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Physical Activity Predicts Higher Physical Function in Older Adults: The Osteoarthritis Initiative

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Abstract

Objectives—Physical activity reduces mobility impairments in elders. We examined the association of physical activity on risk of subjective and objective physical function in adults with and at risk for osteoarthritis (OA).

Methods: Adults aged≥60years from the longitudinal Osteoarthritis Initiative(OAI), a prospective observational study of knee OA, were classified by sex-specific quartiles of Physical Activity Score for the Elderly (PASE) scores.Using linear mixed models, we assessed 6-year data on self-reported health, gait speed, Late-Life Disability Index(LLDI) and chair stand.

Results—Of 2,252 subjects, mean age ranged from 66-70 years. Within each quartile, physical component(PCS) of the Short Form-12 and gait speed decreased from baseline to follow-up in both sexes (all $p<0.001$),yet the overall changes across PASE quartiles between these two time points were no different($p=0.40$ and 0.69, males and females, respectively).Decline in PCS occurred in the younger age group, but rates of change between quartiles over time were no different in any outcomes in either sex.LLDI scores declined in the 70+ age group.Adjusting for knee extensor strength reduced the strength of association.

Discussion—Higher physical activity is associated with maintained physical function, and is mediated by muscle strength highlighting the importance of encouraging physical activity in older adults with and at risk for osteoarthritis.

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Keywords

Exercise; Disability; Strength; Elderly

INTRODUCTION

Osteoarthritis (OA) is a leading cause of functional impairment[1] and is increasingly observed in an aging population[2]. In elders, the observed risk of impairment and disability occurs partly due to sex-specific changes in body composition[3] but also because of complex changes in joint cartilage and bone, as well as other articular and periarticular tissues[4]. This leads to declining mobility, increasing risk of falls[5], and dependency on others for assistance. Understanding the interplay between groups with and at risk for osteoarthritis may provide important answers to incident disability and its time course that is observed in clinical practice.

While disability and impairment are common outcomes of the aging process, there is a critical need to identify key factors that slow impending functional decline and preserve activities of daily living. Providers routinely recommend physical activity (PA) in patients as a key element to healthy aging[6]. In fact, physical activity is recommended at all ages[7], and is relevant in older adults since it has been strongly associated with improved physical function[8], gait speed[9], muscle strength[7], and cardiometabolic variables[10, 11]. Preserved performance on such measures leads to enhanced quality of life[12], mobility, reduced institutionalization[13], and mortality[14].

PA is a well established non-pharmacological treatment that reduces pain from OA[15], which can favorably improve quality of life and physical function. Commonly, clinicians are reluctant to encourage older patients about engaging in regular and sustained physical activity primarily because they fear injury in addition to the unclear consequences on long-term physical function[16]. Whether ‘too much’ physical activity is detrimental also requires examination. The aim of this study was to assess the association of high levels of self-reported physical activity on functional measures in an older adult population with and at risk for osteoarthritis and to determine whether the rate of change of these measures differs over time.

METHODS

We performed a secondary analysis of data from the Osteoarthritis Initiative (OAI), a multi-center, longitudinal, prospective observational study of adults with osteoarthritis which began in 2004. The central purpose of this study was to examine the natural history of knee osteoarthritis in community-dwelling adults. There were four clinical sites: Baltimore, MD; Pawtuckett, RI; Pittsburgh, PA; and Columbus, OH.

Data and procedure manuals are available online at http://oai.epi-ucsf.edu. Briefly, participants were recruited through mailings, advertisements, and community meetings. Eligibility was determined by telephone interview, and subjects attended a screening clinic visit if eligible. Exclusion criteria consisted of: rheumatoid arthritis; severe joint space

narrowing; bilateral total knee replacements; inability to undergo an MRI; unable to provide blood samples; comorbidity preventing study participation; other research participation and unwillingness to sign an informed consent. The enrollment clinic visit collected baseline demographic and questionnaire data and physical assessments within a six-week period. The study recruited subjects aged 45-79 years, an equal number in each sex, and all ethnic groups. Individuals who were unlikely to be residing in the area for at least 3 years were also excluded. Funding was provided by a public-private partnership of the National Institute of Arthritis, Musculoskeletal and Skin Diseases and private industry. OAI had a separate IRB approval process. Our local Institutional Review Board deemed the study exempt for research purposes.

Study Population

At baseline, subjects were classified into three cohorts: clinically significant knee osteoarthritis at risk of disease progression (progression cohort); high risk of developing clinically significant knee OA (incident cohort); and controls. Progression subjects complained of frequent knee symptoms and radiographic tibiofemoral knee OA in at least one native, non-replaced knee. Incident cohort was free of baseline symptomatic knee OA, but had established risk factors including the presence of Heberden's nodes in both hands; increased weight; previous knee operation; previous knee injury; family history of end-stage osteoarthritis; and pain in the knee on most days of the preceding month. Control patients did not have pain nor radiographic findings or risk factors for OA. After limiting our subjects to those aged ≥60years, we excluded those with incident total knee arthroplasty (n=196) and those who died at follow-up (n=137) to allow the ascertainment of the progression of osteoarthritis in the absence of surgical intervention for the knee. We deliberately excluded participants <60years since this population is known to have a lesser degree of functional impairment and disability[17] and increased capacity for homeostasis[18]. The final cohort consisted of 2,252 subjects (Figure 1). Data was collected as part of this study at baseline, and yearly intervals up to six years.

Study Measures

Demographic, medical, and social characteristics were collected via self-reported questionnaire. Age at the initial visit was considered age at baseline in years. We categorized subjects according to age range (60-69years and ≥70years). Marital status was dichotomized as ‘married’ or ‘single’, with the latter consisting of widow, divorced, separated or never married. We categorized education as follows: high school (graduated or not); attended college; college graduate; graduate level. Ever smokers were considered patients who smoked >100 cigarettes in their life. Self-reported knee pain was assessed using the Western Ontario and McMaster University OA Index (WOMAC) Pain Scale on a 5-point Likert scale, ranging from 0-20. Subjects with x-ray defined knee osteoarthritis were considered to have knee OA. Co-morbidity was assessed using the Charlson co-morbidity index[19]. Knee extensor strength was measured with patients sitting in a Good Strength chair with their back supported, and the knee joint at a 60° angle measured by a goniometer for transducer placement. Each participant performed two practice trials at 50% effort, performed after a 15-20minute warm-up session. A transducer was placed behind the participant's leg, centered behind the leg, with the bottom 2cm above the calcaneous. The

leg was strapped and the participant was instructed to do three trials at maximum effort. Measurements were indicated in newtons (N) and full details of the study protocol are available online at http://oai.epi-ucsf.org. Maximum knee strength was considered the greater of the left or right knee extensor strength, in newtons.

Primary Predictor

We assessed physical activity using the 26-item in-person Physical Activity Scale for the Elderly (PASE)[20], which is a measure of occupational, household, and leisure activities during a one-week period in older adults. The leisure activities require participants to self report the number of days per week, and hours per day of performing an activity. All study assessments were performed by self-reported questionnaire. A greater score indicates greater level of activity. There is no minimal clinically important difference score available for PASE for clinicians to use when determining patient response to treatment and to guide clinical decision-making, although there are minimally detectable changes based on 40 individuals with hip osteoarthritis[21]. This validation study defined a minimal detectable change of 87 points for total PASE score. Population normative data are available for those ≤70years (142.9points), and those >70 years (110.8points)[22].

Outcome Measures

We identified both objective and subjective measures of physical function. Gait speed (m/s) was measured using the 20m walk test, a validated measure of functional status in people with knee osteoarthritis[22]. Participants walked 20m in an unobstructed corridor at their usual walking speed and were timed. Long-term disability was measured using the validated Late-Life Function and Disability Instrument (LLDI)[23] which focuses on functional limitations and frequency limitations based on a wide variety of life tasks. Functional limitations focus on instrumental and management domain scores, while frequency limitations focus on personal and social role domains. These domains parallel Nagi's disablement framework[24] on disability in community-dwelling adults. A person's inability to perform daily activities reflects functional limitations, while frequency limitations characterize the inability to engage in social environments and major life tasks. Higher scores correlate with higher functional levels (less disability) and is scored on a 0-100 scale. The scale corresponds to both the physical functioning subscale of the SF-36 and London Handicap Scale[25]. The Short-Form 12 (SF12) is an easily administered, self-reported, valid, and reliable, measure of a person's perceived health status[26] comprised of Physical and Mental component scores assessed on a Likert scale. For the purposes of this study focusing on physical function, we represent only the physical component score (PCS). A score of 50 is the mean of the general population. Chair stand test is a validated measure of leg strength[27] measured using a straight-backed chair without arms, with the seat height of 45cm, placed against a wall for stability. Participants were asked to fold their arms, stand up as quickly as they can five times, rising until they are in a fully standing position. The test was timed and measured to the hundredth of a second.

Statistical Analysis

We stratified PASE by sex-specific quartiles [males: <97, 98-144, 145-187, >188; females: <85, 86-124, 125-170, >171]. Our univariate analysis assessed differences between the four

quartiles of PASE (low, 25-50, 50-75, >75% percentile (high)) on all baseline characteristics. Data was presented as means ± standard deviations or counts (percent). One-way ANOVA assessed differences among categories.

Separate models were performed by sex as functional decline differs by sex with age[17] as we demonstrated in previous analyses. Linear mixed models tested these associations including both PASE quartile and time-main effects as well as PASE quartiles*time interaction terms. In this way, both differences at baseline and 6 years could be examined along with differences in change over time between the PASE quartiles. Data was available at a number of times points including baseline, 12, 24, 36, 48, 60 and 72 months for SF-12 and gait speed, and only at six-years for LLDI. Unadjusted models were used to estimate baseline and 6-year means for each outcome. For each model, we performed: 1) within PASE quartile, a comparison of mean outcome at baseline and 6-years; 2) within time-point, a comparison of mean outcome across all categories; 4) mean change from baseline to 6-years, a comparison across all PASE quartiles. Each of these tests were performed by creating appropriate contrasts of model parameter estimates from the unadjusted models. Linear mixed models adjusting for age, education, race, cohort type (incidence, progression, control), Charlson co-morbidity score [19], and smoking status were fit. Within these models, we compared both the main effect of PASE quartile (representing differences between PASE quartiles at baseline) as well as the interaction between PASE quartiles and time (representing differences between PASE quartiles in change over time). We additionally incorporated knee extensor strength in our models as a surrogate for sarcopenia in our modeling[28]. We fit the adjusted models and also stratified by age group based on our previous analysis that suggested differences in physical function based on age[17, 29]. Sensitivity analyses compared baseline characteristics in those with and without missing data. Multicollinearity was assessed using variance inflation factor and a value greater than 5.0 was considered collinear. As an exploratory analysis, we performed sex-specific analysis by cohort type (progression and incidence only). Data was analyzed using STATA version 12 (STATACorp, College Station, TX). A p-value <0.05 was considered statistically significant.

RESULTS

Mean age ranged from 66.8 to 70.1 years in males, and 65.8 to 68.8 years in females. Of the 2,252 subjects, 1,397 were females. Baseline characteristics of each sex-specific cohort are presented in Table 1. Generally, covariates were different amongst PASE quartile in females than in males. Subjects with incomplete data (n=333) had higher WOMAC scores, slower gait speeds and less yearly income in both males and females than those included in our cohort (Appendix). Table 2 outlines the unadjusted subjective and objective outcomes according to PASE quartile by sex. Trends suggest that the highest quartile of PASE in both males and females had higher LLDI frequency scores, but was significant only for limitations in females. Gait speed, chair stand, and SF-12 physical function scores decreased with PASE quartile, although there were no significant differences among the change in score in the four quartiles between baseline and follow-up scores.

Multivariable modeling is presented in Table 3 and 4. We used knee extensor strength as a surrogate for sarcopenia in our models and found that the estimates were reduced among all outcome variables, although general trends were similar (data not shown). Estimated means for the adjusted models are plotted over time (Figure 2 & 3). In males, higher PASE scores, as represented by increasing quartiles, were associated with higher SF-12 PCS scores, gait speed and LLDI-frequency scores. The decline in PCS scores and chair stand speed, occurred earlier in the 60-70 year age group than in the 70+ year age group. Rates of change (time*PASE quartile interaction) in all models were similar by age cohort , although change in gait speed slope differed in both age groups. In females, declines in PCS occured in both age categories as did gait speed. LLDI scores appeared to decline in the 70+ year age group, while chair stand speeds were higher earlier in life. No collinearity was observed in any of our models other than with Race which consistently had a variance inflation factor greater than 5.0. In our exploratory analysis, notable differences were by PASE quartile in females across all outcomes in the progression cohort, and seen only in PCS and LLDI scores in the incident cohort (Appendix 2). Generally there were no significant changes in the outcomes over time by PASE quartile (time × PASE quartile interaction).

DISCUSSION

Higher self-reported physical activity levels are associated with higher subjective and objective measures of physical function in both males and females in this population with and at risk for osteoarthritis. Our data highlight the importance of encouraging high levels of physical activity in older adults.

Our results confirm the importance of physical activity on longitudinal changes in both objective (gait speed) and subjective (LLDI) functional measures in older adults. Gait speed, in particular, is a marker of disability that is associated with functional decline and mortality[30]. Specifically in a population at risk for osteoarthritis, the results suggest recommending exercise to reduce risk of onset of disability. Importantly, we demonstrated an effect of activity level on physical function. Previous reports in older adults suggested that there may be a ceiling effect of physical activity, and overuse was associated with detrimental outcomes including mortality[31, 32]. Our results suggest that patients should not be deterred from engaging in higher levels of activity. We do caution the reader that the overall PASE score does not discriminate between aerobic and anaerobic activity, or intensity, all of which impact cardiovascular and musculoskeletal systems in different manners. As such, our results provide a prelude of further study of the association of different types of physical activity and their degree of magnitude on the primary outcome of physical function.

We introduced a time × PASE quartile interaction term in our models and surprisingly found that rates of change were no different by age category. We believe that the observed changes in scores (in all our outcome measures), is likely reflected by the specifics of this population, that the magnitude of such declines occur earlier in life. This was further validated in our exploratory results stratified by cohort type where we expected changes over time, particularly in the progression cohort as they had risk factors for osteoarthritis.

Interestingly, our data confirms previous sex-specific impact of muscle mass and strength on long-term physical function by our group[33]. While males have higher muscle strength, after multivariable adjustment, there was attenuation of the results observed, suggesting that physical activity in males is likely, in part, mediated through muscle strength. While sarcopenia is known to impact physical function[28], and may be present in subjects with OA, this modulation of our results requires further exploration.

Physical activity appears to play a mediating role in the relationship with physical function. Our results suggest that high levels of self-reported physical activity may be associated with lower long-term disability scores, in both sexes. The mechanisms that explain this phenomenon are thought to be on the biological level. Physical activity is a known surrogate for cardiovascular fitness[34] may dampen pro-inflammatory cytokines, including IL-1, IL-6, and TNF-a[35], all of which may lead to homeostatic derangements leading to frailty and subsequently disability[18, 36]. Joints of subjects with osteoarthritis[37, 38] may exhibit a similar inflammatory milieu commonly implicated in the aforementioned disorders. While these biomarkers would be helpful in understanding the potential mechanisms of frailty and disability, they were unavailable for analysis in this dataset, but could be the subject of future investigation.

We caution the reader that our estimates may in fact be conservative. Our cohort was relatively young (mean age ~68years) and thus longer follow-up may be needed to observe the changes in physical function observed with aging. Disability and frailty often are preceded by compensated functional decline[17], data that would not be reflected in our findings. Second, participants were ambulatory, community-based adults, which may not be fully representative of the general older adult population. Third, the degree of co-morbidity was modest, implying a healthier population. Fourth, while our estimates are statistically significant, it is unclear whether our results are of clinical significance. Lastly, we purposely created quartiles of PASE to allow us to categorize whether intermediate categories of activity levels were any different than higher categories. We acknowledge that differences may be introduced simply because categories reflect different points in the distribution and thus we presented our data using PASE as a continuous variable as well.

Other limitations in this study exist. The OAI dataset was designed specifically to examine longitudinal outcomes of OA; our analysis may not have coincided with the primary scope of the study design. Both males and females not included had a higher degree of comorbidity and lower functional status at baseline, thereby possibly underestimating the true effect observed in our results. Our study results were also at risk for possible over-adjustment but we deliberately presented unadjusted data to show the similarities after accounting for these *a priori* variables. While race was a highly collinear variable, ethnicity and education can impact both physical activity[39, 40] and disability[41, 42] and hence was included in the model.

CONCLUSION

In older adults, higher levels of physical activity are associated with higher self-reported and objective functional measures. Encouraging patients with OA to be physically active should be strongly considered to improve joint pain and overall walking performance.

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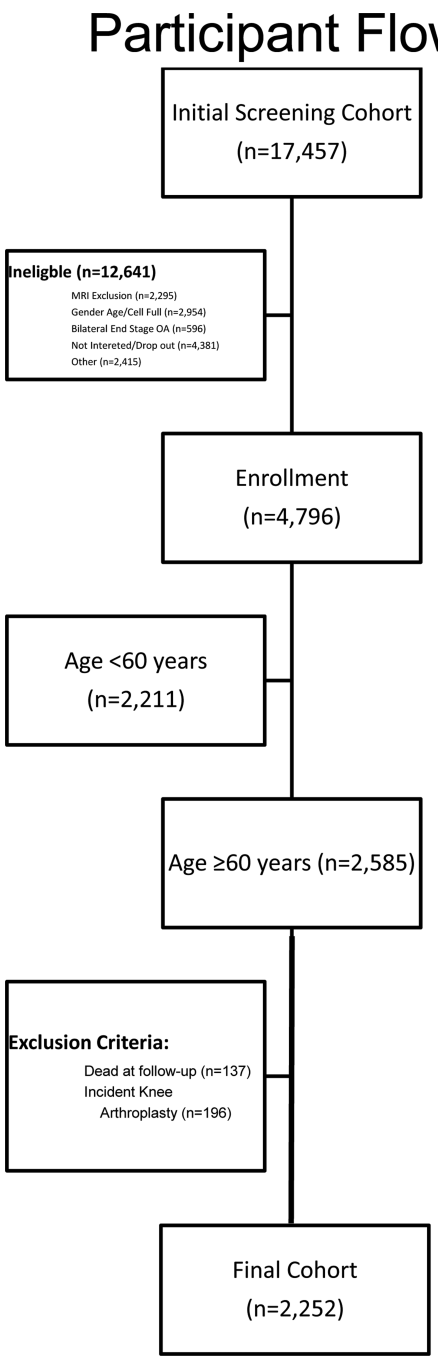

Figure 1. Participant Flow among 17,457 screened in the Osteoarthritis Initiative Protocol

Patient flow is demonstrated from initial telephone screen to cohort included in this study. Abbreviations: BMI – body mass index; MRI – magnetic resonance imaging; OA – osteoarthritis; PASE – physical activity for the elderly survey; SF – short form; WC – waist circumference

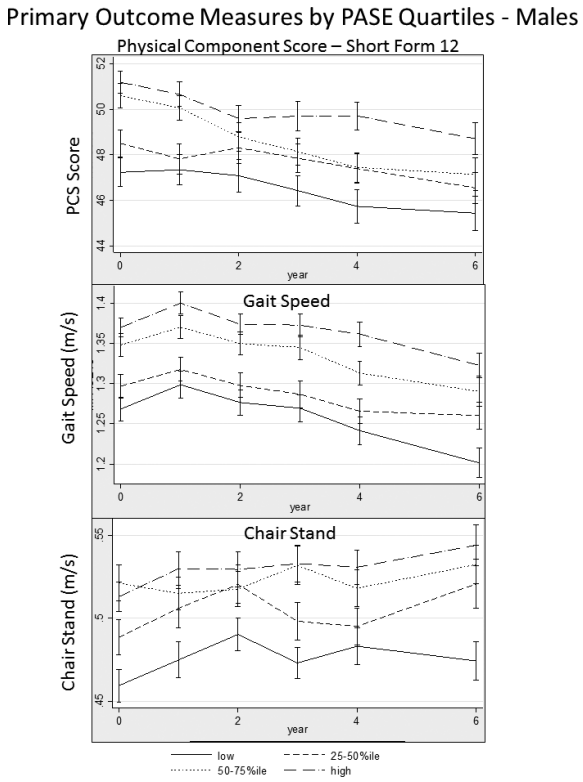

Figure 2.

Time-trends of Primary Outcome Measures Among Older Adult Participants in the Osteoarthritis Initiative in Males

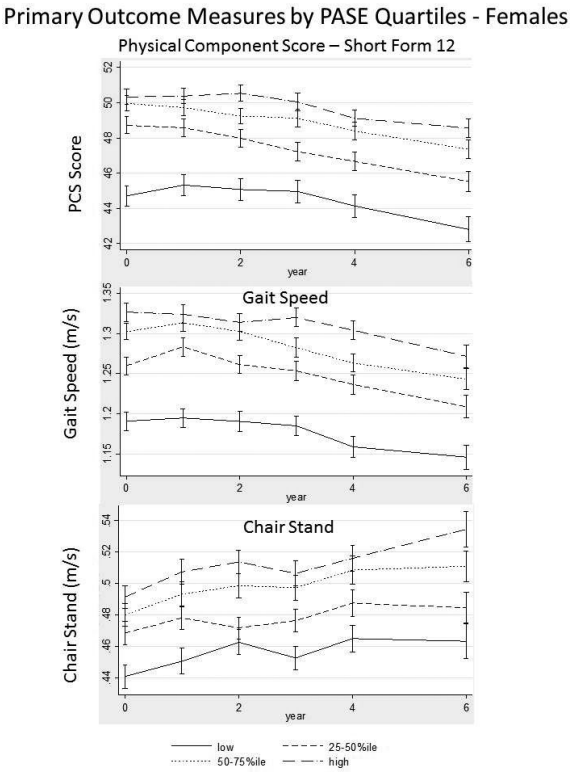

Figure 3.

Time-trends of Primary Outcome Measures Among Older Adult Participants in the Osteoarthritis Initiative in Females

Table #1

Overall Baseline Characteristics of Cohort (n=2252)

	Males (n=842)					Females (n=1,397)				
	Q1 PASE <97 N=214	**Q2 PASE 98-144 N=210**	**Q3 PASE 145-187 N=209**	**Q4 PASE >188 N=209**	**P-value**	**Q1 PASE <85 N=355**	**Q2 PASE 86-124 N=347**	**Q3 PASE 125-170 N=351**	**Q4 PASE >171 N=344**	**P-value**
Age	70.1 ± 5.3	69.9±5.2	68.8±4.9	66.8±5.3	<0.001	68.8±5.6	68.4±5.2	67.7±5.1	65.8±4.9	<0.001
Education Status										
< High School	44 (20.8)	27 (12.9)	32 (14.4)	18 (8.6)		88 (24.8)	91 (25.6)	71 (20.0)	105 (29.6)	
Some College	33 (15.6)	31 (14.8)	33 (15.9)	41 (19.6)	0.04	87 (25.1)	90 (25.9)	68 (19.6)	102 (29.4)	0.02
College	42 (19.8)	55 (26.2)	40 (19.2)	54 (25.8)		78 (22.4)	108 (31.0)	52 (14.9)	110 (31.6)	
>College	93 (43.9)	97 (46.2)	103 (49.5)	96 (45.9)		65 (19.1)	113 (33.1)	42 (12.3)	121 (35.5)	
Yearly Income										
>$50,000	121 (58.7)	135 (65.9)	127 (64.8)	147 (72.4)	0.04	147 (43.9)	144 (43.5)	150 (45.3)	172 (55.0)	0.01
Marital Status										
Married	166 (78.3)	175 (83.3)	165 (79.3)	176 (84.2)	0.32	181 (51.1)	209 (60.2)	209 (60.1)	196 (57.5)	0.05
Race										
White	165 (77.1)	190 (90.5)	182 (87.1)	187 (89.5)		248 (70.1)	279 (80.4)	299 (85.2)	287 (83.4)	
Black	42 (19.6)	16 (7.6)	25 (12.0)	15 (7.2)	0.002	93 (26.3)	63 (18.2)	46 (13.1)	45 (13.1)	<0.001
Asian	3 (1.4)	1 (0.5)	1 (0.5)	1 (0.5)		8 (2.3)	---	3 (0.9)	3 (0.9)	
Charlson Score	0.60 ± 1.08	0.60 ± 1.05	0.53 ± 0.99	0.54 ± 1.08	<0.001	0.46±0.88	0.41±0.85	0.37±0.70	0.28±0.67	0.03
Baseline WOMAC Right	10.9 ± 12.5	9.2 ± 12.0	8.2 ± 11.0	8.9 ± 11.2	0.007	15.4 ± 16.9	12.9±15.6	10.9±13.1	10.9±13.0	<0.001
Baseline WOMAC Left	11.7 ± 15.0	9.8±13.3	7.9±12.7	8.8 ± 13.5	0.03	14.5±17.3	11.7±15.3	10.0±13.8	11.1±14.5	0.001
Ever Smoker	115 (54.3)	123 (58.9)	111 (54.4)	111 (53.4)	0.67	166 (47.2)	153 (44.5)	175 (50.9)	159 (46.8)	0.41
# Medications	4.24 ± 2.77	3.79 ± 2.41	3.63 ± 2.30	**3.32** ± 2.20	0.004	4.29±2.56	3.88±2.41	3.66±2.40	3.50±2.33	<0.001
Body mass index	28.9±3.7	28.8±4.1	28.6±4.0	28.3±3.7	0.46	29.0±5.3	27.9±4.8	27.5±4.5	27.8±4.8	<0.001
Maximum Knee Extensor strength (N)	411.2±108.9	424.1±107.1	434.2±109.0	463.0±110.8	<0.001	262.4±82.2	283.4±77.3	284.3±73.5	302.5±77.7	<0.001
Cohort Allocation										
Incidence	143 (66.8)	153 (72.9)	153 (73.2)	150 (71.8)		235 (66.2)	256 (73.8)	270 (76.9)	262 (76.2)	
Progression	69 (32.2)	54 (25.7)	50 (23.9)	53 (25.4)	0.31	118 (33.2)	91 (26.2)	76 (21.7)	76 (22.1)	0.001
Control	2 (0.93)	3 (1.4)	6 (2.9)	6 (2.9)		2 (0.6)	--	5 (1.4)	6 (1.7)	

All values are represented as mean ± standard deviation, or count (%).

Abbreviations: BMI – body mass index; Q – quartile; WOMAC – Western Ontario McMaster Universities Arthritis Index

p-values represent analysis of variance between four quartile categories in each sex

At baseline, there were 13 subjects without baseline PASE scores

Table 2

Sex-Specific Unadjusted outcomes of Functional Outcomes by Physical Activity Quartile

	Males					Females				
	Q1 PASE	**Q2 PASE**	**Q3 PASE**	**Q4 PASE**	**P-value[B]**	**Q1 PASE**	**Q2 PASE**	**Q3 PASE**	**Q4 PASE**	**P-value[B]**
Quartile Score	**<97 N=214**	**98-144 N=210**	**145-187 N=209**	**>188 N=209**		**<85 N=355**	**86-124 N=347**	**125-170 N=351**	**>171 N=344**	
SF-12 Physical										
Baseline	47.2±9.0	48.5±8.6	50.6±7.6	51.2±6.9	<0.001	44.7±10.9	48.7±8.7	50.0±8.0	50.3±8.1	<0.001
Follow-up	45.4±9.4	46.5±8.7	47.1±9.3	48.7±9.1	0.01	42.8±11.3	45.5±9.9	47.4±9.0	48.6±9.2	<0.001
P-value[A]	<0.001	<0.001	<0.001	<0.001	0.78[C]	<0.001	<0.001	<0.001	<0.001	0.37[C]
SF-12 Mental										
Baseline	55.6±9.0	55.7±8.6	55.4±7.6	55.4±6.9	0.94	54.3±10.9	54.0±8.7	54.4±8.0	54.5±8.1	0.88
Follow-up	55.6±7.5	54.9±7.2	55.4±7.3	55.8±7.5	0.72	53.7±9.3	54.5±8.5	54.6±7.5	54.0±8.8	0.54
P-value[A]	0.18	0.24	0.83	0.40	0.38[C]	0.39	0.82	0.95	0.29	0.86[C]
Gait Speed										
Baseline	1.27 ± 0.22	1.30 ±0.21	1.35±0.20	1.37±0.17	<0.001	1.19 ±0.22	1.26±0.21	1.30±0.19	1.32±0.21	<0.001
Follow-up	1.20 ±0.21	1.26±0.19	1.29±0.22	1.32±0.19	<0.001	1.15±0.21	1.21±0.21	1.24±0.20	1.27±0.22	<0.001
p-value[A]	<0.001	<0.001	<0.001	<0.001	0.40[C]	<0.001	<0.001	<0.001	<0.001	0.69[C]
LLDI										
Frequency	51.7±5.0	52.6±5.8	54.6±6.1	55.4±6.0	<0.001	54.2±6.0	56.2±6.0	56.8±6.1	57.7±6.7	<0.001
Limitation	81.1±15.6	81.5±15.8	82.6±15.7	84.9±14.6	0.10	76.3±15.5	79.6±15.5	81.5±13.9	83.0±14.9	<0.001
Chair Stand										
Baseline	0.46±0.14	0.49±0.15	0.52±0.15	0.51±0.13	<0.001	0.44±0.14	0.47±0.13	0.48±0.13	0.49±0.13	<0.001
Follow-up	0.47±0.13	0.52±0.17	0.53±0.13	0.54±0.15	<0.001	0.46±0.14	0.48±0.14	0.51±0.14	0.53±0.17	<0.001
P-value[A]	0.44	0.02	0.94	0.06	0.26[C]	0.04	0.18	0.29	0.006	0.17[C]

All values represented are means ± standard deviation or count (%)

PASE – Physical Activity Score for the Elderly

LLDI – Late-life function & Disability Index

Q – Quartile

SF-12 – Short form 12

A p-values within PASE quartiles represent significance of change from baseline to follow-up.

B p-values represent overall test of difference in means between PASE quartiles

C P-values represent differences in change from baseline to follow-up between PASE quartiles

Table 3

Multivariable Regression Analysis of Primary Outcome Measures of Quality of Life, Lower Extremity Function and Late Life Disability (n=2,210) – MALES

MALES	SF-12 PCS β (95% CI)	Gait Speed β (95% CI)	LLDI-Frequency β (95% CI)	LLDI-Limitations β (95% CI)	Chair Stand β (95% CI)
Intercept	**43.3 [34.9:51.6]**	**1.49 [1.27:1.70]**	**56.3 [52.9-59.6]**	**100.0 [91.2:108.9]**	**0.42 [0.28:0.57]**
Low PASE	Ref	Ref	Ref	Ref	Ref
25-50 percentile PASE	0.90 [−0.45:2.25]	0.07 [−0.03:0.04]	**0.35 [−0.18:0.87]**	0.02 [−1.39:−1.43]	0.03 [0.004:0.05]
50-75th percentile PASE	**1.43 [0.06:2.79]**	**0.05 [0.02:0.09]**	**2.21 [1.68:2.74]**	−0.15 [−1.56:1.26]	**0.04 [0.01:0.06]**
High PASE	**1.90 [0.52:3.28]**	**0.05 [0.02:0.09]**	**2.74 [2.21:3.28]**	0.76 [−0.66:2.19]	0.02 [−0.001:0.05]
Time	**−0.58 [−0.76:−0.40]**	**−0.015 [−0.02:−0.012]**	--	--	0.0003 [−0.003:0.003]
Time * Low PASE	Ref	Ref	--	--	Ref
Time * 25-50percentile PASE	0.14 [−0.11:0.40]	0.004 [−0.001:0.08]	--	--	0.002 [−0.002:0.006]
Time * 50-75percentile PASE	−0.07 [−0.33:0.18]	0.001 [−0.003:0.006]	--	--	0.0011 [−0.003:0.005]
Time * High PASE	0.11 [−0.14:0.36]	**0.006 [0.001:0.01]**	--	--	0.003 [−0.001:0.007]

Age 60-70 years	SF-12 PCS β (95% CI)	Gait Speed β (95% CI)	LLDI-Frequency β (95% CI)	LLDI-Limitations β (95% CI)	Chair Stand β (95% CI)
Intercept	**36.7 [31.6:41.8]**	**1.15 [1.02:1.28]**	**50.4 [48.4:52.5]**	**73.8 [68.4:79.2]**	**0.30 [0.20:0.40]**
Low PASE	**Ref**	**Ref**	**Ref**	**Ref**	**Ref**
25-50percentile PASE	**2.07 [0.18:3.97]**	0.01 [−0.04:0.06]	**0.83 [0.06:1.60]**	**3.26 [1.24:5.29]**	**0.05 [0.02:0.09]**
50-75percentile PASE	**2.16 [0.34:3.98]**	0.04 [−0.01:0.09]	**2.80 [2.07:3.52]**	**2.79 [0.89:4.70]**	**0.04 [0.01:0.08]**
High PASE	**3.24 [1.52:4.97]**	**0.05 [0.01:0.09]**	**2.70 [2.00:3.39]**	**3.28 [1.46:5.10]**	**0.02 [−0.01:0.05]**
Time	**−0.52 [−0.79:−0.26]**	**−0.01 [−0.02:−0.01]**	--	--	0.0003 [−0.004:0.005]
Time * Low PASE	**ref**	**Ref**	--	--	**Ref**
Time * 25-50percentile PASE	0.27 [−0.10:0.65]	**0.010 [0.004:0.017]**	--	--	**0.009 [0.002:0.015]**
Time * 50-75percentile PASE	−0.021 [−0.38:0.34]	0.0024 [−0.004:0.009]	--	--	−0.0009 [−0.007:0.005]
Time * High PASE	0.23 [−0.11:0.57]	**0.008 [0.002:0.014]**	--	--	0.004 [−0.002:0.09]

Age 70+ years	SF-12 PCS β (95% CI)	Gait Speed β (95% CI)	LLDI-Frequency β (95% CI)	LLDI-Limitations β (95% CI)	Chair Stand β (95% CI)
Intercept	**28.1 [17.0:39.2]**	**0.97 [0.70:1.24]**	**38.8 [34.1:43.6]**	**54.9 [42.2:67.8]**	**0.28 [0.11:0.45]**
Low PASE	Ref	Ref	**Ref**	Ref	Ref
25-50percentile PASE	−0.32 [−2.29:1.65]	0.003 [−0.05:0.05]	−0.05 [−0.78:0.67]	**−3.84 [−5.70:−2.34]**	0.004 [0.03:0.04]

Age 70+ years	SF-12 PCS β (95% CI)	Gait Speed β (95% CI)	LLDI-Frequency β (95% CI)	LLDI-Limitations β (95% CI)	Chair Stand β (95% CI)
50-75percentile PASE	0.59 [−1.47:2.65]	**0.06 [0.01:0.12]**	**1.77 [1.00:2.54]**	**−2.99 [−5.07:−0.91]**	0.03 [−0.006:0.06]
High PASE	0.40 [−1.85:2.64]	**0.07 [0.02:0.13]**	**3.33 [2.50:4.15]**	−0.39 [−1.85:−2.62]	**0.04 [0.004:0.07]**
Time	**−0.63 [−0.87:−0.39]**	**−0.02 [−0.02:−0.01]**	--	--	0.002 [−0.004:0.004]
Time * Low PASE	Ref	Ref	--	--	Ref
Time * 25-50percentile PASE	0.05 [−0.28:0.39]	−0.002 [−0.008:0.004]	--	--	−0.003 [−0.009:0.002]
Time * 50-75percentile PASE	−0.16 [−0.51:0.20]	−0.001 [−0.007:0.006]	--	--	0.004 [−0.002:0.009]
Time * High PASE	−0.18 [−0.55:0.19]	0.002 [−0.005:0.008]	--	--	0.0015 [−0.004:0.007]

All linear mixed models are adjusted for age, education, race, cohort type (incidence, progression, control), Charlson co-morbidity score, smoking status, and maximum knee strength. Referent category is low quartile of Physical Activity Score for the Elderly (PASE) for each sex. Time-dependent co-variates are included in time × PASE quartile interaction. **Boldfaced items indicate p<0.05**. LLDI was only available at 6-year follow-up thereby no time interaction term model was considered for this outcome measure. Abbreviations: CI – Confidence Intervals; LLDI – Late-Life Functional and Disability Index; MCS – Mental Component Score; PASE – Physical Activity Score for the Elderly; PCS – Physical Component Score; SF – Short Form

Table 4

Multivariable Regression Analysis of Primary Outcome Measures of Quality of Life, Lower Extremity Function and Late Life Disability (n=2,210) – Females by age with strength

FEMALES	SF-12 PCS β (95% CI)	Gait Speed β (95% CI)	LLDI-Frequency β (95% CI)	LLDI-Limitations β (95% CI)	Chair Stand β (95% CI)
Intercept	**42.5 [35.3:49.5]**	**1.53 [1.36:1.69]**	**55.4 [52.6-58.1]**	**76.2 [69.8:82.7]**	0.45 [0.34-0.55]
Low PASE	Ref	Ref	Ref	Ref	Ref
25-50percentile PASE	**2.21 [1.05:3.38]**	**0.06 [0.03:0.08]**	**1.69 [1.23:2.14]**	**2.32 [1.24:3.40]**	0.01 [−0.003:0.03]
50-75percentile PASE	**3.52 [2.35:4.69]**	**0.08 [0.05:0.11]**	**2.22 [1.76:2.68]**	**3.65 [2.57:4.73]**	**0.02 [0.007:0.04]**
High PASE	**3.68 [2.48:4.87]**	**0.07 [0.05:0.10]**	**3.13 [2.67:3.60]**	**5.13 [4.03:6.22]**	**0.03 [0.01:0.04]**
Time	**−0.50 [−0.65:−0.35]**	**−0.013 [−0.016:−0.01]**	--	--	0.002 [−0.003:0.004]
Time * Low PASE	ref	Ref	--	--	Ref
Time * 25-50percentile PASE	**−0.20 [−0.40:−0.001]**	0.005 [−0.003:0.004]	--	--	0.0006 [−0.003:0.004]
Time * 50-75percentile PASE	−0.003 [−0.20:0.20]	0.002 [−0.002:0.006]	--	--	0.0008 [−0.0023:0.004]
Time * High PASE	0.08 [−0.12:0.28]	0.002 [−0.002:0.005]	--	--	0.002 [−0.0013:0.005]

Age 60-70 years	SF-12 PCS β (95% CI)	Gait Speed β (95% CI)	LLDI-Frequency β (95% CI)	LLDI-Limitations β (95% CI)	Chair Stand β (95% CI)
Intercept	**35.4 [30.6:40.3]**	**1.06 [0.95:1.17]**	**50.4 [48.3:52.5]**	**55.0 [50.3:59.8]**	**0.32 [0.25:0.40]**
Low PASE	**Ref**	**Ref**	**Ref**	**Ref**	**Ref**
25-50percentile PASE	**2.34 [0.83:3.85]**	**0.07 [0.03:0.10]**	**1.29 [0.67:1.91]**	**1.89 [0.47:3.32]**	0.02 [−0.002:0.05]
50-75percentile PASE	**3.65 [2.16:5.14]**	**0.08 [0.05:0.12]**	**1.37 [0.76:1.99]**	**3.51 [2.10:4.97]**	**0.03 [0.01:0.05]**
High PASE	**3.52 [2.07:4.98]**	**0.08 [0.05:0.11]**	**2.26 [1.66:2.85]**	**4.65 [3.30:6.01]**	**0.04 [0.01:0.06]**
Time	**−0.39 [−0.59:−0.19]**	**−0.01 [−0.013:−0.006]**	--	--	0.002 [−0.001:0.005]
Time * Low PASE	**Ref**	**Ref**	--	--	Ref
Time * 25-50percentile PASE	−0.20 [−0.47:0.07]	0.0004 [−0.005:0.005]	--	--	0.003 [−0.001:0.008]
Time * 50-75percentile PASE	0.02 [−0.25:0.28]	−0.0003 [−0.005:0.004]	--	--	0.001 [−0.003:0.005]
Time * High PASE	0.04 [−0.22:0.29]	0.002 [−0.003:0.007]	--	--	**0.004 [0.00003:0.008]**

Age 70+ years	SF-12 PCS β (95% CI)	Gait Speed β (95% CI)	LLDI-Frequency β (95% CI)	LLDI-Limitations β (95% CI)	Chair Stand β (95% CI)
Intercept	**38.5 [31.6:45.4]**	**0.90 [0.74:1.06]**	**60.7 [58.1:63.1]**	**77.7 [72.5:83.9]**	**0.33 [0.23:0.42]**
Low PASE	Ref	Ref	Ref	Ref	Ref
25-50percentile PASE	2.13 [0.29:3.97]	0.04 [−0.003:0.09]	**1.89 [1.24:2.54]**	**2.53 [0.90:4.17]**	0.007 [−0.019:−0.03]

Age 70+ years	SF-12 PCS β (95% CI)	Gait Speed β (95% CI)	LLDI-Frequency β (95% CI)	LLDI-Limitations β (95% CI)	Chair Stand β (95% CI)
50-75percentile PASE	**3.50 [1.58:5.42]**	**0.07 [0.03:0.12]**	**3.21 [2.55:3.88]**	**3.95 [2.27:5.62]**	0.02 [−0.008:0.05]
High PASE	**4.71 [2.61:6.81]**	**0.09 [0.04:0.14]**	**4.65 [3.93-5.37]**	**7.11 [5.30:8.91]**	0.02 [−0.01:0.05]
Time	**−0.63 [−0.85:−0.42]**	**−0.018 [−0.022:−0.014]**	--	--	0.0014 [−0.002:0.005]
Time * Low PASE	Ref	Ref	--	--	Ref
Time * 25-50percentile PASE	−0.23 [−0.53:0.08]	0.0003 [−0.006:0.006]	--	--	−0.004 [−0.009:0.0007]
Time * 50-75percentile PASE	−0.09 [−0.40:0.23]	0.004 [−0.002:0.01]	--	--	0.001 [−0.004:0.006]
Time * High PASE	0.024 [−0.31:0.36]	−0.004 [−0.011:0.003]	--	--	−0.005 [−0.01:0.00002]

All linear mixed models are adjusted for age, education, race, cohort type (incidence, progression, control), Charlson co-morbidity score, maximum knee strength, smoking status. Referent category is low quartile of Physical Activity Score for the Elderly (PASE) for each sex. Time-dependent co-variates are included in time × PASE quartile interaction. **Boldfaced items indicate p<0.05**. LLDI was only available at 6-year follow-up thereby no time interaction term model was considered for this outcome measure. Abbreviations: CI – Confidence Intervals; LLDI – Late-Life Functional and Disability Index; MCS – Mental Component Score; PASE – Physical Activity Score for the Elderly; PCS –Physical Component Score; SF – Short Form