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Features of Knee and Multi-joint Osteoarthritis by Sex and Race/Ethnicity: A Preliminary Analysis in the Johnston County Health Study

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Abstract

Objective: To evaluate knee and multi-joint osteoarthritis (KOA and MJOA) and compare features by sex and race/ethnicity in a population-based cohort.

Methods: Participants (n=544) enrolled in the Johnston County Health Study (JoCoHS) as of January 2023 were categorized by radiographic and symptomatic KOA and MJOA phenotypes and frequencies were compared by sex and race/ethnicity. Symptoms were assessed according to the Knee and Osteoarthritis Outcomes Scores (KOOS) and pain, aching, stiffness scores (PAS) at various joints. Models produced adjusted (for age, BMI, education) estimates (odds ratios [OR] or mean ratios [MR] and 95% confidence intervals [CI]).

Results: Men had twice the odds of MJOA-6 (at least three lower extremity joints); there were no significant differences in MJOA phenotypes by race. Women had 50% higher odds of KOA along with various features of KOA. Women reported significantly worse KOOS symptoms scores (MR = 1.25). Black participants had higher odds of more severe KOA (OR=1.47), subchondral sclerosis (OR=2.06) and medial tibial osteophytes (OR=1.50). Black participants reported worse KOOS symptoms than White participants (MR= 1.18). Although not statistically significant, Hispanics (versus non-Hispanics) appeared to have lower odds of radiographic changes but reported worse symptoms.

Conclusion: Preliminary findings in the diverse JoCoHS cohort suggest more lower extremity predominant MJOA in men compared to women. Women and Black participants had more KOA features and more severe symptoms. Hispanic participants appear to have higher pain

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None

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and symptoms scores despite having fewer structural changes. Studies in diverse populations are needed to understand the burden of OA.

Key Indexing Terms:

Osteoarthritis; Knee; Arthritis; Sex; Pain; Knee Joint

Background

Osteoarthritis (OA) is a leading cause of disability in the aging population that places notable burden on both the patient and the healthcare system [1,2]. The global prevalence of knee OA alone is estimated to be greater than 20% in individuals over the age of 40 [3]. Compounding the pervasiveness of this disease, the healthcare costs of managing OA introduce considerable socioeconomic burden. In fact, when assessed in 2013 and 2017, OA was consistently the second most expensive medical condition in the U.S., accounting for greater than 5% of hospital costs and second only to sepsis [4,5]. The individual, and by extension socioeconomic, burden is expected to continue increasing in the foreseeable future due to an aging population and a persisting obesity epidemic [6,7]. Though the widespread prevalence of OA is appreciated by many, it is postulated that we are actually underestimating the true burden of disease [8,9].

Considerable heterogeneity in the disease, from its pathological mechanisms to its presentation, makes epidemiological research in OA challenging [10,11]. The extent of disease elements such as mechanical/anatomic abnormalities, physiologic changes, and molecular events leading to onset or progression of OA introduce one challenge. The role of different imaging modalities in the definition of OA present another challenge, especially in those without clinical symptoms of disease activity. To our interest, another challenge includes the variation in symptom presentation in patients with OA. For example, the knee is the most common site of diagnosed arthritis [10,12,13]. It has been shown that clinical signs and symptoms of knee osteoarthritis (KOA) vary in patients with radiographic evidence of disease and poorly correlate with the presence of radiographic features [14–16], prompting investigation into other predictors of pain and disability reporting in patients with OA. Differences between race, ethnicity, and sex are postulated to play a role in symptom presentation. There are robust data revealing that Black patients with KOA experience greater pain and disability as compared to White patients [17–21]. However, such comparisons in radiographic features, pain, and function in other ethnic groups, specifically Hispanic patients, are not well described. We aim to further describe these differences between race/ethnicity and sex.

Additionally, OA often presents in a polyarticular rather than a monoarticular distribution. Although this multi-joint presentation is prevalent in the population, it has suffered from lack of clarity in the literature. Variations in nomenclature such as “generalized osteoarthritis,” “polyarticular osteoarthritis,” “multiple joint osteoarthritis,” and others have been used, though no standardized definition has been widely adopted [22]. A more specific and understandable term, multi-joint osteoarthritis (MJOA), accompanied by the affected joints has been proposed in the recent past [22]. Although there has been a trend towards

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the term, “MJOA,” standardized definitions are lacking. A 2019 systematic review analyzed the literature on MJOA and generated 10 clear definitions of different phenotypes based on joint sites and number of joints/sites involved [23]. Utilizing these definitions, we also aim to determine the association of these generated MJOA definitions between race/ethnicity and sex.

Participants and Methods

This cross-sectional study used data (collected as of January 2023) from the baseline visit of the Johnston County Health Study (JoCoHS), an actively enrolling population-based study in Johnston County, North Carolina with a focus on OA and other common comorbid conditions [24]. JoCoHS recruits White, Black, and Hispanic men and women ages 35 to 70 years old living in the county, who must speak fluent English or Spanish. Members of JoCoHS were invited to an outpatient clinic visit for data collection including demographic information, anthropometric measurements, functional assessments, and radiographs of major joints (Figure 1).

Demographics and Covariables

All participants are asked to self-report their sex at birth as well as their current gender identity; sex at birth (male or female) was used in this analysis. As part of the inclusion criteria for the study, participants self-report their ethnicity (“Are you Hispanic, Latino/a, or of Spanish origin?”) followed by their race (All that apply: White, Black or African American, American Indian or Alaskan Native, Asian, Pacific Islander, Other). The inclusion criteria selected any participant who identified as Hispanic along with non-Hispanic individuals that identified as Black or African American, and/or White if identified as such in their selections. Non-Hispanic individuals who did not identify as White or Black/African American (e.g. American Indians, Alaskan Natives, Asians, Pacific Islanders, Other) were not included in the study. Age was calculated from date of birth in years at enrollment. Weight and standing height were measured at clinic visit to the nearest half centimeter and nearest pound, respectively, and body mass index (BMI) was computed as weight (kilograms, kg) divided by height (meters, m^2). Highest level of education was self-reported as less than high school, high school diploma, some college, college degree, some graduate school, or graduate degree and dichotomized for this analysis as less than a college degree education or a college degree education or higher. Knee injury was self-reported for the right and left knee as having ever injured a knee joint badly enough that it limited ability to walk for at least two days.

Symptom and Radiographic Assessment

Symptoms of pain, aching, and stiffness (PAS) were assessed by asking participants, “On most days of any one month in the last 12 months did you have pain, aching, or stiffness in any of the following joints? Please rate as none, mild, moderate, or severe.” Radiographs were made following defined protocols of the anteroposterior (AP) supine hips, posteroanterior semi-flexed knees, posteroanterior hands, lateral and mortise weight-bearing ankles, and AP and lateral weight-bearing feet. These standardized radiographs were assessed for radiographic OA (rOA) using the Kellgren-Lawrence grade (KLG)

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and other joint features based on the standardized Burnett Atlas [25] by a single blinded musculoskeletal radiologist (JR) with demonstrated high reliability [20,26–28]. Symptomatic rOA was defined as the combination of radiographic features of OA and symptoms of PAS in the same joint. Additional definitions were utilized for specific features or complex sites such as the hands and feet, such that both hand and foot OA required rOA in a minimum of one joint in each of these sites. Symptomatic rOA was defined as the combination of radiographic features of OA and mild, moderate, or severe PAS in the same joint. Participants were excluded from this analysis if they did not complete their clinic visit, radiographic assessment, had knees with joint replacement, or were missing MJOA definitions.

This study was conducted in full compliance with the UNC Institutional Review Board (UNC IRB# 18–0438). All JoCoHS participants provided written informed consent prior to participation and at each study visit.

Evaluation of Multi-Joint Osteoarthritis (MJOA)

We utilized previously established MJOA definitions to classify participants based on phenotype [23]. Spinal radiographs were not obtained during JoCoHS clinic evaluations and thus MJOA-7 (bilateral knees and spine) was excluded from this analysis. Similarly, the use of spine OA in the definition of other MJOA subtypes (MJOA-1, MJOA-3, MJOA-4, MJOA-5, MJOA-MJOA-6, and MJOA-8) was also omitted. Joint sites included: distal interphalangeal (DIP), proximal interphalangeal (PIP), carpometacarpal (CMC), hips, knees, ankles, and feet. For each MJOA phenotype, participants were defined using a “radiographic” (MJOA-r) or “symptomatic” (MJOA-s) classification based on imaging results and symptomatology at joint sites. Refer to (Table 1) for the full list of MJOA definitions used in this study.

Participants were assessed for symptoms by asking them the previously defined questions for PAS. For the hand joints, a clinical examination was performed by two experienced examiners to assess for tenderness and bony enlargement at each joint. Reliability was determined by having both examiners independently assess a randomly selected subset of 40 patients. Proportional agreement ranged from 0.57 to 0.97 for nodes and 0.86 to 0.97 for tenderness [23]. To be considered symptomatic MJOA, any subtype needed to have radiographic evidence of OA in each joint and any of the previously mentioned symptoms (for joints other than hands) or hand physical exam abnormalities (tenderness, bony enlargement) in at least one joint.

Evaluation of Knee Osteoarthritis (KOA)

Fixed-flexion posteroanterior knee radiographs were read for KLG and other features as described above [29]. Knee rOA was defined as KLG ≥2 (mild, moderate, or severe KLG) and symptomatic knee OA (sxKOA) was defined as rOA and PAS in the same knee. Other radiographic feature outcomes included osteophytes (medial/lateral and tibial/femoral), sclerosis, subchondral cysts, medial/lateral chondrocalcinosis, and medial/lateral joints space narrowing. Pain, function, and other symptoms (such as swelling, decreased range of motion, etc.) were assessed via self-reported questionnaires including the Knee and

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Osteoarthritis Outcomes Scores (KOOS) [30]. KOOS was self-reported and computed from answers regarding the participant's worst knee and reported for the separate subscales for KOOS Pain (9 items), KOOS Symptoms (7 items), KOOS Function (9 items), and KOOS Quality of Life (QOL, 4 items). KOOS scores ranged from 0 to 100 with a score of 0 representing extreme knee problems and 100 representing no knee problems. PAS symptoms were collected and graded by severity (none, mild, moderate, or severe).

Statistical Analysis

Descriptive statistics were computed for the analytic sample with counts and percentages provided for categorical variables, means and standard deviation (SD) provided for continuous variables, and median and interquartile range (IQR) provided for count or score variables. Some variables were at the person-level and descriptive statistics were provided out of the total number of participants. Other variables were at the knee-level and descriptive statistics were provided out of total number of knees in the analysis.

The 18 person-level MJOA dichotomous outcomes were each modeled using logistic regression to produce adjusted odds ratios (OR) and 95% confidence intervals (CI) to quantify the association of sex and race with MJOA. All models included the following variables: sex, race/ethnicity, age, BMI, and education. Effects were non-estimable (ne) if cross-cell counts were smaller than 5.

The four person-level KOOS subscale outcomes were each modeled using zero-inflated negative binomial distribution to produce adjusted mean ratios (MR) and 95% CI to quantify the association of sex and race with KOOS. The log of the mean KOOS was modeled and the MR was interpreted as how much worse the KOOS score is on average between two groups (e.g. how much worse the KOOS score is on average for women compared to men). To account for excess number of scores equal to 100, KOOS subscale scores were reversed as 100 minus score so the higher the score the worse the knee assessment. This allowed the fit of a zero-inflated model that can account for the excess zeros (in this case corresponding to excess 100 scores). All models included the following variables: sex, race/ethnicity, age, BMI, education, and knee injury (given that this is KOOS and is a knee specific outcome).

Two knee-level outcomes for knee PAS were dichotomous: any PAS and ordinal severity PAS. Any knee PAS was modeled using logistic regression and ordinal severity PAS was modeled using cumulative logit regression to produce adjusted OR and 95% CI (using generalized estimating equations (GEE) to estimate an exchangeable correlation between knees within a person) to quantify the association of sex and race with knee PAS. All models included the following variables: sex, race/ethnicity, age, BMI, education, and knee injury (given that knee PAS and is a knee specific outcome). All other 13 knee-level radiographic outcomes were either dichotomous (knee rOA, sxKOA, sclerosis, subchondral cysts, medial/lateral chondrocalcinosis) or ordinal (KLG, medial/lateral and tibial/femoral osteophytes, and medial/lateral joint space narrowing). Dichotomous outcomes were modeled using logistic regression and ordinal outcomes were modeled using cumulative logit regression to produce adjusted OR and 95% CI (using generalized estimating equations (GEE) to estimate an exchangeable correlation between knees within a person) to quantify the association of sex and race with knee radiographic outcomes. All models included the following variables:

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sex, race/ethnicity, age, BMI, education, and knee injury (given that knee radiographic outcomes are knee specific outcomes).

All analyses were conducted using the statistical software package SAS version 9.4 (SAS Institute Inc., Cary, NC) and R package multgee: GEE solver for correlated nominal or ordinal multinomial responses [31]). Alpha level of statistical significance was considered at 0.05 and effects shown as such where the 95% confidence interval excludes the null value of 1.

Results

As of January 29th, 2023, 544 participants (1073 knees) completed their clinic visits and had at least one radiograph (excluded were 180 participants who did not complete their clinic visits, 6 participants and 15 knees without radiographs, 10 participants/20 knees with bilateral joint replacement, 19 knees involved in unilateral joint replacement, and 44 participants missing all MJOA definitions, Figure 1). This group had a mean age of 55 years and 33% were men. Sixty-eight percent of the population identified as White, 23% Black, and 9% Hispanic (Table 1).

MJOA Outcomes

The most common MJOA subtypes in our population were MJOA-4: at least 2 lower body joint sites (22% MJOA-4r and 17% MJOA-4s), MJOA-8: at least 3 joint sites (19% MJOA-8r and 14% MJOA-8s), and MJOA-5: knee or hip and ankle or foot (16% MJOA-5r and 13% MJOA-5s). The least common MJOA subtypes included MJOA-2: at least 2 interphalangeal and at least one CMC with knee or hip (5% MJOA-2r and 3% MJOA-2s), MJOA-9: at least 1 CMC and bilateral nodes (5% MJOA-9r and 2% MJOA-9s), and MJOA-3: at least 5 joint sites (3% MJOA-3r and 2% MJOA-3s, Table 1).

MJOA Outcomes by Sex—Men had statistically significant higher odds of displaying MJOA-6 (at least 3 sites out of the hip, knee, ankle, or foot), both radiographically and symptomatically (OR = 2.27 and OR = 2.33 respectively). Higher odds for men were also observed, though not statistically significant, in MJOA-1 and MJOA-3. Lower odds for men, though not statistically significant, were observed in MJOA-2 and MJOA 10r (Table 2).

MJOA Outcomes by Ethnicity—Black participants showed no statistically significant differences compared to White participants. Given the low census of Hispanic participants, we were unable to assess comparisons between Hispanic and White participants.

Knee Osteoarthritis (KOA) - Person Level Outcomes

For the worse knee, the median KOOS pain was 92, symptoms 86, function 92, and quality-of-life 81, respectively, in the overall analysis population (Table 1). Women reported significantly worse KOOS symptoms scores (MR = 1.25; 95% CI: 1.08, 1.43). Both Black and Hispanic participants reported worse KOOS in most subscales than White participants, though this effect only reached the level of statistical significance in KOOS symptoms between Black and White participants (MR = 1.18; 95% CI: 1.00, 1.38, Table 3).

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Knee Osteoarthritis (KOA) - Knee Level Outcomes

A history of injury was reported in 15% of knees. An absence of PAS symptoms (on most days) was reported in 53% of knees, while 20% of knees had mild, 19% had moderate, and 9% had severe symptoms. Radiographic KOA was present in 28% of knees. Symptomatic KOA (evidence of radiographic KOA with any PAS) was present in 18% of knees. The most common radiographic features of KOA were medial tibial osteophytes, which were found in 55% (n=586) of knees and lateral tibial osteophytes, which were found in 34% (n=367) of knees. The least common radiographic KOA features included medial and lateral chondrocalcinosis in 2.3% and 2.6% of knees respectively. The distribution of all assessed radiographic features can be found in Table 4.

Knee Level Outcomes by Sex—Women tended towards greater PAS severity (Table 3), though this did not reach statistical significance (odds ratio [OR] = 1.35; 95% CI: 0.98, 1.86). Women had significantly higher odds of knee rOA than men (OR = 1.56; 95% CI: 1.04, 2.35). Additionally, women had higher odds of displaying advanced grades of most radiographic features of KOA, significantly so for lateral joint space narrowing (OR = 1.88; 95% CI: 1.00, 3.54), medial tibial osteophytes (OR = 1.67; 95% CI:1.21, 2.30), and sclerosis (OR = 1.61; 95% CI: 1.07, 2.44, Table 5).

Knee Level Outcomes by Ethnicity—We found no evidence of differences in PAS symptoms severity by race/ethnicity (Table 3). Black participants had significantly higher odds of knee rOA than White participants (OR = 1.63; 95% CI: 1.06, 2.51). Overall, Black participants had higher odds of displaying advanced grades of most radiographic features than White participants, such as sclerosis (OR = 2.06; 95% CI: 1.36, 3.14), more severe KLG (OR = 1.47; 1.02, 2.11), and more severe medial tibial osteophytes (OR = 1.50; 95% CI: 1.01, 2.22). They also had higher, although not statistically significant, odds of subchondral cysts (OR = 1.96; 95% CI: 0.89, 4.32), more severe lateral femoral osteophytes (OR = 1.89; 95% CI: 0.85, 4.22), and more severe medial joint space narrowing (OR=1.54; 95% CI: 0.99, 2.38). Hispanic participants overall had lower odds of having advanced radiographic features of KOA compared to White participants. This was significant in KLG grade severity (OR = 0.60; 95% CI: 0.36, 1.00, Table 5).

Discussion

Using preliminary data from the actively enrolling JoCoHS, we compared multiple aspects of KOA and MJOA by race/ethnicity and sex. Our findings represent an interim analysis of ongoing cross-sectional research into OA using this diverse cohort. We discuss our major findings here, and as our sample size increases, we hope to further elucidate some of the initial results discovered in future comparisons.

Multi-Joint Osteoarthritis

The most common MJOA phenotypes in our sample were those with greater involvement of lower extremity, weight-bearing joints. Specifically, MJOA-4 (at least 2 lower extremity joints) was the most common phenotype. MJOA-5 (knee or hip plus either ankle or foot) and MJOA-8 (at least 3 joint sites including DIP, PIP, CMC, hip, knee, ankle, or foot) were

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also highly represented. These findings feature some of the most common joints affected by OA such as the knees, hips, and hands and are thus consistent with our expectations [2, 32, 33]. However, some findings challenged these expectations. MJOA-6 (at least 3 lower extremity joints), for example, interestingly was not as consistent with this trend despite its similarity to MJOA-4. Perhaps this reflects the overall prevalence of knee and hip involvement in lower extremity OA as compared to the foot and ankle [32, 34]. Further attention to the discrepancy between MJOA-4 and MJOA-6 expression will be necessary in repeat examinations.

Our least represented MJOA phenotype overall unsurprisingly was the one representing the greatest burden of disease. Both radiographic and symptomatic MJOA-3, involving at least 5 joint sites between the DIP, PIP, CMC, hip, knee, ankle, and foot were only represented in 2–3% of the population each. While MJOA-3 has a more “generalized” definition, we attribute this to high number of affected joints required to meet its criteria, which would be expected to be less frequent in this younger, population-based cohort. Compared to most MJOA phenotypes in our sample, symptomatic subtypes primarily involving the hand appear to be expressed less often compared to their radiographic subtypes. Examples include MJOA-9 (with at least 1 CMC joint and bilateral nodes) and MJOA-10 (at least 3 interphalangeal joints or bilateral nodes). We will continue to dedicate attention to this as our sample size grows, given the known and significant disability that can be associated with hand OA [35].

Observing for sex-specific differences, Men had more than double the odds of expressing MJOA-6 (at least 3 lower extremity joint sites), both radiographically and symptomatically. While this phenotype has heavy representation of the lower extremities, other leg or foot predominant phenotypes were not consistent with this finding. Notably the more common MJOA-4, which includes at least 2 lower extremity sites had an OR of around 1 for both radiographic and symptomatic presentations. As previously discussed, the commonly involved knees and hips are presumably well-represented in both MJOA-4 and MJOA-6, but this discrepancy implies that men with lower extremity predominant MJOA may have more extensive involvement, such as in the ankles and feet, introducing opportunity for more focused investigation. In our sample, 38% of men reported injury in at least one knee. Specific additional data including nature of injury, surgeries/procedures, and other injury of the lower extremity were not accounted for. Additionally, detailed social factors such as activity, exercise, and sports history were not included in this analysis. We will continue to closely follow this data as this study expands.

We found no statistically significant association between race and MJOA phenotype.

Knee Osteoarthritis

Consistent with prior epidemiologic evidence, the medial knee compartment appears to be affected significantly more in KOA, with a higher prevalence of osteophytes and joint space narrowing compared to the lateral compartment of the knee [36]. Likewise, tibial involvement appears more common than femoral involvement. Women in our sample had significantly greater odds of KOA compared to men, including all radiographic features assessed, although this was only significant in medial tibial osteophytes, sclerosis, and

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lateral joint space narrowing. Similarly, women also had greater PAS scores and KOOS than men for each category, though findings were only significant for non-pain KOOS symptoms. Overall, this is an expected result of our study given the abundance of available data detailing that women have a greater likelihood of developing OA than men, especially with regards to KOA.

We note that Blacks follow an overall similar pattern to the above, having higher odds of knee rOA, more severe KLG grade, and presence of more radiographic features in multiple outcomes, most significant for medial tibial osteophytes and sclerosis. Additionally, Blacks reported worse KOOS in all categories, though only significant in non-pain symptoms. There was also a non-significant trend towards more moderate/severe PAS compared to Whites. Hispanics, on the other hand, were noted overall to have the opposite trend, with significantly lower KLG and non-significantly lower odds of multiple radiographic features. However, we observed a paradoxical increase in symptoms, as KOOS was non-significantly worse in all categories. Similar to Blacks, there was also non-significant trend towards more severe PAS. It must be noted that due to a relatively low sample size of Hispanic participants, this data is limited, but overall, our data suggest a potential association between race and multiple aspects of KOA. Previous studies have indicated that KOA may be more common in Blacks than in Whites [17, 20] and the few available studies on OA-related pain and disability suggest that Hispanics are more likely to experience activity limitation, work limitation, and more severe joint pain compared to Whites [37, 38]. Furthermore, studies focused on non-OA chronic pain have also suggested that Hispanics report more severe pain symptoms and activity limitation [39, 40]. However, there is an overall paucity of data relevant to OA-related pain in this population. Thus, we plan to dedicate particular attention to the apparent discrepancy between fewer knee rOA findings in Hispanics and the general trend towards worse KOOS and PAS scores.

This study has important strengths and limitations. Key strengths include the population-based nature of the JoCoHS cohort and its diversity, allowing for valuable representation and therefore better generalizability. We anticipate that this growing and diverse cohort will allow flexibility in the study of OA outcomes and associations. Our most significant limitation is sample size. This limitation is notable in our Hispanic population, making it difficult to draw strong and reliable conclusions. We anticipate this limitation to be mitigated as JoCoHS grows. Additionally, in our observational study, there may be unmeasured or uncontrolled confounding factors, and the possibility of multiple testing problems may potentially inflate results to appear more significant. However, given the exploratory nature of this study, corrections of the significance level to account for this are often meaningless as there is no clear hypothesis with aim to maintain a specified significance level [41]. Another possible limitation may include the use of radiographs as the primary imaging modality for assessing OA, as it may miss early signs of OA compared to MRI and may also lead to skewing of some of our results if symptomatic patients also had other causes of joint pain (such as a meniscal injury or ligamental injury of the knee). However, radiographs are widely considered to be the most appropriate initial imaging modality for musculoskeletal abnormalities such as OA and the use of radiographs correlate to what is often initially explored in the evaluation of patients with suspected joint abnormalities. Lastly, excluding spinal imaging (and by extension MJOA-7) in our analysis may have also resulted in

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slight variations in MJOA classification between participants as compared to the original definitions which included the spine.

Conclusion

This preliminary analysis of an actively enrolling cohort describes many characteristics of note, with some findings consistent with current epidemiological trends and some unique findings as well. Men were found to more commonly express MJOA-6, suggesting a possible association between lower extremity-predominant MJOA compared to women in this younger group. We found no statistically significant association in MJOA phenotypes by race. Regarding KOA, women and Blacks generally had more features of KOA and more severe pain and symptom outcomes, consistent with the literature. Interestingly, our preliminary data suggests that Hispanics may express most MJOA subtypes less frequently than Whites along with fewer knee level outcomes, despite typically reporting higher pain and symptoms scores. While our data is currently limited by sample size, we expect the growing and diverse JoCoHS cohort to allow us the opportunity to contribute unique and beneficial knowledge to the OA literature.

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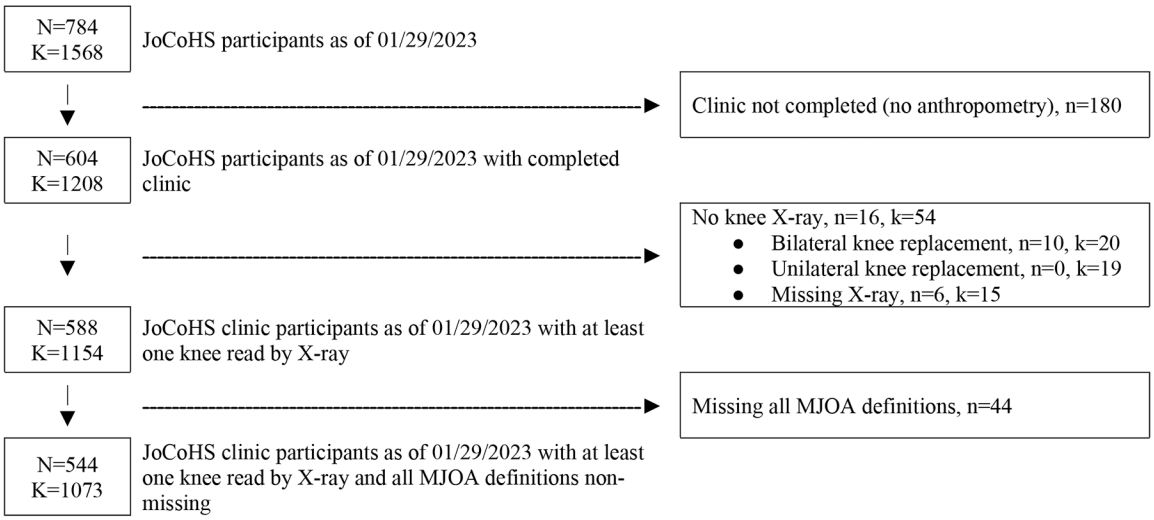

N = Number of Persons
K = Number of Knees

Figure 1.
Strobe Diagram of Patient Selection

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Table 1.

Descriptive Statistics on Person-level Characteristics of JoCoHS Sample

Person-level characteristics	**Overall (N=544)**	
Demographics and Anthropometry	**n or mean**	**% or ±SD**
Men, n %	180	33.1
Age, mean±SD years, range=35–70	55.3	±9.5
Age group (years), n %		
35–44	93	17.1
45–54	148	27.2
55–64	191	35.1
65–74	112	20.6
Race, n %		
White	371	68.2
Black	124	22.8
Hispanic	49	9.0
Education: less than College degree, n % (missing=3)	276	50.7
BMI, mean±SD kg/m^2, range=17–54	32.0	±6.9
KOOS subscales on the worst side knee	**median**	**(IQR)**
KOOS Pain (9 items), range=19–100 (missing=2)	91.7	(75.0–100)
KOOS Symptoms (7 items), range=14–100 (missing=2)	85.7	(67.9–96.4)
KOOS Function (9 items), range=6–100 (missing=2)	91.7	(72.2–100)
KOOS QOL (4 items), range=0–100 (missing=1)	81.3	(56.3–100)
MJOA Definitions	**n**	**%**
1r. ≥1 IP node and ≥2 other sites (hip, knee, ankle, foot)	51	9.4
1s. ≥1 IP node and ≥2 other sites (hip, knee, ankle, foot) (≥1 Sx / T/ BE)	38	7.0
2r. ≥2 IP and ≥1 CMC and knee or hip	28	5.1
2s. ≥2 IP and ≥1 CMC and knee or hip (≥1 Sx / T/ BE)	18	3.3
3r. ≥5 joint sites (DIP, PIP, CMC, hip, knee, ankle, foot)	14	2.6
3s. ≥5 joint sites (DIP, PIP, CMC, hip, knee, ankle, foot) (≥1 Sx / T/ BE)	11	2.0
4r. ≥2 lower body joint sites (hip, knee, ankle, foot)	118	21.7
4s. ≥2 lower body joint sites (hip, knee, ankle, foot) (≥1 Sx / T/ BE)	91	16.7
5r. Knee or hip and 1 other joint site: (ankle or foot)	85	15.6
5s. Knee or hip and 1 other joint site: (ankle or foot) (≥1 Sx / T / BE)	69	12.7
6r. ≥3 sites (hip, knee, ankle, or foot)	39	7.2
6s. ≥3 sites (hip, knee, ankle, or foot) (≥1 Sx / T / BE)	34	6.3
8r. ≥3 joint sites (DIP, PIP, CMC, hip, knee, ankle, foot)	104	19.1
8s. ≥3 joint sites (DIP, PIP, CMC, hip, knee, ankle, foot) (≥1 Sx / T/ BE)	76	14.0
9r. ≥1 CMC and bilateral nodes	29	5.3
9s. ≥1 CMC and bilateral nodes (≥1 Sx / T/ BE)	8	1.5
10r. ≥3 IPs or bilateral nodes	72	13.2
10s. ≥3 IPs or bilateral nodes (≥1 Sx / T / BE)	17	3.1

SD=standard deviation; IQR=interquartile range, KOOS=Knee injury and osteoarthritis outcome score, MJOA=multi-joint osteoarthritis, IP=interphalangeal, DIP=distal interphalangeal, PIP=proximal interphalangeal, CMC=carpometacarpal, Sx=symptom(s), T=tenderness, BE=bony enlargement

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Table 2.

Descriptive and adjusted associations for differences in sex and race/ethnicity for MJOA outcome models

MJOA outcomes*	Women	Men	Men [vs Women]	White	Black	Hispanic	Black [vs White]	Hispanic [vs White]
	%	%	OR (95% CI)	%	%	%	OR (95% CI)	OR (95% CI)
MJOA-1r	8.2	11.7	1.21 (0.64, 2.29)	8.9	13.7	2.0	1.27 (0.64, 2.53)	ne
MJOA-1s	6.0	8.9	1.32 (0.65, 2.69)	7.3	8.1	2.0	0.81 (0.36, 1.81)	ne
MJOA-2r	4.9	5.6	0.86 (0.37, 1.98)	6.2	3.2	2.0	ne	ne
MJOA-2s	3.3	3.3	0.81 (0.29, 2.28)	4.3	1.6	.	ne	ne
MJOA-3r	2.2	3.3	1.28 (0.43, 3.87)	3.2	1.6	.	ne	ne
MJOA-3s	1.6	2.8	1.48 (0.43, 5.07)	2.7	0.8	.	ne	ne
MJOA-4r	21.7	21.7	0.97 (0.59, 1.57)	20.5	30.6	8.2	1.12 (0.67, 1.88)	ne
MJOA-4s	16.8	16.7	1.06 (0.62, 1.80)	16.4	21.0	8.2	0.82 (0.46, 1.46)	ne
MJOA-5r	15.9	15.0	0.92 (0.53, 1.58)	14.6	23.4	4.1	1.23 (0.71, 2.14)	ne
MJOA-5s	12.6	12.8	1.09 (0.60, 1.96)	12.1	17.7	4.1	1.01 (0.55, 1.87)	ne
MJOA-6r	5.8	10.0	**2.27 (1.10, 4.69)**	7.0	9.7	2.0	0.97 (0.45, 2.09)	ne
MJOA-6s	4.9	8.9	**2.33 (1.07, 5.07)**	5.9	8.9	2.0	1.06 (0.47, 2.39)	ne
MJOA-8r	18.7	20.0	0.88 (0.53, 1.45)	19.4	23.4	6.1	0.85 (0.49, 1.48)	ne
MJOA-8s	13.5	15.0	1.02 (0.58, 1.79)	14.3	17.7	2.0	0.81 (0.44, 1.49)	ne
MJOA-9r	5.5	5.0	0.65 (0.28, 1.52)	6.5	3.2	2.0	ne	ne
MJOA-9s	1.9	0.6	ne	2.2	.	.	ne	ne
MJOA-IOr	13.2	13.3	0.73 (0.41, 1.29)	14.3	12.9	6.1	0.68 (0.35, 1.33)	ne
MJOA-IOs	3.8	1.7	ne	3.2	3.2	2.0	ne	ne

MJOA=multi-joint osteoarthritis; OR=odds ratio; CI=confidence interval; ne=non estimable due to small cell counts (<5) OR>1 indicates higher odds of MJOA outcome prevalence and OR<1 indicates lower odds of MJOA outcome prevalence for group indicated; significant effects at alpha=0.05 shown in **BOLD**;

*Models 1–18: Each row shows results from a logistic model for MJOA outcome using logit regression to produce adjusted odds ratios and 95% confidence intervals, OR (95% CI); All models include covariables for: sex, race/ethnicity, age, BMI, and <College degree education

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Table 3.

Descriptive and adjusted associations for differences in sex and race/ethnicity for separate, self-reported knee outcome models

Model*	Self-Reported outcome	Women	Men	Women [vs Men]	White	Black	Hispanic	Black [vs White]	Hispanic [vs White]
	Knee-level	%	%	OR (95% CI)	%	%	%	OR (95% CI)	OR (95% CI)
1	*Any PAS*	47.8	45.7	1.18 (0.84, 1.65)	47.5	46.1	46.3	0.77 (0.52, 1.13)	0.88 (0.49, 1.57)
2	*Severity*			1.35 (0.98, 1.86)				0.86 (0.59, 1.25)	0.97 (0.55, 1.70)
	none	52.2	54.3		52.5	53.9	53.7		
	mild	19.0	21.8		23.6	12.0	11.6		
	moderate	18.6	18.2		16.0	23.7	24.2		
	severe	10.2	5.6		7.9	10.4	10.5		
	Person-level	**median (IQR)**	**median (IQR)**	**MR (95% CI)**	**median (IQR)**	**median (IQR)**	**median (IQR)**	**MR (95% CI)**	**MR (95% CI)**
3	*KOOS Pain*	89 (72–100)	92 (75–100)	1.12 (0.95, 1.33)	92 (75–100)	86 (65–100)	86 (72–100)	1.15 (0.94, 1.39)	1.27 (0.95, 1.68)
4	*KOOS Symptoms*	86 (68–96)	86 (71–96)	**1.25 (1.08, 1.43)**	89 (71–96)	79 (64–96)	82 (71–96)	**1.18 (1.00, 1.38)**	1.08 (0.85, 1.37)
5	*KOOS Function*	92 (70–100)	93 (74–100)	1.07 (0.90, 1.26)	94 (75–100)	83 (67–100)	86 (75–100)	1.14 (0.94, 1.37)	1.22 (0.91, 1.63)
6	*KOOS QOL*	81 (56–100)	81 (63–100)	1.04 (0.91, 1.19)	81 (63–100)	75 (56–100)	81 (56–100)	1.06 (0.91, 1.24)	1.11 (0.88, 1.40)

PAS=pain, aching, or stiffness; KOOS=knee injury and osteoarthritis outcome score; QOL=quality of life; IQR=interquartile range; OR=odds ratio; MR=mean ratio; CI=confidence interval; OR>1 indicates higher odds of knee outcome and OR<1 indicates lower odds of knee outcome for group indicated; MR>1 indicates how many times worse the KOOS subscale score is and MR<1 indicates how many times better the KOOS subscale score is for group indicated; significant effects at alpha=0.05 shown in **BOLD;** All models include covariables for: sex, race/ethnicity, age, BMI, <College degree education, and knee injury

*Model 1: Population-averaged, binomial model for correlated, *knee-level* outcome using logit regression and generalized estimating equations (GEE) with an exchangeable working correlation structure to produce adjusted odds ratios and 95% confidence intervals, OR (95% CI); Model 2: Population-averaged, multinomial model for correlated, ordinal *knee-level* outcome using cumulative logit regression and generalized estimating equations (GEE) with an exchangeable working correlation structure to produce adjusted odds ratios and 95% confidence intervals, OR (95% CI); Models 3–6: Zero-inflated negative binomial model for *person-level* outcome modeling log of the mean (KOOS values were reversed as 100-score so that 0 is best and 100 is worst) to produce adjusted mean ratios and 95% confidence intervals, DR (95% CI)

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Table 4.

Descriptive Statistics on Knee-level Characteristics

Self-reported Knee features (n=1073 knees)	n	%
Any history of knee injury	159	14.8
Pain, aching, and stiffness (PAS) on most days		
none	568	52.9
mild	214	19.9
moderate	198	18.5
severe	93	8.7
Radiographic features	**n**	**%**
Radiographic Knee Osteoarthritis (rOA)	305	28.4
Symptomatic Knee Osteoarthritis: rOA + PAS	192	17.9
Kellgren Lawrence Grade (KLG)		
0: no osteoarthritis	408	38.0
1: questionable	360	33.6
2: mild	151	14.1
3: moderate	98	9.1
4: severe	56	5.2
Medial Tibial Osteophytes		
0: normal	487	45.4
1: mild	538	50.1
2: moderate	38	3.5
3: severe	10	0.9
Medial Femoral Osteophytes		
0: normal	1011	94.2
1: mild	44	4.1
2: moderate	17	1.6
3: severe	1	0.1
Lateral Tibial Osteophytes		
0: normal	709	66.1
1: mild	328	30.6
2: moderate	30	2.8
3: severe	6	0.6
Lateral Femoral Osteophytes		
0: normal	1030	96.0
1: mild	38	3.5
2: moderate	4	0.4
3: severe	1	0.1
Sclerosis	243	22.6
Subchondral cysts	36	3.4
Medial Chondrocalcinosis	25	2.3
Lateral Chondrocalcinosis	28	2.6

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Self-reported Knee features (n=1073 knees)	n	%
Medial Joint Space Narrowing		
0: normal	798	74.4
1: mild	149	13.9
2: moderate	77	7.2
3: severe	49	4.6
Lateral Joint Space Narrowing		
0: normal	1003	93.5
1: mild	40	3.7
2: moderate	21	2.0
3: severe	9	0.8

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Table 5.

Descriptive and adjusted associations for differences in sex and race/ethnicity for separate, knee radiographic outcome models

Model*	Radiographic Knee outcomes	Women	Men	Women [vs Men]	White	Black	Hispanic	Black [vs White]	Hispanic [vs White]
		%	%	OR (95% CI)	%	%	%	OR (95% CI)	OR (95% CI)
1	*Knee rOA*	29.9	25.5	**1.56 (1.04, 2.35)**	25.8	42.7	12.6	**1.63 (1.06, 2.51)**	0.61 (0.28, 1.32)
2	*sxKOA*	19.6	14.6	1.51 (0.88, 2.60)	16.7	24.9	9.5	1.03 (0.60, 1.78)	0.65 (0.24, 1.80)
3	*KLG*			1.34 (1.00, 1.81)				**1.47 (1.02, 2.11)**	**0.60 (0.36, 1.00)**
	0	36.7	40.6		39.8	26.6	53.7		
	1	33.4	33.9		34.5	30.7	33.7		
	2	14.8	12.6		14.2	15.8	8.4		
	3	9.6	8.1		7.2	17.8	2.1		
	4	5.4	4.8		4.3	9.1	2.1		
4	*Medial Tibial Osteophytes*			**1.67 (1.21, 2.30)**				**1.50 (1.01, 2.22)**	0.60 (0.35, 1.05)
	0	43.0	50.1		47.8	32.0	61.1		
	1	51.4	47.6		48.4	59.8	38.9		
	2	4.3	2.0		3.4	5.4	.		
	3	1.3	0.3		0.4	2.9	.		
5	*Medial Femoral Osteophytes*			1.47 (0.65, 3.31)				1.38 (0.65, 2.92)	1.77 (0.41, 7.58)
	0	93.3	96.1		95.3	90.5	95.8		
	1	4.2	3.9		3.5	5.8	4.2		
	2	2.4	.		1.1	3.7	.		
	3	0.1	.		0.1	.	.		
6	*Lateral Tibial Osteophytes*			1.22 (0.86, 1.73)				1.06 (0.72, 1.56)	0.58 (0.29, 1.14)
	0	64.8	68.6		66.9	58.1	80.0		
	1	31.4	28.9		30.3	36.1	18.9		
	2	2.9	2.5		2.4	4.6	1.1		
	3	0.8	.		0.4	1.2	.		
7	*Lateral Femoral Osteophytes*			1.06 (0.50, 2.25)				1.89 (0.85, 4.22)	ne
	0	95.8	96.4		96.6	92.5	100		
	1	3.5	3.6		3.1	6.2	.		
	2	0.6	.		0.3	0.8	.		

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Model*	Radiographic Knee outcomes	Women	Men	Women [vs Men]	White	Black	Hispanic	Black [vs White]	Hispanic [vs White]
		%	%	OR (95% CI)	%	%	%	OR (95% CI)	OR (95% CI)
	3	0.1	.		.	0.4	.		
8	*Sclerosis*	24.7	18.5	**1.61 (1.07, 2.44)**	19.4	37.8	9.5	**2.06 (1.36, 3.14)**	0.60 (0.26, 1.39)
9	*Subchondral Cysts*	3.6	2.8	1.47 (0.67, 3.24)	2.6	6.6	1.1	1.96 (0.89, 4.32)	ne
10	*Medial Chondrocalcinosis*	2.2	2.5	1.26 (0.46, 3.42)	2.6	2.1	1.1	0.87 (0.25, 3.03)	ne
11	*Lateral Chondrocalcinosis*	2.8	2.2	1.65 (0.58, 4.72)	2.6	3.3	1.1	1.33 (0.43, 4.10)	ne
12	*Medial Joint Space Narrowing*			1.02 (0.68, 1.55)				1.54 (0.99, 2.38)	0.52 (0.23, 1.19)
	0	74.3	74.5		76.8	61.0	89.5		
	1	13.7	14.3		14.0	16.2	7.4		
	2	7.3	7.0		5.2	15.4	2.1		
	3	4.7	4.2		4.1	7.5	1.1		
13	*Lateral Joint Space Narrowing*			**1.88 (1.00, 3.54)**				1.61 (0.85, 3.05)	1.02 (0.28, 3.77)
	0	92.6	95.2		94.2	90.5	95.8		
	1	4.1	3.1		3.4	5.0	3.2		
	2	2.4	1.1		2.0	2.5	.		
	3	1.0	0.6		0.4	2.1	1.1		

OA=osteoarthritis; rOA=radiographic osteoarthritis sxKOA=symptomatic knee OA; KLG=Kellgren-Lawrence grade; OR=odds ratio; CI=confidence interval, ne=non estimable.

OR>1 indicates higher odds of knee outcome and OR<1 indicates lower odds of knee outcome for group indicated; significant effects at alpha=0.05 shown in **BOLD**

*Models 1–2 and 8–11: Population-averaged, binomial model for correlated, *knee-level* outcome using logit regression and generalized estimating equations (GEE) with an exchangeable working correlation structure to produce adjusted odds ratios and 95% confidence intervals, OR (95% CI); Models 3–7 and 12–13: Population-averaged, multinomial model for correlated, ordinal *knee-level* outcome using cumulative logit regression and generalized estimating equations (GEE) with an exchangeable working correlation structure to produce adjusted odds ratios and 95% confidence intervals, OR (95% CI); All models include covariables for: sex, race/ethnicity, age, BMI, <College degree education, and knee injury