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However, to clarify whether high salt intake or sodium itself increases the risk of OSA, further studies comparing differences between daytime and nighttime sodium excretion and their relationship with OSA are required.

<u>Author disclosures</u> are available with the text of this letter at www.atsjournals.org.

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8 Reply: Salt, Diuretics, and Obstructive Sleep Apnea

From the Authors:

We fully appreciated the interest in discussing our recent findings pointing to an independent association of sodium excretion with obstructive sleep apnea (OSA) in participants with hypertension but not in the normotensive ones (1). Until recently, it was not clear whether we could extrapolate the role of dietary sodium and related fluid retention on the OSA pathogenesis to all myriad of patients with this important and prevalent sleep-disordered breathing. The main take-home message from our study is that the role of sodium and related fluid retention is probably limited to hypervolemic conditions (1).

Drs. Tabara and Chin (2) appropriately argued that our strategy for limiting the sodium excretion analysis to 12 hours (7 P.M. to 7 A.M.) is not

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ideal, to which we agree. This strategy was chosen to minimize the inaccuracy of the urine volume collected and stored during working periods and to avoid the influence of significant sodium loss in sweat in this large sample size (1). As discussed in the paper, the ELSA-Brasil study previously validated the 12-hour urine collected at night to estimate 24-hour excretion of sodium (3, 4). Moreover, it is also important to stress that the 12-hour urine sample certainly surpasses the sleep time. Most of the participants from the ELSA-Brasil study slept 6–7 hours (5). In our study, we had the opportunity to perform additional analysis using 24h sodium intake instead of sodium excretion. The consistent results reinforce the main study message (1). Despite these arguments, we agree that additional analysis using daytime and nighttime sodium excretion may provide incremental findings for improving our current understanding of sodium's impact on OSA according to the hypertension and blood pressure dipping

The influence of the individual susceptibility to the effects of salt intake (salt sensitivity) is another interesting point discussed by Tabara and Chin. Salt-sensitive individuals usually present an abnormal kidney reaction to salt intake (6) and have been estimated to be present in approximately half of the patients with hypertension and a quarter of normotensives (7); in this scenario, it is conceivable that salt-sensitive patients may be more susceptible to the fluid retention and therefore more susceptible to the upper airway collapse during sleep. The major

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challenge for pursuing this hypothesis is the lack of feasible and straightforward methods for measuring salt sensitivity in clinical practice due to multiple confounders (6).

We also are grateful for the comments provided by Revol and colleagues (8). They highlighted the potential role of diuretics on ameliorating OSA severity based on the overnight rostral fluid shift phenomenon. Their huge propensity-matched analysis data showed that the presence of diuretics reduced the severity of OSA only in patients with hypertension but not in the entire population (9). Our results are, therefore, in line with this real-life observation. The authors argued that these combined properties—a well-established antihypertensive treatment (10) and the effects on chronic fluid retention as a mediator of OSA severity—make diuretics one of the preferable choices for hypertensive patients with comorbid OSA. Although we agreed about this attractive strategy, definitive evidence from head-to-head comparisons between diuretics and other classes would be ideal. It is important to note, however, that the vast majority of available studies showed modest effects of diuretics on OSA severity (11, 12), underscoring the need for combined and personalized treatments as suggested by Revol and colleagues (8).

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