Electronic Administration of a Clinical Trials Version of the MMSE (eMMSE-CT)

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INTRODUCTION
The MMSE is a brief assessment that assesses Orientation, Registration, Attention and Calculation, Recall, Naming, Repetition, Comprehension, Reading, Writing and Drawing. The assessment is widely used in clinical practice as well as clinical trials. Many clinicians have adopted their “own” way of administering this relatively simple test. In clinical trials, paper MMSE administration by trained raters is subject to procedural inconsistencies, including scoring, administration and transcription errors. Independent clinical reviews of MMSE source documents have been part of data quality control in trials. Our published research has shown that one-third of MMSE completed at inclusion visits in Alzheimer’s trials contain procedural errors related to improper scale administration or, for example, addition errors. In a clinical trial, these errors can impact study eligibility and trial interpretability.

METHODS
■ We sought to create an electronic version of the MMSE for clinical trials (eMMSE-CT) by first obtaining a software license and agreement with Psychological Assessment Resources, Inc. (PAR), the copyright holder of the scale. With PAR’s agreement and encouragement, we looked to develop an electronic clinical trials version that went beyond other electronic versions of the scale, which functioned as electronic CPF and offered little ability to reduce administration errors and improve outcome reliability. Our version of the eMMSE-CT integrates instructions to raters, training reminders, enforces scoring rules, and has the flexibility to incorporate, for example, alternative questions and cultural adaptations of questions. The eMMSE-CT would use approved translations of the MMSE scale for non-English speaking raters and subjects.
■ The eMMSE-CT requires raters to ask each obligatory question and record a response to each question. The eMMSE-CT automatically calculates scores based on the recorded responses and enforces administration conventions. For example, the eMMSE-CT will display the ‘serial 7s’ correct score for the rater, and, in the next release, automatically determine if the response entered was correct or incorrect.

RESULTS
Table 1 shows the scores and discrepancies of the paired MMSE interviews.
■ The total scores on the paired administrations were the same when the eMMSE-CT was administered first.
■ The eMMSE-CT scores were slightly higher when the paper MMSE was administered first.
■ Although this was not designed as a research project, we did calculate the ICC (Pearson) between the paired eMMSE and paper MMSE at .89.
■ Word recall was the most common source of discrepancies in the test/retest format.

Table 1: Results of the paired paper MMSE and eMMSE-CT

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender, Age</th>
<th>Scores</th>
<th>Items that produced different scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>JKL (M, 54), paper MMSE first</td>
<td>22</td>
<td>36</td>
<td>Orientation to place: 5 of 5 correct, Orientation to time: 1 of 2 correct, Word Recall: 3 of 3 correct</td>
</tr>
<tr>
<td>DEF (F, 65), eMMSE-CT first</td>
<td>22</td>
<td>33</td>
<td>Orientation to time: 2 of 2 correct, Orientation to place: 4 of 5 correct</td>
</tr>
<tr>
<td>GHI (M, 69), eMMSE-CT first</td>
<td>25</td>
<td>36</td>
<td>Orientation to place: 5 of 5 correct, Orientation to time: 4 of 4 correct</td>
</tr>
<tr>
<td>DEF (F, 65), paper MMSE first</td>
<td>25</td>
<td>30</td>
<td>Word Recall: 1 of 3 correct, Orientation to time: 2 of 2 correct</td>
</tr>
<tr>
<td>DEF (F, 65), paper MMSE first</td>
<td>25</td>
<td>30</td>
<td>Word Recall: 1 of 3 correct, Orientation to time: 2 of 2 correct</td>
</tr>
<tr>
<td>DEF (F, 65), paper MMSE second</td>
<td>25</td>
<td>30</td>
<td>Word Recall: 1 of 3 correct, Orientation to time: 2 of 2 correct</td>
</tr>
</tbody>
</table>

Scoring is automatically calculated and displayed to raters at the conclusion of the interview.

■ The eMMSE-CT underwent extensive internal user acceptance and regulatory compliance testing. The eMMSE-CT qualifies as a electronically administered Clinical and, when administered on a closed system such as the Rater Station platform at Bracket, meets electronic medical records guidelines for clinical trials (FDA 21 CFR part 11).
■ To support internal UAT, we conducted a small test/retest comparison of the eMMSE-CT with traditional paper MMSE administration. The comparison was designed to generate rater and patient feedback for the next release of the scale, not as a research study of the administration. Five patients ranging from age 50 to 79 were interviewed in an outpatient clinic. Two patients had been diagnosed with MCI, another with post-concussion after MVI, and the other two had no complaints of memory loss.
■ A paper version and the eMMSE-CT were administered by clinical experts that have conducted rater training on the MMSE in dozens of trials throughout the world. The versions were administered by a different rater approximately 30 minutes apart in counterbalanced order. Word recall lists were varied in each pair of interviews. Patients and raters were asked to provide feedback about their experiences with the two administration methods.

CONCLUSIONS
■ The eMMSE-CT is a feasible method of administering the scale, and produced equivalent ratings to the standard, paper-based MMSE in this small sample.
■ The eMMSE-CT may decrease the likelihood of addition error on the scale and in structured items such as the serial 7s. As noted, in one of our interviews, a very experienced rater made an addition error using the paper MMSE that the eMMSE-CT would have prevented. The eMMSE-CT may also decrease the need for external reviews of paper worksheets for administrative errors.
■ The eMMSE-CT standardizes the administration of the scale and could be a useful tool to enhance data quality across sites and raters in large clinical trials.
■ Patients generally found rater administration of the MMSE using a computer acceptable.

Electronic Administration of a Clinical Trials Version of the MMSE (eMMSE-CT) - Figure 1: Screen shot of eMMSE-CT Serial 7s item

Electronic Administration of a Clinical Trials Version of the MMSE (eMMSE-CT) - Table 1: Results of the paired paper MMSE and eMMSE-CT

Electronic Administration of a Clinical Trials Version of the MMSE (eMMSE-CT) - Table 2: Patient feedback on administration of MMSE and eMMSE-CT

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