

## What Does a Serum Sodium Cost?

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The article by Shea *et al.*<sup>1</sup> in this issue of *JASN* uses observational techniques to define the association between disordered serum sodium concentration and the cost of medical care in the 6- and 12-mo periods after diagnosis. Most significant, they find patients with hyponatremia have highly elevated costs despite the relatively mild hyponatremia in most patients. Although the magnitude of the univariate relationship declines substantially after adjustment for comorbidities, it remains economically significant. To their credit, the authors make no specific claim that their estimate of the relationship between serum sodium and costs is causal; however, they also fail to raise the standard caveats regarding observational studies and, by emphasizing that hyponatremia remains a significant, independent predictor of costs after adjustment for case mix, do little to dissuade the reader from reaching such a conclusion. Some key issues regarding the analysis and its limitations remain largely unaddressed in the article. In this editorial, we raise several of these issues as a stimulus for clarifying future research.

One issue related to this study lies in determining whether the results can be generalized. Given the information reported in the article, it is impossible to ascertain how likely it is that the results will generalize to broader populations. The authors draw their analytic sample from a large, managed care claims database including over 25 million enrollees; however, other than an apparent concentration in the Middle Atlantic region, we are given no information about how these enrollees compare with the entire population with private insurance or the United States population as a whole. Because laboratory values on serum sodium levels are necessary for the study, the authors restrict attention to the 10% of enrollees for whom outpatient laboratory data were available. Again, we are not told how that 10% compares with the enrollee population as a whole. Presumably, only a few of the 30 managed care plans in the database provided this information. It would be useful to know how the features of those plans and the characteristics of their

enrollees compared with the larger database. Finally, attention is limited to patients with two serum sodium laboratory results within a 60-d window. This results in an analytic sample that includes about two thirds of 1% of the enrollee population.

A second technical issue with this study relates to potential limitations of the case-mix adjustment. Assessing success of case-mix adjustment is crucial to interpretation of the results and ultimately to assessing the clinical implications of the study. To avoid biased estimates of the effects of hyponatremia and hypernatremia on costs, a researcher would ideally measure and control for all other variables that affect costs and are correlated with the abnormal level of serum sodium. In practice, the extent that such biases have been avoided, it is neither certain nor directly testable; therefore, it is necessary to assess which factors were measured and how well they were measured. Shea *et al.*<sup>1</sup> used diagnoses reported on the claims to ascertain the presence of a variety of underlying conditions; however, they examined claims for services only within the 60 d preceding the reference serum sodium date. Most of the conditions they considered are relatively long term or chronic, such as diabetes or cerebrovascular disease, calling the 60-d interval into question. Such conditions could readily be present without being reported on a medical claim during a short time interval. Other comorbidities that may affect costs over the subsequent 6 or 12 mo (*e.g.*, nonmetastatic carcinoma, HIV infection, psychiatric disease) are not reported at all. Finally, even if all relevant comorbidities were measured and accurately identified as present or absent, their severity could still vary in unmeasured ways. For example, if hyponatremia is a marker for a more severe than average case of congestive heart failure, then higher costs associated with hyponatremia may simply reflect this correlation with severity. Taken together, these limitations leave open the very real possibility that the observed relationships between serum sodium and costs remain biased by unobserved case mix.

Interestingly, case-mix adjustment had a substantial effect on the results, with the magnitude of the association between hyponatremia and costs declining by nearly 60% after the potential demographic and clinical confounders were added to the model (the association between hypernatremia and costs declined even more). An optimistic interpretation is that case-mix adjustment “did its job,” and the remaining association reflects the true, independent contribution of serum sodium status to costs; however, given the substantial limitations in the measurement of comorbidities noted, there also exists a plausible—but more pessimistic—interpretation. If this imperfect case-mix adjustment had such a large effect on the measured associations, then it is quite possible that an ideal case-mix adjustment would account for much or all of the remaining associations.

So, what is the practitioner to make of these findings? Certainly, a belief that treating sodium imbalances, absent treat-

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ment for underlying conditions that may be correlated with these imbalances, will produce substantial savings could not be held with great confidence on the basis of these limited observational data. Furthermore, to the extent that the sodium imbalances were treated in the studied patients, the estimated associations with cost are those that remain after treatment (notably because some enrollees did not have pharmacy benefits, pharmacy costs were excluded from the cost measures, or the direct costs of pharmaceutical treatment for sodium imbalances are not captured). Clearly, this study presents some new data and can serve as the springboard for useful, further research; however, readers should take care not to misinterpret the findings and their implications for practice.

## DISCLOSURES

None.

## REFERENCES

1. Shea AM, Hammill BG, Curtis LH, Szczech LA, Schulman KA: Medical costs of abnormal serum sodium levels. *J Am Soc Nephrol* 19: 764–770, 2008

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See related article, "Medical Costs of Abnormal Serum Sodium Levels," on pages 764–770.