strategies adopted at the global and European level to contribute to the reduction of premature mortality from non-communicable diseases (NCDs). It is one of the targets to be achieved in 2025 of the Global Action Plan for the Prevention and Control of Non-Communicable Diseases of the WHO (2013) and is an integral part of the WHO European Action Plan for Food and Nutrition Policy (2014). Also at European Union level, the EU High Level Group on Diet, Physical Activity and Health

supports EU Member States to achieve the WHO targets of salt intake. Such international attention underlines the importance of salt reduction.

Concluding remarks

The research described in this thesis illustrates that to achieve a daily salt intake below the recommended intake of 6 g/d in the Netherlands, sodium levels should be reduced by on average 50% or substantial changes in dietary behaviour should be made. The efforts by the food industry that have been implemented between 2006 and 2010 have not yet resulted in a lower salt intake in the Netherlands. Considerably more effort will be needed to have a successful salt intake reduction. If substantial salt reduction is achieved, this would delay the development of cardiovascular disease and considerably reduce the burden of disease in the Netherlands, as well as in nine European countries. However, the total of health gain that can be achieved can differ between the population health models used, depending on the parameters used, intrinsic model characteristics or data included. This illustrates the need for clear documentation and transparency of the models used.

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Annex I

Supplement to chapter 2 – Impact of sodium reduction strategies on salt intake

Table I.1 Overview of the evidence of technologically feasible sodium levels per food subcategory levels

Food group	Food subcategory	Added sodium	Main functions of sodium			Specific sodium reduction strategies	Reasonable sodium reduction [%] in 5 years	Remarks	References
			Processing	Microbiological	Sensory				
Bread	Dutch rusk, Swedish crackers, crackers and toast	Salt added to dough	Dough processability - control yeast fermentation	Low Aw	Flavour/ texture	Salt reduction, salt replacement	50		(1–5)
	Sandwich bread	Salt added to dough	Dough processability - control yeast fermentation	Mainly consumed fresh	Flavour/ texture	Salt reduction, salt replacement	50		
	Filled bread	Salt added to dough	Dough processability - control yeast fermentation	Mainly consumed fresh or reduced Aw	Flavour/ texture	Salt reduction, salt replacement	35	Sodium level is already lower due to the filling content.	
	Croissants	Salt added to dough - Present in margarine/fat	Dough processability - control yeast fermentation	Mainly consumed fresh or reduced Aw	Flavour/ texture	Salt reduction, salt replacement	50		

Table I.1 continues on next page

Table I.1 ***Continued***

Food group	Food subcategory	Added sodium	Main functions of sodium			Specific sodium reduction strategies	Reasonable sodium reduction [%] in 5 years	Remarks	References
			Processing	Microbiological	Sensory				
Pies and cakes	Biscuits	Salt added to dough - Sodium based leavening agents	Chemical leavening	Low Aw	Flavour/ texture	Salt reduction, salt replacement, substitution chemical leavening agents	60		
	Gingerbread	Salt added to dough - Sodium based leavening agents	Chemical leavening	Mainly depends on sugar	Flavour/ texture	Salt reduction, salt replacement, substitution chemical leavening agents	50		
	Cakes	Salt added to dough - Sodium based leavening agents	Chemical leavening	Mainly depends on sugar	Flavour/ texture	Salt reduction, salt replacement, substitution chemical leavening agents	60		(6)
	Filled cakes	Salt added to dough - Sodium based leavening agents	Chemical leavening	Mainly depends on sugar	Flavour/ texture	Salt reduction, salt replacement, substitution chemical leavening agents	40	Sodium level is already lower due to the filling content.	

Table I.1 continues on next page

Table I.1 ***Continued***

Food group	Food subcategory	Added sodium	Main functions of sodium			Specific sodium reduction strategies	Reasonable sodium reduction [%] in 5 years	Remarks	References
			Processing	Microbiological	Sensory				
Cheese	Aged, (semi) hard cheese	Brined for 3 to 8 days	Water expulsion from the curd, control ripening process	Changes microbial ecology (e.g. butyric acid fermentation)	Flavour (increased acidity, bitterness), increased brittleness	Salt reduction, salt replacement by minerals to control ripening	50		
	Processed cheese	Sodium from cheese and emulsifying agents	Emulsification	Shelf life	Stability of product (emulsion breakdown)	Salt reduction, substitution emulsifiers	50	Reduction or replacement of stabilizers may require lower shear forces during processing	
	Soft cheese	Salted after molding	Control ripening process	Changes in microbial ecology	Flavour, development of bitterness	Some cheeses are washed with either dry salt or salt slurry during aging. Decreasing the salt levels may result in problems with ripening	50		(11-18)
	Fresh cheese	Direct salting	N/A	Shelf life	Flavour	Salt reduction, salt replacement	50		
	Blue cheese	Surface dry salting	Control ripening process	Changes in microbial ecology	Flavour (increased acidity, bitterness), increased brittleness	Salt reduction, salt replacement by minerals to control ripening	50		

Table I.1 continues on next page

Table I.1 ***Continued***

Food group	Food subcategory	Added sodium	Main functions of sodium			Specific sodium reduction strategies	Reasonable sodium reduction [%] in 5 years	Remarks	References
			Processing	Microbiological	Sensory				
Soups	All	Added as salt or indirect via ingredients	N/A	N/A	Flavour	Salt reduction, salt replacement, flavour enhancers	50		(19)
Nuts, seeds and snacks	Chips	Added salt, Seasoning	N/A	N/A	Flavour	Salt reduction, salt replacement, flavour enhancers	50	Taste will be decisive factor	
	Baked	Added salt, Seasoning	N/A	N/A	Flavour	Salt reduction, salt replacement, flavour enhancers	50		No literature
	Meat snacks	Added salt, Seasoning	Process modification	Frozen storage	Flavour	See meat products below	50		
	Cheese snacks	Added salt, Seasoning	Process modification	Low Aw	Flavour	Salt reduction, salt replacement, flavour enhancers	50		
Soy and vegetarian products	Soy sauce	Added as salt during processing	Fermentation occurs under brine conditions	Correct microbial ecology during fermentation	Soy sauce is supposed to be salty	Separation of sodium by ion exchange technologies	50		(20)

Table I.1 continues on next page

Table I.1 ***Continued***

Food group	Food subcategory	Added sodium	Main functions of sodium			Specific sodium reduction strategies	Reasonable sodium reduction [%] in 5 years	Remarks	References
			Processing	Microbiological	Sensory				
Soy and vegetarian products	Meat replacers	Added as salt during processing and from functional ingredients	Changes in water binding, emulsion capacity	N/A	Flavour and texture changes	Salt reduction, salt replacement	50		(20)
	Soy milk	Added salt	N/A	N/A	Flavour enhancer	Salt reduction, salt replacement	50		
Herbs and spices	Herb mix	Added salt	N/A	N/A	Flavour	Salt reduction, salt replacement, flavour enhancement	50	Low-sodium products are available on the market	No literature
	Mustard	Added salt	N/A	N/A	Flavour		50		
	Red pepper hot paste	Added salt	Brine fermentation process	Correct microbial ecology	Flavour		30		

Table I.1 continues on next page

Table I.1 ***Continued***

Food group	Food subcategory	Added sodium	Main functions of sodium			Specific sodium reduction strategies	Reasonable sodium reduction [%] in 5 years	Remarks	References
			Processing	Microbiological	Sensory				
Fats, oils and savoury sauces	Formulated products	Added salt, mainly from ingredients	N/A	N/A	Flavour	Salt reduction, salt replacement, flavour enhancers	50	Taste will be decisive factor	
	Emulsion	Added salt, mainly from ingredients	N/A	N/A	Flavour	Salt reduction, salt replacement, flavour enhancers	50		No literature
	Brined	Added salt, mainly from ingredients	N/A	N/A	Flavour	Salt reduction, salt replacement, flavour enhancers	50		
	Dried	Added salt, mainly from ingredients	N/A	N/A	Flavour	Salt reduction, salt replacement, flavour enhancers	50		

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Annex II

Supplement to chapter 4 – Impact of salt reduction in foods on public health

1. Calculations to estimate discretionary salt use and total salt intake

In food consumption surveys salt intake is often not assessed due to lack of information on discretionary salt use. Verkaik-Kloosterman *et al.* developed a simulation model in which habitual salt intake could be estimated including discretionary salt use (1; 2). In brief, the model takes into account the three main sources of sodium intake: sodium present in (industrially) processed foods, sodium present in supplements and sodium added during meal preparation and seasoning. The intake of sodium present in foods and supplements is calculated with a deterministic approach: the consumed amount of a food or supplement in the DNFCS 2007–2010 is multiplied with the concentration of sodium in the food in supplement as available in the food composition table of 2011 or in the Dutch supplement database. The salt intake from foods is the sum of salt intakes from all foods per subject per day, and the salt intake from supplements is the sum of salt intakes from all supplements per subjects per day. In **Table II.1** the percentage of subjects not using discretionary salt is presented.

Table II.1 Percentage of non-users of discretionary salt

Age category	Sex	Non-users of discretionary salt (%)
7–8y	Boys	16
	Girls	15
9–13y	Boys	7
	Girls	16
14–18y	Boys	5
	Girls	8
19–30y	Men	13
	Women	14
31–50y	Men	9
	Women	16
51–69y	Men	17
	Women	17

We assumed that no salt was added to foods already containing industrially added salt, like canned vegetables or processed meat. Based on recipes and guidelines of the food composition table, the amount of discretionary salt added per 100 g consumed product was estimated (see **Table II.2**).

The uncertainties related to the use of discretionary salt are estimated based on Monte Carlo simulations and the presented salt intake distributions are the mean value of the calculations based on 10 repetitions (see **Table II.3**).

Table II.2 Use of discretionary salt for various food groups

Food groups	% users	g salt /100g
Potatoes	85	0.4
Mashed potatoes	85	0.6
Rice and pasta	85	0.4
Vegetables	75	0.6
Meat	95	1.8
Fish	95	1.8
Meat substitutes	95	1.8
Eggs	75	1.8
Home prepared sauces	80	0.8
Pancakes	85	0.2

Table II.3 Salt intake distributions of men and women in the various scenarios

	Men			Women		
Age	P5	P50	P95	P5	P50	P95
Current salt intake scenario						
20–29y	6.6	9.7	13.5	5.0	7.5	10.3
30–39y	6.7	9.9	13.6	5.1	7.6	10.4
40–49y	6.8	9.8	13.4	4.8	7.4	10.3
50–59y	5.9	9.2	12.9	5.0	7.4	10.2
≥60y	5.3	8.6	12.2	4.6	7.2	10.9
Salt reduction in processed foods scenario						
20–29y	4.5	7.1	9.9	3.4	5.3	7.5
30–39y	4.7	7.2	10.0	3.5	5.4	7.6
40–49y	4.8	7.2	10.0	3.2	5.3	7.5
50–59y	4.0	6.7	9.6	3.4	5.4	7.5
≥60y	3.5	6.2	9.1	3.0	5.1	7.3
Recommended maximum intake scenario						
20–29y	6.0	6.0	6.0	5.0	6.0	6.0
30–39y	6.0	6.0	6.0	5.1	6.0	6.0
40–49y	6.0	6.0	6.0	4.8	6.0	6.0
50–59y	5.9	6.0	6.0	5.0	6.0	6.0
≥60y	5.3	6.0	6.0	4.6	6.0	6.0
Substitution processed foods scenario						
20–29y	3.7	6.2	8.9	2.7	4.6	6.5
30–39y	4.0	6.4	9.1	2.9	4.7	6.7
40–49y	4.2	6.6	9.2	2.7	4.7	6.7
50–59y	3.4	6.2	9.0	3.0	4.9	6.9
≥60y	3.1	5.9	8.7	2.8	4.9	7.0

2. Health effect calculations of salt reduction on systolic blood pressure and CVD in more detail

2.1 From measured systolic blood pressure to usual systolic blood pressure

Systolic blood pressure (SBP) data were based on data from two surveys in the Netherlands (the Morgen study and the ERGO study) (3; 4). In these studies SBP is measured during a single examination. The variation of SBP measurement from a single examination contains both within person day-to-day variation as well as between persons variation of the usual SBP. We used the method described by Klungel *et al.* (5) to transform the distribution of measured SBP values into a distribution of usual SBP values, including using a factor 0.76 for the ratio K of the between person variance (usual) to total variance (measured).

The second step in our calculations is to use the distribution of usual SBP to calculate the percentage of the population in the different SBP categories (<120, 120–139, 140–159 and ≥160 mmHg).

More in detail, the calculation steps used are

1. We fitted a log-normal distribution to the proportion in each SBP category as measured in the surveys, separately by gender and age. This resulted in values $\mu_{log,measured}$ and $\sigma_{log,measured}^2$ of the mean and total variance (on the log scale) respectively.

2. We calculated the values of the mean ($\mu_{measured}$) and variance ($\sigma_{measured}^2$) of the untransformed SBP values.

$$\mu_{measured} = \exp(\mu_{log,measured} + \tfrac{1}{2}\, \sigma_{log,measured}^2)$$

$$\sigma_{measured}^2 = \mu_{measured}^2 * (\exp(\sigma_{log,measured}^2) - 1) \qquad \text{(II.1)}$$

3. We calculated the mean and variance for the usual instead of measured SBP values as

$$\mu_{usual} = \mu_{measured}$$

$$\sigma_{usual}^2 = K * \sigma_{measured}^2 \qquad \text{(II.2)}$$

4. We assumed that the usual distribution is still log-normal, and we calculated the new parameters of the corresponding lognormal distribution as

$$\sigma_{log,usual}^2 = \sqrt{\log(1 + \sigma_{usual}^2 / \mu_{usual}^2)}$$

$$\mu_{log,usual} = \exp(\mu_{usual}) - \tfrac{1}{2} * \sigma_{log,usual}^2 \qquad \text{(II.3)}$$

5. Using this new distribution we calculated for each age and gender the part of the population in each SBP category (<120, 120–139, 140–159 or ≥160) (see **Table II.4**).

6. As well as the mean usual and measured SBP value in each of these categories for later use in section 2.5 as:

$$\mu_{log,usual,i} = \mu_{log,usual} + \sigma_{log,usual} * (f_i - f_{i+1}) / (F_{i+1} - F_i) \quad \text{(II.4)}$$

with: i: index over classes, $\mu_{log,usual}$, $\mu_{log,usua,il}$: overall and class-specific mean value respectively, $\sigma l_{og,usual}^2$: variance, f_i: value of probability density function for lower cut-off point of class i, F_i: value of cumulative probability function for lower cut-off point of class i.

Table II.4 Baseline usual SBP prevalence of men and women in the various scenarios

	Men				Women			
Age[a]	<120 mmHg	120–139 mmHg	140–159 mmHg	≥160 mmHg	<120 mmHg	120–139 mmHg	140–159 mmHg	≥160 mmHg
Current salt intake scenario								
20y	0.54	0.44	0.03	0.00	0.86	0.13	0.00	0.00
40y	0.46	0.46	0.08	0.00	0.72	0.25	0.03	0.00
60y	0.15	0.42	0.32	0.11	0.22	0.42	0.27	0.09
80y	0.02	0.21	0.42	0.35	0.02	0.20	0.39	0.38
Salt reduction in processed foods scenario								
20y	0.57	0.42	0.01	0.00	0.89	0.11	0.00	0.00
40y	0.48	0.48	0.04	0.00	0.72	0.26	0.02	0.00
60y	0.17	0.43	0.33	0.07	0.23	0.44	0.28	0.06
80y	0.04	0.23	0.44	0.29	0.04	0.21	0.41	0.34
Recommended maximum intake scenario								
20y	0.60	0.40	0.01	0.00	0.88	0.12	0.00	0.00
40y	0.50	0.47	0.03	0.00	0.72	0.26	0.02	0.00
60y	0.17	0.44	0.33	0.06	0.23	0.42	0.29	0.06
80y	0.04	0.24	0.45	0.28	0.04	0.20	0.40	0.36
Substitution of processed foods scenario								
20y	0.59	0.40	0.01	0.00	0.89	0.11	0.00	0.00
40y	0.49	0.47	0.04	0.00	0.73	0.25	0.02	0.00
60y	0.17	0.44	0.32	0.06	0.23	0.44	0.28	0.05
80y	0.04	0.24	0.45	0.28	0.04	0.22	0.41	0.33

[a] CDM is divided into one-year age categories. Numbers presented only for selected ages.

2.2 Deriving the dose-response relationship between salt intake and SBP

We reformulated the findings of He and MacGregor (6) in formula II.5 in which we assumed that the change in SBP per additional amount of salt in the diet is linearly related to the usual SBP levels:

$$\frac{dSBP}{dSI} = \beta(\alpha + SBP) \qquad \text{(II.5)}$$

where *SI* is salt intake (g/d), *SBP* is usual SBP level (mmHg), and α and β are regression coefficients of the dose-response curve.

Solving equation II.5 results in the following formula of the SBP level as a function of salt intake:

$$SBP = c\, e^{\beta SI} - \alpha \qquad \text{(II.6)}$$

with *c* a stochastic parameter depending on age and sex. According to He and MacGregor, the SBP level of 127 mmHg (normal SBP) corresponds to a *dSBP/dSI* of 0.6 mmHg/g salt and a SBP levels of 149 mmHg (hypertension) corresponds to a *dSBP/dSI* of 1.2 mmHg/g salt. Using these two findings as conditions, the regression coefficients α and β are estimated; α = -105, and β = 0.03. The variation of the SBP level in the population is larger than that resulting from the variation of the salt intake. Therefore, we assumed that c is a stochastic parameter that is lognormally distributed. We estimated the mean and variance of c using data on the distribution of salt intake given in **Table II.3** and on SBP (7, 8), specified by gender and age-class. **Table II.5** shows the mean and standard deviation men and women for selected ages.

Table II.5 Mean and standard deviation of *c* for selected ages

	Men	Women
Age[a]	Mean (sd)	Mean (sd)
20y	12.0 (8.2)	3.2 (8.9)
40y	13.9 (10.2)	6.6 (12.3)
60y	27.7 (14.9)	25.5 (15.9)
80y	41.3 (15.5)	43.8 (17.1)

[a] CDM is divided into one-year age categories. Numbers presented only for selected ages.

In these calculations we assumed the parameters α and β are fixed. In an uncertainty analysis, we varied these parameters (see the section on uncertainty analysis below).

2.3 The RIVM Chronic Disease Model (CDM) in more detail

The RIVM Chronic Disease Model (CDM) describes the changes in morbidity and mortality from diseases that result from changes in risk factor levels, i.e. SBP level in our model application. CDM is a multi-state Markov model (9). The model time-step was 1 year.

The model states are defined by the SBP classes and the presence or absence of three chronic diseases. The SBP classes were defined by the cut-off points 120, 140, and 160 mmHg. The chronic diseases included were those causally related to SBP, i.e. acute myocardial infarction (AMI), stroke (CVA), and congestive heart failure (CHF). Persons can move between model states: there are transitions between SBP classes, and disease incidence. The model did not allow recovery from disease (transitions from the state "with disease" to the state "without disease). Disease incidence probabilities depend on SBP class (s) and for CHF incidence also on AMI status. They were calculated as follows using relative risks:

$$P(inc_{AMI}|SBP = s) = P_0(inc_{AMI})RR^{AMI}(s) \quad \text{(II.7)}$$

$$P(inc_{CVA}|SBP = s) = P_0(inc_{CVA})RR^{CVA}(s) \quad \text{(II.8)}$$

those with AMI

$$P(inc_{CHF}|SBP = s, AMI = 1) = P_0(inc_{CHF})RR^{CHF}_{SBP}(s)R^{CHF}_{AMI}(1) \quad \text{(II.9)}$$

those without AMI

$$P(inc_{CHF}|SBP = s, AMI = 0) = P_0(inc_{CHF})RR^{CHF}_{SBP}(s) \quad \text{(II.10)}$$

with: $P(inc_I)$: the incidence probability of disease *i*, that depends on SBP class. CHF also depends on the presence of AMI, $P_0(inc_i)$: calculated reference value of incidence probability of disease *i*, i.e. the incidence probability for those with SBP<120 mmHg, $RR^{CHF}(SBP)$: relative risk for the SBP class, $RR^{CHF,AMI}$: relative risk on CHF in those with AMI. For the baseline SBP class (<120 mmHg) and those without AMI, the relative risks are equal to 1. Formulas (II.9 and II.10) show that we assumed that SBP class and the presence of AMI have independent effects on CHF incidence.

Table II.6 shows the overall population incidence for AMI, CHF and CVA at the start of simulation.

The simulation starts with disease probabilities as shown in **Table II.7**. The resulting prevalence is updated with the new cases (incidence) each year.

Table II.6 One year incidence rates of AMI, CHF and CVA

	Men			Women		
Age[a]	AMI	CHF	CVA	AMI	CHF	CVA
20y	0.000006	0	0.00004	0.000006	0	0.00003
40y	0.000883	0.000122	0.000473	0.000327	0.000177	0.000354
60y	0.004426	0.002429	0.003529	0.001212	0.001399	0.002644
80y	0.012421	0.020271	0.017084	0.00487	0.015213	0.012843

[a] CDM is divided into one-year age categories. Numbers presented only for selected ages.

Table II.7 Current prevalence of AMI, CHF and CVA

	Men			Women		
Age[a]	AMI	CHF	CVA	AMI	CHF	CVA
20y	0.00005	0.000005	0.000229	0.00005	0.00005	0.000172
40y	0.004116	0.000283	0.002589	0.00153	0.000397	0.001939
60y	0.055251	0.00738	0.018877	0.015717	0.004227	0.014197
80y	0.146528	0.075954	0.085441	0.062621	0.05917	0.065358

[a] CDM is divided into one-year age categories. Numbers presented only for selected ages.

The one-year probability of mortality depends on the presence or absence of the diseases using an additive model:

$$\begin{aligned} P(mort \mid AMI = i, CVA = j, \quad CHF = k, \quad SBP = s) \\ = (1-i)P(inc_{AMI}|SBP = s)P(cf_{AMI}) + \Delta P_{AMI}(mort|AMI = i) \\ + (1-j)P(inc_{CVA}|SBP = s)P(cf_{CVA}) \\ + \Delta P_{CVA}(mort|CVA = I_{CVA}) + (1-k))P(inc_{CHF}|SBP = s)P(cf_{CHF}) \\ + \Delta P_{CHF}(mort|CHF = k) + P_0(mort)) \end{aligned} \quad \text{(II.11)}$$

with: $P(mort)$: the one-year probability of mortality that depends on SBP class and on the presence of diseases, $\Delta P(mort)$: the excess mortality probability that is uniquely attributable to AMI, CVA and CHF (9, 10), which equals 0 if the disease is not present; $P_0(mort)$: the mortality probability due to other causes, $P(inc_{AMI})$ and $P(inc_{CVA})$ the incidence probability of AMI, and CVA, cf_{AMI} and cf_{CVA}: the 1-year mortality probability directly after onset (case

fatalities) of AMI and CVA. The indicators *i*, *j*, and *k* equal 1 when a person suffers from AMI, CVA and CHF, respectively and equals 0 otherwise. The equation (II.11) shows that the mortality probability consists of three types of terms: the excess mortality related to the diseases, the mortality related to all other causes, and the 1-year mortality (case fatality) directly after disease onset. For more details of the calculated of the uniquely attributable excess mortality, see Van Baal *et al.* (10). The disease incidence probabilities were worked out in formula (II.7-II.10). The model equation shows that we assumed that the all-cause mortality probability depends on SBP level only through the three forms of cardiovascular diseases that we distinguished. All model parameters were specified by gender and age. For illustration purposes chronic and acute mortality probabilities for some ages are shown in **Table II.8a** and **II.8b**.

Table II.8a Uniquely attributable excess mortality probabilities of AMI, CHF and CVA

	Men			Women		
Age[a]	AMI	CHF	CVA	AMI	CHF	CVA
20y	0.000609	0.179991	0.002017	0.0	0.130012	0.001022
40y	0.000522	0.179778	0.004204	0.0	0.129789	0.003257
60y	0.004239	0.177961	0.022314	0.00297	0.128243	0.01527
80y	0.034202	0.188657	0.052761	0.010073	0.126783	0.023877

[a] CDM is divided into one-year age categories. Numbers presented only for selected ages.

Table II.8b Case fatality of AMI and CVA and other causes mortality probability values

	Case fatality				Other causes mortality	
	Men		Women		Men	Women
Age[a]	AMI	CHF	CVA	AMI		
20y	0.29	0.06	0.30	0.07	0.00046	0.00024
40y	0.28	0.09	0.28	0.10	0.00090	0.00074
60y	0.37	0.21	0.37	0.23	0.00497	0.00508
80y	1.00	0.65	1.00	0.71	0.03916	0.03722

[a] CDM is divided into one-year age categories. Numbers presented only for selected ages.

2.4 The 1-year transition probabilities between the SBP classes

The SBP levels change over age and time. We did not have longitudinal data to calculate the 1-year transition probability values between the SBP classes. Therefore, we calculated them from cross-sectional data specified by gender and age. The one-year transition probability values were chosen so that they move the distribution of an age class to the distribution of

the one-year older age class. We included mortality in different SBP classes in the calculations and assumed the transition takes place when half of the mortality has happened. This problem of calculating transition probability values, given the proportions at the start and end of the 1-year interval is interpreted as a mathematical transportation problem. We applied the integer programming solution for this transportation problem (lp.transport from R-package lpsolve, CRAN (2011)) to estimate the transition probabilities, minimizing the number of movements between SBP classes, and favouring changes to neighbouring classes over those two classes further apart. For more details, see Van de Kassteele *et al.*, who implemented the same method but ignored mortality (11). See **Table II.9** for the resulting transition probabilities.

Table II.9 Transition probabilities (percentages) between SBP classes

	Men			Women		
Age[a]	<120 mmHg to 120–139 mmHg	120–139 mmHg to 140–159 mmHg	140–159 mmHg to ≥160 mmHg	<120 mmHg to 120–139 mmHg	120–139 mmHg to 140-159 mmHg	140–159 mmHg to ≥160 mmHg
20y	0.21	0.00	1.95	0.00	0.25	1.95
40y	2.01	1.72	2.50	2.56	2.68	2.14
60y	7.99	6.07	5.96	9.26	7.41	5.50
80y	0.19	0.24	1.26	1.43	1.91	1.08

[a] CDM is divided into one-year age categories. Numbers presented only for selected ages.

Applying this method to estimate transition probabilities for SBP classes implies that during the simulation, the age-specific SBP distribution remains constant. We used a separate set of transition probabilities for each scenario, reproducing the SBP distribution over the classes in that scenario.

2.5 Relative risks for disease incidence

We used the relative risks for incidence of AMI and CVA that were presented by Lewington *et al.* (12). In this paper relative risks are given per 20 mmHg. As in Lewington *et al.* we calculated the relative risk in each SBP category, $RR(SBP_i)$ as:

$$RR\ (SBP_i) = RR_{20mmHg}^{\frac{\mu_{log,usuak,i} - \mu_{log,usual,1}}{20}} \qquad \text{(II.12)}$$

where RR_{20mmHg} is the relative risk per 20 mmHg difference in SBP according to Lewington *et al*., and μ_i is the mean SBP in category *i* (see equation II.4). For outcome incidence of CHF we used relative risk values from literature. The selection criteria we applied to include studies were: cohort study, end-point incidence of or mortality from CHF, (mainly) Caucasian population, adjusted for confounding risk factors, and year of baseline measurements at least 1980. As a result, we included the following cohort studies: Cardiovascular Health Study (13), Health ABC Study (14), EPESE East Boston Study (15), EPESE New Haven Study (16), Framingham Study (17), and Physicians Health Study (18). The relative risk observed in these studies were combined in a mixed effects model, with study as a random coefficient, and age as a fixed coefficient, using the mixed-effects model package in R (http://www.metafor-project.org). This mixed effects model resulted in age-dependent relative risks per 20 mmHg of measured SBP values. We applied the regression dilution ratio of 0.76 (5) in order to get the relative risk per 20 mmHg of usual SBP. We used these relative risks to calculate the relative risks in each SBP category as described above (equations II.4 and II.12). **Table II.10** presents the RRs.

Table II.10 Relative risks for usual SBP and outcomes for selected ages

		Men				Women			
	Age[a]	<120 mmHg	120–139 mmHg	140–159 mmHg	≥160 mmHg	<120 mmHg	120–139 mmHg	140–159 mmHg	≥160 mmHg
AMI	20y	1	1.62	2.23	3.13	1	1.89	2.63	3.74
	40y	1	1.62	2.25	3.16	1	1.89	2.64	3.77
	60y	1	1.47	1.97	2.80	1	1.52	2.04	2.91
	80y	1	1.28	1.59	2.10	1	1.29	1.60	2.15
CHF	20y	1	2.64	5.07	10.04	1	3.63	7.07	14.39
	40y	1	2.71	5.30	10.66	1	3.73	7.41	15.46
	60y	1	1.86	2.92	4.96	1	2.01	3.26	5.83
	80y	1	1.22	1.45	1.80	1	1.23	1.48	1.88
CVA	20y	1	1.32	1.59	1.93	1	1.44	1.75	2.14
	40y	1	1.34	1.63	2.00	1	1.47	1.79	2.22
	60y	1	1.53	2.11	3.11	1	1.59	2.20	3.25
	80y	1	1.40	1.90	2.78	1	1.42	1.92	2.86

[a] CDM is divided into one-year age categories. Numbers presented only for selected ages.

2.6 Calculation of the DALYs over the simulation time period

Using the model results we calculated the Disability Adjusted Life Years lived (DALYlived) over the time period by multiplying the time spend in each disease state with a disability weight:

$$DALYlived = \sum_{n,g,a} N(g,a,n) \prod_{d} 1 - p_d(g,a,n)\, w_d(g,a) \qquad \text{(II.13)}$$

with: n: time-step, g: gender, a: age, $p_d(g,a;n)$: probability of disease d, $w_d(g,a)$: disease d disability weight, $N(g,a;n)$: calculated population number. Disability weights are taken from Stouthard *et al.* (19). We calculated the gain or loss in total DALYs of a scenario compared with the current scenario, as the difference in the number of DALYlived.

2.7 Uncertainty analysis

The results of CDM indirectly depend on the results of the meta-analysis of He and MacGregor (6) giving the change in SBP per gram of salt intake for two groups: normotensives (SBP = 127 mmHg, (v_1)) and hypertensives (SBP = 142 mmHg (v_2)). The parameters α, β and c in the dose response function (equation II.6) that relates salt intake to SBP, are estimated based on v_1 and v_2. So, a different value for v_1 and v_2 will result in a different value for parameters α, β and c and consequently in a different SBP distribution in a scenario. Both values, v_1 and v_2, are uncertain and according to He and MacGregor normally distributed with mean μ_{v1}, μ_{v2} and variance σ_{v1}^2, σ_{v2}^2 respectively. As a measure of uncertainty we calculated the variance of CDM results (f) that results from the uncertainty of v_1 and v_2.

We used the following procedure for this: We calculated the parameters α, β and c first using the values μ_{v1} and $\mu_{v2} + \sigma_{v2}$ and fitted the CZM using SBP values derived from this new α, β and c, yielding the model result $f(\mu_{v1}, \mu_{v2} + \sigma_{v2}^2)$. Secondly, we repeated this using μ_{v2} and $\mu_{v1} + \sigma_{v1}$ yielding $f(\mu_{v1} + \sigma_{v1}, \mu_{v2})$. We calculated the variance of the model result $f(v_1,v_2)$ (equation II.15) by combining both, using the delta-method (20).

$$\frac{df}{dv_1}(\mu_{v1},\mu_{v2}) \approx \frac{f(\mu_{v1}+\sigma_{v1},\mu_{v2}) - f(\mu_{v1},\mu_{v2})}{\sigma_{v1}}$$

$$\frac{df}{dv_2}(\mu_{v1},\mu_{v2}) \approx \frac{f(\mu_{v1},\mu_{v2}+\sigma_{v2}) - f(\mu_{v1},\mu_{v2})}{\sigma_{v2}} \qquad \text{(II.14)}$$

$$Var\big(f(v_1, v_2)\big) \approx \frac{df}{dv_1}(\mu_{v1}, \mu_{v2})^2 \sigma_{v1}^2 + \frac{df}{dv_2}(\mu_{v1}, \mu_{v2})^2 \sigma_{v2}^2 \qquad \text{(II.15)}$$

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Annex III

Supplement to chapter 5 – Health gain by salt reduction in Europe

1. Salt intake distribution

The prevalence of salt intake over the salt intake categories in the current situation, 30% salt reduction and in 5 grams per day for men and women are presented in **Table III.1** and **Table III.2**.

Table III.1 Prevalence of salt intake over the salt intake categories in the current situation, 30% salt intake reduction and in 5 grams per day for men

		Men								
		<4 g/d	4–6 g/d	6–8 g/d	8–10 g/d	10–12 g/d	12–14 g/d	14–16 g/d	16–18 g/d	>18 g/d
Finland	Current	0.1	3.4	18.1	28.8	24.2	14.2	6.7	2.8	1.8
	30% reduction	2.4	27.4	39.3	21.2	7.2	2.0	0.5	0.1	0.0
	5 g/d	0.1	99.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0
France	Current	0.0	1.0	11.2	27.1	28.3	18.2	8.7	3.5	1.9
	30% reduction	0.6	18.5	41.8	27.0	9.2	2.3	0.5	0.1	0.0
	5 g/d	0.0	100	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ireland	Current	0.0	0.81	12.9	33.1	30.5	15.3	5.4	1.5	0.5
	30% reduction	0.5	21.8	48.4	23.4	5.1	0.8	0.1	0.0	0.0
	5 g/d	0.0	100	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Italy	Current	0.3	5.5	17.0	22.9	20.3	14.3	8.8	5.0	5.8
	30% reduction	4.5	25.0	31.7	21.0	10.4	4.5	1.8	0.7	0.5
	5 g/d	0.3	99.7	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Netherlands	Current	0.5	6.9	19.1	23.9	19.8	13.2	7.8	4.3	4.6
	30% reduction	5.4	27.2	31.9	19.9	9.4	3.9	1.5	0.6	0.4
	5 g/d	0.5	99.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Poland	Current	0.0	0.3	4.3	14.2	22.0	21.7	16.2	10.1	11.2
	30% reduction	0.2	7.1	26.1	31.0	20.3	9.6	3.8	1.4	0.7
	5 g/d	0.0	100	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Spain	Current	0.7	7.0	16.4	20.1	18.0	13.5	9.2	5.9	9.2
	30% reduction	5.9	23.3	27.6	19.9	11.5	6.0	3.0	1.4	1.4
	5 g/d	0.7	99.3	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sweden	Current	0.0	0.7	9.2	24.9	28.5	19.8	10.1	4.3	2.5
	30% reduction	0.4	14.7	39.6	29.7	11.5	3.2	0.7	0.2	0.0
	5 g/d	0.0	100	0.0	0.0	0.0	0.0	0.0	0.0	0.0
UK	Current	2.5	14.1	22.8	21.4	15.6	9.9	5.9	3.4	4.3
	30% reduction	14.0	32.3	26.7	14.7	6.9	3.1	1.3	0.6	0.5
	5 g/d	2.5	97.5	0.0	0.0	0.0	0.0	0.0	0.0	0.0

Table III.2 Prevalence of salt intake over the salt intake categories in the current situation, 30% salt intake reduction and in 5 grams per day for women

		Women								
		<4 g/d	4–6 g/d	6–8 g/d	8–10 g/d	10–12 g/d	12–14 g/d	14–16 g/d	16–18 g/d	>18 g/d
Finland	Current	0.9	21.7	42.9	24.7	7.7	1.8	0.3	0.1	0.0
	30% reduction	16.5	57.6	22.3	3.3	0.3	0.0	0.0	0.0	0.0
	5 g/d	0.9	99.1	0.0	0.0	0.0	0.0	0.0	0.0	0.0
France	Current	0.4	14.7	39.6	29.7	11.5	3.2	0.7	0.2	0.0
	30% reduction	11.2	54.6	28.2	5.3	0.6	0.1	0.0	0.0	0.0
	5 g/d	0.4	99.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Ireland	Current	0.4	17.9	45.2	27.1	7.7	1.5	0.2	0.0	0.0
	30% reduction	13.5	61.0	22.7	2.6	0.2	0.01	0.0	0.0	0.0
	5 g/d	0.4	99.6	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Italy	Current	3.0	18.8	28.1	22.7	13.7	7.2	3.5	1.6	1.4
	30% reduction	17.6	39.0	26.1	11.2	4.0	1.4	0.5	0.2	0.1
	5 g/d	3.0	97.0	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Netherlands	Current	3.6	23.5	32.2	22.1	11.0	4.5	1.9	0.7	0.4
	30% reduction	21.2	45.4	23.7	7.3	1.8	0.4	0.1	0.0	0.0
	5 g/d	3.6	96.4	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Poland	Current	0.0	3.3	19.9	31.8	24.6	12.6	5.1	1.8	0.9
	30% reduction	2.2	30.3	41.8	19.2	5.2	1.1	0.2	0.0	0.0
	5 g/d	0.0	100	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Spain	Current	7.2	22.2	25.1	18.7	11.7	6.7	3.7	2.0	2.5
	30% reduction	25.9	34.9	21.5	10.1	4.3	1.8	0.8	0.3	0.3
	5 g/d	7.2	92.8	0.0	0.0	0.0	0.0	0.0	0.0	0.0
Sweden	Current	0.1	6.4	33.1	36.4	17.3	5.2	1.2	0.2	0.1
	30% reduction	4.3	47.7	38.3	8.5	1.0	0.1	0.0	0.0	0.0
	5 g/d	0.1	99.9	0.0	0.0	0.0	0.0	0.0	0.0	0.0
UK	Current	19.8	24.7	19.8	13.3	8.4	5.1	3.2	2.0	3.7
	30% reduction	40.7	27.6	15.4	7.8	4.0	2.0	1.1	0.6	0.8
	5 g/d	19.8	80.2	0.0	0.0	0.0	0.0	0.0	0.0	0.0

2. Dose-response association between salt intake and blood pressure

We reformulated the findings of He and MacGregor (1) in which we assumed that the change in SBP per additional amount of salt in the diet is linearly related to the SBP levels:

$$\frac{dSBP}{dSI} = \beta(\alpha + SBP)$$

where *SI* is salt intake (g/d), *SBP* is SBP level (mmHg), and α and β are regression coefficients of the dose-response curve. Solving equation (5) results in the following formula of the SBP level as a function of salt intake:

$$SBP = ce^{\beta SI} - \alpha$$

with *c* a stochastic parameter depending on age and sex. According to He and MacGregor, the SBP level of 127 mmHg (normal SBP) corresponds to a $\frac{dSBP}{dSI}$ of 0.6 mmHg/g salt and a SBP level of 149 mmHg (hypertension) corresponds to a $\frac{dSBP}{dSI}$ of 1.2 mmHg/g salt. Using these two findings as conditions, the regression coefficients α and β are estimated; α = 105, and β = 0.028. We assumed that blood pressure levels of ≥160 mmHg lead to a maximal reduction of 1.5 mmHg per gram salt intake reduction.

The variation of the SBP level in the population is larger than the variation resulting from the variation in salt intake. Therefore, we assumed that *c* is a stochastic parameter that is lognormally distributed. The mean and standard deviation of log(C) was estimated by equating the mean and variance of the SBP calculated from salt intake using the formulae above to the observed mean and variance in the population.

3. Blood pressure distribution within each salt intake category

Salt intake categories were further subdivided into salt intake categories of 0.5 g/d. In each salt intake category, 100 blood pressure values were calculated representing the current blood pressure distribution.

4. Relative risks for disease incidence

For each of the 100 blood pressures representing the blood pressure in a salt category, a single relative risk was calculated using the dose-response relation between blood pressure and IHD or stroke. We used the relative risks for incidence of IHD and stroke that were presented by Lewington (2). For each broader salt category, the average of these relative risks was taken. This average was weighted for the blood pressure distribution over these

subcategories. All relative risks were divided by the relative risk for the salt category 4–6 g/d, in order to make the latter the reference category.

Table III.3 and **Table III.4** give the resulting relative risks at the ages of 40, 60 and 80 years for stroke and IHD.

Table III.3 Combined relative risks between salt intake and stroke for a selection of salt intake categories and for selected ages

		Men				Women			
	Age[a]	<4 g/d[b]	4–6 g/d	8–10 g/d	14–16 g/d	<4 g/d	4–6 g/d	8–10 g/d	14–16 g/d
Finland	40y	0.93	1	1.18	1.60	0.99	1	1.00	1.00
	60y	0.92	1	1.20	1.67	0.99	1	1.00	1.00
	80y	0.96	1	1.10	1.29	0.99	1	1.00	1.00
France	40y	0.93	1	1.16	1.54	0.94	1	1.16	1.52
	60y	0.92	1	1.20	1.67	0.93	1	1.19	1.64
	80y	0.96	1	1.09	1.28	0.96	1	1.09	1.27
Ireland	40y	0.94	1	1.15	1.51	0.94	1	1.15	1.50
	60y	0.92	1	1.20	1.68	0.92	1	1.22	1.73
	80y	0.96	1	1.10	1.30	0.96	1	1.10	1.30
Italy	40y	0.94	1	1.16	1.53	0.94	1	1.16	1.50
	60y	0.92	1	1.20	1.65	0.92	1	1.21	1.68
	80y	0.96	1	1.09	1.27	0.96	1	1.10	1.29
Netherlands	40y	0.94	1	1.15	1.50	0.95	1	1.14	1.46
	60y	0.93	1	1.20	1.64	0.93	1	1.19	1.61
	80y	0.96	1	1.09	1.27	0.97	1	1.08	1.25
Poland	40y	0.94	1	1.15	1.49	0.94	1	1.15	1.48
	60y	0.92	1	1.19	1.61	0.91	1	1.22	1.74
	80y	0.97	1	1.08	1.24	0.96	1	1.11	1.32
Spain	40y	0.94	1	1.16	1.51	0.94	1	1.15	1.47
	60y	0.92	1	1.22	1.69	0.92	1	1.21	1.67
	80y	0.96	1	1.09	1.27	0.96	1	1.10	1.30
Sweden	40y	0.94	1	1.14	1.48	0.94	1	1.15	1.48
	60y	0.93	1	1.17	1.54	0.93	1	1.17	1.58
	80y	0.97	1	1.07	1.21	0.97	1	1.08	1.23
UK	40y	0.93	1	1.20	1.64	0.93	1	1.17	1.53
	60y	0.92	1	1.21	1.66	0.91	1	1.21	1.68
	80y	0.96	1	1.09	1.26	0.95	1	1.09	1.28

[a] DYNAMO-HIA is divided into one-year age categories. Numbers presented only for selected ages.
[b] Salt intake is divided into nine salt intake categories. Numbers presented only for selected categories.

Table III.4 Combined relative risks between salt intake and IHD for a selection of salt intake categories and for selected ages

		Men				Women			
	Age[a]	<4 g/d[b]	4–6 g/d	8–10 g/d	14–16 g/d	<4 g/d	4–6 g/d	8–10 g/d	14–16 g/d
Finland	40y	0.95	1	1.12	1.35	0.99	1	1.00	1.00
	60y	0.95	1	1.12	1.38	0.99	1	1.00	1.00
	80y	0.97	1	1.08	1.24	0.99	1	1.00	1.00
France	40y	0.96	1	1.10	1.31	0.97	1	1.07	1.23
	60y	0.95	1	1.12	1.38	0.96	1	1.11	1.35
	80y	0.96	1	1.09	1.24	0.97	1	1.08	1.23
Ireland	40y	0.96	1	1.09	1.30	0.97	1	1.08	1.26
	60y	0.95	1	1.13	1.39	0.95	1	1.13	1.40
	80y	0.96	1	1.08	1.25	0.97	1	1.08	1.25
Italy	40y	0.96	1	1.09	1.30	0.97	1	1.08	1.24
	60y	0.95	1	1.12	1.37	0.95	1	1.12	1.38
	80y	0.97	1	1.08	1.23	0.97	1	1.08	1.25
Netherlands	40y	0.96	1	1.10	1.30	0.97	1	1.07	1.22
	60y	0.95	1	1.12	1.36	0.96	1	1.11	1.33
	80y	0.97	1	1.08	1.23	0.97	1	1.07	1.21
Poland	40y	0.96	1	1.09	1.29	0.96	1	1.09	1.27
	60y	0.95	1	1.11	1.33	0.94	1	1.14	1.42
	80y	0.97	1	1.07	1.20	0.96	1	1.10	1.27
Spain	40y	0.96	1	1.09	1.28	0.97	1	1.08	1.23
	60y	0.95	1	1.12	1.38	0.95	1	1.13	1.38
	80y	0.97	1	1.08	1.23	0.96	1	1.09	1.25
Sweden	40y	0.96	1	1.09	1.27	0.97	1	1.07	1.22
	60y	0.96	1	1.09	1.29	0.96	1	1.10	1.31
	80y	0.97	1	1.06	1.17	0.97	1	1.06	1.19
UK	40y	0.95	1	1.12	1.37	0.96	1	1.10	1.29
	60y	0.95	1	1.12	1.37	0.94	1	1.12	1.37
	80y	0.97	1	1.08	1.22	0.96	1	1.08	1.23

[a] DYNAMO-HIA is divided into one-year age categories. Numbers presented only for selected ages.
[b] Salt intake is divided into nine salt intake categories. Numbers presented only for selected categories.

5. DYNAMO-HIA model in more detail

The DYNAMIC MODEL for Health Impact Assessment (DYNAMO-HIA) is a Markov model combining micro-simulation of the exposure variable with macro-simulation of the disease and survival. For more details, see Boshuizen *et al.*, who published a detailed description

of the model (3). In the present study, we used DYNAMO-HIA version 1.2 (available at the website www.dynamo-hia.eu). We simulated the effect of the population aged 18 years and older and our simulated population size was 100 subjects in each salt intake category. We did not include any newborns in our simulation. The transition rates between the risk factor categories were assumed to be zero. We only included chronic diseases in our model that were causally related to systolic blood pressure: IHD and stroke.

Incidence, prevalence and excess mortality data included in the DYNAMO-HIA model

A detailed description of the data collection of the prevalence, incidence and excess mortality can be found at the website of DYNAMO-HIA (www.dynamo-hia.eu; Report on the data collection for cardiovascular disease and diabetes and related relative risks, 2010).

In short, generally data collection of IHD differs widely and different definitions and procedures are in use to select events (f.e. population based registries, or GP networks). GP networks are considered to provide the best data for estimating prevalence and incidence, excess mortality and 28-day case fatality, and are available in UK (UK GPRD) and the Netherlands.

In order to obtain comparable IHD data across countries, IHD mortality and incidence rates were extracted for each country (based on the available registries) and a ratio was calculated in relation to the UK. This ratio was then applied to the UK GPRD IHD incidence data for all other countries (except the Netherlands). All incidence data was subject to incidence-prevalence and mortality modelling in order to obtain consistent estimates for prevalence and excess mortality (using RR from UK GPRD registry). In addition, 28 day case fatality was obtained from GPRD as well.

Stroke incidence and prevalence was obtained from GP registries from the UK and the Netherlands. A review of available stroke incidence and prevalence data in Europe was available (4) and provided best estimates in the other countries.

6. Uncertainty analyses

Monte Carlo simulations were used to estimate the uncertainties around the model estimates. We used the lower and upper estimates of the effects of reduction on blood pressure based

on the confidence intervals of He and MacGregor (1), and the lower and upper estimates of the association between blood pressure and IHD and stroke based on the confidence intervals of the log(RR) of Lewington (2). The intervals of both associations were assumed to have a normal probability distribution. The mean and 95% confidence interval of 100 simulations are presented.

References

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4. Truelsen T, Piechowski-Jozwiak B, Bonita R *et al.* (2006) Stroke incidence and prevalence in Europe: a review of available data. *Eur J Neurol* **13**, 581-598.

Annex IV

Supplement to chapter 6 – Sources of heterogeneity and its consequences in health impact assessments

Table IV.1 Combined relative risks between salt intake and stroke for a selection of salt intake categories and for selected ages

		Men					Women			
		Age[a]	<4 g/d[b]	4–6 g/d	8–10 g/d	14–16 g/d	<4 g/d	4–6 g/d	8–10 g/d	14–16 g/d
	Default	40	0.95	1	1.14	1.43	0.96	1	1.10	1.34
		60	0.94	1	1.17	1.56	0.94	1	1.16	1.57
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
General input of the model										
Population of model	35–80y	40	0.95	1	1.14	1.43	0.96	1	1.10	1.34
		60	0.94	1	1.17	1.56	0.94	1	1.16	1.57
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
Disease sources	CVD data from 2010	40	0.95	1	1.14	1.43	0.96	1	1.10	1.34
		60	0.94	1	1.17	1.56	0.94	1	1.16	1.57
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
Modelling effect of salt reduction on blood pressure										
Salt intake – SBP	Linear association, with RR from Law, 1991	40	0.91	1	1.22	1.72	0.92	1	1.23	1.73
		60	0.90	1	1.26	1.82	0.91	1	1.25	1.82
		80	0.96	1	1.09	1.26	0.96	1	1.09	1.26
Modelling effect of blood pressure on CVD										
SBP-CVD	RR from Framingham	40	0.98	1	1.06	1.18	0.99	1	1.04	1.11
		60	0.96	1	1.09	1.29	0.97	1	1.08	1.26
		80	0.96	1	1.11	1.34	0.95	1	1.13	1.41
Attenuation correction	No correction usual SBP	40	0.95	1	1.14	1.43	0.96	1	1.10	1.34
		60	0.94	1	1.17	1.56	0.94	1	1.16	1.57
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29

Table IV.1 continues on next page

Table IV.1 ***Continued***

			Men				Women			
		Age[a]	<4 g/d[b]	4–6 g/d	8–10 g/d	14–16 g/d	<4 g/d	4–6 g/d	8–10 g/d	14–16 g/d
Modelling effect of CVD on mortality										
Mortality also depends on SBP directly[b]	Other cause of death mortality depends on salt intake/SBP	40	0.95	1	1.14	1.43	0.96	1	1.10	1.34
		60	0.94	1	1.17	1.56	0.94	1	1.16	1.57
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
Reported outcomes										
Period of simulation	Extended to 20y	40	0.95	1	1.14	1.43	0.96	1	1.10	1.34
		60	0.94	1	1.17	1.56	0.94	1	1.16	1.57
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
	Extended to 50y	40	0.95	1	1.14	1.43	0.96	1	1.10	1.34
		60	0.94	1	1.17	1.56	0.94	1	1.16	1.57
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29

[a] DYNAMO-HIA is divided into one-year age categories. Numbers presented only for selected ages.
[b] Salt intake is divided into nine salt intake categories. Numbers presented only for selected categories.

Table IV.2 Combined relative risks between salt intake and stroke for a selection of blood pressure categories and for selected ages

		Age[a]	Men						Women					
			Baseline			3 gram salt			Baseline			3 gram salt		
			<120 mmHg[b]	120–140 mmHg	≥160 mmHg	<120 mmHg	120–140 mmHg	≥160 mmHg	<120 mmHg	120–140 mmHg	≥160 mmHg	<120 mmHg	120–140 mmHg	≥160 mmHg
Main model structures														
Risk factor distribution	Change in prevalence in categories	40	0.88	1.50	9.89	0.84	1.36	6.90	0.67	1.39	10.2	0.65	1.27	7.79
		60	0.95	1.65	7.90	0.92	1.52	6.05	0.88	1.44	8.69	0.85	1.34	6.84
		80	0.96	1.24	2.92	0.94	1.20	2.58	0.96	1.25	2.98	0.94	1.20	2.65
	Change in mean SBP in categories	40	0.88	1.50	9.89	0.84	1.36	6.90	0.67	1.39	10.2	0.65	1.27	7.79
		60	0.95	1.65	7.90	0.92	1.52	6.05	0.88	1.44	8.69	0.85	1.34	6.84
		80	0.96	1.24	2.92	0.94	1.20	2.58	0.96	1.25	2.98	0.94	1.20	2.65
Combined approach														
	Similar to CHD policy model	40	0.94	1.22	3.2	0.92	1.17	2.64	0.82	1.18	3.22	0.81	1.13	2.81
		60	0.97	1.36	3.52	0.95	1.29	3.00	0.92	1.25	3.74	0.90	1.19	3.23
		80	0.95	1.32	3.96	0.93	1.26	3.38	0.95	1.33	4.06	0.93	1.26	3.50

[a] DYNAMO-HIA is divided into one-year age categories. Numbers presented only for selected ages.

[b] Blood pressure is divided into four blood pressure categories. Numbers presented only for selected categories.

Table IV.3 Combined relative risks between salt intake and IHD for a selection of salt intake categories and for selected ages

			Men				Women			
		Age[a]	<4 g/d[b]	4–6 g/d	8–10 g/d	14–16 g/d	<4 g/d	4–6 g/d	8–10 g/d	14–16 g/d
	Default	40	0.97	1	1.09	1.27	0.98	1	1.06	1.18
		60	0.95	1	1.12	1.36	0.96	1	1.11	1.34
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
General input of the model										
Population of model	35–80y	40	0.97	1	1.09	1.27	0.98	1	1.06	1.18
		60	0.95	1	1.12	1.36	0.96	1	1.11	1.34
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
Disease sources	CVD data from 2010	40	0.97	1	1.09	1.27	0.98	1	1.06	1.18
		60	0.95	1	1.12	1.36	0.96	1	1.11	1.34
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
Modelling effect of salt reduction on blood pressure										
Salt intake – SBP	Linear association, with RR from Law, 1991	40	0.95	1	1.13	1.39	0.95	1	1.13	1.40
		60	0.93	1	1.16	1.50	0.94	1	1.16	1.49
		80	0.96	1	1.09	1.26	0.96	1	1.09	1.26

Table IV.3 continues on next page

Table IV.3 ***Continued***

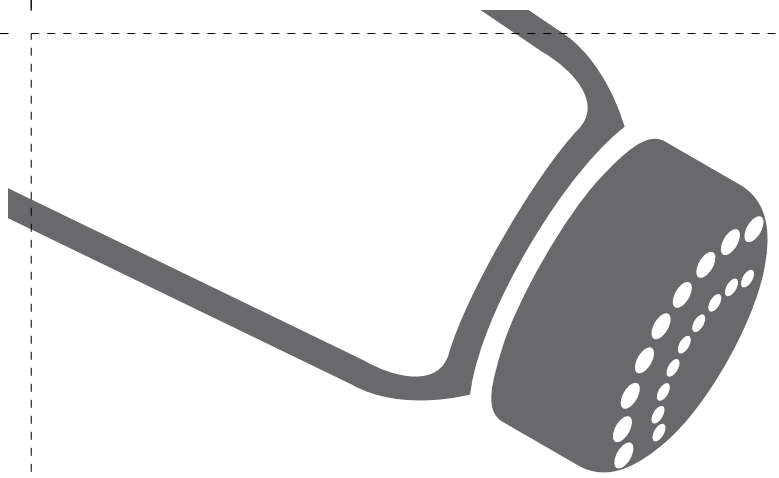
			Men				Women			
		Age[a]	<4 g/d[b]	4–6 g/d	8–10 g/d	14–16 g/d	<4 g/d	4–6 g/d	8–10 g/d	14–16 g/d
Modelling effect of blood pressure on CVD										
SBP-CVD	RR from Framingham	40	0.98	1	1.04	1.12	0.99	1	1.02	1.07
		60	0.97	1	1.06	1.19	0.98	1	1.06	1.17
		80	0.97	1	1.07	1.22	0.97	1	1.09	1.26
Attenuation correction	No correction usual SBP	40	0.97	1	1.09	1.27	0.98	1	1.06	1.18
		60	0.95	1	1.12	1.36	0.96	1	1.11	1.34
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
Modelling effect of CVD on mortality										
Mortality also depends on SBP directly[b]	Other cause of death mortality depends on salt intake/SBP	40	0.97	1	1.09	1.27	0.98	1	1.06	1.18
		60	0.95	1	1.12	1.36	0.96	1	1.11	1.34
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
Reported outcomes										
Period of simulation	Extended to 20y	40	0.97	1	1.09	1.27	0.98	1	1.06	1.18
		60	0.95	1	1.12	1.36	0.96	1	1.11	1.34
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29
	Extended to 50y	40	0.97	1	1.09	1.27	0.98	1	1.06	1.18
		60	0.95	1	1.12	1.36	0.96	1	1.11	1.34
		80	0.97	1	1.08	1.24	0.97	1	1.09	1.29

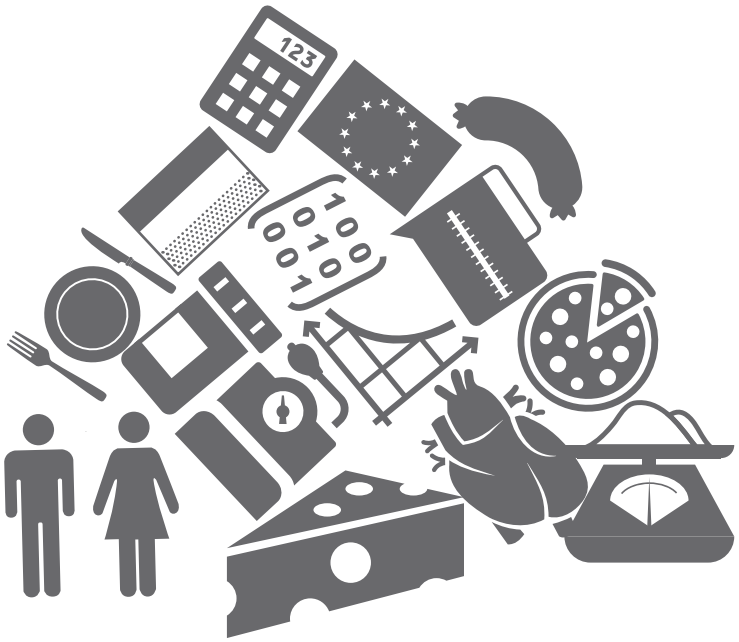
[a] DYNAMO-HIA is divided into one-year age categories. Numbers presented only for selected ages.
[b] Salt intake is divided into nine salt intake categories. Numbers presented only for selected categories.

Table IV.4 Combined relative risks between salt intake and stroke for a selection of blood pressure categories and for selected ages

			Men						Women					
		Age[a]	Baseline			3 gram salt			Baseline			3 gram salt		
			<120 mmHg[b]	120–140 mmHg	≥160 mmHg	<120 mmHg	120–140 mmHg	≥160 mmHg	<120 mmHg	120–140 mmHg	≥160 mmHg	<120 mmHg	120–140 mmHg	≥160 mmHg
Main model structures														
Risk factor distribution	Change in prevalence in categories	40	0.91	1.32	4.95	0.89	1.24	3.85	0.76	1.26	5.07	0.74	1.18	4.19
		60	0.96	1.44	4.52	0.94	1.35	3.72	0.91	1.31	4.85	0.89	1.24	4.07
		80	0.96	1.24	2.92	0.94	1.20	2.58	0.96	1.25	2.98	0.94	1.20	2.65
	Change in mean SBP in categories	40	0.91	1.32	4.95	0.89	1.24	3.85	0.76	1.26	5.07	0.74	1.18	4.19
		60	0.96	1.44	4.52	0.94	1.35	3.72	0.91	1.31	4.85	0.89	1.24	4.07
		80	0.96	1.24	2.92	0.94	1.20	2.58	0.96	1.25	2.98	0.94	1.20	2.65
Combined approach														
	Similar to CHD policy model	40	0.95	1.16	2.29	0.94	1.12	2.01	0.97	1.13	2.32	0.86	1.09	2.10
		60	0.98	1.24	2.58	0.96	1.20	2.20	0.95	1.18	2.58	0.93	1.14	2.33
		80	0.96	1.22	2.69	0.95	1.18	2.40	0.96	1.23	2.74	0.95	1.18	2.46

[a] DYNAMO-HIA is divided into one-year age categories. Numbers presented only for selected ages.
[b] Blood pressure is divided into four blood pressure categories. Numbers presented only for selected categories.

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Summary

Cardiovascular diseases (CVD) contribute substantially to the burden of diseases worldwide, including the Netherlands. An important risk factor for cardiovascular disease is hypertension. There is convincing evidence that high salt intake has an adverse effect on blood pressure. Salt intake in the Netherlands is far above recommended levels. The majority of daily salt intake comes from processed foods. Reducing sodium contents in processed foods and changing dietary behaviour is necessary to reduce salt intake. Reducing daily salt intake will likely result in lower blood pressure levels and fewer cardiovascular disease events in the population. The magnitude of the impact of salt reduction strategies on daily salt intake and on long-term health is not known for the Netherlands and Europe.

The research described in this thesis aims to investigate the health benefits of salt reduction in the Netherlands and Europe. First, we studied the potential impact of two possible salt reduction strategies on daily salt intake in the Netherlands using scenario analysis. Second, we monitored the progress on salt reduction initiatives in the Netherlands between 2006 and 2010 using 24h urine samples. Third, we assessed the long-term health benefits of reduction of salt intake in the Netherlands using the RIVM Chronic Disease Model, and in Europe using DYNAMO-HIA. Finally, we explored the effect of underlying assumptions of seven health impact models for salt reduction in different populations.

In **Chapter 2**, we study how far low-sodium alternatives as well as the current minimum feasible sodium levels can reduce daily salt intake in a hypothetical situation. In this simulation study, data from the Dutch National Food Consumption Survey 2007–2010 (N=3819) and the Food Composition Table (2011) was used to estimate the current sodium intake from foods. We created two scenarios: 1) sodium contents in processed foods were reduced to their minimum feasible sodium level (on average 50% reduction) and 2) foods consumed were replaced by low-sodium alternatives. Daily salt intake from processed foods may be reduced by 38% to 1886 mg/d in men and 1449 mg/d in women if the sodium content in processed foods is at their lowest possible level. Consuming low-sodium alternatives may reduce sodium intake by 47% to 1627 mg/d in men and to 1215 mg/d in women. Thus, both strategies would substantially reduce sodium intake, provided that strategies are successfully implemented.

In **Chapter 3** the effort of the food industry to reduce the level of sodium in processed foods is evaluated by monitoring the change in daily salt intake between 2006 and 2010. Two cross-sectional studies in 317 subjects (year 2006) and 342 subjects (year 2010) aged 19 to 70 years were conducted. Participants collected a single 24h urine sample and daily salt and

iodine intake was estimated from sodium and iodine excreted in the urine. We observed no difference in daily salt intake between 2006 (8.7 g/d) and 2010 (8.5 g/d). Daily iodine intake was reduced from 257 µg/d in 2006 to 179 µg/d in 2010. Despite the initiatives of the food industry to lower sodium content in processed foods, salt intake is well above the recommended intake of 6 g/d. Iodine intake could still be considered adequate.

In **Chapter 4** the potential impact of the lower salt intake through food reformulation or behavioural changes on long-term health in the Dutch population is evaluated. A health impact assessment model was developed in which the long-term health benefits of salt reduction in the Netherlands could be estimated. First, the effects of salt reduction on blood pressure levels were quantified and in a following step the RIVM Chronic Disease Model was used to translate the changed blood pressures into incidence of cardiovascular diseases, disability adjusted life years (DALYs) and life expectancy. Technologically minimal sodium levels would reduce the incidence of acute myocardial infarction (AMI) by 4.4%, the incidence of stroke by 6.0%, and 56,000 averted DALYs. For behavioural change, there would be 5.3% less AMI, 7.2% less stroke, and 67,900 averted DALYs. We concluded that for the Netherlands, sodium reduction may substantially contribute to a reduced burden of cardiovascular disease.

In **Chapter 5**, the potential health impact of World Health Organization recommendation on salt intake (30% reduction or maximum of 5 g/d) in nine European countries is assessed. In this study, the salt intake and blood pressure levels were collected for the selected countries and used in the DYNAMO-HIA model. In a two-step approach we first estimated the effect of salt reduction on blood pressure, which was subsequently translated to changes in CVD prevalence. Based on our model, a 30% salt reduction would reduce the prevalence of stroke by 6.4% (Finland) to 13.5% (Poland) and ischemic heart disease (IHD) by 4.1% (Finland) to 8.9% (Poland). For a maximum salt intake of 5 g/d, estimated reductions would be larger for stroke (10.1% for Finland to 23.1% for Poland) and IHD (6.6% for Finland to 15.5% for Poland).

Chapter 6 provides an overview of seven published population health models of salt reduction. Here, the seven population health modelling tools were compared with a set of four predefined characteristics. Comparison of the population health models showed that there is much variation in the underlying assumptions. The extent to which variation in several of the underlying assumptions could affect the outcome of the population health models was assessed in alternative simulations. This revealed that especially the assumptions on

the way salt intake is related to blood pressure and the sizes of the relative risks for the relation between blood pressure and cardiovascular diseases could change the estimated health impact for stroke by -33% and +19% respectively and for IHD by -40% and +22% respectively. Also an intrinsic model characteristic, which relates to modelling blood pressure as a categorical rather than a continuous entity could change the health impact estimate for stroke by -31% and for IHD by 32%. This showed a clear need for transparency in model calculations. However, in all alternative simulations the health impact of salt reduction remained substantial.

In **Chapter 7**, the research findings are summarized and discussed, and the implications for public health policy are considered. The research findings showed that to achieve a daily salt intake below the recommended maximum intake of 6 g/d, sodium contents in processed foods should be reduced by on average 50% in the Netherlands. Efforts by food industry to reduce sodium contents in processed foods between 2006 and 2010 did not yet result in a lower salt intake in the Netherlands. The outcomes of this thesis showed that if daily salt intake is in line with the recommended maximal intake, this would lead to considerable health gain in the Netherlands and in other European countries. However, there is a clear need for transparency of included data and assumptions of population health models, to be able to interpret and compare the estimated health impacts of salt reduction strategies across populations.

Samenvatting

Hart- en vaatziekten dragen wereldwijd substantieel bij aan de totale ziektelast. In Nederland veroorzaken coronaire hartziekten en beroerte de hoogste ziektelast. Hypertensie, een te hoge bloeddruk, is een belangrijke risicofactor voor hart- en vaatziekten. Er is overtuigend bewijs dat een hoge zoutinname bijdraagt aan het risico op hypertensie. In Nederland ligt de zoutinname ruim boven de aanbevolen maximale hoeveelheid van 6 gram per dag (g/d). Ongeveer 80% van de dagelijkse zoutinname komt uit bewerkte voedingsmiddelen. Verwacht mag worden dat een verlaging van de zoutinname, onder andere door het verlagen van het zoutgehalte in voedingsmiddelen, leidt tot een lagere bloeddruk en daardoor tot minder gevallen van hart- en vaatziekten in de bevolking. De grootte van het effect van zoutverlaging in voedingsmiddelen op de dagelijkse zoutinname en de invloed van een verlaagde dagelijkse zoutinname op de volksgezondheid op de lange termijn is voor de Nederlandse en Europese situatie niet duidelijk.

In dit proefschrift is de impact van zoutverlaging op de volksgezondheid onderzocht voor de Nederlandse en Europese bevolking. Hiertoe is als eerste het effect van twee mogelijke zoutverlagingsstrategieën op de dagelijkse Nederlandse zoutinname geschat door middel van een scenarioanalyse. Vervolgens is tussen 2006 en 2010 de voortgang van het effect van de initiatieven van de levensmiddelenindustrie om het zoutgehalte in voedingsmiddelen te verlagen gemonitord in een steekproef van de bevolking met behulp van 24-uurs urineverzamelingen. Daarnaast zijn de langetermijneffecten van zoutverlaging op de volksgezondheid voor Nederland geschat met behulp van het RIVM Chronische Ziekten Model en voor Europa met behulp van het DYNAMO-HIA Model. Verder is onderzocht wat in zeven gepubliceerde modellen de effecten van gemaakte aannames zijn op de verwachte gezondheidswinst door zoutverlaging.

In **Hoofdstuk 2** is onderzocht in hoeverre veranderingen in de dagelijkse voeding de dagelijkse zoutinname kunnen verlagen. De bestudeerde veranderingen hebben betrekking op het verlagen van het zoutgehalte in de huidige voedingsmiddelen of op aanpassingen in het voedingspatroon. In deze simulatiestudies zijn gegevens gebruikt uit de Nederlandse Voedselconsumptie Peiling 2007–2010, uitgevoerd bij 3.819 personen van 7 tot 69 jaar, en uit de Nederlandse Voedingsmiddelentabel (NEVO) uit 2011. Met deze gegevens werd de huidige zoutinname uit voedingsmiddelen (dus exclusief het zout dat de consument zelf toevoegt bij de voedselbereiding of aan tafel) geschat op 7,7 g/d voor mannen en op 5,8 g/d voor vrouwen. Vervolgens hebben we twee mogelijke scenario's opgesteld: in het eerste scenario werd het zoutgehalte van bewerkte voedingsmiddelen verlaagd tot een niveau dat technologisch gezien haalbaar is (gemiddeld een verlaging met 50%). In het tweede scenario

werden geconsumeerde voedingsmiddelen vervangen door vergelijkbare en verkrijgbare voedingsmiddelen maar met een lager zoutgehalte. De dagelijkse zoutinname van bewerkte voedingsmiddelen lag 38% lager (4,8 g/d voor mannen en 3,7 g/d voor vrouwen) wanneer het zoutgehalte in voedingsmiddelen op het technologisch laagst haalbare niveau lag. Wanneer werd gekozen voor alternatieve voedingsmiddelen met een lager zoutgehalte daalde de zoutinname met 47% (naar 4,1 g/d voor mannen en 3,1 mg/d voor vrouwen). Deze resultaten laten zien dat met beide strategieën de zoutinname substantieel verlaagd zou kunnen worden. Het is dan wel van belang dat deze strategieën succesvol worden geïmplementeerd.

In **Hoofdstuk 3** is het effect geëvalueerd van de inspanningen van de voedingsmiddelenindustrie om het zoutgehalte in bewerkte voedingsmiddelen te verlagen op de dagelijkse zoutinname over de periode tussen 2006 en 2010. Hiervoor voerden wij twee cross-sectionele studies uit onder inwoners van Doetinchem in de leeftijd van 19–70 jaar (317 personen in 2006 en 342 personen in 2010). De deelnemers verzamelden 24 uur lang alle urine. Op basis van natrium- en jodiumuitscheiding in de urine werd de dagelijkse zout- en jodiuminname berekend. We vonden geen statistisch significant verschil in dagelijkse zoutinname (8,7 g/d in 2006 en 8,5 g/d in 2010; p=0,75). De dagelijkse jodiuminname was significant gedaald (257 µg/d in 2006 en 179 µg/d in 2010; p<0,0001). Deze resultaten laten zien dat de zoutverlagingsinitiatieven nog niet hebben geleid tot een daling in de dagelijkse zoutinname. De inname van jodium is ondanks de daling nog steeds voldoende.

De verwachte langetermijneffecten van zoutverlaging op de volksgezondheid in Nederland zijn berekend in **Hoofdstuk 4**. Als eerste werden de effecten van zoutverlaging op de bloeddruk berekend. Vervolgens werd met behulp van het RIVM Chronische Ziekten Model het effect van de verlaagde bloeddruk op het aantal hart- en vaatziekten, de ziektelast (in DALYs) en de levensverwachting berekend over een periode van 20 jaar. Het aantal Nederlanders met een hartinfarct zal met 4,4% dalen, het aantal Nederlanders met een beroerte zal met 6,0% dalen en de ziektelast zal met 56.000 DALYs worden verminderd bij een technologisch haalbaar minimaal zoutgehalte in voedingsmiddelen. Bij een verlaging van de zoutinname door te kiezen voor laag-zout alternatieven krijgen 5,3% minder Nederlanders een hartinfarct, 7,2% minder Nederlanders een beroerte en zal de ziektelast met 67.900 DALYs afnemen. Deze resultaten tonen aan dat zoutverlaging in Nederland, mits succesvol geïmplementeerd, een substantiële bijdrage kan leveren aan een daling van het aantal personen met hart- en vaatziekten en kan bijdragen aan een verminderde ziektelast ten gevolge van deze hart- en vaatziekten.

In **Hoofdstuk 5** hebben wij voor negen Europese landen de langetermijneffecten van de doelstelling en aanbeveling van de Wereldgezondheidsorganisatie (WHO) voor zoutinname (30% zoutverlaging in 2025 en een maximum inname van 5 g/d) geschat. In dit onderzoek hebben wij de zoutinname en bloeddrukgegevens van deze landen verzameld en ingevoerd het DYNAMO-HIA model. In een tweetraps benadering hebben wij eerst de effecten van zoutverlaging op de bloeddruk geschat en vervolgens het effect van de bloeddrukverlaging op het aantal personen met hart- en vaatziekten. Gebaseerd op de uitkomsten van ons model zal een 30% daling in de zoutinname leiden tot een daling van het aantal personen met een beroerte variërend van 6,4% in Finland tot 13,5% in Polen. Het aantal personen met ischemische hartziekten zal dalen variërend van 4,1% in Finland tot 8,9% in Polen. Wanneer de gehele bevolking voldoet aan de aanbeveling van 5 g/d zal het aantal personen met een beroerte dalen met 10,1% in Finland tot 23,1% in Polen. Het aantal personen met ischemische hartziekten zal dalen met 6,6% in Finland tot 15,5% in Polen. Op basis van deze resultaten concluderen wij dat ook in andere landen in Europa zoutverlaging zal kunnen leiden tot een aanzienlijke daling aan het aantal hart- en vaatziekten.

Hoofdstuk 6 geeft een overzicht van de aannames van zeven gepubliceerde gezondheidswinstmodellen waarmee de gezondheidsimpact van zoutverlaging is geschat. Een vergelijking tussen deze modellen liet zien dat deze modellen op meerdere onderliggende aannames van elkaar verschillen. Vervolgens is onderzocht in hoeverre deze verschillen zouden kunnen leiden tot andere uitkomsten. Hiervoor hebben we gebruik gemaakt van het DYNAMO-HIA model, waarbij we steeds hebben gerekend met de Nederlandse inputgegevens. Uit deze berekeningen bleek dat afhankelijk van de aannames die worden gedaan om de relatie tussen zout en bloeddruk te berekenen, de geschatte gezondheidswinst voor beroerte met 33% kunnen verschillen en voor ischemische hartziekten met 40%. De grootte van relatieve risico's in de relatie tussen bloeddruk en hart- en vaatziekten leidde tot een verschil in effectschatting van 19% voor een beroerte en van 22% voor ischemische hartziekten. De modellering van bloeddruk in een beperkt aantal categorieën resulteerde in een 31% lagere effectschatting voor beroerte en 32% lagere effectschatting voor ischemische hartziekte vergeleken met een modellering van bloeddruk als continue invoervariabele. Deze resultaten laten zien dat er behoefte is aan transparantie in modelberekeningen en aan een duidelijke beschrijving van alle aannames. Ondanks de effecten van de verschillen in aannames, bleken de effecten van zoutverlaging op de volksgezondheid onder alle aannames te blijven bestaan.

In **Hoofdstuk 7** zijn de bevindingen samengevat en bediscussieerd en zijn de gevolgen voor het Nederlandse volksgezondheidsbeleid besproken. De onderzoeksresultaten tonen aan dat

in Nederland het zoutgehalte in voedingsmiddelen met gemiddeld 50% moet dalen om de Nederlandse aanbevolen maximale hoeveelheid van 6 g/d te halen. De inspanningen van de levensmiddelenindustrie om het zoutgehalte in bewerkte voedingsmiddelen te laten dalen hebben zich tussen 2006 en 2010 nog niet vertaald in een lagere dagelijkse zoutinname. Wanneer de inname van zout voldoet aan de aanbevolen maximale dagelijkse hoeveelheid is er een aanzienlijke gezondheidswinst te behalen in Nederland en in andere Europese landen. Er is behoefte aan transparantie van de gegevens en aannames die gebruikt worden in de gezondheidswinstmodellen zodat men de uitkomsten op een juiste manier kan interpreteren en tussen populaties kan vergelijken.

Abbreviations

/d	/day
AMI	Acute myocardial infarction
BP	Blood pressure
DCS	Doetinchem Cohort Study
CDM	Chronic Disease Model
CHD	Coronary heart disease
CHF	Congestive heart failure
CI	Confidence interval
CV	Coefficients of variability
CVA	Cerebrovascular accident
CVD	Cardiovascular diseases
DALYs	Disability-adjusted life years
DNFCS	Dutch National Food Consumption Survey
DPP	Deaths Prevented or Postponed
DYNAMO-HIA	DYNAMIC MODEL for Health Impact Assessment
EPIC	European Prospective Investigation into Cancer and Nutrition
g	gram
GBD	Global burden of disease
GDPS	General Doetinchem Population Sample
GP	General practitioner
GPRD	General Practice Research Database
HF	Heart failure
HIA	Health impact assessments
IHD	Ischemic heart disease
IOM	Institute of Medicine
IQR	Interquartile range
LYG	Life years gained
MI	Myocardial infarction
mmHg	Millimeters of mercury
MORGEN	Monitoring project on Chronic Disease Risk Factors
N/A	Not available
NCDs	Non-communicable diseases
QALY	Quality adjusted life years
PABA	Para-aminobenzoic acid

PIF	Potential impact fraction
PCR	Polymerase chain reactor
PMSLT	Proportional MultiState Life-Table
PRIME	Preventable Risk Integrated Model
RIVM	Rijksinstituut voor Volksgezondheid en Milieu (National Institute for Public Health and the Environment)
RR	Relative risk
SBP	Systolic blood pressure
SD	Standard deviation
SI	Salt intake
UK	United Kingdom
YLD	Years lived disease
YLL	Years live lost
WHO	World Health Organization

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Dankwoord

Het proefschrift is klaar! Eindelijk kan ik beginnen aan het leukste gedeelte van het proefschrift: het dankwoord. Ik wil dit laatste hoofdstuk gebruiken om iedereen te bedanken die mij in dit traject heeft geholpen, gemotiveerd en gestimuleerd.

In de eerste plaats mijn promotor en co-promotoren. Beste Joop, je hebt je altijd bijzonder ingespannen om mijn onderzoek op het RIVM te laten resulteren in een promotie. Je had geduld met me als ik minder tijd had om aan het proefschrift te werken, maar je zorgde er ook voor dat ik de draad weer oppakte door harde deadlines voor te stellen. Je hebt me veel mogelijkheden gegeven om mezelf te ontwikkelen. Heel erg bedankt daarvoor! Beste Hendriek, je werd in een iets later stadium betrokken bij dit project, maar je was meteen onmisbaar. Ik bewonder je kennis over de statistiek en de manier waarop je heel snel een, in mijn ogen groot, probleem weet op te lossen. Het was ook heel fijn dat ik een periode bij jou op de kamer mocht werken aan mijn proefschrift, weg van de hectiek in G22. Ik vind het bijzonder dat ik je eerste promovenda mag zijn. Beste Marianne, bedankt voor alle kritische opmerkingen en stevige discussies. Jouw commentaar op mijn wollige schrijfstijl kwam de leesbaarheid alleen maar ten goede!

Ik wil graag Hans en Nynke en Jantine en Matthijs bedanken voor de mogelijkheid die ik heb gekregen om te kunnen promoveren op mijn werkzaamheden voor het RIVM. Matthijs, dank voor je vertrouwen en de mogelijkheden die je mij biedt. Je enthousiasme werkt aanstekelijk.

Veel collega's hebben bijgedragen aan de verschillende hoofdstukken in dit proefschrift. Daphne, ik vind het altijd leuk om met je samen te werken. Dank je wel dat ik altijd met je mag meerijden als de NS me weer in de steek laat. Rudolf, zonder jou waren er geen getallen in hoofdstuk 4. Je moet regelmatig wanhopig zijn geworden als er weer een sommetje op een net iets andere manier moest worden berekend. Dank je wel voor je hulp. Jeljer, ik bewonder je gave om de complexe berekeningen in simpele en voor mij begrijpelijke taal uit te leggen. Janneke, Caroline W en Marga, dank jullie wel voor jullie bijdragen aan mijn manuscripten. Martijn Noort, het duurde een hele tijd voordat we het supplement bij hoofdstuk 2 hadden afgerond, maar daardoor werd het manuscript uiteindelijk wel gepubliceerd. Zonder de technologische kennis van jou en jouw collega's was ons dit nooit gelukt. Heel erg bedankt!

De eerste ideeën om aan een proefschrift te beginnen ontstonden tijdens het parapluproject Herformulering, een samenwerking tussen TNO, Wageningen UR en het RIVM. Martijn, Anke, Liesbeth en Joop, ik vond onze projectoverleggen altijd erg interessant en gezellig.

Dear Joao, thank you for giving me the opportunity to work together on several WHO projects. It was an honour to organize the WHO workshop on methodological aspects of salt reduction modelling together with you. I am looking forward to continue our collaboration on salt. Dear participants of the WHO workshop on salt modelling issues, it was a pleasure to discuss the challenges of salt modelling with you. Thank you all for your input on chapter 6 of this thesis. In particular, Pamela Coxson, I really enjoyed that I could show you and your colleague Antoinette the Dutch way of commuting to work.

Ik wil graag de leden van de leescommissie, hoogleraar Cees de Graaf, lector Annet Roodenburg en dr. Wilma Nusselder bedanken voor het kritisch lezen van mijn proefschrift en het opponeren. Dear professor Franco Cappuccio, thank you for reviewing my thesis and coming from the UK for my thesis defence. It is an honour to have you as an opponent.

De studenten Frederike, Ettje, Farah, Aziz, Maud, Saartje, Dieuwke en Ellen hebben allen in verschillende fases bijgedragen aan mijn proefschrift: thank you for your contributions.

Mijn (oud)collega's bij CVG en VPZ wil ik bedanken voor de fijne samenwerking. In het bijzonder Caroline W, sinds het @nders werken mis ik je als kamergenootje. Gelukkig vinden we soms tijd om samen bij te kletsen tijdens een wandeling in het bos. Heidi, Frederike en Fränzel, ik ben erg blij dat we, nadat jullie bij het RIVM vertrokken, nog steeds contact hebben. Susanne, Sander, Elly, Caroline v R, Wanda, Djoeke en alle anderen, dank voor jullie interesse in de voortgang van mijn proefschrift. Ivon, bedankt voor al je opbeurende woorden tijdens de laatste loodjes van mijn proefschrift. Debra, thanks for correcting the general discussion! Marianne en de andere dames van het secretariaat, bedankt voor alle secretariële ondersteuning. Arnold, ik voelde me meteen welkom toen ik aan aantal maanden bij jou op de kamer kwam zitten. Ik kom binnenkort echt een keer langs in Nieuwkuijk.

Gelukkig bestaat het leven niet alleen uit werken. Lieve vrienden en familie, bedankt voor alle ontspanning naast het werk. Lieve Esmee, het zijn voor ons allebei tropenjaren en we zien elkaar veel te weinig, maar ik weet dat ik altijd bij je terecht kan. Je bent een heel dierbare vriendin! Oud-Di-Et-Tri, het is zo gezellig dat we elkaar nog steeds zien. Michel, je was een trouwe en kritische volger van mijn onderzoek. Zo leuk dat je voor even mijn collega bij het RIVM bent (of is het inmiddels was?)! Lieve Magda, onze afspraken worden er alleen maar leuker op als onze meiden samen spelen! Lieve Sarah, ook jou zie ik veel te weinig, maar ik ben blij dat we al zo lang vriendinnen zijn. Beste Coenraad, onze lunches op het RIVM gaven me altijd veel energie. Bedankt voor je interesse in mij als persoon en mijn onderzoek. Tim, wat heb je een gave voorkant ontworpen!

Een speciaal woord van dank aan mijn paranimfen Simone en Janneke. Lieve Simone, ik bewonder je positieve levenshouding; je bent een geweldige vriendin! Waar gaat ons volgende weekendje weg naar toe? Liefste Jans, jij bent alles-in-een: herbergier voor een gestrande reiziger, discussiegenoot over proefschrift-gerelateerde zaken, mede-mollenvanger, (t)huisarts, fietsmaatje, huisfotograaf en ook nog mijn kleine zus. Onze schrijfdagen aan het eind van mijn traject waren niet alleen nuttig, maar ook erg gezellig. Succes met jouw laatste loodjes! Lieve dames, het geeft mij een prettig gevoel dat jullie naast mij staan!

Het schrijven aan je proefschrift naast je normale baan, een flinke reistijd naar je werk en het krijgen van een kindje vraagt niet alleen veel van jezelf, maar in mijn geval ook van de personen om mij heen. Vooral in de afrondende fase heb ik vaak een beroep gedaan op de beide oma's om voor Rosalie te zorgen. Ook Tessel, klein groot nichtje, het is zo lief van je dat je heel graag op Rosalie wilt passen. Dank jullie wel! Mijn schoonfamilie wil ik bedanken voor hun gastvrijheid, gezelligheid en hulp. Lieve Marita, jij staat altijd voor ons klaar, en niets is te gek. Ik waardeer dat enorm en kan je daar niet genoeg voor bedanken.

Lieve Coen, gelukkig woon je weer in de buurt; het is leuk om je weer zo dicht bij ons te hebben. Lieve Mariët, je brengt echt leven in de brouwerij. Dank jullie wel voor alle gezelligheid en lang leve de spontane acties! Lieve papa, ik mis je enorm, zeker bij alle belangrijke gebeurtenissen. Lieve mama, jij en papa hebben me altijd gestimuleerd om door te leren en mezelf te blijven ontwikkelen. De afgelopen jaren waren niet gemakkelijk, maar ik bewonder je veerkracht. Bedankt voor jouw liefde, interesse en hulp bij alles. Ik geniet van je als oma van Rosalie.

En dan als laatste de twee hoofdrolspelers in mijn leven. Lieve, lieve John. De afronding van mijn proefschrift was een pittige tijd. Bedankt voor de ruimte die je me hebt gegeven. Maar uiteindelijk wil ik je het meest bedanken voor al je energie, je onvoorwaardelijke steun en je liefde. Jij bent degene die me uitdaagt en stimuleert om net dat stapje extra te zetten.

Lieve kleine vrolijke Rosalie, in ons gezinnetje ben jij de échte onderzoeker. Gelukkig hoeft mama nu niet meer alleen maar te werken en kan ik samen met jou en papa op avontuur!

Marieke

About the author

Curriculum Vitae

Marieke Hendriksen was born in Elst (Gld), the Netherlands on the 14th of December 1982. After completing secondary school at "Stedelijk Gymnasium" in Nijmegen (2001), she started her study "Nutrition and Health" at Wageningen University. During her Master program she specialized in Epidemiology and Public Health. She wrote a Master's thesis at the National Institute for Public Health and the Environment (RIVM), the Netherlands, where she investigated the association between maternal overweight and breastfeeding in the PIAMA cohort. During a 4-month internship at the National Institute for Public Health (former KTL) in Helsinki, Finland, she compared the national overweight and diabetes prevention programs of Finland and the Netherlands. For her second thesis, she examined the association between dairy products and hypertension in the Rotterdam Study. Her abstract was awarded with the Student price during the WEON congress in Maastricht, 2007.

After she graduated in March 2007, she worked for 3 months at the Municipal Health Service 'GGD Rivierenland' in Tiel. In July 2007, she started to work for the Centre for Nutrition and Health at the RIVM in Bilthoven. She worked as a researcher at the umbrella-project "Food reformulation", which was a collaboration between RIVM, Wageningen University and Research Centre and TNO. Within this project, she started to focus on the public health benefits of salt reduction in the Netherlands, and soon the idea to start a PhD was born. She was one of the researchers that conducted the 24h urine study in Doetinchem in 2010. In collaboration with the WHO Regional Office for Europe she wrote a protocol to estimate the health benefits of salt reduction in Europe and performed an actual health impact assessment for nine European countries. In 2013, she and her colleagues organized a workshop on the Methodological aspects of health effect projections of salt reduction, in collaboration with the WHO Regional Office for Europe. The work described in this thesis is a result of these activities.

Besides the work described in this thesis, Marieke was and is involved in several European projects, such as DiOGenes, the JPI project DEDIPAC and Joint Action CHRODIS-JA. Other activities included benefit-risk assessments of foods, research of the nutritional status of the Dutch population and monitoring the progress of food reformulation in the Netherlands. She will continue her work as a researcher at the Centre for Nutrition, Prevention and Health Services at RIVM after completion of this PhD thesis.

Publications described in the present thesis

Sources of heterogeneity and its consequences in health impact assessments of salt reduction
MAH Hendriksen, JM Geleijnse, JMA van Raaij, participants workshop, HC Boshuizen.
In preparation

Health gain by salt reduction in Europe: a modelling study.
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Monitoring salt and iodine intakes in Dutch adults between 2006 and 2010 using 24 h urinary sodium and iodine excretions.
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Other publications

Good practice characteristics of diet and physical activity interventions and policies: an umbrella review.
Horodyska K, Luszczynska A, van den Berg M, Hendriksen M, Roos G, De Bourdeaudhuij I, Brug J.
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State of the art in benefit-risk analysis: food and nutrition.
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A tiered approach for risk-benefit assessment of foods.
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van Raaij J, Hendriksen M, Verhagen H.
Public Health Nutr. 2009 Mar;12(3):325-30. doi: 10.1017/S1368980008003376.

Overview of completed training activities

Discipline specific courses and activities		
Masterclass DYNAMO-HIA	Rotterdam, the Netherlands	2014
Workshop 'Methodological consequences of salt impact assessment' (oral presentation)	Bilthoven, the Netherlands	2013
Medical demography	Rotterdam, the Netherlands	2013
Exposure Assessment in Nutrition Research	Wageningen, the Netherlands	2012
Course on 'Health Impact Assessment'	Bilthoven, the Netherlands	2011
Workshop 'Estimation of habitual intake'	Bilthoven, the Netherlands	2008
Conferences and meetings		
European Salt Action Network meeting	Ankara, Turkey	2013
International congress on Nutrition (poster presentation)	Granada, Spain	2013
World Nutrition Congress (3 oral presentations)	Rio de Janeiro, Brazil	2012
2nd World Congress Public Health Nutrition (2 poster presentations)	Porto, Portugal	2010
Wageningen Nutritional Science Forum	Arnhem, the Netherlands	2009
Symposium ' Sodium reduction in foods: a matter of desire or ability'	Wageningen, the Netherlands	2008
Annual meeting NWO nutrition	Deurne, the Netherlands	2008
General courses		
RIVM Academy 'Expert 2020'	Bilthoven, the Netherlands	2015
RIVM masterclass 'Statistical prediction'	Bilthoven, the Netherlands	2015
RIVM course 'Starters R'	Bilthoven, the Netherlands	2012
RIVM course 'Scientific writing in English'	Amsterdam, the Netherlands	2008
Optionals		
Preparation research proposal	Bilthoven, the Netherlands	2012
RIVM Research presentations	Bilthoven, the Netherlands	2012–2015

Financial support from RIVM, WHO Regional office for Europe, and Wageningen UR is gratefully acknowledged.

Cover design Tim Jacobs, Identim
Layout Renate Siebes, Proefschrift.nu
Printed by Ridderprint, Ridderkerk