Urinary sodium excretion, blood pressure, cardiovascular disease, and mortality: a community-level prospective epidemiological cohort study

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Summary

Background WHO recommends that populations consume less than 2 g/day sodium as a preventive measure against cardiovascular disease, but this target has not been achieved in any country. This recommendation is primarily based on individual-level data from short-term trials of blood pressure (BP) without data relating low sodium intake to reduced cardiovascular events from randomised trials or observational studies. We investigated the associations between community-level mean sodium and potassium intake, cardiovascular disease, and mortality.

Methods The Prospective Urban Rural Epidemiology study is ongoing in 21 countries. Here we report an analysis done in 18 countries with data on clinical outcomes. Eligible participants were adults aged 35–70 years without cardiovascular disease, sampled from the general population. We used morning fasting urine to estimate 24 h sodium and potassium excretion as a surrogate for intake. We assessed community-level associations between sodium and potassium intake and BP in 369 communities (all >50 participants) and cardiovascular disease and mortality in 255 communities (all >100 participants), and used individual-level data to adjust for known confounders.

Findings 95 767 participants in 369 communities were assessed for BP and 82 544 in 255 communities for cardiovascular outcomes with follow-up for a median of 8·1 years. 82 (80%) of 103 communities in China had a mean sodium intake greater than 5 g/day, whereas in other countries 224 (84%) of 266 communities had a mean intake of 3–5 g/day. Overall, mean systolic BP increased by 2·86 mm Hg per 1 g increase in mean sodium intake, but positive associations were only seen among the communities in the highest tertile of sodium intake (p<0·0001 for heterogeneity). The association between mean sodium intake and major cardiovascular events showed significant deviations from linearity (p=0·043) due to a significant inverse association in the lowest tertile of sodium intake (lowest tertile <4·43 g/day, mean intake 4·04 g/day, range 3·42–4·43; change –1·00 events per 1000 years, 95% CI –2·00 to –0·01, p=0·0497), no association in the middle tertile (middle tertile 4·43–5·08 g/day, mean intake 4·70 g/day, 4·44–5.05; change 0·24 events per 1000 years, –2·12 to 2·61, p=0·8391), and a positive but non-significant association in the highest tertile (highest tertile >5·08 g/day, mean intake 5·75 g/day, >5·08–7·49; change 0·37 events per 1000 years, –0·03 to 0·78, p=0·0712). A strong association was seen with stroke in China (mean sodium intake 5·58 g/day, 0·42 events per 1000 years, 95% CI 0·16 to 0·67, p=0·0020) compared with in other countries (4·49 g/day, –0·26 events, –0·46 to –0·06, p=0·0124; p<0·0001 for heterogeneity). All major cardiovascular outcomes decreased with increasing potassium intake in all countries.

Interpretation Sodium intake was associated with cardiovascular disease and strokes only in communities where mean intake was greater than 5 g/day. A strategy of sodium reduction in these communities and countries but not in others might be appropriate.

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Introduction

Reduction of sodium intake as a population-level intervention to reduce cardiovascular disease and mortality is recommended by WHO.[1] The recommended mean population-level sodium intake is 2 g/day (equivalent to 5 g/day salt), but has not been achieved in any country.[1] The rationale, however, is based on the association between sodium intake and blood pressure (BP) and the

Research in context

Systematic review

We searched PubMed for papers published between Jan 1, 1960, and April 1, 2018, using the term "('sodium' OR 'salt' AND 'mortality' OR 'cardiovascular' OR 'myocardial' OR' stroke' OR 'heart failure' OR 'sudden cardiac death')". We screened papers by title and abstract to identify full-text reports that were relevant to the study aims. We also screened citation lists from retrieved papers to identify further relevant research. We considered papers if they assessed the relation between sodium intake and at least one of the outcomes of interest. The papers cited in this Article were selected to be representative of the existing evidence base but do not comprise an exhaustive list of relevant research. WHO recommends that all populations consume less than 2 g/day sodium as a preventive measure against cardiovascular disease, but the target has not been achieved in any country. This recommendation is based on individual-level data from short-term trials of blood pressure, with no data from randomised trials or observational studies showing significantly lower rates of clinical cardiovascular events or mortality with sodium intake less than 3 g/day compared with 3–5 g/day. J-shaped or inverse associations between sodium and cardiovascular events or mortality have been observed in cohort studies estimating sodium intake by 24 h urine collection, morning fasting urine, or diet.

Added value of the study

We investigated community-level mean sodium intake and associations with cardiovascular disease and mortality among individuals enrolled from the general population in a large number and range of communities in 18 different countries followed up for around 8 years. We recorded standardised and detailed data on exposure, confounders, and outcomes, which allowed individual-level and group-level analyses.

Implications of all the available data

We found a positive association between sodium intake and systolic blood pressure across communities. Sodium intake and stroke were associated, but only significantly among communities in the upper third of sodium intake, which were largely confined to China. By contrast we found an inverse relation with myocardial infarction and mortality. The rates of stroke, cardiovascular death, and total mortality decreased with increasing potassium intake in all communities. A strategy of sodium reduction that targets communities and countries with high mean sodium intake (eg, >5 g/day) might be preferable to a global strategy. By contrast, a strong case can be made for increasing the consumption of potassium-rich foods (eg, fruits and vegetables) worldwide.

assumption that any approach to reducing BP will translate into fewer clinical cardiovascular outcomes.[2–5] Nevertheless, the claim that the effects of salt on cardiovascular disease are exclusively mediated through its effects on BP has never been proven.[6,7] Increased mean sodium intake was associated with a modestly raised mean BP at the community level in one study,[5] but the study cohort was too small to assess the association at all levels of sodium intake. Additionally, no study has reported on the association between community-level sodium intake and cardiovascular disease or mortality. The effect of sodium on BP is small and, therefore, only slight reductions in cardiovascular disease could be expected.[3–5] However, sodium affects numerous physiological processes and, therefore, its net effects on cardiovascular events cannot be predicted solely from its effects on BP.[6,8,9] Thus, direct data are lacking for population-level effects of mean sodium intake on cardiovascular disease or death.

The Prospective Urban Rural Epidemiology (PURE) study[10] provides a unique opportunity to assess associations between community-level mean sodium intake and cardiovascular disease and mortality in a large sample of individuals from the general population in different countries and communities. Standardised and detailed data on exposure, confounders, and outcomes have been recorded to permit both individual-level and group-level analyses. Here we report an analysis of PURE data on sodium intake and outcomes at the community (or centre) level and extend our previous analyses with greater numbers of cardiovascular events obtained with additional follow-up.

Methods

Study design and participants

PURE is a large-scale epidemiological cohort study that has enrolled 168 067 individuals aged 35–70 years from the general populations of 664 communities, 51 study centres (89 urban and rural subcentres) in 21 low-income (n=5), middle-income (n=12), and high-income (n=4) countries.[10,12–15] We define communities in urban areas as groups of people with common characteristics in defined geographical areas (eg, sets of contiguous postal codes or groups of streets) and those in rural areas as groups, generally in villages (appendix). We have used an unbiased method to sample individuals based on representativeness and likelihood of long-term follow-up (appendix).

All participants provided written informed consent. The study protocol was approved by the ethics committee at each participating centre.

Procedures

A morning fasting midstream urine sample was collected from every participant, frozen at –20°C to –70°C,

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See Online for appendix

and shipped in batches at ambient temperature to a central laboratory in Canada, China, India, or Turkey, in STP 250 ambient specimen shipping boxes (Saf-T-Pak, Edmonton, AB, Canada).[11,16] The Kawasaki formula was used to estimate 24 h urinary sodium and potassium excretion, and these values were used as surrogates of intake (appendix).[17–19]

Information about demographic factors, lifestyle, health history, and medication use were recorded in face-to-face interviews at the study centres. We also measured weight and height, and took two measurements of BP with an Omron HEM-757 automatic digital monitor (Omron, Tokyo, Japan) after 5 min of sitting. Data were collected by research assistants, who were trained with comprehensive manuals, videos, and workshops to ensure standardised methods of data collection. Data were transferred electronically to the coordinating centre at the Population Health Research Institute, Hamilton, ON, Canada, where additional checks of the quality of data were made.

Participants were followed up face to face or by telephone at 3, 6, and 9 years, when we gathered data on selected risk factors (eg, weight, height, and blood pressure), health outcomes, and community. Major cardiovascular events and deaths during follow-up were recorded and adjudicated centrally in each country by trained local researchers. To ensure a standard approach and accuracy for classification of events across all countries and over time, the first 100 cardiovascular events (deaths, myocardial infarctions, strokes, heart failure, or cancers) for China and India and the first 50 cases for other countries were adjudicated locally and by the central adjudication committee. Thereafter, 50 cases for China and India and 25 cases for the remaining countries were adjudicated by the same method once per year. If necessary, further training was provided.

Of 110 600 individuals enrolled in PURE with completed morning fasting urine assessments, 101 008 (14 492 from high-income, 77 695 from middle-income, and 8821 from low-income countries) in 36 study centres (70 urban and rural subcentres) covering 548 communities in 21 countries had no history of cardiovascular disease (appendix). For this analysis we focused on the first wave of 18 countries enrolled into PURE from 2003 to 2013 with at least one completed follow-up cycle, and included communities larger than 50 people for BP analyses and larger than 100 people for assessment of cardiovascular events to minimise imprecision. We included all outcome events known until Sept 30, 2017. We also did assessments at the centre and subcentre levels, but these analyses had far fewer units than the community level analyses. We therefore present data primarily at the community level, as they had the greatest power to examine the shape of associations, with centre-level and subcentre-level data presented mostly in the appendix.

Statistical analysis

We calculated mean estimated 24 h urinary values of sodium and potassium intake and mean systolic and diastolic BP, adjusted for age, sex, body-mass index, education, alcohol intake, and smoking status, for each community and centre. We used individual-level data to fully adjust for known confounders in all group-level analyses. When reporting mean intakes for individuals, we adjusted for regression dilution bias (the regression dilution ratio was calculated on the basis of baseline measurement and repeat measurements at 30–90 days in 448 participants), as described previously.[16] We first used the individual-level data in time-to-event analyses in Cox proportional hazards models to calculate probability values for each participant. These models were adjusted for age, sex, and country in univariable analyses, and for these factors plus body-mass index, smoking status, diabetes, educational level, alcohol consumption, physical activity, and use of anti-hypertensive or statin medications in multivariable analyses. The predicted values for individuals were divided by duration of follow-up in years (ie, annualised probability of an event) and multiplied by 1000 to obtain the probability of an event per 1000 years in individuals. The means adjusted probability values in each community represent the multivariable adjusted mean event rate in that community.

We used linear regression to determine the slope describing the relations between mean sodium and potassium intake (exposures; per 1 g increase in intake for each), the sodium-to-potassium ratio, and the mean adjusted probability values across communities (outcomes), with tests for linearity and deviation from linearity. To assess the shape of the association between estimated sodium intake and the outcomes, we used locally weighted scatterplot smoothing. To assess whether the associations at community level varied by mean sodium or potassium intake, we assessed subgroups by subdividing the communities into tertiles of intake and estimated associations within each. Given that the slope estimates for sodium intake versus systolic BP by centre paralleled the results by community, but with higher precision in the latter, the main analyses on sodium intake and clinical outcomes are presented at the community level.

China had a markedly higher intake of sodium than other countries in PURE and, therefore, we did a separate assessment of associations in communities in China versus those in other countries, with tests for heterogeneity.

In sensitivity analyses, we excluded individuals who were taking antihypertensive medications. Additional analyses included an assessment adjusted for BP to check whether the associations between sodium or potassium and clinical cardiovascular events would be attenuated, given that BP is assumed to be the main mediating pathway for the relation with cardiovascular

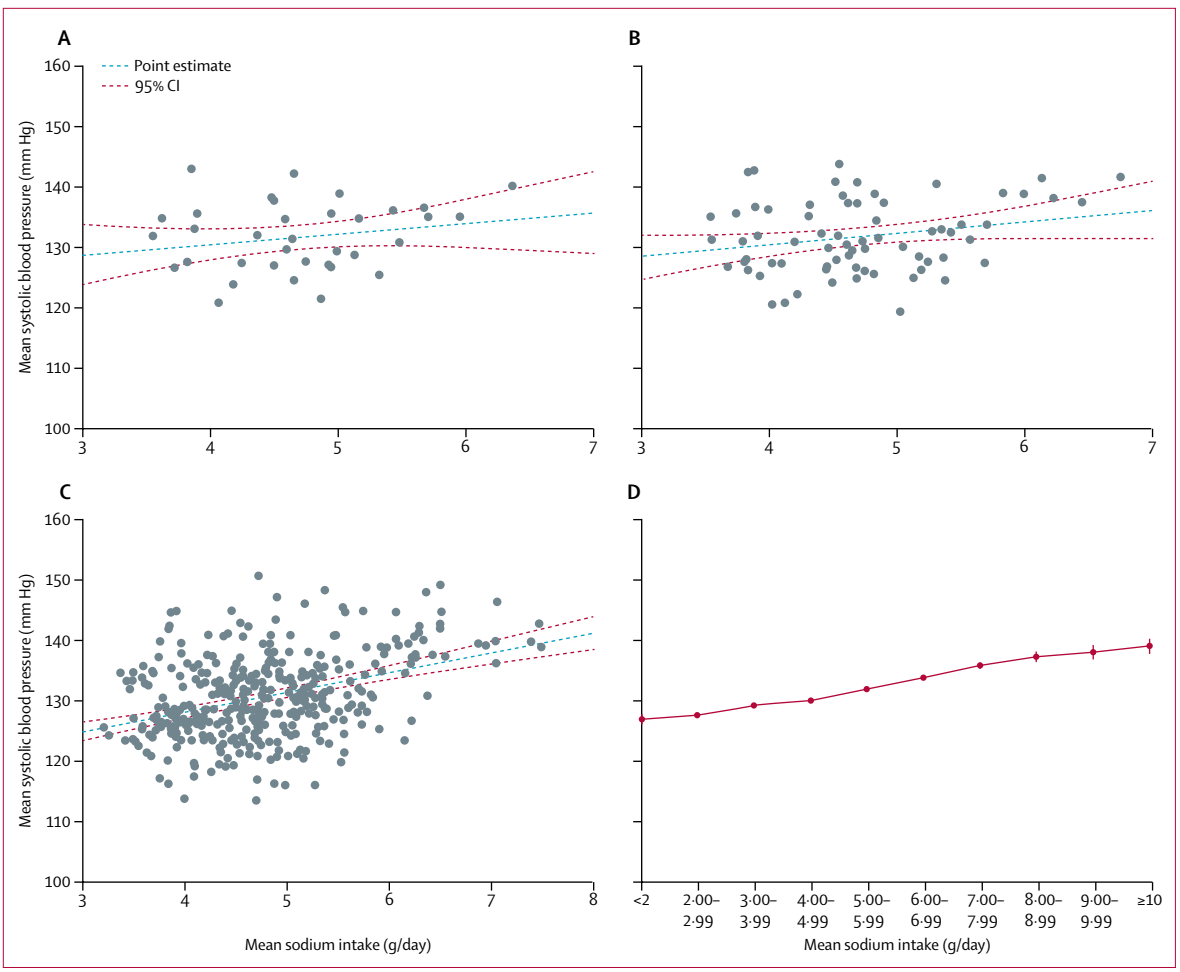

Figure 1: **Change in mean systolic blood pressure per 1 g increase in mean sodium intake**
Data are from 369 communities (70 urban and rural subcentres, 95 767 individuals). (A) Centre-level change 2·45 mm Hg (95% CI 0·09–4·82, p=0·0427). (B) Subcentre-level change 2·58 mm Hg (95% CI 0·95–4·20, p=0·0023). (C) Community-level change 2·86 mm Hg (95% CI 2·12–3·60, p<0·0001). (D) Individual-level change 2·11 mm Hg (95% CI 2·00–2·22). The results remained similar with all four different approaches.

disease. Statistical analyses were done with SAS software, version 9.3.

Role of the funding source

The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Results

The sample for the community-level analysis consisted of 95 767 participants in 369 communities (average 260 individuals per community) for the BP analyses 82 544 participants in 255 communities (average 324 per community) for the cardiovascular events analyses (appendix). The mean number of individuals in the centre-level analyses was 2501 and the mean number in the subcentre-level analyses was 1290 (appendix).

Median follow-up was 8·1 years (IQR 5·8–9·4), during which 3695 people died, 3543 had major cardiovascular events (myocardial infarction n=1372, stroke n=1965, heart failure n=343, and cardiovascular death n=914; some individuals are counted in more than one cause category), and 6281 had the composite outcome of a cardiovascular event or death. At least one follow-up visit was completed for 89 659 (95%) participants.

The mean sodium intake across 369 communities (36 centres, 70 subcentres) was 4·77 g/day (range 3·22–7·52). At the individual level, sodium intake varied much more (ie, 5th percentile 2·53 g/day, 95th percentile 7·97 g/day, range 1·92–19·2 after correction for regression dilution bias). Sodium intake was substantially higher in communities from China than those in other countries (5·58 g/day *vs* 4.45 g/day). The mean intake was greater than 5 g/day in 82 (80%) of 103 communities in China and was 5 g/day or less in 224 (84%) of 266 communities outside China. The mean potassium intake was

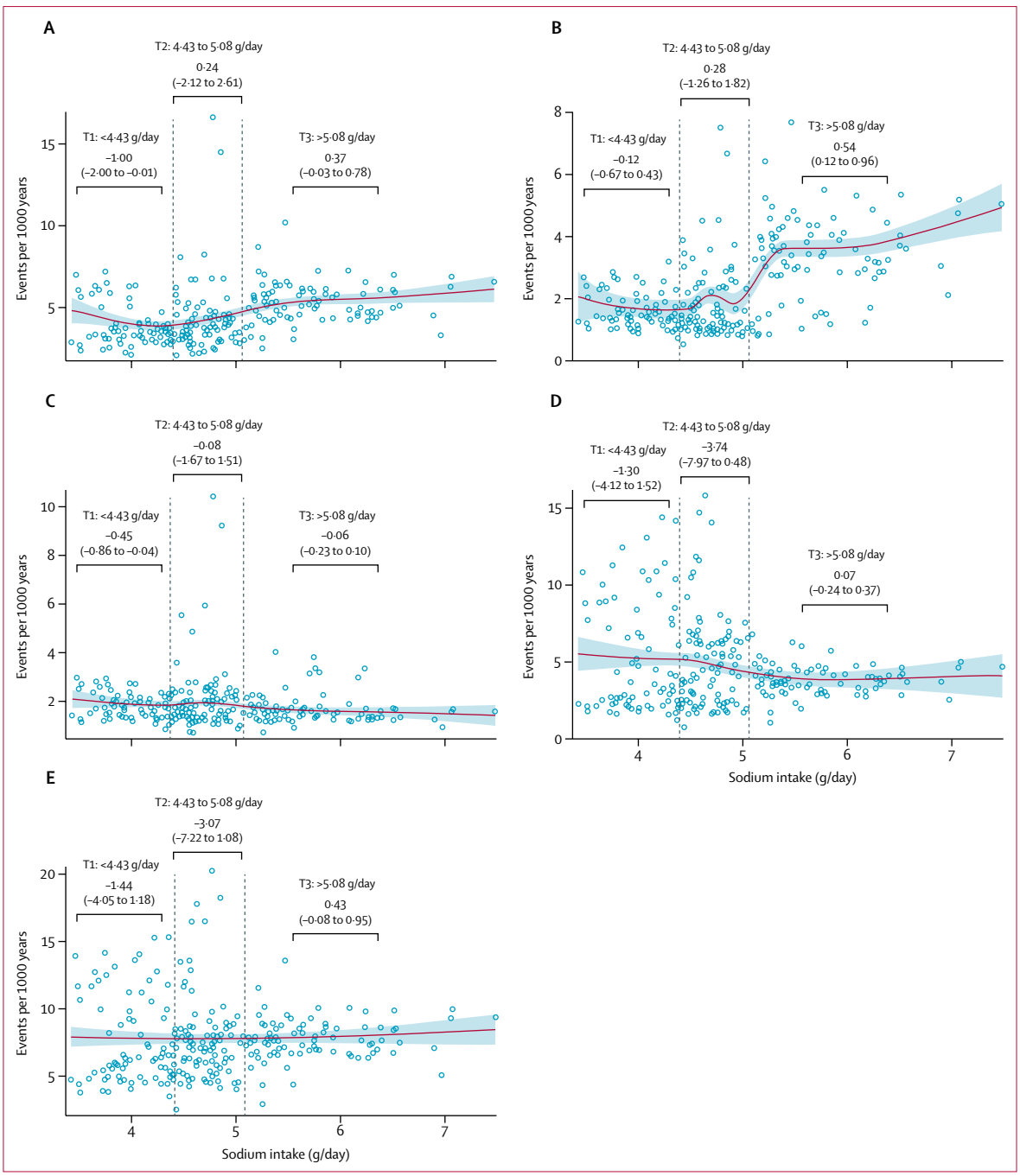

Figure 2: **Mean changes in cardiovascular event rates per 1 g increase in mean sodium intake**
Data are from 255 communities, calculated as point estimates with 95% CIs after multivariable adjustment for confounders with individual-level data, and shown by tertile of sodium intake. (A) Major CVD. (B) Stroke. (C) Myocardial infarction. (D) Total mortality. (E) Composite major CVD or death. T=tertile.

2·16 g/day (range 1·25–3·11) across 369 communities, and 2·12 g/day (0·90–7·69) in individuals after correction for regression dilution bias. Mean potassium intake did not differ between communities in and outside China (2·11 *vs* 2·18 g/day).

At all group levels, we found positive associations between estimated sodium intake and systolic BP, but precision increased with increasing numbers of data points (ie, greatest in communities and least in subcentres figure 1). For each 1 g increase in estimated sodium intake, systolic BP increased by an 2·86 mm Hg (95% CI 2·12–3·60, p<0·0001). The slope estimates in group-level analyses were stronger than those in individual-level analyses, even after adjustment for regression dilution

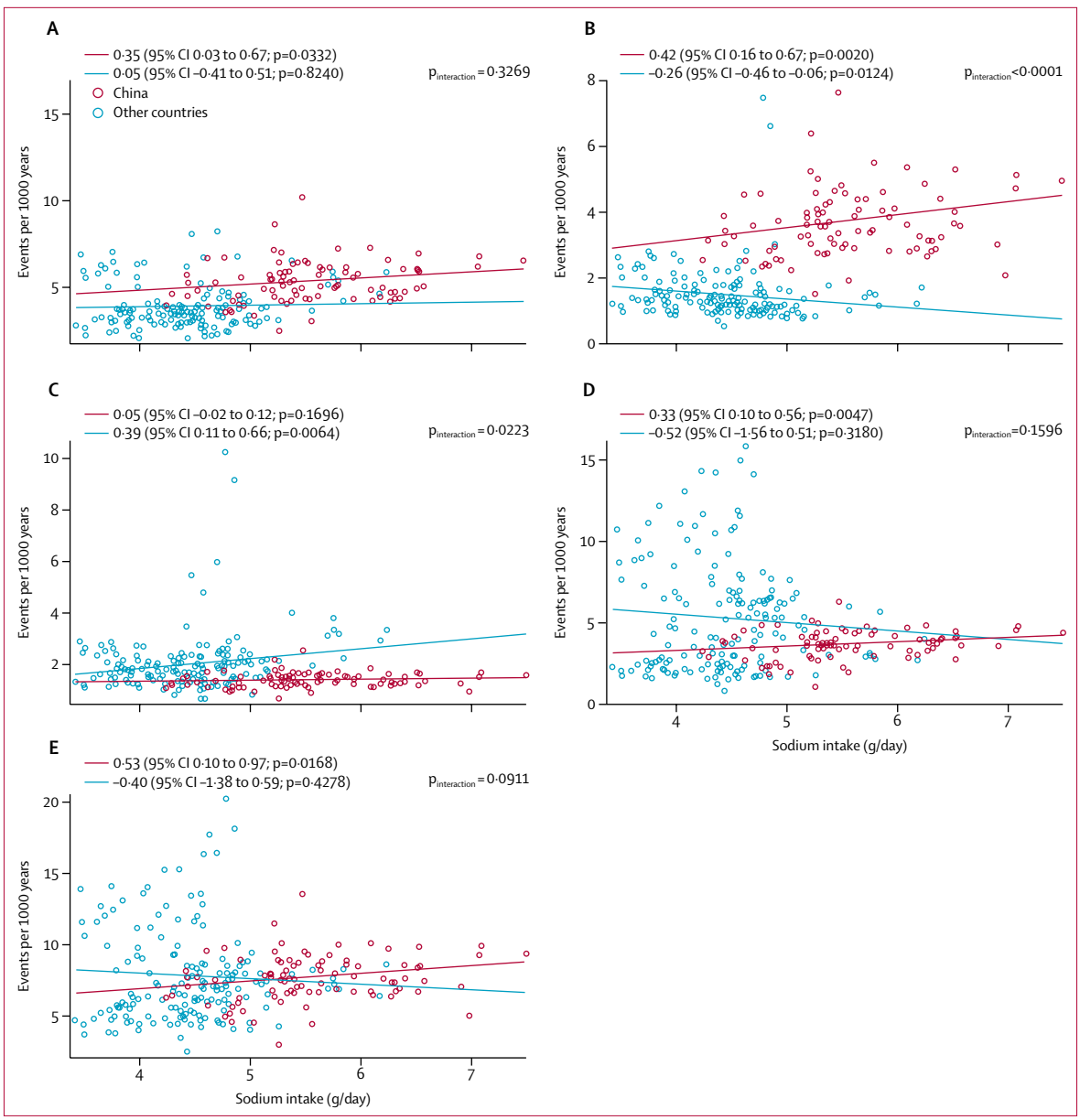

***Figure 3*: Adjusted mean cardiovascular event rates per 1 g increase in mean sodium intake**
Data are from 255 communities (China n=89, other countries n=166) and calculated as point estimates with 95% CIs. (A) Major cardiovascular disease. (B) Stroke. (C) Myocardial infarction. (D) Total mortality. (E) Composite major cardiovascular disease or death.

bias (change in systolic BP per 1 g increase in sodium intake 2·86 mm Hg *vs* 2·10 mm Hg; appendix). The associations between community-level systolic BP and sodium intake were positive, large, and significant in communities in the highest sodium intake tertile, but we saw an inverse and non-significant association in the communities with sodium intakes in the middle and lower tertiles (p<0·0001 for heterogeneity). Similar results were found for diastolic BP. Potassium intake was not significantly associated with systolic or diastolic BP.[16]

In 255 communities (33 centres, 64 subcentres), we found a positive association (p<0·0001) between mean sodium intake and the mean overall cardiovascular event rate (0·66 (95% CI 0·46–0·87) events per 1000 years per 1 g increase in sodium intake. Similar results were found in analyses at the centre and subcentre levels (appendix). After multivariable adjustment for known confounders, the positive association between sodium intake and major cardiovascular events remained similar across communities (0·73, 95% CI 0·53–0·93, p<0·0001). The association between sodium intake and major cardiovascular events showed significant deviation from linearity, having a significant inverse association in the lowest tertile of sodium intake, no association in the

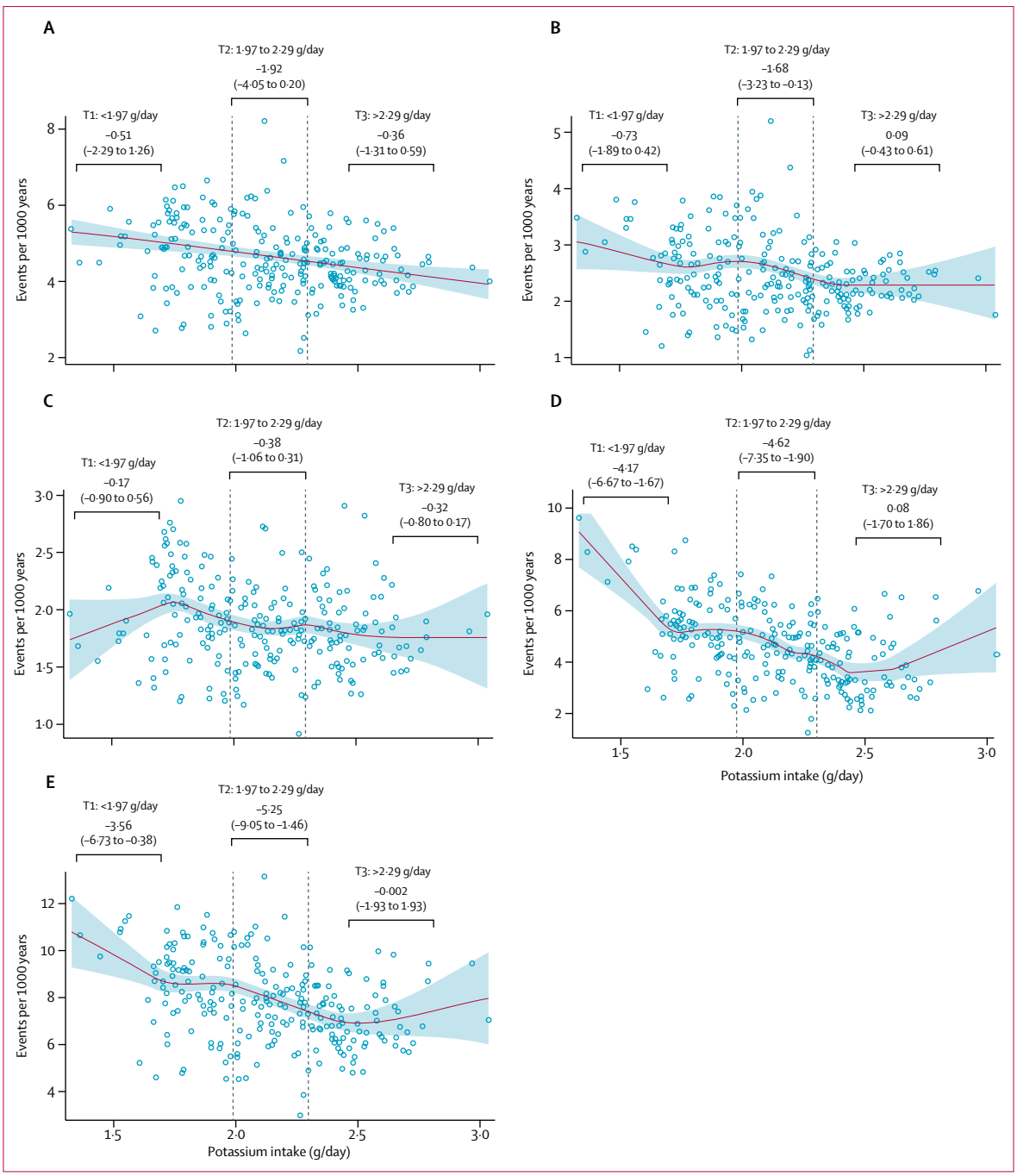

Figure 4: **Mean changes in cardiovascular outcomes per 1 g increase in mean potassium intake**
Data are from 255 communities, calculated as point estimates with 95% CIs after multivariable adjustment for confounders using individual-level data, and shown by tertile of potassium intake. (A) Major cardiovascular disease −0·77 (95% CI −1·16 to −0·38, p=0·0001; p=0·66 for deviation from linearity). (B) Stroke −0·53 (95% CI −0·80 to −0·27, p<0·0001; p=0·54 for deviation from linearity). (C) Myocardial infarction −0·28 (95% CI −0·43 to −0·13, p=0·0003; p=0·10 for deviation from linearity). (D) Total mortality −2·31 (95% CI −2·86 to −1·75, p<0·0001; p=0·97 for deviation from linearity). (E) Composite of major cardiovascular disease or death −2·39 (95% CI −3·09 to −1·68, p<0·0001; p=0·86 for deviation from linearity). T=tertile.

middle tertile, and a non-significant positive association in the highest tertile (p=0·1267 for heterogeneity of slopes estimates, p=0·043 for deviation from linearity; figure 2).

The association between each 1 g increase in sodium intake and all major cardiovascular events was primarily due to stroke (0·97, 95% CI 0·81–1·13 events per 1000 years, p<0·0001), which remained similar after

multivariable adjustment (1·01, 0·86–1·17, p<0·0001). Similarly, the association between sodium intake and stroke showed significant deviations from linearity, with a positive association found only among communities in the highest tertile of sodium intake (>5·08) and no significant association found in the middle or lowest tertiles (p=0·3437 for heterogeneity of slopes estimates, p<0·0001 for deviation from linearity; figure 2).

We found no significant association between mean sodium intake and mean rates of myocardial infarction, total mortality, or the composite outcome of major cardiovascular events or mortality after adjustment for age, sex, and country (data not shown). After multivariable adjustment, we found inverse associations between each 1 g increase in sodium intake and myocardial infarction (–0·15; 95% CI, –0·26 to –0·04, p=0·0030) and total mortality (–0·66, –1·04 to –0·29, p=0·0006), and no significant association with the composite outcome (0·09, –0·29 to 0·46, p=0·65). For myocardial infarction a significant inverse association with sodium intake was found in the lowest tertile but no association was found in the middle or highest tertiles, and for total mortality and the composite outcome of major cardiovascular events or death, inverse associations were seen in the lowest two tertiles of sodium intake (<5·08, figure 2).

When adjusted for age, sex, and BP, the associations between sodium intake and cardiovascular events did not change (appendix). This finding suggests that the effects of sodium intake on cardiovascular events is largely unrelated to the effects of sodium intake on BP.

A positive association was seen between sodium intake and stroke among the communities in China but not among those in other countries (figure 3). Similar but less significant differences were seen for all cardiovascular events, death, and the composite outcome of major cardiovascular events or death (figure 3). Conversely, we found no significant association between sodium intake and myocardial infarction in communities in China, even in the communities with high sodium intake. By contrast, we found a significant positive association with those in other countries, but this association was not found among the communities with sodium intake less than 5 g/day (figure 3).

We saw inverse relations between increasing mean potassium intake and all major cardiovascular events after adjustment for age, sex, and country (data not shown) and after multivariable adjustment, with no significant deviation from linearity (figure 4, and appendix). The associations did not differ between communities in China and those in other countries (appendix).

The sodium-to-potassium ratio showed a positive and linear association with all cardiovascular events, stroke, death, and the composite endpoint of major cardiovascular events or death, but not with myocardial infarction (appendix). Additionally, we found marked heterogeneity by region for associations with stroke, with communities in China having a significantly positive association with sodium-to-potassium ratio, but not those in other countries (p<0·0001 for heterogeneity, appendix).

Discussion

We found a positive and significant association between sodium intake and systolic BP at community, centre, and subcentre levels. This association was strong in communities with high sodium intake (>5 g/day) but not in communities with lower intake. Among the 255 communities assessed for cardiovascular outcomes, sodium intake was associated with a significantly increased rate of stroke, but inverse associations were seen with myocardial infarction and mortality. The association with stroke, however, was found only among communities in the highest tertile of sodium intake, most of which were in China. Increased potassium intake had inverse associations with all cardiovascular outcomes in all regions.

We report a stronger magnitude of association between sodium intake and systolic BP across communities (2·86 mm Hg per 1 g increase in sodium intake) than the INTERSALT study (1·94 mm Hg)[5] and other international studies (eg, INTERMAP 0·22 mm Hg).[20] In our study, the positive associations with BP at the community level were only seen in the highest tertile of sodium intake. A similar pattern was seen for stroke, which showed a positive association with sodium intake in China (mean sodium intake 5·58 g/day) but no increase in risk in other countries (mean sodium intake 4·49 g/day). By contrast, we found inverse associations between sodium intake and major cardiovascular events and myocardial infarction.

Rather than a population-wide approach, our data suggest that a targeted approach of intervening in communities and countries with high mean sodium intakes (>5 g/day) might improve reduction of cardiovascular disease (and strokes). Such an approach would avoid diversion of resources to communities with lower sodium intakes, where no correlation with increased rates of clinical events are seen, and those in which associations with BP are small. If the inverse associations between low sodium intake and increased rates of myocardial infarction and death are real, such a targeted strategy would minimise the potential for harm by sodium reductions in populations with average sodium intake.

Community-level sodium-reduction strategies have not been well assessed in clinical trials. One report indicated that reductions in mean sodium intake in the UK by around 0·4 g/day was associated with a decline in mortality,[21] but this finding was not observed in a later study.[22] Furthermore, the original report was confounded by the decline in mortality preceding the reductions in sodium and by marked decline in smoking rates and increased use of preventive therapies, such as statins. In the USA, exhortations to limit sodium intake have been ineffective.[23,24] In China, where mean intake of sodium is markedly higher than in most countries, mean sodium

intake declined by 1·9 g from 1991 to 2009 with reduced use of discretionary salt intake,[25] but no correlating changes in stroke incidence have been reported. At the community level, findings from clinical trials have been mixed. A cluster-randomised controlled trial in China involving 120 villages and 1295 participants reported a significant 0·3 g reduction in sodium intake but no significant reduction in BP.[26] A larger 5-year cluster-randomised controlled trial in 600 villages with 21000 participants is being done in China to assess the effects on stroke of using potassium-rich salt.[27] Nevertheless, even if that trial shows a reduction in strokes, the findings should not automatically be assumed to apply to countries or communities with lower sodium consumption. Rather, the data should provide impetus for similar trials of salt substitution in countries where mean sodium intake is lower than 5 g/day.[2]

Meta-analyses of individual participant data in cohort studies have revealed a J-shaped association between sodium intake and cardiovascular disease,[28,29] mirroring findings from physiological studies reporting adverse cardiovascular biomarker effects at extremes of sodium intake.[3,8,9,30,31] J-shaped or inverse associations have been seen in several studies assessing sodium intake by 24 h urine collection,[32–35] morning fasting urine,[11,36–38] or diet,[39–41] and in different types of populations (elderly people, patients with vascular disease or diabetes, and the general population).[11,32–41] Furthermore, no study has shown significantly reduced rates of clinical events with sodium intake less than 3 g/day versus 3–5 g/day.[29,42] Collectively, these findings suggest that sodium intake has a physiological role in cardiovascular health at moderate intake ranges and a pathological role when intake is high or low, which is the expected relationship between an essential nutrient and health.[30] Even when sodium intake is high, numerous studies suggest that the adverse effects are largely independent of BP,[43,44] which is consistent with our results. The inverse associations we found between sodium intake and myocardial infarction and mortality are similar to those in several individual-level data studies.[11,32–35]

We observed consistent decreases in cardiovascular disease and mortality with increasing potassium intake, without evidence of a J-shaped association. Similar associations have been reported in individual-level and group-level analyses.[45,46] Diets rich in fruit and vegetables are high in potassium and have frequently been associated with improved health outcomes, suggesting that high potassium concentrations might simply be a marker of a healthy dietary pattern.[47] Moreover, high potassium intake appears to diminish the cardiovascular risk associated with high sodium intake.[48,49] If potassium is protective, substitution of potassium for sodium in salt might be a particularly effective intervention. If, however, the health associations with potassium intake are simply markers of a better quality diet, substitutions in salt might not necessarily reduce stroke or cardiovascular disease.

Strengths of our study include our hybrid approach combining community-level analyses with individual-level data. The use of these two approaches is complementary and overcomes some of the limitations of using either alone, meaning that this method might be superior and likely to provide more robust results. The strengths and limitations of the PURE sodium study have been discussed previously[11,16,50] and are presented in the appendix.

Our findings suggest that a population-specific strategy for sodium reduction targeted at countries or communities with sodium intake greater than 5 g/day would be preferable to a population-wide strategy of sodium reduction to reduce cardiovascular disease and premature deaths. In contrast, there is a stronger case for increasing the consumption of foods that are rich in potassium (eg, fruits and vegetables) population wide.

Contributors

SY conceived and started the overall Prospective Urban Rural Epidemiology (PURE) study, SR coordinated the study, and KT was the co-principal investigator. AM and SY designed and SY supervised the present study. AM did the statistical analysis and wrote the first draft of the manuscript. SY supervised the study conduct and data analysis and provided critical comments on all drafts of the manuscript. MO'D reviewed and provided critical comments on drafts. All other authors coordinated the study and collected the data in their respective countries and provided comments on drafts of the manuscript.

Declaration of interests

We declare no competing interests.

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