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COMMENTS AND OPINIONS

Reanalysis of NHANES III Data on Sodium Association With Mortality: Appropriate Adjustment for Potassium Not Performed

In their reanalysis of the Third National Health and Nutrition Examination Survey (NHANES III), Yang et al[1] reached an opposite conclusion from the first NHANES III analysis of almost the same data[2] and other recent population studies,[3,4] which show that low sodium intake is associated with increased mortality.

According to eTable 7 in their article, all-cause mortality decreases with increasing sodium intake: quintile (Q)1, 699; Q2, 509; Q3, 450; Q4, 372; and Q5, 240 (based on single 24-hour dietary recall). Remarkably, the adjustments performed by Yang et al[1] not only attenuated this trend but reversed it. This may be because Yang et al, in contrast to the majority of similar studies, did not adjust for potassium.

The creation of the sodium-potassium ratio gives the impression of adjusting sodium for potassium, but in fact allows potassium to drive the association rather than adjust it. This allows the authors to make a statement about sodium only based on the ratio, which they might not be able to make based on a sodium model adjusted for potassium. The ratio is in fact a multiplicative product interaction term of sodium with the inverse of potassium, and it is conventional in regression analyses to test such a term for significance in the presence of both main effect terms (ie, sodium and the inverse of potassium). If the product term does not add significantly or meaningfully to a model while simultaneously adjusting for both main effect terms, the general practice is not to use the more complicated product term when simpler main effects will do. We suggest the results of such a test be reported.

Furthermore, we suggest that eTable 7 be shown as quartiles consistent with the rest of the article instead of quintiles and, for comparison, that the numbers of all-cause deaths in the 4 quartiles of Table 2 (corrected for a second 24-hour dietary recall of sodium intake) be given.

The different interpretations of the NHANES III data show that the result of a multivariable regression analysis depends on which confounders are included in the model. Furthermore, they illustrate the lack of unambiguous evidence and robustness that characterizes the attempts to relate sodium intake to morbidity and mortality. Such data are not sufficient to recommend a general reduction in sodium intake.[5]

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Financial Disclosure: None reported.

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Method of Estimating Sodium Intake and Its Possible Influence on NHANES III Outcome

One justification for the repeated analysis of the Third National Health and Nutrition Examination Survey (NHANES III)[1] is that the original analysis[2] only used 1-day dietary recall data to estimate sodium intake. According to the authors, a single dietary recall estimation of salt intake is insufficient compared with a method based on 2 estimations. However, Caggiula et al[3] found that the difference between a single and the average of 2 dietary recall estimations was minimal, but that the estimation by both recall methods was significantly smaller than the 24-hour urine sodium excretion (approximately 60 mEq/L [to convert to mmol/L, multiply by 1.0]). Consequently, the major difference is not between different recall methods but between dietary sodium recall and urine sodium excretion, the latter being considered the gold standard. However, to evaluate the quantitative significance of the method used by Yang et al[1] to correct sodium intake, which they based on only 7.2% of the participants, it would be important for the authors to provide the number and percentage of participants changing sodium intake quartile as a result of this correction.

The results of Yang et al[1] are not only in contrast to the previous interpretation of NHANES III but also to a number of other reports.[4] Finally, according to eTable 5, the findings are not general but limited to overweight persons, and thus, the data do not justify a general recommendation of sodium reduction.

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