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Monitoring the South African population's salt intake: spot urine *v.* 24 h urine

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Abstract

Objective: The present study set out to determine whether morning spot urine samples can be used to monitor Na (and K) intake levels in South Africa, instead of the 'gold standard' 24 h urine sample.

Design: Participants collected one 24 h and one spot urine sample for Na and K analysis, after which estimations using three different formulas (Kawasaki, Tanaka and INTERSALT) were calculated.

Setting: Between 2013 and 2015, urine samples were collected from different population groups in South Africa.

Subjects: A total of 681 spot and 24 h urine samples were collected from white (*n* 259), black (*n* 315) and Indian (*n* 107) subgroups, mostly women.

Results: The Kawasaki and the Tanaka formulas showed significantly higher ($P \leq 0{\cdot}001$) estimated Na values than the measured 24 h excretion in the whole population (5677·79 and 4235·05 *v.* 3279·19 mg/d). The INTERSALT formula did not differ from the measured 24 h excretion for the whole population. The Kawasaki formula seemed to overestimate Na excretion in all subgroups tested and also showed the highest degree of bias (−2242 mg/d, 95 % CI − 10 659, 6175) compared with the INTERSALT formula, which had the lowest bias (161 mg/d, 95 % CI − 4038, 4360).

Conclusions: Estimations of Na excretion by the three formulas should be used with caution when reporting on Na intake levels. More research is needed to validate and develop a specific formula for the South African context with its different population groups. The WHO's recommendation of using 24 h urine collection until more studies are carried out is still supported.

Keywords
Spot urine
24h urine
Sodium
Potassium
Salt
South Africa

Hypertension is an important contributor to the burden of disease in South Africa. There is convincing evidence that a high Na intake contributes to the development of hypertension[1,2]. Accurate estimation of population Na intake is crucial for monitoring trends in Na intake. Estimating Na intake by means of dietary questionnaires does not accurately reflect actual Na intake[3–5]. The amount of Na excreted in the urine is, however, a more acceptable method.

Twenty-four hours is the minimum time required to characterise the pattern of urinary excretion for a given individual[6]. The 24 h urine collection method (one or more) is considered the 'gold standard' in determining Na intake in individuals as well as in population groups[7]. It should be noted that for estimation of individual Na excretion, a single measurement would not be sufficient as highlighted by Ji *et al.*[8]. However, alternative methods have been proposed due to the high methodological burden of a 24 h urine collection in large population-based studies. As reported in a recent systematic review, initiatives for finding a replacement for 24 h urinary collection, that do not compromise data accuracy, are high on the agenda[9].

Mente *et al.* indicated in 2014 that spot urine samples from the Prospective Urban and Rural Epidemiological (PURE) study may be representative of the Na intake of the group despite the fluctuations in values for individuals[10]. This was also shown earlier by Tanaka *et al.*[11] in 2002.

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However, this methodology was greatly criticised[12–14] when the PURE study authors used spot urine samples to indicate the potentially harmful effects of very low salt intake on cardiovascular health and mortality[2,15].

As spot urine samples are affordable and easy to obtain, they would be valuable in monitoring Na intake particularly in resource-poor settings or where 24 h urine collections are not deemed feasible. Validity is also needed in terms of estimating a population's Na intake above a specific threshold, i.e. classifying what percentage of the population is above the recommended 2000 mg of Na or 5 g of salt per day[16]. However, the validity of spot urine samples is still inconclusive[6,9] and specific ethnic subgroup analyses are also needed to determine whether certain equations are better suited for a specific population. Recently, South Africa developed a national strategy to reduce the Na intake of the population[17] and has implemented a national Na reduction regulation (R.214) to regulate the Na content in certain processed foods[18]. Therefore, reliable, ongoing population-wide data on Na intake are necessary to monitor the progress and the effectiveness of public health efforts to curb the high hypertension rates.

For this reason, the first objective of the present study was to estimate the proportion of the population 'below' the 2000 mg Na/d threshold, using a single spot urine sample compared with a 24 h urine sample. The second objective was to provide some clarity on how to estimate the absolute difference in South Africans' salt consumption (i.e. the effectiveness of the Na reduction regulation) in terms of using a single spot urine sample or not.

Methods

Participants

Participants were recruited from three ongoing studies, two in the North West Province and one in KwaZulu-Natal, and included individuals of different age categories, ethnicity and gender. All relevant data were collected between 2013 and 2015. In all studies, the data were cross-sectional in nature. Details concerning the studies are summarised elsewhere[19].

First, we collected data from the African PRospective study on the Early Detection and Identification of Cardiovascular disease and hyperTension (African-PREDICT study). The participants included black and white men and women (aged between 20 and 30 years) who were apparently healthy and normotensive, and not using chronic medication. The Thusa-Bothle study included older black women (35–65 years), who were apparently healthy, from an urban community in the North West Province of South Africa. Lastly, data were collected in an urban area in the KwaZulu-Natal Province of South Africa. The latter study included apparently healthy Indian women between the ages of 18 and 50 years.

Urine collection

Participants from all three studies were given the same collection instructions by a trained field researcher. Each participant was provided with the necessary equipment (collection kit) to collect both a 24 h urine and a spot urine sample. On a day that was convenient for the participant, he/she was instructed to discard the 'first pass urine' on the morning of the start of his/her collection and collect all the urine passed thereafter, ending with the first urine of the following morning. This first urine collection of the following morning was collected and divided into a spot urine sample (collected in a separate container) and the rest of the urine, which was added to the larger container (with the rest of the 24 h urine). The start and end times were also recorded. After an aliquot was taken from the spot urine sample, the remaining urine in the spot urine sample was also added to the large container before aliquoting of the 24 h urine sample.

To check for completeness of the 24 h urine samples, the following cut-off points were used: volume of the 24 h urine collection >500 ml and urinary creatinine (Cr) >4·0 mmol/d for women or >6·0 mmol/d for men[20].

Biochemical analysis, blood pressure and anthropometric measurements

After careful aliquoting of the 24 h and spot urine samples, the samples were stored at −20 °C until analysis. For 24 h and spot urine samples, Na, K and Cr were measured as described in Swanepoel *et al.*[19].

The measurements of blood pressure, height and weight in the African-PREDICT study were performed using appropriate methods, and are described elsewhere[21]. As described in Thompson *et al.*[21], with the participants seated, clinic blood pressure recordings were measured at the brachial artery, twice on each arm (DINAMAP; GE Healthcare, Buckinghamshire, UK)[22], and a mean of the four readings was then used for all subsequent analyses. There was a rest period of 5 min between each measurement and appropriate-sized blood pressure cuffs were used. Blood pressure of the black and Indian women was measured on a semi-automatic blood pressure device (M3W-HEM7202; OMRON Healthcare, Kyoto, Japan)[19] using the participants' right arm after a 5 min rest in the sitting position with legs uncrossed. Readings were done in duplicate with a 3 min interval between the two readings.

BMI was calculated as [weight (kg)]/[height (m)]^2. The participants' weight was measured to the nearest 0·01 kg (in duplicate) with a digital scale (Seca 813, Hamburg, Germany) and height to the nearest 0·1 cm using a stadiometer (Seca 264, Hamburg, Germany). The waist circumference of both the black and Indian women was measured in triplicate to the nearest 0·1 cm at the midpoint between the lowest rib and the top of the iliac crest, using a steel tape (Lufkin, Apex, NC, USA).

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Calculation formulas used

Na and K from the 24 h urine collections were converted from mmol/d to mg/d by multiplying by 23 and 39, respectively. Salt was calculated by multiplying the mmol Na by 58·9 (combined molecular weight of Na and Cl).

To estimate 24 h urinary Na from spot urine the following three formulas were used.

Kawasaki formula[23]:

$$\text{Estimated 24 h Na (mmol/d)} = 16{\cdot}3 \times \sqrt{\text{spot Na(mmol/l)} / (\text{spot Cr (mg/dl)} \times 10)} \times (\text{predicted 24 h urinary Cr (mg/d)}),$$

where

$$\text{Predicted Cr (mg/d)} = -4{\cdot}72 \times \text{age (years)} + 8{\cdot}58 \times \text{weight (kg)} + 5{\cdot}09 \times \text{height (cm)} - 74{\cdot}5 \text{ (women)}$$

and

$$\text{Predicted Cr (mg/d)} = -12{\cdot}63 \times \text{age (years)} + 15{\cdot}12 \times \text{weight (kg)} + 7{\cdot}39 \times \text{height (cm)} - 79{\cdot}9 \text{ (men)}.$$

INTERSALT formula[24]:

$$\text{Estimated 24 h Na (mg/d)} = 23 \times [5{\cdot}07 + (0{\cdot}34 \times \text{spot Na (mmol/l)}] - (2{\cdot}16 \times \text{spot Cr (mmol/l)}) - (0{\cdot}09 \times \text{spot K (mmol/l)}) + (2{\cdot}39 \times \text{BMI (kg/m}^2)) + (2{\cdot}35 \times \text{age (years)}) - (0{\cdot}03 \times \text{age}^2\text{(years)})] \text{ (women)}$$

and

$$\text{Estimated 24 h Na (mg/d)} = 23 \times [25{\cdot}46 + (0{\cdot}46 \times \text{spot Na (mmol/l)}] - (2{\cdot}75 \times \text{spot Cr (mmol/l)}) - (0{\cdot}13 \times \text{spot K(mmol/l)}) + (4{\cdot}10 \times \text{BMI(kg/m}^2)) + (0{\cdot}26 \times \text{age (years)})] \text{ (men)}.$$

Tanaka formula[11]:

$$\text{Estimated 24 h Na (mmol/d)} = 21{\cdot}98 \times \text{XNa}^{0{\cdot}392},$$

where

$$\text{XNa} = [\text{spot Na (mmol/l)} / (\text{spot Cr (mg/dl)} \times 10)] \times (\text{predicted 24 h urinary Cr (mg/d)})$$

and

$$\text{Predicted Cr (mg/d)} = (-2{\cdot}04 \times \text{age (years)}) + (14{\cdot}89 \times \text{weight (kg)}) + (16{\cdot}14 \times \text{height (cm)}) - 2244{\cdot}45.$$

To estimate 24 h K excretion, the Kawasaki and Tanaka formulas were used. The INTERSALT formula is not designed to estimate K excretion and was therefore not used.

Kawasaki formula[23]:

$$\text{Estimated 24 h K (mmol/d)} = 7{\cdot}2 \times \sqrt{\text{spot K (mmol/l)} / (\text{spot Cr (mg/dl)} \times 10)} \times (\text{predicted 24 h urinary Cr (mg/d)}),$$

where

$$\text{Predicted Cr (mg/d)} = -4{\cdot}72 \times \text{age (years)} + 8{\cdot}58 \times \text{weight (kg)} + 5{\cdot}09 \times \text{height (cm)} - 74{\cdot}5 \text{ (women)}$$

and

$$\text{Predicted Cr (mg/d)} = -12{\cdot}63 \times \text{age (years)} + 15{\cdot}12 \times \text{weight (kg)} + 7{\cdot}39 \times \text{height (cm)} - 79{\cdot}9 \text{ (men)}.$$

Tanaka formula[11]:

$$\text{Estimated 24 h K (mmol/d)} = 7{\cdot}59 \times \text{XK}^{0{\cdot}431},$$

where

$$\text{XK} = [\text{spot K (mmol/l)} / (\text{spot Cr (mg/dl)} \times 10)] \times (\text{predicted 24 h urinary Cr (mg/d)})$$

and

$$\text{Predicted Cr (mg/d)} = (-2{\cdot}04 \times \text{age (years)}) + (14{\cdot}89 \times \text{weight (kg)}) + (16{\cdot}14 \times \text{height (cm)}) - 2244{\cdot}45.$$

Statistical analyses

The population was stratified according to the different studies, ethnicity and gender. To analyse agreement between the measured Na (and K) excretion (24 h urine sample) and the estimated Na (and K) excretion (spot urine samples, for all three (two) formulas), Bland–Altman plots were used[25]. The degree of bias was also calculated with the 95 % CI. The bias for each individual is the measured Na or K intake (24 h urine sample) minus the predicted (using Kawasaki, Tanaka and INTERSALT formulas) Na or K intake divided by the mean of the predicted and measured 24 h urinary Na or K excretion. We further calculated the possibility of proportional bias by

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conducting a linear regression with the difference (between the measured and predicted Na or K excretion) and the mean (between the predicted and measured Na or K intake). The β value of the regression should be as close to zero as possible with an insignificant P value to indicate no proportional bias. Correlations between estimated Na (and K) excretion from a spot urine sample (using the three (two) different formulas) and the measured 24 h urine sample were calculated using intraclass correlation coefficients.

Sensitivity and specificity of the estimated Na excretion (based on spot urine samples) to correctly classify the mean Na intake of this population as above or below the WHO's recommended 2000 mg Na/d were also assessed by using the following equations:

$$\text{Sensitivity} = \frac{\text{Na}_{\text{spot}} > 2000\,\text{mg/d} \times \text{Na}_{24\text{h}} > 2000\,\text{mg/d}}{\text{Na}_{24\text{h}} > 2000\,\text{mg/d}}$$

and

$$\text{Specificity} = \frac{\text{Na}_{\text{spot}} < 2000\,\text{mg/d} \times \text{Na}_{24\text{h}} < 2000\,\text{mg/d}}{\text{Na}_{24\text{h}} < 2000\,\text{mg/d}}.$$

Results

We collected 24 h urine as well spot urine samples from 470, 104 and 107 participants from the African-PREDICT, Thusa-Bothle and KwaZulu-Natal study, respectively. The characteristics of the three populations studied are summarised in Table 1. The average age and BMI of this population was 35·5 years and 27·8 kg/m^2, respectively. More women (n 476) than men (n 205) were included in the present study. Further details of the characteristics of this population and the differences between subgroups are described elsewhere[19].

In Table 2 we compare Na excretion obtained from 24 h collections with estimated Na values from spot samples, based on the three formulas described. The Kawasaki and Tanaka formulas showed significantly higher ($P \leq 0{\cdot}001$) estimated Na values than the measured 24 h excretion in the whole population (5677·79 and 4235·05 $v.$ 3279·19 mg/d, respectively). In the younger white (3547·81 $v.$ 3352·27 mg/d) and black individuals (3560·6 $v.$ 3417·57 mg/d), the Tanaka formula did not differ from the 24 h measurement. The INTERSALT formula also did not differ from the measured 24 h excretion, for the whole population. In all population groups except for the Indian population (3523·12 $v.$ 2683·08 mg/d), the INTERSALT formula underestimated the Na excretion. The Kawasaki formula seemed to overestimate Na excretion in all subgroups tested and also showed the highest degree of bias (−2242 mg/d, 95 % CI −10 659, 6175), whereas the INTERSALT formula had the lowest bias (161 mg/d, 95 % CI −4038, 4360).

The β values of the linear regression were above zero and significant in the INTERSALT formula, but not in the Kawasaki and Tanaka formulas. There were no significant and strong correlations (interclass correlation coefficients) observed, except for the INTERSALT (0·2, 95 % CI − 0·5, 0·3) formula in the whole population.

More importantly, analysis of sensitivity and specificity showed more or less the same pattern in all three formulas when estimating Na excretion, with a high sensitivity (>90 %) and a very low specificity (<10 %).

K excretion was estimated only by the Kawasaki and Tanaka formulas (Table 3). The Kawasaki formula overestimated K excretion in the young white (2355·28 $v.$ 1722·71 mg/d) and black (2290·24 $v.$ 1632·59 mg/d) populations. The Tanaka underestimated the K value in all population groups. The degree of bias was the lowest in the Kawasaki formula (−782 mg/d, 95 % CI −6930, 5366). There were also no significant correlations observed in either of the two formulas. Analysis of both sensitivity (8·11 %) and specificity (7·35 %) showed low values when estimating K excretion with the Kawasaki formula; corresponding values were 0·0 and 0·2 % with the Tanaka formula, respectively.

Bland–Altman plots (Fig. 1) showed inconsistent Na estimations across low and high levels of 24 h Na excretion. The mean difference of the Kawasaki and Tanaka formula was −2221 and −836·8 mg/d, respectively, with a wide limit of agreement. The INTERSALT formula overestimated 24 h Na excretion between 0 and 5000 mg/d (0–12·5 g salt) and underestimated Na excretion above 5000 mg/d (>12·5 g of salt). For 24 h K excretion, the

Table 1 Characteristics of the populations analysed in the present study

	African-PREDICT study				Thusa-Bothle study		KwaZulu-Natal study		Total					
	White (n 259)		Black (n 211)		Black (n 104)		Indian (n 107)		Men (n 205)		Women (n 476)		All (n 681)	
	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD	Mean	SD
Age (years)	25·5	2·9	24·5	3·2	50·2	9·0	40·2	11·6	25·0	3·1	38·6	13·9	35·5	13·6
Weight (kg)	76·4	18·0	66·1	14·9	76·0	21·8	68·7	14·8	73·4	18·3	72·7	19·2	72·9	19·0
Height (cm)	172·4	8·4	163·4	8·3	156·7	5·6	155·4	13·6	171·7	9·1	159·4	9·9	161·9	10·9
BMI (kg/m^2)	25·6	5·3	24·9	6·1	30·9	8·7	28·1	5·8	24·8	5·4	28·6	7·7	27·8	7·4
WC (cm)	82·0	14·0	77·4	11·9	87·9	15·2	91·8	14·2	81·4	13·5	85·6	15·2	84·8	14·9
SBP (mmHg)	117·6	12·4	119·3	11·7	135·5	17·7	123·4	19·9	122·5	11·4	126·4	18·8	125·6	17·6
DBP (mmHg)	77·2	7·7	79·4	7·7	83·2	11·2	81·8	12·2	79·5	7·9	80·9	10·7	80·6	10·2

WC, waist circumference; SBP, systolic blood pressure; DBP, systolic blood pressure.

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Table 2 Summary of results: comparison between the different methods of estimating 24 h sodium excretion *v.* measured excretion in different population groups in South Africa

	24 h measured excretion		Kawasaki formula		Tanaka formula		INTERSALT formula	
Na excretion (mg/d), mean and SD								
All	3279·19	2077·00	5677·79*	2936·41	4235·05*	1777·15	3140·32	730·86
AP, white	3352·27	1762·0	4551·75*	2026·56	3547·81	3241·26	2887·85‡	742·43
AP, black	3417·57	1919·49	4828·74*	2216·12	3560·60	1216·75	3047·35‡	710·47
TB, black	3477·39	3308·26	7485·42*	3256·53	5487·03*	1993·68	3254·33	585·98
KNZ, Indian	2683·08	1459·46	6446·32*	3344·56	4754·03*	1926·46	3523·12*	714·73
Range of excretion (mg/d)	271·3–21 568·6		1248·5–19 795·6		1292·9–11 226·9		868·1–51 75·5	
Degree of bias (mg/d) and 95 % CI	Reference		−2242†	−10 659, 6175	−837†	−6476, 4802	161	−4038, 4360
Degree of bias (salt g/d) and 95 % CI	Reference		−5·6†	−26·6, 15·4	−2·1†	−16·2, 12·0	0·4	−10·1, 10·9
Linear regression and 95 % CI	Reference		0·11	−0·04, 0·06	0·03	−0·06, −0·11	0·48§	0·25, 0·70
Validation, ICC and 95 % CI								
All	Reference		0·03	−0·14, 0·18	0·05	−0·12, 0·19	0·20‖	−0·50, 0·31
AP, white	Reference		0·17	−0·09, 0·37	0·14	−0·14, 0·34	0·29	0·06, 0·46
AP, black	Reference		0·24	−0·02, 0·43	0·12	−0·08, 0·39	0·26	0·03, 0·44
TB, black	Reference		0·04	−0·43, 0·36	0·06	−0·40, 0·37	0·15	−0·26, 0·43
K Indian	Reference		−0·07	−0·60, 0·29	−0·13	−0·69, 0·25	0·03	−0·48, 0·35
Sensitivity (%)	Reference		99·30		98·59		95·44	
Specificity (%)	Reference		2·60		3·90		11·39	

AP, African-PREDICT study; TB, Thusa-Bothle study; KNZ, KwaZulu-Natal study; ICC, intraclass correlation coefficient.
*Significantly higher than 24 h measured excretion.
†Greater bias than INTERSALT.
‡Significantly lower than 24 h measured excretion.
§Significant ($P \leq 0{\cdot}001$), indicating proportional bias.
‖ P value = 0·005.

Table 3 Summary of results: comparison between the different methods of estimating 24 h potassium excretion *v.* measured excretion in different population groups in South Africa

	24 h measured excretion		Kawasaki method		Tanaka method	
K excretion (mg/d), mean and SD						
All	1594·18	1181·04	2422·45*	2719·72	587·54‡	478·69
AP, white	1722·71	1117·72	2355·28*	3362·51	562·84‡	576·32
AP, black	1632·59	1037·17	2290·24*	2765·96	527·09‡	479·18
TB, black	1502·40	1521·71	2450·87*	1009·57	635·04‡	236·10
KZN, Indian	1271·14	946·15	2671·37*	2942·31	653·52‡	517·18
Range of excretion (mg/d)	206·1–11 341·55		418·9–36 087·9		133·6–5809·6	
Degree of bias (mg/d) and 95 % CI	Reference		−782	−6930, 5366	1039§	−1577, 3657
Degree of bias (mmol/d) and 95 % CI	Reference		−20·1	−177·7, 137·6	26·6	−40·4, 93·8
Linear regression and 95 % CI	Reference		−1·34†	−1·48, −1·24	1·41†	1·30, 1·53
Validation, ICC and 95 % CI						
All	Reference		0·07	−0·05, 0·12	0·08	−0·09, 0·22
AP, white	Reference		0·06	−0·24, 0·29	0·10	−0·19, 0·32
AP, black	Reference		0·00	−0·33, 0·26	0·02	−0·32, 0·26
TB, black	Reference		0·20	−0·20, 0·46	0·07	−0·38, 0·38
KZN, Indian	Reference		−0·03	−0·55, 0·31	−0·06	−0·59, 0·29
Sensitivity (%)	Reference		8·11		0·00	
Specificity (%)	Reference		7·35		0·20	

AP, African-PREDICT study; TB, Thusa-Bothle study; KNZ, KwaZulu-Natal study; ICC, intraclass correlation coefficient.
*Significantly higher than 24 h measured excretion.
†Significant ($P \leq 0{\cdot}001$), indicating proportional bias.
‡Significantly lower than 24 h measured excretion.
§Greater bias than Kawasaki.

Kawasaki formula both overestimated and underestimated K intake and the Tanaka formula overestimated K intake at high levels.

Discussion

The present study set out to estimate the proportion of the population 'below' the 2000 mg Na/d threshold, using a single spot urine sample compared with a 24 h urine sample, and to provide some evidence on how to estimate the absolute difference in South Africans' salt consumption in terms of using a single spot urine sample.

From the results presented, one might be tempted to conclude that the INTERSALT formula can be used to estimate Na excretion in the South African population because of non-significant difference compared with the

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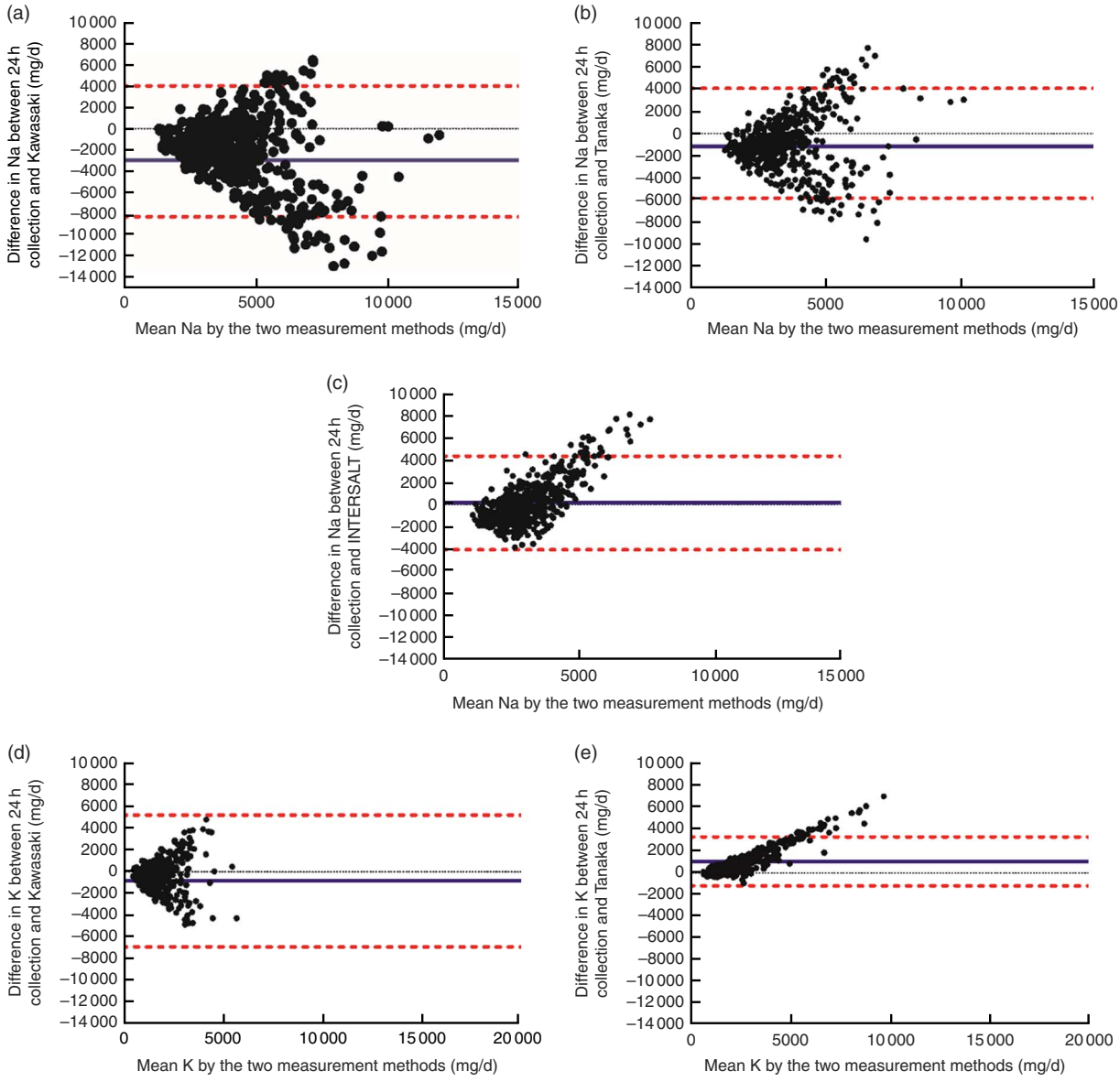

Fig. 1 (colour online) Bland–Altman plots comparing measured *v.* estimated 24 h sodium and potassium excretion using different formulas: (a) measured *v.* Kawasaki formula for sodium; (b) measured *v.* Tanaka formula for sodium; (c) measured *v.* INTERSALT formula for sodium; (d) measured *v.* Kawasaki formula for potassium; (e) measured *v.* Tanaka formula for potassium. ------, upper and lower limits of agreement calculated as the mean difference ± 1·96 × SD; ——, mean difference between the measured and predicted intake

24 h excretion. The same can be said for the Tanaka formula in young black and white populations. However, when we look at the totality of the results (i.e. degree of bias, sensitivity and specificity), this is not true. Even though the INTERSALT formula provided a non-significant difference with the 24 h excretion and showed the least biased information about the group mean 24 h Na excretion, it should be noted that a bias of approximately 0·4 g salt equivalent/d was still present. This suggests that the INTERSALT formula would be unable to detect an average change in salt consumption at two time points in the evaluation of the Na reduction regulation. This formula will therefore be unable to detect small changes in population salt consumption (~0·4 g/d) and unable to detect small increases in the proportion of the population below the stated threshold. The same can be seen in both the Kawasaki (bias of 5·6 g salt) and the Tanaka (bias of 2·1 g salt) formulas.

Our results are different from those reported by Mente *et al.*[10], who found that the Kawasaki formula showed the best agreement and the least bias when compared with the other two formulas. The INTERSALT had the highest degree of bias and the weakest correlation compared with the Kawasaki and Tanaka formulas[10]. Cogswell *et al.*[26] conducted a cross-sectional study to evaluate the validity of these three formulas with a 24 h

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urine sample in young Americans. They reported that the INTERSALT formula provided the least bias when compared with Kawasaki and Tanaka formulas and would be recommended in America for the monitoring of Na intake. As observed in our study, it must still be noted that even though the bias was smaller compared with the other formulas, a bias of 0·4 g salt/d was still present, which is the same as reported in the current study and is unable to detect differences.

In terms of the correlations of the three formulas, the INTERSALT had a weak but significant correlation in the whole group. Kawasaki *et al.*[23] reported a correlation of 0·53 and Tanaka *et al.*[11] a correlation of 0·54 between the predicted and actual 24 h excretion. Our study reported much weaker correlations (Kawasaki = 0·03 and Tanaka = 0·05). The hypothesis on which the Kawasaki and Tanaka formulas are based does not seem to relate to the South African population and could be a possible reason for not observing the same correlations. Cr values are highly influenced by weight (and BMI) and are used to form the hypothesis of these two formulas. The same issues of Cr and the variability thereof was raised by Campbell[14], who stated that Cr, among other parameters, is highly impacted by variation in assessment methods. The Kawasaki and Tanaka formulas were developed and tested in a Japanese population with a mean BMI (in women) of 21·4 and 22·1 kg/m^2, respectively. The mean BMI of the women included in the present population was 28·6 kg/m^2; therefore, a population that was overweight *v.* a population of normal weight. Both the Tanaka and INTERSALT formulas were developed and validated in young populations[11,24], whereas the Kawasaki formula[23] was validated in a wider age group.

According to a systematic review done by Ji *et al.*[9], the INTERSALT study[27] produced the most convincing evidence with regard to the feasibility and usefulness of the 24 h urine collection. The INTERSALT study was conducted in fifty-two different populations. As mentioned, the method of Tanaka[11] and Kawasaki[23] is population specific (Japanese individuals) and requires internal calibration with age, weight and Cr. It also has been reported to overestimate low intakes and underestimate high intakes[28].

Even though the INTERSALT formula showed the least bias and did not differ from the measured Na intake in a South African population, research on developing a formula based on the INTERSALT should be approached with caution. The INTERSALT was carried out in the 1980s in different low- and middle-income countries. The age, BMI and Cr distributions have changed substantially with the epidemiological transition, resulting in these parameters perhaps not being directly applicable today and in this population. As suggested by Cogswell *et al.*, designing a study to standardise mean estimated Na intake from spot urine samples among a small group within the larger population may better inform monitoring at a population level and could be viable in South Africa[26]. Furthermore, research should investigate differences of the predictions of spot urine samples that were collected at different times in the day within this population. Kawasaki *et al.*[23] reported an even stronger correlation when participants collected three 24 h urine samples, and this should also be considered for future research.

Sensitivity is the proportion of true positives that are correctly identified by the estimation formulas[29] and can be seen as not that important in this context. In other words, 99·30, 98·59 and 95·44 % of the estimations from the Kawasaki, Tanaka and INTERSALT formulas correctly classified individuals who had Na intake above 2000 mg/d. Specificity, on the other hand, is the proportion of true negatives that are correctly identified by the estimation formulas[29] and can be seen as paramount in this context. Only 2·60, 3·90 and 11·39 % of the estimations by the Kawasaki, Tanaka and INTERSALT formulas correctly identified individuals having Na excretion below 2000 mg/d. Therefore, the different formulas are able to identify true positives (sensitivity), but fail to identify true negative individuals (specificity). This will translate into the formulas overestimating Na excretion and classifying individuals with low Na intake as having high Na intake (low specificity). In other words, all three formulas will be unable to detect successful outcome of the Na reduction strategy in the population, with immediate risk to the continuation of the programme. This is of extreme importance, not only for South Africa as a country in establishing the success of its Na regulation, but also globally to report and assess which interventions are more likely to be achievable. All these considerations should be kept in mind when using these formulas in estimating Na excretion in a population setting.

With regard to K intake estimations, the Kawasaki formula overestimated and the Tanaka formula underestimated the K intake compared with the 24 h excretion. No correlation was found for either of these formulas; however, the Kawasaki reported the lowest degree of bias. These formulas are also based on the same hypothesis as explained earlier and were developed for a population with a much lower BMI than the current population (which means the Cr values will differ significantly). A formula should be developed for estimating K accurately in the South African or similar population, as K is crucial in monitoring health in a country. The sensitivity and specificity of the formulas to correctly identify true positive and negatives were very low, and therefore it is not advised to use these two formulas in estimating K excretion.

Our study had some limitations. Our sample was not representative of the whole of South African population and we collected only one 24 h urine sample from each participant. Another limitation of the study is that the spot urine sample was collected as part of the 24 h urine sample and not as an independent sample. This makes it difficult to compare the results of our INTERSALT

formula with the original INTERSALT results as these latter samples were collected as independent samples and poses a potential problem when comparing studies and formulas[8,9,28]. Although the heterogeneity of the present study is a limitation on the one hand, it provides us with the opportunity to review our findings in different settings and populations and closely imitates a 'real-world' situation.

To conclude, in most countries of the world, programmes of population salt reduction will be likely to reduce salt consumption – although they may not be able to bring levels below thresholds in the short term. Therefore, it is important that the measure of salt intake used is able to detect absolute changes in salt consumption, irrespective of thresholds. Our findings suggest that not one of the formulas is suitable to use in a South African population and efforts need to be made to investigate modern internal validation within the population when developing a new formula. If inaccurate methods are used for estimating Na excretion and establishing changes over time, the continuation of an Na reduction programme could be wrongfully ended or misinterpreted.

We agree with other authors[2,24,26], in that estimated Na excretion from spot urine samples may possibly be used to monitor trends in the population, but the WHO's statement of 'until more studies are carried out to assess simpler but reliable methods of urine collection for the purpose of estimating daily excretions [of sodium], 24-hour urine collections are recommended' is still supported until more conclusive evidence is produced with regard to the use of spot urine in Na intake monitoring.

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References

1. Kotchen TA, Cowley AW & Frohlich ED (2013) Salt in health and disease – a delicate balance. *N Engl J Med* **368**, 1229–1237.
2. O'Donnell M, Mente A, Rangarajan S *et al.* (2014) Urinary sodium and potassium excretion, mortality, and cardiovascular events. *N Engl J Med* **371**, 612–623.
3. Espeland MA, Kumanyika S, Wilson AC *et al.* (2001) Statistical issues in analyzing 24-hour dietary recall and 24-hour urine collection data for sodium and potassium intakes. *Am J Epidemiol* **153**, 996–1006.
4. Caggiula AW, Wing RR, Nowalk MP *et al.* (1985) The measurement of sodium and potassium intake. *Am J Clin Nutr* **42**, 391–398.
5. Clark AJ & Mossholder S (1986) Sodium and potassium intake measurements: dietary methodology problems. *Am J Clin Nutr* **43**, 470–476.
6. Elliot P & Brown I (2007) *Sodium Intakes Around the World*. Geneva: WHO.
7. Bingham SA (2002) Biomarkers in nutritional epidemiology. *Public Health Nutr* **5**, 821–827.
8. Ji C, Dary O, Campbell NR *et al.* (2013) Spot and overnight urine are inappropriate to assess population sodium intake. *Rev Panam Salud Publica* **34**, 283–283.
9. Ji C, Sykes L, Paul C *et al.* (2012) Systematic review of studies comparing 24-hour and spot urine collections for estimating population salt intake. *Rev Panam Salud Publica* **32**, 307–315.
10. Mente A, O'Donnell MJ, Dagenais G *et al.* (2014) Validation and comparison of three formulae to estimate sodium and potassium excretion from a single morning fasting urine compared to 24-h measures in 11 countries. *J Hypertens* **32**, 1005–1015.
11. Tanaka T, Okamura T, Miura K *et al.* (2002) A simple method to estimate populational 24-h urinary sodium and

potassium excretion using a casual urine specimen. *J Hum Hypertens* **16**, 97–103.
12. Cogswell ME, Mugavero K, Bowman BA *et al.* (2016) Dietary sodium and cardiovascular disease risk – measurement matters. *N Engl J Med* **375**, 580–586.
13. Cook NR, Appel LJ & Whelton PK (2014) Lower levels of sodium intake and reduced cardiovascular risk. *Circulation* **129**, 981–989.
14. Campbell N (2014) Validation and comparison of three formulae to estimate sodium and potassium excretion from a single-morning fasting urine compared to 24-h measures in 11 countries. *J Hypertens* **32**, 2499–2500.
15. Mente A, O'Donnell M, Rangarajan S *et al.* (2016) Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies. *Lancet* **388**, 465–475.
16. World Health Organization (2012) *Guideline: Sodium Intake for Adults and Children*. Geneva: WHO.
17. South African Government, Department of Health (2013) Strategic Plan for the Prevention and Control of Non-Communicable Diseases 2013–17. https://www.health-e.org.za/wp-content/uploads/2013/09/NCDs-STRAT-PLAN-CONTENT-8-april-proof.pdf (accessed September 2017).
18. South African Government, Department of Health (2013) Government Gazette: No. R. 214 Foodstuffs, Cosmetics and Disinfectants Act, 1972 (Act 54 of 1972) Regulations Relating to the Reduction of Sodium in Certain Foodstuffs and Related Matters. http://extwprlegs1.fao.org/docs/pdf/saf122848.pdf (accessed September 2017).
19. Swanepoel B, Schutte AE, Cockeran M *et al.* (2016) Sodium and potassium intake in South Africa: an evaluation of 24-hour urine collections in a white, black, and Indian population. *J Am Soc Hypertens* **10**, 829–837.
20. Stolarz-Skrzypek K, Kuznetsova T, Thijs L *et al.* (2011) Fatal and nonfatal outcomes, incidence of hypertension, and blood pressure changes in relation to urinary sodium excretion. *J Am Med Assoc* **305**, 1777–1785.
21. Thompson JES, Smith W, Ware LJ *et al.* (2016) Masked hypertension and its associated cardiovascular risk in young individuals: the African-PREDICT study. *Hypertens Res* **39**, 158–165.
22. Reinders A, Reggiori F & Shennan AH (2006) Validation of the DINAMAP ProCare blood pressure device according to the international protocol in an adult population. *Blood Press Monit* **11**, 293–296.
23. Kawasaki T, Itoh K, Uezono K *et al.* (1993) A simple method for estimating 24 h urinary sodium and potassium excretion from second morning voiding urine specimen in adults. *Clin Exp Pharmacol Physiol* **20**, 7–14.
24. Brown IJ, Dyer AR, Chan Q *et al.* (2013) Estimating 24-hour urinary sodium excretion from casual urinary sodium concentrations in Western populations: the INTERSALT study. *Am J Epidemiol* **177**, 1180–1192.
25. Altman DG & Bland JM (1983) Measurement in medicine: the analysis of method comparison studies. *J R Stat Soc Ser D* **32**, 307–317.
26. Cogswell ME, Wang C-Y, Chen T-C *et al.* (2013) Validity of predictive equations for 24-h urinary sodium excretion in adults aged 18–39 y. *Am J Clin Nutr* **98**, 1502–1513.
27. Intersalt International Collaborative Group (1988) Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. Intersalt Cooperative Research Group. *BMJ* **297**, 319–328.
28. Ji C, Miller MA, Venezia A *et al.* (2014) Comparisons of spot vs 24-h urine samples for estimating population salt intake: validation study in two independent samples of adults in Britain and Italy. *Nutr Metab Cardiovasc Dis* **24**, 140–147.
29. Altman DG & Bland JM (1994) Diagnostic tests 1: sensitivity and specificity. *BMJ* **308**, 1552.