

## Methodologic Issues Relating to Outcomes in Severe Hyponatremia With and Without Desmopressin



To the Editor:

We read the article by MacMillan and Cavalcanti with great interest.<sup>1</sup> They proposed to compare outcomes in hyponatremia on the basis of desmopressin (DDAVP) usage. They found that baseline characteristics are statistically different between the groups with and without DDAVP; but we wonder why they compared outcomes between these 2 groups using univariable models and why no confounders were controlled between the groups. Additionally, it should be stated that the number of patients in each group was high, and many confounders could be controlled in their study. Hence, their results may be biased owing to confounding effects.<sup>2</sup>

Our second point is that the authors stated that the quantitative variables were compared by using Wilcoxon and Kruskal-Wallis tests, which is problematic. The Wilcoxon test is used when nonnormally distributed quantitative variables are compared in related or dependent samples, whereas the samples in their study were independent and the Mann-Whitney *U* test should be used to obtain valid results.<sup>3</sup>

Finally, the multivariable logistic regression model was used to predict odds of in-hospital death, but confounders were not selected according to the defined criteria. It has been suggested that variables for which the estimated effect size (odds ratio in their study) is changed more than 10% in the univariable and corresponding multivariable model should be selected as confounders and imported into the multivariable model.<sup>4</sup> Otherwise nonconfounders may be imported into multivariable model and lead to over-parameterization of the

model; and on the other hand, some confounders may be missed.

The take-home message for readers is that multivariable regression models should be applied when the distribution of confounders is different between studied groups. Additionally, the confounders should be detected according to the standard criteria to obtain a parsimonious model with efficient controlling of confounders. Finally, nonparametric tests should be used appropriately considering the dependency of samples.

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## References

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