Normal Range of Human Dietary Sodium Intake: A Perspective Based on 24-Hour Urinary Sodium Excretion Worldwide

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BACKGROUND
The recommendation to restrict dietary sodium for management of hypertensive cardiovascular disease assumes that sodium intake exceeds physiologic need, that it can be significantly reduced, and that the reduction can be maintained over time. In contrast, neuroscientists have identified neural circuits in vertebrate animals that regulate sodium appetite within a narrow physiologic range. This study further validates our previous report that sodium intake, consistent with the neuroscience, tracks within a narrow range, consistent over time and across cultures.

METHODS
Peer-reviewed publications reporting 24-hour urinary sodium excretion (UNaV) in a defined population that were not included in our 2009 publication were identified from the medical literature. These datasets were combined with those in our previous report of worldwide dietary sodium consumption.

RESULTS
The new data included 129 surveys, representing 50,060 participants. The mean value and range of 24-hour UNaV in each of these datasets were within 1 SD of our previous estimate. The combined mean and normal range of sodium intake of the 129 datasets were nearly identical to that we previously reported (mean = 158.3 ± 22.5 vs. 162.4 ± 22.4 mmol/d). Merging the previous and new datasets (n = 190) yielded sodium consumption of 159.4 ± 22.3 mmol/d (range = 114–210 mmol/d; 2,622–4,830 mg/d).

CONCLUSIONS
Human sodium intake, as defined by 24-hour UNaV, is characterized by a narrow range that is remarkably reproducible over at least 5 decades and across 45 countries. As documented here, this range is determined by physiologic needs rather than environmental factors. Future guidelines should be based on this biologically determined range.

Keywords: blood pressure; dietary sodium; hypertension; normal range; sodium intake; worldwide.

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Few public health policies have been as widely endorsed for lowering cardiovascular disease (CVD) morbidity and mortality as dietary sodium restriction.1 The origins of this policy date back 7 decades to Kempner’s observation that extreme sodium restriction tempered the hypertensive crisis associated with renal insufficiency.2 Subsequently, sodium restriction was gradually incorporated into the management of many patients with essential hypertension as adjunct therapy to antihypertensive drugs.3

The recommended levels of sodium intake by American health organizations have been gradually but significantly decreased over the past 40 years.4–8 Those increasingly restrictive guidelines have occurred against the backdrop of several critical scenarios:

1. No consistent data had appeared in the scientific literature specifically demonstrating that lower sodium intake was associated with a reduction in either all-cause or CVD mortality.9
2. An increasing number of consumer food products were reduced in their sodium content in response to the government's effort directed at lowering the sodium intake.10
3. There was no evidence that sodium intake was declining in the United States.11,12
4. Basic research, particularly in the neurosciences, indicated that vertebrate sodium intake was a physiologically determined parameter.13

Our 2009 report of estimated worldwide daily sodium intake, based on 24-hour urinary sodium excretion (UNaV) data in 19,151 participants, introduced evidence into this longstanding scientific dialogue that human sodium intake was defined by a very narrow range.14 That range was consistent across 3–4 decades and over 30 different countries and their unique food cultures. Thus, our analysis indicated that there is a “normal” range of human sodium intake defined by physiology and biological needs and not by the food supply. This report is intended to expand by numbers, duration, and cultures our original characterization of the normal range of human sodium intake.

METHODS

Types of studies

Published studies that contained 24-hour UNaV datasets from free-living persons and that were not previously included in our initial report were used as the source of the new datasets. PubMed and other publicly available search mechanisms were used to identify such reports.

Data extraction

From each publication's dataset of 24-hour UNaV, the following were extracted: sample size, mean SD of the reported 24-hour UNaV, sex composition of sample, time period of data collection, and country of origin.

Statistical analysis

Twenty-four-hour UNaV was assessed using the mean values for each dataset reported in each publication. Several of the publications provided multiple datasets, which were entered separately into the overall analysis. Twenty-four-hour UNaV mean values were weighted by each study's sample size to generate an overall mean. When separate male and female 24-hour UNaVs were provided, the overall mean for the dataset was derived based on the relative contribution of each sex to the dataset sample size. The final analysis does not include 7 studies (788 participants, 1.1% of the total) in which the mean UNaV was greater than ±2 SD from the mean of all other combined samples (Table 1).15 The range of the excluded lower UNaV values was 90–108 mmol/d, whereas the upper range was 212–248 mmol/d. Analyses and a descriptive graph (Figure 1) showing 1 and 2 SDs from the mean of all 24-hour UNaV were generated with StatView version 5.0 (SAS Institute, Cary, NC).

RESULTS

From 8 publications, 129 datasets that were not included in our 2009 publication were identified.15–22 These new 24-hour UNaV datasets represented samples from 50,060 participants and an additional 12 countries to those we identified previously. Six publications added 1 dataset each. One of 8 publications provided 37 additional datasets,22 and the eighth contributed 86 datasets to the analysis.15 The collections of the 24-hour UNaV were done primarily for population surveys or as baseline collections before entering a clinical trial. All the datasets estimated dietary sodium based on 24-hour UNaV collections. One dataset relied on 12 yearly surveys of sodium intake as determined by food frequency questionnaires that were calibrated on total salt intake using an independent validation substudy of 100 volunteers who also provided 24-hour urine collections.18 Inclusion of this specific dataset did not significantly modify the mean or range of the final analysis. Its inclusion provided the only repetitive yearly estimate of sodium intake validated by 24-hour UNaV collections over a prolonged period of 12 years.

The means and ranges of 24-hour UNaV from each of the new datasets were within 1 SD of our previous estimate. These reports generated a mean ±1 SD of 158.3 ± 22.5 mmol/d (3,641 mg/d) (range = 114–210 mmol/d; 2,622–4,830 mg/d). The mean of the new datasets is nearly identical to our previous estimate of 162.4 ± 22.4 mmol/d (range = 117–212 mmol/d; 2,691–4,876 mg/d) (Table 1). The composite of our previous and the new datasets represents a total of 69,011 participants, 190 collection sites in 45 countries, and a span of more than 5 decades (1957–2010). The composite of these datasets (Figure 1) yields an estimated intake with a mean value of 159.4 ± 22.3 mmol/d (3,666 mg/d) and range

| Table 1. Comparison of urinary sodium excretion (UNaV) values and number of sites and participants among 2009, 2013, and combined datasets with and without 7 outliers |
|---------------|---------------|---------------|---------------|---------------|
| Measure          | Initial report datasets (2009) | Additional datasets (2013) | All datasets combined | All datasets excluding 7 outliers |
| Mean UNaV, mmol/d | 162.4          | 157.7          | 159.2          | 159.4          |
| SD, mmol/d       | 22.4           | 26.1           | 25.1           | 22.3           |
| Range, mmol/d    | 117–208        | 90–248         | 90–248         | 114–210        |
| No. of datasets  | 62             | 135            | 197            | 190            |
| No. of participants | 19,151       | 50,648         | 69,799         | 69,011         |
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of 114–210 mmol/d. Figure 2 depicts the distribution of the 69,011 participants by quintiles of reported 24-hour UNaV and documents the “normal” nature of that distribution.

Two of the reports specifically assessed trends with time, age, ethnicity, and sex. In both, there was no change over time—12 years in one and 5 decades in the other. These 24-hour UNaV collections were carried out in 45 countries and over 5 decades, thus representing exposure to substantive variations in the food supply that occurs over time and across cultures. Likewise, there was no significant variation based on age or ethnicity. Where the 24-hour UNaV data was reported separately by sex, females uniformly consumed less sodium. This difference reflects the well-established lower caloric intake of females and, thus, lower daily intake of all nutrients among women.

DISCUSSION

This report significantly expands our previous analysis of worldwide 24-hour UNaV data and establishes that human sodium intake follows a classic “normal” distribution that depicts a narrow range with strict lower and upper limits of normality. The extensive nature of our data addresses the major limitations of 24-hour UNaV collections as a measure of daily sodium intake—individual day-to-day variations as well as incomplete collection. Because all the datasets were obtained as part of research protocols for governmental surveys or research studies and represent a large and diverse sample, both potential limitations are likely addressed. The finding that sodium intake has been unchanged over decades of observation and a wide array of societies challenges the entrenched perceptions that sodium intake is increasing and that the postulated increase is due to the sodium content of the food supply. These data do not support those often-expressed opinions.

The existence of a normal range for sodium intake is evidenced in several previous studies. First, in the Trials of Hypertension Prevention II (TOHP II), the protocol for the sodium restriction limbs called for a target sodium intake of 80 mmol/d to be achieved by intensive, frequent dietary counseling and behavioral change. Neither the sodium restriction (104 mmol/d) nor the combined weight loss and sodium restriction (124 mmol/d) cohorts achieved the target sodium intake. These respective minimal sodium intakes are remarkably similar to the lower limit of normal our data established (114 mmol/d). Furthermore, over the ensuing 30 months of the trial, in spite of continued counseling and contact, participants’ dietary sodium intake regressed toward a mean of sodium (135 mmol/d and 145 mmol/d, respectively) well within the normal range our data described.

Second, in a multicenter, double-blind, crossover, randomized trial intended to test whether sodium intake influenced a calcium channel blocker’s antihypertensive effect, 99 patients with mild hypertension were studied in 6 university clinical research centers and received nutrition counseling and a previously tested reference manual for a 75 mmol/d sodium diet for 2 weeks. At the end of the 2 weeks, mean 24-hour UNaV of the cohort was 76.2 mmol/d. They remained on their sodium-restricted diet and were randomized to receive either a 100 mmol/d tablet of slow-release sodium or a placebo for 4 weeks, at which time the slow-release sodium treatment was crossed over for an additional 4 weeks. On placebo, 24-hour UNaV increased to 121.2 mmol/d. Thus, while on placebo, the sodium intake from the diet increased 45 mmol/d. In contrast, at the end of 4 weeks on the slow-release sodium, mean 24-hour UNaV increased to 176.2 mmol/d. The change in 24-hour UNaV precisely reflected the sodium in the slow-release sodium tablets, indicating that participants continued their adherence to the very low sodium diet (i.e., they had not increased their sodium intake from food sources). As with TOHP II, these study participants in a randomized, double-blind, cross-over trial, who were counseled to consume 75 mmol/d of sodium, regressed to a comparable mean sodium intake of 121.2 mmol/d, virtually identical to the lower limit of the normal distribution of worldwide sodium intake.
Third, a 12-year sodium consumption surveillance study that involved 13,335 residents of Geneva, Switzerland, documented an approximate lower limit of tolerable sodium intake of 117 mmol/d with <1% of the cohort below this value. Neither the mean (161.2 mmol/d) nor this lower limit of sodium intake varied significantly over the 12-year period of observation in this large cohort.

Collectively, these findings from the largest and longest National Institutes of Health–sponsored randomized control trial of sodium restriction, from the only randomized, double-blind, crossover trial of sodium restriction testing the approximate lower limit of current US sodium restriction guideline, and the longest and largest continuous surveillance study of a defined free-living population have yielded virtually identical estimates of the lower limit of adult sodium intake—an approximately 115–120 mmol/d—a lower limit that is consistent with our estimate of 114 mmol/d.

The apparent existence of a normal range of human sodium intake is consistent with the neural control of sodium appetite, a principle that neuroscience research has explored and documented over the past 80 years. Since the 1930s, it has been known that animals adjust their sodium intake to maintain homeostasis. Under extreme conditions, this mechanism is critical for life. This homeostatic mechanism is referred to as sodium appetite. The neural circuitry responsible for sodium appetite is the subject of active investigation, but its existence across many species and some of its basic mechanisms are well established. The most prominent influence on sodium appetite is exerted through the circulation, by the renin-angiotensin-aldosterone system (RAAS). Increases in angiotensin II and aldosterone stimulate sodium appetite, whereas increased salt intake suppresses the RAAS. The RAAS component and sodium intake/appetite are physiologically coordinated in experimental animal models such that conditions that increase plasma renin activity/angiotension II/aldosterone increase sodium appetite; exogenous angiotensin II/aldosterone induce the appetite, and ultimately, sodium ingestion leads to suppression of plasma renin activity/angiotensin II/aldosterone.

The normal distribution of 24-hour UNaV among adults worldwide (Figure 2) is consistent with a long-established principle of nutritional physiology originally outlined by Bertrand in 1912. Bertrand’s rule characterized a normal distribution parabola, such as the one our 24-hour UNaV data describes, for essential nutrients whose consumption is critical for optimal organ function. The plateau of such a parabolic relationship describes the point at which optimal function is maintained through homeostatic feedback systems. The normal distribution of human sodium intake simply follows the basic principle that Bertrand first hypothesized for all essential nutrients, although each has its own specific curve.

The recent reports that have characterized an increase in CVD and all-cause mortality associated with reduced sodium intake may reflect the impairment of organ function that Bertrand’s rule proposed would occur when intake of an essential nutrient is insufficient or deficient. It is noteworthy that 2 independent summary analyses of the CVD and all-cause mortality data associated with lower sodium intake have arrived at an estimated healthy range of sodium intake comparable with the range we describe (130–220 mmol/d or 3,000–5,000 mg/d).

Our findings have important implications for US nutritional policy. The recent Institute of Medicine (IOM) report Sodium Intake in Populations—Assessment of Evidence found “no evidence for benefit and some evidence suggesting risk of adverse health outcomes associated with sodium intake levels in ranges approximating 1,500–2,300 mg per day,” a range well below the lower limit of normal that our data defines. Furthermore, the IOM committee found “that evidence from studies on direct health outcomes is inconsistent and insufficient to conclude that lowering sodium intakes below 2,300 mg per day either increases or decreases risk of CVD outcomes (including stroke and CVD mortality) or all-cause mortality.
in the general US population.\(^9\) These findings of the IOM committee indicate the previously established\(^6–^8,^23\) upper limit of sodium intake deemed safe (2,300 mg/d or 100 mmol/d) is not supported by scientific evidence. This conclusion is consistent with what our data would predict (i.e., sodium intake <115–120 mmol/d likely confers no physiologic benefit).

The IOM committee had the opportunity to review\(^33\) both our data and those of the 2 laboratories\(^31,^32\) noted above that independently arrived at essentially the same normal range for sodium intake in humans. However, the committee specifically stated that it was not in its charge to define the normal range of human sodium intake, and, therefore, the report was silent on what defined “excessive” or inadequate intake.\(^9,^34\) With the findings of this report and the cited studies that identified similar values of 24-hour UNaV for the mean and lower and upper limits of the normal distribution of human sodium intake, it is reasonable to conclude that the estimated healthy range for human sodium intake is 120–220 mmol/d (2,800–5,000 mg/d).

The existence of a normal range with a reproducible mean value for sodium intake in humans is consistent with several facts. First, it provides clinical validation of the functional importance of neuroscience research that has defined the central control of sodium appetite.\(^13\) Second, when combined with the neuroscience evidence, it accounts for the failure of public policy efforts to lower sodium intake in the US population.\(^35\) No matter how well intended, public policy simply cannot alter a physiologically set parameter. Third, when combined with the Bertrand rule, it provides plausibility as to why sodium intakes outside this normal range have been associated with adverse health outcomes at both extremes, inadequate and excessive. Fourth, in a 1972 New England Journal of Medicine article, Brunner et al.\(^28\) first characterized the relationship of 24-hour UNaV to plasma renin activity. The parabolic nature of the 24-hour UNaV–vascular regulatory system relationship is readily evident (Figure 3). What is also apparent, although not previously acknowledged, is that Brunner et al’s figure predicted the optimal 24-hour UNaV for plasma renin activity suppression and, therefore, an estimate of what constituted an optimal sodium intake based on physiology. The optimal 24-hour UNaV value in this analysis is defined by where the asymptote intersects the confidence interval of the regression line (Figure 3). This analysis of 1972 data estimates that the minimal 24-hour UNaV for optimal suppression of plasma renin activity is approximately 156 mmol/d. This value is virtually identical to the worldwide population mean sodium intake (159 mmol/d) our analysis has documented.

Although these data describe a physiologic range for human sodium consumption and the apparent limits such a range imposes on therapeutic interventions to lower sodium intake, they do not indicate that certain patient groups should not be encouraged to moderate dietary sodium. Specifically, individuals being treated for high blood pressure or diabetes might benefit by moving from the higher end of this normal intake range to the lower end.\(^36\) The definitive understanding of the effectiveness of such an approach, however, will require appropriate controlled clinical trials.

Our analysis defines the normal range and mean value for sodium intake in humans. It further documents that the range has not changed over 5 decades, is not influenced by ethnicity, exhibits remarkably narrow lower and upper limits, and is comparable across 45 societies and their unique dietary practices. Diverse clinical studies provide confirmatory data regarding both the range and mean of 24-hour UNaV we have identified. The biologic plausibility is supported by the scientific characterization of sodium appetite and physiological evidence involving a critical hormone system, the renin-angiotensin system, which is involved in both cardiovascular homeostasis and the neural control of sodium appetite.

Although the recent IOM report did not define “excessive” sodium intake or comment on what constituted a normal range, these data, which were presented to the IOM committee, address that critical assessment. Based on our data and the wide array of published data from the basic sciences through clinical investigation cited herein, it is reasonable to conclude that a normal range for human sodium intake exists. If future guidelines are to be effective and feasible, they must be based on that scientific reality.\(^37\)

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**DISCLOSURE**

The authors declared no conflict of interest.

**REFERENCES**