Challenging PANSS Items for Raters in Adolescent Schizophrenia Trials: Expansion of Earlier Findings

Busner, J[1,2], Daniel, DG[1], Findling, RL[2]

[1]Signant Health, [2]Virginia Commonwealth University School of Medicine, Department of Psychiatry

ABSTRACT

OBJECTIVE: Measures designed for adults, such as the PANSS, are frequently used in adolescent schizophrenia trials. To identify PANSS items for which raters in pediatric trials might have particular difficulty, we previously reported PANSS item scoring variability from 2 standardized videos in 3 adolescent schizophrenia industry trials.[1] We have since secured data from 2 additional trials and videos, allowing for combined analysis and expansion of our findings. **DESIGN:** Standard deviations (SDs) were calculated for each of the 30 PANSS items scored by 408 investigators/raters from 23 countries who had viewed one of four standardized adolescent patient videos as part of the qualification process for their respective clinical trial. PANSS item SDs were rank ordered by variability, per video, and compared for cross-video similarity using Kendall W. **RESULTS:** Variability rankings of the 30 PANSS items for the 4 videos was statistically similar, W=0.57, p<.0001. Three PANSS items were ranked among the 10 most variable in all 4 videos: N4, P7, and P4, and two were ranked among the 10 least variable in all 4 videos: P3 and G14. **CONCLUSIONS:** Variability rankings across four adolescent videos were statistically similar, suggesting that scoring ease or difficulty of individual PANSS items is independent of the specifics of the patients rated. Identification of challenging PANSS items for pediatric raters allows targeted training and in-study intervention. Findings differed from those noted in adult videos[2], making even more clear the need for focused attention and perhaps modification for PANSS items when applied to the pediatric age range. **DISCLOSURES:** Presented in part at the 2021 Congress of the Schizophrenia International Research Society (SIRS) virtual meeting, April 17-21, 2021. Financial support provided by Signant Health. **REFERENCES:** [1]Busner, J., Daniel, D.G., Findling, R.L. Identification of PANSS Items of Particular Challenge to Raters in Adolescent Schizophrenia Clinical Trials. Presented as a poster at the 2013 Autumn International Society of Clinical Trials Methodology (ISCTM) Conference, Philadelphia, PA, 30 September - 2 October, 2013.; [2]Daniel, D.G., and Dries, J. What PANSS Items Do Site Raters Have the Most Trouble Rating? Presented as a poster at the 53rd Annual Meeting of the New Clinical Drug Development Unit (NCDEU), May 28-31, 2013, Hollywood, FL USA.

OBJECTIVE

- Measures designed for adults, such as the PANSS, are frequently used in adolescent schizophrenia trials.
- To identify PANSS items for which raters in pediatric trials might have particular difficulty, we previously reported PANSS item scoring variability from 2 standardized videos in 3 adolescent schizophrenia industry trials.[1]
- We have since secured data from 2 additional trials and videos, allowing for combined analysis and expansion of our findings.

DESIGN

- Standard deviations (SDs) were calculated for each of the 30 PANSS items scored by 408 investigators/raters from 23 countries who had viewed one of four standardized adolescent patient videos as part of the qualification process for their respective clinical trial.
- PANSS item SDs were rank ordered by variability, per video, and compared for cross-video similarity using Kendall W.

RESULTS

- Variability rankings of the 30 PANSS items for the 4 videos were statistically similar, W=0.57, p<.0001.
- Three PANSS items were ranked among the 10 most variable in all 4 videos: N4, P7, and P4, and two were ranked among the 10 least variable in all 4 videos: P3 and G14.

TABLE 1. RANKS FROM SMALLEST TO LARGEST SDS BY PANSS ITEM #

panss item#	Video 1	Video 2	Video 3	Video 4
P1	11	6	4	8
P2	14	10	25	10
P3	2	7	1	4
P4	21	21	23	24
P5	3	4	12	1
P6	5	13	6	3
P7	28	27	30	29
N1	8	2	18	16
N2	23	11	9	27
N3	12	20	8	13
N4	22	28	21	30
N5	6	17	14	7
N6	15	8	19	21
N7	13	9	24	22
G1	18	29	29	20
G2	1	25	17	23
G3	25	1	22	5
G4	9	18	11	25
G5	26	14	28	17
G6	7	26	7	6
G7	10	12	10	12
G8	29	15	26	28
G9	24	22	20	26
G10	16	3	3	19
G11	19	30	13	14
G12	20	24	16	11
G13	17	19	27	9
G14	4	5	2	2
G15	30	23	15	15
G16	27	16	5	18

Kendall W=0.57, p<.0001

TABLE 2. TOP 10 MOST DIFFICULT (HIGHEST INTERRATER VARIABILITY) ITEMS

Video 1	Video 2	Video 3	Video 4
P4	P4	P7	N4
N4	G9	G1	P7
N2	G15	G5	G8
G9	G12	G13	N2
G3	G2	G8	G9
G5	G6	P2	G4
G16	P7	N7	P4
P7	N4	P4	G2
G8	G1	G3	N7
G15	G11	N4	N6

Green = item in top ten all 4 videos Blue = item in top ten for 3 of the 4 videos

TABLE 3. TOP 10 EASIEST (LOWEST INTERRATER VARIABILITY) ITEMS

Video 1	Video 2	Video 3	Video 4
G2	G3	G7	P2
P3	N1	N2	G13
P5	G10	N3	P1
G14	P5	G6	N5
P6	G14	P6	G6
N5	P1	G16	G3
G6	P3	P1	P3
N1	N6	G10	P6
G4	N7	G14	G14
G7	P2	P3	P5

Green = item in top ten all 4 videos Blue = item in top ten for 3 of the 4 videos

CONCLUSIONS

- Variability rankings across four adolescent videos were statistically similar, suggesting that scoring ease or difficulty of individual PANSS items is independent of the specifics of the patients rated.
- Identification of challenging PANSS items for pediatric raters allows targeted training and in-study intervention.
- Findings differed from those noted in adult videos[2], making even more clear the need for focused attention and perhaps modification for PANSS items when applied to the pediatric age range.

REFERENCES

- [1]Busner, J., Daniel, D.G., Findling, R.L. Identification of PANSS Items of Particular Challenge to Raters in Adolescent Schizophrenia Clinical Trials. Presented as a poster at the 2013 Autumn International Society of Clinical Trials Methodology (ISCTM) Conference, Philadelphia, PA, 30 September - 2 October, 2013.
- [2]Daniel, D.G., and Dries, J. What PANSS Items Do Site Raters Have the Most Trouble Rating? Presented as a poster at the 53rd Annual Meeting of the New Clinical Drug Development Unit (NCDEU), May 28-31, 2013, Hollywood, FL USA.

Presentation and associated analyses financially supported by Signant Health

Presented in part at the 2021 Congress of the Schizophrenia International Research Society (SIRS) virtual meeting, April 17-21, 2021.

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

Identification of PANSS items of particular challenge to raters in adolescent schizophrenia clinical trials: Expansion of initial findings

Busner, J[1,2], Daniel, DG[1], Findling, RL[2]

[1] Signant Health, [2] Virginia Commonwealth University School of Medicine, Department of Psychiatry

ABSTRACT

BACKGROUND: Global regulatory initiatives have resulted in an increasing number of psychopharmacology trials in the pediatric age range. Among the challenges in ensuring valid and reliable data in such trials are developmental limitations in symptom description, the need to integrate and weight information from varied sources including parents/caregivers and other informants, and the global shortage of child-trained clinical investigators (Busner, 2013; Farchione, 2013). Moreover, few efficacy measures have been developed and validated specifically for pediatric trials. As a result, measures designed for and validated in adults such as the Positive and Negative Syndrome Scale (PANSS) are frequently used in adolescent schizophrenia trials. The PANSS is a complex 30-item measure that has been extensively studied and shown to pose ratings challenges even in the adult patients for whom it was designed (e.g., Daniel and Dries, 2013). To identify PANSS items for which raters in pediatric trials might have particular difficulty, we examined and reported PANSS item scoring variability of 171 worldwide raters from several large adolescent schizophrenia trials who had watched one of two standardized patient videos (Busner, Daniel, Findling, 2013). We have since secured data from 2 additional sponsors' international adolescent schizophrenia trials, with 2 additional standardized videos and 237 additional raters, allowing for new analyses and expansion of our initial findings.
METHODS: Using data from multiple adolescent schizophrenia clinical trials by multiple sponsors, standard deviations were calculated for each of the 30 PANSS items scored by 408 clinical trials investigators/raters from 23 countries who had viewed one of four separate standardized adolescent patient videos as part of the qualification process for their respective clinical trial. The clinical trials investigators/raters had been trained extensively in live sessions on adolescent-specific conventions immediately prior to viewing and scoring the video. PANSS item standard deviations from each video, separately, were calculated and rank ordered from lowest to highest variability. The variability rank order of the 30 PANSS items for each of the 4 videos was then compared across videos using Kendall W. **RESULTS:** The variability (SD) rankings of the 30 PANSS items for the 4 videos was statistically similar, Kendall W=0.57, p<.0001 (See Table 1 for rankings by video). Three PANSS items were ranked among the 10 most variable in all 4 videos: N4 (Passive/apathetic social withdrawal), P7 (Hostility), and P4 (Excitement) (See Table 2), and two PANSS items were ranked among the 10 least variable in all 4 videos: P3 (Hallucinatory Behavior), and G14 (Preoccupation) (See Table 3). **DISCUSSION:** Scoring variability of a standardized video reflects lack of agreement among raters and suggests challenges in item scoring. Identification of PANSS items that reflect scoring challenges and scoring disagreement for pediatric trials investigators allows targeted training and in-study intervention to help improve consistency. The work extends our earlier findings despite the addition of 2 new videos and 11 new countries. Item variability rankings across four different adolescent videos were statistically similar, suggesting that scoring ease or difficulty of individual PANSS items is independent of the specifics of the patients rated. As occurred with our earlier work, the high variability items in these adolescent videos continue to differ from those noted in with videos of adults (Daniel and Dries, 2013), making even more clear the need for focused attention and perhaps modification for these items when applied to the pediatric age range.

BACKGROUND

- Global regulatory initiatives have resulted in an increasing number of psychopharmacology trials in the pediatric age range.
- Among the challenges in ensuring valid and reliable data in such trials are developmental limitations in symptom description, the need to integrate and weight information from varied sources including parents/caregivers and other informants, and the global shortage of child-trained clinical investigators (Busner, 2013; Farchione, 2013).
- Moreover, few efficacy measures have been developed and validated specifically for pediatric trials.
- As a result, measures designed for and validated in adults such as the Positive and Negative Syndrome Scale (PANSS) are frequently used in adolescent schizophrenia trials.
- The PANSS is a complex 30-item measure that has been extensively studied and shown to pose ratings challenges even in the adult patients for whom it was designed (e.g., Daniel and Dries, 2013).
- To identify PANSS items for which raters in pediatric trials might have particular difficulty, we examined and reported PANSS item scoring variability of 171 worldwide raters from several large adolescent schizophrenia trials who had watched one of two standardized patient videos (Busner, Daniel, Findling, 2013).
- We have since secured data from 2 additional sponsors' international adolescent schizophrenia trials, with 2 additional standardized videos and 237 additional raters, allowing for new analyses and expansion of our initial findings.

METHODS

- Using data from multiple adolescent schizophrenia clinical trials by multiple sponsors, standard deviations were calculated for each of the 30 PANSS items scored by 408 clinical trials investigators/raters from 23 countries who had viewed one of four separate standardized adolescent patient videos as part of the qualification process for their respective clinical trial.
- The clinical trials investigators/raters had been trained extensively in live sessions on adolescent-specific conventions immediately prior to viewing and scoring the video.
- PANSS item standard deviations from each video, separately, were calculated and rank ordered from lowest to highest variability.
- The variability rank order of the 30 PANSS items for each of the 4 videos was then compared across videos using Kendall W.

RESULTS

- The variability (SD) rankings of the 30 PANSS items for the 4 videos was statistically similar, Kendall W=0.57, p<.0001 (See Table 1 for rankings by video).
- Three PANSS items were ranked among the 10 most variable in all 4 videos: N4 (Passive/apathetic social withdrawal), P7 (Hostility), and P4 (Excitement) (See Table 2), and two PANSS items were ranked among the 10 least variable in all 4 videos: P3 (Hallucinatory Behavior), and G14 (Preoccupation) (See Table 3).

TABLE 1. RANKS FROM SMALLEST TO LARGEST SDS BY PANSS ITEM #

panss item#	Video 1	Video 2	Video 3	Video 4
P1	11	6	4	8
P2	14	10	25	10
P3	2	7	1	4
P4	21	21	23	24
P5	3	4	12	1
P6	5	13	6	3
P7	28	27	30	29
N1	8	2	18	16
N2	23	11	9	27
N3	12	20	8	13
N4	22	28	21	30
N5	6	17	14	7
N6	15	8	19	21
N7	13	9	24	22
G1	18	29	29	20
G2	1	25	17	23
G3	25	1	22	5
G4	9	18	11	25
G5	26	14	28	17
G6	7	26	7	6
G7	10	12	10	12
G8	29	15	26	28
G9	24	22	20	26
G10	16	3	3	19
G11	19	30	13	14
G12	20	24	16	11
G13	17	19	27	9
G14	4	5	2	2
G15	30	23	15	15
G16	27	16	5	18

Kendall W=0.57, p<.0001

TABLE 2. TOP 10 MOST DIFFICULT (HIGHEST INTERRATER VARIABILITY) ITEMS

Video 1	Video 2	Video 3	Video 4
P4	P4	P7	N4
N4	G9	G1	P7
N2	G15	G5	G8
G9	G12	G13	N2
G3	G2	G8	G9
G5	G6	P2	G4
G16	P7	N7	P4
P7	N4	P4	G2
G8	G1	G3	N7
G15	G11	N4	N6

Green = item in top ten all 4 videos Blue = item in top ten for 3 of the 4 videos

TABLE 3. TOP 10 EASIEST (LOWEST INTERRATER VARIABILITY) ITEMS

Video 1	Video 2	Video 3	Video 4
G2	G3	G7	P2
P3	N1	N2	G13
P5	G10	N3	P1
G14	P5	G6	N5
P6	G14	P6	G6
N5	P1	G16	G3
G6	P3	P1	P3
N1	N6	G10	P6
G4	N7	G14	G14
G7	P2	P3	P5

Green = item in top ten all 4 videos Blue = item in top ten for 3 of the 4 videos

DISCUSSION

- Scoring variability of a standardized video reflects lack of agreement among raters and suggests challenges in item scoring.
- Identification of PANSS items that reflect scoring challenges and scoring disagreement for pediatric trials investigators allows targeted training and in-study intervention to help improve consistency.
- The work extends our earlier findings despite the addition of 2 new videos and 11 new countries. Item variability rankings across four different adolescent videos were statistically similar, suggesting that scoring ease or difficulty of individual PANSS items is independent of the specifics of the patients rated.
- As occurred with our earlier work, the high variability items in these adolescent videos continue to differ from those noted in with videos of adults (Daniel and Dries, 2013), making even more clear the need for focused attention and perhaps modification for these items when applied to the pediatric age range.

Presentation and associated analyses financially supported by Signant Health

Presented at the 2021 Congress of the Schizophrenia International Research Society, April 17-21, 2021.

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

New analyses in the development of an abbreviated PANSS for pediatric trials:
Criterion validity and treatment sensitivity of an abbreviated PANSS using an NIMH adolescent schizophrenia study sample

Busner, J[1,3], Youngstrom, EA[2], Daniel, DG[1], Findling, RL[3]

[1] Signant Health, Blue Bell, PA [2] University of North Carolina, Chapel Hill, NC [3] Virginia Commonwealth University, Richmond, VA,

ABSTRACT

BACKGROUND: What are the psychometric properties of the PANSS in a pediatric sample, and do they support abbreviation of this instrument for pediatric trials? Pediatric schizophrenia trials, with few exceptions, have used for primary efficacy assessment the PANSS, a complex and lengthy 30-item (adult) measure that has been extensively studied and shown to pose ratings challenges even when used with the adult patients for whom it was designed. For adult populations, there have been a variety of efforts to shorten the PANSS while retaining its clinical and research value. As presented to ACNP in 2020, we developed a psychometrically sound abbreviated 10 item pediatric PANSS derived from the baseline data of the NIMH Treatment of Early Onset Schizophrenia (TEOSS) study. The present study extends this work by testing the criterion validity and treatment sensitivity of our 10-item version compared with the original 30-item version using TEOSS on-treatment observations and associated measures. **METHOD:** As part of a NIMH multisite study (completed and previously described), 118 male and female youths with schizophrenia/schizoaffective disorder (mean age=14.26, SD=2.41 years) were administered the 30 item PANSS, the Brief Psychotic Rating Scale for Children (BRPS-C), and the Clinical Global Impressions – Severity (CGI-S) at baseline and weekly throughout an 8-week randomized double-blind study of three antipsychotic agents. In the present study, we examined the baseline correlation of our psychometrically derived 10-item abbreviated PANSS (Busner et al, ACNP 2020 poster) with the BPRS-C and CGI-S scales and then compared these with the BPRS-C and CGI-S correlations obtained using the 30-item PANSS. To examine treatment sensitivity, we computed effect sizes for the 30-item vs 10- item PANSS LOCF change from baseline. We also examined the correlation of the CGI-S LOCF changes from baseline with those of the 30-item and 10-item PANSS. **RESULTS:** Convergent correlations of the 10-item PANSS version with the BRPS-C and the CGI-S were similar to those found with the original 30-item PANSS. The 10-item version correlated .71 with the BPRS-C (versus .75 for the 30-item version); this difference was not statistically significant, t=1.43, p=.155, per Steiger's test. Similarly, the CGI-S correlations were .57 with the 10-item versus .62 with the 30-item versions, also not significantly different per Steiger's test, t=1.69, p=.093. The 10-item and 30-item versions produced essentially identical estimates of treatment effects: the eta-squared for baseline to LOCF change was .55 for the 30-item PANSS and .51 for the 10-item version, both indicating large treatment effects. The time-by-treatment interaction was not significant, eta-squared <.01, for either version (consistent with published results, finding no separation between active comparators). CGI-S change from baseline correlated similarly with LOCF change from baseline for both the 10-item (.63) and 30-item (.66) PANSS versions. **CONCLUSIONS:** The results support the utility of our previously reported 10 item "optimized" PANSS for use in pediatric trials. For pediatric trials, the 10-item PANSS should maintain treatment sensitivity and precision while reducing costs, shortening interviews, and reducing burden. In this randomized and blinded adolescent schizophrenia treatment study, the proposed 10-item empirically derived version of the PANSS performed similarly to the original 30-item version with respect to treatment sensitivity and measures of criterion validity. Next steps include examination of the optimized pediatric PANSS in larger samples and placebo-controlled trials.

BACKGROUND

- Pediatric schizophrenia trials, with few exceptions, have used for primary efficacy assessment the PANSS, a complex and lengthy 30-item (adult) measure that has been extensively studied and shown to pose ratings challenges even when used with the adult patients for whom it was designed.
- For adult populations, there have been a variety of efforts to shorten the PANSS while retaining its clinical and research value.
- As presented to ACNP in 2020, we developed a psychometrically sound abbreviated 10 item pediatric PANSS derived from the baseline data of the NIMH Treatment of Early Onset Schizophrenia (TEOSS) study.
- The present study extends this work by testing the criterion validity and treatment sensitivity of our 10-item version compared with the original 30-item version using TEOSS on-treatment observations and associated measures.

METHOD

- As part of a NIMH multisite study (completed and previously described), 118 male and female youths with schizophrenia/schizoaffective disorder (mean age=14.26, SD=2.41 years) were administered the 30 item PANSS, the Brief Psychotic Rating Scale for Children (BRPS-C), and the Clinical Global Impressions – Severity (CGI-S) at baseline and weekly throughout an 8-week randomized double-blind study of three antipsychotic agents.
- In the present study, we examined the baseline correlation of our psychometrically derived 10-item abbreviated PANSS (Busner et al, ACNP 2020 poster) with the BPRS-C and CGI-S scales and then compared these with the BPRS-C and CGI-S correlations obtained using the 30-item PANSS.
- To examine treatment sensitivity, we computed effect sizes for the 30-item vs 10- item PANSS LOCF change from baseline.
- We also examined the correlation of the CGI-S LOCF changes from baseline with those of the 30-item and 10-item PANSS.

RESULTS

TABLE 1. CONVERGENT CORRELATIONS OF 10 ITEM AND 30 ITEM PANSS

	10 Item Optimized	30 Item Standard PANSS	Comparison
Baseline BPRS-C	r=.71	r=.75	NS
Baseline CGI-S	r=.57	r=.62	NS

TABLE 2. TREATMENT SENSITIVITY

	10 Item Optimized	30 Item Standard PANSS	Comparison
PANSS Baseline to LOCF Change	eta^2=.51	eta^2=.55	NS
CGI-S Baseline to LOCF Change	r=.63	r=.66	NS

- Convergent correlations of the 10-item PANSS version with the BRPS-C and the CGI-S were similar to those found with the original 30-item PANSS.
- The 10-item version correlated .71 with the BPRS-C (versus .75 for the 30-item version); this difference was not statistically significant, t=1.43, p=.155, per Steiger's test.
- Similarly, the CGI-S correlations were .57 with the 10-item versus .62 with the 30-item versions, also not significantly different per Steiger's test, t=1.69, p=.093.
- The 10-item and 30-item versions produced essentially identical estimates of treatment effects: the eta-squared for baseline to LOCF change was .55 for the 30-item PANSS and .51 for the 10-item version, both indicating large treatment effects.
- The time-by-treatment interaction was not significant, eta-squared <.01, for either version (consistent with published results, finding no separation between active comparators). CGI-S change from baseline correlated similarly with LOCF change from baseline for both the 10-item (.63) and 30-item (.66) PANSS versions.

CONCLUSIONS

- The results support the utility of our previously reported 10 item "optimized" PANSS for use in pediatric trials.
- For pediatric trials, the 10-item PANSS should maintain treatment sensitivity and precision while reducing costs, shortening interviews, and reducing burden.
- In this randomized and blinded adolescent schizophrenia treatment study, the proposed 10-item empirically derived version of the PANSS performed similarly to the original 30-item version with respect to treatment sensitivity and measures of criterion validity.
- Next steps include examination of the optimized pediatric PANSS in larger samples and placebo-controlled trials.

REFERENCES

- Streiner DL, Norman GR, Cairney J. Health measurement scales: A practical guide to their development and use. 5th ed. New York, NY: Oxford University Press; 2015.
- Santor DA, Ascher-Svanum H, Lindenmayer JP, Obenchain RL. Item response analysis of the Positive and Negative Syndrome Scale. BMC Psychiatry. 2007;7:66.
- Lindenmayer JP. Are Shorter Versions of the Positive and Negative Syndrome Scale (PANSS) Doable? A Critical Review. Innov Clin Neurosci. 2017;14(11-12):73-76.
- Busner J, Youngstrom EA, Daniel, DG, Findling, RL. Toward development of an abbreviated PANSS for pediatric trials: New analyses of PANSS TEOSS data. ACNP 59th Annual Meeting: Poster Session III. Neuropsychopharmacol. 45, 278–382 (2020). https://doi.org/10.1038/s41386-020-00892-5

Presentation and associated analyses financially supported by Signant Health

Presented in part at the 2021 60th ACNP Annual Meeting December 5-8, 2021

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

Independent Replication of Reliability, Convergent Validity, and Treatment Sensitivity of an Abbreviated PANSS in an Adolescent Schizophrenia Double-Blind RCT

Joan Busner, Ph.D.[1,3]; Eric A. Youngstrom, Ph.D.,[2]; David G., Daniel, M.D.[1]; Robert L. Findling, M.D.[3]

[1]Signant Health, Wayne PA; [2]University of North Carolina, Chapel Hill, NC; [3]Virginia Commonwealth University, Richmond, VA

ABSTRACT

Background: Global regulatory initiatives have increased the number of pediatric psychopharmacology trials. Challenges in ensuring valid and reliable data in such trials include developmental limitations in symptom description, the need to combine and calibrate information from varied sources, including patients and parents/caregivers, and a dearth of pediatric-specific scales [1,2]. Pediatric schizophrenia trials, with few exceptions, have used for primary efficacy assessment the (adult) Positive and Negative Syndrome Scale (PANSS) [3], a complex and lengthy 30 item measure that has been extensively studied and shown to pose ratings challenges even in the adult populations for whom it was designed. For this reason, using data from an NIMH pediatric psychosis trial [4], we previously conducted a retrospective study using confirmatory factor analysis and graded response item response theory to develop and explore the validity of a short form of the PANSS optimized for use with youths [5]. Results suggested that a 10 item version could still produce reliable information about five different symptom dimensions and a good overall total score estimate highly correlated with the 30 item version. Replication in an independent sample, however, is crucial before recommending wider adoption. Therefore, the present study performed secondary analyses on a separate large, double-blind, placebo-controlled trial to investigate and confirm the psychometric properties in a second sample. As with the initial work, the hypotheses were that the reliability would be acceptable and that sensitivity to treatment effects would not differ significantly from the 30 item version. **Method**. The 6-week, double-blind, parallel group, acute phase data from the Johnson & Johnson sponsored completed, positive, paliperidone study [6] were accessed from the YODA secure data environment. The trial included 201 12-17 year olds randomly allocated to placebo or one of three fixed doses of paliperidone. Analyses were performed using the mirt, lavaan, sjstat and psych packages in R, using the same syntax and methods as the prior analyses [4], with mixed regressions using random intercepts and partial eta-squared as the effect size estimate for time, treatment, and time x treatment interaction effects. **Results**. The 10 item vs. 30 item versions had similar average interitem correlations (.25 and .25), as well as similar partial eta-squared values for time – .37 [.32 to .41] versus .41 [.36 to .45], treatment (all .00) and time x treatment (.007 versus .003 for the full length). IRT models indicated similar reliability as in the development sample, with good precision across a similar range of severity. **Conclusion**. The 10 item version of the PANSS replicated well in an independent, larger sample using double-blind RCT data. The similar sensitivity to treatment effects is particularly promising given the substantial reduction in scale length and corresponding decreases in required rater training, interview length, and respondent burden.

BACKGROUND

- Global regulatory initiatives have increased the number of pediatric psychopharmacology trials.
- Challenges in ensuring valid and reliable data in such trials include developmental limitations in symptom description, the need to combine and calibrate information from varied sources, including patients and parents/caregivers, and a dearth of pediatric-specific scales [1,2].
- Pediatric schizophrenia trials, with few exceptions, have used for primary efficacy assessment the (adult) Positive and Negative Syndrome Scale (PANSS) [3], a complex and lengthy 30 item measure that has been extensively studied and shown to pose ratings challenges even in the adult populations for whom it was designed.
- For this reason, using data from an NIMH pediatric psychosis trial [4], we previously conducted a retrospective study using confirmatory factor analysis and graded response item response theory to develop and explore the validity of a short form of the PANSS optimized for use with youths [5].
- Results suggested that a 10 item version could still produce reliable information about five different symptom dimensions and a good overall total score estimate highly correlated with the 30 item version.
- Replication in an independent sample, however, is crucial before recommending wider adoption.
- Therefore, the present study performed secondary analyses on a separate large, double-blind, placebo-controlled trial to investigate and confirm the psychometric properties in a second sample.
- As with the initial work, the hypotheses were that the reliability would be acceptable and that sensitivity to treatment effects would not differ significantly from the 30 item version.

METHOD

- The 6-week, double-blind, parallel group, acute phase data from the Johnson & Johnson sponsored completed, positive, paliperidone study [6] were accessed from the YODA secure data environment.
- The trial included 201 12-17 year olds randomly allocated to placebo or one of three fixed doses of paliperidone.
- Analyses were performed using the mirt, lavaan, sjstat and psych packages in R, using the same syntax and methods as the prior analyses [4], with mixed regressions using random intercepts and partial eta-squared as the effect size estimate for time, treatment, and time x treatment interaction effects.

RESULTS

- The 10 item vs. 30 item versions had similar average interitem correlations (.25 and .25), as well as similar partial eta-squared values for time – .37 [.32 to .41] versus .41 [.36 to .45], treatment (all .00) and time x treatment (.007 versus .003 for the full length)
- IRT models indicated similar reliability as in the development sample, with good precision across a similar range of severity

CONCLUSION

- The 10 item version of the PANSS replicated well in an independent, larger sample using double-blind RCT data.
- The similar sensitivity to treatment effects is particularly promising given the substantial reduction in scale length and corresponding decreases in required rater training, interview

REFERENCES

1. Busner J. Challenges in child and adolescent psychopharmacology clinical trials. Child Adolesc Psychopharmacol News 2013; 18(3): 1-3.
2. Farchione T. A regulatory perspective on clinical trials: FDA 101 for clinicians. Child Adolesc Psychopharmacol News 2013; 18(3):4-7.
3. Kay SR, Fiszbein A, Opler LA. The positive and negative syndrome scale (PANSS) for schizophrenia. Schizophr Bull. 1987;13(2):261-76.
4. Sikich L, Frazier JA, McClellan J, Findling RL, et al: Double-blind comparison of first- and second-generation antipsychotics in early-onset schizophrenia and schizoaffective disorder: findings from the treatment of early-onset schizophrenia spectrum disorders (TEOSS) study. Am J Psychiatry 2008; 165(11):1420-31.
5. Busner J, Youngstrom EA, Daniel DG, Findling, RL. Toward development of an abbreviated PANSS for pediatric trials: New analyses of PANSS TEOSS data. Presented at ISCTM Autumn Conference, Boston MA 2020
6. Singh J, Robb A, Vijapurkar U, Nuamah I, Hough D. A randomized, double-blind study of paliperidone extended-release in treatment of acute schizophrenia in adolescents. Biol Psychiatry. 2011 Dec 15;70(12):1179-87.

ACKNOWLEDGEMENTS

This study, carried out under YODA Project Protocol # 2020-4528, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C.. The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C..

Presentation and associated analyses financially supported by Signant Health

Presented at the American Society of Clinical Psychopharmacology (ASCP) May 31- June 3, 2022

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

Optimized 10 Item PANSS for Pediatric Trials: Comparison to 30 Item Version in a Multi-Site Trial for Adolescent Schizophrenia

Busner, J[1,2]; Youngstrom, EA[3]; Langfus, JA[3]; Findling, RL[2]; Findling, DG[1]

[1]Signant Health; [2]Virginia Commonwealth University School of Medicine, Department of Psychiatry; [3]University of North Carolina, Chapel Hill

ABSTRACT

The methodological question being addressed: Will a 10 item PANSS optimized for pediatric trials perform similarly to the 30 item PANSS in an independent placebo-controlled multi-site trial? **Introduction:** Global regulatory initiatives have resulted in an increasing number of psychopharmacology trials in the pediatric age range. Among the challenges in ensuring valid and reliable data in such trials are developmental limitations in symptom description, the need to integrate and weight information from varied sources (including the patient, parents/caregivers and other informants, and the global shortage of child-trained clinical investigators (Busner, 2013; Farchione, 2013). Moreover, few efficacy measures have been developed and validated specifically for pediatric trials. As a result, measures designed for and validated in adults, such as the Positive and Negative Syndrome Scale (PANSS), are frequently used in adolescent schizophrenia trials. The PANSS is a complex 30-item measure that has been extensively studied and shown to pose ratings challenges even in the adult patients for whom it was designed (e.g., Daniel and Dries, 2013). Our group has developed a 10-item PANSS based on psychometric analyses of NIMH TEOSS study data. The 10-item PANSS was reliable and sensitive to treatment changes. In the present study we attempt to replicate the findings using an independent multi-site trial. **Methods**: The 6-week, double-blind, parallel group, acute phase data from the Johnson & Johnson-sponsored completed, positive, paliperidone study [6] were accessed from the YODA secure data environment. The trial included 201 12-17 year olds randomly allocated to placebo or one of three fixed doses of paliperidone. Analyses were performed using the mirt, lavaan, sjstat, rstatix and psych packages in R, using the same syntax and methods as the prior analyses (Findling et al., under review), with mixed regressions using random intercepts and partial eta-squared as the effect size estimate for time, treatment, and time x treatment interaction effects. **Results**: The 10-item vs. 30-item versions had similar average inter-item correlations (.25 and .25), as well as similar partial eta-squared values for time – .37 (.32 to .41) versus .41 (.36 to .45), treatment (all .00) and time x treatment (.007 versus .003 for the full length). IRT models indicated similar reliability as in the development sample, with good precision across a similar range of severity. LOCF analyses found separation from placebo using both the 10 and 30-item versions on multiple, identical arms; ANCOVAs controlling for PANSS at phase entry produced similar eta-squared at subsequent weeks (largest difference = .005, favoring 10-item version). **Conclusions**: The 10-item version of the PANSS replicated well in an independent, larger adolescent sample using double-blind RCT data. The similar sensitivity to treatment effects is particularly promising given the substantial reduction in scale length and corresponding decreases in required rater training, interview length, and respondent burden.

METHODOLOGICAL QUESTION

Will a 10 item PANSS optimized for pediatric trials perform similarly to the 30 item PANSS in an independent placebo-controlled multi-site trial?

INTRODUCTION

- Global regulatory initiatives have resulted in an increasing number of psychopharmacology trials in the pediatric age range.
- Among the challenges in ensuring valid and reliable data in such trials are developmental limitations in symptom description, the need to integrate and weight information from varied sources (including the patient, parents/caregivers and other informants, and the global shortage of child-trained clinical investigators (Busner, 2013; Farchione, 2013).
- Moreover, few efficacy measures have been developed and validated specifically for pediatric trials. As a result, measures designed for and validated in adults, such as the Positive and Negative Syndrome Scale (PANSS), are frequently used in adolescent schizophrenia trials.
- The PANSS is a complex 30-item measure that has been extensively studied and shown to pose ratings challenges even in the adult patients for whom it was designed (e.g., Daniel and Dries, 2013).
- Our group has developed a 10-item PANSS based on psychometric analyses of NIMH TEOSS study data.
- The 10-item PANSS was reliable and sensitive to treatment changes.
- In the present study we attempt to replicate the findings using an independent multi-site trial.

METHODS

- The 6-week, double-blind, parallel group, acute phase data from the Johnson & Johnson- sponsored completed, positive, paliperidone study [6] were accessed from the YODA secure data environment.
- The trial included 201 12-17 year olds randomly allocated to placebo or one of three fixed doses of paliperidone.
- Analyses were performed using the mirt, lavaan, sjstat, rstatix and psych packages in R, using the same syntax and methods as the prior analyses (Findling et al., under review), with mixed regressions using random intercepts and partial eta-squared as the effect size estimate for time, treatment, and time x treatment interaction effects.

RESULTS

- The 10-item vs. 30-item versions had similar average inter-item correlations (.25 and .25), as well as similar partial eta-squared values for time – .37 (.32 to .41) versus .41 (.36 to .45), treatment (all .00) and time x treatment (.007 versus .003 for the full length).
- IRT models indicated similar reliability as in the development sample, with good precision across a similar range of severity.
- LOCF analyses found separation from placebo using both the 10 and 30-item versions on multiple, identical arms; ANCOVAs controlling for PANSS at phase entry produced similar eta-squared at subsequent weeks (largest difference = .005, favoring 10-item version).

CONCLUSIONS

- The 10-item version of the PANSS replicated well in an independent, larger adolescent sample using double-blind RCT data.
- The similar sensitivity to treatment effects is particularly promising given the substantial reduction in scale length and corresponding decreases in required rater training, interview length, and respondent burden.

ACKNOWLEDGEMENTS

- This study, carried out under YODA Project Protocol # 2020-4528, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C..
- The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C.

Presentation and associated analyses financially supported by Signant Health

Presented at The International Society For CNS Clinical Trials and Methodology (ISCTM) September 8 - 9, 2022

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

Utility of an optimized 10 item pediatric PANSS: Comparison to 30 item PANSS in a large multi-site industry sponsored trial for adolescent schizophrenia

Joan Busner, Ph.D., [1,2] Eric A. Youngstrom, Ph.D[3]., Joshua A. Langfus[3], Robert L. Findling, M.D[2]., David G. Daniel, M.D.[1]

[1]Signant Health; [2]Virginia Commonwealth University School of Medicine, Department of Psychiatry; [3]University of North Carolina, Chapel Hill

ABSTRACT

Objective: The Positive and Negative Syndrome Scale (PANSS) is a lengthy 30-item psychosis measure designed for adults. Our group has developed a 10-item PANSS for pediatric trials based on psychometric analyses of the NIMH Treatment of Early Onset Schizophrenia Study (TEOSS). Our 10-item PANSS compared well to the 30- item version and was reliable and sensitive to treatment changes in that study. In the present study we attempt to replicate the findings using an independent multi-site placebo-controlled trial. **Design**: Unblinded data from the 6-week, double-blind, parallel group, acute phase data from the Johnson & Johnson-sponsored positive paliperidone study were accessed from the Yale Open Data Access (YODA) secure data environment. The trial included 201 12-17 year olds randomly allocated to placebo or one of three fixed doses of paliperidone. Analyses included mixed regressions using random intercepts and partial eta-squared as the effect size estimate for time, treatment, and time x treatment interaction effects. **Results**: The 10 vs. 30-item versions had similar average inter-item correlations as well as similar partial eta-squared values for time, treatment, and time x treatment. LOCF analyses found similar 10 vs 30 item separation from placebo on multiple, identical arms; week by week effect sizes for the 10 and 30 items versions were similar. **Conclusions**: The 10-item version of the PANSS replicated well in an independent, larger adolescent sample using double-blind RCT data. The similar sensitivity to treatment effects is particularly promising given the decreases in scale length, required rater training, interview length, and respondent burden.

OBJECTIVE

- The Positive and Negative Syndrome Scale (PANSS) is a lengthy 30-item psychosis measure designed for adults.
- Our group has developed a 10-item PANSS for pediatric trials based on psychometric analyses of the NIMH Treatment of Early Onset Schizophrenia Study (TEOSS).
- Our 10-item PANSS compared well to the 30- item version and was reliable and sensitive to treatment changes in that study.
- In the present study we attempt to replicate the findings using an independent multi-site placebo-controlled trial.

DESIGN

- Unblinded data from the 6-week, double-blind, parallel group, acute phase data from the Johnson & Johnson-sponsored positive paliperidone study were accessed from the Yale Open Data Access (YODA) secure data environment.
- The trial included 201 12-17 year olds randomly allocated to placebo or one of three fixed doses of paliperidone.
- Analyses included mixed regressions using random intercepts and partial eta-squared as the effect size estimate for time, treatment, and time x treatment interaction effects.

RESULTS

- The 10 vs. 30-item versions had similar average inter-item correlations as well as similar partial eta-squared values for time, treatment, and time x treatment.
- LOCF analyses found similar 10 vs 30 item separation from placebo on multiple, identical arms; week by week effect sizes for the 10 and 30 items versions were similar.

CONCLUSIONS

- The 10-item version of the PANSS replicated well in an independent, larger adolescent sample using double-blind RCT data.
- The similar sensitivity to treatment effects is particularly promising given the decreases in scale length, required rater training, interview length, and respondent burden.

ACKNOWLEDGEMENTS

- This study, carried out under YODA Project Protocol # 2020-4528, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C..
- The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C.

Presentation and associated analyses financially supported by Signant Health. Drs. Busner and Daniel are full time employees of Signant Health. Mr. Langfus has no financial disclosures. Financial disclosures of Drs. Findling and Youngstrom are available on request.

Thie poster was presented in part at the ISCTM Autumn Conference, September 8-9, Boston, MA and presented at the Collaborating for Novel Solutions Summit (CNS) November 17 - 20, 2022

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

Sensitivity to time and treatment effects of new short forms of the PANSS in an outpatient pediatric randomized controlled trial

*Busner, J[1,3], Youngstrom, EA[2], Daniel, DG[1], Langfus, JA[2], Findling, RL[3]

[1]Signant Health, Blue Bell, PA; [2]University of North Carolina, Chapel Hill, NC; [3]Virginia Commonwealth University, Richmond, VA

*presenting author

ABSTRACT

Background: Global regulatory initiatives have resulted in an increasing number of psychopharmacology trials in the pediatric age range. Among the challenges in ensuring valid and reliable data in such trials are developmental limitations in symptom description, the need to integrate and weight information from varied sources (including the patient, parents/caregivers and other informants, and the global shortage of child-trained clinical investigators (Busner, 2013; Farchione, 2013). Moreover, few efficacy measures have been developed and validated specifically for pediatric trials. As a result, measures designed for and validated in adults, such as the Positive and Negative Syndrome Scale (PANSS), are frequently used in adolescent schizophrenia trials. The PANSS is a complex 30-item measure that has been extensively studied and shown to pose ratings challenges even in the adult patients for whom it was designed (e.g., Daniel and Dries, 2013). Our group has developed a 10-item PANSS based on psychometric analyses of NIMH TEOSS study data. The 10-item PANSS was reliable and sensitive to treatment changes. In the present study we attempt to replicate the findings using an independent multi-site trial (Findling et al., in press). Will a 10 item PANSS optimized for pediatric trials perform similarly to the 30 item PANSS in an independent placebo-controlled multi-site trial? **Method**: The 6-week, double-blind, parallel group, acute phase data from the Johnson & Johnson- sponsored completed, positive, paliperidone study (Singh et al., 2011) were accessed from the YODA secure data environment. The trial included 201 12-17 year olds randomly allocated to placebo or one of three fixed doses of paliperidone. Analyses were performed using the mirt, lavaan, sjstat, rstatix and psych packages in R, using the same syntax and methods as the prior analyses (Findling et al., in press), with mixed regressions using random intercepts and partial eta-squared as the effect size estimate for time, treatment, and time x treatment interaction effects. **Results**: The 10-item vs. 30-item versions had similar average inter-item correlations (.25 and .25), as well as similar partial eta-squared values for time – .37 (.32 to .41) versus .41 (.36 to .45), treatment (all .00) and time x treatment (.007 versus .003 for the full length). IRT models indicated similar reliability as in the development sample, with good precision across a similar range of severity. LOCF analyses found separation from placebo using both the 10 and 30-item versions on multiple, identical arms; ANCOVAs controlling for PANSS at phase entry produced similar eta-squareds at subsequent weeks (largest difference = .005, favoring 10-item version). **Conclusions**: The 10-item version of the PANSS replicated well in an independent, larger adolescent sample using double-blind RCT data. The similar sensitivity to treatment effects is particularly promising given the substantial reduction in scale length and corresponding decreases in required rater training, interview length, and respondent burden.

BACKGROUND

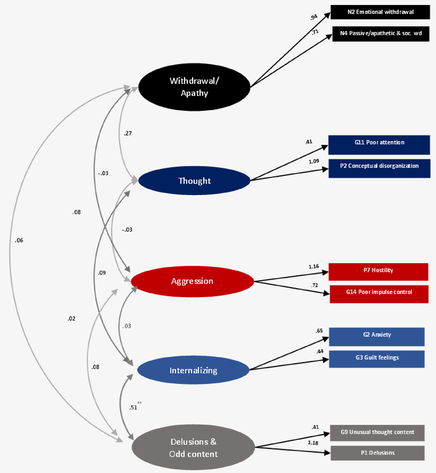
- Global regulatory initiatives have resulted in an increasing number of psychopharmacology trials in the pediatric age range.
- Among the challenges in ensuring valid and reliable data in such trials are developmental limitations in symptom description, the need to integrate and weight information from varied sources (including the patient, parents/caregivers and other informants, and the global shortage of child-trained clinical investigators (Busner, 2013; Farchione, 2013).
- Moreover, few efficacy measures have been developed and validated specifically for pediatric trials. As a result, measures designed for and validated in adults, such as the Positive and Negative Syndrome Scale (PANSS), are frequently used in adolescent schizophrenia trials.
- The PANSS is a complex 30-item measure that has been extensively studied and shown to pose ratings challenges even in the adult patients for whom it was designed (e.g., Daniel and Dries, 2013).
- Our group has developed a 10-item PANSS based on psychometric analyses of NIMH TEOSS study data.
- The 10-item PANSS was reliable and sensitive to treatment changes.
- In the present study we attempt to replicate the findings using an independent multi-site trial (Findling et al., in press).
- *Will a 10 item PANSS optimized for pediatric trials perform similarly to the 30 item PANSS in an independent placebo-controlled multi-site trial?*

METHOD

- The 6-week, double-blind, parallel group, acute phase data from the Johnson & Johnson- sponsored completed, positive, paliperidone study (Singh et al., 2011) were accessed from the YODA secure data environment.
- The trial included 201 12-17 year olds randomly allocated to placebo or one of three fixed doses of paliperidone.
- Analyses were performed using the mirt, lavaan, sjstat, rstatix and psych packages in R, using the same syntax and methods as the prior analyses (Findling et al., in press), with mixed regressions using random intercepts and partial eta-squared as the effect size estimate for time, treatment, and time x treatment interaction effects.

RESULTS

- The 10-item vs. 30-item versions had similar average inter-item correlations (.25 and .25), as well as similar partial eta-squared values for time – .37 (.32 to .41) versus .41 (.36 to .45), treatment (all .00) and time x treatment (.007 versus .003 for the full length).
- IRT models indicated similar reliability as in the development sample, with good precision across a similar range of severity. LOCF analyses found separation from placebo using both the 10 and 30-item versions on multiple, identical arms; ANCOVAs controlling for PANSS at phase entry produced similar eta-squareds at subsequent weeks (largest difference = .005, favoring 10-item version).



CONCLUSIONS

- The 10-item version of the PANSS replicated well in an independent, larger adolescent sample using double-blind RCT data.
- The similar sensitivity to treatment effects is particularly promising given the substantial reduction in scale length and corresponding decreases in required rater training, interview length, and respondent burden.

REFERENCES

1. Streiner DL, Norman GR, Cairney J. Health measurement scales: A practical guide to their development and use. 5th ed. New York, NY: Oxford University Press; 2015.
2. Santor DA, Ascher-Svanum H, Lindenmayer JP, Obenchain RL. Item response analysis of the Positive and Negative Syndrome Scale. BMC Psychiatry. 2007;7:66.
3. Lindenmayer JP. Are Shorter Versions of the Positive and Negative Syndrome Scale (PANSS) Doable? A Critical Review. Innov Clin Neurosci. 2017;14(11-12):73-76.
4. Findling, R.L., Youngstrom, E.A., McClellan, J., Frazier, J.A., Sikich, L., Daniel, D., Busner, J. (in press). An Optimized Version of the Positive and Negative Symptoms Scale (PANSS) for Pediatric Trials. J Am Acad Child Adol Psychiatry
5. Singh J, Robb A, Vijapurkar U, Nuamah I, Hough D. A randomized, double-blind study of paliperidone extended-release in treatment of acute schizophrenia in adolescents. Biol Psychiatry. 2011 Dec 15;70(12):1179-87.

ACKNOWLEDGEMENTS

- This study, carried out under YODA Project Protocol # 2020-4528, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C..
- The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C.

Presentation and associated analyses financially supported by Signant Health. Drs. Busner and Daniel are full time employees of Signant Health.Mr. Langfus has no financial disclosures. Financial disclosures of Drs. Findling and Youngstrom are available on request.

Presented at The American College of Neuropsychopharmacology Meeting (ACNP) December 4 - 7, 2022

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

Calibrating the Optimized Pediatric PANSS10 Short Form in Three Independent Pediatric Clinical Trials

Joshua A Langfus[1], Joan Busner[2,3], David Daniel[2], Eric A Youngstrom[4], Robert L Findling[3]

[1]University of North Carolina at Chapel Hill, [2]Signant Health, [3]Virginia Commonwealth University, [4]Institute of Mental and Behavioral Health Research, Nationwide Children's Hospital and The Ohio State University

INTRODUCTION

- The Positive and Negative Syndrome Scale (PANSS) is the most-used primary efficacy measure for schizophrenia trials
- Limitations of the original 30-item PANSS:
- Developed for adults
- Long, complex; requires trained raters
- The optimized PANSS10 short form was developed to address these challenges

GOALS

- **AIM1:** Demonstrate calibration of the PANSS10 vs. full 30-item PANSS
- **AIM 2:** Show PANSS10 scores detect treatment effects equally well

METHODS

- Data from three independent pediatric schizophrenia clinical trials[1,2,3]
  - One study[1] had placebo control arm
  - Two compared established compounds
- Examined scores on extracted 10-item short form (PANSS10) vs. full form
- Bland-Altman analyses tested for bias
- ANCOVA probed effect of treatment

RESULTS

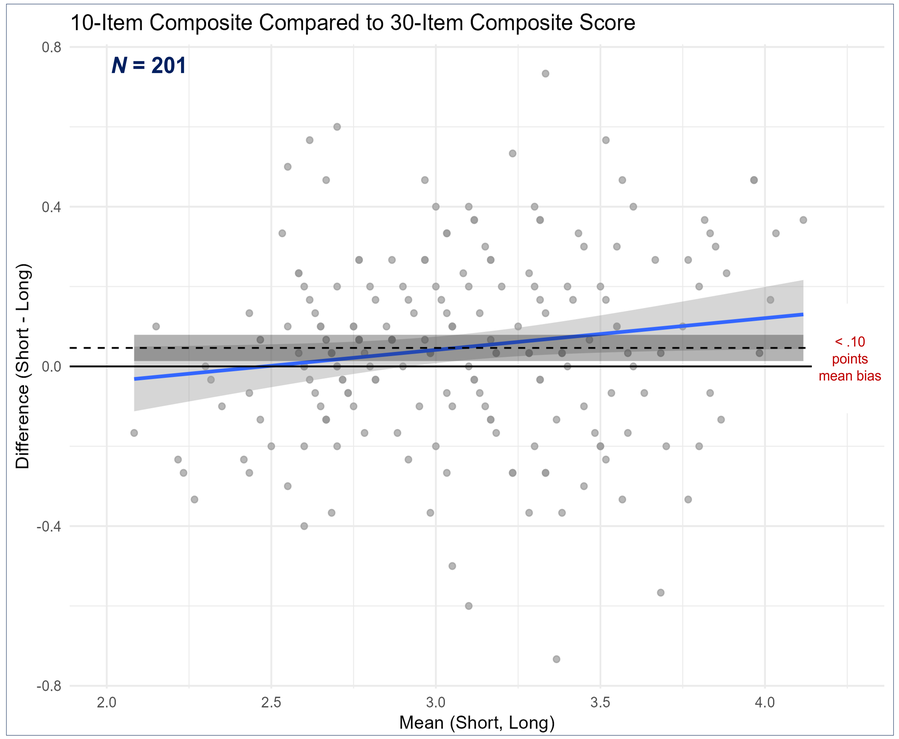
- Good calibration for PANSS10 vs. PANSS30 across all studies
  - On average, minimal overall (mean) difference
  - Some evidence of enhanced sensitivity
- PANSS10 replicates original efficacy results in trial with placebo arm

DISCUSSION

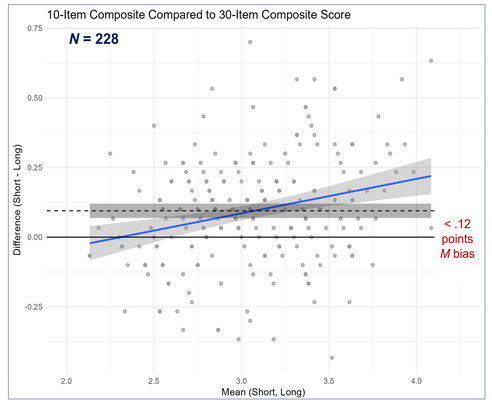
- The optimized PANSS10 is well-calibrated compared to original PANSS
- The PANSS10 is equally sensitive to treatment effects

THE PANSS10 IS WELL-CALIBRATED TO THE FULL PANSS AND SHOWS EQUAL SENSITIVITY TO TREATMENT FOR CHILDREN

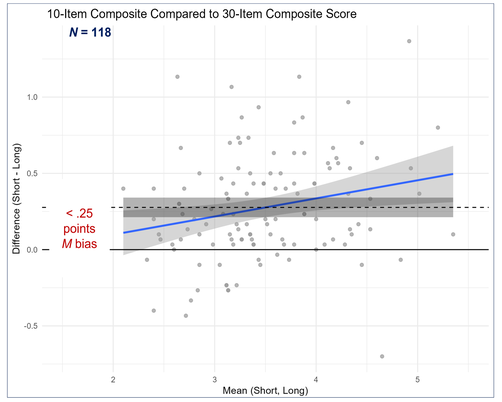
CALIBRATION IN SAMPLE 1 (SINGH ET AL. 2011) COMPARING ITEM AVERAGES



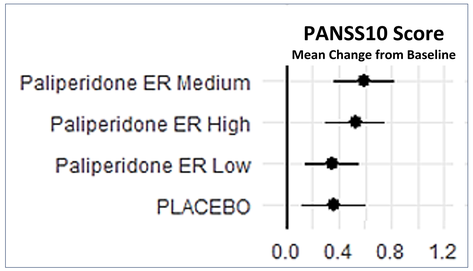
CALIBRATION IN SAMPLE 2 (SAVITZ ET AL. 2015)



CALIBRATION IN SAMPLE 3 (SIKICH ET AL. 2008)



SAMPLE 1 RESULTS REPLICATION



Mean Change in PANSS10 Scores from Baseline to Endpoint

As in Singh et al. (2011), change in Medium Dose group significantly greater than in Placebo group

ANCOVA RESULTS (SAMPLE 1 REPLICATION)

```
lm(formula = panssk10.end ~ panssk10.bl + TRTGRP + SEX + DCOUNTRY +
    DAGE, data = bl.endpoint)

Residuals:
     Min       1Q   Median       3Q      Max
-1.6260 -0.3615  0.0112  0.3381  1.9532

Coefficients:
                                Estimate Std. Error t value Pr(>|t|)
(Intercept)                       2.7360     0.1126   24.29  < 2e-16 ***
panssk10.bl                       0.3412     0.0407    8.38  1.1e-14 ***
TRTGRPPaliperidone ER Low        -0.0105     0.1104   -0.10   0.9242
TRTGRPPaliperidone ER High       -0.1780     0.1150   -1.55   0.1233
TRTGRPPaliperidone ER Medium     -0.2661     0.1145   -2.32   0.0212 *
SEXMALE                           0.0323     0.0837    0.39   0.7001
DCOUNTRYEUROPE and Other          0.0440     0.0997    0.44   0.6591
DCOUNTRYNORTH AMERICA            -0.4372     0.1346   -3.25   0.0014 **
DAGE12-<=15                       0.0583     0.0813    0.72   0.4737
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Residual standard error: 0.559 on 192 degrees of freedom
Multiple R-squared:  0.308,  Adjusted R-squared:  0.279
F-statistic: 10.7 on 8 and 192 DF,  p-value: 2.12e-12
```

DISCLOSURES

- One or more authors report potential conflicts which are described in the program
- This study, carried out under YODA Project 2020-4528, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C.. The interpretation and reporting of research using this data are solely the responsibility of the authors and do not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C

REFERENCES

1. Singh J, Robb A, Vijapurkar U, Nuamah I, Hough D. A randomized, double-blind study of paliperidone extended-release in treatment of acute schizophrenia in adolescents. Biol Psychiatry. 2011;70(12):1179-1187. doi:10.1016/j.biopsych.2011.06.021
2. Savitz AJ, Lane R, Nuamah I, Gopal S, Hough D. Efficacy and Safety of Paliperidone Extended Release in Adolescents With Schizophrenia: A Randomized, Double-Blind Study. J Am Acad Child Adolesc Psychiatry. 2015;54(2):126-137.e1. doi:10.1016/j.jaac.2014.11.009
3. Sikich L, Frazier JA, McClellan J, et al. Double-Blind Comparison of First- and Second-Generation Antipsychotics in Early-Onset Schizophrenia and Schizo-affective Disorder: Findings From the Treatment of Early-Onset Schizophrenia Spectrum Disorders (TEOSS) Study. Am J Psychiatry. 2008;165(11):1420-1431. doi:10.1176/appi.ajp.2008.08050756

Presentation and associated analyses financially supported by Signant Health

Presented at the 20th Annual ISCTM Scientific Meeting, Feb 21 - 23, 2023, Washington, D.C.

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

New Shortened Pediatric PANSS 10 item Scale: Extension and Replication of Findings in the Paliperidone Adolescent Schizophrenia Clinical Trial Dataset

Joan Busner, Ph.D.[1], Eric A. Youngstrom, Ph.D.[2], Joshua Langfus. M.A.[3], David G. Daniel, M.D.,[4], Robert L. Findling, M.D.[5]

[1]Signant Health and Virginia Commonwealth University School of Medicine, [2]University of North Carolina at Chapel Hill, Psychology Department, Chapel Hill, NC, 3University of North Carolina at Chapel Hill, [4]Signant Health, [5]Virginia Commonwealth University School of Medicine

ABSTRACT

OBJECTIVE: Pediatric studies of schizophrenia have relied on the 30-item Positive and Negative Syndrome Scale (PANSS) as a primary outcome measure. The scale was designed for adults. Our group developed and published in 2023[1] a psychometrically sound 10-item version using pediatric data from the NIMH Treatment of Early Onset Schizophrenia (TEOSS) study[2]. A 20 item version was also developed. We wished to replicate and extend the findings in an independent large placebo controlled trial. **DESIGN**: We applied the same psychometric and treatment sensitivity analyses of our earlier work to the international placebo-controlled adolescent schizophrenia paliperidone randomized clinical trial, accessed via the YODA secure data environment. Analyses included confirmatory factor analyses, graded response models, omega reliability coefficients, tests of convergent criterion validity, sensitivity to change, and Bland-Altman plots to evaluate score reproducibility. **RESULTS**: The 10-item and 20-item versions were similar to the 30-item version for average interitem correlations, ωTotal reliabilities, with reliability >.80 across patient presentations from mild residual symptoms to severe pathology, correlations of .92 and .98 with the 30-item total, similar partial eta-squared values for time, treatment, and time x treatment, and similar correlations with CGI-severity and CGAS ratings. CONCLUSIONS: The 10- and 20-item PANSS short forms replicated strong reliability and validity in this large international positive RCT. The short forms demonstrated treatment sensitivity and convergent validity equivalent to that of the 30 item form, supporting their future use and offering the promise of substantial savings of rater and patient time and burden.

OBJECTIVE

- Pediatric studies of schizophrenia have relied on the 30-item Positive and Negative Syndrome Scale (PANSS) as a primary outcome measure
- The scale was designed for adults
- Our group developed and published in 2023[1] a psychometrically sound 10-item version using pediatric data from the NIMH Treatment of Early Onset Schizophrenia (TEOSS) study[2]
- A 20 item version was also developed
- We wished to replicate and extend the findings in an independent large placebo controlled trial

DESIGN

- We applied the same psychometric and treatment sensitivity analyses of our earlier work to the international placebo-controlled adolescent schizophrenia paliperidone randomized clinical trial, accessed via the YODA secure data environment
- Analyses included confirmatory factor analyses, graded response models, omega reliability coefficients, tests of convergent criterion validity, sensitivity to change, and Bland-Altman plots to evaluate score reproducibility

RESULTS

- The 10-item and 20-item versions were similar to the 30-item version for average interitem correlations, ωTotal reliabilities, with reliability >.80 across patient presentations from mild residual symptoms to severe pathology, correlations of .92 and .98 with the 30-item total, similar partial eta-squared values for time, treatment, and time x treatment, and similar correlations with CGI-severity and CGAS ratings

CONCLUSIONS

- The 10- and 20-item PANSS short forms replicated strong reliability and validity in this large international positive RCT
- The short forms demonstrated treatment sensitivity and convergent validity equivalent to that of the 30 item form, supporting their future use and offering the promise of substantial savings of rater and patient time and burden

REFERENCES

1. Findling, R.L., Youngstrom, E.A., Frazier, J.A., Sikich, L., Daniel, D.G., Busner, J. (2023). An optimized version of the Positive and Negative Symptoms Scale (PANSS) for pediatric trials. J American Academy Child and Adolescent Psychiatry. 62 (4): 427-434.
2. Sikich L, Frazier JA, McClellan J, Findling RL, et al. Double-blind comparison of first- and second-generation antipsychotics in early-onset schizophrenia and schizo-affective disorder: findings from the treatment of early-onset schizophrenia spectrum disorders (TEOSS) study. Am J Psychiatry. 2008 Nov;165(11):1420-31.

These findings were presented at the ASCP Annual Meeting, June, 2023, Miami, FL. Drs. Busner and Daniel are employees of Signant Health; financial disclosures of other authors available upon request.

Presented at CNS Summit, November 8-11, Boston, MA

SIGNANTHEALTH
THE EVIDENCE GENERATION COMPANY

Replicating and Extending the Reliability, Criterion Validity, and Treatment Sensitivity of the PANSS10 and PANSS20 for Pediatric Trials

Joan Busner, Ph.D.[1], Eric A. Youngstrom, Ph.D.[2], Joshua Langfus. M.A.[3], David G. Daniel, M.D.,[4], Robert L. Findling, M.D.[5]

[1]Signant Health and Virginia Commonwealth University School of Medicine, [2]University of North Carolina at Chapel Hill, Psychology Department, Chapel Hill, NC, [3]University of North Carolina at Chapel Hill, [4]Signant Health, [5]Virginia Commonwealth University

ABSTRACT

Background: Pediatric studies of schizophrenia have relied on the 30-item Positive and Negative Syndrome Scale (PANSS) as a primary outcome measure. There have been many efforts to create shorter versions of it to reduce costs and burden while keeping good reliability and validity. The present aim is to conduct a confirmatory investigation of the reliability and validity of 10 and 20 item abbreviated versions developed in another pediatric sample that reflect the five-factor structure underlying the PANSS, adding more detailed examination of patient-level score reproducibility. **Method**: We applied the same psychometric and treatment sensitivity analyses as in Findling et al., (2023) to an international placebo-controlled adolescent schizophrenia paliperidone randomized clinical trial, accessed via the YODA secure data environment. Analyses included confirmatory factor analyses, graded response models, omega reliability coefficients, tests of convergent criterion validity, sensitivity to change, and Bland-Altman plots to evaluate score reproducibility. **Results**: Using the paliperidone RCT dataset, the 10-item or 20-item vs. 30-item versions had similar average interitem correlations (.11 to .15), ωTotal reliabilities of .78 to .89 with reliability >.80 across patient presentations from mild residual symptoms to severe pathology, correlations of .92 and .98 with the 30-item total, partial eta-squared values for time, treatment, and time x treatment, and similar correlations with CGI-severity and CGAS ratings. Patient scores differed by 0.04 points on average on the 10- and 0.01 for the 20-item version versus the 30-item, all not significant. **Conclusions**: The 10- and 20-item PANSS short forms replicated strong reliability and validity in a large international RCT. Besides replication and generalization to an international sample, findings extend prior work by being the first to apply modern reliability models (omega) for multi-factor composites, also using Bland-Altman methods to evaluate patient-level score reproducibility. Scores based on the 10- or 20-item version reproduce traditional scores with high fidelity, offering substantial savings in terms of time, cost, and burden, especially when used for tracking progress or outcomes.

BACKGROUND

- Pediatric studies of schizophrenia have relied on the 30-item Positive and Negative Syndrome Scale (PANSS) as a primary outcome measure.
- There have been many efforts to create shorter versions of it to reduce costs and burden while keeping good reliability and validity.
- The present aim is to conduct a confirmatory investigation of the reliability and validity of 10 and 20 item abbreviated versions developed in another pediatric sample that reflect the five-factor structure underlying the PANSS, adding more detailed examination of patient-level score reproducibility.

METHOD

- We applied the same psychometric and treatment sensitivity analyses as in Findling et al., (2023) to an international placebo-controlled adolescent schizophrenia paliperidone randomized clinical trial, accessed via the YODA secure data environment.
- Analyses included confirmatory factor analyses, graded response models, omega reliability coefficients, tests of convergent criterion validity, sensitivity to change, and Bland-Altman plots to evaluate score reproducibility.

RESULTS

- Using the paliperidone RCT dataset, the 10-item or 20-item vs. 30-item versions had similar average interitem correlations (.11 to .15), ωTotal reliabilities of .78 to .89 with reliability >.80 across patient presentations from mild residual symptoms to severe pathology, correlations of .92 and .98 with the 30-item total, partial eta-squared values for time, treatment, and time x treatment, and similar correlations with CGI-severity and CGAS ratings.
- Patient scores differed by 0.04 points on average on the 10- and 0.01 for the 20-item version versus the 30-item, all not significant.

CONCLUSIONS

- The 10- and 20-item PANSS short forms replicated strong reliability and validity in a large international RCT.
- Besides replication and generalization to an international sample, findings extend prior work by being the first to apply modern reliability models (omega) for multi-factor composites, also using Bland-Altman methods to evaluate patient-level score reproducibility.

REFERENCES

1. Findling RF, Youngstrom EA, McClellan JM, Frazier JA, Sikich L, Daniel DG, Busner, J. An optimized version of the Positive and Negative Symptoms Scale (PANSS) for pediatric trials. J Amer Acad Child Adolesc Psychiatry, Published online: December 12, 2022, DOI:https://doi.org/10.1016/j.jaac.2022.07.864
2. Busner J. Challenges in child and adolescent psychopharmacology clinical trials. Child Adolesc Psychopharmacol News, 2013; 18(3): 1-3.

Presentation and associated analyses financially supported by Signant Health. Drs. Busner and Daniel are full time employees of Signant Health.Mr. Langfus has no financial disclosures. Financial disclosures of Drs. Findling and Youngstrom are available on request.

Presented at the American Society for Clinical Pathology Meeting (ASCP) May 30 - June 2, 2023

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY™

Initial psychometric evaluation of the pediatric short Positive and Negative Syndrome Scale (PANSS) version in an adult, acutely exacerbated clinical trial population with schizophrenia

Daniel DG[1], Kott A[1], Busner J[1,4], Wang X[1], Langfus J[2], Youngstrom EA[3], Findling R[4]

[1]Signant Health, [2]University of North Carolina at Chapel Hill, [3]University of North Carolina at Chapel Hill & Helping Give Away Psychological Science, 501c3,[4]Virginia Commonwealth University

OBJECTIVE

Psychometric evaluation of the pediatric short Positive and Negative Syndrome Scale (PANSS) version in an adult, acutely exacerbated clinical trial population with schizophrenia.

INTRODUCTION

The Positive and Negative Syndrome Scale (PANSS) is the most frequently used instrument to measure severity of schizophrenia in clinical research. The scale is long, takes a lot of time to administer, and appears to have many item redundancies. Several attempts were conducted to shorten the instrument to reduce administrative burden yet retain the validity and reliability of the original PANSS. In the current study we assessed the performance of the recently developed PANSS10 scale for pediatric studies (Findling et al, 2023) in adult acute schizophrenia trials.

METHODS

The Positive and Negative Syndrome Scale (PANSS) is the most frequently used instrument to measure severity of schizophrenia in clinical research. The scale is long, takes a lot of time to administer, and appears to have many item redundancies. Several attempts were conducted to shorten the instrument to reduce administrative burden yet retain the validity and reliability of the original PANSS. In the current study we assessed the performance of the recently developed PANSS10 scale for pediatric studies (Findling et al, 2023) in adult acute schizophrenia trials. We used Bland-Altman analysis to examine the calibration of the PANSS10 versus the original PANSS.

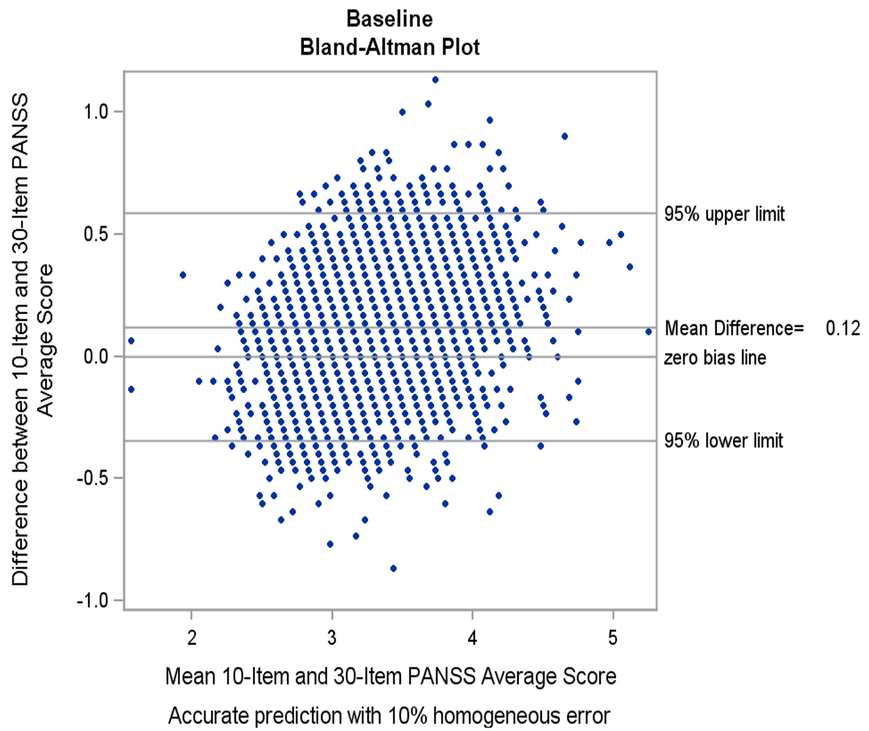
RESULTS

- The average inter-item correlation for the PANSS10 was 0.09.
- The PANSS10 showed a strong correlation with the full PANSS, r=0.96, p<.0001.
- The Spearman correlation between the PANSS10 and the CGI-S was 0.46, p<.0001; and between the full PANSS and the CGI-S was 0.52, p<.0001.
- Figure 1 shows the Bland-Altman plot. The x-axis represents the average of a patient's PANSS10 and original 30-item PANSS scores and the y-axis shows the difference between these scores. The average discrepancy was 0.12 points, indicating a slight tendency for higher scores on the PANSS10.

CONCLUSION

The 10-item version of the PANSS developed for pediatric population shows promising psychometric qualities even in adult population of acutely exacerbated clinical trial participants with schizophrenia.

FIGURE 1. BLAND-ALTMAN PLOT OF PATTERNS OF AGREEMENT BETWEEN THE PANSS10 AND THE FULL PANSS



Alan Kott, Xingmei Wang and Joan Busner are employees of Signant Health. David Daniel is an Executive Advisor to Signant Health. Dr. Youngstrom 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. Joshua Langfus reports no relevant conflict of interest. Dr. Robert Findling's disclosures are available by request.

SIGNANT HEALTH
THE EVIDENCE GENERATION COMPANY