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Letters to the Editor

Comments on decreased mortality in patients prescribed vancomycin after implementation of an antimicrobial stewardship program

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To the Editor:

We read the article by Conway et al[1] with great interest; however, we think some methodologic and statistical issues should be taken into account to avoid misinterpretation.

The authors[1] stated that predictors with P values < .05 in univariate analysis were considered further for multivariable analysis. It is important to emphasize that such a univariate criterion can increase the risk of Testimation bias in the resulting effect estimates.[2,3] Testimation bias will occur when a conservative univariate P value is considered in multivariable analysis.[2] The authors studied the effect of several baseline and clinical patient characteristics on death in univariate analysis.[1] Some of them had a relatively large effect; for example, those with $P < .05$ and some others had a relatively small effect (eg, body mass index with $P = .06$ in univariate analysis).[1] When predictors with relatively large effect only are included in multivariable analysis, the effect of such predictors will be overestimated.[2] Such overestimation of effects of strong predictors is known as Testimation bias.[2] To reduce this bias several strategies have been suggested. For example, a liberal univariate P value < .10 or < .20 can be considered in multivariable analysis or predictors can be selected based on both statistical test and clinical relevancy.[2]

Moreover, the authors[1] point out that external validity of the results may be low. We think internal validity of the results is still questionable. Cross-validation and bootstrapping are efficient strategies for checking internal validity of results.[2]

A take-home message for readers is that the estimated odds ratios for the predictors of death in patients treated with intravenous vancomycin therapy should be considered along with the degree of Testimation bias.

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Conflicts of interest: None to report.

Decreased mortality in patients prescribed vancomycin after implementation of an antimicrobial stewardship program

To the Editor:

Thank you to Drs Safiri and Ayubi for their response to our article on the topic of mortality associated with vancomycin after implementation of an antimicrobial stewardship program.[1] We agree that a conservative P value of <.05 can increase the risk of testimation bias for univariate analysis included into a multivariate analysis. However, we feel that you are confusing effect size with P value.

By using a P value of <.05, 5 predictors were included into our multivariate model in accordance with the commonly accepted rule of 10 events per variable (EPV) in logistic regression models. We had 11 events for every variable included in the model. Furthermore, a study done by Vittinghoff and McCulloch concluded the rule of 10 EPV could be further relaxed because they found uncommon

statistical issues with 5-9 EPV.[2] Bootstrapping is unnecessary in studies with a large sample size.

References

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Conflicts of interest: None to report.

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