

Letter to the Editor

Stroke welcomes Letters to the Editor and will publish them, if suitable, as space permits. Letters must reference a Stroke published-ahead-of-print article or an article printed within the past 4 weeks. The maximum length is 750 words including no more than 5 references and 3 authors. Please submit letters typed double-spaced. Letters may be shortened or edited.

Letter by Dijkland et al Regarding Article, “Development and Validation of a Predictive Model for Functional Outcome After Stroke Rehabilitation: The Maugeri Model”

To the Editor:

With great interest, we read the study by Scrutinio et al,¹ which describes the development and validation of the Maugeri model that predicts functional outcome after inpatient stroke rehabilitation based on easily obtainable clinical characteristics. We agree with the authors that prediction of functional outcome after stroke rehabilitation is important to inform patients and relatives on prognosis and to identify rehabilitation goals. The authors performed external validation of the model, which is crucial to evaluate generalizability. However, we noted opportunities for methodological improvement in the development and validation of the Maugeri model. More specifically, do the modeling strategies that were used support the authors' conclusion on applicability in clinical practice? We will address some key methodological concepts and provide recommendations for future stroke prediction research.

First, Scrutinio et al¹ dichotomized the primary and secondary ordinal outcome measures (motor Functional Independence Measure score >61 points and physical independence grade ≥ 5 according to the Functional Independence Staging system). However, dichotomization of ordinal and continuous outcome measures reduces statistical power.² Statistical approaches preserving the ordinal or continuous nature of outcome measures, such as proportional odds logistic regression or linear regression, have been recommended.

Second, an effective sample size and adequate selection of predictors are necessary to develop a robust model for prediction purposes. Scrutinio et al¹ considered 19 candidate predictors for potential inclusion in the models. For binary or categorical outcome measures, a minimum of 10 events (ie, patients with the defined outcome) per variable is required for an effective sample size.³ The derivation cohort had a sample size of 717 patients, with 206 patients achieving the primary outcome and 100 patients achieving the secondary outcome. Therefore, an effective sample size is only just attained for the primary outcome (10 events per variable), and sample size is insufficient for the secondary outcome (5 events per variable). Furthermore, the final model for each outcome was derived with a forward stepwise selection approach. Stepwise selection methods have the disadvantage of causing unstable predictor selection and biased estimates of regression coefficients.⁴ The combination of a relatively small sample size and the forward stepwise selection approach causes overfitting, resulting in an overoptimistic impression of model performance. This

is confirmed by a relatively large decrease in area under the curve between the development and validation data, especially for the model predicting physical independence (area under the curve of 0.913 in development data and 0.850 in external validation).

Third, the Hosmer–Lemeshow test for the model predicting physical independence showed substantial miscalibration (χ^2 statistic, 34.50; $P=0.001$).¹ Thus, although the Maugeri model was externally validated, the results are unsatisfactory. How did the authors incorporate this finding in the final model and the conclusion of their study? To obtain the best estimates for the regression coefficients, a preferable approach would be to fit the Maugeri model on the combined data of both cohorts.

In conclusion, there are potential methodological improvements in the development and validation of the Maugeri model. Therefore, the current study results should be interpreted with caution. Application of the Maugeri model in rehabilitation research and stroke management can only be recommended after thoroughly performed external validation and incorporation of the validation results in the model.

Acknowledgments

We thank Prof Gerard M. Ribbers, Erasmus MC University Medical Center Rotterdam, who provided helpful comments on this letter.

Disclosures

None.

Simone A. Dijkland, MD
Diederik W.J. Dippel, MD, PhD
Hester F. Lingsma, PhD
Erasmus MC University Medical Center
Rotterdam, the Netherlands

References

1. Scrutinio D, Lanzillo B, Guida P, Mastropasqua F, Monitillo V, Pusineri M, et al. Development and validation of a predictive model for functional outcome after stroke rehabilitation: the Maugeri model. *Stroke*. 2017;48:3308–3315. doi: 10.1161/STROKEAHA.117.018058.
2. Altman DG, Royston P. The cost of dichotomising continuous variables. *BMJ*. 2006;332:1080. doi: 10.1136/bmj.332.7549.1080.
3. Wynants L, Bouwmeester W, Moons KG, Moerbeek M, Timmerman D, Van Huffel S, et al. A simulation study of sample size demonstrated the importance of the number of events per variable to develop prediction models in clustered data. *J Clin Epidemiol*. 2015;68:1406–1414. doi: 10.1016/j.jclinepi.2015.02.002.
4. Steyerberg EW, Eijkemans MJ, Habbema JD. Stepwise selection in small data sets: a simulation study of bias in logistic regression analysis. *J Clin Epidemiol*. 1999;52:935–942.