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Are mandatory salt reduction policies and universal salt iodisation programmes at loggerheads? A cross-sectional analysis from the WHO-SAGE South Africa cohort

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3 **1 Are mandatory salt reduction policies and universal salt iodisation programmes at**
4 **2 loggerheads? A cross-sectional analysis from the WHO-SAGE South Africa cohort**
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8 **Short title:** Salt reduction and universal salt iodisation
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56 **Abstract**
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Objective: The World Health Organization's (WHO) global targets for non-communicable disease (NCD) reduction recommend consumption of <5g salt/day. In 2016, South Africa was the first country to legislate maximum salt levels in processed foods. South Africa's universal salt iodization (USI) fortification programme has successfully eradicated iodine deficiency. Simultaneous monitoring of sodium reduction and iodine status is required to ensure compatibility of the two public health interventions.

Design/setting/participants: A nested cohort design within WHO's 2015 Study on global AGEing and adult health (SAGE, n=2887) including individuals from households across South Africa. Randomly selected adults (n=875) provided 24-hour and spot urine samples for sodium and iodine concentration (UIC) analysis (the primary and secondary outcome measures respectively). Median 24-hour and spot UIC were compared by salt intakes <5g/day, 5 – 9 g/day and ≥9g/day.

Results: Median daily salt excretion was 6.3g salt/day (range 1-43 g/day); 35% had urinary sodium excretion values within the desirable range (< 5g salt/day), 37% had high values (5 – 9 g salt/day) and 28% had very high values (≥ 9g salt/day). Median UIC was 130 µg/L (IQR=58-202), indicating population iodine sufficiency (≥100 µg/L). Both spot and 24hr iodine excretion differed across urinary sodium categories (p<0.001) and were positively correlated with 24h urinary sodium (r= 0.170 and 0.528 respectively; both p<0.001).

Conclusions: 24hr urinary sodium and iodine within a nationally representative cohort study allows simultaneous assessment of the compatibility of both salt reduction strategies and USI. Iodine status of populations undergoing salt reduction strategies needs to be closely monitored to prevent re-emergence of iodine deficiency.

Strengths and limitations of this study

- The study uses the current gold standard of 24-hour urine to assess sodium intake
- The large sample size includes coastal and inland populations from across the country
- Lack of dietary data precludes assessment of sources of iodine or sodium
- The data is only for adults and not children
- The sample includes 14% women of approximate child bearing age (18-49y; n=121)

Keywords: iodine; sodium, dietary; policy; nutritional requirements; legislation, food

Introduction

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3 57 Iodine deficiency remains the largest preventable cause of brain damage and mental
4 58 impairment worldwide. Thyroid hormone production requires an adequate supply of iodine
5 59 from the diet, and is essential to metabolism and growth across the lifecycle. As well as
6 60 cretinism in its most severe form, iodine deficiency can also result in miscarriages, stillbirths,
7 61 and impaired psychomotor development and behavioural problems in children born to iodine
8 62 deficient mothers¹. To prevent iodine deficiency disorders, the World Health Organization
9 63 (WHO) has endorsed universal salt iodization (USI), where all salt for human and animal
10 64 consumption is iodized². USI is hailed as a public health success story, as 70% of the world's
11 65 population is estimated to use iodized salt in a total of 130 countries³. However, 2 billion
12 66 individuals worldwide still have insufficient iodine intake, with many in south Asia and sub-
13 67 Saharan Africa particularly affected⁴.

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21 68 In South Africa, mandatory iodization of table salt, at a level of 40 to 60 ppm, replaced
22 69 voluntary iodization in December 1995, using potassium iodate as the fortificant⁵ because of
23 70 its stability in warm climates⁶, rather than potassium iodide that is used in North America and
24 71 Europe. The level of fortification was subsequently revised in 2007 to allow a wider range,
25 72 namely 35 to 65 ppm². The iodization program has effectively eliminated iodine deficiency in
26 73 the country, but there are some loopholes in the program, such as the domestic use of non-
27 74 iodized agricultural salt in the northern provinces⁷. Under the legislation, salt used in the
28 75 manufacturing of processed foods and salt packaged in bags of at least 20 kg are also
29 76 exempted from mandatory iodization⁵. In 2005, 77% of households in the country used
30 77 adequately iodized salt, described as salt containing more than 15 ppm of iodine⁸. However,
31 78 data on the iodine status of the South African population is outdated and a national survey
32 79 was last conducted in 2005⁷. At that time, South African women and children aged 6 to 9 y
33 80 old were found to have an optimal iodine status (i.e., MUIC 100–199 mg/L, <20% with UIC
34 81 levels <50 mg/L)⁹ which indicated a well-functioning salt iodization program¹⁰.

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45 82 At the same time as salt iodization efforts around the world are being celebrated, there is a
46 83 global focus on salt reduction efforts to lower population level blood pressure. The World
47 84 Health Organization (WHO) and World Health Assembly targets to reduce non
48 85 communicable diseases (NCDs) include a 30% reduction in population salt intake by 2025¹¹
49 86 ¹². South Africa was the first country to implement mandatory legislation in July 2016 for
50 87 maximum salt levels permitted in a wide range of processed foods¹³ that are significant
51 88 contributors to the sodium intake of the population¹⁴⁻¹⁷. The legislation is predicted to
52 89 decrease population-level salt intake by 0.85 grams per day¹⁸ and reduce annual deaths from

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3 90 cardiovascular diseases by 11%. This public health strategy is estimated to save the
4 91 government US\$51.25 million/year in health care costs; and save households more than
5 92 US\$4 million/year in out-of-pocket medical expenses¹⁹.

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8 93 Since salt is the vehicle for iodine fortification, successful campaigns to reduce salt intake
9 94 would also likely result in reduced iodine intake²⁰. Dietary modelling conducted in the
10 95 Netherlands estimated the effect of 12%, 25%, and 50% decreases in salt from processed
11 96 foods and table salt²⁰. Only at a 50% salt decrease would iodine intake become inadequate for
12 97 a small percentage of the population which, at that time, confirmed a lack of conflict between
13 98 population-wide strategies of decreasing salt while ensuring adequate consumption of iodized
14 99 salt to prevent iodine deficiency. We have previously reported no difference in median UIC
15 100 across categories of sodium excretion equivalent to salt intakes lower than 5g/day, 5 - 9
16 101 g/day, and greater than or equal to 9 g/d in a convenience sample of 262 adult men and
17 102 women in Cape Town in 2004²¹. It was concluded that this was because much of the dietary
18 103 salt consumed was provided from non-iodinated sources, presumably in salt added to
19 104 processed foods. Given the introduction of the salt reduction legislation, it is timeous to
20 105 assess the iodine status of the South African population, according to salt intakes.

21 106 The aim of the current study was to simultaneously measure sodium (Na) and iodine in 24hr
22 107 and spot urinary collections in an adult cohort cohort to determine whether lower salt intakes
23 108 are associated with a suboptimal iodine status.

24 109 **Methods**

25 110 A nested observational study was conducted as part of Wave 2 of the World Health
26 111 Organization Study on global AGEing and adult health (WHO SAGE). WHO-SAGE is a
27 112 multinational cohort study examining the health and wellbeing of adult populations and the
28 113 ageing process. Two waves of this longitudinal study have been completed in China, Ghana,
29 114 India, Mexico, Russia and South Africa²². In total, 42,464 respondents were recruited across
30 115 the six countries for Wave 1 (2007-2010), including 4223 respondents in South Africa (9%
31 116 18-49 years; 40% 50-59 years; 51% 60+ years). Respondents were recruited from selected
32 117 probability sampled enumeration areas (EAs) using a multi-stage cluster sampling strategy,
33 118 with stratification by province, residence and race. Urine capture was included as part of
34 119 SAGE South Africa Wave 2 data collection. The sampling strategy was designed to account
35 120 for attrition, where households were classified into the following mutually exclusive
36 121 categories: 1) SAGE Wave 1 follow-up households with one or more members aged 50 years

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3 122 or more targeted for selection; 2) new households with one or more members aged 50 years
4 123 or more; 3) SAGE Wave 1 follow-up households which include residents aged 18-49 targeted
5 124 for selection; or, 4) new households which include residents aged 18-49. Further detail on the
6 125 sampling and recruitment strategy can be found in the study protocol paper²³.
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10 126 For Wave 2 data collection in 2015, twenty survey teams (one nurse and three interviewers
11 127 per team) simultaneously collected data and samples from respondents across all provinces in
12 128 the country over a five-month period. Respondents that were recruited to provide urine
13 129 samples (n=1200) were sampled from among the first households visited within each EA, as
14 130 a means to simplify logistics and reduce sample transit time to the central Durban laboratory.
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19 131 Inclusion criteria for urine collection were: respondent must be part of the WHO SAGE
20 132 cohort, with no indication of urinary incontinence or other condition that could impede 24-
21 133 hour urine collection; and if female, not menstruating, pregnant, or breastfeeding on the day
22 134 of collection.
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26 135 **Study Measures**

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28 136 All survey teams were trained with support from WHO Geneva. As part of the larger survey,
29 137 anthropometry, household and individual questionnaires, blood sampling, blood pressure
30 138 (BP) and physical function tests were completed as described previously in SAGE Wave 1²².
31 139 Interviewers spoke the respondents' home languages with consent forms available in the most
32 140 widely spoken languages for each area. All respondents gave free and informed consent prior
33 141 to taking part. The study complied with ethical principles²⁴ and all procedures involving
34 142 human subjects were approved by the WHO Ethics Review Committee [RPC149], and
35 143 North-West University and University of Witwatersrand research ethics committees in South
36 144 Africa.
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44 145 **Urine collection**

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46 146 The protocol used for collection of 24-hour urine samples followed the WHO/PAHO
47 147 guidelines²⁵. Respondents were requested to collect all urine produced for 24 hours,
48 148 excluding the first pass urine on day 1, but including the first urine of the following morning
49 149 (day 2) in a 5-litre plastic container containing 1g thymol as preservative in South Africa. The
50 150 spot sample was collected without preservative from the second urine passed on day 1
51 151 (marking the start of the 24-hour collection) and decanted into three 15 ml Porvair tubes
52 152 (Porvair Sciences, Leatherhead, UK) then kept in a cool box powered by the fieldwork
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3 153 vehicles. The next morning, the 24-hour sample volumes were recorded and aliquots (4 x
4 154 Porvair tubes) generated with all samples then shipped to the laboratory, maintaining the cold
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6 155 chain. Thymol, a crystalline natural derivative of the Thyme plant, was used as a
7
8 156 preservative. Thymol has been shown to prevent changes in urinary creatinine, sodium and
9
10 157 potassium concentrations for up to five days²⁶. Incomplete 24-hour urine collections were
11
12 158 assumed if: total volume ≤ 300 ml; or creatinine excretion ≤ 4 mmol/day (women) or ≤ 6
13 159 mmol/day (men)²⁷.

14 15 160 **Urine analysis**

16
17 161 Sodium and potassium were determined using the indirect Ion Selective Electrode method
18
19 162 and creatinine analysed using the standardised urinary Jaffe kinetic method (Beckman
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21 163 Coulter Synchron DXC600/800 System). The WHO population target for salt intake is 5g salt
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23 164 (NaCl) per day, equivalent to urinary sodium excretion 85 mmol/24hr. With the exception of
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25 165 iodine, all South African samples were analysed at a single laboratory in Durban, South
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27 166 Africa (Global Clinical and Viral Laboratories). Urine samples for iodine analysis were
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29 167 stored at -20° C and batch analysed using the Sandell-Kolthoff method with ammonium
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31 168 persulfate digestion and microplate reading²⁸ at the North-West University Centre of
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33 169 Excellence for Nutrition. The laboratory participates successfully in the Program to Ensure
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35 170 the Quality of Urinary Iodine Procedures (EQUIP, U.S. Centres for Disease Control and
36
37 171 Prevention, Atlanta GA, USA)²⁹. A median of $<100\mu\text{g}$ iodine/L indicates population-level
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39 172 deficiency (there are no reference ranges for individuals)³⁰.

40 41 173 **Data capture, analysis and statistical power**

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43 174 All data was captured using an electronic data capture system and uploaded to a secure
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45 175 central server for data cleaning and analysis. The nested cohort sample size for the primary
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47 176 outcome measure of 24-hour urine sodium was calculated as previously described.²³
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49 177 Allowing for error in 24-hour sample collection (incomplete or missing samples) in this
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51 178 complex field study, a target sub-sample size of 1200 was randomly selected from the main
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53 179 SAGE-Wave 2 cohort, and those with incomplete or missing samples excluded from the
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55 180 analysis. The sample size used for this analysis was deemed adequate based on
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57 181 recommendations of WHO (2007) that states a sample size between 600 and 900 is sufficient
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59 182 to have a reasonable confidence interval around the coverage estimate for urinary iodine
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183 concentration².

184 Both spot urinary iodine analyses (UIC) and 24hr urinary iodine excretion (UIE) were
185 compared across three categories of 24hr urinary Na excretion intake, equivalent to salt
186 intakes <5g/day, 5 – 9 g/day and ≥9g/day. Normality of data was assessed by visual
187 inspection of histograms and the Kolmogorov-Smirnov test. All non-parametric data were
188 reported as median and interquartile range (IQR; 25th, 75th percentile) and continuous
189 variables compared using independent Samples Mann-Whitney U test or Independent
190 Samples Kruskal-Wallis test. Categorical variables were compared across groups using
191 Pearson Chi-Square and Fisher's Exact Test. Data were also analysed according to urinary Na
192 excretion values and by iodine category (sub-optimal: UIC <100 µg/L; iodine replete: 100 –
193 299 µg/L; and excessive: >300µg/L). To assess the association between salt intake, body size,
194 UIC and UIE, Spearman's rank order and partial correlations were conducted.

195 **Results**

196 Complete urinary Na and iodine data were available in n = 874 participants.
197 Sociodemographic characteristics and health indicators of the sub-sample are compared to the
198 total SAGE-Wave 2 cohort (n = 2887) in Table 1. The sub-sample had a higher proportion of
199 women and more black/coloured respondents than the main cohort, which may explain
200 differences in smoking, education and BP.

201 Median 24hr Na excretion (n=874) was equivalent to a median salt intake of 6.3gsalt/day
202 (range 1-43 g/day); 35% had values within the desirable range (< 5g salt/day), 37% had high
203 values (5 – 9 g salt/day) and 28% had very high values (≥ 9g salt/day) (Table 2). MUIC
204 (n=875) was 130 µg/L (IQR=58-202), indicating iodine sufficiency (≥100 µg/L) while
205 median 24hr UIE (n=866) was 117 ug/day (IQR 138).

206 Both UIC and 24hr iodine excretion differed across urinary Na categories and were positively
207 correlated with urinary Na (r= 0.172 and 0.533; both P<0.001) (Table 2). In the lowest salt
208 category of <5g/d, median UIC indicated borderline deficiency of 102 µg/L. Based on 24hr
209 UIE, participants with a salt intake of <5g/day would be considered to be iodine deficient
210 (<100 ug/day).

211 When the data was analysed according to urinary Na excretion values by iodine category,
212 those in the sub-optimal category (<100 ug/day) had significantly lower salt equivalent
213 excretion values compared to those that were classified as being iodine replete (median (IQR)
214 = 5.4 (2.9; 7.9) vs 6.9 (4.0; 9.9) g/day) (Table 3). Those in the category considered to be

215 excessive (>300ug/L) had similar urinary Na excretion values to those in the sufficient
216 category (100 – 299 ug/L), namely 6.9 (4.0, 9.9) and 7.3 (4.7, 10.0) g salt/day, respectively (P
217 = 0.854). Similarly, the median UIC of those with the highest salt excretion (>9g/day) was
218 within the normal range (ie.149 (78, 220) ug/L).

219 Responses to questions on salt behaviours did not differ between participants across median
220 UIC categories (data not shown), nor according to UIE (Figure 1).

221

222 Discussion

223 Our study found that, although the population are on the whole iodine sufficient, iodine
224 intake is associated with salt intake. With two thirds of the population consuming more than
225 the recommended daily salt intake, and the low salt intake group already exhibiting
226 borderline iodine status, there is a risk that sodium reduction strategies may also impact
227 iodine intake.

228 Concerted efforts are being made in many countries to lower salt consumption¹². Because the
229 primary food vehicle for iodine fortification is salt, there is concern that decreasing salt
230 consumption will increase the risk of iodine deficiency. Our study findings indicate that this
231 is a potential public health problem. The findings of the current study are in contrast to
232 previous findings from a sample of adult men and women surveyed in Cape Town in 2004,
233 when UIC did not differ across categories of salt intake⁽²¹⁾. This discrepancy may be
234 explained by an increasing number of food manufacturers that have knowingly or
235 unknowingly included iodized salt for food processing over the past decade, or alternatively
236 by an increased consumption of salt provided from processed foods, relative to discretionary
237 salt intake.

238 The South African strategic plan to reduce cardiovascular disease includes the target to
239 reduce the population intake of salt to less than 5 grams/day. At present the salt intake is
240 higher than this level with an estimated 40% coming from discretionary salt intake¹⁶. Our
241 study was conducted immediately prior to introduction of the mandatory salt targets in
242 processed foods. Despite iodised salt not being required by law to be used as an ingredient in
243 the manufacturing of processed foods, a study³¹ that investigated the iodine content of salt
244 used in bread, margarine, and salty snack flavourings in 2002 provided surprising results.
245 Even though 11 of the 12 manufacturers surveyed at that time reported that they used non-

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3 246 iodized salt in their products, substantial amounts of iodine were found in the salt used by a
4 247 third of these manufacturers' products, with a mean content of 39 to 69 ppm, and these were
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6 248 the items that were mostly distributed countrywide. An appreciable percentage of the food
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8 249 companies used iodized salt unknowingly in the manufacturing of frequently consumed
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10 250 processed foods, and this may have had a considerable impact on the daily iodine intake of
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12 251 consumers. To our knowledge, there is no updated information on the use of iodised salt by
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14 252 food manufacturers. The salt intake estimations in the current study include both added
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16 253 (discretionary) and non-discretionary salt intakes but the lack of data on dietary intakes of the
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18 254 participants prevents further investigation of the source of the salt.

19 255 We hypothesize that food manufacturers may have already reduced salt content in processed
20 256 foods at the time of the study (2015), and that some of these products may have been
21
22 257 produced with iodized salt. If this is the case, this would result in lowered iodine intake at the
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24 258 same time as lowered salt intake, as would any reduction in discretionary salt use.

25 259 Considering the latter, there have been many accompanying health education strategies that
26 260 target salt reduction behaviours, alongside the salt legislation in processed foods³². In 2015, a
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28 261 mass media campaign (Saltwatch), using television, radio advertisement and other platforms
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30 262 for information dissemination was undertaken to increase public awareness related to the
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32 263 association between a high salt intake, blood pressure and cardiovascular disease in South
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34 264 Africa. The campaign, conducted by the Heart and Stroke Foundation of South Africa with
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36 265 funding from the Department of Health, focused on the need to reduce discretionary salt
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38 266 intake. Evaluation of the programme undertaken in 550 black women, aged 18-55 years in
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40 267 three provinces identified that there was an increase in most of the indicators of knowledge,
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42 268 attitudes and behaviour change towards considering and initiating reduced salt consumption
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44 269 following the campaign³³. Significant increases were found for knowledge items related to
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46 270 high salt intake and its health outcomes. Participants also reported that they added less salt
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48 271 while cooking and at the table. In the current study, responses to questions on salt behaviours
49
50 272 did not differ between participants across median UIC categories, nor according to 24-hr
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52 273 UIE. This could mean that the questions are not sufficiently sensitive to discern between salt
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54 274 intake behaviours, or that the contribution of discretionary salt to total iodine intake is
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56 275 influenced by other food sources of iodised salt.

57 276 A strength of the study was use of the gold standard method for assessment of salt intake,
58
59 277 namely 24hr urinary collections. Limitations relate to the high number of respondents with
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278 missing or incomplete urine samples. The difficulty in obtaining complete 24-hour urine

279 samples is well-known, and the comparison between the main study cohort and those
280 providing complete samples shows that men, and those with higher education less frequently
281 provided complete 24-hour urine. This may also reflect the nature of the survey as
282 fieldworkers visited the respondent's homes and those that were away with work were less
283 likely to have taken part or would have potentially had more difficulty with the urine
284 collection, creating a selection bias in the data towards the population with lower
285 employment levels. Future research may consider work-based data collection. A further
286 limitation is the lack of dietary data on sources of iodine provided by foods other than iodised
287 salt. Iodine-rich dietary sources include fish and seafood, and dairy products and it is possible
288 that some of these foods may also be high in salt, as in the case of salted dried fish commonly
289 consumed by the coloured population (known as "*bokkems*"). However, generally these foods
290 are not major contributors to sodium in the South African diet¹⁶. Interestingly, in women,
291 both UIC and UIE correlated positively with body mass index, independently of salt intake.
292 Looking at changes in food consumption patterns in South Africa over time, it seems that
293 there is not only an increase in processed foods but also other foods that may contribute to
294 iodine intake independently of iodized salt such as fish, eggs, seafood, and dairy foods³⁴. The
295 contribution of food sources, other than iodized salt, to total iodine intake warrants further
296 investigation in the context of evaluating the universal salt iodization programme in South
297 Africa. Furthermore, this study presents limited data for women of child bearing age and no
298 data for children. Further work is needed to determine if there is an impact of the sodium
299 reduction legislation in these particularly iodine-sensitive groups.

300 **Conclusion**

301 This study highlights the need to closely monitor the iodine status of populations as they
302 undergo population-level reductions in salt intake, in countries where universal salt iodisation
303 is implemented. If salt intake levels drop to the WHO target of <5g/day, there may be a need
304 to increase the level of iodine in fortified table salt. Alternatively, compulsory iodisation of
305 salt used in the production of some staple foods such as bread may be considered. In a
306 country where some sectors of the population may be over-iodised, this strategy would
307 require careful dietary modelling before being pursued. It is recommended that surveys that
308 measure urinary Na excretion also simultaneously measure urinary iodine concentration.

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324 implemented research; JB analysed iodine samples; MC, LJW, KC analysed data; KC, LJW,
325 JB, AES, MC, PK, wrote the paper; KC takes responsibility for the contents of this article.
326 All authors read and approved the final manuscript.

327 Data sharing statement: The dataset is available on request and will form part of the data
328 catalogue of the World Health Organization Study on Global AGEing and Adult Health
329 (SAGE) (<http://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/sage/about>)

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427 **Table 1.** Characteristics of the main (SAGE South Africa Wave 2, 2015) and subsample
428 study cohort.

	Main SAGE cohort		Subsample ^a		p value
	n=2887		n=875		
	median	IQR	median	IQR	
Female, n (%)	1939	67	671	77	<0.001
Age years	57	46, 69	55	44, 67	0.468
Aged over 50 years, n (%)	1979	69	567	65	0.171
Ethnicity, n (%)					
Black	1988	69	410	74	<0.001
Coloured, mixed race	465	16	96	17	
Indian	306	11	41	7	
White	128	1	11	2	
Rural, n (%)	792	28	163	29	0.418
Education years	10	7, 13	9	6, 12	0.028
Never been to school, n (%)	495	18	109	20	0.180
Never had paid employment, n (%)	1101	55	238	56	0.403
BMI, kg/m ²	28.8	23.9, 33.7	29.1	24.0, 34.2	0.540
Waist to height ratio	0.59	0.52, 0.67	0.58	0.50, 0.66	0.070
Never used alcohol, n (%)	1576	80	353	83	0.052
Never used tobacco, n (%)	1635	83	367	86	0.023
Systolic BP mmHg	131	118, 144	128	116, 141	0.073
Diastolic BP mmHg	81	73, 89	79	71, 87	0.029
Hypertension, n (%)	1233	45	232	43	0.239
Diabetes, n (%)	248	13	46	11	0.355

429 BMI, body mass index. ^aSubsample: all respondents with spot UIC, valid 24-hour urine, sex
430 and age recorded. Some variables may contain missing data as indicated by percentages. Data
431 shown as median and interquartile range (IQR; 25th, 75th percentile) unless otherwise
432 indicated. Hypertensive by measured BP \geq 140 and/or 90mmHg or previous diagnosis.
433 Education, tobacco/alcohol use, ethnicity, employment and diabetes prevalence by self-
434 report. Continuous variables compared using Independent Samples Mann-Whitney U test,
435 categorical variables compared using Pearson Chi-Square and Fisher's Exact Test.

436

437 **Table 2.** Spearman's rank order and partial correlations between salt, body size and urine
 438 iodine concentration (UIC), SAGE South Africa Wave 2 (2015).

		All	Men	Women
<i>Correlations with spot UIC $\mu\text{g/l}$</i>				
Salt intake g/day	<i>rho</i>	0.172(***)	0.201(**)	0.156(***)
	<i>p</i>	0.000	0.002	0.000
	<i>n</i>	879	203	671
24-hr iodine $\mu\text{g/day}$	<i>rho</i>	0.469(***)	0.510(***)	0.456(***)
	<i>p</i>	0.000	0.000	0.000
	<i>n</i>	871	203	663
BMI kg/m^2	<i>r</i>	0.038	0.004	0.097(*)
	<i>p</i>	0.207	0.484	0.034
	<i>n</i>	461	109	350
Weight kg	<i>r</i>	0.041	0.016	0.058
	<i>p</i>	0.184	0.433	0.133
	<i>n</i>	482	112	368
Waist circumference cm	<i>r</i>	0.019	0.032	0.034
	<i>p</i>	0.339	0.369	0.260
	<i>n</i>	477	111	364
Hip circumference cm	<i>r</i>	0.065	0.203(*)	0.046
	<i>p</i>	0.078	0.015	0.187
	<i>n</i>	481	112	367
<i>Correlations with 24-hr UIE $\mu\text{g/d}$</i>				
Salt intake g/day	<i>rho</i>	0.533(***)	0.467(***)	0.546(***)
	<i>p</i>	0.000	0.000	0.000
	<i>n</i>	872	202	665
BMI kg/m^2	<i>r</i>	0.079(*)	0.051	0.137(**)
	<i>p</i>	0.046	0.299	0.005
	<i>n</i>	460	109	349
Weight kg	<i>r</i>	0.090(*)	-0.015	0.132(**)
	<i>p</i>	0.024	0.436	0.006
	<i>n</i>	481	112	367
Waist circumference cm	<i>r</i>	0.035	-0.004	0.064
	<i>p</i>	0.226	0.484	0.111
	<i>n</i>	476	111	363
Hip circumference cm	<i>r</i>	0.070	0.083	0.097(*)
	<i>p</i>	0.062	0.191	0.031
	<i>n</i>	479	112	365

439 BMI, body mass index; UIC, spot urine iodine concentration; UIE, 24-hour urine iodine
 440 excretion. Correlations between iodine and body size controlled for salt intake. Correlation is
 441 significant at the 0.05 level (*); at the 0.01 level (**); or at the 0.001 level (***)

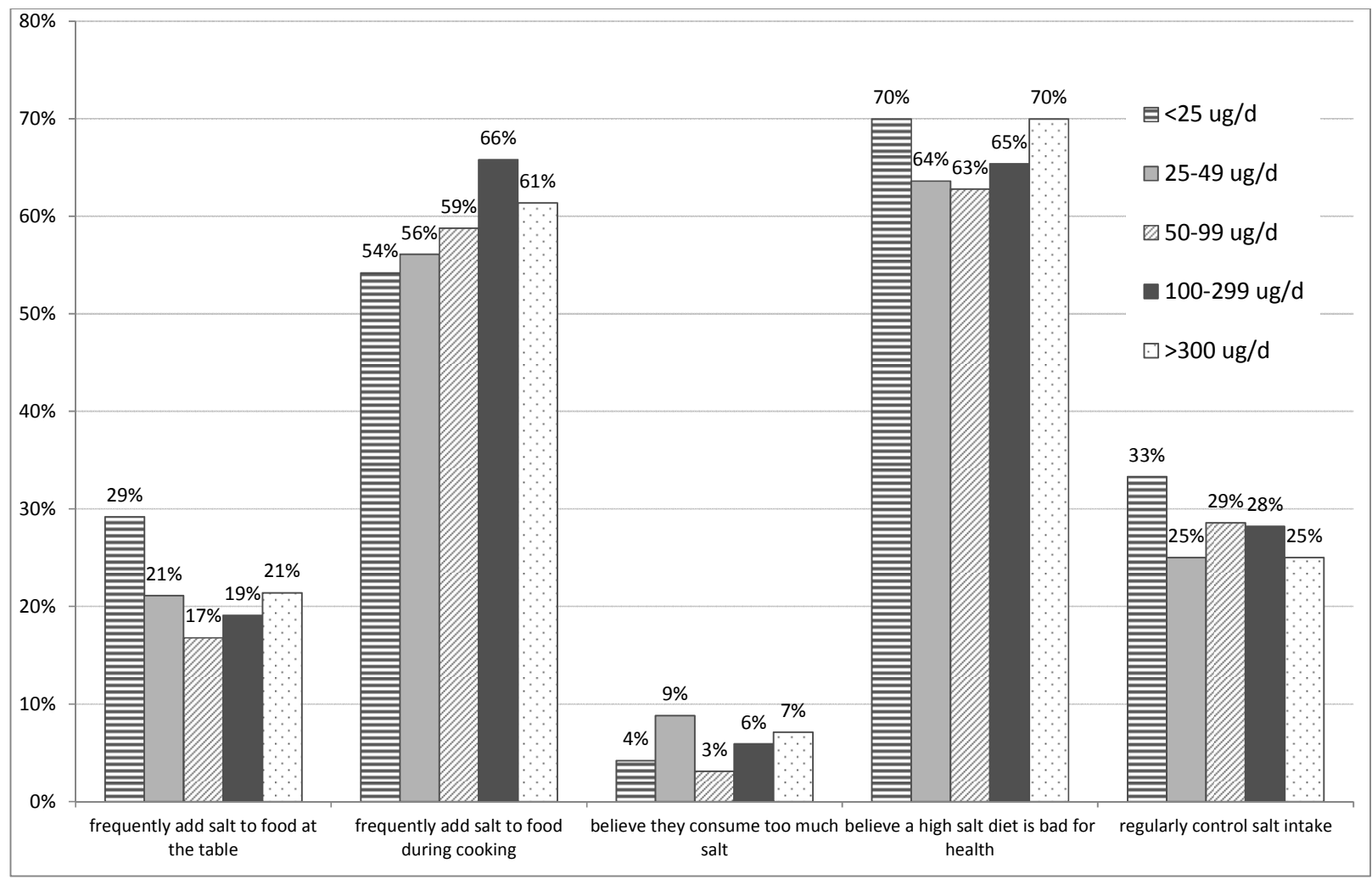
442 **Table 3.** Urinary iodine and sodium excretion by salt and iodine categories

	24-hour urinary sodium excretion								
	All n=874 ^a		Salt <5g/d n=307		Salt 5-9g/d n=322		Salt >9g/d n=245		p value
	median	IQR	median	IQR	median	IQR	median	IQR	
Sodium mg/day	2471	1434, 3506	1393	1068, 1719	2638	2219, 3057	4799	3607, 5993	<0.001
Salt g/day	6.3	3.7, 9.0	3.6	2.8, 4.5	6.8	5.7, 7.9	12.3	9.3, 15.4	<0.001
UIC µg/l	130	58, 202	102	32, 172	131	56, 206	149	78, 220	<0.001
UIC µg/g creatinine	102	48, 157	95	41, 150	105	48, 163	109	58, 161	0.076
24hr UIE µg/day	117	48, 186	74	37, 111	119	57, 181	195	117, 273	<0.001
	Spot urine iodine concentration (UIC)								
	All n=874 ^a		UIC <100 µg/l n=343		UIC 100-299 µg/l n=408		UIC >300 µg/l n=107		p value
	median	IQR	median	IQR	median	IQR	median	IQR	
Sodium mg/day	2471	1434, 3506	2102	1144, 3061	2703	1547, 3860	2855	1811, 3899	<0.001
Salt g/day	6.3	3.7, 9.0	5.4	2.9, 7.9	6.9	4.0, 9.9	7.3	4.7, 10.0	<0.001
UIC µg/l	130	58, 202	55	37, 73	169	132, 206	400	332, 469	<0.001
UIC µg/g creatinine	102	48, 157	63	37, 89	119	72, 166	247	169, 325	<0.001
24hr UIE µg/day	117	48, 186	78	38, 119	134	69, 199	240	148, 332	<0.001

443 UIC, spot urine iodine concentration; UIE, 24-hour urine iodine excretion. ^aOne individual in subsample with missing 24-hour sodium analysis.
 444 Data shown as median and interquartile range (IQR; 25th, 75th percentile). Continuous variables compared using Independent Samples Kruskal-
 445 Wallis test.

446 **Figure 1.** Self-reported salt knowledge, attitudes and behaviour by 24-hour urinary iodine excretion (UIE; n=539)

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STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(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	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
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	5-6
Bias	9	Describe any efforts to address potential sources of bias	4-6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	6
		(d) If applicable, describe analytical methods taking account of sampling strategy	7
		(e) Describe any sensitivity analyses	none
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	6-7
		(b) Give reasons for non-participation at each stage	6-7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, p 14
		(b) Indicate number of participants with missing data for each variable of interest	Table 1, p 14
Outcome data	15*	Report numbers of outcome events or summary measures	Table 3, p 16
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	none
		(b) Report category boundaries when continuous variables were categorized	7-8; Table 3, p 16; Figure 1, p 17
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	none
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10; Table 1, p 14
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
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.

BMJ Open

How will South Africa's mandatory salt reduction policy affect its salt iodisation programme? A cross-sectional analysis from the WHO-SAGE Wave 2 Salt & Tobacco study

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Keywords:	sodium, iodine, dietary, policy, nutritional requirements

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3 **1 How will South Africa's mandatory salt reduction policy affect its salt iodisation**
4 **2 programme? A cross-sectional analysis from WHO-SAGE Wave 2 Salt & Tobacco**
5 **3 study**
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9 **Short title:** Salt reduction and table salt iodisation
10

11
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25 Abstract

26 **Objective:** The World Health Organization's (WHO) global targets for non-communicable
27 disease (NCD) reduction recommend consumption of <5g salt/day. In 2016, South Africa
28 was the first country to legislate maximum salt levels in processed foods. South Africa's salt
29 iodization fortification programme has successfully eradicated iodine deficiency.
30 Simultaneous monitoring of sodium reduction and iodine status is required to ensure
31 compatibility of the two public health interventions.

32 **Design/setting/participants:** A nested cohort design within WHO's 2015 Study on global
33 AGEing and adult health (SAGE, n=2887) including individuals from households across
34 South Africa. Randomly selected adults (n=875) provided 24-hour and spot urine samples for
35 sodium and iodine concentration analysis (the primary and secondary outcome measures
36 respectively). Median 24-hour iodine excretion (UIE) and spot urinary iodine concentrations
37 (UIC) were compared by salt intakes <5g/day, 5 – 9 g/day and ≥9g/day.

38 **Results:** Median daily sodium excretion was equivalent to 6.3g salt/day (range 1-43 g/day);
39 35% had urinary sodium excretion values within the desirable range (< 5g salt/day), 37% had
40 high values (5 – 9 g salt/day) and 28% had very high values (≥ 9g salt/day). Median UIC was
41 130 µg/L (IQR=58-202), indicating population iodine sufficiency (≥100 µg/L). Both UIC and
42 UIE differed across salt intake categories (p<0.001) and were positively correlated with 24h
43 urinary sodium (r= 0.170 and 0.528 respectively; both p<0.001). Participants with salt intakes
44 <5g/day were not meeting the EAR for iodine intake (95 µg/day).

45 **Conclusions:** In a nationally representative sample of South African adults, the association
46 between indicators of population iodine status (UIC and UIE) and urinary sodium excretion
47 indicate that low salt intakes may compromise adequacy of iodine intakes in a country with
48 mandatory iodisation of table salt. The iodine status of populations undergoing salt reduction
49 strategies need to be closely monitored to prevent re-emergence of iodine deficiency.

51 Strengths and limitations of this study

- 52 • The study uses the current gold standard of 24-hour urine to assess sodium intake
- 53 • Timing of the study was immediately prior to legislation of maximum permitted salt
54 levels in processed foods
- 55 • The large sample size includes coastal and inland populations from across the country
- 56 • Lack of dietary data precludes assessment of sources of iodine or sodium
- 57 • The data is only for adults and not children

58

59 **Keywords:** iodine; sodium, dietary; policy; nutritional requirements; legislation, food

60 **Introduction**

61 Iodine deficiency remains the largest preventable cause of brain damage and mental
62 impairment worldwide. Thyroid hormone production requires an adequate supply of iodine
63 from the diet, and is essential to metabolism and growth across the lifecycle. As well as
64 cretinism in its most severe form, iodine deficiency can also result in miscarriages, stillbirths,
65 and impaired psychomotor development and behavioural problems in children born to iodine
66 deficient mothers¹. To prevent iodine deficiency disorders, the World Health Organization
67 (WHO) has endorsed universal salt iodization (USI), where all salt for human and animal
68 consumption is iodized^{2,3}. USI is hailed as a public health success story, as 75% of the
69 world's population was estimated in 2016 to use iodized salt in a total of 130 countries^{4,5}.
70 The 2016 global estimate of iodine nutrition, based on surveys of school-age children
71 conducted between 2002 and 2016, shows that the iodine intake is insufficient in 15
72 countries, sufficient in 102, and excessive in 10 countries^{6,7}. Among the 15 countries with
73 insufficient intake, only two are classified as moderately deficient and 13 as mildly deficient.
74 This represents a reduction in the number of countries with insufficient iodine intake, from 32
75 in 2011⁸, to 25 countries in 2015⁹, to 15 countries in 2016⁶ which reflects continuing progress
76 to improved coverage of iodized salt at the national level.¹⁰

77

78 In South Africa, mandatory iodization of table salt, at a level of 40 to 60 ppm, replaced
79 voluntary iodization in December 1995, using potassium iodate as the fortificant¹¹ because of
80 its stability in warm climates¹², rather than potassium iodide that is used in North America
81 and Europe. The level of fortification was subsequently revised in 2007 to allow a wider
82 range, namely 35 to 65 ppm¹³. The iodization program has effectively addressed iodine
83 deficiency in the country, but there are some loopholes in the program, such as the domestic
84 use of non-iodized agricultural salt in some regions^{14,13}. In 2005, 78% of households
85 nationwide purchased salt for household uses from typical food stores. At the same time, 8-
86 37% of households across all the provinces of South Africa obtained salt for household use
87 from "unconventional" channels such as agricultural and other sources of non-iodized salt.
88 Under the legislation, salt used in the manufacturing of processed foods and salt packaged in
89 bags of at least 20 kg are also exempted from mandatory iodization¹¹. In 2005, 77% of
90 households in the country used adequately iodized salt, described as salt containing more than

1
2
3 91 15 ppm of iodine¹³. However, data on the iodine status of the South African population is
4 92 outdated and a national survey was last conducted in 2005¹⁴. At that time, South African
5 93 women and children aged 6 to 9 y old were found to have an optimal iodine status (i.e.,
6 94 MUIC 100–199 mg/L, <20% with UIC levels <50 mg/L)¹⁵ which indicated a well-
7
8 95 functioning salt iodization program^{6,16}.

9
10
11 96 At the same time as salt iodization efforts around the world are being celebrated, there is a
12 97 global focus on salt reduction efforts to lower population level blood pressure. The World
13 98 Health Organization (WHO) and World Health Assembly targets to reduce non
14
15 99 communicable diseases (NCDs) include a 30% reduction in population salt intake by 2025¹⁷
16
17 100¹⁸. South Africa was the first country to implement mandatory legislation in July 2016 for
18
19 101 maximum salt levels permitted in a wide range of processed foods¹⁹ that are significant
20
21 102 contributors to the sodium intake of the population²⁰⁻²³. The legislation is predicted to
22
23 103 decrease population-level salt intake by 0.85 grams per day²⁴ and reduce annual deaths from
24
25 104 cardiovascular diseases by 11%. This public health strategy is estimated to save the
26
27 105 government US\$51.25 million/year in health care costs; and save households more than
28
29 106 US\$4 million/year in out-of-pocket medical expenses²⁵.

30
31 107 Since salt is the vehicle for iodine fortification, successful campaigns to reduce salt intake
32
33 108 would also likely result in reduced iodine intake²⁶. Dietary modelling conducted in the
34
35 109 Netherlands estimated the effect of 12%, 25%, and 50% decreases in salt from processed
36
37 110 foods and table salt²⁶. Only at a 50% salt decrease would iodine intake become inadequate for
38
39 111 a small percentage of the population which, at that time, confirmed a lack of conflict between
40
41 112 population-wide strategies of decreasing salt while ensuring adequate consumption of iodized
42
43 113 salt to prevent iodine deficiency. We have previously reported no difference in median UIC
44
45 114 across categories of sodium excretion equivalent to salt intakes lower than 5g/day, 5 - 9
46
47 115 g/day, and greater than or equal to 9 g/d in a convenience sample of 262 adult men and
48
49 116 women in Cape Town in 2004²⁷. It was concluded that this was because much of the dietary
50
51 117 salt consumed was provided from non-iodinated sources, presumably in salt added to
52
53 118 processed foods. Given the introduction of the salt reduction legislation, it is timeous to
54
55 119 assess the iodine status of the South African population, according to salt intakes.

56
57 120 The aim of the current study was to simultaneously measure sodium (Na) and iodine in 24hr
58
59 121 and spot urinary collections in an adult cohort to determine whether lower salt intakes are
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122 associated with a suboptimal iodine status.

123 **Methods**

124 A nested observational study was conducted as part of Wave 2 of the World Health
125 Organization Study on global AGEing and adult health (WHO SAGE). WHO-SAGE is a
126 multinational cohort study examining the health and wellbeing of adult populations and the
127 ageing process. Two waves of this longitudinal study have been completed in China, Ghana,
128 India, Mexico, Russia and South Africa²⁸. In total, 42,464 respondents were recruited across
129 the six countries for Wave 1 (2007-2010), including 4223 respondents in South Africa (9%
130 18-49 years; 40% 50-59 years; 51% 60+ years). Respondents were recruited from selected
131 probability sampled enumeration areas (EAs) using a multi-stage cluster sampling strategy,
132 with stratification by province, residence and race. Urine capture was included as part of
133 SAGE South Africa Wave 2 data collection. The sampling strategy was designed to account
134 for attrition, where households were classified into the following mutually exclusive
135 categories: 1) SAGE Wave 1 follow-up households with one or more members aged 50 years
136 or more targeted for selection; 2) new households with one or more members aged 50 years
137 or more; 3) SAGE Wave 1 follow-up households which include residents aged 18-49 targeted
138 for selection; or, 4) new households which include residents aged 18-49. Further detail on the
139 sampling and recruitment strategy can be found in the study protocol paper²⁹.

140 For Wave 2 data collection in 2015, twenty survey teams (one nurse and three interviewers
141 per team) simultaneously collected data and samples from respondents across all provinces in
142 the country over a five-month period. Respondents that were recruited to provide urine
143 collections (n=1200) were sampled from among the first households visited within each EA,
144 as a means to simplify logistics and reduce sample transit time to the central Durban
145 laboratory.

146 Inclusion criteria for urine collection were: respondent must be part of the WHO SAGE
147 cohort, with no indication of urinary incontinence or other condition that could impede 24-
148 hour urine collection; and if female, not menstruating, pregnant, or breastfeeding on the day
149 of collection.

150 **Study Measures**

151 All survey teams were trained with support from WHO Geneva. As part of the larger survey,
152 anthropometry, household and individual questionnaires, blood sampling, blood pressure
153 (BP) and physical function tests were completed as described previously in SAGE Wave 1²⁸.

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3 154 Interviewers spoke the respondents' home languages with consent forms available in the most
4 155 widely spoken languages for each area. All respondents gave free and informed consent prior
5 156 to taking part. The study complied with ethical principles³⁰ and all procedures involving
6 157 human subjects were approved by the WHO Ethics Review Committee [RPC149], and
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8 158 North-West University and University of Witwatersrand research ethics committees in South
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10 159 Africa.

13 160 **Urine collection**

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16 161 The protocol used for collection of 24-hour urine samples followed the WHO/PAHO
17 162 guidelines³¹. Respondents were requested to collect all urine produced for 24 hours,
18 163 excluding the first pass urine on day 1, but including the first urine of the following morning
19 164 (day 2) in a 5-litre plastic container containing 1g thymol as preservative in South Africa. The
20 165 spot sample was collected without preservative from the second urine passed on day 1
21 166 (marking the start of the 24-hour collection) and decanted into three 15 ml Porvair tubes
22 167 (Porvair Sciences, Leatherhead, UK) then kept in a cool box powered by the fieldwork
23 168 vehicles. The next morning, the 24-hour sample volumes were recorded and aliquots (4 x
24 169 Porvair tubes) generated with all samples then shipped to the laboratory, maintaining the cold
25 170 chain. Thymol, a crystalline natural derivative of the Thyme plant, was used as a
26 171 preservative. Thymol has been shown to prevent changes in urinary creatinine, sodium and
27 172 potassium concentrations for up to five days³². Incomplete 24-hour urine collections were
28 173 assumed if: total volume ≤ 300 ml; or creatinine excretion ≤ 4 mmol/day (women) or ≤ 6
29 174 mmol/day (men)³³.

32 175 **Urine analysis**

33 176 Sodium was determined using the indirect Ion Selective Electrode method and creatinine
34 177 analysed using the standardised urinary Jaffe kinetic method (Beckman Coulter Synchron
35 178 DXC600/800 System). The WHO population target for salt intake is 5g salt (NaCl) per day,
36 179 equivalent to urinary sodium excretion 1950mg (or 85mmol)/24hr. Sodium (mmol/l) in the
37 180 24 h urine sample was converted to salt (g/d) using the formula: Na mmol/l * 24 h volume
38 181 (litres) * 23.1 (molecular weight of sodium)/390 (390 mg sodium per 1 g sodium chloride
39 182 (salt)). With the exception of iodine, all South African samples were analysed at a single
40 183 laboratory in Durban, South Africa (Global Clinical and Viral Laboratories). Urine samples
41 184 for iodine analysis were stored at -20° C and batch analysed using the Sandell-Kolthoff
42 185 method with ammonium persulfate digestion and microplate reading³⁴ at the North-West

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3 186 University Centre of Excellence for Nutrition. The laboratory participates successfully in the
4 187 Program to Ensure the Quality of Urinary Iodine Procedures (EQUIP, U.S. Centres for
5 188 Disease Control and Prevention, Atlanta GA, USA)³⁵. To convert urinary excretion values to
6 189 estimated daily iodine intake (ug/day), UIE (ug/24hr) values were divided by 0.92 to account
7 190 for the 92% bioavailability (approximately 8% of consumed dietary iodine consumption is
8 191 absorbed). A median of <100µg iodine/L indicates population-level deficiency (there are no
9 192 reference ranges for individuals)³⁶.
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16 194 **Data capture, analysis and statistical power**

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19 195 All data was captured using an electronic data capture system and uploaded to a secure
20 196 central server for data cleaning and analysis. The nested cohort sample size for the primary
21 197 outcome measure of 24-hour urine sodium was calculated as previously described.²⁹
22 198 Allowing for error in 24-hour sample collection (incomplete or missing samples) in this
23 199 complex field study, a target sub-sample size of 1200 was randomly selected from the main
24 200 SAGE-Wave 2 cohort, and those with incomplete or missing samples excluded from the
25 201 analysis. The sample size used for this analysis was deemed adequate based on
26 202 recommendations of WHO (2007) that states a sample size between 600 and 900 is sufficient
27 203 to have a reasonable confidence interval around the coverage estimate for urinary iodine
28 204 concentration². More recently, Karmisholt (2014) recommends that 400 urine samples are
29 205 required to determine the median UIC of a group with 5% precision³⁷.
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38 206 Both spot urinary iodine analyses (UIC) and 24hr urinary iodine excretion (UIE) were
39 207 compared across three categories of 24hr urinary Na values, equivalent to salt intakes
40 208 <5g/day, 5 – 9 g/day and ≥9g/day. Normality of data was assessed by visual inspection of
41 209 histograms and the Kolmogorov-Smirnov test. All non-parametric data were reported as
42 210 median and interquartile range (IQR; 25th, 75th percentile) and continuous variables compared
43 211 using independent Samples Mann-Whitney U test or Independent Samples Kruskal-Wallis
44 212 test. Categorical variables were compared across groups using Pearson Chi-Square and
45 213 Fisher's Exact Test. Data were also analysed according to urinary Na excretion values and by
46 214 iodine category (sub-optimal: UIC <100 ug/L; iodine replete: 100 – 299 ug/L; and excessive:
47 215 >300ug/L). To assess the association between salt intake, body size, UIC and UIE,
48 216 Spearman's rank order and partial correlations were conducted.
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218 Results

219 Complete urinary Na and iodine data were available in n = 874 participants.
220 Sociodemographic characteristics and health indicators of the sub-sample are compared to the
221 total SAGE-Wave 2 cohort (n = 2887) in Table 1. The sub-sample had a higher proportion of
222 women and more black/coloured respondents than the main cohort, which may explain
223 differences in smoking, education and BP.

224 Median 24hr Na excretion (n=874) was equivalent to a median salt intake of 6.3gsalt/day
225 (range 1-43 g/day); 35% had values within the desirable range (< 5g salt/day), 37% had high
226 values (5 – 9 g salt/day) and 28% had very high values (\geq 9g salt/day). We have previously
227 reported that median salt intakes are higher in younger than older (50+ y) adults in this cohort
228 (8.6 g vs 6.1 g/day; $p < 0.001$), and in urban compared to rural dwellers (7.0 g vs 6.0 g/day;
229 $p=0.033$)³⁸ but further analysis of Na vs iodine excretion, by demographic breakdown is
230 outside the scope of the current analysis. No significant difference in median UIE was found
231 according to age category (18-49y; 50+y) or sex, however median UIE was significantly
232 higher in urban compared to rural dwellers (128 (IQR147) vs 115 (IQR 119); $p=0.041$). No
233 demographic differences were found for median UIC. In the total sample, median UIC
234 (n=875) was 130 $\mu\text{g/L}$ (IQR=58-202), indicating iodine sufficiency ($\geq 100 \mu\text{g/L}$) while
235 median 24hr UIE (n=866) was 117 $\mu\text{g/day}$ (IQR 138).

236
237 Both UIC and 24hr iodine excretion differed across urinary salt categories and were
238 positively correlated with urinary Na ($r= 0.172$ and 0.533 ; both $P<0.001$) (Table 2). In the
239 lowest salt category of <5g/d, median UIC indicated borderline deficiency of 102 $\mu\text{g/L}$
240 (Table 3). According to median 24hr UIE values, the group of participants with a salt intake
241 of <5g/day are not meeting their dietary n Estimated Average Requirement (EAR) of
242 95 $\mu\text{g/day}$ (IOM 2003).³⁹, with 58.4% having intakes below this value (Table 3). Responses to
243 questions on salt behaviours did not differ between participants across median UIC categories
244 (data not shown), nor according to UIE (Figure 1).

245

246 Discussion

247 Our study found that in a sample of South African adults, those with a salt intake within the
248 WHO recommended range of less than 5g/day had urinary iodine excretion values indicative

249 of suboptimal iodine intakes, whereas those with higher salt intakes were shown to have
250 adequate intakes using 24hour urinary iodine excretion as a biomarker of intake. . Thus, there
251 is a risk that sodium reduction strategies may impact adversely on iodine intakes and result in
252 populations being at risk of inadequate iodine intakes unless fortificant levels of iodine in salt
253 are revised accordingly.

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255 This data was collected immediately prior to introduction of South Africa's mandatory salt
256 reduction legislation, that requires food manufacturers to comply with maximum salt targets
257 across a wide range of processed foods. The impact of the salt reduction policy on iodised
258 salt intake is unknown. South Africa has had a well functioning table salt iodisation
259 programme since 2005, but salt used in food processing is exempt from mandatory iodisation.
260 Despite iodised salt not being required by law to be used as an ingredient in the
261 manufacturing of processed foods, a study⁴⁰ that investigated the iodine content of salt used
262 in bread, margarine, and salty snack flavourings in 2002 provided surprising results. Even
263 though 11 of the 12 manufacturers surveyed at that time reported that they used non-iodized
264 salt in their products, substantial amounts of iodine were found in the salt used by a third of
265 these manufacturers' products, with a mean content of 39 to 69 ppm, and these were the items
266 that were mostly distributed countrywide. An appreciable percentage of the food companies
267 used iodized salt unknowingly in the manufacturing of frequently consumed processed foods,
268 and this may have had a considerable impact on the daily iodine intake of consumers. To our
269 knowledge, there is no updated information on the use of iodised salt by food manufacturers.
270 Thus, it is feasible that the salt reduction legislation may also impact on contribution of
271 iodine intake from iodised salt.

272
273 As well as changes to the food supply, nutrition education activities undertaken by the
274 Department of Health and non-governmental organizations in South Africa aim to change
275 consumer behaviour related to table salt use^{41 42}. The timing of the WHO SAGE Salt &
276 Tobacco sub-study in South Africa was planned to provide a baseline population salt intake³⁸
277 one year before mandatory salt legislation, in order for comparison in the same cohort one
278 year after introduction of the legislation²⁹ in SAGE Wave 3. The data reported in this paper
279 relate to the pre-salt reduction legislation baseline timepoint. Inclusion of iodine analyses in
280 Wave 3 in 2018 will further allow evaluation of the compatibility of iodine fortification and
281 salt reduction policies.

282

283 Concerted efforts are being made in many countries to lower salt consumption¹⁸. Because the
284 primary food vehicle for iodine fortification is salt, there is concern that decreasing salt
285 consumption will increase the risk of iodine deficiency. Our study findings indicate that this
286 is a potential public health problem. The findings of the current study are in contrast to
287 previous findings from a sample of adult men and women surveyed in Cape Town in 2004,
288 when UIC did not differ across categories of salt intake²¹. Reasons for this are unclear but
289 may reflect an increased consumption of salt provided from non-iodised sources in processed
290 foods, accompanied by a reduction in discretionary iodised salt intake, since 2004.
291 However, data is not available to further postulate in this regard.

292 The South African strategic plan to reduce cardiovascular disease includes the target to
293 reduce the population intake of salt to less than 5 grams/day. At present the salt intake is
294 higher than this level, with older reports from the early 2000s estimating that 40% salt was
295 provided from discretionary salt intake²². Our study was conducted immediately prior to
296 introduction of the mandatory salt targets in processed foods. The salt intake estimations in
297 the current study include both added (discretionary) and non-discretionary salt intakes but the
298 lack of data on dietary intakes of the participants prevents further investigation of the source
299 of the salt.

300 We hypothesize that food manufacturers may have already reduced salt content in processed
301 foods at the time of the study (2015), and that some of these products may have been
302 produced with iodized salt. If this is the case, this would result in lowered iodine intake at the
303 same time as lowered salt intake, as would any reduction in discretionary salt use.
304 Considering the latter, there have been many accompanying health education strategies that
305 target salt reduction behaviours, alongside the salt legislation in processed foods⁴². In 2015, a
306 mass media campaign (Saltwatch), using television, radio advertisement and other platforms
307 for information dissemination was undertaken to increase public awareness related to the
308 association between a high salt intake, blood pressure and cardiovascular disease in South
309 Africa. The campaign, conducted by the Heart and Stroke Foundation of South Africa with
310 funding from the Department of Health, focused on the need to reduce discretionary salt
311 intake. Evaluation of the programme undertaken in 550 black women, aged 18-55 years in
312 three provinces identified that there was an increase in most of the indicators of knowledge,
313 attitudes and behaviour change towards considering and initiating reduced salt consumption
314 following the campaign. Significant increases were found for knowledge items related to high
315 salt intake and its health outcomes. Participants also reported that they added less salt while

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3 316 cooking and at the table. In the current study, responses to questions on salt behaviours did
4 317 not differ between participants across median UIC categories, nor according to 24-hr UIE.
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6 318 This could mean that the questions are not sufficiently sensitive to discern between salt intake
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8 319 behaviours, or that the contribution of discretionary salt to total iodine intake is influenced by
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10 320 other food sources of iodised salt.

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12 321 A strength of the current study was use of the gold standard method for assessment of salt
13 322 intake, namely 24hr urinary collections. Limitations relate to the high number of respondents
14 323 with missing or incomplete urine samples. The difficulty in obtaining complete 24-hour urine
15 324 samples is well-known, and the comparison between the main study cohort and those
16 325 providing complete samples shows that men, and those with higher education less frequently
17 326 provided complete 24-hour urine. This may also reflect the nature of the survey as
18 327 fieldworkers visited the respondent's homes and those that were away with work were less
19 328 likely to have taken part or would have potentially had more difficulty with the urine
20 329 collection, creating a selection bias in the data towards the population with lower
21 330 employment levels. Future research may consider workplace-based data collection. An
22 331 assumption was made regarding cut-off values for completeness of 24hr urine collection
23 332 whereby urinary volume < 300ml/day or creatinine excretion ≤ 4 mmol/day (women) or ≤ 6
24 333 mmol/day (men)³³ were the criteria used for exclusion purposes. In populations with low
25 334 protein intakes, daily creatinine excretion is more variable than in well nourished populations,
26 335 and often lower than 1 g (8.84 mmol)per day.⁴³ A limitation of the study is that neither
27 336 dietary protein intake, nor lean body mass was assessed which makes it difficult to account
28 337 for these two confounding variables when deciding on how to interpret low urinary creatinine
29 338 concentrations.

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42 340 A further limitation is the lack of dietary data on sources of iodine provided by foods other
43 341 than iodised salt. Iodine-rich dietary sources include fish and seafood, and dairy products and
44 342 it is possible that some of these foods may also be high in salt, as in the case of salted dried
45 343 fish commonly consumed by the coloured population (known as "*bokkems*"). However,
46 344 generally these foods are not major contributors to sodium in the South African diet²².
47 345 Interestingly, in women, both UIC and UIE correlated positively with body mass index,
48 346 independently of salt intake. Looking at changes in food consumption patterns in South
49 347 Africa over time, it seems that there is not only an increase in processed foods but also other
50 348 foods that may contribute to iodine intake independently of iodized salt such as fish, eggs,

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3 349 seafood, and dairy foods⁴⁴. The contribution of food sources, other than iodized salt, to total
4 350 iodine intake warrants further investigation in the context of evaluating the mandatory salt
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6 351 iodization programme in South Africa. Furthermore, this study presents limited data for
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8 352 women of child bearing age and no data for children. Further work is needed to determine if
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10 353 there is an impact of the sodium reduction legislation in these particularly iodine-sensitive
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12 354 groups.

13 355 **Conclusion**

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16 356 This study highlights the need to closely monitor the iodine status of populations as they
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18 357 undergo population-level reductions in salt intake, in countries where mandatory salt
19
20 358 iodisation is implemented. If salt intake levels drop to the WHO target of <5g/day, there may
21
22 359 be a need to increase the level of iodine in fortified table salt. Alternatively, compulsory
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24 360 iodisation of salt used in the production of some staple foods such as bread may be
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26 361 considered. In a country where some sectors of the population may be exposed to excessive
27
28 362 iodine intakes, this strategy would require careful dietary modelling before being pursued. It
29
30 363 is recommended that surveys that measure urinary Na excretion also simultaneously measure
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32 364 urinary iodine concentration and determine the iodine content in table salt collected from
33
34 365 households.

35
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383 All authors read and approved the final manuscript.

384 Data sharing statement: The dataset is available on request and will form part of the data
385 catalogue of the World Health Organization Study on Global AGEing and Adult Health
386 (SAGE) (<http://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/sage/about>)
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510 **Table 1.** Characteristics of the main (SAGE South Africa Wave 2, 2015) and subsample
511 study cohort.

	Main SAGE cohort		Subsample ^a		p value
	n=2887		n=875		
	median	IQR	median	IQR	
Female, n (%)	1939	67	671	77	<0.001
Age years	57	46, 69	55	44, 67	0.468
Aged over 50 years, n (%)	1979	69	567	65	0.171
Ethnicity, n (%)					
Black	1988	69	410	74	<0.001
Coloured, mixed race	465	16	96	17	
Indian	306	11	41	7	
White	128	4	11	2	
Rural, n (%)	792	28	163	29	0.418
Education years	10	7, 13	9	6, 12	0.028
Never been to school, n (%)	495	18	109	20	0.180
Never had paid employment, n (%)	1101	55	238	56	0.403
BMI, kg/m ²	28.8	23.9, 33.7	29.1	24.0, 34.2	0.540
Waist to height ratio	0.59	0.52, 0.67	0.58	0.50, 0.66	0.070
Never used alcohol, n (%)	1576	80	353	83	0.052
Never used tobacco, n (%)	1635	83	367	86	0.023
Systolic BP mmHg	131	118, 144	128	116, 141	0.073
Diastolic BP mmHg	81	73, 89	79	71, 87	0.029
Hypertension, n (%)	1233	45	232	43	0.239
Diabetes, n (%)	248	13	46	11	0.355

512 BMI, body mass index. ^aSubsample: all respondents with spot UIC, valid 24-hour urine, sex
513 and age recorded. Some variables may contain missing data as indicated by percentages. Data
514 shown as median and interquartile range (IQR; 25th, 75th percentile) unless otherwise
515 indicated. Hypertensive by measured BP \geq 140 and/or 90mmHg or previous diagnosis.
516 Education, tobacco/alcohol use, ethnicity, employment and diabetes prevalence by self-
517 report. Continuous variables compared using Independent Samples Mann-Whitney U test,
518 categorical variables compared using Pearson Chi-Square and Fisher's Exact Test.

519

520 **Table 2.** Spearman's rank order and partial correlations between urine iodine concentration,
 521 salt, and body size SAGE South Africa Wave 2 (2015).

		All n=456	Men n=110	Women n=346
<i>Correlations with spot UIC $\mu\text{g/l}$</i>				
Salt intake g/day	<i>rho</i>	0.166(***)	0.164	0.153(**)
	<i>p</i>	0.000	0.088	0.004
24-hr iodine $\mu\text{g/day}$	<i>rho</i>	0.423(***)	0.483(***)	0.392(***)
	<i>p</i>	0.000	0.000	0.000
BMI kg/m^2	<i>r</i>	0.036	0.001	0.096
	<i>p</i>	0.448	0.988	0.076
Weight kg	<i>r</i>	0.043	0.035	0.056
	<i>p</i>	0.365	0.716	0.299
Waist circumference cm	<i>r</i>	0.001	0.027	0.008
	<i>p</i>	0.991	0.784	0.878
Hip circumference cm	<i>r</i>	0.040	0.213(*)	0.008
	<i>p</i>	0.389	0.026	0.883
<i>Correlations with 24-hr UIE $\mu\text{g/d}$</i>				
Salt intake g/day	<i>rho</i>	0.552(***)	0.504(***)	0.561(***)
	<i>p</i>	0.000	0.000	0.000
BMI kg/m^2	<i>r</i>	0.092	0.030	0.168(**)
	<i>p</i>	0.051	0.758	0.002
Weight kg	<i>r</i>	0.130(**)	-0.023	0.193(***)
	<i>p</i>	0.005	0.814	0.000
Waist circumference cm	<i>r</i>	0.032	-0.011	0.069
	<i>p</i>	0.491	0.911	0.200
Hip circumference cm	<i>r</i>	0.052	0.056	0.094
	<i>p</i>	0.269	0.563	0.080

522 BMI, body mass index; UIC, spot urine iodine concentration; UIE, 24-hour urine iodine
 523 excretion. Correlations between iodine and body size controlled for salt intake. Correlation is
 524 significant at the 0.05 level (*); at the 0.01 level (**); or at the 0.001 level (***)

525 **Table 3.** Urinary iodine, estimated iodine intake and sodium excretion values by salt intake equivalent categories

	24-hour urinary sodium excretion								p value
	All n=874 ^a		Salt <5g/d n=307		Salt 5-9g/d n=322		Salt >9g/d n=245		
	median	IQR	median	IQR	median	IQR	median	IQR	
Sodium mg/day	2471	1434, 3506	1393	1068, 1719	2638	2219, 3057	4799	3607, 5993	<0.001
Salt g/day	6.3	3.7, 9.0	3.6	2.8, 4.5	6.8	5.7, 7.9	12.3	9.3, 15.4	<0.001
UIC µg/l	130	58, 202	102	32, 172	131	56, 206	149	78, 220	<0.001
24hr UIE µg/day	117	48, 186	74	37, 111	119	57, 181	195	117, 273	<0.001
Estimated iodine intake µg/day	127	52, 202	80	40, 120	130	63, 197	212	127, 297	<0.001
% with daily iodine intake below EAR for iodine (95 µg/day)†	37.1%		58.4%		34.7%		13.5%		

526 UIC, spot urine iodine concentration; UIE, 24-hour urine iodine excretion. ^aOne individual in subsample with missing 24-hour sodium analysis.
 527 Data shown as median and interquartile range (IQR; 25th, 75th percentile). Continuous variables compared using Independent Samples Kruskal-
 528 Wallis test.

529 † Daily iodine intake assumed as 24hr UIE (µg/day)/0.92 to account for bioavailability

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532 **Figure Legend: Self-reported salt knowledge, attitudes and behaviour by 24-hour urinary iodine excretion (UIE; n=539)**
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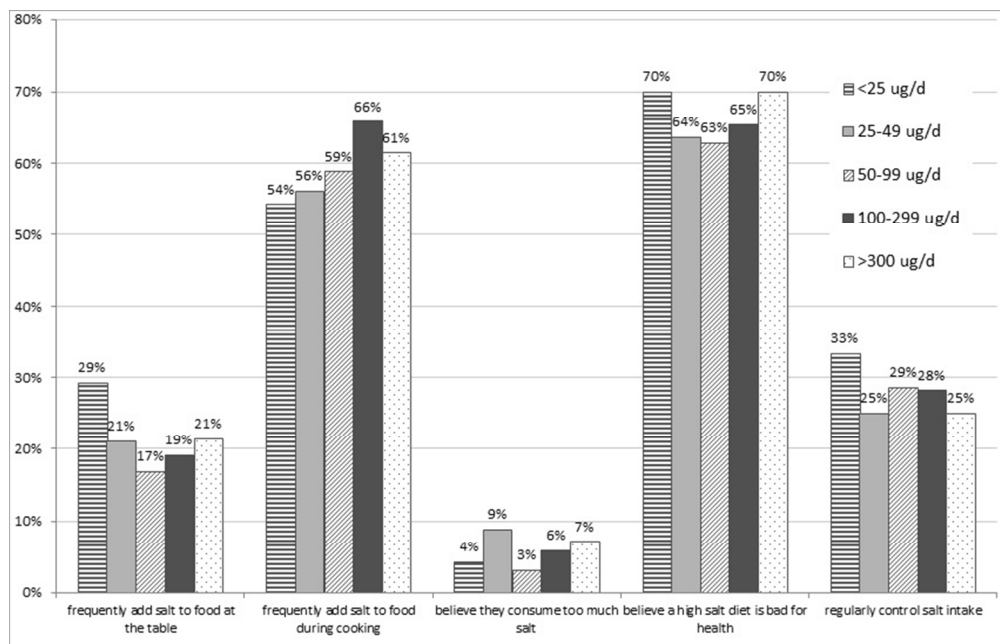


Figure 1. Self-reported salt knowledge, attitudes and behaviour by 24-hour urinary iodine excretion (UIE; n=539)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study’s design with a commonly used term in the title or the abstract	1
		(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	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
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	5-6
Bias	9	Describe any efforts to address potential sources of bias	4-6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	6
		(d) If applicable, describe analytical methods taking account of sampling strategy	7
		(e) Describe any sensitivity analyses	none
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	6-7
		(b) Give reasons for non-participation at each stage	6-7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, p 14
		(b) Indicate number of participants with missing data for each variable of interest	Table 1, p 14
Outcome data	15*	Report numbers of outcome events or summary measures	Table 3, p 16
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	none
		(b) Report category boundaries when continuous variables were categorized	7-8; Table 3, p 16; Figure 1, p 17
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	none
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10; Table 1, p 14
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
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.

BMJ Open

How will South Africa's mandatory salt reduction policy affect its salt iodisation programme? A cross-sectional analysis from the WHO-SAGE Wave 2 Salt & Tobacco study

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Secondary Subject Heading:	Nutrition and metabolism, Public health
Keywords:	sodium, iodine, dietary, policy, nutritional requirements

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3 **1 How will South Africa's mandatory salt reduction policy affect its salt iodisation**
4 **2 programme? A cross-sectional analysis from the WHO-SAGE Wave 2 Salt & Tobacco**
5 **3 study**
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9 **Short title:** Salt reduction and table salt iodisation
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3 264
5 276 28 **Abstract**

7
8 29 **Objective:** The World Health Organization's (WHO) global targets for non-communicable
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10 30 disease (NCD) reduction recommend consumption of <5g salt/day. In 2016, South Africa
11 31 was the first country to legislate maximum salt levels in processed foods. South Africa's salt
12 32 iodization fortification programme has successfully addressed iodine deficiency but
13
14 33 information is dated. Simultaneous monitoring of sodium reduction and iodine status is
15
16 34 required to ensure compatibility of the two public health interventions.

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18 35 **Design/setting/participants:** A nested cohort design within WHO's 2015 Study on global
19 36 AGEing and adult health (SAGE, n=2887) including individuals from households across
20 37 South Africa. Randomly selected adults (n=875) provided 24-hour and spot urine samples for
21 38 sodium and iodine concentration analysis (the primary and secondary outcome measures
22 39 respectively). Median 24-hour iodine excretion (UIE) and spot urinary iodine concentrations
23 40 (UIC) were compared by salt intakes <5g/day, 5 – 9 g/day and ≥9g/day.

24
25 41 **Results:** Median daily sodium excretion was equivalent to 6.3g salt/day (range 1-43 g/day);
26 42 35% had urinary sodium excretion values within the desirable range (< 5g salt/day), 37% had
27 43 high values (5 – 9 g salt/day) and 28% had very high values (≥ 9g salt/day). Median UIC was
28 44 130 µg/L (IQR=58-202), indicating population iodine sufficiency (≥100 µg/L). Both UIC and
29 45 UIE differed across salt intake categories (p<0.001) and were positively correlated with
30 46 estimated salt intake (r= 0.166 and 0.552 respectively; both p<0.001). Participants with salt
31 47 intakes <5g/day were not meeting the EAR for iodine intake (95 µg/day).

32 48 **Conclusions:** In a nationally representative sample of South African adults, the association
33 49 between indicators of population iodine status (UIC and UIE) and salt intake, estimated using
34 50 24hr urinary sodium excretion, indicate that low salt intakes may compromise adequacy of
35 51 iodine intakes in a country with mandatory iodisation of table salt. The iodine status of
36 52 populations undergoing salt reduction strategies need to be closely monitored to prevent re-
37 53 emergence of iodine deficiency.

38 54

39 55 **Strengths and limitations of this study**

- 40 56
- 41 57 • The study uses the current gold standard of 24-hour urine to assess sodium intake
 - 42 58 • Timing of the study was immediately prior to legislation of maximum permitted salt
43 59 levels in processed foods
- 44 60

- 59 • The large sample size includes coastal and inland populations from across the country
- 60 • Lack of dietary data precludes assessment of sources of iodine or sodium
- 61 • The data is only for adults and not children

62
63 **Keywords:** iodine; sodium, dietary; policy; nutritional requirements; legislation, food

64 **Introduction**

65 Iodine deficiency remains the largest preventable cause of brain damage and mental
66 impairment worldwide. Thyroid hormone production requires an adequate supply of iodine
67 from the diet, and is essential to metabolism and growth across the lifecycle. As well as
68 cretinism in its most severe form, iodine deficiency can also result in miscarriages, stillbirths,
69 and impaired psychomotor development and behavioural problems in children born to iodine
70 deficient mothers¹. To prevent iodine deficiency disorders, the World Health Organization
71 (WHO) has endorsed universal salt iodization (USI), where all salt for human and animal
72 consumption is iodized^{2,3}. USI is hailed as a public health success story, as 75% of the
73 world's population was estimated in 2016 to use iodized salt in a total of 130 countries^{4,5}.
74 The 2016 global estimate of iodine nutrition, based on surveys of school-age children
75 conducted between 2002 and 2016, shows that the iodine intake is insufficient in 15
76 countries, sufficient in 102, and excessive in 10 countries^{6,7}. Among the 15 countries with
77 insufficient intake, only two are classified as moderately deficient and 13 as mildly deficient.
78 This represents a reduction in the number of countries with insufficient iodine intake, from 32
79 in 2011⁸, to 25 countries in 2015⁹, to 15 countries in 2016⁶ which reflects continuing progress
80 to improved coverage of iodized salt at the national level.¹⁰

81
82 In South Africa, mandatory iodization of table salt, at a level of 40 to 60 ppm, replaced
83 voluntary iodization in December 1995, using potassium iodate as the fortificant¹¹ because of
84 its stability in warm climates¹², rather than potassium iodide that is used in North America
85 and Europe. The level of fortification was subsequently revised in 2007 to allow a wider
86 range, namely 35 to 65 ppm¹³. The iodization program has effectively addressed iodine
87 deficiency in the country, but there are some loopholes in the program, such as the domestic
88 use of non-iodized agricultural salt in some regions^{14,13}. In 2005, 78% of households
89 nationwide purchased salt for household uses from typical food stores. At the same time, 8-
90 37% of households across all the provinces of South Africa obtained salt for household use

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3 91 from “unconventional” channels such as agricultural and other sources of non-iodized salt.
4 92 Under the legislation, salt used in the manufacturing of processed foods and salt packaged in
5 93 bags of at least 20 kg are also exempted from mandatory iodization¹¹. In 2005, 77% of
6 94 households in the country used adequately iodized salt, described as salt containing more than
7 95 15 ppm of iodine¹³. However, data on the iodine status of the South African population is
8 96 outdated and a national survey was last conducted in 2005¹⁴. At that time, South African
9 97 women and children aged 6 to 9 y old were found to have an optimal iodine status (i.e.,
10 98 MUIC 100–199 mg/L, <20% with UIC levels <50 mg/L)¹⁵ which indicated a well-
11 99 functioning salt iodization program^{6,16}.

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18 100 At the same time as salt iodization efforts around the world are being celebrated, there is a
19 101 global focus on salt reduction efforts to lower population level blood pressure. The World
20 102 Health Organization (WHO) and World Health Assembly targets to reduce non
21 103 communicable diseases (NCDs) include a 30% reduction in population salt intake by 2025¹⁷
22 104 ¹⁸. South Africa was the first country to implement mandatory legislation in July 2016 for
23 105 maximum salt levels permitted in a wide range of processed foods¹⁹ that are significant
24 106 contributors to the sodium intake of the population²⁰⁻²³. The legislation is predicted to
25 107 decrease population-level salt intake by 0.85 grams per day²⁴ and reduce annual deaths from
26 108 cardiovascular diseases by 11%. This public health strategy is estimated to save the
27 109 government US\$51.25 million/year in health care costs; and save households more than
28 110 US\$4 million/year in out-of-pocket medical expenses²⁵.

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37 111 Since salt is the vehicle for iodine fortification, successful campaigns to reduce salt intake
38 112 would also likely result in reduced iodine intake²⁶. Dietary modelling conducted in the
39 113 Netherlands estimated the effect of 12%, 25%, and 50% decreases in salt from processed
40 114 foods and table salt²⁶. Only at a 50% salt decrease would iodine intake become inadequate for
41 115 a small percentage of the population which, at that time, confirmed a lack of conflict between
42 116 population-wide strategies of decreasing salt while ensuring adequate consumption of iodized
43 117 salt to prevent iodine deficiency. We have previously reported no difference in median UIC
44 118 across categories of sodium excretion equivalent to salt intakes lower than 5g/day, 5 - 9
45 119 g/day, and greater than or equal to 9 g/d in a convenience sample of 262 adult men and
46 120 women in Cape Town in 2004²⁷. It was concluded that this was because much of the dietary
47 121 salt consumed was provided from non-iodinated sources, presumably in salt added to
48 122 processed foods. Given the introduction of the salt reduction legislation, it is timeous to
49 123 assess the iodine status of the South African population, according to salt intakes.

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3 124 The aim of the current study was to simultaneously measure sodium (Na) and iodine in 24hr
4 125 and spot urinary collections in an adult cohort to determine whether lower salt intakes are
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6 126 associated with a suboptimal iodine status.
7

8 127 **Methods**

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11 128 A nested observational study was conducted as part of Wave 2 of the World Health
12 129 Organization Study on global AGEing and adult health (WHO SAGE). WHO-SAGE is a
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14 130 multinational cohort study examining the health and wellbeing of adult populations and the
15
16 131 ageing process. Two waves of this longitudinal study have been completed in China, Ghana,
17 132 India, Mexico, Russia and South Africa²⁸. In total, 42,464 respondents were recruited across
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19 133 the six countries for Wave 1 (2007-2010), including 4223 respondents in South Africa (9%
20 134 18-49 years; 40% 50-59 years; 51% 60+ years). Respondents were recruited from selected
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22 135 probability sampled enumeration areas (EAs) using a multi-stage cluster sampling strategy,
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24 136 with stratification by province, residence and race. Urine capture was included as part of
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26 137 SAGE South Africa Wave 2 data collection. The sampling strategy was designed to account
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28 138 for attrition, where households were classified into the following mutually exclusive
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30 139 categories: 1) SAGE Wave 1 follow-up households with one or more members aged 50 years
31 140 or more targeted for selection; 2) new households with one or more members aged 50 years
32 141 or more; 3) SAGE Wave 1 follow-up households which include residents aged 18-49 targeted
33 142 for selection; or, 4) new households which include residents aged 18-49. Further detail on the
34
35 143 sampling and recruitment strategy can be found in the study protocol paper²⁹.

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38 144 For Wave 2 data collection in 2015, twenty survey teams (one nurse and three interviewers
39 145 per team) simultaneously collected data and samples from respondents across all provinces in
40
41 146 the country over a five-month period. Respondents that were recruited to provide urine
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43 147 collections (n=1200) were sampled from among the first households visited within each EA,
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45 148 as a means to simplify logistics and reduce sample transit time to the central Durban
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47 149 laboratory.

48 150 Inclusion criteria for urine collection were: respondent must be part of the WHO SAGE
49 151 cohort, with no indication of urinary incontinence or other condition that could impede 24-
50 152 hour urine collection; and if female, not menstruating, pregnant, or breastfeeding on the day
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52 153 of collection.
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54 154 **Study Measures**

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3 155 All survey teams were trained with support from WHO Geneva. As part of the larger survey,
4 156 anthropometry, household and individual questionnaires, blood sampling, blood pressure
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6 157 (BP) and physical function tests were completed as described previously in SAGE Wave 1²⁸.
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8 158 Interviewers spoke the respondents' home languages with consent forms available in the most
9
10 159 widely spoken languages for each area. All respondents gave free and informed consent prior
11
12 160 to taking part. The study complied with ethical principles³⁰ and all procedures involving
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14 161 human subjects were approved by the WHO Ethics Review Committee [RPC149], and
15
16 162 North-West University and University of Witwatersrand research ethics committees in South
17
18 163 Africa.

164 **Urine collection**

165 The protocol used for collection of 24-hour urine samples followed the WHO/PAHO
166 guidelines³¹. Respondents were requested to collect all urine produced for 24 hours,
167 excluding the first pass urine on day 1, but including the first urine of the following morning
168 (day 2) in a 5-litre plastic container containing 1g thymol as preservative in South Africa. The
169 spot sample was collected without preservative from the second urine passed on day 1
170 (marking the start of the 24-hour collection) and decanted into three 15 ml Porvair tubes
171 (Porvair Sciences, Leatherhead, UK) then kept in a cool box powered by the fieldwork
172 vehicles. The next morning, the 24-hour sample volumes were recorded and aliquots (4 x
173 Porvair tubes) generated with all samples then shipped to the laboratory, maintaining the cold
174 chain. Thymol, a crystalline natural derivative of the Thyme plant, was used as a
175 preservative. Thymol has been shown to prevent changes in urinary creatinine, sodium and
176 potassium concentrations for up to five days³². Incomplete 24-hour urine collections were
177 assumed if: total volume ≤ 300 ml; or creatinine excretion ≤ 4 mmol/day (women) or ≤ 6
178 mmol/day (men)³³.

179 **Urine analysis**

180 Sodium was determined using the indirect Ion Selective Electrode method and creatinine
181 analysed using the standardised urinary Jaffe kinetic method (Beckman Coulter Synchron
182 DXC600/800 System). The WHO population target for salt intake is 5g salt (NaCl) per day,
183 equivalent to urinary sodium excretion 1950mg (or 85mmol)/24hr. Sodium (mmol/l) in the
184 24 h urine sample was converted to salt (g/d) using the formula: Na mmol/l * 24 h volume
185 (litres) * 23.1 (molecular weight of sodium)/390 (390 mg sodium per 1 g sodium chloride
186 (salt)). With the exception of iodine, all South African samples were analysed at a single

187 laboratory in Durban, South Africa (Global Clinical and Viral Laboratories). Urine samples
188 for iodine analysis were stored at -20°C and batch analysed using the Sandell-Kolthoff
189 method with ammonium persulfate digestion and microplate reading³⁴ at the North-West
190 University Centre of Excellence for Nutrition. The laboratory participates successfully in the
191 Program to Ensure the Quality of Urinary Iodine Procedures (EQUIP, U.S. Centres for
192 Disease Control and Prevention, Atlanta GA, USA)³⁵. To convert urinary excretion values to
193 estimated daily iodine intake (ug/day), UIE (ug/24hr) values were divided by 0.92, based on
194 the assumption that approximately 92% of dietary iodine is excreted in urine. A median of
195 $<100\mu\text{g}$ iodine/L indicates population-level deficiency (there are no reference ranges for
196 individuals)³⁶.

198 **Data capture, analysis and statistical power**

199 All data was captured using an electronic data capture system and uploaded to a secure
200 central server for data cleaning and analysis. The nested cohort sample size for the primary
201 outcome measure of 24-hour urine sodium was calculated as previously described.²⁹
202 Allowing for error in 24-hour sample collection (incomplete or missing samples) in this
203 complex field study, a target sub-sample size of 1200 was randomly selected from the main
204 SAGE-Wave 2 cohort, and those with incomplete or missing samples excluded from the
205 analysis. The sample size used for this analysis was deemed adequate based on
206 recommendations of WHO (2007) that states a sample size between 600 and 900 is sufficient
207 to have a reasonable confidence interval around the coverage estimate for urinary iodine
208 concentration². More recently, Karmisholt (2014) recommends that 400 urine samples are
209 required to determine the median UIC of a group with 5% precision³⁷.

210 Both spot urinary iodine analyses (UIC) and 24hr urinary iodine excretion (UIE) were
211 compared across three categories of 24hr urinary Na values, equivalent to salt intakes
212 $<5\text{g/day}$, $5 - 9\text{g/day}$ and $\geq 9\text{g/day}$. Normality of data was assessed by visual inspection of
213 histograms and the Kolmogorov-Smirnov test. All non-parametric data were reported as
214 median and interquartile range (IQR; 25th, 75th percentile) and continuous variables compared
215 using independent Samples Mann-Whitney U test or Independent Samples Kruskal-Wallis
216 test. Categorical variables were compared across groups using Pearson Chi-Square and
217 Fisher's Exact Test. Data were also analysed according to urinary Na excretion values and by
218 iodine category (sub-optimal: UIC $<100\text{ug/L}$; iodine replete: $100 - 299\text{ug/L}$; and excessive:

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3 219 >300ug/L). To assess the association between salt intake, body size, UIC and UIE,
4 220 Spearman's rank order and partial correlations were conducted.
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8 9 222 **Results**

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11 223 Complete urinary Na and iodine data were available in n = 874 participants.
12 224 Sociodemographic characteristics and health indicators of the sub-sample are compared to the
13 225 total SAGE-Wave 2 cohort (n = 2887) in Table 1 which included participants aged between
14 226 18 and 102y with a BMI of 13.5-69.9. The sub-sample had a higher proportion of women and
15 227 more black/coloured respondents than the main cohort, which may explain differences in
16 228 smoking, education and BP.

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18 229 In the subsample that provided urine collections, median 24hr urine volume was 1385 (IQR
19 230 900, 2278) ml/day, with a range from 500 – 4900ml/day. Median urinary creatinine excretion
20 231 was 1097 (IQR 790, 1682) mg/24hr, with a range from 460 – 6441 mg/24hr. Median 24hr Na
21 232 excretion (n=874) was equivalent to a median salt intake of 6.3gsalt/day (range 1-43 g/day);
22 233 35% had values within the desirable range (< 5g salt/day), 37% had high values (5 – 9 g
23 234 salt/day) and 28% had very high values (\geq 9g salt/day). We have previously reported that
24 235 median salt intakes are higher in younger than older (50+ y) adults in this cohort (8.6 g vs 6.1
25 236 g/day; $p < 0.001$), and in urban compared to rural dwellers (7.0 g vs 6.0 g/day; $p=0.033$)³⁸ but
26 237 further analysis of Na vs iodine excretion, by demographic breakdown is outside the scope of
27 238 the current analysis. No significant difference in median UIE was found according to age
28 239 category (18-49y; 50+y) or sex, however median UIE was significantly higher in urban
29 240 compared to rural dwellers (128 (IQR147) vs 115 (IQR 119); $p=0.041$). No demographic
30 241 differences were found for median UIC. In the total sample, median UIC (n=875) was 130
31 242 $\mu\text{g/L}$ (IQR=58-202), indicating iodine sufficiency ($\geq 100 \mu\text{g/L}$) while median 24hr UIE
32 243 (n=866) was 117 ug/day (IQR 138).
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48 245 Both UIC and 24hr iodine excretion differed across salt intake categories and were positively
49 246 correlated with 24hr salt intake, estimated from urinary Na excretion ($r= 0.166$ and 0.552 ;
50 247 both $P<0.001$) (Table 2). In the lowest salt category of <5g/d, median UIC indicated
51 248 borderline deficiency of 102 $\mu\text{g/L}$ (Table 3). According to median 24hr UIE values, the
52 249 group of participants with a salt intake of <5g/day are not meeting their dietary Estimated
53 250 Average Requirement (EAR) of 95 $\mu\text{g/day}$ (IOM 2003).³⁹, with 58.4% having intakes below
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251 this value (Table 3). Even in those with salt intakes in the moderately raised category of 5 –
252 9g/day, a considerable proportion (34.7%) had intakes below the EAR. Responses to
253 questions on salt behaviours did not differ between participants across median UIC categories
254 (data not shown), nor according to UIE (Figure 1).

255

256 Discussion

257 Our study found that in a sample of South African adults, those with a salt intake within the
258 WHO recommended range of less than 5g/day had urinary iodine excretion values indicative
259 of suboptimal iodine intakes, whereas those with higher salt intakes were shown to have
260 adequate intakes using 24hour urinary iodine excretion as a biomarker of intake. . Thus, there
261 is a risk that sodium reduction strategies may impact adversely on iodine intakes and result in
262 populations being at risk of inadequate iodine intakes unless fortificant levels of iodine in salt
263 are revised accordingly.

264

265 This data was collected immediately prior to introduction of South Africa’s mandatory salt
266 reduction legislation, that requires food manufacturers to comply with maximum salt targets
267 across a wide range of processed foods. The impact of the salt reduction policy on iodised
268 salt intake is unknown. South Africa has had a well functioning table salt iodisation
269 programme since 2005, but salt used in food processing is exempt from mandatory iodisation.
270 Despite iodised salt not being required by law to be used as an ingredient in the
271 manufacturing of processed foods, a study⁴⁰ that investigated the iodine content of salt used
272 in bread, margarine, and salty snack flavourings in 2002 provided surprising results. Even
273 though 11 of the 12 manufacturers surveyed at that time reported that they used non-iodized
274 salt in their processed foods, substantial amounts of iodine were found in the salt used by a
275 third of these manufacturers’ products, with a mean content of 39 to 69 ppm, and these were
276 the items that were mostly distributed countrywide. An appreciable percentage of the food
277 companies used iodized salt unknowingly in the manufacturing of frequently consumed
278 processed foods, and this may have had a considerable impact on the daily iodine intake of
279 consumers. To our knowledge, there is no updated information on the use of iodised salt in
280 food processing by food manufacturers. Thus, it is feasible that the salt reduction legislation
281 may also impact on contribution of iodine intake from iodised salt.

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3 283 As well as changes to the food supply, nutrition education activities undertaken by the
4 284 Department of Health and non-governmental organizations in South Africa aim to change
5 285 consumer behaviour related to table salt use^{41 42}. The timing of the WHO SAGE Salt &
6 286 Tobacco sub-study in South Africa was planned to provide a baseline population salt intake³⁸
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8 287 one year before mandatory salt legislation, in order for comparison in the same cohort one
9 288 year after introduction of the legislation²⁹ in SAGE Wave 3. The data reported in this paper
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11 289 relate to the pre-salt reduction legislation baseline timepoint. Inclusion of iodine analyses in
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13 290 Wave 3 in 2018 will further allow evaluation of the compatibility of iodine fortification and
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15 291 salt reduction policies.
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20 293 Concerted efforts are being made in many countries to lower salt consumption¹⁸. Because the
21 294 primary food vehicle for iodine fortification is salt, there is concern that decreasing salt
22 295 consumption will increase the risk of iodine deficiency. Our study findings indicate that this
23 296 is a potential public health problem. The findings of the current study are in contrast to
24 297 previous findings from a sample of adult men and women surveyed in Cape Town in 2004,
25 298 when UIC did not differ across categories of salt intake²¹. Reasons for this are unclear but
26 299 may reflect an increased consumption of salt provided from non-iodised sources in processed
27 300 foods, accompanied by a reduction in discretionary iodised salt intake, since 2004.
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29 301 However, data is not available to further postulate in this regard.
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35 302 The South African strategic plan to reduce cardiovascular disease includes the target to
36 303 reduce the population intake of salt to less than 5 grams/day. At present the salt intake is
37 304 higher than this level, with older reports from the early 2000s estimating that 40% salt was
38 305 provided from discretionary salt intake²². Our study was conducted immediately prior to
39 306 introduction of the mandatory salt targets in processed foods. The salt intake estimations in
40 307 the current study include both added (discretionary) and non-discretionary salt intakes but the
41 308 lack of data on dietary intakes of the participants prevents further investigation of the source
42 309 of the salt.
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49 310 We hypothesize that food manufacturers may have already reduced salt content in processed
50 311 foods at the time of the study (2015), and that some of these products may have been
51 312 produced with iodized salt. If this is the case, this would result in lowered iodine intake at the
52 313 same time as lowered salt intake, as would any reduction in discretionary salt use.
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54 314 Considering the latter, there have been many accompanying health education strategies that
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3 315 target salt reduction behaviours, alongside the salt legislation in processed foods⁴². In 2015, a
4 316 mass media campaign (Saltwatch), using television, radio advertisement and other platforms
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6 317 for information dissemination was undertaken to increase public awareness related to the
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8 318 association between a high salt intake, blood pressure and cardiovascular disease in South
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10 319 Africa. The campaign, conducted by the Heart and Stroke Foundation of South Africa with
11 320 funding from the Department of Health, focused on the need to reduce discretionary salt
12 321 intake. Evaluation of the programme undertaken in 550 black women, aged 18-55 years in
13 322 three provinces identified that there was an increase in most of the indicators of knowledge,
14 323 attitudes and behaviour change towards considering and initiating reduced salt consumption
15 324 following the campaign. Significant increases were found for knowledge items related to high
16 325 salt intake and its health outcomes. Participants also reported that they added less salt while
17 326 cooking and at the table. In the current study, responses to questions on salt behaviours did
18 327 not differ between participants across median UIC categories, nor according to 24-hr UIE.
19 328 This could mean that the questions are not sufficiently sensitive to discern between salt intake
20 329 behaviours, or that the contribution of discretionary salt to total iodine intake is influenced by
21 330 other food sources of iodised salt.

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29 331 A strength of the current study was use of the gold standard method for assessment of salt
30 332 intake, namely 24hr urinary collections. Limitations relate to the high number of respondents
31 333 with missing or incomplete urine samples. The difficulty in obtaining complete 24-hour urine
32 334 samples is well-known, and the comparison between the main study cohort and those
33 335 providing complete samples shows that men, and those with higher education less frequently
34 336 provided complete 24-hour urine. This may also reflect the nature of the survey as
35 337 fieldworkers visited the respondent's homes and those that were away with work were less
36 338 likely to have taken part or would have potentially had more difficulty with the urine
37 339 collection, creating a selection bias in the data towards the population with lower
38 340 employment levels. Future research may consider workplace-based data collection. An
39 341 assumption was made regarding cut-off values for completeness of 24hr urine collection
40 342 whereby urinary volume < 300ml/day or creatinine excretion ≤ 4 mmol/day (women) or ≤ 6
41 343 mmol/day (men)³³ were the criteria used for exclusion purposes. In populations with low
42 344 protein intakes, daily creatinine excretion is more variable than in well nourished populations,
43 345 and often lower than 1 g (8.84 mmol)per day.⁴³ A limitation of the study is that neither
44 346 dietary protein intake, nor lean body mass was assessed which makes it difficult to account
45 347 for these two confounding variables when deciding on how to interpret low urinary creatinine

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3 348 concentrations. It is possible that the use of higher creatinine excretion cut-off reference
4 349 values as a measure of completeness of urine collection may have resulted in a somewhat
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6 350 lower number of subjects considered to be at risk of inadequate iodine nutrition, as well as a
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8 351 higher estimated salt intake.

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10 353 A further limitation is the lack of dietary data on sources of iodine provided by foods other
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12 354 than iodised salt. Iodine-rich dietary sources include fish and seafood, and dairy products and
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14 355 it is possible that some of these foods may also be high in salt, as in the case of salted dried
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16 356 fish commonly consumed by the coloured population (known as “*bokkems*”). However,
17 357 generally these foods are not major contributors to sodium in the South African diet²².
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19 358 Interestingly, in women, both UIC and UIE correlated positively with body mass index,
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21 359 independently of salt intake. Looking at changes in food consumption patterns in South
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23 360 Africa over time, it seems that there is not only an increase in processed foods but also other
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25 361 foods that may contribute to iodine intake independently of iodized salt such as fish, eggs,
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27 362 seafood, and dairy foods⁴⁴. The contribution of food sources, other than iodized salt, to total
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29 363 iodine intake warrants further investigation in the context of evaluating the mandatory salt
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31 364 iodization programme in South Africa. Furthermore, this study presents limited data for
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33 365 women of child bearing age and no data for children. Further work is needed to determine if
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35 366 there is an impact of the sodium reduction legislation in these particularly iodine-sensitive
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37 367 groups.

368 **Conclusion**

38 369 This study highlights the need to closely monitor the iodine status of populations as they
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40 370 undergo population-level reductions in salt intake, in countries where mandatory salt
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42 371 iodisation is implemented. Even at salt intake levels currently above the WHO target of
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44 372 5g/day, there was a considerable proportion with iodine intakes below the EAR. This
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46 373 indicates there may be a need to increase the level of iodine in fortified table salt.
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48 374 Alternatively, compulsory iodisation of salt used in the production of some staple foods such
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50 375 as bread may be considered. In a country where some sectors of the population may be
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52 376 exposed to excessive iodine intakes, this strategy would require careful dietary modelling
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54 377 before being pursued. It is recommended that surveys that measure urinary Na excretion also
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56 378 simultaneously measure urinary iodine concentration and determine the iodine content in
57
58 379 table salt collected from households.

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396 JB, AES, MC, PK, wrote the paper; KC takes responsibility for the contents of this article.
397 All authors read and approved the final manuscript.

398 Data sharing statement: The dataset is available on request and will form part of the data
399 catalogue of the World Health Organization Study on Global AGEing and Adult Health
400 (SAGE) (<http://apps.who.int/healthinfo/systems/surveydata/index.php/catalog/sage/about>)

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524 **Table 1.** Characteristics of the main (SAGE South Africa Wave 2, 2015) and subsample
525 study cohort.

	Main SAGE cohort		Subsample ^a		p value
	n=2887		n=875		
	median	IQR	median	IQR	
Female, n (%)	1939	67	671	77	<0.001
		46, 69		44, 67	0.468
	57		55		
Age years					
Aged over 50 years, n (%)	1979	69	567	65	0.171
Ethnicity, n (%)					
Black	1988	69	410	74	<0.001
Coloured, mixed race	465	16	96	17	
Indian	306	11	41	7	
White	128	4	11	2	
Rural, n (%)	792	28	163	29	0.418
Education years	10	7, 13	9	6, 12	0.028
Never been to school, n (%)	495	18	109	20	0.180
Never had paid employment, n (%)	1101	55	238	56	0.403
		23.9, 33.7		24.0, 34.2	0.540
BMI, kg/m ²	28.8		29.1		
Waist to height ratio	0.59	0.52, 0.67	0.58	0.50, 0.66	0.070
Never used alcohol, n (%)	1576	80	353	83	0.052
Never used tobacco, n (%)	1635	83	367	86	0.023
Systolic BP mmHg	131	118, 144	128	116, 141	0.073
Diastolic BP mmHg	81	73, 89	79	71, 87	0.029
Hypertension, n (%)	1233	45	232	43	0.239
Diabetes, n (%)	248	13	46	11	0.355

526 BMI, body mass index. ^aSubsample: all respondents with spot UIC, valid 24-hour urine, sex
527 and age recorded. Some variables may contain missing data as indicated by percentages. Data
528 shown as median and interquartile range (IQR; 25th, 75th percentile) unless otherwise
529 indicated. Hypertensive by measured BP \geq 140 and/or 90mmHg or previous diagnosis.
530 Education, tobacco/alcohol use, ethnicity, employment and diabetes prevalence by self-

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3 531 report. Continuous variables compared using Independent Samples Mann-Whitney U test,
4 532 categorical variables compared using Pearson Chi-Square and Fisher's Exact Test.
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535 **Table 2.** Spearman's rank order and partial correlations between urine iodine concentration,
 536 estimated salt intake, and body size SAGE South Africa Wave 2 (2015).

		All n=456	Men n=110	Women n=346
<i>Correlations with spot UIC $\mu\text{g/l}$</i>				
Salt intake g/day	<i>rho</i>	0.166(***)	0.164	0.153(**)
	<i>p</i>	0.000	0.088	0.004
24-hr iodine $\mu\text{g/day}$	<i>rho</i>	0.423(***)	0.483(***)	0.392(***)
	<i>p</i>	0.000	0.000	0.000
BMI kg/m^2	<i>r</i>	0.036	0.001	0.096
	<i>p</i>	0.448	0.988	0.076
Weight kg	<i>r</i>	0.043	0.035	0.056
	<i>p</i>	0.365	0.716	0.299
Waist circumference cm	<i>r</i>	0.001	0.027	0.008
	<i>p</i>	0.991	0.784	0.878
Hip circumference cm	<i>r</i>	0.040	0.213(*)	0.008
	<i>p</i>	0.389	0.026	0.883
<i>Correlations with 24-hr UIE $\mu\text{g/d}$</i>				
Salt intake g/day	<i>rho</i>	0.552(***)	0.504(***)	0.561(***)
	<i>p</i>	0.000	0.000	0.000
BMI kg/m^2	<i>r</i>	0.092	0.030	0.168(**)
	<i>p</i>	0.051	0.758	0.002
Weight kg	<i>r</i>	0.130(**)	-0.023	0.193(***)
	<i>p</i>	0.005	0.814	0.000
Waist circumference cm	<i>r</i>	0.032	-0.011	0.069
	<i>p</i>	0.491	0.911	0.200
Hip circumference cm	<i>r</i>	0.052	0.056	0.094
	<i>p</i>	0.269	0.563	0.080

537 BMI, body mass index; UIC, spot urine iodine concentration; UIE, 24-hour urine iodine
 538 excretion. Correlations between iodine and body size controlled for salt intake. Correlation is
 539 significant at the 0.05 level (*); at the 0.01 level (**); or at the 0.001 level (***)

540 **Table 3.** Urinary iodine, estimated iodine intake and sodium excretion values by salt intake equivalent categories

	24-hour urinary sodium excretion								p value
	All n=874 ^a		Salt <5g/d n=307		Salt 5-9g/d n=322		Salt >9g/d n=245		
	median	IQR	median	IQR	median	IQR	median	IQR	
Sodium mg/day	2471	1434, 3506	1393	1068, 1719	2638	2219, 3057	4799	3607, 5993	<0.001
Salt g/day	6.3	3.7, 9.0	3.6	2.8, 4.5	6.8	5.7, 7.9	12.3	9.3, 15.4	<0.001
UIC µg/l	130	58, 202	102	32, 172	131	56, 206	149	78, 220	<0.001
24hr UIE µg/day	117	48, 186	74	37, 111	119	57, 181	195	117, 273	<0.001
Estimated iodine intake µg/day	127	52, 202	80	40, 120	130	63, 197	212	127, 297	<0.001
% with daily iodine intake below EAR for iodine (95 µg/day)†	37.1%		58.4%		34.7%		13.5%		

541 UIC, spot urine iodine concentration; UIE, 24-hour urine iodine excretion. ^aOne individual in subsample with missing 24-hour sodium analysis.
 542 Data shown as median and interquartile range (IQR; 25th, 75th percentile). Continuous variables compared using Independent Samples Kruskal-
 543 Wallis test.

544 † Daily iodine intake assumed as 24hr UIE (µg/day)/0.92 to account for bioavailability

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547 **Figure Legend: Self-reported salt knowledge, attitudes and behaviour by 24-hour urinary iodine excretion (UIE; n=539)**
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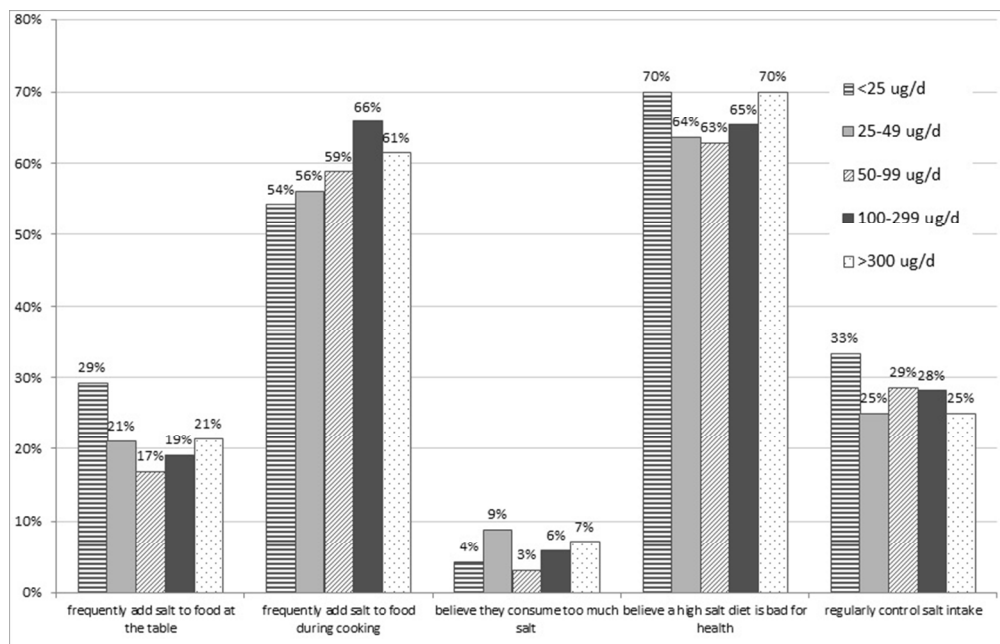


Figure 1. Self-reported salt knowledge, attitudes and behaviour by 24-hour urinary iodine excretion (UIE; n=539)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cross-sectional studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(a) Indicate the study's design with a commonly used term in the title or the abstract	1
		(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	3-4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4-5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(a) Give the eligibility criteria, and the sources and methods of selection of participants	5
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	5-6
Bias	9	Describe any efforts to address potential sources of bias	4-6
Study size	10	Explain how the study size was arrived at	6
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(a) Describe all statistical methods, including those used to control for confounding	7
		(b) Describe any methods used to examine subgroups and interactions	7
		(c) Explain how missing data were addressed	6
		(d) If applicable, describe analytical methods taking account of sampling strategy	7
		(e) Describe any sensitivity analyses	none
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	6-7
		(b) Give reasons for non-participation at each stage	6-7
		(c) Consider use of a flow diagram	
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1, p 14
		(b) Indicate number of participants with missing data for each variable of interest	Table 1, p 14
Outcome data	15*	Report numbers of outcome events or summary measures	Table 3, p 16
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	none
		(b) Report category boundaries when continuous variables were categorized	7-8; Table 3, p 16; Figure 1, p 17
		(c) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	none
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10; Table 1, p 14
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
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	8-11
Generalisability	21	Discuss the generalisability (external validity) of the study results	10
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.