Incorporating Patient Perspectives into a Composite Score for Measuring Disease Progression in Spinocerebellar Ataxia (SCA)

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CONCLUSIONS

1. The items' weights from the partial least squares (PLS)-derived SCACOMS differed from the weights assigned by patients, with the Clinician Global Impression of Change (CGI-C) receiving greater importance in the PLS-derived SCACOMS.
2. The combined scale, with an updated set of SCACOMS item weights, effectively balances scale responsiveness with patient-relevance.
3. Incorporating the patient's perspective into the adoption and derivation of SCACOMS could increase the patient-centricity of an optimized measure for detecting disease progression, potentially enhancing its acceptance and adoption.

References:

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Data Acknowledgment:
Researchers can submit requests for the CRC-SCA data at https://www.ataxia.org/crc-sca/academic-research/ and EUROSCA data at https://www.eurosca.org.

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INTRODUCTION

- Spinocerebellar ataxia (SCA) is a group of rare genetic diseases that cause progressive loss of motor function and coordination.[1]
- The SCA composite score (SCACOMS) is a statistically derived composite measure of disease progression in participants with SCA, with more progressive items given higher weights.[2]
- While SCA patients value a therapy that can slow disease progression, the details regarding measuring this concept is of interest to explore.
- Though SCACOMS has been optimized to detect disease progression with increased sensitivity as compared to the parent measures, patient input is critical to contextualize the items selected and respective weights assigned in the score.

OBJECTIVE To incorporate patients' perspective into SCACOMS

METHODS

- Item weights derived by statistical analysis were compared to relative importance assigned to the items by patients with SCA.

PLS-derived SCACOMS

- Two natural history datasets were used to develop SCACOMS: the Clinical Research Consortium for Spinocerebellar Ataxias (CRC-SCA; NCT01060371) and the European Integrated Project on Spinocerebellar Ataxias (EUROSCA; NCT02440763).
- Five items from validated measures used in clinical practice were included in SCACOMS: 4 items from the Modified Functional Scale for the Assessment and Rating of Ataxia (f-SARA [gait, stance, sitting, speech]) and CGI-C.
- Sensitivity of individual items to progression in the natural history datasets was assessed using PLS regression, with responsive items objectively selected and summed to create the PLS-derived SCACOMS.
- Item weights reflected sensitivity to decline.

Qualitative interview

- Semi-structured interviews were conducted with United States-based participants with SCA (n=24) between April and May 2024.
- Participants were asked to review and discuss the items contributing to the PLS-derived SCACOMS in the context of importance of these items as a measure of disease progression.
- Patients ranked items by importance and assigned a relative weighting.[3]

Data Analysis

- Adjustments to SCACOMS item weights to incorporate the patient perspective were explored using several approaches:
  1. 50/50 combination of PLS and patient weights
  2. reducing maximum weight of CGI-C to 20% before rescaling the remaining item weights.
- Scales were assessed for ability to detect disease progression using the 1-year mean-to-standard deviation ratios (MSDRs) derived from the Global natural history data (combined CRC-SCA and EUROSCA).
- Larger MSDRs indicated greater sensitivity to measure disease progression.

RESULTS

- CGI-C at 53.1% was the highest contributor to the PLS-derived SCACOMS, whereas participants with SCA assigned the highest importance to the f-SARA Gait item (33.0%; **Figure 1)**.
- The stance and sitting items were assigned similar weights by SCA participants than the weights observed in the PLS-derived scale.
- The PLS-derived scale had the highest 1-year MSDR **(Figure 2**), indicating the greatest sensitivity to clinical decline**.**
- The scale combining PLS-derived and patient weights still maintained a relatively high MSDR of 0.91.
- Reducing the percentage contribution of CGI-C to 20% in the combined weights score (to better align with the patient assigned weights of the CGI) reduced the MSDR further to 0.79, however this is still a marked improvement over responsiveness of original f-SARA of 0.50.

Figure 1. Relative weightings of scale items in (A) PLS-derived SCACOMS and (B) assigned by patients with SCA

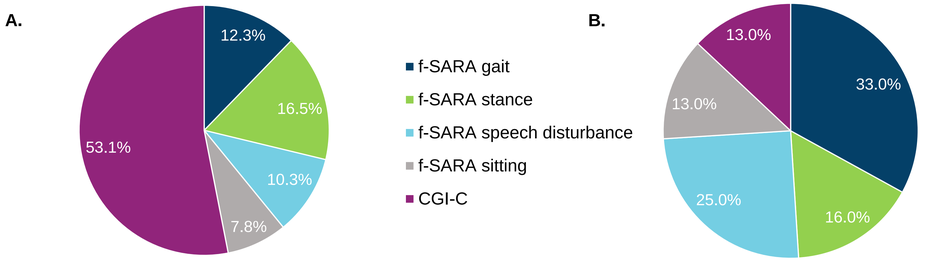
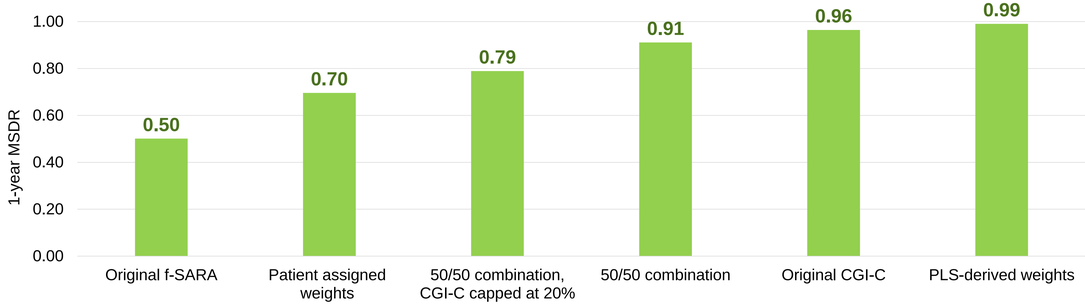


Figure 2. 1-year MSDRs in pooled natural history data



Abbreviations: CGI-C, Clinician Global Impression of Change; f-SARA, Modified Functional Scale for the Assessment and Rating of Ataxia; MSDR, mean-to-standard deviation ratio; PLS, partial least square; SCA, Spinocerebellar ataxia; SCACOMS, SCA composite score

DISCUSSION

- This study took a novel approach to enhance the validity of a composite measure SCACOMS by incorporating the patient's perspective into a statistically derived composite scale.
- The combined scale, though had lower sensitivity than the PLS-derived scale as measured by MSDR, was more sensitive to detect progression than the original f-SARA.
- The combined scale provided a balanced approach between incorporating the lived experiences of SCA participants while still being more sensitive to measuring disease progression.
- Depending on the trial scenario, the decision to lower a study's power to measure disease progression by incorporating patient preferences should be balanced with trial feasibility considerations.