Correspondence

Response to Letter Regarding Article, "Lower Levels of Sodium Intake and Reduced Cardiovascular Risk"

We welcome further discussion of our article on sodium and cardiovascular disease (CVD).[1] The methodology used in analyzing the Trials of Hypertension Prevention (TOHP) follow-up in the current article was prespecified. For those in the active sodium intervention, levels of sodium changed over time, and for some reflected short-term compliance with the intervention. Average sodium excretion would not reflect long-term usual intake for these participants and would introduce error. For this reason, we conducted our analysis solely among those who were not assigned to a reduced sodium intervention. In addition, as Drs Cohen and Alderman acknowledge,[2] we previously found a 25% lower rate of CVD in the sodium reduction arms in an analysis that took advantage of the randomized design.[3] By focusing only on the control arm in the current analysis, the results are independent of intervention effects that we have already reported.

Our previous analyses, which compared the experience in those randomized to the sodium reduction intervention with those randomized to usual care, included all outcome events during the trial periods as well as during long-term follow-up. For the current observational analysis we prespecified use of the end of the 1- to 4-year trial periods as the start of our long-term follow-up for ascertainment of CVD. Our exposure was defined as the average sodium excretion throughout the trials, and those with outcome events during these exposure periods were not included. This was again to enhance the quality of our exposure definition by using all collected excretion data.

Although the line in Figure 2 appears linear, the analysis makes no assumption of linearity. Outliers and extreme values can influence a straight line, but Figure 2 depicts a flexible spline curve. The increased risk of CVD at high levels of sodium excretion thus does not influence the estimated risk at the lowest levels. Our findings provide strong evidence that the effect is linear throughout the range of sodium intake, with no evidence of a J-shaped curve.

Finally, we would like to stress that sodium intake is notoriously difficult to measure.[4] Single measures of excretion, particularly spot urines, provide limited capacity to obtain a valid estimate of usual sodium intake. Even 24-hour excretions are subject to problems related to undercollection and variations in daily diet. In TOHP, our goal was to obtain an accurate measure of usual sodium intake by averaging the values for sodium excretion from several carefully collected 24-hour urine specimens obtained over several years in each participant. This approach reduces measurement error as well as seasonal, daily, and diurnal variation. Most of the studies that have been reported have suffered from imprecise measurement of the exposure and a variety of other methodological errors that have the potential to yield spurious results.[5] Such studies have led to confusion on the effects of sodium on CVD by introducing imprecision and bias. We strongly believe that TOHP data provide the most methodologically sound evidence on this important question.

Disclosures

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Nancy R. Cook, ScD
Division of Preventive Medicine
Brigham and Women's Hospital
Harvard Medical School
Boston, MA

Lawrence J. Appel, MD, MPH
Welch Center for Prevention, Epidemiology, and Clinical Research
The Johns Hopkins School of Medicine
Baltimore, MD

Paul K. Whelton, MB, MD, MSc
Department of Epidemiology
Tulane University School of Public Health and Tropical Medicine
New Orleans, LA

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