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Original Article

Factors Associated with Trajectories of Physical Activity Over 8 Years in Knee Osteoarthritis

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Abstract

Objective: The aim of the study was to investigate (1) trajectories of physical activity (PA) over 96 months and (2) study to what extent knee pain, muscle strength, physical function, and radiographic disease were associated with PA trajectories in adults with or at risk of knee osteoarthritis (KOA).

Methods: Using the Osteoarthritis Initiative (OAI) database, we described PA trajectories with the Physical Activity Scale for the Elderly (PASE) over 96 months. Knee pain was categorized into three groups: "no pain" [visual numeric pain rating scale (VAS = 0)], "little to some pain" (VAS = 1-3), or "moderate to severe pain" (VAS ≥ 4). Knee extensor strength was classified into high [>16.21 (men) and >10.82 (women) N/kg/m^2] and low [<16.21 (men) and <10.82 (women) N/kg/m^2] groups. Gait speed was classified into slow (<1.22 m/s) and fast (≥1.22 m/s) groups. Chair stand time was classified into slow (>12 seconds) and fast (<12 seconds) groups. Radiographic disease was classified as present [Kellgren–Lawrence (KL) ≥2] or absent (KL grade <2) of KOA.

Results: Among 3755 participants (age 61.0 ± 9.0 years, body mass index 28.5±4.8 kg/m^2, 58% female), we identified three trajectories: sedentary PA with slow decline (44.3%), low PA with slow decline (41.3%), and high PA with slow decline (14.4%). Poorer gait speed (OR: 2.32; 95% CI: 1.71-3.16), chair stand time (OR: 1.45; 95% CI: 1.07-1.96), and knee extensor strength (OR: 1.35; 95% CI: 1.03-1.76), but not pain or radiographic disease, were associated with PA trajectory of sedentary PA with slow decline.

Conclusion: Physical function and strength, but not pain and radiographic disease, were associated with a trajectory of decline in PA among adults with or at risk of KOA.

Keywords: Knee osteoarthritis, physical activity, pain, muscle strength, physical function

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Introduction

Osteoarthritis is the 11th most common cause of disability worldwide in adults,[1] and knee osteoarthritis (KOA) is the most common cause of functional limitation.[2] Decline in physical activity (PA) is also common among adults with KOA,[3] despite evidence showing improved health outcomes in those that remain physically active.[4] While the level of PA naturally decreases with age, excessive inactivity is associated with higher rates of obesity, coronary heart disease, type II diabetes mellitus, and dementia.[5,6] Decline in PA is a public health concern due to the strong association of risk of future hospitalization, loss of independence, and need for assistive care.[7,8]

Decline in PA over time is not uniform as some adults with KOA decrease faster than others.[9] However, little is known about decline in PA in adults with KOA, independent of age and how modifiable risk factors relate to the trajectory of decline in PA. Knee joint pain is assumed to be the primary driver of decline in PA in adults with KOA; however, other potential contributors may also exist. Adults with KOA also have 20-45% lower muscle strength, particularly of the quadriceps muscle, compared to age- and gender-matched peers.[10,11] Quadriceps weakness is clinically important and could likely be a determinant of decline in PA over time. Another potential barrier to increasing PA is functional limitation, such as slow walking,[12] which has been shown to hinder how often one participates in PA.[13] Knee joint pain,[14] quadriceps weakness,[15] and functional limitation[16] are all known symptoms of KOA, though it is unknown how these relate to decline in PA.

To date, little is known on how radiographic disease influences PA trajectories in older adults with and at risk for KOA. This is a major gap given that joint structural changes on radiography are a common clinical indicator of disease progression,[17] though the consequences on physical activity (PA) are unclear. Given that many patients with radiographic evidence of KOA have no knee pain symptoms,[18] we will study the

relationship of radiographic disease with PA trajectories separate from knee pain.

Therefore, the purpose of our study was to (1) describe trajectories of self-reported PA over 96 months and (2) investigate to what extent knee joint pain, muscle strength, and performance-based physical function at baseline are associated with PA trajectories in adults with or at high risk of KOA. Because knee pain,[14] muscle weakness,[10] and gait speed[16] are all modifiable risk factors for potential change in PA trajectories, we focused on these risk factors for study. Further, we examined radiographic disease to determine if joint structure is related to a faster decline in PA over time. We hypothesized that poorer knee pain, muscle strength, and performance-based physical function would be associated with trajectories of decline in PA, after controlling for potential confounders. If the identified risk factors were influential on PA trajectories, this could help inform targeted KOA interventions. We also hypothesized that the severity of radiographic KOA would be associated with a decline in PA. Understanding how clinical risk factors impact PA trajectories could offer important insight into the impact of disease and help inform appropriate treatment plans for adults with KOA.

Methods

Study Sample

Annual clinic visits from baseline to 96 months were used from the Osteoarthritis Initiative (OAI). Details of the study are described elsewhere.[19] In brief, adults between ages of 45 to 79 years who had or were at high risk of KOA were eligible. Participants were recruited from five clinical sites (Baltimore MD, Pittsburgh PA, Pawtucket RI, San Francisco, CA and Columbus OH). Participants were excluded if they were diagnosed with rheumatoid or inflammatory arthritis, unilateral or bilateral total knee arthroplasty or had positive pregnancy test. Data were obtained on all participants at the baseline visit and over 96 months of follow-up visits. In order to have an adequate number of data points for the trajectory analysis, study participants were required to have a baseline Physical Activity Scale for the Elderly (PASE) data point and a minimum of two follow-up PASE data points.[20] Institutional Review Board approval was obtained from all four OAI collaborating centers for the parent OAI study and ethics approval was granted from the Committee on Human Research, University of Maryland, The Ohio State University, University of Pittsburgh, Memorial Hospital of Rhode Island and University of California, San Francisco (IRB approval number 10-00532).

Study Outcome

The Physical Activity Scale for the Elderly (PASE) score measures PA performed by older adults (walking, recreational activities, exercise, housework, yard work, and caring for others).[21] A score, ranging from 0 to 793, is assigned based on frequency, duration, and intensity level of activity over the previous week, with higher scores indicating a greater PA.[21] The PASE survey is a validated instrument that has shown moderate (Spearman rho = 0.43) convergent validity to digital PA monitors (Actigraph Monitors Inc.).[22] To date, there is no minimal clinically important difference score available for the PASE for KOA; however, a minimal detectable change of 87 points was found for hip OA.[17] Normative data are available for healthy older adults ≤70 years (142.9 points) and those >70 years (110.8 points).[18]

Study Exposure

A priori risk factors were identified prior to analysis and defined as three domains: knee joint pain [visual numeric pain rating scale (VAS)], muscle strength (knee extensor force output and repeated chair stand test), and performance-based physical function (gait speed).

Knee joint pain was rated on an 11-point ordinal scale (0 = no pain and 10 = worst possible pain imaginable) and used as a proxy for perception of knee pain intensity.[23] Participants were asked to rate their pain in each knee over the last 7 days. The knee with worst pain rating served as the index knee and was used to categorize participants into one of three groups: "no pain" (VAS = 0), "little to some pain" (VAS = 1-3), "moderate to severe pain" (VAS ≥ 4). We categorized VAS to provide clinically distinct groups of knee pain. The visual analog pain scale has shown high test–retest reliability in patients with arthritis ($r = 0.96$)[23] and is commonly used for adults with KOA.[24]

Muscle strength was defined as maximal isometric knee extensor force output and repeated chair stand test. Isometric knee extensor force testing was performed with the participants placed in a seated position with the knee flexed to 60° using the Good Strength Chair (Metitur Oy).[25] Participants were asked to perform two warm-up trials at 50% maximal effort, followed by three trials at maximum effort. The average of the three trials was used for analysis. Participants were dichotomized into either a low- or high-strength group based on sex-specific means normalized by body mass index (BMI) [≥16.21 N/kg/m^2 for males and ≥10.82 N/kg/m^2 for females = high strength group, <16.21 N/kg/m^2 for males and <10.82 N/kg/m^2 for females = low strength group]. The cutoff for strength groups was based on a mean split of this strength metric as no study has examined categorization of low and high strength within people with KOA. However, women with KOA have less strength[26] and have lower BMI[27] compared to their male counterparts, which can influence strength outcomes. Strength measures normalized to BMI have been established as a common method for evaluating quadricep deficits over time in knee pathology.[28] Maximum isometric strength testing has shown good to excellent reliability ($r = .81$-$.98$).[29] The repeated chair stand test is a validated measure of lower body function.[30] It is measured using a straight-backed chair without arms, with the seat height of 45 cm.[30] Participants were asked to fold their arms, stand up as quickly as they can five times, rising until they are in a full upright standing position. The test was timed and measured to the hundredth of a second. The average of two trials was used for analysis. Participants were dichotomized into either a slow or fast repeated chair stand group based on a cutoff score of 12 seconds (≥12 seconds = slow repeated chair stand group, <12 seconds = fast repeated chair stand group), as times greater than or equal to 12 seconds are associated with the inability to be physically active in adults with KOA.[13] Community-dwelling older adults who took more than 12 seconds to compete the five times sit to stand test had double (OR = 2.0, 95% CI [1.3, 3.0]) the risk for multiple falls compared with those who took <12 seconds to complete the test.[31]

Performance-based physical function was defined as the average gait speed at baseline, which is associated with future health outcomes in older adults, including mortality.[32] Gait speed was collected by a certified OAI assessor using a standard protocol detailed with specific course setup, measurement procedures and scripted instructions. Gait speed [meters per second (m/s)] was determined based on the average self-selected speed over two 20-m trials and used as a valid index of physical capacity in older adults.[33] Participants were dichotomized into either a slow or fast gait speed group based on a cutoff score of 1.25 m/s (<1.25 m/s = slow group >1.25 m/s = fast group), which is the speed needed to safely cross a timed crosswalk.[34] Gait speed recommendations for community-dwelling older adults vary widely.[35] However, recommendations of speeds of 1.25 m/s have been used as a baseline for timing walk signals traffic crossing.[35]

Baseline radiographic KOA was assessed from weight-bearing posteroanterior and lateral fixed flexion radiographic evaluations. Radiographic images were independently graded twice among three experts (two rheumatologists and a musculoskeletal radiologist) for tibiofemoral joint space narrowing and osteophytes using the Kellgren–Lawrence (KL) 0-4 criteria,[36] with adjudication of a third rater if necessary. The knee with the worst KL grade served as the index knee and was used to classify participants into either presence (KL grade ≥2) or absence (KL grade <2) of radiographic KOA.

Potential Confounders

The following variables were considered as potential confounders based on their association with decline in PA in previous studies [37-39] and were obtained at the baseline OAI clinic visit: age, sex, BMI, race (non-White vs. White), education (<college degree vs. ≥college degree), marital status (married or non-married), comorbidities (≥1 vs. none, measured from the modified Charlson comorbidity index), and depressive symptoms (depressed >16 vs. non-depressed <16, measured from the Center for Epidemiologic Studies Depression Scale).

Statistical Analysis

First, the number of PA trajectory groups was determined using a group-based trajectory model (PROC TRAJ),[40] which applies a multinomial modeling strategy to identify relatively homogeneous clusters of developmental trajectories within a sample population. In other words, the modeling strategy allows for the emergence of trajectories based on the data rather than forcing a set number of trajectories determined a priori. Trajectory groups were also modeled using one of the following polynomial orders of time: intercept only or by linear, quadratic, or cubic terms. We selected a censored normal model, as this model is appropriate for the physical activity data from the PASE (i.e., psychometric scale data). PASE values were confirmed to be normally distributed via histograms overlaid with a density plot curve for each time point. To determine the number of trajectory groups, the order of the polynomial was varied until the best-fitting model was obtained that met statistical significance.[41] Each participant was classified into a specific trajectory group that had the highest estimated probability compared with other trajectory groups. To select the optimal number of trajectory groups, we required the smallest trajectory group to include >10% of the participants in the analytic dataset.

Second, the associations of baseline risk factors with PA trajectories were determined using odd ratios and 95% CIs, calculated from separate multinomial logistic regression models. The baseline risk factors included radiographic KOA, knee joint pain (VAS), muscle strength (knee extensor force output and repeated chair stands), and performance-based physical function (gait speed) for those participants that met the study eligibility requirements. In the primary analyses, we categorized exposure variables using cut-points from the literature. As a sensitivity analysis, we used tertiles to categorize exposure variables. All analyses were adjusted for potential confounders (i.e., age, sex, BMI, race, education, marital status, depressive symptoms, presence of comorbidity, and radiographic KOA) in multivariable models. In addition, radiographic KOA and knee pain were added as covariates in the models investigating muscle strength and performance-based tests of physical function. Knee joint pain was not adjusted for as a potential confounder in the radiographic KOA model, as pain is an intermediate on the causal pathway between radiographic KOA and PA. All analyses were performed using SAS software, version 9.4 (SAS Institute Inc., Cary, NC, USA, Copyright 2016).

Results

Participants

Of the 4796 OAI participants at baseline, 3755 participants met our analytic eligibility requirements (i.e., had a baseline visit and at least two follow-up visits). The average age (standard deviation) was 61.0 (9.0) years, 58.3% were female, 81.9% were White, 62.9% had at least a college education, and 22.8% had at least one comorbidity. At baseline, 56.4% had radiographic KOA. The average (standard deviation) knee pain was 3.2 (2.7) and 23.3% rated their knee pain as 0 or 1 on the 11-point VAS scale. The average BMI (standard deviation) was 28.5 (4.8) kg/m^2 with 25.6% having a BMI <25 kg/m^2, 39.8% considered overweight, and 34.6% classified as obese. Less than 9% of participants had depressive symptoms (Table 1). We found that 370 study participants (10.3%) had a total or partial knee arthroplasty over the follow-up. Compared to those included in the analytic dataset (n=3755), those not included (n=1041) were older, less white, less college educated, had more depressive symptoms, were more likely to have a comorbidity, had a higher BMI, were less physically active, had a slower gait speed and repeated chair stand test time, had higher pain, and had lower strength (Supplemental Table 1).

Trajectories of Physical Activity

We identified three PA trajectories over 96 months (Figure 1 and Table 2). Figure 1 shows the superimposed mean decline of each trajectory along with a random sample of 100 individual PASE values within each trajectory group. The *sedentary PA with slow decline* trajectory included 44.3% of participants, was cubic in shape, and was characterized by a minimal decline throughout the 96 months of follow-up that met statistical significance [mean (95% CI) PASE=−2.30/year (−2.71, −1.87)]. The *low PA with slow decline* trajectory included 41.4% of participants, was linear in shape, and was characterized by minimal decline throughout the 96 months of follow-up that met statistical significance [mean (95% CI) PASE=−2.81/year (−3.37, −2.26)]. The *high PA with slow decline* trajectory included 14.4% of participants, was linear in shape, and was characterized by minimal decline throughout the 96 months of follow-up that met statistical significance [mean (95% CI) PASE=−2.49/year (−3.57, −1.41)]. The posterior probabilities of assigning each participant into one of the three trajectories were all >0.90, indicating there was a 90% probability, on average, of each individual trajectory fitting the respective group trajectory. A sensitivity trajectory analysis was performed with only participants who had complete PASE data at each time point (n=3394) and produced three trajectories of similar intercept, slope, shape, posterior probabilities, and percent distribution of the sample between the three trajectory groups. As well, we found three trajectories of similar intercept, slope, shape, posterior probabilities, and percent distribution when restricting the sample to participants who had not received a knee replacement at any point during the study (n=3229).

Association of Knee Joint Pain, Muscle Strength, and Performance-Based Physical Function with Trajectory Groups

Slower gait speed (Table 3 and Supplemental Table 2), longer repeated chair stand time (Table 3 and Supplemental Table 3), and less knee extensor strength (Table 3 and Supplemental Table 4) at baseline were associated with the *sedentary PA with slow decline* trajectory. Participants walking less than 1.22 m/s had twice the odds of being in the *sedentary PA with slow decline* trajectory group [odd ratio (OR) 2.32; 95% CI (1.71, 3.16)] and 1.5 times the odds of being in the *low PA with slow decline* group [OR 1.56; 95% CI (1.16, 2.11)] compared with those walking at least 1.22 m/s. Those that completed the repeated chair stand test in greater than or equal to 12 seconds at baseline had 1.4 times the odds of being in the

Table 1. Baseline Participant Characteristics

	Entire Sample (n=3755)	High PA with slow decline (n=534)	Low PA with slow decline (n=1557)	Sedentary PA with slow decline (n=1664)	*P* value*
Age [mean (SD; min-max)]	61.0 (9.0; 45.0-79.0)	54.0 (5.8; 45.0-78.0)	59.3 (8.3,45.0-79.0)	64.8 (8.6, 45.0-79.0)	<.0001
Women [%]	58.3	37.8	56.4	66.8	<.0001
White [%]	81.9	84.8	83.2	79.7	.01
College graduate [%]	62.9	69.8	64.2	59.4	<.0001
Depressive Sx (CES-D) [mean (SD; min-max)]	6.2 (6.6; 0.0-57.0)	5.8 (6.7; 0.0-57.0)	6.0 (6.3; 0.0-46.0)	6.6 (6.9; 0.0-55.0)	.01
1+ comorbidities [%]	22.8	14.2	22.5	25.9	<.0001
BMI [kg/m^2] [mean (SD; min-max)]	28.5 (4.8; 16.9-48.7)	28.5 (4.7; 16.9-44.2)	28.1 (4.7; 17.7-46.8)	28.8 (4.9; 17.2-48.7)	.0001
Radiographic KOA [%]	56.4	48.9	53.5	61.7	<.0001
PASE score [mean (SD; min-max)]	164.6 (82.1; 0.0-531.0)	275.6 (70.4; 56.0-504.0)	185.8 (62.6; 8.0-531.0)	109.0 (49.9; 0.0-328.0)	<.0001
Gait speed (m/s) [mean (SD; min-max)]	1.33 (0.21; 0.24-2.17)	1.43 (0.20; 0.94-2.10)	1.36 (0.20; 0.68-2.17)	1.28 (0.21; 0.24-2.08)	<.0001
Repeated chair stands (sec) [mean (SD; min-max)]	10.6 (3.3; 3.0-36.9)	9.6 (2.6; 3.6-21.8)	10.4 (3.0; 3.0-27.7)	11.3 (3.6; 4.4-36.9)	<.0001
Knee pain, last 7 days [0-10] [mean (SD; min-max)]	3.2 (2.7; 0.0-10.0)	3.1 (2.7; 0.0-10.0)	3.2 (2.6; 0.0-10.0)	3.3 (2.7; 0.0-10.0)	.36
Normalized strength (N/BMI) [mean (SD; min-max)]	13.3 (4.9; 0.9-37.8)	15.9 (5.2; 3.3-34.8)	13.8 (4.9; 2.8-37.8)	12.0 (4.3; 0.9-30.0)	<.0001
Posterior probabilities [%]	-	93.5	90.4	93.4	-

Sx, symptoms; CES-D, Center for Epidemiologic Studies Depression Scale; BMI, body mass index; KOA, knee osteoarthritis; PASE, Physical Activity Scale for the Elderly; PA, physical activity; *p-value for overall model comparing trajectory groups for respective baseline characteristic.

sedentary PA with slow decline group [OR 1.45 95% CI (1.07, 1.96)] compared with those completing the test in less than 12 seconds. Those classified into the low strength group at baseline had 1.3 times the odds of being in the *sedentary PA with slow decline* group [OR 1.35; 95% CI (1.03, 1.76)] and 1.3 times the odds of being in the *low PA with slow decline* group [OR 1.29; 95% CI (1.00, 1.66)]. Severity of radiographic KOA and knee joint pain at baseline was not associated with trajectory groups, as odds of membership were similar across groups (Table 4).

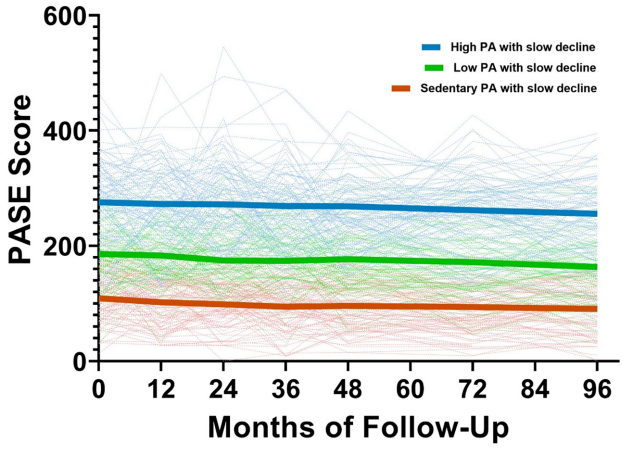
Discussion

We found three unique PA trajectories over 96 months with 44.3% of our sample being on a trajectory of *sedentary PA with slow decline*. We also found that those with slow gait speed, longer repeated chair stand time, and less knee extensor strength at baseline had greater odds of being in the sedentary PA with slow decline group. Knee joint pain and severity of radiographic KOA at baseline did not increase the odds of membership into the *sedentary PA with slow decline* trajectory group. These findings show that physical function and strength may be more potent modifiable risk factors for change in PA than knee pain and severity of radiographic KOA, though future clinical studies would need to confirm this relationship.

We also found an 18.4 PASE point reduction over the 96-month period (i.e., 2.3 point decline/year over 8 years). The average decline in the *high PA with slow decline* and *low PA with slow decline* trajectories, which had decreases of 19.9 and 22.5 points on average over 8 years, respectively, is consistent with previous systematic reviews of healthy adults.[4,42] Hence, our findings indicate a steady decline in PA for all groups over time. PASE score compared to both the *low and sedentary PA with slow decline* trajectory groups, shown by the linear average change of each trajectory sample over time based on the parameter estimates, and not the cubic component, which reflects the statistical significance of the polynomial model and the individual-level variation. These small annual changes over time can have large ramifications on future disability for adults with KOA.

Our findings indicate that adults walking slower than 1.22 m/s (i.e., the speed needed to safely cross a timed crosswalk) were twice as likely to be in the *sedentary PA with slow decline* group compared to those walking above this threshold. This finding may point a decline in PA being a downstream consequence of limited physical function. In particular, the inability to walk fast enough to get across the street may likely be a barrier to walking in the community and result in declining PA over time. This is consistent with prior literature demonstrating a strong relationship between gait speed and PA in adults with and at risk of KOA.[13,43] Our findings add support for the notion that walking at a speed necessary for mobility in the community setting may be an important predictor of future PA.

Whether it is isolated knee extensor strength deficit or impaired ability to perform repeated chair stands, muscle weakness leads to increased risk of a rapid trajectory of decline in PA. Decline in PA is mediated by muscle weakness in male adults with or at risk of KOA.[43] While sarcopenia, the age-related reduction in muscle mass has also shown to be associated with functional decline[44] and poor physical health[45] in older adults, rehabilitation may be indicated to address these underlying impairments limiting physical function. Physical activity promotion and resistive



		BL	12M	24M	36M	48M	72M	96M
Trajectory Groups	High PA with slow decline (n)	534	527	531	526	533	528	517
	Low PA with slow decline (n)	1557	1534	1531	1537	1550	1547	1505
	Sedentary PA with slow decline (n)	1664	1643	1637	1650	1660	1651	1562

Figure 1. Trajectories of Physical Activity Scale for the Elderly (PASE) score. Note: PASE, Physical Activity Scale for the Elderly; PA, physical activity; values in table indicate the number of participants at each time point within each trajectory group; sedentary PA with slow decline trajectory (baseline PASE = 109.0, PASE decline = −2.30/year [−2.71, −1.87]); low PA with slow decline trajectory (baseline PASE = 185.8, PASE = −2.81/year [−3.37, −2.26]); high PA with slow decline trajectory (baseline PASE = 275.6, PASE = −2.49/year [−3.57, −1.41]).

resistance training are effective in improving cardiovascular fitness and muscle strength in adults with KOA,[46] however, further study is needed to determine how these interventions relate to future PA participation.

Knee pain and the severity of radiographic KOA did not increase the risk of being in a trajectory group with decline in PA. Indeed, adults with KOA report that knee pain is a barrier to an active lifestyle[47] and participate in less PA than healthy adults.[48,49] However, more recent studies using accelerometry-based measures of PA show mixed results and show that adults with KOA have similarly low levels of PA as the general population.[3,50] Even after total knee replacement, which results in large clinically meaningful improvements in knee pain and physical function, PA has small to moderate improvements 12 months post-surgery.[51]

Our findings should be considered with caution as several limitations were present with our study. First, given the observational design, there is a possibility of confounding and reverse-causation. We have attempted to mitigate these by adjusting for potential confounders (i.e., age, sex, BMI, race, education,

Table 2. Physical Activity Scale for the Elderly (PASE) Scores at Each Time Point

	High PA with slow decline (n=534)	Low PA with slow decline (n=1557)	Sedentary PA with slow decline (n=1664)
PASE score, BL [mean (SD; min-max)]	275.6 (70.4; 56.0-504.0)	185.8 (62.6; 8.0-531.0)	109.0 (49.9; 0.0-328.0)
PASE score, 12 M [mean (SD; min-max)]	272.6 (69.9; 91.0-580.0)	183.4 (62.5; 5.0-462.0)	102.0 (47.3; 0.0-327.0)
PASE score, 24 M [mean (SD; min-max)]	272.2 (71.0; 58.0-553.0)	174.7 (57.3; 25.0-381.0)	98.6 (45.3; 0.0-291.0)
PASE score, 36 M [mean (SD; min-max)]	269.2 (67.9; 24.0-548.0)	174.0 (57.4; 0-376.0)	94.3 (46.4; 0.0-299.0)
PASE score, 48 M [mean (SD; min-max)]	268.7 (67.5; 82.0-498.0)	176.8 (59.8; 25.0-438.0)	95.9 (46.1; 0.0-314.0)
PASE score, 72 M [mean (SD; min-max)]	261.9 (73.3; 0.0-570.0)	171.6 (62.0; 0.0-499.0)	93.8 (47.0; 0.0-291.0)
PASE score, 96 M [mean (SD; min-max)]	255.7 (71.0; 41.0-488.0)	163.3 (60.9; 3.0-399.0)	90.7 (45.1; 0.0-288.0)

PA, physical activity; PASE, Physical Activity Score for the Elderly.

Table 3. Odds Ratios for Gait Speed, Isometric Quadriceps Strength, and Repeated Chair Stand

Trajectory Group	Gait Speed <1.22 m/s [%]	Unadj. OR [95% CI] <1.22 m/s vs. ≥1.22 m/s	Adj.* OR [95% CI] <1.22 m/s vs. ≥1.22 m/s	Low Strength [%]	Unadj. OR [95% CI] Low Strgth vs. High Strgth	Adj.* OR [95% CI] Low Strgth vs. High Strgth	RCS ≥12 sec [%]	Unadj. OR [95% CI] ≥ 12 sec vs. < 12 sec	Adj.* OR [95% CI] ≥ 12 sec vs. < 12 sec
High PA with slow decline (n=534)	14.2	1.0 (REF)	1.0 (REF)	58.8	1.0 (REF)	1.0 (REF)	15.7	1.0 (REF)	1.0 (REF)
Low PA with slow decline (n=1557)	23.3	1.84 [1.40, 2.40]	1.56 [1.16, 2.11]	47.7	1.58 [1.27, 1.95]	1.29 [1.00, 1.66]	22.6	1.57 [1.20, 2.05]	1.20 [0.90,1.61]
Sed. PA with slow decline (n=1664)	38.6	3.78 [2.91, 4.92]	2.32 [1.71, 3.16]	36.7	2.46 [1.99, 3.05]	1.35 [1.03, 1.76]	32.1	2.54 [1.96, 3.30]	1.45 [1.07, 1.96]

Adj, adjusted; OR, odds ratio; m/s, meters/second; RCS, repeated chair stand test; sec, seconds; strgh, strength; PA, Physical Activity; Sed, sedentary; Unadj, unadjusted.
*Adjusted for age, sex, body mass index, race, education, marital status, depressive symptoms, comorbidity, and radiographic knee osteoarthritis.

Table 4. Odd Ratios for Radiographic Knee Osteoarthritis and Numeric Pain Rating Scale

Trajectory Group	Knee ROA present [%]	Unadj. OR [95% CI] ROA present vs. No ROA	Adj.* OR [95% CI] ROA present vs. No ROA	Little to Some (1-3) pain [%]	Unadj. OR [95% CI] Little (1-3) pain vs. No (0) pain	Adj.* OR [95% CI] Little (1-3) pain vs. No (0) pain	Moderate to Severe (4+) pain [%]	Unadj. OR [95% CI] High (4+) pain vs. No (0) pain	Adj.* OR [95% CI] High (4+) pain vs. No (0) pain
High PA with slow decline (n=534)	48.8%	1.0 (REF)	1.0 (REF)	39.0%	1.0 (REF)	1.0 (REF)	38.0%	1.0 (REF)	1.0 (REF)
Low PA with slow decline (n=1557)	53.5%	1.21 [0.99, 1.47]	1.01 [0.80, 1.28]	37.6%	0.97 [0.75, 1.25]	1.21 [0.90, 1.62]	39.4%	1.04 [0.80, 1.35]	1.18 [0.86, 1.63]
Sed. PA with slow decline (n = 1664)	61.7%	1.69 [1.39, 2.06]	0.98 [0.76, 1.26]	34.7%	0.87 [0.67, 1.12]	1.23 [0.90, 1.68]	41.6%	1.06 [0.82, 1.37]	1.17 [0.84, 1.64]

Adj, adjusted; OR, odds ratio; PA, physical activity; ROA, radiographic knee osteoarthritis; Unadj, unadjusted.
*Adjusted for age, sex, body mass index, race, education, marital status, depressive symptoms, and comorbidity.

marital status, depressive symptoms, presence of comorbidity and radiographic KOA) and studied changes in PA that occurred after our exposures of interest were collected. Other factors, particularly pain in other joints beyond the knee and previous knee injury, could have influenced the results of the study, which will need to be considered in future study. Nevertheless, there is a possibility of residual confounding. Second, caution should be taken when generalizing our study findings to adults with KOA. The OAI includes adults that were generally healthy, younger, well educated, and predominantly White. Third, we employed a self-reported measure of PA, which is subject to recall bias and has limited precision compared to objective measures of PA using accelerometers. While the OAI does include objective measures of PA, these were taken only at two time points, which precludes the ability to study trajectories of PA.

Conclusion

We found limited physical function and lower body strength to be associated with a trajectory of decline in PA among adults with or at risk of KOA. We did not find knee pain and the severity of radiographic KOA to be associated with trajectories of PA. Given that physical function and lower body strength are modifiable, these may be more promising targets for intervention than knee pain to mitigate decline in PA in adults with KOA.

Ethics Committee Approval: Ethical committee approval was received from the Ethics Committee of Memorial Hospital of Rhode Island Institutional Review Board, The Ohio State University's Biomedical Sciences Institutional Review Board, University of Pittsburgh Institutional Review Board, University of Maryland Baltimore – Institutional Review Board, and Committee on Human Research at University of California, San Francisco (IRB approval number 10-00532).

Informed Consent: Written informed consent was obtained from all participants who participated in this study.

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Supplemental Table 1. Baseline Participant Characteristics: Analytic Sample vs Excluded Sample

	Analytic Sample (n=3755)	Excluded Sample (n=1041)	*P* value
Age [mean (SD; min-max)]	61.0 (9.0; 45.0-79.0)	61.7 (9.8; 45.0-79.0)	.046*
Women [%]	58.3	58.8	.756
White [%]	81.9	69.1	<.0001*
College graduate [%]	62.9	47.5	<.0001*
Depressive Sx (CES-D) [mean (SD; min-max)]	6.2 (6.6; 0.0-57.0)	8.1 (8.1; 0.0-48.0)	<.0001*
At least 1 comorbidity [%]	22.8	31.3	<.0001*
BMI [kg/m^2] [mean (SD; min-max)]	28.5 (4.8; 16.9-48.7)	29.2 (5.0; 18.3-47.7)	<.0001*
Radiographic KOA [%]	56.4	58.9	.215
PASE score [mean (SD; min-max)]	164.6 (82.1; 0.0-531.0)	147.1 (82.3; 0.0-516.0)	<.0001*
Gait speed (m/s) [MEAN (SD; min-max)]	1.33 (0.21; 0.24-2.17)	1.27 (0.23; 0.41-2.13)	<.0001*
Repeated chair stands (sec) [mean (SD; min-max)]	10.6 (3.3; 3.0-36.9)	11.7 (4.6; 3.3-50.9)	<.0001*
Knee pain, last 7 days [0-10] [mean (SD; min-max)]	3.2 (2.7; 0.0-10.0)	4.1 (2.8; 0.0-10.0)	<.0001*
Normalized strength (N/BMI) [mean (SD; min-max)]	13.3 (4.9; 0.9-37.8)	12.3 (4.7; 1.9-35.0)	<.0001*

BMI, body mass index; CES-D, Center for Epidemiologic Studies Depression Scale; KOA, knee osteoarthritis; PASE, Physical Activity Scale for the Elderly; Sx, symptoms.
*Denotes excluded sample is statistically significantly different from the analytic sample at $\alpha = 0.05$ using independent samples *t*-tests for continuous variables and chi-square tests for categorical variables.

Supplemental Table 2. Odds Ratios for Gait Speed Tertiles

Trajectory Group	Unadjusted OR [95% CI] Medium Gait Speed vs Fast Gait Speed^	Adjusted* OR [95% CI] Medium Gait Speed vs Fast Gait Speed^	Unadjusted OR [95% CI] Slow Gait Speed vs Fast Gait Speed^	Adjusted* OR [95% CI] Slow Gait Speed vs Fast Gait Speed^
High PA with slow decline (n=534)	1.0 (REF)	1.0 (REF)	1.0 (REF)	1.0 (REF)
Low PA with slow decline (n=1557)	1.46 [1.16, 1.82]	1.30 [1.02, 1.66]	2.04 [1.57, 2.66]	1.73 [1.28, 2.33]
Sedentary PA with slow decline (n=1664)	1.91 [1.52, 2.41]	1.40 [1.07, 1.83]	4.72 [3.63, 6.14]	2.57 [1.87, 3.52]

OR, odds ratio; PA, physical activity.
^fast [mean (SD): 1.56 (0.12) m/s], medium [mean (SD): 1.33 (0.05) m/s] and slow [mean (SD): 1.11 (0.12) m/s] gait speed tertiles.
*Adjusted for age, sex, body mass index, race, education, marital status, depressive symptoms, comorbidity, and radiographic knee osteoarthritis.

Supplemental Table 3. Odds Ratios for Repeated Chair Stand Test Tertiles

Trajectory Group	Unadjusted OR [95% CI] Medium RCS Time vs Fast RCS Time^	Adjusted* OR [95% CI] Medium RCS Time vs Fast RCS Time^	Unadjusted OR [95% CI] Slow RCS Time vs Fast RCS Time^	Adjusted* OR [95% CI] Slow RCS Time vs Fast RCS Time^
High PA with slow decline (n=534)	1.0 (REF)	1.0 (REF)	1.0 (REF)	1.0 (REF)
Low PA with slow decline (n=1557)	1.41 [1.12, 1.78]	1.17 [0.91, 1.50]	1.73 [1.34, 2.24]	1.29 [0.97, 1.73]
Sedentary PA with slow decline (n=1664)	1.84 [1.45, 2.33]	1.21 [0.92, 1.60]	3.31 [2.56, 4.28]	1.65 [1.21, 2.24]

PA, Physical Activity; RCS, repeated chair stand test; OR, odds ratio.
^fast [mean (SD): 7.6 (1.1) sec], medium [mean (SD): 10.2 (0.6) sec], and slow [mean (SD): 14.1 (3.0) sec] repeated chair stand test tertiles.
*Adjusted for age, sex, body mass index, race, education, marital status, depressive symptoms, comorbidity, visual numeric pain rating scale, and radiographic knee osteoarthritis.

Supplemental Table 4. Odds Ratios for Isometric Quadriceps Strength Tertiles

Trajectory Group	Unadjusted OR [95% CI] Medium Strength vs High Strength^	Adjusted* OR [95% CI] Medium Strength vs High Strength^	Unadjusted OR [95% CI] Low Strength vs High Strength^	Adjusted* OR [95% CI] Low Strength vs High Strength^
High PA with slow decline (n=534)	1.0 (REF)	1.0 (REF)	1.0 (REF)	1.0 (REF)
Low PA with slow decline (n=1557)	1.40 [1.10, 1.79]	1.12 [0.87, 1.46]	2.25 [1.71, 2.97]	1.55 [1.15, 2.09]
Sedentary PA with slow decline (n=1664)	2.15 [1.69, 2.75]	1.45 [1.10, 1.93]	3.88 [2.95, 5.11]	1.93 [1.41, 2.65]

OR, odds ratio; PA, physical activity.
^Sex-specific high [mean (SD): females – 208.7 (41.2) N, males – 339.1 (51.9) N], medium [mean (SD): females – 298.8 (20.6) N, males – 457.8 (30.8) N] and low [mean (SD): females – 398.6 (51.8) N, males – 605.6 (84.6) N] strength tertiles of isometric quadriceps strength.
*Adjusted for age, sex, body mass index, race, education, depressive symptoms, comorbidity, and radiographic knee osteoarthritis.