Does the 1-year Decline in Walking Speed Predict Mortality Risk Beyond Current Walking Speed in Adults With Knee Osteoarthritis?

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ABSTRACT. **Objective.** To investigate whether walking speed at 1 timepoint, decline over the past 12 months, or both predict mortality risk over 11 years in adults with, or at risk of, knee osteoarthritis (OA).

Methods. Using the data from the Osteoarthritis Initiative, we defined slow versus adequate walking speed as walking < 1.22 versus ≥ 1.22 m/s on a 20m walk test during the 12-month follow-up visit. We defined meaningful decline (yes/no) as slowing ≥ 0.08 m/s over the past year. At the 12-month visit, we classified adequate sustainers as those with adequate walking speed and no meaningful decline, slow sustainers as slow walking speed and no meaningful decline, adequate decliners as adequate walking speed and meaningful decline, and slow decliners as slow walking speed and meaningful decline. Mortality was recorded over 11 years. To examine the association of walking speed with mortality, HR and 95% CI were calculated using Cox regression, adjusted for potential confounders.

Results. Of 4229 participants in the analytic sample (58% female, age 62 ± 9 yrs, BMI 29 ± 5 kg/m^2), 6% (n = 270) died over 11 years. Slow sustainers and slow decliners had 2-times increased mortality risk compared to adequate sustainers (HR 1.96, 95% CI 1.44–2.66 for slow sustainers, and HR 2.08, 95% CI 1.46–2.96 for slow decliners). Adequate decliners had 0.43 times the mortality risk compared with adequate sustainers (HR 0.57, 95% CI 0.32–1.01).

Conclusion. In adults with, or at risk of, knee OA, walking slower than 1.22 m/s in the present increased mortality risk, regardless of decline over the previous year.

Key Indexing Terms: decline, knee osteoarthritis, mortality, walking speed

Over 250 million people worldwide have knee osteoarthritis (OA)[1], which is a leading cause of pain and functional limitation[2,3,4] (e.g., slow walking). Subsequently, premature mortality is 55–90% more likely for people with knee OA compared to the general population[5,6,7]. Walking plays a significant role in overall health in adults with knee OA, given those who report walking difficulty have a 51% higher risk for all-cause mortality compared to those with no difficulty[8]. Speed is one method to quantify difficulty walking. In particular, slow walking is associated with an increased risk of all-cause mortality, prolonged hospitalization, and other markers of health in well-functioning older adults[9,10,11,12] and other patient populations[13,14,15]. For this reason, walking speed is considered a "functional" vital sign of overall health[12], and assessing walking speed in clinical practice is important.

Slow walking speed is associated with all-cause mortality

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in older adults[9,10,11,12]. Walking slower than specific thresholds indicates the risk of future poor health outcomes. For instance, walking slower than 1.22 m/s is associated with difficulty crossing the streets using timed signals in well-functioning older adults[16] and is predictive of the inability to be physically active in adults with, or at risk of, knee OA[17]. At the same time, walking speed typically declines with age[18,19,20,21], though changes over time are not uniform. There are different rates or trajectories of change in walking speed (i.e., some decline quickly, whereas others decline gradually or remain stable). Moreover, community-dwelling older adults who experienced a fast decline in walking speed over 2 years have a 90% greater risk of all-cause mortality compared with those who experienced a slow decline over 2 years[22].

Clinically, however, gaps remain with the utility of walking speed measured over points in time. In particular, the relative importance of current speed versus change in speed over the previous year is not known. For instance, adults may have a slow walking speed that is not new but has been sustained over time, which we have defined as a slow sustainer. This is different from someone who has a slow walking speed and has declined in walking speed over the past year, which we have defined as a slow decliner. While both groups have current slow walking speed, it is unclear if the recent decline over the past year increases the risk of mortality independent of risk due to current walking speed. This is important to study, as clinicians may be unsure how to weigh the importance of change in walking speed and current walking speed for predicting future health. Therefore, the purpose of this study was to investigate whether walking speed at 1 timepoint, decline over 1 year, or both were associated with mortality risk over 11 years in adults with, or at risk of, knee OA.

MATERIALS AND METHODS

Study participants. We used publicly available data from the Osteoarthritis Initiative (OAI). The OAI is a large prospective multicenter observational cohort study of 4796 people with, or at risk of, knee OA. Detailed descriptions of the study protocol and eligibility criteria have been published elsewhere[23] and can be found on the NIH website (nda.nih.gov/oai). Briefly, people were excluded from the OAI study if they had rheumatoid or inflammatory arthritis, or bilateral endstage disease, defined as severe joint space narrowing or total knee replacements in both knees, or if they used ambulatory aids other than a cane at baseline. The OAI study had institutional review board (IRB) approval from each recruitment site and the OAI coordinating center (Memorial Hospital/Brown University, the Ohio State University, University of Maryland and Johns Hopkins University joint center, University of Pittsburgh, and University of California San Francisco; approval #10-00532). All participants provided written informed consent before enrollment in the OAI study. In this study, since publicly available data was used to investigate the research question, IRB exemption was obtained from the site where the analysis was conducted (University of Delaware, approval #1125357).

The current analysis included data from participants who completed enrollment and 12-month follow-up clinic visits conducted in 2004–2006 and 2005–2007, respectively. For this analysis, the publicly available data was downloaded from the Website hosted by the National Institutes of Health (nda.nih.gov/oai).

Study outcome. Time to all-cause mortality was quantified from the 12-month clinic visit to 11 years later. The date of death was confirmed through obituary or death certificates, when available. We censored participants who were lost to follow-up anytime between 12 months to 11 years later.

Study exposure. Self-selected walking speed was calculated from the 20-m walk test at enrollment and at the 12-month follow-up clinic visit. During the test, participants were instructed to walk at their usual speed over a marked 20-m course in an unobstructed and dedicated corridor. A digital stopwatch was used to record time (seconds) to complete the test. Timing began at the initial movement from standing and stopped when participants crossed the 20-m mark. Walking speed was calculated in m/s by dividing the total distance (20 m) by the total time to complete the test. Slower walking speed indicates worse physical function[16]. The 20-m walk test has high test-retest reliability (intraclass or Spearman correlation coefficients > 0.9) for measuring walking speed in adults with knee OA[24,25].

For the purpose of this study, walking speed at the 12-month visit was considered as current walking speed. The decline in walking speed was calculated by subtracting walking speed at the 12-month follow-up visit from walking speed at study enrollment. Subjects were categorized as having a 12-month decline for walking speed if they declined ≥ 0.08 m/s from enrollment to the 12-month visit, representing a clinically meaningful decline[26,27].

We classified study subjects into 1 of 4 categories of current walking speed and change in walking speed over 1 year. The first category was adequate sustainers, defined as those whose walking speed was ≥ 1.22 m/s at the 12-month follow-up visit and who had < 0.08 m/s decline in walking speed over 1 year. The second category was slow sustainers, defined as those whose walking speed was < 1.22 m/s and who had < 0.08 m/s decline in walking speed over 1 year. The third category was adequate decliners, defined as those whose walking speed was ≥ 1.22 m/s at a 12-month follow-up visit and who had ≥ 0.08 m/s decline in walking speed over 1 year. The fourth category was slow decliners, defined as those whose walking speed at 12-month follow-up visit was < 1.22 m/s and who had ≥ 0.08 m/s decline in walking speed over 1 year.

Potential confounders. We considered the following factors as potential confounders based on their association with walking speed and all-cause mortality[10,28,29,30,31,32]: age, sex (female vs male), race/ethnicity (White vs. non-White), education (< college graduate vs ≥ college graduate), BMI (kg/m²) computed from weight and height assessment, comorbidities measured using the modified Charlson Comorbidity Index[33], depressive symptoms measured using the Center for Epidemiologic Studies Depression (CES-D) Scale (≥ 16 vs < 16)[34], symptomatic knee OA defined as the presence of knee pain, aching, or stiffness on most days in past month during the previous year in either right or left knee (present vs absent), and radiographic knee OA defined as the presence of Kellgren–Lawrence grade ≥ 2 on radiograph in 1 or both knees (present vs absent). These factors were ascertained at the study enrollment by interview, questionnaire, and/or direct measurement, as appropriate.

Statistical analysis. We described the study sample using means and SD for continuous variables and percentages for categorical variables. The Kaplan-Meier method[35] was used to generate survival curves to determine the cumulative mortality risk for each of the categories of walking speed measured at 1 timepoint and change over 1 year within exposure categories (i.e., adequate sustainers, slow sustainers, adequate decliners, and slow decliners). Specifically, cumulative incidence curves were plotted for each of the exposure groups and all-cause mortality. Further, the 4-sample log-rank test was applied to test for a survival difference.

After testing the proportional hazards assumptions using the Supremum Test, we examined the association of the 4-level exposure group (derived using current walking speed at one time and history of a clinically meaningful decline in walking speed) with all-cause mortality over 11 years by calculating HR and 95% CI from Cox regression model adjusted for potential confounders. In these analyses, participants classified as adequate sustainers were being regarded as a reference group. We also investigated the association of the 4-level exposure group with mortality risk using a Cox model stratified by radiographic knee OA status and adjusted for potential confounders. The stratified Cox model was used to account for different baseline hazards for each exposure group by the disease severity because the presence of radiographic knee OA is an irreversible condition.

We repeated this analysis, restricting the sample to those who walked < 1.3 m/s at the 12-month follow-up visit. We chose this threshold to remove study participants who were high-functioning at the 12-month follow-up visit. This threshold represents those walking above the 45th percentile. The intent of this sensitivity analysis was to examine if findings were similar in a sample that did not include individuals with high physical function. Knee OA severity may affect walking speed[2,34] and mortality risk[5,6,7]. Therefore, we repeated the analysis restricting the sample to adults with radiographic knee OA at study enrollment. The intent of this sensitivity analysis was to investigate the stability of the study findings in the sample who are at higher risk of mortality and slow walking speed. All analyses were performed using SAS, version 9.4 (SAS Institute Inc.).

RESULTS

Of 4796 participants recruited for the study, 4229 completed the 20-m walk test at study enrollment and the 12-month follow-up visit. The average age was 62.3 ± 9.2 years, BMI was 28.5 ± 4.8 kg/m², over half were women (57.6%), the majority (81.3%) were White, and 61.5% were college graduates. Over 6% of the analytic sample (270/4229) died over 11 years (Table 1).

The average walking speed at the 12-month visit was 1.45 ± 0.16 m/s, 1.41 ± 0.14 m/s, 1.10 ± 0.11 m/s, and 1.06 ± 0.15 m/s in the adequate sustainers, adequate decliners, slow sustainers, and slow decliners groups, respectively. The change in walking speed over a previous year was 0.07 ± 0.11 m/s (increase), −0.15 ± 0.07 m/s (decline), 0.03 ± 0.08 m/s (increase), and −0.19 ± 0.11 m/s (decline) in the adequate sustainers, adequate decliners, slow sustainers, and slow decliners groups, respectively (Table 1). The average follow-up time was highest in adequate

sustainers (114 ± 35 mos) and adequate decliners (114 ± 37 mos), followed by slow sustainers (105 ± 40 mos), and the least in the slow decliners (102 ± 43 mos). The probability of survival during the course of this study was 95%, 96%, 85%, and 85% for participants in the adequate sustainers, adequate decliners, slow sustainers, and slow decliners groups, respectively (Figure 1). The survival probabilities for the groups were significantly different (log-rank test $P < 0.01$).
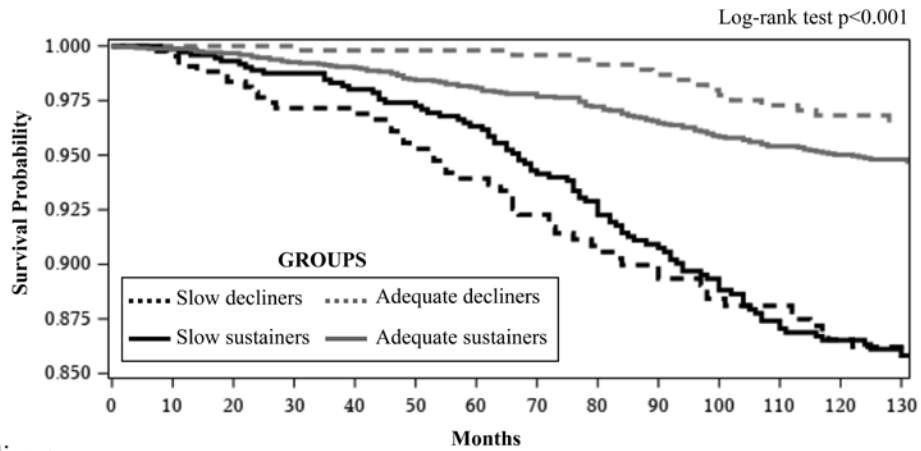
Slow sustainers had a 96% increased hazard of all-cause mortality compared with adequate sustainers (adjusted HR 1.96, 95% CI 1.44–2.66; Table 2). Slow decliners had about twice (or 108%) increased hazard of all-cause mortality compared with adequate sustainers (adjusted HR 2.08, 95% CI 1.46–2.96; Table 2). Adequate decliners had a 43% lower hazard of all-cause mortality compared with the adequate sustainers; this did not meet statistical significance (adjusted HR 0.57, 95% CI 0.32–1.01). Similar effects and 95% CI were obtained for each of the exposure group compared to the reference group (i.e., adequate sustainers) when using the stratified Cox regression model by radiographic knee OA (Table 2) and when the sample was restricted to adults with radiographic knee OA only (Table 4). The effect estimates (HR) and 95% CI for slow sustainers and slow decliners were similar after restricting the sample to adults with, or at risk of, knee OA who walked < 1.3 m/s at the 12-month visit (Table 3). However, the effect estimates for adequate decliners became less precise with wider 95% CI when the sample was restricted to adults who walked < 1.3 m/s at the 12-month follow-up visit (Table 3).

Table 1. Characteristics of study participants who completed a 20-m walk test at study enrollment (baseline) and at the 12-month follow-up visit (n = 4229).

	All	Slow Decliners[a]	Adequate Decliners[b]	Slow Sustainers[c]	Adequate Sustainers[d]
Total sample	4229	439	532	751	2507
Age, yrs, mean ± SD	62.3 ± 9.2	65.0 ± 9.4	60.6 ± 8.7	65.5 ± 9.4	61.2 ± 8.8
Women, % (n)	57.6 (2437)	66.7 (293)	56.6 (301)	67.1 (504)	53.4 (1339)
Race, White, % (n)	81.3 (3438)	70.2 (308)	87.4 (465)	65.8 (494)	86.6 (2171)
Education, at least college graduate, % (n)	61.5 (2600)	45.6 (200)	69.9 (372)	47.0 (353)	66.0 (1675)
BMI, kg/m², mean ± SD	28.5 ± 4.8	29.9 ± 5.3	27.5 ± 4.6	30.2 ± 5.3	28.0 ± 4.5
Presence of knee pain, aching or stiffness[e]					
Right, % (n)	29.7 (1252)	45.0 (197)	28.8 (153)	38.1 (284)	24.7 (618)
Left, % (n)	29.2 (1229)	41.7 (182)	29.4 (156)	37.0 (276)	24.6 (615)
Comorbidities, mean ± SD	0.4 ± 0.8	0.6 ± 1.0	0.3 ± 0.76	0.6 ± 1.0	0.3 ± 0.7
At least 1 comorbidity, % (n)	24.4 (1032)	31.7 (139)	20.7 (139)	37.6 (282)	20.0 (501)
Depression[f], % (n)	10.1 (426)	17.3 (76)	7.9 (42)	16.6 (125)	7.3 (183)
ROA, % (n)	56.6 (2394)	64.5 (283)	51.1 (272)	65.9 (495)	53.6 (1344)
SxOA, % (n)	27.1 (1146)	41.5 (182)	25.6 (136)	38.1 (286)	21.6 (542)
Walking speed, m/s					
Baseline, mean ± SD	1.33 ± 0.22	1.24 ± 0.15	1.56 ± 0.16	1.07 ± 0.14	1.38 ± 0.17
1-yr follow-up, mean ± SD	1.34 ± 0.22	1.06 ± 0.15	1.41 ± 0.14	1.10 ± 0.11	1.45 ± 0.16
Change over previous year, mean ± SD	0.01 ± 0.14	−0.19 ± 0.11	−0.15 ± 0.07	0.03 ± 0.08	0.07 ± 0.11
Time in the study, mos, mean ± SD	111 ± 38	102 ± 43	114 ± 37	105 ± 40	114 ± 35
Deaths, % (n)	6.4 (270)	11.6 (51)	2.8 (15)	11.7 (88)	4.6 (116)

[a] Slow decliners walked < 1.22 m/s at 12-month follow-up and ≥ 0.08 m/s annual decline in walking speed. [b] Adequate decliners walked ≥ 1.22 m/s at 12-month follow-up and ≥ m/s annual decline in walking speed. [c] Slow sustainers walked < 1.22 m/s at 12-month follow-up and < 0.08 m/s annual decline in walking speed. [d] Adequate sustainers walked ≥ 1.22 m/s at 12-month follow-up and < 0.08 m/s annual decline in walking speed. [e] More than half the days of a month, in the past 12 months. [f] Presence of depression was defined as score ≥16 on Center for Epidemiologic Studies Depression Scale. ROA: radiographic knee osteoarthritis; SxOA: symptomatic knee osteoarthritis.

Figure 1. The probability of survival during the course of this study for participants in the adequate sustainers (walked at least 1.22 m/s at 12-month follow-up and < 0.08 m/s annual decline in walking speed), adequate decliners (walked at least 1.22 m/s at 12-month follow-up and ≥ 0.08 m/s annual decline in walking speed), slow sustainers (walked slower than 1.22 m/s at 12-month follow-up visit and < 0.08 m/s annual decline in walking speed), and slow decliners (walked slower than 1.22 m/s at 12-month follow-up and had ≥ 0.08 m/s annual decline in walking speed) groups.

Table 2. Association of adults with, or at risk of, knee osteoarthritis (OA) who were defined as adequate sustainers, slow sustainers, adequate decliners, and slow decliners using a 20-m walk test, to the risk of all-cause mortality over 11 years (n = 4229).

	Slow Decliners[a]	Adequate Decliners[b]	Slow Sustainers[c]	Adequate Sustainers[d]
Sample size, n	439	532	751	2507
Walking speed, m/s, mean ± SD				
At study enrollment (baseline)	1.24 ± 0.15	1.56 ± 0.16	1.07 ± 0.14	1.38 ± 0.17
At 12-month follow-up visit	1.06 ± 0.15	1.41 ± 0.14	1.10 ± 0.11	1.45 ± 0.16
Change over 1 yr	−0.19 ± 0.11	−0.15 ± 0.07	0.03 ± 0.08	0.07 ± 0.11
Deaths, % (n)	11.6 (51)	2.8 (15)	11.7 (88)	4.6 (116)
Unadjusted HR (95% CI)	2.88 (2.07–4.00)	0.61 (0.34–1.05)	2.79 (2.12–3.69)	1.00 (Ref)
Adjusted HR (95% CI)[e]	2.08 (1.46–2.96)	0.57 (0.32–1.01)	1.96 (1.44–2.66)	1.00 (Ref)
Adjusted HR (95% CI)[f]	2.06 (1.44–2.94)	0.56 (0.32–1.00)	1.94 (1.43–2.64)	1.00 (Ref)

[a] Slow decliners walked < 1.22 m/s at 12-month follow-up and ≥ 0.08 m/s annual decline in walking speed. [b] Adequate decliners walked ≥ 1.22 m/s at 12-month follow-up and ≥ 0.08 m/s annual decline in walking speed. [c] Slow sustainers walked < 1.22 m/s at 12-month follow-up and < 0.08 m/s annual decline in walking speed. [d] Adequate sustainers walked ≥ 1.22 m/s at 12-month follow-up and < 0.08 m/s annual decline in walking speed. [e] Adjusted for baseline age, BMI, sex, race, education, comorbidities, the presence of depression (≤ vs ≥ 16 on the Center for Epidemiologic Studies Depression Scale), and symptomatic knee OA (yes or no; defined as presence of Kellgren-Lawrence grade ≥ 2 on radiograph in 1 or both knees, and pain, aching, or stiffness on most days of a month during the previous year). [f] Cox model stratified by radiographic knee OA status and adjusted for baseline age, BMI, sex, race, education, comorbidities, the presence of depression (≤ vs ≥ 16), and symptomatic knee OA (yes or no).

DISCUSSION

Slow walking speed was related to increased risk of all-cause mortality over 11 years, regardless of decline over the previous year, in people with, or at risk of, knee OA. These findings were consistent for adults who did not have fast walking speeds (i.e., those who walked < 1.3 m/s at the 12-month visit as well as those who had radiographic knee OA at study enrollment.

Our findings further support the notion that walking speed is a vital sign of health in older adults[12] and should be objectively measured in all adults with, or at risk of, knee OA. In particular, we

Table 3. Association of adults with, or at risk of, knee osteoarthritis (OA) who walked < 1.3 m/s at the 12-month follow-up visit and were defined as adequate sustainers, slow sustainers, adequate decliners, and slow decliners using a 20-m walk test to the risk of all-cause mortality over 11 years (n = 1798).

	Slow Decliners[a]	Adequate Decliners[b]	Slow Sustainers[c]	Adequate Sustainers[d]
Sample size, n	439	139	751	469
Walking speed, m/s, mean ± SD				
At study enrollment (baseline)	1.24 ± 0.15	1.42 ± 0.09	1.07 ± 0.14	1.21 ± 0.09
At 12-month follow-up visit	1.06 ± 0.15	1.25 ± 0.23	1.10 ± 0.11	1.26 ± 0.02
Change over 1 yr	−0.19 ± 0.11	−0.16 ± 0.08	0.03 ± 0.08	0.05 ± 0.09
Deaths, % (n)	11.6 (51)	3.6 (5)	11.7 (88)	5.3 (25)
Unadjusted HR (95% CI)	2.43 (1.50–3.92)	0.66 (0.25–1.73)	2.35 (1.51–3.67)	1.00 (Ref)
Adjusted HR (95% CI)[e]	2.06 (1.26–3.38)	0.56 (0.19–1.61)	1.96 (1.24–3.09)	1.00 (Ref)

[a] Slow decliners walked < 1.22 m/s at 12-month follow-up and had ≥ 0.08 m/s annual decline in walking speed. [b] Adequate decliners walked ≥ 1.22 m/s at 12-month follow-up and ≥ 0.08 m/s annual decline in walking speed. [c] Slow sustainers walked < 1.22 m/s at 12-month follow-up visit and < 0.08 m/s annual decline in walking speed. [d] Adequate sustainers walked ≥ 1.22 m/s at 12-month follow-up and < 0.08 m/s annual decline in walking speed. [e] Adjusted for baseline age, BMI, sex, race, education, comorbidities, the presence of depression (≤ vs ≥ 16 on the Center for Epidemiologic Studies Depression Scale), and symptomatic knee OA (yes or no; defined as presence of Kellgren-Lawrence grade ≥ 2 on radiograph in 1 or both knees, and pain, aching, or stiffness on most days of a month during the previous year).

Table 4. Association of adults with, or at risk of, knee osteoarthritis (OA) who had radiographic knee OA[a] (n = 2394) at study enrollment (baseline) and who were defined as adequate sustainers, slow sustainers, adequate decliners, and slow decliners using a 20-m walk test to the risk of all-cause mortality over 11 years (n = 2394).

	Slow Decliners[b]	Adequate Decliners[c]	Slow Sustainers[d]	Adequate Sustainers[e]
Sample size, n	283	272	495	1344
Walking speed, m/s, mean ± SD				
At study enrollment (baseline)	1.21 ± 0.15	1.54 ± 0.14	1.05 ± 0.14	1.36 ± 0.16
At 12-month follow-up visit	1.03 ± 0.15	1.39 ± 0.13	1.09 ± 0.11	1.43 ± 0.15
Change over 1 yr	−0.19 ± 0.12	−0.15 ± 0.07	0.03 ± 0.09	0.07 ± 0.11
Deaths, % (n)	11.3 (32)	2.0 (8)	12.5 (62)	4.3 (58)
Unadjusted HR (95% CI)	2.92 (1.89–4.49)	0.69 (0.33–1.45)	3.18 (2.22–4.55)	1.00 (Ref)
Adjusted HR (95% CI)[f]	2.38 (1.50–3.80)	0.73 (0.35–1.54)	2.62 (1.76–3.90)	1.00 (Ref)

[a] Radiographic knee OA defined as presence of Kellgren-Lawrence grade ≥ 2 on radiograph in 1 or both knees. [b] Slow decliners walked < 1.22 m/s at 12-month follow-up and ≥ 0.08 m/s annual decline in walking speed. [c] Adequate decliners walked ≥ 1.22 m/s at 12-month follow-up and ≥ 0.08 m/s annual decline in walking speed. [d] Slow sustainers walked < 1.22 m/s at 12-month follow-up and < 0.08 m/s annual decline in walking speed. [e] Adequate sustainers walked ≥ 1.22 m/s at 12-month follow-up and < 0.08 m/s annual decline in walking speed. [f] Adjusted for baseline age, BMI, sex, race, education, comorbidities, the presence of depression (< vs ≥ 16 on the Center for Epidemiologic Studies Depression Scale), and symptomatic knee OA (yes or no; defined as presence of radiographic knee OA, and pain, aching, or stiffness on most days of a month during the previous year).

found that those with persistently slow walking speed (i.e., slow sustainers) had almost twice the risk of mortality compared with those with persistently adequate walking speed (i.e., adequate sustainers). These findings are consistent with the notion that slow current walking speed is consistently a strong predictor for adverse health outcomes (i.e., mortality and prolonged hospitalization) in older adults[9,10,11,12] and poor response to rehabilitation in adults after stroke[11,12,13]. Slow walking speed is associated with increased risk of radiographic and symptomatic knee OA[36]. Slow walking speed reflects impairments in a wide range of body systems[37] (e.g., impaired vision, lower extremity strength[38,39], lower aerobic capacity[40], poor postural control[39]), and reduced ability to engage in daily walking (i.e., taking more steps per day[17]).

One inconsistency with previous literature was our finding that the presence of previous history of a clinically meaningful decline in walking speed was not associated with increased mortality risk among adults whose current walking speed

was more than 1.22 m/s. Specifically, participants classified as adequate decliners did not have increased mortality risk compared to those who were classified as adequate sustainers. Previous studies found that older adults who reported a fast decline in walking speed over 2 years had increased risk of poor future health outcomes, including all-cause mortality[22] and cardiovascular disease[41]. One possible reason for the inconsistency can be explained by the difference in time frame over which the change in walking speed was observed (i.e., 1 year in this study as opposed to 2 years in the prior study)[22]. The second plausible reason can be explained by the fact that previous studies did not mutually adjust for current walking speed differences. We acknowledge that adjusting the absolute value and rate of change in walking speed in one model may not be statistically appropriate given there was a moderate correlation between these variables. Nevertheless, from a clinical perspective, we wanted to understand the independent association of change in walking speed and current walking speed at one time with mortality

risk. Further, when we restricted the sample to adults with the slower walking speed at the 12-month visit, we found that the mortality risk in adults who were classified as adequate decliners was not as precise as the overall sample. Our finding of decreased mortality risk in adults who were classified as adequate decliners may be attributed to the presence of higher physical functioning at study enrollment visit, which subsequently declined at the next clinic visit. This is consistent with the regression of the mean. Specifically, adequate decliners had high walking speed on average (i.e., 1.56 m/s at study enrollment visit) and were slower at the next visit (i.e., 1.41 m/s). Thus, even though there was a meaningful decline, the average walking speed at the 12-month visit was above the threshold known to predict adverse health outcomes. Therefore, though both slow walking speed at 1 timepoint and decline over the previous year may be independently associated with mortality risk, the slow walking speed at one time will give important information regarding mortality risk regardless of the patient's history.

The major strength of our study is that we used a large dataset and 11 years of follow-up, providing a powerful means to study our primary research purpose. However, this study had several limitations. First, we were not able to methodologically test for the association of walking speed at 1 timepoint and change over 1 year with mortality in a single mutually adjusted model. This is because our measure of the change in walking speed from baseline to the 12-month visit is correlated with walking speed at the 12-month visit. As well, 12-month walking speed is an intermediate in the pathway of the relationship of change in walking speed with mortality and methodologically, it is incorrect to adjust for intermediates. Hence, we examined the relationship between current walking speed and decline in walking speed as a multilevel categorical variable. This method uses the same time period during which walking speed was collected for each exposure level [i.e., all levels use both study enrollment (baseline) and 12-month clinic visits) and circumvents the issues of collinearity and adjustment for an intermediate. Second, we caution generalizing the results of our study, since the average age of the sample was 62 years, the majority were White and had a college education, and nearly 75% had no comorbidities. Therefore, the analytical sample was healthy and relatively young. Third, we did not account for intercurrent events such as hospitalization or knee replacement, which may have occurred during the follow-up period. We believe understanding how such events alter the joint association of the current walking speed at one time and decline over the previous year with the risk of all-cause mortality is essential and needed in future research. Fourth, a limited proportion (6%) of the analytical sample died during the follow-up, which limits the precision of the estimated relationship between the walking speed measured at 1 timepoint versus change over 1 year with all-cause mortality. Fifth, the change in walking speed was measured over a 1-year time frame; therefore, we were not able to identify trajectories of decline. Given that the incidence of mortality was low in the sample, we were not able to investigate the association of different walking speed trajectories over 3 or 4 years. However, we used the minimal clinically important difference to identify whether the decline

in walking speed over 1 year was clinically important. Future studies are needed to investigate the joint association of walking speed trajectories and walking speed measured at 1 timepoint with mortality risk in adults with, or at risk of, knee OA. Last, walking speed was measured using a 20-m walk test. Therefore, we cannot generalize the study findings to walking speeds taken over shorter distances such as a 10-m or 4-m walk test given the difference in acceleration and deceleration phases needed to complete it[12,42,43,44].

In people with, or at risk for, knee OA, we found that assessing the walking speed at 1 timepoint was predictive for all-cause mortality, regardless of decline in the walking speed over the previous year. Healthcare professionals should consider assessing walking speed in routine clinical practice, as it may aid in clinical decision making and tailoring goals and care needs for people with, or at risk of, knee OA.

REFERENCES

1. Vos T, Flaxman AD, Naghavi M, Lozano R, Michaud C, Ezzati M, et al. Years lived with disability (YLDs) for 1160 sequelae of 289 diseases and injuries 1990–2010: a systematic analysis for the Global Burden of Disease study 2010. Lancet 2012;380:2163-96.
2. Murray CJ, Richards MA, Newton JN, Fenton KA, Anderson HR, Atkinson C, et al. UK health performance: findings of the Global Burden of Disease study 2010. Lancet 2013;381:997-1020.
3. Guccione AA, Felson DT, Anderson JJ, Anthony JM, Zhang Y, Wilson PW, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham study. Am J Public Health 1994;84:351-8.
4. Hubertsson J, Petersson IF, Thorstensson CA, Englund M. Risk of sick leave and disability pension in working-age women and men with knee osteoarthritis. Ann Rheum Dis 2013;72:401-5.
5. Nüesch E, Dieppe P, Reichenbach S, Williams S, Iff S, Jüni P. All cause and disease specific mortality in patients with knee or hip osteoarthritis: Population based cohort study. BMJ 2011;342:d1165.
6. Liu Q, Niu J, Huang J, Ke Y, Tang X, Wu X, et al. Knee osteoarthritis and all-cause mortality: the Wuchuan osteoarthritis study. Osteoarthritis Cartilage 2015;23:1154-7.
7. Losina E, Walensky RP, Reichmann WM, Holt HL, Gerlovin H, Solomon DH, et al. Impact of obesity and knee osteoarthritis on morbidity and mortality in older Americans. Ann Intern Med 2011;154:217-26.
8. Hawker GA, Croxford R, Bierman AS, Harvey PJ, Ravi B, Stanaitis I, et al. All-cause mortality and serious cardiovascular events in people with hip and knee osteoarthritis: a population based cohort study. PLoS One 2014;9:e91286.
9. Studenski S, Perera S, Patel K, Rosano C, Faulkner K, Inzitari M, et al. Gait speed and survival in older adults. JAMA 2011;305:50-8.
10. Cesari M, Kritchevsky SB, Penninx BWHJ, Nicklas BJ, Simonsick EM, Newman AB, et al. Prognostic value of usual gait speed in well-functioning older people—results from the Health, Aging and Body Composition study. J Am Geriatr Soc 2005;53:1675-80.
11. Fritz S, Lusardi M. White paper: "walking speed: the sixth vital sign." J Geriatr Phys Ther 2009;32:46-9.
12. Middleton A, Fritz SL, Lusardi M. Walking speed: the functional vital sign. J Aging Phys Act 2015;23:314.
13. Goldie PA, Matyas TA, Evans OM. Deficit and change in gait velocity during rehabilitation after stroke. Arch Phys Med Rehabil 1996;77:1074-82.
14. Ekström H, Dahlin-Ivanoff S, Elmståhl S. Effects of walking speed

and results of timed get-up-and-go tests on quality of life and social participation in elderly individuals with a history of osteoporosis-related fractures. J Aging Health 2011;23:1379-99.

15. van Hedel HJ, Dietz V, Curt A. Assessment of walking speed and distance in subjects with an incomplete spinal cord injury. Neurorehabil Neural Repair 2007;21:295-301.

16. Langlois JA, Keyl PM, Guralnik JM, Foley DJ, Marottoli RA, Wallace RB. Characteristics of older pedestrians who have difficulty crossing the street. Am J Public Health 1997;87:393-7.

17. Master H, Thoma LM, Christiansen MB, Polakowski E, Schmitt LA, White DK. Minimum performance on clinical tests of physical function to predict walking 6,000 steps/day in knee osteoarthritis: an observational study. Arthritis Care Res 2018;70:1005-11.

18. Payette H, Gueye NR, Gaudreau P, Morais JA, Shatenstein B, Gray-Donald K. Trajectories of physical function decline and psychological functioning: the Quebec longitudinal study on nutrition and successful aging (NuAge). J Gerontol B Psychol Sci Soc Sci 2011;66:i82-90.

19. Himann JE, Cunningham DA, Rechnitzer PA, Paterson DH. Age-related changes in speed of walking. Med Sci Sports Exerc 1988;20:161-6.

20. Kanehisa H, Fukunaga T. Age-related change in sit-to-stand power in Japanese women aged 50 years or older. J Physiol Anthropol 2014;33:26.

21. Øiestad BE, White DK, Booton R, Niu J, Zhang Y, Torner J, et al. Longitudinal course of physical function in people with symptomatic knee osteoarthritis: data from the multicenter osteoarthritis study and the osteoarthritis initiative. Arthritis Care Res 2016;68:325-31.

22. White DK, Neogi T, Nevitt MC, Peloquin CE, Zhu Y, Boudreau RM, et al. Trajectories of gait speed predict mortality in well-functioning older adults: the Health, Aging and Body composition study. J Gerontol A Biol Sci Med Sci 2013;68:456-64.

23. Riddle DL, Kong X, Jiranek WA. Two-year incidence and predictors of future knee arthroplasty in persons with symptomatic knee osteoarthritis: preliminary analysis of longitudinal data from the osteoarthritis initiative. Knee 2009;16:494-500.

24. Villadsen A, Roos EM, Overgaard S, Holsgaard-Larsen A: Agreement and reliability of functional performance and muscle power in patients with advanced osteoarthritis of the hip or knee. Am J Phys Med Rehabil 2012,91:401-10.

25. Motyl JM, Driban JB, McAdams E, Price LL, McAlindon TE. Test-retest reliability and sensitivity of the 20-meter walk test among patients with knee osteoarthritis. BMC Muscoskelet Disord 2013;14:166.

26. Perera S, Mody SH, Woodman RC, Studenski SA. Meaningful change and responsiveness in common physical performance measures in older adults. J Am Geriatr Soc 2006;54:743-9.

27. Kwon S, Perera S, Pahor M, Katula JA, King AC, Groessl EJ, et al. What is a meaningful change in physical performance? Findings from a clinical trial in older adults (the LIFE-P study). J Nutr Health Aging 2009;13:538-44.

28. Cesari M, Kritchevsky SB, Newman AB, Simonsick EM, Harris TB, Penninx BW, et al. Added value of physical performance measures in predicting adverse health-related events: Results from the Health, aAging and Body composition study. J Am Geriatr Soc 2009;57:251-9.

29. Haas SA, Krueger PM, Rohlfsen L. Race/ethnic and nativity disparities in later life physical performance: the role of health and socioeconomic status over the life course. J Gerontol B Psychol Sci Soc Sci 2012;67:238-48.

30. Penninx BW, Guralnik JM, Ferrucci L, Simonsick EM, Deeg DJ, Wallace RB. Depressive symptoms and physical decline in community-dwelling older persons. JAMA 1998;279:1720-6.

31. Hannan MT, Anderson JJ, Pincus T, Felson DT. Educational attainment and osteoarthritis: differential associations with radiographic changes and symptom reporting. J Clin Epidemiol 1992;45:139-47.

32. Felson DT, Lawrence RC, Dieppe PA, Hirsch R, Helmick CG, Jordan JM, et al. Osteoarthritis: new insights. Part 1: the disease and its risk factors. Ann Intern Med 2000;133:635-46.

33. Katz JN, Chang LC, Sangha O, Fossel AH, Bates DW. Can comorbidity be measured by questionnaire rather than medical record review? Med Care 1996;73-84.

34. Radloff LS. The CES-D scale: a self-report depression scale for research in the general population. Appl Psychol Meas 1977; 1:385-401.

35. Allison PD. Survival analysis using SAS: a practical guide. SAS Institute; 2010.

36. Purser JL, Golightly YM, Feng Q, Helmick CG, Renner JB, Jordan JM. Association of slower walking speed with incident knee osteoarthritis-related outcomes. Arthritis Care Res 2012; 64:1028-35.

37. Park YH, Kim YM, Lee BH. An ankle proprioceptive control program improves balance, gait ability of chronic stroke patients. J Phys Ther Sci 2013;25:1321-4.

38. Bohannon RW. Comfortable and maximum walking speed of adults aged 20–79 years: Reference values and determinants. Age Ageing 1997;26:15-9.

39. Clark DJ, Manini TM, Fielding RA, Patten C. Neuromuscular determinants of maximum walking speed in well-functioning older adults. Exp Gerontol 2013;48:358-63.

40. Fiser WM, Hays NP, Rogers SC, Kajkenova O, Williams AE, Evans CM, et al. Energetics of walking in elderly people: factors related to gait speed. J Gerontol A Biol Sci Med Sci 2010;65:1332-7.

41. Corsi M, Alvarez C, Callahan LF, Cleveland RJ, Golightly YM, Jordan JM, et al. Contributions of symptomatic osteoarthritis and physical function to incident cardiovascular disease. BMC Musculoskelet Disord 2018;19:393.

42. Peters DM, Fritz SL, Krotish DE. Assessing the reliability and validity of a shorter walk test compared with the 10-meter walk test for measurements of gait speed in healthy, older adults. J Geriatr Phys Ther 2013;36:24-30.

43. Najafi B, Helbostad JL, Moe-Nilssen R, Zijlstra W, Aminian K. Does walking strategy in older people change as a function of walking distance? Gait Posture 2009;29:261-6.

44. Johnson RT, Hafer JF, Wedge RD, Boyer KA. Comparison of measurement protocols to estimate preferred walking speed between sites. Gait Posture 2020;77:171-4.