

Spot urine samples compared to 24-hour urine samples for estimating changes in urinary sodium and potassium excretion in the China Salt Substitute and Stroke Study

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ABSTRACT

Background: The capacity of spot urine samples for detecting changes in population sodium and potassium excretion is unclear.

Methods: Changes in urinary sodium and potassium excretion, over a 6-month to 2-year interval, were measured from 24-hour urine samples and estimated from spot urine samples using several published methods in 3270 Chinese. Additional estimates were made by multiplying individual spot sodium and potassium concentrations by a single estimated 24-hour urine volume derived from external data.

Results: The measured difference in 24-hour urinary excretion between intervention and control groups was -0.35g (95%CI: -0.68 to -0.02g; $p=0.039$) for sodium and 0.66g (95%CI: 0.52 to 0.80g; $p<0.001$) for potassium, based upon 24-hour urine samples. The corresponding estimates of sodium differences for the Tanaka (-0.06g), Kawasaki (-0.09g), Intersalt without potassium (-0.09g) and Intersalt with potassium (-0.14g) equations were all smaller and not clearly different (all $p>0.10$). The estimates were -0.65g for sodium and 1.11g for potassium using individual spot urine concentrations and an externally derived standard urine volume (both $p<0.01$).

Conclusions: The published equations were unable to detect the differences in sodium excretion measured by 24-hour urine samples in our study. A simpler method based upon spot urine electrolyte concentrations and a standard urine volume may offer an alternative approach to measuring differences in sodium and potassium excretion between population groups without requiring 24-hour urine, but will need further investigation.

Keywords Sodium, potassium, spot urine, 24-hour urine, controlled trial, random allocation

Key Messages

- Published equations that use spot urine samples to estimate daily sodium intake were unable to detect a difference in urinary sodium excretion between population groups
- There were detectable differences between groups in the mean concentration of sodium and potassium in spot urine samples
- Multiplication of the sodium concentration in spot urine by the measured 24-hour urine volume provided a slight over-estimate of the difference in sodium excretion compared to that determined from 24-h urine samples
- Multiplication of the concentration in spot urine by a standard single externally derived urine volume detected differences in excretion between groups for both sodium and potassium, though resulted in over-estimates of the differences
- Serial cross-sectional surveys of spot urine sodium and potassium concentrations, without collection of 24-hour urine samples may provide a mechanism for measuring difference in population intake levels of sodium and potassium.

INTRODUCTION

It is well established that excessive dietary salt (sodium chloride) intake raises blood pressure, which is a leading risk factor for stroke and other cardiovascular diseases (1-3). Reducing average population salt intake has been identified as a strategy for preventing these diseases (4), and member states of the World Health Organization (WHO) are seeking to reduce population salt intake by 30% by 2025 (5). Implementation of this strategy requires baseline and serial follow-up measurements of mean population salt intake to document progress towards this goal. In addition, supplementation of dietary potassium has also been proved to be helpful with controlling high blood pressure (6).

The usual approach to measuring mean dietary sodium and potassium intake in the population is through collection of 24-hour urine samples in a representative sample (7-9). However, collection of 24-hour urine samples is burdensome to participants resulting in low response rates, non-representative population samples (10) and poor quality urine collections. Many nations find this method expensive and difficult to use (11). By comparison, spot urine samples collected at one time point during the day are easier for patients to provide and simpler for research teams to collect and analyze. Spot urine samples are already the basis for estimations of pesticide exposure (12, 13) and iodine intake (14).

Prior studies have demonstrated the capacity of several different estimating equations that incorporate measures of spot urine sodium concentration to provide an indication of mean daily population sodium intake (15). The capacity of these equations to detect differences in sodium intake over time is, however, unknown. The primary objective of this study was to understand

whether spot urine can be used to replace 24-hour urine in estimating sodium and potassium intake at population level by comparing estimates of differences in mean 24-hour sodium and potassium excretion determined from standard 24-hour urine collections and alternative estimates derived from methods based upon the urinary sodium concentration in spot urine samples.

METHODS

This investigation was done within the China Salt Substitute and Stroke Study (SSaSS) (16), an on-going large-scale cluster-randomized trial investigating the effects of a reduced-sodium, added-potassium salt substitute compared to usual salt on the risk of stroke (clinicaltrials.gov identifier: NCT02092090). Effects of the salt substitute on urinary sodium and potassium excretion are being monitored during the course of the study to check the integrity of the randomized intervention, through the collection of 24-hour urine samples in a randomly sampled subset of villages every 12 months. Prior to commencement, we made plans to use the trial to test questions about the potential use of spot urine samples for making estimates of daily sodium intake, and we collected parallel spot urine samples for this purpose. The study commenced in 2014 and is scheduled to complete in 2020. Approval for the trial, including the collection and evaluation of urine samples, was obtained from both Peking University Health Science Center Institutional Review Board and the University of Sydney Ethics Committee. All participants have provided written informed consent.

Participants

Participants of the SSaSS study are individuals 60 years old or above with uncontrolled high

blood pressure or individuals with a history of stroke resident in 600 villages in Northern China (Liaoning, Shanxi, Hebei, Ningxia, Shaanxi). There are about 35 participants in each village involved. The SSaSS participating villages (half intervention, half control) were randomly selected for baseline (36 villages), 12- (60 villages) and 24- (140 villages) month follow-up surveys to collect urine samples, with an additional 12 villages in Shanxi province surveyed at 6 months. A randomly sampled 20 participants from each selected village were invited to provide urine samples with replacement from other participants within the village to achieve that number in the event that selected individuals were unavailable. Because villages and participants were randomly selected at each time point, there are a few villages and participants that have been surveyed on multiple occasions. Participants were excluded from participation in the urine collection survey if they reported urinary incontinence, inability to collect urine samples as required, genito-urinary infection, current menstruation, pregnancy or breastfeeding.

Urine collection and analysis

Participants were seen face-to-face in their village and first instructed to empty their bladder while providing a mid-stream urine sample into a disposable urine cup, from which 2x2 ml aliquots of urine were extracted (the spot urine sample). Participants were then directed to immediately commence their 24-hour urine collection and the time was recorded - collection of the spot urine sample and commencement of the 24-hour collection could be at any time during the day. Six 1000ml urine containers were provided and participants were asked to collect all voids of urine for the next 24 hours. Instructions were communicated orally with supporting printed materials. An appointment was made for the next day about 23½ hours after commencement of the 24-hour urine collection at which time the return of all 6 containers was

sought, regardless of whether they contained urine. Participants were also asked to void one last time at that visit and the time was recorded. Enquiry about missed voids and spillage was also made. Urine from all containers was then thoroughly mixed in a single large container, urine volume was measured and 2x2 ml aliquots were extracted. Urine samples were not collected if participants reported diarrhea or vomiting on the day of collection or if the urine was seen to be contaminated with blood or faeces. Samples were refrigerated and transported to a central laboratory in Beijing for analysis. Assays of sodium and potassium were done by the ion selective electrode method and creatinine was assayed by the sarcosine oxidase method using the HITACHI 7600 automated biochemistry analyzer.

Statistical analysis

The primary outcome was the difference in estimated change of mean 24-hour urinary sodium excretion (g) between intervention and control groups from baseline to follow up. Secondary outcomes were differences in estimated change of mean 24-hour urinary potassium excretion (g), mean concentration of sodium (mmol/L), mean concentration of potassium (mmol/L) and mean urine volume (ml) from baseline to follow up. The estimating methods that were compared were based upon:

- Standard 24-hour urine samples: i.e. sodium concentration in individual 24-hour urine sample x volume of individual 24-hour urine sample.
- Published estimating equations that use spot urine samples: i.e. Intersalt (17), Kawasaki (18) and Tanaka (Appendix 1) equations (19). The Intersalt equation estimates were made separately with and without inclusion of potassium concentration and in the absence of a

Chinese intercept, using the extensively validated North America intercept.

- Simple calculations using spot urine samples and urine volumes done in two ways: (1) individual volume spot = sodium concentration in individual spot urine sample x volume of individual 24-hour urine sample; (2) standard volume spot = sodium concentration in individual spot urine sample x 1.55L. This was the mean urine volume recorded for a comparable Northern Chinese population in Shandong province (20). Estimates were also made using volumes 10% greater (1.71L) and 10% lesser (1.40L). Of note, the source of this externally derived 24-hour urine volume was retracted due to an oversight of the author not including body mass index in the multiple linear regression analysis between urinary sodium or potassium excretion and blood pressure in adults (21). However, the estimate of the 24-hour urine volume should not be affected and is the best estimate we could obtain.

Each of these methods (except for the estimating equations) was also used to estimate differences in the change of 24-hour potassium excretion between randomized groups from baseline to follow-up since the salt substitute would be anticipated to also increase daily potassium intake. Findings for each method were compared by plotting point estimates of effect and 95% confidence intervals.

The 24-hour urine samples were included only if (1) less than 10% of the 24-hour urine was self-reported as missing through spillage or uncollected voids; (2) 24-hour urine volume was between 500ml and 6000ml; (3) 24-hour creatinine excretion was between 4mmol and 25mmol for women, or 6mmol and 30mmol for men (22); and (4) 24-hour urine collection duration was between 22 and 26 hours (Figure 1). These are criteria for completeness of collection used in a

prior study (23) though are unlikely to be as effective as the use of PABA (24-27), which was not done in this project. In each case a valid 24-hour urine had to have an accompanying spot urine sample collected for the same participant at the same time point for the data point to be included in the analyses.

For participants with baseline and follow-up urine samples a paired analysis strategy was used to estimate the differences between baseline and follow up excretion and for the remainder an unpaired methodology was used to control for baseline excretion levels. Overall differences were estimated by using a fixed effect meta-analytic approach to combine the data from the paired and unpaired analyses. To maximize power, the follow-up data were treated as a single time point regardless of whether measures were made at 6, 12 or 24-months. If participants were included in more than one follow-up survey the last measurement was used. Analyses used SAS Enterprise version 7.1 and Stata version 13.1.

RESULTS

There were 961, 298, 1778 and 4325 (total 7362) participants invited to participate in the baseline, 6, 12 and 24-month follow-up surveys, respectively, with 4931 (67%) of invitations resulting in the collection of one or more urine samples. After exclusions (583 with only a spot urine sample or with only a 24-hour urine sample and 843 for other reasons, Figure 1) there were 3396 sets of 24-hour urine collections and corresponding spot urine samples that contributed to the analyses. Of these 3396 sets of samples, 252 were paired samples collected from 126 individuals with measurements made at both baseline and follow-up, and 3144 were unpaired samples (406 collected at baseline and 2738 collected at follow up). Characteristics of

participants were broadly comparable across intervention and control groups and at baseline and follow-up (Table 1). There were two provinces (Liaoning and Shanxi) from which samples were only collected during the follow-up period.

Estimated differences in sodium excretion between randomized groups

The mean difference in urinary sodium concentration in the intervention group compared to the control group was $-14.3(\text{mmol/L})$ (95% confidence interval (CI): -23.5 to $-5.1(\text{mmol/L})$; $p=0.002$) for the 3396 assays of 24-hour urine samples, and $-18.4(\text{mmol/L})$ (95% CI: -29.9 to $-6.9(\text{mmol/L})$; $p=0.002$) for the 3396 assays of spot urine samples (Table 2). The 24-hour urine volumes measured for the 3396 assays of 24-hour urine samples were not different between randomized groups with a mean difference of $71(\text{ml})$ (95% CI: -50 to $192(\text{ml})$; $p=0.248$).

The estimated difference in 24-hour urinary sodium excretion between intervention and control groups was $-0.35(\text{g})$ (95%CI: -0.68 to $-0.02(\text{g})$; $p=0.039$) based upon the standard 24-hour urine collections (Figure 2). The corresponding estimates obtained from the four published equations based upon spot urine samples were all smaller (all $p>0.100$), though directionally similar (Figure 2). The estimate of difference using the ‘individual volume spot’ method was comparable in magnitude ($-0.48(\text{g})$) but not obvious (95% CI: -0.98 to 0.02 ; $p=0.062$). The estimate of difference based upon the ‘standard volume spot’, ($-0.65(\text{g})$, 95% CI: -1.06 to $-0.25(\text{g})$) was greater than that obtained from the 24-hour urine collection and identified a clear difference between groups ($p=0.002$). Estimates of the difference using the ‘standard urine volume’ approach with volumes 10% lesser or greater were $-0.59(\text{g})$, 95%CI: -0.96 to $-0.22(\text{g})$ and $-0.72(\text{g})$, 95%CI: -1.17 to $-0.27(\text{g})$ respectively (both $p=0.002$).

Estimated differences in potassium excretion between randomized groups

The difference in urinary potassium concentration between the intervention group compared to the control group was 11.7(mmol/L) (95% CI: 8.6 to 14.8(mmol/L); $p<0.001$) for the 3396 assays of the 24-hour urine samples and 18.4(mmol/L) (95%CI: 12.4 to 24.4(mmol/L); $p<0.001$) for the 3396 spot urine samples.

The estimated difference in 24-hour urinary potassium excretion between intervention and control groups was 0.66(g) (95%CI: 0.52 to 0.80(g); $p<0.001$) based upon the standard 24-hour urine collections. The estimates made using the ‘individual volume spot’ and the ‘standard volume spot’ methods all identified clear differences (all $p<0.001$) though the point estimates of effect were all approximately two-fold over-estimates compared to that obtained from the 24-hour urine collections (Figure 2).

DISCUSSION

These data suggest significant potential for a greatly simplified approach to monitoring population sodium excretion based upon the collection of spot urine samples rather than 24-hour urine samples. Differences in population sodium and potassium excretion resulting from the administration of a reduced-sodium added-potassium salt substitute were clearly reflected in the mean concentrations of sodium and potassium in both spot and 24-hour urine samples. Given no corresponding differences in mean urine volume between groups, it was possible to apply an externally derived estimate of mean population urine volume and detect a difference in urinary sodium and potassium excretion. While the magnitude of the estimates in difference for mean population daily sodium and potassium excretion obtained from the simple method

based upon spot urine samples and a standard urine volume varied in comparison to those obtained from the 24-hour urine collections, the data provide initial proof of principle. Replication of the approach in other datasets will be required to confirm these findings and determine the extent to which methods based upon this approach might be biased or prone to random errors compared to methods based upon 24-hour urine samples. If the findings are confirmed then this would greatly simplify the measurement of population salt intake around the world and offer policy makers a practical, low cost and easily implemented new way to monitor the effectiveness of intervention programs.

The published equations that have been used to estimate the mean population level of sodium intake at a single time point were in this study ineffective for detecting differences in sodium intake between groups. The magnitudes of difference calculated were substantial underestimates of the results obtained from the 24-hour urine. Prior cross-sectional analyses of daily excretion estimates based upon these equations showed that estimates based upon spot urine samples were able to provide reasonable approximations of sodium excretion at a given time point, but also that there was a tendency to underestimate excretion at high excretion levels and to overestimate excretion at low excretion levels (15). Over- and under-estimation of this type would be expected to produce systematic underestimation of the true difference in excretion between two groups and may, in part at least, explain the smaller effects observed here.

The results of these analyses are aligned with the findings from a previous study that used data from two Australian States (New South Wales and Victoria) to estimate differences in sodium intake over time using spot and 24 hour urine samples (28). That study also showed that methods based upon spot urine samples were able to detect a difference in sodium excretion,

although in that study the estimates of effect obtained were derived from the published equations, albeit only for the subset of analyses based on paired data. The published equations include multiple variables and in unpaired analyses small differences in spot urine sodium concentrations may be masked by differences in covariates such as age, gender, body mass index and urine creatinine. In the paired analyses, by comparison, differences in such covariates would be removed or substantially reduced. The unpaired nature of the great majority of the data in the current report may explain why we were unable to detect differences using the published equations in contrast to the prior study. Paired samples were available for only 126 individuals in the present study and were too few to enable a robust assessment of effects in that subset.

The potential to detect differences in daily sodium (and potassium) excretion using simple calculations based upon only spot urine electrolyte concentrations and an externally derived standard estimate of mean population urine volume is important because it might preclude the need for assessment of urinary creatinine or direct measurement of 24-hour urine volume. Urinary creatinine, unlike sodium and potassium concentrations, cannot easily be measured in the field and 24-hour urine volume measurement is onerous for participants and prone to error. Further, collecting paired data from the same individuals at multiple time points, as appears to be necessary for estimation of differences using the published equations, is difficult to achieve. Accordingly, a method based upon unpaired data with no requirement for direct measurement of 24-hour urine volume would be preferable.

Statistical power to detect differences in mean population sodium excretion would require a greater sample size for methods based upon spot urine samples compared to 24 hour urine

samples. To detect a 0.35g difference in sodium with 80% power and 95% confidence using 24-hour urine samples would require a total sample size of 420 (210 per group) based upon paired samples and a sample size of 832 (416 per group) based upon unpaired samples assuming a standard deviation of 1.8g for sodium excretion. For methods based upon 'standard volume spot', corresponding power would be achieved with 624 samples for a study based upon paired samples and 1242 samples for a study based upon unpaired samples, assuming a standard deviation of 2.2g for sodium excretion. In practice, because the collection of paired samples is likely to be impractical in most settings, unpaired analyses and larger samples will be required. While the required sample size is larger, the much greater feasibility of spot urine sample collection may nonetheless make studies based upon unpaired spot urine samples more plausible.

Key strengths of this study are the large sample size and the standardized approach to the collection and analysis of both the spot and 24-hour urine samples at multiple time points. The broad coherence of the findings for the spot-urine based methods across both sodium and potassium provides reassurance that the main findings are unlikely to be attributable to chance. The generalizability of the results beyond rural China cannot be directly assessed, although the physiology underpinning sodium and potassium regulation is similar across diverse ethnic groups. Likewise the generalizability of the method for the assessment of sodium reduction strategies that use approaches other than salt substitution requires confirmation. The estimates obtained from the spot urine samples did not exactly match the estimates obtained from the 24-hour urine samples and further data are required to understand whether this reflects random errors or biases. If the latter, as seems likely for potassium at least, then adjustment to methods

will need to be developed such that the magnitude of the difference derived from the spot urine-based methods more closely approximates that obtained from the 24-hour urine samples. For example, the large difference between the concentrations of potassium in spot and 24-hour urine specimens likely reflects the known diurnal variation of urinary potassium excretion, and this could be controlled for by specifying collection times and adjustments during analyses (29). The simple methods described in this study depend upon there being no substantive difference in mean urine volume between the populations being compared and there are reports indicating that a decrease in sodium intake can result in a decrease in 24-hour urine volume (30). Additional data describing the changes in mean population urine volume associated with changes in mean population salt intake, and confirmation that any changes in urine volume do not importantly bias estimates of change in salt intake, are needed. Also as the external urine volume was a variance-free constant, the result will not incorporate any allowance for variance or uncertainty in the volume estimate. Refinements that estimate mean population urine volume based upon characteristics such as age, sex and weight or apply strata-specific estimates of urine volume may enhance the methodology. Finally, these analyses provide a basis for the assessment of mean population sodium excretion and not for sodium excretion levels amongst individuals.

These data affirm prior reports that spot urine-based methods may be effective not just for estimating mean population sodium excretion at a single time point, but also for measuring differences in mean sodium excretion between population samples (28). The primary implication of this finding is that a much simpler and more practical method for monitoring the effectiveness of sodium reduction programs may be feasible. While there is a need for

confirmation and refinement of the methods outlined here before they can be used at scale, these data provide a strong rationale for the further exploration of the approach.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest

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Table 1 Participant characteristics at baseline and follow-up, overall and for each randomized group

	Baseline			Follow up		
	Intervention	Control	All	Intervention	Control	All
Total number of participants included in analysis	272 (100%)	260 (100%)	532 (100%)	1524 (100%)	1340 (100%)	2864 (100%)
<i>Participants from each province, n (%)</i>						
<i>Liaoning</i>	0 (0%)	0 (0%)	0 (0%)	169 (11%)	135 (10%)	304 (11%)
<i>Shanxi</i>	0 (0%)	0 (0%)	0 (0%)	436 (291%)	345 (26%)	781 (27%)
<i>Hebei</i>	90 (33%)	84 (32%)	174 (33%)	291 (199%)	288 (21%)	579 (20%)
<i>Ningxia</i>	100 (37%)	96 (37%)	196 (37%)	301 (20%)	297 (22%)	598 (21%)
<i>Shaanxi</i>	82 (30%)	80 (31%)	162 (30%)	327 (21%)	275 (21%)	602 (21%)
Male, n (%)	125 (45%)	131 (50%)	256 (48%)	758 (50%)	676 (51%)	1,434 (50%)
Age, yrs (mean, SD)	65.9 (7.4)	66.8 (7.2)	66.3 (7.4)	66.1 (7.7)	66.7 (7.9)	66.4 (7.8)
Height, cm (mean, SD)	159.6 (7.9)	160.4 (8.1)	160 (8)	160.9 (7.9)	161.3 (8.2)	161.1 (8)
Weight, kg (mean, SD)	66.1 (12.2)	65.8 (10.3)	66 (11.3)	64.8 (11)	65.8 (10.9)	65.3 (10.9)
BMI, kg/m² (mean, SD)	25.9 (4.3)	25.5 (3.3)	25.7 (3.9)	25.0 (3.6)	25.2 (3.5)	25.1 (3.6)
24-hour sodium excretion, g/day (mean, SD)	4.4 (1.9)	4.2 (1.8)	4.3 (1.8)	3.8 (1.6)	4.0 (1.9)	3.9 (1.7)
24-hour potassium excretion, g/day (mean, SD)	1.4 (0.6)	1.4 (0.6)	1.4 (0.6)	2.1 (0.9)	1.4 (0.6)	1.8 (0.9)

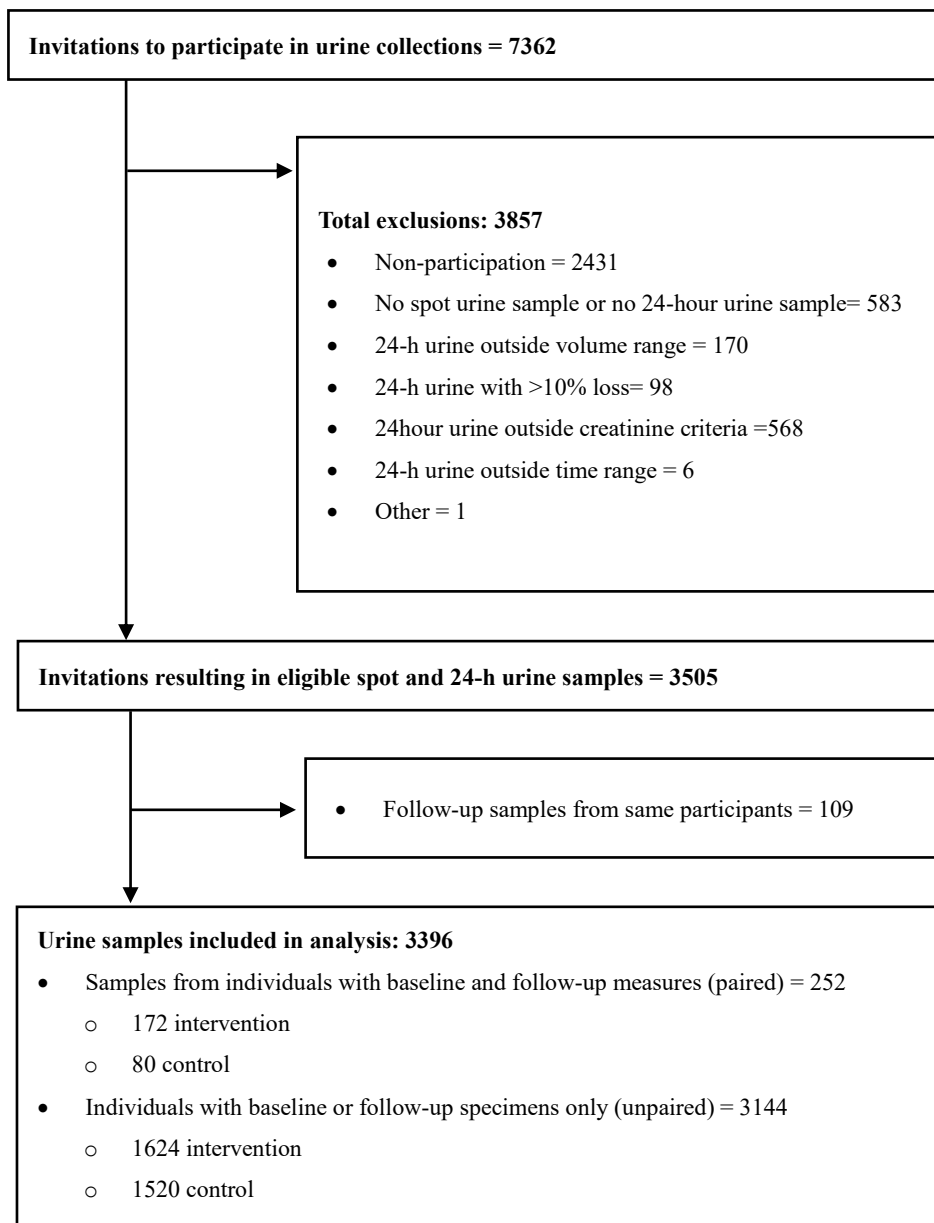
Intervention was use of reduced-sodium, added-potassium salt substitute. Control was continued use of usual salt. BMI= body mass index

Table 2 Urine concentration and volume parameters at baseline and follow-up for each randomized group

	Intervention			Control			Difference between intervention and control (95% CI)	P-value
	Baseline	Follow up	Change from baseline (95% CI)	Baseline	Follow up	Change from baseline (95% CI)		
Spot urine electrolyte and creatinine concentrations (mmol/L)								
Potassium	43.9 (24.4)	67.2 (36.7)	22.1 (17.6, 26.5)	42.6 (26.2)	47.9 (27.9)	5.4 (1.7, 9.1)	18.4(12.4, 24.4)	<0.001
Sodium	130.6 (58.8)	123.6 (58.4)	-7.8 (-15.5, -0.1)	118.5 (55.6)	131.3 (63.3)	12.1 (3.7, 20.4)	-18.4 (-29.9, -6.9)	0.002
Creatinine	10.1 (6.5)	10.2 (6.4)	0.3 (-0.6, 1.1)	9.8 (6.8)	10.7 (6.7)	0.7 (-0.2, 1.6)	-0.4 (-1.7, 0.8)	0.519
24-hour urine electrolyte and creatinine concentrations (mmol/L)								
Potassium	23.6 (10.5)	40.1 (20.7)	15.8 (13.4, 18.2)	22.5 (10.7)	26.6 (14.3)	4.4 (2.7, 6.2)	11.7 (8.6, 14.8)	<0.001
Sodium	122.3 (46.6)	119.8 (51.3)	-3.0 (-9.1, 3.1)	113.7 (47.7)	125.4 (51.9)	11.5 (4.8, 18.3)	-14.3 (-23.5, -5.1)	0.002
Creatinine	5.9 (3.0)	6.5 (3.4)	0.6 (0.2, 1.0)	5.7 (2.7)	6.5 (3.4)	0.7 (0.3, 1.2)	-0.2 (-0.8, 0.4)	0.612
24-hour volume (mls)								
Urine	1700.1 (713.4)	1512.3 (670.2)	-188.3 (-265.3, -111.2)	1757.2 (715.2)	1509.3 (689.7)	-244.6 (-334.8, -154.4)	71.0 (-50.0, 192.0)	0.248

Values are expressed as mean (SD) if not otherwise specified.

Figure 1 Flowchart



Appendix 1 Published predictive equations that use spot urine sodium concentration to estimate 24-hour sodium intake

Method	Urine Sample	Formula to predict 24 hour sodium intake (g)
Tanaka	Casual spot urine	$23 \div 1000 \times 21.98 \times \{\text{spot Na (mmol/l)} / [\text{spot creatinine (mg/dl)} \times 10] \times [-2.04 \times \text{age (years)} + 14.89 \times \text{weight (kg)} + 16.14 \times \text{height (cm)} - 2244.45]\}^{0.392}$
Kawasaki	Second morning urine	
Male		$23 \div 1000 \times 16.3 \times \{\text{Spot Na (mmol/l)} / [\text{Spot Cr (mg/dl)} \times 10] \times [-12.63 \times \text{age (years)} + 15.12 \times \text{weight (kg)} + 7.39 \times \text{height (cm)} - 79.9]\}^{0.5}$
Female		$23 \div 1000 \times 16.3 \times \{\text{Spot Na (mmol/l)} / [\text{Spot Cr (mg/dl)} \times 10] \times [-4.72 \times \text{age (years)} + 8.58 \times \text{weight (kg)} + 5.09 \times \text{height (cm)} - 74.5]\}^{0.5}$
Intersalt with K	Casual spot urine	
Male		$23 \div 1000 \times \{25.46 + [0.46 \times \text{spot Na (mmol/L)}] - [2.75 \times \text{spot Cr (mmol/L)}] - [0.13 \times \text{spot K (mmol/L)}] + [4.10 \times \text{BMI (kg/m}^2\text{)}] + [0.26 \times \text{age (y)}]\}$
Female		$23 \div 1000 \times \{5.07 + [0.34 \times \text{spot Na (mmol/L)}] - [2.16 \times \text{spot Cr (mmol/L)}] - [0.09 \times \text{spot K (mmol/L)}] + [2.39 \times \text{BMI (kg/m}^2\text{)}] + [2.35 \times \text{age (y)}] - [0.03 \times \text{age}^2\text{ (y)}]\}$
Intersalt without K	Casual spot urine	
Male		$23 \div 1000 \times \{23.51 + [0.45 \times \text{spot Na (mmol/L)}] - [3.09 \times \text{spot Cr (mmol/L)}] + [4.16 \times \text{BMI (kg/m}^2\text{)}] + [0.22 \times \text{Age (y)}]\}$
Female		$23 \div 1000 \times \{3.74 + [0.33 \times \text{spot Na (mmol/L)}] - [2.44 \times \text{spot Cr (mmol/L)}] + [2.42 \times \text{BMI (kg/m}^2\text{)}] + [2.34 \times \text{Age(y)}] - [0.03 \times \text{Age}^2\text{(y)}]\}$