Impact of Obesity on Disability, Function and Physical Activity: Data from the Osteoarthritis Initiative

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Abstract

Objective—Older adults with obesity are at risk for osteoarthritis(OA) and are predisposed to functional decline and disability. We examined the association of obesity on disability, physical activity and quality of life at six years.

Methods—Using data from the longitudinal Osteoarthritis Initiative, we analyzed older adults (age 60years) with a body mass index at baseline (BMI) 18.5kg/m2 (n=2,378) using standard BMI categories. Outcomes were assessed at 6year follow-up and included:Late-life Disability Index (LLDI), Short Form-12 (SF-12) questionnaire and the Physical Activity Scale for the Elderly (PASE). Linear regression predicted outcomes based on BMI category, adjusting for age, sex, race, education, smoking, cohort status, radiographic knee osteoarthritis, co-morbidity scores and baseline scores when available.

Results—Follow-up data were available on 1,727(71.9%) participants. Mean age was 67.9±5.3years, and 61.6% were female. At baseline, obese subjects compared to overweight and normal, were on a greater number of medications(4.28 vs. 3.63 vs. 3.32), had lower gait speeds(1.22 vs. 1.32 vs. 1.36m/s), higher Charlson (0.59 vs 0.37 vs. 0.30) and higher WOMAC scores (right: 14.8 vs. 10.3 vs. 7.5; left: 14.4 vs. 9.9 vs. 7.5). SF-12 scores at 6-years were lower in obese patients than overweight or normal(99.5 [98.7–100.4] vs. 101.1 [100.4–101.8] vs. 102.8 [101.8–103.8]), as were PASE scores (115.1 [110.3–119.8] vs. 126.2 [122.2–130.2] vs. 131.4[125.8–137.0]).The LLDI-limitation component demonstrated differences in obese compared to overweight or normal (78.6 [77.4–79.9] vs. 81.2[80.2–82.3] vs. 82.5[81.1–84.0].

Conclusion—Obesity was associated with worse physical activity scores, lower quality of life, and higher risk of 6-year disability.

Keywords

Obesity; Elderly; Osteoarthritis; Physical Function

INTRODUCTION

Osteoarthritis (OA) is a leading cause of functional impairment[1] and is increasingly observed in an aging population[2]. Aging leads to a number of physiological changes characterized by a reduced ability to participate in one's activities of daily living, leading to further disability, institutionalization and death[3]. Epidemiologic surveys demonstrate rises in the prevalence of knee osteoarthritis (OA) in the elderly[4]. Parallel trends have been observed in the prevalence of obesity as measured by body mass index (BMI)[5]. While obesity impacts cardiometabolic factors[6], it importantly leads to impairment in quality of life[7] by decreasing functional status and leading to disability[8]. Additionally, increased fat is associated with institutionalization and premature death[9, 10].

The interplay of muscle and function is likely a modulating factor in incident disability[11]. Subjects with knee osteoarthritis often decline in their ability to function due to muscle weakness, pain and a reduced ability to engage in physical activity[12, 13]. Obesity can exacerbate the development of knee OA[14, 15] which, left untreated or unmanaged, can place patients at risk for of worsening pain leading to chronic musculoskeletal disorders[16].

Few longitudinal studies have examined the impact of obesity on physical activity, quality of life, and disability in older adults with obesity at risk for knee OA, and none to our knowledge have examined functional capabilities over a six year period of time. We examined the impact of baseline obesity measured using body mass index (BMI) on long-term (six year) outcomes in a population at risk for progression and development of OA. We hypothesized that older adults with obesity, as compared to overweight or normal weight patients had worse functional outcomes at six-years.

MATERIALS AND METHODS

The Osteoarthritis Initiative (OAI) is a multi-center, longitudinal, prospective observational study of knee OA which began in 2004. The primary purpose of this cohort study was to

evaluate biomarkers as potential endpoints for disease onset and progression. The dataset is prospectively gathered and includes questionnaires, examination data, imaging and biological specimens. The four clinical recruitment sites included Baltimore, MD, Pawtuckett, RI, Pittsburgh, PA, and Columbus, OH. Recruitment and enrollment at baseline involved an initial contact to reach persons in an intended targeted population through mailings, advertisements, and community meetings. An initial eligibility interview occurred by telephone to determine if interested individuals qualified for the study and those qualifying attended a screening clinic visit where additional assessments were performed. An enrollment clinic visit where the majority of baseline data were collected was then performed. All visits took place within a six-week time frame. Data and study protocols were obtained from the OAI database, which is available for public access at http://www.oai.ucsf.edu/. Specific datasets used in this analysis were at baseline and at six years. The study analysis was exempt from local review due to the de-identified nature of the data.

Study Population

The study consists of three distinct subgroups: participants with clinically significant knee OA who are at risk of disease progression; those at high risk of developing clinically significant knee OA; and a control group. The initial sample included an ethnically diverse sample of both sexes aged 45–79 years. Following the eligibility interview, subjects were classified according to subcohort based on data collected. The progression cohort consisted of subjects with frequent knee symptoms and radiographic tibiofemoral knee OA in at least one native knee. The incidence cohort did not have symptomatic knee OA in either knee at baseline but had established risk factors: presence of heberden's node in both hands; weight defined by using gender and age-specific cutpoints; previous knee operation; previous knee injury; family history; and pain in knee on most days of the preceding month. The nonexposed subcohort had no pain, radiographic findings or risk factors. Exclusion criteria were: rheumatoid arthritis; severe joint space narrowing; bilateral total knee replacements; inability to undergo an MRI; unable to provide a blood sample; co-morbid conditions interfering with participation in the study; unlikely to reside in the area for at least 3 years; other research participation; or unwilling to sign informed consent. Participant flow is shown in Figure 1.

Study Measures

All data were obtained from either self-report or measurements. Age was determined at initial visit. Marital status was defined as married or single, where the latter consisted of widowed, divorced, separated or never married. Education status was re-classified in four categories: attended high school (with or without graduation), attended college, college graduate, graduate level. Any person who smoked >100 cigarettes in their lifetime was considered an ever smoker. Self-reported knee pain was measured using the Western Ontario and McMaster University OA Index (WOMAC) using a 5-point Likert scale asking questions about both knees separately in the past 7 days. Pain scores ranged from 0–20 with higher scores representing worse symptoms. Hip pain was assessed by self-report. Subjects with documented knee osteoarthritis OA on X-ray were considered to have radiographic knee OA. Co-morbidity score was calculated based on the Charlson index[17]. Death was

identified based on reporting to the Osteoarthritis Initiative Coordinating Center and confirmed through a formal adjudication process.

Measurements

Standing height was measured with a wall-mounted stadiometer. Weight was measured without participant's shoes or heavy jewelry and in light weight clothing, using a calibrated standard balance beam scale. We calculated BMI as weight (in kilograms) divided by height (in meters) squared, and categorized as underweight ($<18.5 \text{kg/m}^2$), normal (18.5–24.9kg/m^2), overweight (25–29.9kg/m^2), and obese ($>30 \text{kg/m}^2$). Waist circumference was measured at the level between the lower rib and the iliac crest, normally at the level of the umbilicus in centimeters.

Mobility Measures

The chair stand test is a measure of balance and measure of strength of knee extensor and back muscles. It is a test of overall physical performance[18]. Subjects are seated with their arms folded across their chest and stand up and sit down five times. Chair stands were administered by a certified examiner and timed (measured in seconds). This test has excellent test-retest reliability (0.81–0.92) and responsiveness to change[19, 20]. The 20meter walk test (gait speed) is a standard outcome measure of subjects with osteoarthritis and a measure of functional performance[21], consisting of a course length of 20m, in an unobstructed, dedicated corridor. The participant is asked to walk at their usual speed in a 20m cooridor turns around walks in the opposite direction. Both the chair stand and 20m walk test have excellent reliability and intraclass correlations ranging from 0.93 to 0.98 within and between testers in patients with moderate to severe knee OA[22].

Outcome Measures

The Late-Life Function and Disability Instrument (LLDI)[23] parallels Nagi's disablement framework on disability in community dwelling adults[24]. This self-reported instrument has two main domains each scored on a scale of 0–100, with higher scores indicating higher levels of function: functional limitations characterized by the inability to perform daily activities, and frequency limitations reflecting the inability to engage in social environments and major life tasks. The scale correlates well with the physical functioning subscale of the Medical Outcomes Study 36-item Short Form (SF) Health Survey[25] and the London Handicap Scale[26].

Quality of life was ascertained using the SF-12, a self-reported measure of a person's perceived health status and a reasonable alternative to the lengthier SF-36[25]. The shorter form accounts for >90% of the statistical variance of the SF-36 and is reliable, valid, and easily self-administered[25]. The SF-12 uses Likert scales divided into both physical (PCS) and mental (MCS) components scores, both standardized and weighted to a mean of 50 ± 10 in the general population[27, 28] with higher scores signify better health. The overall SF-12 score combines the PCS and MCS scoring.

The Physical Activity Scale for the Elderly (PASE) is a 26-item instrument measuring occupational, household and leisure activities during a one-week period in elderly (65year

old) persons. It can be administered by telephone, mail or in-person and is reliable and valid. Scores increase with greater intensity of activity time. Population-based means are available with the general population having a mean score of 103±64.1. No known minimally clinically important differences are available[29].

Statistical Analysis

All baseline six year data were downloaded in March 2013 and merged into a single dataset for analysis. Continuous variables are represented as means ± standard deviations, and categorical values as counts (percent). A one-way ANOVA compared baseline and follow-up values across all three BMI categories. An ANOVA was also used to compare within-person differences from baseline across BMI categories. Post-hoc Bonferroni adjustments were performed for unadjusted mean variables between BMI-categories. Standard statistical tests compared subjects included vs. those excluded for the purposes of the analysis. Our primary six-year outcomes of interest included SF-12, PASE, and LLDI scores (frequency and limitation domains). As LLDI frequency and limitations scores only had follow-up data, we tested significances across all BMI categories. Within each BMI category, paired t-tests were used to compare baseline and follow-up values within-person

Using our primary outcomes as the dependent variable, we determined the mean follow-up scores in each baseline BMI category (referent=normal BMI), after adjusting for age, sex, education level, race, presence of radiographic knee OA, hip pain, cohort type (incidence, progression), Charlson co-morbidity score and current smoking status. To account for differences in baseline measures between BMI categories, we adjusted for baseline scores where data was available. As disability advances with age[3], we stratified our cohort by age group (60–70 and ≥70years). We explored similar models in those with and without radiographic knee OA. A secondary analysis determined the impact of clinically significant weight loss/gain of 5%[30] on our primary outcomes, and stratified both by age and OA status. Due to the extent of missing data over the six-year time period, we performed a sensitivity analysis using inverse probability weighting. Adjusted mean differences with 95% confidence intervals were calculated. All estimates were calculated using STATA version 12 (STATACorp, College Station, TX). A p-value <0.05 was considered statistically significant.

RESULTS

We identified 1,742 subjects (72.6%) with complete follow-up data at six years on our primary outcomes and included them in our final analysis. Obese subjects at baseline were younger and had lower education and socioeconomic status than overweight or normal subjects (Table 1). Baseline WOMAC scores were higher in the obese category as compared to the overweight or normal. A higher proportion of obese subjects had radiographic OA. We compared included and excluded subjects and found that the excluded cohort were less educated, were less likely to be Caucasian, had higher WOMAC and Charlson scores and had lower gait speed, PASE scores and SF-12 scores (Appendix 1).

Table 2 presents our univariate baseline and follow-up outcome measures. Table 3 demonstrates our modeling representing mean adjusted scores in each BMI category.

Specifically, obese subjects had worse overall and physical function SF-12 and PASE scores over time. Self-reported function, PASE, gait speed, and chair stands were all lower in the 70+ age group as compared to the 60–70year age group. The limitation component of the LLDI scores were markedly lower in the obese category, as compared to the overweight or referent categories, in the 60–70 year age group but not in other groups. We present in Appendix 2 the analysis stratified by osteoarthritis. Patients with obesity and OA consistently had lower scores in all domains as compared to those without OA. Appendix 3 and 4 represent the exploratory analysis demonstrating the impact of weight change on the primary outcomes. A 5% weight gain is associated with lower SF-12, PASE and LLDI-limitation scores, as compared to those who lost weight or those with no change in weight.

DISCUSSION

In an older adult population at risk for developing and progressing to osteoarthritis, obesity places subjects at risk for lower physical activity scores, quality of life and disability indices than overweight or normal BMI. These results provide estimates of the degree of functional impairment elderly persons with obesity may expect over time.

Previous studies have demonstrated the impact of obesity on pain scores[31] and progression of osteoarthritis[32], all of which may can impact our outcomes. Cross-sectional data have consistently demonstrated associations between obesity and quality of life, physical function and exercise[33–36]. Very few studies have examined the impact of obesity in a longitudinal manner on physical activity, quality of life, and disability, and none have utilized the PASE and LLDI. A study utilizing National Health and Nutrition Examination Surveys demonstrated that obesity predicts long-term disability in knee OA[1]. The three scales used in OAI are well validated in the elderly suggesting that osteoarthritis will inevitably impact one's ability to engage in physical activity, and may lead to compromised limitation scales of the LLDI in addition to lower quality of life scores. Our findings taken together with those of previous studies suggest the importance of preventing weight gain in knee OA [37–40].

Knee OA impacts quality of life, physical activity, and disability [41]. Our results suggest that as compared to normal BMI, subjects with obesity differed across measures with lower self-reported physical function, PASE scores and gait speeds. We explored a number of secondary outcomes of function, such as gait speed and chair stand. Notably, these dropped with increasing age consistent with other studies that demonstrate gradual decline with aging [42]. Interestingly, SF-12 and LLDI both had subscales that are related to mental health. Our data suggest that any impact of obesity was solely due to physical limitations and not psychological. While controversy exists with respect to obesity impacting mental health[43], our longitudinal data analysis suggests that there may not be any association.

While our results provide some additional credence to the relationship between obesity and important geriatric outcomes on a longitudinal basis, we caution that our results indeed may underestimate the natural history of the demonstrated decline. Our cohort excluded 677 subjects (28.1%) due to missing outcome data, a group noted in our sensitivity analysis to be associated with increased comorbidity, lower socioeconomic class, and higher WOMAC

scores, all of which negatively impact our outcomes of choice. One may argue that the magnitude of the changes, while statistically significant, may not necessarily be clinically significant. While a 10-point difference in SF-12 is considered clinically significant[28], to our knowledge there are no clinically meaningful differences in PASE or the LLDI. One potential explanation for lower magnitude in change could be the baseline characteristics of our study population, which may be considered healthier and/or have lower degrees of co-morbidity. Disability is known to increase in prevalence as one ages[3]; our population's mean age was 68years and in part, this 'young' population may not fully reflect the degree of potential disability people with obesity are subject to. A six-year follow-up may be too short for this phenomenon considering the examined cohort included those both with knee OA but also those with risk factors for OA (and no OA). Stratifying by age further demonstrated that age in fact plays a large role in functional decline. As increased co-morbidity may lead to frailty and disability, it often is preceded by many years of preserved or minimally declining function. The cohort enrolled in this observational cohort may not be typically representative of older adults in the community. Future studies should focus on cohorts with varied medical and social demographics to correctly ascertain the natural history of overweight and obesity on quality of life, physical activity and functional limitations.

CONCLUSION

Obesity measured by BMI leads to reduced physical function, physical activity and disability in a six year period in subjects with or at risk for OA.

ACKNOWLEDGEMENT

ABBREVIATIONS

BMI	body mass index
LLDI	Late Life Function and Disability Instrument
MCS	mental component scale

OA	osteoarthritis
OAI	Osteoarthritis Initiative
PASE	Physical Activity Score for the Elderly
PCS	physical component score
SF	Short form
WC	Waist circumference
WOMAC	Western Ontario and McMaster University OA Index

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Appendix 1: Baseline Characteristics of Subjects Included for Outcome Analysis Compared to those Excluded

Variable	Included 1,729 (71.9)	Excluded 677 (28.1)	p-value
Age	67.9 ± 5.3	69.0 ± 5.4	<0.001
Female Sex (%)	1,065 (61.6)	438 (64.7)	0.17
Education			
< High School	306 (17.7)	167 (25.0)	
Some College	403 (23.3)	177 (26.5)	
College	344 (19.9)	113 (17.1)	<0.001
>College	676 (39.1)	207 (31.4)	
Yearly Income >$50,000	919 (55.5)	303 (48.6)	0.003
Marital Status	1,168 (67.6)	425 (63.6)	0.07
Race			
White	1,445 (83.6)	533 (79.0)	
Black	247 (14.3)	115 (17.0)	0.005
Other	37 (2.1)	27 (4.0)	
WOMAC Right	11.1 ±13.4	14.2 ±16.0	<0.001
WOMAC Left	10.8 ± 14.6	14.2 ± 16.6	<0.001
Charlson Comorbidity	0.43 ± 0.86	0.55 ± 1.0	0.004

Variable	Included 1,729 (71.9)	Excluded 677 (28.1)	p-value
Medication Number	3.78 ± 2.43	4.03 ± 2.57	0.04
Smoker (yes/no)	858 (49.9)	332 (50.2)	0.93
Radiographic Knee OA Present/Absent	447 (29.6)	230 (25.7)	0.04
Hip Pain (yes/no)	187 (10.8)	89 (13.2)	0.14
20M Gait Speed, m/s	1.30 ± 0.21	1.25 ± 0.22	<0.001
PASE	141.5 ± 67.1	127.4 ± 68.3	<0.001
SF-12			
Total	104.4 ± 10.1	100.2 ±12.9	<0.001
Physical	49.3 ± 8.3	45.8 ± 10.3	<0.001
Mental	55.1 ± 7.1	54.4 ± 8.4	0.06

All values represent mean ± SD, or count (%)

P-value represents the difference between the excluded and included analytical cohort

PASE - Physical Activity Scale for the Elderly; SF - Short Form 12; WOMAC – Western Ontario and McMaster University Arthritis Index

Appendix 2: Multivariable Analysis of Follow-up Primary Outcome Measures Stratified by Osteoarthritis

		BMI					
		Normal (18.5–24.9kg/m^2)	95% CI	Overweight (25.0–29.9kg/m^2)	95% CI	Obese (30kg/m^2)	95% CI
Short-Form 12 Score							
Overall Score	OA +	101.7	100.2–103.1	100.3	99.4–101.3	98.5	97.5–99.6
	OA −	104.5	103.2–105.8	102.3	101.3–103.4	101.4	99.9–103.0
Physical	OA +	46.4	45.2–47.7	45.5	44.7–46.3	43.5	42.7–44.4
	OA −	49.8	48.6–50.8	47.8	46.9–48.7	46.4	45.1–47.6
Mental	OA +	55.4	54.5–56.4	55.0	54.3–55.6	54.8	54.0–55.5
	OA −	54.9	53.9–55.9	54.5	53.7–55.4	54.3	53.2–55.4
Physical Activity Scale for Elderly	OA +	128.4	120.5–136.3	126.2	121.1–131.2	112.6	107.1–118.1
	OA −	135.4	127.4–143.4	125.9	119.2–132.6	120.3	111.1–129.5
Late-Life Disability Index							
Frequency	OA +	55.64	54.6–56.3	55.2	54.7–55.8	54.7	54.1–55.2
	OA −	56.2	55.3–57.0	55.5	54.8–56.2	55.5	54.5–56.4
Limitation	OA +	80.4	78.3–82.5	81.5	80.1–82.9	77.9	76.4–79.4
	OA −	84.8	82.8–86.9	80.9	79.2–82.6	79.8	77.5–82.1
Gait Speed	OA +	1.24	1.22–1.27	1.22	1.21–1.24	1.18	1.17–1.20
	OA −	1.29	1.27–1.31	1.25	1.23–1.27	1.24	1.22–1.27

		BMI					
		Normal (18.5–24.9kg/m^2)	95% CI	Overweight (25.0–29.9kg/m^2)	95% CI	Obese ($\geq$30kg/m^2)	95% CI
Chair Stand	OA +	0.50	0.48–0.52	0.50	0.48–0.51	0.48	0.47–0.49
	OA −	0.55	0.53–0.57	0.52	0.50–0.53	0.51	0.49–0.53

OA + : radiographic knee osteoarthritis present; OA − : radiographic knee osteoarthritis absent

Values represent mean score (95% confidence interval) of the indicated metric adjusted for: Age, sex, education level, race, Charlson co-morbidity index, smoking status, hip pain and cohort type (incidence, progression), and baseline scoring (Short Form 12, Physical Activity Scale for the Elderly) where available. Models stratified by age adjust for the similar co-variates other than age.

Cohort included in the modeling includes all eligible subjects with follow-up data on outcomes of Short Form 12, Physical Activity Scale for the Elderly and Late-Life Function and Disability Instrument (n=1,729)

BMI – Body mass index

Appendix 3: Impact of Weight Change on Primary Outcomes and Age

		5 % Weight Loss N=598	95% CI	No Change in Weight N=916	95% CI	5 % Weight Gain N=215	95% CI
Short-Form 12 Score							
Overall Score	Overall	100.5	99.7–101.3	101.7	101.1–102.3	99.0	97.7–100.3
	60–70	101.3	100.2–102.3	102.5	101.7–103.3	99.2	97.7–100.7
	70+	99.4	98.1–100.6	100.6	99.5–101.7	99.4	96.7–102.1
Physical	Overall	46.2	45.5–46.8	46.5	45.9–47.0	44.5	43.4–45.6
	60–70	46.8	45.9–47.7	7.1	46.4–47.8	44.7	43.4–46.0
	70+	45.2	44.2–46.3	45.6	44.7–46.4	44.6	42.4–46.8
Mental	Overall	54.3	53.7–54.9	55.2	54.8–55.7	54.4	53.4–55.4
	60–70	54.4	53.6–55.2	55.4	54.8–56.0	54.4	53.3–55.5
	70+	54.2	53.3–55.0	55.0	54.3–55.8	54.6	52.7–56.5
Physical Activity Scale for Elderly	Overall	122.3	117.7–126.8	126.7	123.0–130.3	115.4	107.8–123.0
	60–70	127.7	121.3–134.1	137.7	132.7–142.8	127.0	117.6–136.3
	70+	112.9	106.8–119.0	110.3	105.1–115.5	95.3	82.0–108.6
Late-Life Disability Index							
Frequency	Overall	54.8	54.3–55.2	55.8	55.4–56.1	54.9	54.0–55.7
	60–70	55.3	54.6–55.9	56.1	55.6–56.6	55.5	54.5–56.5
	70+	54.1	53.4–54.8	55.2	54.6–55.8	53.6	52.0–55.2
Limitation	Overall	80.1	79.0–81.3	81.6	80.6–82.5	78.2	76.2–80.2
	60–70	81.8	80.3–83.4	82.6	81.3–83.8	79.9	77.6–82.2
	70+	77.9	76.1–79.7	79.9	78.4–81.4	75.5	71.7–79.4
Gait Speed	Overall	1.23	1.22–1.24	1.24	1.23–1.25	1.19	1.17–1.21
	60–70	1.26	1.24–1.28	1.27	1.26–1.28	1.23	1.21–1.25

		5 % Weight Loss N=598	95% CI	No Change in Weight N=916	95% CI	5 % Weight Gain N=215	95% CI
	70+	1.19	1.16–1.21	1.19	1.17–1.20	1.13	1.09–1.17
Chair Stand	Overall	0.51	0.49–0.52	0.50	0.50–0.51	0.49	0.47–0.51
	60–70	0.52	0.51–0.53	0.51	0.49–0.53	0.52	0.51–0.54
	70+	0.48	0.46–0.49	0.48	0.47–0.49	0.47	0.44–0.50

Values represent mean score (95% confidence interval) of the indicated metric adjusted for: Age, sex, education level, race, Charlson co-morbidity index, smoking status, radiographic knee pain, hip pain and cohort type (incidence, progression), and baseline scoring (Short Form 12, Physical Activity Scale for the Elderly) where available. Models stratified by age adjust for the similar co-variates other than age. Cohort included in the modeling includes all eligible subjects with follow-up data on outcomes of Short Form 12, Physical Activity Scale for the Elderly and Late-Life Function and Disability Instrument (n=1,729)

Appendix 4: Impact of Weight Change on Primary Outcome Measures Stratified by Osteoarthritis status

		5 % Weight Loss N=598	95% CI	No Change in Weight N=916	95% CI	5 % Weight Gain N=215	95% CI
Short-Form 12 Score							
Overall Score	OA+	99.7	98.7–100.7	100.5	99.7–101.4	97.7	95.9–99.4
	OA−	103.5	102.5–104.5	101.2	99.2–103.2	101.8	100.6–103.1
Physical	OA+	45.1	44.2–45.9	45.2	44.5–45.9	43.2	41.8–44.8
	OA−	48.0	46.9–49.0	48.5	47.6–49.3	46.4	44.8–48.2
Mental	OA+	54.6	53.8–55.3	55.4	54.8–56.0	54.4	53.1–55.6
	OA−	53.9	52.9–54.8	55.1	54.4–55.8	54.5	52.9–56.0
Physical Activity Scale for Elderly	OA+	119.1	113.5–124.7	125.8	121.3–130.4	108.6	99.1–118.2
	OA−	127.7	120.0–135.4	127.9	121.8–134.0	125.7	113.3–138.2
Late-Life Disability Index							
Frequency	OA+	54.6	54.0–55.2	55.4	54.9–55.9	54.6	53.6–55.7
	OA−	55.0	54.2–55.8	56.3	55.6–56.9	55.1	53.8–56.4
Limitation	OA+	79.4	77.9–80.9	80.9	79.7–82.1	77.1	74.5–79.6
	OA−	81.3	79.3–83.2	82.7	81.1–84.3	80.2	77.0–83.4
Gait Speed	OA+	1.21	1.19–1.23	1.22	1.21–1.23	1.16	1.14–1.19
	OA−	1.26	1.24–1.29	1.27	1.25–1.28	1.24	1.21–1.27
Chair Stand	OA+	0.49	0.48–0.51	0.49	0.48–0.50	0.48	0.46–0.50
	OA−	0.52	0.50–0.54	0.52	0.51–0.54	0.51	0.48–0.54

OA + : radiographic knee osteoarthritis present; OA − : radiographic knee osteoarthritis absent

Values represent mean score (95% confidence interval) of the indicated metric adjusted for: Age, sex, education level, race, Charlson co-morbidity index, smoking status, hip pain and cohort type (incidence, progression), and baseline scoring (Short

Form 12, Physical Activity Scale for the Elderly) where available. Models stratified by age adjust for the similar co-variates other than age.

Cohort included in the modeling includes all eligible subjects with follow-up data on outcomes of Short Form 12, Physical Activity Scale for the Elderly and Late-Life Function and Disability Instrument (n=1,729)

Appendix 5 – Impact of Weight Change on Primary Outcome Measures Stratified by Osteoarthritis status

		Normal (18.5–24.9kg/m^2)	95% CI	Overweight (25.0–29.9kg/m^2)	95% CI	Obese (30kg/m^2)	95% CI
Short-Form 12 Score							
Overall Score	Overall	101.9	100.4–103.3	100.9	100.2–101.7	99.6	98.6–100.6
Physical	Overall	47.2	46.2–48.2	46.3	45.6–46.9	44.9	44.2–45.7
Mental	Overall	55.2	54.4–55.9	54.7	54.2–55.3	54.5	53.8–55.1
Physical Activity Scale for Elderly	Overall	128.7	121.3–136.0	125.8	121.5–130.0	116.9	111.6–122.1
Late-Life Disability Index							
Frequency	Overall	55.4	54.8–56.1	55.2	54.8–55.7	54.9	54.4–55.4
Limitation	Overall	81.9	80.3–83.4	80.9	79.9–82.0	78.8	77.5–80.0
Gait Speed, m/s	Overall	1.26	1.23–1.28	1.23	1.22–1.25	1.20	1.18–1.22

Values represent mean score (95% confidence interval) of the indicated metric adjusted for: Age, sex, education level, race, Charlson co-morbidity index, smoking status, radiographic knee osteoarthritis, hip pain and cohort type (incidence, progression), and baseline scoring (Short Form 12, Physical Activity Scale for the Elderly) where available. All subjects included in the modeling with missing values accounted for using Inverse probability weighting

Participant Flow Diagram

Study Enrolment

Assessed for eligibility (n= 17,457)

Ineligible for Study (n = 12,641)
- MRI Exclusion (n = 2,295)
- Gender Age/Cell Full (n = 2,954)
- Bilateral End-Stage Osteoarthritis (n = 596)
- Not Interested or Dropout (n = 4,381)
- Other (n = 2,415)

Enrolment (n = 4.796)

Exclusion Criteria

- Age < 60 years (n= 2,211)
- Missing Body Mass Index (n = 1)
- Missing Waist Circumference (n = 38)
- Body Mass Index <18.5kg/m^2 (n = 4)
- Dead at Follow-up (n = 136)
- Control cohort (n = 10)
- Missing Baseline data
  - PASE (n = 10)
  - SF-12 (n = 8)
- Missing 6-year data (n = 649)
  - LLDFI (n = 500)
  - SF- 12 (n = 1)
  - PASE (n = 148)

Analysis

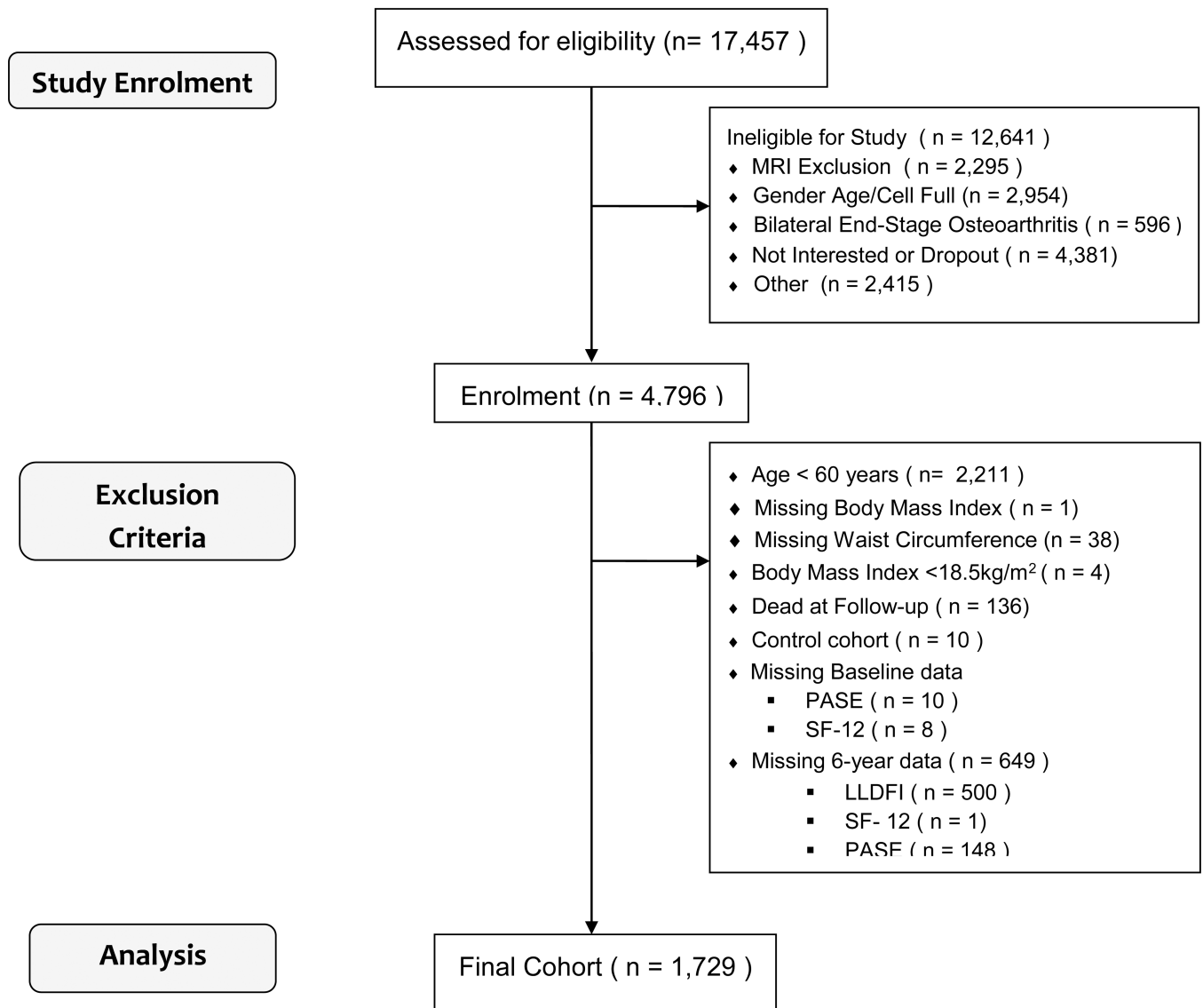Final Cohort (n = 1,729)

Figure 1. Participant Flow: 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: LLDFI – Late-Life Function and Disability Instrument; MRI – magnetic resonance imaging; PASE – Physical Activity Scale for the Elderly; SF – Short Form;

Table 1

Baseline Characteristics of all subjects 60 years old (n=1,729)

| | BMI Category | | | |
Variable	Normal 18.5–25kg/m^2	Overweight 25–29.9kg/m^2	Obese 30kg/m^2	p-value
	N=408	N=747	N=574	
Age, years	68.3 ± 5.6	68.4 ± 5.2	67.1 ± 5.2	<0.001
Female Sex, %	303 (74.3)	405 (54.2)	357 (62.2)	<0.001
Education Status				
< High School	57 (14.0)	136 (18.2)	113 (19.7)	
Some College	77 (19.1)	162 (21.7)	164 (28.5)	
College	89 (21.8)	150 (20.1)	105 (18.3)	<0.001
>College	185 (45.4)	299 (40.0)	192 (33.5)	
Yearly Income				
>$50,000	239 (61.1)	406 (56.6)	274 (49.9)	0.002
Marital Status				
Married	287 (70.3)	525 (70.3)	356 (62.1)	0.003
Race				
White	377 (92.4)	649 (86.9)	419 (73.0)	
Black	20 (4.9)	83 (11.1)	144 (25.1)	<0.001
Other	11 (2.7)	15 (2.0)	11 (1.9)	
Charlson Score	0.30 ± 0.66	0.37 ± 0.80	0.59 ± 1.0	<0.001
Baseline WOMAC Right	7.5 ± 9.4	10.3 ± 12.0	14.8 ± 16.3	<0.001
Baseline WOMAC Left	7.5 ± 11.8	9.9 ± 13.5	14.4 ± 16.9	<0.001
Ever Smoker (y/n)	186 (45.8)	387 (52.1)	285 (50.1)	0.13
# Medications	3.32 ± 2.23	3.63 ± 2.34	4.28± 2.57	<0.001
Radiographic Knee Osteoarthritis	197 (48.3)	456 (61.0)	412 (71.8)	<0.001
Hip Pain	32 (7.8)	83 (11.1)	72 (12.5)	0.06
Waist circumference, cm	90.6 ± 7.7	101.4 ± 7.6	113.7±10.1	<0.001
Cohort Allocation[*]				
Progression	63 (15.4)	205 (27.4)	214 (37.3)	
Incidence	345 (84.6)	542 (72.6)	360 (62.7)	<0.001

All values represent mean ± SD, or count (%)

P-value represents the ANOVA across all body mass index categories

OA – defined as having radiographic knee osteoarthritis on either knee or both knees

Some fields may not add up to overall cohort totals due to missing values

WOMAC – Western Ontario and McMaster University Arthritis Index

[*] controls were not included in this analysis

Table 2

Primary and Follow-up outcome Measures - Unadjusted

Variable	Overall Cohort	BMI Category			p-value
		Normal 18.5–25kg/m²	Overweight 25–29.9kg/m²	Obese 30kg/m²	
		N=408	N=747	N=574	
Short Form12 Score					
Total					
Baseline	104.4 ± 10.1	106.6 ± 8.3^{NS}	$105.2 \pm 9.5^{\#\#}$	$101.8 \pm 11.4^{\#\#\#}$	$<0.001^*$
Follow-up	101.0 ± 12.3	$104.3 \pm 10.2^{\#\#}$	$101.6 \pm 12.2^{\#\#}$	$97.7 \pm 13.2^{\#\#}$	$<0.001^*$
p-value	$<0.001^\dagger$	$<0.001^\dagger$	$<0.001^\dagger$	$<0.001^\dagger$	$0.022^\#$
% of Difference	-3.04 ± 10.3	-1.89 ± 9.2^{NS}	-3.23 ± 9.9^{NS}	$-3.61 \pm 11.5^{\#\#}$	$0.029^{\dagger\dagger}$
Physical					
Baseline	49.3 ± 8.3	$51.9 \pm 6.9^{\#\#\#}$	$49.7 \pm 7.9^{\#\#}$	$47.1 \pm 9.3^{\#\#\#}$	$<0.001^*$
Follow-up	46.2 ± 9.8	$49.2 \pm 8.5^{\#\#\#}$	$46.6 \pm 9.6^{\#\#}$	$43.3 \pm 10.2^{\#\#}$	$<0.001^*$
p-value	$<0.001^\dagger$	$<0.001^\dagger$	$<0.001^\dagger$	$<0.001^\dagger$	$0.20^\#$
% of Difference	-5.29 ± 19.9	-4.2 ± 17.9^{NS}	-5.0 ± 20.3^{NS}	-6.3 ± 20.7^{NS}	$0.24^{\dagger\dagger}$
Mental					
Baseline	55.1 ± 7.1	54.7 ± 6.9^{NS}	55.5 ± 6.9^{NS}	54.7 ± 7.6^{NS}	0.06^*
Follow-up	54.8 ± 8.0	55.1 ± 7.2^{NS}	55.0 ± 7.7^{NS}	54.3 ± 8.8^{NS}	0.20^*
p-value	$0.20^\dagger$	$0.31^\dagger$	$0.07^\dagger$	$0.28^\dagger$	$0.16^\#$
% of Difference	0.66 ± 17.4	2.3 ± 19.9^{NS}	0.05 ± 16.3^{NS}	0.29 ± 16.9^{NS}	$0.09^{\dagger\dagger}$
Physical Activity Score for Elderly					
Baseline	141.5 ± 67.1	149.3 ± 67.7^{NS}	$143.3 \pm 65.5/$	$133.6 \pm 68.2^{\#\#}$	$<0.001^*$
Follow-up	123.8 ± 63.4	132.3 ± 63.6^{NS}	$127.0 \pm 62.4^{\#\#}$	$113.8 \pm 63.3^{\#\#}$	$<0.001^*$
p-value	$<0.001^\dagger$	$<0.001^\dagger$	$<0.001^\dagger$	$<0.001^\dagger$	$0.64^\#$
% of Difference	-5.18 ± 91.9	-6.0 ± 83.4^{NS}	-5.5 ± 93.8^{NS}	-4.2 ± 95.1^{NS}	$0.95^{\dagger\dagger}$

Late-life Disability Index

Variable	Overall Cohort	BMI Category			p-value
		Normal 18.5–25kg/m²	Overweight 25–29.9kg/m²	Obese 30kg/m²	
		N=408	N=747	N=574	
Frequency	55.3 ± 6.3	56.5 ± 6.3##	55.1 ±6.2NS	54.7 ± 6.4##	<0.001*
Limitation	80.6 ± 15.1	82.9 ± 14.3NS	81.3 ± 15.2##	78.1 ± 15.1##	<0.001*
Gait Speed, m/s					
Baseline	1.30 ± 0.21	1.36 ± 0.20/	1.32 ± 0.20/	1.22 ± 0.20##	<0.001*
Follow-up	1.23 ± 0.21	1.30 ± 0.10##	1.25 ± .20##	1.16 ± 0.21##	<0.001*
p-value	<0.001†	<0.001†	<0.001†	<0.001†	0.16#
% of Difference	−4.51 ± 15.9	−3.2 ± 12.5NS	−4.74 ± 15.0NS	−5.2 ±18.9NS	0.19††
Chair Stand Pace					
Baseline	0.48 ± 0.13	0.52 ± 0.13##	0.48 ± 0.13##	0.45 ± 0.13##	<0.001*
Follow-up	0.50 ± 0.15	0.54 ± 0.15##	0.50 ±0.14/	0.47 ± 0.14##	<0.001*
p-value	<0.001†	0.03†	0.008†	0.008†	0.99#
% of Difference	6.18 ± 30.2	1.5 ± 12.7NS	1.4 ± 13.0NS	1.6 ± 12.3NS	0.45††

All values represent mean ± standard deviation, or count (percent)

A drop (negative change) in Short-form 12 score (Total, physical and mental) represents a reduction in self-reported health status. A decrease in Physical Activity for the Elderly Score and Gait Speed, represent reductions in physical activity and mobility speeds. An increase in chair stand pace represents a slower speed. Higher scores of Late-life function and disability scores represent better function (or less disability).

* represents an analysis of variance across each BMI category within a specified time period (baseline or follow-up);

† represents a paired t-test within each BMI category between baseline and follow-up;

\# represents the difference across all BMI categories between baseline and follow-up.

†† represents an analysis of variance across all BMI categories comparing the percent change in scores between baseline and follow-up of a measure

Post-hoc Bonferroni adjustments are presented within each BMI category and the mean score of each outcome represented by symbols

p<0.001;

/ p<0.05;

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*NS*NS – non-significant. Those represented in the normal BMI column represent values comparing normal BMI *vs.* obese BMI; symbols in the overweight column represent values comparing normal BMI vs. overweight BMI; symbols in the obese column represent overweight BMI vs. normal BMI.

Table 3

Multivariable Analysis of Follow-up Primary Outcome Measures

		BMI Category					
		Normal (18.5–24.9kg/m²)	95% CI	Overweight (25.0–29.9kg/m²)	95% CI	Obese (≥30kg/m²)	95% CI
Short-Form 12 Score							
Overall Score	Overall	102.8	101.8–103.8	101.1	100.4–101.8	99.5	98.7–100.4
	60–70	103.2	102.0–104.5	102.1	101.2–103.0	100.1	99.1–101.0
	70+	102.3	100.7–103.8	99.6	98.4–100.7	98.7	97.1–100.2
	Physical Overall	47.8	46.9–48.6	46.4	45.8–47.0	44.7	44.0–45.3
	60–70	48.1	47.0–49.3	47.2	46.4–48.0	45.2	44.3–46.0
	70+	47.3	46.1–48.6	45.2	44.3–46.1	43.7	42.5–45.0
	Mental Overall	55.2	54.5–55.9	54.8	54.3 – 55.3	54.6	54.0–55.2
	60–70	55.2	54.2–56.2	55.0	54.3–55.7	54.7	54.0–55.4
	70+	55.1	54.1–56.2	54.5	53.7–55.2	54.6	53.5–55.6
Physical Activity Scale for Elderly	Overall	131.4	125.8–137.0	126.2	122.2–130.2	115.1	110.3–119.8
	60–70	140.6	132.5–148.7	136.4	130.7–142.1	124.4	118.3–130.6
	70+	118.3	110.9–126.1	110.7	105.2–116.2	100.8	93.3–108.3
Late–Life Disability Index							
	Frequency Overall	55.8	55.2–56.4	55.3	54.9–55.7	55.0	54.5–55.5
	60–70	56.3	55.5–57.1	55.7	55.2–56.3	55.4	54.8–56.0
	70+	55.1	54.2–56.0	54.6	53.9–55.3	54.3	53.4–55.2
	Limitation Overall	82.5	81.1–84.0	81.2	80.2–82.3	78.6	77.4–79.9
	60–70	84.1	82.1–86.1	82.6	81.2–84.0	79.9	78.4–81.4
	70+	80.9	78.7–83.1	79.0	77.4–80.6	76.4	74.2–78.6
Gait Speed	Overall	1.26	1.25–1.28	1.23	1.22–1.24	1.20	1.19–1.22
	60–70	1.29	1.27–1.31	1.27	1.25–1.28	1.24	1.23–1.26
	70+	1.22	1.20–1.24	1.18	1.16–1.20	1.14	1.12–1.17
Chair Stand	Overall	0.52	0.50–0.53	0.50	0.49–0.51	0.49	0.48–0.50

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			BMI Category				
	Normal	**95% CI**	**Overweight**	**95% CI**	**Obese**	**95% CI**
	(18.5–24.9kg/m^2)		(25.0–29.9kg/m^2)		(30kg/m^2)	
60–70	0.53	0.51–0.55	0.52	0.50–0.53	0.51	0.49–0.52
70+	0.50	0.48–0.52	0.47	0.46–0.49	0.46	0.44–0.48

Values represent mean score (95% confidence interval) of the indicated metric adjusted for: Age, sex, education level, race, Charlson co-morbidity index, smoking status, radiographic knee OA, hip pain and cohort type (incidence, progressionl), and baseline scoring (Short Form 12, Physical Activity Scale for the Elderly) where available. Models stratified by age adjust for the similar co-variates other than age.

Cohort included in the modeling includes all eligible subjects with follow-up data on outcomes of Short Form 12, Physical Activity Scale for the Elderly, and Late-Life Function and Disability Instrument (n=1,729)

BMI – Body Mass Index