2016

Older Adults with Elevated BMI are at Greater Risk of Accelerated Knee Osteoarthritis: Data from the Osteoarthritis Initiative

Kyle D. Wallace
Wright State University - Main Campus

Older adults with elevated BMI are at greater risk of accelerated knee osteoarthritis: Data from the Osteoarthritis Initiative

Kyle D. Wallace, MPH

Wright State University

Acknowledgements

I would like to thank Dr. Naila Khalil and Dr. Ramzi W. Nahhas for their outstanding guidance and support, and for being pleasant co-chairs to work with on this project. Also, a special thanks to Dr. Andrew Froehle for his consult and expertise.

“The OAI is a public-private partnership comprised of five contracts (N01-AR-2-2258; N01-AR-2-2259; N01-AR-2-2260; N01-AR-2-2261; N01-AR-2-2262) funded by the National Institutes of Health, a branch of the Department of Health and Human Services, and conducted by the OAI Study Investigators. Private funding partners include Merck Research Laboratories; Novartis Pharmaceuticals Corporation, GlaxoSmithKline; and Pfizer, Inc. Private sector funding for the OAI is managed by the Foundation for the National Institutes of Health. This manuscript was prepared using an OAI public use data set and does not necessarily reflect the opinions or views of the OAI investigators, the NIH, or the private funding partners” (Osteoarthritis initiative guidelines for publications using public use datasets, 2006, p. 2).

Table of Contents

Abstract

Background: Around 35% of adults with osteoarthritis (OA) have knee osteoarthritis (KOA), which generally progresses over several years; however, some individuals experience accelerated KOA (AKOA), a rapid progression to end-stage disease within 48-months.

Purpose: To assess baseline differences among those who develop the different types of KOA, and to determine if baseline characteristics and measures can be used to predict an individual's KOA status (Common KOA or AKOA) 48 months later.

Methods: Cross-sectional analysis of data from the Osteoarthritis Initiative (OAI) was completed. At baseline, 4,769 participants were enrolled. Data from individuals (n = 1,561) free of radiographic KOA (Kellgren-Lawrence [KL] <2) at baseline were included. These participants were categorized into three disease progression groups based on KL score at 48-month follow-up (No KOA, Common KOA, and AKOA). Multinomial logistic regression was used to determine the magnitude of association between baseline risk factors and 48-month KOA status.

Results: Age ($p = 0.049$), BMI ($p < 0.001$), and gender ($p = 0.018$) were significantly associated with KOA status. Older age was associated with a greater risk of AKOA (RRR = 1.46, $p = 0.021$), but not common KOA (RRR = 0.93, $p = 0.481$). BMI was associated with a greater risk of both, but the magnitude of association was stronger with AKOA (RRR = 1.73, $p = 0.001$) compared to common KOA (RRR = 1.40, $p < 0.001$).

Conclusion: KOA reduces quality of life and thus is an important public health concern. Older, obese individuals are at greater risk of developing AKOA.

Keywords: age, gender, body mass index, public health, quality of life

Older adults with elevated BMI are at greater risk of accelerated knee osteoarthritis: Data from the Osteoarthritis Initiative

Osteoarthritis (OA), the most common form of arthritis, affects more than 10% of the U.S. adult population (Murphy & Helmick, 2012). According to Hirsch and Hochberg (2010), the defining characteristics of OA include defects in the integrity of articular (joint) cartilage; more specifically, degeneration of the cartilage at the joint, thickening of underlying bone, formation of spurs and osteophytes (bony outgrowths due to cartilage degeneration), and inflammation of varying degrees. OA is not only a biomechanical process but also a biochemical one, which affects all of the tissues of the joint (Hirsch & Hochberg, 2010). OA is known to occur as a localized condition in the hip, foot, ankle, knee, hand, shoulder, spine or neck, but it is not uncommon for OA to occur as a generalized condition in which three or more joint groups are affected simultaneously (Murphy & Helmick, 2012). OA impairs quality of life; therefore it is of great importance within the realm of public health. According to Murphy and Helmick (2012), OA is the third most significant cause of disability in the U.S. due to the functional limitations it elicits and the slew of comorbidities that arise with it.

Advanced OA is treated surgically with joint replacement in certain anatomical regions such as the knee and hip joints. Otherwise, generally management of OA is focused on symptomatic pain relief (Hensor, Dube, Kingsbury, Tennant, & Conaghan, 2015). Because of very limited treatment options, it is of the utmost importance to raise awareness for early detection of OA. Early detection of the disease may enable effective interventions before structural damage becomes too severe (Hensor et al., 2015).

Among the adult population affected by OA, greater than 35% of them have knee osteoarthritis (KOA); KOA is one of the most debilitating forms of OA (Centers for Disease

Control and Prevention, 2015). Typically, KOA is characterized by slow progression, designated as common KOA (Driban et al., 2014). However, recent studies have acknowledged that about 3% to 17% of individuals with knees that rapidly progress from normal structure to end-stage KOA within 48 months (Driban, Price et al., 2016). This rapidly progressing form of the disease is classified as accelerated KOA (AKOA). This study will distinguish between common KOA and AKOA, and how it relates to Body Mass Index (BMI) and physical activity.

Purpose Statement

The purpose of this study was to assess whether there are baseline differences among those who develop the different types of KOA (AKOA, common KOA, and no KOA) in terms of demographic characteristics (age, ethnicity, gender, income, and education), BMI, physical performance and pain measures, and to determine if baseline characteristics and measures could be used to predict an individual's KOA status (common KOA or AKOA) 48 months later.

Literature Review

Definitions of OA

OA is not limited to a single definition; published OA research in the United States employed at least three definitions for establishing OA: radiographic, symptomatic, and clinical. The basis of radiographic OA stems from information found on x-rays, and is usually defined by the Kellgren-Lawrence (KL) scale (Murphy & Helmick, 2012). The KL scale assesses the severity of joint degeneration as normal (grade 0), doubtful (grade 1) mild (grade 2), moderate (grade 3), or severe/end-stage (grade 4). Radiographic OA is often utilized to track the disease process (Murphy & Helmick, 2012). The combination of radiographic evidence of OA and symptoms of the disease (i.e. pain, swelling, and stiffness) in the radiographically affected joint are used to define symptomatic OA (Centers for disease Control and Prevention, 2015). The

prevalence of symptomatic OA is the most commonly used definition for describing the burden of OA on the health of the population (Felson & Nevitt, 2004). Clinical OA is solely based on clinical information such as patient history and physical examination; clinical diagnoses are not commonly used to study the burden of OA (Murphy & Helmick, 2012).

KOA and Gender

KOA affects men and women differently; according to Hame and Alexander (2013), KOA is expressed in different manners between males and females, and studies have shown that certain parts of the knee are affected disproportionately between the two sexes due to anatomic differences in knee structure. This is apparent in the patellofemoral joint; women tend to have a higher prevalence of isolated patellofemoral arthritis compared to men (McAlindon, Snow, Cooper, & Dieppe, 1992). Also, knee cartilage degenerates at a faster rate in women than it does in men (O'Connor & Hooten, 2011). Men tend to have a greater volume of total tibial and patellar cartilage as well (Hame & Alexander, 2013). Lower volumes of cartilage, coupled with an increased loss of cartilage volume are likely contributing factors to the higher prevalence of KOA in women. In addition to gender differences in the anatomy of the knee joint, the stage in which KOA is diagnosed tends to be more advanced in women than in men (Hame & Alexander, 2013). Moreover, females report higher levels of pain and more disability than their male counterparts (O'Connor & Hooten, 2011). A study of female and male recreational athletes explains another possible factor contributing to these gender discrepancies in KOA. The study found that females experience increased force and extension on their knees during stop-jump tasks, which may potentially place more stress on the joint for female athletes (Chappell, Yu, Kirkendall, & Garret, 2002). It has also been well-established that young, active women are 35 times more likely to suffer anterior cruciate ligament (ACL) injuries compared to young, active

men when participating in contact sports. Regardless of gender, these injuries lead to future KOA (Friel & Chu, 2013). Men and women also differ in age at which KOA is diagnosed. Among those younger than 45 years, KOA is more common among men, but among those older than 54 years, it is more common among women (Hirsch & Hochberg, 2010). This gender associated age difference in KOA may be due to hormonal changes in postmenopausal women. Postmenopausal women have lower estrogen levels than adult women and lower estrogen is linked with an increased risk of KOA (Hame & Alexander, 2013).

KOA and Age

Age itself greatly impacts OA. According to Hirsch and Hochberg (2010), the incidence of OA increases with age. In addition, the prevalence of moderate and severe cases of the disease increases with age through 65 to 74 years. Similar findings have also been observed in other studies. Data from the Framingham Heart Study showed that radiographic OA was present in 27% of participants younger than 70 years; in participants older than 80 years OA prevalence was 44% (Hame & Alexander, 2013). It is also well-known that KOA is quite common among older adults; the risk of KOA and its severity increases with age. Hame and Alexander (2013) estimated that more than 33% of adults over the age of 65 are affected by KOA. Using data from the Third National Health and Nutrition Examination Survey, Lo et al. (2015), documented that the prevalence of radiographic KOA was 37.4% among U.S. adults older than 60 years.

There may be differences in age among those who develop AKOA when compared to those with common KOA. Older age has been identified as a key risk factor for AKOA; however, age is a known risk factor for common KOA as well (Driban, Eaton et al., 2016). Studies have shown that individuals who develop AKOA are older than those with the common

form of the disease (Driban, Eaton et al., 2016). The results from Driban, Eaton's et al. (2016) study showed that older age was independently associated with AKOA.

KOA Race, Education, and SES

Along with older adults, there may be other subgroups that are considered high-risk for developing KOA. Very few studies have explored racial differences among those who develop KOA as race is not generally considered a major risk factor. However, limited studies report significant racial differences in KOA. Anderson and Felson (1988) published the first study in which racial differences in KOA were assessed within the United States. They found that Black women, compared to White women and women of other races, had an increased risk of KOA; however, this race difference in KOA was not observed in men. Another study found Blacks to have higher odds of developing KOA when compared to Whites and other races, regardless of gender (Dillon, Rasch, Gu, & Hirsch, 2006). These racial differences in KOA are explained by Blacks being more likely to suffer from joint space narrowing along with developing more osteophytes than whites (Jordan, 2015). According to Jordan's (2015) research, Blacks may also present with elevated biomarkers for KOA development compared to their White counterparts.

Education and socioeconomic status (SES) are considered important risk factors for OA. These variables have been commonly analyzed in OA research studies. Hirsch and Hochberg (2010) documented that having less than 12 years of formal education was associated with a higher prevalence of clinical diagnosis of OA. This same study also reported that low SES was associated with a greater risk of OA. An explanation for these associations may be that low educational attainment and low SES are consequently linked to a lack of access to health resources, and are often accompanied with blue collar jobs such as construction and farming, which are generally associated with repetitive use of specific joints and thus more joint strain

(Hirsch and Hochberg, 2010). However, on the basis of radiographic KOA, only low educational attainment has been associated with the disease (Luong, Cleveland, Nyrop & Callahan, 2012).

Symptoms of KOA

Pain, swelling, and stiffness are the most common symptoms of KOA. Other symptoms such as functional impairments and reduced quality of life, which are associated with pain, are evident among those suffering from KOA, as well (Bindawas & Vennu, 2015). According to Murphy and Helmick (2012), results from the Johnston County OA project indicated that 43.3% of individuals with KOA reported pain, aching or stiffness on most days. This same study reported higher pain levels with increasing age, and higher pain among Blacks compared to Whites and in women compared to men. Among the elderly, KOA is the most significant cause of pain and disability (Mansournia et al., 2012). Davison, Ioannidis, Maly, Adachi, and Beattie (2016), identified two types of KOA pain: constant aching pain and intermittent pain. Constant pain is considered 'background' pain that is manageable, whereas intermittent pain has been established as more severe and emotionally draining, and is associated with avoidance of social and recreational activities (Davison, Ioannidis, Maly, Adachi, & Beattie, 2016). Both types of pain lead to functional limitations and reduced quality of life, although intermittent pain has the greatest impact on an individual's quality of life and physical function (Gooberman-Hill et al., 2007). These symptoms of KOA may vary among those with different forms of the disease. Driban, Price et al. (2016) found that individuals with AKOA were more likely to report greater pain and functional limitations than those with common KOA. These reports are in accordance with findings from another study assessing the differences in KOA symptoms based on KOA severity (Wesseling, Bierman-Zeinstra, Kloppenburg, Meijer, & Bijlsma, 2015). Overall, the symptoms of KOA can be quite debilitating to the individual.

KOA and Joint Injuries

Injuries to the knee joint play a significant role in the development and progression of KOA. According to Hirsch and Hochberg (2010), the strongest risk factor for KOA is a history of joint trauma. Common joint injuries result from sports and work, and in either case they increase the risk of developing KOA (Murphy & Helmick, 2012). Knee injury is a risk factor for common KOA and AKOA. According to Driban, Eaton et al. (2016) older adults with a recent knee injury are more likely to develop AKOA, more so if they have an elevated BMI.

KOA and BMI

Another very strong risk factor of KOA is obesity (Murphy & Helmick, 2012). The prevalence of older adults with obesity has steadily increased over the past several decades, thus rendering it a significant public health concern (Batsis, Zbehlik, Barre et al., 2015). Therefore, as the population of older adults continues to increase so will the number of individuals with obesity. According to Batsis, Zbehlik, Barre et al. (2015), obesity based on BMI has been linked to functional limitations and disability in subjects with KOA. As demonstrated by numerous studies, obesity plays a causal role in KOA (Hirsch & Hochberg, 2010). Higher BMI is a key risk factor for developing KOA, and has been linked to AKOA regardless of any other contributing factors of the disease (Driban, Eaton et al, 2016). Driban, Eaton et al. (2016) found that older individuals with a higher BMI were more likely to develop AKOA than common KOA. Obesity has been shown to exacerbate the symptoms of KOA such as pain (Batsis, Zbehlik, Barre et al., 2015). Moreover, a study evaluating the effects of obesity on physical function and quality of life in individuals with KOA found that obesity (defined as having a BMI greater than 30) leads to a reduction of physical function, greater levels of disability, and a lower quality of life (Batsis, Zbehlik, Barre et al., 2015). Furthermore, obesity predicts the progression of KOA in both sexes

as demonstrated by longitudinal studies (Hirsch & Hochberg, 2010). Many studies have also shown that weight loss not only decreases the risk of developing KOA, but also alleviates symptoms and functional impairments in individuals with the disease (Hirsch & Hochberg, 2010).

KOA and Physical Activity

Physical activity is documented to relieve the symptoms of OA not only by improving joint mobility directly but also indirectly by weight loss (Hirsch & Hochberg, 2010). The relationship between physical activity and KOA is of significant public health importance. Physical activity limitations are common among those suffering from KOA; the most frequent functional limitations among individuals with KOA are bending, standing, and walking (Murphy & Helmick, 2012). Obesity is known to accelerate disability and deteriorate physical activity levels, especially in those with KOA (Batsis, Zbehlik, Pidgeon, & Bartels 2015). Many studies have demonstrated that obesity negatively impacts gait speed in individuals with KOA. Gait speed is measured by the 20-meter walk test. Reports from these studies show that older, obese individuals have slower gait speeds and greater declines in gait speeds when assessed at multiple time points (Batsis, Zbehlik, Pidgeon et al., 2015; Bindawas & Vennu, 2015; Lee et al., 2015). These same studies reported similar findings concerning the chair stand test; older, obese individuals with KOA had slower chair stand rates and more drastic declines compared to their younger, normal weight counterparts. Batsis, Zbehlik, Pidgeon, and Bartels (2015) found obese individuals and those older than 70 years to have significant declines in 400-meter walk time assessed at different time points (i.e. baseline and 48-month follow-up).

Many individuals with KOA often worry that exercise will exacerbate the disease, and this is why they abstain from such activities (Murphy & Helmick, 2012). Numerous studies have

shown this concern to be unfounded; physical activity, including exercise, has been shown to decrease pain, improve physical function and, thus, improve quality of life in those with KOA (Brady, Jernick, Hootman, & Sniezek, 2009). Others who are at risk of the disease feel that exercising will lead to the development of KOA, but Hirsch and Hochberg (2010) explain that exercise (including running and other sports activities) have not been associated with the development of KOA in those without previous joint trauma. Regular physical activity has many health benefits and is a known protective factor for several chronic diseases including KOA (Lee et al., 2015).

Methods

Background

Data for this cross-sectional study were obtained from the publicly available Osteoarthritis Initiative (OAI) database, which can be accessed online (http://www.oai.ucsf.edu/). Specific datasets used were database release versions: 23, 0.2.2, and 6.2.2.

The OAI is a multicenter prospective cohort study of older adults (ages 45 to 79 years) who had existing OA or were at risk of developing OA (n = 4,796). Four clinical sites for this study were Baltimore, Maryland; Pawtucket, Rhode Island; Pittsburgh, Pennsylvania; and Columbus, Ohio. Data collection began in 2004 and participant enrollment was completed in 2006; follow-up visits have been conducted every 12 months since.

The current study utilized information from radiographic assessments of KOA in order to track the disease process and to determine risk factors for the two subtypes (common KOA and AKOA) of the disease. Radiographic assessment of knee degeneration was evaluated using

Kellgren-Lawrence (KL) score (grade 0 to 4) at enrollment (baseline) through 48-month follow-up.

Inclusion Criteria for Participants

Data from individuals (n = 1,561) free of radiographic KOA (KL < 2) at baseline were included. These participants were categorized into three disease progression groups based on KL score at 48-month follow-up:

1) **No KOA:** no change in KL score in either knee
2) **Common KOA:** KL score increase in at least one knee from zero to one (0 to 1) or one to two (1 to 2)
3) **AKOA:** at least one knee progressed to end-stage KOA (KL grade three [3] or four [4])

Study Measures

All study related data were obtained from patient self-reports or from measurements based on the OAI protocol (Nevitt, Felson, & Lester, 2006). Data regarding demographic, medical, social, and ethnic characteristics of subjects were collected using questionnaires. Age, gender, race, and education were self-reported. Age recorded at the initial screening was considered age at baseline. Gender was reported as male or female at the initial visit. Race was dichotomized as ‘White’ or ‘All Others’ (non-White individuals were grouped together due to a small number of individuals in any single other racial/ethnic group). Education status of participants was classified as having high school or further education versus less than high school, and income was divided into $50,000 or more versus less than $50,000 of annual household income.

Physical activity level of study participants was assessed using the Physical Activity Scale for the Elderly (PASE) (2010), a questionnaire assessing leisure-time, household, and occupational activities in the last seven days (scoring from 0 to 361; increasing score indicates more physical activity). Participants' self-reported pain was assessed using the Western Ontario and McMaster University OA index for pain (WOMAC), which uses a five-point Likert scale inquiring about knee pain in the last seven days, (sum of five questions each scored from zero to four [0 to 4] for a total score of zero to twenty [0 to 20] where increasing score indicates more pain; each participant's average score of right and left knee scores was utilized) (Western Ontario and McMaster Universities Osteoarthritis Index [WOMAC], 2016). Self-reported disability was assessed via WOMAC index for disability, which uses a five-point Likert scale inquiring about physical function limitations in performing everyday tasks (sum of 17 questions each scored from zero to four [0 to 4] for a total score of zero to sixty-eight [0 to 68] where increasing score indicates greater disability; each participant's average score of right and left knee scores was utilized) (WOMAC, 2016).

Measurements included BMI, which was calculated as weight in kilograms divided by the square of height in meters. Three different performance measures for each participant were assessed: 20-meter walk test, repeated chair stand test, and 400-meter walk test. The 20-meter walk test was the speed (m/sec) at which it took an individual to complete a walk of 20 meters. Repeated chair stand test assessed ability to stand up from a chair from the seated position without using any type of aid; the pace was measured in number of stands/sec for a 30 second period. The 400-meter walk test assessed the total time (in seconds) it took for the participant to walk 400 meters.

Statistical Analysis

Analyses were performed using Statistical Package for the Social Science (SPSS, Version 23.0). The significance cutoff for hypothesis tests was $\alpha = 0.05$ (two-tailed). Measures of centrality and dispersion included mean and standard deviation for normally distributed continuous variables and median and interquartile range for non-normally distributed continuous variables. Categorical variables were examined via frequency distributions. For continuous variables, baseline differences between groups (no KOA, Common KOA, and AKOA) were tested using Analysis of Variance (ANOVA). When groups had very serious non-normality or very different group variances (determined by Levene's Test for Equality of Variances), the Kruskal-Wallis test (non-parametric alternative to ANOVA) was used. If groups were normally distributed, but had unequal variances for a specific continuous variable, then the Welch F test was used for the test of association. Baseline differences between groups for categorical variables were tested using the chi-square (X^2) test.

Multinomial logistic regression was used to determine the magnitude of association between baseline risk factors and 48-month KOA status (AKOA and common KOA, compared to no KOA). Univariate regression analyses were conducted first to estimate the crude associations between the predictors and the outcome. A multivariable model was obtained via stepwise regression (criteria for inclusion was set at $p \leq 0.05$, and for removal at $p > 0.10$), beginning with all predictors included. The final model was developed from backwards stepwise regression excluding cases list wise, but the final parameter estimates were obtained after refitting with all cases with non-missing values of age, gender, BMI, and 400m time. The continuous variables of the final model (age, BMI, and 400m time) were adjusted in order to make the relative risk ratios (RRR) more comprehensible. To ease interpretation, the RRRs were

constructed to correspond to a 10-year difference in age, a five-unit difference in BMI, and a 60-second difference in 400m time.

Results

Baseline Characteristics

The baseline characteristics of study participants who were assessed at 48 month follow-up for their KOA status are presented in Table 1. There were significant group differences observed in mean age ($p = 0.032$), BMI ($p = 0.001$), WOMAC pain score ($p = 0.034$), and WOMAC disability score ($p = 0.031$). On average, individuals with AKOA compared to those with common KOA and no KOA were older (61.81 years vs 58.13 and 59.24 years, respectively), had a higher BMI (28.89 vs 27.92 and 27.04, respectively), and reported more pain (2.08 vs 1.74 and 1.50, respectively) and functional disability (6.66 vs 5.58 and 4.74, respectively). Across increasing severity of 48-month KOA status, an increasing trend in BMI was observed. A similar trend was observed in WOMAC pain and disability scores, higher severity was associated with greater pain and functional disability.

Table 1. *Baseline Characteristics by 48-Month KOA Status*

Variable:	**No KOA (n = 1,320)**	**Common KOA (n = 187)**	**AKOA (n = 54)**	**p-value**
Age (years)	58.00 (15)	56.00 (12)	63.00 (14)	0.032[a]
Male	567 (43.0%)	65 (34.8%)	20 (37.0%)	0.081[b]
White	1,139 (86.5%)	156 (83.4%)	46 (85.2%)	0.518[b]
Education ≥ High school	1,167 (88.7%)	162 (87.6%)	44 (84.6%)	0.622[b]
Income ≥ $50K	877 (68.6%)	130 (72.6%)	29 (56.9%)	0.100[b]
BMI (kg/m^2)	27.04 ± 4.42	27.92 ± 4.39	28.89 ± 4.67	0.001[c]
PASE (0-361)[e]	168.71 ± 82.14	178.47 ± 82.47	182.04 ± 91.03	0.182[c]
20m test (m/sec)	1.37 ± 0.21	1.38 ± 0.19	1.34 ± 0.19	0.583[c]
Chair stand test (stands/sec)	0.54 ± 0.15	0.54 ± 0.16	0.50 ± 0.12	0.265[c]
400m time (secs)	296.55 ± 49.77	293.19 ± 40.79	296.74 ± 37.20	0.610[d]
WOMAC pain (0-20)[f]	0.50 (2)	1.00 (3)	1.50 (3)	0.034[a]
WOMAC disability (0-68)[g]	1.50 (6)	2.06 (9)	2.66 (11)	0.031[a]

Note. Values given as mean ± SD, median (IQR), or n (%).
[a] p-value from Kruskal-Wallis test
[b] p-value from chi-square test
[c] p-value from ANOVA F test
[d] p-value from Welch F test
[e] PASE: increasing score indicates more physical activity
[f] WOMAC pain: increasing score indicates more pain; average of right and left knee scores
[g] WOMAC disability: increasing score indicates greater disability; average of right and left knee scores

Univariate Multinomial Regression

Table 2 illustrates the results from the univariate multinomial regression analyses. Age (p = 0.029) and BMI (p = 0.001) were the only two variables significantly associated with KOA status.

Table 2. *Results from Univariate Multinomial Regression Analyses*

	KOA Status			
Predictor	**No KOA (reference): RRR (n)**	**Common KOA: RRR (95% CI) p-value[a] (n)**	**AKOA: RRR (95% CI) p-value[a] (n)**	**p-value[b]**
Age	1.00 (1320)	0.99 (0.97, 1.00) 0.115 (187)	1.03 (1.00,1.06) 0.042 (54)	0.029
Male vs Female	1.00 (1320)	0.71 (0.51, 0.98) 0.034 (187)	0.78 (0.45, 1.37) 0.390 (54)	0.077
White vs All Others	1.00 (1317)	0.79 (0.52, 1.19) 0.258 (187)	0.90 (0.42, 1.94) 0.785 (54)	0.531
≥ High school vs < High school	1.00 (1316)	1.11 (0.70, 1.78) 0.657 (185)	1.42 (0.66, 3.08) 0.370 (52)	0.641
≥ $50K vs <$50K	1.00 (1279)	0.82 (0.58, 1.17) 0.272 (179)	1.66 (0.94, 2.92) 0.081 (51)	0.107
BMI	1.00 (1320)	1.05 (1.01, 1.08) 0.011 (187)	1.09 (1.03, 1.16) 0.003 (54)	0.001
PASE	1.00 (1314)	1.00 (1.00, 1.01) 0.131 (186)	1.00 (1.00, 1.01) 0.243 (54)	0.187
20m test	1.00 (1318)	1.20 (0.57, 2.52) 0.630 (186)	0.55 (0.15, 2.07) 0.376 (54)	0.582
Chair stand test	1.00 (1277)	1.09 (0.39, 3.05) 0.866 (179)	0.19 (0.03, 1.44) 0.107 (51)	0.243
400m time	1.00 (1236)	0.99 (0.99, 1.00) 0.390 (179)	1.00 (0.99, 1.01) 0.977 (52)	0.681
WOMAC Pain	1.00 (1320)	1.05 (0.98, 1.13) 0.146 (187)	1.12 (1.00, 1.24) 0.045 (54)	0.076
WOMAC Disability	1.00 (1318)	1.02 (1.00, 1.04) 0.139 (186)	1.03 (1.00, 1.06) 0.061 (53)	0.092

Note. RRRs for continuous predictors compare relative risk of Common KOA or AKOA vs. no KOA for a one-unit difference in the predictor

[a] p-value for RRR for each KOA status vs. reference group

[b] Overall p-value for predictor

Multivariate Multinomial Regression

Table 3 presents the final model from the multinomial logistic regression. Note that all of the variables of this model were significant at $\alpha = 0.05$ level, except 400m time; it was kept in the model because we found it interesting that the RRRs for 400m time changed so much compared to the univariate (from RRR ≈ 1.00 to ≈ 0.80). The parameter estimates for age, BMI, and sex remained essentially the same whether 400m time was included in the final model or not,

and their statistical significance was unaffected ($p < 0.05$ either way). Age was significantly associated with KOA status ($p = 0.049$) in the overall model; however, older age was associated with a significantly greater risk of AKOA (RRR = 1.46, $p = 0.021$) only. Baseline BMI was significantly associated with 48-month KOA status ($p < 0.001$). Higher BMI was associated with a greater risk of common KOA and AKOA compared to no KOA; however, the magnitude of association was stronger for AKOA (RRR = 1.73, $p = 0.001$) compared to common KOA (RRR = 1.40, $p < 0.001$). Also, a significant association between gender and KOA status was observed ($p=0.018$). Being male was protective against common KOA (RRR = 0.63, $p = 0.009$) when compared to no KOA. Although the RRR for males was similar for AKOA (RRR = 0.70, $p = 0.239$), it was not significantly different from zero for this smaller sized group. The association between 400m time and KOA status was not significant ($p = 0.081$); however, a negative association was observed indicating that the longer the 400m time the less risk of AKOA (RRR = 0.76) and common KOA (RRR = 0.81).

Table 3. *Predicting KOA Status*

	KOA Status			
Predictor	**No KOA (reference) n = 1236 RRR**	**Common KOA: n = 174 RRR (95% CI) p-value[a]**	**AKOA: n = 52 RRR (95% CI) p-value[a]**	**p-value[b]**
Age/10	1.00	0.93 (0.77, 1.13) 0.481	1.46 (1.06, 2.02) 0.021	0.049
BMI/5	1.00	1.40 (1.16, 1.67) <0.001	1.73 (1.26, 2.38) 0.001	<0.001
Male vs Female	1.00	0.63 (0.45, 0.89) 0.009	0.70 (0.39, 1.27) 0.239	0.018
400m Time/60	1.00	0.81 (0.64,1.02) 0.074	0.76 (0.51, 1.13) 0.167	0.081

Note. RRRs for continuous predictors compare relative risk of Common KOA or AKOA vs. no KOA for a 10-year difference in age, a 5-unit difference in BMI, and a 60-second difference in 400m time

[a] p-value for RRR for each KOA status vs. reference group

[b] Overall p-value for predictor

Discussion

This analysis showed that, at baseline, individuals who developed AKOA 48-months later tended to be older, had higher BMI, and were more likely to report greater pain and functional limitations compared to those who developed common KOA and those who did not develop KOA. Older age was associated with a greater risk of AKOA, and it was an important risk factor for progression to AKOA. Being male was protective against common KOA and AKOA (though not significantly so for this smaller sized group). Individuals with higher BMI were at a greater risk of developing AKOA and common KOA compared to no KOA, but having an elevated BMI was a key risk factor for AKOA development. Overall, AKOA is more disabling, is associated with more pain, and a greater reduction in quality of life compared to common KOA, thus AKOA warrants more public health attention (Driban, Price et al., 2016).

The findings from this study coincide with the literature. At baseline, individuals who developed AKOA 48-months later reported higher levels of pain and disability than those who developed common KOA; this is in accordance with reports from two different studies assessing the differences in KOA symptoms based on KOA severity. Driban, Price et al. (2016) and Wesseling et al. (2015) reported that individuals with AKOA suffer from greater pain and more functional limitations than those with common KOA and no KOA. Pain and functional limitations tend to worsen with increasing severity of KOA (Driban, Price, et al., 2016; Wesseling et al., 2015).

Our results also suggest that KOA is associated with gender. Being male was protective against the different types of KOA. This is concurrent with existing literature. According to Hame and Alexander (2013), the prevalence of KOA is higher among women, and women are diagnosed at a more advanced KOA stage compared to men. This same study also discussed the

relationship of low estrogen levels with increased risk of KOA among post-menopausal women. This may help explain our findings, since our cohort of study participants is older (age range 45 to 79 years) the majority of women will likely be post-menopausal, thus having a greater risk of KOA compared to men. Age itself was also associated with KOA status in current analysis.

The risk of KOA as well as its severity increases with age (Hame & Alexander 2013). Our findings support this claim. Results from univariate regression analysis suggest that age is associated with AKOA; this is in accordance with the findings from Driban, Eaton's et al. (2016) research. Our multivariate regression results suggest that older age was associated with a greater risk of AKOA, even after controlling for gender, BMI, and 400m time. Age is a known risk factor for both common KOA and AKOA, but evidence has shown that individuals who develop AKOA are older than those with common KOA and no KOA (Driban, Eaton et al., 2016).

Perhaps the most prominent finding from our study is the association of BMI with KOA status. Our results depict an increasing trend in baseline BMI among those who develop more severe KOA at 48-months. According to our univariate regression analysis, BMI is associated with common KOA and AKOA; multivariate regression results indicate that after controlling for age, gender, and 400m time individuals with an elevated BMI were at an increased risk of common KOA and AKOA development, versus no KOA. Our findings also indicate that BMI is a stronger risk factor for AKOA (RRR = 1.73) than it is for common KOA (RRR = 1.40). These findings are consistent with the literature. Obesity plays a causal role in the development of KOA, and higher BMI in general is a key risk factor for KOA development (Hirsch & Hochberg, 2010). Driban, Eaton et al. (2016) reported that having a higher BMI is associated with AKOA regardless of any other factors. They also reported a higher risk of AKOA compared to common KOA in individuals with a higher BMI.

Study Limitations

Our study offers valuable insight into the public health implications of KOA, and more specifically the differences between common KOA and AKOA; however, as with any study there are some important limitations to be considered. First, we observed only a small number of individuals with AKOA. The generalizability of our findings as well as our ability to identify significant associations may be limited by this small sample size. An example of this is the association between gender and AKOA; with a larger sample size this association may have been significant. Despite our small sample size of individuals with AKOA, we found significant associations between AKOA and age and BMI. A second limitation could be recall bias associated with self-reported study measures (i.e. PASE and WOMAC scores). There is also a potential for confounding with comorbidity scores and previous joint injuries, not taken into account, which may have skewed results. Another noteworthy, yet puzzling finding from our study was the negative association between 400m meter time and KOA status. We found it to be anomalous that a longer 400m meter time was protective against common KOA and AKOA compared to no KOA. However, this finding was not statistically significant at the 0.05 level. It is highlighted here due to its inclusion in the final model at $\alpha = 0.10$ level. Aside from this counterintuitive result, our findings agree with the literature, and add additional insight to the different implications of risk factors for AKOA versus common KOA.

Conclusion

KOA is a debilitating disease shown to reduce quality of life, rendering it an important public health concern. Early detection of the disease may help prevent severe structural damage. KOA is quite common among the older population and affects women disproportionately. Higher BMI is a key risk factor for developing KOA. KOA is typically a slowly progressing

disease, but recently the rapid, more severe form AKOA has gained significant research interest. AKOA is very similar to common KOA in terms of risk factors and end-stage outcomes; however, AKOA warrants more public health attention due to its aggressive nature and its key risk factors. Older individuals, especially those with elevated BMIs may be at greater risk of developing AKOA. We recommend that individuals at risk of KOA maintain an active lifestyle and a normal BMI in order to preserve a higher quality of life and mitigate their risk of common KOA and AKOA.

References

Anderson, J. J., & Felson, D. T. (1988). Factors associated with osteoarthritis of the knee in the first national health and nutrition examination survey (HANES I). Evidence for an association with overweight, race, and physical demands of work. *American Journal of Epidemiology, 128*(1), 179-189.

Batsis, J. A., Zbehlik, A. J., Barre, L. K., Bynum, J. P., Pidgeon, D., & Bartels, S. J. (2015). Impact of obesity on disability, function, and physical activity: Data from the osteoarthritis initiative. *Scandinavian Journal of Rheumatology, 44*(6), 495-502. doi:10.3109/03009742.2015.1021376

Batsis, J. A., Zbehlik, A. J., Pidgeon, D., & Bartels, S. J. (2015). Dynapenic obesity and the effect on long-term physical function and quality of life: Data from the Osteoarthritis Initiative. *BMC Geriatrics, 15,* 118-015-0118-9. doi:10.1186/s12877-015-0118-9

Bindawas, S. M., & Vennu, V. (2015). Longitudinal effects of physical inactivity and obesity on gait speed in older adults with frequent knee pain: Data from the Osteoarthritis Initiative. *International Journal of Environmental Research and Public Health, 12*(2), 1849-1863. doi:10.3390/ijerph120201849

Brady, T. J., Jernick, S. L., Hootman, J. M., & Sniezek, J. E. (2009). Public health interventions for arthritis: Expanding the toolbox of evidence-based interventions. *Journal of Women's Health, 18*(12), 1905-1917. doi:10.1089/jwh.2009.1571

Centers for Disease Control and Prevention (CDC). (2015). Osteoarthritis (OA). Retrieved on June 3, 2016 from http://www.cdc.gov.ezproxy.libraries.wright.edu/arthritis/basics/osteoarthritis.htm

Chappell, J. D., Yu, B., Kirkendall, D. T., & Garrett, W. E. (2002). A comparison of knee kinetics between male and female recreational athletes in stop-jump tasks. *The American Journal of Sports Medicine, 30*(2), 261-267.

Davison, M. J., Ioannidis, G., Maly, M. R., Adachi, J. D., & Beattie, K. A. (2016). Intermittent and constant pain and physical function or performance in men and women with knee osteoarthritis: Data from the Osteoarthritis Initiative. *Clinical Rheumatology, 35*(2), 371-379. doi:10.1007/s10067-014-2810-0

Dillon, C. F., Rasch, E. K., Gu, Q., & Hirsch, R. (2006). Prevalence of knee osteoarthritis in the United States: Arthritis data from the third National Health and Nutrition Examination Survey 1991-94. *The Journal of Rheumatology, 33*(11), 2271-2279. doi:06/13/1011

Driban, J. B., Eaton, C. B., Lo, G. H., Price, L. L., Lu, B., Barbe, M. F., & McAlindon, T. E. (2016). Overweight older adults, particularly after an injury, are at high risk for accelerated knee osteoarthritis: Data from the Osteoarthritis Initiative. *Clinical Rheumatology, 35*(4), 1071-1076. doi:10.1007/s10067-015-3152-2

Driban, J. B., Eaton, C. B., Lo, G. H., Ward, R. J., Lu, B., & McAlindon, T. E. (2014). Association of knee injuries with accelerated knee osteoarthritis progression: Data from the Osteoarthritis Initiative. *Arthritis Care & Research, 66*(11), 1673-1679. doi:10.1002/acr.22359

Driban, J. B., Price, L. L., Eaton, C. B., Lu, B., Lo, G. H., Lapane, K. L., & McAlindon, T. E. (2016). Individuals with incident accelerated knee osteoarthritis have greater pain than those with common knee osteoarthritis progression: Data from the Osteoarthritis Initiative. *Clinical Rheumatology, 35*(6), 1565-1571. doi:10.1007/s10067-015-3128-2

Felson, D. T., & Nevitt, M. C. (2004). Epidemiologic studies for osteoarthritis: New versus conventional study design approaches. *Rheumatic Diseases Clinics of North America, 30*(4), 783-97, vii. doi:S0889-857X(04)00082-1

Friel, N. A., & Chu, C. R. (2013). The role of ACL injury in the development of posttraumatic knee osteoarthritis. *Clinics in Sports Medicine, 32*(1), 1-12. doi:10.1016/j.csm.2012.08.017

Gooberman-Hill, R., Woolhead, G., Mackichan, F., Ayis, S., Williams, S., & Dieppe, P. (2007). Assessing chronic joint pain: Lessons from a focus group study. *Arthritis and Rheumatism, 57*(4), 666-671. doi:10.1002/art.22681

Hame, S. L., & Alexander, R. A. (2013). Knee osteoarthritis in women. *Current Reviews in Musculoskeletal Medicine, 6*(2), 182-187. doi:10.1007/s12178-013-9164-0

Hensor, E. M., Dube, B., Kingsbury, S. R., Tennant, A., & Conaghan, P. G. (2015). Toward a clinical definition of early osteoarthritis: Onset of patient-reported knee pain begins on stairs. Data from the Osteoarthritis Initiative. *Arthritis Care & Research, 67*(1), 40-47. doi:10.1002/acr.22418

Hirsch, R., & Hochberg, M. C. (2010). Arthritis and other musculoskeletal diseases. In P. L. Remington, C. R. Brownson & M. V. Wegner (Eds.). *Chronic Disease Epidemiology and Control* (3rd ed., pp. 571-592). Washington, DC: American Public Health Association.

Jordan, J. M. (2015). An ongoing assessment of osteoarthritis in African Americans and Caucasians in North Carolina: The Johnston County osteoarthritis project. *Transactions of the American Clinical and Climatological Association, 126*, 77-86.

Lee, J., Chang, R. W., Ehrlich-Jones, L., Kwoh, C. K., Nevitt, M., Semanik, P. A., . . . Dunlop, D. D. (2015). Sedentary behavior and physical function: Objective evidence from the Osteoarthritis Initiative. *Arthritis Care & Research, 67*(3), 366-373. doi:10.1002/acr.22432

Lo, G. H., McAlindon, T. E., Hawker, G. A., Driban, J. B., Price, L. L., Song, J., . . . Dunlop, D. D. (2015). Symptom assessment in knee osteoarthritis needs to account for physical activity level. *Arthritis & Rheumatology, 67*(11), 2897-2904. doi:10.1002/art.39271

Luong, M. L., Cleveland, R. J., Nyrop, K. A., & Callahan, L. F. (2012). Social determinants and osteoarthritis outcomes. *Aging Health, 8*(4), 413-437. doi:10.2217/ahe.12.43

Mansournia, M. A., Danaei, G., Forouzanfar, M. H., Mahmoodi, M., Jamali, M., Mansournia, N., & Mohammad, K. (2012). Effect of physical activity on functional performance and knee pain in patients with osteoarthritis: Analysis with marginal structural models. *Epidemiology, 23*(4), 631-640. doi:10.1097/EDE.0b013e31824cc1c3

McAlindon, T. E., Snow, S., Cooper, C., & Dieppe, P. A. (1992). Radiographic patterns of osteoarthritis of the knee joint in the community: The importance of the patellofemoral joint. *Annals of the Rheumatic Diseases, 51*(7), 844-849.

Murphy, L., & Helmick, C. G. (2012). The impact of osteoarthritis in the United States: A population-health perspective. *The American Journal of Nursing, 112*(3 Suppl 1), S13-19. doi:10.1097/01.NAJ.0000412646.80054.21

Nevitt, M. C., Felson, D. T. & Lester, G. (2006). The Osteoarthritis Initiative: Protocol for the cohort study. Retrieved from https://oai.epi-ucsf.org/datarelease/docs/StudyDesignProtocol.pdf

O'Connor, M. I., & Hooten, E. G. (2011). Breakout session: Gender disparities in knee osteoarthritis and TKA. *Clinical Orthopaedics and Related Research, 469*(7), 1883-1885. doi:10.1007/s11999-010-1743-4

Osteoarthritis Initiative Guidelines for Publications using Public Use Datasets. (2006). Retrieved from https://oai.epi-ucsf.org/datarelease/Docs/OAIPubsGuidePublicData.pdf

Physical Activity Scale for the Elderly (PASE). (2010). Retrieved from http://www.framinghamheartstudy.org/share/protocols/bmd1_7s_protocol.pdf

Wesseling, J., Bierma-Zeinstra, S. M., Kloppenburg, M., Meijer, R., & Bijlsma, J. W. (2015). Worsening of pain and function over 5 years in individuals with 'early' OA is related to structural damage: Data from the Osteoarthritis Initiative and CHECK (cohort hip & cohort knee) study. *Annals of the Rheumatic Diseases, 74*(2), 347-353. doi:10.1136/annrheumdis-2013-203829

Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC). (2016). Retrieved on July 22, 2016 from http://www.rheumatology.org/I-Am-A/Rheumatologist/Research/Clinician-Researchers/Western-Ontario-McMaster-Universities-Osteoarthritis-Index-WOMAC

Appendix A – List of Competencies Met in CE

Tier 1 Core Public Health Competencies

Domain #1: Analytic/Assessment Skills
Describes factors affecting the health of a community (e.g., equity, income, education, environment)
Identifies quantitative and qualitative data and information (e.g., vital statistics, electronic health records, transportation patterns, unemployment rates, community input, health equity impact assessments) that can be used for assessing the health of a community
Applies ethical principles in accessing, collecting, analyzing, using, maintaining, and disseminating data and information
Uses information technology in accessing, collecting, analyzing, using, maintaining, and disseminating data and information
Selects valid and reliable data
Selects comparable data (e.g., data being age-adjusted to the same year, data variables across datasets having similar definitions)
Identifies gaps in data
Collects valid and reliable quantitative and qualitative data
Describes public health applications of quantitative and qualitative data
Uses quantitative and qualitative data
Describes how evidence (e.g., data, findings reported in peer-reviewed literature) is used in decision making
Domain #2: Policy Development/Program Planning Skills
Identifies current trends (e.g., health, fiscal, social, political, environmental) affecting the health of a community
Domain #3: Communication Skills
Suggests approaches for disseminating public health data and information (e.g., social media, newspapers, newsletters, journals, town hall meetings, libraries, neighborhood gatherings)
Conveys data and information to professionals and the public using a variety of approaches (e.g., reports, presentations, email, letters)
Communicates information to influence behavior and improve health (e.g., uses social marketing methods, considers behavioral theories such as the Health Belief Model or Stages of Change Model)
Domain #4: Cultural Competency Skills
Describes the concept of diversity as it applies to individuals and populations (e.g., language, culture, values, socioeconomic status, geography, education, race, gender, age, ethnicity, sexual orientation, profession, religious affiliation, mental and physical abilities, historical experiences)
Describes the ways diversity may influence policies, programs, services, and the health of a community
Domain #5: Community Dimensions of Practice Skills
Recognizes relationships that are affecting health in a community (e.g., relationships among health departments, hospitals, community health centers, primary care providers, schools, community-based organizations, and other types of organizations)
Suggests relationships that may be needed to improve health in a community
Supports relationships that improve health in a community
Describes the importance of community-based participatory research
Domain #6:Public Health Sciences Skills
Describes the scientific foundation of the field of public health
Identifies prominent events in the history of public health (e.g., smallpox eradication, development of vaccinations, infectious disease control, safe drinking water, emphasis on hygiene and hand washing, access to health care for people with disabilities)
Describes how public health sciences (e.g., biostatistics, epidemiology, environmental health sciences, health services administration, social and behavioral sciences, and public health informatics) are used in the delivery of the 10 Essential Public Health Services
Retrieves evidence (e.g., research findings, case reports, community surveys) from print and electronic sources (e.g., PubMed, Journal of Public Health Management and Practice, Morbidity and Mortality Weekly Report, The World Health Report) to support decision making
Recognizes limitations of evidence (e.g., validity, reliability, sample size, bias, generalizability)
Describes evidence used in developing, implementing, evaluating, and improving policies, programs, and services
Contributes to the public health evidence base (e.g., participating in Public Health Practice-Based Research Networks, community-based participatory research, and academic health departments; authoring articles; making data available to researchers)

Domain #7: Financial Planning and Management Skills
Motivates colleagues for the purpose of achieving program and organizational goals (e.g., participating in teams, encouraging sharing of ideas, respecting different points of view)
Domain #8: Leadership and Systems Thinking Skills
Describes public health as part of a larger inter-related system of organizations that influence the health of populations at local, national, and global levels
Describes the ways public health, health care, and other organizations can work together or individually to impact the health of a community
Contributes to development of a vision for a healthy community (e.g., emphasis on prevention, health equity for all, excellence and innovation)

Concentration Specific Competencies

Public Health Management
Be capable of applying communication and group dynamic strategies to individual and group interaction
Be capable of applying decision-making processes
Know strategies for promoting teamwork for enhanced efficiency
Have an understanding of effective mentoring methods
A knowledge of ethical principles relative to data collection, usage, and reporting results