Associations of urinary sodium excretion with cardiovascular events in individuals with and without hypertension: a pooled analysis of data from four studies

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Summary

Background Several studies reported a U-shaped association between urinary sodium excretion and cardiovascular disease events and mortality. Whether these associations vary between those individuals with and without hypertension is uncertain. We aimed to explore whether the association between sodium intake and cardiovascular disease events and all-cause mortality is modified by hypertension status.

Methods In this pooled analysis, we studied 133 118 individuals (63 559 with hypertension and 69 559 without hypertension), median age of 55 years (IQR 45–63), from 49 countries in four large prospective studies and estimated 24-h urinary sodium excretion (as group-level measure of intake). We related this to the composite outcome of death and major cardiovascular disease events over a median of 4·2 years (IQR 3·0–5·0) and blood pressure.

Findings Increased sodium intake was associated with greater increases in systolic blood pressure in individuals with hypertension (2·08 mm Hg change per g sodium increase) compared with individuals without hypertension (1·22 mm Hg change per g; $p_{interaction}<0·0001$). In those individuals with hypertension (6835 events), sodium excretion of 7 g/day or more (7060 [11%] of population with hypertension: hazard ratio [HR] 1·23 [95% CI 1·11–1·37]; p<0·0001) and less than 3 g/day (7006 [11%] of population with hypertension: 1·34 [1·23–1·47]; p<0·0001) were both associated with increased risk compared with sodium excretion of 4–5 g/day (reference 25% of the population with hypertension). In those individuals without hypertension (3021 events), compared with 4–5 g/day (18 508 [27%] of the population without hypertension), higher sodium excretion was not associated with risk of the primary composite outcome (≥7 g/day in 6271 [9%] of the population without hypertension; HR 0·90 [95% CI 0·76–1·08]; p=0·2547), whereas an excretion of less than 3 g/day was associated with a significantly increased risk (7547 [11%] of the population without hypertension; HR 1·26 [95% CI 1·10–1·45]; p=0·0009).

Interpretation Compared with moderate sodium intake, high sodium intake is associated with an increased risk of cardiovascular events and death in hypertensive populations (no association in normotensive population), while the association of low sodium intake with increased risk of cardiovascular events and death is observed in those with or without hypertension. These data suggest that lowering sodium intake is best targeted at populations with hypertension who consume high sodium diets.

Funding Full funding sources listed at end of paper (see Acknowledgments).

Published Online
May 20, 2016
http://dx.doi.org/10.1016/S0140-6736(16)30467-6

See Online/Comment
http://dx.doi.org/10.1016/S0140-6736(16)30510-4

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Introduction

Several prospective cohort studies[1–7] have reported that the association between sodium consumption and cardiovascular disease or mortality is U-shaped, with increased risk at both high and low sodium intake. This finding has been reported in studies done in different countries, in studies using different methods to estimate sodium intakes, and in different types of populations (ie, people with diabetes, those with vascular disease, and in the general population). A meta-analysis of 23 epidemiological studies (n=274 683) also reported a U-shaped relation.[8] Subsequently, findings from the PURE study[7] were consistent with findings from this previous meta-analysis, such that the collective data for 376 628 people involving more than 15 000 clinical events, showing a U-shaped association, are robust. In view that increasing sodium intake is related to increased blood pressure, and that this is steeper in those individuals with hypertension compared with in those without hypertension,[9,10] we hypothesised that there might be differences in the association between sodium intake and cardiovascular disease outcomes in individuals with hypertension compared with in those without hypertension. In this analysis, we explore whether the association between sodium intake and cardiovascular disease events and all-cause mortality is modified by hypertension status. We also compare the observed magnitude (and pattern) of association between sodium intake and clinical events with the predicted hazard ratio (HR) derived