

Assessing Interview Quality and Scoring Accuracy in Clinical Trials with Continuous Quality Control (CQC)

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ABSTRACT

Introduction: CNS clinical trials fail more often than their a priori powering indicates they should. Quality assurance/quality control (QA/QC) safeguards for clinical (including primary) outcome measures have rarely been utilized. The large number of raters performing assessments in multi-site trials increases the probability of variability in ratings. Rater drift over time is well-documented and common¹, and superior interview performance as measured by the Rater Applied Performance Scale (RAPS) is associated with drug-placebo separation². We report the first findings using Continuous Quality Control (CQC), a new approach to monitoring and remediating the administration and scoring of clinical outcome measures.

Methods: 17 calibrated quality reviewers were rigorously trained and continuously calibrated on scale scoring and interview quality. This cohort was tightly calibrated on the MADRS, HAM-A and HAM-D, with ICCs = .91-.94. Data from two on-going clinical trials were pooled. Site raters audio recorded all MADRS, and HAM-A/HAM-D (SIGH-AD) administrations and uploaded the recordings to a central server. A priori scoring accuracy and RAPS interview quality criteria were established. Calibrated quality reviewers independently scored 448 site raters' assessments and rated interview quality using the RAPS. Only after scores and RAPS were submitted was the calibrated quality reviewer given access to the site raters' scores. Feedback was provided to the site raters on both interview quality and scoring accuracy before their next reviewed assessment.

Results: 448 assessments were reviewed. At the first review of 110 site ratings, 58% met the a priori criteria for scoring accuracy, 64% for interview quality and 45% met both criteria. By review six or later (n=78) there were substantial improvements: 79% met criteria for scoring accuracy, 87% for interview quality and 77% met both criteria. Improvements generally occurred by month four of the study. Analysis of RAPS domains showed Follow-up difficulties most commonly compromised interview quality.

Conclusions: QA/QC of clinical assessments identified significant scale administration and scoring issues. Repeated feedback improved rater performance substantially. Study outcomes will be evaluated to determine if continuous QA/QC of study assessments assists sponsors in identifying risks that contribute to CNS trial failures.

INTRODUCTION

Khan (2005) recently showed that 51-52% of clinical trials failed with known effective antidepressants and anxiolytics.

Possible reasons for failed trials include:

- Variability in ratings of clinical scales due in part to the sheer number of raters performing assessments in multi-site trials.
- Rater drift over time: study start-up rater standardization does not persist and rater calibration drops off after a short time. Raters drift occurs in scale administration interviewing techniques and scoring.

Fair to unsatisfactory interview performance, as measured by the Rater Applied Performance Scale (RAPS) (Lipsitz, 2004) has been associated with a failure in drug-placebo separation (Kobak, 2007).

Quality assurance/quality control (QA/QC) safeguards for clinical (including primary) outcome measures have rarely been utilized in clinical trials.

We report the first findings from two major depression randomized clinical trials using Continuous Quality Control (CQC), a new approach to monitoring and remediating the administration and scoring of clinical outcome measures.

METHODS

Calibrated Quality Reviewers:

- 17 calibrated quality reviewers were extensively trained and calibrated on the MADRS, HAM-A, and HAM-D
- Reviewers were calibrated to clinical scale scoring, assessing quality and delivery of feedback
- Reviewers were calibrated prior to study start and quarterly throughout the study

MADRS Scoring ICC = .94

HAM-D Scoring ICC = .93

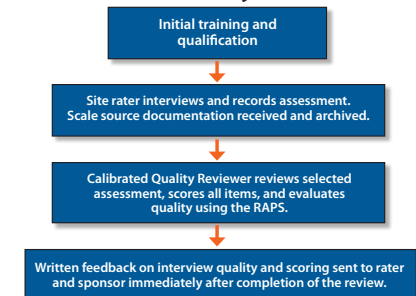
HAM-A Scoring ICC = .91

METHODS (continued)

Study Design:

- 110 site raters were selected by the sponsors to interview patients in these studies.
- All site raters were trained and qualified prior to study start.
- All study assessments are audio recorded.
- Assessments are uploaded to a central server where they can be accessed by the calibrated quality reviewer.
- A study-specific algorithm determines which assessments are reviewed.
- The calibrated quality reviewer listens to the assessment, scores all items, assesses interview quality with the RAPS, and enters their scores into the system.
- The calibrated quality reviewer is given access to the site rater scores after all item and RAPS scores entered.
- Reviewer scores are compared with site raters' scores and scoring feedback as well as interview quality feedback are prepared and sent to rater and sponsor.
- The RAPS is used to assess interview quality (Adherence, Follow-up; Clarification; Neutrality, and Rapport) with a pre-specified definition of "meets criteria."
- Scale-specific criteria defining the necessary level of scoring agreement between the site rater and the reviewer were pre-specified.

Continuous Quality Control (CQC)



RESULTS

% Assessments Meeting Scoring Criteria

| Reviews | Meets Criteria | Does Not Meet Criteria | Total Assessments | % Meets Criteria |
|---------|----------------|------------------------|-------------------|------------------|
| 1 | 64 | 46 | 110 | 58% |
| 2 | 54 | 36 | 90 | 60% |
| 3 | 43 | 33 | 76 | 57% |
| 4 | 34 | 20 | 54 | 63% |
| 5 | 26 | 14 | 40 | 65% |
| 6+ | 62 | 16 | 78 | 79% |

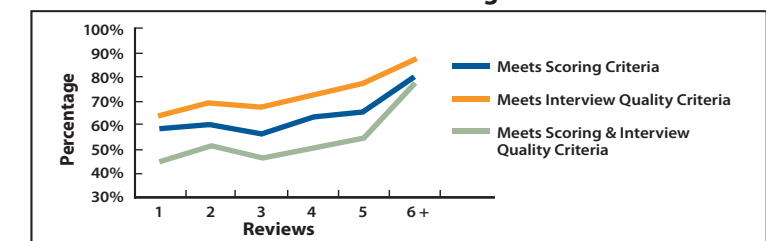
% Assessments Meeting Interview Quality Criteria

| Reviews | Meets Criteria | Does Not Meet Criteria | Total Assessments | % Meets Criteria |
|---------|----------------|------------------------|-------------------|------------------|
| 1 | 70 | 40 | 110 | 64% |
| 2 | 62 | 28 | 90 | 69% |
| 3 | 51 | 25 | 76 | 67% |
| 4 | 39 | 15 | 54 | 72% |
| 5 | 31 | 9 | 40 | 78% |
| 6+ | 68 | 10 | 78 | 87% |

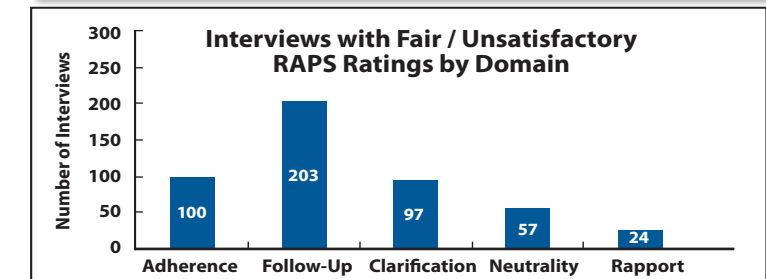
% Assessments Meeting Both Scoring & Interview Quality Criteria

| Reviews | Meets Criteria | Does Not Meet Criteria | Total Assessments | % Meets Criteria |
|---------|----------------|------------------------|-------------------|------------------|
| 1 | 49 | 25 | 110 | 45% |
| 2 | 46 | 20 | 90 | 51% |
| 3 | 35 | 17 | 76 | 46% |
| 4 | 27 | 8 | 54 | 50% |
| 5 | 22 | 5 | 40 | 55% |
| 6+ | 60 | 8 | 78 | 77% |

Percent of Assessments Meeting A Priori Criteria



Interviews with Fair / Unsatisfactory RAPS Ratings by Domain



CONCLUSION

- Multi-site trials may pose special challenges in standardizing administration and scoring of clinical outcome measures across many raters.
- At first review CQC of clinical assessments identified significant scale administration and scoring issues. Interview quality was most impacted by the Follow-up domain of the RAPS.
- These challenges can be remediated through continuous feedback and monitoring.
- Rater performance improved substantially in both scoring and interview quality with application of the CQC of clinical assessments by a closely and continuously calibrated cohort of quality reviewers.
- Scoring and interview quality may require ongoing monitoring and training to achieve an acceptable standard.

Indicated Next Step:

- Rater performance throughout the remainder of these studies will continue to be monitored to determine the degree to which continued monitoring and training maintains the acceptable standards of interview quality and scoring.

References

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