INTERSALT Study Findings
Public Health and Medical Care Implications
Jeremiah Stamler, Geoffrey Rose, Rose Stamler, Paul Elliott, Alan Dyer, and Michael Marmot

INTERSALT found a significant association between 24-hour urine sodium excretion and systolic blood pressure in individuals. There was also a significant association between sodium and slope (increase) of blood pressure with age across population samples. The weight of evidence from animal-experimental, clinical, intervention, and epidemiological data favors a causal relation. INTERSALT data from 52 centers in 32 countries permit an estimate of effect on average population blood pressure of lower sodium intake. Based on the sodium-blood pressure association in individuals, it was estimated that a habitual population sodium intake that was lower by 100 mmol/day (e.g., 70 vs. 170 mmol/day) would correspond to an average population systolic pressure that was lower by at least 2.2 mm Hg. This size difference in systolic blood pressure in major US and UK population studies is associated with 4% lower risk of coronary death and 6% lower risk of stroke death in middle age. If habitual diet is both lower in sodium and higher in potassium with lower alcohol intake and less obesity, INTERSALT data estimate average population systolic pressure would be lower by 5 mm Hg. This was calculated to correspond to a 9% lower risk of coronary death and a 14% lower risk of stroke death. INTERSALT cross-population data also suggest that, with a 100 mmol/day lower sodium intake over the life span, the average increase in population systolic pressure from age 25 to 55 years would be less by 9 mm Hg, corresponding at age 55 to a 16% lower risk of subsequent coronary death and 23% lower risk of stroke death. These findings have importance in long-term population strategy for reduction of cardiovascular mortality. (Hypertension 1989;14:570-577)

INTERSALT was a large international epidemiological study on the relation of electrolyte excretion and other aspects of lifestyle to blood pressure. Associations between 24-hour urinary sodium and potassium excretion and blood pressure were examined in the 10,079 individual participants (men and women age 20–59 years) both within centers and in ecological analyses across the study’s 52 centers located in 32 countries. Body mass index and alcohol intake (assessed by questionnaire) were also studied, and their independent contribution to blood pressure estimated. Field work was based on a common protocol, with rigorous efforts to assure standardized data collection.1,2 The main overall findings have been published and are summarized below.3 The present paper assesses their implications for public health and medical care.

Main INTERSALT Results

Qualitative Findings

1. Sodium excretion was significantly and independently related to the systolic blood pressure (SBP) of individuals. Across populations, the level of sodium excretion correlated with the slope (increase) of blood pressure with age. In four remote populations, sodium excretion was very low, and blood pressure was low at all ages.

2. Potassium had a significant independent inverse association with blood pressure of individuals.

3. Sodium/potassium ratio was significantly related to the blood pressure of individuals.

4. Body mass index (BMI) and high alcohol intake were also significantly and independently related to blood pressure of individuals.

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Supported by grants from the Wellcome Trust (United Kingdom); the National Heart, Lung, and Blood Institute (United States); the International Society of Hypertension; the World Health Organization; the Heart Foundations of Canada, Great Britain, Japan, and The Netherlands; the Chicago Health Research Foundation; the FWGO-FMRS (Belgian National Research Foundation); and the ASLK-CGER (Parastatal Insurance Co., Brussels).

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TABLE 1. Pooled Coefficients for Systolic Blood Pressure and 24-Hour Urinary Sodium and Potassium, Sodium/Potassium Ratio, Body Mass Index, and Reported Heavy Intake of Alcohol from 52 INTERSALT Centers

<table>
<thead>
<tr>
<th>Variable</th>
<th>Combined within-center coefficients*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na (mm Hg SBP per 10 mmol Na)</td>
<td>+0.217</td>
</tr>
<tr>
<td>K (mm Hg SBP per 10 mmol K)</td>
<td>−0.446</td>
</tr>
<tr>
<td>Na/K (mm Hg SBP per unit Na/K)</td>
<td>+1.608</td>
</tr>
<tr>
<td>BMI (mm Hg SBP per unit BMI)</td>
<td>+0.775</td>
</tr>
<tr>
<td>Alcohol (mm Hg SBP for difference between ≥300 ml/wk and 1–299 ml/wk)</td>
<td>+2.809</td>
</tr>
</tbody>
</table>

Body mass index (BMI) was calculated as: weight (kg)/height² (m²). Na, sodium; SBP, systolic blood pressure; K, potassium; Na/K, sodium/potassium ratio.

*From multiple linear regression. Coefficients are adjusted for age and sex with each variable (Na, K, alcohol, and BMI) adjusted also for the remaining variables. These relations were unchanged when urinary calcium and magnesium were included as possible additional confounders. For the electrolytes, coefficients are also adjusted for reliability, based on repeat urine measurements in 8% of participants.

5. These associations were not as strong or consistent for diastolic pressure (e.g., sodium and sodium/potassium ratio were related to diastolic blood pressure (DBP) of individuals in analyses adjusted for age and sex, but not significantly so for sodium when also adjusted for BMI and alcohol). In cross-population comparison, sodium was significantly related to the slope of DBP with age with adjustment for BMI and alcohol intake were also related to average DBP, but not as strongly as to SBP.

6. In cross-center (ecological) analyses, the association of median sodium excretion with center median SBP as well as with prevalence of hypertension was significant for 52 centers, positive but not significantly so when the four low sodium centers (which strongly influenced the cross-center association) were excluded. This might reflect, at least in part, limited variability across the 48 centers in sodium excretion but wide differences between centers in such confounding variables as climate, physical activity, and social factors.

Quantitative Findings

Analysis within each center yielded 52 separate multiple regression coefficients for the relation of SBP to each of the lifestyle variables. For each variable, these center coefficients were then combined (pooled) to yield the whole-study coefficients given in Table 1. Each coefficient indicates the estimated difference in SBP per unit of the independent variable (e.g., a 10 mmol lower sodium output was associated with a 0.2 mm Hg lower SBP for individuals).

All pooled coefficients were significant, indicating that each of these aspects of lifestyle was independently related to systolic pressure of individuals.

In a further analysis of the INTERSALT data, within-center regression coefficients were recalculated with hypertensive individuals excluded (systolic 140+, or diastolic 90+, or treated with antihypertensive medication). This analysis sought to determine whether these associations between lifestyle variables and SBP applied mainly (or only) to hypertensive individuals or were present across the entire population. After hypertensive individuals were excluded, all these variables continued to be related significantly to the SBP of individuals.

In addition to these within-center findings, a significant positive association was also found across centers between the slope of blood pressure with age and the median center levels of sodium excretion. The regression coefficient indicated that over a 10-year period SBP would be higher by an additional 0.34 mm Hg for each 10 mmol increment of 24-hour sodium excretion.

Implications of INTERSALT Findings

Expected Quantitative Effect on Blood Pressure of Improved Lifestyle

Our estimates of the average effect on population blood pressure of lower intake of sodium, higher

TABLE 2. Predicted Differences in Population Average Systolic Blood Pressure With Given Differences in Lifestyle Variables

<table>
<thead>
<tr>
<th>Lifestyle variable</th>
<th>Present level*</th>
<th>Improved level</th>
<th>Predicted difference</th>
</tr>
</thead>
<tbody>
<tr>
<td>Na</td>
<td>170 mmol*</td>
<td>70 mmol</td>
<td>−2.17 mm Hg</td>
</tr>
<tr>
<td>K</td>
<td>55 mmol*</td>
<td>70 mmol</td>
<td>−0.67</td>
</tr>
<tr>
<td>Na/K</td>
<td>3.09*</td>
<td>1.00</td>
<td>−3.36</td>
</tr>
<tr>
<td>BMI</td>
<td>25.0*</td>
<td>23.0</td>
<td>−1.55</td>
</tr>
<tr>
<td>High alcohol</td>
<td>≥300 ml/wk†</td>
<td>1–299 ml/wk</td>
<td>−2.81</td>
</tr>
<tr>
<td>Improved levels of both Na/K and BMI</td>
<td>. . .</td>
<td>. . .</td>
<td>−4.91</td>
</tr>
<tr>
<td>Expected difference if heavy drinkers also reduced alcohol</td>
<td>. . .</td>
<td>. . .</td>
<td>−5.33</td>
</tr>
</tbody>
</table>

*Approximate median level found in INTERSALT.
†Reported by about 15% of respondents.
Na, sodium; K, potassium; Na/K, sodium/potassium ratio; BMI, body mass index.
intake of potassium, less obesity, and avoidance of heavy alcohol consumption are based on the judgment that these factors are causally related to blood pressure. The estimates relate to the expected effect of a lifetime exposure at improved levels of these factors.

Table 2 translates the coefficients derived from the INTERSALT data into an estimated decrease of population SBP if, for example, by progressive improvement, average daily sodium were lower by 100 mmol and potassium were higher by 15 mmol, with a sodium/potassium ratio of 1.00 (instead of the 3.09 observed in the INTERSALT study). Average systolic pressure would be lower by an estimated 3.4 mm Hg. If BMI were also lower by 2 units (approximately 13 lb or 6 kg), population mean SBP could be lower by approximately 5 mm Hg. If heavy drinkers (about 15% of the population) also moderated alcohol intake, the improved level of all these lifestyle factors could yield an average population SBP lower by more than 5 mm Hg.

The difference in slope of blood pressure with age with lower sodium intake can also be calculated, based on the coefficient from the cross-center ecological analysis. With a daily sodium intake lower by 100 mmol, average population increase in SBP from age 25 to 55 years would be less by an estimated 9 mm Hg.

**Estimated Effect on Mortality of Lower Population Systolic Blood Pressure**

Since INTERSALT was a cross-sectional study, one must turn to long-term follow-up studies of defined populations to assess the impact on mortality of a reduction in population average pressure through improved lifestyles. Estimated effects on risk of death with lower pressures were obtained from several large longitudinal population studies: Framingham, Whitehall, Chicago Heart Association, Western Electric, and Multiple Risk Factor Intervention Trial (MRFIT) Primary Screenees (References 33–36 and personal communication with Martin Shipley in 1989). Follow-up was from 6 years (MRFIT) to 19 years (Western Electric). In these studies, the multivariate coefficients expressing the relation of systolic blood pressure to subsequent mortality were similar and were therefore averaged for each of three mortality end points—coronary heart disease, stroke, and all causes. These combined coefficients were then used to estimate percentage reductions in mortality corresponding to the lower blood pressure levels described above. Results are displayed in Table 3. The difference in mortality estimated for each 2 mm Hg difference in SBP is about 4% for coronary heart disease, the most common cause of death, and about 6% for stroke. Thus, seemingly small differences in population average pressure can mean notable differences in population mortality.

These projected reductions in mortality risk can be used to estimate the potential number of lives saved in particular countries (Table 3). For example, based on the published death data for US men and women age 45–64 years in 1985, a 3% decrease of total mortality (corresponding to a 2 mm Hg lower average population SBP) could mean 11,800 fewer annual deaths; a 4% reduction could mean 15,800 fewer deaths; and a 7% reduction in mortality could mean 27,600 fewer deaths in that age group alone in a single year.

These same calculations for England and Wales (with a similar all-cause death rate but a population about one quarter that of the United States) showed a potential annual reduction of 2,900, 3,900, and 6,800 deaths from all causes, in the group 45–64 years of age in 1985, if population SBP were lower by 2, 3, or 5 mm Hg, respectively. The INTERSALT data also permit an estimate of the effect on mortality of a smaller increase of blood pressure with age (9 mm Hg smaller increase in SBP from age 25 to 55 years with a 100 mmol/day lower lifetime sodium intake). This corresponds, by age
55 years, to a reduction in mortality rates of 16% for coronary heart disease, 23% for stroke, and 13% for death from all causes.

It is probable that for a variety of reasons, mainly methodological, the quantitative estimates, derived from the INTERSALT data, of the size of the associations (e.g., of sodium and potassium intake with blood pressure, and therefore the impact of these lifestyle variables on mortality) are likely to be too low. These reasons include:

1. A single 24-hour urine collection is a weak method of quantifying habitual intake that, because of day-to-day individual variability, can result in misclassification of individuals. The adjustments that were made based on within-study reliability (from repeat urine collections in an 8% subsample) probably do not completely eliminate the underestimation of associations with use of a single 24-hour collection.

2. Despite all precautions, completeness of urine collection must still have varied, tending to reduce true associations.

3. The study was cross-sectional, relating current levels of explanatory variables to current blood pressure. It is likely that exposure from childhood onward is important, and lifetime exposure is here unknown.

4. Many populations in the study (e.g., those in Japan and the United States) have been part of medical care and health efforts against high salt intake. This would also introduce bias if hypertensive individuals were selectively reducing sodium intake. In fact, among the 1,732 hypertensive persons included in the INTERSALT study, 36% reported reduced salt intake, compared with 16% of the normotensive persons. Recent changes in intake would also tend to mask any effects related to lifetime exposure.

5. Some individuals in the study (in some centers the majority of the older people) were on antihypertensive medication, and hence blood pressures as measured were artificially low. This again would lead to underestimation of the correlates of blood pressure.

For reasons not fully explicable from the study data, the associations observed for diastolic pressure were weaker and less consistent than for systolic pressure. This might relate to the greater ease and accuracy in identifying the systolic sound. In any case, systolic pressure is predictive of morbidity and mortality in population studies independent of diastolic pressure; thus, it is reasonable to use the INTERSALT coefficients for SBP and lifestyle for prediction of risk.

We conclude that our estimates of the effects of these lifestyle variables on population blood pressure are conservative; the potential impact on mortality is nonetheless considerable.

Who Needs to Be Concerned About Lifestyle and Blood Pressure?

Improved levels of sodium, potassium, body weight, and alcohol—and thereby of blood pressure—are desirable goals not solely for those with hypertension, who are at highest risk. Excess risk related to blood pressure is also present for a majority of middle-aged persons in such countries as the United States and the UK. Across virtually the whole range, risk is related to blood pressure in a progressive, graded manner. For example, in the MRFIT follow-up of 348,000 middle-aged, screened men, if the coronary heart disease death rate for the lowest blood pressure stratum (SBP less than 115 mm Hg) had prevailed for the entire cohort, then the total number of coronary heart disease deaths would have been reduced by 46%. Of the excess deaths attributable to SBP above optimal levels, 28% were in the group with baseline SBP 115–139 mm Hg, almost one half were in the group at 140–159 mm Hg, and less than one third were in the group with levels of 160+ mm Hg. Only 15% of the men had systolic blood pressure less than 115 mm Hg, the level associated with the lowest coronary mortality.

Thus, the blood pressure problem in populations has two parts: the problem of those already hypertensive, and the excess risk in the much higher number of persons described as nonhypertensive but with pressure above optimal levels. Therefore, the goal of more desirable dietary patterns in regard to sodium, potassium, alcohol, and calorie balance is a matter not only for hypertensive patients but also for the majority of the population with blood pressures above optimal levels. The study finding of a significant association between these dietary factors and SBP in normotensive as well as hypertensive individuals adds weight to this conclusion.

Prevalence of hypertension is highly correlated with a population mean or median blood pressure; in the INTERSALT study, in the five centers with median SBP of 125 mm Hg or higher, more than one quarter of those examined were hypertensive (Table 4). In contrast, hypertension was markedly lower in the centers with the lowest median blood pressure. A reduction in average population blood pressure could be expected to reduce the prevalence of hypertension. Thus, improved lifestyle patterns relate to both components of the population blood pressure challenge.

INTERSALT data also help put the issue of salt sensitivity in a more appropriate framework. There

### Table 4. Median Systolic Blood Pressure in INTERSALT Centers and Percent Hypertensive at Different Median Levels

<table>
<thead>
<tr>
<th>Center median SBP (mm Hg)</th>
<th>Average median</th>
<th>Centers (no.)</th>
<th>Average percent hypertensive*</th>
</tr>
</thead>
<tbody>
<tr>
<td>95.0–109.9</td>
<td>105.3</td>
<td>7</td>
<td>5.2%</td>
</tr>
<tr>
<td>110.0–114.9</td>
<td>112.5</td>
<td>7</td>
<td>12.2%</td>
</tr>
<tr>
<td>115.0–119.9</td>
<td>117.2</td>
<td>17</td>
<td>15.8%</td>
</tr>
<tr>
<td>120.0–124.9</td>
<td>122.3</td>
<td>16</td>
<td>23.1%</td>
</tr>
<tr>
<td>125.0+</td>
<td>127.2</td>
<td>5</td>
<td>26.8%</td>
</tr>
</tbody>
</table>

* Systolic blood pressure (SBP) ≥140 mm Hg, or diastolic ≥90 mm Hg, or treated with antihypertensive medication.

† If the four remote low sodium centers are excluded, percent hypertensive is 10.0.
is very likely a varying response of individuals to sodium. But it is most unlikely that salt sensitivity can explain why populations differ widely in average blood pressure or prevalence of hypertension. It is not reasonable to believe that differing population levels of salt sensitivity explain why the INTERSALT study found hypertension present in only 1% of the Xingu sample (Brazil) but in 31% of the Hungarian sample. More plausible reasons are the differences in sodium intake (6 mmol/day in Brazil vs. 190 mmol/day in Hungary), the differences in body mass index (23.1 vs. 25.8), and the differences in prevalence of alcohol drinking (0 vs. 58%). Similarly, differing levels of salt sensitivity are an unlikely explanation for the finding that one population sample in China (Tianjin) had almost twice as much hypertension as another (Beijing) (15 vs. 8%) and had an average systolic pressure 10 mm Hg higher. Again, a more reasonable explanation is the finding that the Tianjin sample had a 25% higher sodium intake than the Beijing sample, as well as a higher BMI and alcohol intake. On a population basis, the INTERSALT data indicate that improved levels of these lifestyle variables are likely to result in lower average population blood pressure (and therefore lower prevalence of hypertension), despite individual variability.

Are Lower Average Population Sodium/Potassium Ratio, Less Obesity, and Lower Alcohol Intake Realistic Long-term Goals?

Both the study data and current nutrition trends indicate that such goals are achievable once based on a concerted public health effort, with interim goals determined by conditions in each country.

Lower sodium intake. In every center in the present study, many individuals were already near the goals described here, at least at the time of the study. In more than half of all centers at least 15% had a daily sodium output less than 100 mmol. About 20% of all participants reported some reduction in salt intake. This, with the expanded availability and sale in several countries of lower sodium products, indicates a widespread interest among the public and a growing part of the food industry to decrease sodium consumption. Commercial addition of salt in food processing and discretionary personal addition of salt in cooking and at table are the main sources of salt intake in most populations, and these are all amenable to progressive change.

Increased potassium intake. Eight INTERSALT centers had a mean daily excretion of 70 mmol potassium or more. In an additional 18 centers, 70 mmol was only 1 SD away from the center mean, indicating that approximately 15% were at 70 mmol or higher when the urine sample was collected.

Sodium/potassium ratio. A sodium/potassium ratio of 1.0 or less was, in fact, recorded by at least some participants in most INTERSALT centers. For most populations, it is unlikely that average daily potassium intake will be increased much above 70–80 mmol, and therefore achievement of the lower sodium/potassium ratio will depend mainly on lowering sodium intake.

Avoidance of obesity. A high prevalence of obesity, including obesity in childhood, is relatively new historically and is not now universal. In the INTERSALT study, nine of the 52 centers had a mean BMI of 23.0 or lower, and almost all the remaining centers had 15% or more of individuals at that level. In regard to weight loss, there is some evidence from intervention trials that moderate sustained reduction is possible. US population surveys indicate that the modest reductions in weight achieved in recent years have occurred mainly among the more educated and affluent; among other adults average weight has increased. Thus, this aspect of improving lifestyle continues to be difficult. It may be crucial to start early in childhood to establish more favorable dietary and exercise patterns in all social strata.

Alcohol intake. Excessive alcohol intake remains a difficult problem in many countries, but there are indications of progress in its control. In the United States, for example, after many years of an increase in average alcohol consumption, there is some evidence of a decrease. Average population alcohol intake has been found to relate to the prevalence of excess drinking, so that a reduction in average alcoholic intake is a possible—and perhaps necessary—means to influence the high end of the distribution. A recent trial in the UK found that personal physicians can significantly influence drinking behavior.

Are Population Changes in These Aspects of Lifestyle Safe?

Few would disagree that reduction in high alcohol intake, or avoidance of overweight through improved nutrition and regular exercise, are generally safe recommendations. A potassium intake of 70 mmol or more daily is already the norm in many countries and for many individuals in most countries. Patients in whom it could be harmful (such as those with renal failure) are likely to be under regular medical care and dietary guidance.

It is clear that in most countries present average sodium consumption is many times greater than physiological need. Throughout our main evolutionary history, humans lived under conditions where addition of salt to food was virtually unknown. In the present study, populations such as the four centers with very low sodium intake engaged in normal daily activities, including a level of physical activity higher than in most other study populations. As in all public health recommendations, there will be exceptions—for example, the temporary need for higher salt intake where there is a great deal of sweating (such as for the marathon runner). But a recommendation to reduce the aver-
Average sodium intake should be reduced substantially over time. Availability of commercial products lower in sodium, health education to promote less addition of salt in cooking and at table, and efforts starting in infancy and childhood to provide a lower sodium diet, should be encouraged. There should be encouragement of increased consumption of fruits, vegetables, and other natural foodstuffs with high potassium content. A sodium/potassium ratio of 1.00 should be a long-term goal.

Avoidance of obesity, beginning in childhood, through balance of caloric intake and appropriate physical activity, should be promoted. All possible steps should be taken to avoid heavy alcohol consumption, including appropriate measures among young people. Public policy commitment, allocation of adequate resources, professional and consumer support, agriculture and industry cooperation, are all part of the public health effort needed to accomplish these long-term goals. Their achievement through relevant and realistic programs (local, regional, and national) can make an important contribution to reduction of unnecessary cardiovascular disease.

Acknowledgments
Although this paper represents the personal views of the Principal Investigators and Co-Investigators in the two INTERSALT Coordinating Centers (Chicago and London), we wish to acknowledge the study leadership bodies, the local investigators, and the financial supporters who made INTERSALT possible. The study was launched under the auspices of the Council on Epidemiology and Prevention of the International Society and Federation of Cardiology (ISFC).

Appendix
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KEY WORDS • INTERSALT study • blood pressure • electrolytes • body mass index • alcohol
INTERSALT study findings. Public health and medical care implications.
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Hypertension. 1989;14:570-577
doi: 10.1161/01.HYP.14.5.570

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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