

Original Article

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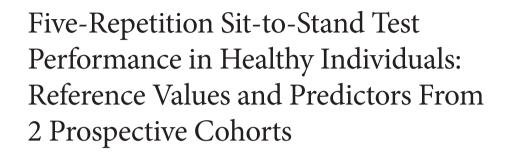
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Objective: The 5-repetition-sit-to-stand (5R-STS) test is an objective test of functional impairment- commonly used in various diseases, including lumbar degenerative disc diseases. It is used to measure the severity of disease and to monitor recovery. We aimed to evaluate reference values for the test, as well as factors predicting 5R-STS performance in healthy adults. Methods: Healthy adults (>18 years of age) were recruited, and their 5R-STS time was measured. Their age, sex, weight, height, body mass index (BMI), smoking status, education level, work situation and EuroQOL-5D Healthy & Anxiety category were recorded. Linear regression analysis was employed to identify predictors of 5R-STS performance. Results: We included 172 individuals with mean age of 39.4 ± 14.1 years and mean BMI of $24.0 \pm 4.0 \text{ kg/m}^2$. Females constituted 57%. Average 5R-STS time was 6.21 ± 1.92 seconds, with an upper limit of normal of 12.39 seconds. In a multivariable model, age (regression coefficient [RC], 0.07; 95% confidence interval [CI], 0.05/0.09; p < 0.001), male sex (RC, -0.87; 95% CI, -1.50 to -0.23; p = 0.008), BMI (RC, 0.40; 95% CI, 0.10–0.71; p = 0.010), height (RC, 0.13; 95% CI, 0.04–0.22; p = 0.006), and houseworker status (RC, -1.62; 95% CI, -2.93 to -0.32; p = 0.016) were significantly associated with 5R-STS time. Anxiety and depression did not influence performance significantly (RC, 0.82; 95% CI, -0.14 to 1.77; p = 0.097).

Conclusion: The presented reference values can be applied as normative data for 5R-STS in healthy adults, and are necessary to judge what constitutes abnormal performance. We identified several significant factors associated with 5R-STS performance that may be used to calculate individualized expected test times.

Clinical Trial Registration: Clinical Trials.gov Identifier: NCT03303300 and NCT03321357

Keywords: Sit-to-stand, Objective test, Degenerative disc disease, Lumbar stenosis, Lumbar disc herniation, Functional impairment



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INTRODUCTION

The sit-to-stand (STS) action is very common and performed by individuals of all ages up to 60 times a day or more.¹ This movement is an important determinant of physical function and independence.² In 1985, Csuka and McCarty³ were among the first to introduce the 5-repetition-sit-to-stand test (5R-STS) as a way of measuring lower leg strength. It involves measuring how quickly an individual will repeat the sitting-to-standing action 5 times.³⁻⁵ Since then, it has been applied to patients with

a range of medical conditions, including lumbar degenerative spine disease, stroke, chronic obstructive pulmonary disease (COPD), Parkinson disease, rheumatoid arthritis, postkidney transplant, and posttotal knee replacement to not only objectively assess functional impairment, but also to monitor recovery and progress. It is also used in the pediatric setting. Objective functional tests can eliminate subjectivity that is at times captured in questionnaires, and account for symptoms such as foot drop missed by common Patient-Reported Outcome Measures. The popularity of tests for objective functional impairment (OFI) has increased rapidly during the past years. Other OFI tests include the Timed Up and Go (TUG) test and the 6-minute walk test (6MWT).

To assess what should be considered as a pathological performance in any test for OFI, normative reference values from a healthy population need to be established. Only few data are available on normative values for the 5R-STS in healthy individuals, only focusing on elderly individuals.¹⁶ In addition, it is important to understand which factors govern test performance. For example, if body height significantly influences test performance because of a standardized chair height that may benefit shorter individuals, this effect needs to be considered. In addition, knowledge of these predictive factors allows generation of individualized expected test statistics for patients with e.g., degenerative disease of the lumbar spine. Lower extremity muscle strength and sense of balance are the mostly commonly studied predictive factors, although only few studies analyzed variables such as age, sex, or height as determinants of the 5R-STS test time.^{7,17-22} Additionally, the majority of 5R-STS studies concentrate on patients with specific diseases or elderly patients, creating a gap in understanding the younger adult population. In addition, sociodemographic factors such as work status, education level, and anxiety and depression are frequently not considered.²³ We aimed to evaluate reference values for the test, as well as factors predicting 5R-STS performance in healthy adults.

MATERIALS AND METHODS

1. Study Design

In 2 prospective studies, carried out between October and December of 2017 and between December 2017 and June 2018, healthy volunteers were seen at a Dutch specialized short-stay outpatient spine surgery clinic. The prospective studies (ClinicalTrials.gov Identifier: NCT03303300 and NCT03321357) were approved by the local Institutional Review Board (Medical Research Ethics Committees United, Registration Number: W17.107

and W17.134) and were conducted according to the Declaration of Helsinki. Informed consent was obtained from all participants.

2. Study Population

Healthy individuals aged > 18 years were recruited and were either volunteers or employees of the department. Most volunteers were partners of patients scheduled for surgery, and thus demonstrated comparable sociodemographic features. Some volunteers were also acquittances and relatives of authors. Participants disclosing spinal conditions, hip- or knee replacements, other lower extremity-related complaints, or that required walking aides were excluded.

3. Testing Protocol

The 5R-STS test was performed as previously described. $^{4,5,8,12,15,24-26}$ Participants were asked to sit down on an armless chair of standard height (48 cm) with a hard seat, firmly placed against a wall. The participants were instructed to fold their arms across their chest, and to keep their feet flat on the ground. Participants were required to wear stable shoes for this test. To become familiar with the maneuver, participants were asked to stand up fully and sit back down again once without using their upper limbs. If assistance was required, or if the maneuver could not be completed, the test was abandoned. Otherwise, the patients were asked to stand up fully and sit down again, landing on the seat firmly, 5 times as fast as possible, starting on the command "go." Using a stopwatch, the 5 repetitions were timed from the initial command to the completed fifth stand. This time was recorded as the participant's score. If the patient was unable to perform the test in 30 seconds, or not at all, this was captured, and the test score was recorded as 30 seconds. Volunteers and patients were also asked to complete questionnaires containing baseline sociodemographic data: age, sex, body mass index (BMI), height, weight, smoking status, education level, work situation, and EuroQOL-5D (EQ-5D) questionnaire - containing the EQ-Anxiety and Depression category, which has been demonstrated to correlate adequately with anxiety and depression.²⁷ Participants filled in the questionnaires right after initially performing the test.

4. Statistical Analysis

Continuous variables are reported as mean ± standard deviation, and categorical variables as numbers and percentages. The 2 cohorts were pooled. The upper limit of normal (ULN) was arrived at by calculating the 99th percentile of this normative

population.^{5,28} Missing data, which was presumed to be missing at random, was imputed using 5-nearest neighbor imputation.²⁹ To identify univariable predictors of 5R-STS performance in healthy individuals, linear regression models were fitted for each of the baseline variables. Subsequently, a multivariable linear regression model was fitted to identify factors independently associated with 5R-STS performance. The primary analysis was based on the purposeful variable selection procedure described by Bursac et al.³⁰ In more detail, variables were considered for primary inclusion at univariable $p \le 0.25$. Subsequently, an initial multivariable model was built, and variables that did not have a significant effect (defined as $p \le 0.1$) or that did not demonstrate confounding (defined using a change-in-estimate criterion of 20% or greater) were iteratively removed from the model. Finally, any variable not eligible for the initial multivariable model was added iteratively, and the model was subsequently reduced in the same way as described above by iterative removal of only those variables that were additionally added.²⁹ Spearman rank correlation was applied to describe the correlation among continuous variables and 5R-STS performance. All analyses were carried out using R version 3.6.2 (The R Foundation for Statistical Computing, Vienna Austria).³¹ A 2-tailed p≤0.05 was considered significant. The statistical code is provided (Supplementary Content 1).

RESULTS

1. Cohort

The cohort consisted of 172 healthy adult participants (Table 1) with a mean age of 39.4 ± 14.1 years. The ratio of females to males was 57:43. A mean BMI of 24.0 ± 4.0 kg/m² was observed. Only 13.4% were active smokers. In terms of work situation, 35.5% of participants were students, 39.5% of participants were employed, and 13% were retired, among others. A vast majority (94.2%) of the cohort scored 1 in EQ-5D Anxiety & Depression, indicating no signs of anxiety or depression, while the rest scored at 2 indicating mild anxiety or depression. ²⁷ Fifteen indi-

viduals (8.7%) had missing data on anxiety and depression.

2. Reference Values

A detailed account of normative reference values for healthy adults is provided in Table 2, including stratifications for male

Table 1. Basic demographic data for healthy adult participants

Characteristic	All participants (n = 172)	pants $(n = 98)$			
Age (yr)	39.4 ± 14.1	63.3 ± 18.5	41.7 ± 19.5		
Sex					
Female	98 (57.0)	-	-		
Male	74 (43.0)	-	-		
BMI (kg/m ²)	24.0 ± 4.0	23.3 ± 4.5	25.0 ± 3.0		
Height (cm)	171.0 ± 10.0	164.9 ± 6.6	179.2 ± 7.7		
Weight (kg)	70.5 ± 14.1	63.3 ± 11.7	80.0 ± 11.1		
Smoking status					
Active smoker	23 (13.4)	10 (10.2)	13 (17.6)		
Ceased smoking	37 (21.5)	19 (19.4)	18 (24.3)		
Never smoked	112 (65.1)	69 (70.4)	43 (58.1)		
Education level					
Elementary	6 (3.4)	2 (20.0)	4 (50.4)		
High-school	59 (34.3)	34 (34.7)	25 (33.8)		
Higher	103 (60.0)	59 (60.2)	44 (59.5)		
Postdoctoral	4 (2.3)	3 (30.1)	1 (1.3)		
Work situation					
Employed	68 (39.5)	37 (37.8)	31 (41.9)		
Self-employed	13 (7.6)	3 (3.1)	10 (13.5)		
Retired	22 (12.8)	11 (11.2)	11 (14.9)		
Houseworker	5 (2.9)	5 (5.1)	0 (0.0)		
Unemployed	3 (1.7)	1 (1.0)	2 (2.7)		
Student	61 (35.5)	41 (41.8)	20 (27.0)		
EQ5D Anxiety & Depression					
1	162 (94.2)	90 (91.8)	72 (97.3)		
2	10 (5.8)	8 (8.2)	2 (2.7)		

Values are presented as mean \pm standard deviation and number (%). BMI, body mass index.

Table 2. Reference values for the 5R-STS test time (second) in healthy individuals

Age (yr) —	Male		Female		Overall	
	Mean ± SD	ULN	Mean ± SD	ULN	Mean ± SD	ULN
≤60	5.98 ± 1.54	8.7	5.60 ± 1.43	9.31	5.76 ± 1.50	9.11
>60	8.23 ± 2.26	11.85	9.00 ± 1.98	13.36	8.63 ± 2.12	13.36
Overall	6.38 ± 1.88	11.10	6.09 ± 1.95	13.36	6.21 ± 1.92	12.39

 $\label{eq:mean provided} Mean \pm standard\ deviation\ (SD)\ and\ ULN\ (upper\ limits\ of\ normal)\ are\ provided\ for\ each\ subpopulation.$ 5R-STS, 5-repetition sit-to-stand test.

and female individuals, for those aged under and over 60 years, as well as for combinations of these factors. In the overall population, the average 5R-STS test time was 6.21 ± 1.92 seconds, with an ULN of 12.39 seconds.

We have additionally provided normative reference values for healthy adults further stratified by age groups \leq 60 years of age (Supplementary Table 1).

3. Factors Associated With 5R-STS Performance

Results of the univariable analysis are demonstrated in Table 3. In the multivariable model (Table 4) including confounders,

Table 3. Univariable linear regression analysis of predictive factors for the 5R-STS in healthy adult individuals

	<u> </u>		
Variable		Univariate analysis	
variable	RC	95% CI	p-value
Age	0.06	0.05 to 0.08	< 0.001*
Sex			
Male	0.29	-0.29 to 0.87	0.335
Female		Reference	
BMI (kg/m²)	0.21	0.14 to 0.27	< 0.001*
Height (cm)	0.02	-0.01 to 0.04	0.265
Weight (kg)	0.05	0.03-0.07	< 0.001*
Smoking status			
Active smoker	-0.20	-1.06 to 0.67	0.653
Ceased smoking	0.07	-0.64 to 0.79	0.838
Never smoked		Reference	
Education level			
Elementary	3.03	-8.08 to 2.86	< 0.001*
High-school	-0.37	-0.58 to 2.94	0.224
Higher		Reference	
Postdoctoral	0.56	-4.49 to 4.13	0.553
Work situation			
Employed		Reference	
Self-employed	0.72	-0.28 to 1.72	0.158
Retired	2.30	1.49-3.10	< 0.001*
Houseworker	-0.15	-1.68 to 1.37	0.846
Unemployed	-0.17	-2.11 to 1.77	0.862
Student	-0.81	-1.39 to -0.23	0.007
EQ-5D Anxiety &Depres	sion		
1		Reference	
2	2.04	0.85-3.23	< 0.001*

5R-STS, 5-repetition sit-to-stand test; RC, regression coefficient; CI, confidence interval; BMI, body mass index; EQ-5D, EuroQOL-5D.

higher age (regression coefficient [RC], 0.07; 95% confidence interval [CI], 0.05/0.09; p < 0.001) (Fig. 1), higher BMI (RC, 0.40; 95% CI, 0.10–0.71; p = 0.010), and greater height (RC, 0.13; 95% CI, 0.04–0.22; p = 0.006) were significantly associated with a higher 5R-STS test time, and thus with worse performance. In contrast, male sex (RC, -0.87; 95% CI, -1.50 to -0.23; p = 0.008) (Fig. 2) and houseworker status (RC, -1.62; 95% CI, -2.93 to -0.32; p = 0.016) were associated with lower 5R-STS test time, and thus with greater performance. Body weight and education level were included in the model as confounding variables – as was anxiety and depression, which did not influence 5R-STS performance significantly (RC, 0.82; 95% CI, -0.14 to 1.77; p = 0.097). The *post hoc* power analysis demonstrated a power of 1- β approaching 1.

Table 4. Multivariable linear regression analysis of predictive factors for the 5R-STS in healthy adult individuals

37 - 11		S		
Variable	RC	95% CI	p-value	
Age	0.07	0.05-0.09	< 0.001*	
Sex				
Male	-0.87	-1.50 to -0.23	0.008*	
Female		Reference		
BMI (kg/m²)	0.40	0.10-0.71	0.010*	
Height (cm)	0.13	0.04-0.22	0.006*	
Weight (kg)	-0.10	-0.21 to 0.01	0.088	
Education level				
Elementary	1.07	-0.12 to 2.26	0.081	
High-school	-0.02	-0.48 to 0.43	0.918	
Higher		Reference		
Postdoctoral	-0.03	-1.39 to 1.34	0.971	
Work situation				
Employed		Reference		
Self-employed	0.02	-0.83 to 0.87	0.967	
Retired	-0.17	-1.15 to 0.80	0.731	
Houseworker	-1.62	-2.93 to -0.32	0.016*	
Unemployed	-0.21	-1.83 to 1.41	0.802	
Student	0.71	0.11-1.31	0.022*	
EQ-5D Anxiety &De	pression			
1		Reference		
2	0.82	-0.14 to 1.77	0.097	

Variables for inclusion in this final model were selected according to the purposeful variable selection algorithm.

5R-STS, 5-repetition sit-to-stand test; RC, regression coefficient; CI, confidence interval; BMI, body mass index; EQ-5D, EuroQOL-5D.

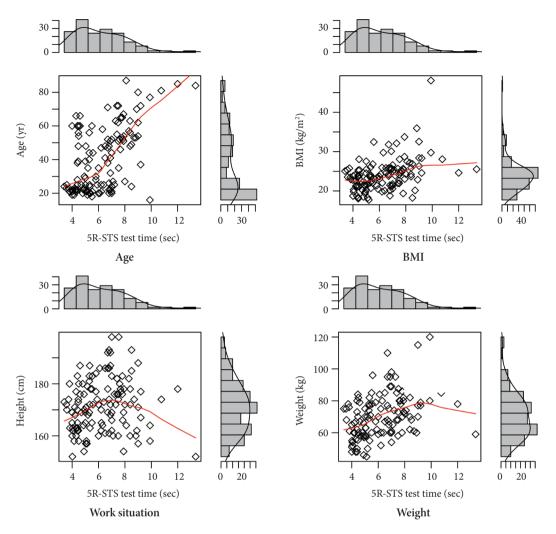


Fig. 1. Scatter plots with marginal histograms demonstrating continuous factors associated with 5-repetition sit-to-stand test (5R-STS) test time in healthy adult individuals using Spearman rank correlation. BMI, body mass index.

DISCUSSION

The purpose of this study was to describe reference values and to identify predictive factors of 5R-STS test time in healthy individuals. It was found that age, BMI, and body height correlated positively with 5R-STS test time, while male sex and houseworker status correlated negatively with test times. Anxiety and depression, body weight, and education level were identified as confounders of 5R-STS performance and were thus included in the multivariable model, however without a significant influence on performance.

Establishing normative data in the form of reference values—derived from healthy "normal" population—is crucial for 2 reasons: First, it allows judgement of what is normal and what is abnormal. Commonly, the ULN is calculated to base this deci-

sion on. Our reference values (Table 2) allow application of the 5R-STS in most pathological populations, as the age- and sex-stratified ULNs can determine what is objectively normal and what is pathological performance. The degree to which abnormal 5R-STS performance correlates with disease progression (construct validity) for particular diseases such as COPD or lumbar degenerative disease can however only be judged after validation in those specific populations. Second, these data allow generation of models that can calculate expected 5R-STS test times for each individual, even if their performance is pathological – Much akin to spirometry reporting in pulmonary functional testing or t-scores for bone density in osteoporosis. This can both help to quantify the degree of abnormality, as well as enable setting targets, for example when it comes to recovery of functional status after lumbar spine surgery or pro-

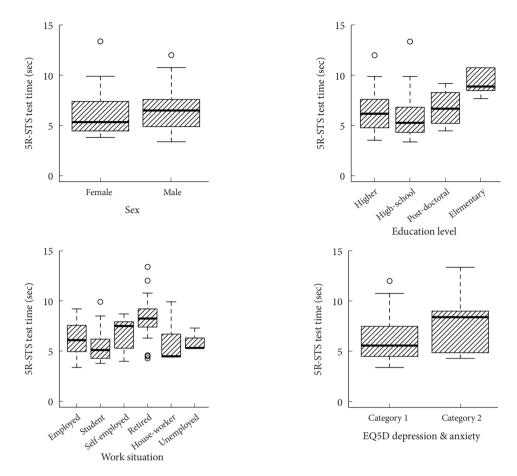


Fig. 2. Boxplots of categorical factors associated with 5-repetition sit-to-stand test (5R-STS) test time in healthy adult individuals.

longed intensive care unit stays.

The statistical analysis of factors associated with 5R-STS performance was performed using the purposeful variable selection algorithm, which substantiates that variables included in the final model significantly influence the 5R-STS test time either by statistical significance of a low p-value or by providing adjustment for other variables, known as confounding.³⁰ This method is often deemed superior to forward and backward stepwise selection models, or those based on simple univariate filtering, as it reduces the risk of missing meaningful variables that failed to have a p-value of <0.05—or any other threshold for that matter—initially. 30,32,33 Many question the validity of the commonly used p-value cutoff of < 0.05, often suggesting that it is an arbitrary threshold creating a fallacious reassurance of significance. 34,35 Through the use of this approach in this study, all relevant variables that were collected are ascertained to be included in the multivariable model, without missing out on important confounders.

The identified age-associated increase in 5R-STS test time is multifactorial and is in agreement with available literature. 17-19

Firstly, older individuals experience progressive loss of skeletal muscle mass and power.³⁶⁻³⁸ Multiple studies confirmed that the quadriceps strength is one of the most important determinants of the test performance.^{10,19,22,39} On the other hand, some data suggested that sense of balance is as crucial while other found no significant association between the 5R-STS test and the Berg Balance Scale.^{10,19,20,40} Nonetheless, all of the aforementioned components including sensorimotor and cognitive status decline with age may contribute not only to increased 5R-STS test time, but also to poorer performance across other OFI tests such as 6MWT.^{18,41-43} Therefore, it is highly recommended to include age in any proposed baseline severity stratification, or in algorithms predicting individual expected 5R-STS test time.⁵

We found that higher BMI was associated with longer 5R-STS test times. Albeit this is contrary to what Lord et al. reported in their study in an elderly population—the mean age of their participants was 80 years —this difference in results may be rationalised by increased weight in younger individuals reflecting muscle mass. ^{19,21,22} Currently, there is no consensus on the independent impact of height on OFI test's, such as the 5R-STS test. ^{19,25,44}

Performance related to height appears dependent also on standardized seat height—in our population, a standardized seat with 48-cm height was used, corresponding to a normal seat height in continental Europe. As decreased chair height increases test time, some testing protocols strongly recommended to seat an individual at their knee height to optimize the test. 45,46

In our study, level of education did not significantly influence test performance, although it was included as a confounding variable, with elementary-level education leading to marginally longer test times. It has been previously demonstrated that less educated individuals were at greater risk of decreasing their physical activity.⁴⁷ This finding was suggested to be linked to perceived control, where participants with lower education had lower self-esteem and less confidence in achieving a desired outcome, as well as being more likely to face challenges of multiple-child families and financial struggles.^{43,47}

There is a bidirectional relationship between mood and functional mobility.⁴⁸ Multiple sources have found that increased physical activity positively affects people's mental health, while other studies demonstrated presence of depressive symptoms as a strong predictor of decreased mobility and indirectly functional impairment. 48-52 In this study, the EQ-5D was utilized—a validated tool for depression and anxiety symptoms assessment that is commonly used to assess patients' psychological status.^{27,53} In patients with degenerative disease of the lumbar spine, a stepwise increase in OFI measured by the TUG test demonstrated a drop in EQ-5D by -0.073.54 A similar relationship was identified between the 6MWT and psychological status. 19,55,56 While the influence of depression and anxiety on the 5R-STS performance in our study was minimal in the multivariable model suggesting that the 5R-STS test is relatively robust towards mood factors, in contrast to many subjective questionnaires—the univariable analysis demonstrated a weak influence of depression and anxiety on 5R-STS test performance. However, this statistically significant influence disappeared after inclusion in a multivariable model.

In contrast to results of Bohannon et al.¹⁷ and Lord et al.¹⁹ in elderly patients, findings of this study —at least in the multivariable model—demonstrated a strong relationship between male sex and lower 5R-STS test times. Interestingly, studies on the 6 MWT did not identify gender differences.^{44,57} The gender difference identified in our study may be partially explained through the 5R-STS's more prominent focus on rapid lower limb muscle torque and knee extension strength, which undergoes more accelerated age-related decline in women compared to men.^{58,59}

Intriguingly, the smoking status was not a significant predictive factor for the 5R-STS test time in healthy individuals. A cross-sectional study by Heydari et al.⁶⁰ demonstrated that smokers were 4.88 more likely to experience decreased physical function compared to nonsmokers. However, they did not differentiate between 'never smokers' and 'ex-smokers,' as we did – an important distinction as irreversible airway gene expression changes persist years after smoking cessation.⁶¹ The relatively quick performance of the 5R-STS test may not be sufficient to elicit decreased physical function as a result of smoking, although it has been effectively used in COPD.⁴ Additionally, it is crucial to highlight that this study's cohort comprised of healthy individuals only without mobility issues. Smoking is said to affect physical function as result of developing severe chronic conditions which were not applicable for this cohort.⁶²

First, some categories were low in sample size. Only 3.4% of the cohort had elementary-level education, while around 63% had a higher or postdoctoral education. This statistical power may have influenced the effect size. This also applies to work situation and anxiety and depression - future studies should include a higher number of patients with anxious and depressive symptoms to more accurately study the robustness of the 5R-STS in this population. In addition, the presence of chronic conditions in volunteers was not clearly reported, which may have influenced their 5R-STS performance. However, our criteria for inclusion led to an exclusion of individuals with comorbidities typically influencing 5R-STS performance markedly. Also, we were limited in our analysis to the variables collected within the 2 prospective cohorts - any other variables such as presence of regular exercise or polypharmacy could thus not be considered. We did not include any individuals aged under 18, although the test could potentially also be used in adolescents. Finally, our data may only generalize to a Dutch population. As has been observed for other measurements, such as the EQ-5D or the 6MWT, different populations may require different normative values. Further studies should aim to distinguish between different nationalities and ethnicities. 63,64

CONCLUSION

The presented reference values can be applied as normative data for the 5R-STS in healthy adult individuals of all age groups, and are necessary to judge what constitutes abnormal performance. We identified several factors associated with 5R-STS performance that must be taken into account and that may be applied to calculate individualized expected test times. Notably,

the 5R-STS does not appear to be significantly influenced by anxiety and depression.

CONFLICT OF INTEREST

The authors have nothing to disclose.

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SUPPLEMENTARY MATERIALS

Supplementary Content 1 and Table 1 can be found via https: //doi.org/10.14245/ns.2142750.375.

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Supplementary Content 1. Statistical code. R Code for the statistical analysis figure rendering. The code was executed in R Version 3.5.2 (The R Foundation for Statistical Computing, Vienna, Austria) on a machine running macOS Catalina Version 10.15.6. The raw data will be made available by the authors on request.

Supplementary Table 1. Reference values for the 5R-STS test time (second) in healthy individuals ≤ 60 years of age

Age (yr)	Mal	Male		Female		Overall	
	Mean ± SD	ULN	Mean ± SD	ULN	Mean ± SD	ULN	
20-30 yr	5.24 ± 1.36	8.15	5.18 ± 1.08	7.59	5.20 ± 1.18	8.13	
31-40 yr	5.89 ± 1.10	7.49	5.60 ± 1.68	9.01	5.73 ± 1.47	9.0	
41-50 yr	7.01 ± 1.88	8.49	5.91 ± 1.19	7.66	6.46 ± 1.25	8.48	
51-60 yr	7.02 ± 1.44	8.91	6.64 ± 1.82	8.83	6.83 ± 1.63	8.95	

Mean \pm standard deviation (SD) and ULN (upper limits of normal) are provided for each subpopulation. 5R-STS, 5-repetition sit-to-stand test.