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Estimating 24-Hour Urinary Sodium Excretion From Casual Urinary Sodium Concentrations in Western Populations

The INTERSALT Study

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High intakes of dietary sodium are associated with elevated blood pressure levels and an increased risk of cardiovascular disease. National and international guidelines recommend reduced sodium intake in the general population, which necessitates population-wide surveillance. We assessed the utility of casual (spot) urine specimens in estimating 24-hour urinary sodium excretion as a marker of sodium intake in the International Cooperative Study on Salt, Other Factors, and Blood Pressure. There were 5,693 participants recruited in 1984–1987 at the ages of 20–59 years from 29 North American and European samples. Participants were randomly assigned to test or validation data sets. Equations derived from casual urinary sodium concentration and other variables in the test data were applied to the validation data set. Correlations between observed and estimated 24-hour sodium excretion were 0.50 for individual men and 0.51 for individual women; the values were 0.79 and 0.71, respectively, for population samples. Bias in mean values (observed minus estimated) was small; for men and women, the values were −1.6 mmol per 24 hours and 2.3 mmol per 24 hours, respectively, at the individual level and −1.8 mmol per 24 hours and 2.2 mmol per 24 hours, respectively, at the population level. Proportions of individuals with urinary 24-hour sodium excretion above the recommended levels were slightly overestimated by the models. Casual urine specimens may be a useful, low-burden, low-cost alternative to 24-hour urine collections for estimation of population sodium intakes; ongoing calibration with study-specific 24-hour urinary collections is recommended to increase validity.

nutrition assessment; population surveillance; sodium intake

Abbreviations: INTERSALT, International Cooperative Study on Salt, Other Factors, and Blood Pressure; NHANES, National Health and Nutrition Examination Survey.

Editor's note: *An invited commentary on this article appears on page 1193, and the authors' response appears on page 1196.*

High levels of dietary sodium (mostly consumed as the food additive salt (sodium chloride)) are associated with raised blood pressure and an increased risk of cardiovascular disease (1). Animal experiments, epidemiologic studies, and clinical trials have provided compelling evidence for a detrimental association of sodium intake and the blood pressure levels of individuals across the population (2–8). In addition to its impact on blood pressure, excess dietary sodium consumption has been linked to an increased risk of coronary heart disease (9, 10) and stroke (11), as well as noncardiovascular conditions, including stomach cancer, renal stones, and osteoporosis (12).

National and international guidelines have called for reductions in average sodium intakes at the population level to tackle the population-wide burden of adverse blood pressure levels and the associated cardiovascular risks. The report of a joint World Health Organization–Food and Agriculture

Organization Expert Consultation recommended that adults consume less than 85 mmol/day (<2 g/day) of sodium (13). In the United States, the Dietary Guidelines for Americans recommend a reduction of sodium intake to less than 100 mmol/day (<2.3 g/day) in the general population, with a further reduction to 65 mmol/day (1.5 g/day) for individuals with hypertension, diabetes, or chronic kidney disease, as well as for African Americans and adults over 50 years of age (14).

Population-based surveys are required to monitor population sodium intakes and assess the effectiveness of public health efforts to reduce sodium intakes. Because of difficulties in estimating sodium intakes using dietary surveys, measurement of 24-hour urinary sodium excretion has become the preferred method in population surveys (15–17). However, 24-hour collections are expensive and relatively burdensome to individuals. Estimating sodium excretion from casual (spot) urine specimens is cheaper and less burdensome but has not been extensively evaluated for use in population surveys of sodium intake.

In the present study, we used casual and 24-hour urinary sodium data collected in the International Cooperative Study on Salt, Other Factors, and Blood Pressure (INTERSALT) (8, 18, 19) to assess the utility of casual urine specimens for estimation of sodium intake in Western (North American and European) populations. The primary aim was to evaluate whether casual urinary specimens are useful for estimation of group mean sodium intakes; we also examined their relationship with individual intakes.

MATERIALS AND METHODS

Population samples and field methods

INTERSALT investigators collected standardized data on casual urinary sodium concentrations and timed 24-hour urinary sodium excretion for 10,079 men and women 20–59 years of age from 52 population samples in 32 countries (8, 18–20). Field work took place between 1985 and 1987. Each study center was asked to recruit 200 men and women, stratified by age and sex, from samples selected randomly or by sampling from whole population groups (e.g., village dwellers). Institutional ethics committee approval was obtained for each collaborating center, and all participants gave informed consent.

Before the onset of 24-hour urine collection, participants were asked to provide a casual urine specimen. To guard against under- and over-collection, start and end times of the 24-hour urine collections were supervised by clinic staff. Urine collections were rejected if the participant reported that "more than a few drops" were missing from the collection, if 24-hour urinary volumes were less than 250 mL, or if the timing of the collection fell outside the range of 20–28 hours. A randomly selected 8% of the study sample provided a second 24-hour urinary specimen 3–6 weeks later for estimation of within-individual variability of sodium excretion. Aliquots of the casual and 24-hour urinary specimens were frozen and sent to a central laboratory (Leuven, Belgium) where several analytes were measured during 1985–1987, including sodium, potassium (measured using emission flame photometry), and creatinine (measured using Jaffé reaction). Quality-control measures included repeated analyses of specially collected "stock" urine specimens with "low," "medium," and "high" sodium and potassium concentrations and analyses in which investigators were blinded to which samples were split specimens. Technical error of the laboratory measurements, based on split specimens, was calculated for each population sample using the formula $\sqrt{\sum d^2/2N}$, where d is the difference between a pair of measurements and N is the number of split pairs. The percentage of technical error per population sample (defined as 100 times the technical error divided by the mean value of the split samples) was then calculated and averaged over the samples, weighted by N. The averaged percentages of technical errors were 1.4% (sodium), 1.9% (potassium), and 2.3% (creatinine) (21). Urinary excretions over 24 hours were calculated as analyte concentration × urinary volume corrected to 24 hours.

In the present study, we focused on data from the Western population samples in INTERSALT. We excluded 2 samples from Goodman, United States, with low mean urinary volumes that indicated systematic under-collection; an Innuit population from Labrador, Canada, who were unrepresentative of the wider North-American population; and a sample from a coastal fishing village in St. John's, Canada, who had high sodium intakes that were found to be a marked population outlier in the regression equations. This left data for the analyses herein from 5,693 participants in 29 Western population samples.

Statistical methods

Participants were assigned randomly (stratified by center, age, and sex) to either test ($n = 2{,}948$) or validation ($n = 2{,}745$) data sets. For the regression analyses, centers were divided into 5 regions: North America, Northern Europe, Eastern Europe, Southern Europe, and Western Europe. Sex-specific regression equations estimating individual 24-hour urinary sodium excretion from casual urinary sodium, potassium, and creatinine concentrations, age, age^2, region, and body mass index (weight (kg)/height (m)^2) were obtained for participants from the test data set. Utility of inclusion of specific variables in the models was assessed using Student's t test, and model fit was assessed using adjusted R^2; regional interactions in the slope of the casual sodium–24-hour sodium regression association were tested using analysis of variance.

Regression coefficients obtained from the test data set were applied to the validation data set; observed and estimated 24-hour sodium excretion levels were compared at the individual and mean population sample levels. Observed population standard deviations were corrected for overdispersion due to within-person variability by multiplying observed standard deviations by the square root of the reliability coefficient previously derived for 24-hour sodium excretion, 0.387 (21, 22); reliability $= s_b^2/(s_b^2 + s_w^2)$, where s_b^2 is the between-person variance (i.e., an estimate of the "true" population variance, which is unknown), s_w^2 is the within-person variance, and $s_b^2 + s_w^2$ is the observed variance. Estimated and observed proportions of the population

with urinary sodium excretions greater than 65 mmol in 24 hours and greater than 100 mmol in 24 hours were estimated assuming normal distributions. Bland-Altman plots, showing the mean of observed and estimated 24-hour sodium excretion values versus the difference between the 2 values, were used to assess bias (23).

To provide equations based on the totality of available data, overall models using data from all 5,693 participants were also computed. Statistical analyses were done by I.J.B. and Q.C. using SAS, version 9.2 (SAS Institute, Inc., Cary, North Carolina).

RESULTS

Descriptive statistics

Comprehensive descriptive statistics have been published previously (24). Among the 29 North American and European population samples analyzed here, the mean 24-hour sodium excretions for men ranged from 147.2 mmol (Charleroi, Belgium) to 240 mmol (Krakow, Poland) (Web Table 1, available at http://aje.oxfordjournals.org/); for women, they ranged from 117.8 mmol (Cottbus, Germany) to 167.5 mmol (Bassiano, Italy) (Web Table 2). Mean casual urinary sodium concentrations for men ranged from 109.2 mmol/L (Glostrup, Denmark) to 191.3 mmol/L (Krakow, Poland); for women, they ranged from 82.7 mmol/L (Glostrup, Denmark) to 186.8 mmol/L (Bassiano, Italy).

Regression models

Regression coefficients from individual-level linear regression models estimating 24-hour sodium excretion from casual urinary concentrations (sodium, potassium, and creatinine), region, body mass index, age, and age^2 based on the test data set are shown in Web Table 3, and those based on data for all 5,693 participants are shown in Table 1. Consistently, all terms were significantly related to 24-hour sodium excretion except age and age^2 in the men-only model. The intercept represents the β coefficient for North America, and the region β coefficients are with respect to North America. There was no interaction by region. For both men and women, coefficients were positive for casual urinary sodium concentration and body mass index and negative for casual urinary creatinine and potassium concentrations. The adjusted R^2 was 0.27 for men and 0.23 for women in the overall model (Table 1).

Models derived from the test data set (Web Table 3) were used to estimate 24-hour sodium excretion in the validation data set. Pearson r correlations between individual observed and estimated 24-hour sodium excretions in the validation data set were 0.50 and 0.51, with β regression coefficients of 1.03 mmol and 0.86 mmol, among men and women, respectively (Figure 1A and 1B). Individual estimated 24-hour sodium excretions ranged from 11.9 mmol to 573.6 mmol in men and 7.7 mmol to 532.9 mmol in women. Bland-Altman plots showed overestimation of observed 24-hour sodium

Table 1. Sex-Specific Multiple Linear Regression Analyses of Individual 24-Hour Urinary Sodium Excretion in Test and Validation Data Sets Combined, International Cooperative Study on Salt, Other Factors, and Blood Pressure, 1984–1987

Variable	Men (n = 2,841)[a]			Women (n = 2,852)[b]		
	β (SE)	Student's t Test	P Value	β (SE)	Student's t Test	P Value
Intercept (North America)[c]	25.46 (16.63)	1.53	0.1	5.07 (13.42)	0.38	0.7
Casual sodium, mmol/L	0.46 (0.02)	20.24	3.6×10^{-85}	0.34 (0.02)	18.66	2.1×10^{-73}
Casual creatinine, mmol/L	−2.75 (0.22)	−12.70	5.7×10^{-36}	−2.16 (0.20)	−10.74	2.1×10^{-26}
Casual potassium, mmol/L	−0.13 (0.04)	−3.14	0.002	−0.09 (0.03)	−2.71	0.007
Body mass index[d]	4.10 (0.31)	13.32	2.5×10^{-39}	2.39 (0.20)	11.98	2.8×10^{-32}
Age, years	0.26 (0.78)	0.34	0.7	2.35 (0.65)	3.60	3.3×10^{-4}
Age^2, years^2	0.00 (0.01)	−0.30	0.8	−0.03 (0.01)	−3.60	3.2×10^{-4}
Region						
Northern Europe	23.17 (4.51)	5.13	3.0×10^{-7}	15.73 (3.62)	4.34	1.4×10^{-5}
Eastern Europe	39.56 (4.54)	8.71	5.1×10^{-18}	16.94 (3.58)	4.73	2.4×10^{-6}
Southern Europe	23.08 (4.03)	5.73	1.1×10^{-8}	23.79 (3.20)	7.44	1.3×10^{-13}
Western Europe	17.05 (3.96)	4.31	1.7×10^{-5}	12.82 (3.12)	4.10	4.2×10^{-5}

Abbreviation: SE, standard error.
[a] Adjusted R^2 = 0.27.
[b] Adjusted R^2 = 0.23.
[c] Coefficients for region are with respect to North America.
[d] Weight (kg)/height (m)^2.

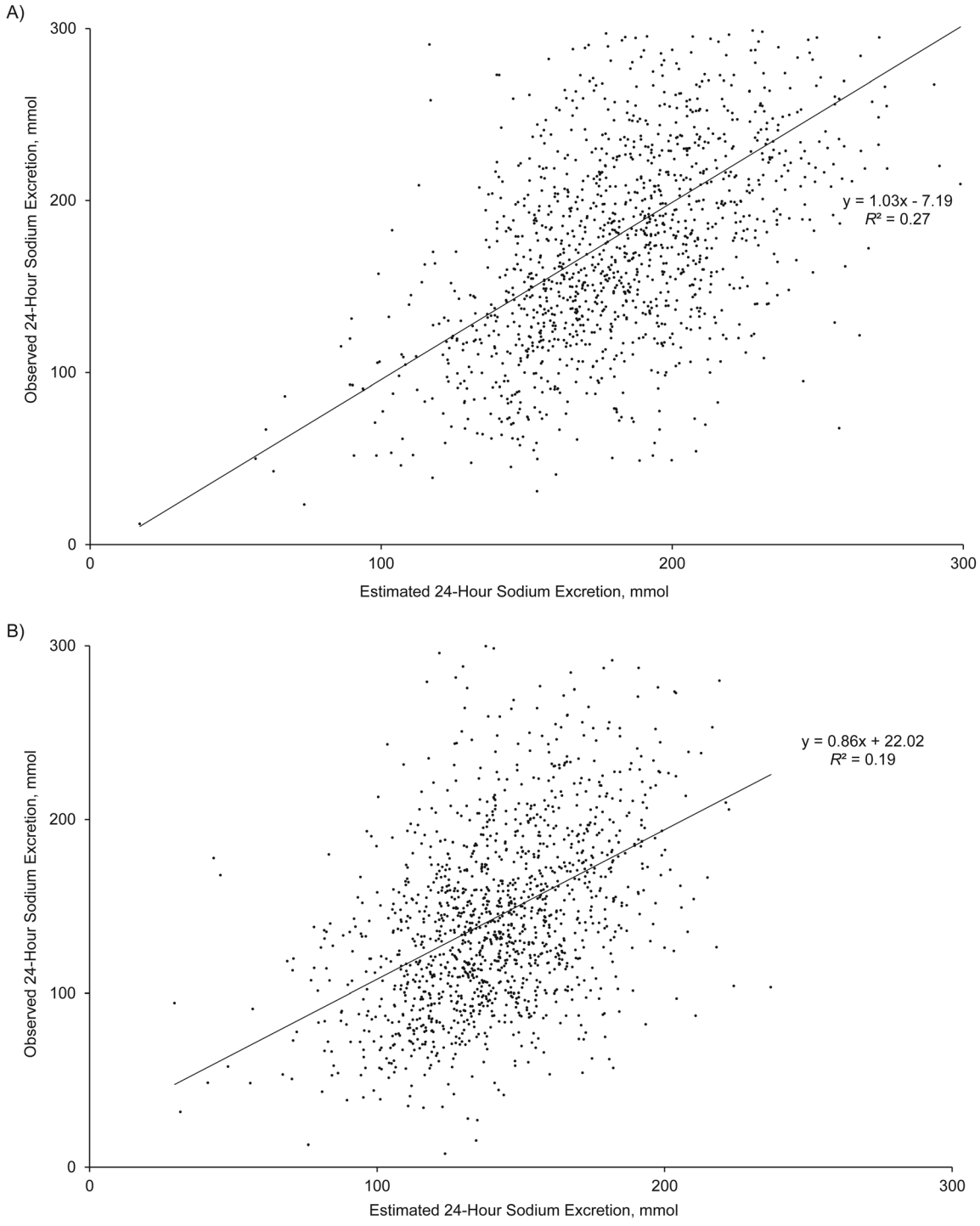

Figure 1. Observed and estimated (casual urine) individual 24-hour sodium excretion levels in men (A; $n = 1{,}369$) and women (B; $n = 1{,}376$) in the validation data set for the International Cooperative Study on Salt, Other Factors, and Blood Pressure, 1984–1987.

excretion at lower levels and underestimation at higher levels for both men and women (Figure 2A and 2B), with some marked outliers at high levels of sodium; however, the difference between observed and estimated mean 24-hour sodium excretion (i.e., bias) was small (−1.6 mmol and 2.3 mmol for men and women, respectively).

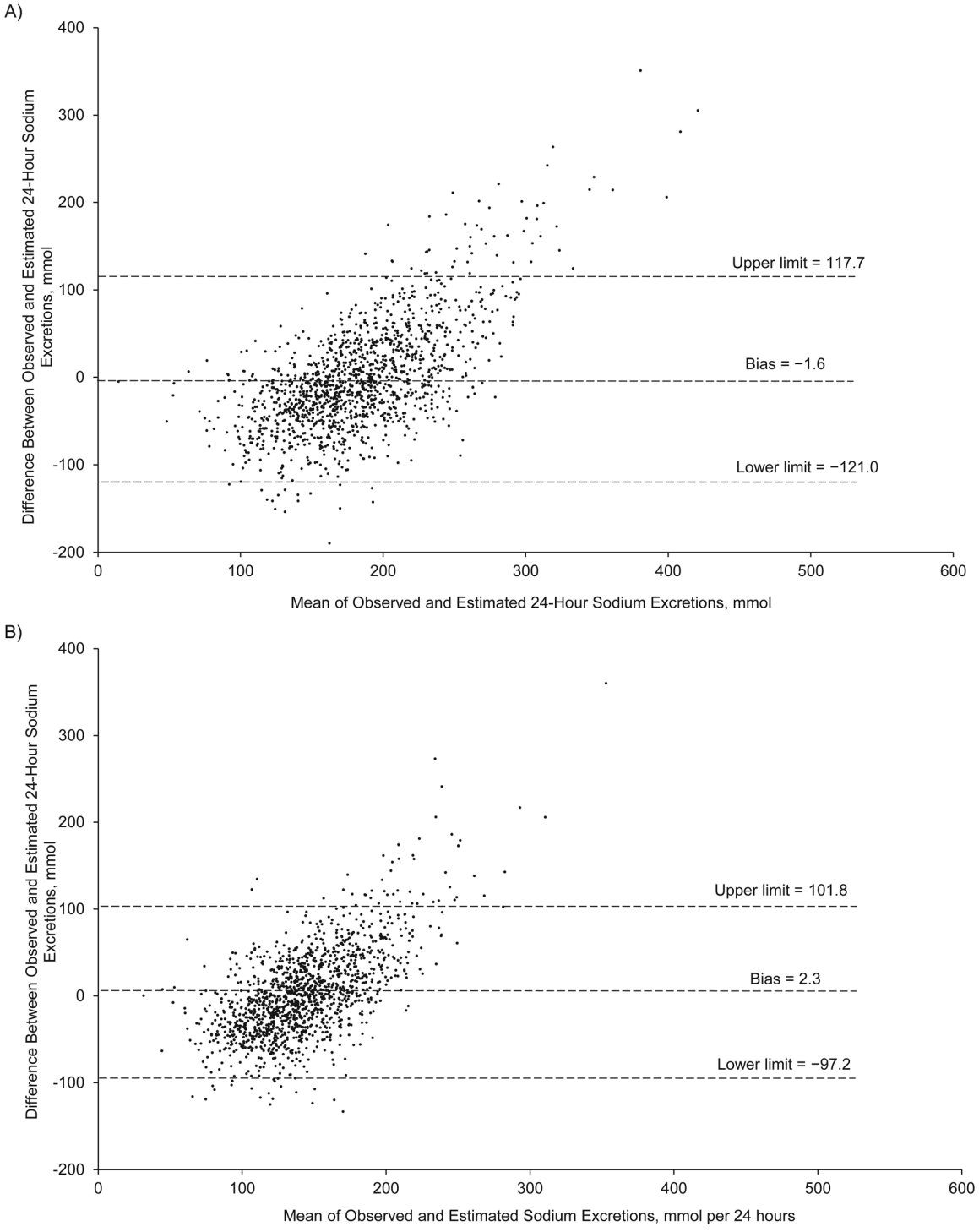

Figure 2. Bland-Altman plots comparing observed and estimated (casual urine) individual 24-hour sodium excretion levels in men (A; $n = 1{,}369$) and women (B; $n = 1{,}376$) in the validation data set for the International Cooperative Study on Salt, Other Factors, and Blood Pressure, 1984–1987. The upper limit of agreement equals the mean difference + 1.96 × standard deviation of the difference, and the lower limit equals the mean difference – 1.96 × standard deviation of the difference.

Sample-level validation

Pearson *r* correlations between observed and estimated sample mean 24-hour sodium excretions were 0.79 and 0.71, with β regression coefficients of 1.17 mmol and 0.80 mmol, among men and women, respectively (Figure 3A and 3B). Bland-Altman plots did not indicate over- or underestimation of observed 24-hour sodium excretion, and bias in mean values (observed minus estimated) was small at −1.8 mmol and 2.2 mmol for men and women, respectively (Figure 4A and 4B). Two samples (from Moscow, Russia, and Hawaii, United States) fell outside the limits of agreement of the Bland-Altman plots for men, as did 2 (Cottbus and Heidelberg, Germany) for women. The pattern of results for observed and estimated sample median 24-hour sodium excretions was similar to that seen in analyses of sample means, though the adjusted R^2 was lower and the bias was larger (Web Figures 1 and 2).

Estimated sample standard deviations were mostly smaller than were observed 24-hour sodium excretion standard deviations (Table 2), despite correction of observed standard deviations for overdispersion based on the reliability estimate (see Materials and Methods). As a result, estimated proportions of individuals with 24-hour sodium intakes above 65 mmol and 100 mmol were generally higher for estimated 24-hour sodium excretion than for observed levels (Table 2). For example, based on the estimated standard deviations, the proportion of participants with a 24-hour sodium excretion greater than 100 mmol ranged from 96.4% to 100% for men and from 76.1% to 99.9% for women, as compared with 86.5% to 99.8% and 70.1% to 98.6% for men and women, respectively, based on observed standard deviations (corrected for overdispersion).

DISCUSSION

INTERSALT data indicated that models based on sodium, potassium, and creatinine concentrations from casual urine specimens may be useful for estimation of sample mean 24-hour sodium excretion. Using either threshold (65 mmol or 100 mmol), the 24-hour sodium excretion of the majority of North American and European individuals analyzed here was in excess of current recommended limits (14).

For both men and women, bias in estimated mean values was small for individual- and sample-based models. This may have relevance not only for estimation of mean population sodium excretion values using casual urine samples but also for population-based surveys with a cluster design, such as the ongoing US National Health and Nutrition Examination Survey (NHANES). In NHANES, casual urine specimens are collected, but sodium intake is estimated from 24-hour dietary recalls (25), which may be less accurate than estimates based on urinary data (15–17). Also, analysis of casual urine specimens at the cluster (sample) level in NHANES and other studies of similar design may result in less bias than analysis at individual level, but this would need to be validated with study-specific 24-hour urine collections.

Distributions of sodium excretion levels estimated by the regression models were typically less dispersed than were estimates based on the observed means and standard deviations, despite correction of the observed standard deviations for overdispersion due to within-person variability in sodium excretion. (Without such correction, the standard deviations of the observed data are too large; we recommend that the proposed simple correction procedure based on the reliability coefficient (intra-class correlation) of sodium excretion be applied to population data on urinary sodium excretion.) Accordingly, the proportion of individuals with values of urinary 24-hour sodium excretion above recommended levels of 65 mmol and 100 mmol tended to be slightly overestimated by the models; however, the extent of the bias varied by country and sex.

We did not set out to assess the validity of casual specimens for estimating 24-hour sodium excretion at the individual level. Compared with sample means, individual measurements of casual and 24-hour sodium are much more prone to "measurement error" because of intra-individual variability in sodium intakes, which contribute to the lower Pearson *r* correlations for individual-level analyses compared with the group-level analyses. Nonetheless, despite wide variations in individual 24-hour sodium excretion, bias in the estimation of group mean levels from individual data was small.

There was a wide range of populations represented among the INTERSALT North American and European samples. The lack of significant regional interaction for the casual urinary sodium–24-hour sodium association suggests that our findings may be broadly generalizable. Despite this and the small bias overall in estimation of mean intakes, there may be error in estimation of intakes for individual population samples of more than 10 percentage points; we therefore recommend that in future studies, 24-hour urinary sodium specimens collected from representative subsamples of study participants be used to calibrate data from casual urine specimens. We have previously estimated for samples with a standard deviation of 24-hour urinary sodium excretion of approximately 60 mmol that a single 24-hour urine collection from 100 individuals would be sufficient to provide an estimate of the mean population sodium intake with 95% confidence intervals of plus or minus 12 mmol around the mean (26). Precision could be improved by using larger samples or by obtaining more than 1 specimen per person (27). The combination of casual urine specimens obtained from all participants in a study, with calibration against 24-hour collections from subsamples, could provide accurate estimates of mean 24-hour urinary sodium excretion while achieving a considerable saving in cost, logistics, and participant burden compared with use of 24-hour collections alone.

The inclusion of casual urinary creatinine concentrations, sex, age, and body mass index in the regression models was informed by previous work by Joossens et al. (28), who similarly developed equations for estimation of 24-hour urinary sodium excretion based on casual urinary data. We estimated 24-hour urinary sodium excretion directly from the regression models rather than working through an intermediate step based on estimation of 24-hour urinary creatinine; removal of 1 step should help reduce statistical error in the estimation procedure. In addition, we found that casual urinary potassium concentration (readily available at minimal

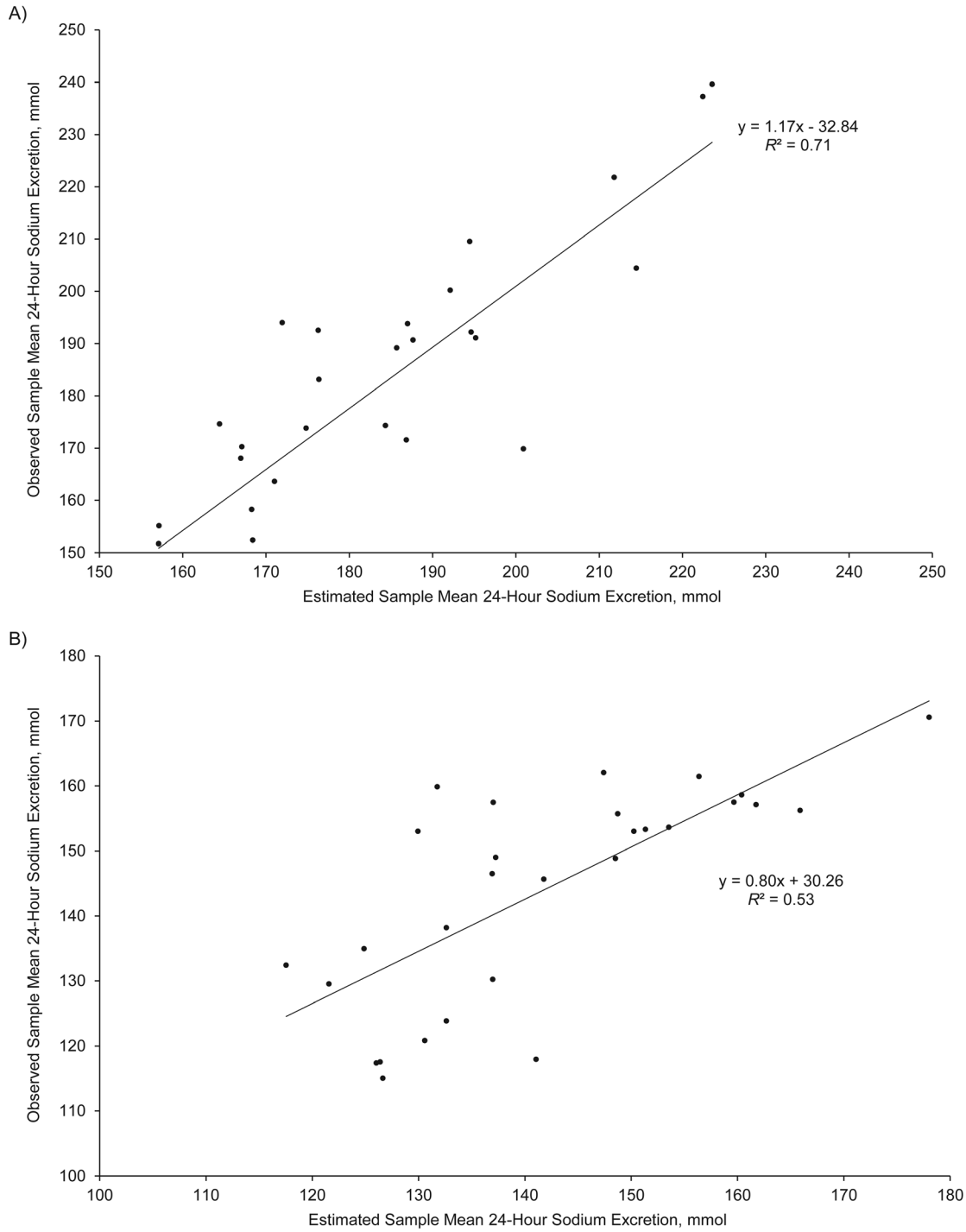

Figure 3. Observed and estimated (casual urine) sample-level mean 24-hour sodium excretion for 29 samples in men (A) and women (B) in the validation data set for the International Cooperative Study on Salt, Other Factors, and Blood Pressure, 1984–1987.

cost from standard urinary biochemistry) and age^2 (for women) added significantly to the regression models. The significant age^2 term observed for women is indicative of a curvilinear association between age and 24-hour sodium excretion. The association between urinary potassium concentration and 24-hour urinary sodium was inverse; the model therefore results in a lower estimated 24-hour sodium excretion for a given casual urinary sodium concentration when

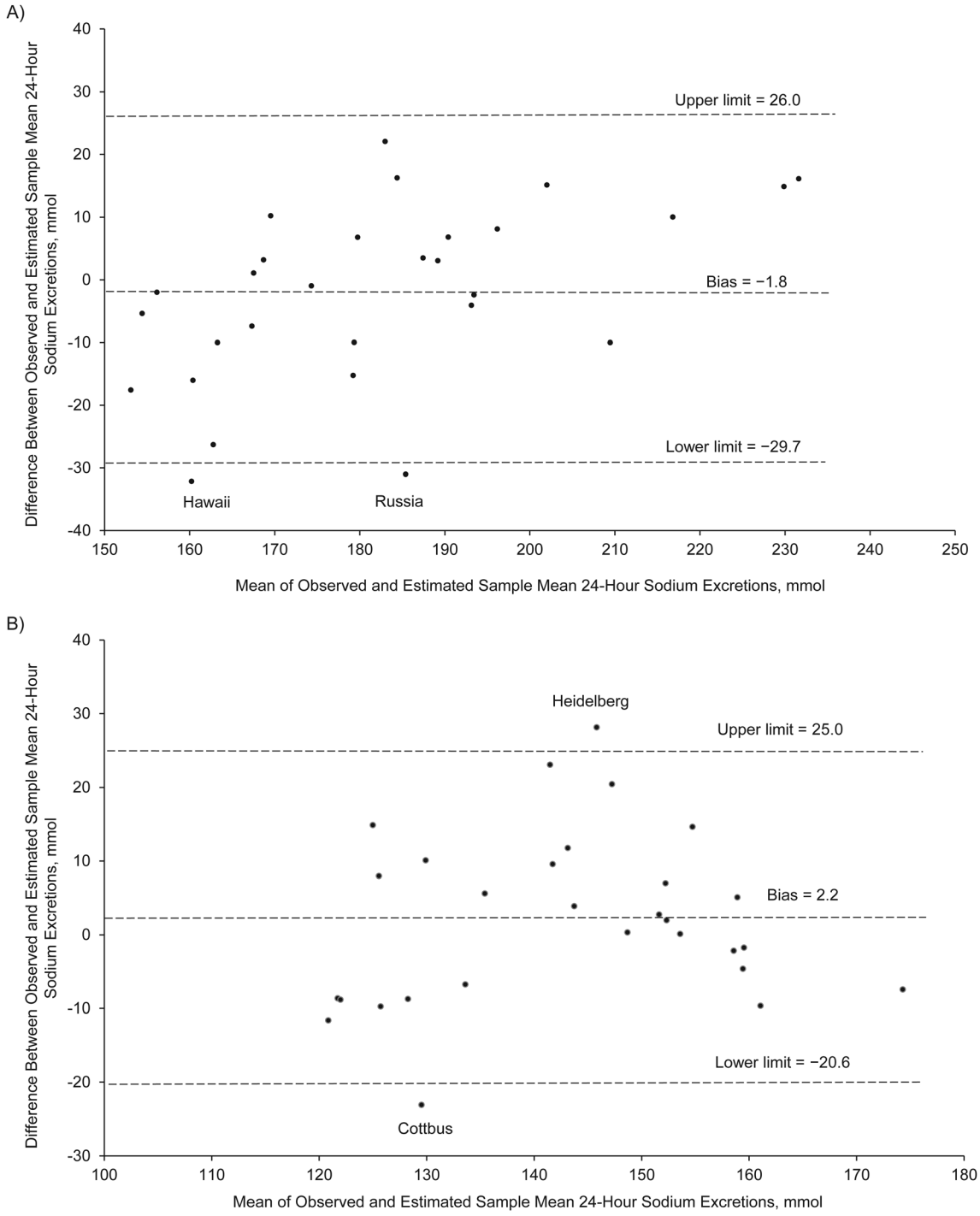

Figure 4. Bland-Altman plots comparing observed and estimated (casual urine) sample-level mean 24-hour sodium excretion for 29 samples in men (A) and women (B) in the validation data set for the International Cooperative Study on Salt, Other Factors, and Blood Pressure, 1984–1987. The upper limit of agreement equals the mean difference + 1.96 × standard deviation of the difference, and the lower limit equals the mean difference – 1.96 × standard deviation of the difference.

accompanied by higher urinary potassium concentration. This could reflect the fact that higher potassium concentrations are indicative of a "healthier" diet that is richer in fruit and vegetables and lower in salt (29).

In other studies, investigators have reported significant positive correlations among casual urinary sodium concentrations, sodium/creatinine ratios, and 24-hour urinary sodium excretion (30–33). Using an analytical strategy similar to

Table 2. Observed and Estimated 24-Hour Sodium Excretion by Sample in Men in the Validation Data Set ($n = 1,369$), International Cooperative Study on Salt, Other Factors, and Blood Pressure, 1984–1987

Country and Sample	No. of Men	Mean		Standard Deviation[a]		Median		% >65 mmol[b]		% >100 mmol[b]	
		Observed	Estimated	Observed	Estimated	Observed	Estimated	Observed	Estimated	Observed	Estimated
Belgium, Charleroi	39	149.6	175.9	33.5	30.5	140.8	174.2	99.1	100.0	93.1	99.4
Belgium, Ghent	48	163.6	171.0	32.1	25.0	158.9	164.6	99.8	100.0	97.6	99.8
Denmark, Glostrup	48	158.3	168.3	40.2	35.5	152.3	171.1	98.6	99.7	92.6	97.3
Finland, Joensuu	48	193.8	187.0	35.8	29.2	189.6	184.9	100.0	100.0	99.6	99.9
Finland, Turku	48	173.8	174.8	38.3	25.2	159.1	173.7	99.7	100.0	97.3	99.9
Germany, Bernried	48	192.5	176.3	42.0	30.8	182.9	177.4	99.8	100.0	98.6	99.3
Germany, Cottbus[c]	48	174.3	184.3	44.9	31.9	152.8	187.2	99.0	100.0	95.1	99.6
Germany, Heidelberg	47	194.0	171.9	46.7	35.3	193.0	170.4	99.6	99.8	97.8	97.9
Hungary, Porcsalma	48	237.3	222.4	60.6	35.9	224.0	225.3	99.7	100.0	98.8	100.0
Iceland, Reykjavik	48	152.4	168.4	30.2	26.7	148.3	174.0	99.7	100.0	95.8	99.5
Italy, Bassiano	47	204.5	214.4	40.4	31.5	199.2	210.8	100.0	100.0	99.5	100.0
Italy, Gubbio	48	192.2	194.6	41.2	30.2	190.2	196.9	99.9	100.0	98.7	99.9
Italy, Mirano	48	189.2	185.7	37.5	32.9	183.6	184.8	99.9	100.0	99.1	99.5
Italy, Naples	48	171.6	186.8	31.9	27.2	173.2	186.2	99.9	100.0	98.8	99.9
Malta, Dingli	48	191.1	195.2	35.6	30.4	192.0	196.7	100.0	100.0	99.5	99.9
Netherlands, Zutphen	48	174.6	164.4	38.5	29.3	168.3	167.4	99.7	99.9	97.4	98.6
Poland, Krakow	48	239.7	223.6	48.6	27.3	235.6	227.6	100.0	100.0	99.8	100.0
Poland, Warsaw	48	221.8	211.8	59.4	37.5	210.6	208.4	99.5	100.0	98.0	99.9
Portugal, Cartaxo	48	200.2	192.1	51.8	33.9	199.6	195.6	99.4	100.0	97.3	99.7
Russia, Moscow	48	169.9	200.9	34.6	28.8	178.4	201.3	99.8	100.0	97.8	100.0
Spain, Manresa	48	209.5	194.4	39.8	34.1	212.5	193.2	100.0	100.0	99.7	99.7
Spain, Torrejon	48	190.7	187.6	50.6	37.6	184.7	192.9	99.1	99.9	96.3	99.0
United Kingdom, Belfast	48	151.7	157.1	36.8	31.5	150.9	155.8	98.7	99.7	92.0	96.5
United Kingdom, Birmingham	48	168.1	167.0	26.9	17.1	163.0	163.5	100.0	100.0	99.4	100.0
United Kingdom, South Wales	48	183.1	176.4	37.2	31.0	185.1	172.7	99.9	100.0	98.7	99.3
United States, Chicago	47	144.3	161.9	38.1	33.6	150.4	162.8	97.5	99.7	87.8	96.7
United States, Hawaii	45	144.2	176.3	40.1	42.3	127.5	178.9	96.8	99.4	86.5	96.4
United States, Jackson (Black)	40	170.3	167.1	59.7	29.2	152.9	161.3	95.3	100.0	88.0	98.9
United States, Jackson (White)	48	155.2	157.1	40.7	32.2	147.5	157.2	98.2	99.7	91.2	96.2

[a] Observed standard deviation corrected for overdispersion by multiplying by $\sqrt{0.387}$.
[b] Calculated from the mean and standard deviation, assuming a normal distribution.
[c] Former German Democratic Republic (East Germany).

Table 3. Observed and Estimated 24-Hour Sodium Excretion by Sample in Women in the Validation Data Set ($n = 1,376$), International Cooperative Study on Salt, Other Factors, and Blood Pressure, 1984–1987

Country and Sample	No. of Women	Mean		Standard Deviation[a]		Median		% >65 mmol[b]		% >100 mmol[b]	
		Observed	Estimated	Observed	Estimated	Observed	Estimated	Observed	Estimated	Observed	Estimated
Belgium, Charleroi	37	123.9	132.6	31.6	22.2	116.4	131.7	95.6	99.8	77.5	92.9
Belgium, Ghent	48	120.8	130.6	24.2	21.5	112.8	126.8	98.2	99.8	80.6	92.3
Denmark, Glostrup	48	117.4	126.0	24.4	20.5	112.2	126.4	97.4	99.7	76.2	89.8
Finland, Joensuu	48	149.0	137.2	32.4	23.4	146.5	136.7	99.3	99.8	93.5	94.5
Finland, Turku	48	138.2	132.6	33.1	19.6	131.8	131.8	98.0	99.9	87.6	95.2
Germany, Bernried	47	157.5	137.0	34.3	23.2	150.1	137.3	99.5	99.8	95.3	94.5
Germany, Cottbus[c]	48	118.0	141.1	24.7	18.9	113.9	142.9	97.4	100.0	76.7	98.5
Germany, Heidelberg	48	159.9	131.7	31.4	20.3	158.7	130.3	99.8	99.9	97.2	94.1
Hungary, Porcsalma	48	156.2	165.9	33.1	27.6	156.6	171.9	99.5	100.0	95.6	99.2
Iceland, Reykjavik	48	115.0	126.6	24.1	22.8	113.4	126.1	96.9	99.4	73.3	87.9
Italy, Bassiano	48	170.6	178.0	39.0	25.0	162.7	182.0	99.5	100.0	96.5	99.9
Italy, Gubbio	48	161.5	156.4	32.7	23.3	159.3	159.6	99.7	100.0	97.0	99.2
Italy, Mirano	48	153.3	151.3	29.5	23.2	156.0	148.4	99.8	100.0	96.5	98.6
Italy, Naples	48	153.6	153.5	30.2	23.5	141.7	154.8	99.7	100.0	96.2	98.9
Malta, Dingli	48	153.0	150.2	38.0	25.0	136.8	152.8	98.6	99.9	91.8	97.8
Netherlands, Zutphen	48	129.5	121.6	25.5	23.8	126.6	123.8	99.0	98.5	87.6	81.7
Poland, Krakow	48	157.5	159.7	38.0	21.1	147.4	158.9	98.9	100.0	93.5	99.8
Poland, Warsaw	48	162.1	147.4	46.7	24.6	150.0	141.5	97.6	99.9	90.8	97.3
Portugal, Cartaxo	49	157.1	161.7	42.4	28.1	144.3	162.6	98.0	99.9	91.1	98.6
Russia, Moscow	47	148.9	148.5	38.6	27.6	145.9	149.8	97.9	99.8	89.7	96.1
Spain, Manresa	48	155.7	148.7	35.1	24.8	149.0	149.2	99.3	99.9	94.4	97.5
Spain, Torrejon	48	158.6	160.4	26.5	27.4	149.8	160.7	100.0	100.0	98.6	98.6
United Kingdom, Belfast	48	153.0	129.9	30.9	28.9	149.1	131.5	99.6	98.1	95.7	85.0
United Kingdom, Birmingham	48	146.5	136.9	28.4	25.5	142.4	132.5	99.6	99.6	94.9	92.6
United Kingdom, South Wales	48	130.2	137.0	28.7	22.5	126.7	134.2	98.2	99.9	85.3	95.0
United States, Chicago	48	135.0	124.9	48.6	24.0	120.4	126.7	90.9	98.9	76.4	85.0
United States, Hawaii	44	145.7	141.8	42.5	33.0	138.6	143.9	96.3	98.5	85.9	89.7
United States, Jackson (Black)	48	117.6	126.4	33.4	33.3	123.0	132.6	92.3	95.5	70.1	78.6
United States, Jackson (White)	48	132.4	117.5	34.5	24.7	119.9	117.9	96.5	97.3	82.7	76.1

[a] Observed standard deviation corrected for overdispersion by multiplying by $\sqrt{0.387}$.
[b] Calculated from the mean and standard deviation, assuming a normal distribution.
[c] Former German Democratic Republic (East Germany).

that from our study, Tanaka et al. (34) developed an equation to estimate 24-hour urinary sodium excretion from casual specimens from 591 Japanese INTERSALT participants and validated the equation in a sample of 513 individuals from another Japanese population sample. The authors noted that circadian patterns in sodium excretion would likely lead to under- or overestimation of 24-hour sodium excretion for some individuals, but if the casual specimen collection times were distributed randomly through the day, the impact on group means would be small. Consistent with our findings and those of others (35), Tanaka et al. concluded that casual urinary specimens may be useful for estimating the mean population 24-hour sodium excretion and charting trends in population means over time.

Overnight urine collection has also been proposed as a low-burden alternative to 24-hour collection (36–38). However, differential diurnal excretion patterns have been observed for nonhypertensive and hypertensive individuals, by sex, and by race (37, 39, 40). Thus, estimates of sodium intake from overnight urine collections may be biased by, for example, the mix of hypertensive and normotensive individuals in the sample.

Our study has limitations. It is based on casual and 24-hour urinary data collected from multiple locations in North America and Europe in the 1980s. Since then, urinary excretion patterns, as well as correlations between casual and 24-hour urinary data, may have altered, reflecting changes in dietary and lifestyle habits over the ensuing 20–30 years. On the other hand, all specimens were collected using standardized methods according to strict protocol; these will have minimized differences between samples and countries. Casual urinary specimens taken at different times of day can be influenced by diurnal variation, including in urinary creatinine concentrations (41), because creatinine excretion is influenced by meat intake (42, 43), with potentially high within-person diurnal variation (44, 45). Fluid intake can also vary over the day, possibly impacting urinary concentrations (46). In addition, we did not have sufficient data to test whether our equations were suitable for important population subgroups, for example, African Americans or hypertensive individuals. Calibration against 24-hour urinary excretion data is recommended to check performance of the equations in subgroups if specific data on these strata are required.

In summary, casual urinary specimens may be a valid low-burden, low-cost alternative to 24-hour collections for estimation of mean population sodium intakes (and by extension, estimation of trends over time), though study-specific calibration against 24-hour collections to increase validity is recommended. Also, these data may be used to estimate the proportion of the population with dietary sodium intakes above specific threshold values within a few percentage points. Reliable, ongoing population-wide data on sodium intakes are necessary to monitor the effectiveness of public health efforts to reduce sodium intakes for the prevention of high blood pressure and major cardiovascular diseases (47).

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REFERENCES

1. Conlin PR. Eat your fruits and vegetables but hold the salt. *Circulation*. 2007;116(14):1530–1531.
2. Sacks FM, Svetkey LP, Vollmer WM, et al. Effects on blood pressure of reduced dietary sodium and the Dietary Approaches to Stop Hypertension (DASH) diet. *N Engl J Med*. 2001;344(1):3–10.
3. Elliott P, Walker LL, Little MP, et al. Change in salt intake affects blood pressure of chimpanzees: Implications for human populations. *Circulation*. 2007;116(14):1563–1568.
4. Cutler JA. Randomized trials of sodium reduction: An overview. *Am J Clin Nutr*. 1997;65(suppl):643S–651S.

5. Midgley JP, Matthew AG, Greenwood CM, et al. Effect of reduced dietary sodium on blood pressure: a meta-analysis of randomized controlled trials. *JAMA*. 1996;275(20): 1590–1597.
6. Graudal NA, Galløe AM, Garred P. Effects of sodium restriction on blood pressure, renin, aldosterone, catecholamines, cholesterols, and triglyceride: a meta-analysis. *JAMA*. 1998;279(17):1383–1391.
7. Elliott P. Observational studies of salt and blood pressure. *Hypertension*. 1991;17(suppl I):I3–I8.
8. Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion. *BMJ*. 1988;297(6644):319–328.
9. He J, Whelton PK, Appel LJ, et al. Long-term effects of weight loss and dietary sodium reduction on incidence of hypertension. *Hypertension*. 2000;35(2):544–549.
10. Cook NR, Cutler JA, Obarzanek E, et al. Long term effects of dietary sodium reduction on cardiovascular disease outcomes: observational follow-up of the Trials of Hypertension Prevention (TOHP). *BMJ*. 2007;334(7599):885–888.
11. Perry IJ, Beevers DG. Salt intake and stroke: a possible direct effect. *J Hum Hypertens*. 1992;6(1):23–25.
12. Antonios TFT, MacGregor GA. Salt—more adverse effects. *Lancet*. 1996;348(9022):250–251.
13. World Health Organization and Food and Agriculture Organization. Diet, nutrition and the prevention of chronic diseases. Report of a joint WHO/FAO expert consultation. Technical Report Series 916. Geneva, Switzerland: World Health Organization; 2003.
14. US Department of Agriculture and US Department of Health and Human Services. *Dietary Guidelines for Americans, 2010*. Washington, DC: US Government Printing Office; 2010.
15. Bingham S. The dietary assessment of individuals; methods, accuracy, new techniques and recommendations. *Nutr Abstr Rev Ser Hum Exp*. 1987;57(10):705–742.
16. Bates CJ, Thurnham DI. Biochemical markers of nutrient intake. In: Margetts BM, Nelson M, eds. *Design Concepts in Nutritional Epidemiology*. Oxford, United Kingdom: Oxford University Press; 1991:192–265.
17. Hunter D. Biochemical indicators of dietary intake. In: Willett W, ed. *Nutrional Epidemiology*. Oxford, United Kingdom: Oxford University Press; 1998:174–243.
18. Rose G, Stamler J. The INTERSALT Study: background, methods and main results. *J Hum Hypertens*. 1989;3(5): 283–288.
19. Elliott P, Stamler J, Nichols R, et al. Intersalt revisited: Further analyses of 24 hour sodium excretion and blood pressure within and across populations. Intersalt Cooperative Research Group. *BMJ*. 1996;312(7041):1249–1253.
20. Elliott P, Stamler R. Manual of operations for "INTERSALT", an international cooperative study on the relation of sodium and potassium to blood pressure. *Control Clin Trials*. 1988; 9(suppl):1S–117S.
21. Dyer AR, Shipley M, Elliott P. Urinary electrolyte excretion in 24 hours and blood pressure in the INTERSALT Study. I. Estimates of reliability. The INTERSALT Cooperative Research Group. *Am J Epidemiol*. 1994;139(9):927–939.
22. Dyer AR, Elliott P, Shipley M. Urinary electrolyte excretion in 24 hours and blood pressure in the INTERSALT Study. II. Estimates of electrolyte-blood pressure associations corrected for regression dilution bias. The INTERSALT Cooperative Research Group. *Am J Epidemiol*. 1994;139(9):940–951.
23. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet*. 1986;1(8476):307–310.
24. INTERSALT Co-operative Research Group. Appendix tables. Centre-specific results by age and sex. *J Hum Hypertens*. 1989;3(5):331–407.
25. Sodium intake among adults—United States, 2005–2006. *MMWR Morb Mortal Wkly Rep*. 2010;59(24):746–749.
26. Elliott P, Brown IJ. Sodium intakes around the world. Background document prepared for the Forum and Technical meeting on Reducing Salt Intake in Populations (Paris 5–7th October 2006). Geneva, Switzerland: World Health Organization Press; 2007. (http://www.who.int/dietphysicalactivity/reducingsalt/en/index1.html). (Accessed May 6, 2013.)
27. Liu K, Cooper R, McKeever J, et al. Assessment of the association between habitual salt intake and high blood pressure: methodological problems. *Am J Epidemiol*. 1979;110(2):219–226.
28. Joossens JV, Claessens J, Geboers J, et al. Electrolytes and creatinine in multiple 24-hour urine collections (1970–1974). In: Kesteloot H, Joossens JV, eds. *Epidemiology of Arterial Blood Pressure*. The Hague, Netherlands: Martinus Nijhoff Publishers; 1980:45–63.
29. Lampe JW. Health effects of vegetables and fruit: assessing mechanisms of action in human experimental studies. *Am J Clin Nutr*. 1999;70(suppl):475S–490S.
30. Walker WG, Whelton PK, Saito H, et al. Relation between blood pressure and renin, renin substrate, angiotensin II, aldosterone and urinary sodium and potassium in 574 ambulatory subjects. *Hypertension*. 1979;1(3):287–291.
31. Moore M, Burgess R, Volosin K. Spot urinary sodium/creatinine ratio predicts previous day's 24 hour sodium excretion in young essential hypertensives [abstract]. *Prev Med*. 1979;8(2):200.
32. Milne FJ, Gear JSS, Laidley L, et al. Spot urinary electrolyte concentrations and 24 hour excretion [letter]. *Lancet*. 1980; 2(8204):1135.
33. Khaw KT, Bingham S, Welch A, et al. Blood pressure and urinary sodium in men and women: The Norfolk Cohort of the European Prospective Investigation into Cancer (EPIC-Norfolk). *Am J Clin Nutr*. 2004;80(5):1397–1403.
34. Tanaka T, Okamura T, Miura K, et al. A simple method to estimate populational 24-h urinary sodium and potassium excretion using a casual urine specimen. *J Hum Hypertens*. 2002;16(2):97–103.
35. Widdowson EM, McCance RA. Use of random specimens of urine to compare dietary intakes of African and British children. *Arch Dis Child*. 1970;45(242):547–552.
36. Watson RL, Langford HG. Usefulness of overnight urines in population groups. Pilot studies of sodium, potassium, and calcium excretion. *Am J Clin Nutr*. 1970;23(3):290–304.
37. Pietinen PI, Findley TW, Clausen JD, et al. Studies in community nutrition: estimation of sodium output. *Prev Med*. 1976;5(3):400–407.
38. Liu K, Dyer AR, Cooper RS, et al. Can overnight urine replace 24-hour urine collection to assess salt intake? *Hypertension*. 1979;1(5):529–536.
39. Dyer AR, Stamler J, Grimm R, et al. Do hypertensive patients have a different diurnal pattern of electrolyte excretion? *Hypertension*. 1987;10(4):417–424.
40. Dyer AR, Martin GJ, Burton WN, et al. Blood pressure and diurnal variation in sodium, potassium, and water excretion. *J Hum Hypertens*. 1998;12(6):363–371.
41. Pollack H. Creatinine excretion as an index for estimating urinary excretion of micronutrients or their metabolic end products. *Am J Clin Nutr*. 1970;23(7): 865–867.

42. Bleiler RE, Schedl HP. Creatinine excretion: variability and relationships to diet and body size. *J Lab Clin Med*. 1962; 59(6):945–955.
43. Lykken GI, Jacob RA, Munoz JM, et al. A mathematical model of creatine metabolism in normal males—comparison between theory and experiment. *Am J Clin Nutr*. 1980; 33(12):2674–2685.
44. Ram MM, Reddy V. Variability in urinary creatinine [letter]. *Lancet*. 1970;2(7674):674.
45. Bingham S, Cummings JH. The use of 4-aminobenzoic acid as a marker to validate the completeness of 24 h urine collections in man. *Clin Sci*. 1983;64(6):629–635.
46. Cummins RO, Shaper AG, Walker M. Methodological problems with estimation of salt intake. *Lancet*. 1981; 1(8234):1373–1374.
47. He FJ, MacGregor GA. Reducing population salt intake worldwide: from evidence to implementation. *Prog Cardiovasc Dis*. 2010;52(5):363–382.