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Conflicts of interest

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REFERENCES

1. Palatini P. Extreme dipping: is the nocturnal blood pressure fall modulated by age? *J Hypertens* 2023; 41:867.
2. Parati G, Stergiou G, O'Brien E, Asmar R, Beilin L, Bilo G, *et al.* European Society of Hypertension practice guidelines for ambulatory blood pressure monitoring. *J Hypertens* 2014; 32:1359–1366.
3. Omboni S, Ballatore T, Rizzi F, Tomassini F, Campolo L, Panzeri E. Age-related patterns of ambulatory blood pressure in a large cohort of individuals referred to Italian community pharmacies: results from the templar project. *J Hypertens* 2023; 41:336–343.
4. Kaul U, Bhagwat A, Omboni S, Pancholia AK, Hardas S, Bardoloi N, *et al.* Blood pressure and heart rate related to sex in untreated subjects: the India ABPM study. *J Clin Hypertens (Greenwich)* 2020; 22:1154–1162.
5. Omboni S, Parati G, Palatini P, Vanasia A, Muiesan ML, Cuspidi C, *et al.* Reproducibility and clinical value of nocturnal hypotension: prospective evidence from the SAMPLE study. Study on Ambulatory Monitoring of Pressure and Lisinopril Evaluation. *J Hypertens* 1998; 16:733–738.
6. Kario K, Shimada K. Risers and extreme-dippers of nocturnal blood pressure in hypertension: antihypertensive strategy for nocturnal blood pressure. *Clin Exp Hypertens* 2004; 26:177–189.

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Spot urine samples and estimation of population salt intake: the return of the phoenix?

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We agree with the conclusions by Du Toit *et al.* [1] that using a formula for predicting 24-h sodium is not to be used for 'individuals' to infer causality in observational studies between sodium consumption and both blood pressure and vital outcomes. Du Toit *et al.* [1] also renew the suggestion that formulas (in particular INTERSALT without K) to estimate sodium excretion obtained from spot urine collections are well suited and cost-effective alternatives to 24-h urine collections to accurately evaluate population 24-h sodium excretion.

Du Toit *et al.* [1] assessed the accuracy of using spot urines to determine 24-h sodium excretion in their population group using several analytical tools (correlation, Bland–Altman method, regression). Their results show that sodium intake (whether measured by 24-h urines or estimated by formulas), as expected [2], exceeded the 5 g per day salt targets (2 g of sodium) recommended by the WHO [3]; formulas overestimated sodium at the lower end of the sodium distribution and underestimated it at the high end [4–9]; estimated median values were not statistically different from those measured in 24-h urines collections (best performer being INTERSALT without K), with a mean difference of −0.21 g of sodium. On the basis of such results, Du Toit *et al.* [1] conclude that the INTERSALT formula (without K) may have the utility to assess sodium excretion at a population level over time.

The main question to answer in the framework of the global action plan to reduce population sodium intake for the prevention of cardiovascular disease (CVD) is not so much to estimate the average population mean [10,11], or the proportion of the population with a salt intake 'above' the WHO threshold [12], as the majority of the populations are above that threshold [2].

How will an accurate, unbiased and reliable measurement of 'average' dietary sodium intake in population groups help public health professionals? First, it will establish the size of the problem by assessing average population sodium consumption. Second, it will provide the size of the gap from set targets, telling us how much average reduction is necessary. Third, it will help evaluate public health interventions by detecting changes in average intake over time. Fourth, it will inform health economic evaluations of health impact and motivate continuous political commitment [13]. To answer the last two points, a validation should compare the ability of two alternative methods to detect a significant difference in sodium intake measured in two independent samples of the same population between two time points, hence assessing the effectiveness of the population programme of sodium reduction. The degree of bias and its proportionality shown by Du Toit *et al.* [1] indicate that none of the formulas are suitable. Such bias could be much greater than any expected difference in population average over time following a programme of sodium reduction, therefore missing smaller but meaningful reductions [11,14].

Du Toit *et al.* [1] do not present a cost-effectiveness analysis, yet they claim the use of spot urines could be a cost-effective alternative. In the framework of the global action plan to reduce population sodium intake for the prevention of CVD, a much smaller sample of individuals would be needed to measure effectiveness when using 24-h urines compared with spot urines. A real scenario was reported in a head-to-head comparison of an evaluation of the effectiveness of a 6 to 24-month salt-substitution programme in China within the framework of a well controlled randomized clinical trial [14]. Over the time of intervention, there was a statistically significant reduction in average sodium consumption of 0.35 g per day ($P = 0.039$) when assessed by 24-h urinary sodium excretion. However, when spot urines with the INTERSALT (without K) equation was used, the change was detected as −0.09 g per day ($P = 0.307$), a quarter of the effect measured with the current gold standard method [13–14].

TABLE 1. Differences in measured (by 24-h urine collection) and estimated (by spot urine collections with INTERSALT without K formula) sodium intake in six population studies.

Ref.	Population	Sample size (*n*)	Measured 24-h UNa (SD) g/day	Estimated 24-h UNa by INTERSALT (SD) g/day
Cogswell *et al*. [4]	USA	339	3.32 (1.44)	3.16 (0.89)[a]
Peng *et al*. [5]	Chinese (PURE)	116	6.34 (2.47)	3.54 (0.87)[a]
Ma *et al*. [6]	Rural China	365	3.73 (1.62)	2.99 (0.95)[a]
Swanepoel *et al*. [7]	S Africa*WhiteBlack_1Black_2Indian*	259211104107	3.35 (1.76)3.42 (1.92)3.48 (3.31)2.68 (1.46)	2.89 (0.74)*3.05 (0.71)*3.25 (0.58)3.52 (0.71)[a]
Charlton *et al*. [8]	S Africa	438	2.76 (1.73, 4.13)[b]	1.18 (0.98, 1.38)[a]
Zhang *et al.* [9]	Chinese Tibetans	323	4.57 (0.89)	3.26 (0.76)[a]

Results are expressed as mean (SD) of sodium in g per day with the exception of [b]expressed as median (IQR).
[a] Statistically significant vs. measured 24-h urinary sodium.

In their study, Du Toit *et al*. [1] do not apply stringent quality control criteria for accepting or refuting 24-h urine collections regarding time of collection, minimum urinary volume, allowance for missing voids and sex-specific urinary creatinine cut-offs, as indicated by the WHO protocol [15], nor do they apply criteria of 'credibility' when using estimated values from spot urines, via a formula, allowing for unlikely daily intakes as low as 0.2 g of sodium (0.5 g of salt). Furthermore, the use of imputed BMI can add further bias. The alluded risk of selection bias due to poor response or reliability of 24-h urine collections is equally present in studies using spot urines. In the PURE study, the largest population-based study applying spot urine collections to obtain a proxy for 24-h sodium intake, out of 156 424 participants aged 35–70 years from 17 countries including South Africa, 101 945 (65%) provided spot urines sample, 42% from China [16]. Their yield of 65% is fully comparable with the yield obtained in well conducted population studies [17–19] in which 24-h urine collections have been used following the WHO-recommended protocol [15]. In the study by Du Toit *et al*. [1] in 2015, 78% (1947/2486) of the eligible cohort collected unspecified urines. The authors then randomly selected 400 individuals for the present validation, but there is no mention of the yield to obtain the final sample from the original 1947 participants. This single study, which shows agreement in estimated population sodium consumption using spot samples with that measured in 24-h urine collections is not a proof that the formulas are a reliable method. On the contrary, there are numerous studies [4–9] reporting that none of the equations used with spot urines, including the INTERSALT without K, provide unbiased estimates of 24-h sodium excretion, leading to differences in population means that are statistically significant (Table 1). Furthermore, the authors of two studies in South Africa [7,8] conclude that these equations are not suitable for public health monitoring at the population level.

In conclusion, the formulas to estimate population sodium intake based on spot urine collections are not suitable alternatives to 24-h urinary sodium to evaluate the effectiveness of public health programmes in populations. Missing the effectiveness of the intervention would have crucial negative implications for further political and industrial support and commitment, undermining public health efforts.

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REFERENCES

1. Du Toit JD, Kapaon D, Crowther NJ, Abrahams-Gessel S, Fabian J, Kabudula CW, *et al*. Estimating population level 24-h sodium excretion using spot urine samples in older adults in rural South Africa. *J Hypertens* 2023; 41:280–287.
2. Kwong EJL, Whiting S, Bunge AC, Leven Y, Breda J, Rakovac I, *et al*. Population level salt intake in the WHO European Region in 2022: a systematic review. *Public Health Nutr* 2022; doi: 10.1017/S136898002200218X [Open access; Online ahead of print].
3. World Health Organization. Guideline: sodium intake for adults and children. Geneva: World Health Organization (WHO); 2012. pp.1–56.
4. Cogswell ME, Wang C-Y, Chen T-C, Pfeiffer CM, Elliott P, Gill CD, *et al*. Validity of predictive equations for 24-h urinary sodium excretion in adults aged 18-39 y. *Am J Clin Nutr* 2013; 98:1502–1513.
5. Peng Y, Li W, Wang Y, Chen H, Bo J, Wang X, *et al*. Validation and assessment of three methods to estimate 24-h urinary sodium excretion from spot urine samples in Chinese adults. *PLoS One* 2016; 11:e0149655.
6. Ma W, Yin X, Zhang R, Liu F, Yang D, Fan Y, *et al*. Validation and assessment of three methods to estimate 24-h urinary sodium excretion from spot urine samples in high-risk elder patients of stroke from the rural areas of Shaanxi Province. *Int J Environ Res Public Health* 2017; 14:1211.
7. Swanepoel B, Schutte AE, Cockeran M, Steyn K, Wentzel-Viljoen E. Monitoring the South African population's salt intake: spot urine v. 24 h urine. *Public Health Nutr* 2018; 21:480–488.
8. Charlton K, Ware LJ, Chidumwa G, Cockeran M, Schutte AE, Naidoo N, *et al*. Prediction of 24-h sodium excretion from spot urine samples in South African adults: a comparison of four equations. *J Hum Hypertens* 2020; 34:24–33.
9. Zhang X, Liao H, Ye R, Li X, Gou Q, Zhang Z, *et al*. Assessment and validation of three spot urine assay methods for the estimation of 24-h urinary sodium excretion in Chinese Tibetan adults living in the mountains. *J Clin Hypertens* 2021; 23:1588–1598.
10. Cappuccio FP, D'Elia L. Evaluating population salt reduction programmes worldwide: the risk of cutting corners!. *Public Health Nutr* 2017; 21:2161–2163.

11. Petersen KS, Wu JH, Webster J, Grimes C, Woodward M, *et al*. Estimating mean change in population salt intake using spot urine samples. *Int J Epidemiol* 2017; 46:1542–1550.
12. Huang L, Crino M, Wu JHY, Woodward M, Barzi F, Land M-A, *et al*. Mean population salt intake estimated from 24-h urine samples and spot urine samples: a systematic review and meta-analysis. *Int J Epidemiol* 2016; 45:239–250.
13. Cappuccio FP. Sever PS on behalf of the British and Irish Hypertension Society. The importance of a valid assessment of salt intake in individuals and populations. A scientific statement of the British and Irish Hypertension Society. *J Hum Hypert* 2019; 33:345–348.
14. Huang L, Woodward M, Stepien S, Tian M, Yin X, Hao Z, *et al*. Spot urine samples compared with 24-h urine samples for estimating changes in urinary sodium and potassium excretion in the China Salt Substitute and Stroke Study. *Int J Epidemiol* 2018; 47:1811–1820.
15. World Health Organization. How to obtain measures of population-level sodium intake in 24-h urine samples. Copenhagen: WHO Office for Europe; 2021. pp. 1–39.
16. O'Donnell M, Mente A, Rangarajan S, McQueen MJ, Wang X, Liu L, *et al*. Urinary sodium and potassium excretion, mortality, and cardiovascular events. *N Engl J Med* 2014; 371:612–623.
17. D'Elia L, Brajovic M, Klisic A, Breda J, Jewell J, Cadjenovic V, *et al*. Sodium and potassium intake, knowledge attitudes and behaviour towards salt consumption, amongst adults in Podgorica, Montenegro. *Nutrients* 2019; 11:160.
18. D'Elia L, Obreja G, Ciobanu A, Breda J, Jewell J. Cappuccio FP on behalf of the Salt Consumption Survey in the Republic of Moldova Study Group. Sodium, potassium and iodine intake in a national adult population sample of the Republic of Moldova. *Nutrients* 2019; 11:2896.
19. Zakauskiene U, Macioniene E, Zabuliene L, Sukackiene D, Linkeviciute-Dumce A, Banys V, *et al*. Sodium, potassium and iodine intake in an adult population in Lithuania. *Nutrients* 2022; 14:3817.

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