

## Leveraging Remote Assessments and Central Raters to Optimize Data Quality in Rare Neurodevelopmental Disorders Clinical Trials

**Authors :** Pamela Ventola, Laurel Bales, Sara Florczyk

**Abstract :** Background: Fully remote or hybrid administration of clinical outcome measures in rare neurodevelopmental disorders trials is increasing due to the ongoing pandemic and recognition that remote assessments reduce the burden on families. Many assessments in rare neurodevelopmental disorders trials are complex; however, remote/hybrid trials readily allow for the use of centralized raters to administer and score the scales. The use of centralized raters has many benefits, including reducing site burden; however, a specific impact on data quality has not yet been determined. Purpose: The current study has two aims: a) evaluate differences in data quality between administration of a standardized clinical interview completed by centralized raters compared to those completed by site raters and b) evaluate improvement in accuracy of scoring standardized developmental assessments when scored centrally compared to when scored by site raters. Methods: For aim 1, the Vineland-3, a widely used measure of adaptive functioning, was administered by site raters (n= 52) participating in one of four rare disease trials. The measure was also administered as part of two additional trials that utilized central raters (n=7). Each rater completed a comprehensive training program on the assessment. Following completion of the training, each clinician completed a Vineland-3 with a mock caregiver. Administrations were recorded and reviewed by a neuropsychologist for administration and scoring accuracy. Raters were able to certify for the trials after demonstrating an accurate administration of the scale. For site raters, 25% of each rater's in-study administrations were reviewed by a neuropsychologist for accuracy of administration and scoring. For central raters, the first two administrations and every 10th administration were reviewed. Aim 2 evaluated the added benefit of centralized scoring on the accuracy of scoring of the Bayley-3, a comprehensive developmental assessment widely used in rare neurodevelopmental disorders trials. Bayley-3 administrations across four rare disease trials were centrally scored. For all administrations, the site rater who administered the Bayley-3 scored the scale, and a centralized rater reviewed the video recordings of the administrations and also scored the scales to confirm accuracy. Results: For aim 1, site raters completed 138 Vineland-3 administrations. Of the 138 administrations, 53 administrations were reviewed by a neuropsychologist. Four of the administrations had errors that compromised the validity of the assessment. The central raters completed 180 Vineland-3 administrations, 38 administrations were reviewed, and none had significant errors. For aim 2, 68 administrations of the Bayley-3 were reviewed and scored by both a site rater and a centralized rater. Of these administrations, 25 had errors in scoring that were corrected by the central rater. Conclusion: In rare neurodevelopmental disorders trials, sample sizes are often small, so data quality is critical. The use of central raters inherently decreases site burden, but it also decreases rater variance, as illustrated by the small team of central raters (n=7) needed to conduct all of the assessments (n=180) in these trials compared to the number of site raters (n=53) required for even fewer assessments (n=138). In addition, the use of central raters dramatically improves the quality of scoring the assessments.

**Keywords :** neurodevelopmental disorders, clinical trials, rare disease, central raters, remote trials, decentralized trials

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