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It is strongly recommended to not conduct, fund, or publish research studies that use spot urine samples with estimating equations to assess individuals' sodium (salt) intake in association with health outcomes: a policy statement of the World Hypertension League, International Society of Hypertension and Resolve to Save Lives

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Spot urine samples with estimating equations have been used to assess individuals' sodium (salt) intake in association with health outcomes. There is large random and systematic error in estimating sodium intake using this method and spurious health outcome associations. Substantial controversy has resulted from false claims the method is valid. Hence, the World Hypertension League, International Society of Hypertension and Resolve to Save Lives, supported by 21 other health organizations, have issued this policy statement that strongly recommends that research using spot urine samples with estimating equations to assess individuals' sodium (salt) intake in association with health outcomes should not be conducted, funded or published. Literature reviews on the health impacts of reducing dietary sodium that include studies that have used spot and short duration timed urine samples with estimating equations need to explicitly acknowledge that the method is not recommended to be used and is associated with spurious health outcome associations.

Keywords: diet, hypertension, prevention, public health, salt, sodium

Abbreviations: CVD, cardiovascular disease

EVIDENCE SUPPORTING DIETARY SODIUM (SALT) REDUCTION

Reducing dietary sodium is estimated to be one of the most effective interventions to improve population health and is also one of the most cost-effective population health interventions [1–4]. Extensive scientific evidence reviewed for international and national dietary recommendations, consistently support dietary sodium reductions to less than 2400 mg/day [5]. The WHO recommends reducing dietary sodium to less than 2000 mg/day in adults [6]. A meta-analysis of three randomized controlled trials (including posttrial follow-up) reported that reducing dietary sodium from an average intake of approximately 3650–2700 mg/day, was associated with a 26% decrease in cardiovascular disease (CVD) [7]. There was a linear association between sodium intake (2300–4100 mg/day) and CVD [7]. Similarly, a meta-analysis of cohort studies in healthy populations, which defined sodium intake using multiple 24-h urine samples (the current recommended standard to assess usual intake) showed a linear association between sodium intake (1846–5230 mg/day) and CVD [8]. An 18–27% CVD decline per 1000 mg decrease in sodium

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was reported in the cohort [8] and randomized controlled trials, respectively [7]. Dietary sodium reductions are consistent with decreasing CVD by reducing blood pressure [9,10]. Meta analyses of randomized controlled trials show blood pressure-lowering effect with dietary sodium intake as low as 800 mg/day [10]. Sodium reduction meta-analyses do not define a lower sodium intake threshold that decreases CVD or blood pressure.

ASSESSING DIETARY SODIUM

One of the more difficult aspects of clinical research on dietary sodium is accurate assessment of average levels of intake in individuals. The sodium content of different processed foods is highly variable, as is the quantity of sodium added during cooking and at the table [11]. Diets also include a wide and changing variety and quantity of foods. Sodium content of food samples that are eaten can be measured along with the weight of the food ingested to provide an accurate estimate of intake, but this method of assessment is expensive and labor-intensive. Hence, it is rarely used outside of carefully conducted metabolic studies [11]. Dietary surveys that are based on a recall of food intake or use of a food frequency questionnaire are widely employed in research and can provide estimates of sodium intake based on the amounts and types of food eaten and database estimates of their sodium content [11]. Systematic reviews indicate these food survey techniques do not provide a valid estimate of an individual's sodium intake because of errors in recalling the types and amount of food eaten, limitations of the database estimates for sodium content of foods consumed and lack of an accurate estimate of sodium added during the preparation and cooking of food and use of salt at the table [12,13]. Over 24-h, on average 93% of ingested sodium is excreted in urine, with the average sodium excretion being subject to cyclic variations in aldosterone excretion, with the caveat that it takes several days to reach steady-state excretion of sodium following substantive changes to usual sodium intake [14–17]. A series of complete 24-h urine samples taken on nonconsecutive days to represent usual variation in sodium intake is currently recommended to assess individual sodium intake [18].

SPOT AND SHORT DURATION-TIMED URINE SAMPLES TO ASSESS DIETARY SODIUM

Most sodium is excreted within hours of ingestion hence short-term urine sodium excretion largely reflects the sodium content of recently ingested foods and does not account for long-term dietary sodium ingestion [18,19]. Sodium excretion is also regulated by factors other than diet, including hydration status, body position (standing vs. recumbent), time of day, common substances with natriuretic or diuretic action (e.g. caffeine), neurohormonal activation (e.g. early morning rises in adrenaline), and cyclic changes in aldosterone [18,20]. Excretion is also influenced by several common diseases (e.g. cardiac and renal disease) and drug treatments (e.g. diuretics) [18,20]. Spot and short duration-timed urine samples are impacted by both dietary and nondietary sources of variation in sodium excretion.

VALIDATION STUDIES OF SPOT AND SHORT DURATION TIMED URINE SAMPLES

Validation studies repeatedly demonstrated that spot and short duration timed urine samples with estimating equations have both large systematic and random errors in relation to the sodium content in 24-h urine collections [18,21–24]. The degree of systematic error changes with the level of measured 24-h urine sodium. There is increasing error with higher and lower than average sodium intake [18,21–24]. Further, spot urine sample estimates of 24-h urinary sodium excretion are not reproducible within individuals [18,21–23,25,26]. Some investigators have falsely claimed spot samples provide a valid estimate of an individual's sodium intake but these claims have been based on validation studies that peers have deemed to be methodologically flawed, to have employed inappropriate statistical methods and incomplete analyses [23,27].

DISEASE ASSOCIATIONS WITH SPOT AND SHORT DURATION-TIMED URINE SAMPLES

Several studies that employed spot urine sample estimates of sodium intake have reported 'J' curves with cardiovascular disease or total mortality [28]. Many of these studies have used estimating formulae to convert the sodium concentration in the spot or short duration urine sample to an estimate of 24-h urine sodium. The conversion formulae employ risk factors, such as age, gender, BMI, urine creatinine (which is closely correlated with muscle mass) that are known to be strongly related to CVD and mortality, and some add urine potassium. When formulae used to convert spot urine sodium concentrations to estimate 24-h urine sodium were used in place of multiple 24-h measured urine sodium, the linear association for sodium intake with total mortality was changed to a J curve [29,30]. In a separate study, when formulae used to convert spot urine sodium concentrations to estimate 24-h urine sodium was employed instead of multiple 24-h urine sodium measurements, the linear association for sodium intake with blood pressure was also changed to a curve [31]. Further, the formulae had associations with blood pressure and mortality when a constant sodium value was entered into the equations [30,31]. Hence, the formulae are a source of spurious associations with disease outcomes that are independent of dietary sodium.

'CONTROVERSY' ABOUT REDUCING DIETARY SODIUM

Although national and international scientific organizational reviews and dietary recommendations consistently endorse sodium reduction, there is an aura of controversy about reducing dietary sodium. Specifically, it has been suggested that lowering dietary sodium below 3000 mg/day may increase CVD [28]. One major source of the controversy

has been identified as low-quality research prone to spurious findings [7,23,32–37]. Although there are many methodological issues that can cause spurious findings, one prominent source that can be addressed is the inaccurate assessment of dietary sodium consumption [18,37–39]. In an effort to reduce controversy related to low-quality research, this World Hypertension League, International Society of Hypertension and Resolve to Save Lives statement calls on scientific journals to stop publishing manuscripts with findings based on associations of disease when dietary sodium has been assessed using spot urine or short duration-timed urine samples and for funding agencies to stop funding such research.

SCIENTIFIC POSITIONS

Major health and scientific organizations have strongly recommended against using spot and short duration-timed urine collections to estimate sodium intake in individuals [18,39]. These organizations include the British and Irish Hypertension Society, Chinese Regional Office of the World Hypertension League, George Institute for Global Health, Hypertension Canada, International Council of Cardiovascular Prevention and Rehabilitation, International Society of Hypertension, International Society of Nephrology, Resolve To Save Lives, WHO Collaborating Centre on Population Salt Reduction, WHO Collaborating Centre on Nutrition Policy for Chronic Disease Prevention, the World Hypertension League and the European Salt Network [18,39].

RECOMMENDATION

The World Hypertension League, International Society of Hypertension, and Resolve to Save Lives strongly recommend that researchers not use spot urine samples with estimating equations to assess an individual's sodium (salt) intake in association with health outcomes. We also recommend funding agencies to not support studies that assess individuals' dietary sodium excretion using spot and short duration-timed urine samples with estimating equations in association with health outcomes. Only the recommended method of assessing sodium intake should be funded (i.e. multiple carefully collected complete 24-h urine samples) in these types of studies. Journals and peer reviewers should only publish studies that use recommended methods of assessing an individual's usual sodium intake in association with disease outcomes. Manuscripts reviewing the literature on the health impacts of reducing dietary sodium that include studies that have used spot and short duration-timed urine samples with estimating equations to assess individual sodium intake in association with health outcomes need to fully acknowledge the limitations of this method (i.e. that the method is recommended not to be used and that it is associated with spurious associations). There is an ongoing need to establish more feasible and accurate methods to estimate sodium intake in individuals.

CONCLUSION

Dietary sodium estimates from spot and short duration-timed urine collections that use estimating equations have large systematic and random error and so are not reproducible. There is little scientific rationale to support such short-term urine collections predicting long-term sodium intake. Consistent evidence indicates spot samples with estimating equations are not a valid method of assessing an individual's sodium intake, cause spurious associations with disease, and major scientific and health organizations have recommended against their use to assess individual sodium intake and the association of intake to disease outcomes.

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Conflicts of interest

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REFERENCES

1. World Health Organization. *The updated Appendix 3 of the WHO Global NCD Action Plan 2013-2020. Best Buys*. Geneva, Switzerland: World Health Organization; 2017.
2. Wang G, Labarthe D. The cost-effectiveness of interventions designed to reduce sodium intake. *J Hypertens* 2011; 29:1693–1699.
3. World Health Organization. Saving lives, spending less: a strategic response to noncommunicable diseases. Geneva, Switzerland; World Health Organization; 2018. (WHO/NMH/NVI/18.8). Licence: CC BY-NC-SA 3.0 IGO.:1-20.
4. Lee C, Kim D-I, Hong J, Koh E, Kang B-W, Kim JW, *et al*. Cost-benefit analysis of sodium intake reduction policy in Korea. *KJCN* 2012; 17:341–352.

5. Campbell NRC, Whelton PK, Orias M, Wainford RD, Cappuccio FP, Ide N, *et al.* 2022 World Hypertension League, Resolve To Save Lives and International Society of Hypertension dietary sodium (salt) global call to action. *J Hum Hypertens* 2022.
6. World Health Organization. *SHAKE the salt habit. The SHAKE Technical Package for Salt Reduction*. Geneva: World Health Organization; 2016; 1-60.
7. National Academies of Sciences, Engineering, and, Medicine, 2019. Dietary reference intakes for sodium and potassium. Washington, DC: The National Academies Press.
8. Ma Y, He FJ, Sun Q, Yuan C, Kieneker LM, Curhan GC, *et al.* 24-h urinary sodium and potassium excretion and cardiovascular risk. *N Engl J Med* 2022; 386:252–263.
9. Huang L, Trieu K, Yoshimura S, Neal B, Woodward M, Campbell NRC, *et al.* Effect of dose and duration of reduction in dietary sodium on blood pressure levels: systematic review and meta-analysis of randomised trials. *BMJ* 2020; 368:m315.
10. Filippini T, Malavolti M, Whelton PK, Naska A, Orsini N, Vinceti M. Blood pressure effects of sodium reduction: dose-response meta-analysis of experimental studies. *Circulation* 2021; 143: 1542–1567.
11. McLean RM. Measuring population sodium intake: a review of methods. *Nutrients* 2014; 6:4651–4662.
12. McLean RM, Farmer VL, Nettleton A, Cameron CM, Cook NR, Woodward M, *et al.* Twenty-four-hour diet recall and diet records compared with 24-h urinary excretion to predict an individual's sodium consumption: a systematic review. *J Clin Hypertens* 2018; 20:1360–1376.
13. McLean RM, Farmer VL, Nettleton A, Cameron CM, Cook NR, Campbell NRC. Assessment of dietary sodium intake using a food frequency questionnaire and 24-h urinary sodium excretion: a systematic literature review. *J Clin Hypertens* 2017; 19:1214–1230.
14. Lucko AM, Doktorchik C, Woodward M, Cogswell M, Neal B, Rabi D, *et al.* Percentage of ingested sodium excreted in 24-h urine collections: a systematic review and meta-analysis. *J Clin Hypertens* 2018; 20:1220–1229.
15. Birukov A, Rakova N, Lerchl K, Engberink RH, Johannes B, Wabel P, *et al.* Ultra-long-term human salt balance studies reveal interrelations between sodium, potassium, and chloride intake and excretion. *Am J Clin Nutr* 2016; 104:49–57.
16. Rakova N, Juttner K, Dahlmann A, Schroder A, Linz P, Kopp C, *et al.* Long-term space flight simulation reveals infradian rhythmicity in human Na(+) balance. *Cell Metab* 2013; 17:125–131.
17. Sagnella GA, Markandu ND, Singer DR, MacGregor GA. Kinetics of renal sodium excretion during changes in dietary sodium intake in man–an exponential process? *Clin Exp Hypertens* 1990; 12:171–178.
18. Campbell NRC, He FJ, Tan M, Cappuccio FP, Neal B, Woodward M, *et al.* The International Consortium for Quality Research on Dietary Sodium/Salt (TRUE) position statement on the use of 24-h, spot, and short duration (<24 h) timed urine collections to assess dietary sodium intake. *J Clin Hypertens* 2019; 21:700–709.
19. Strauss MB, Lamdin E, Smith WP, Bleifer DJ. Surfeit and deficit of sodium; a kinetic concept of sodium excretion. *Arch Intern Med* 1958; 102:527–536.
20. Bie P. Mechanisms of sodium balance: total body sodium, surrogate variables, and renal sodium excretion. *Am J Physiol Regul Integr Comp Physiol* 2018; 315:R945–R962.
21. Ji C, Sykes L, Paul C, Dary O, Legetic B, Campbell NRC, *et al.* Systematic review of studies comparing 24-h and spot urine collections for estimating population salt intake. *Rev Panam Salud Publica* 2012; 32:307–315.
22. Huang L, Crino M, Wu JH, Woodward M, Barzi F, Land MA, *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.
23. Campbell NRC, He FJ, McLean RM, Cappuccio FP, Woodward M, MacGregor GA. Dietary sodium and cardiovascular disease in China: addressing the authors' response, statements and claims. *J Hypertens* 2022; 40:1831–1836.
24. Zhang Y, Peng Y, Li K, Peng X. Assessing whether a spot urine specimen can predict 24-h urinary sodium excretion accurately: a validation study. *J Hypertens* 2019; 37:99–108.
25. Re F, Hammami I, Littlejohns TJ, Arnold M, Lewington S, Clarke RJ, *et al.* Effects of within-person variability in spot urinary sodium measurements on associations with blood pressure and cardiovascular disease. *Hypertension* 2021; 78:1628–1636.
26. Charlton KE, Schutte AE, Wepener L, Corso B, Kowal P, Ware LJ. Correcting for intra-individual variability in sodium excretion in spot urine samples does not improve the ability to predict 24-h urinary sodium excretion. *Nutrients* 2020; 12:2026.
27. Liu X, Yusuf S, O'Donnell M, Li W. Reply. *J Hypertens* 2021; 39:1467–1469.
28. O'Donnell M, Mente A, Alderman MH, Brady AJB, Diaz R, Gupta R, *et al.* Salt and cardiovascular disease: insufficient evidence to recommend low sodium intake. *Eur Heart J* 2020; 41:3363–3373.
29. He FJ, Campbell NRC, Ma Y, MacGregor GA, Cogswell ME, Cook NR. Errors in estimating usual sodium intake by the Kawasaki formula alter its relationship with mortality: implications for public health. *Int J Epidemiol* 2018; 47:1784–1795.
30. He FJ, Ma Y, Campbell NRC, MacGregor GA, Cogswell ME, Cook NR. Formulas to estimate dietary sodium intake from spot urine alter sodium-mortality relationship. *Hypertension* 2019; 74:572–580.
31. Naser AM, He FJ, Rahman M, Campbell NRC. Spot urine formulas to estimate 24-h urinary sodium excretion alter the dietary sodium and blood pressure relationship. *Hypertension* 2021; 77:2127–2137.
32. Campbell N, L'Abbe MR, McHenry EW. Too much focus on low-quality science? *CMAJ* 2015; 187:131–132.
33. Campbell NR, Lackland DT, Niebylski ML, Nilsson PM. Is reducing dietary sodium controversial? Is it the conduct of studies with flawed research methods that is controversial? A perspective from the World Hypertension League Executive. *J Clin Hypertens* 2015; 17:85–86.
34. Cappuccio FP, Campbell NRC, He FJ, Jacobson MF, MacGregor GA, Antman E, *et al.* Sodium and health: old myths, and a controversy based on denial. *Curr Nutr Rep* 2022; 11:172–184.
35. Campbell NRC, He FJ, Cappuccio FP, MacGregor GA. Dietary sodium 'controversy'—issues and potential solutions. *Cur Nutr Rep* 2021; 10:188–199.
36. He FJ, Campbell NRC, Woodward M, MacGregor GA. Salt reduction to prevent hypertension: the reasons of the controversy. *Eur Heart J* 2021; 42:2501–2505.
37. Cobb LK, Anderson CA, Elliott P, Hu FB, Liu K, Neaton JD, *et al.*, American Heart Association Council on Lifestyle and Metabolic Health. Methodological issues in cohort studies that relate sodium intake to cardiovascular disease outcomes: a science advisory from the American Heart Association. *Circulation* 2014; 129:1173–1186.
38. Cappuccio FP, Sever PS, 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 Hypertens* 2019; 33:345–348.
39. Cappuccio FP, Beer M, Strazzullo P, European Salt Action Network. Population dietary salt reduction and the risk of cardiovascular disease. A scientific statement from the European Salt Action Network. *Nutr Metab Cardiovasc Dis* 2018; 29:107–114.