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Quantifying Mediators of Racial Disparities in Knee Osteoarthritis Outcome Scores

A Cross-Sectional Analysis

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Background: Studies on symptomatic osteoarthritis suggest that Black patients report worse pain and symptoms compared with White patients with osteoarthritis. In this study, we aimed to quantify the relationship among variables such as overall health and socioeconomic status that may contribute to disparities in patient-reported outcomes.

Methods: A total of 223 patients were enrolled. A mediation analysis was used to evaluate cross-sectional associations between race and the Knee injury and Osteoarthritis Outcome Score (KOOS) questionnaire, which was administered to patients prior to undergoing primary total knee arthroplasty.

Results: Black patients had worse KOOS pain, symptoms, and activities of daily living subscale scores than White patients. In our cohort, Black patients were younger, more likely to be female, and more likely to report lower educational status. We identified age, sex, Charlson Comorbidity Index, and education as partial mediators of racial disparities in KOOS subscale scores. Insurance status, deformity, radiographic (Kellgren-Lawrence) grade, C-reactive protein level, marital status, body mass index, and income did not show mediating effects. We found that, if age and sex were equal in both cohorts, the racial disparity in KOOS symptom scores would be reduced by 20.7% and 9.1%, respectively (95% confidence intervals [CIs], −5.1% to 47% and −5.5% to 26.3%). For KOOS pain scores, age and education level explained 18.9% and 5.1% of the racial disparity (95% CIs, −0.6% to 37% and −10.8% to 22.9%). Finally, for KOOS activities of daily living scores, education level explained 3.2% of the disparity (95% CI, −19.4% to 26.6%).

Conclusions: No single factor in our study completely explained the racial disparity in KOOS scores, but our findings did suggest that several factors can combine to mediate this disparity in outcome scores. Quantification of variables that mediate racial disparity can help to build models for risk adjustment, pinpoint vulnerable populations, and identify primary points of intervention.

Level of Evidence: Prognostic Level III. See Instructions for Authors for a complete description of levels of evidence.

Patients with osteoarthritis (OA) who report a higher level of pain and worse symptoms are at a greater risk for reduced mobility, sleep complications, poorer general health, and less satisfaction with total joint replacement than patients with less symptomatic OA[1-6]. They are also more likely to leave the workforce and experience loss of income[7-9]. Thus, symptomatic OA (high level of pain and poor symptom status) puts the patient at a disadvantage as well as contributes to rising health-care costs.

With a few exceptions[10-12], the majority of studies show that symptomatic OA is more prevalent and more severe in Black American populations compared with White American populations[13-15]. This disparity is evident in the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) and the Knee injury and Osteoarthritis Outcome Score (KOOS) in civilian and veteran populations[16-21], in cross-sectional analyses[14,22], in longitudinal analyses[17,23,24], and for knee OA specifically[8,9,25,26]. Despite 40 years of research describing this racial

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disparity, where to start addressing this problem is not clear. To identify primary points of intervention, we aimed to quantify the relationship among variables that may contribute to disparities in patient-reported outcomes. We build on the findings of previous studies that have identified several variables associated with poor outcome scores, including the overall physical health of the patient, socioeconomic status, sex, age, and marital status, as described below.

Poor patient physical health—high obesity and a greater number of comorbidities—is often associated with worse WOMAC scores, a higher incidence of symptomatic OA, and faster OA disease progression[17,27-29]. Low socioeconomic status, as measured by education level, household income, and insurance status, is associated with OA progression, worse OA patient-reported outcome (PRO) scores, and reports of work limitations due to OA[9,10,17,23,30]. Living with a partner in a healthy relationship, however, is associated with better pain reports in rheumatoid arthritis and following total knee arthroplasty (TKA)[31,32]. Most of the above factors are unequally distributed in White and Black cross-sectional cohorts, with Black populations more likely to experience lower socioeconomic status, worse overall health, and a lack of support systems[8,30,33]. The skewed distribution suggests these factors mediate the racial disparity in symptomatic OA. However, which factor should be prioritized for interventions is unknown. On the basis of these previous studies, we aimed to identify the largest mediators of this racial disparity.

We hypothesized that the association of race with lower outcome scores is mediated by demographic factors (age, sex), socioeconomic status (insurance status, education level, and household income), overall health status (body mass index [BMI], comorbidities as measured by the Charlson Comorbidity Index [CCI][34], and C-reactive protein [CRP] level), and disease progression measurements (Kellgren-Lawrence [KL] score, deformity type). To test this hypothesis, we conducted a mediation analysis of a cross-sectional cohort of patients with knee osteoarthritis in the New Orleans area. Specifically, we used a multiple mediation analysis method described by Yu et al. that incorporates linear and nonlinear modeling to determine whether a combination of factors can explain the racial disparity in KOOS outcomes[35]. This quantification of variables that mediate racial disparity can help build models for risk adjustment, pinpoint vulnerable populations, and identify primary points of intervention.

Materials and Methods

Patient Selection and Measures

This was a prospective cross-sectional sample of adult patients (≥18 years of age) undergoing primary TKA performed by a single surgeon at a university-based, safety-net hospital in New Orleans, Louisiana, from 2015 to 2019. Patients were enrolled in the study during their clinical visit prior to TKA; patient consent was obtained by the primary surgeon. Patients were placed into cohorts on the basis of self-reporting as African American/Black or White (n = 223). Patients who identified as Hispanic or Latino, Asian, American Indian or Alaska Native, Native Hawaiian or Other Pacific Islander, or Other were not included in this specific study. This study was approved by, and conducted under guidance from, the Louisiana State University Health institutional review board.

Patients completed the KOOS questionnaire during the clinical visit prior to TKA. The KOOS consists of 42 items assessing 5 subscales: pain, other symptoms, function in daily living (activities of daily living), function in sport and recreation (sport/rec), and knee-related quality of life (QoL)[36]. Raw KOOS scores are transformed to a 0-to-100 scale, with 0 representing extreme problems and 100 representing no problems. Surveys with incomplete answers (missing ≥2 answers) were not included in final analysis. Patients also completed demographic and health-behavior surveys regarding ethnicity, race, sex, education level, marital status, and income level as shown in Table I. For analysis, annual household income was grouped into 10 categories, with category 1 corresponding to <$10,000 and category 10 corresponding to ≥$150,000. Education was analyzed as 5 categories, as shown in Table I, and marital status was consolidated into 2 categories (living with or without a partner).

Variables obtained from patients' medical charts included age, insurance type (private, Medicare, Medicare Advantage), BMI, CCI, KL grade, overall deformity, and CRP level. KL grade was assessed by a board-certified, fellowship-trained orthopaedic surgeon using anteroposterior standing knee radiographs of patients as part of the routine work-up. Overall deformity was measured as the angle formed between the femoral mechanical axis and the tibial-shaft axis using hip-to-ankle standing radiographs.

Statistical Analysis

Data were analyzed using SAS/STAT version 9.4 (SAS Institute) and R (version 3.6.2, MMA [Multiple Mediation Analysis] package; R Project for Statistical Computing). Analysis of covariance (ANCOVA) was performed to examine the main effect of race on the KOOS subscales.

To identify specific risk factors that may help to explain differences in KOOS scores by race, we performed mediation analyses[35]. Mediation analysis tests a hypothetical path where 1 variable X (risk factor) associates a second variable M (mediator), and, in turn, that variable affects the outcome variable Y. A mediator must satisfy 2 conditions. First, the variable must be significantly correlated with the risk factor (race, in this case). We examined this hypothesis using a chi-square, analysis of variance (ANOVA), or Pearson correlation coefficient test, depending on the variable type. Second, the variable must be significantly correlated with the outcome (KOOS subscore). This second analysis was performed again using a chi-square test, ANOVA, or Pearson correlation coefficient test, depending on the variable type. Variables that are significantly correlated with the outcome but not with the mediator are considered as covariates. To capture candidates that may have even small mediating effects, the significance level for testing these correlations was set at $p < 0.2$. For identifying important mediators, the significance level was set at $p < 0.05$ with adjustment for multiple comparisons using Bonferroni adjustment.

TABLE I Survey Questions

Question	Answer Options
(1) Do you consider yourself to be Hispanic or Latino?	Hispanic or Latino; Not Hispanic or Latino; Don't want to answer
(2) What race do you consider yourself to be?	American Indian or Alaska Native; Asian; Black or African American; Native Hawaiian or Other Pacific Islander; White; Other; Don't want to answer
(3) What is your sex?	Female; Male; Don't want to answer
(4) What is the highest grade of education you have completed and received credit for?	Less than 9th grade (Category 1); 9th-11th grade, includes 12th grade with no diploma (Category 2); High school graduate/general equivalency diploma (GED) or equivalent (Category 3); Some college or Associate of Arts (AA) degree (Category 4); College graduate or above (Category 5); Don't want to answer
(5) What is your current marital status?	Married; Widowed; Divorced; Separated; Single; Living with partner; Don't want to answer
(6) Thinking about your income and the income of everyone who lives in your household and contributes to the household budget, what was the total household income before taxes and deductions in the previous year? Include all sources of income, including non-legal sources.	<$10,000; $10,000-$14,999; $15,000-$19,999; $20,000-$24,999; $25,000-$34,999; $35,000-$49,000; $50,000-$74,999; $75,000-$99,999; $100,000-$149,999; ≥$150,000

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Results

Patient Characteristics and KOOS

A total of 223 patients with end-stage knee OA undergoing TKA were prospectively enrolled in the database (40.3% Black and 59.7% White). Patients who self-identified as a race or ethnicity other than African American/Black or White were not included in this study (Table II). Analysis of the KOOS by

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TABLE II Outcomes Comparison of African American/Black and White Patients

	African American/Black		White		
KOOS Subscale	N	Score*	N	Score*	P Value
Symptoms	88	37.2 (20.9)	131	47.7 (19.1)	0.0002
Pain	86	34.2 (19.5)	129	45.1 (17.4)	<0.0001
Activities of daily living	87	35.8 (19.7)	129	45.9 (19.2)	0.0002
QoL	87	21.4 (18.7)	130	25.2 (18.9)	0.140

*The values are given as the mean and standard deviation.

ANCOVA demonstrated that Black patients with OA were more likely to report worse pain ($p < 0.0001$), symptoms ($p = 0.0002$), and limitations in activities of daily living ($p = 0.0002$) than White patients with OA (Table II). KOOS QoL scores did not differ significantly by race (Table II).

To determine whether variables associated with disease severity, socioeconomic status, and health could explain racial differences in KOOS subscale scores, a mediation analysis was performed (Fig. 1). To be included in a mediation analysis, potential mediators (M) must meet 2 criteria, as previously explained. First, in the case of our analysis, a significant correlation between race and the potential mediator had to be demonstrated. Second, the potential mediator must demonstrate a significant correlation with the outcome (e.g., KOOS symptoms). To check the first criterion, the correlation between race and age, BMI, CCI, CRP, overall deformity, median income, sex, educational attainment, marital status, insurance type, and KL grade was investigated (Table III, p value 1). Age ($p < 0.01$), sex ($p = 0.07$), BMI ($p = 0.03$), CCI ($p = 0.06$), CRP ($p = 0.04$), education level ($p < 0.0001$), and marital status ($p < 0.01$) differed significantly between races in our cohort (Table III, p value 1). Severity of disease (KL grade, deformity) did not differ significantly between races, nor did insurance type (Table III, p value 1). These variables therefore were not considered mediators of an effect of race on the KOOS subscales.

Mediation: KOOS Symptoms

A potential mediator must show a significant correlation with the outcome variable (in this case, the KOOS symptoms subscale). As shown in Table III (p value 2), age ($p = 0.12$), sex ($p = 0.13$), and CCI ($p = 0.14$) were significantly correlated with symptoms such that patients who were younger, female, or had a higher CCI were more likely to report worse symptoms. Patients with an overall more severe deformity were also more likely to report worse symptoms ($p = 0.07$). Because deformity was not correlated with race and therefore did not meet the first criterion to be considered a mediator, deformity was included as a covariate in the final model. Age, CCI, and sex were all included as mediators in the final model for the effect of race on symptoms (Fig. 2-A).

Results of the final model show KOOS symptom scores were mediated by age, sex, and CCI to varying degrees (Fig. 2). The relative direct effect of race on KOOS symptom scores was 76.2%, with age, sex, and CCI mediating at 20.7% (95% CI, −5.1% to 47.0%), 9.1% (−5.5% to 26.3%), and −7% (−26.8% to 10.7%), respectively. We found that KOOS symptom scores increased (improved) with age (Fig. 2-A′), that male patients had higher KOOS symptom scores than female patients (Fig. 2-A″), and that KOOS symptom scores decreased with increasing CCI (Fig. 2-A‴). Together, these results suggest that, if age and sex were equally distributed between African American/Black and White patient groups, the disparity in symptoms would decrease by a combined 29.8%. If CCI was equally distributed, the disparity would increase by 7%.

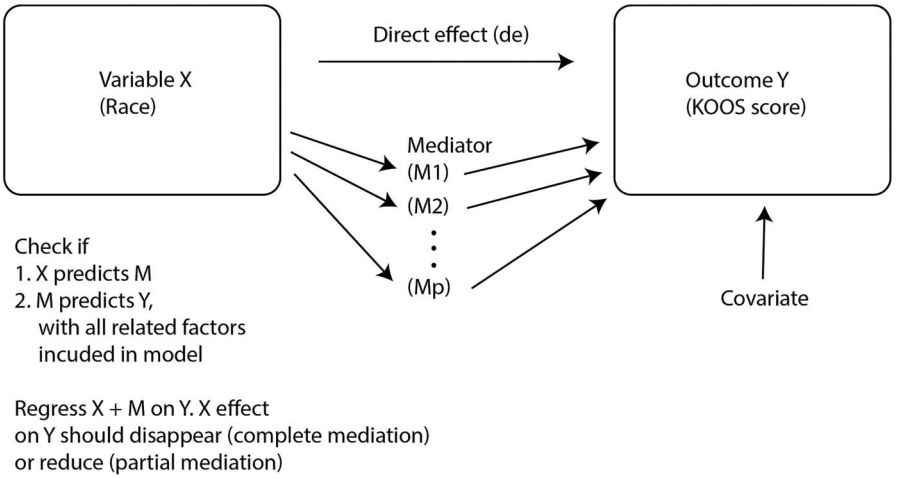

Fig. 1

Schematic of mediation analysis to quantify factors that mediate an interaction between a predictor (race) and an outcome (KOOS subscale). "M1, M2… Mp" denotes variables that act as multiple mediators between race and KOOS score. A covariate is a variable that affects outcome without being affected by the predictor.

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TABLE III Potential Mediators/Confounders and Covariates

Item	N	African American/Black†	White†	P Values for Association with the Row Variable†			
				1: Race	2: Symptoms	3: Pain	4: Activities of Daily Living
Age *(yr)*	223	66.4 (9.1)	70.2 (8.3)	<0.01	0.12*	0.06*	0.45
BMI *(kg/m²)*	222	33.5 (5.9)	31.8 (5.0)	0.03	0.57	0.45	0.24
CCI	223	2.9 (1.4)	3.3 (1.5)	0.06	0.14*	0.04*	0.14*
CRP *(mg/L)*	207	6.6 (8.3)	4.5 (6.0)	0.04	0.62	0.92	0.88
Overall deformity *(deg)*	213	8.4 (4.7)	8.6 (4.6)	0.84	0.07§	0.03§	0.07§
Median income category	144	3	6		0.98	0.96	0.86
Sex *(% [no.])*				0.07	0.13*	0.41	0.57
Male	70	24.7 (22)	36.4 (48)				
Female	151	75.3 (67)	63.6 (84)				
Education level *(% [no.])*				<0.0001	0.51	0.02*	0.06*
Less than 9th grade	4	0 (0)	3.3 (4)				
9th-11th grade	27	28.6 (20)	5.8 (7)				
High school graduate/ GED or equivalent	60	37.1 (26)	28.1 (34)				
Some college or Associate of Arts (AA) degree	46	18.6 (13)	27.3 (33)				
College graduate or above	54	15.7 (11)	35.5 (43)				
Live with partner *(% [no.])*	216	37.2 (32)	58.5 (76)	<0.01	0.36	0.46	0.96
Insurance type *(% [no.])*				0.38	0.24	0.03§	0.13§
Private	89	37.8 (34)	41.4 (55)				
Medicare	54	21.1 (19)	26.3 (35)				
Medicare Advantage	80	41.1 (37)	32.3 (43)				
KL grade *(% [no.])*				0.58	0.52	0.98	0.70
1	0	0 (0)	0 (0)				
2	2	0 (0)	1.6 (2)				
3	24	12.9 (11)	10.1 (13)				
4	188	87.1 (74)	88.4 (114)				

†P value 1 shows the p value from testing the association between race and the row variables. P values 2, 3, and 4 are the p values of a Type-III test for the row variable in the full model for predicting KOOS symptoms (2), pain (3), or activities of daily living (4). *The variable was chosen as a mediator/confounder. §The variable was chosen as a covariate. ‡The values for age, BMI, CCI, CRP, and overall deformity are given as the mean and standard deviation.

Mediation: KOOS Pain

We next examined the relationship of race-correlated variables (age, sex, education level, marital status, BMI, CCI, and CRP level) and the KOOS pain subscale. Age (p = 0.06), education (p = 0.02), and CCI (p = 0.04) showed a correlation with KOOS pain and were therefore identified as potential mediators of race on pain. Deformity (p = 0.03) and insurance status (p = 0.03) were included as covariates because they met our significance level in correlation with KOOS pain but not with race (Table III, p values 1 and 3). The final mediation model showed that race had an 85.4% relative direct effect on KOOS pain scores, while age (18.9%; 95% CI ,−0.6% to 37.0%), education (5.1%; 95% CI, −10.8% to 22.9%), and CCI (−11.5%; 95% CI, −27.8% to 6.9%) showed varying levels of mediation (Fig. 2-B). Similar to KOOS symptoms, as age increased, KOOS pain scores increased (Fig. 2-B′). A higher education level was correlated with better pain outcome scores (Fig. 2-B″), and as CCI increased, pain scores decreased (Fig. 2-B‴). Therefore, if age and education were equally distributed among African American/Black and White patient groups, the disparity in KOOS pain would decrease by 24%. If CCI were equally distributed, the disparity would increase by 11.5%.

Mediation: KOOS Activities of Daily Living

As with the other 2 KOOS subscales, we examined the relationship of sex, education level, marital status, BMI, age, CCI,

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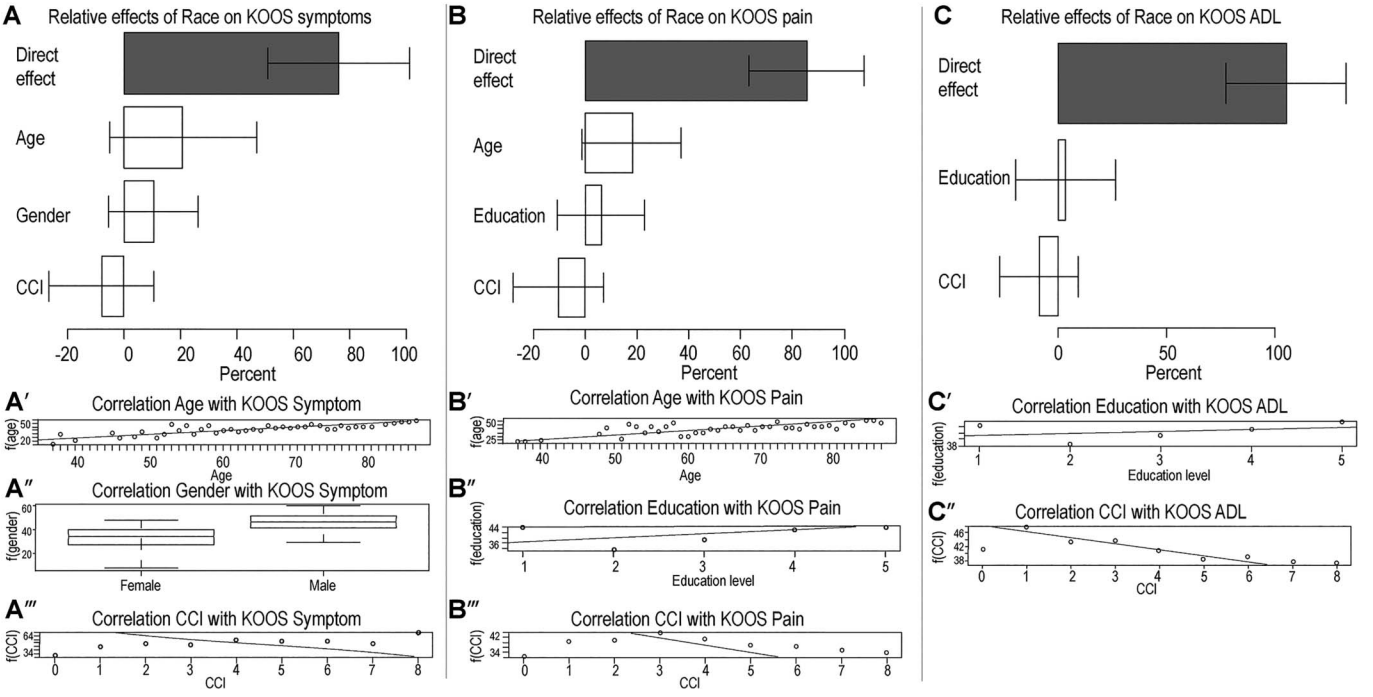

Fig. 2

Mediation analysis results for KOOS symptoms, pain, and activities of daily living (ADL) subscales. **Fig. 2-A** KOOS symptom scores were mediated by age, sex, and CCI to varying degrees. The correlation of age (**Fig. 2-A′**), sex (**Fig. 2-A″**), and CCI (**Fig. 2-A‴**) with KOOS symptoms is shown. **Fig. 2-B** KOOS pain scores were mediated by age, education level, and CCI to varying degrees. The correlation of age (**Fig. 2-B′**), education (**Fig. 2-B″**), and CCI (**Fig. 2-B‴**) with KOOS pain is shown. **Fig. 2-C** KOOS activities of daily living (ADL) scores were mediated by education level and CCI to varying degrees. The correlation of education (**Fig. 2-C′**) and CCI (**Fig. 2-C″**) with KOOS ADL is shown. Relative effects of each variable are listed as the percentage of the total effect. The I bars in the upper panels represent the 95% confidence interval. The y axes in the lower panels indicate KOOS scores. Age values are given in years. The 5 values for "Education Level" correspond to the categories shown for education level in Table I.

and CRP level with the KOOS activities of daily living subscale score. This analysis identified education (p = 0.06) and CCI (p = 0.14) as potential mediators of KOOS activities of daily living (Table III, p value 4). Deformity (p = 0.07) and insurance status (p = 0.13) were included as covariates, as they met our significance level in correlation with KOOS activities of daily living but not with race. Mediation analysis showed that education level accounted for 3.2% (95% CI, −19.4% to 26.6%) of the relative effect of race on KOOS activities of daily living scores (Fig. 2-C), where education level was negatively correlated with KOOS activities of daily living (Fig. 2-C′). CCI again had a negative relative effect (−10.3%, 95% CI, −26.6% to 9.7%) (Fig. 2-C). Patients with a higher CCI had lower KOOS activities of daily living scores (Fig. 2-C″).

Discussion

In this study, we used mediation analysis to identify primary drivers of the racial disparity in KOOS scores. We found that age contributed the most to the racial disparity in our cohort. Sex and educational status (a proxy for socioeconomic status) explained a smaller percentage of the disparities. We also found that CCI played a mediating role. However, in our cohort, White patients were more likely to have a higher CCI than Black patients. This finding is counter to results reported in previous studies[25,37,38]. Our analysis suggests that the racial disparity would, in fact, increase if CCI were equally distributed between African American/Black and White patient groups. Of note, factors that did not show a mediating effect included insurance status, deformity, KL grade, CRP value, marital status, BMI, and income.

The racial disparity in patient-reported knee pain and stiffness has been well documented[13]. The current study helps refine a model for how race is associated with outcome scores. For example, a well-designed study performed by Allen et al. showed, with multiple regression, that race is associated with lower outcome scores for patients with a high number of comorbidities[22]. Mediation analysis refines this model to suggest that these variables are connected in a linear path. Our findings suggest that race is correlated with CCI, which is correlated with outcome scores. This updated model is useful in that it identifies that race, comorbidities, and outcomes are all linked, and that changing the first variable (patient race) will have an effect on the second, the prevalence of comorbidities, which will have an effect on the third, outcome scores. One might hypothesize, based on a moderation analysis like multiple regression, that interventions to reduce comorbidities in

the Black population will reduce the racial disparity in pain scores; however, mediation analysis helps predict by how much this targeted intervention could reduce the disparity.

Among the factors that we analyzed, age was the greatest mediator of the racial disparity in pain and symptoms. In our cohort, Black patients were more likely to be younger than White patients, and pain decreased as age increased. In parallel, there is a greater national trend for Black Americans undergoing TKA to be younger[22,25,39-41]. These data suggest that interventions with a focus on age would show a greater reduction in the racial disparity than interventions focused on other factors (e.g., socioeconomic divides). In the same vein, research that focuses on what drives pain in younger patients has the potential to greatly reduce observed disparities.

The variables that we included in our model were able to explain 30% of the racial disparity, leaving 70% of the disparity explained by unknown factors. This fact points to 2 ideas: (1) racial disparities arise because of complex variables, many of which cannot be explained by socioeconomic status or other patient-level factors[42], and (2) there are notable limitations in the variables we included in our study.

In terms of limitations of the study, we were not able to capture patient variables that have been connected to pain in other studies. For instance, depressive symptoms are often associated with higher pain levels reported by patients with OA, and we were unable to evaluate this variable in our cohort[17,22,43]. We were also unable to evaluate the influence of biological factors, such as vitamin-D levels or the presence of osteophytes, which has also been suggested to influence OA pain and often is unequally distributed across racial cohorts[44,45]. Social determinants of health (e.g., where a patient lives and works, access to transportation, nutrition, and access to health care) and factors related to systemic bias within a hospital system have been identified as cofactors of racial disparities in other diseases[46-48] but were not evaluated in this study. Both are potentially large mediators of the disparities in KOOS scores. Future mediation analysis could quantify the extent to which these additional factors contribute.

Our analysis focused on a relatively small sample of patients treated by a single surgeon, and our findings may not be generalizable to a national patient population. Previous studies suggest that each patient population has unique attributes and faces unique challenges. In some studies, the observed racial disparity in reported pain was eliminated or reduced when controlling for depressive symptoms, BMI, education, and socioeconomic status[8,11,23,45]. However, other studies have reported a persistent disparity in pain between Black and White patients even after controlling for these same risk factors[37-41]. This discrepancy in the literature highlights differences in each cohort analyzed. Mediation analysis would help quantify the relationships between these cofactors and the racial disparity for each unique population.

Without proper intervention for patients with OA with a high level of pain, we risk continued rising health-care costs and loss to our workforces. For decades, studies have shown that symptomatic OA is more prevalent in the population of Black Americans[13-15]. Therefore, interventions to reduce pain and osteoarthritis symptoms specifically in Black populations would have a greater impact on reducing health-care costs. Where to start targeting interventions is not well defined. This study highlights the complexity of factors that mediate pain and symptoms in knee OA and provides evidence that mediation analysis can pinpoint primary areas for intervention. ■

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