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Comparison of Percent Change from Baseline using 10 vs. 30 Items of the PANSS in an Adult, Acutely Exacerbated Clinical Trial Population with Schizophrenia

David G. Daniel[1], Alan Kott[1], Xingmei Wang[1], Robert L. Findling[2], Eric A. Youngstrom,[3] Joshua A. Langfus[4], Joan Busner1,2

Signant Health[1], Virginia Commonwealth University[2], Nationwide Children's Hospital, The Ohio State University & Helping Give Away Psychological Science, 501c3[3]. University of California, San Francisco[4]

THE METHODOLOGICAL ISSUE BEING ADDRESSED

How do change from baseline and categorical measures of change compare for an abbreviated 10-item vs. the full 30-item PANSS in an acutely exacerbated adult schizophrenia clinical trial population?

INTRODUCTION

The Positive and Negative Syndrome Scale (PANSS) is the gold standard for assessing symptom severity and treatment response in schizophrenia clinical trials. The length and complexity of the 30-item PANSS are sometimes perceived as burdensome in both research and clinical settings. We have previously reported and replicated promising psychometric qualities for an abbreviated 10-item version of the PANSS extracted post-hoc from the full PANSS in both pediatric (Findling et al, 2023; Youngstrom et al, 2024; Langfus et al, 2024; Busner et al, 2025) and adult clinical trial populations (Daniel et al, 2023; Daniel et al, 2025). In the current retrospective analysis, we compare change from baseline and categorical measures of change for the 10-item and 30-item versions of the PANSS in an acutely exacerbated adult schizophrenia clinical trial population.

METHODS

Data were obtained from 12 acute adult schizophrenia clinical trials (N=3,067), with baseline and last-visit PANSS scores extracted for all participants. For each subject, percent change from baseline to last visit was calculated for the full 30-item PANSS and the abbreviated 10-item PANSS extracted post-hoc from the full PANSS.

To compare the 10- and 30-item PANSS versions, we conducted linear regression analyses of percent change scores, including clinical trial protocol as a categorical predictor.

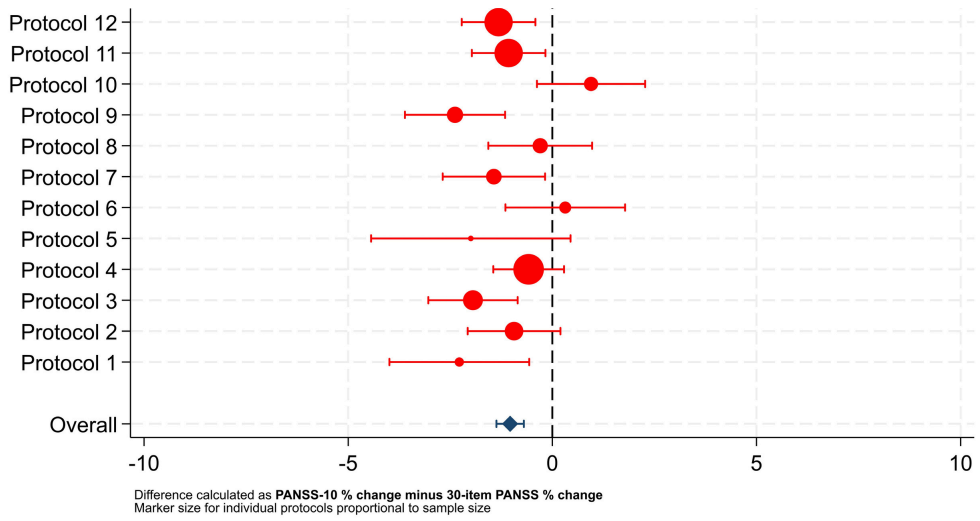
Percent change was further classified into worsening or improvement from baseline (up to 10%, 20%, 30%, 40%, 50%, and above 50%) for both PANSS versions.

Agreement between the two scales was assessed using polychoric correlations for the ordinal categories and Spearman rank correlations.

RESULTS

- Data from 3,067 adult subjects across 12 clinical trials were analyzed. The mean percent change in the 30-item PANSS total score was -23.8% (SD = 24.3), while the mean percent change for the PANSS-10 total was -24.9% (SD = 27.4).
- Welch's ANOVA revealed a statistically significant difference in end-of-treatment change across protocols for both scales.
- As shown in Figure 1, the mean difference in percent change between the 30-item PANSS total and the PANSS-10 total was -1.0% (95% CI: -1.40 to -0.70), with significant variability observed across different protocols.
- Agreement between categorical change classifications for the 30 item PANSS total and PANSS-10 was very strong, with a polychoric correlation coefficient of 0.94 and a Spearman's rho of 0.92 (both $p < 0.001$).

FIGURE 1: CONCORDANCE IN PERCENT CHANGE BETWEEN THE PANSS-10 TOTAL AND THE 30-ITEM PANSS TOTAL



DISCUSSION

- Our results demonstrate that the total score of the abbreviated PANSS-10 scale performs comparably to the total score of the full PANSS in assessing symptom change among adult patients with acute schizophrenia similar to what we found in pediatric patients.
- The observed mean difference in percent change between the two scales was minimal, and the correlations between categorical change classifications were exceptionally strong. These findings are consistent with clinical utility for PANSS-10 in adult acutely exacerbated clinical trial populations with schizophrenia. Moreover, the brevity of the PANSS-10 makes it likely less fatiguing to both raters and patients compared to the full PANSS.
- This study has several strengths, including a large and diverse sample size (N = 3,067) drawn from 12 clinical trials, the use of both continuous and categorical analytical approaches, and adjustment for protocol differences to account for trial heterogeneity.
- There are important limitations to consider. The PANSS-10 was derived post-hoc from the full PANSS and it is possible that scoring of the 10 items was influenced by the administration of the full PANSS; analyses were conducted post hoc and were not pre-specified; the categorization of change thresholds was somewhat arbitrary; and the findings may not generalize to stable or chronic schizophrenia populations with prominent negative symptoms, as only acute cases were included. Moreover, the data were blinded and do not provide insight as to the relative ability to distinguish drug from placebo.
- In summary, the PANSS-10 appears to offer practical advantages, such as reduced rater burden and faster administration, while maintaining measurement fidelity. Future research should aim to determine if these findings extend to the PANSS-10 administered as a standalone scale and to real-world clinical settings and more diverse patient populations.

DISCLOSURES

Alan Kott, Xingmei Wang and Joan Busner are employees of Signant Health and may hold stock/equity shares. David Daniel is an Executive Advisor to Signant Health, holds stock/equity shares in Signant Health and is a consultant to Merck and Abbvie.

In the past 36 months, Dr. Findling receives or has received research support, acted as a consultant and/or has received honoraria from Abbvie, Ajna, Akili, Aluco, American Academy of Child & Adolescent Psychiatry, American Psychiatric Press, Bioproject, BioXcel, Bristol Myers Squibb, Corium, Elsevier, Intra-Cellular Therapies, Iqvia, Karuna, Lundbeck, Maplight, Merck, MJH Life Sciences, NIH, Novartis, Otsuka, Oxford University Press, PaxMedica, PCORI, Pfizer, Radius, Sage, Signant Health, Sumitomo Pharma, Sunovion, Supernus Pharmaceuticals, Takeda, Tris, Viatris and Xenon.

Eric Youngstrom is Director, Institute for Mental and Behavioral Health research at Nationwide Children's Hospital and Ohio State University; he is the co-founder and Executive Director of Helping Give Away Psychological Science, a 501c3; he has consulted about psychological assessment with Signant Health and received royalties from the American Psychological Association and Guilford Press, and he holds equity in Joe Startup Technologies and AI Measures.

Joshua Langfus reports no relevant conflict of interest.

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The prevalence and relationship of anxiety and depression in acute schizophrenia clinical trials.

Kott, Alan; Wang, Xingmei; Daniel, David G

Signant Health

INTRODUCTION

- DSM-5 TR notes that mood symptoms are common in patients with schizophrenia and may occur concurrently with active-phase symptoms.
- In both, real world and research settings, mood and anxiety symptoms may influence the clinical presentation of non-affective symptoms and influence broader treatment outcomes.
- We previously demonstrated that the presence of baseline anxiety was associated with drug-placebo separation in an acute schizophrenia clinical trial (Kott et al, 2023).
- The current analysis aims to characterize the prevalence of clinically meaningful anxiety and depressive symptoms, as measured by the Positive and Negative Syndrome Scale (PANSS), in a large sample of subjects entering acute schizophrenia clinical trials.
- We also examined the relationship between anxiety and depression and assessed how these symptoms contribute to the severity of the PANSS and its subscales.

METHODS

- Baseline PANSS data were analyzed from 12 clinical trials involving patients with acute schizophrenia (N = 3,924).
- Clinically meaningful anxiety and depression were operationally defined as PANSS Anxiety (G2) and Depression (G6) scores of 4 or higher.
- We determined the frequency of these symptoms across the dataset and within individual studies.
- The association between anxiety and depression was evaluated using polychoric and Spearman's correlations.
- To assess the impact of anxiety and depression on PANSS subscales and total scores (excluding G2 and G6 items), we used linear mixed-effects models, with G2 and G6 as fixed effects and random intercepts for each study. Parameter estimates were obtained using restricted maximum likelihood.

RESULTS

- Of the 3,924 subjects, the mean baseline anxiety score was 3.81 (SD = 1.27) and the mean depression score was 3.10 (SD = 1.02), with significant variability among studies.
- Clinically meaningful anxiety was present in 64% of subjects, while clinically meaningful depression was observed in 39%.
- Clinically meaningful anxiety often appeared independently of clinically meaningful depression (31%), whereas clinically meaningful depression rarely occurred alone (6%), most commonly co-occurring with clinically meaningful anxiety (33%). (Figure 1)
- The polychoric correlation between anxiety and depression was 0.51, and Spearman's rho was 0.49 (both $p < 0.05$).
- Anxiety was associated with significantly increased positive symptoms (+0.4 per point), decreased severity of negative symptoms (-0.4 per point), increased general psychopathology (+0.8 per point) and total PANSS scores (+0.8 per point). (Figure 2 - Anxiety)
- Depression contributed significantly only to the general psychopathology subscore (+0.2 per point). (Figure 2 – Depression)

FIGURE 1: PRESENCE OF CLINICALLY MEANINGFUL ANXIETY AND DEPRESSION IN RANDOMIZED SUBJECTS AT BASELINE (N = 3,924 SUBJECTS)

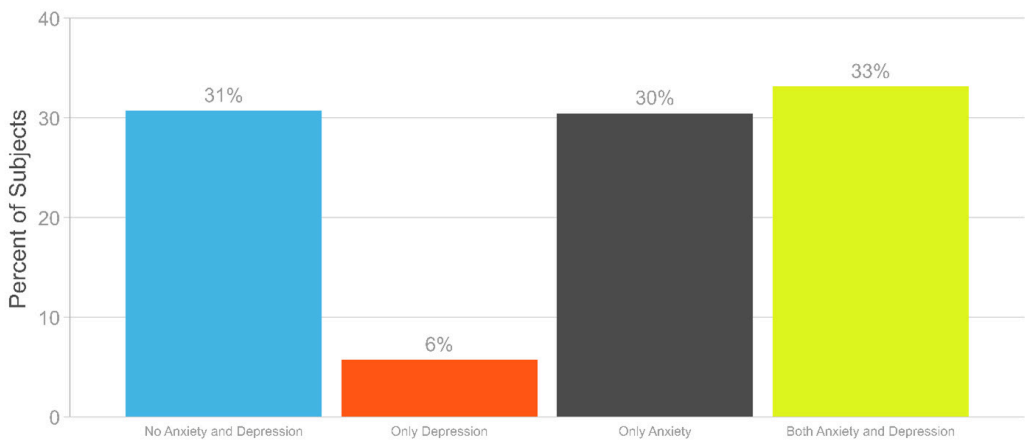
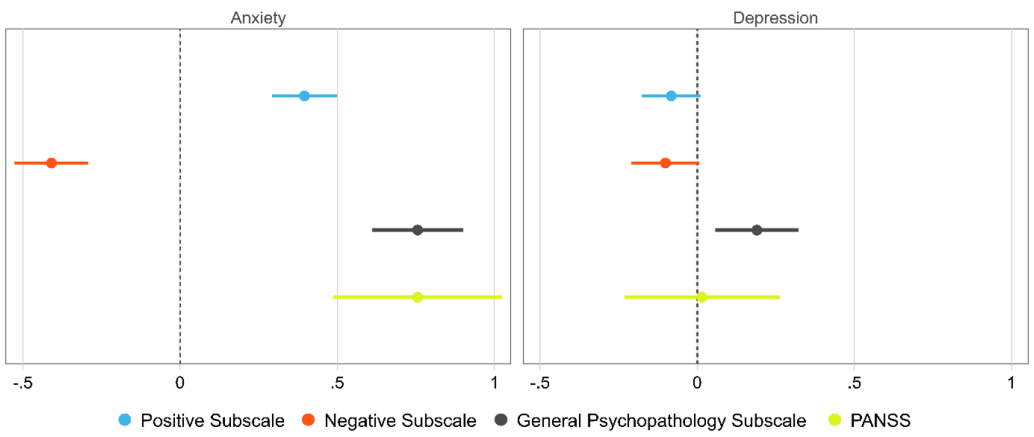


FIGURE 2: LS MEAN CHANGE PER POINT INCREASE IN ANXIETY OR DEPRESSION IN THE PANSS AND PANSS SUBSCALES.



DISCUSSION

- This study shows that anxiety is highly prevalent in acute schizophrenia and frequently occurs independently of depression, whereas depression is most often seen in combination with anxiety.
- Anxiety was found to have a broader and more significant impact on overall symptom severity than depression.
- Notably, our previous research demonstrated that the presence of baseline anxiety was associated with drug-placebo separation in an acute schizophrenia clinical trial (Kott et al, 2023).
- Interpretation of this analysis is limited by its retrospective design and by relying solely on PANSS items to assess affective symptom severity.
- Overall, these findings underscore the multifaceted impact of anxiety on a broad range of other symptomology in acute exacerbation of schizophrenia.
- Future work could focus on expanding these analyses using unblinded datasets, assessment of impact on the Clinical Global Impression (CGI) and non-acute as well as acute schizophrenia populations.

REFERENCES

- Kott A, Brannan S, Wang X, Daniel D. The Impact of Baseline Anxiety on Drug Placebo Separation and Drug/Placebo Response in an Acute Schizophrenia Clinical Trial—A Post-hoc Analysis. Schizophrenia Bulletin Open. 2023;4(1):811. doi:10.1093/schizbullopen/sgad003.

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Ensuring Data Quality Through Calibrated Central Quality Reviewers

Roy, M., Pavel, A., Iraheta, S., Ivanova, E., Wang, X., Sachs, G., Kott, A

BACKGROUND

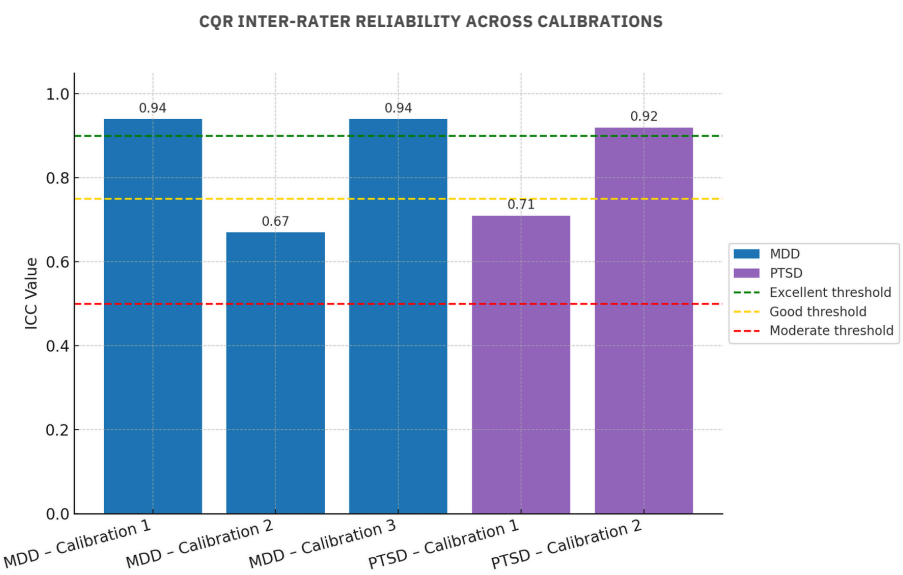
- In clinical trials, Clinical Quality Reviewers (CQRs) play a critical role in ensuring the accuracy and consistency of key efficacy data, directly impacting signal detection and drug evaluation outcomes.
- By identifying and remediating suboptimal scale administration or scoring, reliable CQRs help reduce measurement noise, thereby improving data quality, strengthening regulatory compliance, and enhancing reproducibility.
- Like the well-documented rater drift phenomenon, CQR drift can occur over time, potentially undermining trial integrity.
- This study evaluated whether periodic calibration exercises can mitigate drift and sustain high CQR reliability, addressing a methodological need for standardized procedures, defined benchmarks, and validated frameworks for reviewer performance monitoring.

METHOD

- CQR quality data were sourced from two global, double-blind, randomized, placebo-controlled studies:
  - Major Depressive Disorder (MDD) using the Montgomery–Åsberg Depression Rating Scale (MADRS)
  - Post-Traumatic Stress Disorder (PTSD) using the Clinician-Administered PTSD Scale for DSM-5 (CAPS-5).
- CQRs were selected based on qualifications and clinical experience with the relevant assessments, trained to high proficiency, and tasked with evaluating both scoring quality and subject eligibility, with remediation provided to raters as needed.
- Inter-rater reliability was assessed via intraclass correlation coefficients (ICCs) using a two-way random-effects model with absolute agreement.
- ICC values were interpreted using standard thresholds:
  - <0.5 = poor
  - 0.5–0.75 = moderate
  - 0.75–0.9 = good
  - >0.9 = excellent

RESULTS

- In the MDD study, 19 CQRs completed Calibration 1; 17 completed Calibration 2, and 16 completed Calibration 3.
- In the PTSD study, 17 CQRs completed Calibration 1, but only 8 completed Calibration 2.
- Periodic calibrations yielded sustained or improved reliability.
- MDD CQRs demonstrated inter-rater ICCs of 0.94 (excellent), 0.67 (moderate), and 0.94 (excellent) across the three calibrations.
  - Intra-rater ICCs average was 0.89 (good).
- PTSD CQRs achieved inter-rater ICCs of 0.71 (moderate) and 0.92 (excellent) across two calibrations.



CONCLUSION

- These findings suggest that even in the presence of CQR attrition, periodic calibrations are effective in sustaining high reliability, supporting their use as a standard practice to mitigate drift.
- Implementing defined ICC benchmarks and structured calibration schedules can be broadly applied to improve trial quality across therapeutic areas.
- Future research should validate these approaches in other conditions, such as schizophrenia and bipolar disorder, to further standardize quality metrics in clinical research.

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