ORIGINAL ARTICLE

# Association of self-reported physical function with survival in patients with chronic kidney disease

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## ABSTRACT

**Background.** Reduced physical function is associated with an increased risk of mortality among patients with chronic kidney disease (CKD) not requiring renal replacement therapy (RRT). Assessments of physical performance can help to identify those at risk for adverse events. However, objective measures are not always feasible and self-reported measures may provide a suitable surrogate.

**Methods.** We performed a cohort study examining associations between self-reported physical function and walking behaviour with survival in patients with CKD not requiring RRT. Data were analysed from the QCKD study (Physical activity opinions in kidney disease) (ISRCTN 87066351), a prospective observational mixed methods study of physical activity in patients with CKD. A total of 450 patients with CKD not requiring RRT, ages 17–93 years, were followed up for a median of 43 months. Upon enrolment, participants completed two questionnaires: Duke Activity Status Index (DASI) (physical function) and General Practice Physical Activity Questionnaire (GPPAQ) (habitual activity). Mortality data were collected from electronic records in September 2016; RRT was considered a competing event.

**Results.** A total of 74 deaths occurred during follow-up and 101 participants were started on RRT. The adjusted subdistribution hazard ratio (SHR) of mortality in participants scoring >19.2 on the DASI was 0.51 [95% confidence interval (CI) 0.30–0.88] while a one-unit increase in the DASI was associated with an SHR of 0.97 (95% CI 0.95–0.99). The adjusted SHRs of mortality were 0.48 (95% CI 0.26–0.90), 0.25 (0.11–0.57) and 0.48 (0.23–0.80) for participants walking <1, 1–3 and ≥3 h/week, respectively, compared with no walking. A walking pace >3 mph was associated with a reduced risk of mortality [SHR 0.37 (95% CI 0.20–0.71)] compared with a walking pace <3 mph.

**Conclusions.** Physical function and walking behaviours were independently associated with survival in CKD and may help to identify patients at risk for adverse events.

**Keywords:** chronic kidney disease, mortality, physical function, survival, walking

## INTRODUCTION

Chronic kidney disease (CKD) is associated with reduced physical function, independent of age, gender and traditional vascular and cardiovascular risk factors [1]. Physical function refers to an individual's functional ability to perform activities of daily living (ADLs), instrumental activities and other discretionary activities [2]. Furthermore, reduced exercise capacity has been shown to be a strong predictor of survival among ambulatory patients with end-stage renal disease (ESRD) [3]. This is important since a reduction in physical function is not exclusive to haemodialysis patients but has also been demonstrated in patients prior to requiring renal replacement therapy (RRT) [4]. When compared with age-matched controls, patients with CKD have greater levels of impairment across all aspects of physical function [5]. Roshanravan *et al.* [6] reported an association between reduced lower limb function (including gait speed and timed up and go) and increased risk of mortality among patients with CKD Stages 2–4. However, upper limb function assessed using grip strength was not shown to be a significant predictor of mortality.

Performing objective tests of physical performance, such as those reported by Roshanravan *et al.* [6], may not always be clinically applicable due to time and space constraints, and the need for an observer to record measurements. In contrast, self-reported measures may offer a more practical and cost-effective way of assessing physical function. Patient-reported outcome measures have the potential to assess the effect of declining physical function on the ability to participate in ADLs, which is often the prominent concern of patients [2]. The Duke Activity Status Index (DASI) is a short 12-item validated patient-reported outcome measure designed to assess functional capacity via an individual's ability to participate in life activities [7]. The DASI was originally designed to assess physical function and aspects of quality of life in patients with cardiovascular disease [7] but has since been widely used in several clinical populations. This includes patients with CKD not requiring RRT, where the DASI has been shown to be reliable and have high agreement with the gold standard measure of cardiorespiratory fitness [8]. Alternative measures of self-reported physical function, such as the Human Activity Profile (HAP) and 36-item Short Form Health Survey (SF-36), have been shown to correlate well with performance measures in patients requiring dialysis treatment [9], but to our knowledge they have not been validated as a measure of physical function in non-dialysis CKD patients. Furthermore, the HAP is often criticized for its length (94 items) and the time required to complete it [10]. When considering the choice of outcome measures, certain factors should be taken into consideration, including patient burden, accuracy of the measure, cost and ability to implement the measure into routine practice [2]. The DASI is quick to complete, has been shown to be an accurate measure in the target population and has the potential to be distributed in large numbers and assess the physical function of most patients at routine clinic appointments. However, currently it is unknown if a self-reported measure of physical function incorporating activities requiring both upper and lower body strength is associated with adverse outcomes in CKD patients.

Physical inactivity may contribute to reduced levels of physical function and exercise capacity in CKD, although the nature of the relationship is likely to be bidirectional. Physical activity refers to any movement produced by the skeletal muscles that increases energy expenditure above resting [2], and is strikingly low among CKD patients [11]. Evidence suggests that despite guideline recommendations [9, 12], almost 60% of patients with CKD are insufficiently active to experience health benefits [13]. Beddhu *et al.* [13] conducted a prospective follow-up analysis of physical activity and mortality among patients with non-CKD and CKD patients and reported that within the CKD cohort, achieving physical activity goals set by international guidelines was associated with a 56% reduction in mortality risk over a 7-year follow-up. Patients with CKD often describe walking as their preferred form of physical activity [14]; regular walking has been shown to be cardioprotective [15] and is associated with a reduced risk of RRT [16] and all-cause mortality among CKD patients [16]. Furthermore, walking speed has been shown to predict a decline in physical function, hospitalization and all-cause mortality in ESRD [17]. However, the association between walking behaviours and survival has not been explored previously among a UK CKD population. Based on the available literature, we hypothesize that better levels of self-reported physical function (assessed by the DASI and self-reported walking pace) and greater volume of weekly walking will be associated with a reduced risk of mortality among non-dialysis CKD.

The aim of this study was to investigate if self-reported physical function and walking behaviours are associated with survival among patients with CKD not requiring RRT.

## MATERIALS AND METHODS

We analysed data from the QCKD study (Physical activity opinions in kidney patients; ISRCTN 87066351), a prospective observational mixed methods study of physical activity in patients with CKD Stages 1–5 not requiring RRT. Participants were recruited from a single-centre, secondary-care National Health Service outpatient unit within the UK between September 2012 and June 2013.

### Recruitment and inclusion

Participants were invited to participate by a researcher in the outpatient clinic while awaiting their appointment. All patients >18 years of age with CKD Stages 1–5 not requiring RRT were eligible to participate. During the recruitment period we visited 54 outpatient clinics and approached 563 patients. This study was approved by the National Research Ethics Service Committee East Midlands–Northampton on 13 June 2012.

### Procedures

Upon entry to the study, participants were asked to complete a survey pack that included questionnaires assessing self-reported levels of physical function and physical activity. Demographic and clinical data including age, gender, ethnicity, estimated glomerular filtration rate (eGFR; Modification of Diet in Renal Disease equation), haemoglobin and comorbidities were obtained from patient medical records. The extraction of clinical data was performed in temporal proximity to questionnaire completion. Written consent was obtained prior to accessing medical records.

### Self-reported physical function

Physical function was assessed via self-reports using the DASI. This is a brief 12-item questionnaire that enquires about an individual's capability to complete ADLs [10]. Each activity is weighted with a metabolic equivalent of tasks (METs) value, which is then summed to produce a continuous measure

ranging from 0 to 58.2. The DASI has previously been used in patients with CKD not requiring RRT and has been shown to be both a valid and reliable predictor of exercise capacity [8]. A higher DASI score is associated with better physical functioning.

### Self-reported walking behaviours

The General Practice Physical Activity Questionnaire (GPPAQ) is a screening tool used to classify individuals to one of four physical activity levels: inactive, moderately inactive, moderately active or active [18]. However, certain subcategories within the questionnaire such as walking, gardening, housework and walking pace are not included in the classification system. Instead, this relies on employment status, hours of gym work and cycling. As the majority of participants in this study were of retirement age, and walking is often cited as the most common form of physical activity among CKD patients, we extracted hours of walking and walking pace from the GPPAQ. As part of the GPPAQ, participants were asked to report the number of hours spent walking per week, including walking to work, shopping and walking for pleasure. Responses were recorded categorically: none, some but <1, 1–3 or ≥3 h. In addition, participants were asked to self-report their walking pace as slow (<3 mph), steady, brisk or fast (>4 mph).

### Outcome assessment

Mortality data were extracted from an electronic patient medical record used for renal patients in September 2016. Patient records are routinely accessed and updated by the clinical team. Time zero in the survival models was taken as the point where patients were consented to the study and completed the survey questions. Patients were right censored if they had not experienced the event (death) at the time of data extraction (the end of study); RRT was considered a competing risk event.

## STATISTICAL ANALYSIS

Descriptive statistics were summarized as median [interquartile range (IQR)] for continuous variables and percentages for categorical variables. Categorical variables, including hours of walking (0, <1, 1–3 and ≥3 h) and self-reported walking pace [slow (<3 mph), steady, brisk and fast (>4 mph)] were extracted from the GPPAQ. Due to the small number of participants reporting brisk or fast walking, the categories were merged for analysis to create two walking pace groups: <3 and ≥3 mph.

The main outcome of interest was mortality after study enrolment. We estimated the cumulative incidence function and tested differences across categorical variables using a modified log-rank test [19]. A receiver operating characteristics (ROC) curve was constructed to plot the performance of the DASI continuous scores as a binary classifier for survival in order to identify a potential clinical marker for risk stratification. Sensitivity and specificity analyses were performed to identify the best cut-off score to predict mortality. We fitted Fine and Gray [20] models to examine the association between physical function, hours of walking per week, walking pace and mortality in both unadjusted and adjusted models considering the competing risk of RRT; the proportional subhazards assumption was tested using Schoenfeld residuals. Models were constructed to explore DASI scores as both binary and continuous variables. The models were then adjusted to control for the following covariates: age, gender, ethnicity, eGFR, haemoglobin, diabetes mellitus,

hypertension and ischaemic heart disease. In addition, four sensitivity analyses were conducted: (i) using a modified inclusion criterion of CKD, that is, including only participants with an eGFR <60 mL/min/1.73 m$^2$; (ii) removing deaths within the first 6 months to reduce the potential of reverse causation; (iii) imputing missing data to generate 10 imputed datasets with results combined using Rubin's rules [21] and (iv) to estimate mortality hazard ratios (HRs) for variables of interest a standard Cox regression model was conducted, where competing events were censored.

Assuming a binary variable (high versus low DASI score or walking pace) with roughly equal numbers within each category, a 90% survival in one group and 70% survival in the other group, a significance of 0.05 and a log-rank test power of 90%, an overall sample size of at least 178 participants was required.

Statistical analyses were performed using SPSS Statistics for Windows, version 22 (IBM, Armonk, NY, USA) and Stata version 13 (StataCorp, College Station, TX, USA) [22]. Statistical significance was accepted as a P-value <0.05 and results are reported with 95% confidence intervals (CIs) unless stated otherwise.

## RESULTS

Data from 450 participants were available for analysis (Figure 1 shows the flow of participants through the study). Follow-up data were obtained covering a median of 43 (IQR 42–45) months. During the follow-up period, 74 (16.4%) deaths occurred and 101 (22.4%) patients started RRT. The rate (per 1000 person-years) was 58 for mortality and 79 for starting RRT. No patients were lost to follow-up. Missing data for all variables of interest were <5%. Participant characteristics are detailed in Table 1. Cumulative incidence curves for self-reported physical function, walking pace and hours of walking are shown in Figure 2.

### Associations between physical function and survival

Data on self-reported physical function were available for 450 participants, 74 of whom died over the follow-up period. The ROC curve showed that a DASI score of 19.2 predicted mortality with 60% sensitivity and 77% specificity [area under the curve 0.76 (95% CI 0.71–0.81), P < 0.001]. The rate (per 1000 person-years) was 22 for patients scoring >19.2 and 36 for patients scoring ≤19.2. After adjustment for age, gender, ethnicity, eGFR, haemoglobin, hypertension, diabetes mellitus and ischaemic heart disease, participants with a DASI score >19.2 had a lower incidence of death [subdistribution hazard ratio (SHR) 0.51 (95% CI 0.30–0.88)] (Table 2). When used continuously, a 1-unit higher DASI was associated with a 3% reduction in mortality [SHR 0.97 (95% CI 0.95–0.99), P = 0.004] (Table 2).

### Associations between hours of walking and survival

Data on the number of hours walked were available for 437 participants, 70 of whom died over the follow-up period. Compared with 0 h weekly, any amount of walking (<1, 1–3 and ≥3 h) was associated with a reduced risk of mortality before and after adjustment (Table 2).

### Associations between walking pace and survival

Self-reported walking pace data were available for 431 participants, 71 of whom died during the follow-up period. A self-reported walking pace ≥3 mph was associated with a 63% lower risk of death [SHR 0.37 (95% CI 0.20–0.71)] (Table 2).
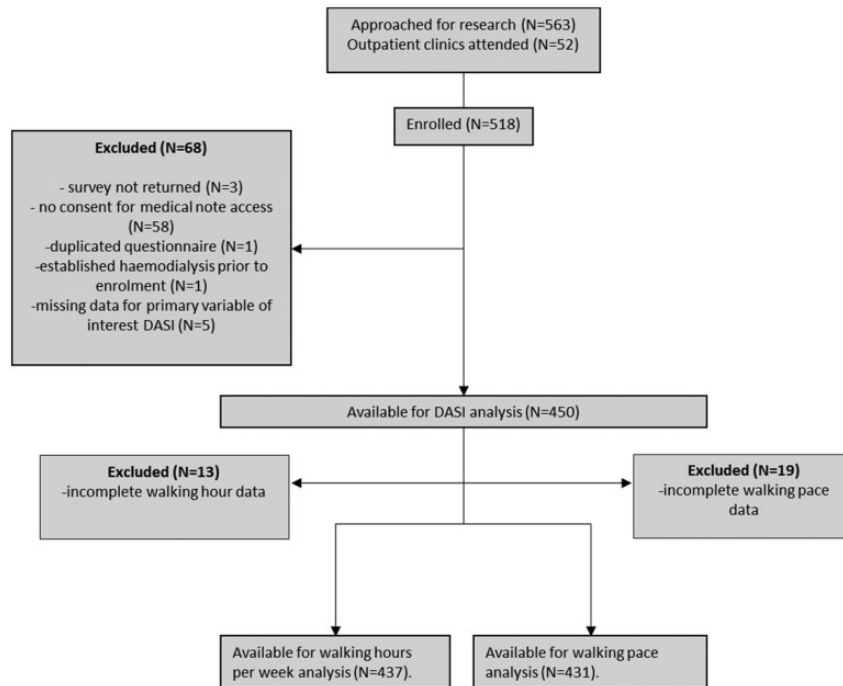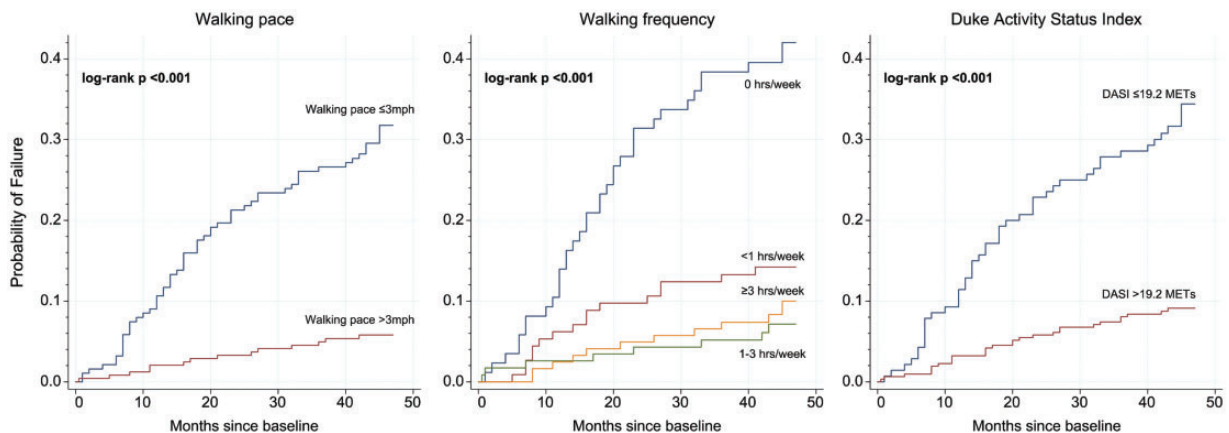
FIGURE 1: Study flow diagram.



FIGURE 2: Cumulative incidence curves.

## SENSITIVITY ANALYSES

Sensitivity analyses restricted to patients with an eGFR >60 mL/min/1.73 m², removing death in the first 6 months, imputing missing values or using Cox HRs rather than a competing risk model largely demonstrated a consistent pattern of results, particularly for the DASI as a continuous score and walking pace, with associations seen with mortality across all models (Table 3).

## DISCUSSION

Objective measures of physical performance have been shown to associate with an increased risk of mortality [23]. This study aimed to explore whether self-reported measures of physical function and walking behaviours are associated with survival among a CKD cohort not requiring RRT. We found that self-reported physical function is independently associated with mortality. Specifically, when using competing risk models for

RRT, self-reported levels of physical function indicated by a DASI score >19.2 and walking pace >3 mph were associated with a 49 and 63% reduced risk of mortality. This suggests that the DASI score or self-reported walking pace may be a useful prognostic factor when used alongside clinical and other known risk markers for identifying patients who are at risk for adverse outcomes. Using an equation previously validated in this population [8], a DASI score of 19.2 equates to an estimated peak oxygen consumption ($VO_{2peak}$) score of 17.86 mL/min/kg, similar to the median cut-off of 17.5 mL/min/kg reported by Sietsema *et al.* [3] that predicted survival in a relatively healthy subset of ESRD patients. Baseline $VO_{2peak}$ scores were determined by a standardized cycle ergometry exercise protocol and were shown to significantly contribute to an explanatory model relating clinical variables to mortality [3]. The DASI is a validated, quick and simple measure of exercise capacity that has been widely utilized within CKD research studies [24, 25] and could be incorporated relatively easily into routine clinical assessment.

**Table 1. Baseline characteristics**

| Characteristics | Total (N = 450) | Event-free (n = 275) | RRT (n = 101) | Deceased (n = 74) |
|---|---|---|---|---|
| Age (years), median (IQR) | 62 (48–75) | 61 (45–73) | 57 (48–68) | 79 (68–83) |
| Gender (male), n (%) | 258 (57) | 147 (54) | 60 (59) | 51 (69) |
| Ethnicity (white), n (%) | 360 (80) | 226 (82) | 63 (62) | 71 (96) |
| eGFR (mL/min/1.73 m$^2$), median, (IQR) | 29 (19–54) | 43 (27–74) | 16 (11–19) | 23 (17–34) |
| Haemoglobin (g/L), median (IQR) | 122 (108–135) | 129 (115–139) | 111 (102–123) | 114 (111–126) |
| Diabetes, n (%) | 121 (27) | 62 (23) | 32 (32) | 27 (37) |
| Hypertension, n (%) | 247 (55) | 128 (47) | 77 (76) | 42 (57) |
| Ischaemic heart disease, n (%) | 82 (18.2) | 36 (13) | 18 (18) | 28 (38) |
| DASI summed METs, median (IQR) | 35.7 (18.95–50.70) | 42.7 (23.45–58.2) | 31.45 (15.45–50.2) | 18.48 (9.95–28.7) |
| Walking hours (weekly), n (%) | | | | |
| 0 | 86 (19) | 32 (12) | 19 (19) | 35 (47) |
| <1 | 113 (25) | 72 (26) | 25 (25) | 16 (22) |
| 1–3 | 116 (26) | 83 (30) | 25 (25) | 8 (11) |
| ≥3 | 122 (27) | 81 (30) | 30 (30) | 11 (15) |
| Missing | 13 (3) | 7 (3) | 2 (2) | 4 (5) |
| Walking pace | | | | |
| <3 mph | 188 (42) | 86 (31) | 45 (45) | 57 (77) |
| ≥3 mph | 243 (54) | 177 (64) | 52 (52) | 14 (19) |
| Missing | 19 (4) | 12 (4) | 4 (4) | 3 (4) |

**Table 2. Competing risk analysis for mortality (n = 450)**

| Measures | Crude SHRs (95% CI) | Adjusted SHRs (95% CI) |
|---|---|---|
| DASI (0–58.2) (per 1-unit increase) | 0.95 (0.94–0.97)** | 0.97 (0.95–0.99)** |
| DASI (>19.2 summed METs versus ≤19.2) | 0.24 (0.15–0.38)** | 0.51 (0.30–0.88)* |
| Walking hours (weekly) (reference 0 h) | | |
| <1 | 0.30 (0.17–0.54)** | 0.48 (0.26–0.90)* |
| 1–3 | 0.14 (0.06–0.30)** | 0.25 (0.11–0.57)** |
| ≥3 | 0.18 (0.09–0.36)** | 0.48 (0.23–0.80)* |
| Walking pace (reference <3 mph) | | |
| ≥3 mph | 0.17 (0.09–0.30)** | 0.37 (0.20–0.71)** |

Adjusted for age, gender, ethnicity, eGFR, haemoglobin, diabetes mellitus, hypertension and ischaemic heart disease.
*P < 0.05; **P < 0.01.

Furthermore, the benefits of regular walking among patients with CKD are well documented [26]. To our knowledge, this is the first study to report the association between walking behaviours and survival in a UK CKD cohort. The results of this study indicate that participants reporting 1–3 h of walking per week had the greatest reduction in risk of mortality. Previous research from a large observational study conducted in China indicated that walking frequency was associated with survival among patients with CKD Stages 3–5 [16], independent of age, eGFR and comorbidities. The authors reported a relationship between walking frequency and lower mortality, however, they did not specifically state the relationship between walking duration and mortality. In our study, any reported walking activity was associated with a reduction in mortality, with no clear evidence of a dose–response relationship. The lack of a clear linear dose response may be due to uncaptured confounders such as exercise intensity and other known comorbidities, for example, peripheral vascular disease and cerebrovascular disease. The cross-sectional nature of the current study precludes our ability to draw any conclusions regarding the dose–response

relationship between physical activity and mortality in patients with CKD. However, a meta-analysis of 22 studies undertaken in the general population showed that walking 2.5 h/week was associated with a 19% reduction in all-cause mortality risk, whereas walking 7 h/week was associated with an increase of 24% [27]. This indicated that the greatest benefits to health may be found when encouraging patients to move from sedentary to low levels of activity, although further health benefits were still accrued from additional activity in patients reporting greater levels of physical activity [28]. Further work, including walking frequency, duration and intensity, is required to explore the dose–response relationship in patients with CKD.

Gait speed is known to be associated with survival in older adults [29] and patients with CKD [6]. However, objective measures of gait speed are not readily available in a clinical setting. Therefore self-reported measures of walking pace may offer an alternative that is quick and simple to complete and could be easily implemented into routine clinical assessment. Recent evidence has suggested that self-reported walking pace may provide a good surrogate measure of walking speed when direct measurement is unavailable [30], while also being associated with cardiorespiratory fitness and mortality within the general population [31]. Our results suggest that patients who reported a walking speed ≥3 mph had a reduced risk of mortality. Indeed, the reduction in risk for walking pace was more pronounced than the threshold of physical function (DASI score 19.2) derived from this study, suggesting a simple self-reported walking pace question could also be used to predict future morality risk in CKD patients. Furthermore, in somewhat of a contradiction to the relationship between physical activity and mortality, the association between walking pace and risk of mortality has been shown to be linear. Reasons for this are not fully understood, however, faster walking pace may be an indicator of vitality and multiple organ system function, thus offering a proxy measure of overall health [29]. Roshanravan et al. [6] demonstrated in fully adjusted models that for every 1-s increase on the timed up and go, the risk of death increased by 8%. Slowness is also a defining characteristic of frailty syndrome, which has been shown to increase the risk of mortality [32]. However, further

Table 3. Sensitivity analyses

| Measures | 1 Adjusted SHRs (95% CI) | P-value | 2 Adjusted SHRs (95% CI) | P-value | 3 Adjusted SHRs (95% CI) | P-value | 4 Adjusted HRs (95% CI) | P-value |
|---|---|---|---|---|---|---|---|---|
| DASI (per 1-unit increase) | 0.97 (0.95–0.99)** | 0.003 | 0.97 (0.95–1.00)** | 0.016 | 0.97 (0.95–0.99)** | 0.011 | 0.97 (0.95–0.99)* | 0.006 |
| DASI (>19.2 summed METs versus ≤19.2) | 0.47 (0.27–0.83)** | 0.009 | 0.56 (0.32–1.01) | 0.054 | 0.53 (0.30–0.92)* | 0.023 | 0.52 (0.30–0.90)* | 0.019 |
| Walking hours (weekly) (reference 0 h) | | | | | | | | |
| <1 | 0.43 (0.22–0.82)** | 0.01 | 0.55 (0.29–1.05) | 0.068 | 0.57 (0.30–1.10) | 0.074 | 0.54 (0.29–1.00)* | 0.049 |
| 1–3 | 0.24 (0.11–0.55)** | 0.001 | 0.60 (0.28–1.27)** | 0.002 | 0.30 (0.13–0.68)** | 0.004 | 0.28 (0.12–0.62)* | 0.002 |
| ≥3 | 0.44 (0.21–0.94)* | 0.034 | 0.23 (0.09–0.58) | 0.18 | 0.54 (0.27–1.09) | 0.083 | 0.48 (0.23–1.00)* | 0.051 |
| Walking pace (reference <3 mph) | | | | | | | | |
| ≥3 mph | 0.35 (0.18–0.68)** | 0.002 | 0.37 (0.19–0.74)** | 0.005 | 0.40 (0.20–0.78)** | 0.009 | 0.38 (0.20–0.72)* | 0.003 |

Adjusted for age, gender, ethnicity, eGFR, haemoglobin, diabetes mellitus, hypertension and ischaemic heart disease.

Sensitivity analysis 1 (participants, $n = 348$; events, $n = 65$): proportional subhazards model conducted for mortality after excluding patients with an eGFR >60 mL/min/1.73 $m^2$.

Sensitivity analysis 2 (participants, $n = 441$; events, $n = 65$): proportional subhazards model conducted for mortality after excluding patients who died within the first 6 months after enrolment to the study.

Sensitivity analysis 3 (participants, $n = 455$; events, $n = 74$): proportional subhazards model conducted for main analysis using multiple imputation to control for missing data.

Sensitivity analysis 4 (participants, $n = 450$; events, $n = 74$): Cox proportional hazards model conducted for main analysis where competing events were censored.

*$P < 0.05$; **$P < 0.01$.

work is now required to determine if interventions targeting walking pace are associated with improved outcomes in CKD patients at risk of adverse events.

To our knowledge this is the largest CKD cohort utilized to investigate the association between self-reported physical function and survival. However, this study is not without its limitations. Due to the observational study design, caution should be exercised when assigning a causal relationship between self-reported physical function and walking behaviours and an increased risk of mortality. Moreover, although we adjusted for some factors (e.g. age, sex, haemoglobin), residual confounding or confounding by unmeasured factors remains a possibility. Data regarding causes of death were not obtainable, and as such we were limited in our ability to perform additional analyses regarding cardiovascular mortalities, which would have been of interest. Furthermore, it remains unclear from this study and the literature if positive changes to walking behaviour and physical function are associated with improved rates of survival. Previous research has demonstrated that both physical function and physical activity in patients with CKD can be successfully targeted via exercise [33] and behavioural intervention [34]. Therefore further longitudinal and interventional studies are required to assess the rate at which function declines and how this associates with adverse outcomes, to investigate the effect of increasing levels of physical activity and improving physical function on adverse events and to determine the optimal dose response for walking with regards to frequency, duration and intensity associated with survival. In addition, as with all self-reported data, there may be tendencies for participants to over- or underestimate physical capabilities and levels of physical activity. However, in the absence of objective assessment, we have shown that self-reported measures can be incorporated into routine clinical assessment and help to identify patients at risk of adverse events.

Self-reported physical function, hours of walking and walking pace are independent predictors of mortality in non-dialysis CKD patients. This suggests that the DASI and self-reported measures of walking behaviour, when used alongside clinical information, may be a useful prognostic clinical tool to identify participants at risk of adverse events.

## AUTHORS' CONTRIBUTIONS

A.L.C., T.Y., A.C.S and J.O.B. contributed to the research idea and study design. A.L.C and K.L.H. contributed to data acquisition. A.L.C., D.W.G., T.Y. and J.O.B. helped in data analysis/interpretation. A.L.C., T.Y. and F.Z. performed the statistical analysis. A.C.S., T.Y. and J.O.B. were involved in supervision or mentorship. Each author contributed important intellectual content during manuscript drafting or revision and accepts responsibility for the overall work by ensuring that questions pertaining to the accuracy or integrity of any portion of the work are appropriately investigated and resolved.

## CONFLICT OF INTEREST STATEMENT

## REFERENCES

1. Smyth A, Glynn LG, Murphy AW et al. Mild chronic kidney disease and functional impairment in community-dwelling older adults. *Age Ageing* 2013; 42: 488–494
2. Painter P, Marcus R. Assessing physical function and physical activity in patients with CKD. *Clin J Am Soc Nephrol* 2013; 8: 861–872
3. Sietsema KE, Amato A, Adler SG et al. Exercise capacity as a predictor of survival among ambulatory patients with end-stage renal disease. *Kidney Int* 2004; 65: 719–724
4. Segura-Orti E, Gordon PL, Doyle JW et al. Correlates of physical functioning and performance across the spectrum of kidney function. *Clin Nurs Res* 2018; 27: 579–596
5. Plantinga LC, Johansen K, Crews DC et al. Association of CKD with disability in the United States. *Am J Kidney Dis* 2011; 57: 212–227
6. Roshanravan B, Robinson-Cohen C, Patel KV et al. Association between physical performance and all-cause mortality in CKD. *J Am Soc Nephrol* 2013; 24: 822–830
7. Hlatky MA, Boineau RE, Higginbotham MB et al. A brief self-administered questionnaire to determine functional capacity (the Duke Activity Status Index). *Am J Cardiol* 1989; 64: 651–654
8. Ravani P, Kilb B, Bedi H et al. The Duke Activity Status Index in patients with chronic kidney disease: a reliability study. *Clin J Am Soc Nephrol* 2012; 7: 573–580
9. Johansen KL, Chertow GM, Ng AV et al. Physical activity levels in patients on hemodialysis and healthy sedentary controls. *Kidney Int* 2000; 57: 2564–2570
10. Hayhurst WS, Ahmed A. Assessment of physical activity in patients with chronic kidney disease and renal replacement therapy. *Springerplus* 2015; 4: 536
11. Brawner CA, Churilla JR, Keteyian SJ. Prevalence of physical activity is lower among individuals with chronic disease. *Med Sci Sports Exerc* 2016; 48: 1062–1067
12. Kidney Disease: Improving Global Outcomes (KDIGO) Blood Pressure Work Group. KDIGO clinical practice guideline for the management of blood pressure in chronic kidney disease. *Kidney Int Suppl* 2012; 2: 337–414
13. Beddhu S, Baird BC, Zitterkoph J et al. Physical activity and mortality in chronic kidney disease (NHANES III). *Clin J Am Soc Nephrol* 2009; 4: 1901–1906
14. Clarke AL, Young HM, Hull KL. Motivations and barriers to exercise in chronic kidney disease: a qualitative study. *Nephrol Dial Transplant* 2015; 30: 1885–1892
15. Viana JL, Kosmadakis GC, Watson EL et al. Evidence for anti-inflammatory effects of exercise in chronic kidney disease. *J Am Soc Nephrol* 2014; 25: 2121–2130
16. Chen I-R, Wang S-M, Liang C-C et al. Association of walking with survival and RRT among patients with CKD stages 3–5. *Clin J Am Soc Nephrol* 2014; 9: 1183–1189
17. Kutner NG, Zhang R, Huang Y et al. Gait speed and mortality, hospitalization, and functional status change among hemodialysis patients: a US Renal Data System special study. *Am J Kidney Dis* 2015; 66: 297–304
18. National Collaborating Centre for Nursing and Supportive Care (UK). *Irritable Bowel Syndrome in Adults: Diagnosis and Management of Irritable Bowel Syndrome in Primary Care*. NICE Clinical Guidelines No. 61. Appendix J, The General Practice Physical Activity Questionnaire (GPPAQ). London: Royal College of Nursing, 2008. https://www.ncbi.nlm.nih.gov/books/NBK51962/ (13 July 2018, date last accessed)
19. Gray RJ. A class of k-sample tests for comparing the cumulative incidence of a competing risk. *Ann Stat* 1988; 16: 1141–1154
20. Fine JP, Gray RJ. A proportional hazards model for the subdistribution of a competing risk. *J Am Stat Assoc* 1999; 94: 496–509
21. Royston P, White IR. Multiple imputation by chained equations (MICE): implementation in Stata. *J Stat Softw* 2011; 45: 1–20
22. Lambert P. The estimation and modeling of cause-specific cumulative incidence functions using time-dependent weights. *Stata J* 2017; 17: 181–207
23. Painter P, Roshanravan B. The association of physical activity and physical function with clinical outcomes in adults with chronic kidney disease. *Curr Opin Nephrol Hypertens* 2013; 22: 615–623
24. Kurella M, Ireland C, Hlatky MA et al. Physical and sexual function in women with chronic kidney disease. *Am J Kidney Dis* 2004; 43: 868–876
25. Cook SA, MacLaughlin H, Macdougall IC. A structured weight management programme can achieve improved functional ability and significant weight loss in obese patients with chronic kidney disease. *Nephrol Dial Transplant* 2008; 23: 263–268
26. Kosmadakis GC, John SG, Clapp EL et al. Benefits of regular walking exercise in advanced pre-dialysis chronic kidney disease. *Nephrol Dial Transplant* 2012; 27: 997–1004
27. Kelly P, Kahlmeier S, Götschi T et al. Systematic review and meta-analysis of reduction in all-cause mortality from walking and cycling and shape of dose response relationship. *Int J Behav Nutr Phys Act* 2014; 11: 1
28. Woodcock J, Franco OH, Orsini N et al. Non-vigorous physical activity and all-cause mortality: systematic review and meta-analysis of cohort studies. *Int J Epidemiol* 2011; 40: 121–138
29. Studenski S, Perera S, Patel K et al. Gait speed and survival in older adults. *JAMA* 2011; 305: 50–58
30. Syddall HE, Westbury LD, Cooper C et al. Self-reported walking speed: a useful marker of physical performance among community-dwelling older people? *J Am Med Dir Assoc* 2015; 16: 323–328
31. Yates T, Zaccardi F, Dhalwani NN et al. Association of walking pace and handgrip strength with all-cause, cardiovascular, and cancer mortality: a UK Biobank observational study. *Eur Heart J* 2017; 38: 3232–3240
32. Walker SR, Gill K, Macdonald K et al. Association of frailty and physical function in patients with non-dialysis CKD: a systematic review. *BMC Nephrol* 2013; 14: 228–2369
33. Greenwood SA, Lindup H, Taylor K et al. Evaluation of a pragmatic exercise rehabilitation programme in chronic kidney disease. *Nephrol Dial Transplant* 2012; 27(Suppl 3): iii126–iii134
34. Kao Y-H, Huang Y-C, Chen P-Y et al. The effects of exercise education intervention on the exercise behaviour, depression, and fatigue status of chronic kidney disease patients. *Health Educ* 2012; 112: 472–484