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Race and Sex Specific Incidence Rates and Predictors of Total Knee Arthroplasty: Seven Year Cumulative Data from the Osteoarthritis Initiative

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Abstract

Objective—To determine race- and sex-specific rates of total knee arthroplasty (TKA) and document independent effects of demographic factors on TKA incidence in a population with radiographically confirmed osteoarthritis (OA).

Methods—We used data from the Osteoarthritis Initiative (OAI), a US-based, multicenter, longitudinal study of knee OA. We selected subjects with radiographic, symptomatic OA at baseline and determined TKA incidence rates (ratio of TKAs to time at risk for TKA) over eighty-four months of follow-up. We used multivariable Poisson regression to identify independent associations between demographics factors and TKA utilization.

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Collection and assembly of data: Collins, OAI
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Results—During study period there were 223 TKAs among 1,915 subjects for an incidence of 1.9% (95% CI: 1.7%–2.2%). The overall rate was 1.9% (95% CI: 1.5%–2.3%) in men vs. 2.0% (95% CI: 1.7%–2.3%) in women, and 2.2% (95% CI: 1.9%–2.6%) in Whites vs. 1.0% (95% CI: 0.7%–1.5%) in non-Whites. We observed a statistically significant interaction between sex and age (stratified at <65 and ≥65 years at end of follow-up), wherein male sex was associated with decreased risk of TKA for younger participants (RR 0.32) but not for older participants. Non-White race was associated with a decreased risk of TKA for both younger (RR 0.32) and older (RR 0.43) participants.

Conclusion—Our finding that non-Whites were less likely to undergo TKA than Whites in adjusted analyses confirm racial differences observed in population-based studies and underscore the need for interventions to address lower use of TKA among non-Whites with OA.

Keywords

Knee osteoarthritis; total knee arthroplasty; total knee replacement; Osteoarthritis Initiative; race; sex; health disparities

Knee osteoarthritis (OA) is one of the most prevalent chronic medical conditions in the United States.[1] Patients with symptomatic, advanced knee OA often turn to total knee arthroplasty (TKA), an elective surgical procedure, to restore functional ability and reduce pain.[2–4] Over 600,000 TKAs are performed annually in the US to treat OA,[5] and about 80% of TKA recipients experience substantial improvement in symptoms and function.[6,7]

TKA utilization rates have increased dramatically over the past two decades in the United States,[8,9] with much of the increase not fully explained by the growing obesity epidemic and overall aging of the population.[10] Many studies have pointed to lower TKA utilization in Hispanics and African Americans, while the role of sex is less clear, with some studies suggesting a differentially greater uptake of TKA in women and others finding no sex effect.[11–14] However, many of these studies did not restrict analyses to subjects with OA, and therefore were unable to distinguish between the effects of demographic factors on the prevalence of knee OA versus the uptake of TKA among those with knee OA.[13–16] Studies that did focus on patients with OA often used self-report or administrative data to identify OA status. These studies did not have a measure of disease severity and were unable to adjust for potential differences in disease severity among demographic groups.[12,17–21]

The Osteoarthritis Initiative (OAI) has previously been used to determine a variety of clinical features associated with knee OA, including progression to arthroplasty.[11,22,23] However, previous studies have not examined in detail age-, sex- and race-stratified incidence and predictors of arthroplasty. In this analysis, we seek to estimate sex- and race-stratified TKA incidence rates over eighty-four months of follow-up and document the independent effect of demographic and clinical factors on TKA incidence in a population with radiographically confirmed knee OA. The comprehensive OAI database will allow us to adjust for baseline OA severity and to incorporate changes in disease severity over time.

Patients and Methods

Sample

We selected data from the OAI, a US multicenter, longitudinal, prospective observational study of knee OA that enrolled men and women ages 45–79 between 2004 and 2006. Subjects were recruited at four clinical centers in the United States: (1) Ohio State University, (2) University of Maryland/Johns Hopkins University joint center, (3) University of Pittsburgh, and (4) Memorial Hospital of Rhode Island. The OAI enrolled subjects with, or at high risk for, knee OA. Exclusion criteria included inflammatory arthritis, bilateral total joint replacement or end-stage OA in both knees, unlikely contraindication or inability to undergo MRI, and use of ambulatory aids other than a single cane for more than 50% of the time. The study protocol was approved by Institutional Review Boards at all participating institutions.[24] Subjects were assessed annually; as of January 2015, clinical data were available for the entire cohort through the 84 month visit and image assessment data, including central reader assessment of standardized fixed-flexion knee x-rays, were available through the 48 month visit. De-identified data and additional study details are publicly available online at https://oai.epi-ucsf.org, and the study is registered on ClinicalTrials.gov under identifier NCT00080171.

We selected subjects from the OAI with radiographic, symptomatic knee OA at baseline, defined by a Kellgren-Lawrence (KL) grade of 2–4 based on the central reading of a standardized fixed-flexion radiograph and a Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain subscale score pertaining to that knee of greater than zero.[25–27] For subjects with two knees with radiographic, symptomatic OA, we selected the knee with the highest KL grade at baseline. If both knees were of the same KL grade, we selected the knee with the highest baseline WOMAC Pain, and if those were identical, we selected one at random. We excluded all subjects in the healthy control subcohort.

Primary outcome

Our primary outcome was total knee arthroplasty (TKA) adjudicated by the OAI team. Time at risk was defined from time of enrollment to time of TKA or to the last available visit date for those without TKA. We determined the TKA incidence rate as the ratio of the number of TKAs in a specific subgroup over the associated time at risk for TKA.

Factors associated with TKA

We examined the impact of age, sex, race, and education on the incidence of TKA. Age was stratified into <65 and >65 years at the 84 month clinic visit date in order to group together subjects becoming eligible at age 65 for Medicare over the course of follow-up. Race was classified as White vs. non-White, and education as high school or less vs. some college or more.

Statistical methods

Primary Analysis—We computed the overall incidence rate (IR) of TKA per person-year with 95% confidence intervals using Poisson regression. In addition to the overall IR, we present unadjusted stratified rates by baseline age, sex, race, and education. In order to evaluate the independent contribution of each factor to TKA incidence, we used multivariable Poisson regression. In multivariable models we adjusted evaluated the effect of our covariates of interest: sex, race, and education, adjusting for baseline KL grade, baseline WOMAC Pain, baseline body mass index (BMI), and the number of baseline comorbidities (measured by the Charlson index and grouped into scores of 0, 1, and 2+). We used interaction terms in our multivariable models to identify subgroups with differential rates of TKA: we hypothesized that the association between TKA and sex may depend on age and race, and that the association between TKA and race may depend on age. Significance was set at $p<0.05$ for main effects.

Secondary Analysis—As a secondary analysis, we conducted a time to event analysis. In initial analyses we used Kaplan-Meier survival curves to visualize time to TKA by race, using the log-rank test to evaluate differences among curves. We used a multivariable Cox proportional hazards regression model to evaluate the effect of demographic and clinical factors on time to TKA, adjusting for baseline KL grade, baseline WOMAC Pain, baseline BMI, and the number of baseline comorbidities. We assessed the proportional hazards assumption graphically and with time by covariate interaction effects. We first included KL grade at baseline as an independent variable and then, in additional analysis, included KL grade as a time-varying covariate. Since knees can progress in KL grade over time, this allowed us to distinguish periods of time with different KL grades where the hazard of TKA may be different.

At the time of analysis, KL grade data were only available through the 48 month time point. In order to include time-varying KL grade we restricted our analysis to the baseline through 48 month data. Subjects undergoing TKA prior to 48 months were counted as TKAs (with time up until TKA counted as time at risk) while subjects not undergoing TKA or undergoing TKA after 48 months were censored at the last study visit if prior to 48 months or at 48 months.

Sensitivity Analyses—We conducted a number of sensitivity analyses to investigate the robustness of our conclusions. First, to address the concern that most TKAs are performed in persons with more advanced OA, we re-ran the analysis including only knees with advanced radiographic, symptomatic OA, defined as KL grade 3 or 4 at baseline with WOMAC Pain greater than zero.[28,29] In our primary analysis we required that TKAs be adjudicated by the OAI team; that is confirmed by OAI study staff using medical records or X-ray. In a second sensitivity analysis we also considered knees as having TKA if the subject self-reported TKA, if TKA was awaiting adjudication, or if the knee received unicompartamental knee arthroplasty (UKA).To address the concern that all non-Whites were grouped together, and that this group may be heterogeneous, we ran a third sensitivity analysis including only White and African American participants. As a fourth sensitivity analysis, in order to use all available data we included all knees meeting inclusion criteria of radiographic, symptomatic knee OA at baseline. Subjects could contribute 0, 1, or 2 knees to this analytic sample. In this analysis we used Poisson regression with repeated measures to account for multiple knees per person.

We conducted a final sensitivity analysis to examine the impact of subject dropout on TKA incidence rates. We used multiple imputation (MI) to impute TKA for those subjects dropping out of the study.[30,31] First, we used logistic regression to compute each subject's predicted probability p of TKA using the covariates deemed important in the primary analysis and then adjusted p based on time dropout: e.g., a subject completing 4 out of 7 years of follow-up TKA-free would have 3/7 * p probability of TKA in years 4–7. We imputed TKAs in two ways: (1) for each subject dropping out, we used the subject's adjusted predicted probability p to assign TKA status and (2) we increased p assuming that subjects dropping out had a 15% higher probability of TKA than assigned by the logistic regression model. To more accurately reflect the uncertainty in missing values we created 25 imputed datasets and then used the MIANALYZE procedure in SAS to combine the results across the 25 imputations.

Software

Data analyses were performed using SAS 9.4 (SAS Institute, Inc., Cary, NC).

Results

Sample

Among the 4,796 participants in the OAI, 1,915 participants had at least one knee meeting inclusion criteria. Of these, 1,200 participants had one eligible knee and 715 participants had two eligible knees. For participants with two eligible knees, we selected one as described above for a final analytic sample of 1,915. Thirty-five percent of subjects were under 65 years of age at 84 months follow-up, 41% were male and 26% were non-Whites. 970 (51%) knees were KL 2, 676 (35%) knees were KL 3, and 269 knees (14%) were KL 4. Eighty-one percent of subjects had at least some college education (Table 1).

Primary Analysis

Overall incidence rate of TKA—There were 223 TKAs over 11,645 person years, for an overall annual incidence rate of 1.9% (95% confidence interval [CI]: 1.7%–2.2%). Among those who had TKA, 8% had surgery prior to the 12 month visit, 12% between 12 and 24 months, 19% between 24 and 36 months, 16% between 36 and 48 months, 17% between 48 and 60 months, 16% between 60 and 72 months, and 13% between 72 and 84 months. Of those not undergoing TKA, 342 (20%) discontinued the study prior to the 84 month visit.

Race- and sex-specific incidence rates of TKA—The annual incidence rate of TKA among Whites was estimated at 2.2% (95% CI: 1.9%–2.6%) compared to 1.0% (95% CI: 0.7%–1.5%) in non-Whites. The annual incidence rate of TKA among those who were younger than 65 at follow-up was estimated at 1.3% (95% CI: 1.0%–1.8%) compared to 2.2% (95% CI: 1.9%–2.6%) among older persons. In race–sex subgroup analysis, White females had the highest incidence rate of TKA at 2.3% (95% CI: 1.9%–2.8%) while non-White males had the lowest observed rate at 0.9% (95% CI: 0.4%–1.7%). Race–age subgroup analysis identified older whites as having an annual incidence rate of 2.6% (95% CI: 2.2%–3.0%), higher than any of the three other groups (Table 2). Finally, in age–sex subgroup analysis, younger males had the lowest incidence rate at 1.1% (95% CI: 0.7%–1.7%).

Multivariable models—In adjusted analysis we found a statistically significant interaction between age, sex, and TKA incidence (p=0.025). For this reason, we present results stratified by age. The other subgroup comparisons (race–age, race–sex, and race–age–sex) were not statistically significant, meaning that the association between TKA and race did not depend on age or sex. For those younger than 65 at follow-up, lower incidence of TKA was significantly associated with non-White race and male sex: non-Whites had 0.32 times the rate of TKA compared to Whites, and males had 0.32 times the rate of TKA compared to females (Table 3A). For those older than 65 at follow-up, lower incidence of TKA was significantly associated with non-White race, but not with sex: non-Whites had 0.43 times the rate of TKA compared to Whites, while males and females were similarly likely to undergo TKA (Table 3A).

Secondary Analysis

Time to TKA—The unadjusted comparison of time to TKA by race using Kaplan-Meier survival curves demonstrated a statistically significant difference, with non-Whites less likely to undergo TKA (p<0.001, Figure 1). In Cox regression, we again observed the interaction between TKA, age and sex (p=0.079) and therefore present age-stratified results. This interaction can be visualized in the Kaplan-Meier survival curves for the unadjusted comparison of time to TKA by KL and sex, stratified by age (Figure 2). For participants younger than 65 at follow-up, within each KL grade the figure demonstrates a marked difference in the survival curves for men and women, with women more likely to undergo TKA. For participants older than 65 at follow-up, within each KL grade the survival curves for men and women are very close together, indicating that men and women are equally likely to undergo TKA.

For the younger age group, multivariable Cox regression adjusting for time-varying KL grade demonstrated that male sex was significantly associated with decreased hazard of TKA in the adjusted model (HR=0.41). The hazard ratio comparing rates of TKA for non-Whites vs. Whites was 0.27, but did not reach statistical significance (p=0.093). For the older age group, race (non-White vs. White HR=0.17) was significantly associated with hazard of TKA, while sex (p=0.626) and education (p=0.989) were not significant (Table 4).

Sensitivity Analyses

In sensitivity analysis restricted to knees with KL 3–4 at baseline, there were 185 TKAs over 84 months of follow-up, for an overall annual incidence rate of 3.4% (95% CI: 2.9%–3.9%). The associations between TKA and covariates were similar to primary analysis. Adjusted analysis demonstrated a statistically significant interaction between age and sex (p=0.009). (Table 3B).

In addition to the 223 adjudicated TKAs in our cohort, there were 5 self-reported knee replacements, 6 TKAs awaiting adjudication, and 17 UKAs. Including these raised the TKA incidence rate from 1.9% to 2.2% among the entire cohort and from 3.4% to 3.8% in the KL

3–4 subgroup. Including these additional surgeries did not change the observed relationships among variables of interest.

Of the non-Whites in our analytic cohort, 89% were African American. Our results did not change appreciably in sensitivity analysis that restricted the sample to Whites and African Americans only.

Among all 2,630 eligible knees there were 281 TKAs over 16,068 person-years, for an overall annual incidence rate of 1.7% (95% CI: 1.5%–2.0%). In sensitivity analysis restricted to knees with KL 3–4 at baseline, there were 211 TKAs over 84 months of follow-up, for an overall annual incidence rate of 3.2% (95% CI: 2.8%–3.7%). The associations between TKA and covariates were similar to primary analysis (Supplemental Table 1).

Twenty percent (342 subjects) of the cohort not receiving TKA dropped out of the study prior to the 84 month visit. The average follow-up time for these patients was 4 years (SD 1.6). Subjects dropping out of the study had higher mean baseline WOMAC pain than completers (28 (SD 19) vs. 24 (SD 19)) and lower mean baseline WOMAC pain than subjects undergoing TKA (30 (SD 17)). Ten percent of completers were KL grade 4 at baseline, compared to 13% of dropouts and 40% of TKAs. Associations between covariates and TKA were similar to the primary analysis. The relative risk of TKA for non-Whites vs. Whites for those aged less than 65 was 0.33 (95% CI: 0.15, 0.74) using the first imputation method and 0.35 (95% CI: 0.15, 0.78) using the second method.

Discussion

We used a large prospective, longitudinal cohort of persons with diagnosed knee OA to determine the incidence of TKA in specific demographic subgroups. We estimated the unadjusted annual incidence rate of TKA to be 1.9% among subjects with radiographic (KL 2–4), symptomatic OA and 3.4% among subjects with advanced radiographic (KL 3–4), symptomatic OA. Non-Whites had a lower rate of TKA as compared to Whites in analyses adjusted for baseline knee OA radiographic severity, pain, BMI, number of comorbidities, age, sex and education. We also noted a statistically significant interaction between age, sex, and TKA rates, with female sex associated with greater TKA uptake in younger (<65 at end of follow-up) persons but not in older persons. Finally, among younger persons more education (at least some college) was associated with a decreased risk for TKA. To our knowledge this study is the first to evaluate predictors of incident TKA adjusting for radiographic and symptomatic severity and the first to incorporate time-varying KL grade.

A number of population-based studies have suggested differential utilization of TKA by race and by sex, but these studies were not done in persons with confirmed knee OA and therefore could not distinguish between the effects of demographic factors on the prevalence of knee OA versus the uptake of TKA among those with OA.[12–16,18–21] Our study is one a few that have evaluated persons at risk for TKA due to OA. In a large prospective longitudinal study in Ontario, Canada, Hawker and colleagues did not observe a difference by sex or race for total joint arthroplasty.[20] However, 96% of their cohort was White, limiting our ability to compare it to the US-based OAI, which specifically targeted racial and ethnic minorities for enrollment. The Multicenter Osteoarthritis Study (MOST) is another long-term US-based multicenter, longitudinal, prospective observational study of knee OA.[32] In an analysis of MOST subjects with radiographic, symptomatic knee OA, Niu et al. found that 26% of subjects underwent TKA over 60 months of follow-up. We found a cumulative 9.6% (95% CI: 8.2%–11.1%) at 60 months in our OAI cohort. Subjects in MOST were heavier than those in the OAI, more frequently had other musculoskeletal conditions and comorbidities, and had more severe knee symptoms at baseline.[24] Riddle et al. used a subset of the OAI progression subcohort and found a 2-year incidence of TKA of 3.7% (95% CI: 2.6%–5.3%).[11] Due to the small sample size and large number of predictors examined, the authors used the nonparametric random forest method and found that females and subjects with a high school education or less were more likely to undergo TKA, while African Americans were less likely to undergo TKA. Riddle and colleagues conducted their study at an earlier time in the evolution of the OAI, and therefore less data were available. Specifically, at the time of the analysis a subset of the progression subcohort (778 out of 1389 persons) had two year follow-up data available for public use and was included in the analysis. As of January 2015, follow-up data are available through 84 months, and our sample was comprised of all knees with pain and radiographic OA at baseline according to the central reading of a fixed-flexion radiograph. We found a cumulative incidence of 2.4% (95% CI: 1.7%–3.1%) at 24 months. Differences in cumulative incidences may be due to temporal trends, or due to the fact that we used slightly different inclusion criteria.

Across all analyses, we found that non-Whites were significantly less likely to undergo TKA as compared to Whites, controlling for important confounders such as disease severity, education, and pain. This difference has previously been suggested by population-based cohort studies that could not restrict the analysis to persons truly at risk by virtue of having OA, and was also noted in Riddle and colleagues' OAI-based investigation of predictors of TKA over a two year period.[11] Our work adds to these prior studies by using a sample of persons affected by OA and also by extending follow up to seven years, permitting a more extensive picture of TKA use. An additional goal of this analysis was to compute incidence rates in the population truly at risk (those with OA), which are presented here for the first time. We found that female sex was associated with an increased risk for TKA, but only for the younger (<65 at follow-up) age group. A possible explanation for this finding is that surgeons may be more reticent to perform surgery on younger men, who may be at greater risk of eventually requiring revision surgery.[33] Finally less educational attainment was associated with an increased risk of TKA, again only for the younger age group. Less education may be a proxy for having a manual labor job. Heavy physical work or manual labor has been shown to be associated with increased risk of developing knee OA.[34–37] Younger persons with lower levels of education may therefore both be at greater risk of knee OA and more inclined to opt for TKA in order to return to work. This proposition warrants further investigation, since details regarding occupation are not well captured by OAI demographic information.

Numerous previous studies have attempted to understand this racial disparity in TKA utilization.[38,39] African American patients appear to have lower expectations of the benefit of TKA and higher perception of risks, which is reflected in a reduced willingness to consider surgery.[40–44] Ibrahim et al. found that African Americans were less familiar with joint replacement compared to whites, and in particular were less likely to have friends or family who had undergone joint replacement.[43,44] African American patients in the Johnston County Osteoarthritis Project, both with and without symptomatic OA, were less likely than Whites to consider joint arthroplasty even if recommended by their physician.[45] A randomized controlled trial testing the efficacy of an educational intervention found that the intervention was successful in increasing the willingness of African Americans with knee OA to consider surgery, suggesting that this lack of willingness, or reduced expectations, is modifiable.[46]

Our analysis has several limitations. Over seven years of observation, we observed approximately 300 knee arthroplasties. Because we stratified the analyses by age group, some of our subgroups had very few outcomes (e.g., there were 12 TKAs among 217 non-White participants younger than 65 at end of follow-up). This limited our ability to demonstrate statistical significance with moderate effect sizes. We were also unable to stratify by location, though location was not significant when added to multivariable models. Approximately one-fifth of the cohort not receiving TKA dropped out of the study prior to the 84 month visit; however, Poisson regression takes into account person-time when calculating incidence rates, and participants contributed person-time up until the time of dropout. Further, sensitivity analysis using multiple imputation to gauge the impact of dropouts on incidence of TKA demonstrated this impact to be relatively minor. As of the time of analysis, data for the radiographic progression of OA among the OAI cohort was only available through 48 months; therefore, models with time-varying KL were truncated at the 48 month time point. We did not examine effects of health insurance coverage on TKA use as only a small proportion of the cohort was uninsured. The OAI excluded persons who were unlikely to demonstrate measurable loss of joint space, including persons that had plans to undergo bilateral TKA within three years, end-stage knee OA in both knees, or TKA in one knee and severe joint space narrowing in the contralateral knee. This could bias any estimates of TKA rates downwards as persons with more advanced disease were excluded.[22] However, this should not affect associations found between covariates and TKA, since we adjusted for degree of radiographic severity. Finally, as these are publically available data we could not assess the rate of TKA at these centers among persons not enrolling in the OAI and were unable to assess selection bias.

In this study we examined differences in TKA incidence by age, sex, race, and education. Further, the associations between TKA and sex as well as TKA and education depended on age. Whereas females were more likely to have TKA than males among those under 65, among older patients females and males have similar rates. This finding remains largely unexplained and is an area for future research. Our data will help physicians and their patients discuss and plan for the likely need for TKA. These data also will assist health planners (e.g., in managed care organizations) to anticipate TKA utilization among members with knee OA. Our data confirm racial differences in TKA utilization suggested by population-based estimates in a sample of subjects with confirmed OA and underscore the need for interventions to address the lower use of TKA among non-Whites with OA.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Significance and Innovation

- We determined the incidence rates of total knee arthroplasty (TKA) over seven years of follow-up in a population with radiographically confirmed, symptomatic knee OA. Unlike many population-based studies, we were able to compute a true incidence rate using time at risk for TKA.
- This is the first long-term analysis of TKA utilization that takes radiographic disease severity into consideration
- We found that non-Whites were significantly less likely to undergo TKA as compared to Whites. Female sex and less education were associated with an increased risk of TKA for younger subjects but not for older subjects. The interaction between age and TKA is largely unexplained.

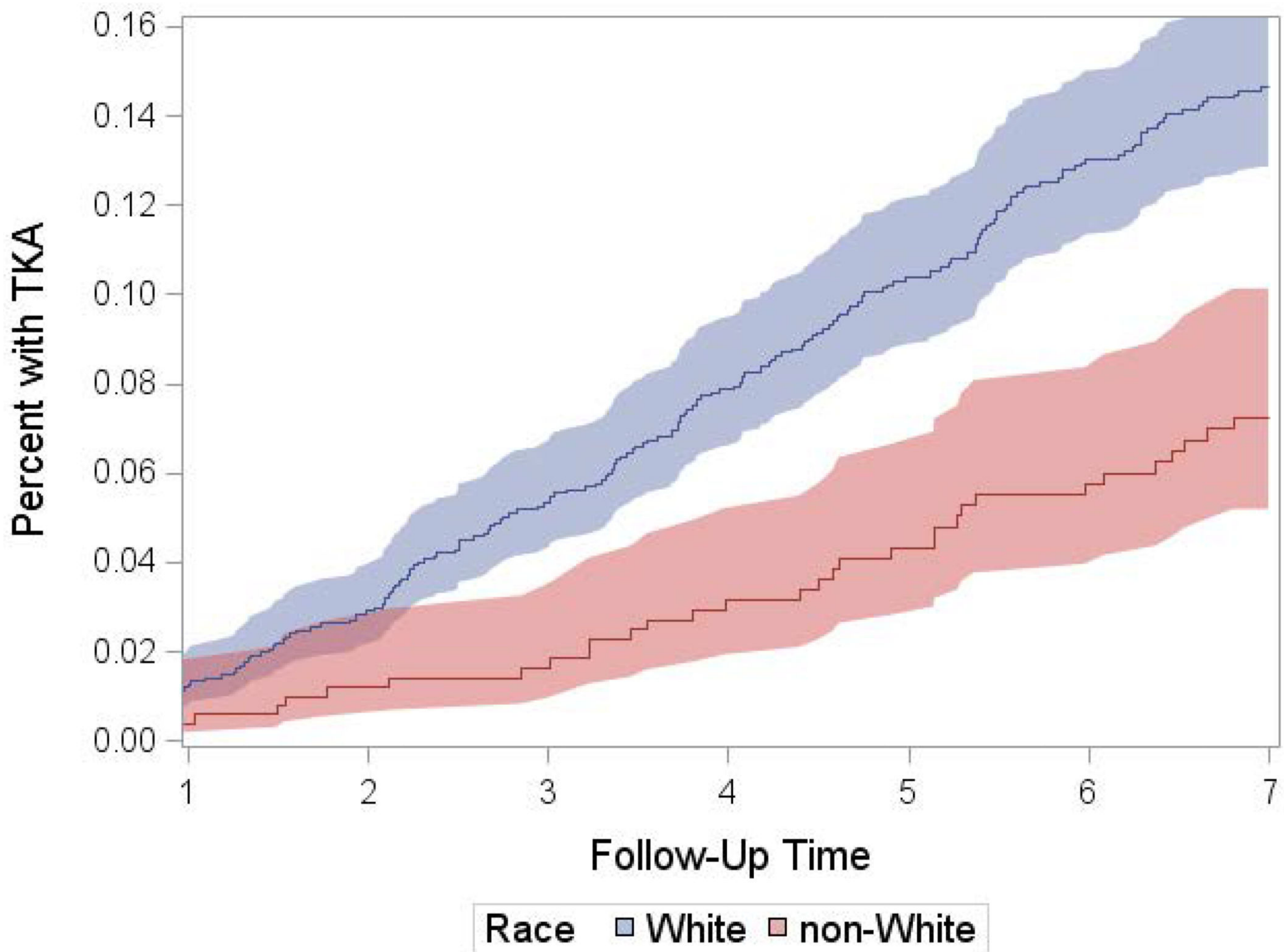

Figure 1. Kaplan-Meier Survival Estimates with 95% Confidence Bands

Follow-up time is along the x-axis and percent with TKA is along the y-axis. Each line represents the probability of undergoing TKA over time, stratified by race (blue line for Whites, red line for non-Whites). The shaded area around each line is the 95% confidence band. The log-rank *p*-value for the difference in the survival curves is <0.001.

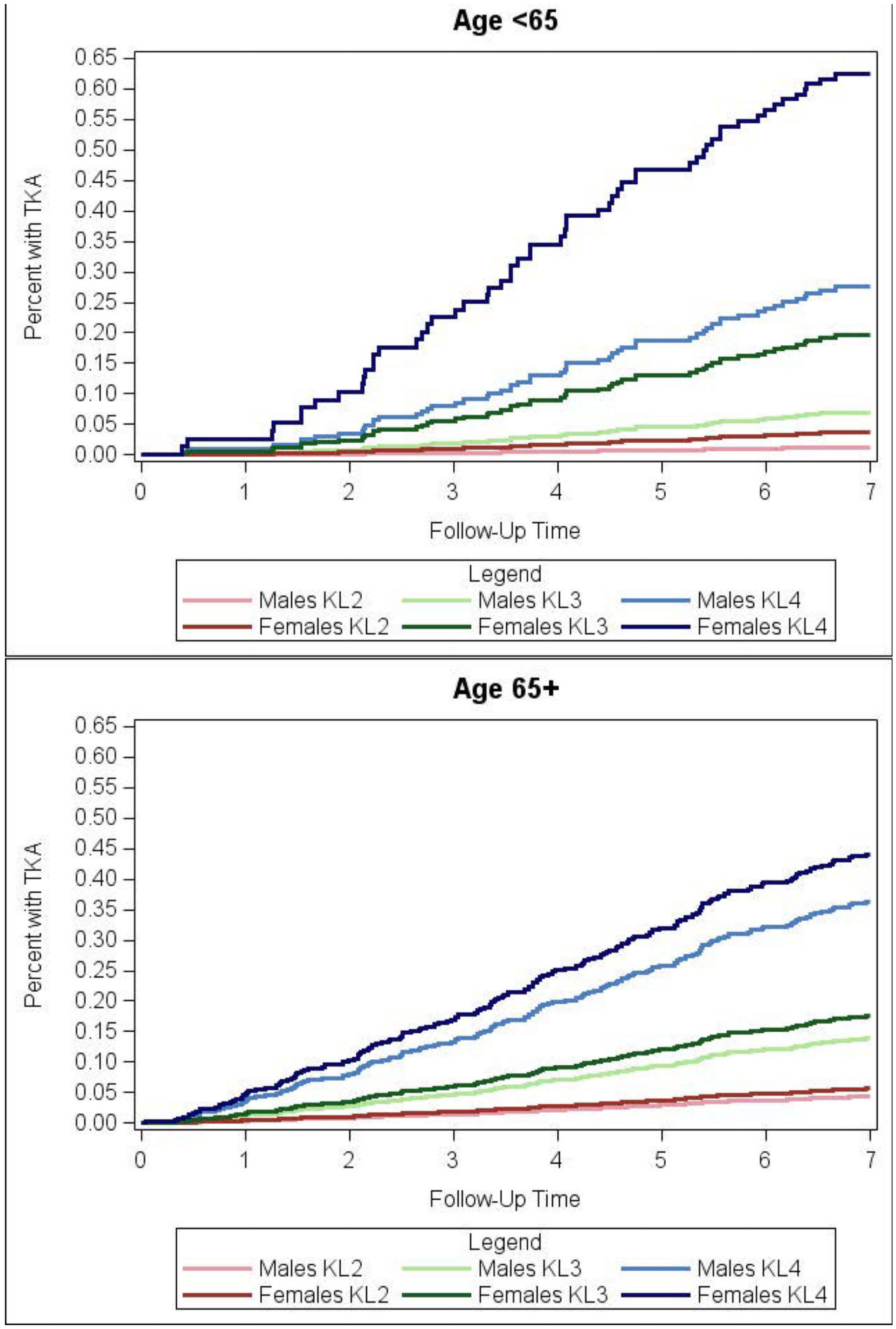

Figure 2. Kaplan-Meier Survival Estimates for Age-Sex Subgroups by Baseline KL. (A) Those less 65 years at 7-years follow-up; (B) Those greater than 65 years at 7-years follow-up

Follow-up time is along the x-axis and percent with TKA is along the y-axis. Each line represents the probability of undergoing TKA over time, stratified by baseline KL (red lines are baseline KL 2, green lines are baseline KL 3, and blue lines are baseline KL 4) and sex (lighter lines are males and darker lines are females). Figure A includes participants in the younger age group (<65 at follow-up) and Figure B includes participants in the older age group (>65 at follow-up). In Figure A, within each baseline KL grade (within each color), the dark line is substantially above the light line, indicating that women are more likely to undergo TKA as compared to men. In Figure B, within each baseline KL grade (within each color), the light and dark lines are much closer together, indicating that there is not a substantial difference in TKA utilization over time between men and women.

Table 1

Description of Sample

Characteristic	Level	Total Persons	Persons with one knee	Persons with two knees	Total knees
Age, end of follow-up period	<65	664 (35%)	417 (35%)	247 (35%)	911 (35%)
	65+	1251 (65%)	783 (65%)	468 (65%)	1719 (65%)
Sex	Male	786 (41%)	546 (46%)	240 (34%)	1026 (39%)
	Female	1129 (59%)	654 (55%)	475 (66%)	1604 (61%)
Race	White	1412 (74%)	951 (79%)	461 (64%)	1873 (71%)
	Non-White	502 (26%)	248 (21%)	254 (36%)	756 (29%)
Education	High school or less	364 (19%)	197 (17%)	167 (23%)	531 (20%)
	Some college or more	1538 (81%)	994 (83%)	544 (77%)	2082 (80%)
Baseline KL grade	2	970 (51%)	--	--	1488 (57%)
	3	676 (35%)	--	--	871 (33%)
	4	269 (14%)	--	--	271 (10%)

* Note: one participant is missing information on sex. 13 participants are missing information on education.

Table 2

Unadjusted Incidence Rates of TKA

Characteristic	Level	n (%)	Number of TKAs	Years at Risk	Incidence Rate (IR)	IR 95% CI
Age, end of follow-up period	<65	664 (35%)	56	4148.9	1.3%	1.0%, 1.8%
	65+	1251 (65%)	167	7496.1	2.2%	1.9%, 2.6%
Sex	Male	786 (41%)	88	4729.0	1.9%	1.5%, 2.3%
	Female	1129 (59%)	135	6916.0	2.0%	1.7%, 2.3%
Race	White	1412 (74%)	191	8551.7	2.2%	1.9%, 2.6%
	Non-White	502 (26%)	32	3086.8	1.0%	0.7%, 1.5%
Sex–Age	Males <65	295 (15%)	21	1848.6	1.1%	0.7%, 1.7%
	Males 65+	491 (26%)	67	2880.4	2.3%	1.8%, 3.0%
	Females <65	369 (19%)	35	2300.2	1.5%	1.1%, 2.1%
	Females 65+	760 (40%)	100	4615.7	2.2%	1.8%, 2.6%
Race–Age	Whites <65	447 (23%)	44	2803.3	1.6%	1.2%, 2.1%
	Whites 65+	965 (50%)	147	5748.4	2.6%	2.2%, 3.0%
	Non-Whites <65	217 (11%)	12	1345.6	0.9%	0.5%, 1.6%
	Non-Whites 65+	285 (15%)	20	1741.2	1.1%	0.7%, 1.8%
Race–Sex	White Males	633 (33%)	80	3797.7	2.1%	1.7%, 2.6%
	White Females	779 (41%)	111	4754.0	2.3%	1.9%, 2.8%

Characteristic	Level	n (%)	Number of TKAs	Years at Risk	Incidence Rate (IR)	IR 95% CI
	Non-White Males	152 (8%)	8	924.9	0.9%	0.4%, 1.7%
	Non-White Females	350 (18%)	24	2161.9	1.1%	0.7%, 1.7%
Race–Sex–Age	White Males <65	228 (12%)	17	1441.7	1.2%	0.7%, 1.9%
	White Males 65+	405 (21%)	63	2356.0	2.7%	2.1%, 3.4%
	White Females <65	219 (11%)	27	1361.6	2.0%	1.4%, 2.9%
	White Females 65+	560 (29%)	84	3392.4	2.5%	2.0%, 3.1%
	Non-White Males <65	67 (4%)	4	407.0	1.0%	0.4%, 2.6%
	Non-White Males 65+	85 (4%)	4	517.9	0.8%	0.3%, 2.1%
	Non-White Females <65	150 (8%)	8	938.6	0.9%	0.4%, 1.7%
	Non-White Females 65+	200 (10%)	16	1223.3	1.3%	0.8%, 2.1%
Baseline KL grade	2	970 (51%)	38	6205.7	0.6%	5.3%, 8.0%
	3	676 (35%)	95	4057.4	2.3%	1.9%, 2.9%
	4	269 (14%)	90	1381.9	6.5%	0.4%, 0.8%
Education	High school or less	364 (19%)	46	2097.7	2.2%	1.6%, 2.9%
	Some college or more	1538 (81%)	175	9472.8	1.8%	1.6%, 2.1%

Table 3

Independent predictors* of incident TKA Stratified by Age at End of Follow-up. Part A: all sample; Part B: Restricted to knees at baseline KL 3 or 4

ALL SAMPLE	<65			65+		
	RR	95% CI	p-value	RR	95% CI	p-value
Race: non-White vs. White	0.32	0.15 , 0.70	0.004	0.43	0.26 , 0.71	<.001
Sex: Male vs. Female	0.32	0.17 , 0.60	<.001	0.79	0.57 , 1.1	0.155
Education: Some college or more vs. high school or less	0.52	0.27 , 1.0	0.052	1.04	0.68 , 1.6	0.866

KL 3–4 only	<65			65+		
	RR	95% CI	p-value	RR	95% CI	p-value
Race: non-White vs. White	0.33	0.13 , 0.79	0.014	0.46	0.26 , 0.79	0.005
Sex: Male vs. Female	0.28	0.14 , 0.55	<.001	0.75	0.53 , 1.1	0.108
Education: Some college or more vs. high school or less	0.48	0.24 , 0.96	0.038	1.07	0.66 , 1.7	0.792

*Results from multivariate Poisson regression, adjusted for baseline KL grade, baseline WOMAC Pain, baseline BMI, and baseline number of comorbidities

Table 4

Hazard Ratios* Stratified by Age at End of Follow-up

	<65			65+		
	HR	**95% CI**	**p-value**	**HR**	**95% CI**	**p-value**
Race: non-White vs. White	0.27	0.06, 1.2	0.093	0.17	0.06, 0.48	<0.001
Sex: Male vs. Female	0.41	0.17, 0.99	0.047	0.89	0.57, 1.4	0.626
Education: Some college or more vs. high school or less	0.54	0.19, 1.5	0.237	1.0	0.56, 1.8	0.989

*Hazard Ratios (HR) from multivariable Cox regression, adjusted for time-varying KL grade, baseline WOMAC Pain, baseline BMI, and baseline number of comorbidities.