

Validity of remote evaluation of the North Star Ambulatory Assessment in patients with Duchenne muscular dystrophy

LP Lowes,^{1,2} LN Alfano,^{1,2} MA Iammarino,¹ NF Reash,¹ K Giblin,³ L Hu,³ L Yu,³ S Wang,³ JR Mendell^{1,2}

¹Center for Gene Therapy, Nationwide Children’s Hospital, Columbus, OH, USA; ²The Ohio State University, Columbus, OH, USA; ³Sarepta Therapeutics, Inc., Cambridge, MA, USA.



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Objective

To assess the validity of remote evaluation of the NSAA, 10MWR and Time to Rise in patients with DMD.

What does this study mean for the DMD community?



Onsite functional assessments conducted during clinical trials can be burdensome to patients with DMD and their families. Conducting functional assessments remotely, rather than in-clinic or at study sites, can help alleviate some of this burden. However, it is important to establish the validity and reliability of remote versus in-person testing.



CONCLUSIONS

- These findings suggest that remote assessment of function in patients with DMD is not statistically or clinically different from in-person assessment.
- Given the significant burden that in-person assessment and monitoring places on patients with DMD and their caregivers, remote assessment may be beneficial in future research, clinical trials and clinical settings.



BACKGROUND

- In-person assessment and monitoring places a significant burden on patients with DMD and their caregivers, and these difficulties have been exacerbated by the COVID-19 pandemic.
- Remote assessment may be beneficial in future research, clinical trials and clinical settings.
- We assessed the reproducibility and validity of remote NSAA, 10MWR and Time to Rise scores against in-person scores using pre-specified statistical analyses.



METHODS

- In ongoing delandistrogene moxeparvovec Studies SRP-9001-101 (Study 101; NCT03375164)¹ and SRP-9001-102 (Study 102; NCT03769116)², remote functional assessments were initiated during the COVID-19 pandemic, in accordance with USFDA guidance.
- The reproducibility of remote versus in-person scores on the NSAA, 10MWR and Time to Rise was assessed using ICC, Pearson, Spearman and Bland-Altman analyses.
- The analyzed remote and in-clinic assessments were ≤2 weeks apart.
- The remote and in-clinic NSAA assessments were considered comparable if total scores from these two visits were ≤3 points different.
- If a patient’s one remote assessment was evaluated as comparable, all their remote assessments were considered comparable.



- Remote assessments were conducted via the NCH telehealth system, facilitated by video conferencing; participants were boys with DMD aged 4 to 7 years.
- The NCH clinical evaluator (CE) recorded the live session.
- If the CE determined there was insufficient space to safely conduct the training/in-home assessment session, the 10MWR was not performed as part of the NSAA (time marked as 0 seconds).
- The CE made necessary adjustments during the live assessment to ensure they could see what they needed to see to score.
- The functional assessments that could not be performed remotely (e.g., 10MWR, 100MWR, and Time to Ascend 4 steps) were documented as invalid and a protocol deviation was noted.
- The CE scored the assessment in real time, if possible. If poor video conferencing quality prevented accurate scoring, the CE could review items from the video as necessary, score those items from the video, and document this in the source.

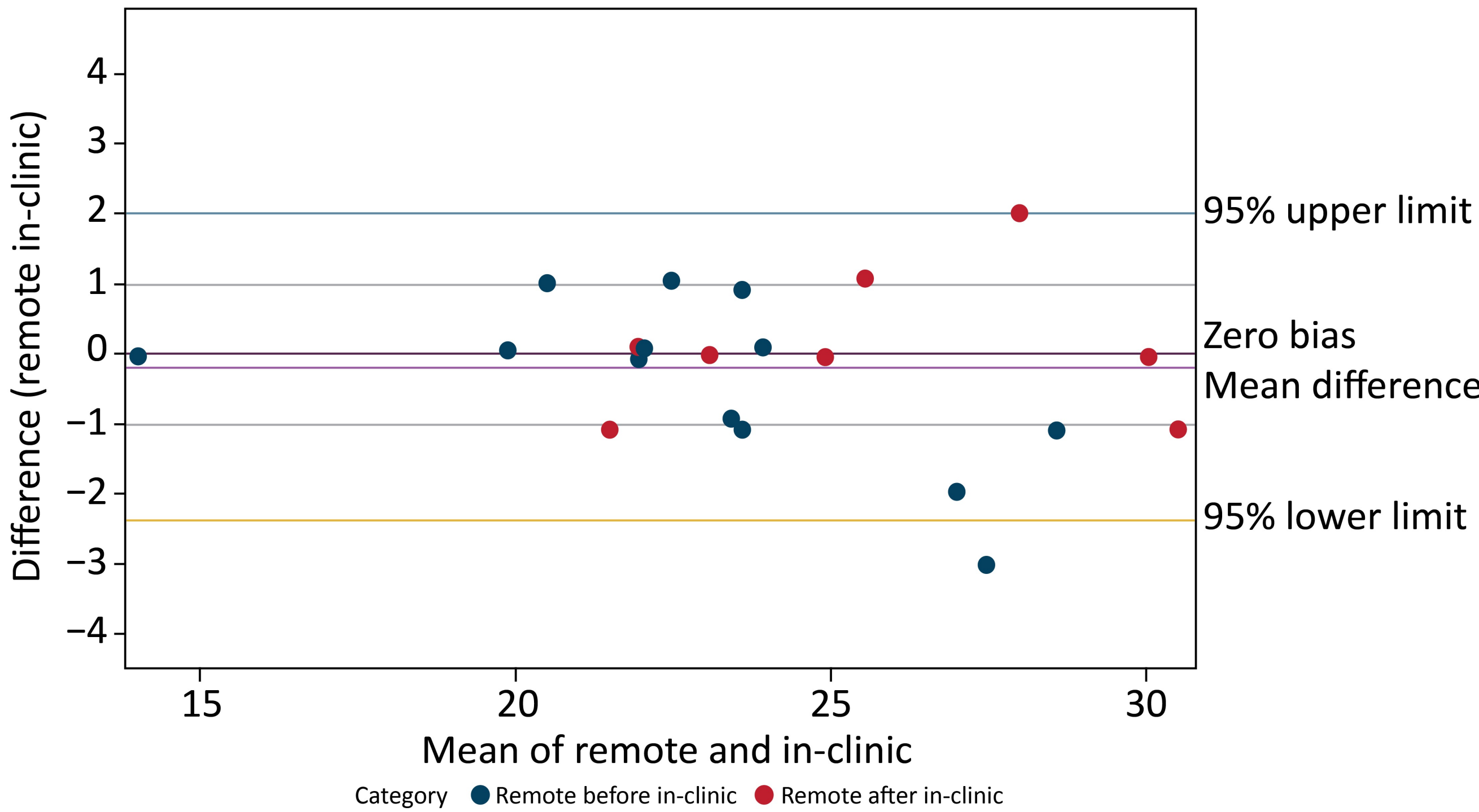


RESULTS

NSAA	Study 101	Study 102		Both
	Delandistrogene moxeparvovec N=4	Delandistrogene moxeparvovec in Part 1 (N=20)	Delandistrogene moxeparvovec in Part 2 (N=21)	Total N=45
Number of patients with remote assessments	2	12	9	23
Number of patients with remote and in-clinic assessments	1	9	8	18
Comparable remote and in-clinic assessments				
Number of patients with comparable assessments	1	9	8	18
Number of instances (pairs of assessments)	2	10	9	21

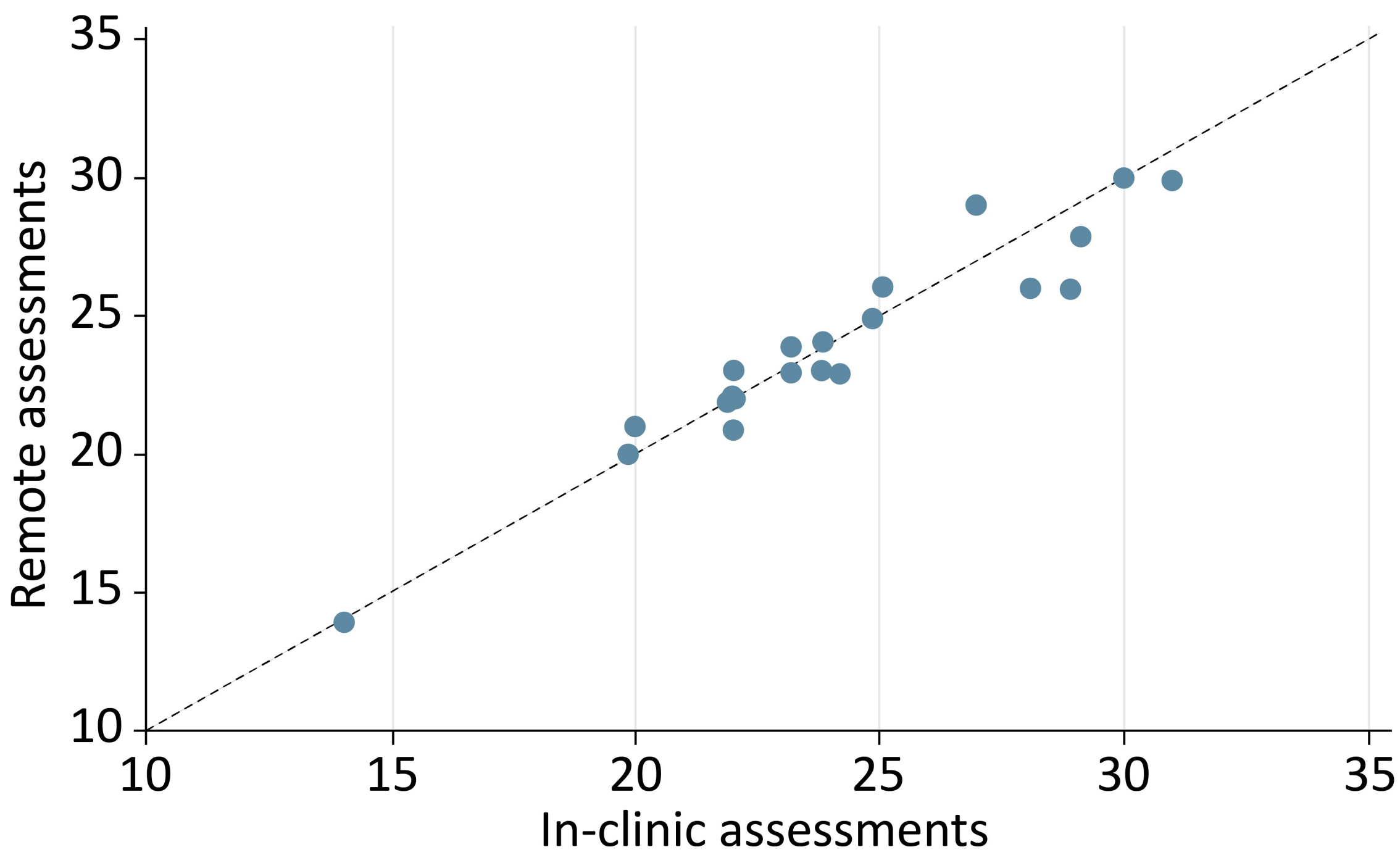
- The least consistent items between remote/in-clinic visits were climb box step, descend box step, stand on heels, and hop.
- The most consistent items were stand, stand up from chair, jump, and run.
- Mean number of days between assessments: 5.29.

Bland-Altman analysis showed agreement between NSAA assessments conducted at home and in-person (N=21)



- Bland-Altman analyses similarly showed agreement between remote and in-person assessments of Time to Rise and 10MWR (see supplemental poster).

Results obtained from NSAA assessed remotely strongly correlated with those attained within 2 weeks via in-person assessment (N=21)



NSAA (N=21)	Correlation	95% confidence interval
ICC	0.96	0.91–0.98
Pearson correlation	0.96	0.90–0.98
Spearman correlation	0.96	0.90–0.98

- Variability appears to increase as NSAA increases.
- Strong correlations were also observed in the results of timed function tests (Time to Rise and 10MWR) that were assessed remotely versus those conducted via in-person assessment (see supplemental poster).

Limitations

- Influence of recall:
 - Most paired assessments are within 1 week; therefore, there could be recall bias.
- Results are from a single center and a limited sample size; additional data may further support generalizability.
- Due to the need for a long, flat running surface, the 10m and 100m frequently could not be collected.
- We choose not to collect the 4SC due to differences between clinic and home stairs, and to minimize risk of injury.

REFERENCES

- ClinicalTrials.gov. NCT03375164 (Accessed February 2022);
- ClinicalTrials.gov. NCT03769116 (Accessed February 2022).

ABBREVIATIONS

4SC, 4-Stair Climb; 10MWR, 10 Meter Walk/Run; 100-meter walk/run; AAVrh74, adeno-associated virus serotype rh74; CI, confidence interval; COVID-19, coronavirus disease 2019; DMD, Duchenne muscular dystrophy; MHCK, myosin-heavy-chain kinase; NSAA, North Star Ambulatory Assessment; ICC, intraclass correlation coefficient; USFDA, United States Food and Drug Administration.

ACKNOWLEDGMENTS & DISCLOSURES

We would like to thank the patients and their families for participation in this study, as well as the investigators and trial staff involved in EMBARK. This study is sponsored by Sarepta Therapeutics & funded by Sarepta Therapeutics & F. Hoffmann-La Roche. Writing and editorial assistance was provided by Jen Claroche, PhD, of Nucleus Global in accordance with Good Publication Practice guidelines (<http://www.ismpp.org/gpp3>). LPL reports receiving salary support from Sarepta Therapeutics through Nationwide Children’s Hospital to support training and quality control activities for ongoing clinical trials and licensing fees for natural history data. LNA reports receiving salary support from Sarepta Therapeutics through Nationwide Children’s Hospital to support training and quality control activities for their ongoing clinical trials. MAI reports no conflicts of interest. NFR reports receiving salary support from Sarepta for Clinical Evaluator training for ongoing and upcoming clinical trials. KG is an employee of Eli Lilly and was previously an employee of Sarepta Therapeutics and may have stock options. LH, LY and SW are employees of Sarepta Therapeutics and may have stock options. JRM has received study funding from Sarepta Therapeutics and has a service agreement with Sarepta to provide training on ongoing studies. JRM is a co-inventor of AAVrh74.MHCK7-micro-dys technology. This study was funded by Sarepta Therapeutics, Inc.

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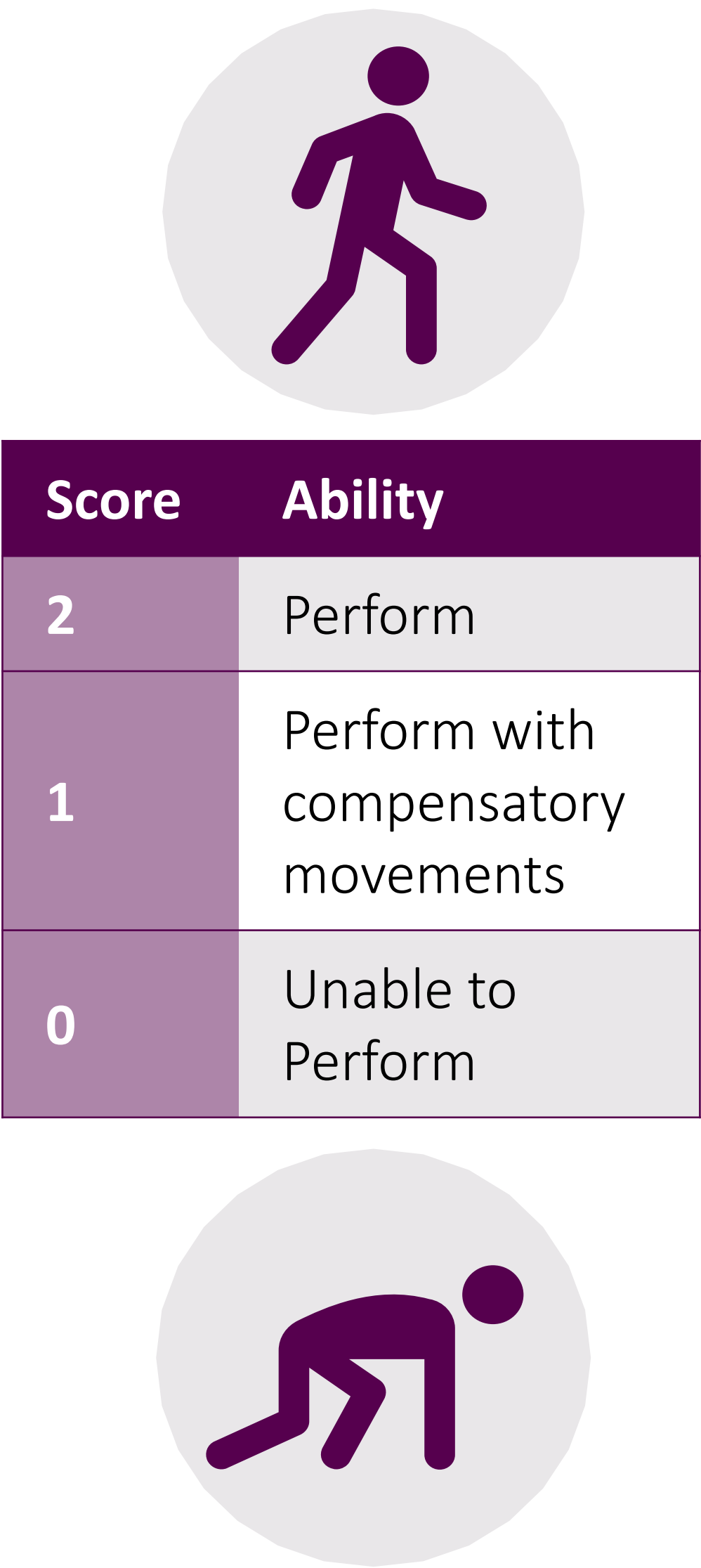
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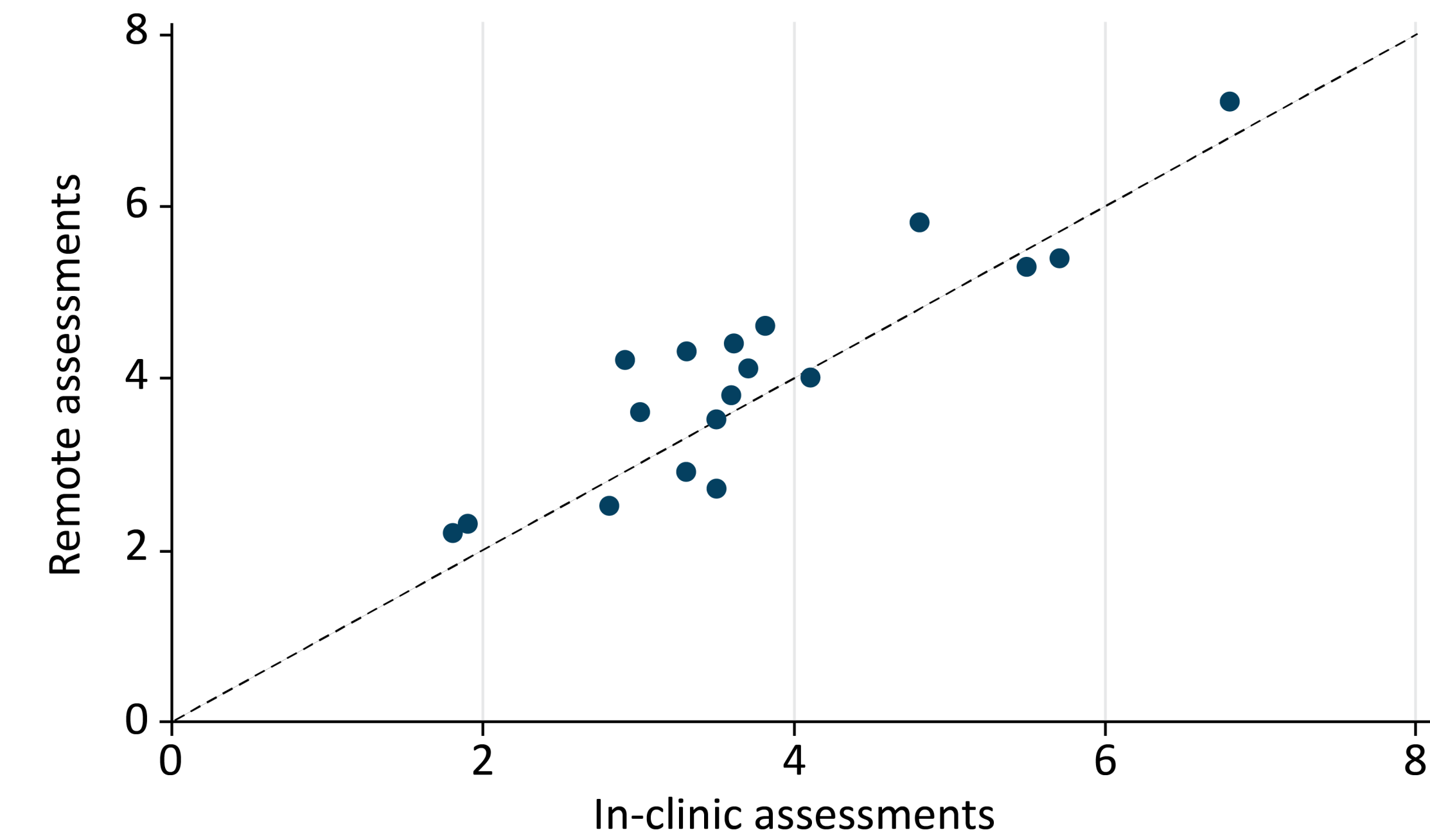
SUPPLEMENTARY MATERIAL

NSAA is a composite endpoint evaluating physical function across 17 tests with increasing difficulty



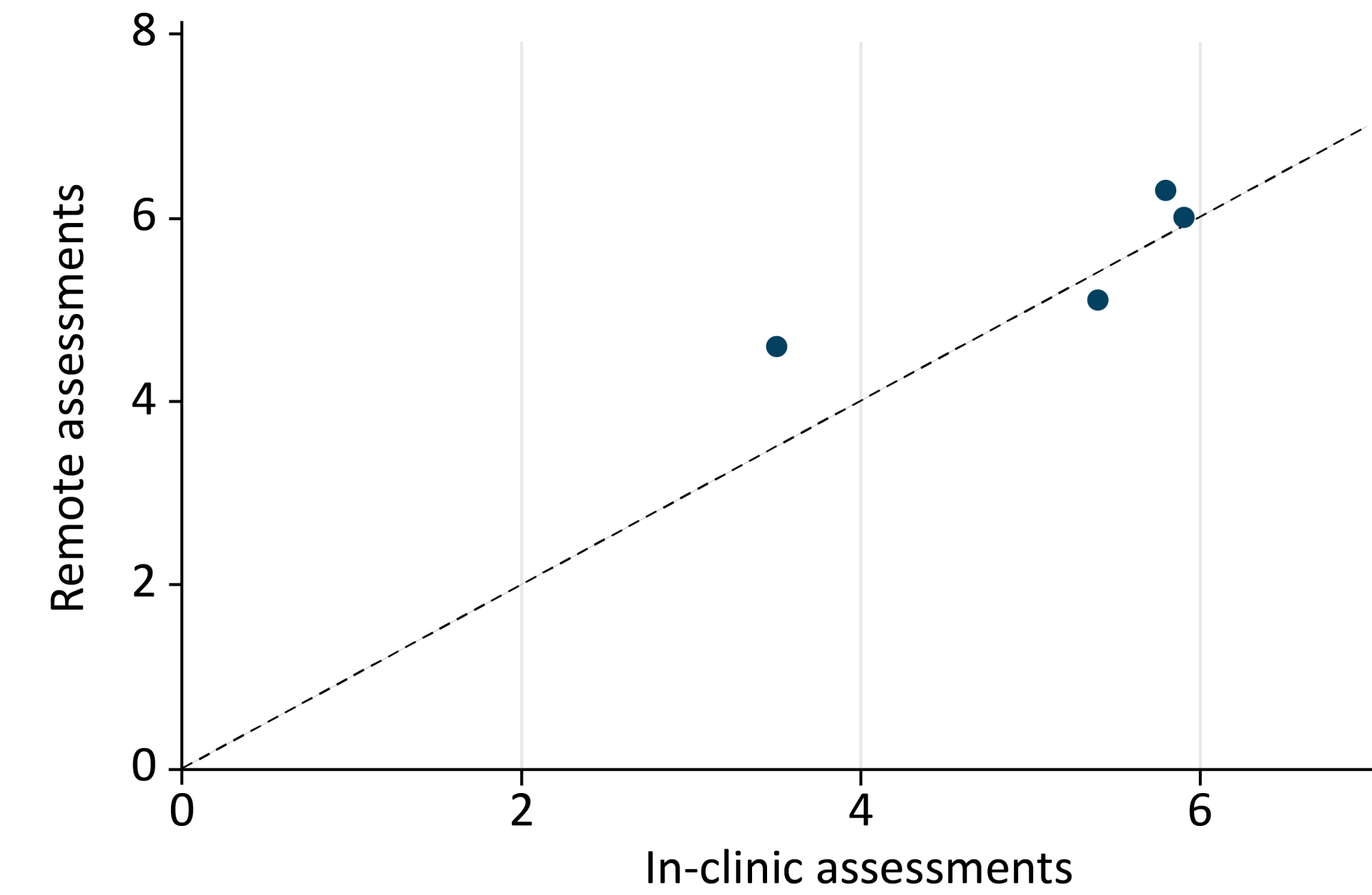
Assessment	Relevant activities of daily living
Items 14–17: Jump, hop, run	Playing, accessing sports, keeping up socially and physically with peers, skipping, hopscotch
Item 13: Stand on heels	Walking on uneven or hilly ground, cycling more easily, getting out of chair and stepping more easily
Item 11: Rise from floor	Getting up after falling down, sitting on floor with classmates without needing help to get up
Item 10: Gets to sitting	Sitting up in bed, assuming a safer position if fall occurs
Items 6–9: Climb on and off box step	Independent outdoor mobility (curbs in particular)
Items 4 & 5: Stand on one leg	Kicking a ball, stepping off a curb, putting on pants, shoes and socks while standing
Item 3: Stand up from chair	Moving from class to class, using a toilet, getting out of bed or a car
Item 2: Walk	Participating in peer related activities, mobility in the home, school and community
Item 1: Stand	Standing to pee, groom, prepare meals, or access high items like elevator buttons, light switches and cupboards

Scatter plot of remote and in-clinic Time to Rise assessments (seconds)



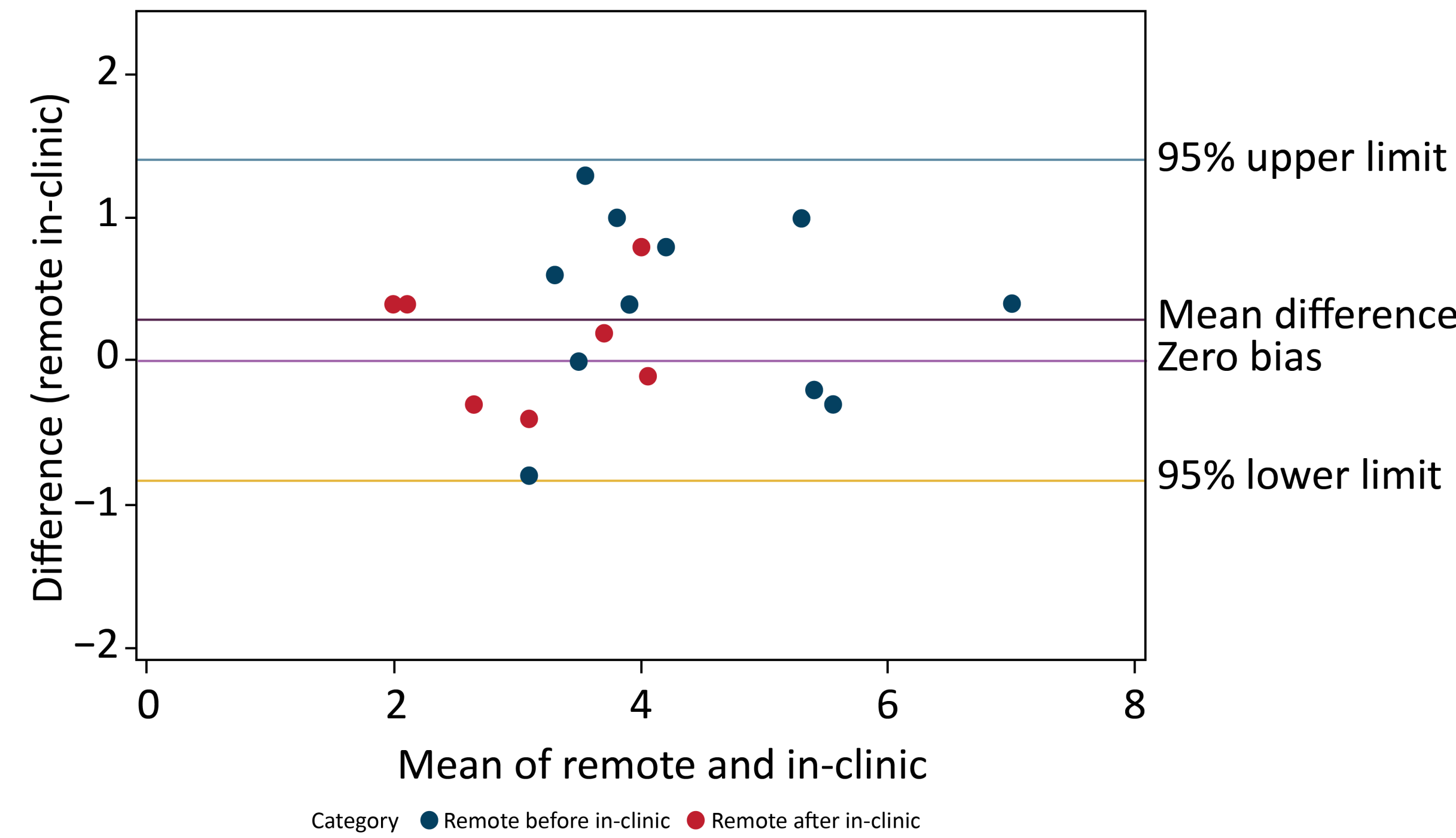
Time to Rise from Floor	Correlation	95% CI
ICC	0.88	0.72–0.95
Pearson correlation	0.90	0.74–0.96
Spearman correlation	0.83	0.59–0.93

Scatter plot of remote and in-clinic 10MWR assessments (seconds)

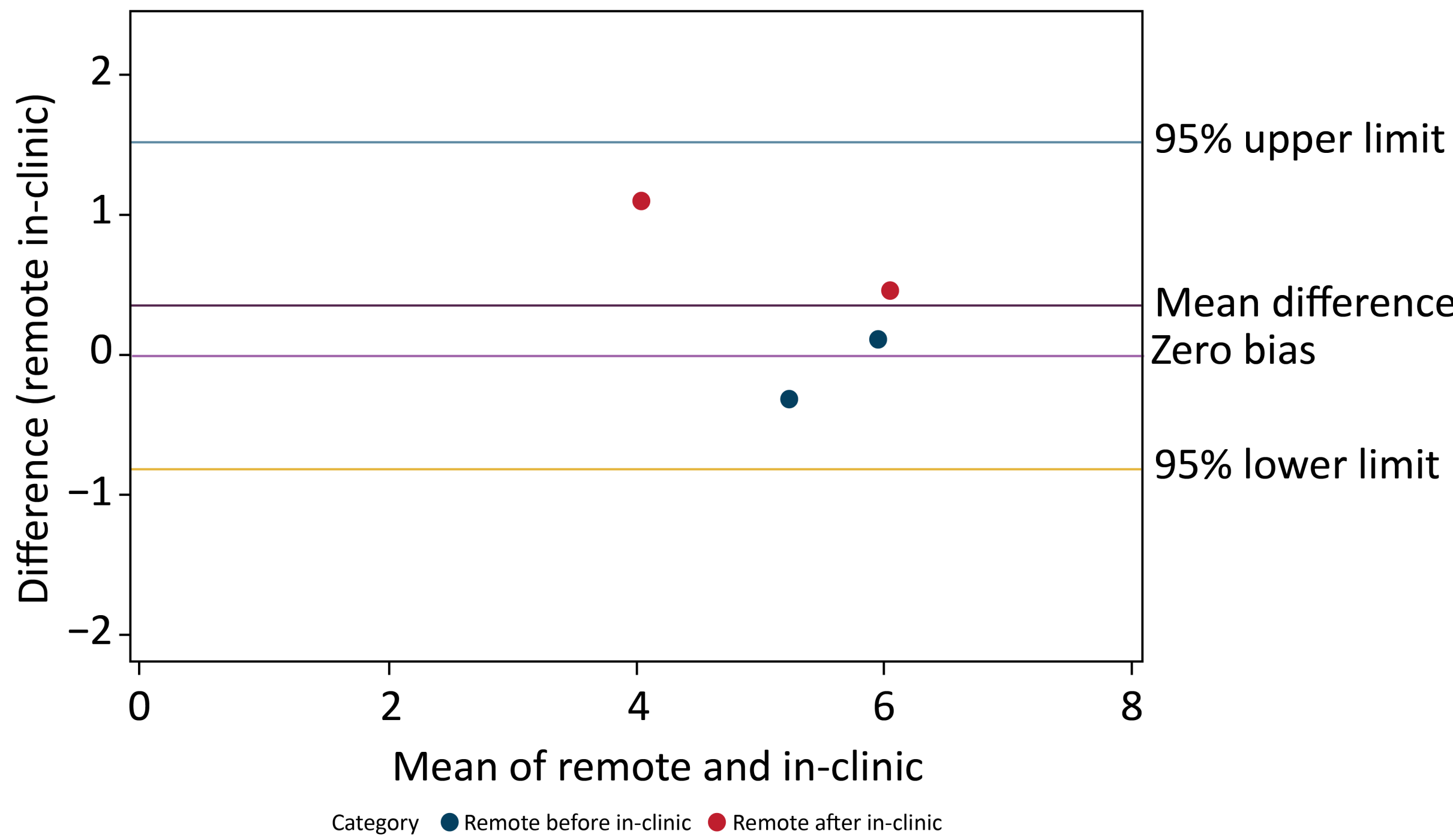


10MWR	Correlation	95% CI
ICC	0.79	0.01–0.97
Pearson correlation	0.86	-0.67–1.00
Spearman correlation	0.80	-0.76–0.99

Bland-Altman plot of remote and in-clinic Time to Rise assessments



Bland-Altman plot of remote and in-clinic 10MWR assessments



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