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The Prevalence of Knee Symptoms, Radiographic, and Symptomatic Osteoarthritis at Four Time Points: The Johnston County Osteoarthritis Project, 1999-2018

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Objective. To describe point prevalence of knee symptoms, radiographic knee osteoarthritis (rKOA), severe rKOA, and symptomatic rKOA at four time points in the longitudinal, population-based Johnston County Osteoarthritis Project (JoCo OA).

Methods. Data were from 2573 JoCo OA participants with up to 18 years of follow-up (1999-2018) and standardized fixed-flexion knee radiographs read by a single, reliable expert musculoskeletal radiologist. The four outcomes were 1) self-reported knee symptoms, defined by "On most days, do you have pain, aching, or stiffness in your right/left knee?"; 2) rKOA, defined as a Kellgren-Lawrence grade (KLG) of 2 to 4); 3) severe rKOA, defined as a KLG of 3 or 4; and 4) symptomatic rKOA, defined as both symptoms and rKOA in the same joint. Weighted prevalence estimates and 95% confidence intervals (CIs) were generated overall and by age group, sex, race, and body mass index (BMI).

Results. Most recently (2017-2018, T4), the overall prevalence (percentage) of knee symptoms, rKOA, severe rKOA, and symptomatic rKOA was 41% (95% CI: 35-47%), 61% (95% CI: 56-67%), 35% (95% CI: 30-40%), and 30% (95% CI: 24-35%), respectively. From time point T1 to T4, prevalence increased for rKOA, severe rKOA, and symptomatic rKOA but not for knee symptoms. The prevalence of both severe rKOA (17-39%) and symptomatic rKOA (23-30%) was consistently higher among women. The prevalence of all outcomes was higher among those with higher BMI and among Black participants at all time points, particularly rKOA (35-69%) and severe rKOA (22-46%).

Conclusion. These updated estimates demonstrate a large and increasing burden of knee OA, particularly among women and Black individuals.

INTRODUCTION

The lifetime risk of developing symptomatic radiographic knee osteoarthritis (rKOA) by the age of 85 years has been estimated at 45%, meaning that nearly 1 in 2 US adults will develop this debilitating condition; the risk has been estimated to be higher among women (47%), those with prior knee injury (57%), and those with obesity (61%) (1). It is also apparent that those

with knee symptoms, with or without rKOA, experience premature mortality (2), emphasizing the magnitude of knee osteoarthritis (KOA) as a public health issue.

Estimates of disease point prevalence provide an assessment of disease burden in a population at a given time, adjusted for the size of the source population (3, 4). The prevalence of osteoarthritis (OA) is known to depend on the definition, with radiographic being OA more frequent than symptomatic OA (5).

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Importantly, population-based studies, such as those described below, are necessary to estimate point prevalence in the general population in contrast to symptom-based or other clinical cohorts, which may have limited generalizability. Specifically, multicenter osteoarthritis study and osteoarthritis initiative, which are composed only of individuals with OA or at increased risk of developing it, are not able to provide prevalence estimates, as these are not population-based studies. A seminal early study of older White participants (aged 63-94 years) in the Framingham Heart Study cohort (1983-1985) showed that the overall prevalence of rKOA was 33%, and it increased from 27% in those under the age of 70 years to 44% in those aged 80 years or older; symptomatic rKOA (overall prevalence of 10%) increased from 7% to 11%, and both rKOA and symptomatic rKOA were more common in women (6). Another early study using data from the third National Health and Nutrition Examination Survey (NHANES) (1991-1994) found rKOA in 37% of adults aged 60 years or older and symptomatic rKOA in 12% (7), although the study used non-weight-bearing radiographs. The initial report from the baseline visit of the Johnston County Osteoarthritis Project (JoCo OA, 1991-1997) of adults aged 45 years or older estimated that 43% of the cohort had knee symptoms, 28% had rKOA, 16% had symptomatic rKOA, and 8% had severe rKOA, with all outcomes generally more frequent in older participants, women, and Black individuals (8). The relatively higher prevalence estimates in the JoCo OA study were thought to be related to age differences, geographic and racial differences, and the higher prevalence of obesity compared with other studies (8).

More recently, using data from the National Health Interview Survey and the Osteoarthritis Policy Model, Deshpande et al estimated that 7% (14 million) of people aged 25 years or older in the United States had symptomatic KOA, with the majority of these (4% of the total US population) having severe (Kellgren-Lawrence grade [KLG] of 3 or 4) disease (9). From 1983 to 2005, an increasing prevalence of symptomatic rKOA was noted among White Framingham participants aged 70 years old or greater, independent of age and attributable in that cohort to increasing knee symptoms rather than rKOA (10). Additionally, data from the Chingford cohort of 516 older White women (median age of 53 years at baseline) with 14 years of follow-up showed that the prevalence of rKOA increased from 14% at baseline (1988-1989) to nearly half of participants (48%) by Year 15 (11). Because of differences in study design and population characteristics, estimates across the studies described above are not directly comparable but suggest an overall increase in KOA over time.

Estimating OA point prevalence, especially at multiple time points, is useful for describing the burden of this chronic disease, understanding differences in disease frequencies across sociodemographic groups, and informing policy decisions. Few recent population-based cohort studies can provide point prevalence estimates for OA at multiple time points across almost two decades, including contemporary estimates for Black individuals. We aimed to describe the cross-sectional, population-based point prevalence of four knee outcomes (symptoms, rKOA, severe rKOA, and symptomatic rKOA) separately at four time points from 1999 to 2018 in a large US cohort comprising Black and White men and women.

PATIENTS AND METHODS

The JoCo OA, a prospective population-based cohort of Black and White residents of six townships in Johnston County, North Carolina, who were 45 years old or older at baseline, has been described in detail previously (8). In brief, the probabilitysampled JoCo OA cohort was designed to be representative of this noninstitutionalized civilian population. The design included oversampling of Black individuals and undersampling of White women over the age of 65 years to facilitate analyses of racial differences. The selected townships included those with the largest proportions of Black residents, and each included both a town and a surrounding rural area. The primary sampling unit was the streets in these townships, stratified by rural or urban status, predominant race, and socioeconomic status. Households were enumerated for each street; age, sex, race, and marital status were collected from each individual. Of 5138 individuals in eligible households, 72% completed at least one interview. Given this design, sampling weights were calculated using the following three steps: 1) raw weights were used as the reciprocal of the selection probability, 2) these were then multiplied by the inverse of predicted probabilities of response to adjust for nonresponse, 3) and they were adjusted after stratification to the appropriate US Census counts. All participants gave written informed consent prior to participation. The JoCo OA has been continuously approved by the University of North Carolina institutional review board (#92-0583).

For the current analysis, data were collected from the following four time points: the first (T1) was 1999 to 2003, including cohort enrichment (T1*: 2003-2004) (n = 2573); the second (T2) was 2006 to 2011 (n = 1595); the third (T3) was 2013 to 2015 (n = 785); and the fourth (T4) was 2017 to 2018 (n = 506) (Table 1). The mean time between participant assessments was 6.5 years for T1 to T2, 5.5 years for T2 to T3, and 3.5 years for T3 to T4. The baseline visit of the JoCo OA (T0, 1991-1997; n = 3086) was not included, as only anteroposterior extended knee radiographs were obtained at that visit, and it has been previously described (8). Otherwise, all visits included standardized posteroanterior fixedflexion radiographs obtained using the SynaFlexer (CCBR-Synarc) frame; all radiographs were read by a single experienced musculoskeletal radiologist (JBR) with high reliability (12).

For this study, there were four outcomes of interest, as follow: 1) knee symptoms, using self-reported knee symptoms defined using the question "On most days, do you have pain, aching, or stiffness in your right/left knee?" 2) rKOA, defined as a KLG (13) of 2 or more; 3) severe rKOA, defined as a KLG of 3 or more; and 4) symptomatic rKOA, defined as the presence of both symptoms

Table 1. Onweighted sample on				
		Time P	Point	
Characteristic	T1 (1999-2004; n = 2573)	T2 (2006-2011; n = 1595)	T3 (2013-2015; n = 785)	T4 (2017-2018; n = 506)
Age, mean ± SD (range)	63.8 ± 10.6 (45-102)	68.7 ± 9.2 (50-95)	71.7 ± 7.7 (55-94)	73.5 ± 7.4 (59-95)
Age group, n (%) 45-54 years 55-64 years 65-74 years ≥75 years	627 (24) 837 (33) 664 (26) 445 (17)	74 (4) 586 (35) 571 (34) 430 (26)	0 (0) 140 (18) 383 (49) 262 (33)	0 (0) 55 (11) 237 (47) 214 (42)
Sex, n (%) Men Women	878 (34) 1695 (66)	537 (33) 1114 (67)	251 (32) 534 (68)	148 (29) 358 (71)
Race, n (%) Black White	834 (32) 1739 (68)	522 (32) 1129 (68)	245 (31) 540 (69)	170 (34) 336 (66)
BMI, ^b mean ± SD (range), kg/m ²	30.5 ± 6.7 (15-71)	31.4 ± 7.1 (15-78)	30.9 ± 6.6 (16-61)	30.9 ± 6.5 (15-57)
BMI, ^b n (%) Underweight (<18.5 kg/m ²) Normal (18.5-24.9 kg/m ²) Overweight (25-29.9 kg/m ²) Obese (≥30 kg/m ²)	19 (1) 471 (18) 902 (35) 1177 (46)	9 (1) 250 (15) 543 (33) 847 (51)	6 (1) 117 (15) 274 (35) 388 (49)	3 (1) 88 (17) 158 (31) 257 (51)
Either knee injury, ^c n (%)				
Yes	712 (28)	468 (29)	243 (31)	46 (9)
No	1854 (72)	1169 (71)	538 (69)	458 (91)

Table 1. Unweighted sample characteristics of the JoCo OA cohort across four time points^a

Abbreviation: BMI, body mass index; JoCo OA, Johnston County Osteoarthritis Project; T1, time point 1; T2, time point 2; T3, time point 3; T4, time point 4.

^a Time points in the JoCo OA are as follows: baseline (T0), 1991-1997 (not included here because of differences in xray assessment); first follow-up (T1)/cohort enrichment (T1*), 1999 to 2004; second follow-up (T2), 2006 to 2011; third follow-up (T3), 2013 to 2015; and fourth follow-up (T4), 2017 to 2018. ^b By World Health Organization category.

^c Self-report of knee injury measures by time point as follows: at T1, "Have you ever injured your [right/left] knee?"; at T2, "Since your last visit, other than a fracture, have you injured [your right/left knee] enough to require a crutch, cast, cane, sling, or brace?"; and at T3 and T4, "Have you ever injured [your right/left knee] badly enough that it limited your ability to walk for at least 2 days?"

and rKOA (as defined above) in the same knee. Less than 3% of knees at any time point had undergone replacement, so this outcome was not analyzed separately (these individuals were included in the symptomatic rKOA category).

Cross-sectional, person-based, weighted point prevalence analyses were performed using the SURVEYFREQ procedure in SAS version 9.4, taking the stratified sampling design and survey weights into account, as detailed below. Sampling weights were calibrated separately for each time point to the respective US Census population counts for Johnston County. Streets (defined as the full length of a named thoroughfare from start to end) were the primary sampling unit. The sampling rates differed by township and depended on each township's relative size, racial makeup, rural/urban status, and socioeconomic status, with the goal of oversampling Black individuals.

Each set of cross-sectional survey weights was constructed using a three-step process, which was detailed in Jordan et al (8) and summarized here. First, the inverse of the probability of selection, as determined by the sampling scheme at T0, the time of enrollment, was taken as the raw weight for T0; raw weights were set to 1 for the supplemental sample (T1*), drawn to enrich the size of the cohort, as this sample was considered a convenience sample. Second, the raw weights from T0 were adjusted for nonresponse at T0 and T1 using logistic regression; T1* weights were not adjusted for nonresponse. Third, all adjusted weights were calibrated to the Johnston County population values from the US Census for the year closest to the time point of data collection by a post-stratification adjustment; these values were from 1990 for T0, from 2000 for T1, and from 2010 for T2 to T4. To standardize all timepoints to the same census values to enhance comparability, a sensitivity analysis was conducted calibrating T1 to the 2010 census rather than the 2000 census (to make the estimates more comparable). The weights were calibrated on four stratifying variables: age group (45-54 years, 55-64 years, 65-74 years, and \geq 75 years), sex, race, and township of residence. Finally, point prevalence estimates and corresponding 95% confidence intervals (CIs) of the knee outcomes at each time point were generated for the overall sample and by age group, sex, race, and body mass index (BMI) category (normal weight: 18.5-24.9 kg/m²; overweight: 25-29.9 kg/m²; and obese: \geq 30 kg/m²) (14). The analysis of each wave incorporates a set of cross-sectional survey weights to more accurately reflect the population of Johnston County at the corresponding point in time. We did not perform formal statistical testing comparing point prevalence between waves but rather



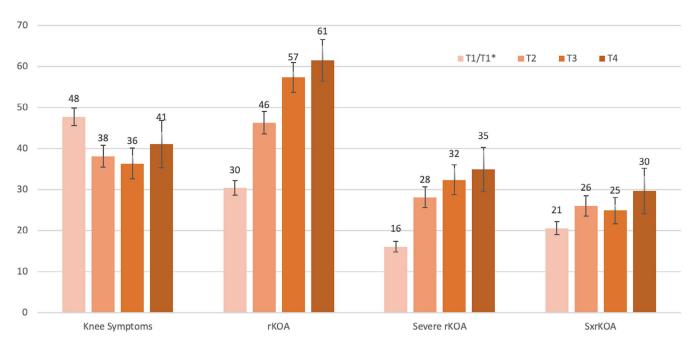


Figure 1. Weighted prevalence of knee outcomes over 18 years (percentage with 95% confidence interval) in the overall cohort, for four time points. Timepoints in the Johnston County Osteoarthritis Project are as follows: baseline (T0), 1991 to 1997 (previously reported in reference 8, not included here because of differences in x-ray assessment); first follow-up (T1)/cohort enrichment (T1*), 1999 to 2004; second follow-up (T2), 2006 to 2011; third follow-up (T3), 2013 to 2015; and fourth follow-up (T4), 2017 to 2018. Estimates are weighted to the US Census for Johnston County, North Carolina. rKOA, radiographic knee osteoarthritis; sxKOA, symptomatic knee osteoarthritis. [Color figure can be viewed at wileyonlinelibrary.com]

provided Cls to reflect precision (15) and to allow for the assessment of the degree of their overlap.

RESULTS

As shown in Table 1, approximately two-thirds of the sample were women, two-thirds were White, and four-fifths were overweight or obese at all time points. The mean age at each time point increased over time; because of aging, there were no cohort members in the youngest age group for the last two follow-up periods. One-quarter to one-third of participants reported any knee injury.

All estimates reported below are for point prevalence. As expected, the overall point prevalence of rKOA, severe rKOA, and symptomatic rKOA increased with aging of the cohort (Figure 1); however, knee symptoms were somewhat less frequent at subsequent time points compared with the initial time point. In contrast to earlier time points, the last two (T3 and T4) time points were closer in time, and therefore the changes in estimates were smaller for most outcomes. At the most recent follow-up time point (T4, 2017-2018), the overall prevalence of knee symptoms, rKOA, severe rKOA, and symptomatic rKOA was 41% (95% CI: 35-47%), 61% (95% CI: 56-67%), 35% (95% CI: 30-40%), and 30% (95% CI: 24-35%), respectively (Table 2).

The weighted point prevalence estimates overall and by subgroups of age, sex, race, and BMI category are shown for T1 to T4 in Table 2. For each time point, the prevalence of rKOA and severe rKOA increased with older age; symptomatic rKOA also increased with older age, but less so, particularly at later time points. In contrast, the prevalence of knee symptoms increased with age at T1 but actually decreased with age at T3 and T4. Compared with men at all time points, higher percentages of women had knee symptoms, severe rKOA, and symptomatic KOA, and similar percentages of women and men had radiographic KOA (Table 2). Compared with Whites, Blacks had more of all four knee outcomes at most time points. The point prevalence of all four outcomes increased in higher BMI categories, most dramatically among the group with obesity (BMI ≥30 kg/m²). Results by age within sex categories are reported in Table 3.

In the sensitivity analysis in which T1 was instead calibrated to the 2010 (rather than the 2000) Johnston County census, the results did not change substantially, and trends were preserved (results not shown).

DISCUSSION

We report weighted point prevalence estimates for four knee outcomes in a large, population-based cohort of middle-aged and older Black and White men and women for four time points with up to 18 years of follow-up data. The point prevalence of rKOA, severe rKOA, and symptomatic rKOA are high and increasing among this general population sample. Older adults, women,

	Knee	Knee Symptoms [% (95% CI)]	IS [% (95%	% CI)]		rkoa [% (95% CI)]	[(I) %56.		Seve	Severe rKOA [% (95%	[% (95%	CI)]	Sympt	omatic rK	Symptomatic rKOA [% (95%	5% CI)]
	Τ1	Τ2	T3	T4	Τ1	T2	T3	T4	Τ1	T2	T3	T4	T1	T2	T3	T4
All participants	48 (46-50)	38 36 41 (35-41) (33-40) (35-47)	36 (33-40)	41 (35-47)	30 (29-32)	46 (44-49)	57 (54-61)	61 (56-67)	16 (15-17)	28 (26-31)	32 (29-36)	35 (30-40)	21 (19-22)	26 (24-28)	25 (22-28)	30 (24-35)
Age group 45-54 years	46 (40-51)	40 (30-50)	n/a ^c	n/a ^c	20 (17-23)	32 (77-47)	n/a ^c	n/a ^c	8 (6-11)	20 (11-29)	n/a ^c	n/a ^c	15 (12-18)	13 (7-18)	n/a ^c	n/a ^c
55-64 years	45	37	(37-47) (31-47) (34-67	48 (24-62)	25	37 (37_47)	45 (38-53)	57	13 (11-15)	21 21 (17_75)	30	29 /18-40)	15-20 18 (15-20)	22 (17_7)	25 (19-31)	32 (19-46)
65-74 years		(34-42) 38 (34-42)	(34-42) (31-44) (34-92) (34-42) (31-44) (30-50)	(30-50) (30-50)		(22-42) 54 (49-59)	(22-02-) 54 (48-61)	(49-65)	(11-1-1) 21 (18-24)	(27-36) 31 (27-36)	(24-36) 30 (24-36)	(10-40) 30 (22-39)	(22-28) (22-28)	(17-27) 29 (25-33)	(19-29) (19-29)	(18-36) (18-36)
≥75 years		41 (36-46)	, 41 , 33 , 39 (36-46) (28-39) (30-47)	39 (30-47)		, 65 (60-69)	69 (63-75)	, 71 (61-81)	, 38 (33-42)	, 44 (39-49)	38 (30-45)	, 45 (34-57)	37 (32-42)	, 36 (31-41)	26 (20-32)	32 (23-41)
Sex Men	43 (40-47)		34 31 40 (79-30) (75-36) (79-50)	40 79-50	29	43 (38-48)	59 (53-66)	62 62	15 (13_17)	23	28	28 170-361	18 115_200	22 (17_76)	19 112_110	28 119-38)
Women	(148-54) (48-54)	(20-02) 42 (39-44)	(20-72) (20-72) (20-72) 42 41 42 (39-44) (36-46) (36-4	(20-72) 42 (36-48)	(20-02) 31 (29-34)	(46-52)	(51-60) (51-60)	(54-68)	(15-19) (15-19)	(12-27) 32 (29-35)	(22-34) 36 (32-41)	(20-20) 39 (32-45)	(21-25) (21-25)	(17-20) 30 (27-32)	(125-24) 30 (26-34)	(24-37) (24-37)
Race	ЦV	LC	9C	1	00	VV	۲ ۲	о С	7	цС	Cr	C C C	0	ц С	, C	Cr
	(42-48)	(42-48) (34-41) (31-40) (34-4	(31-40)	(34-48)	(27-31)	(40-47)	(52-61)	(53-66)	(13-16)	(22-28)	(25-35)	,25-39)	(17-21)	(22-28)	20-28)	(23-37)
Black	56 (52-60)	56 40 39 41 (52-60) (35-45) (31-47) (32-51)	39 (31-47)	41 (32-51)	35 (31-39)	54 (48-59)	60 (52-67)	69 (61-77)	22 (19-25)	36 (31-42)	41 (34-48)	46 (37-56)	25 (22-29)	29 (24-34)	29 (22-36)	28 (19-37)
BMI ^d																
Normal (18.5-24.9 kg/m²)	35 (30-40)	35 29 25 35 (30-40) (21-38) (17-34) (21-4)	25 (17-34)	35 (21-49)	23 (18-27)	32 (24-40)	40 (31-48)	49 (37-62)	11 (8-14)	14 (9-19)	19 (10-27)	17 (10-24)	12 (9-15)	13 (6-21)	8 (3-13)	21 (10-32)
Overweight (25-29.9 kg/m²)	40 (36-44)	25 (21-30)	25 30 26 (21-30) (24-36) (19-34)	26 (19-34)	25 (21-28)	40 (35-45)	52 (45-58)	54 (45-62)	11 (9-13)	18 (15-22)	23 (17-28)	23 (15-31)	14	16 (13-20)	19 (14-24)	15 (8-23)
Obese (≥30 kg/m²)	58 (55-62)		48 45 52 (44-52) (39-50) (43-60)	52 (43-60)	(35-41)	(50-59)	67 (61-72)	70 (62-77)	23 (20-25)	(34-42)	44 (38-49)	47 (39-56)	29 (26-32)	(32-39)	34 (29-40)	41 (32-49)
Abbreviation: BMI, body mass index; CI, confidence interval; n/a, not applicable; rKOA, radiographic knee osteoarthritis; T1, time point 1; T2, time point 2; T3, time point 3; T4, time point 4. ^a Weighted to the US Census for Johnston County, North Carolina. ^b Timepoints in the Johnston County Osteoarthritis Project are as follows: baseline (T0), 1991-1997 (not included here because of differences in x-ray assessment); first follow-up (T1)/cohort enrichment (T1*), 1999-2004; second follow-up (T2), 2006-2011; third follow-up (T3), 2013-2015; and fourth follow-up (T4), 2017-2018. ^c At T3 and T4, no members of the cohort were aged less than 55 years. ^d Estimates among those who were underweight are not included because they have nonestimable variance because of stratum with a single cluster and overall small samole size (1%).	s index; Cl for Johnst County Os : second fc of the coho	, confiden on County teoarthriti sllow-up (1 srt were ag	ce interva /, North Ca is Project a [2], 2006-2 ged less th are not in	ll; n/a, not arolina. are as follk 2011; thirc 1an 55 yea	not applicable; rKOA, radiographic knee osteoarthritis; T1, time poin follows: baseline (T0), 1991-1997 (not included here because of diffe third follow-up (T3), 2013-2015; and fourth follow-up (T4), 2017-2018 years.	e; rKOA, ra ine (T0), 15) (T3), 2015 v have nor	diographic 191-1997 (1 3-2015; an	c knee ost not includ d fourth fr	eoarthriti ed here b ollow-up (s; T1, time ecause of T4), 2017- of stratum	e point 1; differenci 2018. Vwith a si	T2, time p es in x-ray ngle clust	oint 2; T3, ' assessm'	, time poin ent); first f	it 3; T4, tirr ollow-up (1 sample siz	ie point 4. [1]/cohort 7e (1%).

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Table 3. Weighted" point prevalence estimates and corresponding 95% CIs by sex and age group for four time points," 1999 to 2018	t prevalenc	estimat	es and col	rrespondin	g 95% UIS	by sex and	a age grou	p tor tour	time poini	s,~ 1999	to 2018					
Sex and age group	Knee	e Sympto	Knee Symptoms [% (95% CI)]	(I)]		rkoa [% (95% CI)]	95% CI)]		Seve	ere rKOA	Severe rKOA [% (95%	CI)]	Sympto	Symptomatic rKOA [% (95% Cl)]	3A [% (95	% CI)]
subgroups	Τ1	Τ2	T3	74	Τ1	Τ2	T3	Т4	Τ1	Т2	T3	T4	Τ1	T2	T3	Т4
Men																
45-54 years	42 (33-50)	42 34 (33-50) (18-50)	n/a ^c	n/a ^c	17 (11-24)	43 (29-56)	n/a ^c	n/a ^c	7 (3-12)	32 (19-44)	n/a ^c	n/a ^c	10 (5-15)	18 (8-29)	n/a ^c	n/a ^c
55-64 years	42	36	42	60	25	35	43	76	12	19	25	46	17	21	21	44
	(36-48)	(36-48) (27-44) (31-53)	(31-53)	(36-84)	(20-29)	(27-43)	(32-54)	(55-97)	(9-16)	(13-25)	(14-35)	(20-71)	(13-21)	(14-28)	(11-32)	(18-70)
65-74 years	46	27	31	45	41	52	56	58	22	23	28	22	23	18	20	31
	(39-52)	(39-52) (19-35) (23-40)	(23-40)	(27-62)	(35-47)	(43-62)	(47-66)	(44-72)	(17-27)	(17-30)	(20-37)	(10-34)	(18-28)	(12-24)	(13-28)	(15-47)
≥75 years	49	37	23	21 (9-33)	63		75	65		42	29	32	37	32	14	18 (7-28)
	(41-58)	(41-58) (28-47) (13-33)	(13-33)		(54-72)	(57-75)	(66-83)	(51-79)	(29-48)	(33-50)	(16-41)	(18-45)	(28-47)	(23-42)	(5-24)	
Women																
45-54 years	49	44	n/a ^c	n/a ^c	22	25	n/a ^c	n/a ^c	9 (6-12) 12 (3-22)	12 (3-22)	n/a ^c	n/a ^c		9 (1-17)	n/a ^c	n/a ^c
	(43-55)	(43-55) (26-61)			(17-27)	(13-36)							(14-23)			
55-64 years	47	38	37	43	26	39	47	50	14	24	34	23	18	23	27	28
	(43-52)	(43-52) (33-44) (28-46)	(28-46)	(28-58)	(22-30)	(33-45)	(37-57)	(32-68)	(12-17)	(19-29)	(25-42)	(13-34)	(15-21)	(18-28)	(18-37)	(15-41)
65-74 years	53	45	44	80 300	36	55	52	56	21	37	32	36	26	36	28	25
	(48-58)	(48-58) (40-49) (35-53)	(35-53)	(27-48)	(31-41)	(50-60)	(45-60)	(45-68)	(17-25)	(32-42)	(23-40)	(25-47)	(22-30)	(32-41)	(21-36)	(14-36)
≥75 years	60	43	41	48	59	64	65	75	37	45	44	53	37	38	34	40
	(54-65)	(54-65) (37-49) (33-49)	(33-49)	(38-57)	(52-65)	(58-70)	(56-74)	(65-85)	(31-42)	(39-51)	(36-53)	(41-65)	(32-43)	(32-44)	(26-42)	(29-50)
Abbreviation: Cl, confidence interval; n/a, not applicable; rKOA, radiographic knee osteoarthritis; T1, time point 1; T2, time point 2; T3, time point 3; T4, time point 4. ^a Weighted to the US Census for Johnston County, North Carolina. ^b Timepoints in the Johnston County Osteoarthritis Project are as follows: baseline (T0), 1991-1997 (not included here because of differences in x-ray assessment); first follow-up (T1)/cohort enrichment (T1*), 1999-2004; second follow-up (T2), 2006-2011; third follow-up (T3), 2013-2015; and fourth follow-up (T4), 2017-2018. ^c At T3 and T4, no members of the cohort were aged less than 55 years.	ce interval; us for John: nn County C 34; second s of the coh	n/a, not a ston Cour Ssteoarthi follow-up hort were	pplicable; vity, North (ritis Project (T2), 2006	rKOA, radic Carolina. t are as foll -2011; thir than 55 ye.	idiographic kni follows: baselir hird follow-up years.	ее osteoar าе (Т0), 19 <u>5</u> (ТЗ), 2013-	thritis; T1, 91-1997 (ու -2015; and	time poin ot included fourth foll	t 1; T2, tin d here bec low-up (T²	a point 2 ause of d 4), 2017-2	; T3, time ifferences 018.	point 3; T ₄ ; in x-ray a	4, time po Issessmen	int 4. nt); first fol	T) dn-woll	1)/cohort

noints ^b 1999 to 2018 ir tima Ę for C AC Ş <u>v</u> 95% 2 7 C C C estim ĉ noint Weighted^a Table 3. 25785745, 2021, 8, Downloaded from https://actjournals.onlinelibrary.wiley.com/doi/10.1002/act2.11295 by University Of North Carolina, Wiley Online Library on [09/102023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/doi/10.1002/act2.11295 by University Of North Carolina, Wiley Online Library on rules of use; OA articles are governed by the applicable Carolina, Wiley Online Library on [09/102023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/doi/10.1002/act2.11295 by University Of North Carolina, Wiley Online Library on [09/102023]. See the Terms and Conditions (https://onlinelibrary.wiley.com/doi/10.1002/act2.11295 by University Of North Carolina, Wiley Online Library on [09/102023]. See the Terms and Conditions (https://online.library.wiley.com/doi/10.1002/act2.11295 by University Of North Carolina, Wiley Online Library on [09/102023]. See the Terms and Conditions (https://online.library.wiley.com/doi/10.1002/act2.11295 by University Of North Carolina, Wiley Online Library on [09/102023].

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Population-Based Cohort	Location	Age (years)	Women (%)	Black (%)	BMI	XR Method	Prevalence of rKOA/sxKOA (%)
Framingham (6): 1983-1985	Massachusetts	≥60	58	0	Mean (SD): 25 (3-4) kg/m ²	AP WB	33/10
NHANES III (7): 1991-1994	United States	≥60	53	20	26% obese	AP NWB	37/12
Chingford (11): 1988-1989 and 2003-2004	United Kingdom	44-67	100	0	Median (IQR): 25 (23-28) kg/m ²	AP WB	14/nd and 48/nd
JoCo OA (8): 1991-1997	North Carolina	≥45	57	19	36% obese	AP WB	28/16

Table 4. Population-based cohorts with knee osteoarthritis prevalence data

Abbreviation: AP, anteroposterior; BMI, body mass index; IQR, interquartile range; JoCo OA, Johnston County Osteoarthritis Project; nd, no data; NHANES, National Health and Nutrition Examination Survey; NWB, non-weight-bearing; rKOA, radiographic knee osteoarthritis; sxKOA, symptomatic knee osteoarthritis; WB, weight-bearing; XR, x-ray or radiographic.

Black individuals, and participants with obesity had higher point prevalence of all knee outcomes.

This study analyzed JoCo OA data from 1999 to 2018, and the youngest age group in 1999 (T1/T1*) (mean age of 64 years) was much younger than those in many other studies (eg, Framingham or NHANES). By 2018, the mean age was approximately 73 years. During this time, several trends were noted. Although it is known that KOA increases with age, we saw dramatic increases in all age groups over time, particularly for rKOA but also for symptomatic rKOA. In contrast to Nguyen et al (10), we did not see a consistent increase in knee symptoms to account for the increase in symptomatic rKOA, rather observing a relatively steady increase in rKOA and severe rKOA over time. Of note, that study population was older and had a lower BMI, and pain questions differed from those in the present work. The subjective and mutable nature of pain make it a difficult construct to characterize in a longitudinal cohort with data collection years apart.

Our estimates are higher than those in the few other population-based studies available for comparison (Table 4). In the Framingham study, the mean age (73 years) was similar to that of our most recent follow-up (T4; 2017-2018) but completed many years earlier, in 1985; the prevalence of rKOA was 33% and that of severe rKOA was 16%, similar to contemporaneous estimates (6) but much lower than our current estimates of 61% and 35%, respectively. Similarly, we found the point prevalence of symptomatic rKOA to be much higher, 30% compared with 10% in Framingham (6) and 12% in NHANES (7) (completed in 1994). This is likely due to US population trends for age and obesity over this time frame, as well as differences across the cohorts (eg, age, race, BMI, and geographic location represented), imaging techniques, and statistical methodology.

In contrast, the marked increase in rKOA we observed over 18 years of follow-up in our longitudinal cohort (30% to 61%) is similar in magnitude to that seen in the Chingford cohort, in which an increase from 14% to 48% was found over a period of 14 years (11). The Chingford cohort is limited to older (median age 53 years at baseline) White women and therefore could not demonstrate the differences we were able to see by sex and race. However, differences by 5-year follow-up increments suggested a similar increase, with a prevalence of rKOA at 14% at baseline, 24% at Year 5, 36% at Year 10, and 48% at Year 15. Additionally, the BMI reported in other studies is generally much lower than that in JoCo OA (eg, the median BMI in Chingford was approximately 25 kg/m²) (11), with the higher obesity prevalence in JoCo OA likely more accurately reflecting current population trends.

A few studies have reported on the prevalence of OA in recent years using claims or registry data, which, although not directly comparable to our cohort-based estimates, reinforce the growing burden of OA. Using 2014 insurance claims data from Germany including more than 7 million adults (mean age 75 years; 70% women), the frequency of hip or knee OA was estimated at 21% (16). Another study, using Global Burden of Disease data, found that the frequency of hip and knee OA in six Nordic countries (Denmark, Finland, Greenland, Iceland, Norway, and Sweden) increased by 43% to more than 1.5 million adults from 1990 to 2015 (17).

The strengths of this study include the large, longitudinal population-based cohort with standardized follow-up over up to 18 years, the inclusion of Black and White men and women from a range of socioeconomic backgrounds, and the high reliability of the radiographic reads over time (all performed by a single expert musculoskeletal radiologist) using the optimal posteroanterior fixed-flexion protocol. By accounting for the complex sampling strategy and weighting to the US Census figures for Johnston County, we are able to provide more generalizable estimates of population point prevalence than studies without such a sampling strategy. As with any longitudinal study, the main limitation is loss to follow-up (primarily due to death in this aging group), although recalibration of the sampling weights to a common point in time may help in this regard, and this single cohort (with enrichment at T1*) allows for long-term follow-up assessments in ways than multiple cross-sectional samples could not. We performed multi-time point cross-sectional analyses as a first step. Future work will incorporate novel methods for a comprehensive incidence analysis accounting for interval censoring, competing risks, and sample survey features.

In conclusion, we provide longitudinal and updated personbased point estimates of the prevalence of knee symptoms, rKOA, severe rKOA, and symptomatic rKOA. Overall, these estimates are higher than many previously reported estimates from other cohorts but are similar to those from contemporary cohorts of similar age. These high point prevalence estimates support the large and increasing burden of KOA in the general population.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Nelson had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study conception and design. Nelson, Hu, Schwartz, Murphy, Helmick, Jordan, Golightly.

Acquisition of data. Nelson, Renner, Jordan, Golightly.

Analysis and interpretation of data. Nelson, Hu, Arbeeva, Alvarez, Cleveland, Schwartz, Murphy, Helmick, Callahan, Renner, Jordan, Golightly.

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