Measuring Sodium Intake in Populations: Simple Is Best?

Andrew Mente,1,2 Martin J. O’Donnell,1,3,4 and Salim Yusuf1,2

Dietary sodium has long been proposed as a target for population-level interventions to reduce cardiovascular disease (CVD), given its association with blood pressure (BP).1 However, recent evidence from epidemiologic studies shows that low sodium intake (in the range recommended by current guidelines) compared to moderate (average) intake is not associated with lower risk of CVD events and mortality and may even be associated with an increased risk.2–4 In 2013, an Institute of Medicine (IOM) expert panel concluded that the optimum level of sodium intake to reduce CVD is uncertain and called for large epidemiologic studies and randomized controlled trials of sodium intake and clinical events.5 With research on sodium intake undergoing a shift from evaluating its short-term effects on surrogate markers to assess long-term clinical outcomes, there has been growing interest in developing efficient approaches to measuring sodium intake suitable for use in large studies.6–9

In this issue of the journal, Han et al.10 have reported that the Kawasaki formula is valid for estimating population mean levels of sodium excretion from a morning fasting urine. They showed that sodium excretion from a morning urine (collected before breakfast) showed the least bias (2.1 mmol/day) and most agreement with 24-hour measurements of urinary sodium excretion (intraclass correlation coefficient [ICC] = 0.64). These findings are consistent with previous data from our group, based on a study of 1,083 individuals from the general population in 11 countries which also reported good correlation (ICC = 0.71) and the least bias (8.8 mmol/day) with the Kawasaki formula (compared to other formulae).11 Conversely, for the Tanaka formula, Han et al.10 found greater bias (21.1–30.1 mmol/day) and less agreement (ICC of 0.26–0.38) for either morning fasting or late-afternoon/early evening predinner samples, which is in keeping with findings from our study11 and two other studies in Japanese cohorts.12,13 These findings highlight that the Kawasaki formula6 on a morning fasting urinary collection is a good estimate of actual 24-hour urinary excretion of sodium, which is the reference standard for estimating sodium intake. Large studies reduce random error, so the averaged estimates across a large number of people will provide reliable estimates of average sodium intake at a group level, although there may be some variability in estimates for single individuals (e.g., determining adherence to guidelines in an individual).14 The findings of the above two validation studies have important implications for surveys and epidemiologic studies of sodium intake. To describe the association of sodium to health outcomes or to obtain estimates of sodium intake in different populations, large studies are needed, e.g., the Prospective Urban Rural Epidemiology (PURE) study involving >100,000 healthy people from the general population.4,13 Such studies include representative populations, and accrue a few thousand deaths or CVD events within a relatively short time. Similarly monitoring sodium intake in populations over time and comparing intakes between populations require simple methods that are valid in order to study large numbers of people. For instance, in the Prospective Urban Rural Epidemiology (PURE) study, the range of mean sodium excretion (determined using the Kawasaki method) across the 17 different countries was consistent with the findings of a recent meta-analysis of cross-sectional studies from 187 countries, with most populations of the world consuming between 3 and 6 g of sodium per day.15 Lastly, both repeated 24-hour urine measurements or estimates of sodium intake from multiple morning urines may be used to more precisely estimate “usual” sodium intake in groups of people during follow-up in randomized controlled trials. The latter method has the advantage of better adherence (fewer refusals or incomplete collections) and can be done more often than 24-hour urine collections—all of which can lead to more accurate assessments of sodium intake.

A single measurement of urinary sodium by itself (whether this is a spot measure, a fasting measure, or a 24-hour urine) does not provide as good a measure of usual intake as multiple measures, because sodium intake varies from day-to-day, making repeated measurements desirable to estimate “usual”

Correspondence: Andrew Mente (andrew.mente@phri.ca).

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1 Population Health Research Institute, Hamilton Health Sciences, McMaster University, Hamilton, Ontario, Canada; 2Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada; 3Department of Medicine, McMaster University, Hamilton, Ontario, Canada; 4HRB-Clinical Research Facility, NUI Galway, Galway, Ireland.

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sodium intake. However, single measurement (as opposed to multiple measurements) introduces mainly random error and reduces statistical precision and most likely to bias estimates of association between sodium and health measures toward the null, but would not be expected to change the overall pattern (i.e., shape) of association. One practical way to account for this day-to-day variability in large population studies is by obtaining repeated measures in a subset of participants to estimate the correlation between measures obtained on two separate occasions (weeks or months apart) and then use the correlation to correct for the degree of regression-dilution bias. This has been widely used to describe the association between “usual” levels of exposures such as cholesterol or BP and CVD, and is widely accepted as being a valid approach. Since morning fasting urines are convenient, they have the added advantage of allowing easier repeat measures of sodium intake over time, to measure “usual” sodium intake.

While conventional thinking has led people to assume that the 24-hour urine collection is the reference standard for measuring sodium intake, this assumption may have to be reconsidered. First, there is often a bias in volunteers to provide 24-hour urine collection, because it is inconvenient and intrusive, especially in people working outside their homes. This can lead to biases as to who agrees to participate in studies. Second, even in those who agree to obtain 24-hour urine collection, the rates of incomplete collection may be significant and even as high as 30%; and those who complete collections may differ from those who fail to complete collections. Third, participants are more reluctant to provide repeated 24-hour urine collections than simple morning urines. Therefore, while the 24-hour urine collection may be considered the reference standard for individual measurement, Kawasaki formula derived estimates from a single morning void may be a more appropriate reference standard for estimating sodium intake in populations.

Recently, there have been advances in the area of sodium kinetics which question traditional concepts about sodium homeostasis and may have implications for measuring sodium intake. In a series of studies in space simulation flights, Rakova et al. found that aside from the extracellular space and a poorly exchangeable portion in bone, salt is stored largely in the skin interstitium and soft tissue, with immune system cells and lymph capillaries regulating sodium balance and BP. This suggests that sodium excretion on any given day may be only partly influenced by short-term variations in sodium intake but may be substantially influenced by the exchange of sodium across many different compartments. Therefore, on theoretical grounds, multiple “spot” collections of urine obtained some weeks or months apart may be a better indicator of sodium in the body than a single 24-hour collection.

In conclusion, obtaining 24-hour urine collections may not be necessary and also may not be the optimal approach for large studies, as it is impractical and invariably results in the exclusion of a substantial proportion of the population. Instead a formula-derived approach to estimate mean excretion of sodium from morning voids of urine is sufficiently robust and may even be the preferred method for large surveys and epidemiological studies.

DISCLOSURE
The authors declared no conflict of interest.

REFERENCES


