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# Rasch Evaluation of North Star Ambulatory Assessment and North Star Assessment for Limb-Girdle Type Muscular Dystrophies in Becker Muscular Dystrophy

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## Background & Objective

The North Star Ambulatory Assessment (NSAA) and North Star Assessment for Limb-Girdle type muscular dystrophies (NSAD) are motor performance scales specifically developed for Duchenne muscular dystrophy (DMD) and Limb Girdle muscular dystrophy (LGMD), respectively. Both have been used in natural history studies of Becker muscular dystrophy (BMD) a dystrophinopathy sharing clinical characteristics of DMD and LGMD. We examined the suitability of the NSAA and NSAD through psychometric performance across three clinical trials of sevasemten (EDG-5506), an investigational agent.

## Methods

NSAA and NSAD data from 181 assessment screening and baseline visits for participants were examined by Rasch Unidimensional Measurement Model software (RUMM2030). Participants were ambulant BMD patients between 12-65 years old and enrolled across three clinical trials of sevasemten (EDG-5506): ARCH (NCT05160415), CANYON/GRAND CANYON (NCT05291091), and DUNE. Psychometric evaluation was completed examining NSAA and NSAD performance in seven areas: targeting, response categories, fit, reliability, dependency, stability, and unidimensionality.

## Results

NSAA and NSAD demonstrated unidimensional construct of functional motor performance and high reliability with ICC of 0.98 and 0.99, respectively between screen and baseline visits.

Scale	Item fit	Person fit	Reliability	Item Fit		Dependency	Uni-dimensionality
	Mean (SD)	Mean (SD)		Ordered thresholds	Number of items with good fit*		
NSAD	-0.67 (1.77)	-0.28 (0.63)	0.96	28/29	26/29 <sup>a</sup> 4 significant $\chi^2$ <sup>b</sup>	12 pairs >0.3 (PSI 0.96 with one of each pair removed)	acceptable (t-test 0.049)
NSAA	-0.97 (1.94)	-0.37 (0.71)	0.93	14/17	12/17 <sup>a</sup> 3 significant $\chi^2$ <sup>b</sup>	3 pairs >0.3	acceptable (t-test 0.05)

\*Fit: Defined as fit residual inside the recommended range (-2.50 to +2.50)<sup>a</sup> and <sup>b</sup>significant  $\chi^2$  probability (p<0.01)

Adequate targeting, or matching between the distribution of person measurements (upper histogram) and the distribution of item locations (lower histogram) were found for both NSAA and NSAD (Figures 1A & B).

Figure 1A: Person-item location distribution map NSAD

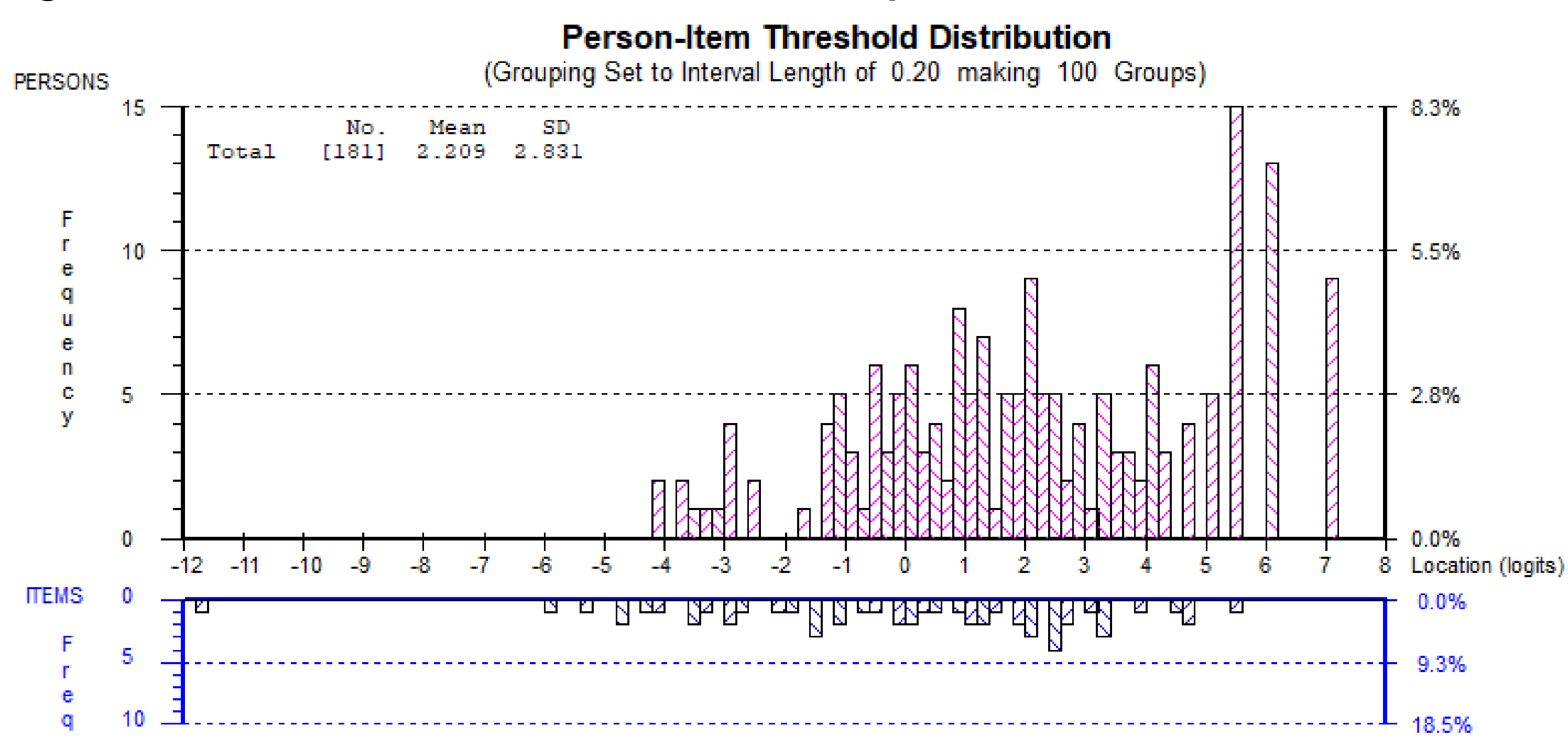
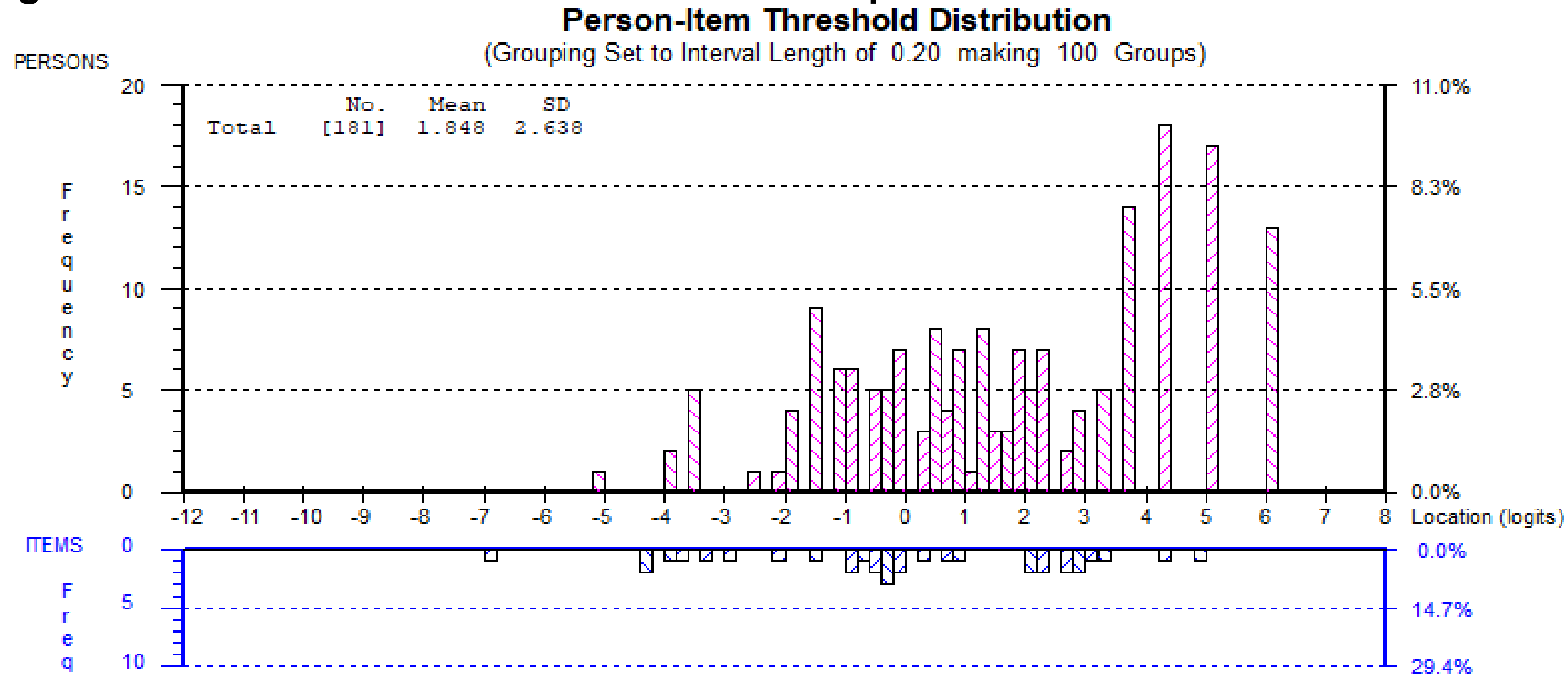


Figure 1B: Person-item location distribution map NSAA



Pink blocks are the individuals in the sample and blue are the items of the NSAD. They are placed on the same ruler, with the easiest items and less able individuals to the left, and the most difficult items and strongest individuals to the right. The ceiling/floor effects are minimal as the range of the person measurements (upper histogram 'blocks') closely matched the item locations (lower histogram 'blocks').

## Results (Continued)

Ordered scoring thresholds were present for 28/29 NSAD items, with the easiest item being "hand to opposite shoulder in supine" and the most difficult item in both NSAA and NSAD being "stand on heels" for this cohort- likely related to calf pseudohypertrophy and early loss of ankle dorsiflexion range of motion. The NSAD provides additional challenges to thigh and pelvic girdle strength compared to the NSAA with the addition of the squat and half kneel to standing items.

Figure 2A: NSAD Item scoring threshold map

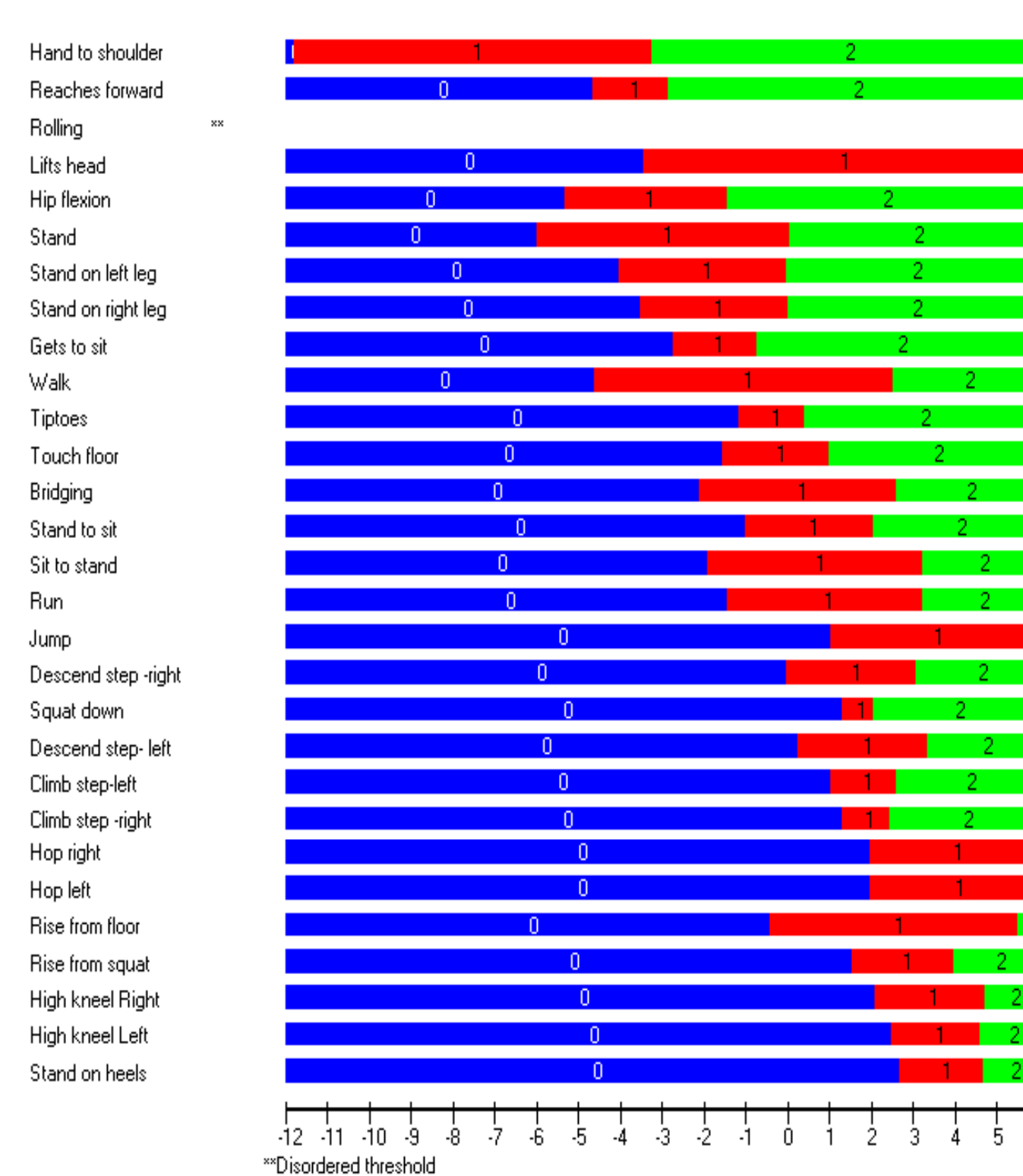
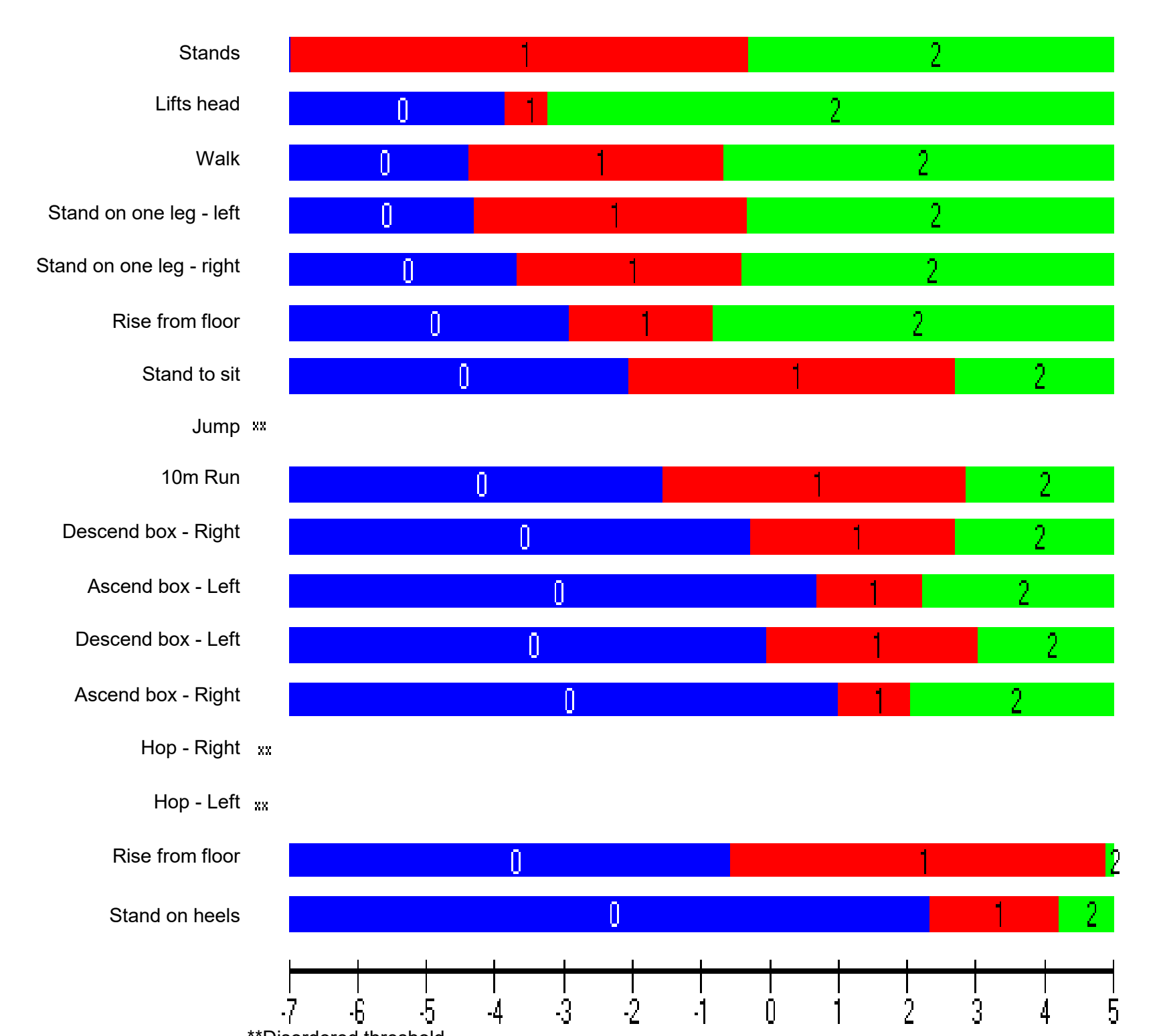


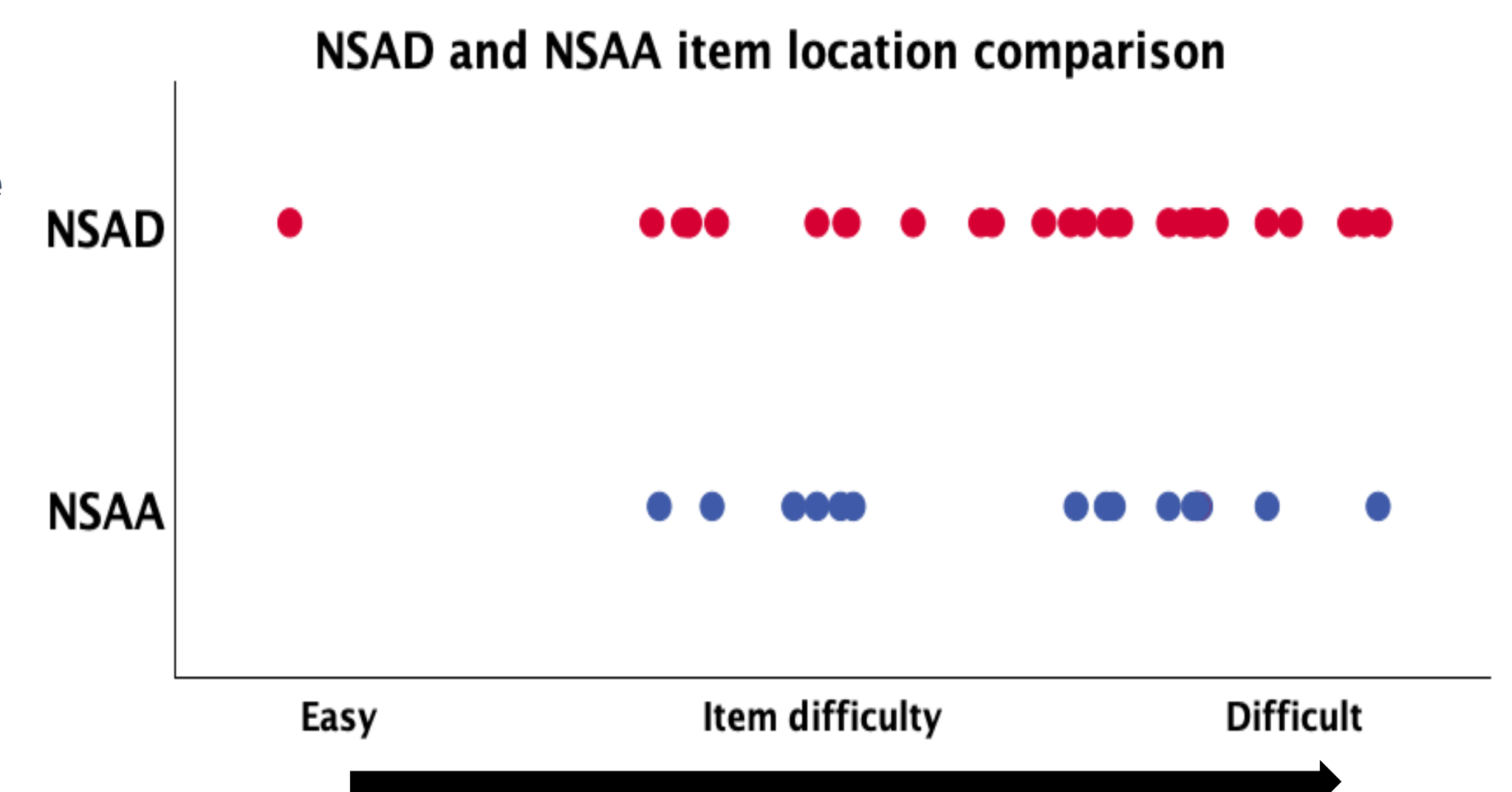
Figure 2B: NSAA Item scoring threshold map



Threshold map for items in ranked order of difficulty according to Rasch analysis. 0, response category labelled 0 (blue block); 1, response category labelled 1 (red block); 2, response category labelled 2 (green block). It would be expected that as an individual's ability increases, they would be more likely to obtain a higher score and that this would increase systematically in a logical progression so that as ability increases they are more likely to score a 0, then a 1, then a 2, or a 0, then a 1 for lifts head, jump and hop items on the NSAD.

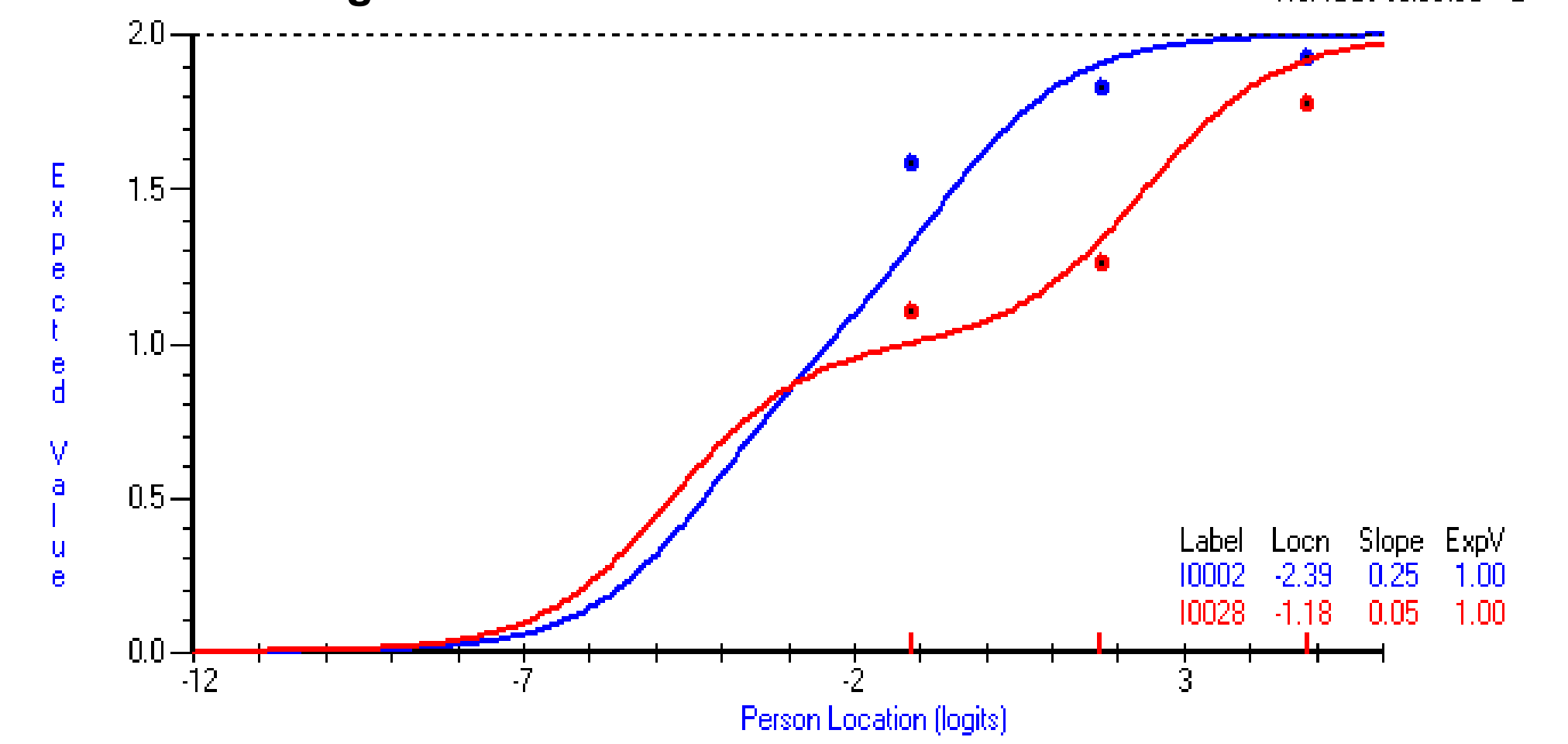
The NSAD items provide a more comprehensive range of easier and more difficult items suitable for ambulant and non-ambulant individuals with BMD compared to the NSAA.

Figure 3 (right) shows NSAA and NSAD item location by scale with each NSAD item in red and NSAA item in blue



Whilst the administration of the item is identical, the scoring is demonstrated to be more difficult in the NSAD (red) and more appropriate for BMD to capture overall change in gait pattern such as wide base support or a waddling gait.

Figure 4. Walk item for NSAD and NSAA. No ICCs selected = 2



## Conclusions

- NSAA and NSAD both demonstrated unidimensional construct of functional motor performance and high reliability with a PSI of 0.93 and 0.96, respectively.
- Although a ceiling effect still existed for the strongest yet still symptomatic patients, the motor performance of ambulant patients was targeted successfully by the items of the NSAA and NSAD.
- 28/29 NSAD items and 14/17 NSAA items demonstrated ordered response categories, meaning the scoring categories for each item are logical and appropriate for BMD. The items fit well together to make use of the total score appropriate.
- The NSAA and NSAD performed well in BMD, with the NSAD providing additional items to test both non-ambulant and those very able individuals with BMD. This analysis supports use of both NSAA and NSAD as measuring clinically meaningful outcomes in clinical trials of BMD.

## References

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### Disclaimer

Some authors are employees or consultants for Edgewise Therapeutics and may hold stock and/or stock options. Sevasemten (EDG-5506) is an investigational agent that is not approved for use by any regulatory authority in any territory. Authors MKJ, AM, LA, LL, and ME provide consultancy services for ATOM International for Edgewise Therapeutics.



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