Blood pressure and cardiovascular mortality in England from 2003 to 2011 – The impact of salt reduction

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Blood pressure and cardiovascular mortality in England from 2003 to 2011 − The impact of salt reduction

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Running title: Impact of salt reduction on BP and CVD mortality

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Abstract

Objectives: To study the trend of stroke and ischemic heart disease(IHD) mortality and blood pressure(BP) between 2003 and 2011 in England, and to determine the extent to which the reduction in salt intake occurred during this period contributed to those changes.

Design: Non-institutionalised population surveys.

Setting and participants: England, 2003 n=14,836, 2006 n=14,142, 2008 n=15,098 and 2011 n=8,610, aged ≥16 years.

Outcomes: Stroke and IHD mortality, BP and 24-hour urinary sodium.

Results: From 2003 to 2011, there was a decrease in mortality from stroke by 42% and IHD by 40%. In parallel, there was a fall in BP of 3.0/1.4mmHg (P<0.001/ P<0.001), a decrease of 0.3mmol/L (P<0.001) in cholesterol, a reduction in smoking from 25% to 20%(P<0.001), an increase in fruit and vegetable consumption (0.2 portion/d, P<0.001), and an increase in body mass index(BMI) (0.4kg/m^2, P<0.001). Salt intake as measured by 24-hour urinary sodium decreased by 1.4 g/d (P<0.01). It is likely that all of these factors, along with improvements in the treatments of BP, cholesterol and CVD contributed to the falls in stroke and IHD mortality. In individuals who were not on BP treatment, there was a fall in BP of 2.7±0.3/1.1±0.2mmHg (P<0.001/ P<0.001) after adjusting for age, sex, ethnic group, education, household income, alcohol consumption, fruit and vegetable intake, and BMI. Although salt intake was not measured in these participants, the fact that the average salt intake in a random sample of the UK population fell by 15% during the same period, suggests that these falls in BP would be largely attributable to the reduction in salt intake.

Conclusions: The reduction in salt intake is likely to be a major contributor to the fall in BP from 2003 to 2011 in England. As a result, it would also have contributed to the decreases in stroke and IHD mortality.

ARTICLE SUMMARY

Article focus

- A modest reduction in salt intake lowers blood pressure (BP) and, thereby, reduces cardiovascular risk.
- In the UK, salt intake as measured by 24-hour urinary sodium excretion decreased from 9.5 to 8.1 g/d from 2003 to 2011. During the same period, there was also a fall in BP and a decrease in stroke and ischemic heart disease (IHD) mortality.

Key messages

- Our analysis of the data from the Health Survey for England showed that, in individuals who were not on any BP treatment or other treatments which might affect BP, there was a significant fall in BP of 2.7/1.1 mmHg from 2003 to 2011 after taking into account almost all factors known to be associated with BP including age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and body mass index. Salt intake, a major determinant of population BP, was not included in this analysis because it was not measured in these participants. However, the fact that salt intake fell by 15% during the same period, would strongly suggest that these falls in BP were largely attributable to the reduction in salt intake.
- As BP throughout its range is a major cause of stroke and IHD, the reduction in salt intake through its effect on BP, would also have played an important role in the reduction in stroke and IHD mortality that occurred in England during this period.

Strengths and limitations of this study

- The study used the best available data in England.
- Various surveys included different sets of participants. Therefore, the results of our study are potentially subject to ecological bias.

Introduction

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide. Unhealthy diet and lifestyle factors are responsible for 80% of CVD.[1] Among all of the risk factors for CVD, raised blood pressure (BP) is a major one, accounting for 62% of stroke and 49% of ischemic heart disease (IHD).[2] The recent analysis of global disease burden shows that raised BP is the leading risk factor accounting for 7% global disability adjusted life-years in 2010 and contributing to 9.4 million deaths per year worldwide.[3]

The Health Survey for England has reported a fall in BP in the adult population between 2003 and 2011.[4] CVD mortality has also reportedly decreased in England.[5] These reductions in BP and CVD mortality could be attributable to various factors such as changes in diet and lifestyle, as well as improvements in the treatments of BP, cholesterol and CVD.[5]

The UK initiated a nationwide salt reduction programme in 2003/2004.[6] The programme has been successful and resulted in a 15% reduction in salt intake of the whole population by 2011.[7] To determine the extent to which the reduction in salt intake contributed to the decreases of BP and CVD mortality, we analysed the data from a series of health surveys carried out in England.

Methods

Data sources

Health Survey for England

We used the BP and other CVD risk factor data from the Health Survey for England,[4 8-11] which is an annual survey of a random sample of the English population living in private households. Data were obtained from the UK Data Service.[12] The methods used in the Health Survey for England were reported in detail elsewhere[4] and only methods relevant to the current analysis are described in brief here.

We used the Health Survey for England data 2003,[8] 2006,[9] 2008[10] and 2011[11]. In all surveys, the interviewers recorded demographic information, smoking status and consumption of alcohol, fruit and vegetables. Trained nurses measured body weight, height and BP. Since 2003, BP has been measured using Omron HEM207 using a standardised protocol in all surveys. In our analysis, we included participants aged ≥16 years.

National Diet and Nutrition Survey

The mean 24-hour urinary sodium was taken from the National Diet and Nutrition Survey.[7] In the 2000/2001 survey, 24-hour urine was collected in a random sample of adults in Great Britain. In the 2005/2006 survey, 24-hour urine was collected in a random sample of adults in England which was part of the Health Survey for England. In 2008, the 24-hour urine collection was made in a random sample of adults in the UK and, in 2011, 24-hour urine was collected in a random sample of adults in England. In all surveys, the completeness of the 24-hour urine collection was assessed using the para-aminobenzoic acid (PABA) recovery method.[7 13]

Office for National Statistics

From the Office for National Statistics, we obtained the number of deaths from IHD (I20-I25), cerebrovascular diseases (I60-I69) and mid-year population estimates aged ≥15 years for England and Wales.[14]

Statistical analysis

IHD and stroke mortality was calculated as the number of IHD or stroke deaths divided by the population. Descriptive data on salt intake, BP and other continuous variables were

reported as mean±SE. Comparisons among the four years (2003, 2006, 2008 and 2011) were made by One-Way ANOVA for continuous variables and by χ^2 test for categorical variables.

To estimate the contribution of salt intake to the changes of BP and to exclude any potential confounding effect of treatments, we performed a separate analysis that included only individuals who were not on any BP treatment or other treatments that might affect BP. We compared BP in 2011 with that in 2003 using multiple regression analysis, with adjustment for potential confounding factors. In the regression model, systolic or diastolic BP was entered as the dependent variable and the independent variables included year (1=2011 and 0=2003), age, sex (1=male and 0=female), ethnic group (1=white and 0=other), education level (1=A level or above and 0=other), household income (1=top 3 quintiles and 0=bottom 2 quintiles), alcohol consumption (1=once or more a month and 0=less than once a month), fruit and vegetable intake, and body mass index (BMI).

As 24-hour urinary sodium was not measured in the participants involved in the Health Survey for England, where BP and other CVD risk factors were recorded, we assumed that the changes in BP from 2003 to 2011, after adjusting for the above variables which included almost all other factors known to be related to BP, were largely attributable to the changes in population salt intake which occurred during the same period.

All statistical analyses were carried out using Statistical Package for Social Science (SPSS).

Results

Stroke and IHD mortality

In 2003, the mortality rates from stroke were 134/100,000 and the mortality rates from IHD were 232/100,000 for the adult population in England. As shown in Figure 1, there had been a gradual reduction in both stroke and IHD mortality. By 2011, stroke mortality decreased to

78/100,000 and IHD mortality decreased to 139/100,000. Therefore, from 2003 to 2011, there was a reduction in mortality by 42% and 40% for stroke and IHD respectively.

BP and other CVD risk factors

Table 1 showed the comparisons among the four years (2003, 2006, 2008 and 2011) in demographics and CVD risk factors. The mean age was slightly but significantly higher in 2011 compared with that in 2003. Despite this, the mean BP fell from 129±0.2/74±0.1 mmHg in 2003 to 126±0.3/73±0.2 mmHg in 2011 (i.e. a fall of 3.0/1.4 mmHg, P<0.001 for both systolic and diastolic BP). From 2003 to 2011, there was a decrease of 0.3 mmol/L (P<0.001) in total cholesterol, a reduction in smoking prevalence from 25% to 20% (P<0.001), and an increase in fruit and vegetable consumption of 0.2 portion/d (P<0.001). At the same time, there was a small but significant increase in body mass index (BMI) by 0.4 kg/m^2 (P<0.001) and a small decrease in HDL (by 0.02 mmol/L, P<0.001).

The average salt intake, as measured by 24-hour urinary sodium excretion in a random sample of the adult population, was 9.5±0.2 g/d in 2000/2001. Salt intake fell to 9.0±0.4 g/d in 2005/2006, 8.64±0.2 g/d in 2008, and fell further to 8.1±0.2 g/d by 2011.[7] Therefore, from 2003 to 2011, salt intake decreased by 1.4 g/d (i.e. 15%, P<0.05 for the downward trend).[7]

It is likely that all of the above factors, i.e. the fall in BP, total cholesterol and smoking, the reduction in salt intake and the increase in the consumption of fruit and vegetables, along with improvements in the treatments of BP, cholesterol and CVD, contributed to the decreases in stroke and IHD mortality.

BP in untreated individuals

To investigate the role of salt reduction in the changes of BP, we compared the BP in 2011 with that in 2003 with adjustment for potential confounding factors. In order to further

exclude any potential confounding effect of BP treatments, we included only individuals who were not on any BP treatment or other treatments that might affect BP.

The results showed that there was a fall in BP of 2.7±0.3/1.1±0.2 mmHg (P<0.001 for both systolic and diastolic BP) from 2003 to 2011 after adjusting for age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and BMI. These variables altogether explained 28% of the variance of systolic BP and 16% of the variance of diastolic BP.

Salt intake was not included in the above regression model because it was not measured in the same participants. However, the fact that after adjusting for almost all other variables known to be associated with BP, there was still a significant fall in BP of 2.7/1.1 mmHg from 2003 to 2011, would suggest that these falls in BP were likely to be attributable to the reduction in population salt intake that occurred during this period.

Discussion

Our analyses showed that the average BP in the adult population in England decreased by 3.0/1.4 mmHg from 2003 to 2011. This could be attributable to various factors such as the reduction in salt intake, the increase in fruit and vegetable consumption, and the improvement in BP treatment and control. However, our findings that, in untreated individuals, there was a fall in BP of 2.7/1.1 mmHg after taking into account age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and BMI, strongly suggest that the reduction in salt intake that occurred from 2003 to 2011 would be the major contributor to the fall in BP. These results are supported by the compelling evidence from various types of studies which have consistently demonstrated that dietary salt is a major determinant of population BP.[15 16]

The question is whether our results would be confounded by the pay for performance programme which was introduced by the UK government in 2004.[17] This programme, known as the Quality and Outcomes Framework, intended to improve hypertension control by making bonus payments to general practitioners for achieving benchmarks for hypertension care, although the efficacy of this programme has been questioned.[18] In spite of this, there had been no change to the antihypertensive drug treatment threshold from 2003 to 2011.[19-21] Therefore, this programme is unlikely to have a big confounding effect on our results in individuals who were not on BP treatment.

Although our analysis focused on individuals who were not on BP treatment, there is clear evidence that, in individuals who are on antihypertensive drug treatments, a reduction in salt intake is additive to drug therapies,[22 23] particularly drugs that block the renin-angiotensin system.[22] Therefore, salt reduction would also have contributed to the falls in BP in those who were on BP treatments.

It is well established that raised BP throughout its range is a major cause of CVD.[24] A reduction in salt intake through its effect on BP would reduce CVD.[25 26] Additionally, increasing evidence suggests that salt reduction may have a direct beneficial effect on reducing CVD.[15] It is therefore, of interest, that we found a decrease in both stroke and IHD mortality in parallel with the reduction in salt intake and the falls in BP from 2003 to 2011 in England. Various other studies have documented a reduction in the incidence of CVD. For example, a study using the South London Stroke Register showed that the incidence of stroke decreased from 247/100,000 in 1995 to 149.5/100,000 in 2010 (i.e. a reduction of 39.5% over 16 years),[27] and an analysis of the General Practice Research Database showed that the incidence of stroke in the UK fell by 29% between 1999 and 2008.[28]

It is difficult to quantify the relative contribution of salt reduction to the decrease of CVD as several other dietary and lifestyle factors as well as treatments all have played a part.

However, based on the meta-analysis of BP treatment trials where a 10 mmHg reduction in systolic BP was related to a decrease of 41% in stroke and 22% in IHD,[29] it was estimated that a 2.7 mmHg reduction in systolic BP that occurred with salt reduction would be predicted to reduce stroke by 11% and IHD by 6%. Therefore, salt reduction is likely to have played an important role in the decreases of stroke and IHD mortality in England. These results are supported by the evidence from both prospective cohort studies and outcome trials which have demonstrated that a reduction in salt intake is related to a decrease in CVD risk.[26 30 31]

Our findings that a reduction in population salt intake led to a fall in population BP and CVD mortality in England are consistent with those observed in Japan and Finland.[32 33] Japan, in the late 1960s, carried out a government-led campaign to reduce salt intake. Over the following decade, salt intake was reduced, particularly in northern areas from 18 to 14 g/d. Paralleling this reduction in salt intake, there were falls in BP and an 80% reduction in stroke mortality[32] in spite of large increases in fat intake, cigarette smoking, alcohol consumption and obesity which occurred during that period. Finland, in the late 1970s, initiated a systematic approach to reducing salt intake through mass media-campaigns, co-operation with the food industry and implementing salt labelling legislation.[33-35] This led to a significant reduction in the average salt intake of the Finnish population[33 35] from ≈14 g/d in 1972 to less than 9 g/d in 2002.[33] The reduction in salt intake was accompanied by a fall of over 10 mmHg in both systolic and diastolic BP and a decrease of 75-80% in both stroke and IHD mortality. Although these results were attributable to several factors, the reduction in salt intake is likely to have played a major role, particularly in the fall in BP as BMI and alcohol consumption increased during that time.

Strengths and limitations: The strength of our analysis is that we used the data from a nationally representative sample of the population in England. However, there are several

potential limitations. First, our study used an ecological design that is subject to various methodological issues.[36] Because we used data from national surveys that included different sets of participants both cross-sectionally and longitudinally, we were unable to work with data at the individual level. Therefore, the results of our study are potentially subject to ecological bias. Second, the trend in 24-hour urinary sodium reported in our paper was taken from the data either for England, Great Britain or the UK, as the original report did not separate the results by countries. Such a difference in the composition of the population surveyed may cause a bias to the trend in 24-hour urinary sodium. However, the small proportion of the population in Scotland, Wales and Northern Ireland (altogether accounting for 16% of the total UK population) would indicate that the bias, if any, would be small.

Conclusions

The reduction in salt intake is likely to be a major contributor to the fall in BP in England from 2003 to 2011. As a result, the decrease in salt intake would also have played an important role in the reduction in stroke and IHD mortality.

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Contributors: FJH and GAM designed the analysis plan. FJH performed statistical analyses and wrote the first draft of the manuscript. SPR contributed to database organisation and variable selections. All authors contributed to the interpretation of the results and revision of the manuscript. FJH is guarantor.

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years. FJH is a member of Consensus Action on Salt & Health (CASH) and World Action on Salt & Health (WASH). Both CASH and WASH are non-profit charitable organisations and FJH does not receive any financial support from CASH or WASH. GAM is Chairman of Blood Pressure UK (BPUK), Chairman of CASH and Chairman of WASH. BPUK, CASH and WASH are non-profit charitable organisations. GAM does not receive any financial support from any of these organisations. SPR is an employee of CASH.

Ethics committee approval: Our study is an analysis of previously collected data and therefore ethical approval was not required for our analysis. Ethical approval for the Health Survey for England was obtained by the survey team.

Data sharing statement: No additional data are available. The data are already in the public domain.

Legend to Figure

Figure 1. Changes in salt intake as measured by 24-hour urinary sodium excretion, blood pressure, stroke and ischemic heart disease (IHD) mortality in England from 2003 to 2011.

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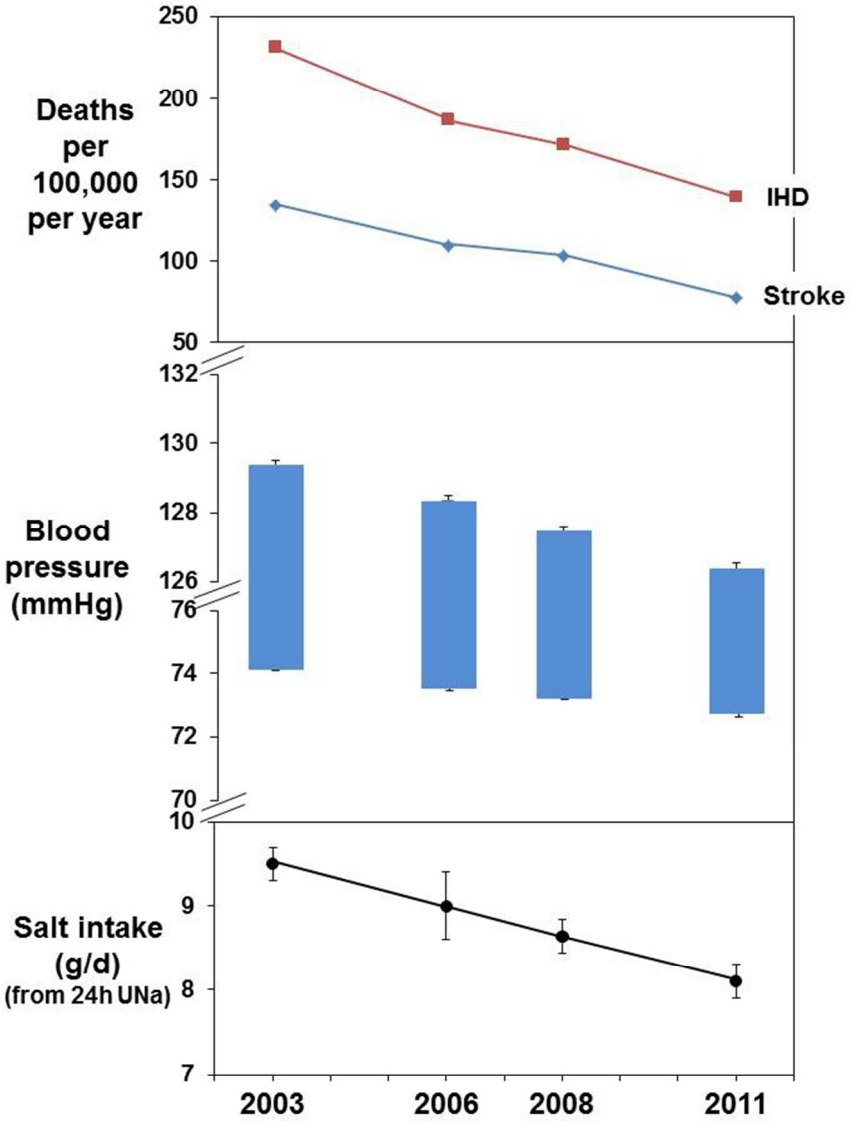
Table 1. Changes in demographic parameters, blood pressure and other variables from 2003 to 2011 in individuals who took part in the Health Survey for England

	2003 (N=14,836)	2006 (N=14,142)	2008 (N=15,098)	2011 (N=8,610)	P value
Age (year)	48.2±0.2	49.3±0.2	49.0±0.2	49.6±0.2	<0.001
Sex, N (%)					
Men	6602 (45)	6324 (45)	6759 (45)	3822 (44)	
Women	8234 (56)	7818 (55)	8339 (55)	4788 (56)	0.928
Ethnic group					
White	13626 (92)	12834 (91)	13639 (91)	7679 (90)	
Black	314 (2)	337 (2)	356 (2)	220 (3)	
Mixed	92 (1)	113 (1)	151 (1)	99 (1)	
Other	769 (5)	823 (6)	893 (6)	572 (6)	<0.001
Highest education qualification					
NVQ4/NVQ5/Degree equivalent	2392 (16)	2711 (19)	2926 (20)	2008 (23)	
Lower than higher education	1576 (11)	1583 (11)	1677 (11)	948 (11)	
NVQ3/GCE A level equivalent	1734 (12)	1806 (13)	2191 (15)	1248 (15)	
NVQ2/GCE O level equivalent	3519 (24)	3146 (22)	3262 (22)	1803 (21)	
NVQ1/GCE other equivalent	778 (5)	678 (5)	745 (5)	395 (5)	
Foreign or other	699 (5)	250 (2)	253 (2)	127 (2)	
No qualification	4097 (28)	3920 (28)	3983 (27)	2037 (24)	<0.001
Household income in quintile (1 to 5, high to low)					
1	2386 (19)	1855 (16)	2132 (18)	1201 (18)	
2	2184 (17)	2321 (20)	2445 (20)	1418 (21)	
3	2732 (22)	2351 (21)	2363 (20)	1358 (20)	
4	2714 (22)	2409 (21)	2468 (21)	1407 (21)	
5	2522 (20)	2414 (21)	2649 (22)	1429 (21)	<0.001

Frequency of alcohol consumption in past 12 months					
Every Day	2116 (14)	1864 (13)	1862 (12)	891 (10)	<0.001
5/6 days/week	670 (5)	674 (5)	699 (5)	337 (4)	
3/4 days/week	2229 (15)	1947 (14)	2212 (15)	1125 (13)	
Once or twice a week	4301 (29)	3797 (27)	4036 (27)	2285 (27)	
Once or twice a month	1745 (12)	1703 (12)	1923 (13)	1159 (14)	
Once every couple of months	939 (6)	1039 (7)	1049 (7)	715 (8)	
Once or twice a year	1156 (8)	1203 (9)	1222 (8)	673 (8)	
Not at all	1594 (11)	1817 (13)	1986 (13)	1343 (16)	
Fruit and vegetable consumption (portion/d)	3.4±0.02	3.8±0.02	3.7±0.02	3.6±0.03	<0.001
Body mass index (kg/m^2)	27.0±0.04	27.2±0.05	27.2±0.05	27.4±0.06	<0.001
Blood pressure (mmHg)					
Systolic	129.3±0.20	128.3±0.19	127.4±0.19	126.3±0.25	<0.001
Diastolic	74.2±0.12	73.6±0.12	73.3±0.12	72.8±0.16	<0.001
Total Cholesterol (mmol/L)	5.6±0.01	5.4±0.01	5.4±0.01	5.3±0.02	<0.001
HDL (mmol/L)	1.52±0.004	1.49±0.005	1.49±0.005	1.50±0.007	<0.001
Smoking Status					
Never smoked cigarettes at all	6476 (44)	6574 (47)	7128 (48)	4032 (47)	
Used to smoke cigarettes occasionally	900 (6)	741 (5)	743 (5)	440 (5)	
Used to smoke cigarettes regularly	3737 (25)	3667 (26)	3965 (26)	2353 (28)	
Current cigarette smoker	3651 (25)	3074 (22)	3158 (21)	1707 (20)	<0.001



190x254mm (96 x 96 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page Number Reported
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Not applicable
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	4-5
Bias	9	Describe any efforts to address potential sources of bias	6
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	6
		(*b*) Describe any methods used to examine subgroups and interactions	Not applicable
		(*c*) Explain how missing data were addressed	Not applicable
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and	Not applicable

		controls was addressed *Cross-sectional study*—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Not applicable
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, 18
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Not applicable
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	6-8
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	7-8
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	Subgroup analysis was not carried out.
Discussion			
Key results	18	Summarise key results with reference to study objectives	8
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	10-11
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	11

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Salt reduction in England from 2003 to 2011 – Its relationship to blood pressure, stroke and ischemic heart disease mortality

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Salt reduction in England from 2003 to 2011 – Its relationship to blood pressure, stroke and ischemic heart disease mortality

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Running title: Salt reduction, BP, stroke and IHD mortality

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Abstract

Objectives: To determine the relationship between the reduction in salt intake that occurred in England, and blood pressure (BP), as well as mortality from stroke and ischemic heart disease (IHD).

Design: Analysis of the data from the Health Survey for England.

Setting and participants: England, 2003 N=9,183, 2006 N=8,762, 2008 N=8,974 and 2011 N=4,753, aged ≥16 years.

Outcomes: BP, stroke and IHD mortality.

Results: From 2003 to 2011, there was a decrease in mortality from stroke by 42%(P<0.001) and IHD by 40%(P<0.001). In parallel, there was a fall in BP of 3.0±0.33/1.4±0.20mmHg (P<0.001/ P<0.001), a decrease of 0.4±0.02mmol/L (P<0.001) in cholesterol, a reduction in smoking from 19% to 14%(P<0.001), an increase in fruit and vegetable consumption (0.2±0.05 portion/d, P<0.001), and an increase in body mass index(BMI)(0.5±0.09kg/m^2, P<0.001). Salt intake as measured by 24-hour urinary sodium decreased by 1.4 g/d (P<0.01). It is likely that all of these factors (with the exception of BMI), along with improvements in the treatments of BP, cholesterol and CVD contributed to the falls in stroke and IHD mortality. In individuals who were not on anti-hypertensive medication, there was a fall in BP of 2.7±0.34/1.1±0.23mmHg (P<0.001/ P<0.001) after adjusting for age, sex, ethnic group, education, household income, alcohol consumption, fruit and vegetable intake, and BMI. Although salt intake was not measured in these participants, the fact that the average salt intake in a random sample of the UK population fell by 15% during the same period, suggests that the falls in BP would be largely attributable to the reduction in salt intake rather than anti-hypertensive medications.

Conclusions: The reduction in salt intake is likely to be an important contributor to the falls in BP from 2003 to 2011 in England. As a result, it would have substantially contributed to the decreases in stroke and IHD mortality.

ARTICLE SUMMARY

Article focus

- A modest reduction in salt intake lowers blood pressure (BP) and, thereby, reduces cardiovascular risk.
- In the UK, salt intake as measured by 24-hour urinary sodium excretion decreased from 9.5 to 8.1 g/d from 2003 to 2011. During the same period, in England there was a fall of 3.0/1.4 mmHg in BP and a decrease of 42% and 40% in stroke and ischemic heart disease (IHD) mortality respectively.

Key messages

- Our analysis of the data from the Health Survey for England showed that, in individuals who were not on any anti-hypertensive medications or other medications which might affect BP, there was a significant fall in BP of 2.7/1.1 mmHg from 2003 to 2011 after taking into account almost all major factors known to be associated with BP, including age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and body mass index. Salt intake, a major determinant of population BP, was not included in this analysis because it was not measured in these participants. However, the fact that salt intake fell by 15% during the same period, would suggest that the falls in BP were largely attributable to the reduction in salt intake.
- As BP throughout its range is a major cause of stroke and IHD, the reduction in salt intake would have played an important role in the reduction in stroke and IHD mortality which occurred in England during this period.

Strengths and limitations of this study

- The study used the best available data in England.
- Various surveys included different sets of participants. Therefore, the results of our study are potentially subject to ecological bias.

Introduction

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide.[1] Unhealthy diet and lifestyle factors are responsible for approximately 80% of CVD.[2] Among all of the risk factors for CVD, raised blood pressure (BP) is a major one, accounting for 62% of stroke and 49% of ischemic heart disease (IHD).[3] The recent analysis of global disease burden shows that raised BP is the leading risk factor, accounting for approximately 7% global disability adjusted life-years in 2010 and contributing to about 9.4 million deaths per year worldwide.[4]

In England, the average population BP has fallen in recent years[5] and CVD mortality has also declined.[6] These could be attributable to various factors such as changes in diet and lifestyle, as well as improvements in the treatments of BP, cholesterol and CVD.[6] An analysis of the data from the Health Survey for England showed that anti-hypertensive medications accounted for less than 25% of the systolic BP decline in man over the period of 1994-2002 and 2003-2009.[7] A population modelling study showed that reductions in major cardiovascular risk factors explained 43% of the recent fall in IHD mortality in England and the single largest contribution to the overall IHD mortality decrease came from falls in population BP with relatively small contributions from anti-hypertensive therapies.[8]

Evidence from various types of studies has consistently shown that a reduction in salt intake lowers BP and thereby reduces CVD risk.[9-12] A meta-analysis of relatively short-term salt reduction trials showed a dose-response relationship with a 1 g/d reduction in salt intake relating to approximately 1 mmHg fall in systolic BP.[9] The UK initiated a nationwide salt reduction programme in 2003/2004.[13] The programme has been successful and resulted in a 15% reduction in population salt intake by 2011.[14] To determine the relationship between this reduction in salt intake and the fall in BP and mortality from stroke and IHD, we

analysed the data from a series of health surveys carried out in a nationally representative sample of the population in England.

Methods

Data sources

Health Survey for England

We used the BP and other CVD risk factor data from the Health Survey for England,[5 15-18] which is an annual survey of a random sample of the English population living in private households. Data were obtained from the UK Data Service. The methods used in the Health Survey for England were reported in detail elsewhere[5] and only methods relevant to the current analysis are described in brief here.

We used the Health Survey for England data for 2003,[15] 2006,[16] 2008[17] and 2011[18]. We included participants aged ≥16 years and who had BP measurements recorded (2003 N=9,183, 2006 N=8,762, 2008 N=8,974 and 2011 N=4,753). In all surveys, the interviewers recorded demographic information, smoking status and consumption of alcohol, fruit and vegetables. Trained nurses measured body weight, height and BP. Since 2003, BP has been measured using Omron HEM207 using a standardised protocol in all surveys. BP was measured in a seated position after the participant had five minutes' rest, using an appropriately sized cuff on the right arm. Three BP readings were taken from each participant at one minute intervals and the mean of the last two readings was used in the analysis.

National Diet and Nutrition Survey

The mean salt intake as measured by 24-hour urinary sodium was taken from the National Diet and Nutrition Survey (NDNS) in participants aged 19-64 years.[14] In the 2000/2001 survey, 24-hour urine was collected in a random sample of adults in Great Britain (N=1147). In the 2005/2006 survey, 24-hour urine was collected in a random sample of adults in

England (N=350) which was part of the Health Survey for England. In 2008, the 24-hour urine collection was made in a random sample of adults in the UK (N=692) and, in 2011, 24-hour urine was collected in a random sample of adults in England (N=547). In all surveys, the completeness of the 24-hour urine collection was assessed using the para-aminobenzoic acid (PABA) recovery method.[19,20]

Office for National Statistics

From the Office for National Statistics, we obtained the number of deaths from IHD (I20-I25), cerebrovascular diseases (I60-I69) and mid-year population estimates aged ≥15 years for England and Wales.[21-24] Deaths were certified by medical practitioners, using the Medical Certificate of Cause of Death.[21]

Statistical analysis

Stroke and IHD mortality was calculated as the number of stroke or IHD deaths divided by the population. Descriptive data on salt intake, BP and other continuous variables were reported as mean±SE. Comparisons among the four years (2003, 2006, 2008 and 2011) were made by One-Way ANOVA for continuous variables and by χ^2 test for categorical variables.

To estimate the contribution of salt intake to the changes of BP and to exclude any potential confounding effect of treatments, we performed a separate analysis that included only individuals who were not on any anti-hypertensive medications or other medications that might affect BP. We compared BP in 2011 with that in 2003 using multiple regression analysis, with adjustment for potential confounding factors. In the regression model, systolic or diastolic BP was entered as the dependent variable and the independent variables included year (1=2011 and 0=2003), age, sex (1=male and 0=female), ethnic group (1=white and 0=other), education level (1=A level or above and 0=other), household income (1=top 3

quintiles and 0=bottom 2 quintiles), alcohol consumption (1=once or more a month and 0=less than once a month), fruit and vegetable intake, and body mass index (BMI).

As 24-hour urinary sodium was not measured in the individuals who participated in the Health Survey for England, where BP and other CVD risk factors were recorded, we assumed that the changes in BP from 2003 to 2011, after adjusting for the above variables which included almost all other major factors known to be related to BP, were largely attributable to the changes in population salt intake which occurred during the same period.

We also performed a separate analysis that included only individuals aged 19-64 years examining the trend of BP and stroke and IHD mortality, as the age range was the same as those participants who had 24-hour urinary sodium measured. All statistical analyses were carried out using Statistical Package for Social Science (SPSS).

Results

Stroke and IHD mortality

In 2003, the mortality rates from stroke were 134/100,000 and the mortality rates from IHD were 232/100,000 for the adult population in England. As shown in Figure 1, there had been a gradual reduction in both stroke and IHD mortality. By 2011, stroke mortality decreased to 78/100,000 ($P<0.001$) and IHD mortality decreased to 139/100,000 ($P<0.001$). Therefore, from 2003 to 2011, there was a reduction in mortality by 42% and 40% for stroke and IHD respectively.

BP and other CVD risk factors

Table 1 showed the comparisons among the four years (2003, 2006, 2008 and 2011) in demographics and CVD risk factors. The mean age was slightly but significantly higher in 2011 compared with that in 2003. Despite this, the mean BP fell from 129.3±0.20/74.2±0.12

mmHg in 2003 to 126.3±0.25/72.8±0.16 mmHg in 2011 (i.e. a fall of 3.0±0.33/1.4±0.20 mmHg, P<0.001 for both systolic and diastolic BP). From 2003 to 2011, there was a decrease of 0.4±0.02 mmol/L (P<0.001) in total cholesterol, a reduction in smoking prevalence from 19% to 14% (P<0.001), and an increase in fruit and vegetable consumption of 0.2±0.05 portion/d (P<0.001). At the same time, there was a small but significant increase in body mass index (BMI) by 0.5±0.09 kg/m^2 (P<0.001) and a small decrease in HDL (by 0.02±0.01 mmol/L, P<0.05).

The average salt intake, as measured by 24-hour urinary sodium excretion in a random sample of the adult population, was 9.5±0.2 g/d in 2000/2001. Salt intake fell to 9.0±0.4 g/d in 2005/2006, 8.64±0.2 g/d in 2008, and fell further to 8.1±0.2 g/d by 2011.[14] Therefore, from 2003 to 2011, salt intake decreased by 1.4 g/d (i.e. 15%, P<0.05 for the downward trend).[14]

It is likely that several factors, i.e. the fall in BP, total cholesterol and smoking prevalence, the reduction in salt intake and the increase in the consumption of fruit and vegetables, along with improvements in the treatments of BP, cholesterol and CVD, contributed to the decrease in stroke and IHD mortality.

BP in untreated individuals

To investigate the role of salt reduction in the changes of BP, we compared the BP in 2011 with that in 2003 with adjustment for potential confounding factors. In order to further exclude any potential confounding effect of BP treatments, we included only individuals who were not on any anti-hypertensive medications or other medications that might affect BP.

The results showed that there was a fall in BP of 2.7±0.34/1.1±0.23 mmHg (P<0.001 for both systolic and diastolic BP) from 2003 to 2011 after adjusting for age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and BMI.

These variables altogether explained 28% of the variance of systolic BP and 16% of the variance of diastolic BP.

Salt intake was not included in the above regression model because it was not measured in the same participants whose BP was recorded. However, the fact that after adjusting for almost all other major factors known to be associated with BP, there was still a significant fall in BP of 2.7/1.1 mmHg from 2003 to 2011, would suggest that these falls in BP were likely to be largely attributable to the reduction in population salt intake which occurred during this period.

BP and stroke and IHD mortality in individuals aged 19-64 years

Our above conclusions were based on the assumption that the 15% reduction in salt intake occurred in the whole adult population in England. However, 24-hour urinary sodium was measured only in individuals aged 19-64 years. We have therefore performed separate analyses on the trend of BP and stroke and IHD mortality in individuals of the same age groups as those who had salt intake measured. The results showed that, from 2003 to 2011, stroke mortality decreased from 128/1,000,000 to 82/1,000,000 (36% reduction, P<0.001) and IHD mortality decreased from 423/1,000,000 to 272/1,000,000 (36% reduction, P<0.001). In individuals who were not on any anti-hypertensive medications or other medications that might affect BP, there was a fall in BP of 1.9±0.34/1.0±0.25 mmHg (P<0.001 for both systolic and diastolic BP) from 2003 to 2011 after adjusting for age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and BMI.

Discussion

Our analyses showed that the average BP in the adult population in England decreased by 3.0/1.4 mmHg from 2003 to 2011. This could be attributable to various factors such as the

reduction in salt intake, the increase in fruit and vegetable consumption, and the improvement in BP treatment and control. However, our findings that, in untreated individuals, there was a fall in BP of 2.7/1.1 mmHg after taking into account age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and BMI, suggest that the reduction in population salt intake which occurred from 2003 to 2011, is likely to be an important contributor to the falls in BP. Although 24-hour urinary sodium was measured in individuals aged 19-64 years, the reduction in salt intake is likely to have occurred across the whole population as it was predominately achieved by a gradual reduction in the amount of salt added to all processed foods, which accounts for approximately 80% of total salt intake.[13]

Our findings that the recent falls in BP occurred in England are largely attributable to the reduction in salt intake rather than drug therapies, are consistent with the analysis by DeWilde et al who showed that anti-hypertensive medications contributed to less than 25% of the systolic BP decline in man.[7]

Although our analysis focused on individuals who were not on any BP medications, there is clear evidence that, in individuals who are on antihypertensive drug treatments, a reduction in salt intake is additive to drug therapies,[25 26] particularly drugs that block the renin-angiotensin system.[25] Therefore, salt reduction would also have contributed to the falls in BP in those who were on BP medications.

The observed fall in systolic BP was larger than that might have been predicted from the meta-analysis of randomised salt reduction trials.[9] This may be due to the difference in age and duration of the studies. It has been shown that, for a given reduction in salt intake, the fall in BP is larger in older people compared with younger individuals.[9] Indeed, our current analysis showed that in individuals aged 19-64 years, the fall in BP from 2003 to 2011 was smaller compared with that observed when all adults were included. Another important factor

which may account for the observed larger fall in BP is the longer duration of the study, i.e. over a period of 8 years. Most salt reduction trials had a duration of only a few weeks and the median duration for the trials included in the meta-analysis was only 5 weeks in hypertensive individuals and 4 weeks in normotensive individuals.[9] Whether salt reduction has exerted its maximum effect by 4-5 weeks is not known, but much evidence would suggest that this is unlikely. It is possible that a long-term reduction in population salt intake as reported in our current analysis, could have a greater effect on BP than that observed in the salt reduction trials with a duration of only a few weeks.

It is well established that raised BP throughout its range is a major cause of CVD.[27] A reduction in salt intake through its effect on BP would reduce CVD.[9 11] Additionally, increasing evidence suggests that salt reduction may have a direct beneficial effect on reducing CVD, independent of BP.[10] It is therefore, of interest, that we found a decrease in both stroke and IHD mortality in parallel with the reduction in salt intake and the falls in BP from 2003 to 2011 in England. Various other studies have documented a reduction in the incidence of CVD. For example, a study using the South London Stroke Register showed that the incidence of stroke decreased from 247/100,000 in 1995 to 149.5/100,000 in 2010 (i.e. a reduction of 39.5% over 16 years),[28] and an analysis of the General Practice Research Database showed that the incidence of stroke in the UK fell by 29% between 1999 and 2008.[29]

It is difficult to quantify the relative contribution of salt reduction to the decrease of CVD as several other dietary and lifestyle factors as well as treatments all have played a part. However, based on the meta-analysis of BP treatment trials where a 10 mmHg reduction in systolic BP was related to a decrease of 41% in stroke and 22% in IHD,[30] it was estimated that a 2.7 mmHg reduction in systolic BP that occurred with salt reduction would be predicted to reduce stroke by approximately 11% and IHD by 6%. Therefore, salt reduction is

likely to have played an important role in the decreases of stroke and IHD mortality in England. These results are supported by the evidence from both prospective cohort studies and outcome trials which have demonstrated that a reduction in salt intake is related to a decrease in CVD risk.[11 12 31] A cost-effective analysis by National Institute for Health and Clinical Excellence (NICE) shows that salt reduction not only saves lives, but also saves money, and the reduction in salt intake achieved in the UK has saved more than £1.5 billion per annum.[32]

Our findings that a reduction in population salt intake was related to a fall in population BP and mortality from stroke and IHD in England are in agreement with those observed in Japan and Finland.[33 34] Japan, in the late 1960s, carried out a government-led campaign to reduce salt intake. Over the following decade, salt intake was reduced, particularly in northern areas from 18 to 14 g/d. Paralleling this reduction in salt intake, there were falls in BP and an 80% reduction in stroke mortality[33] in spite of large increases in fat intake, cigarette smoking, alcohol consumption and obesity which occurred during that period. Finland, in the late 1970s, initiated a systematic approach to reducing salt intake through mass media-campaigns, co-operation with the food industry and implementing salt labelling legislation.[34 35] This led to a significant reduction in the average salt intake of the Finnish population[34 35] from ≈14 g/d in 1972 to less than 9 g/d in 2002.[34] The reduction in salt intake was accompanied by a fall of over 10 mmHg in both systolic and diastolic BP and a decrease of 75-80% in both stroke and IHD mortality. Although these results were attributable to several factors, the reduction in salt intake is likely to have played a major role, particularly in the fall in BP as BMI and alcohol consumption increased during that time.

Strengths and limitations: The strength of our analysis is that we used the data from a nationally representative sample of the population in England. However, there are several potential limitations. First, our study used an ecological design that is subject to various

methodological issues.[36] Because we used data from national surveys that included different sets of participants both cross-sectionally and longitudinally, we were unable to work with data at the individual level, particularly as salt intake was not measured in the same participants who had BP and other CVD risk factors recorded. Therefore, the results of our study are potentially subject to ecological bias. Second, we could not exclude potential confounding effect of some variables which were not measured, such as physical activity levels which were recorded in 2003, but not in the 2011 survey. Third, the trend in 24-hour urinary sodium was taken from the data either for England, Great Britain or the UK, as the original report did not separate the results by countries. It has been shown that salt intake was higher in Scotland and lower in Wales compared with that in England.[14 37] A difference in the composition of the population surveyed at different years may cause a bias to the trend in 24-hour urinary sodium. However, Scotland, Wales and Northern Ireland account for only a small proportion of the UK population (altogether 16%). Additionally, the lower salt intake in Wales and higher salt intake in Scotland might balance each other out to a certain degree in the 2003 NDNS. Therefore, the 24-hour urinary sodium data for 2003 (Great Britain) and 2011 (England only) were likely to be comparable.

Conclusions

The reduction in salt intake is likely to be an important contributor to the falls in BP in England from 2003 to 2011. As a result, the decrease in salt intake would have played an important role in the reduction in stroke and IHD mortality during this period. Despite considerable progress being made on salt reduction, the mean salt intake in the UK population (8.1 g/d in 2011) was still 35% higher than the recommended level of 6 g/d, and 70% of the adult population (80% men and 58% women) had a daily salt intake above the recommended level.[14] Therefore, continuing and much greater efforts are needed to achieve further reductions in salt intake to prevent the maximum number of stroke and IHD deaths.

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Contributors: FJH and GAM designed the analysis plan. FJH performed statistical analyses and wrote the first draft of the manuscript. SPR contributed to database organisation and variable selections. All authors contributed to the interpretation of the results and revision of the manuscript. FJH is guarantor.

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years. FJH is a member of Consensus Action on Salt & Health (CASH) and World Action on Salt & Health (WASH). Both CASH and WASH are non-profit charitable organisations and FJH does not receive any financial support from CASH or WASH. GAM is Chairman of Blood Pressure UK (BPUK), Chairman of CASH and Chairman of WASH. BPUK, CASH and WASH are non-profit charitable organisations. GAM does not receive any financial support from any of these organisations. SPR is an employee of CASH.

Ethics committee approval: Our study is an analysis of previously collected data and therefore ethical approval was not required for our analysis. Ethical approval for the Health Survey for England was obtained by the survey team.

Data sharing statement: No additional data are available. The data are already in the public domain.

Legend to Figure

Figure 1. Changes in salt intake as measured by 24-hour urinary sodium (UNa) excretion, blood pressure (BP), stroke and ischemic heart disease (IHD) mortality in England from 2003 to 2011. * P<0.05, *** P<0.001 for trend.

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Table 1. Changes in demographic parameters, blood pressure and other variables from 2003 to 2011

	2003 (N=9183)	2006 (N=8762)	2008 (N=8974)	2011 (N=4753)	P value
Age (year)	49.5±0.2	50.6±0.2	50.4±0.2	51.0±0.3	<0.001
Sex, N (%)					
Men	4108 (45)	3924 (45)	4040 (45)	2070 (44)	
Women	5075 (55)	4838 (55)	4934 (55)	2683 (56)	0.406
Ethnic group, N (%)					
White	8559 (93)	8118 (93)	8241 (92)	4344 (92)	
Black	148 (2)	158 (2)	170 (2)	95 (2)	
Mixed	41 (0.4)	66 (1)	75 (1)	58 (1)	
Other	429 (5)	418 (5)	483 (5)	251 (5)	<0.001
Highest education qualification, N (%)					
NVQ4/NVQ5/Degree equivalent	1527 (17)	1708 (20)	1803 (20)	1186 (25)	
Lower than higher education	1040 (11)	1078 (12)	1040 (12)	559 (12)	
NVQ3/GCE A level equivalent	1096 (12)	1124 (13)	1312 (15)	698 (15)	
NVQ2/GCE O level equivalent	2198 (24)	1944 (22)	1934(22)	1001 (21)	
NVQ1/GCE other equivalent	467 (5)	420 (5)	437 (5)	207 (4)	
Foreign or other	431 (5)	175 (2)	173 (2)	71 (2)	
No qualification	2416 (26)	2307 (26)	2273 (25)	1026 (22)	<0.001
Household income in quintile (1 to 5, high to low), N (%)					
1	1355 (17)	1111 (15)	1213 (16)	608 (15)	
2	1421 (18)	1437 (20)	1501 (20)	813 (21)	
3	1760 (22)	1567 (22)	1548 (21)	816 (21)	
4	1821 (23)	1596 (22)	1595 (21)	867 (22)	
5	1653 (21)	1592 (22)	1665 (22)	850 (22)	<0.001

Frequency of alcohol consumption in past 12 months, N (%)					
Every Day	1348 (15)	1208 (14)	1137 (13)	511 (11)	<0.001
5/6 days/week	440 (5)	447 (5)	448 (5)	207 (4)	
3/4 days/week	1443 (16)	1292 (15)	1395 (16)	667 (14)	
Once or twice a week	2689 (29)	2392 (27)	2380 (27)	1252 (26)	
Once or twice a month	1098 (12)	1100 (13)	1149 (13)	687 (15)	
Once every couple of months	588 (6)	639 (7)	641 (7)	422 (9)	
Once or twice a year	696 (8)	698 (8)	725 (8)	376 (8)	
Not at all	860 (9)	972 (11)	1075 (12)	619 (13)	
Fruit and vegetable consumption (portion/d)	3.6±0.03	3.9±0.03	3.8±0.03	3.8±0.04	<0.001
Body mass index (kg/m^2)	27.1±0.05	27.3±0.06	27.3±0.06	27.6±0.08	<0.001
Blood pressure (mmHg)					
Systolic	129.3±0.20	128.3±0.19	127.4±0.19	126.3±0.25	<0.001
Diastolic	74.2±0.12	73.6±0.12	73.3±0.12	72.8±0.16	<0.001
Total Cholesterol (mmol/L)	5.7±0.01	5.5±0.01	5.4±0.01	5.3±0.02	<0.001
HDL (mmol/L)	1.53±0.005	1.50±0.005	1.50±0.005	1.51±0.008	<0.001
Smoking Status, N (%)					
Never smoked cigarettes at all	4258 (46)	4256 (49)	4473 (50)	2376 (50)	
Used to smoke cigarettes occasionally	595 (7)	477 (6)	483 (5)	279 (6)	
Used to smoke cigarettes regularly	2565 (28)	2525 (29)	2536 (28)	1410 (30)	
Current cigarette smoker	1749 (19)	1491 (17)	1458 (16)	680 (14)	<0.001

Salt reduction in England from 2003 to 2011 – Its relationship to blood pressure, stroke and ischemic heart disease mortality

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Running title: Salt reduction, BP, stroke and IHD mortality

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Abstract

Objectives: To determine the relationship between the reduction in salt intake that occurred in England, and blood pressure (BP), as well as mortality from stroke and ischemic heart disease (IHD).

Design: Analysis of the data from the Health Survey for England.

Setting and participants: England, 2003 N=9,183, 2006 N=8,762, 2008 N=8,974 and 2011 N=4,753, aged ≥16 years.

Outcomes: BP, stroke and IHD mortality.

Results: From 2003 to 2011, there was a decrease in mortality from stroke by 42%(P<0.001) and IHD by 40%(P<0.001). In parallel, there was a fall in BP of 3.0±0.33/1.4±0.20mmHg (P<0.001/ P<0.001), a decrease of 0.4±0.02mmol/L (P<0.001) in cholesterol, a reduction in smoking from 19% to 14%(P<0.001), an increase in fruit and vegetable consumption (0.2±0.05 portion/d, P<0.001), and an increase in body mass index(BMI)(0.5±0.09kg/m^2, P<0.001). Salt intake as measured by 24-hour urinary sodium decreased by 1.4 g/d (P<0.01). It is likely that all of these factors (with the exception of BMI), along with improvements in the treatments of BP, cholesterol and CVD contributed to the falls in stroke and IHD mortality. In individuals who were not on anti-hypertensive medication, there was a fall in BP of 2.7±0.34/1.1±0.23mmHg (P<0.001/ P<0.001) after adjusting for age, sex, ethnic group, education, household income, alcohol consumption, fruit and vegetable intake, and BMI. Although salt intake was not measured in these participants, the fact that the average salt intake in a random sample of the UK population fell by 15% during the same period, suggests that the falls in BP would be largely attributable to the reduction in salt intake rather than anti-hypertensive medications.

Conclusions: The reduction in salt intake is likely to be an important contributor to the falls in BP from 2003 to 2011 in England. As a result, it would have substantially contributed to the decreases in stroke and IHD mortality.

ARTICLE SUMMARY

Article focus

- A modest reduction in salt intake lowers blood pressure (BP) and, thereby, reduces cardiovascular risk.
- In the UK, salt intake as measured by 24-hour urinary sodium excretion decreased from 9.5 to 8.1 g/d from 2003 to 2011. During the same period, in England there was a fall of 3.0/1.4 mmHg in BP and a decrease of 42% and 40% in stroke and ischemic heart disease (IHD) mortality respectively.

Key messages

- Our analysis of the data from the Health Survey for England showed that, in individuals who were not on any anti-hypertensive medications or other medications which might affect BP, there was a significant fall in BP of 2.7/1.1 mmHg from 2003 to 2011 after taking into account almost all major factors known to be associated with BP, including age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and body mass index. Salt intake, a major determinant of population BP, was not included in this analysis because it was not measured in these participants. However, the fact that salt intake fell by 15% during the same period, would suggest that the falls in BP were largely attributable to the reduction in salt intake.
- As BP throughout its range is a major cause of stroke and IHD, the reduction in salt intake would have played an important role in the reduction in stroke and IHD mortality which occurred in England during this period.

Strengths and limitations of this study

- The study used the best available data in England.
- Various surveys included different sets of participants. Therefore, the results of our study are potentially subject to ecological bias.

Introduction

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide.[1] Unhealthy diet and lifestyle factors are responsible for approximately 80% of CVD.[2] Among all of the risk factors for CVD, raised blood pressure (BP) is a major one, accounting for 62% of stroke and 49% of ischemic heart disease (IHD).[3] The recent analysis of global disease burden shows that raised BP is the leading risk factor, accounting for approximately 7% global disability adjusted life-years in 2010 and contributing to about 9.4 million deaths per year worldwide.[4]

In England, the average population BP has fallen in recent years[5] and CVD mortality has also declined.[6] These could be attributable to various factors such as changes in diet and lifestyle, as well as improvements in the treatments of BP, cholesterol and CVD.[6] An analysis of the data from the Health Survey for England showed that anti-hypertensive medications accounted for less than 25% of the systolic BP decline in man over the period of 1994-2002 and 2003-2009.[7] A population modelling study showed that reductions in major cardiovascular risk factors explained 43% of the recent fall in IHD mortality in England and the single largest contribution to the overall IHD mortality decrease came from falls in population BP with relatively small contributions from anti-hypertensive therapies.[8]

Evidence from various types of studies has consistently shown that a reduction in salt intake lowers BP and thereby reduces CVD risk.[9-12] A meta-analysis of relatively short-term salt reduction trials showed a dose-response relationship with a 1 g/d reduction in salt intake relating to approximately 1 mmHg fall in systolic BP.[9] The UK initiated a nationwide salt reduction programme in 2003/2004.[13] The programme has been successful and resulted in a 15% reduction in population salt intake by 2011.[14] To determine the relationship between this reduction in salt intake and the fall in BP and mortality from stroke and IHD, we

analysed the data from a series of health surveys carried out in a nationally representative sample of the population in England.

Methods

Data sources

Health Survey for England

We used the BP and other CVD risk factor data from the Health Survey for England,[5 15-18] which is an annual survey of a random sample of the English population living in private households. Data were obtained from the UK Data Service.[19] The methods used in the Health Survey for England were reported in detail elsewhere[5] and only methods relevant to the current analysis are described in brief here.

We used the Health Survey for England data for 2003,[15] 2006,[16] 2008[17] and 2011[18]. We included participants aged ≥16 years and who had BP measurements recorded (2003 N=9,183, 2006 N=8,762, 2008 N=8,974 and 2011 N=4,753). In all surveys, the interviewers recorded demographic information, smoking status and consumption of alcohol, fruit and vegetables. Trained nurses measured body weight, height and BP. Since 2003, BP has been measured using Omron HEM207 using a standardised protocol in all surveys. BP was measured in a seated position after the participant had five minutes' rest, using an appropriately sized cuff on the right arm. Three BP readings were taken from each participant at one minute intervals and the mean of the last two readings was used in the analysis.

National Diet and Nutrition Survey

The mean salt intake as measured by 24-hour urinary sodium was taken from the National Diet and Nutrition Survey (NDNS) in participants aged 19-64 years.[14] In the 2000/2001 survey, 24-hour urine was collected in a random sample of adults in Great Britain (N=1147). In the 2005/2006 survey, 24-hour urine was collected in a random sample of adults in

England (N=350) which was part of the Health Survey for England. In 2008, the 24-hour urine collection was made in a random sample of adults in the UK (N=692) and, in 2011, 24-hour urine was collected in a random sample of adults in England (N=547). In all surveys, the completeness of the 24-hour urine collection was assessed using the para-aminobenzoic acid (PABA) recovery method.[14 20]

Office for National Statistics

From the Office for National Statistics, we obtained the number of deaths from IHD (I20-I25), cerebrovascular diseases (I60-I69) and mid-year population estimates aged ≥15 years for England and Wales.[21-24] Deaths were certified by medical practitioners, using the Medical Certificate of Cause of Death.[21]

Statistical analysis

Stroke and IHD mortality was calculated as the number of stroke or IHD deaths divided by the population. Descriptive data on salt intake, BP and other continuous variables were reported as mean±SE. Comparisons among the four years (2003, 2006, 2008 and 2011) were made by One-Way ANOVA for continuous variables and by χ^2 test for categorical variables.

To estimate the contribution of salt intake to the changes of BP and to exclude any potential confounding effect of treatments, we performed a separate analysis that included only individuals who were not on any anti-hypertensive medications or other medications that might affect BP. We compared BP in 2011 with that in 2003 using multiple regression analysis, with adjustment for potential confounding factors. In the regression model, systolic or diastolic BP was entered as the dependent variable and the independent variables included year (1=2011 and 0=2003), age, sex (1=male and 0=female), ethnic group (1=white and 0=other), education level (1=A level or above and 0=other), household income (1=top 3

quintiles and 0=bottom 2 quintiles), alcohol consumption (1=once or more a month and 0=less than once a month), fruit and vegetable intake, and body mass index (BMI).

As 24-hour urinary sodium was not measured in the individuals who participated in the Health Survey for England, where BP and other CVD risk factors were recorded, we assumed that the changes in BP from 2003 to 2011, after adjusting for the above variables which included almost all other major factors known to be related to BP, were largely attributable to the changes in population salt intake which occurred during the same period.

We also performed a separate analysis that included only individuals aged 19-64 years examining the trend of BP and stroke and IHD mortality, as the age range was the same as those participants who had 24-hour urinary sodium measured. All statistical analyses were carried out using Statistical Package for Social Science (SPSS).

Results

Stroke and IHD mortality

In 2003, the mortality rates from stroke were 134/100,000 and the mortality rates from IHD were 232/100,000 for the adult population in England. As shown in Figure 1, there had been a gradual reduction in both stroke and IHD mortality. By 2011, stroke mortality decreased to 78/100,000 ($P<0.001$) and IHD mortality decreased to 139/100,000 ($P<0.001$). Therefore, from 2003 to 2011, there was a reduction in mortality by 42% and 40% for stroke and IHD respectively.

BP and other CVD risk factors

Table 1 showed the comparisons among the four years (2003, 2006, 2008 and 2011) in demographics and CVD risk factors. The mean age was slightly but significantly higher in 2011 compared with that in 2003. Despite this, the mean BP fell from 129.3±0.20/74.2±0.12

mmHg in 2003 to 126.3±0.25/72.8±0.16 mmHg in 2011 (i.e. a fall of 3.0±0.33/1.4±0.20 mmHg, P<0.001 for both systolic and diastolic BP). From 2003 to 2011, there was a decrease of 0.4±0.02 mmol/L (P<0.001) in total cholesterol, a reduction in smoking prevalence from 19% to 14% (P<0.001), and an increase in fruit and vegetable consumption of 0.2±0.05 portion/d (P<0.001). At the same time, there was a small but significant increase in body mass index (BMI) by 0.5±0.09 kg/m^2 (P<0.001) and a small decrease in HDL (by 0.02±0.01 mmol/L, P<0.05).

The average salt intake, as measured by 24-hour urinary sodium excretion in a random sample of the adult population, was 9.5±0.2 g/d in 2000/2001. Salt intake fell to 9.0±0.4 g/d in 2005/2006, 8.64±0.2 g/d in 2008, and fell further to 8.1±0.2 g/d by 2011.[14] Therefore, from 2003 to 2011, salt intake decreased by 1.4 g/d (i.e. 15%, P<0.05 for the downward trend).[14]

It is likely that several factors, i.e. the fall in BP, total cholesterol and smoking prevalence, the reduction in salt intake and the increase in the consumption of fruit and vegetables, along with improvements in the treatments of BP, cholesterol and CVD, contributed to the decrease in stroke and IHD mortality.

BP in untreated individuals

To investigate the role of salt reduction in the changes of BP, we compared the BP in 2011 with that in 2003 with adjustment for potential confounding factors. In order to further exclude any potential confounding effect of BP treatments, we included only individuals who were not on any anti-hypertensive medications or other medications that might affect BP.

The results showed that there was a fall in BP of 2.7±0.34/1.1±0.23 mmHg (P<0.001 for both systolic and diastolic BP) from 2003 to 2011 after adjusting for age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and BMI.

These variables altogether explained 28% of the variance of systolic BP and 16% of the variance of diastolic BP.

Salt intake was not included in the above regression model because it was not measured in the same participants whose BP was recorded. However, the fact that after adjusting for almost all other major factors known to be associated with BP, there was still a significant fall in BP of 2.7/1.1 mmHg from 2003 to 2011, would suggest that these falls in BP were likely to be largely attributable to the reduction in population salt intake which occurred during this period.

BP and stroke and IHD mortality in individuals aged 19-64 years

Our above conclusions were based on the assumption that the 15% reduction in salt intake occurred in the whole adult population in England. However, 24-hour urinary sodium was measured only in individuals aged 19-64 years. We have therefore performed separate analyses on the trend of BP and stroke and IHD mortality in individuals of the same age groups as those who had salt intake measured. The results showed that, from 2003 to 2011, stroke mortality decreased from 128/1,000,000 to 82/1,000,000 (36% reduction, P<0.001) and IHD mortality decreased from 423/1,000,000 to 272/1,000,000 (36% reduction, P<0.001). In individuals who were not on any anti-hypertensive medications or other medications that might affect BP, there was a fall in BP of 1.9±0.34/1.0±0.25 mmHg (P<0.001 for both systolic and diastolic BP) from 2003 to 2011 after adjusting for age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and BMI.

Discussion

Our analyses showed that the average BP in the adult population in England decreased by 3.0/1.4 mmHg from 2003 to 2011. This could be attributable to various factors such as the

reduction in salt intake, the increase in fruit and vegetable consumption, and the improvement in BP treatment and control. However, our findings that, in untreated individuals, there was a fall in BP of 2.7/1.1 mmHg after taking into account age, sex, ethnic group, education level, household income, alcohol consumption, fruit and vegetable intake and BMI, suggest that the reduction in population salt intake which occurred from 2003 to 2011, is likely to be an important contributor to the falls in BP. Although 24-hour urinary sodium was measured in individuals aged 19-64 years, the reduction in salt intake is likely to have occurred across the whole population as it was predominately achieved by a gradual reduction in the amount of salt added to all processed foods, which accounts for approximately 80% of total salt intake.[13]

Our findings that the recent falls in BP occurred in England are largely attributable to the reduction in salt intake rather than drug therapies, are consistent with the analysis by DeWilde et al who showed that anti-hypertensive medications contributed to less than 25% of the systolic BP decline in man.[7]

Although our analysis focused on individuals who were not on any BP medications, there is clear evidence that, in individuals who are on antihypertensive drug treatments, a reduction in salt intake is additive to drug therapies,[25 26] particularly drugs that block the renin-angiotensin system.[25] Therefore, salt reduction would also have contributed to the falls in BP in those who were on BP medications.

The observed fall in systolic BP was larger than that might have been predicted from the meta-analysis of randomised salt reduction trials.[9] This may be due to the difference in age and duration of the studies. It has been shown that, for a given reduction in salt intake, the fall in BP is larger in older people compared with younger individuals.[9] Indeed, our current analysis showed that in individuals aged 19-64 years, the fall in BP from 2003 to 2011 was smaller compared with that observed when all adults were included. Another important factor

which may account for the observed larger fall in BP is the longer duration of the study, i.e. over a period of 8 years. Most salt reduction trials had a duration of only a few weeks and the median duration for the trials included in the meta-analysis was only 5 weeks in hypertensive individuals and 4 weeks in normotensive individuals.[9] Whether salt reduction has exerted its maximum effect by 4-5 weeks is not known, but much evidence would suggest that this is unlikely. It is possible that a long-term reduction in population salt intake as reported in our current analysis, could have a greater effect on BP than that observed in the salt reduction trials with a duration of only a few weeks.

It is well established that raised BP throughout its range is a major cause of CVD.[27] A reduction in salt intake through its effect on BP would reduce CVD.[9 11] Additionally, increasing evidence suggests that salt reduction may have a direct beneficial effect on reducing CVD, independent of BP.[10] It is therefore, of interest, that we found a decrease in both stroke and IHD mortality in parallel with the reduction in salt intake and the falls in BP from 2003 to 2011 in England. Various other studies have documented a reduction in the incidence of CVD. For example, a study using the South London Stroke Register showed that the incidence of stroke decreased from 247/100,000 in 1995 to 149.5/100,000 in 2010 (i.e. a reduction of 39.5% over 16 years),[28] and an analysis of the General Practice Research Database showed that the incidence of stroke in the UK fell by 29% between 1999 and 2008.[29]

It is difficult to quantify the relative contribution of salt reduction to the decrease of CVD as several other dietary and lifestyle factors as well as treatments all have played a part. However, based on the meta-analysis of BP treatment trials where a 10 mmHg reduction in systolic BP was related to a decrease of 41% in stroke and 22% in IHD,[30] it was estimated that a 2.7 mmHg reduction in systolic BP that occurred with salt reduction would be predicted to reduce stroke by approximately 11% and IHD by 6%. Therefore, salt reduction is

likely to have played an important role in the decreases of stroke and IHD mortality in England. These results are supported by the evidence from both prospective cohort studies and outcome trials which have demonstrated that a reduction in salt intake is related to a decrease in CVD risk.[11 12 31] A cost-effective analysis by National Institute for Health and Clinical Excellence (NICE) shows that salt reduction not only saves lives, but also saves money, and the reduction in salt intake achieved in the UK has saved more than £1.5 billion per annum.[32]

Our findings that a reduction in population salt intake was related to a fall in population BP and mortality from stroke and IHD in England are in agreement with those observed in Japan and Finland.[33 34] Japan, in the late 1960s, carried out a government-led campaign to reduce salt intake. Over the following decade, salt intake was reduced, particularly in northern areas from 18 to 14 g/d. Paralleling this reduction in salt intake, there were falls in BP and an 80% reduction in stroke mortality[33] in spite of large increases in fat intake, cigarette smoking, alcohol consumption and obesity which occurred during that period. Finland, in the late 1970s, initiated a systematic approach to reducing salt intake through mass media-campaigns, co-operation with the food industry and implementing salt labelling legislation.[34 35] This led to a significant reduction in the average salt intake of the Finnish population[34 35] from ≈14 g/d in 1972 to less than 9 g/d in 2002.[34] The reduction in salt intake was accompanied by a fall of over 10 mmHg in both systolic and diastolic BP and a decrease of 75-80% in both stroke and IHD mortality. Although these results were attributable to several factors, the reduction in salt intake is likely to have played a major role, particularly in the fall in BP as BMI and alcohol consumption increased during that time.

Strengths and limitations: The strength of our analysis is that we used the data from a nationally representative sample of the population in England. However, there are several potential limitations. First, our study used an ecological design that is subject to various

methodological issues.[36] Because we used data from national surveys that included different sets of participants both cross-sectionally and longitudinally, we were unable to work with data at the individual level, particularly as salt intake was not measured in the same participants who had BP and other CVD risk factors recorded. Therefore, the results of our study are potentially subject to ecological bias. Second, we could not exclude potential confounding effect of some variables which were not measured, such as physical activity levels which were recorded in 2003, but not in the 2011 survey. Third, the trend in 24-hour urinary sodium was taken from the data either for England, Great Britain or the UK, as the original report did not separate the results by countries. It has been shown that salt intake was higher in Scotland and lower in Wales compared with that in England.[14 37] A difference in the composition of the population surveyed at different years may cause a bias to the trend in 24-hour urinary sodium. However, Scotland, Wales and Northern Ireland account for only a small proportion of the UK population (altogether 16%). Additionally, the lower salt intake in Wales and higher salt intake in Scotland might balance each other out to a certain degree in the 2003 NDNS. Therefore, the 24-hour urinary sodium data for 2003 (Great Britain) and 2011 (England only) were likely to be comparable.

Conclusions

The reduction in salt intake is likely to be an important contributor to the falls in BP in England from 2003 to 2011. As a result, the decrease in salt intake would have played an important role in the reduction in stroke and IHD mortality during this period. Despite considerable progress being made on salt reduction, the mean salt intake in the UK population (8.1 g/d in 2011) was still 35% higher than the recommended level of 6 g/d, and 70% of the adult population (80% men and 58% women) had a daily salt intake above the recommended level.[14] Therefore, continuing and much greater efforts are needed to achieve further reductions in salt intake to prevent the maximum number of stroke and IHD deaths.

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Contributors: FJH and GAM designed the analysis plan. FJH performed statistical analyses and wrote the first draft of the manuscript. SPR contributed to database organisation and variable selections. All authors contributed to the interpretation of the results and revision of the manuscript. FJH is guarantor.

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Competing interests: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/coi_disclosure.pdf (available on request from the corresponding author) and declare: no support from any organisation for the submitted work; no financial relationships with any organisations that might have an interest in the submitted work in the previous three years. FJH is a member of Consensus Action on Salt & Health (CASH) and World Action on Salt & Health (WASH). Both CASH and WASH are non-profit charitable organisations and FJH does not receive any financial support from CASH or WASH. GAM is Chairman of Blood Pressure UK (BPUK), Chairman of CASH and Chairman of WASH. BPUK, CASH and WASH are non-profit charitable organisations. GAM does not receive any financial support from any of these organisations. SPR is an employee of CASH.

Ethics committee approval: Our study is an analysis of previously collected data and therefore ethical approval was not required for our analysis. Ethical approval for the Health Survey for England was obtained by the survey team.

Data sharing statement: No additional data are available. The data are already in the public domain.

Legend to Figure

Figure 1. Changes in salt intake as measured by 24-hour urinary sodium (UNa) excretion, blood pressure (BP), stroke and ischemic heart disease (IHD) mortality in England from 2003 to 2011. * P<0.05, *** P<0.001 for trend.

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Table 1. Changes in demographic parameters, blood pressure and other variables from 2003 to 2011

	2003 (N=9183)	2006 (N=8762)	2008 (N=8974)	2011 (N=4753)	P value
Age (year)	49.5±0.2	50.6±0.2	50.4±0.2	51.0±0.3	<0.001
Sex, N (%)					
Men	4108 (45)	3924 (45)	4040 (45)	2070 (44)	
Women	5075 (55)	4838 (55)	4934 (55)	2683 (56)	0.406
Ethnic group, N (%)					
White	8559 (93)	8118 (93)	8241 (92)	4344 (92)	
Black	148 (2)	158 (2)	170 (2)	95 (2)	
Mixed	41 (0.4)	66 (1)	75 (1)	58 (1)	
Other	429 (5)	418 (5)	483 (5)	251 (5)	<0.001
Highest education qualification, N (%)					
NVQ4/NVQ5/Degree equivalent	1527 (17)	1708 (20)	1803 (20)	1186 (25)	
Lower than higher education	1040 (11)	1078 (12)	1040 (12)	559 (12)	
NVQ3/GCE A level equivalent	1096 (12)	1124 (13)	1312 (15)	698 (15)	
NVQ2/GCE O level equivalent	2198 (24)	1944 (22)	1934(22)	1001 (21)	
NVQ1/GCE other equivalent	467 (5)	420 (5)	437 (5)	207 (4)	
Foreign or other	431 (5)	175 (2)	173 (2)	71 (2)	
No qualification	2416 (26)	2307 (26)	2273 (25)	1026 (22)	<0.001
Household income in quintile (1 to 5, high to low), N (%)					
1	1355 (17)	1111 (15)	1213 (16)	608 (15)	
2	1421 (18)	1437 (20)	1501 (20)	813 (21)	
3	1760 (22)	1567 (22)	1548 (21)	816 (21)	
4	1821 (23)	1596 (22)	1595 (21)	867 (22)	
5	1653 (21)	1592 (22)	1665 (22)	850 (22)	<0.001

Frequency of alcohol consumption in past 12 months, N (%)					
Every Day	1348 (15)	1208 (14)	1137 (13)	511 (11)	<0.001
5/6 days/week	440 (5)	447 (5)	448 (5)	207 (4)	
3/4 days/week	1443 (16)	1292 (15)	1395 (16)	667 (14)	
Once or twice a week	2689 (29)	2392 (27)	2380 (27)	1252 (26)	
Once or twice a month	1098 (12)	1100 (13)	1149 (13)	687 (15)	
Once every couple of months	588 (6)	639 (7)	641 (7)	422 (9)	
Once or twice a year	696 (8)	698 (8)	725 (8)	376 (8)	
Not at all	860 (9)	972 (11)	1075 (12)	619 (13)	
Fruit and vegetable consumption (portion/d)	3.6±0.03	3.9±0.03	3.8±0.03	3.8±0.04	<0.001
Body mass index (kg/m^2)	27.1±0.05	27.3±0.06	27.3±0.06	27.6±0.08	<0.001
Blood pressure (mmHg)					
Systolic	129.3±0.20	128.3±0.19	127.4±0.19	126.3±0.25	<0.001
Diastolic	74.2±0.12	73.6±0.12	73.3±0.12	72.8±0.16	<0.001
Total Cholesterol (mmol/L)	5.7±0.01	5.5±0.01	5.4±0.01	5.3±0.02	<0.001
HDL (mmol/L)	1.53±0.005	1.50±0.005	1.50±0.005	1.51±0.008	<0.001
Smoking Status, N (%)					
Never smoked cigarettes at all	4258 (46)	4256 (49)	4473 (50)	2376 (50)	
Used to smoke cigarettes occasionally	595 (7)	477 (6)	483 (5)	279 (6)	
Used to smoke cigarettes regularly	2565 (28)	2525 (29)	2536 (28)	1410 (30)	
Current cigarette smoker	1749 (19)	1491 (17)	1458 (16)	680 (14)	<0.001

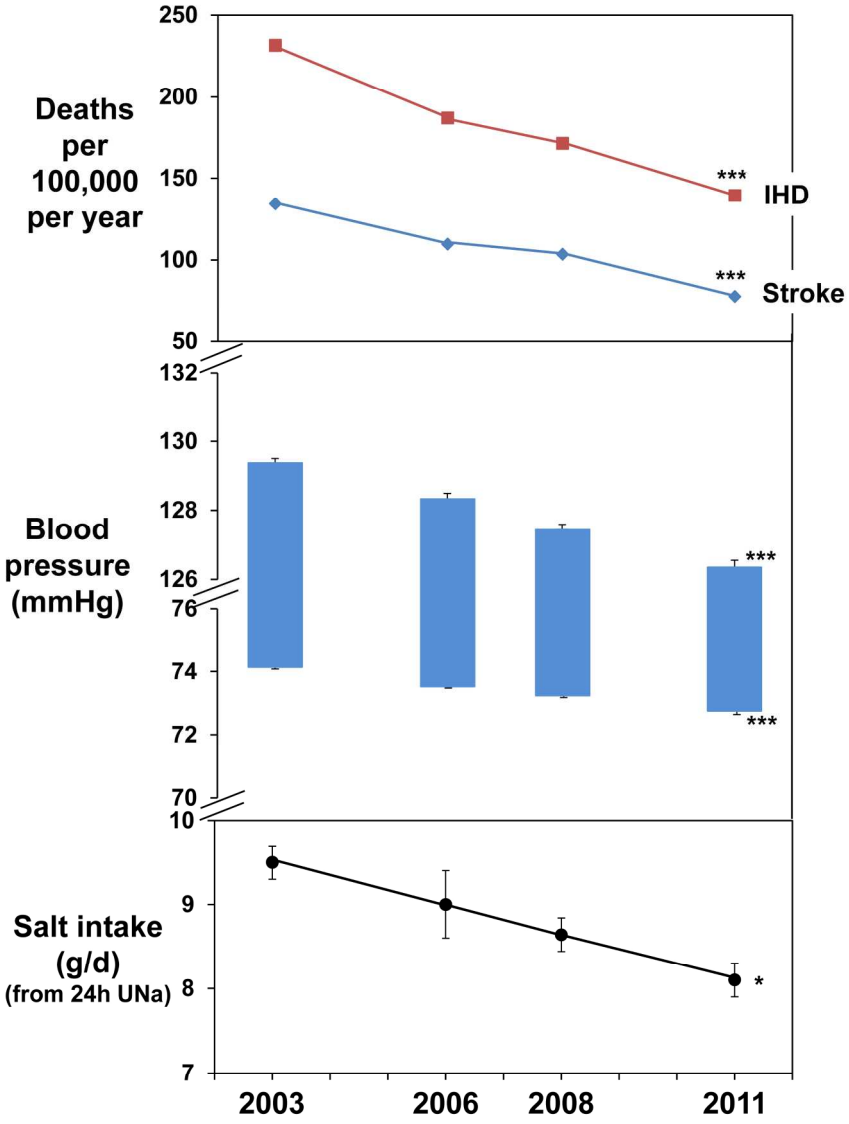

Figure 1
231x308mm (300 x 300 DPI)

STROBE Statement—checklist of items that should be included in reports of observational studies

	Item No	Recommendation	Page Number Reported
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2-3
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2-3
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	5
Objectives	3	State specific objectives, including any prespecified hypotheses	5-6
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5-6
Participants	6	(*a*) *Cohort study*—Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up *Case-control study*—Give the eligibility criteria, and the sources and methods of case ascertainment and control selection. Give the rationale for the choice of cases and controls *Cross-sectional study*—Give the eligibility criteria, and the sources and methods of selection of participants	Not applicable
		(*b*) *Cohort study*—For matched studies, give matching criteria and number of exposed and unexposed *Case-control study*—For matched studies, give matching criteria and the number of controls per case	Not applicable
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6-7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6-7
Bias	9	Describe any efforts to address potential sources of bias	7-8
Study size	10	Explain how the study size was arrived at	Not applicable
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7-8
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7-8
		(*b*) Describe any methods used to examine subgroups and interactions	7-8
		(*c*) Explain how missing data were addressed	Not applicable
		(*d*) *Cohort study*—If applicable, explain how loss to follow-up was addressed *Case-control study*—If applicable, explain how matching of cases and controls was addressed	Not applicable

		Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy	
		(*e*) Describe any sensitivity analyses	Not applicable
Results			
Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	Not applicable
		(b) Give reasons for non-participation at each stage	Not applicable
		(c) Consider use of a flow diagram	Not applicable
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, 21
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) *Cohort study*—Summarise follow-up time (eg, average and total amount)	Not applicable
Outcome data	15*	*Cohort study*—Report numbers of outcome events or summary measures over time	Not applicable
		Case-control study—Report numbers in each exposure category, or summary measures of exposure	Not applicable
		Cross-sectional study—Report numbers of outcome events or summary measures	8-10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	8-10
		(*b*) Report category boundaries when continuous variables were categorized	Not applicable
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	Not applicable
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9-10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10-11
Limitations	19	Discuss limitations of the study, taking into account sources of potential bias or imprecision. Discuss both direction and magnitude of any potential bias	13-14
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	14
Generalisability	21	Discuss the generalisability (external validity) of the study results	10-11,14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.