Vineland Adaptive Behavior Scales in Multicenter International Clinical Trials: Challenges and Solutions for a Successful Implementation

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BACKGROUND

- The assessment of adaptive functioning is critical in clinical trials of individuals with neurodevelopmental disorders, including autism spectrum disorder (ASD).
- The Vineland Adaptive Behavior Scales, Second Edition (Vineland™-II)[1] are the gold-standard measure for assessing adaptive functioning.
- The following components are required to successfully implement the Vineland™-II in multicenter, international clinical trials:
  - Rigorous rater selection.
  - Standardized rater training.
  - Linguistically validated translations with expert clinical review.
  - Specialized data management.
- The specialized data management component is particularly complex, requiring sophisticated processes and expert clinical review to ensure data accuracy.

AIM

- To summarize the challenges and solutions related to data management for successful implementation of the Vineland™-II in multicenter, international clinical trials.

METHODS

- Cogstate provided scientific, data management, and operational expertise and services in the implementation of a rater training and data management program of the Vineland™-II in three industry-sponsored trials:
  - USA trial in Autism Spectrum Disorder (ASD) (27 sites).
  - USA trial in Down Syndrome (10 sites).
  - International trial in Down Syndrome (10 sites; US [3], France [4], Spain [3]).
- Cogstate compiled data from the sites into a single Vineland™-II dataset.
- Data management errors were analyzed, and descriptive statistics of errors are reported.
- A total of 596 Vineland™-II administrations, across 140 raters and 43 sites, were available for analysis.
- Table 1 summarizes the types of data management challenges that were addressed; error types were defined as: data entry, file transfer, or clinical consideration.

Table 1: Data Management Challenges Analyzed.

Error Type	Data Management Challenge	Description
DE	Baseline date	Incorrect date of visit entered in scoring program
DE	Date of birth	Incorrect date of birth entered in scoring program
DE	Scoring software data entry	Incorrect data entered (e.g., visit type, subject identity)
FT	Duplicate files	Two data files uploaded per visit
FT	File transfer data	File title incorrect; mislabeled transfer file
FT	Missing file	Data file not uploaded following visit
CC	Missing standard scores	Standardized scores missing from data file
CC	Personal health information	Failure to exclude information that could identify the patient
CC	Clinical consistency	Unexpected relationship of scores between visits
CC	Respondent change	Change in respondent between visits

CC, clinical consideration; DE, data entry; FT, file transfer.

RESULTS

- The errors that occurred were varied and multifaceted (Figure 1 and Figure 2).
- The predominant error type was inaccurate file transfer procedures by the sites to Cogstate (57% of the total errors; Figure 1).
- Data entry errors were common (26% of the total errors; Figure 1); in particular, incorrect entry of date of birth or visit date, which can have an impact on normative scores.

Figure 1: Distribution of Error Types from Vineland™-II Administrations.

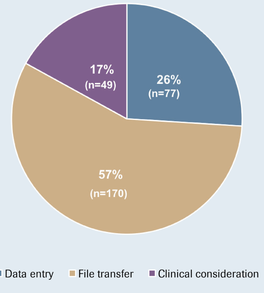
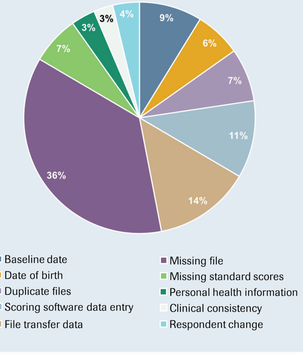


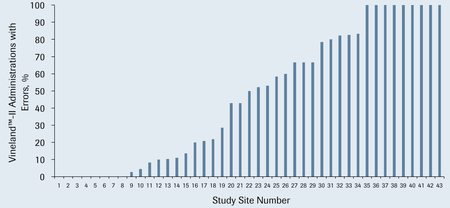
Figure 2: Distribution of Data Management Challenges.



RESULTS CONTINUED

- Clinical consideration errors accounted for 49 of the total errors (17%; Figure 1).
- Clinical consideration errors had the largest impact on data quality. Examples included:
  - Missing standard scores. This could be because of improper administration (data loss) of the Vineland™-II, or because of data entry errors (recoverable data).
  - Identical standardized scores between visits (a score change query). This could be because of mislabeling of the source documents, or because the patient had remained stable.
- Both examples required an expert review of the Vineland™-II source document.
- Remediation of errors, particularly clinical consideration errors, required considerable follow-up and communication with sites and clinical research associates, including:
  - Email follow-up.
  - Phone conferences with data managers.
  - Phone conferences with the expert clinician.
  - Individual rater re-training sessions.
- Some sites needed considerable prompting to transfer data, and substantial variation was evident between sites in the ability to accurately utilize the scoring program and the transfer of data files.
- There were 9 sites (21%) from which every Vineland™-II administration gave rise to a query of some type (Figure 3).
- For some sites in Spain and France it was necessary for clinical research associates to facilitate discussions in Spanish and French.

Figure 3: Percentage of Vineland™-II Submissions with Data Management Errors.



CONCLUSIONS

- Utilization of the Vineland™-II poses unique challenges in multicenter, international clinical trials; data management, in particular, for the Vineland™-II is complex.
- Management of the Vineland™-II-specific queries/errors is time intensive, and requires a high level of expertise.
- Over half of all errors related to file transfers, and over 25% of all errors related to data entry of key variables into the scoring software, highlighting the necessity to train and support study sites and clinical research associates on the Vineland™-II scoring software to ensure accurate calculations of scores and timely data transfers.
- Clinical consideration errors, which accounted for 17% of queries, had the largest impact on data quality and systematic efforts must be made to review data outliers, changes in raters/respondents across visits, unusual patterns of change scores and identical scores across visits.
- Ongoing clinical reviews should be conducted during the study (e.g., identification of patterns of scores for each patient population, review of outliers in the data, and consistency of scores compared with other clinical assessments).
- Given the number of errors (half of all administrations), centralized scoring could be utilized in future trials, instead of relying on site-level scoring, entry, and transfer.

DISCLOSURES

L. R. Kingery, P. Ventola and V. Lo are employees of Cogstate, USA. M. Nallewar was an employee of Cogstate, USA at the time of the study. M. del Valle Rubido, X. Liogier D'ardhuy, Celia Goeldner, F. Bolognani and O. Khwaja are employees of F. Hoffmann-La Roche Ltd, Switzerland.

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REFERENCES

1. Sparrow SS, Cicchetti DV, & Balla DA. Vineland Adaptive Behavior Scales: Survey Forms Manual, 2nd Edition. Pearson Clinical Assessments; Bloomington, MN: 2005.

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