

The MARQ-AD: A New Measure of Interview Quality in Alzheimer's Disease Trials

Weber, C¹ De Santi, S^{1,2} Kirby, L^{1,3} Williams, JBW^{1,4}

MedAvante, Inc.¹, New York University Langone Medical Center², Critical Path Institute³, College of Physicians and Surgeons, Columbia University⁴

ABSTRACT

Introduction: Clinician-administered cognitive assessments in clinical trials of Alzheimer's disease (AD) have multiple sources of variability which can collectively diminish or obscure a treatment effect. Both structured (e.g., ADAS-cog) and semi-structured (e.g., CDR) assessments have significant variability in administration and interpretation of subject responses between sites and between raters. This variability in key outcome measures can undermine the detection of a treatment effect in a randomized clinical trial. Compensating for low signal detection requires increased numbers of subjects, increased time and costs, and may constitute a significant factor in the recent failures seen in AD drug trials.

The challenges of standardized administration and scoring of AD assessments such as the ADAS-cog have been documented.¹ Even experienced raters working on multiple dementia protocols have a substantial likelihood of administration/scoring inconsistency, which decreases signal detection.¹ Furthermore, long trials incur increased rater turnover that can exacerbate these standardization issues. This poster presents a new instrument designed to evaluate variability in the administration of AD outcome measures.

Methods: The MedAvante Analysis of Rating Quality - Alzheimer's Disease (MARQ-AD) was developed to quantify critical domains of rater performance and address reasons for administration and scoring variability encountered in AD assessments. The MARQ-AD was designed to assess raters' clinical interview skills, as a clinical trial qualification and as an ongoing performance assessment tool. AD trainers with at least 10 years of AD assessment experience perform the evaluations with the MARQ-AD. The trainers undergo extensive administration and scoring training on the MARQ-AD and study-specific scales being monitored. Trainers are highly calibrated for administration and scoring on each scale.

Results: Trainer calibration and use of the MARQ-AD provides consistent evaluation and feedback on all reviewed assessments, which, in the context of a research clinical trial, makes detection of a true efficacy signal more likely.

Conclusions: The evaluation of rating quality has been effective in other disease states that utilize subjective assessment instruments.² The benefit to AD and other dementia clinical trials of the MARQ-AD scale is improved interview standardization and quality, resulting in decreased rater drift over the course of a trial and higher rater concordance.

Disclosures: Weber C, DeSanti S, and Williams JBW are employed by MedAvante. Kirby L is a consultant for MedAvante.

INTRODUCTION

Clinician-administered cognitive assessments in clinical trials of Alzheimer's disease (AD) have multiple sources of variability that can collectively diminish or obscure a treatment effect.

Possible sources of variability that can compromise standardization include:

- Inconsistent administration rules and scoring materials across clinical trials
- Poor inter-rater reliability (ICC) of scale administration
- Variability in item order in some scales across clinical trials
- Variability in item selection across clinical trials (e.g., WORLD backwards vs. serial 7s)
- Increased rater turnover in long AD trials (≥18 months)

Ongoing monitoring and feedback have been shown to improve rating quality in psychiatric clinical trials² that share similar sources of variability. Rating quality has been shown to influence signal detection.³ This quality process may mirror the success observed using similar methodology in the psychiatric field.

The purpose of incorporating quality assurance measures in AD trials is to improve:

- Adherence to scale administration guidelines
- Consistency of raters' scoring and clinical interpretation of subject responses
- Quality assurance of interview technique
- Ratings consistency over the course of a trial
- Rating concordance across all study sites

The MARQ-AD is a new instrument designed to evaluate variability in the administration of AD measures. This poster also presents a method for using the MARQ-AD to help evaluate and standardize ratings; Continuous Quality Control (CQC) is presented.

METHODS

Development of the MARQ-AD

- MARQ-AD consists of 3 versions:

- Structured AD scales (e.g., MMSE, ADAS-cog)
- Semi-structured AD scales (e.g., CDR, ADCS-ADL)
- Unstructured AD scales (e.g., ADCS-CGIC)

- Each version is complete with detailed scoring guidelines, including descriptions of each domain and anchor points.

Domains of the MARQ-AD

- The MARQ-AD includes these domains that are important for assessment quality:

- Adherence
- Support and engagement
- Pacing
- Scoring accuracy
- Assessment environment
- Follow-up and qualification
- Neutrality
- Rapport and engagement

- Each domain is scored independently on a 4-point Likert scale

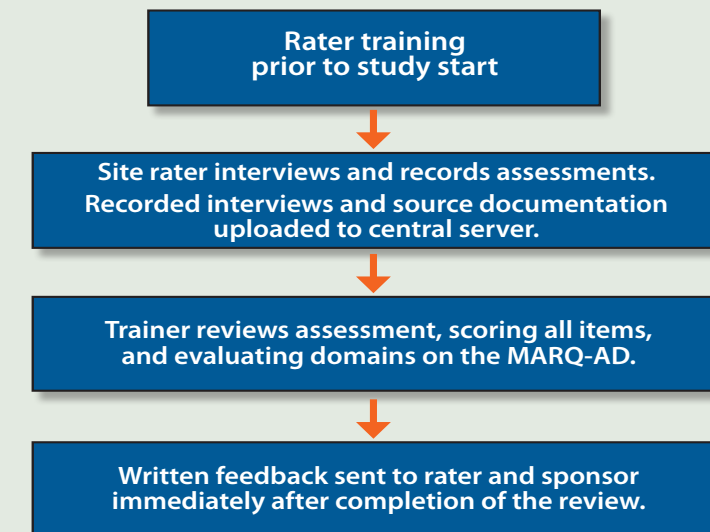
MARQ-AD Administration

- MARQ-AD is performed by experienced clinicians
- Trainers are calibrated on administration and scoring of each AD scale
- Trainers are calibrated on each of the domains and scoring procedures of the MARQ-AD

One example of using the MARQ-AD in a clinical trial

- Site raters participate in didactic and applied training for study specific scales at IM
- Training addresses the MARQ-AD domains which will be evaluated during the trial
- During the trial, site raters digitally record all study assessments to be reviewed
- Centrally trained and calibrated trainers review predetermined percentage of recorded interviews
- Feedback is provided to site and sponsor
- Remediation is administered when necessary

CONTINUOUS QUALITY CONTROL (CQC)



SUMMARY & CONCLUSIONS

The MARQ-AD is a new tool to assess the rater administration and scoring quality of AD clinical scales, and can be utilized at both initial rater training, and as an ongoing performance assessment tool throughout the trial.

There are three versions of the MARQ-AD, each tailored to work with structured (e.g., MMSE and ADAS-cog), semi-structured (e.g., CDR and ADCS-ADL) and unstructured scales (e.g., ADCS-CGIC), providing a structure for the trainer's feedback to the rater and sponsor.

The CQC process can be used to help standardize the quality and consistency of scale administration. CQC also can be used to improve the scoring and interpretation of clinical scales across raters and sites in a multi-center trial.

The benefit of the MARQ-AD to clinical trials in aging and Alzheimer's disease should be improved interview standardization and quality, resulting in improved inter-rater reliability and decreased rater drift over the course of a trial. Using the MARQ-AD in the context of CQC may make detection of a true efficacy signal more likely.

References

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MARQ-AD = MedAvante Assessment of Rating Quality — Alzheimer's Disease

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