Observational Studies of Salt and Blood Pressure

Paul Elliott

The observational data relating salt and blood pressure (excluding ENTERS ALT) are reviewed. Important methodological difficulties and biases are inherent to both across- and within-population studies and confuse their interpretation. Across-population studies are positive but rely on data drawn from the international literature based on a variety of unstandardized field methods; they are prone to unmeasured (ecological) confounding. Within-population studies generally lack statistical power and are subject to major regression-dilution bias (because of considerable day-to-day variation in sodium intake), which could conceal true correlations between sodium and blood pressure. Nevertheless, an overview of reported studies that used 24-hour urine excretion to quantify intake shows positive and highly significant correlations between sodium and blood pressure for both men and women and for systolic and diastolic blood pressures. These results are consistent with the INTERSALT findings and those from trials of sodium restriction. (Hypertension 1991;17[suppl I]:I-3–I-8)

Evidence relating salt and blood pressure (BP) comes from a variety of sources: animal and clinical studies, trials of sodium restriction and supplementation, and epidemiological studies, both across and within populations. In reviewing the observational evidence, my objectives were, first, to discuss some of the complex methodological issues that have confused much of the research in this area, and second, to briefly summarize the contribution of this large body of work to our understanding of the epidemiology of salt and BP. I have excluded consideration of the INTERSALT findings, which are discussed elsewhere in this issue.1-2

Across-Population Studies

A positive across-population association between salt and BP was first described by Dahl in 1960,3 who found, over five population groups, a remarkable straight-line relation between the average sodium intake of a population and the prevalence of hypertension. Dahl also noted that hypertension was uncommon in populations whose members consumed less than 4 or 5 g salt/day (i.e., about 70–80 mmol sodium) and hypothesized that salt intake increased the probability of elevated BP in a group although not necessarily in an individual.

Publication of Dahl's straight-line graph stimulated others to review the international literature for data on mean sodium intake and mean BP of populations.4-8 These studies generally confirmed the Dahl correlation but to a greater or lesser extent suffered from a number of uncertainties and biases. One major concern is that the data were not derived from one standardized source but from a variety of studies in the published literature, in which unstandardized and often unspecified methods were used. Frequently, data on sodium intake and BP for a particular population were derived from different sources, and even the author's own estimates of sodium intake were used (in the well-known paper by Gleibermann in 19734). Systematic error of measurement in a population (e.g., of BP) is another perennial source of bias in across-population (ecological) comparisons. Additionally, few data on confounding variables were available. Because of multiple social, geographic, and environmental differences among populations around the world, which may also relate to differences in BP, correlations in ecological studies are particularly susceptible to major, unmeasured confounding. Under these circumstances, there is the danger of committing an ecological fallacy9 if inappropriate inferences concerning correlations among individuals are made from those among groups.

One of the most comprehensive across-population studies of sodium and BP was published by Froment et al in 19799 and used literature-derived data from 28 populations around the world. The data were presented separately by sex and at approximate ages of 20 and 50 years; values of sodium intake were
derived mostly from 24-hour urine collections although not necessarily from the same studies as the BP data. An example is shown in Figure 1; this gives the correlation between mean systolic blood pressure (SBP) and mean sodium intake for 50-year-old men. The continuous line shows the regression across all 28 populations and is significantly positive, with a slope of 10 mm Hg/100 mmol sodium. However, as discussed elsewhere, the regression analyses are strongly influenced by the nine populations with low average sodium intakes (less than 2 g salt/day). These isolated populations probably had the least adequate data for both sodium intake and BP and likewise probably differed from the remainder in many ways other than sodium intake. When the nine populations are excluded from the analysis, as shown by the interrupted line, the regression slope correlating sodium and BP is reduced and is no longer significant. (This may reflect to some extent the smaller number of populations and the more limited range of sodium intakes in the latter analysis.)

Figure 2, again derived from Froment et al, shows the relation in men between mean sodium intake and population SBP slope with age (estimated from data at approximate ages of 20 and 50 years). The correlation across all 28 populations is positive and significant, as shown by the continuous line. The regression slope indicates an SBP lower by 7.7 mm Hg over a 30-year period for sodium intake lower by 100 mmol. As can be seen, seven of the nine low salt populations (and two others) recorded lower mean BPs with increasing age. When the nine low salt populations are excluded, the size of the regression coefficient relating sodium and BP slope with age is reduced, as shown by the interrupted line.

To summarize, across-population (ecological) studies of sodium and BP generally support Dahl’s salt hypothesis, but they rely on a variety of unstan-
complete 24-hour urine specimens in general popu-
lation samples.15 The effect of these two biases in
deriving quantitative estimates of the sodium-BP rela-
tion is illustrated by the results of a small meth-
odological study conducted in a random sample from a
general practice in North London.16 In this middle-
aged and elderly population with a broad spread of
sodium intakes, the day-to-day variation in individual
sodium excretion was small compared with other stud-
ies.12 Analysis of repeated urine collections in a
subsample indicated that day-to-day, within-indi-
vidual variation in sodium intake biased regression
slopes by only 14% (based on a single 24-hour urine
collection) compared with a downward bias of over
75% in some other studies.12 Under these circum-
stances, whereby individual sodium excretion was
apparently well characterized by a single 24-hour
urine collection, the within-population regression
estimates relating sodium with SBP were similar to
the aforementioned across-population estimates of
Gleibermann4 and Froment et al,5 and the results
were statistically significant even though the sample
size was relatively small.

The results are summarized in Table 1. The regres-
sion slope relating sodium with SBP was 9.1 mm Hg/
100 mmol sodium after adjustment for age, sex, and
body mass index; with correction for reliability, which
statistically adjusts for the regression-dilution bias
introduced by physiological within-person variability
in sodium excretion, the SBP-sodium regression
slope was 10.6 mm Hg/100 mmol sodium. However,
because of the incompleteness of urine collections, it is
probable that this reliability-corrected estimate was
still too low. Although all 58 participants re-
ported complete collections, only 28 of the collec-
tions were found to be complete by excretion of
para-aminobenzoic acid (PABA), a biological marker
orally ingested (as capsules) during the day of the
urine collection. Among the 28 people with complete
urine collections, the regression estimate of the SBP-
sodium relation, after adjustment for confounding
variables, was 14.5 mm Hg/100 mmol sodium. A sim-
ilar progression in the size of regression slopes was
found for sodium and diastolic BP (DBP) (Table 1).

Further methodological problems of within-popu-
lation studies include statistical overadjustment of
the BP-sodium relation for covariates (such as body
weight) that are much more precisely measured than
sodium (giving estimates of the sodium effect that are
biased down toward zero in multiple regression anal-
yses17) and other biases caused by the effects of an-
hypertensive drug treatment on BP and by hyper-
tensive persons selectively reducing their sodium
intakes as a consequence of the diagnosis of high BP.

Within-population studies of salt and BP have
used a variety of dietary methods to estimate sodium
intake, from a salt frequency questionnaire to mul-
tiple 24-hour urine collections. Early reports by Dah-
land Love18 that the frequency of adding salt to food
at table was related to prevalence of high BP were
supported by the findings of one study19 but could not
be confirmed by others.20,21 Recent data from the
United Kingdom suggest that the proportion of non-
discretionary sodium in the diet of Western industri-
alized populations is as high as 85% of intake,22 so
that, given the variation in sodium content of many
processed foods, methods using diet history are un-
likely to yield reliable estimates of the sodium intake
of individuals. Nevertheless, significantly positive
 correlations of dietary sodium with BP have been
described in studies from Belgium,23 Northern Kash-
mir,24,25 and Southern California26 and significantly
negative correlations in one study from the Nether-
lands.27 In analyses of the National Health and
Nutrition Examination Survey (NHANES) study,2 in
which the same data set was used but with different
analytical methods, both positive28 and negative29
correlations of sodium with BP have been described.

Most studies have measured the urinary excretion of
sodium as a proxy for intake. Although the use of casual
(spot) urine samples has been criticized, six30-35 of
eight36-37 population studies that used this method,
which were identified in the literature, reported signifi-
cantly positive sodium-BP correlations. Similarly, with
the use of overnight rather than spot urine collections
to characterize sodium intake, six38-40 of seven41-44 popu-
lation studies (including four with Chinese popula-
tions45-48) reported significantly positive correlations
with BP. No significantly negative associations were
reported, perhaps reflecting a degree of publication
bias toward positive results.

Studies of 24-Hour Urinary Sodium Excretion
and Blood Pressure: Overview Analysis

Most within-population studies have used 24-
hour urine collections to estimate sodium intake.
Both positive and negative correlations with BP
have been described, although many studies have
been too small to show significant associations. The
literature was scanned to identify those studies of
24-hour urinary sodium and BP that could be
incorporated into an overview analysis. The aim was
to include all studies that published a quantitative

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**TABLE 1. Age-, Sex-, and Body Mass Index-Adjusted Regression Coefficients Relating Blood Pressure and Sodium Excretion in a North London Population, With Consideration of the Effects of Within-Person Variability of Sodium Excretion and Incompleteness of Urine Collections**

<table>
<thead>
<tr>
<th>Sample</th>
<th>Regression coefficients (SE) (mm Hg/100 mmol sodium)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All persons (n=58)</td>
<td>9.1* (3.7) 2.5 (2.0)</td>
</tr>
<tr>
<td>All persons, corrected for reliability (point estimate)</td>
<td>10.6 2.9</td>
</tr>
<tr>
<td>Complete collectors by PABA excretion (n=28)</td>
<td>14.5* (5.9) 5.9 (3.0)</td>
</tr>
</tbody>
</table>

Data used is from Reference 16. Correction for reliability is based on repeated measures. BP, blood pressure; PABA, para-aminobenzoic acid.

*p<0.05.
regression or correlation estimate, either positive or negative, of the relation of sodium to both SBP and DBP in populations. Excluded were studies that compared hypertensive with normotensive persons (e.g., studies in Scotland,45 Finland,46 and Australia47) or that reported only significant findings (e.g., studies in China,48 Korea,49 and Sweden50). Because nearly all of these significant findings were positive, inclusion of the latter studies could have introduced a bias toward a positive relation if significantly negative findings were being underreported. Additionally, selective inclusion of significant results (either positive or negative) would tend to enter more extreme values into the overview analysis.

Fourteen studies46-63 (of 16 populations) fulfilled the entry criteria and are listed in Table 2, together with their sample sizes, regression coefficients, and standard errors. From each population, the regression estimates were either directly obtained16,51 or algebraically derived64 from the Pearson r correlation coefficient and the standard deviations of both sodium and BP. Data were available only for simple (unadjusted) regression; where data (e.g., standard deviations) were given stratified by some other variable (e.g., age55), the appropriate unbiased (whole-sample) estimate was obtained by analysis of variance.64 Where possible, regression coefficients were separately obtained for men and women in each population and then averaged to yield an overall estimate of association. Two studies50,63 reported only data for men and women combined. Regression slopes were pooled by weighting with the inverse of the variance; total sample sizes for the three analyses were 7,099 men, 6,136 women, and 12,503 men and women combined.

### Table 2. Overview of Studies of 24-Hour Urinary Sodium Excretion and Blood Pressure: Summary of Abstracted Data

<table>
<thead>
<tr>
<th>Study</th>
<th>Sex</th>
<th>n</th>
<th>Mean age</th>
<th>Systolic BP b(SE)</th>
<th>Diastolic BP b(SE)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Joossens et al, 197151</td>
<td>M</td>
<td>1,314</td>
<td>44.7</td>
<td>3.35* (0.91)</td>
<td>2.29* (0.55)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>713</td>
<td>46.6</td>
<td>4.88† (1.82)</td>
<td>1.53 (0.88)</td>
</tr>
<tr>
<td>2. Sinnett et al, 197352</td>
<td>M</td>
<td>138</td>
<td>30-39†</td>
<td>-10.24 (10.29)</td>
<td>-11.63 (7.55)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>135</td>
<td>30-39†</td>
<td>-3.45 (7.47)</td>
<td>4.93 (4.84)</td>
</tr>
<tr>
<td>3. Karvonen et al, 197753</td>
<td>West Finns</td>
<td>98</td>
<td>63.7</td>
<td>-4.67 (2.94)</td>
<td>-2.20 (1.48)</td>
</tr>
<tr>
<td></td>
<td>East Finns</td>
<td>M</td>
<td>94</td>
<td>62.9</td>
<td>-0.67 (2.32)</td>
</tr>
<tr>
<td>4. Watson et al, 198054</td>
<td>Blacks</td>
<td>F</td>
<td>356</td>
<td></td>
<td>1.78 (1.29)</td>
</tr>
<tr>
<td></td>
<td>Whites</td>
<td>F</td>
<td>104</td>
<td></td>
<td>2.47 (3.08)</td>
</tr>
<tr>
<td>5. Prior et al, 198055</td>
<td>M</td>
<td>234</td>
<td>35-44‡</td>
<td>3.06 (3.85)</td>
<td>0.45 (2.11)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>261</td>
<td>35-44‡</td>
<td>2.25 (6.07)</td>
<td>2.18 (3.30)</td>
</tr>
<tr>
<td>6. Staessen et al, 198156</td>
<td>M</td>
<td>233</td>
<td>41.0</td>
<td>-0.95 (1.25)</td>
<td>0.82 (0.90)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>202</td>
<td>40.4</td>
<td>2.01 (2.03)</td>
<td>-0.38 (1.34)</td>
</tr>
<tr>
<td>7. Staessen et al, 198357</td>
<td>M</td>
<td>273</td>
<td>41.6</td>
<td>-0.59 (1.19)</td>
<td>1.02 (0.88)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>255</td>
<td>39.3</td>
<td>2.07 (1.85)</td>
<td>-0.19 (1.19)</td>
</tr>
<tr>
<td>8. Strazzullo et al, 198358</td>
<td>M</td>
<td>188</td>
<td>40.6</td>
<td>3.99 (2.07)</td>
<td>5.56* (1.45)</td>
</tr>
<tr>
<td>9. Connor et al, 198459</td>
<td>M</td>
<td>170</td>
<td>36</td>
<td>1.79 (1.14)</td>
<td>0.84 (0.92)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>182</td>
<td>36</td>
<td>3.77 (1.99)</td>
<td>2.46† (1.13)</td>
</tr>
<tr>
<td>10. M’Buyamba-Kabangu et al, 198660</td>
<td>M</td>
<td>144</td>
<td>32</td>
<td>1.85 (3.88)</td>
<td>0.99 (2.77)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>169</td>
<td>32</td>
<td>3.27 (3.11)</td>
<td>1.85 (2.04)</td>
</tr>
<tr>
<td>11. Bulpitt et al, 198661</td>
<td>M</td>
<td>459</td>
<td>45</td>
<td>0.29 (1.37)</td>
<td>-0.86 (1.01)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>159</td>
<td>46</td>
<td>2.77 (2.76)</td>
<td>2.08 (1.83)</td>
</tr>
<tr>
<td>12. Smith et al, 198862</td>
<td>M</td>
<td>3,754</td>
<td>40-59‡</td>
<td>0.61 (0.40)</td>
<td>0.39 (0.25)</td>
</tr>
<tr>
<td></td>
<td>F</td>
<td>3,600</td>
<td>40-59‡</td>
<td>1.94† (0.59)</td>
<td>1.04* (0.33)</td>
</tr>
<tr>
<td>13. Pietinen et al, 197963</td>
<td>M and F</td>
<td>50</td>
<td>26.4</td>
<td>7.01† (2.06)</td>
<td>3.75† (1.86)</td>
</tr>
<tr>
<td>14. Elliott et al, 198864</td>
<td>M and F</td>
<td>58</td>
<td>57.9</td>
<td>9.50† (3.60)</td>
<td>4.30† (2.10)</td>
</tr>
</tbody>
</table>

BP, blood pressure; M, male; F, female.
* p<0.0001.
† p<0.01.
‡ Age group, including median age.
§ Young persons (originally screened at high school).
| p <0.05.
| Range.
The results are shown in Table 3, after correction for reliability using the INTERSALT estimate of 0.46. Statistically highly significant positive relations were seen in all analyses. As in INTERSALT, regression coefficients were somewhat larger in the within-population surveys. The results are consistent with the INTERSALT findings and those from trials of sodium restriction.

Acknowledgment

I am grateful to Martin Shipley of the London School of Hygiene and Tropical Medicine for statistical advice.

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KEY WORDS: sodium • blood pressure • ecological studies • epidemiological studies • meta-analysis
Observational studies of salt and blood pressure.
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Hypertension. 1991;17:I3
doi: 10.1161/01.HYP.17.1_Suppl.I3
Hypertension is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0194-911X. Online ISSN: 1524-4563

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