VIRGIL INVESTIGATIVE STUDY PLATFORM MINIMIZES SCORING DISCREPANCIES TO IMPROVE SIGNAL DETECTION

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BACKGROUND

- Clinical trials of Alzheimer's disease (AD) are subject to a very high failure rate, in part due to imprecise endpoint measurements that add noise, reducing signal detection.[1,2]
- Traditional paper-based clinical outcome assessments (COA) are prone to high error rates and require an additional step of manual data entry into an electronic data capture (EDC) system, as well as source data verification monitoring. As such, attempts to implement central oversight typically involve scanning a large volume of paper source, and uploading audio or video files, further adding to the administrative burden at trial sites.
- The use of a tablet device-based electronic COA system for digital data collection has obvious advantages: eliminating calculation errors, flagging missing data, eliminating source data verification and reducing site burden associated with central oversight.
- The Virgil® Investigative Study Platform collects electronic source data and provides real-time clinical guidance to standardize measurements and improve data quality.
- The purpose of this study was to compare error rates on traditional paper-and-pencil administration of clinical rating scales commonly used in AD trials with administration of the same scales using the Virgil tablet device.

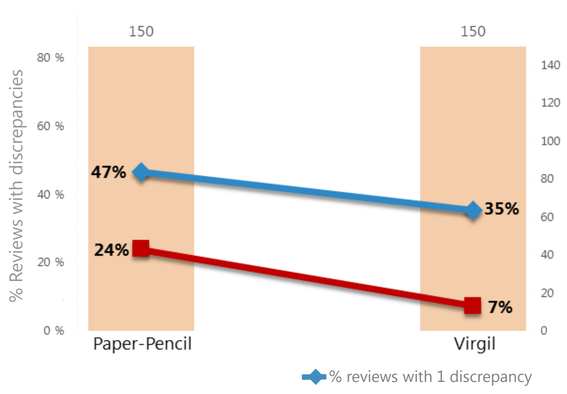
METHODS

- Paper-based assessments from a recent clinical trial of mild cognitive impairment (MCI) due to AD were identified and compared with Virgil tablet administrations of the same scales in two separate MCI trials.
- All studies are phase II/III multinational trials. The following scales were examined: CDR, ADAS-Cog, ADCS-ADL-MCI and MMSE.
- The first 150 administrations of each scale centrally reviewed for the pencil-and-paper trial were compared to the first 150 (or all available at the time of analysis if less than 150) administrations done with the Virgil tablet.
- Score discrepancies in both modes of administration were identified via review of audio recordings and worksheets by the same cohort of expert calibrated reviewers.
- For each scale, the percentage of reviews with one discrepancy, as well as two or more discrepancies, were compared between paper-based and Virgil administrations. Item-level discrepancies were also examined.

RESULTS

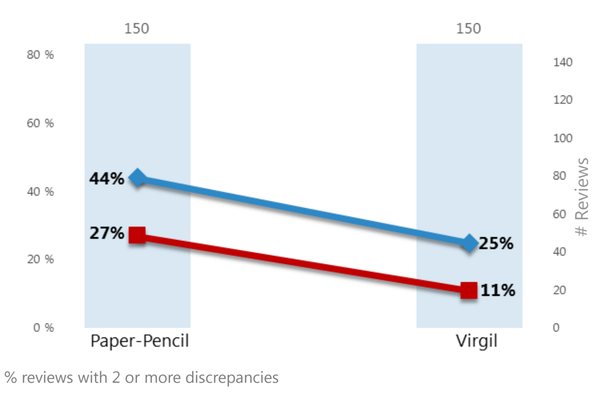
- **Figures 1a-d** show the percentages of reviews with discrepancies for paper-based and Virgil administrations in each scale.
- As the figures indicate, percentages of reviews with at least one discrepancy, as well as those with two or more discrepancies, were substantially lower in Virgil administrations compared to paper-based for all scales.
- Analysis of variance (ANOVA) comparing the number of errors per administration by scale revealed significantly lower error rates on Virgil versus paper-based administration on all scales.

FIG. 1a: CDR



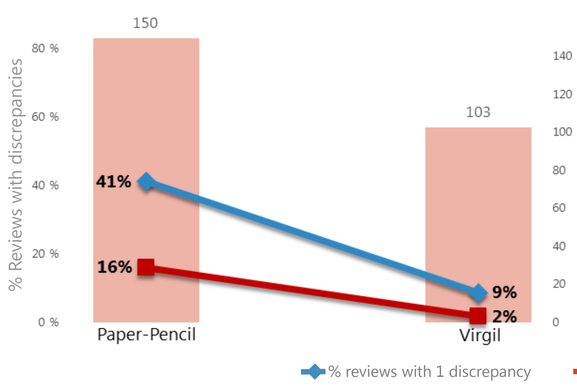
F (1,298) = 15.0 **p<.001**

FIG. 1b: ADAS-Cog



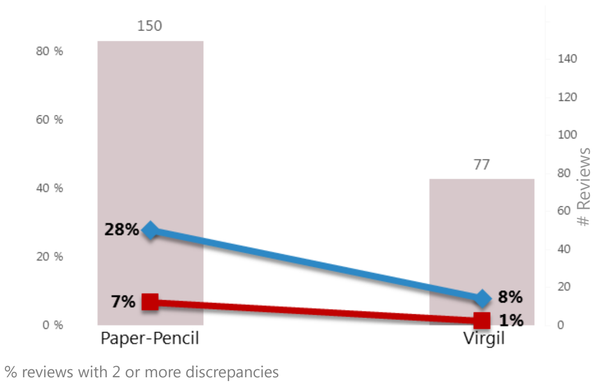
F (1,298) = 8.6 **p=.004**

FIG. 1c: ADCS-ADL-MCI



F (1,251) = 26.0 **p<.001**

FIG. 1d: MMSE



F (1,225) = 11.1 **p<.001**

FIG. 2a: CDR

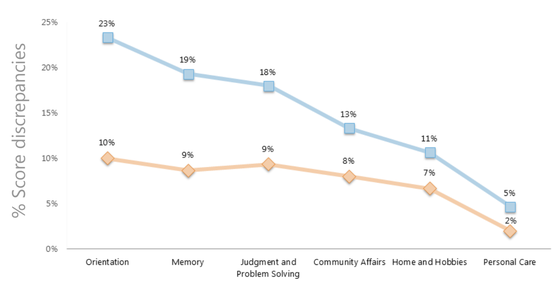


FIG. 2b: ADAS-Cog

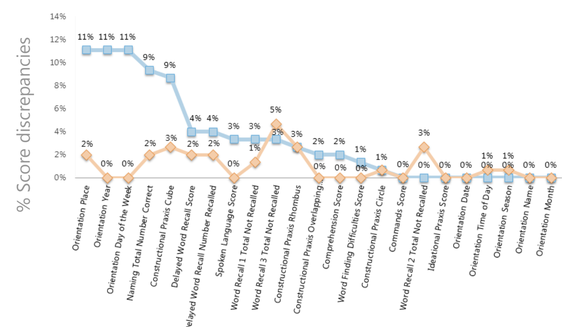


FIG. 2c: ADCS-ADL-MCI

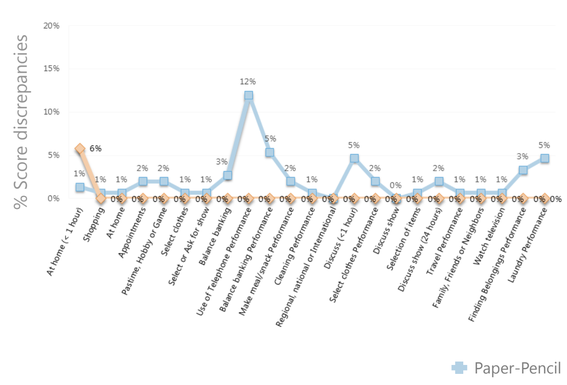
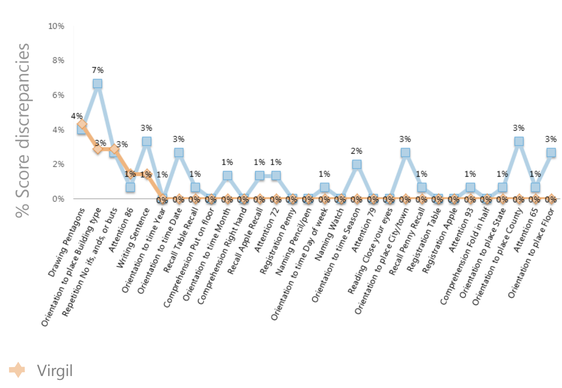


FIG. 2d: MMSE



- Item-level score discrepancies are shown in **Figures 2a-d**.
- Here again, Virgil administrations resulted in consistently lower error rates than paper-based assessments for a vast majority of items in each scale.
- Virgil was also effective at reducing scoring discrepancies in items that are particularly difficult to score, such as the Memory domain in CDR[3]:
  - **19% scoring discrepancies on this item in paper-based assessments, compared to Virgil at 9%.**

DISCUSSION

- The Virgil eCOA platform substantially reduced error rates compared to paper-based administration across all four scales examined in these MCI trials.

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CONCLUSION

Traditional pencil-and-paper based administrations of COAs in AD clinical trials are characterized by high error rates, which contribute to error variance and have the potential to degrade signal detection. This can be attributed to failure of raters to retain information regarding administration and scoring rules and to calculation errors. This mode of administration also requires a separate step of data entry from paper source to EDC systems, and monitoring of that process. Finally, attempts to centrally oversee the quality of assessments done this way involve cumbersome procedures of scanning or faxing and uploading of source data, with significant associated site burden.

eCOA administration involving the use of a tablet to collect these assessments automatically eliminates the EDC transfer step and associated monitoring.

It also has the potential to significantly reduce site-based scoring errors due to the ability to include pop-up clinical guidance for administration and scoring, auto-calculations and consistency checks.

Finally, it eases the process for central oversight as assessments can be seamlessly/simultaneously audio-or video-recorded, with no extra steps for the site such as data transfers or uploads.

This study was the first examination of the actual outcome in terms of error reduction using an eCOA system such as the Virgil tablet. Directly comparable data sets from multinational clinical trials in MCI due to AD were available, and error rates were examined from central review done by the same cohort of calibrated raters. Error reduction was substantial, with reductions from approximately 50% to over 80% by scale, and highly statistically significant.

This is a compelling demonstration of the clinical utility of the Virgil eCOA platform, In addition to the obvious practical advantages delineated above.

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