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Is symptomatic knee osteoarthritis a risk factor for a fast decline in gait speed? Results from the Osteoarthritis Initiative

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Abstract

Objectives—Gait speed is an important marker of health in adults and slows with aging. While knee osteoarthritis (OA) can result in difficulty walking, it is not known if radiographic knee OA (ROA) and/or knee pain are associated with a fast decline trajectory of gait speed over time.

Methods—Gait speed trajectories were constructed using a multinomial modeling strategy from repeated 20-meter walk tests measured annually over four years among participants from the Osteoarthritis Initiative (OAI), a prospective cohort study of adults with or at high risk of knee OA aged 45 to 79 at baseline. We grouped participants into four knee OA categories (having neither ROA nor knee pain, ROA only, knee pain only, or symptomatic knee OA (ROA and pain)) and examined their association with trajectories of gait speed using a multivariable polytomous regression model adjusting for age and other potential confounders.

Results—Of the 4179 participants (mean age (sd) = 61.1 (9.1), women =57.6%, mean BMI =28.5 (4.8) kg/m², 5% (n=205) were in a fast decline trajectory slowing 2.75%/year. People with symptomatic knee OA had almost a 9-fold risk (OR = 8.9, 95% CI [3.1, 25.5]) of being in a fast decline trajectory compared with those with neither pain nor ROA. Participants with knee pain had 4.5 times the odds of fast decline (95% CI [1.4, 14.6]) and those with ROA only had a slight but non-statistically significant increased risk.

Conclusions—People with symptomatic knee OA have the highest risk of fast decline trajectory of gait speed compared with people with ROA or pain alone.

Keywords

Gait speed; Knee Osteoarthritis; Trajectory

INTRODUCTION

Gait speed is a simple yet important indicator of current health and well-being in older adults, and a powerful predictor of mortality(1-4). As such, gait speed has been proposed as a ‘vital sign’. Similar to other vital signs, gait speed changes with aging. Previous studies have reported that gait speed is relatively stable up to age 65, declines 1%/year from age 65 to 69, and by age 80 declines 4%/year(5, 6). Nevertheless, there is substantial variation in the rate of decline across individuals and the presence of certain comorbidities may be a risk factor for premature decline in gait speed(7, 8).

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COMPETING INTERESTS

None

Knee osteoarthritis (OA) is the most common cause of difficulty walking in older adults (9, 10) and subsequently is associated with slow walking(11, 12). Previous cross-sectional studies report that people with both radiographic knee OA and knee pain, also known as symptomatic knee OA, have slower walking speed than healthy age matched controls(12-15). Nevertheless, little is known about trajectories of gait speed in this population over time. In particular, it is unclear if most people with or at high risk of knee OA decline at more or less the same rate or if distinct trajectories of gait speed are present with some declining faster than others. Moreover, while knee pain is the most common symptom of knee OA, substantial discordance has been reported between radiographic findings of disease and knee pain in adults(16). Thus, it is unclear if structural lesions on radiographs, knee pain, or their combination have unique effects on the trajectory of gait speed. Understanding trajectories are important to clarify the natural history of decline expected in this patient population. Furthermore, recognizing disease-related risk for gait speed trajectories helps set realistic expectations for the extent intervention targeting disease and pain may mitigate future decline.

Therefore, the purpose of this study was to examine the association of radiographic disease and/or knee pain with trajectories of gait speed in people with or at high risk of knee OA. Furthermore, we examined these associations across age strata to determine if knee OA was associated with a premature decline in gait speed.

Methods

Sample

The Osteoarthritis Initiative (OAI) is an ongoing longitudinal cohort study of the risk factors and natural history of OA. Adults between 45 to 79 years of age at enrollment who had or were at high risk of knee OA were recruited from four clinical sites: Baltimore MD, Pittsburgh PA, Pawtucket RI, and Columbus OH. Increased risk was identified from age-specific criteria from established risk factors including knee symptoms in the past 12 months(17), being overweight from gender specific cut-points(17-19), knee injury causing difficulty walking for at least one week(17, 20, 21), any knee surgery history(18, 22), family history of a total knee replacement(23, 24), Heberden's nodes(17, 25), or repetitive knee bending at work or outside of work(26, 27). People were excluded who had rheumatoid or inflammatory arthritis, end-stage disease defined as severe joint space narrowing in both knees at baseline, or bilateral total knee replacements, positive pregnancy test, or used ambulatory aids other than a cane. More detail regarding the rationale and approach for these criteria can be found at <http://www.oai.ucsf.edu/datarelease/About.asp>. Participants included in the study were assessed annually. We used data from the baseline visit and the first four years of follow-up for analyses. Institutional Review Board approval was obtained from all OAI sites. In addition, this analysis was approved by the Institutional Review Board at Boston University.

Gait speed

Gait speed was measured over a 20-meter course in an unobstructed corridor and was reported in meters per second (m/s). Participants were instructed to walk at a usual pace from a starting point to an orange cone indicating the end of the course. Timing started with the first step after the starting line and ended after the first step over the finishing line using a stopwatch. Participants were allowed to use walking aids during the test, such as a cane. High test-retest reliability (intraclass correlation coefficients being greater than 0.9) has been reported for gait speed measured over an 8 meter walkway in older adults with radiographic knee OA(28). Study participants performed two 20-meter walks and gait speed was defined as the mean of both walk speeds, i.e. $([20m/time\ 1 + 20m/time\ 2]/2)$.

Knee OA and pain

Radiographic knee osteoarthritis (ROA) was assessed from weight-bearing posteroanterior and lateral fixed flexion radiographic evaluations of both knees(29). Radiographs were independently graded twice among three expert readers (Two rheumatologists and a musculoskeletal radiologist) for joint space narrowing and osteophytes in the tibiofemoral joint according to Kellgren and Lawrence K/L criteria (grades 0-4)(30). Any disagreements were adjudicated among all three expert readers to reach consensus. There was high agreement between readers with kappa statistics ranging from 0.70 to 0.80 for K/L grades. We defined the presence of ROA as a K/L grade ≥ 2 . Knee pain (absent/present) was evaluated by asking participants if they had pain, aching, or stiffness in or around each knee on most days for at least one month within the past year. This definition of knee pain has been employed previously using data from OAI(31) and in combination with ROA to define symptomatic knee OA(32).

Participants were categorized into four groups: neither ROA nor knee pain, the presence of ROA but no knee pain (ROA only), no ROA but with the presence of knee pain (Pain only), or the presence of both ROA and knee pain (symptomatic knee OA). We assigned a participant's knee OA category based on the status of his/her worst knee. For instance, a person with symptomatic knee OA in one knee and pain only in the contralateral knee was classified as having symptomatic knee OA, whereas a person with ROA only in one knee and pain only in the contralateral knee was classified as having pain only.

Knee pain was also examined using a severity scale.(33, 34) Participants were asked to rate the worst pain in each knee from the last 7 days. Pain was rated on an ordinal scale ranging from "0" to "10" with "0" representing "No pain" and "10" being "Pain as bad as you can imagine". We reported values from the knee with higher pain severity.

Potential confounders

We evaluated the following factors as potential confounders given previous literature linking them as risk factors for knee OA or knee pain and slow gait speed. These included age(10, 35), race (Non-White vs White)(10, 36), sex(10, 35), and education level (<some college vs. college)(36, 37) measured from self-report. Body Mass Index (BMI)(10, 38) was computed from standardized weight and height assessments and classified into World Health Organization categories(39). Comorbidities (1 vs none)(40, 41) were measured from the modified Charlson comorbidity index(42) and the presence of depressive symptoms(43, 44) was classified using a score ≥ 16 on the Center for Epidemiologic Studies Depression Scale (CES-D)(45). Isometric knee extensor strength(10, 46) was measured using the "Good Strength Chair" (Metitur Oy, Jycaskyla, Finland) with participants positioned seated with their legs hanging over the edge of the chair. After two warm-up repetitions with 50% effort, three maximum isometric knee extensor repetitions at an angle of 60 degrees were performed and averaged together. We then categorized strength into sex-specific and weight adjusted tertiles since no established strength categories are available. Lastly, physical activity(47-49) was measured from the Physical Activity Scale for the Elderly (PASE)(50) and categorized into tertiles since no established physical activity categories are available from PASE.

Analysis

We compared characteristics of participants across knee OA status categories by performing analysis of variance tests for continuous variables and chi-square tests for categorical variables. Subjects who were included had baseline gait speed and a minimum of two follow-up time points in order to provide an adequate number of data points for trajectory analyses(51, 52). We employed a SAS macro named PROC TRAJ to identify trajectories of

gait speed(53). This approach applies a multinomial modeling strategy to identify relatively homogenous clusters of developmental trajectories within a sample population, i.e. the modeling strategy allows for the emergence of more than two trajectories. Trajectory parameters are derived by latent class analysis using maximum likelihood estimation. In particular, the distinctive trajectories of gait speed were derived by modeling gait speed as a function of time, i.e. the number of years in the study. The number of trajectories were determined by the patterns of change in gait speed, and not forced to fit a particular model. We assumed each trajectory of gait speed had a linear pattern of decline. We tested this by also including a quadratic term, which tests for the possibility that change in gait speed has a curved shape (e.g. faster then slower) and evaluated these patterns of decline from p-values for each trajectory group. Linear but not quadratic model terms were statistically significant ($p < 0.05$), therefore we only included a linear term. The optimal number of groups was assessed using model fit from Bayesian Information Criteria (BIC) and trajectory slopes(2, 3). We considered adjacent trajectory groups with slopes differing by more than 10% to be unique. We used the posterior probabilities of group membership from each individual to assess the fit of the model, which was provided by the PROC TRAJ macro. High probability of membership into a single group represents a good model fit.

Next, we examined the association knee OA categories with trajectories of gait speed using a multivariable polytomous regression model adjusting for potential confounders. We repeated these analyses for each of the following age-strata: 45 to 59 years, 60 to < 69 years, and 70 years.

Results

Of the 4796 subjects at baseline, 87% had at least two years of follow-up and were included in analyses and 20 did not have measures of ROA or pain. Of the remaining participants, 25% had ROA only, 19% pain only, and 30% symptomatic knee OA (ROA and pain). Participants with symptomatic knee OA were more likely to be non-white, have less education, more depressive symptoms, a higher BMI, lower knee strength, and higher knee pain severity compared with those in the other knee OA categories (Table 1). A majority of participants (77%) had gait speed measures at all five time points, while 15% had gait speed measures at four time points, and 8% at three time points.

We identified five distinct trajectories of gait speed. About 5% ($n=205$) of participants were in a fast decline trajectory of gait speed, slowing 0.025 m/s per year (95% CI [-0.020, -0.031]) or 2.70%/year. The remaining participants had either a stable or slightly declining gait speed, slowing less than 1.0%/year (Figure 1). We found the mean posterior probabilities of group assignment to range from 0.90 to 0.94, indicating good fit of the trajectory model.

In general, trajectory groups with faster declines in gait speed had a higher proportion of participants with symptomatic knee OA and a lower proportion of participants with neither ROA nor pain (Figure 2). Participants with symptomatic knee OA had the highest risk of a fast decline in gait speed followed by those with knee pain only and those with ROA only (Table 2). Compared with those with neither pain nor ROA, participants with symptomatic knee OA had almost 9 times the odds (OR = 8.9, 95% CI [3.1, 25.5]) of being in the fastest decline trajectory after adjustment for potential confounders. Participants with knee pain only had an increased risk of being in the fastest decline trajectory, although the magnitude of association was less than those with symptomatic knee OA (OR = 4.5 [1.4, 14.6]). People with ROA only had a slightly increased risk, albeit this was not statistically significant compared with those with neither pain nor ROA (OR = 1.7 [0.6, 4.7]).

For participants 45 to 59 years at baseline, we identified 3 distinct gait speed trajectories. Those in the fastest decline trajectory slowed 0.006 m/s per year (0.72%/year from baseline to the last follow-up visit). Symptomatic knee OA was associated with the highest risk of decline in gait speed (OR=2.3 [1.4, 3.7]) (See Supplementary Figure A, available on the Arthritis Care & Research website). Three distinct gait speed trajectories were also found for participants 60 to 69 years at baseline. Those in the fastest decline group slowed 0.003 m/s per year (0.68%/year from baseline to the last follow-up visit). Symptomatic knee OA and knee pain only had a similar risk of decline in gait speed (OR =3.2, 95% CI [1.7, 6.02], and 3.0 [1.4, 6.1], respectively) (See Supplementary Figure B, available on the Arthritis Care & Research website). For participants 70 years of age or older, we identified five trajectories of gait speed. The fastest decline group slowed 0.038 m/s per year (5.55%/year from baseline to the last follow-up). Participants with symptomatic knee OA again had the highest risk of decline in gait speed (OR=6.0 [1.2, 31.1]) (See Supplementary Figure C, available on the Arthritis Care & Research website).

Discussion

Among people with or at high risk of knee OA, approximately 5% had an underlying trajectory of fast decline in gait speed. People with symptomatic knee OA had the highest risk of being on this trajectory of fast decline compared with those with neither ROA nor knee pain. The current study findings add that people with symptomatic knee OA have a predilection for premature slowing of gait speed. Given the strong link between slow gait speed and mortality, people with a slowing gait speed may also be at risk of morbidity and mortality(4). Moreover, those in the fastest decline trajectory slow at a rate equivalent to what is expected in healthy adults 5 to 12 years older on average. For instance, those in the fastest decline trajectory were 67.4 years old on average and based on normative data around a 1%/year decline gait speed would be expected(6). However, their actual rate of decline was 2.75%/year, which is typically observed in healthy adults aged 75 to 80 years old, which we believe is a difference of clinical relevance.

We find it noteworthy that people with symptomatic knee OA were generally at a higher risk of a fast decline in gait speed than those with pain alone. While previous literature suggests a discordance between radiographic findings and symptoms(16), pain is a subjective factor whose response is unique to each person. A recent study that accounted for between person factors reported a strong association between radiographic severity and pain(54). Therefore, one explanation why people with symptomatic knee OA were at higher risk of a fast decline in gait speed is that they had more severe pain than those with knee pain only. In the present study, the mean pain severity on the 0 to 10 scale for people with symptomatic knee OA was 5, while for those with pain only was 4. While a one unit change in pain may not represent a clinically significant difference for an individual, this mean difference between groups still supports the notion that the effect of knee OA on trajectories of gait speed is perhaps mediated by pain severity, one of the most common symptoms of knee OA.

The study findings show that people with the slowest gait speed at baseline were likely to be in the fast decline gait speed trajectory. Similar phenomenon has also been observed in the other numerical quantities of physiological measures, such as blood pressure in adults and knee cartilage loss among OA participants(55, 56). Nevertheless, the strong correlation between an absolute value and the rate of change is akin to a “horse-racing” effect, i.e. one would expect the fast horses in a race to be out in front at any given time point(57). Thus, it is not that a slow gait speed at baseline causes a trajectory of decline in gait speed, but rather the trajectory of gait speed determines the current gait speed. Symptomatic knee OA may have altered the trajectory of gait speed well before the start of the study, thereby resulting in slower walking at any subsequent point in time.

Despite the fact that increased age is strongly associated with a slower gait speed(35), we consistently found participants with symptomatic knee OA to have the highest risk of a fast decline in gait speed across age stratum. However, it is noteworthy that the rate of decline among those with symptomatic knee OA was by far the fastest within the highest age stratum of participants > 70 years of age (5.55%/year), compared with those 60 to 69 years (0.68%/year) and those 45 to 59 years of age (0.72%/year). Likewise across the overall sample, participants in the fast decline trajectory had the highest mean age (67.4 years) compared with the other trajectory groups (Figure 1). Hence, the presence of symptomatic knee OA may be most detrimental for adults with more advanced age when declines in gait speed are common.

Our study has several limitations. First, since only four years of follow-up were available, we were unable to link membership in trajectory groups with subsequent risk of health outcomes, such as total knee replacement, hospitalization, or mortality. Second, it is important to note that there is still variation of changes in gait speed within each of the five gait speed trajectories despite the fact the methods we employed allowed identification of distinctive trajectories. Finally, an individual's gait speed trajectory is not likely to be discerned in the clinic without collecting standardized measures of gait speed over multiple time points; thus the feasibility of using trajectories in the clinic setting needs to be evaluated in future studies.

Despite these limitations, our study has several strengths. First, we employed a novel methodology whose underlying assumption fits well with gait speed trajectories. Previous longitudinal studies have charted the individual variability of gait speed around a mean population trend(8, 58-60). A limitation to this approach is that meaningful subgroups of change that follow a distinct trajectory cannot be identified(51). As an alternative, a multinomial modeling strategy allows for the emergence of distinct trajectories of gait speed that affords the ability to investigate distinctive patterns within a study population instead of assuming common rate of decline. Furthermore, using this method we found the posterior probability of allocating each study participant into trajectory groups to be over 90%, indicating a good fit of the model of group trajectories to individual trajectories. Second, we used data collected from a large multi-center longitudinal cohort study conducted among people with or at high risk of knee OA. Such data allowed us to describe gait speed trajectories among a large number of people who were likely to experience a decline in gait speed.

Among older adults with or at high risk of knee OA, clinicians should be most concerned about health outcomes in those with symptomatic knee OA given this group is most likely to have a fast decline in gait speed. Currently, clinicians could consider prescribing a walking program to their patients with or at high risk of knee OA in order to promote the preservation or improvement of gait speed. This assertion is based on data from clinical trials that reported improvements in walking performance following the completion of a walking program in people with symptomatic knee OA.(61, 62) In particular, a walking program involving the use of a pedometer to record steps/day paired with a step count goal has been shown to be effective with increasing physical activity and reducing blood pressure in adults.(63) A similar method could be considered to treat people with or at high risk of knee OA. Future research is needed, however, to confirm if such an approach increases gait speed and changes gait speed trajectories in people with or at high risk of knee OA.

In conclusion, 5% of people with or at high risk of knee OA had a fast decline trajectory of gait speed slowing 3% per year in gait speed. This magnitude of slowing is typical in adults 5 to 12 years older on average than our sample. People with symptomatic knee OA had the highest risk of fast decline in gait speed followed by those with pain without ROA. These

findings were consistent across age stratum suggesting that symptomatic knee OA is a risk factor for a premature decline in gait speed independent of age. Future studies should examine if intervention of symptomatic disease, such as walking programs, can prevent future declines in gait speed and whether fast decline in gait speed is associated with poor health outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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SIGNIFICANCE AND INNOVATION

Approximately 5% of participants with or at high risk of knee OA had an underlying trajectory of fast decline in gait speed, which is a strong indicator of future poor health outcomes.

Participants with symptomatic knee OA (radiographic knee OA and knee pain) had almost a 9-fold increased risk of being on a trajectory of fast decline compared with those with neither radiographic knee OA nor knee pain.

Participants with knee pain alone or radiographic knee OA alone also had a higher risk of fast decline, however the magnitude of such risk was less than those with symptomatic knee OA.

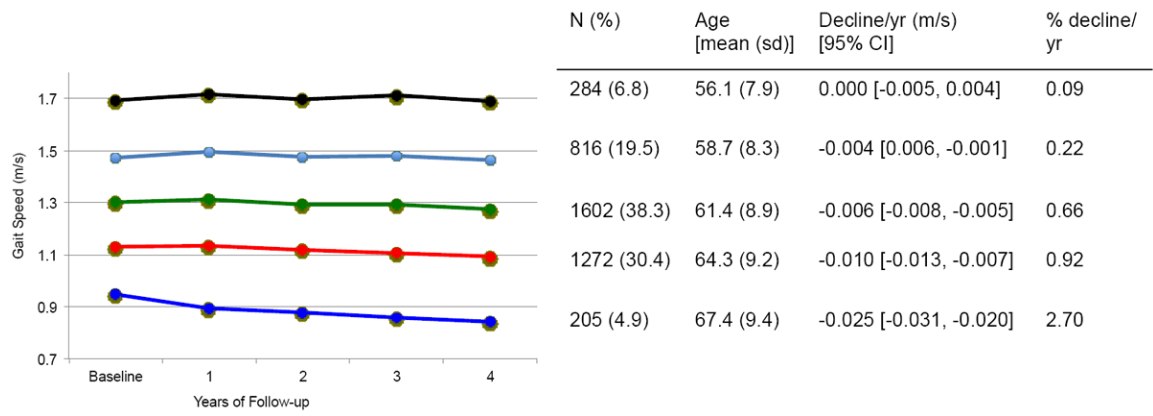


Figure 1. Gait speed trajectory groups and unadjusted absolute and relative decline in gait speed.

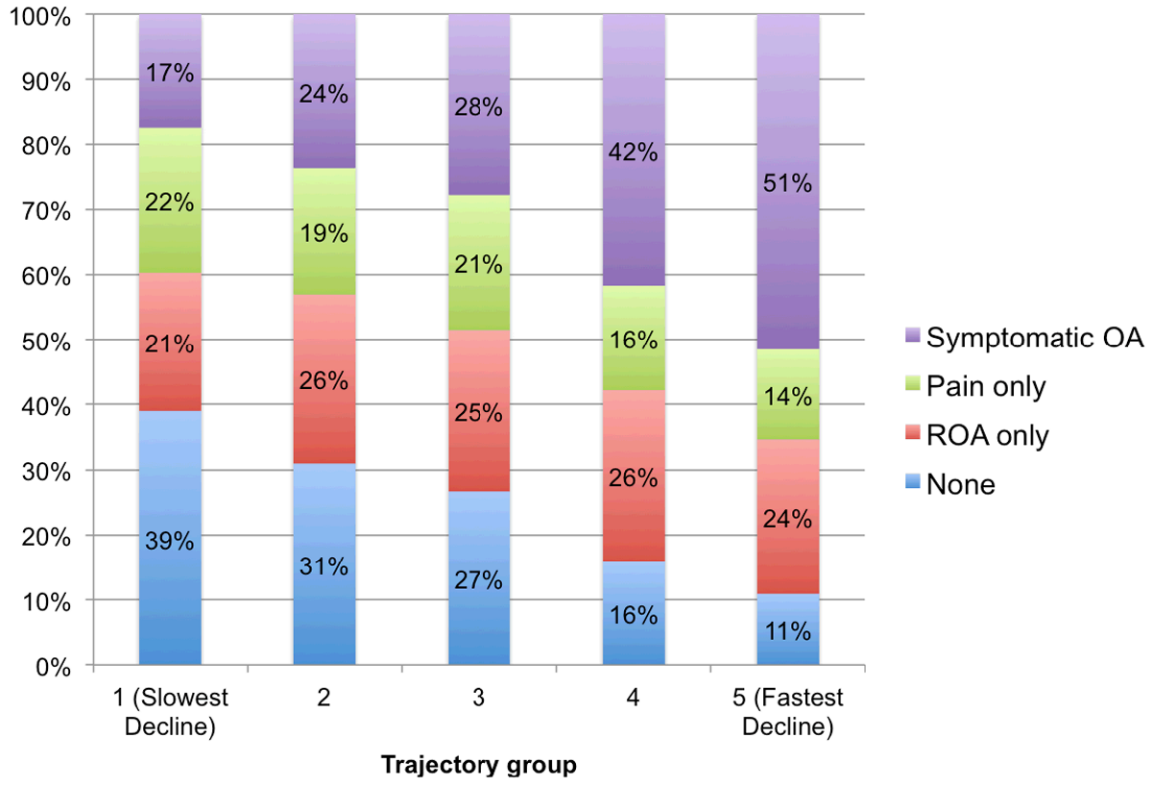


Figure 2. Percentage of participants within each knee OA status category across gait speed trajectory groups.

Table 1

Subject characteristics for all study participants (n=4179) and across knee OA categories.

	Overall (n=4179)	Neither ROA nor no knee pain (n=1079)	ROA only (n=1047)	Pain only (n=797)	Symptomatic OA (n=1236)	p-value
Age [Mean (sd)]	61.1 (9.1)	60.1 (9.1)	63.8 (8.8)	58.4 (8.9)	61.4 (9.0)	<0.0001
Women [%]	57.6	58.4	59.2	57.5	55.7	0.35
Non-White [%]	19.0	10.5	14.2	20.9	28.9	<0.0001
High School [%]	14.6	11.3	13.5	13.7	19.2	<0.0001
Number of Comorbidities [Mean (sd)]	0.4 (0.8)	0.3 (0.7)	0.4 (0.8)	0.4 (0.8)	0.4 (0.9)	<0.0001
CES-D [Mean (sd)]	6.3 (6.7)	5.5 (6.0)	5.3 (5.8)	7.1 (6.9)	7.4 (7.5)	<0.0001
BMI [kg/m] [Mean (sd)]	28.5 (4.8)	26.8 (4.4)	29.0 (4.6)	27.8 (4.5)	30.1 (4.9)	<0.0001
<25 [%]	24.3	36.7	20.7	29.0	13.5	
25-29 [%]	39.7	39.3	39.3	42.8	38.3	
30 [%]	26.2	24.0	40	28.2	48.3	
PASE (Physical activity) [Mean (sd)]	163.2 (82.0)	169.2 (79.5)	151.6 (77.4)	171.6 (86.7)	162.5 (83.8)	<0.0001
Knee extensor strength (Newton/kg) [Mean (sd)]	4.2 (1.5)	4.6 (1.4)	4.1 (1.4)	4.3 (1.5)	3.8 (1.4)	<0.0001
Knee pain intensity (0-10) [Mean (sd)]	3.2 (2.7)	1.7 (2.0)	2.2 (2.2)	4.0 (2.5)	5.0 (2.5)	<0.0001

ROA, Radiographic knee osteoarthritis; OA, Osteoarthritis; CES-D, Center for Epidemiologic Studies Depression Scale; PASE, Physical Activity Scale for the Elderly

Table 2
Adjusted* association knee OA status with membership within each trajectory group

Knee OA Status	1	2	3	4	5
	(Slowest Decline) (n=284) OR	(n=1272) OR (95% CI)	(n=1602) OR (95% CI)	(n=816) OR (95% CI)	(Fastest Decline) (n=205) OR (95% CI)
ROA only vs neither ROA nor pain	1.0	0.9 (0.5, 1.6)	0.9 (0.5, 1.6)	1.3 (0.7, 2.4)	1.7 (0.6, 4.7)
Pain Only vs neither ROA nor pain	1.0	1.2 (0.6, 2.6)	1.9 (0.9, 3.9)	2.0 (0.9, 4.7)	4.5 (1.4, 14.6)
Symptomatic OA vs neither ROA nor pain	1.0	1.7 (0.8, 3.5)	2.5 (1.3, 5.2)	4.1 (1.9, 8.8)	8.9 (3.1, 25.5)

OR, Odds Ratio; 95% CI, 95% Confidence Interval

* Adjusted for age, sex, race, education, comorbidities, depressive symptoms, BMI, Knee extensor strength, and physical activity.