# **BMJ Open** Salt reduction in England from 2003 to 2011: its relationship to blood pressure, stroke and ischaemic heart disease 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 ischaemic heart disease (IHD).

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

**Setting and participants:** England, 2003 N=9183, 2006 N=8762, 2008 N=8974 and 2011 N=4753, aged  $\geq$ 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±0.20 mm Hg (p<0.001/p<0.001), a decrease of 0.4 ±0.02 mmol/L (p<0.001) in cholesterol, a reduction in smoking prevalence from 19% to 14% (p<0.001), an increase in fruit and vegetable consumption (0.2±0.05 portion/day, p<0.001) and an increase in body mass index (BMI;  $0.5\pm0.09$  kg/m<sup>2</sup>, p<0.001). Salt intake, as measured by 24 h urinary sodium, decreased by 1.4 g/ day (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 cardiovascular disease, contributed to the falls in stroke and IHD mortality. In individuals who were not on antihypertensive medication, there was a fall in BP of 2.7±0.34/1.1±0.23 mm Hg (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 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 antihypertensive 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 contributed substantially to the decreases in stroke and IHD mortality.

# **INTRODUCTION**

Cardiovascular disease (CVD) is the leading cause of death and disability worldwide.<sup>1</sup> Unhealthy diet and lifestyle factors are

#### Strengths and limitations of this study

- Salt intake in a random sample of the population was measured by 24 h urinary sodium excretion verified using para-aminobenzoic acid recovery method to ensure the accuracy of the collection.
- Blood pressure was measured in a separate random sample of the population using standardised protocol with the same validated electronic sphygmomanometer.
- The population surveys included different sets of participants. Therefore, the results of our study could possibly be subject to ecological bias.

responsible for approximately 80% of CVD.<sup>2</sup> Among all of the risk factors for CVD, raised blood pressure (BP) is a major one, accounting for 62% of stroke and 49% of ischaemic heart disease (IHD).<sup>3</sup> 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.<sup>4</sup>

In England, the average population BP has fallen in recent years<sup>5</sup> and CVD mortality has also declined.<sup>6</sup> 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.<sup>6</sup> An analysis of the data from the Health Survey for England showed that antihypertensive medications accounted for less than 25% of the systolic BP decline in man over the period of 1994–2002 and 2003–2009.<sup>7</sup> 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 antihypertensive therapies.<sup>8</sup>

Evidence from various types of studies has consistently shown that a reduction in salt intake lowers BP and thereby reduces CVD risk.<sup>9–12</sup> A meta-analysis of relatively short-term salt reduction trials showed a dose –response relationship with a 1 g/day reduction in salt intake relating to an approximately 1 mm Hg fall in systolic BP.<sup>9</sup> The UK initiated a nationwide salt reduction programme in 2003/2004.<sup>13</sup> The programme has been successful and resulted in a 15% reduction in population salt intake by 2011.<sup>14</sup> 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,<sup>5</sup> <sup>15–18</sup> 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.<sup>19</sup> The methods used in the Health Survey for England were reported in detail elsewhere<sup>5</sup> and only methods relevant to the current analysis are described in brief here.

We used the Health Survey for England data for 2003,<sup>15</sup> 2006,<sup>16</sup> 2008<sup>17</sup> and 2011.<sup>18</sup> We included participants aged  $\geq$ 16 years with BP measurements recorded (2003 N=9183, 2006 N=8762, 2008 N=8974 and 2011 N=4753). 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 h urinary sodium, was taken from the National Diet and Nutrition Survey (NDNS) in participants aged 19–64 years.<sup>14</sup> In the 2000/2001 survey, 24 h urine was collected in a random sample of adults in Great Britain (N=1147). As 24 h urine collection was not made in 2003 when the UK salt reduction programme started, it is assumed that salt intake in 2003 was the same as that in 2000/2001. In 2005/2006, 24 h 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 h urine collection was made in a random sample of adults in the UK (N=692), and in 2011, 24 h urine was collected in a random sample of adults in England (N=547). In all surveys, the

completeness of the 24 h urine collection was assessed using the para-aminobenzoic acid 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  $\geq$ 15 years for England and Wales.<sup>21–24</sup> Deaths were certified by medical practitioners, using the Medical Certificate of Cause of Death.<sup>21</sup>

# Statistical analysis

Stroke and IHD mortality rates were 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 4 years (2003, 2006, 2008 and 2011) were made by one-way analysis of variance for continuous variables and by  $\chi^2$  test for categorical variables.

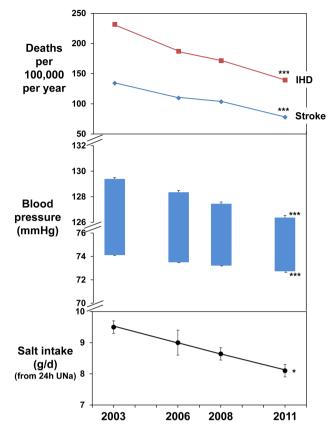
To estimate the contribution of salt intake to the changes of BP and to exclude any potential confounding effect of treatments, we performed a separate analysis that included only individuals who were not on any antihypertensive medications or other medications that might affect BP. We compared BP in 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 h 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 this age range was the same as for those participants who had 24 h 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/



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

100 000 for the adult population in England. As shown in figure 1, there had been a gradual reduction in 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 4 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  $129.3\pm0.20/74.2\pm0.12$  mm Hg in 2003 to  $126.3\pm0.25/72.8\pm0.16$  mm Hg in 2011 (ie, a fall of  $3.0\pm0.33/1.4\pm0.20$  mm Hg, p<0.001 for systolic and diastolic BP). From 2003 to 2011, there was a decrease of  $0.4\pm0.02$  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  $0.2\pm0.05$  portion/day (p<0.001). At the same time, there was a significant increase in BMI by 0.5  $\pm0.09$  kg/m<sup>2</sup> (p<0.001) and a decrease in HDL (by 0.02  $\pm0.01$  mmol/L, p<0.05).

The average salt intake, as measured by 24 h urinary sodium excretion in a random sample of the adult

population, was  $9.5\pm0.2$  g/day in 2003. Salt intake fell to  $9.0\pm0.4$  g/day in 2005/2006,  $8.64\pm0.2$  g/day in 2008 and further to  $8.1\pm0.2$  g/day by 2011.<sup>14</sup> Therefore, from 2003 to 2011, salt intake decreased by 1.4 g/day (ie, 15%, p<0.05 for the downward trend).<sup>14</sup>

It is likely that several factors, that is, 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 antihypertensive medications or other medications that might affect BP.

The results showed that there was a fall in BP of  $2.7 \pm 0.34/1.1 \pm 0.23$  mm Hg (p<0.001 for 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 mm Hg 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 h 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 antihypertensive medications or other medications that might affect BP, there was a fall in BP of 1.9±0.34/1.0  $\pm 0.25$  mm Hg (p<0.001 for 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.

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 (1–5, 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/day)	3.6±0.03	3.9±0.03	3.8±0.03	3.8±0.04	<0.001
Body mass index (kg/m <sup>2</sup> )	27.1±0.05	27.3±0.06	27.3±0.06	27.6±0.08	<0.001
Blood pressure (mm Hg)					
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
HDL, high-density lipoprotein.					

# DISCUSSION

Our analyses showed that the average BP in the adult population in England decreased by 3/1.4 mm Hg 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 mm Hg 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 between 2003 and 2011, is likely to be an important contributor to the falls in BP. Although 24 h 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 predominantly achieved by a gradual reduction in the amount of salt added to all processed foods, which accounts for approximately 80% of total salt intake.<sup>13</sup>

Our findings that the recent falls in BP that 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*<sup>7</sup> who showed that antihypertensive medications contributed to less than 25% of the systolic BP decline in man.

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,<sup>25–26</sup> particularly drugs that block the renin-angiotensin system.<sup>25</sup> 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 which might have been predicted from the meta-analysis of randomised salt reduction trials.<sup>9</sup> 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 of BP in the current report is the longer duration, that is, over a period of 8 years. Most of the 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.<sup>9</sup> 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.<sup>27</sup> A reduction in salt intake through its effect on BP would reduce CVD.<sup>9</sup> <sup>11</sup> Additionally, increasing evidence suggests that salt reduction may have a direct beneficial effect on reducing CVD, independent of BP.<sup>10</sup> It is therefore of interest that we found a decrease in 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 (ie, a reduction of 39.5% over 16 years),<sup>28</sup> 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.<sup>29</sup>

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 mm Hg reduction in systolic BP was related to a decrease of 41% in stroke and 22% in IHD,<sup>30</sup> it was estimated that a 2.7 mm Hg 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 prospective cohort studies and outcome trials, which have demonstrated that a reduction in salt intake is related to a decrease in CVD risk.<sup>11 12 31</sup> A cost-effective analysis by the 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  $\pounds1.5$  billion/annum.<sup>32</sup>

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/ day. Paralleling this reduction in salt intake, there were falls in BP and an 80% reduction in stroke mortality<sup>33</sup> 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.<sup>34 35</sup> This led to a significant reduction in the average salt intake of the Finnish population<sup>34</sup> <sup>35</sup> from  $\approx 14$  g/day in 1972 to less than 9 g/day in 2002.<sup>34</sup> The reduction in salt intake was accompanied by a fall of over 10 mm Hg in systolic and diastolic BP and a decrease of 75-80% in 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 best available data in England. Salt intake in a random sample of the population was measured by 24 h urinary sodium excretion verified using para-aminobenzoic acid recovery method to ensure the accuracy of the collection. Blood pressure was measured in a separate random sample of the population using standardised protocol with the same validated electronic sphygmomanometer. However, there are several potential limitations. First, our study used an ecological design that is subject to various methodological issues.<sup>36</sup> 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 could possibly be subject to ecological bias. Second, we could not exclude the 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 h urinary sodium was taken from the data 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.<sup>14 37</sup> A difference in the composition of the population surveyed at different years may cause a bias to the trend in 24 h 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. Therefore, the 24 h urinary sodium data were likely to reflect the trend of salt intake in England.

# 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 England (8.1 g/day in 2011) was still 35% higher than the recommended level of 6 g/day, and 70% of the adult population (80% men and 58% women) had a daily salt intake above the recommended level.<sup>14</sup> 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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**Competing interests** 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. SP-R is an employee of CASH.

Ethics approval Ethical approval for the Health Survey for England was obtained by the survey team.

Provenance and peer review Not commissioned; externally peer reviewed.

Data sharing statement No additional data are available.

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