Choosing the appropriate rating scale for patient inclusion and primary endpoint definition in MDD trials: MADRS or HAMD?

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Methodological Issue Being Addressed Is there an association between the rating scale we use as severity measure for including major depressive disorder (MDD) patients in a clinical trial, the rating scale we define as primary endpoint, and the success of the trial?

Introduction Among the most established scales to rate severity in major depressive disorder (MDD) are the Hamilton Depression Rating Scale in its 17-item version (HAMD) and the Montgomery Åsberg Depression Rating Scale (MADRS). In clinical trials testing treatment efficacy in MDD patients either one or both scales are usually used as inclusion criteria, and the primary endpoint is often defined as change from baseline in one of these scales . By analyzing recent clinical trials, we are exploring the current practice in MDD trials, and test associations between scales and trial results.

Methods We systematically selected 110 randomized controlled trials of phase 2 or 3 in MDD patients (conducted since 2015, listed on Citeline, industry sponsored, >19 patients, having an NCT-, EUCT- or EUDRACT number and having MADRS or HAMD as inclusion criteria and primary outcome variable) and analyzed frequencies of different clinical trial design features and their associations with trial success.

Results Among the 110 studies analyzed, 87 (79%) defined their primary endpoint based on the MADRS. Regarding inclusion criteria, the MADRS was likewise the predominant measure in 64 (58%) studies. The median cut-off for inclusion was 25 points on MADRS, and 20 on HAMD, respectively. Of the trials, 58 were completed with results published. Trial success (a significant primary endpoint) was more often observed in studies which have used the same scale for both inclusion criteria and outcome definition (55% vs. 45%), and in monotherapy versus adjunctive therapy trials (71% vs. 41%). Also, studies with a higher threshold for inclusion were more successful. None of the associations reached the conventional threshold for statistical evidence ($p<0.05$).

Conclusion Our analysis yielded inconclusive results. While the practice of including on a different scale than the primary efficacy endpoint scale is relatively common (around one third of the trials), no obvious benefit seems to be associated with this approach. Numerically more studies have a significant primary endpoint when using the same scale for inclusion and primary endpoint definition. Monotherapy trials were more successful, but this result might be confounded by less severe depression of included patients. A potential publication bias must be mentioned as a

limitation.

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Keywords

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Guidelines I have read and understand the Poster Guidelines

Disclosures Jonas Huber, Caren Strote, Jonas Henningsen, Annet Glas and Hans Eriksson are full time employees of HMNC. Christine zu Eulenburg is a consultant for HMNC. Christine and Hans hold shares of HMNC. Alan Kott and Xingmei Wang are full time employees and share holders of Signant Health.