Test-retest reliability, validation, and 'minimal detectable change' scores for frequently reported tests of objective physical function in patients with non-dialysis chronic kidney disease

Thomas J. Wilkinson, PhD [1]; Soteris Xenophontos, MSc[1]; Douglas W. Gould, MSc[1]; Barbara P. Vogt, MSc [2]; João L. Viana, PhD [3, 4]; Alice C. Smith, PhD [1, 5]; Emma L. Watson, PhD [1]

[1] Leicester Kidney Exercise Team, Department of Infection, Immunity and Inflammation, University of Leicester, United Kingdom; [2] Department of Clinical Medicine, Faculdade de Medicina de Botucatu, Univ Estadual Paulista, UNESP, Brazil; [3] School of Sport, Exercise and Health Sciences, Loughborough University, United Kingdom; [4] Research Center in Sports Sciences, Health Sciences and Human Development, CIDESD, University Institute of Maia, ISMAI, Portugal; [5] John Walls Renal Unit, Leicester General Hospital, University Hospitals of Leicester Trust, United Kingdom.

Disclosure of interest(s)

The authors report no conflicts of interest. The views expressed are those of the authors and not necessarily those of the National Health Service (NHS), the National Institute for Health Research (NIHR), or the Department of Health. At the time of writing this manuscript, Dr. EL Watson was supported by a Kidney Research UK Post-Doctoral Fellowship. Ms. BP Vogt was sponsored by the CAPES Foundation within the Ministry of Education, Brazil.

This analysis forms part of a larger body of work being completed by our group (ISRCTN registration number: 36489137).

Corresponding author

Dr. Thomas J Wilkinson, Leicester Kidney Exercise Team, Department of Infection, Immunity and Inflammation, University of Leicester, United Kingdom, LE5 4PW. Email: drthomaswilkinson@gmail.com.

ABSTRACT

Physical function is an important outcome in chronic kidney disease (CKD). We aimed to establish the reliability, validity, and the 'minimal detectable change' (MDC) of several common tests used in renal rehabilitation and research. In a repeated measures design, 41 patients with CKD not requiring dialysis (stage 3b to 5) were assessed at an interval of 6 weeks**.** The tests were: the incremental shuttle walk test (ISWT), 'sit-to-stand' (STS) test, estimated 1 repetition maximum for quadriceps strength (e1RM), and VO_{2peak} by cardiopulmonary exercise testing (CPET). Reliability was assessed using intraclass correlation co-efficient (ICC) and Bland-Altman analysis, and absolute reliability by standard error of measurement and MDC. The ISWT, STS-60, e1RM, and CPET had 'good' to 'excellent' reliability (.973, .927, .927, and .866). STS-5 reliability was poor (.676). The MDC are: ISWT, 20 m; STS-5, 7.5 secs; STS-60, 4 reps; e1RM, 6.4 kg; VO_{2peak}, 2.8 ml/kg/min. There was strong correlation between the ISWT and VO_{2peak} (r = 0.73 and 0.74). Whilst there was poor correlation between the STS-5 and e1RM (r = 0.14 and 0.47), better correlation was seen between STS-5 and ISWT (r = 0.55 and 0.74). In conclusion, the ISWT, STS-60, e1RM, and CPET are reliable tests of function in CKD. The ISWT is a valid means of exercise capacity. The MDC can help researchers and rehabilitation professionals interpret changes following an intervention.

Keywords

Chronic Kidney Diseases; Muscle strength; Outcome Assessment**;** Rehabilitation**;** Renal Insufficiency**;** Walking

INTRODUCTION

Chronic kidney disease (CKD) is associated with adverse clinical outcome and reduced quality of life (Levey et al., 2005). CKD patients have reduced physical functioning (Hiraki et al., 2013; Kuo et al., 2015; Segura-Ortí, Gordon, Doyle, and Johansen, 2017), which is partly attributable to fatigue and muscle wasting characteristic of the condition (Wang and Mitch, 2014). Reductions in physical function begin early in the disease process (Hiraki et al., 2013), and are independently associated with mortality (Roshanravan et al., 2013). Consequently, physical function is an important target for research and rehabilitative intervention.

Physical function can be assessed using a range of field tests. The incremental shuttle walk test (ISWT) is a popular measure of exercise capacity, and has been used extensively in patient populations such as chronic obstructive pulmonary disease (COPD) (Singh, Jones, Evans, and Morgan, 2008), haemodialysis (HD) (Wilund et al., 2010), and non-dialysis CKD (Greenwood et al., 2012; Watson et al., 2015). Another well-established measure is the multi-variant 'sit-to-stand' (STS) test. The STS-5 repetition test is an assessment of lower body muscle strength, dynamic balance (Mong, Teo, and Ng, 2010), and exercise capacity (Jones et al., 2013), whilst the STS-60 second test measures lower body muscle endurance (Jones et al., 2013; Mong et al., 2010; Puthoff and Saskowski, 2013; Rikli and Jones, 2013; Segura-Ortí and Martínez-Olmos, 2011). These tests reflect a common activity of daily living (i.e. getting up from a chair), and are widely used in clinical and CKD research (Greenwood et al., 2012; McIntyre et al., 2006; Segura-Ortí et al., 2017; Segura-Ortí and Martínez-Olmos, 2011).

Reliability indicates the degree to which scores of a test are free of measurement errors. Recognising the error inherent in outcome measures is imperative to the understanding of changes and interpretation of research or rehabilitative interventions. Reliability can be expressed in both relative and absolute terms. Relative (or test-retest) reliability can be measured using intraclass correlation co-efficient (ICC). Absolute reliability refers to individual performance variation and measurement error, and is quantified as standard error of measurement (SE_M) (Ries, Echternach, Nof, and Blodgett, 2009; Stratford, 2004).

Using the SE_M, a more clinically useful means of interpreting reliability is the 'minimal detectable change' (MDC) (Haley and Fragala-Pinkham, 2006), defined as the smallest amount of reliable change in a measurement necessary to conclude that the difference is not attributable to error (Segura-Ortí and Martínez-Olmos, 2011). Change exceeding the MDC is considered 'true' change (Haley and Fragala-Pinkham, 2006). The MDC can be calculated at an individual (MDC_{indv}) and group (MDC_{group}) level. The MDC_{indv} shows whether observed changes in the individual's status are greater than variations of chance (Lee et al., 2013), whereas the MDC_{group} is required to determine the relevance of changes across samples (Busija et al., 2008; De Vet, Bouter, Bezemer, and Beurskens, 2001).

Alongside reliability, validity is also an important construct of physical performance tests. Whilst the 'gold standard' measure of exercise capacity is cardiopulmonary exercise testing (CPET) of VO_{2peak}, it is often impractical in rehabilitative settings, particularly in vulnerable clinical patients. As such, the ISWT is frequently used as its surrogate measure (Holland et al., 2014; Singh et al., 1994). Although the ISWT has been validated against CPET (via cycle ergometer and treadmill modality) in other clinical populations (Arnardóttir et al., 2006;

106 Green et al., 2001; Holland et al., 2014; MacSween, Johnson, Armstrong, and Bonn, 2001;
107 Moloney et al., 2003), it has *not* yet been validated in CKD.
108
109 Lower body strength is important in CKD as the muscle of the legs are typically atrophied
110 (Wang and Mitch, 2014). Whilst the STS-5 may act as a surrogate measure of strength
111 (McCarthy, Horvat, Holtsberg, and Wisenbaker, 2004; Mong et al., 2010; Rikli and Jones,
112 2013), calculating 1 rep maximum (1RM) strength using resistance machines may be more
113 applicable in non-laboratory settings (i.e. a gymnasium) where dynamometry is not available
114 (Gail and Künzell, 2014).
115
116 No previous estimates of MDC for physical function tests exist for non-dialysis CKD
117 patients, and neither the ISWT nor STS-5 have not been validated in this group. Despite only
118 ~5% of CKD patients progressing to end-stage renal disease (and requiring renal replacement
119 therapy e.g., HD) (Dalrymple et al., 2011), research, particularly in regard to rehabilitation,
120 into non-dialysis patients often falls behind that of HD (Heiwe and Jacobson, 2014). With
121 reductions in physical function, an independent measure of mortality (Roshanravan et al.,
122 2013), evident in the early stages of CKD (Hiraki et al., 2013), it appears fundamental that
123 interventions designed to improve functional status (e.g., exercise (Heiwe and Jacobson,
124 2014)) are initiated promptly in the disease process and before it can progress. Furthermore,
125 with non-dialysis patients often experiencing differing functional capacities to other disease
126 populations (e.g., COPD), and indeed other CKD groups (e.g., those on HD (Hiraki et al.,
127 2013; Segura-Ortí et al., 2017)), the identification of the reliability and validity of physical
128 function tests specific to the non-dialysis population is vital in the correct interpretation of
129 functional changes.
130

131 The aims of the current study were to: 1) determine the test-retest reliability and estimated
132 MDC of the common physical function tests in patients with non-dialysis CKD; and 2)
133 confirm the validity of the ISWT as a measure of exercise capacity (VO_{2peak}), and the STS as
134 a measure of lower body strength.

METHODS

All assessments took place between December 2013 and June 2016 at Leicester General Hospital, Leicester, UK. Patients were recruited from nephrology outpatient clinics at the University Hospitals of Leicester NHS Trust. Patients gave written informed consent in accordance with the Declaration of Helsinki and local Research Ethics Committee approval was obtained. This analysis forms part of a larger body of work completed by our group (ISRCTN registration 36489137). To ensure accurate reporting of study measurement properties and analysis parameters, the 'COnsensus-based Standards for the selection of health Measurement Instruments' (COSMIN) checklist was adhered to (Mokkink et al., 2010).

Participants

Patients were recruited if they had: CKD stages 3b-5 (i.e. an estimated glomerular filtration rate (eGFR) of ≤44 ml/min/1.73^2) *not* requiring renal replacement therapy (e.g., HD); were aged ≥18; no significant co-morbidity (e.g., unstable hypertension, potentially lethal arrhythmia, myocardial infarction within the previous six months) contraindicative to physical exercise; no significant physical impairment; and sufficient ability to give informed consent. Prior exercise and physical activity level was not a pre-requisite for inclusion.

The severity of comorbidity was recorded and scored according to Charlson Comorbidity Index (CCI). A higher CCI score indicated greater comorbidity, and CCI scores of 1–2 were classified as mild; scores of 3–4 as moderate; and scores ≥ 5 as severe (Huang et al., 2014).

Physical function assessments

Assessments were performed at two time points (test 1 and 2) separated by a six week period in which patients were instructed to maintain their habitual lifestyle. The six week interval forms part of a control period in the main trial, thus we used pre- and post-data as an opportunity to assess the reliability of the tests employed. All researchers performing the tests followed strict operating procedures for each of the tests performed to reduce investigator bias. As different researchers were used, we do not present *intra*-rater reliability, but *inter*-rater reliability. Each test was performed in the same order (STS tests, ISWT, and e1RM). As CPET was used to screen patients for cardio-pulmonary contraindications, and due to the relative exhaustive aspect of the test, CPET was performed on a separate visit several days before. All tests, apart from CPET due to logistic and cost factors, had a familiarisation test several days prior to their first test to minimise learning effect (Holland et al., 2014). The familiarisation testing session involved an explanation of the test to the patient, short demonstration of the basic movement(s) by the researcher present, a practice repetition (if appropriate), and then the full test. On the day of testing, following a re-explanation of the test, patients performed each test once.

ISWT

The ISWT is maximally progressive test that involves walking at a pace externally dictated by an auditory tone (Holland et al., 2014; Singh et al., 1994). During the test, the patient walked a total of 10m back and forth and around two cones. The walking pace was increased by a rate of 0.17m/sec every minute for twelve stages until the patient could no longer keep up with the pace because of breathlessness, pain, or other symptoms. Only completed shuttles were counted. The outcome was distance walked (m).

The ISWT was preferred over other measures of exercise capacity, such as the 6-minute walk test (6MWT), as this test requires at least 30m of walking space (Holland et al., 2014); provisions not available at our research facility. However, along with reducing limitations associated with being self-paced, the ISWT may also provide superiority when prescribing exercise intensity as a % of peak performance (Holland et al., 2014), and thus may be more beneficial in a renal rehabilitation setting when tailoring individualised exercise interventions.

STS tests

The STS-5 and -60 tests were employed as measures of lower body strength and muscle endurance (Mong et al., 2010; Rikli and Jones, 2013; Segura-Ortí and Martínez-Olmos, 2011). The patient sat on a seat (43.2 cm from the ground). With their hands across their chest, patients were asked to: 1) perform five complete STS cycles as fast as possible (STS-5); and 2) perform as many complete STS cycles in 60 secs (STS-60). The STS-5 time was stopped when the patient was seated following their fifth repetition. If the patient was half-way through a stand when STS-60 time had expired, this was counted as one repetition (Rikli and Jones, 2013). The STS-5 test was preferred over other STS versions (e.g., STS-10) as its short duration reduces patient burden during testing sessions involving multiple other outcomes (Nilsagård, Andreasson, Carling, and Vesterlin, 2017).

Lower limb strength

The maximal strength (kg) of the quadriceps muscle was measured using a leg extension machine (TechnoGym, Italy). Performing a true 1RM test is associated with an increased injury risk and stress on the muscles and joints, particularly in untrained (Gail and Künzell, 2014) and clinical groups (Abdul-Hameed, Rangra, Shareef, and Hussain, 2012), therefore

we estimated 1RM (e1RM) for the leg extension exercise from a 5-rep maximum (5RM) (Brzycki, 1993; Dudgeon et al., 2010). During the test, weight was progressively increased by a minimum of 2.5 kg depending on participant feedback and ease of the previous 5 repetitions. To reduce cumulative fatigue and to ensure an accurate 5RM, patients were given a minimum 60 second rest in-between each attempt, although researcher discretion was also used. The 5RM was determined as the maximal weight the patient could lift five times with correct technique.

CPET

Peak exercise capacity (VO_{2peak}) was assessed using CPET. Patients were asked to cycle for as long as possible at a revolutions per minute (RPM) ≥60. Following a 3 minute warm up, the resistance on the static ergometer (Lode Excalibur, Netherlands) increased from 30 Watts by 1 Watt every 3 secs in a ramp protocol. Throughout the test, an echocardiogram was performed and reviewed by an experienced exercise cardiac nurse or doctor. The test was stopped if: RPM <60; the patient reached volitional exhaustion; or at the discretion of the medical professional. Using online direct breath-by-breath measurement (Cortex Metalyzer, Cranlea, UK) of oxygen consumption (VO_2), we calculated relative VO_{2peak} (peak ml/kg/min).

Statistical methods

Test-retest relative reliability of data was assessed using the ICC (*r*). An ICC between .600-.749 is considered 'fair', ≥.750 'good', whilst a value ≥.900 is considered 'excellent' for clinical measures (Cicchetti, 1994). Data is also represented graphically as Bland-Altman plots with mean bias and limits of agreement set at 95% confidence intervals (95CI) (Bland

and Altman, 1999). Here the difference of the two paired measurements is plotted against the mean of the two measurements.

The SE_M and MDC were calculated as a measure of absolute reliability (Haley and Fragala-Pinkham, 2006; Stratford, 2004). The SE_M was calculated as:

$$SE_M = SD * \sqrt{(1-r)}.$$

This method of calculating SE_M has been used previously (Chiu et al., 2016; Ries et al., 2009; Segura-Ortí and Martínez-Olmos, 2011). The MDC at an individual level (MDC_{indv}) was calculated at the 95CI. The equation used was:

$$MDC_{indv} = SE_M * 1.96 * \sqrt{2}.$$

The 1.96 represents the z-score at the 95CI. The 'SE_M * 1.96' is multiplied by the $\sqrt{2}$ to account for errors associated with repeated measures (De Vet et al., 2001; Haley and Fragala-Pinkham, 2006; Segura-Ortí and Martínez-Olmos, 2011; Stratford, 2004). The MDC at group level (Busija et al., 2008; De Vet et al., 2001) (MDC_{group}) was calculated as:

$$MDC_{group} = MDC_{indv} / \sqrt{n}.$$

Construct validity between the ISWT and CPET derived VO_{2peak}, and between the STS-5 and e1RM was assessed using simple linear regression and data are represented as scatterplot graphs with a trend line showing *r* and 95CI interval bands.

A minimum sample size of 39 patients was needed to estimate an ICC *r* of .600 (the minimal acceptable ICC in clinical investigations (Shoukri, Asyali, and Donner, 2004)) with a β of 0.80 at a significance level of $P = 0.050$ (Walter, Eliasziw, and Donner, 1998). Data was assessed using SPSS v24. Data are reported as mean (SD), if normally distributed, or as median (interquartile range, IQR). Distribution was assessed using the Kolmogorov-Smirnov test. Paired comparisons were tested using paired *t*-tests, or non-parametric Wilcoxon signed rank test as appropriate. Difference (with 95CI) is reported as mean (if data were normally distributed), or median (if data were non-normally distributed). Data for some individuals were not collected for different assessments due to missed measures or an inability to complete (see footnote of **Table 2**); consequently, with no comparable data, this patient was excluded (listwise approach) from analysis in that test.

RESULTS

Forty-one patients (23 females, 56%) with non-dialysis CKD were recruited. Mean patient age was 62 (SD: 11) years old with a body mass index of 30.1 (SD: 5.7). The majority of patients were Caucasian (66%). The mean eGFR was 25 (SD: 8) ml/min/1.73^2. Over half of patients (63%) had previously diagnosed hypertension and 22% of patients had diabetes mellitus type II. The mean CCI score was 2.5 (SD: 0.7), with the majority of patients (59%) classified as having a mild CCI score. Full patient clinical and demographic characteristics are shown in **Table 1.** Apart from anticipated exercise-induced fatigue during the tests, no adverse events of complaints were recorded.

Test-retest relative and absolute reliability

There was minimal difference between the two tests for the ISWT, STS-60, e1RM, and VO_{2peak} by CPET with ICC *r* values of .973, .927, .927, (all rated as 'excellent') and .866 (rated 'good'), respectively. Conversely, the ICC for the STS-5 displayed only 'fair' agreement (*r* = .676). Data analysis revealed no statistically significant differences between the two tests for each measure of function **(Table 2)**. **Figure 1A–E** shows Bland-Altman plots with bias and limits of agreement (at 95CI) for each of these tests. Absolute reliability data (both SE_M and MDC) are shown in **Table 3**.

The proportion of patients whom performed best in test 1 was as follows: ISWT (n = 16, 39%), STS-5 (n = 18, 44%), STS-60 (n = 14, 35%), e1RM (n = 9, 23%), and VO_{2peak} (n = 20, 54%). No change between test 1 and 2 was observed in n = 3 (7%) for the ISWT; n = 2 (5%) for the STS-60; n = 9 (23%) for the e1RM; and n = 1 (3%) for VO_{2peak} by CPET.

295 **Validation of the ISWT and STS-5**

296 We found a 'strong' correlation between the ISWT and VO_{2peak} test with an *r* of 0.73 at time
297 point 1 ($P < 0.001$), and an *r* of 0.74 at time point 2 ($P < 0.001$) (**Figure 2A–B**). The
298 correlation between the STS-5 and the e1RM test was 'poor' at time point 1 ($r = 0.14$, $P =$
299 0.371), and (albeit better) 'weak' at time point 2 ($r = 0.47$, $P = 0.003$) (**Figure 2C–D**). When
300 we compared the STS-5 with ISWT, we found 'moderate' correlation at time point 1 ($r =$
301 0.55, $P < 0.001$), and 'strong' correlation at time point 2 ($r = 0.74$, $P < 0.001$) (**Figure 2E–F**).
302

DISCUSSION

This study is the first investigation into the test-retest reliability and identification of the MDC for tests of physical function in a non-dialysis CKD population. Our results have large clinical relevance in CKD research and rehabilitation, and demonstrate that the ISWT, STS-60, e1RM, and VO_{2peak} via CPET have 'good' to 'excellent' reliability in non-dialysis CKD. Conversely, the STS-5 test performed poorly with only 'fair' agreement. Using SEM data, we were able to calculate the MDC at an individual and group level. We also confirmed the ISWT as a valid measure of VO_{2peak}, but found the STS-5 only weakly associated with lower limb strength.

The ISWT in our trial showed excellent test-retest reliability with an ICC of .973. This corresponds well with previous estimates in cardiac rehabilitation patients (.990) (Hanson, Taylor, and McBurney, 2015), patients with peripheral vascular disease (.990) (Cunha-Filho et al., 2008), and non-cystic fibrosis (.950) (Lee et al., 2015). The ISWT is used extensively in research and rehabilitation as a measure of exercise capacity, and as stated previously, was chosen above the 6MWT, another common field test of exercise capacity, for several reasons including space considerations and the limitations associated with self-paced tests. Furthermore, given its progressive nature, the ISWT is superior when prescribing exercise intensity (e.g., % of maximum) (Holland et al. 2014), and thus potentially more useful in a renal rehabilitation setting. Studies validating the ISWT against CPET-measured VO_{2peak} have found good agreement (r = 0.74 to 0.88) regardless of exercise modality (i.e. treadmill versus cycle ergometer) (Arnardóttir et al., 2006; Green et al., 2001; Holland et al., 2014; MacSween et al., 2001; Moloney et al., 2003). Our r values of 0.73 and 0.74 represent a

strong agreement, and confirm the ISWT as a valid and easy means to assess exercise capacity in a CKD population.

The STS-60 had excellent reliability with an ICC of .927. Similarly, Segura-Ortí and Martínez-Olmos (2011) found an ICC of .970 in HD patients; however, other clinical research into the reliability of the STS-60 is limited. Conversely, the STS-5 displayed relatively poor reliability with an ICC of .676 ('fair'). Whilst this contrasts with previous estimates in clinical populations (ICC values between .940 and .990), (Jones et al., 2013; Mong et al., 2010; Thomas and Hageman, 2002), similar reliability (ICC of .640) was reported by Ostchega et al (Ostchega et al., 2000) in older adults. Unfortunately, the authors in this trial offer no explanation for their moderate reliability score. The lack of reliability in our study may be due to the large within-patient variability seen in our sample. Indeed, several patients took considerably longer on their first attempt than on their second: one patient performed 25.8 seconds quicker in the STS-5 at visit 2. When we removed this patient, the ICC for the STS-5 increased to .752 (.577 - .860), and although defined as now 'good', this still lacked the reliability observed relative to our other tests. As the aim of this study was to assess natural variation, and with no clinical justification to remove this patient, we retained this data point in the analysis

As recommended by Nilsagård et al. (2017), the STS-5 was preferred over the STS-10, another commonly reported STS variant, to: 1) ease patient burden (i.e. STS-5 takes ~50% less time); and 2) to isolate the assessment of strength. Given the requirement to complete double the repetitions, the STS-10 has been described as a measure of muscular endurance (Nilsagård et al. 2017), whereas the STS-5 is purported as a measure of lower limb strength. Therefore, to avoid multiple assessments of muscular endurance we used the STS-5.

Nonetheless, we observed a weak relationship between the STS-5 and lower limb strength (by e1RM), suggesting that, in our patients, the STS-5 may not be a comprehensive proxy measure of strength. Whilst this supports previous work which found the STS-5 had only a modest relationships with lower limb strength in COPD (Jones et al., 2013; Roig et al., 2011), it conflicts with research that suggests in both elderly and stroke patients, the STS-5 is a good marker of lower body strength (Mong et al., 2010). Interestingly, although we were unable to demonstrate any strong relationship between STS-5 and lower limb muscle strength, we did observe a strong to moderate association between the STS-5 and the ISWT. Similar observations have been reported by Jones et al (2013) in COPD patients. In CKD clinical practice and research, other methods to measure lower limb strength should be employed over the STS-5.

Limited research exists on the reliability of the e1RM estimated by a 5RM test. Our ICC value of .927 compares well with previous estimates in healthy recreational athletes (.900) (Gail and Künzell, 2014), and in untrained diabetic patients (.990) (Abdul-Hameed et al., 2012). Although dynamometry is considered the 'gold standard' for the assessment of strength, e1RM testing is commonly applied for ease and simplicity, and represents a valid means to assess leg muscle strength (Verdijk, Van Loon, Meijer, and Savelberg, 2009). We experienced no serious difficulties performing a 5RM test, and therefore in gymnasium-based rehabilitative setting, where dynamometers are unavailable, a 5RM test may be a safe and reliable tool in strength measurement in CKD.

As expected, the 'gold standard' of assessing exercise capacity (VO_{2peak}) by CPET showed good (bordering on 'excellent') test-retest reliability. Our ICC of .866 compares well with

previous testing in clinical groups, including patients with multiple sclerosis (.933) (Heine et al., 2015) and coronary heart disease (.970) (Coeckelberghs et al., 2016).

The MDC is the smallest change that falls outside the expected range of error (Segura-Ortí and Martínez-Olmos, 2011), and is invaluable to know as any change from a clinical intervention exceeding the MDC can be considered a 'true' change (Haley and Fragala-Pinkham, 2006). We were able to calculate the MDC at both an individual and group level. An MDC at individual level is should be used to determine whether a single patient has made an improvement, not attributable to error, following an intervention (Haley and Fragala-Pinkham, 2006; Lee et al., 2013). This may be useful to physical therapists, or other allied professionals, whom work with, and interpret changes of, individual patients. Conversely, as the majority of clinical trials compare changes between groups of patients, the MDC_{indv} should be adapted to quantify the MDC of an outcome measure in a group of patients (De Vet et al., 2001). Often the MDC_{group} is smaller than the corresponding MDC_{indv} implying superiority at detecting change at group level (De Vet et al., 2001).

At an individual level, the MDC for the ISWT was 20m. The small MDC_{group} (3m) found suggests that, at group level, small changes in ISWT scores can be reliably identified. To our knowledge, this is the *first* estimate of the MDC for this test in *any* clinical population.

For the STS-60, we found an MDC_{indv} of 4 reps. Similar findings have been reported in HD patients (4 reps) (Segura-Ortí and Martínez-Olmos, 2011). This is perhaps due to the similar mean number of repetitions (26) between their HD patients and our non-dialysis CKD sample. Whilst such comparable functional capacity between HD and non-dialysis CKD patients may be unexpected, the majority of patients in the Segura-Ortí and Martínez-Olmos

trial were almost exclusively male (82%). Male CKD patients (including those on HD) display superior functional capacity than females (Hiraki et al., 2013); as our sample was majority female (56%), this may explain the comparable results observed. At a group level, the high reliability and low measurement error of the STS-60 means the MDC_{group} is just 1 rep.

Whilst an MDC of 3.1 secs has been reported for the STS-5 in patients undergoing cardiac rehabilitation (Puthoff and Saskowski, 2013) and 5.0 secs in those with stroke (Pardo et al., 2013), our data revealed an MDC_{indv} of 7.5 secs and an MDC_{group} of 1.2 secs. Our larger MDC values could be due to the poor reliability for this test as discussed previously.

Whilst no MDC exists for 1RM testing, using dynamometry, in patients with knee osteoarthritis, the MDC using peak isokinetic knee extension torque was estimated at 3.5 kg (Kean et al., 2010). This value is smaller than our estimated MDC_{indv} of 6.4 kg. A possible explanation for the larger value in our trial may be due to equipment limitations. The machine used only increased in increments of 2.5 kg and above, thus limiting the ability to increase weight in smaller increments. Whilst the e1RM has been shown to represent a valid measure of strength assessed by dynamometer (Verdijk et al., 2009), further research is needed to assess the validity in a CKD group.

The MDC_{indv} for VO_{2peak} was 2.8 ml/kg/min, and 0.5 ml/kg/min at group level. Brehm et al. (Brehm, Balemans, Becher, and Dallmeijer, 2014) previously estimated an MDC_{indv} of 5.7 ml/kg/min in patients with cerebral palsy, whilst in patients with multiple sclerosis, Heine et al. (Heine et al., 2015) calculated the MDC_{indv} at 4.6 ml/kg/min and the MDC_{group} at 0.8 ml/kg/min. Like the ISWT, the small MDC_{group} identified suggests that small changes in

427 VO_{2peak} can be identified. This is perhaps unsurprising given the highly technical analysis of
428 CPET.
429
430 We have confirmed the ISWT as a valid assessment of exercise capacity, although
431 disappointingly the STS-5 was not associated with lower limb strength. The low *r* at time
432 point 1 between the STS-5 and e1RM may be attributed to the outlier situated to the far right
433 of the Bland-Altman plot. However, as stated above, with no clinical justification to remove
434 this patient, we retained this data point in the analysis. Nonetheless, even at time point 2, the
435 *r* value (0.47) was still poor. The STS test as a proxy measure of lower limb strength (Mong
436 et al., 2010; Rikli and Jones, 2013) is increasingly being questioned by researchers
437 (McCarthy et al., 2004), and study has shown that only a moderate proportion of STS
438 performance is attributable to strength, with factors such as balance and sensorimotor ability
439 also contributing (McCarthy et al., 2004). Indeed, our data, and that of others (Jones et al.,
440 2013), suggests that the STS-5 may actually be a better measure of exercise capacity than
441 strength. As such, additional physiological factors may be contributing, and further research
442 is required into the identifying these elements and assessing the validity of the STS-5.
443
444 **Study limitations**
445 Our patient population was an opportunistic sample taken from a larger body of work
446 completed by our group. Nonetheless, the 41 patients included in the current analysis was
447 above the minimum sample size of 39 patients required to estimate an ICC r of .600 (the
448 minimal acceptable ICC in clinical investigations). Consequently, our analysis was
449 sufficiently powered to detect any differences between time points.
450

Another limitation in our trial was the six week test-retest interval. However, as our data is derived from the control period the larger trial, this period was unavoidable. Nevertheless, our trial was suitably powered and our data shows even over a six week period, the reliability of our function tests was good. Furthermore, previous test-retest estimates of the reliability of objective function such as the STS (Schaubert and Bohannon, 2005a; Schaubert and Bohannon, 2005b) and strength (Schaubert and Bohannon, 2005b) over a similar six week interval have also established good agreement.

In order to ensure accurate baseline data and to reduce learning effects (Holland et al., 2014; Johnson-Warrington, Sewell, Morgan, and Singh, 2015), patients completing the ISWT at visit 1 did so after a familiarisation test several days before. However, due to time constraints at the second visit, it was feasible that the ISWT, and other outcomes, were repeated only once. Whilst we observed good reliability between the two visits for the ISWT without re-familiarisation at visit 2, it is unclear from our data if lack of re-familiarisation has effected outcome measure scores at the second visit and whether one test is sufficient if the test has previously been conducted is still unclear (Holland et al., 2014). In intervention trials, repeating, or re-familiarising patients with physical function tests may prevent underestimation of the impact of an intervention (Holland et al., 2014). Interestingly however, due to impracticality and costing, patients did not undergo familiarisation CPET at baseline; however, our results show even without this familiarisation test, reliability for CPET is high, perhaps due to the technical accuracy of the method, and a familiarisation is perhaps unnecessary for this test.

In order to further improve the methodology of our study, further research should investigate the identification of the MDC in earlier stages of CKD (1 and 2), as well as potentially

identifying differences in gender or ethnicity. In our sample, a large proportion (46%) of our patients were obese (defined by BMI), with 34% 'overweight'. Whilst more current obesity prevalence statistics are needed to fully determine the demographic of our sample, the external validity of the results may be reduced. Dynamometry, over 1- 5RM testing, should be used to accurately measure strength; as such, associations with the STS-5 should be reassessed. Additional physiological processes that contribute to function, such as balance, should also be considered in future trials assessing performance. The minimally clinical important difference, which is the minimal meaningful important difference from a patient perspective, should also be investigated.

CONCLUSIONS

In conclusion, the ISWT, STS-60, e1RM, and CPET are reliable and valid tests of function in non-dialysis CKD patients. The MDC's we have calculated in this trial are imperative in the interpretation of changes as a result of intervention trials or rehabilitation programmes. In order for a 'true' change to occur, i.e. that above individual performance variability or inherent measurement error, the value should exceed the MDC's presented here. The MDC at an individual level is useful in evaluating changes in a single patient, whilst the MDC at group level should be employed in research comparing changes between groups. The MDC should be used to help clinicians, researchers, and rehabilitation professionals interpret reliable changes in their patients and clinical trials.

Acknowledgments

We are grateful to the Stoneygate Trust for part-funding of this work. The research was supported by the National Institute for Health Research (NIHR) Leicester Biomedical Research Centre (BRC). The views expressed in this publication are those of the author(s) and not necessarily those of the NHS, the National Institute for Health Research Leicester BRC or the Department of Health. We would like to thank Ms. Amy Clarke, Mr. Darren Churchward, Mr. Patrick Highton, and Ms. Charlotte Grantham, researchers at the Leicester Kidney Exercise Team, for collection of some assessment outcome data.

REFERENCES

Abdul-Hameed U, Rangra P, Shareef MY, Hussain ME 2012 Reliability of 1-repetition maximum estimation for upper and lower body muscular strength measurement in untrained middle aged type 2 diabetic patients. Asian Journal of Sports Medicine 3: 267-73. No DOI available.

Arnardóttir RH, Emtner M, Hedenström H, Larsson K, Boman G 2006 Peak exercise capacity estimated from incremental shuttle walking test in patients with COPD: a methodological study. Respiratory Research 7:1. DOI: 10.1186/1465-9921-7-127

Bland JM, Altman DG 1999 Measuring agreement in method comparison studies. Statistical Methods in Medical Research 8: 135-60. No DOI available.

Brehm M-A, Balemans AC, Becher JG, Dallmeijer AJ 2014 Reliability of a progressive maximal cycle ergometer test to assess peak oxygen uptake in children with mild to moderate cerebral palsy. Physical Therapy 94: 121-8. DOI: 10.2522/ptj.20130197

Brzycki M 1993 Strength testing—predicting a one-rep max from reps-to-fatigue. Journal of Physical Education, Recreation & Dance 64: 88-90. No DOI available.

Busija L, Osborne RH, Nilsdotter A, Buchbinder R, Roos EM 2008 Magnitude and meaningfulness of change in SF-36 scores in four types of orthopedic surgery. Health and Quality of Life Outcomes 6: 1. DOI: 10.1186/1477-7525-6-55

533 Chiu E-C, Wu W-C, Chou C-X, Yu M-Y, Hung J-W 2016 Test-retest reliability and minimal
534 detectable change of the Test of Visual Perceptual Skills-in patients with stroke. Archives of
535 Physical Medicine and Rehabilitation. DOI: 10.1016/j.apmr.2016.04.023
536
537 Cicchetti DV 1994 Guidelines, criteria, and rules of thumb for evaluating normed and
538 standardized assessment instruments in psychology. Psychological Assessment 6: 284. No
539 DOI available.
540
541 Coeckelberghs E, Buys R, Goetschalckx K, Pattyn N, Vanhees L, Cornelissen V 2016 Test-
542 Retest Reliability of Maximal and Submaximal Gas Exchange Variables in Patients With
543 Coronary Artery Disease. Journal of Cardiopulmonary Rehabilitation and Prevention. DOI:
544 10.1097/HCR.0000000000000158
545
546 Cunha-Filho ITd, Pereira DAG, Carvalho AMBd, Campedeli L, Soares M, Freitas JdS 2008
547 Reliability of walking tests in claudicating patients: a pilot study. Jornal Vascular Brasileiro
548 7: 106-11. No DOI available.
549
550 Dalrymple, LS, Katz R, Kestenbaum B, Shlipak M, Sarnak MJ, Stehman-Breen C, Seliger S,
551 Siscovick D, Newman AB, Fried L 2011 Chronic kidney disease and the risk of end-stage
552 renal disease versus death. Journal of General Internal Medicine 26: 379-85. DOI:
553 10.1007/s11606-010-1511-x.
554
555 de Vet HC, Bouter LM, Bezemer PD, Beurskens AJ. Beurskens 2001 Reproducibility and
556 responsiveness of evaluative outcome measures. International Journal of Technology
557 Assessment in Health Care 17: 479-87. No DOI available.

Dudgeon WD, Phillips KD, Durstine JL, Burgess SE, Lyerly GW, Davis JM, Hand GA 2010 Individual exercise sessions alter circulating hormones and cytokines in HIV-infected men. Applied Physiology, Nutrition, and Metabolism 35: 560-8. DOI: 10.1139/H10-045

Gail S, Künzell S 2014 Reliability of a 5-repetition maximum strength test in recreational athletes. Deutsche Zeitschrift für Sportmedizin 65: 314-7. No DOI available.

Green D, Watts K, Rankin S, Wong P, O'Driscoll J 2001 A comparison of the shuttle and 6 minute walking tests with measured peak oxygen consumption in patients with heart failure. Journal of Science and Medicine in Sport 4: 292-300. No DOI available.

Greenwood SA, Lindup H, Taylor K, Koufaki P, Rush R, Macdougall IC, Mercer TH 2012 Evaluation of a pragmatic exercise rehabilitation programme in chronic kidney disease. Nephrology Dialysis Transplantation 27: iii126-iii34. DOI: 10.1093/ndt/gfs272

Haley SM, Fragala-Pinkham MA 2006 Interpreting change scores of tests and measures used in physical therapy. Physical Therapy 86: 735-43. No DOI available.

Hanson LC, Taylor NF, McBurney H 2015 The 10m incremental shuttle walk test is a highly reliable field exercise test for patients referred to cardiac rehabilitation: a retest reliability study. Physiotherapy. DOI: 10.1016/j.physio.2015.08.004

Heine M, van den Akker LE, Verschuren O, Visser-Meily A, Kwakkel G, Group T-AS 2015 Reliability and responsiveness of cardiopulmonary exercise testing in fatigued persons with

583 multiple sclerosis and low to mild disability. PloS One 10: e0122260. DOI:
584 10.1371/journal.pone.0122260
585
586 Heiwe S, Jacobson SH 2014 Exercise training in adults with CKD: a systematic review and
587 meta-analysis. American Journal of Kidney Diseases 64: 383-93. DOI:
588 10.1053/j.ajkd.2014.03.020
589
590 Hiraki K, Yasuda T, Hotta C, Izawa KP, Morio Y, Watanabe S, Sakurada T, Shibagaki Y,
591 Kimura K 2013 Decreased physical function in pre-dialysis patients with chronic kidney
592 disease. Clinical and Experimental Nephrology 17: 225-231. DOI: 10.1007/s10157-012-
593 0681-8
594
595 Holland AE, Spruit MA, Troosters T, Puhan MA, Pepin V, Saey D, McCormack MC, Carlin
596 BW, Sciurba FC, Pitta F, Wanger J, MacIntyre N, Kaminsky DA, Culver BH, Revill SM,
597 Hernandes NA, Andrianopoulos V, Camillo CA, Mitchell KE, Lee AL, Hill CJ, Singh SJ.
598 2014 An official European Respiratory Society/American Thoracic Society technical
599 standard: field walking tests in chronic respiratory disease. European Respiratory Society 44:
600 1428-46. DOI: 10.1183/09031936.00150314
601
602 Huang YQ, Gou R, Diao YS, Yin QH, Fan WX, Liang YP, Chen Y, Wu M, Zang L, Li L,
603 Zang J, Cheng L, Fu P, Liu F 2014 Charlson comorbidity index helps predict the risk of
604 mortality for patients with type 2 diabetic nephropathy. Journal of Zhejiang University
605 Science B 15: 58-66. DOI: 10.1631/jzus.B1300109
606

607 Johnson-Warrington V, Sewell L, Morgan M, Singh S 2015 Do we need a practice
608 incremental shuttle walk test for patients with interstitial lung disease referred for pulmonary
609 rehabilitation? Respirology 20: 434-8. DOI: 10.1111/resp.12469
610
611 Jones SE, Kon SS, Canavan JL, Patel MS, Clark AL, Nolan CM, Polkey MI, Man WDC
612 2013 The five-repetition sit-to-stand test as a functional outcome measure in COPD. Thorax
613 68: 1015-20. DOI: 10.1136/thoraxjnl-2013-203576
614
615 Kean CO, Birmingham TB, Garland SJ, Bryant DM, Giffin JR 2010 Minimal detectable
616 change in quadriceps strength and voluntary muscle activation in patients with knee
617 osteoarthritis. Archives of Physical Medicine and Rehabilitation 91: 1447-51. DOI:
618 10.1016/j.apmr.2010.06.002
619
620 Kuo Y-T, Chiu K-M, Tsang Y-M, Chiu C-M, Chien M-Y 2015 Influence of Chronic Kidney
621 Disease on Physical Function and Quality of Life in Patients after Coronary Artery Bypass
622 Grafting. Cardiorenal Medicine 5: 237-45. DOI: 10.1159/000433447
623
624 Lee AL, Cecins N, Holland AE, Hill CJ, McDonald CF, Burge AT, Rautela L, Thompson PJ,
625 Stirling RG, Jenkins S 2015 Field Walking Tests Are Reliable and Responsive to Exercise
626 Training in People With Non–Cystic Fibrosis Bronchiectasis. Journal of Cardiopulmonary
627 Rehabilitation and Prevention 35: 439-45. DOI: 10.1097/HCR.0000000000000130
628
629 Lee P, Liu CH, Fan CW, Lu CP, Lu WS, Hsieh CL 2013 The test–retest reliability and the
630 minimal detectable change of the Purdue Pegboard Test in schizophrenia. Journal of the
631 Formosan Medical Association 112: 332-37. DOI: 10.1016/j.jfma.2012.02.023

Levey AS, Eckardt K-U, Tsukamoto Y, Levin A, Coresh J, Rossert J, Zeeuw DD, Hostetter TH, Lameire N, Eknoyan G 2005 Definition and classification of chronic kidney disease: a position statement from Kidney Disease: Improving Global Outcomes (KDIGO). Kidney International 67: 2089-100. DOI: 10.1038/sj.ki.5002343

MacSween A, Johnson NJ, Armstrong G, Bonn J 2001 A validation of the 10-meter incremental shuttle walk test as a measure of aerobic power in cardiac and rheumatoid arthritis patients. Archives of Physical Medicine and Rehabilitation 82: 807-10. DOI: 10.1053/apmr.2001.23185

McCarthy EK, Horvat MA, Holtsberg PA, Wisenbaker JM 2004 Repeated chair stands as a measure of lower limb strength in sexagenarian women. The Journals of Gerontology Series A: Biological Sciences and Medical Sciences 59: 1207-12. No DOI available.

McIntyre CW, Selby NM, Sigrist M, Pearce LE, Mercer TH, Naish PF 2006 Patients receiving maintenance dialysis have more severe functionally significant skeletal muscle wasting than patients with dialysis-independent chronic kidney disease. Nephrology Dialysis Transplantation 21: 2210-6. DOI: 10.1093/ndt/gfl064

Mokkink LB, Terwee CB, Knol DL, Stratford PW, Alonso J, Patrick DL, Bouter LM, de Vet HCW 2010 The COSMIN checklist for evaluating the methodological quality of studies on measurement properties: A clarification of its content. BMC Medical Research Methodology 6: 2. DOI: 10.1186/1471-2288-6-2

Moloney E, Clayton N, Mukherjee D, Gallagher C, Egan J 2003 The shuttle walk exercise test in idiopathic pulmonary fibrosis. Respiratory Medicine 97: 682-7. No DOI available.

Mong Y, Teo TW, Ng SS 2010 5-repetition sit-to-stand test in subjects with chronic stroke: reliability and validity. Archives of Physical Medicine and Rehabilitation 91: 407-13. DOI: 10.1016/j.apmr.2009.10.030

Nilsagård Y, Andreasson M, Carling A, Vesterlin H 2017 Examining the validity and sensitivity to change of the 5 and 10 sit-to-stand tests in people with multiple sclerosis. Physiotherapy Research International. [Epub ahead of print]. DOI: 10.1002/pri.1681

Ostchega Y, Harris TB, Hirsch R, Parsons VL, Kington R, Katzoff M 2000 Reliability and prevalence of physical performance examination assessing mobility and balance in older persons in the US: data from the Third National Health and Nutrition Examination Survey. Journal of the American Geriatrics Society 48: 1136-41. No DOI available.

Pardo V, Knuth D, McDermott B, Powell J, Goldberg A 2013 Validity, reliability and minimum detectable change of the maximum step length test in people with stroke. Journal of the Neurological Sciences 325: 74-8. DOI: 10.1016/j.jns.2012.11.021

Puthoff ML, Saskowski D 2013 Reliability and responsiveness of gait speed, five times sit to stand, and hand grip strength for patients in cardiac rehabilitation. Cardiopulmonary Physical Therapy Journal 24: 31. No DOI available.

681 Ries JD, Echternach JL, Nof L, Blodgett MG 2009 Test-retest reliability and minimal
682 detectable change scores for the timed “up & go” test, the six-minute walk test, and gait
683 speed in people with Alzheimer disease. Physical Therapy 89: 569-79. DOI:
684 10.2522/ptj.20080258
685
686 Rikli RE, Jones CJ 2013 Development and validation of criterion-referenced clinically
687 relevant fitness standards for maintaining physical independence in later years. The
688 Gerontologist 53: 255-67. DOI: 10.1093/geront/gns071
689
690 Roshanravan B, Robinson-Cohen C, Patel KV, Ayers E, Littman AJ, De Boer IH, Ikizler TA,
691 Himmelfarb J, Katzel LI, Kestenbaum B, Seliger S 2013 Association between physical
692 performance and all-cause mortality in CKD. Journal of the American Society of Nephrology
693 2012070702. DOI: 10.1681/ASN.2012070702.
694
695 Schaubert K, Bohannon RW 2005a Reliability of the sit-to-stand test over dispersed test
696 sessions. Isokinetics and Exercise Science 13: 119-22. No DOI available.
697
698 Schaubert KL, Bohannon RW 2005b Reliability and validity of three strength measures
699 obtained from community-dwelling elderly persons. The Journal of Strength & Conditioning
700 Research 19: 717-20. DOI: 10.1519/R-15954.1
701
702 Segura-Ortí E, PL Gordon, JW Doyle, KL Johansen 2017 Correlates of Physical Functioning
703 and Performance Across the Spectrum of Kidney Function. Clinical Nursing Research
704 1054773816689282. DOI: https://doi.org/10.1177/1054773816689282
705

706 Segura-Ortí E, Martínez-Olmos FJ 2011 Test-retest reliability and minimal detectable change
707 scores for sit-to-stand-to-sit tests, the six-minute walk test, the one-leg heel-rise test, and
708 handgrip strength in people undergoing hemodialysis. Physical Therapy 91: 1244-52. DOI:
709 10.2522/ptj.20100141
710
711 Shoukri M, Asyali M, Donner A 2004 Sample size requirements for the design of reliability
712 study: review and new results. Statistical Methods in Medical Research 13: 251-71. No DOI
713 available.
714
715 Singh SJ, Morgan M, Hardman A, Rowe C, Bardsley P 1994 Comparison of oxygen uptake
716 during a conventional treadmill test and the shuttle walking test in chronic airflow limitation.
717 European Respiratory Journal 7: 2016-20. No DOI available.
718
719 Singh SJ, Jones P, Evans R, Morgan M 2008 Minimum clinically important improvement for
720 the incremental shuttle walking test. Thorax 63: 775-7. DOI: 10.1136/thx.2007.081208
721
722 Stratford PW 2004 Getting more from the literature: estimating the standard error of
723 measurement from reliability studies. Physiotherapy Canada; 56: 27-30. No DOI available.
724
725 Thomas VS, Hageman PA 2002 A preliminary study on the reliability of physical
726 performance measures in older day-care center clients with dementia. International
727 Psychogeriatrics 14: 17-23. No DOI available.
728

729 Verdijk LB, Van Loon L, Meijer K, Savelberg HH 2009 One-repetition maximum strength
730 test represents a valid means to assess leg strength in vivo in humans. Journal of Sports
731 Sciences 27: 59-68. DOI: 10.1080/02640410802428089
732
733 Walter SD, Eliasziw M, Donner A 1998 Sample size and optimal designs for reliability
734 studies. Statistics in Medicine, 17: 101-10. No DOI available.
735
736 Wang XH, Mitch WE 2014 Mechanisms of muscle wasting in chronic kidney disease. Nature
737 Reviews Nephrology 10: 504-16. DOI: 10.1038/nrneph.2014.112
738
739 Watson EL, Greening NJ, Viana JL, Aulakh J, Bodicoat DH, Barratt J, Feehally J, Smith, AC
740 2015 Progressive resistance exercise training in CKD: a feasibility study. American Journal
741 of Kidney Diseases 66: 249-57. DOI: 10.1053/j.ajkd.2014.10.019
742
743 Wilund KR, Tomayko EJ, Wu P-T, Chung HR, Vallurupalli S, Lakshminarayanan B,
744 Fernhall B 2010 Intradialytic exercise training reduces oxidative stress and epicardial fat: a
745 pilot study. Nephrology Dialysis Transplantation 25: 2695-701. DOI: 10.1093/ndt/gfq106
746

747 Table 1. Patient clinical and demographic characteristics

748

	n = 41
Age (years) (SD) [min-max]	62 (11) [27-80]
Females, *n* (%)	23 (56%)
BMI (kg/m^2) (SD) [min-max]	30.1 (5.7) [16.4-41.5]
eGFR (ml/min/1.72^2) (SD) [min-max]	25 (8) [9-41]
Haemoglobin (g/l) (SD) [min-max]	118 (14) [90-161]
Albumin (mg/l) (SD) [min-max]	41 (2.7) [34-47]
Ethnicity	
Caucasian, *n* (%)	27 (66%)
South Asian, *n* (%)	6 (15%)
Indian, *n* (%)	4 (10%)
Black Caribbean, *n* (%)	2 (5%)
Other, *n* (%)	2 (5%)
Cause of disease	
Diabetic nephropathy type II, *n* (%)	5 (12%)
Interstitial nephritis, *n* (%)	5 (12%)
IgA nephropathy, *n* (%)	3 (7%)
Polycystic kidney disease, *n* (%)	3 (7%)
Other, *n* (%)	5 (12%)
Unknown / aetiology uncertain, *n* (%)	20 (49%)

Comorbidities	
Diabetes mellitus type II, *n* (%)	9 (22%)
Hypertension, *n* (%)	26 (63%)
CCI score ($_{SD}$) [min-max]	2.5 (0.7) [2-4]
- Mild CCI score (1-2), *n* (%)	24 (59%)
- Moderate CCI score (3-4), *n* (%)	17 (41%)
- Severe CCI score (≥ 5), *n* (%)	0 (0%)
Median *n* of morbidities [min-max]	3 [0-6]

749

750 Unless stated, data presented as mean and SD: standard deviation; BMI: body mass index;
751 CCI: Charlson Comorbidity Index; eGFR: estimated glomerular filtration rate

752

Table 2. Relative reliability results of physical function tests in patients with CKD

Test	*n*	Test 1 score	Test 2 score	Difference (95CI)	ICC (*r*) †	95CI for ICC (*r*)	*P* †
ISWT (m)	41 ‡	400 (SD: 186)	409 (SD: 185)	9 (-4 – 23)	.973	.950 - .986	0.164
STS-5 (secs)	41 §	11.0 (IQR: 8.8 – 13.4)	10.5 (IQR: 8.7 – 12.4)	-0.1 (-0.9 – 0.4)	.676	.468 - .813	0.248
STS-60 (repetitions)	40 ‖	26 (IQR: 20 – 29)	28 (IQR: 22 – 30)	2 (0 – 2)	.927	.866 - .961	0.093
e1RM (kg)	40 ¶	50.6 (IQR: 34.5 – 64.7)	51.8 (IQR: 36.6 – 64.7)	2.7 (0.0 – 4.3)	.927	.866 - .961	0.053
VO_{2peak} (ml/kg/min)	37 #	19.6 (SD: 5.4)	19.6 (SD: 5.7)	0.0 (-0.9 – 1.0)	.866	.755 - .929	0.936

95CI: 95% confidence interval; e1RM: estimated 1 rep maximum-leg extension strength; ICC: intraclass correlation coefficient; ISWT: incremental shuttle walk test; IQR: interquartile range; SD: standard deviation; STS: sit-to-stand; † refers to test 1 versus test 2 analysis; ‡ 1 (2%) patient removed due to arthritic pain in hips and knees during test, 1 (2%) patient had incomplete data missing at time point 1 or 2; § 1 (2%) patient removed due to arthritic pain in hips and knees during test, 1 (2%) patient had incomplete data missing at time point 1 or 2; ‖ 2 (5%) patients removed due to arthritic pain in hips and knees during test, 1 (2%) patient had incomplete data missing at time point 1 or 2; ¶ 3 (7%) patients had incomplete data missing at time point 1 or 2; # 6 (14%) patients had incomplete data missing at time point 1 or 2

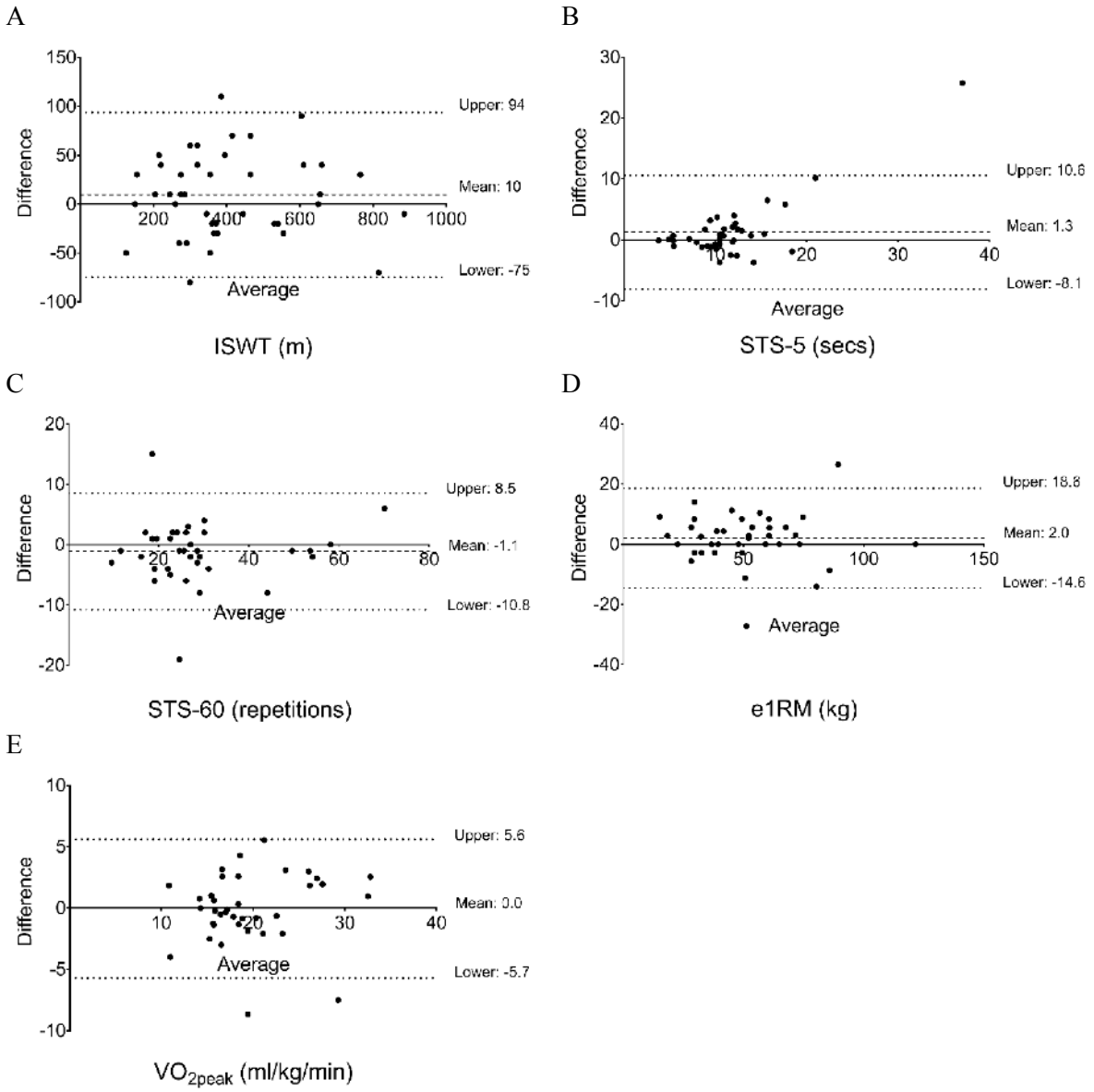
Table 3. SEM and MDC at both individual and group levels at 95CI for physical function tests in patients with CKD

Test	SE_M	MDC_{indv}	MDC_{group}
ISWT (m)	7.1	20	3
STS-5 (secs)	2.7	7.5	1.2
STS-60 (reps)	1.3	4	1
e1RM (kg)	2.3	6.4	1.0
VO_{2peak} (ml/kg/min)	1.0	2.8	0.5

e1RM: estimated 1 rep maximum-leg extension strength; ISWT: incremental shuttle walk test; MDC_{indv}: minimal detectable change at individual level; MDC_{group}: minimal detectable change at group level; SEM: standard error of measurement; STS: sit-to-stand.

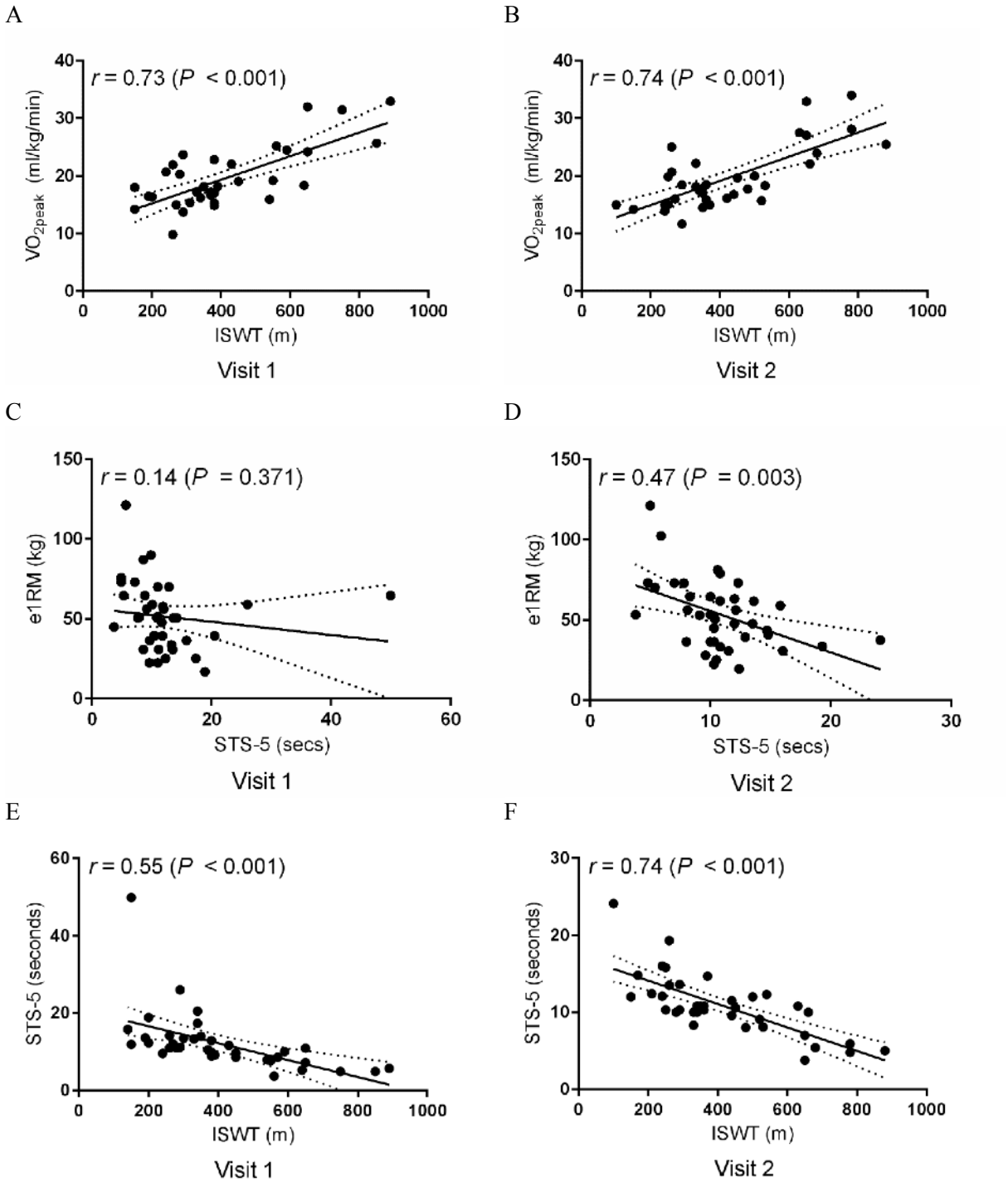
Figures

Figure 1. Bland-Altman plots showing test-retest reliability between test 1 and test 2



e1RM = estimated 1 repetition maximum-leg extension strength; ISWT = incremental shuttle walk test; STS = sit-to-stand. Top and bottom dotted lines represent upper and lower 95% confidence limits of agreement, respectively. Dashed line represents mean bias.

Figure 2. Linear regression line showing the ISWT against VO_{2peak}, and the STS-5 against e1RM and ISWT over the two testing visits



e1RM = estimated 1 repetition maximum-leg extension strength; ISWT = incremental shuttle walk test; STS-5 = sit-to-stand 5 repetition test. 95% confidence interval bands are shown as dotted lines that embrace the regression line in solid black fill.