

Screening Mini Mental State Examination Assessment Duration as a Marker of Possible Score Inflation in Clinical Trials in Alzheimer’s Disease

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Signant Health

BACKGROUND

- Intentional score inflation to meet inclusion criteria represents a serious threat to the success of clinical trials.
- Based on our prior analyses, up to 10% of all subjects entering early Alzheimer’s Disease trials may be affected by score inflation of the inclusionary MMSE. (Kott, 2023).
- This means that these subjects are more cognitively impaired than the protocols require.
- In the population of subjects suffering from early stages AD, MMSE assessment duration is positively related to the severity of cognitive impairment, with longer durations expected in lower MMSE scores (more impaired subjects).
- Current practice of electronic Clinical Outcome Assessment (eCOA) collection of study instruments offers the opportunity to collect at no additional cost and analyze associated metadata, e.g., timestamps.
- In the current analysis we wanted to:
 1. test the hypothesis that those subjects with likely inflated MMSE scores at screening had significantly longer scale administration times corresponding to likely more severe cognitive impairment
 2. estimate a MMSE assessment duration cutoff that would best identify subjects at risk of having their scores inflated.
- This would allow to identify likely inflated subjects at the time of screening and take corrective actions before baseline assessment takes place and these subjects are possibly randomized into the trial.

METHOD

- Screening and Baseline data from 8,081 subjects were pooled from 6 early AD clinical trials.
- Subjects were dichotomized into subjects meeting Screening MMSE criteria at Baseline and subjects who dropped below the Screening MMSE criteria at Baseline.
- A generalized linear model was fitted to the data with the Screening MMSE duration used as the predicted variable and type of subject (drops below criteria yes/no) as the predictor variable correcting for the MMSE score at Screening.
- A ROC analysis was carried out to identify the MMSE assessment duration cutoff that would best identify those subjects who are at risk of having their scores inflated.

RESULTS

- 1,213(15%) subjects no longer met MMSE inclusion criteria at Baseline.
- Correcting for their Screening MMSE score, these subjects had significantly longer MMSE assessment duration by approximately 46 seconds (Figure 1).
- MMSE assessment durations of 8 minutes or longer had the best predictive performance in terms of sensitivity (61.3%) and specificity (60.9%) with the ROC AUC of 65.8% to identify subjects at risk of having their MMSE Screening scores inflated (Figure 2).

FIGURE 1: MMSE DURATION

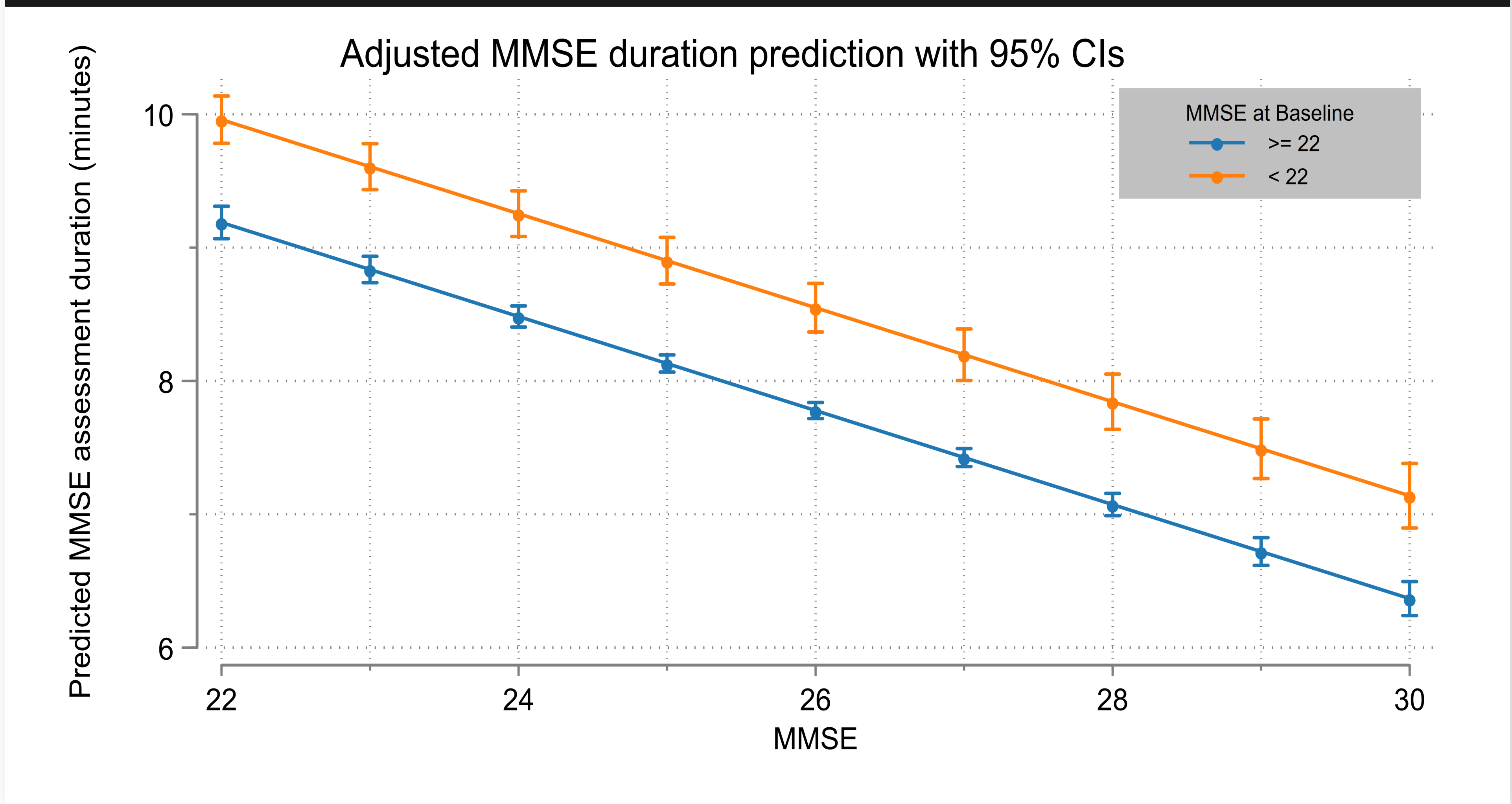
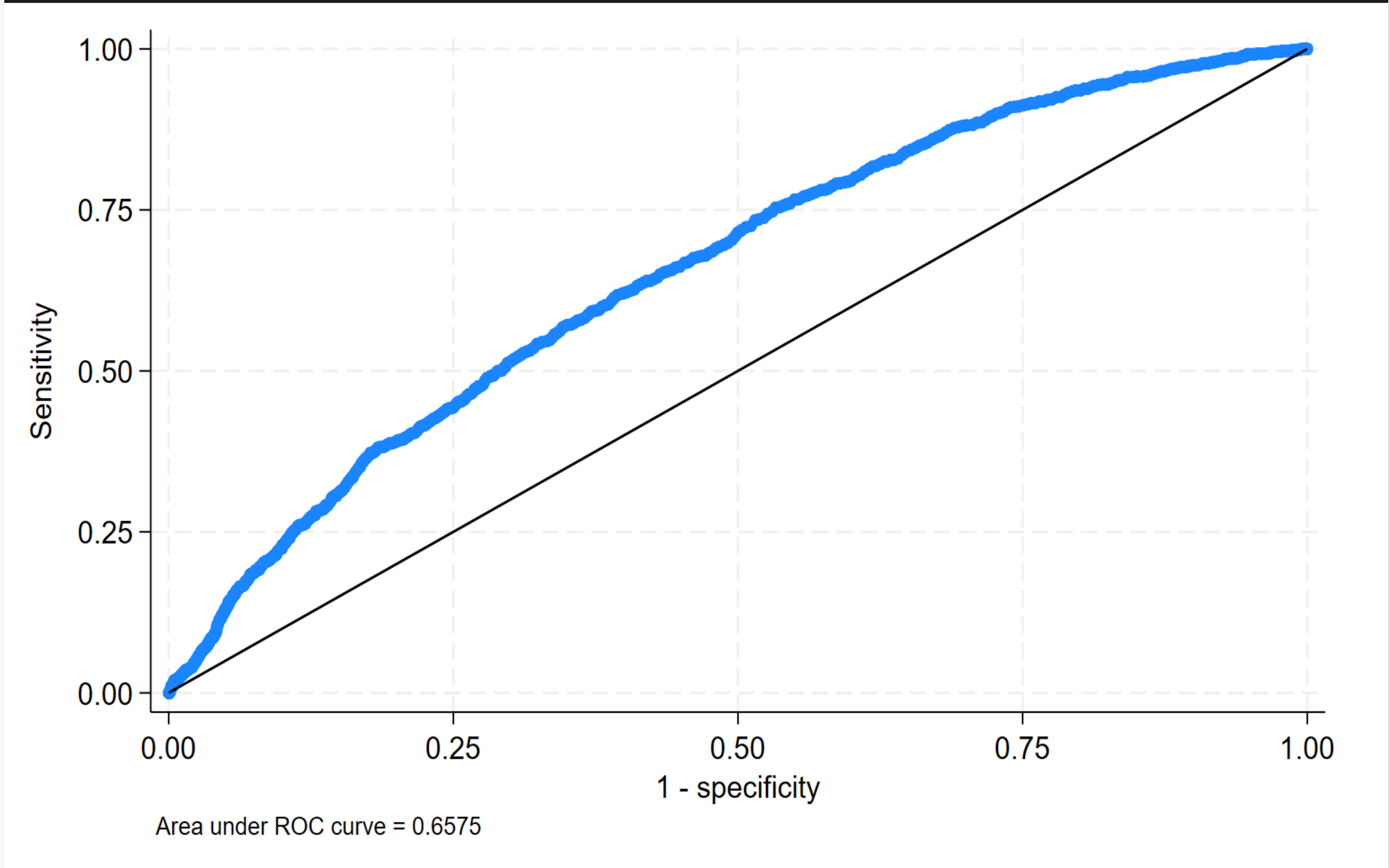


FIGURE 2: ROC ANALYSIS



CONCLUSION

- Our post-hoc analysis of a large dataset found Screening MMSE interview durations significantly longer by roughly 45 seconds in subjects who no longer met MMSE inclusion cutoffs at Baseline.
- The increase is consistent with our hypothesis and likely reflects that these subjects had their Screening MMSE scores inflated to meet inclusion criteria.
- Additionally, we have established a MMSE assessment duration cutoff of 8 minutes to identify a pool of subjects at risk of having their MMSE scores inflated, albeit with only moderate levels of sensitivity and specificity.
- Given the results we suggest MMSE assessment duration be included in analytical programs as a marker of possible MMSE score inflation alongside other markers, such as between scale discordances or performance on diagnostic tests.