Error Rates and Data Integrity: eCOA versus Paper Administration of the PANSS

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METHODOLOGICAL QUESTION:

Does the use of electronic clinical outcomes assessment (eCOA) impact rates of scoring errors as evaluated with the ISCTM working group consensus method for PANSS data?

INTRODUCTION (AIMS)

- Clinical trials of schizophrenia are prone to high rates of failure, in part due to noise in endpoint data from several factors including rater error.
- Scoring inconsistencies are associated with low interrater reliability and low internal consistency.
- In this study, the utility of an electronic platform and consistency checks in improving data quality in clinical trials is compared to paper-based administration in combination with other methods for improving data quality.
- The Positive and Negative Syndrome Scale (PANSS)[1] is a widely used, complex scale that has a very specific set of logical relationships and rules.
- Traditional paper-based administrations, which require manual data entry and source data verification, contribute to poor interrater reliability and inaccurate clinical trial results[2].
- The use of electronic COA (eCOA) has several advantages from operational and clinical standpoint, including eliminating calculation errors, reducing site burden, and standardizing measurements to improve data quality[3].
- We examined the utility of consistency checks in minimizing scoring errors in eCOA versus paper-based administrations.

METHODS

- eCOA administrations of the PANSS were identified from recent schizophrenia trials and compared against paper-based administrations of the same scale in a separate trial.
- All studies were randomized, double-blind, multisite clinical trials.
- Consistency/inconsistency flags assembled from the International Society for CNS Clinical Trials and Methodology (ISCTM) working-group were applied to both paper and eCOA administrations.
- The working-group had identified twenty-four flags, which ranged from within-visit scoring inconsistencies (e.g., a difference of more than two points between related items) to between-visit alerts (e.g., same response on all items from previous visit).
- The flags were divided based on extent to which they represented an error (Possibly, Probably, Very probably/Definitely). The proportions of flags that constituted an error were compared between paper-based and eCOA administrations.

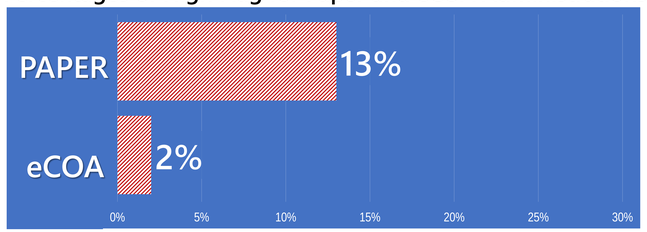
RESULTS

- There were 4,714 paper-based and 4,231 eCOA PANSS assessments.
- The proportion of flags that represented highly probable/ definite error was significantly higher in paper-based (13 percent) compared to eCOA (2 percent) administrations. (Figure 1)

Figure 2
PANSS Inconsistency Flags in Paper and eCOA Administrations

Proportion of ratings with at least one high flag	% Paper (n = 4,714)	% eCOA (n = 4,231)
HIGH FLAG – Very probably (or definitely) an error		
1. Same response on all 30 items from previous visit	0%	0%
2. Same response on 29 items from previous visit	**3%**	**0%**
3. Same response on 28 items from previous visit	**5%**	**1%**
4. Same response on 27 items from previous visit	**7%**	**1%**
5. Change from 1 to 7 on an item from previous visit	0%	0%
6. Change from 7 to 1 on an item from previous visit	0%	0%
7. Change of more than 40 on total score from previous visit	0%	0%
8. Change of 50% or more on total score from previous visit(e.g., (85–40)/80)	0%	0%
9. P5 grandiosity 5, 6 or 7 & P1 delusions less than 3	0%	0%
10. P6 suspiciousness 6 or 7 & P1 delusions less than 3	0%	0%
11. G1 somatic concerns 6 or 7 & P1 delusions less than 3	0%	0%
12. G3 guilt feelings 6 or 7 & P1 delusions less than 3	0%	0%
13. G9 unusual thought 5 or more & P1 delusions less than 3	**0%**	**0%**
MEDIUM FLAG – Probably an error		
14. G4 tension is greater than G2 anxiety	**7%**	**4%**
15. G6 depression 5 or greater and G7 motor retardation less than 3	1%	5%
16. G7 motor retardation 6 or greater & N6 lack of spontaneity less than 5	0%	0%
17. N4 passive social withdrawal & G16 active social avoidance both 7	0%	0%
18. G7 motor retardation 5 or greater & P4 excitement 4 or more	0%	0%
19. Among P5, P6, G1and G3 – more than 1 is 7	0%	0%
LOW FLAG – Possibly an error		
20. N6 lack of spontaneity is 2 pts greater than N3 poor rapport	1%	1%
21. Difference of more than 2 points between G8 uncooperativeness and P7 hostility	0%	0%
22. P7 hostility, G8 uncooperativeness and/or G14 poor impulse control with a score of 4 or greater & at least one of the others with a score 2 points greater or less than that	1%	0%
23. P3 hallucinatory behavior 5 or greater & G15 preoccupation less than 5	**29%**	**56%**
24. P2 conceptual disorganization 5 or greater & N5 difficulty in abstract thinking is less than 5	0%	1%

Figure 1
Percentages of High Flag for Paper and eCOA Administrations



- The flags triggered with most frequency in paper administrations included tension (G4) should not be greater than anxiety (G2) and same response on all items from previous visit. (Figure 2)
- Overall, the inconsistency flags in paper administrations were comparable to those reported in the ISCTM working group, NEWMEDS (14.9 percent)[4], which were both higher than those triggered in eCOA as constituting an error.

CONCLUSION

- Overall, eCOA PANSS administrations are less susceptible to scoring inconsistencies and error compared to those administered on paper.
- The proportion of "low" flags was higher in eCOA than paper administrations. As these flags represented low likelihood of an error, they may reflect a low sensitivity of paper administrations in identifying actual errors. Methodological limitations, including differences in rater training, data monitoring, or study populations, may have also had impact on the findings.
- Clinical trials that utilize consistency checks in conjunction with an eCOA platform can benefit from standardized measurement and flags that alert to errors over the course of a trial.
- The continual data quality monitoring in this setting, coupled with rater training and remediation, can improve data quality and reliability of trials.

References:

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