Comparison Between “Flat” and “Enhanced” eCOA of MMSE Attention and Calculation in Clinical Trials of Alzheimer’s Disease

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INTRODUCTION (AIMS)

- Electronic data capture of clinical outcomes (eCOA) along with audio monitoring of test administrations by trained and calibrated central reviewers significantly improves data quality (Feaster et al., 2017).
- While eCOA provides benefit over paper versions, scales without built-in quality checks (i.e., “flat”) may not reduce errors as much as versions with built-in quality checks (i.e., “enhanced”; Solomon et al., 2016).
- The Mini-Mental State Examination (MMSE) is commonly used as an inclusion criterion for clinical trials of Alzheimer’s disease (AD). This short 30-item screening test measures several aspects of cognition, including working memory (Folstein et al., 1975).
- To assess working memory, subjects mentally subtract 7 from 100 and then keep subtracting 7 from their previous answer. This portion of the MMSE is commonly referred to as “Serial 7s.” One point is awarded for each correct subtraction (maximum score = 5), regardless of whether the previous answer was correct or incorrect. Given the complex nature of administering and scoring this task, it is frequently remediated during quality control checks in clinical trials. Common errors include providing additional instructions, reminding subjects about their last response, and rater incorrectly calculating subtractions.
- Given the various eCOA versions of the MMSE currently in use, it is important to compare their respective ability to reduce rater error and enhance data quality.
- We compared two different eCOA versions of the MMSE which were utilized in similar multinational AD clinical trials in order to determine if an “enhanced” version with built-in quality checks, internal logic and automatic scoring significantly reduced error rates, more than a “flat” version, both overall in the scale and specifically, within Serial 7s.

METHOD

- Administration and scoring error rates on the MMSE between two multinational clinical studies of AD using different eCOA versions of the MMSE were compared.
- Test administrations were reviewed by trained and calibrated, local language, expert central reviewers for both scoring and administration errors. Reviewers evaluated scoring accuracy and listened to audio recordings of the assessment in order to identify additional scoring and/or administration errors.
- In the study using “flat” eCOA, 2,612 screening visit administrations of the MMSE were reviewed. In the study using “enhanced” eCOA, 1,990 screening visit administrations of the MMSE were reviewed.

RESULTS

- Pearson chi-square tests were used to determine differences in scoring and administration errors between the two eCOA versions.
- Scoring errors
  - Overall fewer errors were observed when using the “enhanced” version compared to the “flat” version ($\chi^2 = 9.2, p = .002$)
  - Fewer errors were also observed when using the “enhanced” version compared to the “flat” version on Serial 7s ($\chi^2 = 4.95, p = .026$)
- Administration errors
  - Overall, there were fewer errors observed when using the “enhanced” version when compared to the “flat” version ($\chi^2 = 18.5, p < .001$).
  - No difference in errors on Serial 7s between the two different eCOA versions was found ($\chi^2 = 1, p = .1$).

DISCUSSION

- The use of an “enhanced” eCOA version of the MMSE resulted in a significant reduction in the number of scoring errors overall and with Serial 7s in particular.
- In the “enhanced” eCOA version, audio monitoring identified a small number of scoring errors on Serial 7s (1.75%), which stemmed from differences between the subjects’ oral response and the response entered into the tablet.
- The “enhanced” eCOA version also resulted in fewer administration errors overall, but not on Serial 7s.
- Overall, these findings suggest that employing both intelligently designed, “enhanced” eCOA coupled with audio monitoring is most beneficial for reducing rater error.

REFFERENCES


The authors report no conflicts of interest for this work.