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The health economic consequences of reducing salt and replacing intake of saturated fat with polyunsaturated fat in the adult Finnish population

- Estimates based on the FINRISK and FINDIET studies

Running title: Consequences of reducing salt and improving dietary fat quality

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Abstract

Objectives: To predict the health economic consequences of modest reductions in the daily intake of salt (-1.0g per day) and replacement of saturated fat (SFA, -1.0 energy percent [E%]) with polyunsaturated fat (PUFA, +1.0 E%) in the Finnish population aged 30 to 74 years.

Methods: A Markov model with dynamic population structure was constructed to present the natural history of cardiovascular diseases (CVD) based on the most current information about the age- and sex-specific cardiovascular risk factors, dietary habits, and nutrient intake. To predict the undiscounted future health economic consequences of the reduction of dietary salt and SFA, the model results were extrapolated for the years 2010-2030 by replacing the baseline population in the year 2007 with the extrapolated populations from the official Finnish statistics. Finnish costs (€2009, societal perspective) and EQ-5D utilities were obtained from published references.

Results: During the next twenty years, a population-wide intervention directed at salt intake and dietary fat quality could potentially lead to 8 000-13 000 prevented CVD cases among the Finnish adults compared the situation in year 2007. In addition, the reduced incidence of CVDs could gain 26 000-45 000 quality-adjusted life years and save €150-225 million over the same time period.

Conclusion: A modest reduction of salt and replacement of SFA with PUFA in food products can significantly reduce the burden of CVD in the adult Finnish population. This impact may be even larger in the near future due to the ageing of Finnish population.

Keywords: salt, saturated fat, cardiovascular disease, cost-effectiveness, cost savings, dynamic modelling

Introduction

Cardiovascular disease (CVD) is the leading cause of morbidity and mortality in industrialised countries, causing high health care utilisation costs. Elevated systolic blood pressure (SBP), total cholesterol (TC), and smoking are the best known major risk factors of CVD (Vartiainen et al. 2010). SBP (above 115mmHg) is the single most important cause, responsible for over 60% of strokes and nearly 50% of coronary heart disease (CHD) events, whereas corresponding figures for elevated TC (above 3.8 mmol/l) are around 20% and over 50%, respectively (World Health Report 2002).

The population-wide reduction in dietary salt and replacement of dietary saturated fat (SFA) with polyunsaturated fat (PUFA) are essential in reducing CVD incidence. Their importance is mediated at least in part by the effect of salt on BP and dietary fat quality on total (TLC) and low-density lipoprotein (LDL) cholesterol. The risk of CVD events increases progressively with increasing BP and cholesterol. The major portion of CVD deaths attributable to BP and cholesterol occurs in the upper range of “normal” BP and TC levels (i.e. BP above 130/80 mmHg and TC above 3.8 mmol/l) (He & MacGregor 2009).

In Finland, around 75% of the observed decline in coronary mortality in middle-aged men can be explained by decreases in BP, TC and smoking (Vartiainen et al. 2010). Even though public health interventions aimed at these risk factors have dramatically decreased CVD disability and deaths in developed countries (He & MacGregor 2009), CVD is still the most common cause of death, and stroke and acute myocardial infarction (AMI) are major causes of disability. Despite marked changes in diet since the 1970s, average dietary intake of salt (8.4g/day and 6.1g/day for men and women, respectively) and SFA (12.7 E%/day for both sexes) are still above recommended levels (less than 5 g/d and less than 10 E%), with relatively low PUFA intake (World Health Organisation 2007, Paturi et al. 2008). Therefore, modest reduction of dietary salt and improvement of dietary fat quality, with even small shifts in the population distributions of SBP and TC towards lower values, may improve the health economic consequences of CVD substantially.

No detailed analyses on the economic consequences of reducing dietary salt and improving dietary fat quality intake have been carried out in the adult Finnish population. This study aims to predict the potential health economic consequences of moderate reduction of dietary salt combined with replacing some dietary SFA by polyunsaturated fat (PUFA). Due to data limitations, the analysis was restricted to Finns aged 30-74 years.

Methods

The year 2007 was selected as the baseline year for the CVD risk factors. A previously developed state-transition Markov cohort model (figure 1) for CHD (Martikainen et al. 2007, Peura et al. 2008) was enhanced by adding stroke and population components (Mar et al. 2008). The new model was applied to estimate the incidence and prevalence of CVD events and mortality, impact on quality of life (QoL) and associated costs in the adult Finnish population. First, the most current available national risk factor survey data (Peltonen et al. 2008) and CVD risk functions (Vartiainen et al. 2007) were incorporated into the Markov model. Second, an additional model component (Mar et al. 2008) was built into the Markov model to estimate the total number of CVD patients in the Finnish population in 2007 and to make predictions for the years 2010-2030. Population estimates for adults over age 30 and older in year 2007 and population projections for years 2010-2030 were obtained from official Finnish statistics. To predict the effects of risk-reducing interventions, expected numbers of events were extrapolated for the years 2010-2030 using the corresponding annual extrapolated populations from Finnish statistics. All analyses were implemented in Microsoft Excel.

Event probabilities

For each one-year cycle, the hypothetical cohort of men or women without established CVD were at risk of having of an acute non-fatal CVD event, a fatal CVD event, a fatal non-CVD event, or they might survive to the next year without suffering any event. The annual probabilities for CVD events were determined by logistic risk functions based on the FINRISK study (Vartiainen et al. 2007). After each cycle, CVD risk factors were

updated based on the Finnish age and sex-specific risk factor profile data from the FINRISK 2007 Survey (Peltonen et al. 2008). Since the FINRISK risk functions are developed to predict total CVD risk, information from the National Cardiovascular Disease Register (Laatikainen et al. 2004) was used to determine the age- and gender-based case fatality. Annual risks of non-CVD deaths were estimated from the Causes of Death register by subtracting fraction of deaths due to cardiovascular diseases from the total mortality. **A more detailed description of the methods used to estimate the event probabilities is given in appendix.**

The model was run until all subjects in the cohort entered into terminal states or until 75 years of age was reached. Because the FINRISK 2007 Survey (Peltonen et al. 2008) and its ancillary study FINDIET 2007 Survey (Paturi et al. 2008) did not include information about the levels of CVD risk factors for people aged 75 years and older, the target population was restricted to Finnish adults aged 30 to 74 to ensure the reliability of the model outcomes.

Health care resource use and costs

Costs, estimated from a societal perspective, included direct cost of prevention, morbidity, rehabilitation, and production losses due to non-fatal CVD events. All costs were adjusted to the 2009 price level using the official health care price index determined by Association of Finnish Local and Regional authorities. **All costs were also predicted as future financial streams over time to reflect the actual amount that the reduction of SFA and salt intake can be expected to save in a given year** (Mauskopf et al. 2007, Marshall et al. 2008).

Annual age and sex-specific costs (including costs of hospitalisation, outpatient care, and prescribed outpatient medicines) associated with CVD events were obtained from reports based on the national discharge and prescription registries (Häkkinen et al. 2007, Meretoja et al. 2010). The model assumes that, after hospital discharge, subjects received a prescription for chronic CHD, dyslipidaemia, or hypertension. Average drug treatment costs were weighted by the proportion of subjects receiving reimbursement for those medicines.

Costs of CVD rehabilitation were estimated by weighting the average rehabilitation costs obtained from the national rehabilitation registry at the Social Insurance Institution of Finland (SII) by the proportion (30% to 40%) of CVD patients receiving rehabilitation. Productivity losses due to non-fatal CVD events were estimated by multiplying the average length of sickness leave due to MI (4.78 months) (Vehviläinen et al. 2004) and stroke (8.11 months) (Vohlonen et al. 2002) by the average monthly income in Finland including payroll tax. Productivity losses were applied to patients below the average age of retirement, assumed to be 65 years. All unit cost estimates are summarised in table 1.

Quality-adjusted life years

Age and sex-specific quality of life estimates measured by generic EQ-5D instrument were used represent the average QoL in the Finnish population aged 30 to 75 (Saarni et al. 2006). The disutility weights due to initial or subsequent CVD events were determined from previously published studies (Saarni et al. 2006, Lindgren et al. 2007, Soini et al. 2010).

Estimating the effectiveness of reduced salt and saturated fat intake on the number of CVD events and other outcomes

The reduction of 1 gram of salt per day was assumed to change SBP approximately by -1.185 mmHg among hypertensive subjects and by -0.595 mmHg among normotensive subjects. These changes were estimated based on a dose-response relationship between the changes in dietary salt intake, 24-h urinary sodium and BP (He & MacGregor 2003). These effect estimates were weighted by the age and sex-specific proportions of hypertensive subjects (SBP above 130) in the Finnish population (Peltonen et al. 2008). The effect of salt reduction on SBP was assumed to be linear over the range of 0 to 3 g per day (He & MacGregor 2003).

Effects on serum TC of replacing SFA with PUFA were obtained from a meta-analysis of metabolic ward studies (Clarke et al. 1997). Every 1% increase in energy (E%) from PUFA intake was expected to lead to a -0.026 mmol/l change in TC and 0.005 mmol/l

increase in high-density lipoprotein (HDL). Alternatively, the predicted changes in serum cholesterol were estimated by the Keys equation (Keys et al. 1957), where 1E% increase from PUFA was expected lead to around -0.043 mmol/l reduction in TC. The effect of changing BP and cholesterol levels on CVD events and deaths was then estimated using the FINRISK risk functions (Vartiainen et al. 2007). To simplify the analysis, the full effect of dietary salt and SFA reduction was assumed to be achieved immediately and to persist during the whole time-horizon.

Finally, the proportion of subjects receiving antihypertensive medication was assumed to change as a function of SBP. Based on an estimated logistic regression model, the reduction of 1 mmHg in SBP reduced the probability of receiving antihypertensive medication, with adjustment for age, sex, and body mass index, by approximately 1.5% in men and 2.8% in women (data on file).

Model calibration and sensitivity analyses

The model was calibrated to reproduce the number of key cardiovascular events among the 30-74 years old population in year 2007 in Finland. In addition, uncertainty associated with the model parameters was handled by determining probability distributions for all relevant parameters and then conducting probabilistic sensitivity analysis (PSA) with 1000 iteration rounds (Briggs et al. 2002). **The selection of proper probability distributions for the model parameters has been described in details in technical appendix.** The results of the PSA were used to determine 95% credibility intervals for the model outcomes and the probability of savings as a function of amount of savings. One-way sensitivity analyses were used to test the robustness of model assumptions.

Results

The model was **calibrated** by comparing the model results to the actual number of patient in the different health states in the year 2007. For example, according to the FINRISK 2007 -study the prevalence of people with history of stroke and MI is between 59 900 - 68 800 and 53 800 - 63 300 individuals among the Finnish population

aged 30-74 years old, respectively (Peltonen et al. 2008). The calibrated model estimated that the number of people with history of stroke is around 61 100 and the number of people with history of MI is approximately 58 300. Thus, on average, the calibrated model was considered to be sufficiently accurate to reproduce the baseline population for the year 2007.

Over twenty years, a population-wide intervention could potentially prevent 8 000-13 000 CVD cases among the Finnish adults aged 30 to 74 compared to the status quo scenario, where the CVD risk factors stay at the year 2007 levels over time. In addition, the reduced incidence of CVD cases could yield an additional 26 000-45 000 quality adjusted life years (QALYs) and save 150-225 million Euros over the same time period. Detailed results of base-case and additional one-way sensitivity analyses are presented in table 2. Due to the linearity assumption of effects, the approximations of outcomes with different reduction levels are easily extrapolated based on the results presented in table 2. For example, reducing the daily intake of both dietary salt and saturated fat by 0.5 units would lead to around 74-113 million Euros savings during the next twenty years.

To take the uncertainty of model parameters into account, the probability of obtained cumulative savings was estimated. Figure 2 shows that in the base-case scenario there is over 95% chance that the cumulative total savings with and without productivity losses are at least 130 and 115 million Euros between the years 2010-2030, respectively. In addition, sensitivity analyses showed that the independent effect of salt reduction in the prevention of cardiovascular events is larger than the effect of replacing SFA by PUFA (table 2). The reduction of dietary salt explained over 99 per cent of changes in the incidence of CVD events and their consequences. However, when the Keys equation was used to predict the changes in TC, the reduction of dietary salt explained only around 62 per cent of the changes in the number of CVD cases. Thus, the interpretation of results needs to be done with care, since the results are sensitive to the selection of effect size estimates.

Discussion

Main findings of the study

This study demonstrated that even a modest reduction of dietary salt and replacement of dietary SFA with PUFA would have a great impact on the incidence of CVD events among the population aged 30 to 74 years. The lower number of CVD events would result in substantial gains in QALYs and cost savings.

The results of the present study agree with previous studies (Bibbins-Domingo et al. 2010, Murray et al. 2003, Smith-Spangler et al. 2010, Selmer et al. 2000) that have demonstrated the potential benefits of salt reduction to reduce the burden of CVD. However, none of these previous studies have directly estimated the joint effects of reducing both salt and SFA intake simultaneously, considered here.

Strengths of the study

A strength of this study is that cardiovascular risk factors, dietary habits, and nutrient intake of the Finnish population aged 30 to 74 years were obtained from a well-characterised and representative sample of Finnish adults (Peltonen et al. 2008, Paturi et al. 2008), and the cost and QoL estimates were obtained from representative studies.

In the analysis, the independent role of dietary salt reduction of 1g was larger than the role of a 1 E% change of SFA to PUFA. This is because both the effect sizes obtained from the literature differ and also the beta coefficients of FINRISK functions for the association of SBP with both CVD events and deaths are more significant than for the corresponding association of serum TC with CVD cases. This is in part because serum TC is not included in the FINRISK function that predicts the risk of stroke. In contrast, SBP is a major risk factor for both stroke and MI. The analyses also assume that dietary fat quality mediates its effects on CVD risk solely via effects on lipids. However, dietary fat quality may influence CVD risk by mechanisms other than cholesterol (Erkkilä et al. 2008), and the relatively strong inverse associations of PUFA intake and the PUFA/SFA ratio with CHD or CVD risk from some prospective cohort studies (Erkkilä et al. 2008, Hu et al. 1997, Laaksonen et al. 2005) also implies that dietary fat

quality impact cardiovascular risk more than would be predicted by effects on the lipid profile alone.

This study focused on replacement of SFA with PUFA. Because replacement of SFA with monounsaturated fat yields similar effects on the lipid profile (Clarke et al. 1997), results would have been similar if monounsaturated or other unsaturated fat had been used in place of PUFA.

Limitations of the study

Since the results of the present study are based on statistical computer modelling requiring several assumptions, the results should be interpreted cautiously. The current study did not specify any particular intervention aiming to reduce the dietary salt and SFA intake from daily food. However, the modest reductions presented here could be achieved by voluntary actions of the food industry aimed at reducing the use of salt and saturated fat in processed food, a major source of dietary salt and saturated fat (Paturi et al. 2008). **There are already examples about successful strategies that have managed to reduce the intake of salt and SFA in cooperation with the food industry (Prättälä 2003, Pietinen et al. 2008, Laatikainen et al. 2006, Food Standard Agency 2008). These interventions, for example, have managed to reduce the intake of salt by 10% to 25% (Food Standard Agency 2008, Laatikainen et al. 2006).**

We assumed no changes in consumer behaviour and persistence associated with these modifications, and dramatic changes in consumer behaviour would be unlikely, given that a reduction of dietary salt, for example, by 10-15 per cent is possible without detection (Girgis et al. 2003, Ruusunen & Puolanne 2005). Moreover, after an adaptation period people appear to prefer food with less salt (Blais et al. 1986).

To ensure the robustness of the study results, the study population was restricted to people aged 30 to 74 years. However, over 50 per cent of CVD cases occurs among the population aged 75 and over in Finland, so an important segment of the Finnish population could not be modelled. The impact in the whole population is, thus, clearly underestimated. However, at the moment there are no epidemiological data available to inform the association between CVD risk factors and the risk of CVD events among the

elderly in Finland. The reduction of dietary salt and SFA is likely to benefit also subjects aged less than 30 years, which will potentially decrease the future prevalence of hypertension and hyperlipidaemia in older age groups.

Moreover, there were no relevant estimates available for the proportion of patients provided assisted care or care in institutions such as nursing homes after non-fatal stroke or MI. Therefore the cost of institutionalisation, which is especially important following stroke, has not been considered in the analysis. Also, potential changes in the number of patients with heart failure, end-stage renal disease, or dementia (Kivipelto et al. 2006, Solomon et al. 2010) were not considered in the analysis due to the lack of data.

The current analysis assumes that CVD risk factors stay at the same levels as they were in year 2007. However, if the declining trend in the levels of CVD risk factors seen in 1972-2007 (Vartiainen et al. 2010) will continue unabated, the burden of CVD may not increase as much as presented in this study. On the other hand, the current epidemic of obesity and type II diabetes may have a negative impact on the trends seen in CVD incidence over the past several decades (Poirier et al. 2006). Finally, the assumed linear relationships between salt and SFA intakes and SBP and TC may not hold, and there is evidence that reductions in BP could be even greater at lower levels of salt intake (Sacks et al. 2001). An underestimate of the true amount of future cost savings and improved health at the population level may thus have resulted from these modelling assumptions.

Conclusion

Our findings suggest that even a modest reduction of dietary salt and replacement of SFA content with PUFA in food products can substantially reduce the total burden of cardiovascular diseases in the adult Finnish population, with large cost savings from the societal point of view. The aging of the Finnish population may reinforce this impact.

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Conflict of interest statement:

J.A.M. and E.J.O.S. are consultants and shareholders of ESiOR Oy, commissioned by HK Ruokatalo Oy to perform this study; ESiOR also carries out commissioned studies and health-economic analysis for several other pharmaceutical companies, food industry companies, and hospitals. D.E.L. and L.N. are internal medicine specialists at Kuopio University Hospital and act as medical advisors to ESiOR during the study. LN has held paid lectures and commercially-sponsored research for MSD, Boehringer Ingelheim and AstraZeneca.

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Figure legends

Figure 1. Simplified structure of state-transition model. The model included five health states and death, which was modelled as an absorbing terminal state. The “healthy” state includes subjects without a history of myocardial infarction (MI) or stroke, and they have an annual probability of experiencing an initial non-fatal CVD event (MI or stroke), fatal event (non-CVD death or CVD death), or no CVD event.

Figure 2. Probability of cumulative savings (with and without productivity losses) given a dietary salt and saturated fat reduction of 1g and 1 E% per day (base-case scenario) among Finnish adults aged 30 to 74 between years 2010-2030. PL = Productivity Losses included.

Table 1. Parameters used in the model. Costs are presented in year 2009 values.

	Point estimate		Source
	Men	Women	
Utilities , mean (SE)			
30-44	0.917 (0.003)	0.906 (0.003)	
45-54	0.876 (0.005)	0.865 (0.005)	Estimated based on
55-64	0.821 (0.006)	0.810 (0.006)	Saarni et al. 2006 and
65-74	0.781 (0.008)	0.770 (0.008)	Soini et al. 2010
Disutility due to CVD event, mean (SE)			
Stroke	-0.145 (0.097)		Lindgren et al. 2007
AMI	-0.092 (0.029)		Soini et al. 2010
Post-stroke	-0.090 (0.020)		Saarni et al. 2006
Post-MI	-0.011 (0.009)		Saarni et al. 2006
Costs, mean (SE)			
Stroke, mean (SE) [#]	23 240€		Meretoja et al. 2010
AMI			
30-44	16 245€ (762)	16 215€ (760)	Häkkinen et al. 2007
45-54	14 955€ (701)	17 503€ (820)	
55-64	14 446€ (677)	16 326€ (765)	
65-74	12 995€ (609)	14 958€ (701)	
Fatal AMI*	2294€		Hujanen et al. 2008
Rehabilitation after stroke (first year)	6182€		Assumption based on information from SII's database
Rehabilitation after MI (first year)	2576€		Assumption based on information from SII's database
Antihypertensive medication in the primary prevention per year	314	302	
Dyslipidaemia therapy in the primary prevention per year	195	166	
Monitoring a patient receiving antihypertensive medication	224€		Assumption based on SII data
Monitoring a patient receiving statins	185€		Assumption based on SII data
Monitoring a patient in secondary prevention	388€		Assumption based on SII data
Productivity loses due to non-fatal stroke	11 700€		Vohlonen et al. 2002
Productivity loses due to non-fatal MI	6 884€		Vehviläinen et al. 2004

[#] Estimate is a weighted average cost of treatment of ischemic stroke (79.4%), subarachnoid haemorrhage (13.6%), and intracerebral haemorrhage (7%) * A patient died during a hospitalisation. SII = the Social Insurance Institution of Finland (KELA).

Table 2. Predicted cumulative health and economic changes compared the situation in year 2007 between the years 2010-2030. 95% credibility intervals (CrI) are based on the Monte Carlo simulation.

Scenario	2010 difference (95% CrI)	2020 difference (95% CrI)	2030 difference (95% CrI)
Base-case (salt -1g, SFA -1 E%, PUFA +1 E%)			
Non-fatal CVD	-215 (-348 to -97)	-2 502 (-2 944 to -2 088)	-4 752 (-5 336 to -4 185)
Fatal CVD	-137 (-296 to -60)	-1 684 (-1 980 to -1 395)	-3 271 (-3 662 to -2 897)
Cost (1000 EUR) with productivity losses	-6 786 (-11 506 to -2 926)	-70 507 (-84 489 to -57 924)	-147 094 (-167 364 to -128 731)
without productivity losses	-5 916 (-10 057 to -2 610)	-62 339 (-75 200 to -50 533)	-130 404 (-147 707 to -113 397)
QALYs gained	1 105 (438 to 2 059)	13 444 (10 699 to 16 434)	26 255 (22 498 to 30 102)
Base-case with the Keys equation			
Non-fatal CVD	-341 (-551 to -172)	-3 930 (-4 612 to -3 286)	-7 448 (-8 372 to -6 611)
Fatal CVD	-236 (-385 to -115)	-2 833 (-3 298 to -2 363)	-5 470 (-6 152 to -4 840)
Cost (1000 EUR) with productivity losses	-10 425 (-17 098 to -5 022)	-107 996 (-127 347 to -89 659)	-224 785 (-252 792 to -197 489)
without productivity losses	-8 312 (-13 563 to -4 169)	-88 604 (-105 982 to -74 291)	-185 784 (-207 850 to -164 578)
QALYs gained	1907 (813 to 3 409)	23 232 (18 723 to 28 291)	45 142 (38 586 to 52 421)
Sensitivity analysis[#] (- 1.0 g of salt, -0.0 E% SFA)			
Cost with productivity losses (1000 EUR)	-6 683	-69 923	-146 522
QALYs gained	1 083	13 363	26 142
Baseline risk of CVD event is decreased -10%			
- Cost with productivity losses (1000 EUR)	-6 370	-66 830	-139 471
- QALYs gained	1 016	12 480	24 386
Baseline risk of CVD event is increased +10%			
- Cost with productivity losses (1000 EUR)	-7 158	-7 389	-153 920
- QALYs gained	1180	14 345	27 979

[#] Only deterministic cost-savings and QALYs gained are reported for one-way sensitivity analysis



