# Osteoarthritis and Cartilage



# Differences between race and sex in measures of hip morphology: a population-based comparative study



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# A R T I C L E I N F O

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# SUMMARY

*Objective:* This paper aims to (i) identify differences in measures of hip morphology between four racial groups using anteroposterior (AP) hip x-rays, and (ii) examine whether these differences vary by sex. *Methods:* 912 hip x-rays (456 individuals) from four racial groups (European Caucasians, American Caucasians, African Americans and Chinese) were obtained. Males and females (45–75 years) with no radiographic hip OA (Kellgren and Lawrence < Grade 2 or Croft < Grade 1) were included. Eleven features of hip joint morphology were analysed. Linear regression with generalised estimating equations (GEE) was used to determine race and sex differences in hip morphology. Post-hoc Bonferroni procedure was used to adjust for multiple comparisons.

*Results:* The final analysis included 875 hips. Chinese hips showed significant differences for the majority of measures to other racial groups. Chinese were characterised by more shallow and narrow acetabular sockets, reduced femoral head coverage, smaller femoral head diameter, and a lesser angle of alignment between the femoral neck and shaft. Variation was found between other racial groups, but with few statistically significant differences. The average of lateral centre edge angle, minimum neck width and neck length differed between race and sex (*p*-value for interaction < 0.05).

*Conclusions:* Significant differences were found in measures of morphology between Chinese hips compared to African Americans or Caucasian groups; these may explain variation in hip OA prevalence rates between these groups and the lower rate of hip OA in Chinese. Sex differences were also identified, which may further explain male-female prevalence differences for OA.

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#### Introduction

Hip OA is a leading cause of pain and disability globally due to its effects on functional movement and mobility<sup>1</sup>. The disease also represents a significant economic burden due to associated healthcare costs and loss of work<sup>2,3</sup>. Around 2.46 million adults in England over 45 have hip OA, which is expected to double by 2020 due to population aging<sup>1,3–5</sup>. Identifying predisposing risk factors for hip OA will allow preventative interventions to be designed for at-risk individuals<sup>6</sup>.

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The prevalence of hip OA is known to vary between racial groups<sup>7–9</sup>; in Chinese, hip OA is reportedly 80–90% lower than in American Caucasians<sup>8</sup>. In African American males, prevalence of hip OA appears slightly higher than in American Caucasian males (21% vs  $17\%)^9$ . Therefore, some population groups may be at increased risk of disease development.

Shape and morphological differences of the proximal femur and/or acetabulum are known to be associated with increased risk of hip OA<sup>10–16</sup>. Osseous deformities at the femur head-neck junction create a non-spherical head shape (cam morphology)<sup>11,13,14</sup>, while shape variants of the acetabulum include over-coverage (pincer morphology) and under-coverage (dysplasia)<sup>13,14</sup>. These morphologies may cause abnormal contact between the femur and acetabulum which, when symptomatic, lead to femoroacetabular impingement syndrome<sup>14</sup>. Previous studies have also identified racial differences in cartilage composition at the knee, which has implications for the hip<sup>17</sup>. Identifying variation in hip morphology associated with OA may allow identification of at-risk individuals or population groups.

Differences in hip joint shape and morphology have been identified between racial groups and the sexes. Chinese hips show reduced coverage with a more spherical head shape of the femur than Caucasians<sup>7,18</sup>, while African Americans show differences in proximal femur and acetabular measures to Caucasians<sup>19</sup>. Among African Americans<sup>20</sup>, Chinese<sup>8</sup> and Japanese<sup>21</sup>, males show greater prevalence of radiographic hip OA (RHOA) than females, with Caucasian groups showing mixed results<sup>20,22</sup>. Pincer-type morphologies are more common in women, with cam-type morphologies more prevalent in males<sup>12,23,24</sup>. These differences may lead to increased risk of OA through changes in joint biomechanics and loading<sup>10</sup>.

To date, hip joint morphology has not been compared in European Caucasians, American Caucasians, African Americans and Chinese in a single study. Our aims include (i) to determine which features of hip morphology vary among these groups; and (ii) to investigate the interaction between race and sex on morphological features. Understanding the impact of race and sex on hip morphology will deepen our understanding of pathways to disease development, underlining differences impacting on other OA-related outcomes with reported racial disparities, i.e., pain and function<sup>25,26</sup>, or surgical prosthesis types<sup>27</sup>.

# Methods

#### Description of cohorts

X-Ray data was acquired from three population-based studies; Chingford (European Caucasians), the Johnston County (JoCo) Osteoarthritis Project (American Caucasians, African Americans), and the Beijing Osteoarthritis Study (Chinese). Recruitment and sampling details are reported elsewhere<sup>20,28,29</sup>. Each cohort acquired images using a standardised radiographic protocol.

#### Chingford (CHIN) study

Chingford is a prospective, longitudinal cohort of OA and osteoporosis in women from the general population; all women aged 45–64 years and registered at the London-based practice were invited to participate<sup>29</sup>. Supine AP hip x-rays were obtained with a film-focus distance of 100 cm using a 70 kV peak (KvP).

#### Johnston County (JoCo) osteoarthritis project

The Johnston County Osteoarthritis Project (JoCo OA) is a USbased prospective, longitudinal cohort study of OA in a civilian, non-institutionalised population of African Americans and Caucasians, aged from 45 years, who were permanent residents in one of six townships in Johnston County; age and ethnicity data identified eligible households along streets within each township selected using stratified random sampling methods<sup>20</sup>. Supine AP hip x-rays were taken with feet in 15<sup>0</sup> internal rotation, with a film focus distance of 100 cm and 81KvP.

#### Beijing osteoarthritis (BOA) study

The Beijing Osteoarthritis (BOA) Study enlisted men and women over 60 from 3 central districts of Beijing, China; participants were recruited from randomly selected neighbourhoods in a randomly selected health section from each district<sup>28</sup>. Supine AP pelvic radiographs were obtained with feet in 15-30<sup>0</sup> internal rotation, using a film focus distance of 101 cm and 70-80KvP<sup>8</sup>.

#### Inclusion criteria

We aimed to select a random sample of 120 male hips and 120 female hips from each cohort to ensure adequate representation of each sex and racial group. Minimal sample size was determined *a priori* using Chingford mean ( $30.83^0$ ) and standard deviation ( $6.83^0$ ) data, based on an estimated difference of  $3^0$  in the lateral centre edge angle [LCE]. At 80% power, using a significance level of p = 0.05, the minimal number of hips to be included in each group was 81. Random selection was performed using automated techniques. The demographic details and a supine bilateral anteroposterior (AP) hip radiograph of each selected individual were obtained. Individuals were selected based on the following criteria: aged 45–75 and with no radiographic evidence of hip OA (Kellgren and Lawrence < Grade  $2^{30}$  or Croft < Grade  $1^{31}$ ), as to avoid measurements of interest being affected by bony remodelling from disease processes.

#### Hip morphology assessment

Morphometric data was obtained from included x-rays using OxMorf 2.0.0, a validated software program developed by the University of Oxford that assesses 23 hip morphology parameters. This software has shown high reproducibility for using hip morphology measures to predict incident total hip replacement in a population-based cohort<sup>11,19,32</sup>.

The bilateral hip x-rays of 456 individuals were analysed, with measurements taken from both the right and left hips. A total of 912 single hips were included in the analysis, which was adjusted to factor in two hips from the same person being included. Readers were blinded to race, sex and cohort along with subject demographic and clinical information. Hips were read by three researchers in the field of musculoskeletal imaging (KE, KL and CPA). KE and KL received prior training in the identification of musculoskeletal markers using OxMorf from orthopaedic surgeons specialising in femoroacetabular impingement (FAI), and against whom measurement repeatability was tested. Radiologists and orthopaedic surgeons were available for consultation during the analysis phase.

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Inter- and intra-reader reproducibility was tested between the researchers (KE, KL and CPA) using a subset of 50 images. X-rays were read in two phases; the initial phase was a pilot study designed to identify measures of interest, with the remaining x-rays later added to increase study power. The later x-rays were all read by a single reader (KE) and reproducibility repeated to ensure consistency.

We examined 11 characteristics of hip morphology previously suggested as putative factors in the aetiology of OA or on future risk of total hip arthroplasty (THA). These include measures of acetabular orientation (depth, width, depth to width ratio)<sup>33</sup>, acetabular coverage (LCE)<sup>11,23,32,33</sup>, minimum joint space width as calculated using Bezier curves<sup>30,34,35</sup>, femoral head asphericity (AP alpha angle)<sup>11,33</sup>, femoral morphology (neck length, minimum neck width, head diameter)<sup>36</sup>, femoral alignment (femoral neck shaft angle [FNSA])<sup>37</sup>. Pelvic width (inter-acetabular edge distance) along with the FNSA and acetabular depth to width ratio were measured due to likely sex-differences<sup>19,24</sup>. Hip morphology measures are described in Figs. 1 and 2.

#### Statistical analysis

Inter and intra-observer reliability was tested using intra-class correlation coefficients (ICCs) for continuous variables and kappa tests for non-continuous variables.

Unpaired *t*-tests compared age and BMI differences between individuals included and excluded in the analysis. Age and BMI distributions for each racial group and stratified by sex were summarised using means and standard deviations. Age and BMI differences between racial groups were assessed using Kruskal Wallis tests for non-normally distributed data and one-way analysis of variance (ANOVA) tests for normally distributed data.

To assess the relationship between racial groups and features of hip morphology, linear regression analyses with generalised estimating equations (GEE) were used to obtain mean and standard error (SE) values for each measurement of interest, adjusted by age, side and BMI. The GEE approach was used as it accounts for within person correlation (two hips from the same individual being included in the analysis)<sup>38</sup>. A post-hoc Bonferroni procedure corrected for multiple tests of significance using individual *p*-values<sup>39</sup>. Results were stratified by sex. The interaction between race and sex on each hip morphological measure was tested.

Data analysis was performed in STATA version 13 software<sup>40</sup>.

# Results

Reproducibility was excellent for all measures of femoral morphology (inter-reader ICC range, 0.9-1.0 (95% CI range, 0.8-1.0)). Measures of acetabular morphology showed moderate to excellent reproducibility (inter-reader ICC range, 0.5-1.0 (95% CI range, -0.005-1.0)). Moderate values were found for the alpha angle (kappa, 0.5-0.6 (SE 0.136-0.140)). ICC thresholds are defined as <0.5 (poor), 0.5 to 0.75 (moderate), 0.75 to 0.90 (good) and >0.90 (excellent)<sup>41</sup>.

Included subjects had complete demographic data (age, sex and BMI) and morphometric data available for all assessed variables. From the initial sample of 912 hips, 37 hips were excluded (Fig. 3); 12 due to incomplete demographic data, 15 due to missing morphometric data, 6 due to poor quality images, and 4 were excluded due to outlying data. In total, 875 hips (n = 510 females; n = 365 males) were included. No differences were found for age and BMI between included or excluded individuals.

Demographic characteristics of the included subjects (875 hips) are shown in Table I. Statistically significant differences were identified for age and BMI (p < 0.001) between racial groups in





**Fig. 2.** Description of assessed morphological measures: acetabular width, depth and depth to width ratio.**[AW] Acetabular width**: the length of a line extending from the lateral sourcil (ls) to the inferior medial rim of the acetabulum (rs). **[AD] Acetabular depth**: the length of a line extending from the deepest point of the acetabulum (da) to where it meets the line connecting the lateral sourcil with the inferior acetabular rim at a perpendicular angle. **Acetabular depth to width ratio (not shown)**: calculated from [AD] and [AW].



Fig. 3. Consort Diagram showing selection of included 456 individuals (912 hips). Key: European Caucasians (Chingford), American Caucasians (JoCo AC), African Americans (JoCo AA), Chinese (BOA), Females (F), Males (M). Numbers presented reflect the number of hips. \*Reasons for exclusion include missing demographic data, missing morphometric data, poor quality images or data outliers.

males and females. Mean age was lower among European Caucasians and Chinese, and higher in American Caucasians and African Americans. For BMI, mean values were lowest in Chinese, and highest in African Americans.

# Sex differences

Table II presents adjusted mean and SE data for all hip measures by sex. Male hips showed greater mean values than females for nearly all measures including, acetabular measures (depth and width), LCE, min JSW, AP alpha angle, and femoral measures (head diameter, neck width and length). Female hips were characterised by greater acetabular depth to width ratio, interacetabular distance and FNSA. Statistically significant differences were found for the majority of measurements, except the acetabular depth to width ratio. For unadjusted results, see Appendix 1.

#### Racial differences

Adjusted mean and SE for each hip measure by race and sex is summarised in Table III. Statistically significant differences based on Bonferroni corrected *p*-values are shown between males and females for each racial group by the symbols given; for example, acetabular depth is significantly different for Chinese males and females to each of the other groups, but no significant differences were found between the remaining three groups (Table III). For unadjusted results, see Appendix 2.

Chinese hips had significantly lower mean values for the majority of measures, including measures of acetabular orientation (acetabular depth, width, and depth to width ratio), the proximal femur (head diameter, neck width and neck length), and LCE. Chinese hips had lowest mean values for interacetabular distance, and highest mean values for the minJSW. In Chinese females, significant differences were observed for the minJSW (BOA, mean 4.03 mm; vs CHIN 3.53 mm (p = 0.001), vs JoCo-AA 3.53 mm (p < 0.001), and AP alpha angle (BOA, mean 52.16<sup>0</sup>; vs CHIN 77.54<sup>0</sup> (p < 0.001) compared to some, not all, racial groups.

African Americans had highest mean values for acetabular depth, acetabular depth to width ratio, LCE and FNSA, with the lowest values for minJSW and AP alpha angle. African American males also had highest mean values for femoral neck length. For the majority of measures, statistically significant differences were only identified in comparison to Chinese, except for the AP alpha angle, inter-acetabular distance and FNSA (females only). In females, the inter-acetabular distance and FNSA were statistically significant compared to all other groups; for example, FNSA (JoCo-AA mean 133.36<sup>0</sup>; vs CHIN 128.45<sup>0</sup> (p = 0.008); vs BOA 128.56<sup>0</sup> (p < 0.001); vs JoCo-AC 130.56<sup>0</sup> (p = 0.043)).

Caucasian groups showed higher mean values for interacetabular distance, and statistically significant to African Americans and Chinese (CHIN mean 156 mm; vs JoCo-AA 142.49 mm (p < 0.001); vs BOA 137.05 mm (p < 0.001) and JoCo-AC 150.35 mm; vs JoCo-AA 142.49 mm (p = 0.001); vs BOA 137.05 mm (p < 0.001)). European and American Caucasians showed higher mean values for acetabular width and femoral head diameter than other groups, significant only to Chinese. European Caucasian females and American Caucasian males showed the highest average values for the AP alpha angle and femoral neck width.

Between Caucasian groups, European Caucasian females showed higher mean values for some measures of the acetabulum (depth and width) and proximal femur (head diameter, AP alpha angle, neck width). American Caucasians exhibited greater

#### Table I

Demographic characteristics o	f the included	subjects	(875	hips)
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Characteristic Females ( $n = 510$ )				Males ( <i>n</i> = 365)					
	European Caucasian (CHIN)	American Caucasian (JoCo)	African American (JoCo)	Chinese (BOA)	<i>p</i> -value	American Caucasian (JoCo)	African American (JoCo)	Chinese (BOA)	p-value
n	144	118	118	130		119	112	134	_
Age (years)	54.24 (5.80)	69.85 (3.38)	69.31 (3.05)	64.05 (3.08)	0.0001	68.61 (2.70)	68.89 (2.91)	64.27 (2.46)	0.0001
BMI	25.18 (3.39)	28.29 (4.74)	28.87 (4.90)	24.90 (3.50)	<0.0001	26.62 (3.05)	27.43 (5.40)	24.94 (3.29)	<0.0001

Key: (CHIN) Chingford; (JoCo), Johnston County Cohort, (BOA) Beijing Osteoarthritis Study.

#### Table II

Hip morphology variables between males and females, adjusted for age, BMI and side (n = 875)\*

Variables/Sex	Females	Males	<i>p</i> -value†	
n	510	365		
Acetabular Orientation				
Acetabular depth (mm) (mean/se)	32.81 (.172)	36.68 (.254)	< 0.001	
Acetabular width (mm) (mean/se)	61.08 (.274)	69.20 (.370)	< 0.001	
DWR (mean/se)	.538 (.003)	.530 (.003)	0.082	
Acetabular Coverage				
LCE $(^{0})$ (mean/se)	29.02 (.398)	30.51 (.450)	0.019	
Joint Space Width (jsw)				
Min jsw (mm) (mean/se)	3.72 (.042)	3.92 (.055)	0.007	
Femoral Head Asphericity				
AP AA $(^{0})$ (mean/se)	55.80 (1.12)	62.43 (1.19)	< 0.001	
Femoral Morphology				
Head diameter (mm) (mean/se)	53.52 (.206)	60.55 (.293)	< 0.001	
Neck width (mm) (mean/se)	35.91 (.176)	42.24 (.226)	< 0.001	
Neck length (mm) (mean/se)	55.99 (.395)	59.08 (.526)	< 0.001	
Femoral Alignment				
FNSA ( <sup>0</sup> ) (mean/se)	130.18 (.360)	128.17 (.430)	0.001	
Anatomical Distance				
Inter-ace dist. (mm) (mean/se)	145.16 (.645)	134.16 (.699)	<0.001	

Key: (DWR) Acetabular depth to width ratio, (LCE) Lateral centre edge angle, (Min jsw) Minimum joint space width, (AP AA) Antero-posterior alpha angle, (FNSA) Femoral neck shaft angle, (Inter-ace dist.) Interacetabular edge distance.

\* Data shows means and standard errors adjusted for age, BMI and race, using GEE models to account for within person correlation.

<sup>†</sup> *P*-values for sex differences.

values for femoral neck length, FNSA and minJSW. Statistically significant differences were identified between groups for neck width (CHIN mean 39.27 mm; vs JoCo-AC 36.09 mm (p = 0.002)), and AP alpha angle (CHIN mean 77.54<sup>0</sup>; vs JoCo-AC 51.14<sup>0</sup> (p < 0.001)).

#### Interaction between race and sex

No significant interaction (P < 0.05) was found between race and sex for the majority of measures, with the exception of the LCE, minimum neck width and neck length (Appendix 3, Figs. 4–6). For these measures, the Chinese showed a significant average difference to American Caucasians and African Americans, and this varied by sex; for example, the difference in the LCE was greater in females than males, however, for the other two measures this difference was smaller among females than males.

#### Discussion

This study confirms variation exists in hip morphology measures between European Caucasians, American Caucasians, African Americans and Chinese males and females.

Chinese hips were markedly different, with significant differences for the majority of measures, which is consistent with previous studies<sup>7,42,43</sup>, Chinese hips were characterised by more shallow and narrow acetabular sockets and reduced femoral head coverage. They showed greater joint space width to other groups, and were only significantly different to European Caucasian females for the AP alpha angle.

Racial differences between other groups was less marked. African Americans had the highest mean values for nearly all measures related to acetabular morphology (depth, DWR and LCE), except the acetabular width; this shows African American hips are characterised by wider and deeper acetabular sockets and have greater

#### Table III

Hip morphology variables among race groups and stratified by sex, adjusted for age, BMI and side  $(n = 875)^*$ 

Variables	Females ( $n = 510$ )				Males ( <i>n</i> = 365)		
	European Caucasian (CHIN)	American Caucasian (JoCo)	African American (JoCo)	Chinese (BOA)	American Caucasian (JoCo)	African American (JoCo)	Chinese (BOA)
n	144	118	118	130	119	112	134
Acetabular Orientation	_				_		-
Acetabular depth (mm) (mean/se)	34.36 (.481)♦	33.89 (.383)♦	34.49 (.448)♦	29.65 (.325)† × ●	38.15 (.495)♦	38.61 (.558)♦	32.76 (.472) × ●
Acetabular width (mm) (mean/se)	63.66 (.790)♦	62.45 (.674) ♦	61.93 (.785) ♦	57.86 (.459)† × ●	71.14 (.766)♦	71.11 (.812) ♦	64.27 (.668) × ●
DWR (mean/se)	.540 (.007) ♦	.544 (.005) ♦	.560 (.007) ♦	.514 (.006)† × ●	.537 (.007) ♦	.544 (.006) ♦	.510 (.006) × •
Acetabular Coverage							<b>、</b>
LCE ( <sup>0</sup> ) (mean/se)	30.71 (.987)♦	31.35 (.935)♦	31.73 (1.00) ♦	24.01 (.774)† × ●	31.38 (.792)♦	32.10 (.900)♦	27.03 (.816) × ●
Joint Space Width (jsw)							. ,
Min jsw (mm) (mean/se) Femoral Head Asphericity	3.53 (.119)♦	3.70 (.122)	3.53 (.101)♦	4.03 (.064)†•	4.01 (.107)	3.79 (.099)	4.04 (.095)
AP AA ( <sup>0</sup> ) (mean/se) Femoral Morphology	77.54 (3.70) × ●◆	51.14 (2.90)†	50.14 (2.53)†	52.16 (2.20)†	62.87 (2.17)•	55.46 (2.14) ×	57.11 (2.28)
Head diameter (mm) (mean/se)	55.36 (.672)♦	55.14 (.571)♦	54.41 (.571)♦	50.50 (.340)† × ●	62.21 (.609) ♦	62.14 (.641) ♦	56.50 (.524) × ●
Neck width (mm) (mean/ se)	39.27 (.554) × ◆	36.09 (.444)†◆	36.96 (.526)♦	32.90 (.262)† × ●	43.77 (.449)♦	42.90 (.494)♦	38.54 (.386) × ●
Neck length (mm) (mean/	56.17 (1.23)♦	59.06 (1.06)♦	58.01 (1.08)♦	50.96 (.626)† × ●	60.92 (.976)♦	64.06 (.951)♦	53.50 (.963) × ●
Femoral Alignment							
FNSA ( <sup>0</sup> ) (mean/se)	128.45 (.910)•	130.56 (.888)•	133.36 (.866)† × ♦	128.56 (.691)•	129.58 (.748) ♦	130.05 (.637)♦	125.63 (.831) × ●
Anatomical Distance							. /
Inter-ace dist. (mm) (mean/ se)	/ 156.00 (1.84)•◆	150.35 (1.75)•◆	142.49 (1.77)† × ♦	137.05 (.996)† × ●	137.31 (1.43)•♦	130.24 (1.41) ×	128.64 (1.11) ×

Key: (CHIN) Chingford; (JoCo) Johnston County Cohort, (BOA) Beijing Osteoarthritis Study.

(DWR) acetabular depth to width ratio, (LCE) lateral centre edge angle, (AP AA) Alpha angle, (TIH) triangular index height, (FNSA) femoral neck shaft angle.

Statistically significant differences between racial groups are shown by the following symbols: †European Caucasians (Chin),×American Caucasians (JoCo-AC), • African

Americans (JoCo-AA), Chinese (BOA).

Each racial group is compared against each of the other racial groups for each sex category.

\* Data shows age and BMI adjusted means and standard errors from linear regression analysis, using GEE models to account for within person correlation.

lateral extension of the acetabulum. Findings show African Americans have reduced joint space and femoral head asphericity to other groups.

Our findings correspond to other studies which have evaluated race and sex differences in hip morphology between African Americans and American Caucasians<sup>18</sup>. We similarly found African Americans had more lateral extension of the acetabulum, deeper acetabular sockets, less femoral head asphericity and lesser joint space width than American Caucasians. We also found male hips showed greater mean values for acetabular depth and width<sup>18</sup>, but further that African Americans had overall higher mean values in males and females for these measures than American Caucasians, though non-significant. Our finding of greater femoral head asphericity in African American and American Caucasian males, also corroborates previous studies that found increased prevalence of cam morphology in males for these groups<sup>24</sup>.

The present study shows differences in hip morphology between Caucasian populations. Significant variation was identified between these groups for proximal femur measures (asphericity and neck width). European Caucasians have a wider femoral neck, with a wider and more aspherical femoral head. In American Caucasians, the femoral neck tends to be longer but more narrowed, at a greater degree of angulation to the femur, which may have an impact on weight bearing and distribution.

Concerning sex differences, males showed greater mean values for the majority of assessed hip measures; however, females showed greater average values for the inter-acetabular distance, FNSA and acetabular depth to width ratio, reflecting wider pelvises, a greater neck shaft angle, and a deeper acetabular socket. Our findings are largely consistent with those identified in previous studies between American Caucasians and African Americans<sup>18</sup>.

Our findings showed a statistically significant interaction between race and sex for some measures of hip morphology which, of those assessed here, included the LCE, the femoral neck width and neck length. It would be advisable for future studies on hip morphology to consider these interactions.

Studies have previously investigated the influence of genetic<sup>44,45</sup>, lifestyle<sup>46,47</sup> and cultural<sup>48</sup> factors on OA development; however, given the significant morphological variation in measures of the hip joint shown between racial groups, and their potential effect on weight distribution and biomechanics, differences in hip joint morphology are likely to contribute to hip OA prevalence variation.

This is currently the only study comparing hip morphology between four racial groups including European Caucasians, American Caucasians, African Americans and Chinese; it is also the only study comparing different Caucasian groups within the same study, where significant differences were found in femoral head asphericity and neck width.

Limitations to this study include the use of AP pelvic radiographs, as MRI may be more sensitive to detecting bony changes around the lateral acetabular surface; however, we are not aware of large population-based cohorts using this modality for all racial groups assessed. Given the x-rays were obtained from multiple sites; differences in equipment and calibration may contribute to a degree of technical variation in measurements. All morphologies are affected by patient position, which may change the angle or length of the pelvic bones in relation to the X-ray film; however, each cohort obtained x-rays using a standardised radiographic protocol, and a visual assessment was made to ensure no abnormal pelvic tilt or rotation was present. Pelvic tilt and rotation was not quantified due to the obscurity of the pubic symphysis in a proportion of x-rays.

There are sources of bias that may affect interpretation of the results; hip OA-related morphology would likely already be present for older adults, and by selecting individuals showing no RHOA we may be obtaining a depleted proportion of morphological features related to disease development. Some morphological differences may be influenced by variation in bone size between individuals. Use of a UK-based cohort as representative of a European population was due to logistical reasons and X-ray availability; possible inter-population differences may limit the generalisability of these findings across European groups. Additionally, other confounders than those considered may have an effect on the level of variation in the data; however, we were able to account for a number of the main confounders routinely-collected by cohorts investigating hip OA.

Given there is variation among racial groups and between sexes, future studies investigating hip morphology and OA may want to account for these risk factors. Morphological differences likely indicate different pathways to disease development, which potentially require different treatment. Knowing where the morphological differences lie, future work could explore differences in baseline and follow up in OA subjects to identify if, and to what extent, changes have occurred in these measures along with patterns of expression of OA-related radiographic features; a modelling approach may help identify which changes in morphological features, singly or in combination, are associated with increased risk of hip OA. While this study has confirmed that significant differences exist in hip morphology between racial groups, further work could investigate which differences are clinically meaningful and have an effect on other outcomes for patients with OA, such as pain and function. Given the differences in hip joint morphology, we may also look at introducing standards for defining and classifying RHOA for different racial groups (i.e., standardised use of Kellgren and Lawrence criteria assumes similar presentation and severity of the disease across all groups).

# Conclusion

Hip morphology measures show race and sex differences between European Caucasians, American Caucasians, African Americans and Chinese. Significant differences were identified among all groups, but in particular the Chinese. Importantly, significant differences were identified between races for OA-related measures. Sex differences were present, with larger average values in males for the majority of hip measures. These race and sex differences may help explain prevalence differences in rates of hip OA between these groups.

# Author contributions

Conception and design: KML, KE, NKA; Data acquisition: AEN, JMJ, MN, KE, KML, CPA; Data analysis and interpretation: KE, KML, MTS, NKA; Drafting of article: KE, KML, MS; Review of content: all authors; Approval of submitted version: all authors.

#### **Conflict of Interest**

Within the submitted work; MN reports grants from the NIH (HHSN268201000019C TO); AEN reports grants from NIAMS (K23AR061406 and P60AR30701) and CDC/ASPH (S043 and S3486).

Outside the submitted work; NKA reports personal fees from Pfizer, Regeneron, Eli Lily, Freshfields Bruckhaus and Flexion, with research grants from Merck; AEN reports personal fees from GSK, Flexion, MedScape, Health Press Ltd and the University of Colorado, with research grants from NIAMS, CDC and RRF; JMJ reports board membership of the American College of Rheumatology (2014–2016), and personal fees from Samumed (completed 2015) and Flexion (completed 2016).

Remaining authors declare no conflicts of interest.

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# Appendix 1. Hip morphology variables between males and females, unadjusted for age and BMI $(n = 875)^*$

Variables/Sex	Females	Males	<i>p</i> -value <sup>‡</sup>
n	510	365	
Acetabular Orientation			
Acetabular depth (mm) (mean/se)	32.84 (.173)	36.65 (.258)	< 0.001
Acetabular width (mm) (mean/se)	61.13 (.276)	69.13 (.377)	< 0.001
DWR (mean/se)	.538 (.003)	.531 (.003)	0.088
Acetabular Coverage			
LCE ( <sup>0</sup> ) (mean/se)	29.09 (.401)	30.41 (.448)	0.036
Joint Space Width (jsw)			
Min jsw (mm) (mean/se)	3.72 (.042)	3.92 (.055)	0.005
Femoral Head Asphericity			
AP AA ( <sup>0</sup> ) (mean/se)	55.82 (1.10)	62.41 (1.18)	< 0.001
Femoral Morphology			
Head diameter (mm) (mean/se)	53.56 (.210)	60.49 (.298)	< 0.001
Neck width (mm) (mean/se)	35.97 (.179)	42.15 (.234)	< 0.001
Neck length (mm) (mean/se)	55.97 (.391)	59.10 (.523)	< 0.001
Femoral Alignment			
FNSA ( <sup>0</sup> ) (mean/se)	130.15 (.360)	128.21 (.431)	0.001
Anatomical Distance			
Inter-ace dist. (mm)	145.31 (.643)	133.95 (.712)	< 0.001
(mean/se)			

Key: (DWR) Acetabular depth to width ratio, (LCE) Lateral centre edge angle, (Min jsw) Minimum joint space width, (AP AA) Antero-posterior alpha angle, (FNSA) Femoral neck shaft angle, (Inter-ace dist) Interacetabular edge distance.

\*Data presented means and standard errors adjusted for age, BMI and race, using GEE models to account for within person correlation.

<sup>‡</sup>*P*-values for differences between sex.

# Appendix 2. Hip morphology variables among race groups and stratified by sex, unadjusted $(n = 875)^*$

Variables	Females ( $n = 510$ )		Males ( $n = 365$ )				
	European Caucasian (CHIN)	American Caucasian (JoCo)	African American (JoCo)	Chinese (BOA)	American Caucasian (JoCo)	African American (JoCo)	Chinese (BOA)
n	144	118	118	130	119	112	134
Acetabular Orienta	ation						
Acetabular depth (mm)	34.40 (.291)♦	33.93 (.354)♦	34.61 (.359)♦	29.46 (.320) †×∙	38.20 (.473)♦	38.67 (.473)♦	32.66 (.365) ×∙
Acetabular width (mm)	63.58 (.479)♦	62.61 (.544)♦	62.18 (.638)♦	57.58 (.459)† ×∙	71.07 (.673)♦	71.13 (.730)♦	64.31 (.498) ×∙
DWR (mean/se)	.542 (.005) ♦	.543 (.005) ♦	.559 (.006) ♦	.513 (.006)†×•	.539 (.006) ♦	.545 (.005) ♦	.509 (.005)ו
Acetabular Covera	ge						
LCE ( <sup>0</sup> ) (mean/se)	30.96 (.661)♦	31.36 (.735)♦	31.92 (.852)♦	23.56 (.791)† ×∙	31.49 (.727)♦	32.27 (.835)♦	26.79 (.660) ×∙
Joint Space Width	(jsw)						
Min jsw (mm) (mean/se)	3.57 (.0.75)♦	3.66 (.100)♦	3.49 (.084)♦	4.05 (.062)†∙×	3.98 (.100)	3.76 (.094)♦	4.09 (.083)•
Femoral Head Asp	hericity						
AP AA ( <sup>0</sup> ) (mean/se)	75.80 (2.27)ו◆	52.12 (2.27)†	50.91 (1.91)†	52.50 (2.20)†	62.88 (2.00)•	55.65 (1.94)×	56.94 (1.80)
Femoral Morpholo	ogy						
Head diameter (mm)	55.45 (.353)♦	55.17 (.453)♦	54.54 (.462)♦	50.25 (.340)† ×∙	62.14 (.538)♦	62.14 (.580) ♦	56.56 (.394) ×∙
(mean/se)							
Neck width (mm) (mean/se)	38.71 (.323)× ◆	36.54 (.357)†◆	37.49 (.426)♦	32.63 (.271)† ×∙	43.72 (.397)♦	42.96 (.474)♦	38.54 (.297) ×∙
Neck length (mm) (mean/se)	55.44 (.814) × ◆	59.50 (.776) † <b>◆</b>	58.39 (.889)♦	51.02 (.601)† ×∙	60.50 (1.02)♦	63.52 (.847)♦	54.31 (.723) ×∙
FNSA ( <sup>0</sup> ) (mean/se)	129.67 (.518)∙	129.80 (.787)•	132.67 (.710)†×◆	128.54 (.673)•	129.50 (.750) ♦	129.95 (.582) ♦	125.79 (.779) ×∙
Anatomical Distan	ce						
Inter-ace dist. (mm (mean/se)	) 155.34 (1.05)•◆	150.90 (1.42)•◆	143.16 (1.44)†×◆	136.66 (.984)† ×●	137.57 (1.33)•♦	130.90 (1.35)×	127.86 (.854) ×

\*Data presented means and standard errors unadjusted for confounders, using GEE models to account for within person correlation.

Key:(CHIN) Chingford; Johnston County Cohort (JoCo), Beijing Osteoarthritis Study (BOA). (DWR) acetabular depth to width ratio. (LCE) lateral centre edge angle, (AP AA) Alpha angle, (TIH) triangular index height (FNSA), femoral neck shaft angle.

†European Caucasians (Chin), × American Caucasians (JoCo), • African Americans (JoCo), ◆ Chinese (BOA).

# Appendix 3



Fig. 4. A margins plot showing the effect between race and sex on Lateral Centre Edge Angle.



Fig. 5. A margins plot showing the effect between race and sex on minimum neck width.



Fig. 6. A margins plot showing the effect between race and sex on neck length measure.

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