TECHNICAL APPENDIX

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Section 1. Equations used to fit monthly transition probabilities

Monthly risks of MI and stroke were estimated by fitting exponential curves to data on age- and sex-specific incidence of first MI and stroke from the Framingham Heart Study (1980-2003), published by the National Heart, Lung, and Blood Institute (1).

Fitted exponential for monthly probability of MI, given no history of MI (x is age in years):

Men: \[ y = 0.0001 \times e^{0.0312x} \]
\[ R^2 = 0.864 \]

Women: \[ y = 8E - 06 \times e^{0.0599x} \]
\[ R^2 = 0.990 \]

Fitted exponential for monthly probability of stroke, given no history of stroke (x is age in years):

Men: \[ y = 9E - 06 \times e^{0.0622x} \]
\[ R^2 = 0.960 \]

Women: \[ y = 3E - 06 \times e^{0.0741x} \]
\[ R^2 = 0.953 \]

Age- and sex-specific risk of mortality after MI and stroke was estimated by fitting exponential curves to the ratio of incidence of fatal event to total incidence of event. Fatal MI and total incidence of MI data was from the Framingham Heart Study. The ratio of fatal stroke to stroke incidence was obtained from the Cardiovascular Health Study (1). The Cardiovascular Health Study only reported incidence of fatal versus non-fatal stroke.
for persons age 65+. To estimate ratio of fatal stroke to stroke incidence for ages <65, we assumed that the proportion of persons who die of stroke given stroke increases exponentially with age.

Fitted exponential for probability of mortality after MI ($x$ is age in years):

- **Men:**
  \[ y = 0.0289 \times e^{0.0269x} \]
  \[ R^2 = 0.951 \]

- **Women:**
  \[ y = 0.0013 \times e^{0.0587x} \]
  \[ R^2 = 0.594 \]

Fitted exponential for probability of mortality after stroke ($x$ is age in years):

- **Men:**
  \[ y = 0.0003 \times e^{0.0782x} \]
  \[ R^2 = 0.994 \]

- **Women:**
  \[ y = 0.0034 \times e^{0.0428x} \]
  \[ R^2 = 0.804 \]

The curve fitted to the probability of mortality after MI by age for women had relatively poor fit ($R^2=0.594$). This is because there is an outlier in the data, with the highest mortality seen at age 70. Excluding this data point, the following line may be fitted:

\[ y = 0.0004 \times e^{0.0706x} \]
\[ R^2 = 0.925 \]

Using this alternate equation describing the relationship between age and mortality from MI for women does not significantly change the results. For example, with the alternate equation, cost savings under collaboration with industry is $32.6B (versus $32.1B) and gain in QALYs is 2,043,165 (versus 2,060,790).
Monthly risk of non-CVD mortality was estimated by fitting an exponential curve to annual age- and cause-specific adult mortality data (2).

Fitted exponential for monthly non-CVD mortality risk (x is age in years):

Men:  \( y = 7E - 06 \times e^{0.0773x} \)

\[ R^2 = 0.998 \]

Women:  \( y = 4E - 06 \times e^{0.0825x} \)

\[ R^2 = 0.998 \]
Section 2. Description of distributions used in probabilistic sensitivity analysis

Cost of well state: See Appendix A for a description of how costs in the well state were estimated. Lines were fitted to the estimated monthly costs.

Fitted lines for monthly well costs in dollars (x is age in years):

Men: \[ y = 12.45x - 280.34 \]
\[ R^2 = 0.995 \]

Women: \[ y = 10.44x - 147.14 \]
\[ R^2 = 0.989 \]

The 95% confidence interval for costs in the well state corresponded to +/- 20% of the base case well cost estimates. Hence costs in the well state were multiplied by a constant with a mean of 1, standard deviation 0.15306, gamma distribution.

Cost of CVD state: See Appendix A for a description of how costs in the CVD state were estimated. Lines were fitted to the estimated monthly costs.

Fitted lines for monthly CVD costs in dollars (x is age in years):

Men: \[ y = 15.8x + 19.57 \]
\[ R^2 = 0.998 \]

Women: \[ y = 9.297x + 531.28 \]
\[ R^2 = 0.955 \]

The 95% confidence interval for costs in the CVD state corresponded to +/- 20% of the base case CVD cost estimates. Hence costs in the CVD state were multiplied by a constant with mean of 1, standard deviation 0.15306, gamma distribution.
Cost of acute MI: The acute event cost assigned for the one month individuals remained in the acute MI state had a mean $9,000, standard deviation $3,214, gamma distribution.

Cost of stroke: The acute event cost assigned for the one month individuals remained in the acute stroke state had a mean of $18,800, standard deviation $6,714, gamma distribution.

Cost of UK strategy, per person: See Technical Appendix Section 6 for a detailed description of how this cost was calculated. Monthly cost of UK strategy had a mean of $0.1272, standard deviation $0.017, gamma distribution.

UK strategy % reduction in sodium consumption: Mean reduction in sodium consumption was 9.5%, standard deviation 8.5%, gamma distribution.

Tax strategy % reduction in sodium consumption: Mean reduction in sodium consumption was 6%, standard deviation 5%, gamma distribution.

Probability of first MI, first stroke, non-CVD death, MI death, stroke death: We assumed that these transition probabilities’ 95% CI varied +/- 20%. Hence, these age- and sex-specific transition probabilities were multiplied by a constant with a mean of 1, standard deviation 0.15306, gamma distribution.
Relative risk of death given history of CVD: To calculate the relative risk of death given history of CVD, the relative risk of death given no history of CVD was multiplied by a constant with a mean of 1.5, standard deviation 0.38265, gamma distribution.

Risk of MI or stroke given history of CVD: To calculate the risk of MI (or stroke) given history of CVD, the risk of MI (or stroke) without a history of CVD was multiplied by a constant with a mean of 2, standard deviation 1.0204, gamma distribution.

Monthly utility of MI: We assumed that the 95% CI for annual utility of MI was approximately 0.6-1.0 with mean of 0.85. Hence monthly utility = 0.0708 = 0.85/12. For the monthly utility of MI, we used a beta distribution, with a mean 0.0708, standard deviation 0.0138.

We implemented our model in Matlab and TreeAge and both programs require annual utilities to be divided by 12 to get monthly utilities. Readers should note that some computer programs will automatically divide the annual utility by 12 and hence readers recreating our model in another computer program should be aware of how their computer program handles utilities.

Monthly utility of stroke: We assumed the 95% CI for annual utility of stroke was approximately 0.4-0.85 with mean of 0.64. Hence monthly utility = 0.0533 = 0.64/12. For the monthly utility of stroke, we used a beta distribution, with a mean 0.0533, standard deviation 0.0147.
Monthly utility of CVD: We assumed the 95% CI for annual utility of CVD was approximately 0.75-0.97 with mean of 0.85. Hence monthly utility = 0.0708 = 0.85/12.

For the monthly utility of CVD, we used a beta distribution with a mean 0.0708, standard deviation 0.0068.

Annual utility of low sodium diet: The annual utility of a low sodium diet had a custom distribution, mean: 0.09985. To calculate monthly utility, divide annual utility by 12.
Slope of sodium-SBP dose response curve: The slope of the sodium-SBP dose response curve had a mean of 0.0598, standard deviation 0.015816, beta distribution.
Section 3. Comparison of our model and NHANES estimates of prevalence of cardiovascular disease

Our model's prediction of percent of those alive with a history of MI or stroke ("CVD")

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Men</th>
<th>Women</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>2.5%-8.2%</td>
<td>1%-3.7%</td>
</tr>
<tr>
<td>55-64</td>
<td>9%-16.4%</td>
<td>4.2%-9.1%</td>
</tr>
<tr>
<td>65-74</td>
<td>17.3%-26.2%</td>
<td>9.8%-17.7%</td>
</tr>
<tr>
<td>75-84</td>
<td>27.2%-36%</td>
<td>18.8%-29.9%</td>
</tr>
</tbody>
</table>

Men: Prevalence of history of MI, Stroke, Per NHLBI Chartbook (NHANES data)

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Age</th>
<th>MI</th>
<th>LL</th>
<th>UL</th>
<th>Stroke</th>
<th>LL</th>
<th>UL</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>50</td>
<td>2.8</td>
<td>1.4</td>
<td>4.3</td>
<td>1.2</td>
<td>0.4</td>
<td>1.9</td>
</tr>
<tr>
<td>55-64</td>
<td>60</td>
<td>11.8</td>
<td>8.3</td>
<td>15.3</td>
<td>3.1</td>
<td>1.7</td>
<td>4.5</td>
</tr>
<tr>
<td>65-74</td>
<td>70</td>
<td>12</td>
<td>8.2</td>
<td>15.6</td>
<td>6.7</td>
<td>4.9</td>
<td>8.5</td>
</tr>
<tr>
<td>75-84</td>
<td>80</td>
<td>18.6</td>
<td>15.6</td>
<td>21.7</td>
<td>12.1</td>
<td>9.8</td>
<td>14.4</td>
</tr>
</tbody>
</table>

Women: Prevalence of history of MI, Stroke Per NHLBI Chartbook (NHANES data)

<table>
<thead>
<tr>
<th>Age Range</th>
<th>Age</th>
<th>MI</th>
<th>LL</th>
<th>UL</th>
<th>Stroke</th>
<th>LL</th>
<th>UL</th>
</tr>
</thead>
<tbody>
<tr>
<td>45-54</td>
<td>50</td>
<td>1</td>
<td>0.3</td>
<td>1.7</td>
<td>2.1</td>
<td>0.8</td>
<td>3.4</td>
</tr>
<tr>
<td>55-64</td>
<td>60</td>
<td>3.5</td>
<td>1.9</td>
<td>5</td>
<td>3</td>
<td>1.3</td>
<td>4.7</td>
</tr>
<tr>
<td>65-74</td>
<td>70</td>
<td>5.9</td>
<td>3.9</td>
<td>7.8</td>
<td>6.3</td>
<td>4.2</td>
<td>8.4</td>
</tr>
<tr>
<td>75-84</td>
<td>80</td>
<td>10.7</td>
<td>7.9</td>
<td>13.6</td>
<td>11.5</td>
<td>8.8</td>
<td>14.1</td>
</tr>
</tbody>
</table>

CVD = cardiovascular disease (history of MI OR Stroke), MI = myocardial infarction, NHLBI = National Heart, Lung, and Blood Institute (1), NHANES = National Health and Nutrition Examination Survey, LL = lower limit of 95% confidence interval, UL = upper limit of 95% confidence interval.

Our model keeps track of whether a person has a history of MI or stroke. It does not keep track of which event the person had, or whether they have had both. However, the NHLBI Chartbook reports the prevalence of MI and prevalence of stroke, but not, for example, the prevalence of MI and stroke combined, or of MI without stroke. The prevalence of stroke and MI may be added to estimate the prevalence of both conditions, but will be an overestimate as a portion of the population have had both an MI and stroke.
Section 4. Equations used to estimate change in blood pressure and relative risk of myocardial infarction or stroke

The mmol decrease sodium intake based on the percent change in sodium intake from each strategy was inputted into a linear relationship between sodium-SBP fitted from data reported by Dietary Approaches to Stop Hypertension trial (3). We based our calculation on SBP, which is a better predictor of cardiovascular disease in older adults than diastolic blood pressure and is the parameter used most often by clinicians to adjust blood pressure medications (4). (x= change in mmol of sodium intake)

Equation 1: Decrease in SBP = -0.0598x; R² = 1

This trial reported that greater decreases in SBP were achieved among older persons so an adjustment for age was made by fitting an equation to the data reported on the relationship between age and change in SBP for decreases in sodium intake of approximately 35 mmol per day (5). Mean age among persons included in the data used in Equation 1 was 48 years.

Equation 2: Adjustment in SBP for Age = -0.0431 (age - 48); R² = 0.9068

Hence net change in SBP = Decrease in SBP + Adjustment in SBP for age.

In sensitivity analysis, we applied the decrease in SBP, without the adjustment for age and also used the decrease in SBP per mmol change in sodium reported by the Cochrane Review (6). The Cochrane Review reported mean change in SBP for hypertensives and normotensives, so to estimate a population mean change, we assumed that 24% of the population had hypertension and used the following equation:

Alternate Relationship between Sodium and SBP: Decrease in SBP = -0.04464
Using a more modest relationship between sodium and SBP reported in a older meta-analysis (7) would decrease health benefits and costs savings. However, this meta-analysis included studies of very short duration (less than one week) and the authors did not describe their sensitivity analyses so it was not used as the basis for our analysis.

The relative risk of first MI or stroke from lower SBP was estimated by fitting curves to data from a meta-analysis of prospective patient-level data on blood pressure and CVD mortality from over one million adults without previous cardiovascular disease (8).

Equations to calculate relative risk reduction of MI (x is age in years):

\[
RR \text{ of MI} = 2^{(\text{Net decrease in SBP}\times \text{slope MI})}
\]

\[
\text{slope MI} = -1.1009\times 10^{-5}x^2 + 8.6305\times 10^{-4}x + 3.5176\times 10^{-2}; \ R^2 = 0.995
\]

Equations to calculate relative risk reduction of stroke (x is age in years):

\[
RR \text{ of stroke} = 2^{(\text{Net decrease in SBP}\times \text{slope stroke})}
\]

\[
\text{slope stroke} = -2.5946\times 10^{-5}x^2 + 2.3052\times 10^{-3}x + 2.2168\times 10^{-2}; \ R^2 = 0.997
\]

We were unable to include end stage kidney disease and hypertensive heart failure as outcomes as the mathematical relationship between change in risk of disease and change in SBP by age and sex has not been as clearly worked out as it has been for stroke and MI.
Section 5. Comparison of our model with Strazzullo’s *BMJ* meta-analysis

Our Model’s Age- and Sex-Specific Estimates of RR of Stroke and MI:

<table>
<thead>
<tr>
<th>Age</th>
<th>Stroke</th>
<th></th>
<th></th>
<th>MI</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Men</td>
<td>Women</td>
<td></td>
<td>Men</td>
<td>Women</td>
</tr>
<tr>
<td>40</td>
<td>1.27</td>
<td>1.12</td>
<td></td>
<td>1.18</td>
<td>1.05</td>
</tr>
<tr>
<td>50</td>
<td>1.26</td>
<td>1.18</td>
<td></td>
<td>1.17</td>
<td>1.10</td>
</tr>
<tr>
<td>60</td>
<td>1.22</td>
<td>1.18</td>
<td></td>
<td>1.15</td>
<td>1.11</td>
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<tr>
<td>70</td>
<td>1.16</td>
<td>1.15</td>
<td></td>
<td>1.12</td>
<td>1.10</td>
</tr>
<tr>
<td>80</td>
<td>1.10</td>
<td>1.08</td>
<td></td>
<td>1.09</td>
<td>1.07</td>
</tr>
</tbody>
</table>

*Assume 86 mmol decrease sodium intake, 11 year relative risk
MI= myocardial infarction

Strazzullo's *BMJ* Meta-analysis Estimates of RR Stroke and CVD:

<table>
<thead>
<tr>
<th>mean age</th>
<th>RR Stroke</th>
<th></th>
<th></th>
<th>RR CVD*</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>LL</td>
<td>UL</td>
<td></td>
<td>LL</td>
<td>UL</td>
</tr>
<tr>
<td>not reported</td>
<td>1.23</td>
<td>1.06</td>
<td>1.43</td>
<td>1.17</td>
<td>1.02</td>
</tr>
</tbody>
</table>

* RR of CVD statistically significant once one study was removed. Mean age not reported by authors, mean change in sodium intake was 86 mmol, mean follow-up was 11.3 years. CVD= cardiovascular disease, LL= lower limit of 95% confidence interval, UL= upper limit of 95% confidence interval.

Readers may make rough comparisons of our estimates with Strazzullo’s estimate of RR of stroke. However, Strazzullo and colleagues do not report the mean age nor the proportion of included subjects who were men in their meta-analysis so precise comparisons are not possible. Note that our estimates of RR of stroke are well within the 95% confidence interval reported by these authors. Finally, Strazzullo and colleagues do not state how they defined cardiovascular disease in their meta-analysis so we are unable to make any comparisons with this data. We have included our model’s estimate for RR
of MI in case information about the RR of MI becomes available from future meta-analyses or other sources in the future.
Section 6. Description of cost of collaboration calculation

The 2008-2009 budget of the Food Standards Agency (England) was approximately £137,720,000 (9). There were approximately 20,820,800 adults age 45 and older in England in 2007 (10). Per the World Bank, the purchasing power parity coefficient between the U.S. and the U.K. is £0.65 = 1 international $ (11).

Table 1. The budget of the Food Standard Agency, converted to U.S. dollars (annual cost), and divided by the number of adults in the England age 45 years and older.

<table>
<thead>
<tr>
<th>Percent of FSA budget spent on salt programme</th>
<th>Annual costs $</th>
<th>Annual per person costs</th>
<th>Monthly per persons costs</th>
</tr>
</thead>
<tbody>
<tr>
<td>100%</td>
<td>$211,876,923</td>
<td>$10.18</td>
<td>$0.848018</td>
</tr>
<tr>
<td>67%</td>
<td>$139,838,769</td>
<td>$6.72</td>
<td>$0.559692</td>
</tr>
<tr>
<td>50%</td>
<td>$105,938,462</td>
<td>$5.09</td>
<td>$0.424009</td>
</tr>
<tr>
<td>33%</td>
<td>$69,919,385</td>
<td>$3.36</td>
<td>$0.279846</td>
</tr>
<tr>
<td>15%</td>
<td>$31,781,538</td>
<td>$1.53</td>
<td>$0.127203</td>
</tr>
<tr>
<td>7%</td>
<td>$14,831,385</td>
<td>$0.71</td>
<td>$0.059361</td>
</tr>
<tr>
<td>5%</td>
<td>$10,593,846</td>
<td>$0.51</td>
<td>$0.042401</td>
</tr>
</tbody>
</table>
Section 7. Description of calculation of costs of well and CVD states by age and sex

Adults completing the Medical Expenditure Panel Survey in 2006 were asked whether they had ever had a heart attack or stroke. We used a SAS macro (%SMSUB version 3.1), which provides additional capabilities for PROC SURVEYMEANS to calculate mean medical costs and 95% confidence intervals by age group for men and women with and without a history of heart attack or stroke. The calculated annual medical expenditures for those without a history of heart attack or stroke were used as medical expenditures in the “well” state in the model. To estimate medical expenditures for the cardiovascular disease state (CVD), we subtracted the product of the age-specific incidence of acute heart attack and [per-case] cost of acute heart attack from the calculated medical expenditures of individuals with a history of heart attack and/or stroke. Similarly, the product of the age- and sex-specific incidence of acute stroke was also multiplied by the cost of acute stroke and deducted. By deducting costs attributed to acute heart attack and stroke that may have occurred during the year of measurement, we were able to estimate the chronic costs associated with having a history of heart attack or stroke, not including acute costs. This was done to avoid double counting costs of acute heart attacks and strokes in the model. CVD = history of myocardial infarction or stroke.
Section 8. Technical discussion of the tax strategy

We assume that the tax is approximately neutral, in the following sense. Apart from the changes in QALYs, the welfare losses that individuals suffer because they end up paying more for salty foods are offset by the welfare gains from increased revenues to the government. Arguably this assumption understates the benefits of the tax, since alternative modes of raising tax revenue typically create substantial deadweight losses due to their effects on behavior. For example, an increase in the income tax typically reduces work effort. Thus the salt tax may be a superior mechanism to raise tax revenues as it has the benefit of reducing morbidity and mortality from cardiovascular disease, increasing QALYs.
Section 9. Discussion of mandatory sodium targets

Countries may consider *mandatory* maximum sodium legislation and mandatory laws may be more effective at reducing sodium intake than voluntary regulations. However, government costs may be higher due to enforcement of these laws and if manufacturers encounter difficulty in lowering sodium in some foods, food prices could increase. We have excluded this strategy from our analysis due to the additional uncertainty and lack of data on these issues.
REFERENCES


