

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

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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 (SRP-9001) 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 analysed remote and in-clinic assessments were ≤2 weeks apart.
- Comparability was determined based on the first pair of remote and in-person assessments within two weeks of each other; if a patient had one remote assessment that 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.

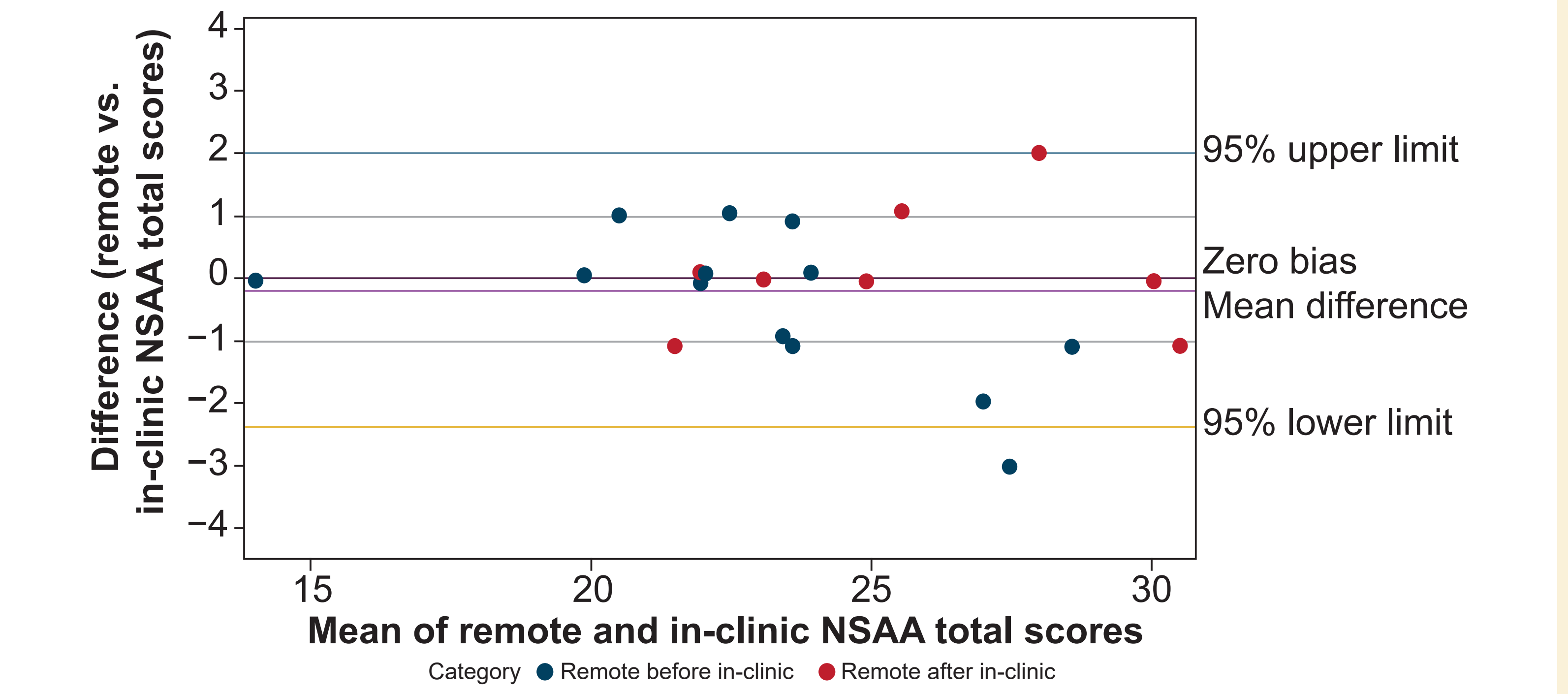
- The NCH clinical evaluator (CE) recorded the live session, making necessary adjustments during the live assessment to ensure they could see what they needed to be able to score.
- The functional assessments that could not be performed remotely (e.g., 10MWR, 100MWR, and 4SC) were documented as invalid 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 and score items from the video, as necessary, 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-clinical assessments				
Number of patients with comparable assessments	1	9	8	18
Number of instances (pairs of assessments)	2	10	9	21

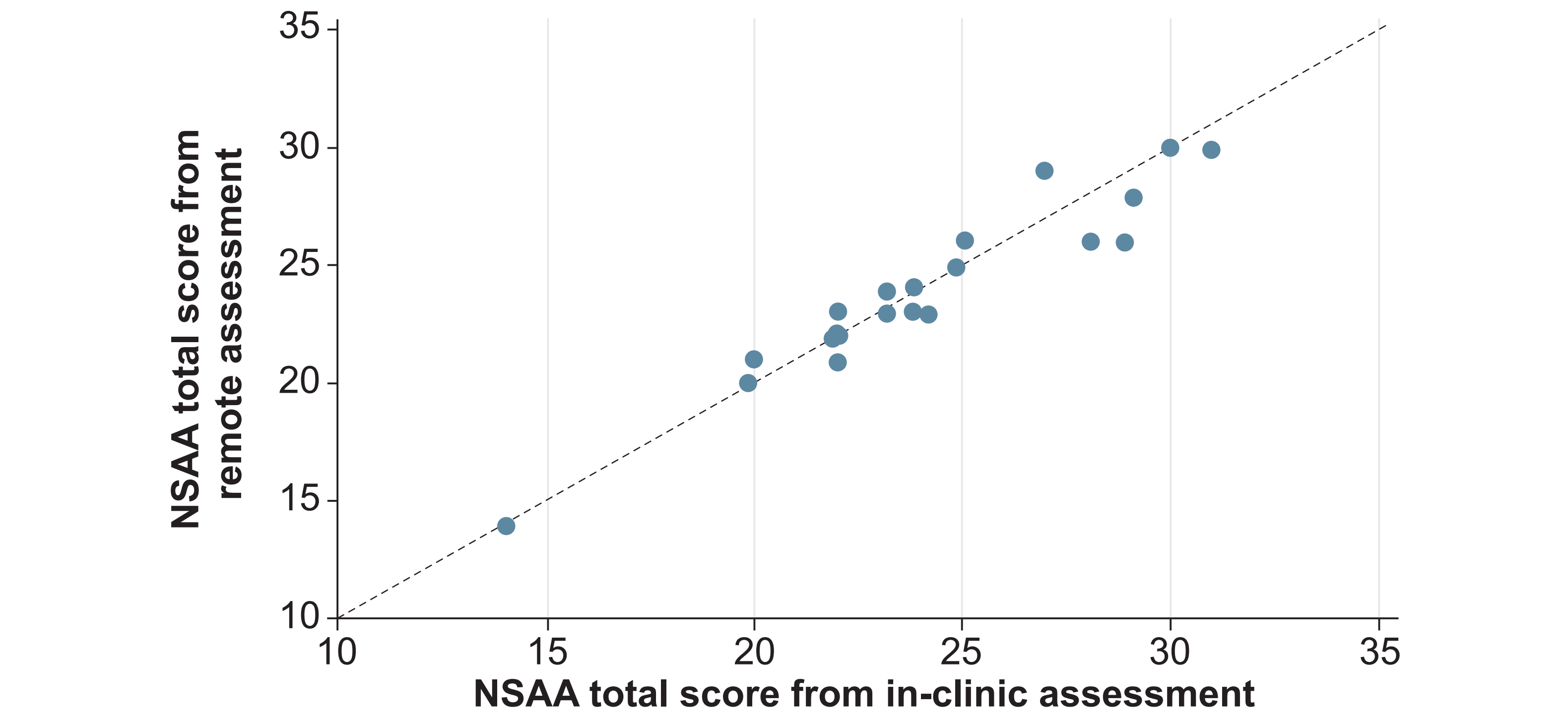
- The least consistent items between remote/in-clinic visits were climb box step, descend box step, stand on heels, and hop.
- The most consistent items were stand, stand up from chair, jump, and run.
- The mean number of days between assessments was 5.29.

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 supplementary material).

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 total score increases.
- Strong correlations were also observed between the results of timed function tests (Time to Rise and 10MWR) that were assessed remotely versus those conducted via in-person assessment (see supplementary material).

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 generalisability.
- Due to the need for a long, flat running surface, the 10MWR and 100MWR frequently could not be evaluated.
- We chose not to collect 4SC data due to differences between clinic and home stairs, and to minimise risk of injury.

REFERENCES

1. ClinicalTrials.gov. NCT03375164 (Accessed August 2022);
2. ClinicalTrials.gov. NCT03769116 (Accessed August 2022).

ABBREVIATIONS

4SC, 4-Stair Climb; 10MWR, 10-Metre Walk/Run; 100MWR, 100-Metre Walk/Run; AAVrh74, adeno-associated virus serotype rh74; CE, clinical evaluator; CI, confidence interval; COVID-19, coronavirus disease 2019; DMD, Duchenne muscular dystrophy; ICC, intraclass correlation coefficient; MHCK, myosin-heavy-chain kinase; NCH, Nationwide Children’s Hospital; NSAA, North Star Ambulatory Assessment; USFDA, United States Food and Drug Administration.

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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. NPR reports receiving salary support from Sarepta Therapeutics 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 Therapeutics to provide training on ongoing studies. JRM is a co-inventor of AAVrh74.MHCK7.micro-dys technology.

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SUPPLEMENTARY MATERIAL

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

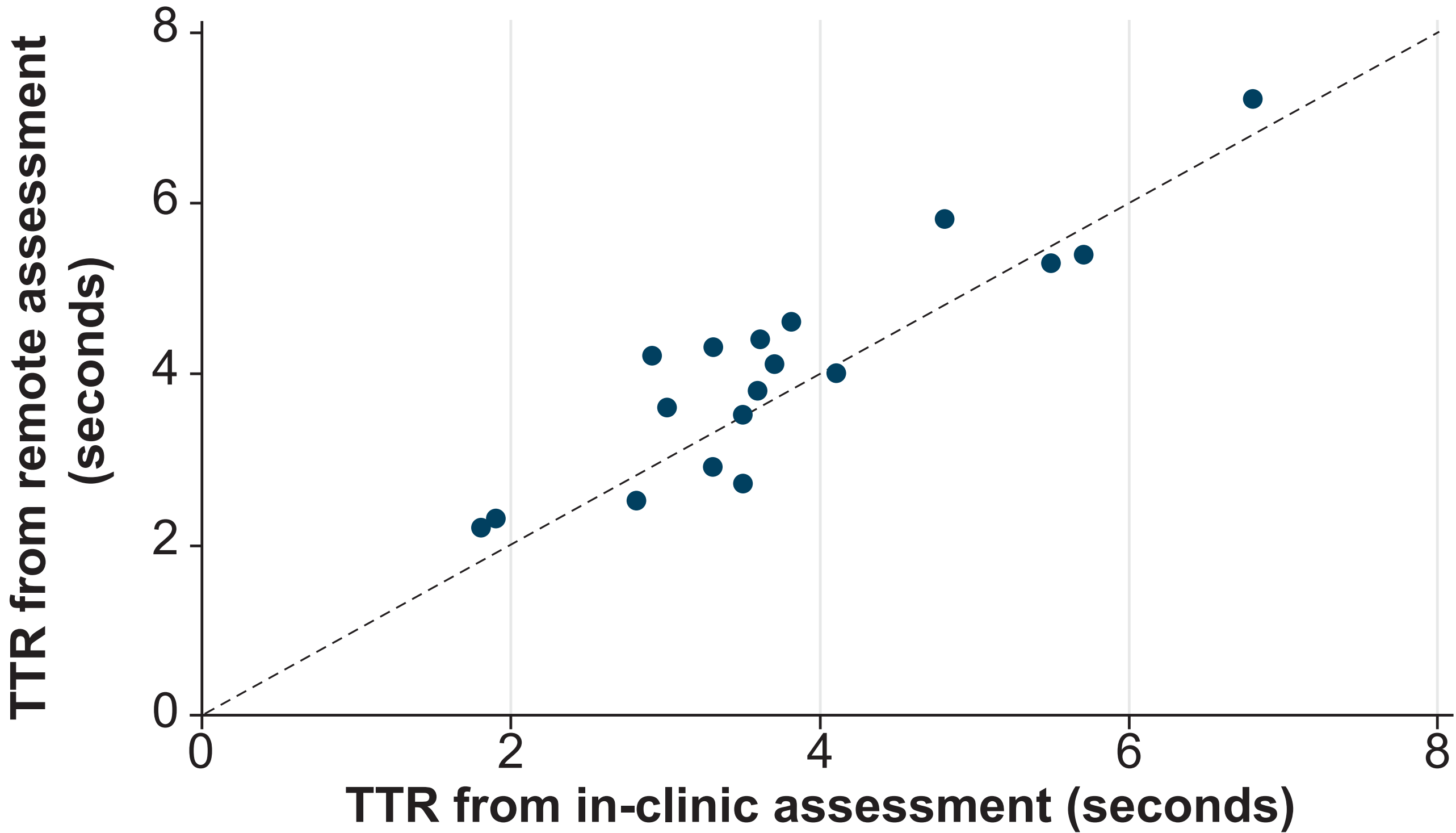


Score	Ability
2	Perform
1	Perform with compensatory movements
0	Unable to Perform



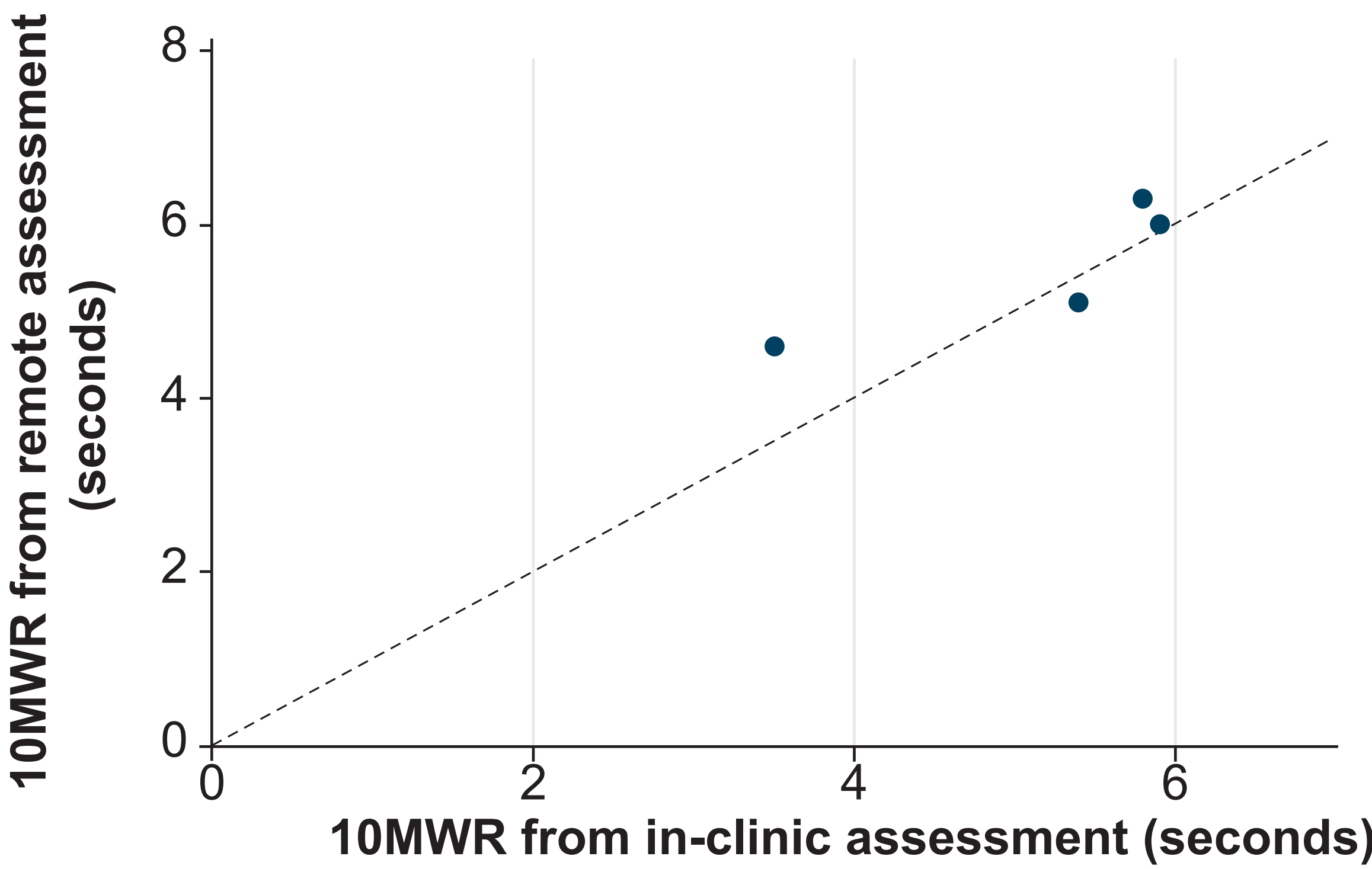
Assessment	Relevant activities of daily living
Items 14–17: Jump, hop, run	Playing, accessing sports, keeping up socially and physically with peers, skipping, hopscotch
Item 13: Stand on heels	Walking on uneven or hilly ground, cycling more easily, getting out of chair and stepping more easily
Item 11: 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)



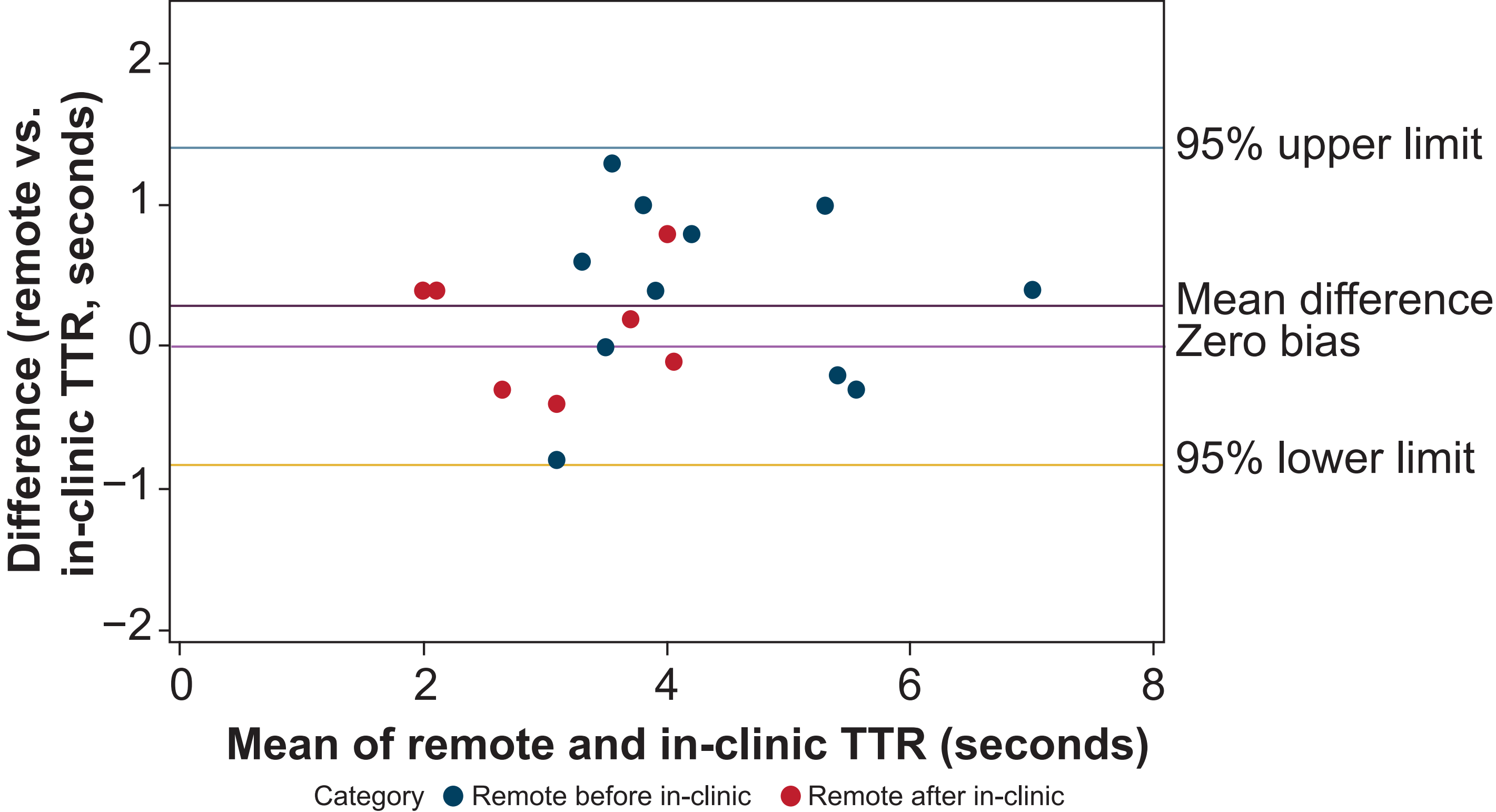
Time to Rise	Correlation	95% confidence interval
ICC	0.88	0.72–0.95
Pearson correlation	0.90	0.74–0.96
Spearman correlation	0.83	0.59–0.93

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

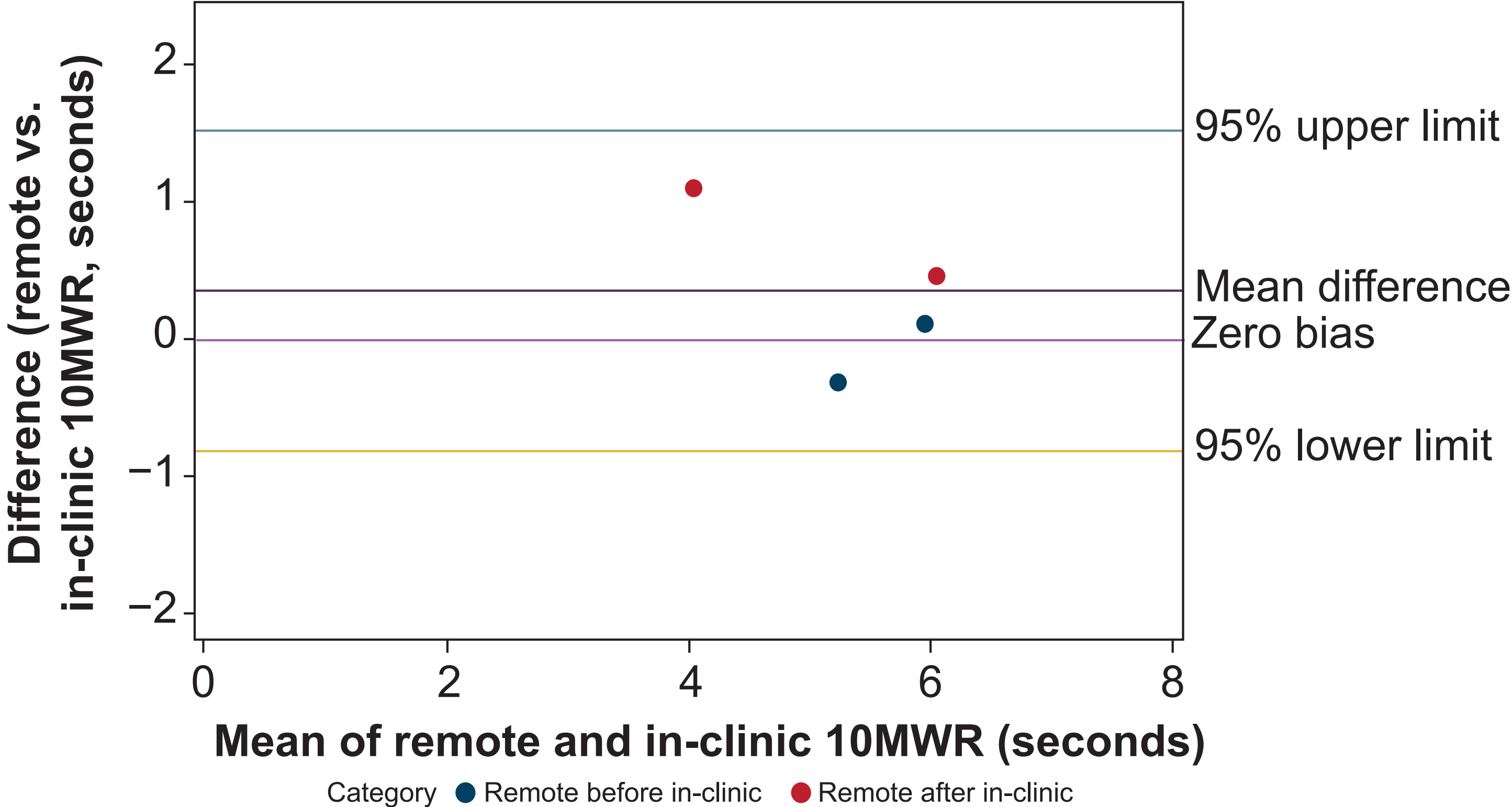


10MWR	Correlation	95% confidence interval
ICC	0.79	0.01–0.97
Pearson correlation	0.86	–0.67–1.00
Spearman correlation	0.80	–0.76–0.99

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



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



REFERENCES

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ABBREVIATIONS

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