Prediction of 24-hour sodium excretion from spot urine samples in South African adults: A comparison of four equations

Journal of Human Hypertension
https://doi.org/10.1038/s41371-019-0210-2

ARTICLE

Prediction of 24-hour sodium excretion from spot urine samples in South African adults: a comparison of four equations

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Received: 7 January 2019 / Revised: 22 February 2019 / Accepted: 13 March 2019

Abstract

Repeated 24-hour urine collection is considered to be the gold standard for assessing salt intake. This is often impractical in large-population studies, especially in low–middle-income countries. Equations to estimate 24-hour urinary salt excretion from a spot urine sample have been developed, but have not been widely validated in African populations. This study aimed to systematically assess the validity of four existing equations to predict 24-hour urinary sodium excretion (24UNa) from spot urine samples in a nationally representative sample of South Africans. Spot and 24-hour urine samples were collected in a subsample ($n = 438$) of participants from the World Health Organisation Study on global AGEing and adult health (SAGE) Wave 2 in South Africa in 2015. Measured 24UNa values were compared with predicted 24UNa values from the Kawasaki, Tanaka, INTERSALT and Mage equations using Bland–Altman plots. In this subsample (mean age 52.8 ± 16.4 years; body mass index 30.2 ± 8.2 kg/m^2; 76% female; 73% black African; 42% hypertensive), all four equations produced a significantly different population estimate compared with the measured median value of 6.7 g salt/day (IQR 4.4–10.5). Although INTERSALT underestimated salt intake (−3.77 g/d; −1.64 to −7.09), the other equations overestimated by 1.28 g/d (−3.52; 1.97), 6.24 g/d (2.22; 9.45), and 17.18 g/d (8.42; 31.96) for Tanaka, Kawasaki, and Mage, respectively. Bland–Altman curves indicated unacceptably wide levels of agreement. Use of these equations to estimate population level salt intake from spot urine samples in South Africans is not recommended.

Introduction

It is widely accepted that excess dietary sodium or salt consumption is a major determinant of population blood pressure (BP) levels [1], contributing to the epidemic of hypertension and cardiovascular disease (CVD) [2]. Of the 56.9 million deaths worldwide in 2016, CVD including ischaemic heart disease and stroke were the world's biggest killers, accounting for over a quarter or 15.2 million deaths in that year alone [3]. Hypertension is estimated to be responsible for around half of these heart disease and stroke deaths, translating to 9.4 million deaths worldwide every year [4], and highlighting the need for prevention and treatment of raised BP to prevent these vascular events [5].

The Global Burden of Disease Study (1990–2016) suggests that, among individual dietary risk factors for CVD mortality and morbidity, a diet high in sodium contributed to 4.2% of deaths [6]. Alongside rapid economic, nutritional and demographic transition, low-to-middle-income countries (LMIC) are experiencing disproportionately rapid increases in hypertension prevalence [7, 8]. With many

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Published online: 10 May 2019

LMICs having no or inadequate universal health coverage [9], preventive public health strategies are urgently needed to reduce the subsequent cardiovascular morbidity and mortality.

An increasing number of countries are recognising the importance of population level salt reduction to reduce hypertension [10]. The WHO global targets to reduce non-communicable disease (NCD) by 2025 [11] list a 30% relative reduction in mean population salt intake of as one of the seven targets defined in the framework. South Africa was the first country to implement legislation on mandatory maximum sodium levels in a wide range of processed foods, with a stepped implementation approach between 2016 and 2019 [12, 13]. Although the impact of the legislation has yet to be evaluated, estimates suggest salt intake should decrease by 0.85 g/person/day, resulting in an 11% reduction in annual CVD deaths and saving the government millions of dollars in health care costs [14, 15]. In many countries, sodium reduction in foods is not through legislation but voluntary reformulation by the food industry. For example, overall salt intake has reduced by ~10% in the UK [16] owing to voluntary efforts by the food industry.

To evaluate the effectiveness of such country-level salt reduction strategies, reliable data are needed showing trends in population salt intake over time [17]. However, obtaining valid measures of population salt intake is challenging. Self-reported dietary data are often inaccurate as salt intake is both obvious (discretionary salt added to foods at the table or during cooking), as well as not-obvious, for example, in processed or packaged foods. Although a number of authors, including ourselves, have developed and validated short dietary assessment food frequency questionnaires to provide an estimate of salt intake that tend to correlate reasonably well with urinary biomarkers [18–21], such instruments tend to underestimate total 24 h urinary excretion.

In many high-income countries, including Australia, UK, and USA, most salt comes from processed foods. As such, it is possible to monitor changes to the salt content in the food supply as a proxy indicator for overall non-discretionary salt intake, although this requires food habits to be known [12, 22]. However, estimating population salt intake from the food supply may also be inaccurate if discretionary salt intake is high, such as in China [23].

The gold standard method for measuring population salt intake is measurement of sodium excretion (as a proxy for intake) in 24-hour urine collections [24]. Although this method has been used to assess the age-specific, sex-specific, and region-specific average sodium and potassium intake‘ and its association with anthropometric characteristics in a sample of 1232 Italian adult hypertensives across 47 centres [25], it is onerous and often impractical for use in large surveys that aim to collect nationally representative data, especially in resource-poor LMICs [26]. Numerous authors have suggested that daily salt intake can be estimated from the sodium concentration in spot urine samples provided there is a measure of either the concentration or dilution of the urine. Other biochemical variables, such as albumin and catecholamines, are routinely measured in spot urine and expressed relative to urinary creatinine concentration, using creatinine concentration as a marker for diuresis [27]. However, the spot urine sodium/creatinine ratio has inherent limitations in estimating daily sodium excretion owing to day to day variability in both sodium and creatinine excretion [28, 29].

Various equations exist to estimate 24-hour sodium excretion from spot urine samples [30–33], many of which are based on 24-hour urinary creatinine estimates. These equations have mostly been developed in Japanese populations and there have been few applications of these equations in African populations [34]. The aim of this study was to investigate the validity of four such equations (INTERSALT [30], Tanaka [31], Kawasaki [32], Mage [33]) to predict 24-hour urinary Na excretion (24Una) from spot urine samples in South African adults.

Methods

Study population and measures

This analysis is based on data collected in a sub-study [35] of the World Health Organisation Study on global AGEing and adult health (WHO–SAGE, Wave 2). WHO–SAGE is a multinational longitudinal study examining the health and wellbeing of adult populations and the ageing process in over 42,000 respondents from six countries (China, Ghana, India, Mexico, Russia, and South Africa) [36]. SAGE South Africa Wave 2 data were collected in 2015 (August–December), following up households from Wave 1 (2007–2010) [37]. Spot and 24-hour urine collection was conducted in a nested subsample of Wave 2 respondents alongside the standard WHO–SAGE data collection (household, individual, and proxy questionnaires; anthropometry; dried blood spot collection; BP; and physical function tests [36, 38]). The WHO/PAHO protocol was used for sodium determination in 24-hour urine [39], with the detailed protocol described previously [35]. In brief, respondents were requested to collect all urine produced for 24-hours, excluding the first pass urine on day 1, but including the first urine of the following morning (day 2) in a 5-litre plastic container containing 1 g thymol as preservative. The spot sample was collected without preservative from the second urine passed on day 1 (marking the start of the 24-hour collection), immediately aliquoted into three 15 ml Porvair tubes (Porvair Sciences,

Leatherhead, UK), then kept in a cool box powered by the fieldwork vehicles. The 24-hour sample was collected the next morning, volumes were recorded, and aliquots generated with all samples then shipped to the central laboratory in Durban, maintaining the cold chain. Sodium and potassium were determined using the indirect Ion Selective Electrode method and creatinine analysed using the standardised urinary Jaffe kinetic method (Beckman Coulter Synchron DXC600/800 System). Incomplete 24-hour urine collections were assumed and excluded from analyses if: total urinary volume ≤ 300 ml; or creatinine excretion ≤ 4 mmol/day (women) or ≤ 6 mmol/day (men) [40].

BP was measured by trained nurses using wrist-worn BP devices with positioning sensor (R6, Omron, Japan). Respondents had been seated for at least 5 minutes before three sequential measures were taken on the left arm (1 minute between each measure), with the wrist resting precisely at the level of the heart and the respondent seated with legs uncrossed. Such wrist BP devices have been shown to meet the validation criteria of the European Society of Hypertension International Protocol [41–43]. Hypertension was determined by systolic BP ≥ 140 mmHg or diastolic BP ≥ 90 mmHg, or current antihypertensive medication use. Mean arterial pressure (MAP) was calculated using the formula: $MAP = (SBP - DBP) \times 0.41 + DBP$ [44].

All respondents provided written informed consent prior to taking part in the study. The study complied with the Declaration of Helsinki [45], with ethical approval from the WHO Ethics Review Committee [RPC149], the North-West University Health Research Ethics Committee (Potchefstroom, South Africa) and the University of the Witwatersrand Human Research Ethics Committee (Johannesburg, South Africa). Interviews were conducted in the respondents' home languages, with consent forms available in the most widely spoken languages for each region.

Data capture and analysis

An electronic data capture system was used during face-to-face interviews. Stata/IC version 15.1 was used for statistical analyses. Categorical data are presented as frequencies and percentages. Data were checked for normality using the Skewness–Kurtosis test, with non-parametric data presented as medians and interquartile ranges and log transformation used for all non-normal outcomes. The following equations were evaluated to assess the accuracy of using spot urine samples to predict 24-hour urinary sodium excretion (24UNa): (1) the INTERSALT equation [30]; (2) the Tanaka equation [31; (3) the Kawasaki equation [32; and (4) the Mage equation [33]. Refer to Table 1 for further details.

Table 1 Equations used to predict 24-hour urinary sodium excretion from spot urine samples[a]

Reference	Cohort	Equation for estimating predicted 24 h urine Na excretion (Pr24UNa mg/day)	Equation for estimating predicted 24 h urine creatinine excretion (Pr24UCr mg/day)
Brown et al., 2013 [25]	Male ($n = 241$) Female ($n = 2852$) Aged 20–59 years	INTERSALT Men: = 23 × {25.46+[0.46 × spot NA (mmol/L)] −[2.75 × spot Cr (mmol/L)]−[0.13 × spot K (mmol/L)]+[4.10 × BMI (kg/m2)]+[0.26 × age (yr)]} Women: = 23 × {5.07+[0.34 × spot NA (mmol/L)]−[2.16 × spot Cr (mmol/L)]−[0.09 × spot K (mmol/L)]+[2.39 × BMI (kg/m2)]+ [2.35 × age (yr)]−[0.03 × age2 (yr)]}	No calculation of Pr24UCr used in equation
Tanaka et al., 2002 [26]	Developed in 591 Japanese adults aged 20–59 years	Tanaka = 23 × (21.98 × $XNa^{0.392}$), where XNA = [spot Na (mmol/l)/spot Creatinine (mg/dL) × 10] × Pr24UCr (mg/day)]	Pr24UCr (mg/day) = (− 2.04 × age (year)) + (14.89 × weight (kg)) + (16.14 × height (cm)) − 2244.45
Kawasaki et al., 1993 [27]	Equation for predicted 24-h urine creatinine excretion developed in a study of 256 male and 231 female participants aged 20–79 year (41) and validated in 20 male and 27 female Japanese and foreign (including 16 American) subjects	Kawasaki = 23 × (16.3 × $XNa^{0.5}$), where XNA = [spot Na (mmol/l)/spot creatinine (mg/dL) × 10] × Pr24UCr (mg/day)	Pr24UCr (mg/day) for men = (12.63 × age (year)) + (15.12 × weight (kg)) + (7.39 × height (cm))− 79.9 Pr24UCr (mg/day) for women = (− 4.72 × age (year)) + (8.58 × weight (kg)) + (5.09 × height (cm))− 74.5
Mage et al., 2003 [28]	The Mage equation was developed to predict urine pesticide and chemical exposure with NHANES urine specimens. Equation for predicted 24-h urine creatinine excretion developed in a separate study (42) of 249 men in Canada with corrections based on the relative amounts of fat and muscle mass in women (25,43) and differences in muscle mass by race and BMI (28,44)	Mage = {[23 × spot NA (mmol/L)]/[spot Cr (mg/dL) × 10]} × [Pr24UCr (mg/day)]	Pr24UCr (mg/day) for men = 0.00179 × (140 − age (year)) − (weight $(kg)^{1.5}$ × height $(cm)^{0.5}$) × (1 + 0.18 × A × (1.366 − 0.0159 × BMI (kg/m^2))) where A is African American or black race = 1, other race = 0. Pr24UCr (mg/day) for women = 0.00163 × (140 − age (year)) × (weight $(kg)^{1.5}$ × height $(cm)^{0.5}$) × (1 + 0.18 × A × (1.429 − 0.0198 × BMI (kg/m^2)))

[a]Adapted from Cogswell et al. [45]

Spearman correlations were conducted to determine the association between observed 24UNa and the predicted 24-hour urinary sodium excretion (Pr24UNa) from each of the four equations with differences assessed using the Wilcoxon signed rank test. Agreement between 24Una and each Pr24UNa was assessed using Bland–Altman plots [46] and assessment of limits of agreement (LOA). Bland–Altman plots compare the mean difference (24UNa minus Pr24UNa) vs. the average of the two values. Both 24UNa and Pr24UNa values were transformed to their natural logarithms (ln) before analyses owing to the skewness in distributions. These are reported as the antilogarithm of the difference, i.e., the geometric mean of the 24UNa/Pr24UNa ratios and the antilogarithms of the LOA, which provide an interval within which 95% of the ratios lie. The LOA approach provides an informative analysis of reliability, including information about the magnitude of errors between the methods. The 95% LOA represent a range of values within which 95% of all differences between methods are expected to fall. Using the standard deviation (sd) of differences between methods, the 95% LOA were calculated for each of the four Pr24UNa values as mean agreement ± 1.96 (sd diff). For example, mean agreement of 100% suggests exact agreement, whereas mean agreement of 80% indicates that the Pr24UNa overestimates observed 24UNa by 20%, on average. All analyses were converted to daily salt (NaCl) equivalents (g/d) for ease of interpretation and consistency of reporting against recommended cutoffs for optimal health [11]. Sensitivity and specificity of each of the equations were calculated to determine their ability to correctly classify participants according to the reference value of 5 g salt per day.

Results

Complete 24-hour urine collections were obtained from 889 of the participants included in the nested sample for urine collection of $n = 1291$, representing 69% response rate. However, missing data reduced the sample size available for the present analysis to $n = 438$. Reasons for missing data related to uploading issues of sociodemographic survey data (age, sex) and anthropometric (weight) and blood pressure measurements by the computer assisted personal interview system. Hypertension prevalence in the total survey sample ($n = 1847$) was 44% in older adults (50-plus years) and 25% in younger adults (18–49 years). The overall weighted prevalence of hypertension was 36% in both the total sample and the subsample, with no significant difference between these. Participant characteristics of the subsample are shown in Table 2. Based on analysis of complete 24-hour urine samples, sodium excretion varied widely with observed values of between 1 and 40 g salt/day, and a group median of 6.7 g salt/day (4.4–10.5). Median salt excretion was higher in the younger group (under 50 years of age; 8.5 (5.1–13.9) g salt/day) compared with the older group (50 years plus; 6.1 (4.2–8.9) g salt/day; $p < 0.001$). No significant differences were observed between men and women, or between respondents living in urban and rural areas.

Predicted urinary creatinine (Pr24UCr) was estimated according to the equations shown in Table 1 (excluding INTERSALT) and then entered into equations to estimate PrUNa.

There were significant differences (Wilcoxon signed rank test) between measured urinary creatinine (24UCr) and Pr24UCr (Table 3). Bland–Altman plots showed that all equations resulted in a systematic bias with higher observed creatinine values, resulting in a greater degree of underestimate in the group as a whole and in men and women independently (data not shown). Log transformation of the values did not remove this systematic bias. Neither BMI, waist-to-height ratio nor age could be used to predict those individuals with high measured daily creatinine excretion, for whom the predictive equations may be less accurate (data not shown). Table 3 shows the median difference between measured and predicted creatinine values, and the poor correlation between the measured value and all estimated values.

Investigating the median differences between the observed and predicted urinary sodium levels (Table 4) showed that the group estimates from the four equations were all significantly different to the measured value. Spearman correlations between 24UNa and Pr24UNa (mmol/L) were significant but weak for all equations. INTERSALT tended to underestimate sodium excretion, especially at lower levels, whereas Kawasaki and Mage overestimated 24UNa (Fig. 1).

The Bland–Altman curves suggest systematic bias for both INTERSALT and Tanaka equations. Geometric means (back transformed logarithmic data of differences) indicate: INTERSALT underestimates 24UNa by 306%; Kawasaki overestimates by 43%, whereas Tanaka performed best with a mean underestimation of 7%. The Mage equation performed the worst, with a mean overestimation of 55% but unacceptably wide limits of agreement (LOA: 57% underestimation to 1321% overestimation). Clearly, this level of bias is outside the scope of an acceptable range [47].

The Tanaka, Kawasaki, and Mage equations had a high sensitivity (95.6–97.7%) for correctly categorising individuals consuming more than the WHO recommendation of a maximum 5 g salt/day (Table 5), because of their bias to overestimate observed intakes. In contrast, specificity was very low (5–12%), demonstrating their inability to correctly detect those individuals consuming <5 g salt/d.

Table 2 Sociodemographic and health characteristics of WHO–SAGE nested salt study sample, South Africa Wave 2 (2015)

	Nested salt study $N = 438$	Male $n = 106$	Female $n = 332$
Age, years	55 (40–65)	52 (37–63)	56 (43–65)
50 years and above, *n* (%)	284 (65)	61 (58)	223 (67)
Ethnicity, *n* (%)			
Black African	319 (73)	78 (74)	241 (73)
Coloured	73 (17)	16 (15)	57 (17)
Indian	36 (8)	7 (7)	29 (9)
White	10 (2)	5 (5)	5 (2)
Rural, *n* (%)	129 (30)	30 (28)	99 (30)
Education, years	9 (7–12)	10 (6–12)	8 (6–12)
BMI, kg/m^2	29.1 (24.2–34.7)	25.6 (22.3–29.7)	30.4 (25.7–35.6)
Waist-to-height ratio	0.58 (0.50–0.66)	0.53 (0.46–0.59)	0.61 (0.52–0.68)
Systolic BP, mmHg	129 (118–142)	129 (119–143)	128 (118–142)
Diastolic BP, mmHg	80 (73–88)	82 (74–89)	80 (72–88)
MAP, mmHg	99 (93–111)	100 (94–111)	99 (93–111)
Hypertensive, *n* (%)	186 (42)	49 (46)	137 (41)
AHT use, *n* (%)	49 (11)	8 (8)	41 (12)
Previous stroke, *n* (%)	4 (1.2)	3 (3.3)	1 (0.4)
Diabetic, *n* (%)	35 (10)	7 (8)	28 (11)
Current smoker, *n* (%)	49 (15)	23 (25)	26 (11)
Alcohol use, *n* (%)	62 (18)	34 (37)	28 (11)

All data shown as median (IQR, interquartile range) unless otherwise indicated. Smokers identified by self-report. Hypertensive categorised as BP ≥ 140/90 mmHg or current medication. *BMI* body mass index, *MAP* mean arterial pressure, *AHT* antihypertensive medication use within the last 2 weeks; alcohol use within the last month

Table 3 Comparison between measured 24-hour (24UCr) and predicted 24 h urinary creatinine excretion (Pr24UCr)

	Median (IQR)	Median difference	*P* value of difference[a]	Spearman correlation coefficient	Spearman correlation *p* value
Measured 24UCr predicted 24UCr using equations	1094.3 (784.6–1679.9)				
Tanaka	1257.6 (1042.4–1496.7)	− 92.8 (− 495.6; 577.0)	0.977	0.1512	0.0015
Kawasaki	1160.9 (1006.9–1639.6)	− 163.7 (− 583.9; 365.2)	<0.001	0.1418	0.0029
Mage	1093.3 (839.3–1422.9)	59.9 (− 344.1; 649.3)	<0.001	0.1841	0.0001

[a]Wilcoxon Signed Rank Test used to compare median values

INTERSALT showed 100% specificity but only 2% sensitivity, thus grossly underestimating observed salt intakes.

Discussion

This study assessed whether four previously published and commonly used equations could be used to estimate 24UNa (as a proxy for daily salt intake) using spot urine samples. The findings indicate that these equations are not appropriate for use in a South African adult population. Tanaka [31], Kawasaki [32], and Mage [33] equations estimate daily creatinine excretion as a proxy for urine 24-hour volume, and were developed in various populations using regression models incorporating age, weight, height, sex, and in some cases, ethnicity. Our findings suggest that both the creatinine and the sodium estimates from these equations are significantly different to measured 24-hour values. Tanaka, Kawasaki, and Mage all overestimated salt intake. In contrast, the INTERSALT equation [30], which does not calculate 24-hour creatinine, systematically underestimated salt intake.

Our findings are supported by previous work in Indian, white, and black subgroups in South Africa, also showing that Tanaka and Kawasaki equations overestimated sodium excretion [48], although that study suggested that

Table 4 Summary of measured 24-hour and predicted 24-hour urinary Na excretion, expressed as salt equivalents[a] per day

	Measured	INTERSALT	Tanaka	Kawasaki	Mage
All, $n = 438$	7.0 (4.4–10.5)	3.0 (2.5–3.5)	8.0 (6.8–9.5)	13.1 (10.2–16.7)	25.5 (15.7–41.7)
Men, $n = 106$	7.7 (4.6–11.2)	3.7 (3.1–4.2)	8.1 (6.9–9.1)	18.5 (14.8–22.3)	25.9 (16.6–42.5)
Women, $n = 332$	6.5 (4.4–10.3)	2.8 (2.4–3.2)	7.9 (6.7–9.6)	11.9 (9.7–14.9)	25.4 (15.2–41.4)
Black, $n = 319$	6.4 (4.4–10.6)	3.0 (0 (2.6–3.5)	8.0 (6.8–9.5)	13.2 (10.2–16.7)	27.0 (16.7–43.1)
Other ethnicity, $n = 119$	7.5 (4.3–10.3)	2.8 (2.4–3.4)	8.0 (6.5–9.7)	12.9 (9.8–16.5)	22.2 (12.0–35.0)
50 years and above, $n = 284$	6.1 (4.2–8.9)	2.9 (2.3–3.4)	8.0 (6.5–9.6)	12.8 (9.9–16.5)	23.1 (13.1–40.0)
Below 50 years, $n = 154$	8.5 (5.1–13.9)	3.1 (2.8–3.5)	8.0 (6.9–9.2)	13.7 (10.5–16.8)	30.7 (20.6–44.2)
Difference[b]		3.77 (1.64; 7.09)	− 1.28 (− 3.52; 1.97)	− 6.24 (− 9.45; − 2.22)	− 17.18 (− 31.96; − 8.42)
P values[b]		< 0.001	0.0118	< 0.001	< 0.001

All data are shown as median (IQR, interquartile range)

[a]24-hour salt (NaCl) equivalent (g/day) = (24-hour Na (mg/day)/1000) × 2.5

[b]Difference is a summary variable of the differences between the measured and predicted 24-hour urinary salt excretion for each participant, assessed using the Wilcoxon Signed Rank Test

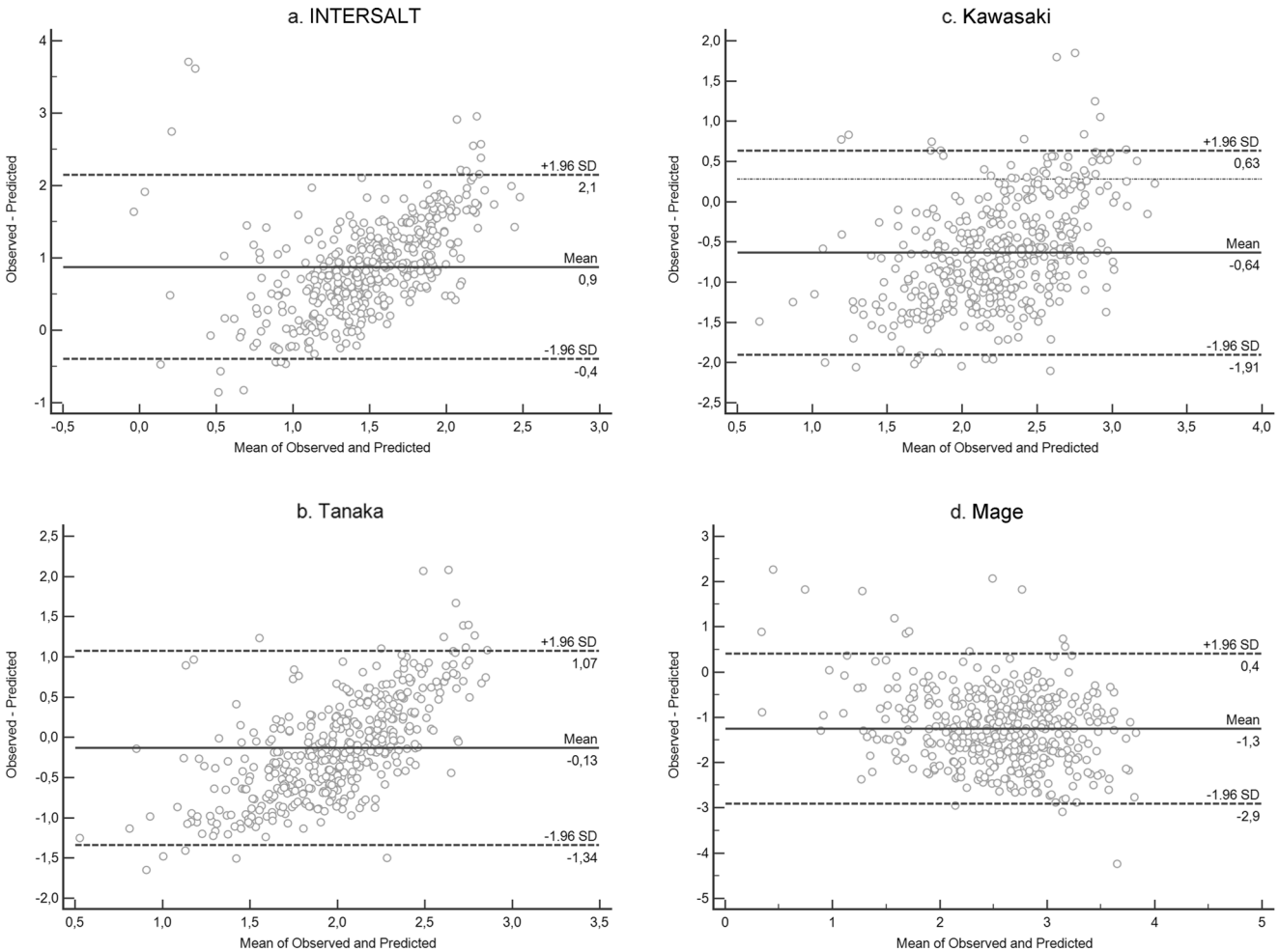

Fig. 1 Bland–Altman plots of log measured vs log predicted 24 h urinary sodium (mg/day). **a** INTERSALT equation. **b** Tanaka equation. **b** Kawasaki equation. **d** Mage equation

INTERSALT performed better, and it did not assess the Mage equation. In the current study, the degree of bias was considerable with all four equations, but smallest with the Tanaka equation. Likewise, in a sample of 554 participants (45–79 years; 58% African American) from the Multi-Ethnic Study of Atherosclerosis (MESA) and the Coronary

Table 5 Sensitivity and specificity of prediction equations vs observed 24-hour urinary salt

Equations	Predicted salt intake equivalent category	Measured (observed) salt intake equivalent category		Specificity%	Sensitivity%
		Less than 5 g/day, $N = 140$	≥ 5 g/day, $N = 298$		
INTERSALT					
< 5 g/day, $n = 432$		140	292	100	2.0
≥ 5 g/day, $n = 6$		0	6		
Tanaka					
< 5 g/day, $n = 30$		17	13	12.1	95.6
≥ 5 g/day, $n = 408$		123	285		
Kawasaki					
< 5 g/day, $n = 12$		7	5	5.0	98.3
≥ 5 g/day, $n = 426$		133	293		
Mage					
< 5 g/day, $n = 19$		12	7	8.6	97.7
≥ 5 g/day, $n = 419$		128	291		

Artery Risk Development in Young Adults (CARDIA) studies in the United States, the Tanaka equation produced the least bias overall in predicting 24-hour sodium excretion. However, the authors also reported that no single equation worked well across subgroups of sex and ethnicity [49]. We did not assess ethnicity- and sex-specific results in the current study as the majority of participants were African and the study was not powered to investigate sex differences.

Even when both the spot and 24-hour urine samples are collected from the same individuals on the same day, validation studies report large differences between estimated and measured 24-hour sodium excretion [50, 51]. The magnitude of bias seen in sodium excretion estimates from spot urine samples varies between different populations. For example, data from the prospective PURE study conducted in eleven LMICs ($n = 1083$; 35–70 years) found good correlation between measured and estimated sodium excretion in the total sample [50], but poor correlations in the Chinese cohort [51]. A further study in Britain and Italy found low agreement between estimated and measured 24UNa, again suggesting ethnic differences [52]. In Japan, the Kawasaki equation produced estimates from second morning void urines that correlated well (correlation coefficient 0.73) with measured values [32]. Although the Tanaka equation applied to random spot urines showed a lower correlation (correlation coefficient 0.54) in a Japanese population sample [31]. This may suggest that the second morning void (as used in our study) gives the best potential for assessing performance of these equations. However, in a US sample, correlation coefficients were moderate (0.4–0.6) for all prediction equations at various times of spot urine collection with Bland–Altman plots indicating significant over- and underestimation across low-to-high values of sodium excretion [53]. Furthermore, poor reproducibility indicates that estimation methods perform inconsistently. Our study found only weak correlations (< 0.22) for all four equations studied.

As highlighted in a recent editorial by Cappuccio and D'Elia [54], there is a need to estimate population salt intakes to support the monitoring and evaluation of population salt reduction initiatives while avoiding the burden of 24-hour urine collections. The WHO NCD Global Action Plan has set voluntary targets for maximum population level salt intakes at 5 g per day [11]. Our study suggests that monitoring of country-level progress toward realising this goal by 2025 cannot be achieved, at least in South Africa, using sodium estimates from spot urine samples.

Furthermore, the South African mandatory salt reduction policy (introduced in June 2016) is expected to result in average reductions in salt intake of 0.85 g per day [8, 9]. The unacceptably large magnitude of error associated with each of these prediction equations indicates their use would not accurately detect such reductions in salt intake. Indeed, the inability of most of the prediction equations to accurately classify individuals with salt intakes below 5 g per day means that incorrect assumptions could be made regarding the success of this salt reduction strategy. Our study is the first to systematically explore the utility of all four equations for use in monitoring the change in South Africa's population salt intake using a nationally representative sample.

The strengths of the study relate to the rigorous random selection procedures of the WHO–SAGE survey within which this study was nested. There are various limitations to the current analysis. Although 24-hour urine collection remains the gold standard for estimating population sodium intake, only a single 24-hour collection was taken as the

standard against which to validate the prediction equations. Other research suggests that multiple consecutive 24-hour samples may be needed (3 days plus) to better estimate individual sodium intake [55]. Although this is clearly a challenge for any large survey, we are currently exploring methods to correct population single 24-hour collection using a smaller subsample of 3-day collections in Wave 3 in South Africa.

An additional limitation is the reduction in sample size from incomplete data. Complete 24-hour urine collections were achieved by 69% of the nested sample ($n = 889$ of 1291), but other missing data reduced the sample size available for analysis to $n = 438$. A further limitation is that the cut-off values used to assess completeness of 24-hour urine collection (24-hour volume ≥ 300 ml/day; creatinine ≥ 4 mmol/day (women) or ≥ 6 mmol/day (men) [40]) may not be optimal for South African adults. For example, populations with low protein intakes exhibit more variability in daily creatinine excretion than well-nourished populations, with values often lower than 1 g (8.84 mmol) per day [56]. As such, it is possible our approach is conservative, though further research is needed to determine optimal thresholds against which to assess urine collection completeness. Another limitation of the study is that neither dietary protein intake, nor lean body mass were assessed. These two variables would inform the interpretation of low urinary creatinine concentrations, though it is well documented that women have lower excretion of creatinine than men and that creatinine excretion reduces with age [57, 58]. The current South African sample is older with higher levels of obesity than the populations in whom these equations were initially validated, and this may explain some of the differences observed. A final limitation was that the spot urine sample was not provided at the same time of day by all participants. Although some researchers suggest afternoon spot urine samples are best [59], the timing of the spot urine sample fails to offset bias and under- or overestimates resulting from the use of prediction equations [53]. Indeed, our results suggest that all of the methods assessed for estimating 24-hour creatinine and/or sodium excretion from a spot urine sample result in significant bias in an African population. A convenient method for estimating population sodium intake is urgently needed in the region, but accurate equations using spot urine samples are yet to be developed for use in South Africans.

Conclusion

Previously published and commonly used equations to predict daily salt intake from sodium concentrations in spot urine samples are inappropriate for use in an adult South African population. Further research is needed to understand why these equations perform so poorly, and to develop population specific methods to accurately assess sodium intake for large surveys. Based on our findings, the use of these prediction equations with spot urine samples to monitor changes in salt intake in South Africa is not recommended.

Summary table

What is known about topic

- Many countries have adopted salt-reduction targets in an attempt to curb hypertension.
- Accurate measurement of population-level salt intake is required to monitor progress toward salt-reduction targets.
- Analysis of 24 h urinary Na excretion is the gold standard measurement to estimate salt intake but this is burdensome.
- Prediction equations based on a casual (spot) urine collection have been developed.
- Validity of these equations for use in African populations remains to be demonstrated.

What this study adds

- In a nationally representative sample of South Africans, the Tanaka, Kawasaki, and Mage prediction equations overestimated 24 h urinary Na excretion.
- The Intersalt equation underestimated 24 h urinary Na.
- All four equations had an unacceptably wide degree of bias and are not recommended for use in South Africans.
- Further research is needed to understand why these equations perform so poorly in this ethnic group.
- Population specific methods to accurately assess sodium intake for large surveys are required.

Acknowledgements We thank all study participants and acknowledge Dr. Stephen Rule, Dr. Robin Richards, and Mr. Godfrey Dlulane of Outsourced Insight who coordinated the data collection. Jordan Stanford and Ezinne Igwe are thanked for editorial assistance.

Funding This work is supported by an agreement with the CDC Foundation with financial support provided by Bloomberg Philanthropies, and a Partnerships & Research Development Fund (PRDF) grant from the Australia Africa Universities Network. SAGE is supported by WHO and the Division of Behavioural and Social Research (BSR) at the National Institute on Aging (NIA), US National Institutes of Health, through Interagency Agreements (OGHA 04034785; YA1323–08-CN-0020; Y1-AG-1005-01) with WHO and a Research Project Grant R01AG034479.

Author contributions KC, PK, NN designed research; LJW implemented research; GC and MC performed analyses; KC, LJW, AES,

MC, PK wrote the paper; KC had primary responsibility for final content. All authors read and approved the final manuscript. The Developmental Pathways for Health Research Unit acknowledges the South African Medical Research Council for support.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

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