Intersalt: an international study of electrolyte excretion and blood pressure. Results for 24 hour urinary sodium and potassium excretion

Intersalt Cooperative Research Group

Abstract

The relations between 24 hour urinary electrolyte excretion and blood pressure were studied in 10 079 men and women aged 20-59 sampled from 52 centres around the world based on a highly standardised protocol with central training of observers, a central laboratory, and extensive quality control. Relations between electrolyte excretion and blood pressure were studied in individual subjects within each centre and the results of these regression analyses pooled for all 52 centres. Relations between population median electrolyte values and population blood pressure values were also analysed across the 52 centres.

Sodium excretion ranged from 0·2 mmol/24 h (Yanomamo Indians, Brazil) to 242 mmol/24 h (north China). In individual subjects (within centres) it was significantly related to blood pressure. Four centres found very low sodium excretion, low blood pressure, and little or no upward slope of blood pressure with age. Across the other 48 centres sodium was significantly related to the slope of blood pressure with age but not to median blood pressure or prevalence of high blood pressure. Potassium excretion was negatively correlated with blood pressure in individual subjects after adjustment for confounding variables. Across centres there was no consistent association. The relation of sodium to potassium ratio to blood pressure followed a pattern similar to that of sodium. Body mass index and heavy alcohol intake had strong, significant independent relations with blood pressure in individual subjects.

Introduction

Evidence relating sodium intake to blood pressure comes from clinical observations, animal experiments, epidemiological investigations, and dietary trials. The weight of evidence favours some causal relation but there are inconsistencies. Studies of individual subjects within populations have been hampered by limited ranges of sodium intake and by large day to day variation in sodium intake and excretion.[1] Nevertheless, some have shown a significant positive association.[2-10] Several trials have disclosed significant falls in blood pressure with reduced sodium intake, but others have not.[11]

Cross sectional studies of isolated populations have found that when sodium intake is low mean blood pressure is low and that among adults blood pressure varies little with age.[12-14] In almost all other populations, with greater intakes of sodium, mean pressure is higher with age. Three reviews have concluded that there is a linear relation between sodium intake and blood pressure across diverse populations with varying levels of sodium intake.[15-17] None of these dealt with data from a systematic, organised international study; no such investigation has been done.[18] Rather, each was based on data from separate, individual studies, with unstandardised measurement of both sodium intake and blood pressure; confounding factors other than age and sex were largely ignored.

The purpose of Intersalt is for the first time to investigate in a systematic and standardised way the relations between electrolyte excretion and blood pressure based on samples from many countries and with assessment of relevant confounding variables. It is also unlike previous international studies in providing data on individual subjects as well as on populations.

This report analyses sodium excretion, potassium excretion, and sodium to potassium ratio in 24 hour urine samples in relation to blood pressure among over 10 000 men and women aged 20-59, taking body mass index and alcohol intake into consideration as confounding variables. Emphasis is placed on electrolyte effects because this was the reason for the study: the important independent effects of body mass index and alcohol will be fully reported later. Relations are examined both within and across the 52 study populations.

Methods

FIELD METHODS

The design of the study and methods have been detailed elsewhere.[19] Briefly, 52 centres from 32 countries participated. Each centre was asked to recruit 200 men and women aged 20-59, 25 in each of eight age and sex groups. Whenever possible the samples were selected at random from population lists or by chunk sampling of defined populations. The population bases included electoral registers, factory or hospital workers, and whole village or island communities. Investigators were trained in standardised field methods at one of five training meetings held around the world. Field methods were described in detail in a manual of operations.[20]

Whenever an unacceptable report—for example, an incomplete urine collection—was identified during data collection the centre was asked to recruit an extra (supplementary) participant from the same age and sex group in strict order of random allocation. This was to facilitate the goal of 200 analysable reports per centre; occasionally, however, fewer than 200 were available. Thus reports were received on 10 648 eligible participants, of whom 569 (5·3%) were excluded, 568 because of problems with the urine collection or forms and one because of incomplete blood pressure measurement. Data on the remaining 10 079 participants (5045 men, 5034 women) are presented; 807 participants chosen at random completed second visits at which blood pressure was remeasured and a repeat 24 hour urine specimen collected.

Blood pressure (sitting) was measured twice with a Hawksley random zero sphygmomanometer[21] with a false zero range of 0-20 mm Hg and the bell

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A full list of participating centres and investigators is given at the end of this paper

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of a Littmann stethoscope. For 30 minutes before measurement participants refrained from eating, smoking, or strenuous activity; they then emptied their bladders and sat quietly for five minutes. A range of cuffs was used to allow for differing arm circumferences. Diastolic pressure was recorded when sounds disappeared (phase V).

Participants were asked to provide both a casual ("spot") urine specimen and a 24 hour urine collection. Standard 1 litre wide mouthed plastic jars were supplied, with a funnel for women, boric acid being used as a preservative. Participants were instructed carefully on the need to collect all urine passed during 24 hours; both the start and end of the collection took place at the examination centre under supervision of clinic staff so as to get exact timing of the collection and eliminate overcollection. At the end of the collection period completeness was assessed by a standardised interview. The height of urine in each jar was measured on a standard platform and scale and later converted into volume by computer in London. Aliquots were refrigerated at 4°C within 24 hours and frozen at −20°C within seven days, then shipped frozen to the central laboratory in Louvain, Belgium.

Height and weight were measured twice, a Stadiometer and beam balance scale being used when possible. Daily intake of alcoholic drinks over the preceding seven days was assessed by questionnaire and converted into volume of absolute alcohol based on local information. The questionnaire also included history of hypertension, current medicines (antihypertensive agents, oral contraceptives, other drugs), education, social state, and changes in diet (including salt intake). When necessary data forms and the questionnaire were translated into the local language and checked by back translation into English. Ambient temperatures outdoors and indoors were recorded.

STUDY ORGANISATION, DATA PROCESSING, AND QUALITY CONTROL

The executive committee has overall responsibility. Coordinating centres at the London School of Hygiene and Tropical Medicine (department of epidemiology) and the Northwestern University Medical School, Chicago (department of community health and preventive medicine) were responsible for the methodology and for enlisting and training investigators. All data forms were sent to London for review, edit, coding, data entry, and analysis. They were checked on receipt for completeness and consistency, queries being referred back to local centres for clarification or correction. The London centre also reviewed each field unit's recruiting documents and urine collection registers as a further check on sampling procedures and data completeness and accuracy. All data were entered twice into the computer. A random 5% of forms were double coded.

URINE ANALYSES

All analyses were carried out by the central laboratory, St Rafäel University, Louvain (department of epidemiology). Sodium and potassium were analysed by emission flame photometry,[22] calcium and magnesium by atomic absorption flame photometry,[23] and creatinine by the Jaffé method.[24] Reference samples were created at the start of the study and included in each day's analyses to check laboratory variation. Quality control was monitored in London by comparing results on anonymous duplicate (split) samples sent to the laboratory under different numbers unknown to the laboratory. Technical error of the laboratory measurements, based on split samples, was calculated for each centre from the formula $\sqrt{(\Sigma d^2/2N)}$, where d is the difference between a pair of measurements and N the number of split pairs. Percentage technical error for each centre (defined as 100 times technical error divided by the mean value of the split samples) was then calculated and averaged over the centres, weighted by N. The averaged percentage technical errors were 1·4% (sodium), 1·9% (potassium), 5·0% (calcium), 3·1% (magnesium), and 2·3% (creatinine).

Laboratory quality control procedures disclosed a systematic underestimate of about 10% in the measurement of sodium concentration for values above 80 mmol/l. Correction of this error did not alter conclusions, and data based on the uncorrected values are presented.

STATISTICAL METHODS

Blood pressure of individual participants was the mean of the two recorded readings. Individual electrolyte excretion was the product of electrolyte concentration in the urine and urinary volume corrected to 24 hours. Body mass index was calculated as weight divided by height squared (kg/m^2). Relations between electrolyte values and blood pressure were assessed both within and across centres in accordance with prior plans.[19] Though the protocol specified one sided hypotheses,[19] a more conservative approach was adopted for this report, two sided tests of significance being presented throughout.

In within centre analyses centre by centre linear regressions of blood pressure on sodium, potassium, and sodium to potassium ratio were calculated, adjusted for age and sex. Adjustments were also made for body mass index and alcohol intake, identified beforehand as important confounding variables, and then potassium was also included in the regression for sodium and sodium in the regression for potassium. Additional exploratory analyses were undertaken with calcium and magnesium in these models. To adjust for alcohol seven day intakes were stratified into three groups (0, 1-299 ml, and ≥300 ml absolute alcohol/week) with two 0,1 variables—that is, no alcohol intake *v* 1-299 ml/week (0,1) and no alcohol intake *v* ≥300 ml/week (0,1).

Within centre regression coefficients for blood pressure and electrolyte values were averaged (pooled) in order to yield overall study estimates, each centre coefficient being weighted by the inverse of its variance; this procedure minimised the variance of the pooled coefficient. Misclassification of individual participants due to within individual variation attenuates true associations[1] and biases regression coefficients towards zero, but corrected estimates of the regression coefficients may be obtained from data on repeat urine measurements. These data yielded coefficients of reliability for each centre and for each urine variable, calculated as the reciprocal of (one plus the ratio of within individual to between individual variances).[25] These centre specific coefficients of reliability were then pooled and the pooled regression coefficient for each urine variable corrected by dividing it by its pooled coefficient of reliability.

The cross centre analyses examined the relations between population median 24 hour urinary electrolyte values and several blood pressure variables. These included slopes of systolic and diastolic blood pressure with age; population median systolic and diastolic pressures; and population prevalence of hypertension, defined for this report as systolic pressure ≥140 mm Hg or diastolic pressure ≥90 mm Hg or use of antihypertensive agents. Medians were used instead of means because they are less affected by extreme values and skewness and, for blood pressure, they avoid bias due to antihypertensive treatment (by assuming that all patients having treatment had blood pressure in the upper half of the distribution). Means and standard deviations were also calculated. Slopes of systolic pressure and diastolic pressure with age were obtained

from regressions of individual blood pressure on age for men and women separately within each centre and then by averaging these two values.

To correct for small differences in age and sex distributions because of varying numbers of participants in the 52 centres (range 157-200) medians were calculated separately for men aged 20-39 and 40-59 and for women aged 20-39 and 40-59 and then averaged over the age and sex groups. Simple regression analyses of the resulting values were carried out unadjusted for other variables. Multiple regression analyses were also done, with adjustment for median body mass index and alcohol intake. For alcohol intake two variables were entered simultaneously into the regression models—percentage of drinkers and median alcohol intake of drinkers.

Four geographically isolated populations with very low sodium excretion and very low blood pressure strongly influenced overall cross centre associations, and so all analyses were done both for all 52 centres and with exclusion of these four. Before the data were analysed adherence of each centre to the protocol and manual of operations[20] was reviewed centrally, and nine centres were judged to have broken one or more of the less critical protocol criteria. These infringements —for example, in recruiting procedures—were not of a nature seriously to affect the study of electrolyte and blood pressure relations, and as exclusion of these nine centres did not materially alter the findings, results presented here are for all centres.

Results

DESCRIPTIVE STATISTICS

Appendices I-III give the data for the 52 centres (men and women combined). Median values of the centres for key study variables had the following ranges (appendix I): urinary sodium excretion 0·2 mmol/24 h (Yanomamo Indians of Brazil) to 242·1 mmol/24 h (Tianjin, north China); potassium excretion 23·4-81·1 mmol/24 h; sodium potassium ratio <0·01-7·27; creatinine excretion 4·0-13·5 mmol/24 h; urine volume 0·58-1·97 l/24 h. Median systolic blood pressure ranged from 95·4 to 132·4 mm Hg, diastolic pressure from 61·4 to 82·1 mm Hg, systolic blood pressure slope with age from −0·149 to 1·326 mm Hg/year, and diastolic blood pressure slope with age from −0·047 to 0·679 mm Hg/year. Prevalence of hypertension varied from nil to 33·5% and of alcohol drinkers from nil to 91·5%. Median body mass index varied from 20·0 to 30·1 kg/m^2. Appendix II gives data on centre means and standard deviations standardised for age and sex.

WITHIN CENTRE ANALYSES

Sodium excretion and blood pressure of individuals

After adjustment for age and sex sodium excretion and systolic pressure of individual participants were positively associated in 39 of the 52 centres, significantly so ($p<0·05$) in 15 (table I). Significant negative associations were found in two centres. After adjustment also for body mass index, alcohol consumption, and potassium excretion positive associations were found in 33 centres (eight significant). Regression slopes for this analysis ranged from −0·040 to 0·085 mm Hg/mmol sodium (appendix III). When these within centre regression slopes were pooled the relation of sodium to systolic pressure was positive and significant ($p<0·001$) (table I). The coefficient of reliability for sodium estimated from the repeat measures was 0·460. Thus the corrected systolic pressure—sodium coefficient (adjusted for age and sex) was the uncorrected coefficient (0·0163) divided by reliability (0·460), giving 0·0354 mm Hg/mmol sodium (table I).

After adjustment for age and sex sodium excretion and diastolic pressure were positively associated in 33 centres (significantly in four) and the pooled regression coefficient was positive and significant ($p<0·001$). Significance was lost when body mass index, alcohol intake, and potassium excretion were added to the analysis (table I).

Sodium to potassium ratio and blood pressure of individuals

The sodium to potassium ratio adjusted for age and sex was positively related to systolic pressure in 40 centres (14 significantly), and in 37 centres (eight significantly) when adjusted also for body mass index

TABLE I—*Summary of within centre associations between 24 hour urinary sodium excretion, sodium:potassium ratio, potassium excretion, and blood pressure (52 centres; all subjects)*

	Systolic pressure		Diastolic pressure	
	Adjusted for age and sex	Adjusted for age, sex, and other confounders†	Adjusted for age and sex	Adjusted for age, sex, and other confounders†
	Sodium			
No of positive coefficients	39	33	33	25
No significant ($p<0·05$)	15	8	4	3
No of negative coefficients	13	19	19	27
No significant ($p<0·05$)	2	2	1	3
Pooled regression coefficient (mm Hg/mmol)	0·0163	0·0100	0·0068	0·0003
SE	0·0023	0·0026	0·0017	0·0019
z Score	6·97***	3·79***	4·08***	0·16
Pooled regression coefficient corrected for reliability‡	0·0354	0·0217	0·0148	0·0006
	Sodium:potassium			
No of positive coefficients	40	37	31	25
No significant ($p<0·05$)	14	8	4	3
No of negative coefficients	12	15	21	27
No significant ($p<0·05$)	0	0	2	3
Pooled regression coefficient (mm Hg)	0·8097	0·6209	0·3188	0·1664
SE	0·1062	0·1045	0·0752	0·0738
z Score	7·62***	5·94***	4·24***	2·26*
Pooled regression coefficient corrected for reliability‡	2·0977	1·6085	0·8259	0·4311
	Potassium			
No of positive coefficients	24	13	29	17
No significant ($p<0·05$)	0	0	2	2
No of negative coefficients	28	39	23	35
No significant ($p<0·05$)	2	3	2	5
Pooled regression coefficient (mm Hg/mmol)	0·0012	−0·0254	−0·0020	−0·0165
SE	0·0065	0·0070	0·0048	0·0052
z Score	0·19	−3·63***	−0·41	−3·18**
Pooled regression coefficient corrected for reliability‡	0·0021	−0·0446	−0·0035	−0·0289

*$p<0·05$. **$p<0·01$. ***$p<0·001$.
†Other confounders were: (for sodium model) body mass index, alcohol consumption, and urinary potassium; (for sodium:potassium model) body mass index and alcohol consumption; and (for potassium model) body mass index, alcohol consumption, and urinary sodium.
‡Coefficient of reliability calculated from data on repeat urine measurements (see text).

and alcohol intake (table I). When the centre data were pooled the relation of the sodium to potassium ratio to systolic pressure was positive and highly significant ($p<0·001$). Though the relation of the sodium to potassium ratio to diastolic pressure was less strong, the pooled regression coefficients adjusted for age and sex and for age, sex, body mass index, and alcohol consumption were positive and significant ($p<0·001$ and $p=0·02$, respectively).

The coefficient of reliability for the sodium to potassium ratio was 0·386, which was used to correct the regression coefficients. For example, the regression coefficient of 0·6209 mm Hg relating systolic pressure to the sodium to potassium ratio (adjusted for age, sex, body mass index, and alcohol consumption) was 1·6085 mm Hg when corrected for reliability (table I).

Potassium excretion and blood pressure of individuals

Most centres showed a negative association between potassium excretion and systolic pressure, which after full adjustment was significant in three centres; none found a significant positive association. The pooled coefficient was small (positive) when only age and sex were in the model but was negative and significant ($p<0·001$) when adjusted for age, sex, body mass index, alcohol intake, and sodium excretion. The coefficient of reliability for potassium was 0·570, so that correction for reliability changed the regression coefficient for this analysis from −0·0254 to −0·0446 mm Hg/mmol potassium (table I).

For potassium and diastolic pressure most centres showed a positive association in the age and sex adjusted analysis but a negative association (significant in five centres) when body mass index, alcohol intake, and sodium excretion were also considered. For both these analyses the pooled findings showed a negative association between potassium and diastolic pressure, which was significant in the analysis adjusted for all confounders ($p<0·01$) (table I).

Within centre results were essentially unchanged by the inclusion of calcium and magnesium in the regression models (data not shown).

Body mass index, alcohol intake, and blood pressure of individuals

Pooled regression coefficients for the relations of both body mass index and heavy alcohol intake (≥300 ml/week) to systolic and diastolic pressure were highly significant in within centre multiple regressions when these included sodium and potassium excretion in the analyses (table II).

ACROSS CENTRE ANALYSES

Median 24 hour sodium excretion and slope of blood pressure with age

In the age and sex standardised analysis a significant linear relation was shown between the median 24 hour urinary sodium excretion for the 52 centres and the slope of systolic blood pressure with age. The regression coefficient was 0·0030 mm Hg/year/mmol sodium ($p<0·001$) (fig 1a).

Four isolated populations—the two Brazilian Indian (Yanomamo and Xingu), the Papua New Guinean, and the Kenyan—had the lowest urinary sodium excretion (0·2, 5·8, 26·8, and 51·3 mmol/24 h respectively) and had decreases or only small increases of systolic pressure with age (−0·079, 0·052, −0·149, and 0·206 mm Hg/year, respectively) (appendix I). The scattergrams of blood pressure variables and median sodium excretion for 52 centres suggested that these four isolated populations substantially influenced associations in linear regression and Pearson correlation analyses (see figs 1a, 2a, 3a, 4a), so analyses were repeated for 48 centres excluding these four. In addition, Spearman rank order correlation coefficients were computed as these do not assume linearity.

In the age and sex standardised analysis for the 48 centres the relation of sodium to systolic blood pressure slope with age remained positive but at a borderline level of significance ($b=0·0019$; $p=0·06$) (fig 1a). Rank order (Spearman) correlation coefficients were significant in the analyses for both 52 and 48 centres ($r=0·451$, $p<0·001$; and $r=0·305$, $p=0·03$, respectively).

Simple correlation analyses of the data for 52 and 48 centres showed that across centres body mass index and alcohol intake were significantly related to key independent and dependent variables (table III). The significant correlations among body mass index, alcohol, and blood pressure variables were all

TABLE II—*Summary of within centre associations† between body mass index, alcohol intake (1-299 ml/week and ≥300 ml/week), and systolic and diastolic blood pressure (52 centres; all subjects)*

	Body mass index†	Alcohol intake‡	
		1-299 ml/week	≥300 ml/week
Systolic blood pressure			
No of positive coefficients	51	28	35
No significant (p<0·05)	40	1	10
No of negative coefficients	1	22	13
No significant (p<0·05)	0	1	0
Pooled regression coefficient	0·7754	0·5272	3·3358
SE	0·0359	0·3536	0·5664
z Score	21·61***	1·52	5·93***
Diastolic blood pressure			
No of positive coefficients	52	26	35
No significant (p<0·05)	44	1	10
No of negative coefficients	0	24	13
No significant (p<0·05)	0	0	0
Pooled regression coefficient	0·5967	0·1138	1·9836
SE	0·0257	0·2507	0·4074
z Score	23·22***	0·45	4·86***

*p<0·05. **p<0·01. ***p<0·001.
†Adjusted for age, sex, sodium, potassium, and the two other explanatory variables—for example, body mass index adjusted for age, sex, sodium, potassium, alcohol intake 1-299 ml/week, and alcohol intake ≥300 ml/week; and alcohol intake ≥300 ml/week adjusted for age, sex, sodium, potassium, alcohol intake 1-299 ml/week and body mass index.
‡For alcohol intake regression coefficients estimate difference in blood pressure for drinkers of 1-299 ml/week and ≥300 ml/week compared with non-drinkers. There were two centres with no drinkers and two other centres with no drinkers of ≥300 ml/week.

TABLE III—*Pearson correlations of systolic blood pressure and diastolic blood pressure slopes with age, median blood pressures, prevalence of hypertension, and 24 hour urinary sodium excretion, sodium:potassium ratio, and potassium excretion with median body mass index, percentage of drinkers, and median alcohol intake of drinkers. (Cross centre analyses; 52 and 48 centres)*

	Body mass index		% Of drinkers		Median alcohol intake of drinkers	
	52 Centres	48 Centres	52 Centres	48 Centres	52 Centres	48 Centres
Systolic blood pressure slope with age	0·313*	0·115	0·182	−0·225	0·202	0·062
Diastolic blood pressure slope with age	0·155	−0·168	0·351*	−0·064	0·219	0·055
Median systolic blood pressure	0·623***	0·572***	0·541***	0·281	0·277*	0·115
Median diastolic blood pressure	0·582***	0·495***	0·437**	0·142	0·230	0·080
Prevalence of hypertension†	0·677***	0·593***	0·343*	0·016	0·168	0·014
24 Hour sodium excretion	0·096	−0·441*	0·452***	−0·022	0·136	−0·163
24 Hour sodium:potassium ratio	−0·029	−0·331*	−0·054	−0·566***	0·095	−0·087
24 Hour potassium excretion	0·022	0·024	0·362**	0·625***	−0·138	−0·071

*p<0·05. **p<0·01. ***p<0·001.
†Hypertension defined as systolic pressure ≥140 mm Hg or diastolic pressure ≥90 mm Hg or use of antihypertensive agents.

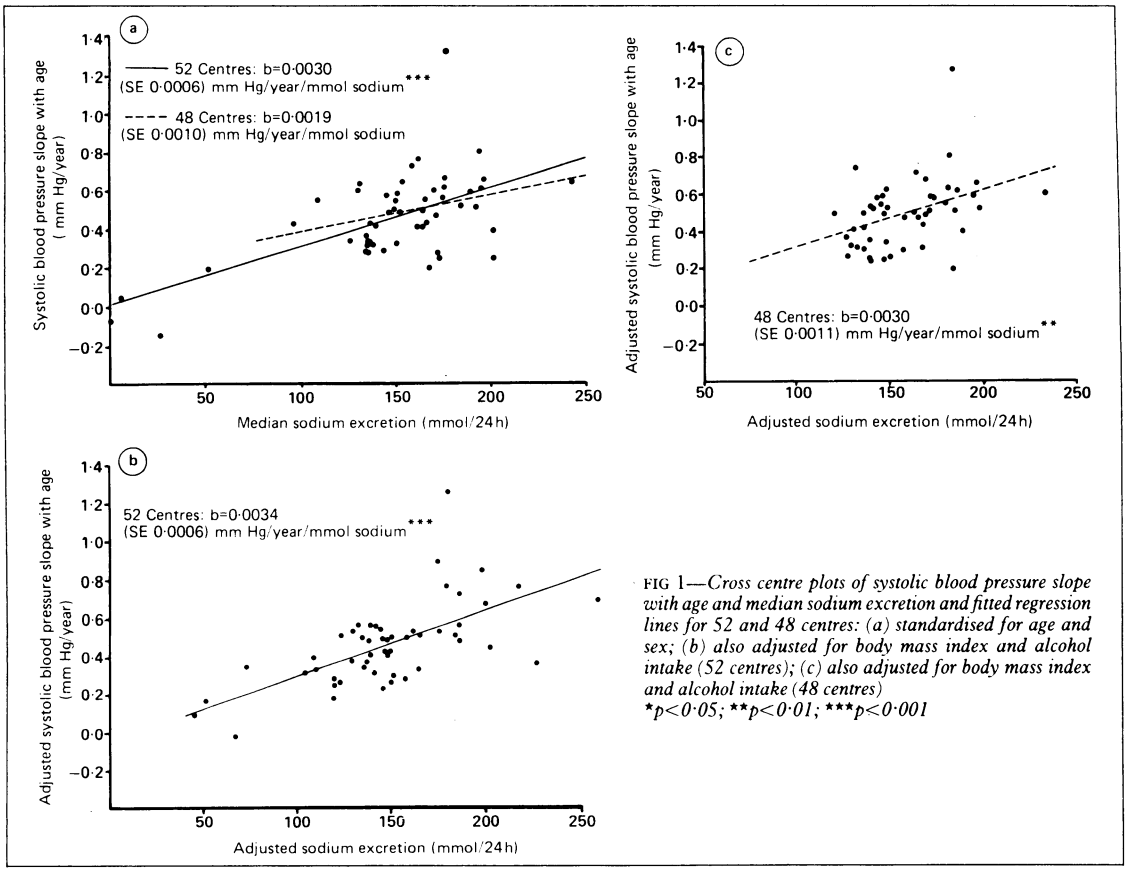

FIG 1—*Cross centre plots of systolic blood pressure slope with age and median sodium excretion and fitted regression lines for 52 and 48 centres: (a) standardised for age and sex; (b) also adjusted for body mass index and alcohol intake (52 centres); (c) also adjusted for body mass index and alcohol intake (48 centres)*
**p<0·05; **p<0·01; ***p<0·001*

positive; those among body mass index, alcohol, and electrolytes were both positive and negative.

After adjustment for body mass index and alcohol intake a significant linear relation was found between sodium excretion and the slope of systolic pressure with age both for 52 centres (b=0·0034; p<0·001) (fig 1b) and for 48 centres (b=0·0030; p<0·01) (fig 1c). The regression coefficient for 48 centres implies that if the relation were causal, then with 100 mmol/day lower habitual sodium intake—for example, 50 rather than 150 mmol/day—the increase in systolic pressure from age 25 to age 55 in a population would be less by 9·0 mm Hg (0·0030 mm Hg/year/mmol sodium × 100 mmol × 30 years).

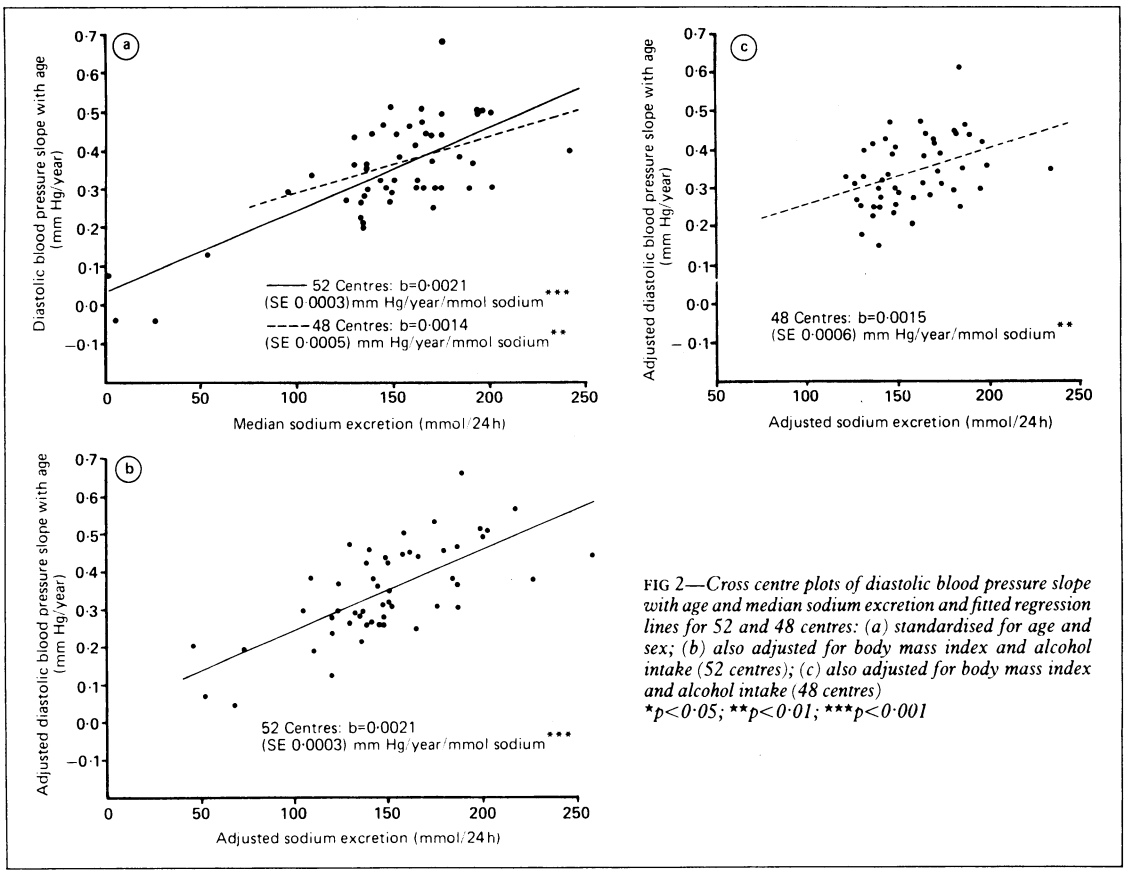

FIG 2—*Cross centre plots of diastolic blood pressure slope with age and median sodium excretion and fitted regression lines for 52 and 48 centres: (a) standardised for age and sex; (b) also adjusted for body mass index and alcohol intake (52 centres); (c) also adjusted for body mass index and alcohol intake (48 centres)*
**p<0·05; **p<0·01; ***p<0·001*

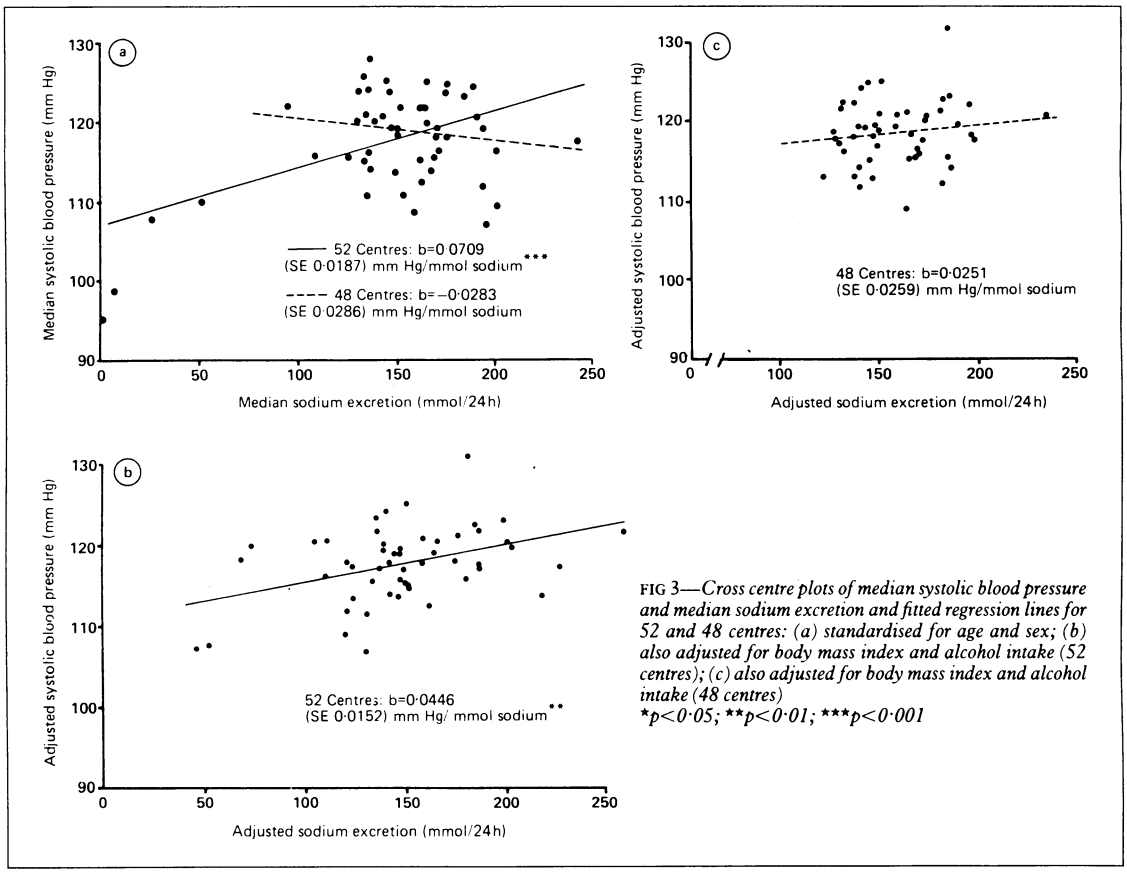

FIG 3—*Cross centre plots of median systolic blood pressure and median sodium excretion and fitted regression lines for 52 and 48 centres: (a) standardised for age and sex; (b) also adjusted for body mass index and alcohol intake (52 centres); (c) also adjusted for body mass index and alcohol intake (48 centres)*
**p<0·05; **p<0·01; ***p<0·001*

All analyses of the relation between median 24 hour urinary sodium excretion and diastolic blood pressure slope with age—that is, both with and without adjustment for body mass index and alcohol intake—yielded significant positive findings for 52 and 48 centres, linear regression coefficients ranging from 0·0014 to 0·0021 mm Hg/year/mmol sodium ($p<0·01$ and $p<0·001$, respectively) (fig 2a-c).

Median 24 hour sodium excretion and median blood pressure

There were positive and significant relations between median sodium excretion and median systolic pressure across 52 centres in both the age and sex standardised regression analysis (b=0·0709 mm Hg/mmol sodium; $p<0·001$) and the analysis also adjusted for body mass index and alcohol intake (b=0·0446; $p<0·01$) (fig 3a, b). For 48 centres, however (excluding the four recording very low sodium excretion), both regression analyses showed no significant associations of sodium with median systolic pressure (fig 3a, c). Rank order correlation analyses showed non-significant associations for both 52 and 48 centres (data not shown).

Significant associations were found between median sodium excretion and median diastolic pressure in age and sex standardised regression analyses for 52 centres (b=0·0379 mm Hg/mmol sodium; $p<0·01$) and, with a sign in the opposite direction, for 48 centres (b=−0·0445; p=0·04) (fig 4a). After adjustment for body mass index and alcohol intake the association was positive and of borderline significance for 52 centres (b=0·0226; p=0·08) but negative and non-significant for 48 centres (fig 4b, c).

Median sodium excretion and prevalence of hypertension

Median sodium excretion and prevalence of hypertension were positively and significantly related in correlation and regression analyses for 52 centres (b=0·0477%/mmol sodium (p=0·01) to b=0·0625%/mmol sodium ($p<0·01$)) but not for 48 centres or on rank order analysis (data not shown).

Data on cross centre analyses for the relation of the sodium to potassium ratio to blood pressure variables (slope with age, median blood pressure, prevalence of hypertension) are not given in this report but are available on request. Though the sodium to potassium ratio was positively related to both slope of blood pressure with age and prevalence of hypertension, this was significant only for the 52 centres and not the 48. Potassium was inconsistently related to blood pressure in these cross centre analyses.

Discussion

Intersalt found significant positive relations between 24 hour urinary sodium excretion and systolic and diastolic blood pressure in individual participants and between individual urinary sodium to potassium ratios and blood pressure. These relations were shown by pooling regression coefficients from 52 separate within centre analyses on 10 079 people world wide after adjustment for age and sex. When also adjusted for body mass index and alcohol consumption of individual subjects and for urinary potassium in the sodium-blood pressure analysis the relation of systolic pressure to both sodium excretion and the sodium to potassium ratio remained significant ($p<0·001$), as did that between diastolic pressure and the sodium to potassium ratio ($p<0·05$). With age, sex, body mass index, alcohol intake, and urinary sodium excretion in the multiple regression analyses, significant negative relations were shown between potassium excretion and blood pressure, both systolic and diastolic.

Body mass index and heavy alcohol intake (≥300 ml/week (≥34 g/day)) were strongly, significantly, and independently related to systolic and diastolic pressure in individual subjects, findings concordant with results of many other studies.[26,27] The effect of body mass index was also strong across centres.

The few previous within population studies of urinary sodium and potassium excretion and blood pressure, each done in one or at most two popula-

tions only, yielded inconsistent and inconclusive findings.[2-10 14] It is therefore relevant to emphasise the methodological basis for the Intersalt results. They are syntheses of data from 52 separate epidemiological studies, each using the same standardised design and methods. For each study centre assessment of the relations between electrolyte and blood pressure was limited by within person variability, especially as only one 24 hour urine collection was used to estimate electrolyte excretion.[1] Ability to combine results from the 52 centres, however, gave the study enough statistical power to overcome this serious problem. Thus for the relation between sodium excretion and systolic pressure, though the multiple regression coefficients were positive in 33 of the 52 centres, they were significant in only eight, and there were negative regression coefficients in 19. Nevertheless, with pooling of the regression coefficients from all 52 of these within centre analyses to take advantage of the large total sample size a significant overall regression coefficient resulted ($p<0{\cdot}001$).

Estimates of the within centre regression coefficients may be seriously diluted by measurement errors. Though correction of this bias may be attempted by using the reliability estimates, adjustment may be incomplete. Nevertheless, after correction of the pooled regression coefficients for unreliability of measurement statistical estimates may be made of the effects of differences in electrolyte intake on blood pressure. These estimates cover a range, depending on the choice of systolic or diastolic pressure and of confounding variables used in the adjustment. Thus it was estimated that a 100 mmol/day lower sodium intake—for example, 70 instead of 170 mmol/day—corresponds statistically (with adjustment for age and sex only) to an average blood pressure lower by 3·5 mm Hg systolic or 1·5 mm Hg diastolic, but adjustment also for potassium excretion, body mass index, and alcohol intake reduces these estimates to 2·2 mm Hg systolic and 0·1 mm Hg diastolic. Important public health benefits may result from even these small changes in blood pressures if applied to the population as a whole.[28]

Cross centre regressions also showed positive linear relations between median 24 hour sodium excretion and slope of both systolic and diastolic pressure with age. After adjustment for body mass index and alcohol intake these relations were significant for all 52 centres and also for the 48 centres exclusive of the four recording low sodium excretion. From the analysis of the 48 centres it is estimated that if the relation were causal, then with a 100 mmol lower daily sodium intake the average increase in blood pressure from age 25 to age 55 would be less by 9·0 mm Hg for systolic pressure and 4·5 mm Hg for diastolic pressure.

In the four isolated centres whose populations had very low sodium excretion (0·2-51·3 mmol/24 h) and low urinary sodium to potassium ratios (<0·01-1·78) median blood pressures were also low (systolic 95-110 mm Hg, diastolic 61-68 mm Hg) and slopes of blood pressure with age were negative or small and positive. All other centres had positive slopes of blood pressure with age and higher median blood pressures. In Intersalt data there was a large gap of 50 mmol/day between median sodium intake in the four populations with low sodium excretion and the population with the next lowest among the other 48 centres. It may be that the relation of sodium with blood pressure is weak in the mid-range of sodium intake and stronger at both the lower and upper extremes of sodium reported in various populations.[29]

In contrast with the significant positive findings for sodium and slope of blood pressure with age, other cross centre results were inconsistent and strongly influenced by the four centres reporting low sodium excretion, so that regression analyses based on 48 centres were no longer significant. Several factors may have contributed to these inconsistencies. Firstly, the statistical power to detect significant associations in the cross centre analyses was low once the four populations with low sodium values were excluded, given a lower than expected upper limit of sodium intake. Secondly, multiple factors might affect blood pressure across populations—for example, climate, physical activity, level of acculturation—but are less likely to confound within centre comparisons; inability to control for

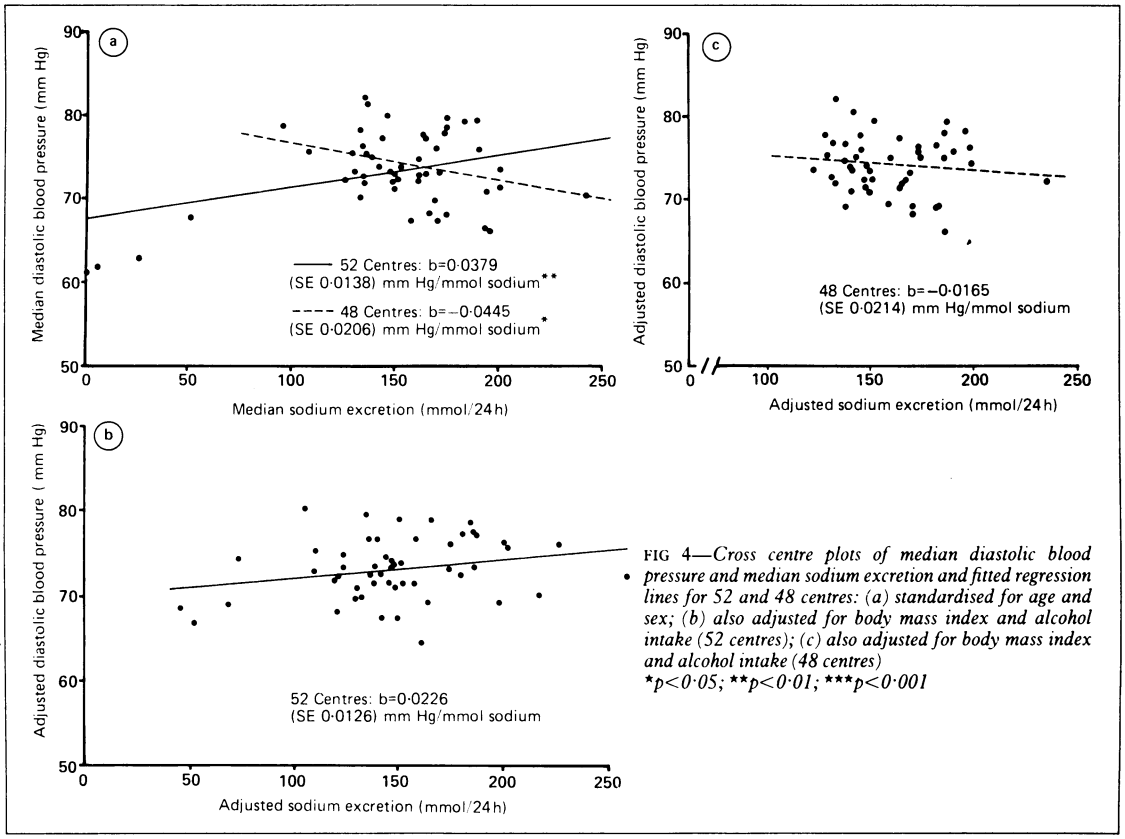

FIG 4—*Cross centre plots of median diastolic blood pressure and median sodium excretion and fitted regression lines for 52 and 48 centres: (a) standardised for age and sex; (b) also adjusted for body mass index and alcohol intake (52 centres); (c) also adjusted for body mass index and alcohol intake (48 centres)*
*$p<0{\cdot}05$; **$p<0{\cdot}01$; ***$p<0{\cdot}001$*

these effects might bias associations in cross centre (ecological) analyses.[30] For one important variable—slope of blood pressure with age—significant positive associations with sodium were found across centres, consistent with the within centre findings. Systematic measurement biases might distort comparisons of medians across centres, but, being similar across age groups and individual subjects within a centre, they would be less likely to bias values of the slope of blood pressure with age or other within centre comparisons.

Analyses are in process for men and women separately and for older and younger ages and of the effects of body mass index, alcohol intake, urinary calcium and magnesium excretion, and social and cultural factors including physical activity, education, and social state.

The following conclusions may be drawn from the Intersalt data:

(1) Within centres sodium excretion was significantly related to blood pressure in individual subjects, and at least in part this relation was independent of body mass index and alcohol intake. Sodium excretion was also significantly related across centres to the slope of blood pressure with age. Thus lower average sodium intake might have a favourable influence on blood pressure, on change of blood pressure with age, and hence on cardiovascular mortality.

(2) The four Intersalt populations with low sodium excretion had low median blood pressures, low prevalence of hypertension, and either a decrease or only a small increase of blood pressure with age.

(3) Cross centre analyses of sodium excretion and median blood pressure and of sodium excretion and the prevalence of hypertension showed a positive association when all 52 centres were included but not when the four populations with low sodium values were excluded. The inconsistency with the findings in individual subjects might reflect the role of confounding variables that differed widely across centres but less so within centres.

(4) Potassium excretion was negatively and independently associated with blood pressure of individual subjects within centres after adjustment for sodium excretion, body mass index, and alcohol intake.

(5) The relation of the urinary sodium to potassium ratio to blood pressure in individual subjects followed a pattern similar to that for sodium but more strongly and consistently.

(6) Body mass index and high alcohol intake were strongly, positively, and independently associated with blood pressure in individual subjects.

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APPENDIX I—*Values of selected variables (52 centres; all subjects)*

Centre	Systolic blood pressure slope with age (mm Hg year)	Diastolic blood pressure slope with age (mm hg year)	Median systolic blood pressure (mm Hg)	Median diastolic blood pressure (mm Hg)	Prevalence of hypertension (%)*	Median urinary sodium (mmol 24 h)	Median urinary sodium: potassium ratio	Median urinary potassium (mmol 24 h)	Median body mass index (kg m^{-2})	Prevalence of drinkers (%)	Median alcohol intake of drinkers (ml week)	Median urinary creatinine (mmol 24 h)	Median urine volume (l 24 h)
Argentina	0·549	0·512	113·5	72·0	13·5	149·3	2·76	55·9	24·1	78·5	173	11·1	1·33
Belgium:													
Charleroi	0·367	0·226	125·6	78·2	19·7	133·0	2·20	58·8	25·6	78·7	88	10·9	1·41
Ghent	0·295	0·316	120·7	73·9	17·0	142·6	2·12	67·1	24·6	78·5	98	12·1	1·47
Brazil:													
Xingu	0·052	0·042	98·9	61·7	1·0	5·8	0·08	81·1	23·1	0	—	9·4	1·53
Yanomamo	0·079	0·086	95·4	61·4	0	0·2	<0·01	57·9	21·3	0	—	4·0	1·07
Canada:													
Labrador	0·500	0·265	119·0	73·4	22·6	148·9	3·34	43·7	24·3	59·1	168	11·9	1·97
St John's	0·529	0·384	123·1	79·2	24·5	184·3	3·36	57·6	24·8	56·0	142	13·3	1·62
Colombia	0·800	0·501	119·1	66·6	17·1	194·1	2·76	67·5	22·6	51·1	145	7·7	1·70
Denmark	0·333	0·352	124·1	82·1	26·6	135·6	2·07	65·7	24·3	89·5	131	12·2	1·54
East Germany	0·425	0·443	120·0	75·0	20·7	138·7	2·64	53·8	24·4	89·4	163	11·7	1·01
Finland:													
Joensuu	0·493	0·508	121·9	77·5	23·0	164·1	2·21	75·9	24·8	60·0	85	12·1	1·45
Turku	0·575	0·465	125·1	77·4	26·0	144·4	1·98	73·7	24·7	60·0	116	12·2	1·45
Hungary	0·593	0·308	124·4	79·2	31·0	189·7	4·03	47·3	25·8	57·5	83	11·2	1·31
Iceland	0·334	0·280	116·0	71·7	12·5	135·1	2·14	63·5	24·0	52·5	86	12·3	1·31
India:													
Ladakh	0·603	0·497	111·9	70·7	10·0	194·4	4·57	45·1	20·0	56·0	346	6·5	1·76
New Delhi	0·647	0·383	110·9	73·9	13·6	153·2	3·37	46·3	23·5	15·0	31	8·4	1·32
Italy:													
Bassiano	0·663	0·436	124·6	79·6	24·6	175·9	3·20	56·6	27·5	90·0	278	11·1	1·06
Gubbio	0·604	0·439	118·1	69·9	16·2	169·9	3·23	54·2	24·8	87·0	147	11·7	1·06
Mirano	0·470	0·370	119·2	76·0	20·5	170·0	2·94	57·6	24·6	84·0	220	12·3	1·15
Naples	0·419	0·321	112·4	72·9	13·0	162·6	2·78	59·5	25·2	91·5	109	11·1	0·94
Japan:													
Osaka	0·196	0·446	113·7	68·4	11·7	167·1	4·01	40·7	21·6	64·2	109	9·8	1·12
Tochigi	0·277	0·254	116·2	67·2	10·9	171·2	4·12	41·9	22·5	62·6	145	9·5	1·02
Tovama	0·395	0·497	116·4	73·5	10·0	201·2	4·49	46·1	22·7	53·0	127	10·3	1·37
Kenya	0·206	0·134	109·9	67·9	5·0	51·3	1·78	29·5	20·5	30·7	122	7·9	0·97
Malta	0·550	0·309	125·1	77·2	23·0	165·6	2·39	68·1	26·5	73·0	64	11·2	1·40
Mexico	0·280	0·215	110·9	72·6	5·9	134·6	3·31	39·9	23·7	86·7	496	7·8	1·43
The Netherlands	0·493	0·301	123·9	79·7	24·2	146·4	2·11	70·9	23·9	67·7	111	12·6	1·43
Papua New Guinea	0·149	0·047	107·7	62·9	0·8	26·8	0·48	63·7	21·7	8·7	85	7·2	0·58
People's Republic of China:													
Beijing	0·663	0·501	107·1	66·1	8·5	196·4	5·80	33·9	22·6	28·0	27	9·4	1·28
Nanning	0·737	0·465	108·9	67·4	13·5	158·1	6·12	26·4	20·8	32·0	11	9·3	1·15
Tianjin	0·640	0·399	117·5	70·2	15·0	242·1	7·27	32·8	23·5	35·5	93	9·7	1·67
Poland:													
Krakow	0·524	0·369	120·5	75·7	19·0	191·8	3·71	50·5	26·1	59·0	70	12·3	1·14
Warsaw	0·563	0·302	123·6	77·9	25·0	174·6	3·85	44·0	26·0	51·5	57	12·1	1·13
Portugal	1·326	0·679	132·4	78·2	32·0	175·4	2·70	61·4	25·4	54·6	256	10·7	1·13
South Korea	0·242	0·303	109·4	71·4	8·1	201·4	4·24	47·5	22·1	23·6	35	9·5	1·47
Soviet Union	0·763	0·411	115·0	72·1	15·5	161·8	3·31	47·1	25·4	33·0	43	11·9	0·98
Spain:													
Manresa	0·438	0·470	119·9	72·7	16·0	165·4	2·63	66·1	24·9	74·5	133	11·6	1·06
Torrejon	0·613	0·490	117·9	68·0	15·5	175·2	2·69	67·3	26·4	72·0	162	11·0	1·28
Taiwan	0·436	0·367	114·0	75·2	17·6	136·2	4·66	29·8	23·1	20·2	63	8·7	1·07
Trinidad and Tobago	0·560	0·340	115·7	75·5	18·0	108·3	2·77	38·0	27·0	36·4	55	12·7	0·87
United Kingdom:													
Belfast	0·338	0·290	119·0	73·1	18·6	149·9	2·63	56·5	24·3	66·9	178	11·0	1·34
Birmingham	0·584	0·320	118·1	71·2	15·0	150·0	2·53	62·3	24·7	74·0	115	11·0	1·67
South Wales	0·492	0·442	121·7	72·4	21·0	151·8	2·38	63·0	24·5	68·8	104	11·4	1·37
United States:													
Chicago	0·287	0·265	115·1	70·0	12·6	133·8	2·60	52·4	25·3	70·4	122	12·1	1·28
Goodman Black	0·433	0·294	122·1	78·5	26·1	95·9	4·15	23·4	28·6	33·8	309	9·9	0·73
Goodman White	0·346	0·270	115·6	72·4	19·2	125·9	3·16	43·1	26·8	27·2	113	10·8	1·14
Hawaii	0·638	0·434	123·7	73·2	23·2	130·3	3·29	39·8	30·1	40·9	263	12·6	1·17
Jackson Black	0·325	0·295	127·9	81·4	33·5	136·6	3·78	38·0	27·0	39·7	89	13·5	1·03
Jackson White	0·320	0·204	120·7	76·2	20·6	134·4	2·56	53·6	24·2	52·2	87	11·0	1·44
West Germany:													
Bernried	0·419	0·300	121·7	74·7	16·6	162·0	2·33	70·7	24·2	81·7	150	12·0	1·40
Heidelberg	0·246	0·303	116·5	73·1	13·1	172·0	2·37	70·6	24·2	84·3	132	11·8	1·55
Zimbabwe	0·611	0·360	120·0	75·6	24·0	129·7	3·77	36·8	25·9	44·3	238	10·5	1·59

*Hypertension defined as systolic pressure ≥140 mm Hg or diastolic pressure ≥90 mm Hg or use of antihypertensive agents.

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APPENDIX II—*Mean (SD) values* of selected variables (52 centres; all subjects)*

Centre	No	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)	Urinary sodium (mmol 24 h)	Urinary sodium: potassium ratio	Urinary potassium (mmol 24 h)	Body mass index (kg/m^2)	Alcohol intake (ml/week)	Urinary creatinine (mmol 24 h)	Urine volume (l 24 h)
Argentina	200	115·1 (14·3)	72·8 (12·6)	155·8 (58·3)	2·91 (1·18)	56·5 (17·0)	25·0 (3·8)	201·6 (253·2)	11·3 (2·2)	1·43 (0·61)
Belgium:										
Charleroi	157	125·1 (14·3)	77·8 (9·9)	141·2 (54·5)	2·34 (0·89)	63·4 (20·2)	25·9 (3·9)	94·3 (121·9)	10·9 (2·2)	1·54 (0·74)
Ghent	200	123·3 (14·3)	74·1 (10·6)	147·7 (54·1)	2·20 (0·75)	70·0 (22·1)	24·9 (3·4)	121·2 (162·9)	12·0 (2·3)	1·58 (0·63)
Brazil:										
Xingu	198	99·8 (10·6)	62·2 (7·8)	12·3 (21·3)	0·20 (0·47)	87·1 (43·2)	23·4 (2·9)	0	9·3 (2·8)	1·58 (0·74)
Yanomamo	195	96·0 (8·6)	60·6 (8·0)	0·9 (2·5)	0·01 (0·04)	63·3 (31·7)	21·2 (1·9)	0	4·2 (2·2)	1·07 (0·44)
Canada:										
Labrador	161	118·1 (14·3)	73·0 (10·5)	151·2 (77·5)	3·60 (1·97)	46·0 (19·9)	25·1 (4·3)	178·5 (372·1)	11·7 (2·8)	2·01 (0·86)
St John's	200	121·1 (13·3)	76·8 (9·1)	200·1 (81·1)	3·59 (1·50)	59·7 (21·9)	25·2 (4·0)	115·7 (185·1)	13·7 (3·9)	1·73 (0·57)
Colombia	191	120·7 (17·3)	67·6 (11·6)	201·4 (73·0)	2·90 (0·92)	71·7 (23·4)	23·0 (3·3)	113·3 (208·4)	8·0 (2·7)	1·72 (0·50)
Denmark	199	124·0 (13·0)	81·6 (9·2)	140·2 (51·8)	2·20 (0·88)	66·7 (20·3)	24·5 (3·7)	147·4 (144·9)	12·2 (2·1)	1·66 (0·68)
East Germany	198	121·8 (14·9)	75·0 (11·1)	147·7 (57·1)	2·73 (0·90)	55·0 (17·2)	24·9 (3·6)	162·0 (155·8)	11·8 (2·2)	1·13 (0·53)
Finland:										
Joensuu	200	121·0 (13·9)	75·4 (10·0)	170·4 (56·6)	2·32 (0·82)	76·6 (21·9)	25·4 (4·0)	78·5 (119·8)	12·2 (2·0)	1·52 (0·56)
Turku	200	127·0 (16·1)	78·4 (10·7)	154·8 (59·0)	2·14 (0·92)	76·1 (23·1)	25·3 (3·8)	110·7 (178·9)	12·1 (2·4)	1·50 (0·56)
Hungary	200	125·7 (16·0)	80·3 (10·3)	198·3 (76·0)	4·14 (1·46)	49·9 (16·3)	26·2 (4·9)	92·8 (156·6)	11·2 (3·0)	1·43 (0·56)
Iceland	200	117·9 (13·4)	71·7 (9·5)	138·3 (44·4)	2·22 (0·77)	65·0 (19·7)	24·5 (3·3)	63·7 (104·9)	12·4 (2·3)	1·43 (0·59)
India:										
Ladakh	200	114·1 (17·0)	71·6 (11·2)	203·7 (75·0)	4·88 (2·00)	47·0 (19·2)	20·1 (2·3)	310·1 (502·5)	6·3 (2·0)	1·79 (0·64)
New Delhi	199	113·7 (13·4)	73·9 (9·6)	160·6 (57·8)	3·51 (1·14)	47·4 (13·8)	23·7 (3·5)	11·6 (46·5)	8·6 (1·7)	1·39 (0·69)
Italy:										
Bassiano	199	125·1 (14·0)	79·6 (9·8)	184·9 (63·1)	3·30 (0·96)	58·1 (17·3)	28·0 (4·3)	300·5 (283·2)	11·4 (2·4)	1·13 (0·37)
Gubbio	199	117·5 (14·3)	69·9 (10·2)	175·4 (62·1)	3·29 (1·13)	55·8 (16·9)	25·4 (3·9)	167·6 (161·9)	11·7 (2·1)	1·14 (0·40)
Mirano	200	119·4 (13·2)	76·0 (9·6)	174·1 (59·7)	3·12 (1·04)	57·4 (15·0)	25·4 (3·9)	228·9 (231·0)	12·4 (2·1)	1·26 (0·52)
Naples	200	114·8 (13·5)	72·5 (10·2)	167·7 (51·3)	2·90 (0·92)	60·2 (16·4)	25·4 (3·2)	119·8 (124·7)	11·1 (1·9)	1·02 (0·34)
Japan:										
Osaka	197	116·5 (14·7)	68·6 (11·5)	168·3 (48·1)	4·05 (1·19)	43·1 (12·5)	21·6 (2·4)	105·1 (146·7)	9·9 (1·5)	1·20 (0·42)
Tochigi	194	117·9 (12·1)	68·4 (12·5)	180·4 (70·7)	4·14 (1·31)	46·0 (18·8)	22·5 (3·2)	156·0 (171·6)	9·6 (2·0)	1·12 (0·45)
Toyama	200	117·3 (12·6)	72·1 (10·9)	212·4 (62·8)	4·61 (1·39)	48·4 (14·9)	23·1 (2·7)	120·4 (185·2)	10·3 (1·8)	1·39 (0·41)
Kenya	176	113·3 (14·7)	66·0 (14·7)	56·8 (33·0)	1·91 (1·06)	33·2 (18·3)	20·8 (2·7)	73·1 (182·8)	7·8 (2·5)	1·07 (0·50)
Malta	200	123·7 (13·4)	76·3 (9·6)	169·8 (57·7)	2·57 (1·18)	73·6 (27·4)	26·9 (4·9)	150·6 (276·1)	11·4 (2·1)	1·56 (0·71)
Mexico	172	112·7 (12·0)	73·6 (9·3)	144·1 (84·0)	3·53 (1·53)	43·2 (23·8)	24·4 (3·1)	543·0 (478·5)	8·7 (4·6)	1·54 (0·55)
The Netherlands	199	125·3 (16·0)	79·6 (9·3)	150·6 (53·4)	2·17 (0·84)	72·5 (20·0)	24·4 (3·4)	108·1 (149·1)	12·6 (2·1)	1·51 (0·58)
Papua New Guinea	162	108·0 (11·9)	62·7 (10·0)	36·8 (31·3)	0·62 (0·57)	70·1 (35·9)	21·7 (1·8)	7·9 (31·4)	7·2 (2·8)	0·65 (0·31)
People's Republic of China:										
Beijing	200	109·4 (14·2)	67·6 (10·0)	204·1 (66·4)	6·01 (1·95)	35·3 (10·4)	22·8 (2·6)	17·8 (44·8)	9·5 (1·5)	1·37 (0·51)
Nanning	200	110·7 (15·0)	67·9 (9·6)	169·2 (61·1)	6·40 (2·10)	27·2 (8·3)	21·3 (2·5)	11·8 (54·4)	9·4 (1·6)	1·22 (0·44)
Tianjin	200	119·4 (18·2)	70·5 (11·7)	245·6 (83·3)	7·58 (2·41)	33·6 (10·4)	23·9 (3·4)	71·0 (144·9)	9·6 (1·9)	1·70 (0·60)
Poland:										
Krakow	200	123·3 (15·1)	76·3 (9·1)	197·7 (66·9)	3·85 (1·19)	52·5 (16·6)	26·4 (3·7)	68·2 (103·9)	12·2 (2·2)	1·24 (0·45)
Warsaw	200	123·3 (16·0)	77·1 (9·7)	181·3 (74·1)	4·06 (1·59)	46·6 (17·3)	26·5 (4·1)	45·6 (82·8)	12·0 (2·4)	1·18 (0·44)
Portugal	198	132·6 (18·3)	76·6 (11·9)	181·9 (73·2)	2·90 (1·07)	65·8 (24·4)	25·8 (3·9)	222·7 (273·4)	10·9 (3·4)	1·19 (0·41)
South Korea	198	112·2 (15·5)	71·9 (12·0)	208·2 (71·9)	4·36 (1·39)	49·3 (15·5)	22·2 (2·6)	26·3 (93·7)	9·7 (2·1)	1·49 (0·50)
Soviet Union	194	117·7 (17·0)	73·4 (10·3)	161·7 (57·7)	3·42 (1·20)	48·9 (15·0)	25·7 (3·7)	21·7 (50·9)	11·6 (2·5)	1·02 (0·31)
Spain:										
Manresa	200	119·7 (12·6)	71·8 (11·3)	174·6 (62·7)	2·69 (0·91)	67·4 (19·8)	25·4 (3·9)	160·0 (219·5)	11·6 (1·8)	1·16 (0·45)
Torrejon	200	119·9 (14·8)	68·6 (10·9)	183·2 (67·4)	2·80 (0·96)	67·1 (18·3)	26·7 (4·4)	164·3 (250·7)	10·9 (2·4)	1·31 (0·43)
Taiwan	181	116·4 (17·2)	76·2 (12·1)	141·4 (60·2)	4·89 (2·15)	31·7 (14·9)	23·1 (2·8)	29·4 (94·7)	8·7 (3·0)	1·16 (0·49)
Trinidad and Tobago	176	118·3 (17·0)	75·0 (13·0)	117·4 (55·8)	3·06 (1·33)	40·8 (17·0)	28·2 (5·9)	73·8 (234·5)	12·7 (4·0)	0·95 (0·44)
United Kingdom:										
Belfast	199	120·3 (13·7)	73·8 (10·7)	150·8 (56·4)	2·79 (1·04)	56·9 (18·4)	24·8 (4·0)	229·7 (597·2)	10·9 (2·3)	1·53 (0·81)
Birmingham	200	119·6 (14·8)	71·2 (10·0)	153·1 (46·4)	2·59 (0·97)	63·0 (18·9)	25·2 (3·8)	124·7 (144·3)	11·0 (2·3)	1·74 (0·65)
South Wales	199	124·3 (16·7)	71·3 (10·7)	152·3 (55·0)	2·54 (0·86)	63·1 (22·0)	25·7 (4·8)	115·8 (169·6)	11·3 (2·7)	1·55 (0·70)
United States:										
Chicago	196	114·0 (12·3)	70·5 (10·3)	140·1 (63·9)	2·81 (1·27)	53·4 (19·7)	26·4 (4·7)	129·0 (177·0)	12·1 (2·5)	1·44 (0·70)
Goodman Black	186	119·5 (12·0)	76·4 (8·8)	103·6 (53·8)	4·78 (2·67)	24·6 (12·1)	30·3 (7·0)	190·1 (498·0)	9·9 (4·0)	0·85 (0·48)
Goodman White	198	114·2 (11·0)	71·5 (8·8)	130·8 (55·7)	3·16 (1·22)	45·3 (21·3)	28·2 (6·6)	45·6 (110·3)	10·6 (3·0)	1·24 (0·55)
Hawaii	187	123·3 (17·5)	73·8 (11·6)	144·1 (76·4)	3·53 (1·84)	44·6 (21·9)	31·2 (7·0)	142·0 (267·4)	12·8 (3·5)	1·39 (0·85)
Jackson Black	184	125·6 (12·6)	79·2 (8·5)	150·9 (76·8)	4·03 (2·13)	40·6 (17·4)	28·0 (5·3)	59·6 (127·1)	14·0 (5·6)	1·22 (0·65)
Jackson White	199	122·2 (13·9)	76·4 (8·7)	141·4 (55·1)	2·77 (1·33)	56·5 (20·9)	25·1 (4·4)	73·2 (115·1)	11·3 (2·7)	1·63 (0·82)
West Germany:										
Bernried	197	122·8 (14·7)	74·9 (9·2)	167·0 (60·6)	2·44 (0·96)	71·6 (20·5)	24·5 (3·6)	135·7 (112·6)	12·3 (2·2)	1·53 (0·63)
Heidelberg	196	117·6 (13·5)	73·6 (10·0)	172·9 (59·8)	2·48 (0·90)	73·0 (23·1)	24·5 (3·1)	146·4 (154·1)	11·8 (2·3)	1·67 (0·73)
Zimbabwe	195	123·7 (18·8)	76·8 (12·6)	140·5 (62·3)	4·02 (2·05)	37·5 (13·9)	26·1 (4·1)	171·7 (270·6)	10·4 (3·1)	1·74 (0·78)

*Means (and SD) calculated for men aged 20-39, men aged 40-59, women aged 20-39, and women aged 40-59 and then averaged over age and sex groups.

Rose, Professor M Marmot, Dr P Elliott, M J Shipley, S Tulloch, L Colwell, B Peachey, and L Tudge.

Members of the Chicago coordinating centre were Professor J Stamler, Professor R Stamler, Professor A Dyer, and G Civinelli.

Members of the central laboratory (Louvain) were Professor H Kesteloot, Professor J Joossens, and J Geboers (laboratory coordinator).

More detailed tabulations of the results presented in this paper may be obtained by writing direct to Dr Paul Elliott.

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APPENDIX III—*Centre by centre regression coefficients of blood pressure-sodium relations adjusted for age and sex and for age, sex, body mass index, alcohol intake, and potassium excretion (52 centres; all subjects)*

Centre	Systolic blood pressure-sodium (mm Hg/mmol): Adjusted for age and sex	Systolic blood pressure-sodium (mm Hg/mmol): Adjusted for age, sex, body mass index, alcohol, and potassium	Diastolic blood pressure-sodium (mm Hg/mmol): Adjusted for age and sex	Diastolic blood pressure-sodium (mm Hg/mmol): Adjusted for age, sex, body mass index, alcohol, and potassium
Argentina	0·0183	0·0081	0·0123	−0·0031
Belgium:				
Charleroi	0·0118	0·0055	−0·0003	−0·0135
Ghent	0·0252	0·0123	0·0182	0·0116
Brazil:				
Xingu	−0·0370	−0·0370	−0·0204	−0·0155
Yanomamo	−0·1731	−0·0398	−0·2407	−0·0853
Canada:				
Labrador	0·0427**	0·0315*	0·0133	−0·0059
St John's	0·0051	0·0033	−0·0010	0·0059
Colombia	−0·0008	−0·0108	−0·0024	−0·0086
Denmark	0·0114	0·0056	−0·0068	−0·0132
East Germany	−0·0067	−0·0097	−0·0027	−0·0097
Finland:				
Joensuu	0·0238	0·0237	0·0090	0·0076
Turku	0·0051	−0·0263	−0·0154	−0·0432**
Hungary	0·0446**	0·0300	0·0137	−0·0014
Iceland	0·0267	0·0159	−0·0071	−0·0197
India:				
Ladakh	0·0190	0·0229	0·0187	0·0207
New Delhi	−0·0150	−0·0198	−0·0192	−0·0276*
Italy:				
Bassiano	0·0169	0·0122	0·0143	0·0030
Gubbio	0·0331*	0·0013	0·0012	−0·0262*
Mirano	−0·0213	−0·0270	−0·0020	0·0021
Naples	0·0151	0·0050	0·0097	−0·0011
Japan:				
Osaka	−0·0828***	−0·0631**	−0·0528**	−0·0288
Tochigi	0·0133	0·0134	0·0138	0·0133
Toyama	0·0315*	0·0263	0·0191	0·0017
Kenya	0·0331	0·0497	0·0059	−0·0031
Malta	−0·0035	−0·0010	0·0055	−0·0008
Mexico	0·0077	0·0085	0·0038	0·0009
The Netherlands	−0·0286	−0·0347	−0·0102	−0·0170
Papua New Guinea	0·0370	0·0382	0·0270	0·0224
People's Republic of China:				
Beijing	0·0295*	0·0394*	0·0079	0·0034
Nanning	0·0788***	0·0848***	0·0398***	0·0414**
Tianjin	0·0347*	0·0367*	0·0399***	0·0415***
Poland:				
Krakow	0·0354*	0·0434*	0·0040	0·0014
Warsaw	0·0639***	0·0537**	0·0162	0·0001
Portugal	−0·0122	−0·0143	0·0053	0·0135
South Korea	0·0225	0·0142	0·0021	−0·0129
Soviet Union	0·0098	−0·0258	0·0063	−0·0102
Spain:				
Manresa	0·0057	−0·0006	0·0086	−0·0040
Torrejon	0·0225	0·0289	0·0034	0·0075
Taiwan	0·0460*	0·0292	0·0332*	0·0226
Trinidad and Tobago	0·0386	0·0406	0·0441*	0·0449*
United Kingdom:				
Belfast	0·0374*	0·0224	0·0119	−0·0038
Birmingham	0·0020	−0·0056	−0·0058	−0·0163
South Wales	0·0461*	0·0494*	−0·0013	0·0021
United States:				
Chicago	0·0005	−0·0096	−0·0036	−0·0056
Goodman Black	−0·0065	0·0049	−0·0100	0·0031
Goodman White	0·0156	−0·0009	0·0094	0·0004
Hawaii	0·0445**	0·0279	0·0110	−0·0030
Jackson Black	−0·0244*	−0·0335*	−0·0044	−0·0080
Jackson White	0·0254	−0·0117	0·0171	0·0023
West Germany:				
Bernried	0·0367*	0·0260	0·0151	0·0050
Heidelberg	−0·0042	−0·0173	−0·0018	−0·0080
Zimbabwe	0·0543*	0·0533*	0·0202	0·0213

*p<0·05. **p<0·01. ***p<0·001.

Correction

Calculating confidence intervals for regression and correlation

Two authors' errors occurred in this paper by Mr Douglas G Altman and Professor Martin J Gardner (30 April, p 1238). In the comparison of two regression lines (p 1239) the standard error of y_{diff} should read:

$$SE(y_{diff}) = S_{par} \times \sqrt{\frac{1}{n_1} + \frac{1}{n_2} + \frac{(\bar{x}_1 - \bar{x}_2)^2}{w}}$$

In the worked example of the vertical distance between two parallel lines (p 1241) the standard error of y_{diff} should read:

$$SE(y_{diff} = 0{\cdot}7786 \times \sqrt{\frac{1}{10} + \frac{1}{10} + \frac{(101{\cdot}2 - 98{\cdot}8)^2}{775{\cdot}22}}$$

$$= 0{\cdot}3546\%.$$

The 95% confidence interval for the population value of y_{diff} is then given by:

$0{\cdot}4548 - (2{\cdot}110 \times 0{\cdot}3546)$ to $0{\cdot}4548 + (2{\cdot}110 \times 0{\cdot}3546)$

that is, from −0·29 to 1·20%.