

Equipercentile Linking Masks Data Quality Concerns in Depression Clinical Trials

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Introduction

- Equipercentile equating or linking is a psychometric method used to align scores from different measures, usually to identify equivalent scores across two different tests that measure the same construct.
- Clinical Outcome Assessment (COA) applications of equipercentile linking have included:
 - Identifying corresponding scores between the Structured Interview Guide for the Montgomery-Asberg Depression Rating Scale (SIGMA/MADRS) with the Clinical Global Impression-Severity Score (CGI-S).¹
 - Equating the Positive and Negative Syndrome Scale (PANSS) with the Brief Psychiatric Rating Scale (BPRS).²
 - Aligning scores from patient-reported outcomes (PROs).³
- Much less attention has been directed at data quality considerations (e.g., errant rater scoring, data entry errors, rater drift) when equating or linking methods are used for clinical trial analyses and decision-making.
- We examined how data quality may impact fundamental psychometric foundations for establishing equipercentile linking across the MADRS and CGI-S, with implications for Risk-Based Data Monitoring (RBDM) in clinical trials discussed.

Methods

- We examined associations between the MADRS and CGI-S using baseline data from 6 Major Depressive Disorder (MDD) clinical trials (n = 2712) using graphical equipercentile linking⁴ to identify corresponding scores across measures.
- All trials used quality improvement interventions prior to the present analysis via Risk-Based Data Monitoring (RBDM).
- Correlation/regression-based analyses were used to examine the strength of the relationship in the context of data quality indicators (flags) from RBDM categorized by severity. (Table 1)

Table 1. Subsamples developed using RBDM procedures (note Severe is a sub-sample within Flagged sample).

	Sample Size	Sample Description
Total Sample	2712	All baseline data across 6 MDD trials
Unflagged	1326	Subsample with no data quality concerns
Flagged	1386	Subsample with any data quality concerns identified
Severe Flags	174	Subsample with only severe quality concerns identified

Results

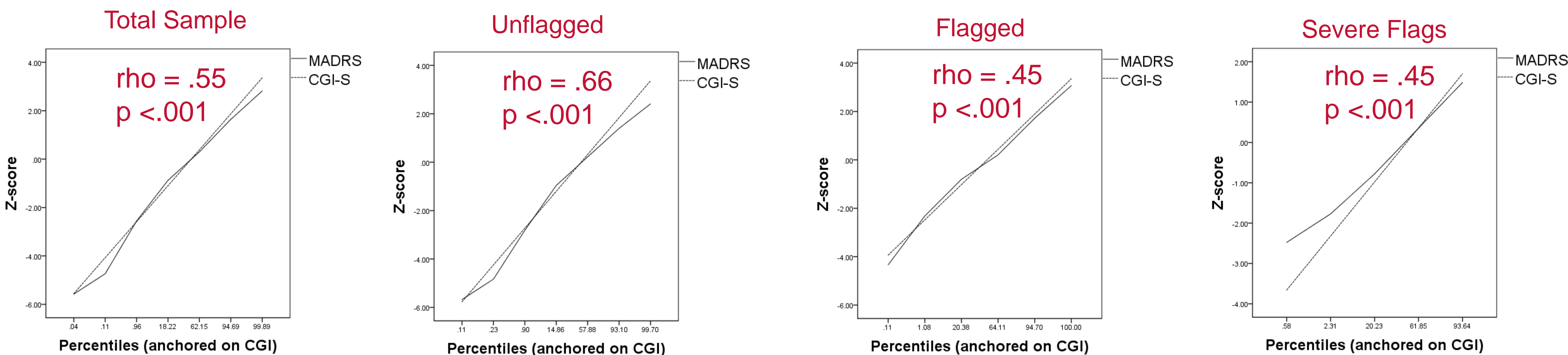


Figure 1. Graphical visualization of equipercentile linking⁴, applied to 4 different subsamples based on data quality.

- Using graphical equipercentile linking alone, there were no appreciable differences across the samples, aside from the Severe Flags group. (Figure 1)
- Correlational and regression analyses did reveal significant differences in the strength of relationship between data quality variables, especially with higher quality data (Unflagged sample). (Figure 1 & Table 2).
- The presence of data quality concerns (Flagged and Severe Flags samples) weakens the relationship between MADRS and CGI-S scores, although it is equal regardless of the magnitude of data quality flags. (Figure 1)
- Post-hoc regression analysis corroborated the initial correlations, noting a stronger relationship between MADRS and CGI-S in the context of better data quality (Unflagged sample). (Table 2)

Table 2. Indicators of Data Quality (Flags) Moderates the association between MADRS and CGI-S.

Predictor	Beta	P	R ²	F _{change}
STEP 1				
MADRS	.56	<.001	.316	626.32**
Flag Present	-.02	.194		
STEP 2				
MADRS	.65	<.001	.324	30.06**
Flag Present	.46	<.001		
Interaction Term	-.49	<.001		

Conclusions

- Our findings (Total Sample) confirm prior research on the overall strength and direction of the correlation between MADRS and CGI-S.¹
- When data quality is high, the observed correlation between baseline MADRS and CGI-S exceeded that reported in previous research. ¹
- Application of equating or linking methods in isolation masks data quality concerns that may be informed using other analyses.
- Rater oversight and intervention may reduce data quality concerns linked to rater performance⁵ which the current results shows can weaken the relationship between MADRS and CGI-S scores.
- These findings support previous work underscoring the important of data monitoring in the context of MDD clinical trials.⁵
- Future research is required to determine if data quality intervention and any resulting changes in scores may impact these findings.

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