

SALT INTAKE ASSESSED BY 24-HOUR URINARY SODIUM EXCRETION IN A RANDOM AND OPPORTUNISTIC SAMPLE IN AUSTRALIA

Journal:	BMJ Open
Manuscript ID:	bmjopen-2013-003720
Article Type:	Research
Date Submitted by the Author:	04-Aug-2013
Complete List of Authors:	Land, Mary-Anne; The George Institute for Global Health, ; The University of Sydney, Webster, Jacqui; The George Institute for Global Health, ; The University of Sydney, Christoforou, Anthea; The George Institute for Global Health, ; The University of Sydney, Praveen, D; The George Institute for Global Health, ; The University of Sydney, Jeffery, Paul; Deakin University, Chalmers, John; The George Institute for Global Health, ; The University of Sydney, Smith, Wayne; New South Wales Health, Woodward, Mark; The George Institute for Global Health, ; The University of Sydney, Barzi, Federica; The George Institute for Global Health, ; The University of Sydney, Nowson, Caryl; Deakin University, Flood, Victoria; The University of Wollongong, Neal, Bruce; The George Institute for Global Health, ; The University of Sydney,
Primary Subject Heading :	Public health
Secondary Subject Heading:	Complementary medicine, Epidemiology, Global health
Keywords:	Hypertension < CARDIOLOGY, NUTRITION & DIETETICS, PUBLIC HEALTH

SCHOLARONE[™] Manuscripts

SALT INTAKE ASSESSED BY 24-HOUR URINARY SODIUM EXCRETION IN A RANDOM AND OPPORTUNISTIC SAMPLE IN AUSTRALIA

Corresponding Author: Miss Mary-Anne Land The George Institute for Global Health PO BOX M201 Missenden Road Camperdown, NSW, AUSTRALIA 2050. T: +61 2 9993 4547 E: maland@georgeinstitute.org.au

Authors: Mary-Anne LAND^{a,b}, Jacqui, WEBSTER^{a,b}, Anthea, CHRISTOFOROU^{a,b}, D PRAVEEN^{a,b}, Paul JEFFERY^c, John CHALMERS^{a,b}, Wayne SMITH^d, Mark WOODWARD^{a,b}, Federica BARZI^{a,b}, Caryl NOWSON^c, Victoria FLOOD^e, Bruce NEAL ^{a,b}.

Affiliations: ^aThe George Institute for Global Health, Sydney, Australia, ^bThe University of Sydney, Sydney, Australia, ^cDeakin University Melbourne, Australia, ^dNew South Wales Health, Sydney, Australia, ^eThe University of Wollongong, Wollongong, Australia.

TABLES: 3

FIGURES: 1

SUPPLEMENTARY: 0

WORD COUNT: 2907

KEY WORDS: Salt, sodium, 24-hour urine, cardiovascular disease prevention

Article Focus

The Global Monitoring Framework for the Prevention and Control of NCDs has set a salt reduction target of 30% by 2025. The assessment of population salt intake underpins the implementation of salt reduction policies and evaluates progress. The gold standard method for assessing population salt intake is the collection of a 24-hour urine specimen. However, because of the high burden, participation rates are generally low and the cost is often high. Hence there is great interest in alternative, yet robust and affordable methods to assess salt intake.

Key Messages

The observation that an opportunistically recruited volunteer population sample appears to provide a reasonable estimate of salt intake is important because this could substantially reduce the cost of future monitoring efforts. If this finding was repeated in other settings this would have global implications, as the reporting of salt intake in 2015, 2020 and 2025 is encouraged as part of the Global Monitoring Framework for the Prevention and Control of NCDs.

Strengths and Limitations

The 'Gold Standard' 24-hour urine method was used to estimate salt intake. The response rate for the random sample was low and the study location was a single town but the response rate and estimated level of salt excretion is not substantively different from that reported in a number of diverse population groups throughout the country.

Abstract

Introduction: The gold standard method for measuring population salt intake is based on a 24-hour urine collection. However, because participant burden is high, response rates are typically low with less than one in four agreeing to provide specimens. At this low level of response it is possible that simply asking for volunteers would produce equally valid results. **Method:** We randomly selected 2152 adults from Lithgow, New South Wales and obtained usable 24-hour urine samples from 306 (response rate 16%). Specimens were also collected from a further 113 volunteers. Estimated salt consumption and the costs for each strategy

were compared.

Results: The characteristics of the 'random' and 'volunteer' samples were moderately different in mean age 58 (standard deviation 14.6) vs. 49(17.7) years respectively; p<0.001) as well as self-reported alcohol use, tobacco use, history of hypertension and prescription drug use (all p<0.04). Overall crude mean 24-hour urinary salt excretion was 8.9(3.6)(g/d) in the random sample vs. 8.5(3.3)g/d for the volunteers (p=0.42). Corresponding age- and sex-adjusted estimates were 9.2(3.3)g/d and 8.8(3.4)g/d (p=0.29). Estimates for men 10.3(3.8) vs. 9.6(3.3)g/d; p=0.26) and women 7.6(3.0) vs. 7.9(3.2)g/d; p=0.43) were also similar for the two samples, as was salt excretion across age groups (p=0.72). The cost of obtaining each 24-hour urine sample was two times greater for the random compared to volunteer samples (A\$62 vs. A\$31).

Conclusion: The estimated salt consumption derived from the two samples were comparable and were not substantively different to estimates obtained from other surveys.

BMJ Open

2
3
1
-
5
6
7
8
0
9
10
11
12
12
13
14
15
16
10
17
18
19
20
20
21
22
23
24
24
25
26
27
21
28
29
30
21
31
32
33
34
25
35
36
37
38
20
39
40
41
42
40
43
44
45
16
40
41
48
49
50
50
51
52
53
51
54
55
56
57
50
20
59

60

In countries were salt is pervasive and cannot easily be avoided, estimates of consumption obtained from volunteer samples may be valid and less costly.

Background

Non-communicable diseases (NCDs) are the leading cause of death accounting for an estimated 35 million (66%) of the 53 million deaths at all ages that occurred in 2010.[1] Raised blood pressure is the leading risk factor for global disease burden, and is estimated to cause 9.4 million deaths every year—more than half of the estimated 17 million deaths a year caused by cardiovascular disease.[2] Much evidence shows that a reduction in salt intake lowers blood pressure and there is a high likelihood that this would reduce the risk of cardiovascular disease.[3] While there is not a current definitive estimate of population dietary salt intake in Australia, it is widely accepted that average consumption is between 7 and 12g/d[4] far above the suggested dietary target for Australians of 4g/d.[5]

The reduction of salt intake and salt content of food has been strongly recommended as a cost effective action that should be undertaken immediately, with expected accelerated results in terms of lives saved, cases of disease prevented and costs avoided.[6] This position has since been historically endorsed by the 2011 Political Declaration of the United Nations High Level Meeting on NCDs[7] which led to the development and adoption of the Global Monitoring Framework and Voluntary Global Targets for the Prevention and Control of NCDs in which salt reduction is a core target.[8]

Measurement of population salt consumption is fundamental for planning and monitoring salt reduction policies and the gold standard method is based upon a 24-hour urine collection from a random community sample. Surveys of this type are, however, complex and expensive and because participant burden is high, randomly selected community

BMJ Open

samples typically have low response rates.[9-11] This has been noted as a significant concern at recent WHO NCD surveillance, monitoring and evaluation consultation meetings in which several member states have expressed doubts about the feasibility of using this method.[12] The potential adverse impact that a low response rate might have on the conclusions drawn was highlighted and the need for further research into practicable methods for defining and monitoring population salt consumption was underlined.[12]

The objective of the present study was to estimate sodium excretion using assays of 24hour urine samples collected from a regional Australian population. A key question about practicality was addressed by using both a standard random sampling approach to make the estimate while simultaneously recruiting an opportunistic (volunteer) sample to make an alternate estimate. The study also examined the costs associated with each strategy.

Methods

The data derived from a random sample and a convenience sample (volunteers) done concurrently in Lithgow, New South Wales, Australia between March and June 2011. Permission to undertake the study was obtained from the Lithgow City Council and the project was approved by the University of Sydney Human Research Ethics Committee.

Inclusion and exclusion criteria

Consenting individuals aged 20 years or above who were resident in Lithgow and listed on the 2009 Federal electoral roll were eligible for inclusion. There was no exclusion based on inter-current illness, use of medications or any other aspect of demography or personal history.

Selection and recruitment process

Random sampling was done by selecting individuals at random from the electoral roll. The electoral roll provided the name and address of each potential participant with electronic databases searched to identify corresponding telephone numbers. Based on the assumption that approximately 25% of invited individuals would participate, 2152 individuals were selected to reach the desired sample size.

Potential participants were first mailed invitations to take part in the survey, with an explanation of the purpose of the study, a participant information sheet and a consent form provided. These individuals were then contacted by telephone to determine their willingness to participate and to schedule an interview time. Where a telephone number could not be obtained, the home address was visited by a member of the research team and willingness to participate was discussed face-to-face.

Volunteer sampling was done by offering participation in the study to individuals at two local shopping centres over several weeks. An information booth was established where those interested could seek further information about participation and arrange a visit by a member of the study team. Recruitment was completed at the time of the inquiry made to the study staff member manning the information booth.

Data collection process

Data collection for randomly selected individuals and the volunteer sample was identical and commenced with a visit to the study participant by a trained research assistant. Once consent was obtained the three components of data collection, comprising a questionnaire, a physical examination and a 24-hour urine collection were initiated. The questionnaire and physical examination were completed at the time of the visit and the urine collection was scheduled to be done within the following three days.

The *questionnaire* was fully structured and administered by research assistants, with all responses based on self-report. The questionnaire recorded information on sociodemographic variables, vascular disease history and current drug treatments. Participants were asked to provide the names of regular medications but if that was not known the purpose of the medication was recorded (for example, anti-hypertensive medication).

The physical examination comprised measurement of body weight (using calibrated Tantia HD-357 portable electronic scales (USA) and height (using a calibrated portable stadiometer Wedderburn WS-HRP model (Australia)) to the nearest 0.1kg and 0.1cm respectively, with body mass index (kg/height(m²)) then calculated. Blood pressure was measured using a manual inflation blood pressure monitor (A&D UA-&704) in triplicate, according to the American Heart Association protocol.[13]

BMJ Open

A single 24-hour urine collection was obtained with the first voided urine upon waking on the day of collection being discarded and participants then collecting all voided urine up to and including the first void the following morning. The time at the beginning and the end of urine collection were recorded. The urine volume was noted and the urinary sodium concentration in an aliquot was measured by ion-selective electrode with the buffered kinetic Jaffe reaction without deproteinisation used for assay of urine creatinine (Cobas Integra 400). Suspected inaccurate urine collections (i.e. urinary creatinine < 4.0 mmol/day for women, or < 6.0mmol/day for men, or a 24-hour urine collection of < 500ml for either sex) and extreme outliers for urinary creatinine (i.e. > 3 standard deviations from the mean) were excluded. The rates of exclusion were similar for the random and volunteer samples. For each individual, the 24-hour sodium excretion value (mmol/day) was calculated as the concentration of sodium in the urine (mmol/L) multiplied by the urinary volume (L/day). The conversion from sodium (Na) to salt (NaCl) was made by multiplying the sodium value by 2.542 (NaCl(g)=Na(g) x 2.542).

Cost data

The pre-interview costs involved staff time in selecting and attempting to reach subjects including accessing the electoral roll, sending participant invitations, follow-up phone calls and door-knocking to schedule interviews with those randomly selected, as well as setting up and manning an information booth to engage the volunteer sample were documented. The post-interview costs comprised primarily of pathology expenses and were the same for each sample.

Statistical analyses

The baseline characteristics of the sample selected at random and the volunteer sample were summarized and compared using t-tests and Chi-square tests as were their average urinary sodium values. In addition to the crude estimates described above, weighted estimates of overall population mean sodium excretion were also made in an effort to account for the non-random sampling of individuals. This was done for both the randomly selected group (to adjust for the poor response rate) and for the volunteer group (to adjust for their non-representative age and sex structure) by calculating age- and sex-specific estimates of salt excretion for 20 year age bands (20-39, 40-59, and 60 plus) for men and women and then weighting these by the age and sex structure of the population to obtain an overall estimate for the community. Regression models were fitted to explore the association between baseline participant characteristics and a range of covariates in the combined (random plus volunteer) sample. Throughout, a p-value of 0.05 or less was taken to indicate a finding unlikely to have arisen solely by chance. Statistical analyses were conducted using SPSS for Windows (Version 21, SPSS Inc, Chicago, IL) and STATA for windows (StataCorp. 2009 Strata Statistical Software: Release 11. College Station, TX: StataCorp LP).

Results

Of 2,152 individuals selected by random sampling of the electoral roll, 853 (40%) were uncontactable after multiple attempts, 126 (5.8%) were ineligible because they had moved out of the study area, 5 (0.2%) had died and 843 (39%) declined to participate. The remaining 329 individuals comprise the 'random' sample with a response rate of 16%. The volunteer

BMJ Open

sample comprised 120 individuals recruited consecutively at a shopping mall over a seven day period. The characteristics of the random and volunteer samples were moderately different in a number of regards, including age, proportion tobacco use, alcohol use , selfreported hypertension and use of any prescription medication (Table 1).

Crude and weighted 24-hour urinary salt excretion in random and volunteer samples

For the analysis there were 306 individuals in the random sample and 113 in the volunteer group with 20 excluded because of suspected incomplete urine collections and 10 for other reasons (Figure 1). The crude mean 24-hour urinary salt excretion was 8.9 (standard deviation 3.6) g/d in the random sample and 8.5 (3.3) g/d in the volunteer group (p=0.42). The corresponding weighted estimates for the Lithgow population were 9.2 (3.9) g/d and 8.8 (3.4) g/d respectively (p=0.29).

The proportion of randomly sampled individuals exceeding the 6 g/d recommended Maximum Level for Australians was 79%, the proportion exceeding the Australian Suggested Dietary Target of 4 g/d was 94% and the proportion exceeding the WHO Maximum Recommended Level of 5 g/d was 87%. The corresponding proportions for the volunteer group were 75%, 93% and 84%. Population-weighted estimates of these proportions were not substantively different.

24-hour urinary salt excretion in participant subgroups

BMJ Open

Urinary sodium excretion in both population samples was significantly higher in men compared to women 10.3 (3.8) g/d vs. 7.6 (3.0) g/d; p<0.001 for random sample and 9.6 (3.3) g/d vs. 7.9 (3.2) g/d; p=0.006 for the volunteer sample (Table 2) and this was also true for every age group. There was an inverse association between daily salt excretion and age (Table 2) such that for every decade increase in age there was 0.3g/d less excretion of salt (p=0.007). The association between salt excretion and BMI was positive with every unit rise in BMI associated with a 0.16g/d greater excretion of salt (p<0.001). Similar patterns were observed in both the random and volunteer population samples. There were no other significant associations observed between salt excretion levels and recorded participant characteristics including education, health status, tobacco use, alcohol use, blood pressure, disease history or prescription drug use (all p>0.05).

Costs associated with random and volunteer survey methods

The two main costs associated with doing the study were staff salaries and pathology expenses. Due primarily to the increased staff time required for the selection and interaction with the randomly selected individuals the estimated average cost associated with obtaining a valid 24-hour urine sample was greater for each participant in the random sample (about AUD\$ 62) compared to each participant in the volunteer sample (about AUD\$ 31).

Discussion

In this population salt intake greatly exceeds the recommended levels, reaffirming the urgent need for concerted action to address salt consumption in Australia. Mean salt

BMJ Open

excretion levels were some 50% higher than maximum recommended levels[5, 14] and only about one in every twenty individuals was found to be consuming the level of salt recommended for good health. Even these data are likely to be an under-estimate of the problem because the approximate 10% of salt excreted by the gastro-intestinal system and the skin will have gone unrecorded.[15] The level of excess salt consumption indicated by this survey would be anticipated to cause substantial disease burden in Australia leading both to large numbers of lives lost prematurely and to many individuals suffering significant disability.[16] With centrally implemented salt reduction programs projected to deliver large population health gains at very low cost [17-19], the implementation of an effective salt reduction program should be a priority for the government of Australia.[20, 21]

The observation that the volunteer sample produced similar findings to the random sample is important because it was much easier and less costly to collect data from the volunteer sample than from the random sample. There are several reasons why a volunteer sample might provide a similar result to a random sample when estimating population salt consumption from 24-hour urine samples. First, the response rate in a random sample from whom a 24-hour urine sample is sought is typically very low, averaging 20% (range 9.7% to 26.8%) in a series of recently reported studies.[9-11, 20] In this situation the random sample effectively becomes a volunteer sample and any biases consequent upon using a volunteer sample might also be apparent in the 'random' sample. That said, there were many differences between the characteristics of the random and volunteer samples included

Page 15 of 28

BMJ Open

in this study but these did not translate into detectable differences in the observed sodium excretion. Another possible explanation therefore is the ubiquitous nature of salt in the food supply[22] and the rather limited capacity of even motivated individuals to meaningfully modify their salt consumption,[23] thereby minimizing the impact of any "healthy volunteer" effect.[24]

In some countries it may be possible to achieve better response rates [25, 26] and in others it may be that specific dietary practices or other cultural factors will mean that a volunteer sample will not give a good measure of true population salt intake. If, however, the findings reported here are observed elsewhere, volunteer sampling might provide a low-cost alternate to traditional random sampling techniques. At the very least it may be possible to use a volunteer sample to demonstrate the need for action - most countries in the world are likely to have salt consumption levels far above the WHO consumption target of <5g/d, and the likelihood that the selection of a volunteer sample will lead to an under-recording of salt consumption of a very large magnitude is probably fairly small.

In addition to the baseline assessment required to justify the commencement of a salt reduction strategy, ongoing monitoring of salt consumption is required to objectively determine program efficacy. If the resources required to conduct high quality surveys of a random population sample can be acquired then this remains the optimal approach both to baseline evaluation and monitoring of progress. If not, then repeat surveys of volunteers are likely to be of value if the methods used for participant selection are identical on each occasion – if the biases are the same on each measurement occasion then any real rise or fall in salt consumption should be clearly apparent.

The cost estimates made for this study showed that recruiting the volunteer sample was a significantly less expensive exercise than recruiting the random population sample. The primary reason for this was the much reduced fieldwork time required for the per capita recruitment of the volunteer sample. Pathology and other recorded costs were otherwise approximately the same. Expenses that were not specifically determined were the costs of computer hardware, computer software, the training of the field staff, and the time required for supervision by the project manager. The last two of these are also likely to have been lower for the volunteer sample due to the simplified and more rapid recruitment process and, as a consequence, the reported difference between costs is likely to have been under-, rather than over-estimated.

Strengths and limitations

The 'Gold Standard' 24-hour urine method was used to estimate salt intake with standard checks for completeness of the specimens based upon urine volume and urine creatinine excretion. The response rate for the random sample was low but comparable to other studies done in similar settings over recent years.[9-11] The sample size was relatively small and results for subgroups are somewhat imprecise as a consequence. It is possible, for this same reason, that the study may have failed to identify small, but real, differences between the salt excretion levels determined by the two different population sampling

Page 17 of 28

BMJ Open

methods. The location of the study in a single town in a regional area of New South Wales compromises the direct generalizability of the study findings to Australia as a whole, although the estimated level of salt excretion is not substantively different from that reported in a number of diverse population groups throughout the country.[27-39]

Conclusion

These data affirm that current efforts to reduce salt intake in Australia are failing, with a large majority of the population studied consuming more than the recommended Australian Upper Limit of 6g/d and almost everyone eating more than the Suggested Dietary Target of 4g/day. The observation that an opportunistically recruited volunteer population sample appears to provide a reasonable estimate of salt intake is important because this could substantially reduce the cost of future monitoring efforts. If this finding was repeated in other settings this would have global implications because sodium reduction has been proposed to all member states by the WHO. Most countries, however, have very limited resources available and any reduction in program cost that can be achieved without seriously adversely affecting program quality will be an important step forward. With population-based salt reduction strategies already shown to be cost effective or cost-saving in most settings, these new data further support the feasibility of widespread rollout of national salt reduction efforts around the world.

3
4
5
6
7
<i>'</i>
8
9
10
11
12
12
13
14
15
16
17
10
10
19
20
21
22
23
24
24 05
25
26
27
28
20
29
30
31
32
33
34
25
35
36
37
38
39
10
40
41
42
43
44
45
16
40
4/
48
49
50
51
51
52
53
54
55
56
57
57
58
59
60

TABLE 1. CHARACTERISTICS OF RANDOM AND VOLUNTEER SAMPLES

	Random sample	Volunteer sample	p-value
	(n=306)	(n=113)	
Female (%)	52.9	61.9	0.10
Age, years (mean)	57.6	49.3	< 0.001
Height, cm (mean)	167.5	167.6	0.85
Weight, kg (mean)	81.8	83.9	0.30
BMI, kg/m ² (mean)	29.1	29.8	0.27
Systolic bp, mmHg (mean)	126.7	123.7	0.16
Diastolic bp, mmHg (mean)	78.7	78.9	0.88
Education			0.22
-Secondary (%)	63.7	55.8	
-Tertiary (%)	25.5	32.7	
-Postgraduate (%)	10.8	11.5	
Health Status			0.21
-Very good (%)	50.3	48.7	
-Good (%)	29.4	23.9	
-Fair (%)	20.2	27.4	
Current smoker (> $1 / day$) (%)	8.2	22.1	< 0.001
Ever smoked (> $1 / day$) (%)	41.2	53.1	0.03
Alcoholic consumption (time since l	ast consumption)		0.04
One week or less (%)	62.1	42.5	
> one week < 12months (%)	19.9	34.5	
12 months or more (%)	11.1	10.6	
Never (%)	6.9	12.4	
Have you ever been told by a doctor	or nurse that you have:	20.1	0.02
-high blood pressure (%)	44.1	30.1	0.03
-low blood pressure (%)	15.4	14.2	0.76
-high cholesterol (%)	37.3	30.0	0.16
-heart attack (%)	8.2	3.5	0.10
-stroke (%)	3.9	1.8	0.37
-angina (%)	6.9	4.4	0.36
-diabetes (%)	11.1	7.1	0.26
Prescription Medication Use*			
Antihypertensive (%)	15 4	15.0	0.54
	1.7.Т	10.0	0.54

BMJ Open

Lipid lowering (%)	11.1	7.1	0.62
Aspirin (%)	8.8	2.7	0.06
Glucose lowering (%)	22.5	7.1	0.17
Any prescription medication (%)	73.9	59.2	0.02

*Participants could be taking more than one prescribed medication

	Rando	m samnla	Volun	toor sampla	
	n (n	=306)	v oluli	n=113)	
	Mean	(SD)	Mean	(SD)	P value
Overall crude	8.9	(3.6)	8.5	(3.3)	0.42
Overall weighted*	9.2	(3.9)	8.8	(3.4)	0.29
Female					0.27
20-39	87	(4)	79	(29)	0,
40-59	8	(3.1)	7.8	(3.8)	
60+	6.8	(2.4)	7.9	(2.6)	
All female	7.6	(3)	7.9	(3.2)	
Male					0.40
20-39	10.8	(4.7)	10.5	(3.9)	
40-59	11.1	(4.2)	9.8	(3.0)	
60+	9.7	(3.1)	8.6	(3.0)	
All male	10.3	(3.8)	9.6	(3.3)	
Education					0.25
Secondary	9.1	(3.7)	8.9	(3.4)	
Tertiary	8.3	(3.0)	8.5	(3.3)	
Post graduate	8.4	(3.6)	8	(3.3)	
Health Status					0.89
Very Good	8.7	(3.8)	8	(2.9)	
Good	8.8	(3.5)	9.3	(3.7)	
Fair	8.7	(2.8)	8.3	(2.6)	
Current Smoker	9	(3.8)	8.8	(3.4)	0.82
Ever Smoked	8.8	(3.6)	9	(3.6)	0.74
Alcohol Consumption					0.45
(time since last consumption)	0.0				0.45
One week or less	8.8	(3.8)	8.7	(3.8)	
> one week < 12months	8.6	(3.2)	8.7	(2.9)	
12 months or more	9.3	(3.8)	7.8	(2.8)	
Never	9.1	(3.2)	8.1	(3.6)	

TABLE 2. URINARY SALT EXCRETION (GRAMS/DAY)

*Adjusted for response rate (random sample) and non-random selection (volunteer sample) by weighting age-and sex-specific estimates to the age and sex structure of the Lithgow population

Random

Volunteer

1	
2	
3	
4	
5	
6	
7	
0	
0	
9	
10	
10	
12	
13	
14	
10	
10	
17	
10	
19	
20	
21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
4/	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	

58 59 60

TABLE 3. COST OF RANDOM COMPARED TO VOLUNTEER SAMPLING(AUD)

	Sample(n=306)	Sample(n=113)
Pre-interview costs		
Sampling from electoral roll	\$2,152	0
Scheduling interviews	\$8,704	\$1,088
	·	,
Post-interview costs		
Pathology costs	\$4,211	\$1,584
<i><i>ov</i></i>		
Other costs		
Postage	\$2.169	0
Telephone	\$1.870	\$818
Shopping centre stand fee	· · · ·	\$10
and the second sec		<i>4</i> - <i>4</i>
TOTAL	\$19.106	\$3,500
COST PER PARTICIPANT*	\$62.44	\$30.96

*Cost per participant calculated by dividing total cost by the number of valid participants in each sample.

BMJ Open

FIGURE 1. RECRUITMENT OF POPULATION SAMPLE



Acknowledgments

The authors thank Lithgow City Council, the Nepean Blue Mountains Local Area Health Network for their support and most importantly all of the participants for their support and interest in the study.

Sources of support

This work was supported by a National Health and Medical Research Council (NHMRC) of Australia partnership project (Neal #13372) which includes The George Institute for Global Health in partnership with the Australian Division of World Action on Salt and Health; the Australian Food and Grocery Council; the New South Wales Food Authority; and New South Wales Health. Bruce Neal was supported by an Australian Research Council Future Fellowship, Mark Woodward by a NHMRC Fellowship and Jacqui Webster by a National Heart Foundation and Stroke Foundation postdoctoral research fellowship.

Conflicts of interest

J.W. is the co-ordinator, and B.N. is the Chairman of the Australian Division of World Action on Salt and Health.

References

- Lozano, R., et al., Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. 380(9859): p. 2095-128.
- Lim, S.S., et al., A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. 380(9859): p. 2224-60.
- 3. He, F.J., N.R. Campbell, and G.A. MacGregor, *Reducing salt intake to prevent hypertension and cardiovascular disease*. Rev Panam Salud Publica, 2012. **32**(4): p. 293-300.
- Keogh, J.B. and P.M. Clifton, *Salt intake and health in the Australian population*. Med J Aust, 2008. 189(9): p. 526.
- 5. National Health and Medical Research Council, *Nutrient Reference Values for Australia and New Zealand.*, 2006, Department of Health and Ageing.
- 6. The World Health Organisation, 2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases, 2008.
- United Nations. 2011 High Level Meeting on Prevention and Control of Non-communicable Diseases. 2011 [cited 2012 12/12/2012]; Available from: http://www.un.org/en/ga/ncdmeeting2011/.
- 8. The World Health Organization, Formal meeting of Member States to conclude the work on the comprehensive global monitoring framework, including indicators, and a set of voluntary global targets for the prevention and control of noncommunicable diseases

Geneva, 5–7 November 2012, 2012: Geneva.

BMJ Open

9.	Ribic, C.H., et al., Salt intake of the Slovene population assessed by 24 h urinary sodium
	excretion. Public Health Nutr, 2010. 13(11): p. 1803-9.
10.	Chappuis, A., et al., Swiss survey on salt intake: main results. 2011.
11.	Ortega, R.M., et al., Estimation of salt intake by 24 h urinary sodium excretion in a
	representative sample of Spanish adults. Br J Nutr, 2011. 105(5): p. 787-94.
12.	The World Health Organisation, European Regional Technical Consultation on
	Noncommunicable Disease Surveillance, Monitoring and Evaluation. 2012.
13.	Perloff, D., et al., Human blood pressure determination by sphygmomanometry. Circulation,
	1993. 88 (5 Pt 1): p. 2460-70.
14.	The World Health Organization, Reducing Salt Intake in Populations, in Report of a WHO
	Forum and Technical Meeting2007, World Health Organisation: Geneva.
15.	Kirkendall, A.M., et al., The effect of dietary sodium chloride on blood pressure, body
	fluids, electrolytes, renal function, and serum lipids of normotensive man. J Lab Clin Med,
	1976. 87 (3): p. 411-34.
16.	Cobiac, L.J., et al., Which interventions offer best value for money in primary prevention of
	cardiovascular disease? PLoS One, 2012. 7(7): p. e41842.
17.	Beaglehole, R., et al., UN High-Level Meeting on Non-Communicable Diseases: addressing
	four questions. Lancet, 2011. 378(9789): p. 449-55.
18.	National Heart Foundation of Australia, Summary of evidence statement on the relationships
	between dietary electrolytes and cardiovascular disease.
	http://www.heartfoundation.org.au/SiteCollectionDocuments/Dietary-Electrolytes-CVD-
	Summary-Evidence.pdf, 2006.

19. Cook, N.R., et al., Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). BMJ, 2007. **334**(7599): p. 885-8. 20. Brown, I.J., et al., Salt intakes around the world: implications for public health. Int J Epidemiol, 2009. **38**(3): p. 791-813. 21. Bibbins-Domingo, K., et al., Projected Effect of Dietary Salt Reductions on Future Cardiovascular Disease. N Engl J Med, 2010: p. NEJMoa0907355. 22. Webster, J.L., E.K. Dunford, and B.C. Neal, A systematic survey of the sodium contents of processed foods. Am J Clin Nutr, 2010. 91(2): p. 413-20. 23. Kumanyika, S., Behavioral aspects of intervention strategies to reduce dietary sodium. Hypertension, 1991. 17(1 Suppl): p. I190-5. 24. Lindsted, K.D., et al., *Healthy volunteer effect in a cohort study: temporal resolution in the* Adventist Health Study. J Clin Epidemiol, 1996. 49(7): p. 783-90. 25. Tuomilehto, J., et al., Community-based prevention of hypertension in North Karelia, Finland. Ann Clin Res, 1984. 16 Suppl 43: p. 18-27. 26. Staessen, J., et al., Salt intake and blood pressure in the general population: a controlled intervention trial in two towns. J Hypertens, 1988. 6(12): p. 965-73. 27. Beard, T.C., et al., The Hobart Salt Study 1995: few meet national sodium intake target. Med J Aust, 1997. 166(8): p. 404-7. 28. Jones, G., et al., A population-based study of the relationship between salt intake, bone resorption and bone mass. Eur J Clin Nutr, 1997. 51(8): p. 561-5. 29. Bao, D.Q., et al., Effects of dietary fish and weight reduction on ambulatory blood pressure *in overweight hypertensives*. Hypertension, 1998. **32**(4): p. 710-7. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

Mori, Y., et al., Effect of highly purified eicosapentaenoic acid ethyl ester on insulin
resistance and hypertension in Dahl salt-sensitive rats. Metabolism, 1999. 48(9): p. 1089-
95.
Cumming, R.G., P. Mitchell, and W. Smith, Dietary sodium intake and cataract: the Blue
Mountains Eye Study. Am J Epidemiol, 2000. 151(6): p. 624-6.
Nowson, C.A., T.O. Morgan, and C. Gibbons, Decreasing dietary sodium while following a
self-selected potassium-rich diet reduces blood pressure. J Nutr, 2003. 133 (12): p. 4118-23.
Nowson, C.A., et al., Blood pressure response to dietary modifications in free-living
individuals. J Nutr, 2004. 134(9): p. 2322-9.
Ward, N.C., et al., Oxidative stress in human hypertension: association with
antihypertensive treatment, gender, nutrition, and lifestyle. Free Radic Biol Med, 2004.
36 (2): p. 226-32.
Hodgson, J.M., et al., Partial substitution of carbohydrate intake with protein intake from
lean red meat lowers blood pressure in hypertensive persons. Am J Clin Nutr, 2006. 83(4):
p. 780-7.
Margerison C and C Nowson Dietary intake and 24-hour excretion of sodium and
notassium Asia Pac I Clin Nutr 2006 15: n S37
Julie Boorman, I.C. Dorothy Mackerras, Salt Intake From Processed Food and
June Boorman, J.C., Dorotny Wackerras., Suit Intuke 170m 170cesseu 1000 und
Discretionary Use in Australia. Food Standards Australia New Zealand, ACT Australia
Available at: <u>http://www.foodstandards.gov.au/_srcfiles/Salt_Intake_5.pdf</u>
26

- Brinkworth, G.D., et al., *Reductions in blood pressure following energy restriction for weight loss do not rebound after re-establishment of energy balance in overweight and obese subjects*. Clin Exp Hypertens, 2008. 30(5): p. 385-96.
- Charlton, K., et al., Urinary sodium excretion, dietary sources of sodium intake and knowledge and practices around salt use in a group of healthy Australian women. Aust N Z J Public Health, 2010. 34(4): p. 356-63.

alth, 2010. 34(+7).



SALT INTAKE ASSESSED BY 24-HOUR URINARY SODIUM EXCRETION IN A RANDOM AND OPPORTUNISTIC SAMPLE IN AUSTRALIA

Journal:	BMJ Open
Manuscript ID:	bmjopen-2013-003720.R1
Article Type:	Research
Date Submitted by the Author:	22-Oct-2013
Complete List of Authors:	Land, Mary-Anne; The George Institute for Global Health, ; The University of Sydney, Webster, Jacqui; The George Institute for Global Health, ; The University of Sydney, Christoforou, Anthea; The George Institute for Global Health, ; The University of Sydney, Praveen, D; The George Institute for Global Health, ; The University of Sydney, Jeffery, Paul; Deakin University, Chalmers, John; The George Institute for Global Health, ; The University of Sydney, Smith, Wayne; New South Wales Health, Woodward, Mark; The George Institute for Global Health, ; The University of Sydney, Barzi, Federica; The George Institute for Global Health, ; The University of Sydney, Nowson, Caryl; Deakin University, Flood, Victoria; The University of Wollongong, Neal, Bruce; The George Institute for Global Health, ; The University of Sydney,
Primary Subject Heading :	Public health
Secondary Subject Heading:	Complementary medicine, Epidemiology, Global health
Keywords:	Hypertension < CARDIOLOGY, NUTRITION & DIETETICS, PUBLIC HEALTH

SCHOLARONE[™] Manuscripts

SALT INTAKE ASSESSED BY 24-HOUR URINARY SODIUM EXCRETION IN A RANDOM AND OPPORTUNISTIC SAMPLE IN AUSTRALIA

Corresponding Author: Miss Mary-Anne Land The George Institute for Global Health PO BOX M201 Missenden Road Camperdown, NSW, AUSTRALIA 2050. T: +61 2 9993 4547 E: maland@georgeinstitute.org.au

Authors: Mary-Anne LAND^{a,b}, Jacqui, WEBSTER^{a,b}, Anthea, CHRISTOFOROU^{a,b}, D PRAVEEN^{a,b}, Paul JEFFERY^c, John CHALMERS^{a,b}, Wayne SMITH^d, Mark WOODWARD^{a,b}, Federica BARZI^{a,b}, Caryl NOWSON^c, Victoria FLOOD^e, Bruce NEAL ^{a,b}.

Affiliations: ^aThe George Institute for Global Health, Sydney, Australia, ^bThe University of Sydney, Sydney, Australia, ^cDeakin University Melbourne, Australia, ^dNew South Wales Health, Sydney, Australia, ^eThe University of Wollongong, Wollongong, Australia.

TABLES: 3

FIGURES: 1

SUPPLEMENTARY: 0

WORD COUNT: 2907

KEY WORDS: Salt, sodium, 24-hour urine, cardiovascular disease prevention

Abstract

Introduction: The gold standard method for measuring population salt intake is based on a 24-hour urine collection. However, because participant burden is high, response rates are typically low with less than one in four agreeing to provide specimens. At this low level of response it is possible that simply asking for volunteers would produce equally valid results. **Method:** We randomly selected 2152 adults from Lithgow, New South Wales and obtained usable 24-hour urine samples from 306 (response rate 16%). Specimens were also collected from a further 113 volunteers. Estimated salt consumption and the costs for each strategy were compared.

Results: The characteristics of the 'random' and 'volunteer' samples were moderately different in mean age 58 (standard deviation 14.6) vs. 49(17.7) years respectively; p<0.001) as well as self-reported alcohol use, tobacco use, history of hypertension and prescription drug use (all p<0.04). Overall crude mean 24-hour urinary salt excretion was 8.9(3.6)(g/d) in the random sample vs. 8.5(3.3)g/d for the volunteers (p=0.42). Corresponding age- and sex-adjusted estimates were 9.2(3.3)g/d and 8.8(3.4)g/d (p=0.29). Estimates for men 10.3(3.8) vs. 9.6(3.3)g/d; p=0.26) and women 7.6(3.0) vs. 7.9(3.2)g/d; p=0.43) were also similar for the two samples, as was salt excretion across age groups (p=0.72). The cost of obtaining each 24-hour urine sample was two times greater for the random compared to volunteer samples (A\$62 vs. A\$31).

Conclusion: The estimated salt consumption derived from the two samples were comparable and were not substantively different to estimates obtained from other surveys.

BMJ Open

In countries were salt is pervasive and cannot easily be avoided, estimates of consumption obtained from volunteer samples may be valid and less costly.

Article Focus

The Global Monitoring Framework for the Prevention and Control of NCDs has set a salt reduction target of 30% by 2025. The assessment of population salt intake underpins the implementation of salt reduction policies and evaluates progress. The gold standard method for assessing population salt intake is the collection of a 24-hour urine specimen. However, because of the high burden, participation rates are generally low and the cost is often high. Hence there is great interest in alternative, yet robust and affordable methods to assess salt intake.

Key Messages

The observation that an opportunistically recruited volunteer population sample appears to provide a reasonable estimate of salt intake is important because this could substantially reduce the cost of future monitoring efforts. If this finding was repeated in other settings this would have global implications, as the reporting of salt intake in 2015, 2020 and 2025 is encouraged as part of the Global Monitoring Framework for the Prevention and Control of NCDs.

Strengths and Limitations

BMJ Open

The 'Gold Standard' 24-hour urine method was used to estimate salt intake. The response rate for the random sample was low and the study location was a single town but the response rate and estimated level of salt excretion is not substantively different from that reported in a number of diverse population groups throughout the country.

Background

Non-communicable diseases (NCDs) are the leading cause of death accounting for an estimated 35 million (66%) of the 53 million deaths at all ages that occurred in 2010.[1] Raised blood pressure is the leading risk factor for global disease burden, and is estimated to cause 9.4 million deaths every year—more than half of the estimated 17 million deaths a year caused by cardiovascular disease.[2] Much evidence shows that a reduction in salt intake lowers blood pressure and there is a high likelihood that this would reduce the risk of cardiovascular disease.[3] While there is not a current definitive estimate of population dietary salt intake in Australia, it is widely accepted that average consumption is between 7 and 12g/d[4] far above the suggested dietary target for Australians of 4g/d.[5]

The reduction of salt intake and salt content of food has been strongly recommended as a cost effective action that should be undertaken immediately, with expected accelerated results in terms of lives saved, cases of disease prevented and costs avoided.[6] This position has since been historically endorsed by the 2011 Political Declaration of the United Nations High Level Meeting on NCDs[7] which led to the development and adoption of the Global Monitoring Framework and Voluntary Global Targets for the Prevention and Control of NCDs in which salt reduction is a core target.[8]

Measurement of population salt consumption is fundamental for planning and monitoring salt reduction policies and the gold standard method is based upon a 24-hour urine collection from a random community sample. Surveys of this type are, however, complex

BMJ Open

and expensive and because participant burden is high, randomly selected community samples typically have low response rates.[9-11] This has been noted as a significant concern at recent WHO NCD surveillance, monitoring and evaluation consultation meetings in which several member states have expressed doubts about the feasibility of using this method.[12] The potential adverse impact that a low response rate might have on the conclusions drawn was highlighted and the need for further research into practicable methods for defining and monitoring population salt consumption was underlined.[12]

The objective of the present study was to estimate sodium excretion using assays of 24hour urine samples collected from a regional Australian population. A key question about practicality was addressed by using both a standard random sampling approach to make the estimate while simultaneously recruiting an opportunistic (volunteer) sample to make an alternate estimate. The study also examined the costs associated with each strategy.

Methods

The data derived from a random sample and a convenience sample (volunteers) done concurrently in Lithgow, New South Wales, Australia between March and June 2011. Permission to undertake the study was obtained from the Lithgow City Council and the project was approved by the University of Sydney Human Research Ethics Committee.

Inclusion and exclusion criteria

Consenting individuals aged 20 years or above who were resident in Lithgow and listed on the 2009 Federal electoral roll were eligible for inclusion. There was no exclusion based on
Selection and recruitment process

Random sampling was done by selecting individuals at random from the electoral roll. The electoral roll provided the name and address of each potential participant with electronic databases searched to identify corresponding telephone numbers. Based on the assumption that approximately 25% of invited individuals would participate, 2152 individuals were selected to reach the desired sample size.

Potential participants were first mailed invitations to take part in the survey, with an explanation of the purpose of the study, a participant information sheet and a consent form provided. These individuals were then contacted by telephone to determine their willingness to participate and to schedule an interview time. Where a telephone number could not be obtained, the home address was visited by a member of the research team and willingness to participate was discussed face-to-face.

Volunteer sampling was done by offering participation in the study to individuals at two local shopping centres over several weeks. An information booth was established where those interested could seek further information about participation and arrange a visit by a member of the study team. Recruitment was completed at the time of the inquiry made to the study staff member manning the information booth.

Data collection process

Data collection for randomly selected individuals and the volunteer sample was identical and commenced with a visit to the study participant by a trained research assistant. Once consent was obtained the three components of data collection, comprising a questionnaire, a physical examination and a 24-hour urine collection were initiated. The questionnaire and physical examination were completed at the time of the visit and the urine collection was scheduled to be done within the following three days.

The *questionnaire* was fully structured and administered by research assistants, with all responses based on self-report. The questionnaire recorded information on sociodemographic variables, vascular disease history and current drug treatments. Participants were asked to provide the names of regular medications but if that was not known the purpose of the medication was recorded (for example, anti-hypertensive medication).

The physical examination comprised measurement of body weight (using calibrated Tantia HD-357 portable electronic scales (USA) and height (using a calibrated portable stadiometer Wedderburn WS-HRP model (Australia)) to the nearest 0.1kg and 0.1cm respectively, with body mass index (kg/height(m²)) then calculated. Blood pressure was measured using a manual inflation blood pressure monitor (A&D UA-&704) in triplicate, according to the American Heart Association protocol.[13]

A single 24-hour urine collection was obtained with the first voided urine upon waking on the day of collection being discarded and participants then collecting all voided urine up to and including the first void the following morning. The time at the beginning and the end of urine collection were recorded. The urine volume was noted and the urinary sodium concentration in an aliquot was measured by ion-selective electrode with the buffered kinetic Jaffe reaction without deproteinisation used for assay of urine creatinine (Cobas Integra 400). Suspected inaccurate urine collections (i.e. urinary creatinine < 4.0 mmol/day for women, or < 6.0mmol/day for men, or a 24-hour urine collection of < 500ml for either sex) and extreme outliers for urinary creatinine (i.e. > 3 standard deviations from the mean) were excluded. The rates of exclusion were similar for the random and volunteer samples. For each individual, the 24-hour sodium excretion value (mmol/day) was calculated as the concentration of sodium in the urine (mmol/L) multiplied by the urinary volume (L/day). The conversion from sodium (Na) to salt (NaCl) was made by multiplying the sodium value by 2.542 (NaCl(g)=Na(g) x 2.542).

Cost data

The pre-interview costs involved staff time in selecting and attempting to reach subjects including accessing the electoral roll, sending participant invitations, follow-up phone calls and door-knocking to schedule interviews with those randomly selected, as well as setting up and manning an information booth to engage the volunteer sample were documented. The post-interview costs comprised primarily of pathology expenses and were the same for each sample.

Statistical analyses

The baseline characteristics of the sample selected at random and the volunteer sample were summarized and compared using t-tests and Chi-square tests as were their average urinary sodium values. In addition to the crude estimates described above, weighted estimates of overall population mean sodium excretion were also made in an effort to account for the non-random sampling of individuals. This was done for both the randomly selected group (to adjust for the poor response rate) and for the volunteer group (to adjust for their non-representative age and sex structure) by calculating age- and sex-specific estimates of salt excretion for 20 year age bands (20-39, 40-59, and 60 plus) for men and women and then weighting these by the age and sex structure of the population to obtain an overall estimate for the community. Regression models were fitted to explore the association between baseline participant characteristics and a range of covariates in the combined (random plus volunteer) sample. Throughout, a p-value of 0.05 or less was taken to indicate a finding unlikely to have arisen solely by chance. Statistical analyses were conducted using SPSS for Windows (Version 21, SPSS Inc, Chicago, IL) and STATA for windows (StataCorp. 2009 Strata Statistical Software: Release 11. College Station, TX: StataCorp LP).

Results

Of 2,152 individuals selected by random sampling of the electoral roll, 853 (40%) were uncontactable after multiple attempts, 126 (5.8%) were ineligible because they had moved out of the study area, 5 (0.2%) had died and 843 (39%) declined to participate. The remaining 329 individuals comprise the 'random' sample with a response rate of 16%. The volunteer Page 11 of 53

BMJ Open

sample comprised 120 individuals recruited consecutively at a shopping mall over a seven day period. The characteristics of the random and volunteer samples were moderately different in a number of regards, including age, proportion tobacco use, alcohol use , selfreported hypertension and use of any prescription medication (Table 1).

Crude and weighted 24-hour urinary salt excretion in random and volunteer samples

For the analysis there were 306 individuals in the random sample and 113 in the volunteer group with 20 excluded because of suspected incomplete urine collections and 10 for other reasons (Figure 1). The crude mean 24-hour urinary salt excretion was 8.9 (standard deviation 3.6) g/d in the random sample and 8.5 (3.3) g/d in the volunteer group (p=0.42). The corresponding weighted estimates for the Lithgow population were 9.2 (3.9) g/d and 8.8 (3.4) g/d respectively (p=0.29).

The proportion of randomly sampled individuals exceeding the 6 g/d recommended Maximum Level for Australians was 79%, the proportion exceeding the Australian Suggested Dietary Target of 4 g/d was 94% and the proportion exceeding the WHO Maximum Recommended Level of 5 g/d was 87%. The corresponding proportions for the volunteer group were 75%, 93% and 84%. Population-weighted estimates of these proportions were not substantively different.

24-hour urinary salt excretion in participant subgroups

Urinary sodium excretion in both population samples was significantly higher in men compared to women 10.3 (3.8) g/d vs. 7.6 (3.0) g/d; p<0.001 for random sample and 9.6 (3.3) g/d vs. 7.9 (3.2) g/d; p=0.006 for the volunteer sample (Table 2) and this was also true for every age group. There was an inverse association between daily salt excretion and age (Table 2) such that for every decade increase in age there was 0.3g/d less excretion of salt (p=0.007). The association between salt excretion and BMI was positive with every unit rise in BMI associated with a 0.16g/d greater excretion of salt (p<0.001). Similar patterns were observed in both the random and volunteer population samples. There were no other significant associations observed between salt excretion levels and recorded participant characteristics including education, health status, tobacco use, alcohol use, blood pressure, disease history or prescription drug use (all p>0.05).

Costs associated with random and volunteer survey methods

The two main costs associated with doing the study were staff salaries and pathology expenses. Due primarily to the increased staff time required for the selection and interaction with the randomly selected individuals the estimated average cost associated with obtaining a valid 24-hour urine sample was greater for each participant in the random sample (about AUD\$ 62) compared to each participant in the volunteer sample (about AUD\$ 31).

Discussion

In this population salt intake greatly exceeds the recommended levels, reaffirming the urgent need for concerted action to address salt consumption in Australia. Mean salt

excretion levels were some 50% higher than maximum recommended levels[5, 14] and only about one in every twenty individuals was found to be consuming the level of salt recommended for good health. Even these data are likely to be an under-estimate of the problem because the approximate 10% of salt excreted by the gastro-intestinal system and the skin will have gone unrecorded.[15] The level of excess salt consumption indicated by this survey would be anticipated to cause substantial disease burden in Australia leading both to large numbers of lives lost prematurely and to many individuals suffering significant disability.[16] With centrally implemented salt reduction programs projected to deliver large population health gains at very low cost [17-19], the implementation of an effective salt reduction program should be a priority for the government of Australia.[20, 21]

The observation that the volunteer sample produced similar findings to the random sample is important because it was much easier and less costly to collect data from the volunteer sample than from the random sample. There are several reasons why a volunteer sample might provide a similar result to a random sample when estimating population salt consumption from 24-hour urine samples. First, the response rate in a random sample from whom a 24-hour urine sample is sought is typically very low, averaging 20% (range 9.7% to 26.8%) in a series of recently reported studies.[9-11, 20] In this situation the random sample effectively becomes a volunteer sample and any biases consequent upon using a volunteer sample might also be apparent in the 'random' sample. That said, there were many differences between the characteristics of the random and volunteer samples included

in this study but these did not translate into detectable differences in the observed sodium excretion. Another possible explanation therefore is the ubiquitous nature of salt in the food supply[22] and the rather limited capacity of even motivated individuals to meaningfully modify their salt consumption,[23] thereby minimizing the impact of any "healthy volunteer" effect.[24]

In some countries it may be possible to achieve better response rates [25, 26] and in others it may be that specific dietary practices or other cultural factors will mean that a volunteer sample will not give a good measure of true population salt intake. If, however, the findings reported here are observed elsewhere, volunteer sampling might provide a low-cost alternate to traditional random sampling techniques. At the very least it may be possible to use a volunteer sample to demonstrate the need for action - most countries in the world are likely to have salt consumption levels far above the WHO consumption target of <5g/d, and the likelihood that the selection of a volunteer sample will lead to an under-recording of salt consumption of a very large magnitude is probably fairly small.

In addition to the baseline assessment required to justify the commencement of a salt reduction strategy, ongoing monitoring of salt consumption is required to objectively determine program efficacy. If the resources required to conduct high quality surveys of a random population sample can be acquired then this remains the optimal approach both to baseline evaluation and monitoring of progress. If not, then repeat surveys of volunteers are likely to be of value if the methods used for participant selection are identical on each

BMJ Open

occasion – if the biases are the same on each measurement occasion then any real rise or fall in salt consumption should be clearly apparent.

The cost estimates made for this study showed that recruiting the volunteer sample was a significantly less expensive exercise than recruiting the random population sample. The primary reason for this was the much reduced fieldwork time required for the per capita recruitment of the volunteer sample. Pathology and other recorded costs were otherwise approximately the same. Expenses that were not specifically determined were the costs of computer hardware, computer software, the training of the field staff, and the time required for supervision by the project manager. The last two of these are also likely to have been lower for the volunteer sample due to the simplified and more rapid recruitment process and, as a consequence, the reported difference between costs is likely to have been under-, rather than over-estimated.

Strengths and limitations

The 'Gold Standard' 24-hour urine method was used to estimate salt intake with standard checks for completeness of the specimens based upon urine volume and urine creatinine excretion. The response rate for the random sample was low but comparable to other studies done in similar settings over recent years.[9-11] The sample size was relatively small and results for subgroups are somewhat imprecise as a consequence. It is possible, for this same reason, that the study may have failed to identify small, but real, differences between the salt excretion levels determined by the two different population sampling

methods. The location of the study in a single town in a regional area of New South Wales compromises the direct generalizability of the study findings to Australia as a whole, although the estimated level of salt excretion is not substantively different from that reported in a number of diverse population groups throughout the country.[27-39]

Conclusion

These data affirm that current efforts to reduce salt intake in Australia are failing, with a large majority of the population studied consuming more than the recommended Australian Upper Limit of 6g/d and almost everyone eating more than the Suggested Dietary Target of 4g/day. The observation that an opportunistically recruited volunteer population sample appears to provide a reasonable estimate of salt intake is important because this could substantially reduce the cost of future monitoring efforts. If this finding was repeated in other settings this would have global implications because sodium reduction has been proposed to all member states by the WHO. Most countries, however, have very limited resources available and any reduction in program cost that can be achieved without seriously adversely affecting program quality will be an important step forward. With population-based salt reduction strategies already shown to be cost effective or cost-saving in most settings, these new data further support the feasibility of widespread rollout of national salt reduction efforts around the world.

	Random sample (n=306)	Volunteer sample (n=113)	p-value
Female (%)	52.9	61.9	0.10
Age, years (mean)	57.6	49.3	< 0.00
Height, cm (mean)	167.5	167.6	0.85
Weight, kg (mean)	81.8	83.9	0.30
BMI, kg/m^2 (mean)	29.1	29.8	0.27
Systolic bp, mmHg (mean)	126.7	123.7	0.16
Diastolic bp, mmHg (mean)	78.7	78.9	0.88
Education			0.22
-Secondary (%)	63.7	55.8	
-Tertiary (%)	25.5	32.7	
-Postgraduate (%)	10.8	11.5	
Health Status			0.21
-Very good (%)	50.3	48.7	
-Good (%)	29.4	23.9	
-Fair (%)	20.2	27.4	
Current smoker (> 1 / day) (%)	8.2	22.1	< 0.00
Ever smoked (> $1 / day$) (%)	41.2	53.1	0.03
Alcoholic consumption (time since l	ast consumption)		0.04
One week or less (%)	62.1	42.5	
> one week < 12months (%)	19.9	34.5	
12 months or more (%)	11.1	10.6	
Never (%)	6.9	12.4	
Have you ever been told by a doctor	or nurse that you have	:	
-high blood pressure (%)	44.1	30.1	0.03
-low blood pressure (%)	15.4	14.2	0.76
-high cholesterol (%)	37.3	30.0	0.16
-heart attack (%)	8.2	3.5	0.10
-stroke (%)	3.9	1.8	0.37
-angina (%)	6.9	4.4	0.30
-diabetes (%)	11.1	7.1	0.26

Lipid lowering (%)	11.1	7.1	0.62
Aspirin (%)	8.8	2.7	0.06
Glucose lowering (%)	22.5	7.1	0.17
Any prescription medication (%)	73.9	59.2	0.02

*Participants could be taking more than one prescribed medication

TABLE 2. U	JRINARY	SALT	EXCRET	ION (GRAMS/DA	4 Y)
------------	---------	------	--------	-------	----------	-------------

	Rando	om sample	Volun	teer sample	
	<u>(n</u>	=306)	(r	n=113)	
	Mean	(SD)	Mean	(SD)	P value
Overall crude	8.9	(3.6)	8.5	(3.3)	0.42
Overall weighted*	9.2	(3.9)	8.8	(3.4)	0.29
Female					0.27
20-39	8.7	(4)	7.9	(2.9)	
40-59	8	(3.1)	7.8	(3.8)	
60+	6.8	(2.4)	7.9	(2.6)	
All female	7.6	(3)	7.9	(3.2)	
Male					0 40
20-39	10.8	(4.7)	10.5	(3.9)	00
40-59	11.1	(4.2)	9.8	(3.0)	
60+	9.7	(3.1)	8.6	(3.0)	
All male	10.3	(3.8)	9.6	(3.3)	
Education					0.25
Secondary	9.1	(3.7)	8.9	(3.4)	
Tertiary	8.3	(3.0)	8.5	(3.3)	
Post graduate	8.4	(3.6)	8	(3.3)	
Health Status					0.89
Very Good	8.7	(3.8)	8	(2.9)	
Good	8.8	(3.5)	9.3	(3.7)	
Fair	8.7	(2.8)	8.3	(2.6)	
Current Smoker	9	(38)	88	(3 4)	0.82
Ever Smoked	8.8	(3.6)	9	(3.6)	0.74
Alcohol Consumption					
(time since last consumption)					0.45
One week or less	88	(3.8)	8.7	(3.8)	0.10
> one week < 12 months	8.6	(3.2)	8.7	(2.9)	
12 months or more	9.3	(3.8)	7.8	(2.8)	
Never	9.1	(3.2)	8.1	(3.6)	

*Adjusted for response rate (random sample) and non-random selection (volunteer sample) by weighting age-and sex-specific estimates to the age and sex structure of the Lithgow population

2
2
3
4
5
5
6
7
Q
0
9
10
11
11
12
13
11
14
15
16
17
17
18
19
20
20
21
22
22
20
24
25
26
20
27
28
20
29
30
31
22
32
33
34
25
30
36
37
20
30
39
40
11
41
42
43
11
45
46
17
4/
48
49
50
50
51
52
52
55
54
55
56
50
57
58
50

1

TABLE 3. COST OF RANDOM COMPARED TO VOLUNTEER SAMPLING(AUD)

	Random	Volunteer
	Sample(n=306)	Sample(n=113)
Pre-interview costs		
Sampling from electoral roll	\$2,152	0
Scheduling interviews	\$8,704	\$1,088
8		
Post-interview costs		
Pathology costs	\$4,211	\$1,584
Other costs		
Postage	\$2,169	0
Telephone	\$1,870	\$818
Shopping centre stand fee		\$10
TOTAL	\$19,106	\$3,500
COST PER PARTICIPANT*	\$62.44	\$30.96

*Cost per participant calculated by dividing total cost by the number of valid participants in each sample.



FIGURE 1. RECRUITMENT OF POPULATION SAMPLE

Acknowledgments

The authors thank Lithgow City Council, the Nepean Blue Mountains Local Area Health Network for their support and most importantly all of the participants for their support and interest in the study.

Contributorship Statement

All authors fulfill the ICMJE guidelines for authorship and have approved the final version of the manuscript submitted to BMJ Open.

Mary-Anne Land - contributed to study concept and design, data collection, analysis and interpretation of the data, drafting the article and final version of the article.

Jacqui Webster - contributed to the study design, revising content and final approval of the version to be published.

Anthea Christoforou – contributed to the analysis of data, revising content and final approval of the version to be published

D Praveen – contributed to the analysis and interpretation of data, revising content and final approval of the version to be published.

Paul Jeffery – contributed to the study design, interpretation of data, revising content and final approval of the version to be published.

John Chalmers – contributed to the conception and study design, revising critically and final approval of the version to be published.

Wayne Smith - contributed to the conception and study design, revising critically and final approval of the version to be published.

BMJ Open

Mark Woodward – contributed to the conception and study design, revising critically and final approval of the version to be published.

Federica Barzi – contributed to the analysis and interpretation of the data, revising critically and final approval of the version to be published.

Caryl Nowson - contributed to the conception and study design, revising critically and final approval of the version to be published.

Victoria Flood - contributed to the conception and study design, revising critically and final approval of the version to be published.

Bruce Neal – contributed to the conception and study design, analysis and interpretation of data, drafting of the article, revising critically and final approval of the version to be published.

Sources of support

This work was supported by a National Health and Medical Research Council (NHMRC) of Australia partnership project (Neal #13372) which includes The George Institute for Global Health in partnership with the Australian Division of World Action on Salt and Health; the Australian Food and Grocery Council; the New South Wales Food Authority; and New South Wales Health. Bruce Neal was supported by an Australian Research Council Future Fellowship, Mark Woodward by a NHMRC Fellowship and Jacqui Webster by a National Heart Foundation and Stroke Foundation postdoctoral research fellowship.

Conflicts of interest

J.W. is the co-ordinator, and B.N. is the Chairman of the Australian Division of World Action on Salt and Health.

References

- Lozano, R., et al., Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. 380(9859): p. 2095-128.
- Lim, S.S., et al., A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. 380(9859): p. 2224-60.
- 3. He, F.J., N.R. Campbell, and G.A. MacGregor, *Reducing salt intake to prevent hypertension and cardiovascular disease*. Rev Panam Salud Publica, 2012. **32**(4): p. 293-300.
- Keogh, J.B. and P.M. Clifton, *Salt intake and health in the Australian population*. Med J Aust, 2008. 189(9): p. 526.
- 5. National Health and Medical Research Council, *Nutrient Reference Values for Australia and New Zealand.*, 2006, Department of Health and Ageing.
- 6. The World Health Organisation, 2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases, 2008.
- United Nations. 2011 High Level Meeting on Prevention and Control of Non-communicable Diseases. 2011 [cited 2012 12/12/2012]; Available from: http://www.un.org/en/ga/ncdmeeting2011/.
- 8. The World Health Organization, *Formal meeting of Member States to conclude the work on the comprehensive global monitoring framework, including indicators, and a set of voluntary global targets for the prevention and control of noncommunicable diseases*

Geneva, 5–7 November 2012, 2012: Geneva.

BMJ Open

9.	Ribic, C.H., et al., Salt intake of the Slovene population assessed by 24 h urinary sodium
	excretion. Public Health Nutr, 2010. 13(11): p. 1803-9.
10.	Chappuis, A., et al., Swiss survey on salt intake: main results. 2011.
11.	Ortega, R.M., et al., Estimation of salt intake by 24 h urinary sodium excretion in a
	representative sample of Spanish adults. Br J Nutr, 2011. 105(5): p. 787-94.
12.	The World Health Organisation, European Regional Technical Consultation on
	Noncommunicable Disease Surveillance, Monitoring and Evaluation. 2012.
13.	Perloff, D., et al., Human blood pressure determination by sphygmomanometry. Circulation,
	1993. 88 (5 Pt 1): p. 2460-70.
14.	The World Health Organization, Reducing Salt Intake in Populations, in Report of a WHO
	Forum and Technical Meeting2007, World Health Organisation: Geneva.
15.	Kirkendall, A.M., et al., The effect of dietary sodium chloride on blood pressure, body
	fluids, electrolytes, renal function, and serum lipids of normotensive man. J Lab Clin Med,
	1976. 87 (3): p. 411-34.
16.	Cobiac, L.J., et al., Which interventions offer best value for money in primary prevention of
	cardiovascular disease? PLoS One, 2012. 7(7): p. e41842.
17.	Beaglehole, R., et al., UN High-Level Meeting on Non-Communicable Diseases: addressing
	four questions. Lancet, 2011. 378(9789): p. 449-55.
18.	National Heart Foundation of Australia, Summary of evidence statement on the relationships
	between dietary electrolytes and cardiovascular disease.
	http://www.heartfoundation.org.au/SiteCollectionDocuments/Dietary-Electrolytes-CVD-
	Summary-Evidence.pdf, 2006.

19. Cook, N.R., et al., Long term effects of dietary sodium reduction on cardiovascular disease

outcomes: observational follow-up of the trials of hypertension prevention (TOHP). BMJ, 2007. **334**(7599): p. 885-8. 20. Brown, I.J., et al., Salt intakes around the world: implications for public health. Int J Epidemiol, 2009. **38**(3): p. 791-813. 21. Bibbins-Domingo, K., et al., Projected Effect of Dietary Salt Reductions on Future Cardiovascular Disease. N Engl J Med, 2010: p. NEJMoa0907355. 22. Webster, J.L., E.K. Dunford, and B.C. Neal, A systematic survey of the sodium contents of processed foods. Am J Clin Nutr, 2010. 91(2): p. 413-20. 23. Kumanyika, S., Behavioral aspects of intervention strategies to reduce dietary sodium. Hypertension, 1991. 17(1 Suppl): p. I190-5. 24. Lindsted, K.D., et al., *Healthy volunteer effect in a cohort study: temporal resolution in the* Adventist Health Study. J Clin Epidemiol, 1996. 49(7): p. 783-90. 25. Tuomilehto, J., et al., Community-based prevention of hypertension in North Karelia, Finland. Ann Clin Res, 1984. 16 Suppl 43: p. 18-27. 26. Staessen, J., et al., Salt intake and blood pressure in the general population: a controlled intervention trial in two towns. J Hypertens, 1988. 6(12): p. 965-73. 27. Beard, T.C., et al., The Hobart Salt Study 1995: few meet national sodium intake target. Med J Aust, 1997. 166(8): p. 404-7. 28. Jones, G., et al., A population-based study of the relationship between salt intake, bone resorption and bone mass. Eur J Clin Nutr, 1997. 51(8): p. 561-5. 29. Bao, D.Q., et al., Effects of dietary fish and weight reduction on ambulatory blood pressure *in overweight hypertensives*. Hypertension, 1998. **32**(4): p. 710-7. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open

2
3
4
5
6
7
1
8
9
10
11
12
12
13
14
15
16
17
18
10
19
20
21
22
23
24
25
20
20
27
28
29
30
31
20
32
33
34
35
36
27
20
38
39
40
41
42
43
11
44 45
45
46
47
48
49
50
50
51
52
53
54
55
56
57
57
20
59
60

Mori, Y., et al., *Effect of highly purified eicosapentaenoic acid ethyl ester on insulin resistance and hypertension in Dahl salt-sensitive rats.* Metabolism, 1999. 48(9): p. 1089-95.

- Cumming, R.G., P. Mitchell, and W. Smith, *Dietary sodium intake and cataract: the Blue Mountains Eye Study*. Am J Epidemiol, 2000. 151(6): p. 624-6.
- 32. Nowson, C.A., T.O. Morgan, and C. Gibbons, *Decreasing dietary sodium while following a self-selected potassium-rich diet reduces blood pressure*. J Nutr, 2003. **133**(12): p. 4118-23.
- 33. Nowson, C.A., et al., *Blood pressure response to dietary modifications in free-living individuals*. J Nutr, 2004. **134**(9): p. 2322-9.
- 34. Ward, N.C., et al., Oxidative stress in human hypertension: association with antihypertensive treatment, gender, nutrition, and lifestyle. Free Radic Biol Med, 2004.
 36(2): p. 226-32.
- 35. Hodgson, J.M., et al., *Partial substitution of carbohydrate intake with protein intake from lean red meat lowers blood pressure in hypertensive persons*. Am J Clin Nutr, 2006. 83(4): p. 780-7.
- 36. Margerison, C. and C. Nowson, *Dietary intake and 24-hour excretion of sodium and potassium*. Asia Pac J Clin Nutr, 2006. **15**: p. S37.
- Julie Boorman, J.C., Dorothy Mackerras., Salt Intake From Processed Food and Discretionary Use in Australia. Food Standards Australia New Zealand, ACT Australia Available at: <u>http://www.foodstandards.gov.au/_srcfiles/Salt_Intake_5.pdf</u>

- Brinkworth, G.D., et al., *Reductions in blood pressure following energy restriction for weight loss do not rebound after re-establishment of energy balance in overweight and obese subjects*. Clin Exp Hypertens, 2008. 30(5): p. 385-96.
- Charlton, K., et al., Urinary sodium excretion, dietary sources of sodium intake and knowledge and practices around salt use in a group of healthy Australian women. Aust N Z J Public Health, 2010. 34(4): p. 356-63.

alth, 2010. 34(+7).

BMJ Open

SALT INTAKE ASSESSED BY 24-HOUR URINARY SODIUM EXCRETION IN A RANDOM AND OPPORTUNISTIC SAMPLE IN AUSTRALIA

Corresponding Author: Miss Mary-Anne Land The George Institute for Global Health PO BOX M201 Missenden Road Camperdown, NSW, AUSTRALIA 2050. T: +61 2 9993 4547 E: maland@georgeinstitute.org.au

Authors: Mary-Anne LAND^{a,b}, Jacqui, WEBSTER^{a,b}, Anthea, CHRISTOFOROU^{a,b}, D PRAVEEN^{a,b}, Paul JEFFERY^c, John CHALMERS^{a,b}, Wayne SMITH^d, Mark WOODWARD^{a,b}, Federica BARZI^{a,b}, Caryl NOWSON^c, Victoria FLOOD^e, Bruce NEAL ^{a,b}.

Affiliations: ^aThe George Institute for Global Health, Sydney, Australia, ^bThe University of Sydney, Sydney, Australia, ^cDeakin University Melbourne, Australia, ^dNew South Wales Health, Sydney, Australia, ^eThe University of Wollongong, Wollongong, Australia.

TABLES: 3

FIGURES: 1

SUPPLEMENTARY: 0

WORD COUNT: 2907

KEY WORDS: Salt, sodium, 24-hour urine, cardiovascular disease prevention

Article Focus

The Global Monitoring Framework for the Prevention and Control of NCDs has set a salt reduction target of 30% by 2025. The assessment of population salt intake underpins the implementation of salt reduction policies and <u>enables_evaluates_evaluation of progress</u>. The gold standard method for assessing population salt intake is the collection of a 24-hour urine specimen from a random population sample. However, because of the high <u>participant</u> burden, <u>participation_response</u> rates are generally low and the cost is often high. Hence there is great interest in alternative, yet robust and affordable methods to assess salt intake.

Key Messages

The observation that an opportunistically recruited volunteer population sample appears tomay provide a reasonable estimate of salt intake is important because this could substantially reduce the cost of future monitoring efforts. If this our finding was repeated in other settings and larger populations this would have be of global implications importance, as because the regular reporting of salt intake in 2015, 2020 and 2025 is encouraged as part of the Global Monitoring Framework for the Prevention and Control of NCDs.

Strengths and Limitations

The 'Gold Standard' 24-hour urine method was used to estimate sodium intake <u>but the</u> <u>sammaple size was small and the</u>. The response rate for the random sample was low-and the study location was a single town but the response rate and estimated level of salt excretion is not substantively different from that reported in a number of diverse population groups throughout the country. The study raises an interesting hypothesis but requires confirmation in other studies.-

BMJ Open

Abstract

Introduction: The gold standard method for measuring population sodium intake is based on a 24-hour urine collection done in a random population sample. However, because participant burden is high, response rates are typically low with less than one in four agreeing to provide specimens. At this low level of response it is possible that simply asking for volunteers would produce equally valid results.

Method: We randomly selected 2152 adults from Lithgow, New South Wales and obtained usable 24-hour urine samples from 306 (response rate 16%). Specimens were also collected from a further 113 volunteers. Estimated salt consumption and the costs for each strategy were compared.

Results: The characteristics of the 'random' and 'volunteer' samples were moderately different in mean age 58 (standard deviation 14.6) vs. 49(17.7) years respectively; p<0.001) as well as self-reported alcohol use, tobacco use, history of hypertension and prescription drug use (all p<0.04). Overall crude mean 24-hour urinary salt excretion was 8.9(3.6)(g/d) in the random sample vs. 8.5(3.3)g/d for the volunteers (p=0.42). Corresponding age- and sex-adjusted estimates were 9.2(3.3)g/d and 8.8(3.4)g/d (p=0.29). Estimates for men 10.3(3.8) vs. 9.6(3.3)g/d; p=0.26) and women 7.6(3.0) vs. 7.9(3.2)g/d; p=0.43) were also similar for the two samples, as was salt excretion across age groups (p=0.72). The cost of obtaining each 24-hour urine sample was two times greater for the random compared to volunteer samples (A\$62 vs. A\$31).

Conclusion: The estimated salt consumption derived from the two samples was comparable and was not substantively different to estimates obtained from other surveys. In countries were salt is pervasive and cannot easily be avoided, estimates of consumption obtained from volunteer samples may be valid and less costly.

Background

Non-communicable diseases (NCDs) are the leading cause of death accounting for an estimated 35 million (66%) of the 53 million deaths at all ages that occurred in 2010.[1] Raised blood pressure is the leading risk factor for global disease burden, and is estimated to cause 9.4 million deaths every year—more than half of the estimated 17 million deaths a year caused by cardiovascular disease.[2] Much evidence shows that a reduction in salt intake lowers blood pressure and there is a high likelihood that this would reduce the risk of cardiovascular disease.[3] While there is not a current definitive estimate of population dietary salt intake in Australia, it is widely accepted that average consumption is between 7 and 12g/d[4] far above the suggested dietary target for Australians of 4g/d.[5]

The reduction of salt intake and sodium content of food has been strongly recommended as a cost effective action that should be undertaken immediately, with expected accelerated results in terms of lives saved, cases of disease prevented and costs avoided.[6] This position has since been historically endorsed by the 2011 Political Declaration of the United Nations High Level Meeting on NCDs[7] which led to the development and adoption of the Global Monitoring Framework and Voluntary Global Targets for the Prevention and Control of NCDs in which salt reduction is a core target.[8]

Measurement of population salt consumption is fundamental for planning and monitoring salt reduction policies and the gold standard method is based upon a 24-hour urine collection from a random community sample. Surveys of this type are, however, complex and expensive and because participant burden is high, randomly selected community samples typically have low response rates.[9-11] This has been noted as a significant

BMJ Open

concern at recent WHO NCD surveillance, monitoring and evaluation consultation meetings in which several member states have expressed doubts about the feasibility of using this method.[12] The potential adverse impact that a low response rate might have on the conclusions drawn was highlighted and the need for further research into practicable methods for defining and monitoring population salt consumption was underlined.[12]

The objective of the present study was to measure sodium excretion using assays of 24hour urine samples collected from a regional Australian population. A key question about practicality was addressed by using both a standard random sampling approach to make the estimate while simultaneously recruiting an opportunistic (volunteer) sample to make an alternate estimate. The study also examined the costs associated with each strategy.

Methods

The data derived from a random sample and a convenience sample (volunteers) done concurrently in Lithgow, New South Wales, Australia between March and June 2011. Permission to undertake the study was obtained from the Lithgow City Council and the project was approved by the University of Sydney Human Research Ethics Committee.

Inclusion and exclusion criteria

Consenting individuals aged 20 years or above who were resident in Lithgow and listed on the 2009 Federal electoral roll were eligible for inclusion. There was no exclusion based on inter-current illness, use of medications or any other aspect of demography or personal history.

Selection and recruitment process

Random sampling was done by selecting individuals at random from the electoral roll. The electoral roll provided the name and address of each potential participant with electronic databases searched to identify corresponding telephone numbers. Based on the assumption that approximately 25% of invited individuals would participate, 2152 individuals were selected to reach the desired sample size.

Potential participants were first mailed invitations to take part in the survey, with an explanation of the purpose of the study, a participant information sheet and a consent form These individuals were then contacted by telephone to determine their provided. willingness to participate and to schedule an interview time. Where a telephone number could not be obtained, the home address was visited by a member of the research team and willingness to participate was discussed face-to-face.

Volunteer sampling was done by offering participation in the study to individuals at two local shopping centres over several weeks. An information booth was established where those interested could seek further information about participation and arrange a visit by a member of the study team. Recruitment was completed at the time of the inquiry made to the study staff member manning the information booth.

Data collection process

Data collection for randomly selected individuals and the volunteer sample was identical and commenced with a visit to the study participant by a trained research assistant. Once consent was obtained the three components of data collection, comprising a questionnaire, a physical examination and a 24-hour urine collection were initiated. The questionnaire and

BMJ Open

physical examination were completed at the time of the visit and the urine collection was scheduled to be done within the following three days.

The *questionnaire* was fully structured and administered by research assistants, with all responses based on self-report. The questionnaire recorded information on sociodemographic variables, vascular disease history and current drug treatments. Participants were asked to provide the names of regular medications but if that was not known the purpose of the medication was recorded (for example, anti-hypertensive medication).

The physical examination comprised measurement of body weight (using calibrated Tantia HD-357 portable electronic scales (USA) and height (using a calibrated portable stadiometer Wedderburn WS-HRP model (Australia)) to the nearest 0.1kg and 0.1cm respectively, with body mass index (kg/height(m²)) then calculated. Blood pressure was measured using a manual inflation blood pressure monitor (A&D UA-&704) in triplicate, according to the American Heart Association protocol.[13]

A single 24-hour urine collection was obtained with the first voided urine upon waking on the day of collection being discarded and participants then collecting all voided urine up to and including the first void the following morning. The time at the beginning and the end of urine collection were recorded. The urine volume was noted and the urinary sodium concentration in an aliquot was measured by ion-selective electrode with the buffered kinetic Jaffe reaction without deproteinisation used for assay of urine creatinine (Cobas Integra 400). Suspected inaccurate urine collections (i.e. urinary creatinine < 4.0 mmol/day for women, or < 6.0mmol/day for men, or a 24-hour urine collection of < 500ml for either sex) and extreme outliers for urinary creatinine (i.e. > 3 standard deviations from the mean)

were excluded. The rates of exclusion were similar for the random and volunteer samples. For each individual, the 24-hour sodium excretion value (mmol/day) was calculated as the concentration of sodium in the urine (mmol/L) multiplied by the urinary volume (L/day). The conversion from mmol to grams was made by dividing by 17 and the conversion from sodium (Na) to salt (NaCl) by multiplying by 2.542.

Cost data

The pre-interview costs involved staff time in selecting and attempting to reach subjects including accessing the electoral roll, sending participant invitations, follow-up phone calls and door-knocking to schedule interviews with those randomly selected, as well as setting up and manning an information booth to engage the volunteer sample. The post-interview costs comprised primarily of pathology expenses and were the same for each sample.

Statistical analyses

The baseline characteristics of the sample selected at random and the volunteer sample were summarized and compared using t-tests and Chi-square tests as were their average urinary sodium values. In addition to the crude estimates described above, weighted estimates of overall population mean sodium excretion were also made in an effort to account for the non-random sampling of individuals. This was done for both the randomly selected group (to adjust for the poor response rate) and for the volunteer group (to adjust for the poor response rate) by calculating age- and sex-specific estimates of salt excretion for 20 year age bands (20-39, 40-59, and 60 plus) for men and women and then weighting these by the age and sex structure of the population to obtain an overall estimate for the community. Regression models were fitted to explore the association between baseline participant characteristics and a range of covariates in the

BMJ Open

combined (random plus volunteer) sample. Throughout, a p-value of 0.05 or less was taken to indicate a finding unlikely to have arisen solely by chance. Statistical analyses were conducted using SPSS for Windows (Version 21, SPSS Inc, Chicago, IL) and STATA for windows (StataCorp. 2009 *Strata Statistical Software: Release 11*. College Station, TX: StataCorp LP).

Results

Of 2,152 individuals selected by random sampling of the electoral roll, 853 (40%) were uncontactable after multiple attempts, 126 (5.8%) were ineligible because they had moved out of the study area, 5 (0.2%) had died and 843 (39%) declined to participate. The remaining 329 individuals comprise the 'random' sample with a response rate of 16%. The volunteer sample comprised 120 individuals recruited consecutively at a shopping mall over a seven day period. The characteristics of the random and volunteer samples were moderately different in a number of regards, including age, proportion <u>using</u> tobacco-use, alcohol use-, self-reported hypertension and use of any prescription medication (Table 1).

Crude and weighted 24-hour urinary salt excretion in random and volunteer samples

For the analysis there were 306 individuals in the random sample and 113 in the volunteer group with 20 excluded because of suspected incomplete urine collections and 10 for other reasons (Figure 1). The crude mean 24-hour urinary salt excretion was 8.9 (standard deviation 3.6) g/d in the random sample and 8.5 (3.3) g/d in the volunteer group (p=0.42). The corresponding weighted estimates for the Lithgow population were 9.2 (3.9) g/d and 8.8 (3.4) g/d respectively (p=0.29).

The proportion of randomly sampled individuals exceeding the 6 g/d recommended Maximum Level for Australians was 79%, the proportion exceeding the Australian Suggested Dietary Target of 4 g/d was 94% and the proportion exceeding the WHO Maximum Recommended Level of 5 g/d was 87%. The corresponding proportions for the volunteer group were 75%, 93% and 84%. Population-weighted estimates of these proportions were not substantively different.

24-hour urinary salt excretion in participant subgroups

Urinary salt excretion in both population samples was significantly higher in men compared to women 10.3 (3.8) g/d vs. 7.6 (3.0) g/d; p<0.001 for random sample and 9.6 (3.3) g/d vs. 7.9 (3.2) g/d; p=0.006 for the volunteer sample (Table 2) and this was also true for every age group. There was an inverse association between daily salt excretion and age (Table 2) such that for every decade increase in age there was 0.3g/d less excretion of salt (p=0.007). The association between salt excretion and BMI was positive with every unit rise in BMI associated with a 0.16g/d greater excretion of salt (p<0.001). Similar patterns were observed in both the random and volunteer population samples. There were no other significant associations observed between salt excretion levels and recorded participant characteristics including education, health status, tobacco use, alcohol use, blood pressure, disease history or prescription drug use (all p>0.05).

Costs associated with random and volunteer survey methods

The two main costs associated with doing the study were staff salaries and pathology expenses. Due primarily to the increased staff time required for the selection and interaction with the randomly selected individuals the estimated average cost associated with obtaining a valid 24-hour urine sample was greater for each participant in the random

sample (about AUD\$ 62) compared to each participant in the volunteer sample (about AUD\$ 31).

Discussion

In this population salt intake greatly exceeds the recommended levels, reaffirming the urgent need for concerted action to address salt consumption in Australia. Mean salt excretion levels were some 50% higher than maximum recommended levels [5, 14] and only about one in every twenty individuals was found to be consuming the level of salt recommended for good health. Even these data are likely to be an under-estimate of the problem because the approximate 10% of salt excreted by the gastro-intestinal system and the skin will have gone unrecorded.[15] An association between blood pressure and salt intake was not observed in this study but this is unsurprising - the substantial day-to-day variability in blood pressure levels and sodium excretion mitigates against the detection of this association and only a much larger study or a study with multiple measures of blood pressure and urinary sodium excretion would have been able to reliably explore this question. The level of excess salt consumption indicated by this survey would be anticipated to cause substantial disease burden in Australia leading both to large numbers of lives lost prematurely and to many individuals suffering significant disability.[16] With centrally implemented managed salt reduction programs projected to deliver large population health gains at very low cost [17-19], the implementation of an effective salt reduction program should be a priority for the government of Australia. [20, 21]

The observation that the volunteer sample produced similar findings to the random sample is potentially important because it was much easier and less costly to collect data from the

volunteer sample than from the random sample. There are several reasons why a volunteer sample might provide a similar result to a random sample when estimating population salt consumption from 24-hour urine samples. First, the response rate in a random sample from whom a 24-hour urine sample is sought is typically very low, averaging 20% (range 9.7%) to 26.8%) in a series of recently reported studies.[9-11, 20] In this situation the random sample effectively becomes a volunteer sample and any biases consequent upon using a volunteer sample might also be apparent in the 'random' sample. That said, there were many differences between the characteristics of the random and volunteer samples included in this study but these did not translate into detectable differences in the observed sodium excretion. Another possible explanation therefore is the ubiquitous nature of salt in the food supply[22] and the rather limited capacity of even motivated individuals to meaningfully modify their salt consumption, [23] thereby minimizing the impact of any "healthy volunteer" effect.[24] It is also possible, of course, that both samples in our study were equally biased and neither gave a robust estimate of true population intake. While this may be true it is of note that the estimates obtained from the present study are not substantially different from prior studies in Australia [25-37] or other countries with broadly similar dietary patterns[38, 39].

In some countries it may be possible to achieve better response rates[40, 41] and in others it may be that specific dietary practices or other cultural factors will mean that a volunteer sample will not give a good measure of true population salt intake. If, however, the findings reported here are observed elsewhere, volunteer sampling might provide a low-cost alternate to traditional random sampling techniques. At the very least it may be possible to use a volunteer sample to demonstrate the need for action - most countries in the world are likely to have salt consumption levels far above the WHO consumption target of

BMJ Open

<5g/d, and the likelihood that the selection of a volunteer sample will lead to an underrecording of salt consumption of a very large magnitude is probably fairly small.

In addition to the baseline assessment required to justify the commencement of a salt reduction strategy, ongoing monitoring of salt consumption is required to objectively determine program efficacy. If the resources required to conduct high quality surveys of a random population sample can be acquired then this remains the optimal approach both to baseline evaluation and monitoring of progress. If not, then repeat surveys of volunteers are likely to be of value if the methods used for participant selection are identical on each occasion – if the biases are the same on each measurement occasion then any real rise or fall in salt consumption should be clearly apparent.

The cost estimates made for this study showed that recruiting the volunteer sample was a significantly less expensive exercise than recruiting the random population sample. The primary reason for this was the much reduced fieldwork time required for the per capita recruitment of the volunteer sample. Pathology and other recorded costs were otherwise approximately the same. Expenses that were not specifically determined were the costs of computer hardware, computer software, the training of the field staff, and the time required for supervision by the project manager. The last two of these are also likely to have been lower for the volunteer sample due to the simplified and more rapid recruitment process and, as a consequence, the reported difference between costs is likely to have been under-, rather than over-estimated.

Strengths and limitations

The 'Gold Standard' 24-hour urine method was used to measure salt intake with standard checks for completeness of the specimens based upon urine volume and urine creatinine excretion. The response rate for the random sample was low but comparable to other studies done in similar settings over recent years.[9-11] The sample size was relatively small and results for subgroups are somewhat imprecise as a consequence. It is possible, for this same reason, that the study may have failed to identify small, but real, differences between the sodium excretion levels determined by the two different population sampling methods. The location of the study in a single town in a regional area of New South Wales compromises the direct generalizability of the study findings to Australia as a whole, although the estimated level of salt excretion is not substantively different from that reported in a number of diverse population groups throughout the country.[25-37]

Conclusion

These data affirm that current efforts to reduce salt intake in Australia are failing, with a large majority of the population studied consuming more than the recommended Australian Upper Limit of 6g/d and almost everyone eating more than the Suggested Dietary Target of 4g/day. The observation that an opportunistically recruited volunteer population sample appears mayto provide a reasonable estimate of salt intake is important worthy of further research because this could substantially reduce the cost of future monitoring efforts. If this finding was repeated in other settings this would have global implications because sodium reduction has been proposed to all member states by the WHO. Most countries, however, have very limited resources available and any reduction in program cost that can be achieved without seriously adversely affecting program quality will be an important step forward. With population based salt reduction strategies already shown to be cost effective
BMJ Open

or cost-saving in most settings, these new data further support the feasibility of widespread

rollout of national salt reduction efforts around the world.

TABLE 1. CHARACTERISTICS OF RANDOM AND VOLUNTEER SAMPLES

	Random sample (n=306)	Volunteer sample (n=113)	p-value
Female (%)	52.9	61.9	0.10
Age, years (mean)	57.6	49.3	< 0.001
Height, cm (mean)	167.5	167.6	0.85
Weight, kg (mean)	81.8	83.9	0.30
BMI, kg/m^2 (mean)	29.1	29.8	0.27
Systolic bp, mmHg (mean)	126.7	123.7	0.16
Diastolic bp, mmHg (mean)	78.7	78.9	0.88
Education			0.22
-Secondary (%)	63.7	55.8	
-Tertiary (%)	25.5	32.7	
-Postgraduate (%)	10.8	11.5	
Health Status			0.21
-Very good (%)	50.3	48.7	
-Good (%)	29.4	23.9	
-Fair (%)	20.2	27.4	
Current smoker (> 1 / day) (%)	8.2	22.1	< 0.001
Ever smoked (> $1 / day$) (%)	41.2	53.1	0.03
Alcoholic consumption (time since	last consumption)		0.04
One week or less (%)	62.1	42.5	
> one week < 12months (%)	19.9	34.5	
12 months or more (%)	11.1	10.6	
Never (%)	6.9	12.4	
Have you ever been told by a docto	r or nurse that you have		
-high blood pressure (%)	44.1	30.1	0.03
-low blood pressure (%)	15.4	14.2	0.76
-high cholesterol (%)	37.3	30.0	0.16
-heart attack (%)	8.2	3.5	0.10
-stroke (%)	3.9	1.8	0.37
-angina (%)	6.9	4.4	0.36
-diabetes (%)	11.1	7.1	0.26
Prescription Medication Use*			
Antihypertensive (%)	15.4	15.0	0.54
			0.00
Lipid lowering (%)	11.1	7.1	0.62
Lipid lowering (%) Aspirin (%)	11.1 8.8	7.1 2.7	0.62 0.06
Lipid lowering (%) Aspirin (%) Glucose lowering (%)	11.1 8.8 22.5	7.1 2.7 7.1	0.62 0.06 0.17

*Participants could be taking more than one prescribed medication

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

TABLE 2. URINARY SALT EXCRETION	(GRAMS/DAY)
--	-------------

	Rando (n	m sample =306)	Va s	lunteer ample 1=113)	
	Mean	(SD)	Mean	(SD)	P value
Overall crude Overall weighted*	8.9 9.2	(3.6) (3.9)	8.5 8.8	(3.3) (3.4)	0.42 0.29
Female					0.27
20-39	8.7	(4)	7.9	(2.9)	
40-59	8	(3.1)	7.8	(3.8)	
60+	6.8	(2.4)	7.9	(2.6)	
All female	7.6	(3)	7.9	(3.2)	
Male					0.40
20-39	10.8	(4.7)	10.5	(3.9)	
40-59	11.1	(4.2)	9.8	(3.0)	
60+	9.7	(3.1)	8.6	(3.0)	
All male	10.3	(3.8)	9.6	(3.3)	
Education					0.25
Secondary	9.1	(3.7)	8.9	(3.4)	
Tertiary	8.3	(3.0)	8.5	(3.3)	
Post graduate	8.4	(3.6)	8	(3.3)	
Health Status					0.89
Very Good	8.7	(3.8)	8	(2.9)	
Good	8.8	(3.5)	9.3	(3.7)	
Fair	8.7	(2.8)	8.3	(2.6)	
Current Smoker	9	(3.8)	8.8	(3.4)	0.82
Ever Smoked	8.8	(3.6)	9	(3.6)	0.74
Alcohol Consumption					
(time since last consumption)					0.45
One week or less	8 8	(3.8)	87	(3.8)	0.43
> one week < 12 months	0.0 8.6	(3.0)	8.7 8.7	(2.0)	
12 months or more	0.0 Q 2	(3.2) (3.8)	0.7 7 8	(2.7)	
Never	9.5 9.1	(3.0)	7.0 & 1	(2.0)	

*Adjusted for response rate (random sample) and non-random selection (volunteer sample) by weighting age-and sex-specific estimates to the age and sex structure of the Lithgow population

TABLE 3. COST OF RANDOM COMPARED TO VOLUNTEER SAMPLING(AUD)

	Random Sample(n=306)	Volunteer Sample(n=113)
Pre-interview costs		
Sampling from electoral roll	\$2 152	0
Scheduling interviews	\$8,704	\$1,088
Post-interview costs		
Pathology costs	\$4,211	\$1,584
Other costs		
Postage	\$2,169	0
Telephone	\$1,870	\$818
Shopping centre stand fee		\$10
TOTAL	\$19,106	\$3,500
COST PER PARTICIPANT*	\$62.44	\$30.96

*Cost per participant calculated by dividing total cost by the number of valid participants in each sample.

Page 47 of 53

BMJ Open

FIGURE 1. RECRUITMENT OF STUDY SAMPLES



Acknowledgments

The authors thank Lithgow City Council, the Nepean Blue Mountains Local Area Health Network for their support and most importantly all of the participants for their support and interest in the study.

Sources of support

This work was supported by a National Health and Medical Research Council (NHMRC) of Australia partnership project (Neal #13372) which includes The George Institute for Global Health in partnership with the Australian Division of World Action on Salt and Health; the Australian Food and Grocery Council; the New South Wales Food Authority; and New South Wales Health. Bruce Neal was supported by an Australian Research Council Future Fellowship, Mark Woodward by a NHMRC Fellowship and Jacqui Webster by a National Heart Foundation and Stroke Foundation postdoctoral research fellowship.

Conflicts of interest

J.W. is the co-ordinator, and B.N. is the Chairman of the Australian Division of World Action on Salt and Health.

BMJ Open

References

- Lozano, R., et al., Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. 380(9859): p. 2095-128.
- 2. Lim, S.S., et al., *A comparative risk assessment of burden of disease and injury attributable* to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. **380**(9859): p. 2224-60.
- 3. He, F.J., N.R. Campbell, and G.A. MacGregor, *Reducing salt intake to prevent hypertension and cardiovascular disease*. Rev Panam Salud Publica, 2012. **32**(4): p. 293-300.
- Keogh, J.B. and P.M. Clifton, *Salt intake and health in the Australian population*. Med J Aust, 2008. 189(9): p. 526.
- 5. National Health and Medical Research Council, *Nutrient Reference Values for Australia and New Zealand.*, 2006, Department of Health and Ageing.
- 6. The World Health Organization, 2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases, 2008.
- United Nations. 2011 High Level Meeting on Prevention and Control of Non-communicable Diseases. 2011. Available from: <u>http://www.un.org/en/ga/ncdmeeting2011/</u>.
- 8. The World Health Organization, *Formal meeting of Member States to conclude the work on the comprehensive global monitoring framework, including indicators, and a set of voluntary global targets for the prevention and control of noncommunicable diseases*

Geneva, 5–7 November 2012, 2012: Geneva.

9. Ribic, C.H., et al., *Salt intake of the Slovene population assessed by 24 h urinary sodium excretion*. Public Health Nutr, 2010. **13**(11): p. 1803-9.

10. Chappuis, A., et al., Swiss survey on salt intake: main results. 2011.

- 11. Ortega, R.M., et al., *Estimation of salt intake by 24 h urinary sodium excretion in a representative sample of Spanish adults*. Br J Nutr, 2011. **105**(5): p. 787-94.
- 12. The World Health Organization, *European Regional Technical Consultation on Noncommunicable Disease Surveillance, Monitoring and Evaluation.* 2012.
- Perloff, D., et al., *Human blood pressure determination by sphygmomanometry*. Circulation, 1993. 88(5 Pt 1): p. 2460-70.
- 14. The World Health Organization, *Reducing Salt Intake in Populations*, in *Report of a WHO Forum and Technical Meeting*2007, World Health Organisation: Geneva.
- 15. Kirkendall, A.M., et al., *The effect of dietary sodium chloride on blood pressure, body fluids, electrolytes, renal function, and serum lipids of normotensive man.* J Lab Clin Med, 1976. 87(3): p. 411-34.
- 16. Cobiac, L.J., et al., *Which interventions offer best value for money in primary prevention of cardiovascular disease?* PLoS One, 2012. **7**(7): p. e41842.
- Beaglehole, R., et al., UN High-Level Meeting on Non-Communicable Diseases: addressing four questions. Lancet, 2011. 378(9789): p. 449-55.
- National Heart Foundation of Australia, Summary of evidence statement on the relationships between dietary electrolytes and cardiovascular disease.
 http://www.heartfoundation.org.au/SiteCollectionDocuments/Dietary-Electrolytes-CVD-

Summary-Evidence.pdf, 2006.

Cook, N.R., et al., Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). BMJ, 2007. 334(7599): p. 885-8.

1		
2 3 4	20.	Brown, I.J., et al., Salt intakes around the world: implications for public health. Int J
5 6 7		Epidemiol, 2009. 38 (3): p. 791-813.
7 8 9	21.	Bibbins-Domingo, K., et al., Projected Effect of Dietary Salt Reductions on Future
10 11		Cardiovascular Disease. N Engl J Med, 2010: p. NEJMoa0907355.
12 13	22.	Webster, J.L., E.K. Dunford, and B.C. Neal, A systematic survey of the sodium contents of
14 15 16		processed foods. Am J Clin Nutr, 2010. 91(2): p. 413-20.
17 18	23.	Kumanyika, S., Behavioral aspects of intervention strategies to reduce dietary sodium.
19 20		Hypertension, 1991. 17(1 Suppl): p. 1190-5.
21 22 23	24.	Lindsted, K.D., et al., <i>Healthy volunteer effect in a cohort study: temporal resolution in the</i>
24 25		Adventist Health Study. J Clin Epidemiol, 1996. 49(7): p. 783-90.
26 27	25.	Beard, T.C., et al., The Hobart Salt Study 1995: few meet national sodium intake target.
28 29 30		Med J Aust, 1997. 166 (8): p. 404-7.
31 32	26.	Jones, G., et al., A population-based study of the relationship between salt intake, bone
33 34 25		resorption and bone mass. Eur J Clin Nutr, 1997. 51(8): p. 561-5.
36 37	27.	Bao, D.Q., et al., Effects of dietary fish and weight reduction on ambulatory blood pressure
38 39		in overweight hypertensives. Hypertension, 1998. 32(4): p. 710-7.
40 41 42	28.	Mori, Y., et al., Effect of highly purified eicosapentaenoic acid ethyl ester on insulin
43 44		resistance and hypertension in Dahl salt-sensitive rats. Metabolism, 1999. 48(9): p. 1089-
45 46		95.
47 48 49	29.	Cumming, R.G., P. Mitchell, and W. Smith, Dietary sodium intake and cataract: the Blue
50 51		Mountains Eye Study. Am J Epidemiol, 2000. 151(6): p. 624-6.
52 53	30.	Nowson, C.A., T.O. Morgan, and C. Gibbons, Decreasing dietary sodium while following a
54 55 56		self-selected potassium-rich diet reduces blood pressure. J Nutr, 2003. 133(12): p. 4118-23.
57 58		22
59 60		

- 31. Nowson, C.A., et al., *Blood pressure response to dietary modifications in free-living individuals*. J Nutr, 2004. **134**(9): p. 2322-9.
- 32. Ward, N.C., et al., Oxidative stress in human hypertension: association with antihypertensive treatment, gender, nutrition, and lifestyle. Free Radic Biol Med, 2004.
 36(2): p. 226-32.
- 33. Hodgson, J.M., et al., *Partial substitution of carbohydrate intake with protein intake from lean red meat lowers blood pressure in hypertensive persons*. Am J Clin Nutr, 2006. 83(4): p. 780-7.
- 34. Margerison, C. and C. Nowson, *Dietary intake and 24-hour excretion of sodium and potassium*. Asia Pac J Clin Nutr, 2006. **15**: p. S37.
- 35. Julie Boorman, J.C., Dorothy Mackerras., Salt Intake From Processed Food and Discretionary Use in Australia. Food Standards Australia New Zealand, ACT Australia Available at: <u>http://www.foodstandards.gov.au/_srcfiles/Salt_Intake_5.pdf</u>
- 36. Brinkworth, G.D., et al., *Reductions in blood pressure following energy restriction for weight loss do not rebound after re-establishment of energy balance in overweight and obese subjects.* Clin Exp Hypertens, 2008. **30**(5): p. 385-96.
- 37. Charlton, K., et al., Urinary sodium excretion, dietary sources of sodium intake and knowledge and practices around salt use in a group of healthy Australian women. Aust N Z J Public Health, 2010. 34(4): p. 356-63.
- 38. Sadler, K., et al. *National Diet and Nutrition Survey Assessment of Dietary Sodium in Adults (Aged 19–64 Years) in England, 2011.* . 2012; Available from:

BMJ Open

3
4
5
6
7
8
å
9
10
11
12
13
14
15
10
10
17
18
19
20
21
22
22
23
24
25
26
27
28
20
29
30
31
32
33
34
35
26
30
37
38
39
40
41
12
42
43
44
45
46
47
<u>18</u>
40
49
50
51
52
53
54
55
55
56
57
58
59
60

https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213420/Sodiu m-Survey-England-2011_Text_to-DH_FINAL1.pdf.

- 39. He, J., et al., *Dietary sodium intake and subsequent risk of cardiovascular disease in overweight adults*. JAMA, 1999. **282**(21): p. 2027-34.
- 40. Tuomilehto, J., et al., Community-based prevention of hypertension in North Karelia, Finland. Ann Clin Res, 1984. 16 Suppl 43: p. 18-27.
- , Su, . and blood , . wris. J Hypertens, . 41. Staessen, J., et al., Salt intake and blood pressure in the general population: a controlled intervention trial in two towns. J Hypertens, 1988. 6(12): p. 965-73.



SALT INTAKE ASSESSED BY 24-HOUR URINARY SODIUM EXCRETION IN A RANDOM AND OPPORTUNISTIC SAMPLE IN AUSTRALIA

Journal:	BMJ Open
Manuscript ID:	bmjopen-2013-003720.R2
Article Type:	Research
Date Submitted by the Author:	13-Dec-2013
Complete List of Authors:	Land, Mary-Anne; The George Institute for Global Health, ; The University of Sydney, Webster, Jacqui; The George Institute for Global Health, ; The University of Sydney, Christoforou, Anthea; The George Institute for Global Health, ; The University of Sydney, Praveen, D; The George Institute for Global Health, ; The University of Sydney, Jeffery, Paul; Deakin University, Chalmers, John; The George Institute for Global Health, ; The University of Sydney, Smith, Wayne; New South Wales Health, Woodward, Mark; The George Institute for Global Health, ; The University of Sydney, Barzi, Federica; The George Institute for Global Health, ; The University of Sydney, Nowson, Caryl; Deakin University, Flood, Victoria; The University of Wollongong, Neal, Bruce; The George Institute for Global Health, ; The University of Sydney,
Primary Subject Heading :	Public health
Secondary Subject Heading:	Complementary medicine, Epidemiology, Global health
Keywords:	Hypertension < CARDIOLOGY, NUTRITION & DIETETICS, PUBLIC HEALTH

SCHOLARONE[™] Manuscripts

SALT INTAKE ASSESSED BY 24-HOUR URINARY SODIUM EXCRETION IN A RANDOM AND OPPORTUNISTIC SAMPLE IN AUSTRALIA

Corresponding Author: Miss Mary-Anne Land The George Institute for Global Health PO BOX M201 Missenden Road Camperdown, NSW, AUSTRALIA 2050. T: +61 2 9993 4547 E: maland@georgeinstitute.org.au

Authors: Mary-Anne LAND^{a,b}, Jacqui, WEBSTER^{a,b}, Anthea, CHRISTOFOROU^{a,b}, D PRAVEEN^{a,b}, Paul JEFFERY^c, John CHALMERS^{a,b}, Wayne SMITH^d, Mark WOODWARD^{a,b}, Federica BARZI^{a,b}, Caryl NOWSON^c, Victoria FLOOD^e, Bruce NEAL^{a,b}.

Affiliations: ^aThe George Institute for Global Health, Sydney, Australia, ^bThe University of Sydney, Sydney, Australia, ^cDeakin University Melbourne, Australia, ^dNew South Wales Health, Sydney, Australia, ^eThe University of Wollongong, Wollongong, Australia.

TABLES: 3

FIGURES: 1

SUPPLEMENTARY: 0

WORD COUNT: 2907

KEY WORDS: Salt, sodium, 24-hour urine, cardiovascular disease prevention

Abstract

Objective: The gold standard method for measuring population sodium intake is based on a 24hour urine collection done in a random population sample. However, because participant burden is high, response rates are typically low with less than one in four agreeing to provide specimens. At this low level of response is it possible that simply asking for volunteers would produce the same results.

Setting: Lithgow, New South Wales Australia.

Participants: We randomly selected 2152 adults and obtained usable 24-hour urine samples from 306 (response rate 16%). Specimens were also collected from a further 113 volunteers. Estimated salt consumption and the costs for each strategy were compared.

Results: The characteristics of the 'random' and 'volunteer' samples were moderately different in mean age 58 (standard deviation 14.6) vs. 49(17.7) years respectively; p<0.001) as well as self-reported alcohol use, tobacco use, history of hypertension and prescription drug use (all p<0.04). Overall crude mean 24-hour urinary salt excretion was 8.9(3.6)g/d in the random sample vs. 8.5(3.3)g/d for the volunteers (p=0.42). Corresponding age- and sex-adjusted estimates were 9.2(3.3)g/d and 8.8(3.4)g/d (p=0.29). Estimates for men 10.3(3.8) vs. 9.6(3.3)g/d; (p=0.26) and women 7.6(3.0) vs. 7.9(3.2)g/d; (p=0.43) were also similar for the two samples, as was salt excretion across age groups (p=0.72). The cost of obtaining each 24-hour urine sample was two times greater for the random compared to volunteer samples (A\$62 vs. A\$31).

Conclusion: The estimated salt consumption derived from the two samples was comparable and was not substantively different to estimates obtained from other surveys. In countries were salt is pervasive and cannot easily be avoided, estimates of consumption obtained from volunteer samples may be valid and less costly.

BMJ Open

Article Focus - The Global Monitoring Framework for the Prevention and Control of NCDs has set a salt reduction target of 30% by 2025 for Australia. Periodic assessments of population salt intake will be required to track progress towards this target. The gold standard method for assessing population salt intake is the collection of 24-hour urine specimens from a random population sample. However, because of the high participant burden, response rates in Australian surveys requiring 24-hour urine collection are very low. When a survey response rate is very low the sample obtained approximates to a volunteer sample.

Key Messages - Population salt intake estimated from a random sample of the Lithgow population with a low response rate was not different to that obtained from opportunistically recruited volunteers. The comparability of the estimates from these two different survey methods may be a consequence of chance or bias. However, it is possible that a volunteer sample provides the same information as a random sample when the response rate is very low. If this is the case, then an argument might be made for using volunteer samples that are much easier and cheaper to recruit.

Strengths and Limitations - The sample size was small. While the random survey method using 24- hour urines represents what can be achieved in practice, it is not a gold standard against which the validity of the volunteer sampling approach can be evaluated. However, the estimates obtained were broadly in line with those anticipated. Since salt is ubiquitous in the food supply and variation in consumption between individuals is driven primarily by factors that can be adjusted for (age, sex and body mass index), volunteer sampling may give a fairly robust estimate.

Background

Non-communicable diseases (NCDs) are the leading cause of death accounting for an estimated 35 million (66%) of the 53 million deaths at all ages that occurred in 2010.[1] Raised blood pressure is the leading risk factor for global disease burden, and is estimated to cause 9·4 million deaths every year—more than half of the estimated 17 million deaths a year caused by cardiovascular disease.[2] Much evidence shows that a reduction in salt intake lowers blood pressure and there is a high likelihood that this would reduce the risk of cardiovascular disease.[3] While there is not a current definitive estimate of population dietary salt intake in Australia, it is widely accepted that average consumption is between 7 and 12g/d[4] which is far above the suggested dietary target for Australians of 4g/d.[5]

The reduction of salt intake and sodium content of food has been recommended as a cost effective action that should be undertaken immediately, with expected accelerated results in terms of lives saved, cases of disease prevented and costs avoided.[6] This position has since been endorsed by the 2011 Political Declaration of the United Nations High Level Meeting on NCDs[7] which led to the development and adoption of the Global Monitoring Framework and Voluntary Global Targets for the Prevention and Control of NCDs in which salt reduction is a core target.[8]

Measurement of population salt consumption is fundamental for planning and monitoring salt reduction policies and the gold standard method is based upon a 24-hour urine collection from a random community sample. Surveys of this type are, however, complex and expensive and because participant burden is high, randomly selected community samples typically have low

BMJ Open

response rates.[9-11] This has been noted as a significant concern at recent WHO NCD surveillance, monitoring and evaluation consultation meetings in which several member states have expressed doubts about the feasibility of using this method.[12] The potential adverse impact that a low response rate might have on the conclusions drawn was highlighted and the need for further research into practicable methods for defining and monitoring population salt consumption was underlined.[12]

The objective of the present study was to measure sodium excretion using assays of 24-hour urine specimens collected from a randomly selected community sample. The response rate was poor, however, and a number of non-randomly selected individuals were interested in participating in the study. Accordingly an opportunistic (volunteer) sample was recruited to investigate whether this alternate approach to sampling might give similar results to a random sample with significant non-response. The study also examined the costs associated with each strategy.

Methods

The data derived from a random sample and a volunteer sample done concurrently in Lithgow, New South Wales, Australia between March and June 2011. Permission to undertake the study was obtained from the Lithgow City Council and the project was approved by the University of Sydney Human Research Ethics Committee.

Inclusion and exclusion criteria

Consenting individuals aged 20 years or above who were resident in Lithgow and listed on the 2009 Federal electoral roll were eligible for inclusion. There was no exclusion based on intercurrent illness, use of medications or any other aspect of demography or personal history.

Selection and recruitment process

Random sampling was done by selecting individuals at random from the electoral roll. The electoral roll provided the name and address of each potential participant with electronic databases searched to identify corresponding telephone numbers. Based on the assumption that approximately 25% of invited individuals would participate, 2152 individuals were selected to reach the desired sample size.

Potential participants were first mailed invitations to take part in the survey, with an explanation of the purpose of the study, a participant information sheet and a consent form provided. These individuals were then contacted by telephone to determine their willingness to participate and to schedule an interview time. Where a telephone number could not be obtained, the home address was visited by a member of the research team and willingness to participate was discussed face-to-face.

Volunteer sampling was done by offering participation in the study to individuals at two local shopping centres over several weeks. An information booth was established where those interested could seek further information about participation and arrange a visit by a member of the study team. Recruitment was completed at the time of the inquiry made to the study staff member manning the information booth.

Data collection process

Data collection for randomly selected individuals and the volunteer sample was identical and commenced with a visit to the study participant by a trained research assistant. Once consent was obtained the three components of data collection, comprising a questionnaire, a physical examination and a 24-hour urine collection were initiated. The questionnaire and physical examination were completed at the time of the visit and the urine collection was scheduled to be done within the following three days.

The *questionnaire* was fully structured and administered by research assistants, with all responses based on self-report. The questionnaire recorded information on socio-demographic variables, vascular disease history and current drug treatments. Participants were asked to provide the names of regular medications but if that was not known the purpose of the medication was recorded (for example, anti-hypertensive medication).

The physical examination comprised measurement of body weight (using calibrated Tantia HD-357 portable electronic scales (USA) and height (using a calibrated portable stadiometer Wedderburn WS-HRP model (Australia)) to the nearest 0.1kg and 0.1cm respectively, with body mass index (kg/height(m²)) then calculated. Blood pressure was measured using a manual inflation blood pressure monitor (A&D UA-&704) in triplicate, according to the American Heart Association protocol.[13]

A single 24-hour urine collection was obtained with the first voided urine upon waking on the day of collection being discarded and participants then collecting all voided urine up to and including the first void the following morning. The time at the beginning and the end of urine collection were recorded. The urine volume was noted and the urinary sodium concentration in an aliquot was measured by ion-selective electrode with the buffered kinetic Jaffe reaction without deproteinisation used for assay of urine creatinine (Cobas Integra 400). Suspected inaccurate urine collections (i.e. urinary creatinine < 4.0 mmol/day for women, or < 6.0mmol/day for men, or a 24-hour urine collection of < 500ml for either sex) and extreme outliers for urinary creatinine (i.e. > 3 standard deviations from the mean) were excluded. The rates of exclusion were similar for the random and volunteer samples. For each individual, the 24-hour sodium excretion value (mmol/day) was calculated as the concentration of sodium in the urine (mmol/L) multiplied by the urinary volume (L/day). The conversion from mmol to grams was made by dividing by 17 and the conversion from sodium (Na) to salt (NaCl) by multiplying by 2.542.

Cost data

The pre-interview costs involved staff time in selecting and attempting to reach subjects including accessing the electoral roll, sending participant invitations, follow-up phone calls and door-knocking to schedule interviews with those randomly selected, as well as setting up and manning an information booth to engage the volunteer sample. The post-interview costs comprised primarily of pathology expenses and were the same for each sample.

Statistical analyses

BMJ Open

The baseline characteristics of the sample selected at random and the volunteer sample were summarized and compared using t-tests and Chi-square tests as were their average urinary sodium values. In addition to the crude estimates described above, weighted estimates of overall population mean sodium excretion were also made in an effort to account for the non-random sampling of individuals. This was done for both the randomly selected group (to adjust for the poor response rate) and for the volunteer group (to adjust for their non-representative age and sex structure) by calculating age- and sex-specific estimates of salt excretion for 20 year age bands (20-39, 40-59, and 60 plus) for men and women and then weighting these by the age and sex structure of the population to obtain an overall estimate for the community. Regression models were fitted to explore the association between baseline participant characteristics and a range of covariates in the combined (random plus volunteer) sample. Throughout, a p-value of 0.05 or less was taken to indicate a finding unlikely to have arisen solely by chance. Statistical analyses were conducted using SPSS for Windows (Version 21, SPSS Inc, Chicago, IL) and STATA for windows (StataCorp. 2009 Strata Statistical Software: Release 11. College Station, TX: StataCorp LP).

Results

Of 2,152 individuals selected by random sampling of the electoral roll, 853 (40%) were uncontactable after multiple attempts, 126 (5.8%) were ineligible because they had moved out of the study area, 5 (0.2%) had died and 843 (39%) declined to participate. The remaining 329 individuals comprise the 'random' sample with a response rate of 16%. The volunteer sample comprised 120 individuals recruited consecutively at a shopping mall over a seven day period.

The characteristics of the random and volunteer samples were moderately different in a number of regards, including age, proportion using tobacco, alcohol use, self-reported hypertension and use of any prescription medication (Table 1).

Crude and weighted 24-hour urinary salt excretion in random and volunteer samples

For the analysis there were 306 individuals in the random sample and 113 in the volunteer group with 20 excluded because of suspected incomplete urine collections and 10 for other reasons (Figure 1). The crude mean 24-hour urinary salt excretion was 8.9 (standard deviation 3.6) g/d in the random sample and 8.5 (3.3) g/d in the volunteer group (p=0.42). The corresponding weighted estimates for the Lithgow population were 9.2 (3.9) g/d and 8.8 (3.4) g/d respectively (p=0.29).

The proportion of randomly sampled individuals exceeding the 6 g/d recommended Maximum Level for Australians was 79%, the proportion exceeding the Australian Suggested Dietary Target of 4 g/d was 94% and the proportion exceeding the WHO Maximum Recommended Level of 5 g/d was 87%. The corresponding proportions for the volunteer group were 75%, 93% and 84%. Population-weighted estimates of these proportions were not substantively different.

24-hour urinary salt excretion in participant subgroups

Urinary salt excretion in both population samples was significantly higher in men compared to women 10.3 (3.8) g/d vs. 7.6 (3.0) g/d; p<0.001 for random sample and 9.6 (3.3) g/d vs. 7.9 (3.2) g/d; p=0.006 for the volunteer sample (Table 2) and this was also true for every age group. There was an inverse association between daily salt excretion and age (Table 3) such that for

every decade increase in age there was 0.3g/d less excretion of salt (p=0.007). The association between salt excretion and BMI was positive with every unit rise in BMI associated with a 0.16g/d greater excretion of salt (p<0.001). Similar patterns were observed in both the random and volunteer population samples. There were no other significant associations observed between salt excretion levels and recorded participant characteristics including education, health status, tobacco use, alcohol use, blood pressure, disease history or prescription drug use (all p>0.05).

Costs associated with random and volunteer survey methods

The two main costs associated with doing the study were staff salaries and pathology expenses. Due primarily to the increased staff time required for the selection and interaction with the randomly selected individuals the estimated average cost associated with obtaining a valid 24-hour urine sample was greater for each participant in the random sample (about AUD\$ 62) compared to each participant in the volunteer sample (about AUD\$ 31).

Discussion

In this population salt intake greatly exceeds recommended levels, reaffirming the urgent need for concerted action to address salt consumption in Australia. Mean salt excretion levels were some 50% higher than the maximum recommended [5, 14] and only about one in every twenty individuals was found to be consuming the level of salt recommended for good health. Even these data are likely to be an under-estimate of the problem because the approximate 10% of salt excreted by the gastro-intestinal system and the skin will have gone unrecorded.[15] An

association between blood pressure and salt intake was not observed in this study but this is unsurprising - the substantial day-to-day variability in blood pressure levels and sodium excretion mitigates against the detection of this association and only a much larger study or a study with multiple measures of blood pressure and urinary sodium excretion would have been able to reliably explore this question. The level of excess salt consumption indicated by this survey would be anticipated to cause substantial disease burden in Australia leading both to large numbers of lives lost prematurely and to many individuals suffering significant disability.[16] With centrally managed salt reduction programs projected to deliver large population health gains at very low cost [17-19], the implementation of an effective salt reduction program should be a priority for the government of Australia.[20, 21]

The observation that the volunteer sample produced similar findings to the random sample is of interest and worthy of further exploration because it was much easier and less costly to collect data from the volunteer sample than from the random sample. There are several reasons why a volunteer sample might provide a similar result to a random sample when estimating population salt consumption from 24-hour urine samples. First, the response rate in a random sample from whom a 24-hour urine sample is sought is typically very low, averaging 20% (range 9.7% to 26.8%) in a series of recently reported studies.[9-11, 20] In this situation the random sample effectively becomes a volunteer sample and any biases consequent upon using a volunteer sample might also be apparent in the 'random' sample. That said, there were many differences between the characteristics of the random and volunteer samples included in this study but these did not translate into detectable differences in the observed sodium excretion. Another possible explanation therefore is the ubiquitous nature of salt in the food supply[22] and the rather limited

BMJ Open

capacity of even motivated individuals to meaningfully modify their salt consumption,[23] thereby minimizing the impact of any "healthy volunteer " effect.[24] It is also possible, of course, that both samples in our study were equally biased and neither gave a robust estimate of true population intake. While this may be true it is of note that the estimates obtained from the present study are not substantially different from prior studies in Australia [25-37] or other countries with broadly similar dietary patterns[38, 39].

In some countries it may be possible to achieve better response rates[40, 41] and in others it may be that specific dietary practices or other cultural factors will mean that a volunteer sample will not give a good measure of true population salt intake. If, however, the findings reported here are observed elsewhere and with larger populations, volunteer sampling might provide a low-cost alternate to traditional random sampling techniques while maintaining the strength of 24-hour urinary collection. At the very least it may be possible to use a volunteer sample to demonstrate the need for action - most countries in the world are likely to have salt consumption levels far above the WHO consumption target of <5g/d, and the likelihood that the selection of a volunteer sample will lead to an under-recording of salt consumption of a very large magnitude is probably fairly small.

In addition to the baseline assessment required to justify the commencement of a salt reduction strategy, ongoing monitoring of salt consumption is required to objectively determine program efficacy. If the resources required to conduct high quality surveys of a random population sample can be acquired then this remains the optimal approach both to baseline evaluation and monitoring of progress. If not, then repeat surveys of volunteers are likely to be of value if the

methods used for participant selection are identical on each occasion – if the biases are the same on each measurement occasion then any real rise or fall in average salt consumption should be clearly apparent. However, we do not advocate for a shift to volunteer-based surveys without sufficient robust evidence that our findings are repeatable.

The cost estimates made for this study showed that recruiting the volunteer sample was a significantly less expensive exercise than recruiting the random population sample. The primary reason for this was the much reduced fieldwork time required for the per capita recruitment of the volunteer sample. Pathology and other recorded costs were otherwise approximately the same. Expenses that were not specifically determined were the costs of computer hardware, computer software, the training of the field staff, and the time required for supervision by the project manager. The last two of these are also likely to have been lower for the volunteer sample due to the simplified and more rapid recruitment process and, as a consequence, the reported difference between costs is likely to have been under-, rather than over-estimated.

Strengths and limitations

The 'Gold Standard' 24-hour urine method was used to measure salt intake with standard checks for completeness of the specimens based upon urine volume and urine creatinine excretion. The response rate for the random sample was low but comparable to other studies done in similar settings over recent years.[9-11] The sample size was relatively small and results for subgroups are somewhat imprecise as a consequence. It is possible, for this same reason that the study may have failed to identify small, but real, differences between the sodium excretion levels determined by the two different population sampling methods. The location of the study in a

BMJ Open

single town in a regional area of New South Wales compromises the direct generalizability of the study findings to Australia as a whole, although the estimated level of salt excretion is not substantively different from that reported in a number of diverse population groups throughout the country.[25-37]

Conclusion

These data affirm that current efforts to reduce salt intake in Australia are failing, with a large majority of the population studied consuming more than the recommended Australian Upper Limit of 6g/d and almost everyone eating more than the Suggested Dietary Target of 4g/day. The observation that an opportunistically recruited volunteer population sample may provide a reasonable estimate of salt intake is worthy of further investigation because this could substantially reduce the cost of future monitoring efforts for some countries.

	Random sample (n=306)	Volunteer sample (n=113)	p-value
Female (%)	52.9	61.9	0.10
Age, years (mean)	57.6	49.3	< 0.001
Height, cm (mean)	167.5	167.6	0.85
Weight, kg (mean)	81.8	83.9	0.30
BMI, $kg/m^2(mean)$	29.1	29.8	0.27
Systolic bp, mmHg (mean)	126.7	123.7	0.16
Diastolic bp, mmHg (mean)	78.7	78.9	0.88
Education			0.22
-Secondary (%)	63.7	55.8	
-Tertiary (%)	25.5	32.7	
-Postgraduate (%)	10.8	11.5	
Health Status			0.21
-Very good (%)	50.3	48.7	
-Good (%)	29.4	23.9	
-Fair (%)	20.2	27.4	
Current smoker (> 1 / day) (%)	8.2	22.1	< 0.001
Ever smoked (> $1 / day$) (%)	41.2	53.1	0.03
Alcoholic consumption (time since la	st consumption)		0.04
One week or less (%)	62.1	42.5	
> one week < 12months (%)	19.9	34.5	
12 months or more (%)	11.1	10.6	
Never (%)	6.9	12.4	
Have you ever been told by a doctor of	or nurse that you have:		
-high blood pressure (%)	44.1	30.1	0.03
-low blood pressure (%)	15.4	14.2	0.76
-high cholesterol (%)	37.3	30.0	0.16
-heart attack (%)	8.2	3.5	0.10
-stroke (%)	3.9	1.8	0.37
			0.20
-angina (%)	6.9	4.4	0.30
-angina (%) -diabetes (%)	6.9 11.1	4.4 7.1	0.36
-angina (%) -diabetes (%) Prescription Medication Use*	6.9 11.1	4.4 7.1	0.36
-angina (%) -diabetes (%) Prescription Medication Use* Antihypertensive (%)	6.9 11.1 15.4	4.4 7.1 15.0	0.36 0.26
-angina (%) -diabetes (%) Prescription Medication Use* Antihypertensive (%) Lipid lowering (%)	6.9 11.1 15.4 11.1	4.4 7.1 15.0 7.1	0.36 0.26 0.54 0.62
-angina (%) -diabetes (%) Prescription Medication Use* Antihypertensive (%) Lipid lowering (%) Aspirin (%)	6.9 11.1 15.4 11.1 8.8	4.4 7.1 15.0 7.1 2.7	0.36 0.26 0.54 0.62 0.06
-angina (%) -diabetes (%) Prescription Medication Use* Antihypertensive (%) Lipid lowering (%) Aspirin (%) Glucose lowering (%)	6.9 11.1 15.4 11.1 8.8 22.5	4.4 7.1 15.0 7.1 2.7 7.1	0.36 0.26 0.54 0.62 0.06 0.17

TABLE 1. CHARACTERISTICS OF RANDOM AND VOLUNTEER SAMPLES

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

TABLE 2. URINARY SALT EXCRETION (GRAMS/DAY)

	Rando	om sample =306)	Volu	nteer sample	
	Mean	(SD)	Mean	(SD)	P value
Overall crude	8.9	(3.6)	8.5	(3.3)	0.42
Overall weighted*	9.2	(3.9)	8.8	(3.4)	0.29
Female					0.27
20-39	8.7	(4)	7.9	(2.9)	
40-59	8.0	(3.1)	7.8	(3.8)	
60+	6.8	(2.4)	7.9	(2.6)	
All female	7.6	(3)	7.9	(3.2)	
Male					0.40
20-39	10.8	(4.7)	10.5	(3.9)	
40-59	11.1	(4.2)	9.8	(3.0)	
60+	9.7	(3.1)	8.6	(3.0)	
All male	10.3	(3.8)	9.6	(3.3)	
Education					0.25
Secondary	9.1	(3.7)	8.9	(3.4)	
Tertiary	8.3	(3.0)	8.5	(3.3)	
Post graduate	8.4	(3.6)	8.0	(3.3)	
Health Status					0.89
Very Good	8.7	(3.8)	8.0	(2.9)	
Good	8.8	(3.5)	9.3	(3.7)	
Fair	8.7	(2.8)	8.3	(2.6)	
Current Smoker	9.0	(3.8)	8.8	(3.4)	0.82
Ever Smoked	8.8	(3.6)	9.0	(3.6)	0.74
Alcohol Consumption					o : -
(time since last consumption)	0.5				0.45
One week or less	8.8	(3.8)	8.7	(3.8)	
> one week < 12months	8.6	(3.2)	8.7	(2.9)	
12 months or more	9.3	(3.8)	7.8	(2.8)	
Never	9.1	(3.2)	8.1	(3.6)	

*Adjusted for response rate (random sample) and non-random selection (volunteer sample) by weighting age-and sex-specific estimates to the age and sex structure of the Lithgow population

	Random Sample(n=306)	Volunteer Sample(n=113)
Pre-interview costs		
Sampling from electoral roll	\$2.152	0
Scheduling interviews	\$8,704	\$1,088
Post-interview costs		
Pathology costs	\$4,211	\$1,584
Other costs		
Postage	\$2,169	0
Telephone	\$1,870	\$818
Shopping centre stand fee		\$10
TOTAL	\$19,106	\$3,500
COST PER PARTICIPANT*	\$62.44	\$30.96

TABLE 3. COST OF RANDOM COMPARED TO VOLUNTEER SAMPLING (AUD)

*Cost per participant calculated by dividing total cost by the number of valid participants in each sample.

Figure legend

FIGURE 1. RECRUITMENT OF STUDY SAMPLES

Acknowledgments

The authors thank Lithgow City Council, the Nepean Blue Mountains Local Area Health Network for their support and most importantly all of the participants for their support and interest in the study.

Sources of support

This work was supported by a National Health and Medical Research Council (NHMRC) of Australia partnership project (Neal #13372) which includes The George Institute for Global Health in partnership with the Australian Division of World Action on Salt and Health; the Australian Food and Grocery Council; the New South Wales Food Authority; and New South Wales Health. Bruce Neal was supported by an Australian Research Council Future Fellowship and an NHMRC Fellowship, Mark Woodward by a NHMRC Fellowship and Jacqui Webster by a National Heart Foundation and Stroke Foundation postdoctoral research fellowship.

Contributorship Statement

All authors fulfill the ICMJE guidelines for authorship and have approved the final version of the manuscript submitted to BMJ Open.

Mary-Anne Land - contributed to study concept and design, data collection, analysis and interpretation of the data, drafting the article and final version of the article.

Jacqui Webster - contributed to the study design, revising content and final approval of the version to be published.

Anthea Christoforou – contributed to the analysis of data, revising content and final approval of the version to be published

D Praveen – contributed to the analysis and interpretation of data, revising content and final approval of the version to be published.

Paul Jeffery – contributed to the study design, interpretation of data, revising content and final approval of the version to be published.

John Chalmers – contributed to the conception and study design, revising critically and final approval of the version to be published.

Wayne Smith - contributed to the conception and study design, revising critically and final approval of the version to be published.

Mark Woodward – contributed to the conception and study design, revising critically and final approval of the version to be published.

Federica Barzi – contributed to the analysis and interpretation of the data, revising critically and final approval of the version to be published.

Caryl Nowson - contributed to the conception and study design, revising critically and final approval of the version to be published.

Victoria Flood - contributed to the conception and study design, revising critically and final approval of the version to be published.

Bruce Neal – contributed to the conception and study design, analysis and interpretation of data, drafting of the article, revising critically and final approval of the version to be published.

Conflicts of interest

J.W. is the co-ordinator, and B.N. is the Chairman of the Australian Division of World Action on

Salt and Health.

Data Sharing Statement

Additional data if available - please email Mary-Anne Land: maland@georgeinstitute.org.au

References 1. Lozano, I

 Lozano, R., et al., Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. 380(9859): p. 2095-128.

- 2. Lim, S.S., et al., *A comparative risk assessment of burden of disease and injury attributable* to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. **380**(9859): p. 2224-60.
- 3. He, F.J., N.R. Campbell, and G.A. MacGregor, *Reducing salt intake to prevent hypertension and cardiovascular disease*. Rev Panam Salud Publica, 2012. **32**(4): p. 293-300.
- 4. Keogh, J.B. and P.M. Clifton, *Salt intake and health in the Australian population*. Med J Aust, 2008. **189**(9): p. 526.
- 5. National Health and Medical Research Council, *Nutrient Reference Values for Australia and New Zealand.*, 2006, Department of Health and Ageing.
- 6. The World Health Organization, 2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases, 2008.
- United Nations. 2011 High Level Meeting on Prevention and Control of Non-communicable Diseases. 2011. Available from: <u>http://www.un.org/en/ga/ncdmeeting2011/</u>.
- 8. The World Health Organization, *Formal meeting of Member States to conclude the work on the comprehensive global monitoring framework, including indicators, and a set of voluntary global targets for the prevention and control of noncommunicable diseases*

Geneva, 5–7 November 2012, 2012: Geneva.

9. Ribic, C.H., et al., *Salt intake of the Slovene population assessed by 24 h urinary sodium excretion*. Public Health Nutr, 2010. **13**(11): p. 1803-9.

BMJ Open

10. Chappuis, A., et al., Swiss survey on salt intake: main results. 2011.

- 11. Ortega, R.M., et al., *Estimation of salt intake by 24 h urinary sodium excretion in a representative sample of Spanish adults*. Br J Nutr, 2011. **105**(5): p. 787-94.
- 12. The World Health Organization, *European Regional Technical Consultation on Noncommunicable Disease Surveillance, Monitoring and Evaluation.* 2012.
- Perloff, D., et al., *Human blood pressure determination by sphygmomanometry*. Circulation, 1993. 88(5 Pt 1): p. 2460-70.
- 14. The World Health Organization, *Reducing Salt Intake in Populations*, in *Report of a WHO Forum and Technical Meeting*2007, World Health Organisation: Geneva.
- 15. Kirkendall, A.M., et al., *The effect of dietary sodium chloride on blood pressure, body fluids, electrolytes, renal function, and serum lipids of normotensive man.* J Lab Clin Med, 1976. 87(3): p. 411-34.
- 16. Cobiac, L.J., et al., *Which interventions offer best value for money in primary prevention of cardiovascular disease?* PLoS One, 2012. **7**(7): p. e41842.
- Beaglehole, R., et al., UN High-Level Meeting on Non-Communicable Diseases: addressing four questions. Lancet, 2011. 378(9789): p. 449-55.
- National Heart Foundation of Australia, Summary of evidence statement on the relationships between dietary electrolytes and cardiovascular disease. <u>http://www.heartfoundation.org.au/SiteCollectionDocuments/Dietary-Electrolytes-CVD-</u>

Summary-Evidence.pdf, 2006.

Cook, N.R., et al., Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). BMJ, 2007. 334(7599): p. 885-8.

- Brown, I.J., et al., Salt intakes around the world: implications for public health. Int J Epidemiol, 2009. 38(3): p. 791-813.
- Bibbins-Domingo, K., et al., Projected Effect of Dietary Salt Reductions on Future Cardiovascular Disease. N Engl J Med, 2010: p. NEJMoa0907355.
- Webster, J.L., E.K. Dunford, and B.C. Neal, A systematic survey of the sodium contents of processed foods. Am J Clin Nutr, 2010. 91(2): p. 413-20.
- 23. Kumanyika, S., *Behavioral aspects of intervention strategies to reduce dietary sodium*.Hypertension, 1991. 17(1 Suppl): p. I190-5.
- 24. Lindsted, K.D., et al., *Healthy volunteer effect in a cohort study: temporal resolution in the Adventist Health Study.* J Clin Epidemiol, 1996. **49**(7): p. 783-90.
- 25. Beard, T.C., et al., *The Hobart Salt Study 1995: few meet national sodium intake target.*Med J Aust, 1997. 166(8): p. 404-7.
- 26. Jones, G., et al., *A population-based study of the relationship between salt intake, bone resorption and bone mass.* Eur J Clin Nutr, 1997. **51**(8): p. 561-5.
- 27. Bao, D.Q., et al., *Effects of dietary fish and weight reduction on ambulatory blood pressure in overweight hypertensives*. Hypertension, 1998. **32**(4): p. 710-7.
- Mori, Y., et al., *Effect of highly purified eicosapentaenoic acid ethyl ester on insulin resistance and hypertension in Dahl salt-sensitive rats*. Metabolism, 1999. 48(9): p. 1089-95.
- 29. Cumming, R.G., P. Mitchell, and W. Smith, *Dietary sodium intake and cataract: the Blue Mountains Eye Study*. Am J Epidemiol, 2000. **151**(6): p. 624-6.
- 30. Nowson, C.A., T.O. Morgan, and C. Gibbons, *Decreasing dietary sodium while following a self-selected potassium-rich diet reduces blood pressure*. J Nutr, 2003. **133**(12): p. 4118-23.
BMJ Open

- 31. Nowson, C.A., et al., *Blood pressure response to dietary modifications in free-living individuals*. J Nutr, 2004. **134**(9): p. 2322-9.
 - 32. Ward, N.C., et al., Oxidative stress in human hypertension: association with antihypertensive treatment, gender, nutrition, and lifestyle. Free Radic Biol Med, 2004.
 36(2): p. 226-32.
 - 33. Hodgson, J.M., et al., *Partial substitution of carbohydrate intake with protein intake from lean red meat lowers blood pressure in hypertensive persons*. Am J Clin Nutr, 2006. 83(4): p. 780-7.
 - 34. Margerison, C. and C. Nowson, *Dietary intake and 24-hour excretion of sodium and potassium*. Asia Pac J Clin Nutr, 2006. **15**: p. S37.
 - 35. Julie Boorman, J.C., Dorothy Mackerras., Salt Intake From Processed Food and Discretionary Use in Australia. Food Standards Australia New Zealand, ACT Australia Available at: <u>http://www.foodstandards.gov.au/_srcfiles/Salt_Intake_5.pdf</u>
 - 36. Brinkworth, G.D., et al., *Reductions in blood pressure following energy restriction for weight loss do not rebound after re-establishment of energy balance in overweight and obese subjects.* Clin Exp Hypertens, 2008. **30**(5): p. 385-96.
- 37. Charlton, K., et al., Urinary sodium excretion, dietary sources of sodium intake and knowledge and practices around salt use in a group of healthy Australian women. Aust N Z J Public Health, 2010. 34(4): p. 356-63.
- 38. Sadler, K., et al. National Diet and Nutrition Survey Assessment of Dietary Sodium in Adults (Aged 19–64 Years) in England, 2011. 2012; Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213420/Sodiu m-Survey-England-2011_Text_to-DH_FINAL1.pdf.

- 39. He, J., et al., Dietary sodium intake and subsequent risk of cardiovascular disease in overweight adults. JAMA, 1999. 282(21): p. 2027-34.
- 40. Tuomilehto, J., et al., Community-based prevention of hypertension in North Karelia, Finland. Ann Clin Res, 1984. 16 Suppl 43: p. 18-27.
- 41. Staessen, J., et al., Salt intake and blood pressure in the general population: a controlled intervention trial in two towns. J Hypertens, 1988. 6(12): p. 965-73.

rial in two towns. .

SALT INTAKE ASSESSED BY 24-HOUR URINARY SODIUM EXCRETION IN A RANDOM AND OPPORTUNISTIC SAMPLE IN AUSTRALIA

Corresponding Author: Miss Mary-Anne Land The George Institute for Global Health PO BOX M201 Missenden Road Camperdown, NSW, AUSTRALIA 2050. T: +61 2 9993 4547 E: <u>maland@georgeinstitute.org.au</u>

Authors: Mary-Anne LAND^{a,b}, Jacqui, WEBSTER^{a,b}, Anthea, CHRISTOFOROU^{a,b}, D PRAVEEN^{a,b}, Paul JEFFERY^c, John CHALMERS^{a,b}, Wayne SMITH^d, Mark WOODWARD^{a,b}, Federica BARZI^{a,b}, Caryl NOWSON^c, Victoria FLOOD^e, Bruce NEAL ^{a,b}.

Affiliations: ^aThe George Institute for Global Health, Sydney, Australia, ^bThe University of Sydney, Sydney, Australia, ^cDeakin University Melbourne, Australia, ^dNew South Wales Health, Sydney, Australia, ^eThe University of Wollongong, Wollongong, Australia.

TABLES: 3

FIGURES: 1

SUPPLEMENTARY: 0

WORD COUNT: 2907

KEY WORDS: Salt, sodium, 24-hour urine, cardiovascular disease prevention

Article Focus - The Global Monitoring Framework for the Prevention and Control of NCDs has set a salt reduction target of 30% by 2025 for Australia. The Periodic assessments of population salt intake will underpins the implementation of salt reduction policies and evaluates progressbe required to track progress towards this target. The gold standard method for assessing population salt intake is the collection of a-24-hour urine specimens from a random population sample. However, because of the high participant burden, participation-response rates in Australian surveys requiring 24-hour urine collection are generally very low and the cost is often high. When a survey response rate is very low the sample obtained approximates to a volunteer sample. Hence there is great interest in alternative, yet robust and affordable methods to assess salt intake.

Key Messages - Population salt intake estimated from a The observation that an random sample of the Lithgow population with a low response rate was not different to that obtained from opportunistically recruited volunteers population sample appears to provide a reasonable estimate of salt intake is importantnoteworthy. The comparability of the estimates from these two different survey methods may be a consequence of chance or bias. However, it is possible that a volunteer sample provides the same information as a random sample when the response rate is very low. -because this could substantially reduce the cost of future increase the feasibility of monitoring efforts. If If this is the case, then an argument might be made for using volunteer samples that are much easier and cheaper to recruit, this finding was repeated in other settings this would have global implications, as the reporting of salt intake in 2015, 2020 and 2025 is encouraged as part of the Global Monitoring Framework for the Prevention and Control of NCDs.

Abstract

Introduction<u>Objective</u>: The gold standard method for measuring population sodium intake is based on a 24-hour urine collection done in a random population sample. However, because participant burden is high, response rates are typically low with less than one in four agreeing to provide specimens. At this low level of response is it possible that simply asking for volunteers would produce equally valid the same results.

MethodSetting: Lithgow, New South Wales Australia.

<u>**Participants:**</u> We randomly selected 2152 adults_<u>from Lithgow, New South Wales</u> and obtained usable 24-hour urine samples from 306 (response rate 16%). Specimens were also collected from a further 113 volunteers. Estimated salt consumption and the costs for each strategy were compared.

Results: The characteristics of the 'random' and 'volunteer' samples were moderately different in mean age 58 (standard deviation 14.6) vs. 49(17.7) years respectively; p<0.001) as well as self-reported alcohol use, tobacco use, history of hypertension and prescription drug use (all p<0.04). Overall crude mean 24-hour urinary salt excretion was 8.9(3.6)(g/d) in the random sample vs. 8.5(3.3)g/d for the volunteers (p=0.42). Corresponding age- and sex-adjusted estimates were 9.2(3.3)g/d and 8.8(3.4)g/d (p=0.29). Estimates for men 10.3(3.8) vs. 9.6(3.3)g/d; (p=0.26) and women 7.6(3.0) vs. 7.9(3.2)g/d; (p=0.43) were also similar for the two samples, as was salt excretion across age groups (p=0.72). The cost of obtaining each 24-hour urine sample was two times greater for the random compared to volunteer samples (A\$62 vs. A\$31).

Conclusion: The estimated salt consumption derived from the two samples was comparable and was not substantively different to estimates obtained from other surveys.

In countries were salt is pervasive and cannot easily be avoided, estimates of consumption obtained from volunteer samples may be valid and less costly.

Strengths and Limitations - The 'Gold Standard' 24-hour urine method was used to estimate sodium intakeam. The response rate for the random sample was low and the study location was a single town but the response rate and estimated level of salt excretion is not substantively different from that reported in a number of diverse population groups throughout the countrysample size was small. While the random survey method using 24hour urines represents what can be achieved in practice, it is not a gold standard against which the validity of the volunteer sampling approach can be evaluated. However, the estimates obtained were broadly in line with those anticipated. Since salt is ubiquitous in the food supply and variation in consumption between individuals is driven primarily by factors that can be adjusted for (age, sex and body mass index), volunteer sampling may give a fairly robust estimate.⁻

Background

Non-communicable diseases (NCDs) are the leading cause of death accounting for an estimated 35 million (66%) of the 53 million deaths at all ages that occurred in 2010.[1] Raised blood pressure is the leading risk factor for global disease burden, and is estimated to cause 9.4 million deaths every year—more than half of the estimated 17 million deaths a year caused by cardiovascular disease.[2] Much evidence shows that a reduction in salt intake lowers blood pressure and there is a high likelihood that this would reduce the risk of cardiovascular disease.[3] While there is not a current definitive estimate of population dietary salt intake in Australia, it is widely accepted that average consumption is between 7 and 12g/d[4] which is far above the suggested dietary target for Australians of 4g/d.[5]

The reduction of salt intake and sodium content of food has been strongly-recommended as a cost effective action that should be undertaken immediately, with expected accelerated results in terms of lives saved, cases of disease prevented and costs avoided.[6] This position has since been historically endorsed by the 2011 Political Declaration of the United Nations High Level Meeting on NCDs[7] which led to the development and adoption of the Global Monitoring Framework and Voluntary Global Targets for the Prevention and Control of NCDs in which salt reduction is a core target.[8]

Measurement of population salt consumption is fundamental for planning and monitoring salt reduction policies and the gold standard method is based upon a 24-hour urine collection from a random community sample. Surveys of this type are, however, complex and expensive and because participant burden is high, randomly selected community

samples typically have low response rates.[9-11] This has been noted as a significant concern at recent WHO NCD surveillance, monitoring and evaluation consultation meetings in which several member states have expressed doubts about the feasibility of using this method.[12] The potential adverse impact that a low response rate might have on the conclusions drawn was highlighted and the need for further research into practicable methods for defining and monitoring population salt consumption was underlined.[12]

The objective of the present study was to measure sodium excretion using assays of 24hour urine samples specimens collected from a randomly selected regional Australian community populationsample. The response rate was poor, however, and -a number of nonrandomly selected individuals were interested in participating in the study. For this reasonAccordingly an opportunistic (volunteer) sample was recruited to investigate the feasibility of a random sample with a poor response rate in which to allwhether this alternate approach to sampling might give similar results to a random sample with significant non-response intents and purposes the random samples are volunteer samples with an opportunistic sample. A key question about practicality was addressed by using both a standard random sampling approach to make the estimate while simultaneously recruiting an opportunistic (volunteer) sample to make an alternate estimate. The study also examined the costs associated with each strategy.-

Methods

The data derived from a random sample and a <u>convenience-volunteer</u> sample (<u>volunteers</u>) done concurrently in Lithgow, New South Wales, Australia between March and June 2011.

BMJ Open

Permission to undertake the study was obtained from the Lithgow City Council and the project was approved by the University of Sydney Human Research Ethics Committee.

Inclusion and exclusion criteria

Consenting individuals aged 20 years or above who were resident in Lithgow and listed on the 2009 Federal electoral roll were eligible for inclusion. There was no exclusion based on inter-current illness, use of medications or any other aspect of demography or personal history.

Selection and recruitment process

Random sampling was done by selecting individuals at random from the electoral roll. The electoral roll provided the name and address of each potential participant with electronic databases searched to identify corresponding telephone numbers. Based on the assumption that approximately 25% of invited individuals would participate, 2152 individuals were selected to reach the desired sample size.

Potential participants were first mailed invitations to take part in the survey, with an explanation of the purpose of the study, a participant information sheet and a consent form provided. These individuals were then contacted by telephone to determine their willingness to participate and to schedule an interview time. Where a telephone number could not be obtained, the home address was visited by a member of the research team and willingness to participate was discussed face-to-face.

Volunteer sampling was done by offering participation in the study to individuals at two local shopping centres over several weeks. An information booth was established where those interested could seek further information about participation and arrange a visit by a member of the study team. Recruitment was completed at the time of the inquiry made to the study staff member manning the information booth.

Data collection process

Data collection for randomly selected individuals and the volunteer sample was identical and commenced with a visit to the study participant by a trained research assistant. Once consent was obtained the three components of data collection, comprising a questionnaire, a physical examination and a 24-hour urine collection were initiated. The questionnaire and physical examination were completed at the time of the visit and the urine collection was scheduled to be done within the following three days.

The *questionnaire* was fully structured and administered by research assistants, with all responses based on self-report. The questionnaire recorded information on sociodemographic variables, vascular disease history and current drug treatments. Participants were asked to provide the names of regular medications but if that was not known the purpose of the medication was recorded (for example, anti-hypertensive medication).

The physical examination comprised measurement of body weight (using calibrated Tantia HD-357 portable electronic scales (USA) and height (using a calibrated portable stadiometer Wedderburn WS-HRP model (Australia)) to the nearest 0.1kg and 0.1cm

BMJ Open

respectively, with body mass index (kg/height(m²)) then calculated. Blood pressure was measured using a manual inflation blood pressure monitor (A&D UA-&704) in triplicate, according to the American Heart Association protocol.[13]

A single 24-hour urine collection was obtained with the first voided urine upon waking on the day of collection being discarded and participants then collecting all voided urine up to and including the first void the following morning. The time at the beginning and the end of urine collection were recorded. The urine volume was noted and the urinary sodium concentration in an aliquot was measured by ion-selective electrode with the buffered kinetic Jaffe reaction without deproteinisation used for assay of urine creatinine (Cobas Integra 400). Suspected inaccurate urine collections (i.e. urinary creatinine < 4.0 mmol/day for women, or < 6.0mmol/day for men, or a 24-hour urine collection of < 500ml for either sex) and extreme outliers for urinary creatinine (i.e. > 3 standard deviations from the mean) were excluded. The rates of exclusion were similar for the random and volunteer samples. For each individual, the 24-hour sodium excretion value (mmol/day) was calculated as the concentration of sodium in the urine (mmol/L) multiplied by the urinary volume (L/day). The conversion from mmol to grams was made by dividing by 17 and the conversion from sodium (Na) to salt (NaCl) by multiplying by 2.542.

Cost data

The pre-interview costs involved staff time in selecting and attempting to reach subjects including accessing the electoral roll, sending participant invitations, follow-up phone calls and door-knocking to schedule interviews with those randomly selected, as well as setting

up and manning an information booth to engage the volunteer sample. The post-interview costs comprised primarily of pathology expenses and were the same for each sample.

Statistical analyses

The baseline characteristics of the sample selected at random and the volunteer sample were summarized and compared using t-tests and Chi-square tests as were their average urinary sodium values. In addition to the crude estimates described above, weighted estimates of overall population mean sodium excretion were also made in an effort to account for the non-random sampling of individuals. This was done for both the randomly selected group (to adjust for the poor response rate) and for the volunteer group (to adjust for their non-representative age and sex structure) by calculating age- and sex-specific estimates of salt excretion for 20 year age bands (20-39, 40-59, and 60 plus) for men and women and then weighting these by the age and sex structure of the population to obtain an overall estimate for the community. Regression models were fitted to explore the association between baseline participant characteristics and a range of covariates in the combined (random plus volunteer) sample. Throughout, a p-value of 0.05 or less was taken to indicate a finding unlikely to have arisen solely by chance. Statistical analyses were conducted using SPSS for Windows (Version 21, SPSS Inc, Chicago, IL) and STATA for windows (StataCorp. 2009 Strata Statistical Software: Release 11. College Station, TX: StataCorp LP).

BMJ Open

Results

Of 2,152 individuals selected by random sampling of the electoral roll, 853 (40%) were uncontactable after multiple attempts, 126 (5.8%) were ineligible because they had moved out of the study area, 5 (0.2%) had died and 843 (39%) declined to participate. The remaining 329 individuals comprise the 'random' sample with a response rate of 16%. The volunteer sample comprised 120 individuals recruited consecutively at a shopping mall over a seven day period. The characteristics of the random and volunteer samples were moderately different in a number of regards, including age, proportion <u>using</u> tobacco-<u>use</u>, alcohol use-, self-reported hypertension and use of any prescription medication (Table 1).

Crude and weighted 24-hour urinary salt excretion in random and volunteer samples For the analysis there were 306 individuals in the random sample and 113 in the volunteer group with 20 excluded because of suspected incomplete urine collections and 10 for other reasons (Figure 1). The crude mean 24-hour urinary salt excretion was 8.9 (standard deviation 3.6) g/d in the random sample and 8.5 (3.3) g/d in the volunteer group (p=0.42). The corresponding weighted estimates for the Lithgow population were 9.2 (3.9) g/d and 8.8 (3.4) g/d respectively (p=0.29).

The proportion of randomly sampled individuals exceeding the 6 g/d recommended Maximum Level for Australians was 79%, the proportion exceeding the Australian Suggested Dietary Target of 4 g/d was 94% and the proportion exceeding the WHO Maximum Recommended Level of 5 g/d was 87%. The corresponding proportions for the volunteer group were 75%, 93% and 84%. Population-weighted estimates of these proportions were not substantively different.

24-hour urinary salt excretion in participant subgroups

Urinary salt excretion in both population samples was significantly higher in men compared to women 10.3 (3.8) g/d vs. 7.6 (3.0) g/d; p<0.001 for random sample and 9.6 (3.3) g/d vs. 7.9 (3.2) g/d; p=0.006 for the volunteer sample (Table 2) and this was also true for every age group. There was an inverse association between daily salt excretion and age (Table 2) such that for every decade increase in age there was 0.3g/d less excretion of salt (p=0.007). The association between salt excretion and BMI was positive with every unit rise in BMI associated with a 0.16g/d greater excretion of salt (p<0.001). Similar patterns were observed in both the random and volunteer population samples. There were no other significant associations observed between salt excretion levels and recorded participant characteristics including education, health status, tobacco use, alcohol use, blood pressure, disease history or prescription drug use (all p>0.05).

Costs associated with random and volunteer survey methods

The two main costs associated with doing the study were staff salaries and pathology expenses. Due primarily to the increased staff time required for the selection and interaction with the randomly selected individuals the estimated average cost associated with obtaining a valid 24-hour urine sample was greater for each participant in the random sample (about AUD\$ 62) compared to each participant in the volunteer sample (about AUD\$ 31).

Discussion

In this population salt intake greatly exceeds the recommended levels, reaffirming the urgent need for concerted action to address salt consumption in Australia. Mean salt excretion levels were some 50% higher than the maximum recommended levels [5, 14] and only about one in every twenty individuals was found to be consuming the level of salt recommended for good health. Even these data are likely to be an under-estimate of the problem because the approximate 10% of salt excreted by the gastro-intestinal system and the skin will have gone unrecorded.[15] An association between blood pressure and salt intake was not observed in this study but this is unsurprising - the substantial day-to-day variability in blood pressure levels and sodium excretion mitigates against the detection of this association and only a much larger study or a study with multiple measures of blood pressure and urinary sodium excretion would have been able to reliably explore this question. The level of excess salt consumption indicated by this survey would be anticipated to cause substantial disease burden in Australia leading both to large numbers of lives lost prematurely and to many individuals suffering significant disability.[16] With centrally implemented managed salt reduction programs projected to deliver large population health gains at very low cost [17-19], the implementation of an effective salt reduction program should be a priority for the government of Australia.[20, 21]

The observation that the volunteer sample produced similar findings to the random sample is <u>of interest potentially important and worthy of further exploration</u> because it was much easier and less costly to collect data from the volunteer sample than from the random

sample. There are several reasons why a volunteer sample might provide a similar result to a random sample when estimating population salt consumption from 24-hour urine samples. First, the response rate in a random sample from whom a 24-hour urine sample is sought is typically very low, averaging 20% (range 9.7% to 26.8%) in a series of recently reported studies.[9-11, 20] In this situation the random sample effectively becomes a volunteer sample and any biases consequent upon using a volunteer sample might also be apparent in the 'random' sample. That said, there were many differences between the characteristics of the random and volunteer samples included in this study but these did not translate into detectable differences in the observed sodium excretion. Another possible explanation therefore is the ubiquitous nature of salt in the food supply[22] and the rather limited capacity of even motivated individuals to meaningfully modify their salt consumption, [23] thereby minimizing the impact of any 'healthy volunteer ' effect. [24] It is also possible, of course, that both samples in our study were equally biased and neither gave a robust estimate of true population intake. While this may be true it is of note that the estimates obtained from the present study are not substantially different from prior studies in Australia [25-37] or other countries with broadly similar dietary patterns [38, 39].

In some countries it may be possible to achieve better response rates[40, 41] and in others it may be that specific dietary practices or other cultural factors will mean that a volunteer sample will not give a good measure of true population salt intake. If, however, the findings reported here are observed elsewhereare observed elsewhere and with larger populations, volunteer sampling might provide a low-cost alternate to traditional random sampling techniques while maintaining the strength of 24-hour urinary collection. At the

BMJ Open

very least it may be possible to use a volunteer sample to demonstrate the need for action - most countries in the world are likely to have salt consumption levels far above the WHO consumption target of <5g/d, and the likelihood that the selection of a volunteer sample will lead to an under-recording of salt consumption of a very large magnitude is probably fairly small.

In addition to the baseline assessment required to justify the commencement of a salt reduction strategy, ongoing monitoring of salt consumption is required to objectively determine program efficacy. If the resources required to conduct high quality surveys of a random population sample can be acquired then this remains the optimal approach both to baseline evaluation and monitoring of progress. If not, then repeat surveys of volunteers are likely to be of value if the methods used for participant selection are identical on each occasion – if the biases are the same on each measurement occasion then any real rise or fall in <u>average</u> salt consumption should be clearly apparent. <u>However, we do not advocate for a shift to volunteer-based surveys without sufficient robust evidence that our findings are repeatable.</u>

The cost estimates made for this study showed that recruiting the volunteer sample was a significantly less expensive exercise than recruiting the random population sample. The primary reason for this was the much reduced fieldwork time required for the per capita recruitment of the volunteer sample. Pathology and other recorded costs were otherwise approximately the same. Expenses that were not specifically determined were the costs of computer hardware, computer software, the training of the field staff, and the time required

for supervision by the project manager. The last two of these are also likely to have been lower for the volunteer sample due to the simplified and more rapid recruitment process and, as a consequence, the reported difference between costs is likely to have been under-, rather than over-estimated.

Strengths and limitations

The 'Gold Standard' 24-hour urine method was used to measure salt intake with standard checks for completeness of the specimens based upon urine volume and urine creatinine excretion. The response rate for the random sample was low but comparable to other studies done in similar settings over recent years.[9-11] The sample size was relatively small and results for subgroups are somewhat imprecise as a consequence. It is possible, for this same reason that the study may have failed to identify small, but real, differences between the sodium excretion levels determined by the two different population sampling methods. The location of the study in a single town in a regional area of New South Wales compromises the direct generalizability of the study findings to Australia as a whole, although the estimated level of salt excretion is not substantively different from that reported in a number of diverse population groups throughout the country.[25-37]

Conclusion

These data affirm that current efforts to reduce salt intake in Australia are failing, with a large majority of the population studied consuming more than the recommended Australian Upper Limit of 6g/d and almost everyone eating more than the Suggested Dietary Target of 4g/day. The observation that an opportunistically recruited volunteer population sample

BMJ Open

appears may to provide a reasonable estimate of salt intake is important-worthy of further investigation because this could substantially reduce the cost of future monitoring efforts for some countries. If this finding was repeated in other settings this would have global implications because sodium <u>salt</u> reduction has been proposed to all <u>M</u>member <u>sS</u>tates by the WHO. Most countries, however, have very limited resources available and any reduction in program cost that can be achieved without seriously adversely affecting program quality will be an important step forward. Although the study design was imperfect, including the limitation of a moderate difference in the participant characteristics, substantial heterogeneity in estimated salt consumption levels is not usually observed between groups unless measures of age, sex or body mass index are substantively different between populations. With population based salt reduction strategies already shown to be cost effective or cost saving in most settings, these new data further support the feasibility of widespread rollout of national salt reduction efforts around the world.

2
2
3
4
5
6
0
7
8
o
3
10
11
12
12
13
14
15
16
10
17
18
19
20
2U
21
22
22
23
24
25
26
20
27
28
29
23
30
31
32
22
33
34
35
26
30
37
38
20
39
40
41
42
40
43
44
45
10
40
47
48
40
49
50
51
52
52
53
54
55
50
90
57
58
50
29
60

TABLE 1. CHARACTERISTICS OF RANDOM AND VOLUNTEER SAMPLES

	Random sample	Volunteer sample	p-value
	(n=306)	(n=113)	
Female (%)	52.9	61.9	0.10
Age, years (mean)	57.6	49.3	< 0.001
Height, cm (mean)	167.5	167.6	0.85
Weight, kg (mean)	81.8	83.9	0.30
BMI, kg/m^2 (mean)	29.1	29.8	0.27
Systolic bp, mmHg (mean)	126.7	123.7	0.16
Diastolic bp, mmHg (mean)	78.7	78.9	0.88
Education			0.22
-Secondary (%)	63.7	55.8	
-Tertiary (%)	25.5	32.7	
-Postgraduate (%)	10.8	11.5	
Health Status			0.21
-Very good (%)	50.3	48.7	
-Good (%)	29.4	23.9	
-Fair (%)	20.2	27.4	
()			
Current smoker (> $1 / day$) (%)	8.2	22.1	< 0.001
Ever smoked (> $1 / day$) (%)	41.2	53.1	0.03
Alcoholic consumption (time since last	consumption)		0.04
One week or less $(\%)$	62 1	42.5	
> one week < 12 months (%)	19.9	34.5	
12 months or more $\binom{0}{2}$	11.1	10.6	
Never $(\%)$	69	12.4	
	0.9	12.7	
Have you ever been told by a doctor or	nurse that you have:		
-high blood pressure (%)	44.1	30.1	0.03
-low blood pressure (%)	15.4	14.2	0.76
-high cholesterol (%)	37.3	30.0	0.16
-heart attack (%)	8.2	3.5	0.10
-stroke (%)	3.9	1.8	0.37
-angina (%)	6.9	4.4	0.36
-diabetes (%)	11.1	7.1	0.26
Prescription Medication Use*			
Antihypertensive $(\%)$	154	15.0	0 54
Linid lowering (%)	11.1	7 1	0.54
$\Delta \operatorname{spirin} (\%)$	× ×	27	0.02
Glucose lowering (%)	22 5	2.7 7 1	0.00
Any prescription medication $(%)$	72.0	50 7	0.17
*D (:: 4 111 (1)	· · · · · · · · · · · · · · · · · · ·	57.4	0.02

*Participants could be taking more than one prescribed medication

1	
2	
3	
4	
5	
6	
7	
0	
0	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18	
19	
20	
20	
2 I 22	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32	
33	
34	
35	
36	
30	
31	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
<u>4</u> 0	
50	
50	
51	
ວ∠ ⊏≏	
53	
54	
55	
56	
57	
58	
59	
60	

TIDLE 2: UNITARI SILLI EXCRETION (UNINS/DITT
--

	Rando	om sample	Volu	nteer sample	
	(n	=306)		(n=113)	
	Mean	(SD)	Mean	(SD)	P value
Overall crude	8.9	(3.6)	8.5	(3.3)	0.42
Overall weighted*	9.2	(3.9)	8.8	(3.4)	0.29
Female					0.27
20-39	8.7	(4)	7.9	(2.9)	
40-59	8.0	(3.1)	7.8	(3.8)	
60+	6.8	(2.4)	7.9	(2.6)	
All female	7.6	(3)	7.9	(3.2)	
Male					0.40
20-39	10.8	(4.7)	10.5	(3.9)	
40-59	11.1	(4.2)	9.8	(3.0)	
60+	9.7	(3.1)	8.6	(3.0)	
All male	10.3	(3.8)	9.6	(3.3)	
Education					0.25
Secondary	9.1	(3.7)	8.9	(3.4)	
Tertiary	8.3	(3.0)	8.5	(3.3)	
Post graduate	8.4	(3.6)	8.0	(3.3)	
Health Status					0.89
Very Good	8.7	(3.8)	8.0	(2.9)	
Good	8.8	(3.5)	9.3	(3.7)	
Fair	8.7	(2.8)	8.3	(2.6)	
Current Smoker	9.0	(3.8)	8.8	(3.4)	0.82
Ever Smoked	8.8	(3.6)	9.0	(3.6)	0.74
Alashal Congressition					
(time since last consumption)					0.45
(unite since last consumption)	00	(2, 8)	07	(2, 9)	0.43
$\sum_{n=1}^{n} \max_{n=1}^{n} \sum_{n=1}^{n} \sum_{n$	0.0 0 <i>C</i>	(3.8)	0./	(3.8)	
\sim one week $<$ 12months	ð.0	(3.2)	ð./	(2.9)	
12 months of more	9.3	(3.8)	/.8	(2.8)	
Inever	9.1	(3.2)	8.1	(3.0)	

*Adjusted for response rate (random sample) and non-random selection (volunteer sample) by weighting age-and sex-specific estimates to the age and sex structure of the Lithgow population

	Random Sample(n=306)	Volunteer Sample(n=113)
Pre-interview costs	\$2.152	0
Sampling from electoral roll	\$2,152	0
Scheduling interviews	\$8,704	\$1,088
Post-interview costs		
Pathology costs	\$4,211	\$1,584
Other costs		
Postage	\$2,169	0
Telephone	\$1,870	\$818
Shopping centre stand fee		\$10
TOTAL	\$19,106	\$3,500
COST PER PARTICIPANT*	\$62.44	\$30.96

TABLE 3. COST OF RANDOM COMPARED TO VOLUNTEER SAMPLING(AUD)

*Cost per participant calculated by dividing total cost by the number of valid participants in each sample.



FIGURE 1. RECRUITMENT OF STUDY SAMPLES



Acknowledgments

The authors thank Lithgow City Council, the Nepean Blue Mountains Local Area Health Network for their support and most importantly all of the participants for their support and interest in the study.

Sources of support

This work was supported by a National Health and Medical Research Council (NHMRC) of Australia partnership project (Neal #13372) which includes The George Institute for Global Health in partnership with the Australian Division of World Action on Salt and Health; the Australian Food and Grocery Council; the New South Wales Food Authority; and New South Wales Health. Bruce Neal was supported by an Australian Research Council Future Fellowship and an NHMRC Fellowship, Mark Woodward by a NHMRC Fellowship and Jacqui Webster by a National Heart Foundation and Stroke Foundation postdoctoral research fellowship.

Conflicts of interest

J.W. is the co-ordinator, and B.N. is the Chairman of the Australian Division of World Action on Salt and Health.

BMJ Open

References

- Lozano, R., et al., Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. 380(9859): p. 2095-128.
- Lim, S.S., et al., A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990-2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet, 2012. 380(9859): p. 2224-60.
- 3. He, F.J., N.R. Campbell, and G.A. MacGregor, *Reducing salt intake to prevent hypertension and cardiovascular disease*. Rev Panam Salud Publica, 2012. **32**(4): p. 293-300.
- Keogh, J.B. and P.M. Clifton, *Salt intake and health in the Australian population*. Med J Aust, 2008. 189(9): p. 526.
- 5. National Health and Medical Research Council, *Nutrient Reference Values for Australia and New Zealand.*, 2006, Department of Health and Ageing.
- 6. The World Health Organization, 2008-2013 Action Plan for the Global Strategy for the Prevention and Control of Noncommunicable Diseases, 2008.
- United Nations. 2011 High Level Meeting on Prevention and Control of Non-communicable Diseases. 2011. Available from: <u>http://www.un.org/en/ga/ncdmeeting2011/</u>.
- 8. The World Health Organization, *Formal meeting of Member States to conclude the work on the comprehensive global monitoring framework, including indicators, and a set of voluntary global targets for the prevention and control of noncommunicable diseases*

Geneva, 5–7 November 2012, 2012: Geneva.

9. Ribic, C.H., et al., *Salt intake of the Slovene population assessed by 24 h urinary sodium excretion*. Public Health Nutr, 2010. **13**(11): p. 1803-9.

10. Chappuis, A., et al., Swiss survey on salt intake: main results. 2011.

- 11. Ortega, R.M., et al., *Estimation of salt intake by 24 h urinary sodium excretion in a representative sample of Spanish adults*. Br J Nutr, 2011. **105**(5): p. 787-94.
- 12. The World Health Organization, *European Regional Technical Consultation on Noncommunicable Disease Surveillance, Monitoring and Evaluation.* 2012.
- Perloff, D., et al., *Human blood pressure determination by sphygmomanometry*. Circulation, 1993. 88(5 Pt 1): p. 2460-70.
- 14. The World Health Organization, *Reducing Salt Intake in Populations*, in *Report of a WHO Forum and Technical Meeting*2007, World Health Organisation: Geneva.
- 15. Kirkendall, A.M., et al., *The effect of dietary sodium chloride on blood pressure, body fluids, electrolytes, renal function, and serum lipids of normotensive man.* J Lab Clin Med, 1976. 87(3): p. 411-34.
- 16. Cobiac, L.J., et al., *Which interventions offer best value for money in primary prevention of cardiovascular disease?* PLoS One, 2012. **7**(7): p. e41842.
- Beaglehole, R., et al., UN High-Level Meeting on Non-Communicable Diseases: addressing four questions. Lancet, 2011. 378(9789): p. 449-55.
- National Heart Foundation of Australia, Summary of evidence statement on the relationships between dietary electrolytes and cardiovascular disease.
 http://www.heartfoundation.org.au/SiteCollectionDocuments/Dietary-Electrolytes-CVD-

Summary-Evidence.pdf, 2006.

Cook, N.R., et al., Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the trials of hypertension prevention (TOHP). BMJ, 2007. 334(7599): p. 885-8.

BMJ Open

20.	Brown, I.J., et al., Salt intakes around the world: implications for public health. Int J
	Epidemiol, 2009. 38 (3): p. 791-813.
21.	Bibbins-Domingo, K., et al., Projected Effect of Dietary Salt Reductions on Future
	Cardiovascular Disease. N Engl J Med, 2010: p. NEJMoa0907355.
22.	Webster, J.L., E.K. Dunford, and B.C. Neal, A systematic survey of the sodium contents of
	processed foods Am I Clin Nutr 2010 $91(2)$: n 413-20
22	Numerviles C. Debryioural amonta of interpretation strategies to unduce distance a diam
23.	Kumanyika, S., Benavioral aspecis of intervention strategies to reduce aletary solium.
	Hypertension, 1991. 17(1 Suppl): p. 1190-5.
24.	Lindsted, K.D., et al., <i>Healthy volunteer effect in a cohort study: temporal resolution in the</i>
	Adventist Health Study. J Clin Epidemiol, 1996. 49(7): p. 783-90.
25.	Beard, T.C., et al., The Hobart Salt Study 1995: few meet national sodium intake target.
	Med J Aust, 1997. 166(8): p. 404-7.
26.	Jones, G., et al., A population-based study of the relationship between salt intake, bone
	resorption and bone mass. Eur J Clin Nutr, 1997. 51(8): p. 561-5.
27.	Bao, D.Q., et al., <i>Effects of dietary fish and weight reduction on ambulatory blood pressure</i>
	in overweight hypertensives. Hypertension, 1998, 32 (4); p. 710-7.
•	
28.	Mori, Y., et al., Effect of highly purified eicosapentaenoic acid ethyl ester on insulin
	resistance and hypertension in Dahl salt-sensitive rats. Metabolism, 1999. 48(9): p. 1089-
	95.
29.	Cumming, R.G., P. Mitchell, and W. Smith, Dietary sodium intake and cataract: the Blue
	Mountains Eye Study. Am J Epidemiol, 2000. 151(6): p. 624-6.
30	Nowson C A T O Morgan and C Gibbons <i>Decreasing dietary sodium while following a</i>
	self-selected potassium-rich diet reduces blood pressure. J Nutr, 2003. 133 (12): p. 4118-23.
	24
	 20. 21. 22. 23. 24. 25. 26. 27. 28. 29. 30.

- 31. Nowson, C.A., et al., *Blood pressure response to dietary modifications in free-living individuals*. J Nutr, 2004. **134**(9): p. 2322-9.
- 32. Ward, N.C., et al., Oxidative stress in human hypertension: association with antihypertensive treatment, gender, nutrition, and lifestyle. Free Radic Biol Med, 2004.
 36(2): p. 226-32.
- 33. Hodgson, J.M., et al., *Partial substitution of carbohydrate intake with protein intake from lean red meat lowers blood pressure in hypertensive persons*. Am J Clin Nutr, 2006. 83(4): p. 780-7.
- 34. Margerison, C. and C. Nowson, *Dietary intake and 24-hour excretion of sodium and potassium*. Asia Pac J Clin Nutr, 2006. **15**: p. S37.
- 35. Julie Boorman, J.C., Dorothy Mackerras., Salt Intake From Processed Food and Discretionary Use in Australia. Food Standards Australia New Zealand, ACT Australia Available at: <u>http://www.foodstandards.gov.au/_srcfiles/Salt_Intake_5.pdf</u>
- 36. Brinkworth, G.D., et al., Reductions in blood pressure following energy restriction for weight loss do not rebound after re-establishment of energy balance in overweight and obese subjects. Clin Exp Hypertens, 2008. 30(5): p. 385-96.
- 37. Charlton, K., et al., Urinary sodium excretion, dietary sources of sodium intake and knowledge and practices around salt use in a group of healthy Australian women. Aust N Z J Public Health, 2010. 34(4): p. 356-63.
- 38. Sadler, K., et al. National Diet and Nutrition Survey Assessment of Dietary Sodium in Adults (Aged 19–64 Years) in England, 2011. 2012; Available from: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/213420/Sodiu m-Survey-England-2011_Text_to-DH_FINAL1.pdf.

1		
2 3 4	39.	He, J., et al., Dietary sodium intake and subsequent risk of cardiovascular disease in
5 6		overweight adults. JAMA, 1999. 282(21): p. 2027-34.
7 8 9	40.	Tuomilehto, J., et al., Community-based prevention of hypertension in North Karelia,
10 11		Finland. Ann Clin Res, 1984. 16 Suppl 43: p. 18-27.
12 13	41.	Staessen, J., et al., Salt intake and blood pressure in the general population: a controlled
14 15 16		intervention trial in two towns. J Hypertens, 1988. 6(12): p. 965-73.
17 18 19		
20 21		
22 23		
24 25 26		
27 28		
29 30		
31 32 22		
33 34 35		
36 37		
38 39		
40 41 42		
43 44		
45 46		
47 48 40		
49 50 51		
52 53		
54 55		
56		



132x90mm (300 x 300 DPI)

