Minimal detectable change in the North Star Ambulatory Assessment (NSAA) in Duchenne muscular dystrophy (DMD)

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Background: The NSAA is a validated functional scale for ambulant boys with DMD used in natural history studies and clinical trials. An important consideration for outcome measures is the magnitude of change that is clinically meaningful. In the present study we used longitudinal analysis of natural history data to identify minimal changes in NSAA scores that can be attributed to DMD disease progression, i.e., to persistent and irreversible changes, rather than measurement variability.

Methods: We analyzed boys with DMD aged 5-15 years at first assessment in the UK North Star Network database. Minimal detectable changes were estimated based on longitudinal mixed effects models for each boy's trajectory of function over time. Trajectories were modeled to allow for periods of both improving and declining function with age. Based on the variation around these patient-specific trajectories, a threshold for NSAA score change was calculated such that declines exceeding that threshold provide >80% confidence that the patient experienced a true decline in function. Distribution-based estimates of clinically important differences were also calculated as 0.5 standard deviations (SD) overall and by age group.

Results: NSAA assessments from 1826 clinic visits among 302 patients were analyzed. Median follow-up was over 1 year and fitted models explained >95% of the variability in NSAA scores. Thresholds corresponding to >80% confidence in disease progression were 3.1 for the NSAA total score and 7.5 for the linearized scores, and were smaller than estimates based on 0.5 SD.

Conclusion: Thresholds for detectable change in NSAA scores can be useful for informing endpoint definitions and interpreting drug effects in clinical trials, and warrant confirmation in other natural history studies and complementary analyses with additional clinical measures.

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