Instead, increasing predictor dimensionality rather increases the risk of overfitting the data, reducing model generalizability and reproducibility. Second, we theoretically agree with Nelson et al that further clinical predictor variables might have improved model performance. However, such improvements usually come with an exploding translational cost of such models, fueled by increased assessment time, clinical skills requirements, missing data, etc, which reduce cost effectiveness and hence clinical utility. Third, the expansion of the variable space proposed by Nelson et al may not only reduce clinical utility, scalability, and generalizability; it bears the significant risk that the variable selection process blindly amalgamates items from different clinical instruments, thus leading to a tool of unknown construct and content validity. Therefore, prospective studies would be needed to test these aspects of tool validity in new patient populations—a clear delay in the implementation of prognostic tools that are urgently needed to improve early recognition and prevention of disability in young patients at risk of poor functional outcomes. The simplicity of a narrow range of well-established predictors, such as we selected, addressed this point on validity.

In the context of these considerations, we believe that the comments by Nelson and colleagues are highly valuable because they lay out a research question of broader interest to the field: what is the optimal balance between model parsimony and complexity for a given predictive end point? This research question will be highly useful to guide analysis efforts in the Personalized Prognostic Tools for Early Psychosis Management (PRONIA) consortium and other projects aiming at developing predictive tools for a future preventive management of psychiatric disorders.

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CORRECTION

Error in Methods and in Figure Axis: In the Original Investigation titled “Effect of Damaging Rare Mutations in Synapse-Related Gene Sets on Response to Short-term Antipsychotic Medication in Chinese Patients With Schizophrenia: A Randomized Clinical Trial,” published online November 7, 2018, and in the December print issue of JAMA Psychiatry, there was an error in the methods section and the y-axis of Figure 2. In the third paragraph of the Methods section, the parenthetical definition “(PANSS score at week 6 – PANSS score at baseline)” should have been “(PANSS score at baseline – PANSS score at week 6).” In Figure 2, the y-axis copy “Minor Allele Frequency, %” should have been “Frequency.” The article has been corrected online.