Sodium and Potassium Intake: A New Statistical Model to Test Their Effects on Health Outcomes

To the Editor: In their article "Urinary Sodium-to-Potassium Ratio and Blood Pressure in CKD," Alencar de Pinho *et al.*[1] report a significant association between urinary sodium and blood pressure among patients with chronic kidney disease from the REIN cohort study. This is an additional piece of evidence in favor of the deleterious effect of sodium intake on blood pressure among patients with chronic kidney disease while this relationship is well documented in numerous populations.[2]

In this study, urinary sodium-to-potassium ratio was associated with blood pressure whereas potassium was not. It can be puzzling to conclude for the significance of a ratio when one of its components is not significant. A similar result was observed in the CoLaus study in which a significant association was observed between urinary sodium and urinary sodium-to-potassium ratio with age-related kidney function decline. Indeed, the authors faced a similar situation when finding no association for urinary potassium.[3]

We propose a new regression model able to solve this issue and to separate the intrinsic effect of sodium and potassium from their respective interaction: one could build a unique regression model with sodium, potassium, and the interaction between each other. The interpretation is greatly facilitated. If the interaction is nonsignificant, the effects of sodium and potassium are additive, whereas if the interaction is positive or negative, the effects are nonadditive. Moreover, this model, which is an alternative to the sodium-to-potassium ratio, is compatible with the physiological literature that suggests that these effects could be nonadditive.[4]

1. Alencar de Pinho N, Kaboré J, Laville M, et al. Urinary sodium-to-potassium ratio and blood pressure in CKD. *Kidney Int Rep*. 2020;5:1240–1250.
2. Huang L, Trieu K, Yoshimura S, et al. Effect of dose and duration of reduction in dietary sodium on blood pressure levels: systematic review and meta-analysis of randomised trials. *BMJ*. 2020;368:m315.
3. Deriaz D, Guessous I, Vollenweider P, et al. Estimated 24-h urinary sodium and sodium-to-potassium ratio are predictors of kidney function decline in a population-based study. *J Hypertens*. 2019;37:1853–1860.
4. Gritter M, Rotmans JI, Hoorn EJ. Role of dietary K+ in natriuresis, blood pressure reduction, cardiovascular protection, and renoprotection. *Hypertension*. 2019;73:15–23.

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The Authors Reply: We thank Deriaz *et al.*[1] for their proposal to use a regression model including sodium, potassium, and an interaction term between the two rather than sodium-to-potassium ratio, to determine whether or not this interaction is significant. We repeated our analysis in the CKD-REIN cohort,[2] using a linear model that included spot urinary sodium-to-creatinine (uNa/Cr), potassium-to-creatinine (uK/Cr), and an interaction term to estimate the effect on systolic blood pressure, while adjusting for potential confounders. In Table 1, we show the adjusted mean difference in systolic blood pressure expressed in mm Hg by quartiles of uNa/Cr for a median uK/Cr, by quartiles of uK/Cr for a median uNa/Cr, and by quartiles combining increasing uNa/Cr quartiles with decreasing uK/Cr quartiles to estimate joint effects.

As in our primary analysis,[2] systolic blood pressure significantly increased across spot uNa/Cr quartiles ($P = 0.003$), up to 5.12 (3.15 to 7.10) mm Hg between the fourth (Q4) and the first quartile (Q1), while it decreased, although