

A Concisely Recorded Ambulatory Assessment for Enhancing Real-World Outcomes Research in Duchenne Muscular Dystrophy: Development and Validation

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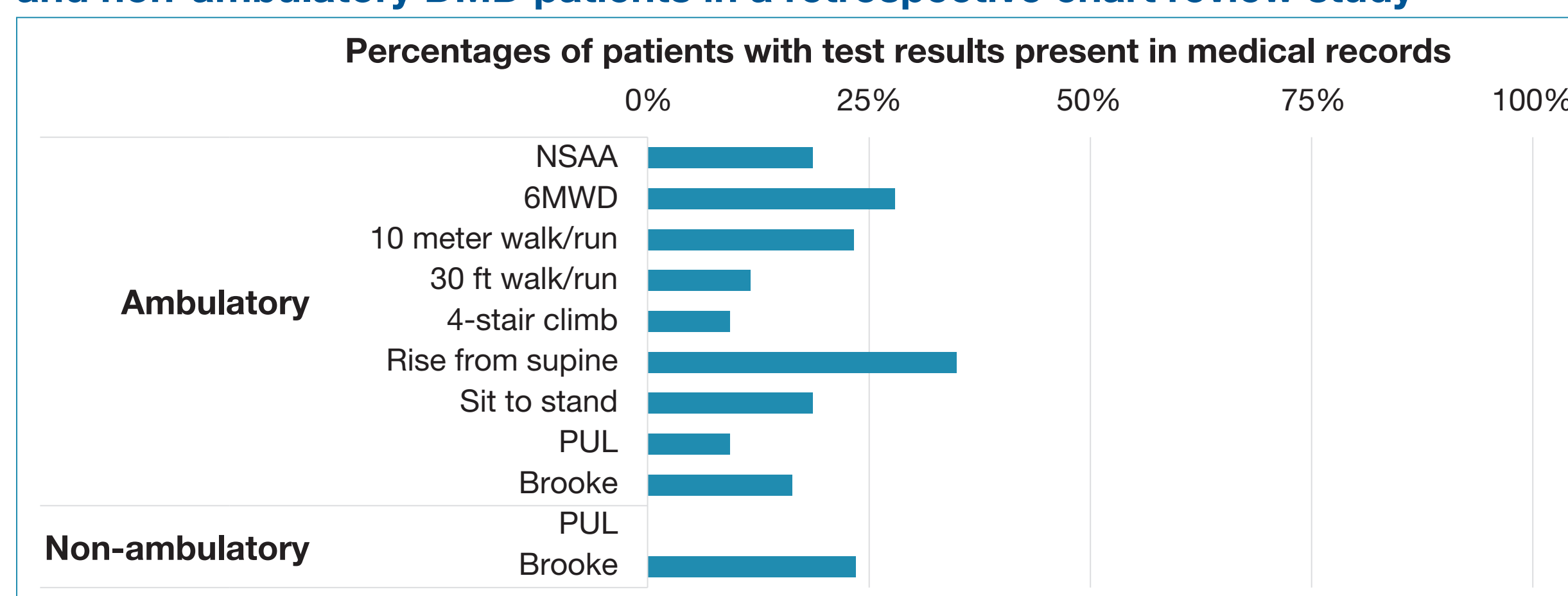
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Introduction

- The North Star Ambulatory Assessment (NSAA) is foundational for ambulatory care in Duchenne muscular dystrophy (DMD)^{1,2}, and is regularly conducted per care guidelines and recorded in medical records throughout the United Kingdom, Europe and elsewhere
- At too many centers and practices, however, recording of standardized motor function assessments in DMD medical records is limited or inconsistent
 - A recent retrospective review of medical records found that no functional measure was consistently recorded for a majority of patients with DMD in the United States³ (Figure 1)
- This hinders retrospective learning from real-world data in this rare, progressive and life-limiting disease
- While optimal clinical management relies on the totality of motor function tasks represented in the NSAA, we aimed to identify a concise subset of motor function tasks that, if consistently recorded in medical records, would adequately proxy for the NSAA total summary score

Figure 1. Availability of functional measures in medical records of ambulatory and non-ambulatory DMD patients in a retrospective chart review study



6MWD = Six minute walk distance; PUL = Performance of upper limb; Data from N=60 DMD patients at 55 care centers in the US³

Objective

- To identify a concise subset of ambulatory assessments for DMD – conducted as part of a complete assessment per care guidelines – that can
 - Be easily recorded in medical records, and
 - Accurately quantify real-world disease progression

Methods

Data Source

- The data used in this study was natural history data from a registry of 20+ clinical centers in the North Star Clinical Network in the United Kingdom
- All patient assessments with complete recording of all 17 NSAA items were used in the analysis (n=320)

Statistical analysis

- LASSO⁴, a machine learning modeling approach, was used to identify subsets of NSAA items that best predicted the NSAA total score
- Models assessed included all NSAA items as predictors, with best scores used for bilateral item pairs

- Models were developed in a training sample of 220 patients, and predictions were evaluated in a held-out sample of 100 patients
- Prediction accuracy was evaluated using the standard error of measurement (SEM) of the NSAA total score as a benchmark (previously estimated as 2.3 units)⁵

Results

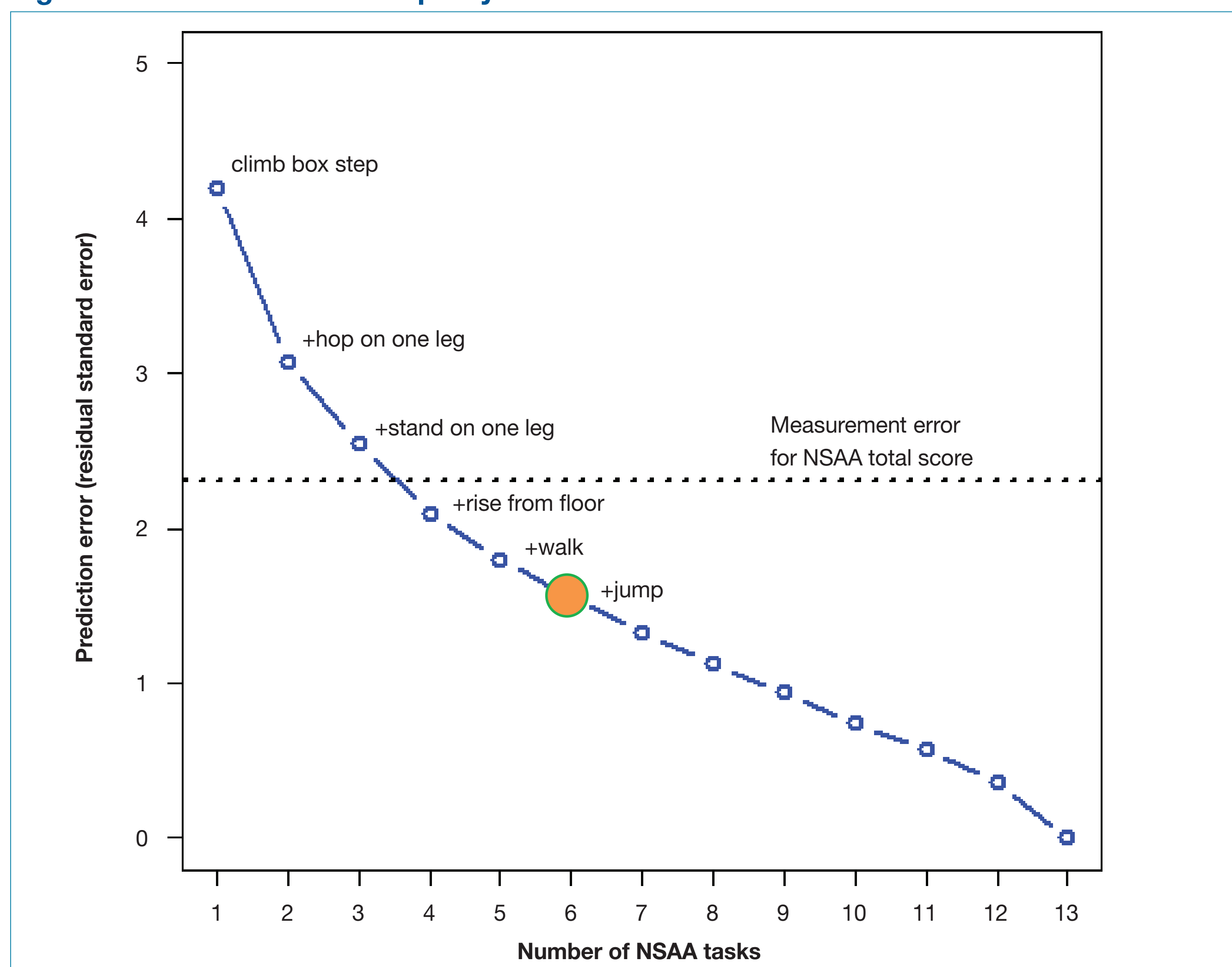
Development of a proxy for NSAA total score

- Models were based on 1,828 complete NSAA assessments among 320 patients
- A proxy score based on the best 6 tasks had a prediction error of 1.6 NSAA units in the training data (1258 assessments from 220 boys)
- The 6 most informative tasks were
 - Walk
 - Rise from floor
 - Stand on one leg
 - Hop on one leg
 - Jump
 - Climb box step
- Findings were similar when the average, best, worst or random choice of the left and right sides was used for bilateral tasks; results presented are for the best side
- The NSAA total score was approximated with prediction error less than the SEM using as few as 4 tasks (Figure 2)

Proxy for NSAA total score

$$\text{NSAA total} \approx 2.7 + 2.00 \times (\text{walk} + \text{rise from floor}) + 2.50 \times (\text{stand on one leg} + \text{hop on one leg}) + 1.75 \times \text{jump} + 4.0 \times \text{climb box step}$$

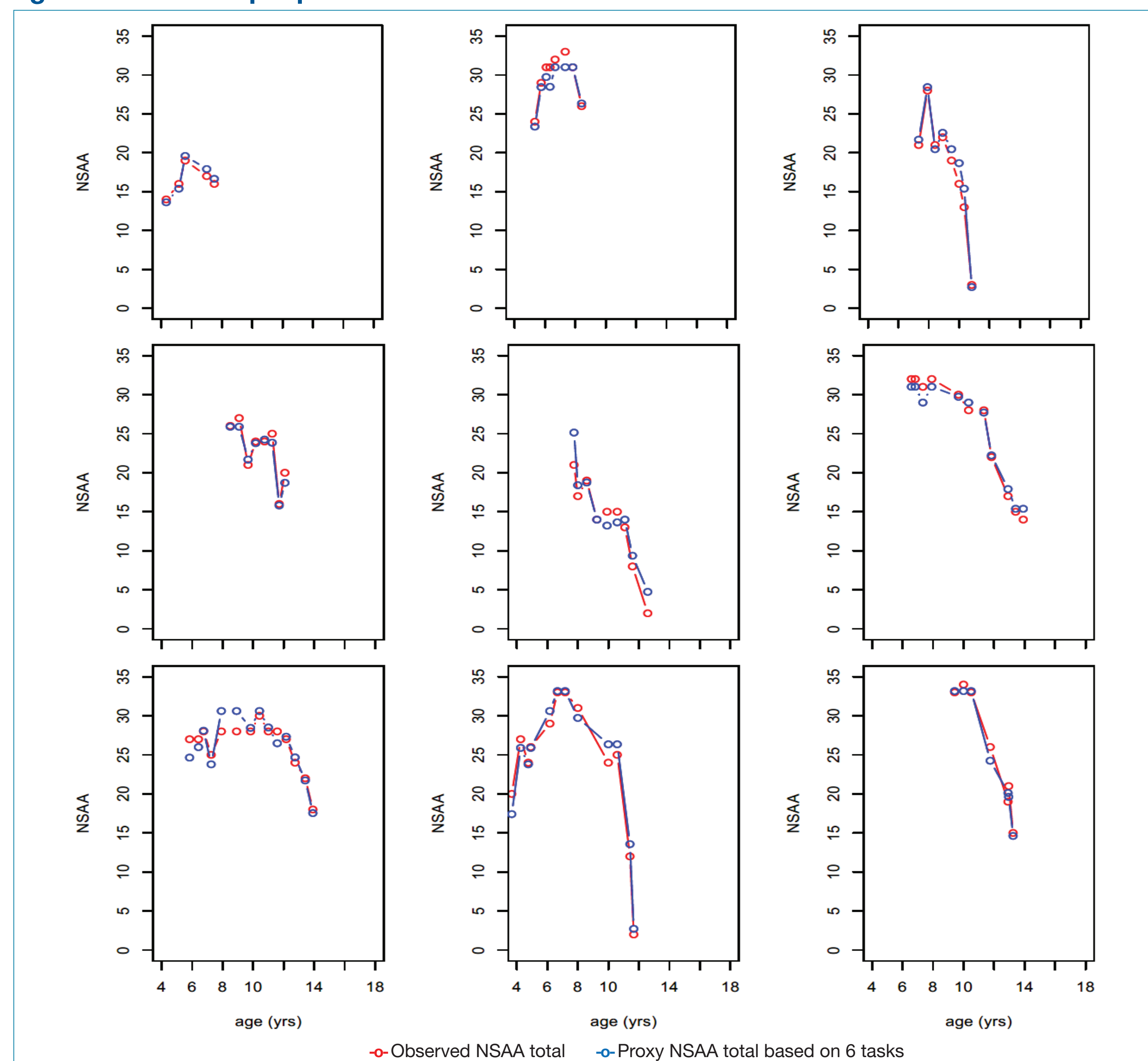
Figure 2. Prediction error for proxy score based on number of NSAA tasks



Validation of a proxy for NSAA total score

- In the held-out validation data (570 assessments from 100 boys), the 6-task proxy for NSAA total score:
 - Explained 95% of the variation in the NSAA total score
 - Had a correlation of 0.97 with the NSAA total score
 - Predicted NSAA total scores within ± 1.8 units, better than the measurement error of NSAA total score (i.e., 2.3 units)
 - Showed similar predictive performance by subgroups of age and NSAA
- Observed and proxied NSAA total score trajectories over time were consistent in the held-out validation set (illustrative trajectories in Figure 3)

Figure 3. Consistency of observed and proxied NSAA total score trajectories versus age for nine example patients



Limitations

- While the 6-task proxy for NSAA total score developed here performed well in the held-out validation sample, validation of its performance in external samples is also needed

Conclusions

- A full ambulatory assessment should be recorded in medical records whenever possible. Consistent with care guidelines, the full NSAA should be conducted by trained assessors to ensure that disease management is not divorced from measurement
- However, when entry of all NSAA items into the medical record is not possible, consistently recording or prioritizing entry of the six NSAA items (i.e., hop on one leg, jump, rise from floor, climb box step, walk, and stand on one leg) would significantly enhance real-world outcomes research in ambulatory patients with DMD

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