Salt and Blood Pressure: Conventional Wisdom Reconsidered

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Abstract

The "salt hypothesis" is that higher levels of salt in the diet lead to higher levels of blood pressure, with attendant risk of cardiovascular disease. Intersalt was designed to test the hypothesis, with a cross-sectional study of salt levels and blood pressures in 52 populations. The study is often cited to support the salt hypothesis, but the data are somewhat contradictory. Thus, four of the populations (Kenya, Papua, and two Indian tribes in Brazil) have very low levels of salt and blood pressure. Across the other 48 populations, however, blood pressures go down as salt levels go up—contradicting the salt hypothesis. Regressions of blood pressure on age indicate that for young people, blood pressure is inversely related to salt intake—another paradox.

This paper discusses the Intersalt data and study design, looking at some of the statistical issues and identifying respects in which the study failed to follow its own protocol. Also considered are human experiments bearing on the salt hypothesis. The effect of salt reduction is stronger for hypertensive subjects than normotensives. Even the effect of a large reduction in salt intake on blood pressure is modest, and publication bias is a concern.

To determine the health effects of salt reduction, a long-term intervention study would be needed, with endpoints defined in terms of morbidity and mortality; dietary interventions seem more promising. Funding agencies and medical journals have taken a stronger position favoring the salt hypothesis than is warranted by the evidence, raising questions about the interaction between the policy process and science.

Key words

Salt, Blood pressure, Diet, Intersalt, Publication bias.

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INTRODUCTION

It is widely believed that dietary salt leads to increased blood pressure, and higher risks of heart attack and stroke. This is the "salt hypothesis." The corollary is that salt intake should be drastically reduced. There are three main kinds of evidence: (i) animal experiments, (ii) observational studies on humans, and (iii) human experiments. Animal experiments are beyond the scope of the present paper, although we give a telgraphic summary of results. A major observational study cited by those who favor salt reduction is Intersalt (1986, 1988). Intersalt is the main topic of the present paper, and we find that the data do not support the primary hypotheses of the study. The other major observational study is Smith et al. (1988), and this too contradicts the salt hypothesis.

There have been many intervention studies on humans, and several meta-analyses. Although publication bias is a concern, the experiments do suggest some reduction in blood pressure for hypertensive subjects from aggressive reduction in salt intake; the effect for normotensives is smaller. Recently, the DASH studies manipulated diet and salt intake. Both have an effect, and there is an interaction. Intervention studies on humans are a second topic of our paper. To document the effect of salt reduction on morbidity or mortality, much larger intervention studies would be needed, with much longer followup. This point is discussed too. Finally, implications for policy analysis are noted.

Animal Studies

Rodents, the best-studied species, show strain-specific effects of salt intake on blood pressure. In some strains, a diet high in salt leads to a marked increase in pressure; but in other strains, there is no effect. Studies of non-human primates, which are more limited, suggest that some animals are salt-sensitive and some are not. In other words, for some animals, blood pressure increases when salt is added to the diet; for other animals, there is no response.

THE INTERSALT STUDY

Intersalt was an observational study, conducted at 52 centers in 32 countries; about 200 subjects age 20–59 were recruited in each center. The two Brazilian centers were Indian tribes, the Yanomamo and Xingu. There was a center in Kenya, and one in Papua New Guinea. In Canada, there were centers in Labrador and in St. John's (Newfoundland). In the United States, there was a center in Hawaii, a center in Chicago, and four centers in Mississippi.

Blood pressure (systolic and diastolic) was measured for each subject, along with urinary sodium and potassium (mmols/24 hrs), and various confounders such as body mass index (weight/ height^2). Other confounders (like alcohol consumption) were obtained by questionnaire. Replicate urine measurements were obtained for a sub-sample of the subjects. Table 1 indicates some of the data available for the various centers; units are explained below.

Within each center, the subjects' blood pressures were regressed on their ages: the slope of the resulting line indicates how rapidly blood pressure increases with age. (Complications will be discussed later.) Slopes were then correlated with salt levels across centers.

The correlation was significant, and seems to be the major finding of Intersalt—as well as the basis for much advice to restrict salt intake.

In each center, the subjects' blood pressures were also regressed on their urinary salt levels. The within-center regression coefficients were variable, some being positive, some negative, and some insignificant. Within-center regression coefficients were "pooled"—averaged—across centers, with weights inversely proportional to estimated variances. Generally, the within-center coefficients were adjusted for age and sex; sometimes, for age, sex, body mass index, alcohol, and potassium intake; the likely size of measurement error in urinary salt was estimated from the replicate measurements, and statistical procedures were sometimes used to adjust results of cross-center regressions for measurement error.

Pooled results were highly significant, especially after correction for measurement error. The estimated effect of salt on blood pressure depends on the statistical adjustments: reduction of salt amounting to 100 mmol per day is estimated to lead to a reduction in systolic pressure in the range from 1 to 6 mm Hg; for diastolic pressure, the estimated reduction ranges from .03 to 2.5 mm Hg. See Intersalt (1988, Table 1) and Elliott et al. (1996, Table 1). By way of comparison, the urinary salt level in the Chicago center was 134 mmol, not far from the current U.S. average; a reduction of 100 mmol gets down to the level in Kenya or Papua New Guinea (Table 1).

Table 1. Intersalt data on systolic blood pressure. Selected centers. Median urinary salt (mmol Na/24 hrs); median blood pressure (mm Hg); slope of blood pressure on age (mm Hg/yr); slope of blood pressure on urinary salt (mm Hg/mmol Na/24 hrs).

	Na	BP	BP on Age	BP on Na
Yanomamo, Brazil	0.2	95	.079	−.173
Xingu, Brazil	6	99	.052	−.037
Papua New Guinea	27	108	.149	+.037
Kenya	51	110	.206	+.033
⋮	⋮	⋮	⋮	⋮
Hawaii	130	124	.638	+.044
Chicago	134	115	.287	+.001
Labrador	149	119	.500	+.043
⋮	⋮	⋮	⋮	⋮
Tianjin, PRC	242	118	.640	+.035

NOTES: Na is sodium, BP is blood pressure, mmol is millimole, and mm Hg is millimeters of mercury.

Units for Salt and Blood Pressure

The units in Table 1 may be unfamiliar and irritating, but they are standard in the field. Relatively little salt intake is retained or excreted other than in the urine, and dietary measurements are quite troublesome, so intake is measured by urinary excretion. Table salt is sodium chloride (NaCl), and urinary salt levels are measured in terms of sodium content, by weight. The unit of weight is the millimole (mmol), that is, 1/1,000 of the gram molecular weight. Sodium (Na) has atomic weight nearly 23; so a mole of Na weighs 23 grams, and 1 gram of Na is $1/23 = .0435$ moles $= 43.5$ mmols. A dietary intake of 2.5 grams per day of table salt corresponds to 1 gram per day of sodium and 43.5 mmols per day of urinary sodium excretion; the other 1.5 grams is the chlorine. By way of calibration, a typical American dietary intake is 8.5 grams per day of salt, which corresponds to $8.5/2.5 = 3.4$ grams per day of sodium, and $3.4 \times 43.5 \doteq 150$ mmols per day of urinary sodium.

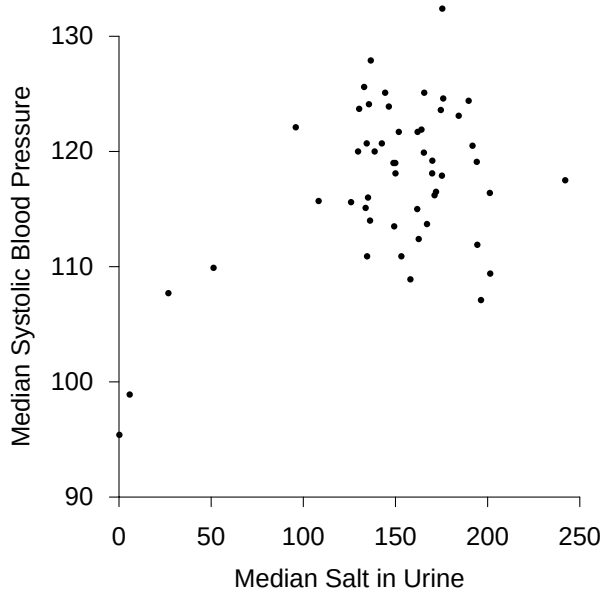
BP is blood pressure, measured in two phases—systolic and diastolic. The systolic phase corresponds to blood being pumped out of the heart, and the pressure is higher; the diastolic phase corresponds to blood flowing back into the heart, and pressure is lower. Pressure is measured relative to the height of a column of mercury; units are millimeters of mercury (mm Hg). Average U.S. systolic pressure for persons over the age of 18 is about 125 mm Hg; average diastolic pressure is about 75 mm Hg: standard deviations are about 20 and 12, respectively. Averages and standard deviations for BP are computed from NHANES III—the third replication of the National Health and Nutrition Examination Survey. Each replication is based on a large probability sample of the U. S. population; subjects fill out questionnaires describing diet, socio-economic status, and so forth; they also undergo a thorough medical examination. (The NHANES data will come up again, later.)

A blood pressure of 140/75 means 140 systolic and 75 diastolic. "Normotensive" persons have normal blood pressures, and "hypertensives" have high blood pressures. Precise definitions vary from one study to another, but 160/95 would generally be considered diagnostic of hypertension. In some studies, even 140/90 would be classified as hypertension.

Patterns in the INTERSALT Data

The correlational pattern across the Intersalt centers between salt level and blood pressure is complex, and has not received the attention it deserves. Figure 1 plots the median systolic blood pressure against the median level of urinary salt. The data are clearly non-linear, because there are four outliers—centers with extremely low levels of salt and BP. These are the two Brazilian tribes, Papua New Guinea, and Kenya; see Table 1. The four outliers show the expected upward trend. In the other 48 centers, the trend is downward, although not significantly. (The adjustments contemplated by Intersalt create a positive slope, but significance is not achieved; with 48 points, adjusted slope is .0251 and $P = .33$; if all 52 points are used, adjusted slope is .0446 and $P < .01$; Intersalt 1988, Figure 3.)

Figure 1. Systolic blood pressure vs urinary salt. Intersalt data, median levels. Excluding the two Brazilian tribes, Papua New Guinea, and Kenya, the trend is downward but not significant ($n = 48, r = -.14, P = .34$, two-sided).



NOTES: The units for the horizontal axis in Figures 1–6 are mmols per day of urinary sodium—not sodium chloride. The data are from summary statistics reported by Intersalt (1988, Appendix I).

Figure 2. Rate of increase of systolic blood pressure with age, plotted against the median level of salt in the urine for subjects at that center. Intersalt data. Even in the 48 centers, there is a significant upward trend ($n = 48, r = .27, P = .05$, two-sided).

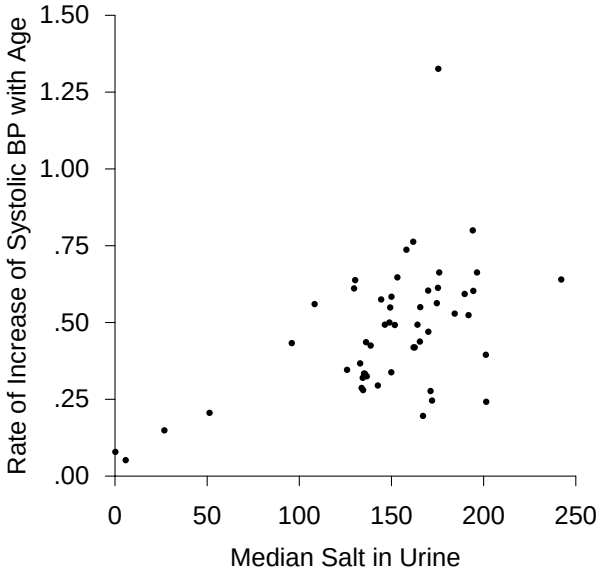


Figure 2 plots the rate of change of systolic blood pressure with age at each center, against the median level of urinary salt. There is a significant, positive relationship: at centers with higher levels of salt, systolic blood pressure generally increases more rapidly with age. In combination, however, Figures 1 and 2 lead to a paradox. For each study center, the regression line of blood pressure on age must pass through the middle of the scatter diagram, so that blood pressure at middle age should equal the average blood pressure. Thus, at middle age, there is at best no cross-center relationship between salt and blood pressures (Figure 1). Since blood pressure increases more rapidly in the centers with higher salt levels (Figure 2), it follows that young people in the high-salt centers must have lower blood pressures than their counterparts in the low-salt centers.

Figure 3. Estimated systolic blood pressure at age 20 plotted against median urinary salt levels. In the 48 centers—excluding the two Brazilian tribes, Papua New Guinea, and Kenya—there is a downward trend, which is significant ($n = 48, r = -.31, P = .02$, two-sided).

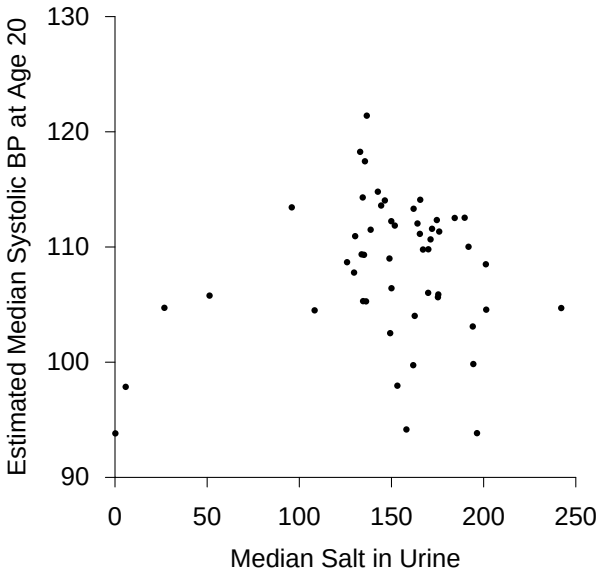


Figure 3 makes the paradox more vivid. The figure plots estimated systolic blood pressure at age 20 in the various centers, against the levels of urinary salt. Excluding the four outliers, the relationship is negative and significant. If dietary advice is to be drawn from these data, it would seem to be the following. Live the early part of your life in a high-salt country, so your blood pressure will be low as a young adult; then move to a low-salt country, so your blood pressure will increase slowly. The alternative position, which seems more realistic, is that differences in blood pressures among the Intersalt study populations are mainly due to uncontrolled confounding—not variations in salt intake.

The underlying Intersalt data do not seem to be available (as discussed below), so Figure 3 involves certain approximations. (i) The average age at each center is taken as the midpoint of the age range, namely, 40. (ii) Blood pressure at age 20 in each center can then be estimated as the overall median at that center, less 20 times the slope of blood pressure on age. Theoretically, of course, regression adjustment should be based on arithmetic averages: if y is regressed on x, the regression line goes through the point of averages $(\overline{x}, \overline{y})$. Medians are used as in Intersalt (1988), but there would be little difference in results if means were used.

Figures 4, 5, and 6 repeat the analysis for diastolic pressure, with similar results. In Figure 4, the downwards slope among the 48 centers is significant; after adjustments recommended by Intersalt (1988, Figure 4), the slope is still downwards, although it is no longer significant. In Figure 5, the slopes of diastolic blood pressure on age are strongly related to salt levels. In Figure 6, the downwards slope among the 48 centers is highly significant: for young people in those centers, estimated diastolic blood pressure is negatively related to salt intake, contradicting the salt hypothesis.

Generally, the Intersalt investigators favor results obtained by combining data from all 52 centers. Any such analysis, however, merely underlines what is obvious from the scatter diagrams: subjects in the four low-salt centers have much lower blood pressures than subjects in the other 48 centers, and slower increase of blood pressure with age.

Figure 4. Diastolic blood pressure vs urinary salt. Intersalt data, median levels. In the 48 centers—excluding the two Brazilian tribes, Papua New Guinea, and Kenya—the downward trend is significant ($n = 48, r = -.31, P = .02$, two-sided).

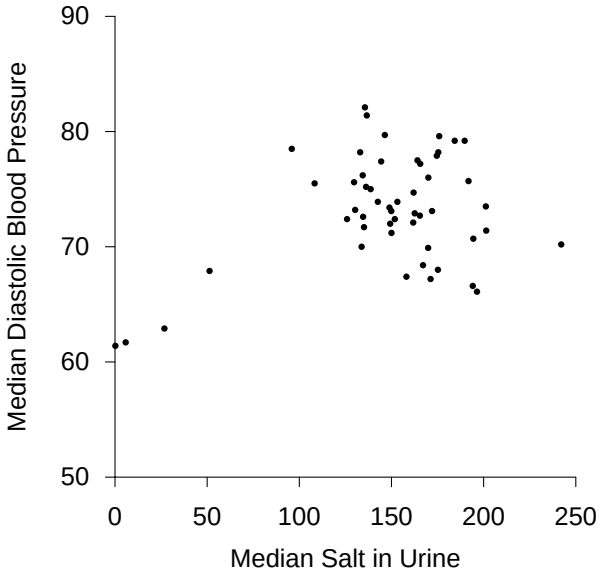


Figure 5. Rate of increase of diastolic blood pressure with age, plotted against the median level of salt in the urine for subjects at that center. Intersalt data. Even in the 48 centers—excluding the two Brazilian tribes, Papua New Guinea, and Kenya—there is a highly significant positive trend ($n = 48, r = .40, P < .01$, two-sided).

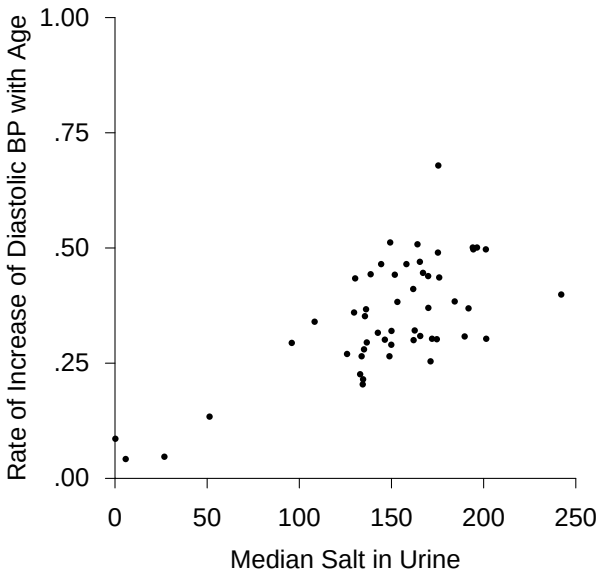
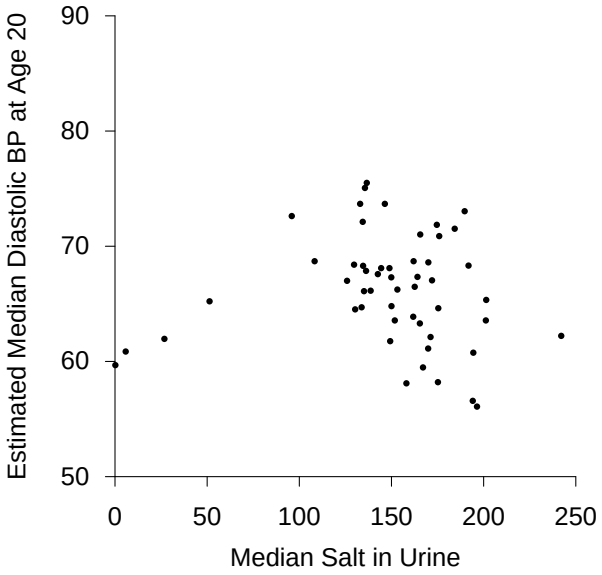


Figure 6. Estimated diastolic blood pressure at age 20 plotted against median urinary salt levels. In the 48 centers—excluding the two Brazilian tribes, Papua New Guinea, and Kenya—there is a downward trend which is highly significant ($n = 48, r = -.42, P < .01$, two-sided).



P-values

The Intersalt investigators use P-values to assess their results; we follow suit, although the interpretation of P may be somewhat problematic in these contexts. (i) The 48 study centers might be viewed as a random sample from some imaginary collection of potential study centers; additional statistical assumptions (such as linearity and homoscedasticity) may need to be imposed on this hypothetical superpopulation, depending on the analysis that is to be rationalized. (ii) It might be assumed that the data were generated in accordance with some linear regression model, with a null hypothesis specifying that a certain coefficient vanishes. Although options (i) and (ii) have their aficionados, we find them unattractive. There is at least one other possibility: for scatter diagrams like those presented here, with the four outliers set aside, P approximates the probability of obtaining larger correlations than the observed ones—if the x- and y-coordinates are randomly paired (Freedman and Lane 1983). In any event, our test statistic was $t = \sqrt{48-2}\, r/\sqrt{1-r^2}$, referred to a normal distribution; equivalently, a straight line is fitted to the 48 points, and the slope is examined to see if it is significantly different from 0.

The Protocol

The Intersalt investigators offered a large number of analyses of the data, and have returned to the topic more than once; see Intersalt (1988), Elliott et al. (1996), and Stamler (1997). The results are not entirely consistent, and the protocol for Intersalt (1986) must now be considered.

(1) "The primary hypothesis to be tested in INTERSALT is that average blood pressure and prevalence of hypertension are linearly related across populations to the average levels of sodium intake, potassium intake (inversely) and the sodium-potassium intake ratio." p. 781

(2) "The variation in electrolyte intake across the study population is judged to be large enough to permit, as a second hypothesis, examining also these same relationships at the level of individuals, despite well known within-individual variability in such intake." p. 782

(3) "It is not expected that useful estimates will be possible ... at the level of particular study populations; but it will be possible to look at the relations in individuals across the study as a whole.... The individual and group relationships will be jointly explored by multi-level analytic techniques." p. 785

(4) Adjustment for measurement error is suggested within center but not across center, p. 783.

(5) Possible confounders include height, weight, physical activity, type of work, socioeconomic status, alcohol, family history, medication. pp. 783–84.

The primary Intersalt hypothesis—point (1) above—is rejected by the data. As Figures 1 and 4 demonstrate, average blood pressure levels are not linearly related to salt intake across the study populations: (i) the four outliers are different from the other 48 centers, and (ii) the relationship between blood pressure and salt is different in the two groups of data—positive in the first, negative in the second. The Intersalt investigators have paid comparatively little attention to prevalence of hypertension, also mentioned as a primary variable in point (1), but the relationship between prevalence and salt is much like that shown in Figures 1–6 for blood pressure and salt. With respect to potassium intake, Intersalt (1988, 324) acknowledges that "potassium was inconsistently related to blood pressure in these cross-center analyses." What they mean is that blood pressure is positively related rather than negatively related to potassium levels. In the 48 centers, $r = .40, P < .01$ for the systolic phase, and $r = .19, P = .19$ for diastolic. For all 52 centers, the correlations are .15 and .03. Dropping the four low-salt centers makes a huge difference to r, because three out of the four have very high potassium levels. In any event, the primary study hypothesis is rejected by the data, for potassium as well as sodium.

Adjusting cross-center regressions for measurement error appears to be a post hoc exercise—point (4). Pooling the within-center coefficients is also post hoc, and seems to replace more obvious regression analyses suggested by (2) and (3). The protocol (Intersalt, 1986) does not mention the idea of pooling within-center regression coefficients. Furthermore, these post-hoc analyses are of doubtful validity, even on their own terms: the weights used to compute the overall average effect depend critically on unverified assumptions about the error structure in the regressions, and there are equally unverified assumptions about the nature of the measurement error in the urine variables. (Taking an average may be harmless, but the force of the assumptions will be felt when calculating standard errors and P-values.)

No adjustment is made for measurement error in confounders such as alcohol consumption. Moreover, numerous confounders remain completely uncontrolled. Diet—apart from

its sodium content—would seem to be one major unmeasured confounding variable, as discussed below. Other potential confounders are listed in the protocol but not controlled in the data analysis, for example, physical activity, type of work, and socio-economic status—point (5). More generally, Intersalt's chief analytic idea is that people in Chicago can be converted to Yanomamo Indians by running a regression with a few control variables, a vision that will commend itself to some observers but not others.

The rate of increase of blood pressure with age versus the salt level is also a post hoc analysis. This has been acknowledged, if indirectly, by the principal figure in the Intersalt group—Stamler (1997, 634S). At scientific meetings where these issues have been raised, Intersalt investigators have responded that age by blood pressure was to have been the primary analysis, according to minutes of the working group. Their response is peculiar—what else is in those minutes? Moreover, Interalt (1988, 320) clearly states that results "were assessed both within and across centres in accordance with prior plans," citing the published protocol (Intersalt, 1986). Finally, the investigators cannot so easily brush aside the paradoxical implications of their models: for young people, blood pressure is negatively related to salt intake.

HUMAN EXPERIMENTS

This section turns to human experiments, where salt intake is manipulated and the effect on blood pressure is determined. There have been many such experiments, and three recent meta-analyses—by Midgley et al. (1996), Cutler et al. (1997), and Graudal et al. (1998). Midgley et al. and Cutler et al. both regress blood pressure reduction on salt reduction and look for a significant slope; reductions are measured by comparing data in the treatment and control conditions. Cutler et al. find significance, Midgley et al. do not. By contrast with Midgley et al., Cutler et al. force their line to go through the origin. Apparently, the decision to force the line through the origin is what leads to significance (Graudal et al. 1998, 1389).

Presumably, the idea behind the constraint is that zero reduction in blood pressure corresponds to zero reduction in salt intake. Notably, however, the control groups in the experiments generally achieve some reduction in blood pressure. Thus, zero reduction in salt intake may well have an effect, depending on attendant circumstances. Generally, confounding due to flaws in experimental design—for instance, lack of blinding—can push the line away from the origin (Cutler et al. 1997, 644S; Midgley et al. 1996, 1592–94; Graudal et al. 1998, 1389).

Table 2 shows the estimated reduction in systolic and diastolic blood pressure (mm Hg) for normotensive and hypertensive subjects, corresponding to a 100 mmol per day reduction in urinary sodium. There is a larger effect on systolic than diastolic pressure, and hypertensives are more affected than normotensives. However, agreement among the three studies is not good. Indeed, Midgley et al. and Graudal et al. report only a minimal effect for normotensives, while Cutler et al. find a bigger effect. As noted before, a typical American dietary intake is 8.5 grams per day of salt (NaCl), which corresponds to 3.4 grams per day of sodium (Na), and 150 mmols per day of urinary sodium excretion. On this scale, a 100 mmol reduction in sodium is striking.

Table 2. Estimated reduction in blood pressure (mm Hg) due to reduction in urinary sodium by 100 mmols per day; three meta-analyses.

	Normotensive		Hypertensive	
	Systolic	Diastolic	Systolic	Diastolic
Cutler et al. (1997)	2.3	1.4	5.8	2.5
Midgley et al. (1996)	1.1	0.1	3.7	0.9
Graudal et al. (1998)	0.8	0.2	3.6	1.6

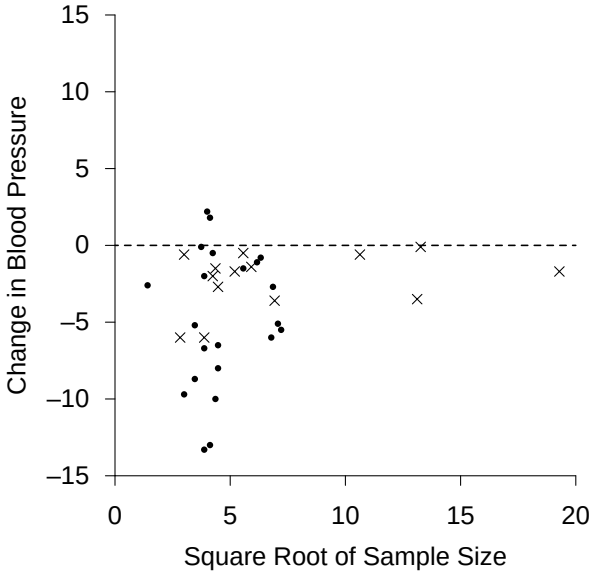
NOTES: "Normotensives" have normal blood pressure, "hypertensives" have high blood pressure.

Given the lack of concordance in Table 2, it will not come as a surprise that the three meta-analyses differ at the bottom line. Cutler et al. are strongly anti-sodium, while the other two papers are relatively neutral. Thus, Cutler et al. (1997, 648S) find "conclusive evidence that moderate sodium reduction lowers systolic and diastolic blood pressure. . . ." However, according to Midgley et al. (1996, 1590), "dietary sodium restriction might be considered for older hypertensive individuals, but ... the evidence in the normotensive population does not support current recommendations for universal dietary sodium restriction." Similarly, Graudal et al. (1998, 1383) conclude that the data "do not support a general recommendation to reduce sodium intake."

Publication Bias

Cutler et al. (1997, 648S) say there was "no indication for diastolic blood pressure from graphic and regression analysis that small negative studies were underrepresented"; for systolic blood pressure, "the graphic plot was more suggestive," although significance is not reached. Midgley et al. conclude that publication bias is evident, using a funnel plot to make the assessment. Figure 7 is a funnel plot showing changes in systolic blood pressure plotted against sample size. (Occasionally, treatment and control groups were of slightly different sizes; then the average of the two was used.) Studies on hypertensives and normotensives are represented by different symbols; data are from Cutler et al. Most of the studies find a reduction in blood pressure, plotted as a negative value. In a few studies, salt reduction leads to increased blood pressure, plotted as a positive value. The smaller studies generally find more dramatic decreases in blood pressure. The difference between estimated effect sizes in the large studies and the small ones is what indicates publication bias: unpublished small studies cannot make it into the picture.

Figure 7. Funnel plot. Studies with hypertensive subjects are marked by dots; normotensives, by crosses. Change in systolic blood pressure plotted against square root of sample size. In some studies, treatment increases blood pressure, plotted as positive values on the y-axis. Smaller studies show bigger effects, suggesting publication bias.



It may be helpful to describe the funnel plot more abstractly. The effect measure is plotted on the vertical axis and a measure of sample size on the horizontal axis. In the absence of publication bias, the graph should—because of sampling variability—have the shape of a funnel with the wide opening to the left. The tip should point to the right and center on the true effect size. The funnel should be horizontal. The large studies and the small ones should be symmetrically distributed around the true effect size. If there is bias against the publication of small studies with null results or results that are unexpected, the wide part of the funnel will be distorted. For more discussion, see Petitti (1999).

Some analysts assess publication bias by estimating the number of imaginary zero-effect trials that would be needed to change the results from significant to non-significant. If the number is large, that is evidence against publication bias. However, this "file-drawer" approach assumes that the missing estimates are centered on zero, and ignores the possibility that smaller studies with contrarian findings—significant or insignificant—are the ones that have been withheld from publication. See Rosenthal (1979), Oakes (1986), Iyengar and Greenhouse (1988), or Petitti (1999). The funnel plot seems preferable.

Another aspect of publication bias is worth mentioning. Smith (1998) notes that "the majority of RCTs were of low methodological quality and bias often tended to increase the changes observed." Swales (2000) makes a similar point with respect to nonrandomized studies, which suggest large effects and are frequently cited. For additional discussion of meta-analysis in the medical context, see for instance Shapiro (1994) and Bailar (1997, 1999).

DASH—Dietary Approaches to Stop Hypertension

DASH-1 assessed the effect on blood pressure of three diets: a control diet, a fruit-and-vegetables diet, and a combination diet; the latter was rich in fruit and vegetables, dairy products, whole grains, with limited amounts of fish, poultry, and meat. All three diets had the same moderate salt levels, 3 grams per day of sodium. The DASH-1 combination diet achieved quite striking reductions in blood pressure among hypertensive subjects (11.4 mm Hg systolic, 5.5 diastolic, relative to the control diet). See Harsha et al. (1999), Moore et al. (1999), or Appel et al. (1997).

The DASH-2 trial has a factorial design with two diets and three levels of daily sodium: 3.3 grams, 2.4 grams, and 1.5 grams. The control diet is meant to resemble what typical Americans eat; the other diet is like the DASH-1 combination diet: compare Svetkey et al. (1999). At the time of writing, data from DASH-2 are not available—not even the mean blood pressures in the $2 \times 3 = 6$ experimental groups. Details on the diets are not available either. However, the investigators did issue a press release on May 17, 2000 (http://www.nhlbi.nih.gov). The impact of salt reduction was emphasized—

> **NHLBI Study Shows Large Blood Pressure Benefit From Reduced Dietary Sodium**
>
> The lower the amount of sodium in the diet, the lower the blood pressure, for both those with and without hypertension, according to a National Heart, Lung, and Blood Institute (NHLBI)-supported clinical study.

But diet has a considerable impact too, and there are interactions. For normotensives on the DASH diet, cutting salt in half reduces systolic blood pressure only by 1 or 2 mm (Taubes 2000). It is not clear how sodium intake can be controlled at the levels indicated without changing the diets in other substantive ways. Such complications have so far been ignored. Further comment must await publication of experimental details and more detailed summary statistics.

HEALTH EFFECTS OF SALT

In essence, the Intersalt investigators argue that substantially reducing salt intake will make a small reduction in blood pressure. Other epidemiologic evidence suggests that lowering blood pressure, even by a small amount in normotensive populations, reduces the risk of heart attack and stroke. However, even if both propositions are accepted, the link between salt and risk remains to be established. See, for instance, the exchange between Psaty et al. (1999) and Temple (1999) on the general usefulness of surrogate endpoints in other contexts.

There is a huge literature on the health effects of salt; some of the more recent and salient papers will now be mentioned. Smith et al. (1988) ran a large observational study in Scotland (7354 men and women age 40–59), and found no effect of salt on blood pressure after adjusting for potassium intake. In other observational studies, Alderman et al. (1991, 1995) find risks in salt reduction; Kumanyika and Cutler (1997) disagree. Also see Graudal et al. (1998) on health risks from salt reduction. He et al. (1999) find adverse health effects

from high salt intake for overweight persons; however, for persons of normal weight, there is no association between health risks and salt intake: data are from long-term followup of subjects in NHANES I, and salt intake was measured by dietary questionnaire. Of course, with better measures of salt intake, the study might have turned out differently. Resnick (1999) stresses the role of calcium; also see McCarron and Reusser (1999).

Port et al. (2000) discuss non-linearities in risk due to blood pressure: their reanalysis of the Framingham data suggests that risk rises more slowly with increasing blood pressure among normotensives, and more rapidly among hypertensives. The U. S. Preventive Services Task Force (1996, 625) finds "There is insufficient evidence to recommend for against conseling the general population to reduce dietary sodum intake ... to improve health outcomes, but recommendations to reduce sodium intake may be made on other grounds." Taubes (1998) has a scathing review of the salt epidemiology.

To determine the effect of salt reduction—or dietary interventions—on mortality or morbidity, large-scale long-term intervention studies would be needed, and diet seems more promising. The DASH trials had a two- or three-month study period, with several hundred subjects, which is adequate only for assessing effects on surrogate endpoints like blood pressure or chemistry. Also see Graudal et al. (1998, 1389).

BACK TO INTERSALT

Hanneman (1996) notes the paradox in the Intersalt data, by estimating the blood pressure of infants. Law (1996) and Stamler et al. (1996) find this argument "bizarre" and think "it is incorrect" to extrapolate beyond the ages in the study. (Hence the decision to use age 20 in the present analysis.) The latter authors call attention to the large range in average blood pressures across centers for subjects age 50–59. The range may be large, but its relevance is obscure. More to the point, predicted blood pressures at age 60 show no relationship to salt levels, when the four outliers in the data are excluded ($n = 48, r = .04$ systolic, $r = -.10$ diastolic). If high salt intake leads to high blood pressure at old age, the correlations should be strongly positive. On the other hand, if the data are non-linear and predictions from regression models are not trustworthy, the investigators should not be using regressions to generate summary statistics, or drawing biological conclusions from model parameters.

The difficulties in correcting for measurement error are discussed by Davey-Smith and Phillips (1996), with a response by Dyer et al. (1996). MacGregeor and Sever (1996) defend Intersalt by reference to other data, but this begs a salient question: do the Intersalt data speak for or against the salt hypothesis? The Intersalt investigators have declined to make the underlying data public, "because of the need to preserve the independence of scientific investigation, the integrity of the data, and the confidentiality of information.... (Elliott et al. 1996, 1249)." We cannot see how releasing data threatens integrity or compromises scientific independence; reversing these propositions makes them more plausible. Moreover, data can be released without identifying subjects, so confidentiality need not be an issue.

Our review of the literature is no doubt incomplete in various respects, but it is sufficient to provide context for questions about the Intersalt data.

The Salt Epidemiologists Respond

The National Heart Lung and Blood Institute convened a workshop to address criticisms of the salt hypothesis (Taubes 1998). However, these criticisms are barely acknowledged in the official report on the workshop (Chobanian and Hill 2000), according to which

> ....studies show unequivocally that lowering high blood pressure can reduce the likelihood of developing or dying from CVD [coronary vascular disease]. Second, dietary factors in individuals and in the population at large have important effects on blood pressure levels, which are generally assumed to translate to CVD risk.... An abundance of scientific evidence indicates that higher sodium consumption is associated with higher levels of blood pressure. This evidence is found in animal studies, observational epidemiologic studies, and clinical studies and trials.
>
> The INTERSALT findings support similar studies that show a relationship between sodium intake and blood pressure. The discussion relative to INTERSALT emphasized that its strengths are its large sample size and sophisticated statistical analyses.... it was noted that difficult statistical issues are involved in the interpretation of the INTERSALT data.

If this is the concession, it's too subtle. And the language is hauntingly similar to Stamler's defense of his study:

> The INTERSALT results, which agree with findings from other diverse studies, including data from clinical observations, therapeutic interventions, randomized controlled trials, animal experiments, physiologic investigations, evolutionary biology research, anthropologic research, and epidemiologic studies, support the judgment that habitual high salt intake is one of the quantitatively important preventable mass exposures causing the unfavorable population-wide blood pressure pattern that is a major risk factor for epidemic cardiovascular disease. (Stamler 1997, 626S).

Next, we quote from the editors of the British Medical Journal. The sentiments seem eminently reasonable to many proponents of the salt hypothesis. Persons not in the fold may react differently.

> Like any group with vested interests, the food industry resists regulation. Faced with a growing scientific consensus that salt increases blood pressure and the fact that most dietary salt (65–85%) comes from processed foods, some of the world's major food manufacturers have adopted desperate measures to try to stop governments from recommending salt reduction. Rather than reformulate their products, manufacturers have lobbied governments, refused to cooperate with expert working parties, encouraged misinformation campaigns, and tried to discredit the evidence. (Godlee 1996, 1239).

Drafts of our paper have been circulated in the community of salt epidemiologists. Reactions can be paraphrased as follows.

> Regression coefficients should have reported, rather than correlations, and significance is obtained only because samples are small.

The regression of blood pressure on age within center doesn't indicate how rapidly blood pressure increases with age, because the data aren't longidutinal. [Fair enough, but then what were the Intersalt people doing?]

The four populations with very low exposure are no more outliers than the highest four, and the relationship *is too* linear: when a line is fitted to all 52 data points, the slope is positive and significant. [They just don't get it: they're fitting one straight line to four points that go up and 48 points that go down—in Figure 1 and again in Figure 4.]

Epidemiologists can never wait for final proof. Instead, recommendations must be made in the interest of promoting good health for the public. The effect of salt reduction may be detectable only in hypertensives, but today's normotensives are tomorrow's hypertensives. Public health guidelines to reduce sodium consumption from three grams to one gram will hurt no one, and may benefit thousands.

Epidemiologists have to make decisions based on the totality of the evidence. [But before deciding which way any particular evidence points, the salt epidemiologist has to look at all the other evidence—and the social implications.]

Access to data can distort, confuse, intimidate, and muddy the waters of medical care and public health.

In summary, the public must be protected from salt, from the machinations of industry, and above all from the data.

POLICY IMPLICATIONS

One segment of the public health community—funded by the the National Heart Lung and Blood Institute and endorsed by many journals in the field—has decided that salt is a public health menace. Therefore, salt consumption must be drastically curtailed. The force with which this conclusion is presented to the public is not in any reasonable balance with the strength of the evidence. Programs, once in place, develop a life of their own; the possibility of health benefits becomes probability, and probability becomes certainty. After all, the public is easily confused by complications, only professionals can weigh the evidence, and where is the harm in salt reduction?

The harm is to public discourse. The appearance of scientific unanimity is a powerful political tool, especially when the evidence is weak. Dissent becomes a threat, which must be marginalized. If funding agencies and journals are unwilling to brook opposition, rational discussion is curtailed. There soon comes about the pretense of national policy based on scientific inquiry—without the substance. In our view, salt is only one example of this phenomenon.

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