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Estimating salt intake in humans: not so easy![1]

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It has long been viewed that the analysis of sodium excretion in a morning "spot" urine sample is a valuable measure to estimate salt intake of the previous day. A study in this issue of the Journal shows that the predictive value of spot urine to correctly estimate urinary 24-h sodium excretion in humans may be little better than a coin-toss. Zhou et al. (1) measured 24-h sodium excretion in 141 Chinese community residents. The investigators used the Kawasaki, the INTERSALT (International Cooperative Study on Salt, Other Factors, and Blood Pressure), and the Tanaka equations to calculate estimates of 24-h sodium excretion from morning spot urine collections. They then compared the agreement between known 24-h sodium excretion and that estimated from morning spot urine collections. The salient result was that hardly every other spot urine–based calculation of sodium excretion was <3 g different from the measured, real 24-h sodium excretion in the urine. Defining a 3-g difference between real and estimated excretion as an "acceptable classification," the spot urine–derived estimation of 24-h sodium excretion was misclassified in >60% of the test subjects. Possibly, these calculated estimates are particularly vulnerable to misclassification when daily salt intake is high. This state of affairs could explain why spot urine–based estimates might have worked more accurately in Western societies with lower salt intakes (9.6 g/d in the United States, 8.6 g/d in the United Kingdom), compared with 13.4 g/d intakes in China or 11.7 g/d in Japan (2). It is also possible that the inclusion of more men into this current study could have influenced the results, although imagining that the predictive value of spot urine collections can be improved in men is difficult. Apparently, none of the above-mentioned equations worked significantly better in subjects from the PURE (Prospective Urban Rural Epidemiology) study (3). The authors conclude that evidence does not support the use of spot urine to estimate 24-h urinary sodium excretion in humans.

The next question could be, "Can matters get worse"? Focusing on the predictive value of spot urine collections to correctly detect real 24-h sodium excretion, Zhou et al. (1) do not question the validity of an accurately collected 24-h urine sample to predict real salt intake. However, the biological patterns of sodium metabolism in humans are apparently not as straightforward as previously believed. Long-term balance studies in which humans not only collected every drop of urine but also ate every meal assigned to them for 105 or 205 d showed that steady state between sodium intake and excretion, in contrast to traditional opinion (4), is not achieved within several days but instead follows weekly and monthly rhythms of body sodium accumulation and release that occur independently of salt intake (5). Coincidentally, this major endogenous biological confounding variable can lead to another coin-toss phenomenon. Every second single, accurately collected 24-h sodium excretion sample failed to detect a 3-g difference in sodium intake (6). For other electrolytes in urine, matters are no different (7). In line with data from earlier clinical dietary intervention studies (8), these findings suggest that multiple 24-h collections are necessary to improve precision, and single spot urine collections are not a valuable tool to assess salt intake in any given individual.

Zhou et al. (1) indicate that "the high burden of labor and difficulty in complete collection of 24-h urine has prompted the search for more practical alternative methods, such as a spot urine sample analysis." This situation may be especially true for "big data" research strategies where excessive increases in numbers of observations may not always be paralleled by excessive primary data quality. Our sodium excretion topic could serve as an example. If we combine the 50% probability to correctly estimate a 3-g difference in 24-h urine excretion in spot urine samples with the 50% likelihood to correctly estimate real salt intake in an accurately collected, single 24-h urine sample, then the probability to correctly estimate a 3-g difference in 24-h salt intake with the help of a spot urine sample will not be higher than $0.50 \times 0.50 = 0.25$, or 25%. Thus, the resulting systematic error may misclassify 3-g differences in salt intake in 75% of the subjects under investigation, regardless of the study population size. Any gambler in Las Vegas will tell you that these are not the odds for projects that will be crowned by long-term success. I have no idea why scientists would have a different view.

If increasingly more data question the currently accepted set of tools used for clinical and epidemiologic investigation of salt

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intake, then how should we proceed? Alternative approaches, such as direct noninvasive measurements of tissue sodium content in humans, may not only lead to a refined understanding of body sodium metabolism (9). The resulting precision approach may additionally provide much faster and more concise information on the relation between salt and health (10) and ultimately outperform unaffordable misclassifications.

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