Received: 12 October 2019 | Revised: 20 February 2020 | Accepted: 21 March 2020

DOI: 10.1002/ajpa.24058

RESEARCH ARTICLE

American Journal of PHYSICAL ANTHROPOLOGY

WILEY

Intrapopulation variation in lower limb trabecular architecture

Bram Mulder[1] | **Jay T. Stock**[1,2,3] | **Jaap P. P. Saers**[1] | **Sarah A. Inskip**[1] | **Craig Cessford**[1] | **John E. Robb**[1]

[1]University of Cambridge, McDonald Institute for Archaeological Research, Cambridge, UK

[2]Department of Anthropology, University of Western Ontario, London, Canada

[3]Department of Archaeology, Max Planck Institute for the Science of Human History, Jena, Germany

Correspondence
Bram Mulder, McDonald Institute for Archaeological Research, Department of Archaeology, University of Cambridge. Downing Street, Cambridge CB2 3ER, UK.
Email: bm509@cam.ac.uk

Funding information
Wellcome Trust, Grant/Award Number: 2000368/Z/15/Z

Abstract

Objectives: Trabecular structure is frequently used to differentiate between highly divergent mechanical environments. Less is known regarding the response of the structural properties to more subtle behavioral differences, as the range of intrapopulation variation in trabecular architecture is rarely studied. Examining the extent to which lower limb trabecular architecture varies when inferred mobility levels and environment are consistent between groups within a relatively homogenous population may aid in the contextualization of interpopulation differences, improve detectability of sexual dimorphism in trabecular structure, and improve our understanding of trabecular bone functional adaptation.

Materials and methods: The study sample was composed of adult individuals from three high/late medieval cemeteries from Cambridge (10th–16th c.), a hospital (n = 57), a parish cemetery (n = 44) and a friary (n = 14). Trabecular architecture was quantified in the epiphyses of the femur and tibia, using high resolution computed tomography.

Results: The parish individuals had the lowest bone volume fraction and trabecular thickness in most regions. Multiple sex differences were observed, but the patterns were not consistent across volumes of interest.

Discussion: Differences between the three groups highlight the great variability of trabecular bone architecture, even within a single sedentary population. This indicates that trabecular bone may be used in interpreting subtle behavioral differences, and suggests that multiple archaeological sites need to be studied to characterize structural variation on a population level. Variation in sex and group differences across anatomical locations further demonstrates the site-specificity in trabecular bone functional adaptation, which might explain why little consistent sexual dimorphism has been reported previously.

KEYWORDS

bone functional adaptation, intrapopulation variation, lower limb, sexual dimorphism, trabecular bone

---

1 | INTRODUCTION

Demonstrable structural differences in trabecular bone exist between species as well as between populations within a species (Christen, Ito, Galis, & van Rietbergen, 2015; Ryan & Ketcham, 2002b, 2005; Ryan & Shaw, 2012, 2015; Saers, Cazorla-Bak, Shaw, Stock, & Ryan, 2016; Saers, Ryan, & Stock, 2019b). Research classifying human populations by behavioral characteristics and comparing their trabecular structure has thus begun to unravel the effects of habitual loading on trabecular morphology (Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2016; Saers et al., 2019b; Scherf, Wahl, Hublin, & Harvati, 2016). Although the complexity of bone functional adaptation and the multitude of factors contributing to trabecular morphology are widely acknowledged (Kivell, 2016, Saers et al., 2019b), structural differences in lower limb trabecular bone between broad categories of subsistence-related mobility suggest that subsistence behavior is a key determinant of overall habitual loading and potentially a major driver of lower limb trabecular variation in humans (Chirchir, Ruff, Junno, & Potts, 2017; Doershuk et al., 2019; Saers et al., 2016; Saers et al., 2019b). This idea is strengthened by a lack of differences found when inferred levels of mobility are similar between populations (Chirchir et al., 2017; Doershuk et al., 2019). However, the interpretation of results is normally confounded by the geographic and temporal diversity of the populations studied. We therefore report variation in the trabecular architecture of a sample with a relatively narrow date range, comprised of individuals from a parish cemetery, a hospital, and an Augustinian friary, all from high/late medieval Cambridge (10th–16th century), United Kingdom. Because the three groups are believed to form a single population, this approach allows us to assess whether groups with similar levels of inferred mobility and from the same geographical and temporal background differ in their trabecular architecture, and whether a single cemetery can serve as representative of an entire population. Using a large sample (n = 115) composed of three groups with similar mobility levels may furthermore provide the statistical power to detect sexual differences in trabecular bone.

1.1 | Bone functional adaptation and terrestrial mobility

Trabecular bone is a highly plastic tissue that adapts its architecture to changes in loading conditions. An optimum strain level is maintained by shifting the balance between bone formation and resorption in response to tissue strains (Frost, 2001, 2003; Lanyon, 1984). The acquisition of trabecular tissue is thus stimulated by enhanced mechanical loading, whereas prolonged limb disuse may lead to net bone loss (Cunningham et al., 2018). Even though the ways in which such mechanical stimuli are sensed and translated into remodeling signals are still somewhat enigmatic, the broad concept of functional adaptation in trabecular bone has been widely demonstrated through a combination of computational modeling (Huiskes, 2000; Tsubota, Adachi, & Tomita, 2002), animal models (Barak, Lieberman, & Hublin, 2011; Sugiyama et al., 2012), and comparisons between groups of athletes (Best, Holt, Troy, & Hamill, 2017; Harrison et al., 2011), archaeological populations (Ryan & Shaw, 2015; Saers et al., 2016) or non-human primates (Dunmore, Kivell, Bardo, & Skinner, 2019; Ryan & Shaw, 2012). These findings indicate a dependency of bone structure on directionality and magnitude of habitual loading, supporting the idea of a trabecular form-function relationship. Anthropologists have drawn on this concept to use trabecular bone as record of loading history, and to employ it in interpreting past behavior (DeSilva & Devlin, 2012; Barak, Lieberman, Raichlen, et al., 2013; Su & Carlson, 2017; Skinner et al., 2015).

The study of skeletal biomechanics and its relationship with loading history has for long revolved around estimations of bone mechanical properties from diaphyseal cross-sections. Such research typically focused on relative activity levels by comparing handedness (Shaw & Stock, 2009; Trinkaus, Churchill, & Ruff, 1994), sexual differences (Ruff, 1987, 2005), degrees of terrestrial mobility (Marchi, Sparacello, & Shaw, 2011; Shaw & Stock, 2013; Stock & Pfeiffer, 2001), or different subsistence strategies (Ruff et al., 2015; Ruff, Larsen, & Hayes, 1984; Sládek et al., 2016; Stock et al., 2011). Increased availability of high-resolution non-invasive imaging over the past two decades has extended this research to include trabecular bone. Trabecular bone has a greater surface-area-to-volume-ratio, which is thought to cause a generally higher turnover rate (Isales & Seeman, 2018; but see Parfitt, 2002). Moreover, the loss of responsivity to loading with age is different in cortical and trabecular bone (Birkhold et al., 2014; Meakin, Galea, Sugiyama, Lanyon, & Price, 2014; Willie et al., 2013). Thus, the functional adaptation of cortical and trabecular bone is not necessarily equally responsive to loading. A better understanding of variation in trabecular bone might complement the reflection of past activity from diaphyseal cross-sections.

Early anthropological work on trabecular variation focused on primates with contrasting locomotor patterns (Fajardo & Müller, 2001; Ryan & Ketcham, 2002a, 2002b, 2005). Such comparative approaches were later used to interpret the trabecular architecture of fossil hominins and its relationship to behavior (Barak, Lieberman, Raichlen, et al., 2013; Skinner et al., 2015; Su & Carlson, 2017). Relatively little attention has been paid to variation within and between human populations. Some studies have looked at ontogenetic changes in humans (Gosman & Ketcham, 2009; Raichlen et al., 2015; Ryan & Krovitz, 2006; Saers, Ryan, & Stock, 2019a), while others have compared trabecular parameters between populations with varying degrees of activity (Chirchir, 2019; Chirchir et al., 2015; Chirchir et al., 2017; Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2016; Saers et al., 2019b; Scherf et al., 2016; Stephens, Kivell, Pahr, Hublin, & Skinner, 2018). These have documented structural differences in trabecular bone across a variety of lifestyles, but within-population variation and the sensitivity of trabecular bone to subtle lifestyle differences is poorly understood.

Studying the effects of contrasting lifestyles as inferred from archaeological, historical, or ethnographical records, on bone robusticity, can be a valuable tool in testing the principles of bone functional adaptation. For example, the extent to which a population's subsistence strategy relies on terrestrial mobility has been positively correlated with lower limb diaphyseal properties (Holt, 2003; Larsen, 1995; Macintosh, Davies, Pinhasi, & Stock, 2015; Macintosh, Pinhasi, & Stock, 2014b; Ruff, 1987; Ruff et al., 1984; Stock, 2006; Stock & Pfeiffer, 2001) and has been shown to affect trabecular bone mass and trabecular thickness (Ryan & Shaw, 2015; Saers et al., 2016; Saers et al., 2019b). It is thought that the decreased bone strength frequently observed in agricultural populations is the result of a relatively sedentary lifestyle associated with food production. This seems to be a temporal trend: even after the adoption of agriculture mobility levels continue to decrease, potentially as a result of technological innovation (Holt et al., 2018; Macintosh, Pinhasi, & Stock, 2014a; Macintosh et al., 2014b; Ruff et al., 2015). Interpretation of such trends is not straightforward, however, as a multitude of factors contribute to skeletal robusticity (Kivell, 2016).

Travel over rugged terrain increases locomotor loads placed on the lower limbs which may complicate the interpretation of interpopulation differences in lower limb structure (Burr et al., 1996). Several studies indicate a correlation between terrain type and lower limb bone strength (Higgins, 2014; Holt & Whittey, 2019; Holt et al., 2018; Ruff, 1999), likely as a result of the greater anterior–posterior bending loads associated with climbing. The assessment of mobility differences between populations thus requires consideration of terrain type, which may remove some of the otherwise significant interpopulation differences, but doing so requires large samples (Holt & Whittey, 2019; Stock & Pfeiffer, 2001). Other ecogeographical factors may similarly affect skeletal phenotype. For example, climate is believed to play a role in determining body composition (Wells, 2012), body breadth (Ruff, 1994), and limb proportions (Temple, Auerbach, Nakatsukasa, Sciulli, & Larsen, 2008), and bone plasticity is in part regulated by temperature (Robbins et al., 2018).

The direct inference of activity patterns from bone strength indices is further challenged by several controlled experiments suggesting that bone is not always remodeled in the regions experiencing the greatest strain (Bertram & Swartz, 1991; Lieberman, Polk, & Demes, 2004; Wallace et al., 2014). Local osteogenic responses to loading depend on a multitude of mechanical variables such as strain rate (Cowin, 2007; LaMothe, Hamilton, & Zernicke, 2005; Turner, Owan, & Takano, 1995), magnitude (Birkhold, Razi, Duda, Checa, & Willie, 2017; Hsieh, Robling, Ambrosius, Burr, & Turner, 2001; but see Judex, Gross, & Zernicke, 1997) and frequency (Birmingham et al., 2015; Hart et al., 2017), while bone tissue may also become desensitized after prolonged sessions of increased loading (Robling, Hinant, Burr, & Turner, 2002; Turner & Robling, 2003). The interplay between these factors rather than their sum is essential in inducing bone formation (see Pivonka, Park, & Forwood, 2018).

The lack of a direct correlation between loading conditions and the adaptive response in bone may to some extent also be attributed to genetic variation. Genetics govern skeletal phenotype but also its responsivity to mechanical loading (Peacock et al., 2018; Robling, Warden, Shultz, Beamer, & Turner, 2007; Wallace, Demes, & Judex, 2017; Wallace, Tommasini, Judex, Garland Jr, & Demes, 2012). In a study of two populations of mice that were bred for genetic heterogeneity, Wallace, Judex, and Demes (2015) found significant differences in their adaptive response to exercise. This corroborates the observation that bone strength indices differ more between populations of inbred mice than between exercised subjects and controls within those same populations (Judex, Zhang, Donahue, & Ozcivici, 2013; Peacock et al., 2018; cf. Ruff, Warden, & Carlson, 2018; see also Judex et al., 2004)

Despite the complexity of the link between behavior and trabecular structure, there is a growing body of evidence that suggests that habitual activity, such as that related to subsistence strategy, is a key driver of trabecular bone remodeling (Chirchir et al., 2015; Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2016; Saers et al., 2019b; Scherf et al., 2016; Stephens et al., 2018). Previous work has found that highly mobile populations had improved trabecular structure in the lower limb compared to more sedentary populations, with greater bone volume fraction and greater trabecular thickness (Chirchir, 2019; Chirchir et al., 2015; Chirchir et al., 2017; Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2016; Saers et al., 2019b). In turn, sedentary populations did not mutually differ in trabecular properties, which reinforces the hypothesized link between trabecular structure and inferred mobility (Chirchir et al., 2017; Doershuk et al., 2019; Ryan & Shaw, 2015). Such findings enhance understanding of past activity as well as bone functional adaptation. However, these studies have been limited in sample size per population (~20), which means that a better appreciation of normal variation in trabecular microstructure within populations is needed to put interpopulation differences into perspective. Here we analyze trabecular variation in a large sample from medieval Cambridge, United Kingdom (n = 115) to advance our understanding of normal variation in trabecular microstructure and to provide the necessary statistical power to detect sexual differences. By composing this single sample of individuals from three separate cemeteries we may furthermore examine the extent to which groups with similar inferred levels of mobility have similar trabecular structure. Since previous studies did not find significant differences between sedentary populations despite differences in their geographical and temporal backgrounds, we expect to find no significant differences between our three groups.

2 | MATERIALS

To investigate the variability in bone structure between subgroups of a single sedentary population we used the skeletal remains from three cemeteries from high/late medieval Cambridge, United Kingdom (10th–16th century). These were associated with a parish church, a hospital, and an Augustinian friary, respectively, and all located within 3 km of each other (Figure 1). Date ranges for each of the sites were derived from a combination of historical documents, radiocarbon dating, and artifact typologies.

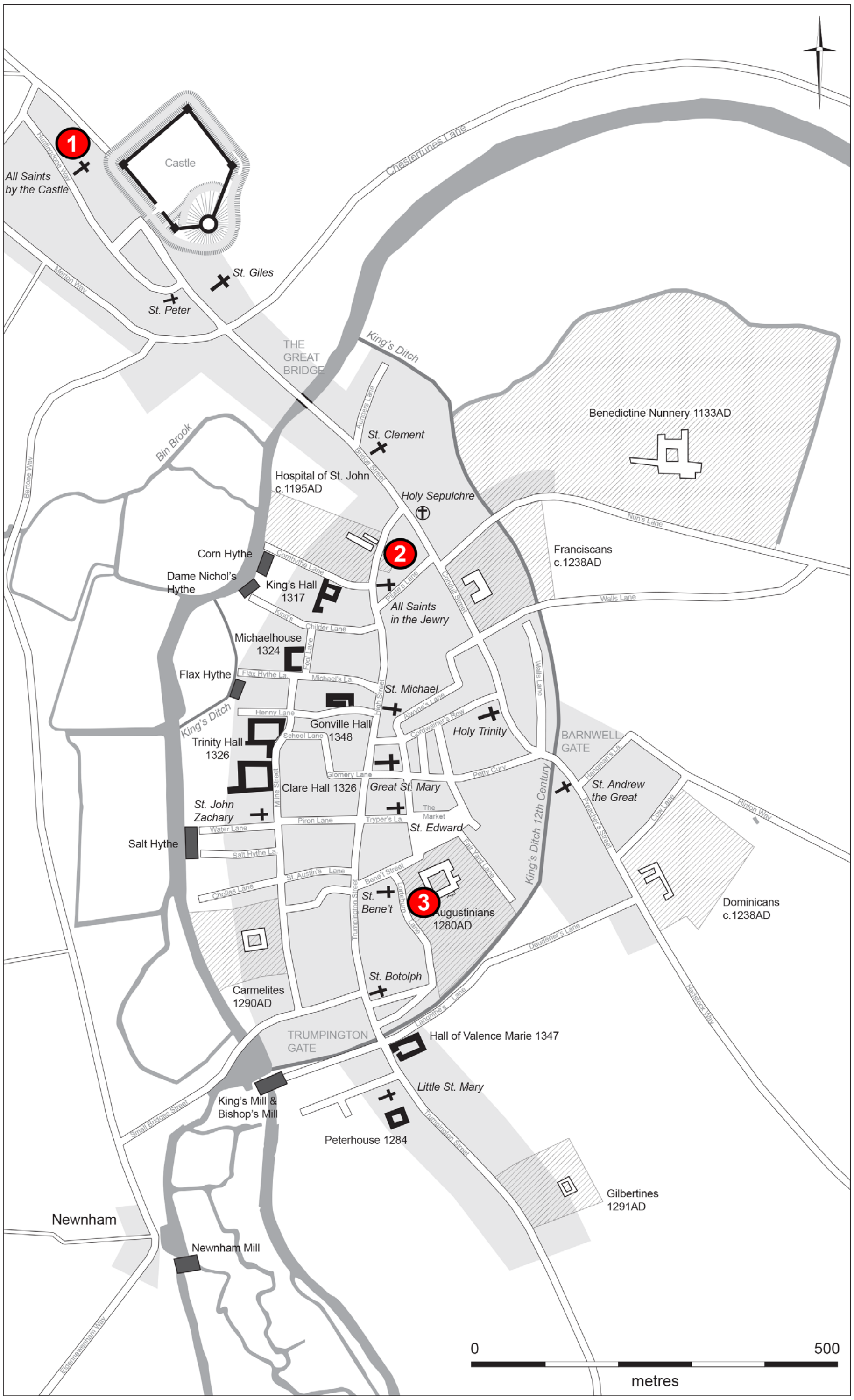

FIGURE 1 Medieval Cambridge c. 1,350 CE. Original map produced by Vicki Herring for the After the Plague project. (1) Parish cemetery of All Saints by the Castle (Comet Place), (2) Cemetery of the Hospital of St. John the Evangelist (Old Divinity School), (3) Augustinian Friary (New Museums)

2.1 | Parish church

Medieval Cambridge accommodated multiple parish churches, one of which was All Saints by the Castle, north of the River Cam. The associated cemetery was in use between the mid-10th and mid-14th centuries and largely consisted of simple, earth-cut graves. Some interments included head support stones, and there was evidence for at least one coffin and one stone lined grave (Cessford & Dickens, 2005). Over 200 skeletons were excavated in 1973 at the site known as Comet Place. As a parish cemetery, All Saints by the Castle is used here to represent the general urban population. The parish had a socioeconomically mixed population, which does appear to be broadly representative of the town as a whole. Although an urban parish, its proximity to the town fields means that a proportion of the population was likely involved in agricultural/rural activities. Their diet may to some extent have been determined by social class, but was generally dominated by bread and ale, in particular prior to the fourteenth century (Dyer, 1989).

2.2 | Hospital of St. John's

On the other side of the river was the hospital of St. John the Evangelist, at the location of what is now St. John's College. The hospital's burial ground was mainly in use between the early 13th and mid/late 15th century, and from this period the remains of 400 individuals were uncovered during excavations, likely representing the hospital residents plus a range of other groups (Cessford, 2015). It is not entirely clear who ended up in the hospital, or for how long people stayed there. Documents mention the care for the poor and infirm among its purposes, as well as the “maintenance of poor scholars and other sick people” (Cessford, 2015). Disabled or wounded people as well as lepers were not admitted to the hospital, nor were pregnant women and the “insane” (Rubin, 1987). As with the parish, bread and ale will have been consumed on a regular basis. Although meat was a luxury product, it was served up to three times a week to the brethren, and likely to the residents as well (Rubin, 1987).

2.3 | Augustinian friary

Further south, at the New Museums Site, was an Augustinian Friary. Accommodating between 20 and 75 friars at any time, the friary was in use between the late 13th and mid-16th century (Cessford, 2017). It was declared a *studium generale*, or international study center, by the papacy, illustrating the status the friary had acquired by the fourteenth century. This involved the presence of foreign students, which indicates a potential diversity of backgrounds of those living in the friary (Laferriere, 2017). The people buried in the excavated areas are believed to have principally been friars, plus some lay individuals (Cessford, 2017). The majority of the studied skeletons derive from a cemetery in use between the late 13th and mid-14th centuries, while others were buried in the friary chapter house between the mid-14th and mid-16th centuries. Some people were buried clothed, as indicated by the recovery of belt buckles, textiles and leather girdles. Although the friars may have carried out manual labor in and around the friary, surviving evidence suggests that they were, or at least should have been, mostly involved in preaching, teaching, studying, and praying (Andrews, 2006). The Augustinian friars were officially not allowed to eat meat, although exceptions were made for the elderly and infirm, but fish, dairy, and eggs appear to have been consumed on a regular basis (Laferriere, 2017).

Previous studies of past behavior have shown bone structural differences between populations by terrain type (e.g., Ruff, 1999), climate (e.g., Stock, 2006), degrees of urbanization (e.g., Holt et al., 2018), and subsistence strategy (e.g., Saers et al., 2019b). The groups in the present study largely overlap geographically and temporally and are here regarded as having formed a single population. While habitual activities arguably varied within medieval Cambridge, there is insufficient support for a distinct classification of activity levels between sites, and each of the three sites can be characterized as urban sedentary.

2.4 | Sample selection

Only individuals whose sex could reliably be determined were included. Sex was determined based on pelvic and skull morphology (Brickley & McKinley, 2004; Buikstra & Ubelaker, 1994) and in some cases confirmed with aDNA analysis (Inskip et al., 2019). Age was estimated based on a combination of methods, including pelvic morphology, dental development, and rib and clavicle morphology. Age was estimated and sex was determined by a single observer (SAI).

The distribution of individuals across age categories was similar between groups when the youngest and oldest age categories were excluded (see Supporting Information 2.1 and 3.1 for distributions). As this exclusion had little effect on the results, we report the results for the full sample. The analyses without the youngest and oldest adults are made available in Supporting Information 3 for comparative purposes.

A total of 115 individuals met the criteria for inclusion: 57 from the hospital, 44 from the parish, and 14 from the friary. Only one female was included in the friary group, which made statistical comparison of means with females from the other sites impossible. Only the friary males were therefore analyzed statistically in comparison to the males from the other two sites.

3 | METHODS

3.1 | Trabecular morphometry

One femur and tibia from each individual were scanned using the Nikon Metrology XT H 225 ST HR computed tomography (CT) scanner at the Cambridge Biotomography Center. Specimens were placed upright in an acrylic tube and scanned with energy source settings of 140 kV and 100 μA, with 708 ms integration time. Epiphyses were scanned with 1,080 projections, 2 frames per projection. The resolution was kept constant for each epiphysis, which was 54 μm for the proximal femur, 48 μm for the distal femur, 45 μm for the proximal tibia, and 38 μm for the distal tibia.

In each epiphysis trabecular bone was analyzed in a spherical volume of interest (VOI), which was scaled to size as recommended (Kivell, 2016; Lazenby, Skinner, Kivell, & Hublin, 2011). These were placed using Avizo Lite (v. 9.0.1) in the following regions: inferolateral to the center of the femoral head (FP), in the centers of the medial femoral condyle (FD) and the medial tibial plateau (TP), and in the center of the distal tibia (TD). FD, TP, and TD were all placed immediately below the subchondral bone. The femoral head is a ball-and-socket joint and may experience more variable loading. Positioning of FP was considered most homologous closer to the femoral neck where primary compressive strains converge. This approach furthermore helped to avoid the ligamentum teres insertion in the fovea capitis.

Figure 2 displays the placement of each of the VOI. The VOI needed to be large enough to be representative of the entire structure, and to limit the effects of placement errors. Conversely, a larger VOI is more likely to include damaged bone matrix and soil, which reduces the sample size. Furthermore, as potential group differences are not necessarily the same throughout an epiphysis,

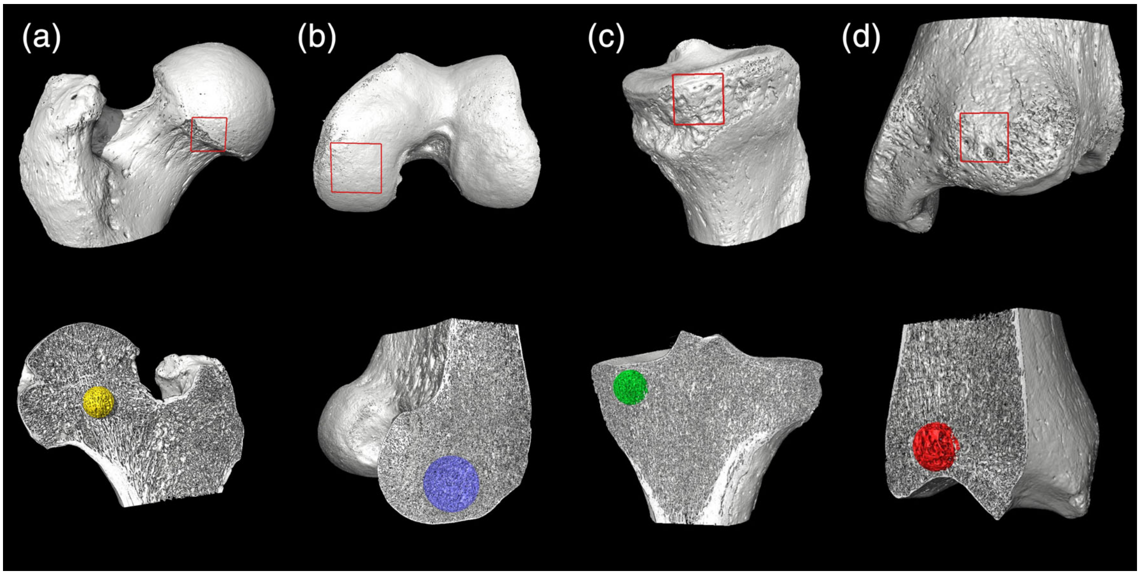

FIGURE 2 Size and location of VOI marked on the surface (top) and in cross-section (bottom). (a) Proximal femur (FP), (b) Distal femur (FD), (c) Proximal tibia (TP), and (d) Distal tibia (TD)

TABLE 1 Means and *SD* for all parameters in each group

		Friary				Hospital				Parish			
		Females *N* = 1		Males *N* = 13		Females *N* = 22		Males *N* = 35		Females *N* = 22		Males *N* = 22	
Stature		155.73		171.13 (5.97)		155.13 (6.92)		165.54 (5.97)		158.02 (5.19)		168.43 (7.41)	
Body mass		62.14		66.70 (5.56)		53.40 (13.44)		65.61 (13.91)		59.41 (3.65)		71.82 (6.73)	
FP	BV/TV	1	0.378	12	0.396 (0.048)	21	0.387 (0.055)	34	0.367 (0.062)	20	0.336 (0.072)	20	0.332 (0.049)
	ConnD		2.041		3.202 (1.023)		3.391 (0.961)		3.317 (1.077)		2.734 (1.082)		3.244 (1.343)
	DA		0.724		0.681 (0.031)		0.685 (0.049)		0.663 (0.053)		0.712 (0.073)		0.674 (0.048)
	Tb.Th		0.365		0.317 (0.028)		0.324 (0.044)		0.308 (0.033)		0.311 (0.039)		0.296 (0.039)
FD	BV/TV	1	0.222	10	0.319 (0.038)	19	0.294 (0.035)	34	0.303 (0.040)	17	0.261 (0.036)	17	0.286 (0.041)
	ConnD		3.356		4.434 (1.216)		5.050 (1.778)		4.685 (2.065)		5.378 (1.569)		4.991 (2.319)
	DA		0.653		0.715 (0.052)		0.692 (0.042)		0.711 (0.047)		0.705 (0.055)		0.718 (0.054)
	Tb.Th		0.262		0.266 (0.020)		0.259 (0.033)		0.267 (0.035)		0.232 (0.019)		0.250 (0.030)
TP	BV/TV	1	0.245	11	0.305 (0.046)	16	0.264 (0.042)	27	0.288 (0.046)	21	0.253 (0.041)	18	0.274 (0.032)
	ConnD		3.696		4.456 (1.796)		4.860 (1.274)		3.638 (1.307)		5.379 (1.214)		4.324 (1.530)
	DA		0.545		0.629 (0.086)		0.603 (0.087)		0.624 (0.084)		0.594 (0.090)		0.621 (0.084)
	Tb.Th		0.268		0.282 (0.031)		0.259 (0.029)		0.290 (0.044)		0.239 (0.034)		0.265 (0.030)
TD	BV/TV	0		10	0.331 (0.062)	18	0.314 (0.054)	24	0.316 (0.066)	20	0.246 (0.065)	16	0.283 (0.041)
	ConnD				5.658 (1.625)		5.987 (2.629)		5.111 (1.911)		7.014 (2.361)		5.651 (1.593)
	DA				0.661 (0.074)		0.597 (0.109)		0.601 (0.084)		0.655 (0.084)		0.633 (0.089)
	Tb.Th				0.253 (0.025)		0.251 (0.032)		0.264 (0.040)		0.204 (0.038)		0.236 (0.031)

Abbreviations: BV/TV, bone volume fraction; ConnD, connectivity density (mm^{-3}); DA, degree of anisotropy; FD, distal femur; FP, proximal femur; Tb.Th, trabecular thickness (mm); TD, distal tibia; TP, proximal tibia.

taking a greater VOI may average out regional structural variation. In finding a balance between all of these factors, the size of the VOI was chosen so that epiphyseal lines could be avoided. A detailed VOI selection protocol is available in Supporting Information 1. Due to the location of the epiphyseal line close to the articular surface, the mean diameter of TD (6.90 mm) was considerably smaller than that of the other VOI (FP: 10.56 mm; FD: 14.36 mm; TP: 11.25 mm). The range of variation in VOI dimensions was similar across epiphyses, with coefficients of variation falling between 0.074 and 0.093.

The spherical VOI were checked for damage and contamination and were excluded from analysis as needed. The total number of VOI included in each comparison is displayed in Table 1. Images were segmented using an iterative thresholding algorithm based on the global histogram, which increments the threshold until the composite average of gray values above and below the threshold is greater than the threshold itself (Ridler & Calvard, 1978). In two instances the result was not representative of the original scan, after which the VOI was excluded from comparison. Trabecular architecture was quantified with the BoneJ plugin (1.4.3) for ImageJ (1.52e) (Doube et al., 2010). The relative bone content or bone volume fraction (BV/TV) and the mean thickness of the trabeculae (Tb.Th) were quantified, as well as the number of connections per cubic millimeter as an indication of connectivity density (ConnD). Degree of anisotropy (DA) was here interpreted as a measure of directionality. Briefly, an ellipsoid is fitted to the point cloud of mean intercept lengths (MIL) in all directions (Harrigan & Mann, 1984), which would have axes of equal length for an isotropic structure. Thus, DA calculated as 1 minus the ratio between the smallest and largest eigenvalue yields a value between 0 (isotropic) and 1 (anisotropic). Consequently, a higher DA indicates a greater degree of directionality in the VOI. The image was sampled on auto mode until a coefficient of variation of 0.005 was reached.

Body mass affects the loads placed on the lower limbs, but there is no standard practice for correcting for the influence of body mass on trabecular bone. Trabecular thickness is commonly scaled with body size in interspecific comparisons (Barak, Lieberman, & Hublin, 2013; Doube, Klosowski, Wiktorowicz-Conroy, Hutchinson, & Shefelbine, 2011; Kivell, 2016; Ryan & Shaw, 2013). Body size has also been reported to affect ConnD within humans (Saers, Ryan, & Stock, 2019c). Body mass may furthermore affect BV/TV (Best et al., 2017) and clinically relevant measures of trabecular structural quality (Berro et al., 2018; Kim et al., 2017; Langsetmo et al., 2016; Looker, Sarafrazi Isfahani, Fan, & Shepherd, 2016). To explore this potential relationship in the present study sample, linear regressions were performed between estimated body mass and trabecular parameters and their natural logarithmic (*ln*) transforms. Body mass was estimated from superoinferior femoral head breadth and bi-iliac breadth following sex-specific equations from Ruff et al. (2012), and the two were averaged if both were available.

3.2 | Statistical methods

Body mass and stature were compared between the three groups of males (ANOVA) and between females from the parish and hospital (Welch's *t*-test).

Because not enough females were present in the friary group to enable statistical comparison, differences in trabecular structural properties were analyzed in two steps. First, the friary was excluded from the dataset and an ANOVA (type 3) was performed on the regression fit on sex and archaeological site. If there was no interaction effect detected between sex and site the interaction level was dropped, and the test was run again. Next, an ANOVA (type 3) was run to compare the means across the three groups of males only. As a consequence of this study design, the parish males and hospital males were analyzed twice. The size of any significant effects was measured by partial eta squared (η_p^2).

Tukey's HSD was used as post hoc test for all ANOVAs. To avoid inflation of type II errors, p values were not corrected for multiple comparisons, but rather interpreted by looking for patterns in all epiphyses instead. Test assumptions were checked on the diagnostic plots of the residuals.

4 | RESULTS

4.1 | Summary statistics

Mean values and standard deviations for all VOI included in the study are displayed in Table 1. Boxplots for these data are given in Figure 3.

4.2 | Body mass

Body mass of parish males was higher than males from the hospital (p = .042), but not from the friary (p = .121). Stature was different between friary and hospital males only (p = .039). For females, stature was not different between the parish and the hospital, while body mass was greater in the parish (p = .030).

There were no consistent correlations between trabecular parameters and body mass or their *ln* transforms. In analyzing the pooled sample, ConnD showed a weak inverse relationship with body mass in TP and TD but not in the femur. Body mass was also correlated with DA in TD (p = .007, r^2 = .08) and inversely related to BV/TV in FP (p = .020, r^2 = .05). In males, BV/TV was correlated with body mass in FP, FD, and TP, but not in TD. However, a similar trend was not observed in the females, where body mass was dependent on BV/TV only in TD (p = .011, r^2 = .17). Correlations in the *ln* transformed data displayed similar patterns. An overview of results from the regressions can be found in Supporting Information 4. While some parameters depended significantly on body mass in some VOI, this was different between males and females, and not consistent across VOI. In effect, results were not standardized.

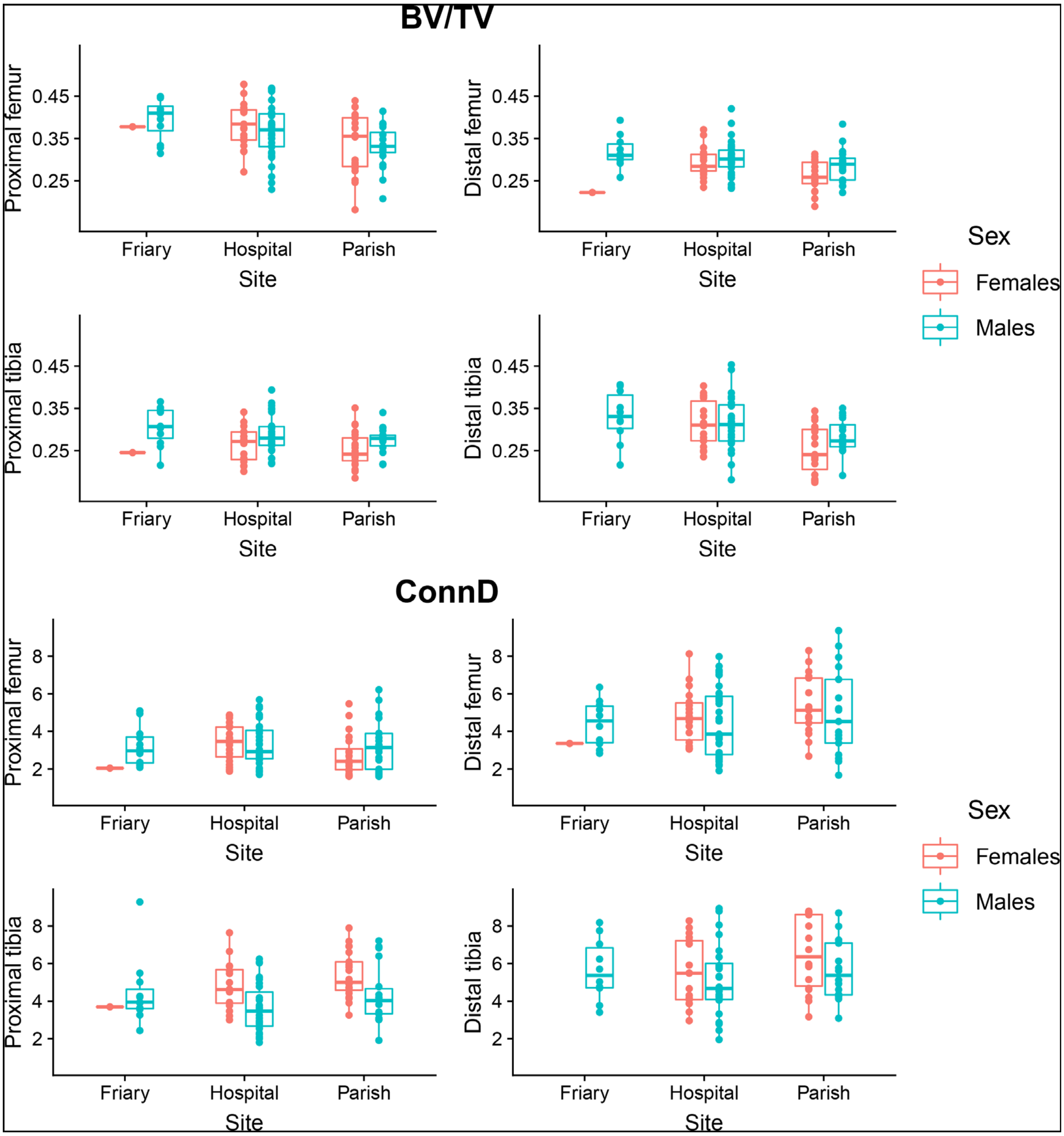

FIGURE 3 (a)–(d) Boxplots with individual data points for each volume of interest, grouped by parameter. BV/TV, bone volume fraction; ConnD, connectivity density (mm^{-3}); DA, degree of anisotropy; Tb.Th, trabecular thickness (mm)

4.3 | Effects of site and sex in the hospital and parish

Table 2 lists the results of the comparison between the males and females from the parish and the hospital, with effect sizes for significant effects. A detailed view of the statistical tests run in this comparison is provided in Supporting Information 2.3. None of the interactions between sex and site rendered significant results. Females had greater connectivity than males in TP ($p < .001$) and TD ($p = .028$). In FP, DA was higher for females than for males ($p = .015$). Males had higher BV/TV in TP ($p = .018$). Tb.Th was greater in males in TP ($p = .001$) and TD ($p = .009$), but not in FD ($p = .085$). Interestingly, FP presented with a trend for higher Tb.Th in females ($p = .051$).

Between the parish and the hospital BV/TV was different for FP ($p = .001$), FD ($p = .006$) and TD ($p < .001$), but not in TP ($p = .165$). In all cases was BV/TV lower in the parish. Tb.Th was also lower in the parish in FD ($p = .002$), TP ($p = .005$), and TD ($p < .001$), but not in FP ($p = .124$). Anisotropy was only different between the sites in TD ($p = .034$).

4.4 | Male differences between the sites

Table 3 lists the results of the comparisons for each VOI between the males from the friary, the hospital, and the parish. A detailed view of the statistical tests run in this comparison is provided in Supporting

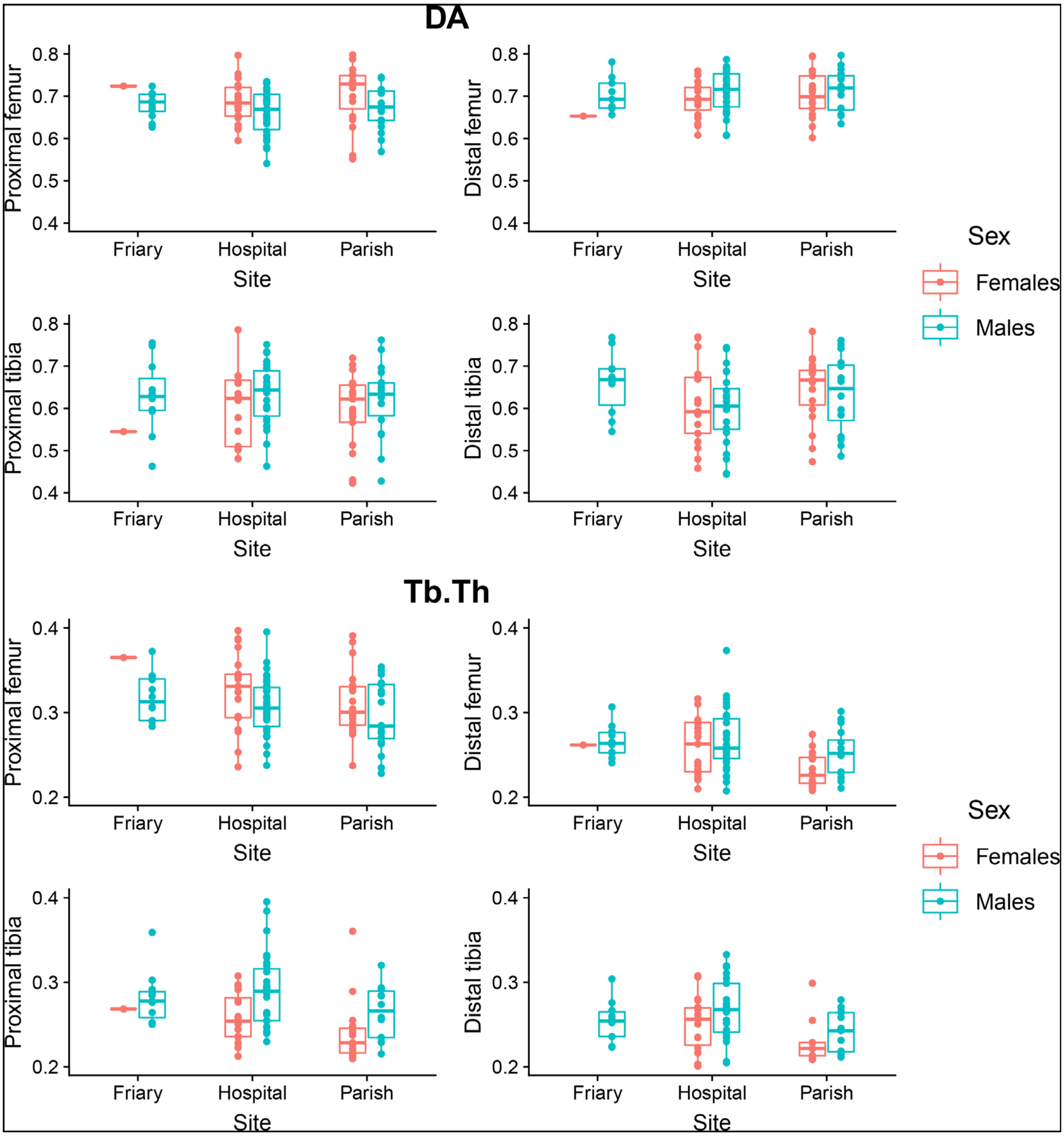

FIGURE 3 (Continued)

Information 2.2. Only the evaluation of BV/TV revealed differences between the three groups in FP, with lower BV/TV in the parish compared with the friary (p = .008).

5 | DISCUSSION

Trabecular architecture in the human lower limb is known to be significantly different between populations with highly divergent inferred behaviors (Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2016; Saers et al., 2019b). Relatively little attention has so far been given to the range of normal variation within populations and the extent to which trabecular architecture may differ between groups from the same region when inferred mobility levels are similar. We therefore analyzed a large sample that was comprised of three separate groups from a single medieval population. Despite the similarity in genetic background, environment, and inferred mobility, the three groups in our study still differed in trabecular structure, with lower BV/TV and Tb.Th in the parish group. This variability of trabecular architecture within a relatively narrow range of behavioral variation can be helpful to put interpopulation differences into context. A second aim of our study was to detect sex differences, by using a large sample from a single population. In contrast with previous findings, we found Tb.Th and ConnD to differ between males and females in multiple VOI. Paradoxically, the observed sexual dimorphism in the femoral head was

TABLE 2 ANOVA results for the comparison of the parish and the hospital

		Sex *p* (*F*)	η_p^2	Site *p* (*F*)	η_p^2	Sex*Site *p* (*F*)
FP	BV/TV	.295 (1.110)		**.001** (10.902)	0.106	.525 (0.408)
	ConnD	.441 (0.598)		.156 (2.044)		.217 (1.544)
	DA	**.015** (6.137)	0.072	.120 (2.457)		.532 (0.394)
	Tb.Th	.051 (3.899)		.124 (2.408)		.905 (0.014)
FD	BV/TV	.069 (3.390)		**.006** (7.925)	0.086	.312 (1.036)
	ConnD	.388 (0.753)		.471 (0.526)		.980 (0.001)
	DA	.118 (2.498)		.353 (0.873)		.808 (0.059)
	Tb.Th	.085 (3.046)		**.002** (10.243)	0.109	.472 (0.522)
TP	BV/TV	**.018** (5.872)	0.084	.165 (1.959)		.839 (0.041)
	ConnD	**<.001** (14.677)	0.185	**.043** (4.230)	0.051	.782 (0.077)
	DA	.230 (1.466)		.762 (0.092)		.879 (0.023)
	Tb.Th	**.001** (12.666)	0.176	**.005** (8.439)	0.097	.745 (0.106)
TD	BV/TV	.170 (1.917)		**<.001** (14.045)	0.158	.194 (1.716)
	ConnD	**.028** (5.037)	0.075	.116 (2.522)		.625 (0.241)
	DA	.705 (0.145)		**.034** (4.662)	0.059	.526 (0.406)
	Tb.Th	**.009** (7.146)	0.125	**<.001** (21.045)	0.219	.250 (1.343)

Notes: Results displayed as *p*-value, followed by the *F*-statistic in parentheses. Significant differences are in bold and followed by the effect size (η_p^2). Abbreviations: BV/TV, bone volume fraction; ConnD, connectivity density (mm^{-3}); DA, degree of anisotropy; FD, distal femur; FP, proximal femur; Tb.Th, trabecular thickness (mm); TD, distal tibia; TP, proximal tibia.

TABLE 3 ANOVA results for the comparison of all males from the three groups

		Site *p* (*F*)	Post hoc	η_p^2
FP	BV/TV	**.008** (5.18)	Parish < Friary	0.14
	ConnD	.948 (0.05)		
	DA	.456 (0.79)		
	Tb.Th	.226 (1.53)		
FD	BV/TV	.120 (2.20)		
	ConnD	.777 (0.25)		
	DA	.869 (0.14)		
	Tb.Th	.166 (1.85)		
TP	BV/TV	.145 (2.00)		
	ConnD	.183 (1.75)		
	DA	.968 (0.03)		
	Tb.Th	.089 (2.53)		
TD	BV/TV	.094 (2.49)		
	ConnD	.557 (0.59)		
	DA	.155 (1.94)		
	Tb.Th	.051 (3.17)		

Notes: Results displayed as *p*-value, followed by the *F*-statistic in parentheses. Significant differences are in bold and followed by the effect size (η_p^2). Abbreviations: BV/TV, bone volume fraction; ConnD, connectivity density (mm^{-3}); DA, degree of anisotropy; FD, distal femur; FP, proximal femur; Tb.Th, trabecular thickness (mm); TD, distal tibia; TP, proximal tibia.

reversed from that observed in the tibia. Exploring sexual dimorphism among other populations for these same anatomical locations would be useful to improve our understanding of the site-specificity of sex differences in trabecular bone.

5.1 | Sedentary lifestyles and trabecular architecture in the human lower limb

Intraspecific variation in trabecular architecture is poorly understood which limits our understanding of trabecular structure as reflection of loading history. Recent anthropological studies have investigated the effects of subsistence behavior and the associated activities on trabecular bone (Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2016; Saers et al., 2019b; Scherf et al., 2016). If the tissue is indeed reflective of loading history, lower limb trabecular properties can be expected to reflect the degrees to which a subsistence strategy relies on terrestrial mobility. Indeed, studies consistently show higher BV/TV in the lower limb of foraging populations compared with agriculturalists, as a result of the relatively sedentary lifestyle associated with food production (Chirchir et al., 2017; Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2016; Saers et al., 2019b). This pattern is observed in the lower but not the upper limb, which supports the idea that a localized response to loading, rather than systemic variation, is the main driver of these population differences (Chirchir et al., 2017; Doershuk et al., 2019). The presumed importance of subsistence-associated mobility to tissue properties is reinforced by the relative homogeneity of the trabecular structure in the lower limb across sedentary populations (Chirchir et al., 2017; Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2019b). This relative homogeneity could suggest that trabecular properties differentiate poorly between more subtle behavioral patterns. However, we found significant differences between groups within a single sedentary population, against our expectations, suggesting that trabecular properties may differentiate between more subtle behavioral differences between groups.

The greatest differences in our sample were found in BV/TV and Tb.Th, with little variation in DA. This is in line with previous comparisons where differences in DA are commonly observed between species (Maga, Kappelman, Ryan, & Ketcham, 2006; Ryan & Shaw, 2012; Stephens et al., 2018; Tsegai et al., 2013) but not between human populations (Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2019b; Scherf et al., 2016; Saers et al., 2016). Animal models yield similar results, with anisotropy rarely being altered by loading interventions even when orientation of the primary loads is changed (Barak et al., 2011; van der Meulen et al., 2006; van der Meulen, Yang, Morgan, & Bostrom, 2009). As anisotropy is mainly interpreted as an indicator of directionality, and variation in lower limb joint loading orientation is likely similar across human groups, homogeneity in DA should be expected.

The lower BV/TV in the parish was regularly accompanied by reduced trabecular thickness. In adulthood, an increase in BV/TV is predominantly achieved through increased Tb.Th, as new trabeculae are not normally formed (Lambers, Schulte, Kuhn, Webster, & Müller, 2011; Meakin et al., 2014; Ruimerman, Hilbers, van Rietbergen, & Huiskes, 2005; van der Meulen et al., 2009). It is therefore possible that the higher BV/TV and Tb.Th in the friary and hospital are the result of an adaptation to greater mechanical loading. However, while the individuals buried at the parish cemetery may have performed less frequent or less intense physical labor compared with the friars and the hospital residents, the group likely included a variety of laborers, which would be expected to have led to an adaptive increase in BV/TV. Moreover, based on documentary evidence, neither the friars nor the hospital residents were expected to have been habitually involved in strenuous physical activities. This means that the observed group differences are poorly explained by inferred loading patterns.

Directly comparing trabecular properties across studies is complicated due to the great variety of methodological approaches. For example, Saers et al. (2016) maximized VOI size in each joint, whereas a relatively dense subvolume of each epiphysis was selected in the present study. As a result, a direct translation of the values we found for BV/TV in the hospital would place St. John's closer to the mixed agriculturalists-foragers than to the more sedentary population studied (Saers et al., 2016). It is therefore more meaningful to compare the range of variation in population means within and between subsistence behaviors, and within and between populations. For the proximal femur, for instance, Saers et al. (2016) found mean BV/TV for the most mobile population to be 1.5 times greater than the mean for the most sedentary population. Selecting a subvolume in each epiphysis, Doershuk et al. (2019) found the highest population mean in BV/TV to be 1.7 times higher than the lowest population mean. The range of variation in both studies is considerably wider than the variation we observed in FP, with a ratio of maximum to minimum group mean in BV/TV of just 1.2.

Doershuk et al. (2019) included 20 individuals from St. John's hospital, finding a mean BV/TV of 0.342, which is lower than the hospital mean in the present study (BV/TV: 0.375). This is likely explained by the choice of analyzing the architecture in the center of the femoral head, in contrast with our placement of the VOI close to the femoral neck. Interestingly, Doershuk et al. (2019) reported a (non-significant) difference between a post-industrial group from Iowa (BV/TV: 0.304) and their hospital group (BV/TV: 0.342), which is of a comparable order to the difference in mean values we found for the parish (BV/TV: 0.334) and hospital (BV/TV: 0.375). While caution must be taken in directly comparing absolute values across studies, this might indicate that variation in BV/TV is as great between groups in medieval Cambridge as it is between the hospital and the post-medieval group from Iowa. Even though this highlights the great intra-population variation in trabecular architecture, overall variation within and between sedentary populations remains considerably less than between subsistence behaviors.

5.2 | Trabecular structural variation in medieval Cambridge

5.2.1 | Sexual dimorphism and body size

In the analysis of sexual dimorphism only the parish and hospital samples could be compared. Some sex differences were observed, but these were not consistent throughout the lower limb. Females had thinner but better-connected trabeculae in the tibial epiphyses, while their femoral head was characterized by a more anisotropic structure with a trend toward thicker trabeculae compared with males. Previous studies failed to uncover straightforward sex differences in trabecular architecture (Doershuk et al., 2019; Saers et al., 2016). In their study of trabecular architecture in the calcaneus, Saers et al. (2019b) found sex differences in connectivity density, but these disappeared when standardizing for body size, suggesting that body size was driving the sexual dimorphism.

In our sample, there was no consistent pattern in the regressions between body mass and trabecular parameters. This supports the findings from other intraspecific studies in which no dependency on body mass was found (Doershuk et al., 2019; Saers et al., 2016), but contrasts with the correlations between body size or body mass and trabecular properties in the foot (Best et al., 2017; Saers et al., 2019b, c). Part of this divergence may have resulted from the bones analyzed, as the foot and the long bones in the lower limb are loaded differently and may be differently affected by body mass. This may explain why the studies of Doershuk et al. (2019) and Saers et al. (2016) did not find any correlations with body mass, despite using some of the same populations as Saers et al. (2019b,c). A study in which trabecular structures of both the foot and the long bones of the lower limb of the same individuals are studied side by side may therefore be a useful step in unraveling the dependency of trabecular bone on body mass.

Any association between trabecular architecture and body mass may be obscured if biological scaling and functional adaptation stimulate opposing trends. For instance, an adaptation to greater body mass-induced loading (e.g., increased Tb.Th) could diminish the effects of a negative scaling with body size (e.g., decreased Tb.Th). A comparison of the trabecular structure in equally sized individuals with varying body masses, or between differently sized individuals with a similar body mass, might help unravel the relationship between trabecular properties and body size and mass in intraspecific analyses. In interpreting the effects of body size on population and/or sex differences, it is important to note that Saers et al. (2019c) found ConnD to scale with body size, but not BV/TV or Tb.Th. Thus, the group and sex differences in BV/TV and Tb.Th in the current study cannot be explained by differences in body mass alone, even if trabecular properties would need to be standardized.

As opposed to the trabecular tissue, sexual dimorphism in mechanical properties of lower limb cortical bone is well documented. Males are generally found to have larger and more robust lower limb diaphyses, but the degree of sexual dimorphism may vary between populations, with more mobile populations displaying greater sexual dimorphism than relatively sedentary populations (Berner, Sládek, Holt, Niskanen, & Ruff, 2018; Brzobohatá, Krajíček, Horák, & Velemínská, 2016; Macintosh et al., 2014b; Ruff, 1987, 2008; Wescott, 2006; but compare Carlson, Grine, & Pearson, 2007). In contrast, no consistent sexual dimorphism has been observed in studies of trabecular bone in the lower limbs. Sex differences found by Saers et al. (2019b) were not the same across populations and anatomical locations. Moreover, in one population they found greater BV/TV in some locations in females, which contrasted with a prior study that found greater diaphyseal rigidity in males in that same population (Nikita, Siew, Stock, Mattingly, & Lahr, 2011; Saers et al., 2019b).

It is surprising that studies of past populations have not yet been able to identify distinctive sex-dependent patterns in trabecular architecture while these are commonly observed in contemporary societies (Gabel, Macdonald, & McKay, 2017; Macdonald, Nishiyama, Kang, Hanley, & Boyd, 2011; Popp et al., 2017; Popp et al., 2019; Sode, Burghardt, Kazakia, Link, & Majumdar, 2010). The reasons for this discrepancy are poorly understood and warrant further research into the effects of sex on trabecular structure and its responsivity to loading. A complicating factor could be the reliance on skeletal collections for the study of past populations, while these do not necessarily mirror the demographics of the community during life. An alternative explanation may be that studies of past populations cover a wide range of ages for which standardization is often problematic, while age may affect males differently than females. This is exemplified by the assessment of the effects of reproduction on sexual dimorphism in bone by de Bakker et al. (2018) in which they analyzed the bone structure of male, reproductive, and non-reproductive female rats on three occasions in a 15-month period. Both groups of female rats initially had greater BV/TV compared to their male counterparts. Age-related loss of bone was observed in each of the three groups, but this was stronger in both female groups. After the first reproductive cycle, the reproductive females had lost more bone than the non-reproductive females, while both groups still displayed greater BV/TV than the males. Only after three cycles was BV/TV greater in males than in the reproductive females, whereas it was still greatest in non-reproductive females. In contrast with the greater BV/TV in females, the authors found more robust femoral midshafts in male rats compared with either of the two groups of females. The authors interpreted the results as an investment of young females in improved trabecular structure to counter future reproductive bone loss (de Bakker et al., 2018). Such an interpretation may explain why Saers et al. (2016) and Saers et al. (2019b) found greater BV/TV in females for a population in which males were found to have more robust diaphyses.

Although the aging process may complicate the study of sexual dimorphism in past populations, it does not explain why the observed dimorphism in our study was different between epiphyses. While the tibial epiphyses were characterized by thicker trabeculae in males, females displayed a trend toward thicker trabeculae with a more anisotropic structure in FP. This sexual dimorphism could not be statistically analyzed for the friary as there was only a single female individual present, but interestingly Tb.Th and DA for her, too, compare differently to the male means in FP than in the other VOI. Moreover, the parish and hospital exhibit this same sexual pattern independently, which makes it unlikely that the inverse patterning in the femoral head appeared by chance, suggesting that sexual dimorphism may differ between sites, even within a single limb.

5.2.2 | Lifestyle beyond mobility

It is unclear to what extent the observed variation in our sample can be attributed to differences in mechanical loading. It follows from previous studies that subsistence strategy plays a major role in the determination of trabecular structural properties (Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2016; Saers et al., 2019b; Scherf et al., 2016). The lack of mutual differences in trabecular properties between sedentary populations (Chirchir et al., 2017; Doershuk et al., 2019; Ryan & Shaw, 2015; Saers et al., 2019b) makes it surprising that the parish and the other two groups in our sample differ despite similarities in subsistence and environment.

Due to the variety of ways in which bone may respond to loading, inferring behavior from trabecular structure is not straightforward. This is further complicated by the multitude of factors contributing to skeletal phenotype we could not control for, such as genetics and diet. Bone quality is highly heritable, with an estimated 60–90% of variation in bone mineral density being attributed to genetic factors. Similarly, bone strength differs more between populations than between trained and untrained subjects within a single population (Peacock et al., 2018; Wallace et al., 2015; Wallace et al., 2012). This means that despite the relative genetic homogeneity of our sample compared to those in interpopulation studies, genetic differences may still be responsible for most of the observed variation in trabecular properties. Although we acknowledge these genetic effects on bone mechanical properties, they may explain the range of variation but not necessarily group differences. As there is no reason to assume genetic isolation for any of the three groups, genetics are unlikely to explain the differences observed in group means.

Diet composition is another factor that needs to be accounted for in interpreting bone microstructure, as adequate nutrition is essential for bone tissue maintenance and therefore contributes to bone structural integrity (Heaney et al., 2000). Moreover, its contribution may even extend beyond what can be considered "adequate" alone. High daily protein intake has for instance frequently been found to correlate with bone mineral density, and this relationship may be further modulated by the availability of calcium (Heaney & Layman, 2008). A recent study on 746 postmenopausal women demonstrated a significant correlation of levels of dietary intake of animal protein with the mechanical properties of the distal tibia and distal radius, while this relationship did not exist with the amounts of vegetable protein consumed (Durosier-Izart et al., 2017). However, excessive ingestion of protein-rich foods has repeatedly been linked to increased fracture risks, indicating a potentially detrimental effect on bone health of overconsumption (cf. Dolan & Sale, 2019; Heaney & Layman, 2008).

Diet in high/late medieval Cambridge was variable, and to some extent determined by social class. The aristocratic diet was composed of a great variety of meat and fish, and dairy to a much lesser extent (Dyer, 1989; Lee, 2003). The Augustinian friars were officially not allowed to eat meat, but fish, dairy, and eggs appear to have been consumed on a regular basis (Laferriere, 2017). In the hospital, meat may have been served up to three times a week, at least to the brethren and corrodians, but most likely to the residents, too (Rubin, 1987). Apart from animal products, the medieval diet was composed of bread and ale, with a minor vegetable component. Few laborers would have had consistent access to animal protein and therefore largely relied on cereals of which to make up their diet. Although nutritional standards appear to have improved in the second half of the fourteenth century, animal protein remained a luxury product (Dyer, 1989). The relatively consistent supply of dairy products and meat or fish in the hospital and friary may explain part of the differences found in the trabecular structure between those two sites and the parish. As such, the bone structure in the parish may reflect a poorer diet on average compared with the friary and the hospital.

As the three groups in our study had similar inferred levels of mobility, variation in nutritional standards may provide an alternative explanation for the observed intrapopulation variation that is more plausible than variation in mechanical loading. It would be of great interest to see this hypothesis tested, for example through a correlation with stable isotope ratios. Since the proportion of animal protein in past diets is believed to be reflected in stable isotope ratios in the skeleton, correlating bone structural parameters with isotopic data from the same individuals could explore the relationship between past diet and trabecular morphology.

Regardless of the causes for the observed variation in trabecular properties, our results are striking on two fronts: first, the thinner trabeculae and lower bone volume fraction in the parish individuals, as well as their higher body mass, questions the accuracy of the initial inference of the parish cemetery as a cross-section of medieval Cambridge. Had the parish been a true cross-section of society, we would expect to see greater similarities with the other sites. Second, the results defy traditional expectations of life within a hospital. Although "crippled" and wounded individuals were excluded from entering the hospital (Cessford, 2015; Rubin, 1987), the presumed care for the poor and the sick may lead to the assumption that its population represents physically less active people with an overall poorer lifestyle. In contrast to these expectations, the trabecular architecture in the hospital individuals does not indicate impairment, a bed-ridden lifestyle, or poor bone maintenance due to nutritional deficiencies. Even though the typical length of stay at the hospital is not known and may not always have been long enough to induce changes to the trabecular architecture, a higher bone mass in the hospital compared to the parish was unexpected. This could indicate a relatively healthy life prior to admission, which suggests that those entering the hospital were not drawn from the poorest layers of society. Moreover, the unexpectedly high BV/TV highlights an important aspect of life in medieval hospitals such as that of St. John, which is that medical care was not among its primary purposes. Rather, the hospital provided bedding, food, and clothing, but most importantly spiritual care (Rubin, 1987; for a review see Watson, 2006).

Our study was limited by a small number of individuals from the friary that could be included, and a greater sample from that site would have improved statistical power. It would therefore be of great interest to see if our analyses can be upheld when the variation within other populations is examined. From the medieval period alone, many more friary, hospital, and parish cemeteries have been excavated, where approaches like the ones used here could be used to explore causes for intrapopulation variation. But outside the medieval realm, too, a better understanding of intrapopulation variation would greatly contribute to our understanding of bone functional adaptation overall and its applicability in inferring behavior from the skeleton.

Our use of VOI assumes the ability to properly define homologous regions in epiphyses between individuals. Given the range of variation in shape and size of epiphyses, our approach brings some obvious limitations. Others have therefore included the entire epiphysis in the analyses which allows a useful visualization of regional trabecular variation (Tsegai et al., 2013). This has been proven to be particularly useful in differentiating limb use between taxa (Dunmore et al., 2019; Stephens et al., 2018; Tsegai et al., 2013), but its usefulness in comparing groups within a single species where joint loading is similar remains doubtful. Rather, the study of trabecular structural variation would benefit from a standardized VOI selection protocol to make results comparable across studies.

6 | CONCLUSIONS

Our study examined whether groups within a sedentary population differ in the structural properties of the lower limb. Differences were apparent in all epiphyses and were mainly observed in bone volume fraction and trabecular thickness. Based on the similarity of inferred mobility levels, we found nutritional differences to better explain the observed variation between groups. Whether diet, mobility, or a combination of factors drove the divergence in trabecular architecture, our results show that trabecular structural properties may capture subtle behavioral differences and can potentially contribute to a more nuanced understanding of past activity patterns. Moreover, our results show that lifestyle in medieval Cambridge can be reflected differently, depending on which skeletal collection is used as a reference. Consequently, studies that examine the effects of lifestyle on the trabecular network are encouraged to include multiple groups for each category to account for variation within activity levels.

Second, we explored the degrees of sexual dimorphism by using a large sample from a single population, as to avoid noise from mechanical and environmental factors in the trabecular structure. We found significant differences between the sexes but failed to identify a consistent sex-dependent pattern in trabecular architecture across VOI. Future analysis of the same VOI in other populations might improve our understanding of sex differences in trabecular bone functional adaptation.

ACKNOWLEDGMENTS

As part of the After the Plague project, this work was funded by the Wellcome Trust (Award no. 2000368/Z/15/Z). We thank the Duckworth Collection for access to the material from Comet Place (All Saints by the Castle), and the Cambridge Archaeological Unit for access to the material from St. John's Hospital and the Augustinian Friary.

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Bram Mulder https://orcid.org/0000-0003-1494-0872
Jaap P. P. Saers https://orcid.org/0000-0003-3209-2969
Sarah A. Inskip https://orcid.org/0000-0001-7424-2094

REFERENCES

Andrews, F. (2006). The Augustinian or Austin friars. In *The other friars: The Carmelite, Augustinian, sack and pied* (pp. 69–172). Woodbridge: Boydell & Brewer.

Barak, M. M., Lieberman, D. E., & Hublin, J. J. (2011). A Wolff in sheep's clothing: Trabecular bone adaptation in response to changes in joint loading orientation. *Bone*, *49*, 1141–1151. https://doi.org/10.1016/j.bone.2011.08.020

Barak, M. M., Lieberman, D. E., & Hublin, J. J. (2013). Of mice, rats and men: Trabecular bone architecture in mammals scales to body mass with negative allometry. *Journal of Structural Biology*, *183*, 123–131. https://doi.org/10.1016/j.jsb.2013.04.009

Barak, M. M., Lieberman, D. E., Raichlen, D., Pontzer, H., Warrener, A. G., & Hublin, J. J. (2013). Trabecular evidence for a human-like gait in *Australopithecus africanus*. *PLoS One*, *8*, e77687. https://doi.org/10.1371/journal.pone.0077687

Berner, M., Sládek, V., Holt, B., Niskanen, M., & Ruff, C. B. (2018). Sexual dimorphism. In C.B. Ruff (Ed.), *Skeletal variation and adaptation in Europeans*. Hoboken: John Wiley & Sons, Inc. https://doi.org/10.1002/9781118628430.ch6

Berro, A.-J., Ayoub, M.-L., Pinti, A., Ahmaidi, S., El Khoury, G., El Khoury, C., … El Hage, R. (2018). Trabecular bone score in overweight and normal-weight young women. In I. Rojas & F. Ortuño (Eds.), *Bioinformatics and biomedical engineering. IWBBIO 2018. Lecture notes in computer science* (Vol. 10814, pp. 59–68). Cham: Springer. https://doi.org/10.1007/978-3-319-78759-6_6

Bertram, J. E. A., & Swartz, S. M. (1991). The 'law of bone transformation': A case of crying Wolff? *Biological Reviews*, *66*, 245–273. https://doi.org/10.1111/j.1469-185X.1991.tb01142.x

Best, A., Holt, B., Troy, K. L., & Hamill, J. (2017). Trabecular bone in the calcaneus of runners. *PLoS One*, *12*, e0188200. https://doi.org/10.1371/journal.pone.0188200

Birkhold, A. I., Razi, H., Duda, G. N., Checa, S., & Willie, B. M. (2017). Tomography-based quantification of regional differences in cortical bone surface remodeling and mechano-response. *Calcified Tissue International*, *100*, 255–270. https://doi.org/10.1007/s00223-016-0217-4

Birkhold, A. I., Razi, H., Duda, G. N., Weinkamer, R., Checa, S., & Willie, B. M. (2014). The influence of age on adaptive bone formation and bone resorption. *Biomaterials*, *35*, 9290–9301. https://doi.org/10.1016/j.biomaterials.2014.07.051

Birmingham, E., Kreipke, T. C., Dolan, E. B., Coughlin, T. R., Owens, P., McNamara, L. M., … McHugh, P. E. (2015). Mechanical stimulation of bone marrow in situ induces bone formation in trabecular explants. *Annals of Biomedical Engineering*, *43*, 1036–1050. https://doi.org/10.1007/s10439-014-1135-0

Brickley, M., & McKinley, J. (2004). *Guidelines to the standards for recording human remains* (Vol. IFA paper no. 7). Southampton: BABAO and the Institute of Field Archaeologists.

Brzobohatá, H., Krajíček, V., Horák, Z., & Velemínská, J. (2016). Sexual dimorphism of the human tibia through time: Insights into shape variation using a surface-based approach. *PLoS One*, *11*, e0166461. https://doi.org/10.1371/journal.pone.0166461

Buikstra, J. E., & Ubelaker, D. H. (1994). *Standards for data collection from human skeletal remains*. Fayetteville: Arkansas Archeological Survey.

Burr, D. B., Milgrom, C., Fyhrie, D., Forwood, M., Nyska, M., Finestone, A., … Simkin, A. (1996). In vivo measurement of human tibial strains during vigorous activity. *Bone*, *18*, 405–410. https://doi.org/10.1016/8756-3282(96)00028-2

Carlson, K. J., Grine, F. E., & Pearson, O. M. (2007). Robusticity and sexual dimorphism in the postcranium of modern hunter-gatherers from Australia. *American Journal of Physical Anthropology*, *134*, 9–23. https://doi.org/10.1002/ajpa.20617

Cessford, C. (2015). The St. John's hospital cemetery and environs, Cambridge: Contextualizing the medieval urban dead. *Archaeological Journal*, *172*, 52–120. https://doi.org/10.1080/00665983.2014.984960

Cessford, C. (2017). Former Old Examination Hall, North Range Buildings, New Museums Site, Cambridge: an archaeological excavation. Report 1377. Cambridge Archaeological Unit.

Cessford, C., & Dickens, A. (2005). Cambridge Castle Hill: Excavations of Saxon, medieval and post-medieval deposits, Saxon execution site and a medieval coinhoard. *Proceedings of the Cambridge Antiquarian Society*, *94*, 73–102.

Chirchir, H. (2019). Trabecular bone fraction variation in modern humans, fossil hominins and other primates. *The Anatomical Record*, *302*, 288–305. https://doi.org/10.1002/ar.23967

Chirchir, H., Kivell, T. L., Ruff, C. B., Hublin, J.-J., Carlson, K. J., Zipfel, B., & Richmond, B. G. (2015). Recent origin of low trabecular bone density in modern humans. *Proceedings of the National Academy of Sciences of the United States of America*, *112*, 366–371. https://doi.org/10.1073/pnas.1411696112

Chirchir, H., Ruff, C. B., Junno, J. A., & Potts, R. (2017). Low trabecular bone density in recent sedentary modern humans. *American Journal of Physical Anthropology*, *162*, 550–560. https://doi.org/10.1002/ajpa.23138

Christen, P., Ito, K., Galis, F., & van Rietbergen, B. (2015). Determination of hip-joint loading patterns of living and extinct mammals using an inverse Wolff's law approach. *Biomechanics and Modeling in Mechanobiology*, *14*, 427–432. https://doi.org/10.1007/s10237-014-0602-8

Cowin, S. C. (2007). The significance of bone microstructure in mechanotransduction. *Journal of Biomechanics*, *40*(Suppl 1), S105–S109. https://doi.org/10.1016/j.jbiomech.2007.02.012

Cunningham, H. C., West, D. W. D., Baehr, L. M., Tarke, F. D., Baar, K., Bodine, S. C., & Christiansen, B. A. (2018). Age-dependent bone loss and recovery during hindlimb unloading and subsequent reloading in rats. *BMC Musculoskeletal Disorders*, *19*(1), 223. https://doi.org/10.1186/s12891-018-2156-x

de Bakker, C. M. J., Zhao, H., Tseng, W. J., Li, Y., Altman-Singles, A. R., Liu, Y., … Liu, X. S. (2018). Effects of reproduction on sexual dimorphisms in rat bone mechanics. *Journal of Biomechanics*, *77*, 40–47. https://doi.org/10.1016/j.jbiomech.2018.06.023

DeSilva, J. M., & Devlin, M. J. (2012). A comparative study of the trabecular bony architecture of the talus in humans, non-human primates, and Australopithecus. *Journal of Human Evolution*, *63*(3), 536–551. https://doi.org/10.1016/j.jhevol.2012.06.006

Doershuk, L. J., Saers, J. P. P., Shaw, C. N., Jashashvili, T., Carlson, K. J., Stock, J. T., & Ryan, T. M. (2019). Complex variation of trabecular bone structure in the proximal humerus and femur of five modern human populations. *American Journal of Physical Anthropology*, *168*, 104–118. https://doi.org/10.1002/ajpa.23725

Dolan, E., & Sale, C. (2019). Protein and bone health across the lifespan. *Proceedings of the Nutrition Society*, *78*, 45–55. https://doi.org/10.1017/S0029665118001180

Doube, M., Kłosowski, M. M., Arganda-Carreras, I., Cordelières, F. P., Dougherty, R. P., Jackson, J. S., … Shefelbine, S. J. (2010). BoneJ: Free and extensible bone image analysis in ImageJ. *Bone*, *47*, 1076–1079. https://doi.org/10.1016/j.bone.2010.08.023

Doube, M., Klosowski, M. M., Wiktorowicz-Conroy, A. M., Hutchinson, J. R., & Shefelbine, S. J. (2011). Trabecular bone scales allometrically in mammals and birds. *Proceedings of the Royal Society B: Biological Sciences*, *278*, 3067–3073. https://doi.org/10.1098/rspb.2011.0069

Dunmore, C. J., Kivell, T. L., Bardo, A., & Skinner, M. M. (2019). Metacarpal trabecular bone varies with distinct hand-positions used in hominid locomotion. *Journal of Anatomy*, *235*, 45–66. https://doi.org/10.1111/joa.12966

Durosier-Izart, C., Biver, E., Merminod, F., van Rietbergen, B., Chevalley, T., Herrmann, F. R., … Rizzoli, R. (2017). Peripheral skeleton bone strength is positively correlated with total and dairy protein intakes in healthy postmenopausal women. *American Journal of Clinical Nutrition*, *105*, 513–525. https://doi.org/10.3945/ajcn.116.134676

Dyer, C. (1989). *Standards of living in the later middle ages: Social change in England c.1200-1520*. Cambridge: Cambridge University Press.

Fajardo, R. J., & Müller, R. (2001). Three-dimensional analysis of nonhuman primate trabecular architecture using micro-computed tomography. *American Journal of Physical Anthropology*, *115*, 327–336. https://doi.org/10.1002/ajpa.1089

Frost, H. M. (2001). From Wolff's law to the Utah paradigm: Insights about bone physiology and its clinical applications. *The Anatomical Record*, *262*, 398–419. https://doi.org/10.1002/ar.1049

Frost, H. M. (2003). Bone's mechanostat: A 2003 update. *The Anatomical Record Part A: Discoveries in Molecular Cellular and Evolutionary Biology*, *275*, 1081–1101. https://doi.org/10.1002/ar.a.10119

Gabel, L., Macdonald, H. M., & McKay, H. A. (2017). Sex differences and growth-related adaptations in bone microarchitecture, geometry, density, and strength from childhood to early adulthood: A mixed longitudinal HR-pQCT study. *Journal of Bone and Mineral Research*, *32*, 250–263. https://doi.org/10.1002/jbmr.2982

Gosman, J. H., & Ketcham, R. A. (2009). Patterns in ontogeny of human trabecular bone from SunWatch Village in the prehistoric Ohio Valley: General features of microarchitectural change. *American Journal of Physical Anthropology*, *138*, 318–332. https://doi.org/10.1002/ajpa.20931

Harrigan, T. P., & Mann, R. W. (1984). Characterization of microstructural anisotropy in orthotropic materials using a second rank tensor. *Journal of Materials Science*, *19*(3), 761–767. https://doi.org/10.1007/bf00540446

Harrison, L. C., Nikander, R., Sikiö, M., Luukkaala, T., Helminen, M. T., Ryymin, P., … Sievänen, H. (2011). MRI texture analysis of femoral neck: Detection of exercise load-associated differences in trabecular bone. *Journal of Magnetic Resonance Imaging*, *34*, 1359–1366. https://doi.org/10.1002/jmri.22751

Hart, N. H., Nimphius, S., Rantalainen, T., Ireland, A., Siafarikas, A., & Newton, R. U. (2017). Mechanical basis of bone strength: Influence of bone material, bone structure and muscle action. *Journal of Musculoskeletal and Neuronal Interactions*, *17*, 114–139.

Heaney, R. P., Abrams, S., Dawson-Hughes, B., Looker, A., Marcus, R., Matkovic, V., & Weaver, C. (2000). Peak bone mass. *Osteoporosis International*, *11*, 985–1009. https://doi.org/10.1007/s001980070020

Heaney, R. P., & Layman, D. K. (2008). Amount and type of protein influences bone health. *American Journal of Clinical Nutrition*, *87*, 1567S–1570S. https://doi.org/10.1093/ajcn/87.5.1567S

Higgins, R. W. (2014). The effects of terrain on long bone robusticity and cross-sectional shape in lower limb bones of bovids, Neandertals, and upper Paleolithic modern humans. In K. J. Carlson & D. Marchi (Eds.), *Reconstructing mobility: Environmental, behavioral, and morphological determinants* (pp. 227–252). Boston, MA: Springer US. https://doi.org/10.1007/978-1-4899-7460-0_13

Holt, B. M. (2003). Mobility in upper Paleolithic and Mesolithic Europe: Evidence from the lower limb. *American Journal of Physical Anthropology*, *122*, 200–215. https://doi.org/10.1002/ajpa.10256

Holt, B. M., & Whittey, E. (2019). The impact of terrain on lower limb bone structure. *American Journal of Physical Anthropology*, *168*, 729–743. https://doi.org/10.1002/ajpa.23790

Holt, B. M., Whittey, E., Niskanen, M., Sládek, V., Berner, M., & Ruff, C. B. (2018). Temporal and geographic variation in robusticity. In C.B. Ruff (Ed.), *Skeletal variation and adaptation in Europeans*. Hoboken: John Wiley & Sons, Inc. https://doi.org/10.1002/9781118628430.ch5

Hsieh, Y. F., Robling, A. G., Ambrosius, W. T., Burr, D. B., & Turner, C. H. (2001). Mechanical loading of diaphyseal bone in vivo: The strain threshold for an osteogenic response varies with location. *Journal of Bone and Mineral Research*, *16*, 2291–2297. https://doi.org/10.1359/jbmr.2001.16.12.2291

Huiskes, R. (2000). If bone is the answer, then what is the question? *Journal of Anatomy*, *197*(Pt 2), 145–156.

Inskip, S., Scheib, C. L., Wohns, A. W., Ge, X., Kivisild, T., & Robb, J. (2019). Evaluating macroscopic sex estimation methods using genetically sexed archaeological material: The medieval skeletal collection from St John's Divinity School, Cambridge. *American Journal of Physical Anthropology*, *168*, 340–351. https://doi.org/10.1002/ajpa.23753

Isales, C. M., & Seeman, E. (2018). Menopause and age-related bone loss. In J.P. Bilezikian (Ed.), *Primer on the metabolic bone diseases and disorders of mineral metabolism* (pp. 155–161). Hoboken: John Wiley & Sons, Inc. https://doi.org/10.1002/9781119266594.ch21

Judex, S., Garman, R., Squire, M., Busa, B., Donahue, L. R., & Rubin, C. (2004). Genetically linked site-specificity of disuse osteoporosis. *Journal of Bone and Mineral Research*, *19*, 607–613. https://doi.org/10.1359/JBMR.040110

Judex, S., Gross, T. S., & Zernicke, R. F. (1997). Strain gradients correlate with sites of exercise-induced bone-forming surfaces in the adult skeleton. *Journal of Bone and Mineral Research*, *12*, 1737–1745. https://doi.org/10.1359/jbmr.1997.12.10.1737

Judex, S., Zhang, W., Donahue, L. R., & Ozcivici, E. (2013). Genetic loci that control the loss and regain of trabecular bone during unloading and reambulation. *Journal of Bone and Mineral Research*, *28*, 1537–1549. https://doi.org/10.1002/jbmr.1883

Kim, Y. S., Han, J. J., Lee, J., Choi, H. S., Kim, J. H., & Lee, T. (2017). The correlation between bone mineral density/trabecular bone score and body mass index, height, and weight. *Osteoporosis and Sarcopenia*, *3*, 98–103. https://doi.org/10.1016/j.afos.2017.02.001

Kivell, T. L. (2016). A review of trabecular bone functional adaptation: What have we learned from trabecular analyses in extant hominoids and what can we apply to fossils? *Journal of Anatomy*, *228*, 569–594. https://doi.org/10.1111/joa.12446

Laferriere, A. (2017). *The Austin Friars in pre-Reformation English society*. (DPhil.). University of Oxford.

Lambers, F. M., Schulte, F. A., Kuhn, G., Webster, D. J., & Müller, R. (2011). Mouse tail vertebrae adapt to cyclic mechanical loading by increasing bone formation rate and decreasing bone resorption rate as shown by time-lapsed in vivo imaging of dynamic bone morphometry. *Bone*, *49*, 1340–1350. https://doi.org/10.1016/j.bone.2011.08.035

LaMothe, J. M., Hamilton, N. H., & Zernicke, R. F. (2005). Strain rate influences periosteal adaptation in mature bone. *Medical Engineering & Physics*, *27*, 277–284. https://doi.org/10.1016/j.medengphy.2004.04.012

Langsetmo, L., Vo, T. N., Ensrud, K. E., Taylor, B. C., Cawthon, P. M., Schwartz, A. V., … Osteoporotic Fractures in Men (MrOS) Research Group. (2016). The association between trabecular bone score and lumbar spine volumetric BMD is attenuated among older men with high body mass index. *Journal of Bone and Mineral Research*, *31*, 1820–1826. https://doi.org/10.1002/jbmr.2867

Lanyon, L. E. (1984). Functional strain as a determinant for bone remodeling. *Calcified Tissue International*, *36*(Suppl 1), S56–S61.

Larsen, C. S. (1995). Biological changes in human populations with agriculture. *Annual Review of Anthropology*, *24*, 185–213. https://doi.org/10.1146/annurev.an.24.100195.001153

Lazenby, R. A., Skinner, M. M., Kivell, T. L., & Hublin, J. J. (2011). Scaling VOI size in 3D μCT studies of trabecular bone: A test of the over-sampling hypothesis. *American Journal of Physical Anthropology*, *144*, 196–203. https://doi.org/10.1002/ajpa.21385

Lee, J. S. (2003). Feeding the colleges: Cambridge's food and fuel supplies, 1450–1560. *The Economic History Review*, *56*, 243–264. https://doi.org/10.1046/j.1468-0289.2003.00249.x

Lieberman, D. E., Polk, J. D., & Demes, B. (2004). Predicting long bone loading from cross-sectional geometry. *American Journal of Physical Anthropology*, *123*, 156–171. https://doi.org/10.1002/ajpa.10316

Looker, A. C., Sarafrazi Isfahani, N., Fan, B., & Shepherd, J. A. (2016). Trabecular bone scores and lumbar spine bone mineral density of US adults: Comparison of relationships with demographic and body size variables. *Osteoporosis International*, *27*, 2467–2475. https://doi.org/10.1007/s00198-016-3550-6

Macdonald, H. M., Nishiyama, K. K., Kang, J., Hanley, D. A., & Boyd, S. K. (2011). Age-related patterns of trabecular and cortical bone loss differ between sexes and skeletal sites: A population-based HR-pQCT study. *Journal of Bone and Mineral Research*, *26*, 50–62. https://doi.org/10.1002/jbmr.171

Macintosh, A. A., Davies, T. G., Pinhasi, R., & Stock, J. T. (2015). Declining tibial curvature parallels ~6150 years of decreasing mobility in central European agriculturalists. *American Journal of Physical Anthropology*, *157*, 260–275. https://doi.org/10.1002/ajpa.22710

Macintosh, A. A., Pinhasi, R., & Stock, J. T. (2014a). Divergence in male and female manipulative behaviors with the intensification of metallurgy in Central Europe. *PLoS One*, *9*, e112116. https://doi.org/10.1371/journal.pone.0112116

Macintosh, A. A., Pinhasi, R., & Stock, J. T. (2014b). Lower limb skeletal biomechanics track long-term decline in mobility across ~6150 years of agriculture in Central Europe. *Journal of Archaeological Science*, *52*, 376–390. https://doi.org/10.1016/j.jas.2014.09.001

Maga, M., Kappelman, J., Ryan, T. M., & Ketcham, R. A. (2006). Preliminary observations on the calcaneal trabecular microarchitecture of extant large-bodied hominoids. *American Journal of Physical Anthropology*, *129*, 410–417. https://doi.org/10.1002/ajpa.20276

Marchi, D., Sparacello, V. S., & Shaw, C. N. (2011). Mobility and lower limb robusticity of a pastoralist Neolithic population from North-Western Italy. In R. Pinhasi & J. T. Stock (Eds.), *Human bioarchaeology of the transition to agriculture* (pp. 317–346). Chichester: John Wiley & Sons, Ltd. https://doi.org/10.1002/9780470670170.ch13

Meakin, L. B., Galea, G. L., Sugiyama, T., Lanyon, L. E., & Price, J. S. (2014). Age-related impairment of bones' adaptive response to loading in mice is associated with sex-related deficiencies in osteoblasts but no change in osteocytes. *Journal of Bone and Mineral Research*, *29*, 1859–1871. https://doi.org/10.1002/jbmr.2222

Nikita, E., Siew, Y. Y., Stock, J., Mattingly, D., & Lahr, M. M. (2011). Activity patterns in the Sahara Desert: An interpretation based on cross-sectional geometric properties. *American Journal of Physical Anthropology*, *146*, 423–434. https://doi.org/10.1002/ajpa.21597

Parfitt, A. M. (2002). Misconceptions (2): Turnover is always higher in cancellous than in cortical bone. *Bone*, *30*, 807–809. https://doi.org/10.1016/S8756-3282(02)00735-4

Peacock, S. J., Coats, B. R., Kirkland, J. K., Tanner, C. A., Garland, T., & Middleton, K. M. (2018). Predicting the bending properties of long bones: Insights from an experimental mouse model. *American Journal of Physical Anthropology*, *165*, 457–470. https://doi.org/10.1002/ajpa.23363

Pivonka, P., Park, A., & Forwood, M. R. (2018). Functional adaptation of bone: The mechanostat and beyond. In P. Pivonka (Ed.), *Multiscale mechanobiology of bone remodeling and adaptation* (pp. 1–60). Cham: Springer International Publishing. https://doi.org/10.1007/978-3-319-58845-2_1

Popp, K. L., Hughes, J. M., Martinez-Betancourt, A., Scott, M., Turkington, V., Caksa, S., … Bouxsein, M. L. (2017). Bone mass, microarchitecture and strength are influenced by race/ethnicity in young adult men and women. *Bone*, *103*, 200–208. https://doi.org/10.1016/j.bone.2017.07.014

Popp, K. L., Xu, C., Yuan, A., Hughes, J. M., Unnikrishnan, G., Reifman, J., & Bouxsein, M. L. (2019). Trabecular microstructure is influenced by race and sex in black and white young adults. *Osteoporosis International*, *30*, 201–209. https://doi.org/10.1007/s00198-018-4729-9

Raichlen, D. A., Gordon, A. D., Foster, A. D., Webber, J. T., Sukhdeo, S. M., Scott, R. S., … Ryan, T. M. (2015). An ontogenetic framework linking locomotion and trabecular bone architecture with applications for reconstructing hominin life history. *Journal of Human Evolution*, *81*, 1–12. https://doi.org/10.1016/j.jhevol.2015.01.003

Ridler, T. W., & Calvard, S. (1978). Picture thresholding using an iterative selection method. *IEEE Transactions on Systems, Man, and Cybernetics*, *8*(8), 630–632. https://doi.org/10.1109/TSMC.1978.4310039

Robbins, A., Tom, C. A. T. M., Cosman, M. N., Moursi, C., Shipp, L., Spencer, T. M., … Devlin, M. J. (2018). Low temperature decreases bone mass in mice: Implications for humans. *American Journal of Physical Anthropology*, *167*, 557–568. https://doi.org/10.1002/ajpa.23684

Robling, A. G., Hinant, F. M., Burr, D. B., & Turner, C. H. (2002). Improved bone structure and strength after long-term mechanical loading is greatest if loading is separated into short bouts. *Journal of Bone and Mineral Research*, *17*, 1545–1554. https://doi.org/10.1359/jbmr.2002.17.8.1545

Robling, A. G., Warden, S. J., Shultz, K. L., Beamer, W. G., & Turner, C. H. (2007). Genetic effects on bone mechanotransduction in congenic mice harboring bone size and strength quantitative trait loci. *Journal of Bone and Mineral Research*, *22*, 984–991. https://doi.org/10.1359/jbmr.070327

Rubin, M. (1987). *Charity and community in medieval Cambridge*. Cambridge: Cambridge University Press.

Ruff, C. B. (1987). Sexual dimorphism in human lower limb bone structure: Relationship to subsistence strategy and sexual division of labor. *Journal of Human Evolution*, *16*, 391–416. https://doi.org/10.1016/0047-2484(87)90069-8

Ruff, C. B. (1994). Morphological adaptation to climate in modern and fossil hominids. *American Journal of Physical Anthropology*, *37*, 65–107. https://doi.org/10.1002/ajpa.1330370605

Ruff, C. B. (1999). Skeletal structure and behavioral patterns of prehistoric Great Basin populations. In B. E. Hemphill & C. S. Larsen (Eds.), *Prehistoric lifeways in the Great Basin wetlands: Bioarchaeological reconstruction and interpretation* (pp. 290–320). Salt Lake City: University of Utah Press.

Ruff, C. B. (2005). Mechanical determinants of bone form: Insights from skeletal remains. *Journal of Musculoskeletal and Neuronal Interactions*, *5*, 202–212.

Ruff, C. B. (2008). Biomechanical analyses of archaeological human skeletons. In: M.A. Katzenberg & S.R. Saunders (Eds.), *Biological Anthropology of the Human Skeleton*, 183–206. Hoboken: John Wiley & Sons, Inc. https://doi.org/10.1002/9780470245842.ch6

Ruff, C. B., Holt, B., Niskanen, M., Sladek, V., Berner, M., Garofalo, E., … Whittey, E. (2015). Gradual decline in mobility with the adoption of food production in Europe. *Proceedings of the National Academy of Sciences of the United States of America*, *112*, 7147–7152. https://doi.org/10.1073/pnas.1502932112

Ruff, C. B., Holt, B. M., Niskanen, M., Sladék, V., Berner, M., Garofalo, E., … Tompkins, D. (2012). Stature and body mass estimation from skeletal remains in the European Holocene. *American Journal of Physical Anthropology*, *148*, 601–617. https://doi.org/10.1002/ajpa.22087

Ruff, C. B., Larsen, C. S., & Hayes, W. C. (1984). Structural changes in the femur with the transition to agriculture on the Georgia coast. *American Journal of Physical Anthropology*, *64*, 125–136. https://doi.org/10.1002/ajpa.1330640205

Ruff, C. B., Warden, S. J., & Carlson, K. J. (2018). Of mice and men (and women): Comment on Peacock et al., 2018. *American Journal of Physical Anthropology*, *167*, 185–189. https://doi.org/10.1002/ajpa.23615

Ruimerman, R., Hilbers, P., van Rietbergen, B., & Huiskes, R. (2005). A theoretical framework for strain-related trabecular bone maintenance and adaptation. *Journal of Biomechanics*, *38*, 931–941. https://doi.org/10.1016/j.jbiomech.2004.03.037

Ryan, T. M., & Ketcham, R. A. (2002a). Femoral head trabecular bone structure in two omomyid primates. *Journal of Human Evolution*, *43*, 241–263. https://doi.org/10.1006/jhev.2002.0575

Ryan, T. M., & Ketcham, R. A. (2002b). The three-dimensional structure of trabecular bone in the femoral head of strepsirrhine primates. *Journal of Human Evolution*, *43*, 1–26. https://doi.org/10.1006/jhev.2002.0552

Ryan, T. M., & Ketcham, R. A. (2005). Angular orientation of trabecular bone in the femoral head and its relationship to hip joint loads in leaping primates. *Journal of Morphology*, *265*, 249–263. https://doi.org/10.1002/jmor.10315

Ryan, T. M., & Krovitz, G. E. (2006). Trabecular bone ontogeny in the human proximal femur. *Journal of Human Evolution*, *51*, 591–602. https://doi.org/10.1016/j.jhevol.2006.06.004

Ryan, T. M., & Shaw, C. N. (2012). Unique suites of trabecular bone features characterize locomotor behavior in human and non-human anthropoid primates. *PLoS One*, *7*, e41037. https://doi.org/10.1371/journal.pone.0041037

Ryan, T. M., & Shaw, C. N. (2013). Trabecular bone microstructure scales allometrically in the primate humerus and femur. *Proceedings of the Royal Society B: Biological Sciences*, *280*, 20130172. https://doi.org/10.1098/rspb.2013.0172

Ryan, T. M., & Shaw, C. N. (2015). Gracility of the modern *Homo sapiens* skeleton is the result of decreased biomechanical loading. *Proceedings of the National Academy of Sciences of the United States of America*, *112*, 372–377. https://doi.org/10.1073/pnas.1418646112

Saers, J. P. P., Cazorla-Bak, Y., Shaw, C. N., Stock, J. T., & Ryan, T. M. (2016). Trabecular bone structural variation throughout the human lower limb. *Journal of Human Evolution*, *97*, 97–108. https://doi.org/10.1016/j.jhevol.2016.05.012

Saers, J. P. P., Ryan, T. M. & Stock, J. T. (2019a). Baby steps towards linking calcaneal trabecular bone ontogeny and the development of bipedal human gait. *Journal of Anatomy*, 10.1111/joa.13120. doi:https://doi.org/10.1111/joa.13120, *236*, 474, 492

Saers, J. P. P., Ryan, T. M., & Stock, J. T. (2019b). Trabecular bone functional adaptation and sexual dimorphism in the human foot. *American Journal of Physical Anthropology*, *168*, 154–169. https://doi.org/10.1002/ajpa.23732

Saers, J. P. P., Ryan, T. M., & Stock, J. T. (2019c). Trabecular bone structure scales allometrically in the foot of four human groups. *Journal of Human Evolution*, *135*, 102654. https://doi.org/10.1016/j.jhevol.2019.102654

Scherf, H., Wahl, J., Hublin, J.-J., & Harvati, K. (2016). Patterns of activity adaptation in humeral trabecular bone in Neolithic humans and present-day people. *American Journal of Physical Anthropology*, *159*, 106–115. https://doi.org/10.1002/ajpa.22835

Shaw, C. N., & Stock, J. T. (2009). Habitual throwing and swimming correspond with upper limb diaphyseal strength and shape in modern human athletes. *American Journal of Physical Anthropology*, *140*, 160–172. https://doi.org/10.1002/ajpa.21063

Shaw, C. N., & Stock, J. T. (2013). Extreme mobility in the late Pleistocene? Comparing limb biomechanics among fossil *Homo*, varsity athletes and Holocene foragers. *Journal of Human Evolution*, *64*, 242–249. https://doi.org/10.1016/j.jhevol.2013.01.004

Skinner, M. M., Stephens, N. B., Tsegai, Z. J., Foote, A. C., Nguyen, N. H., Gross, T., … Kivell, T. L. (2015). Human-like hand use in *Australopithecus africanus*. *Science*, *347*, 395–399. https://doi.org/10.1126/science.1261735

Sládek, V., Ruff, C. B., Berner, M., Holt, B., Niskanen, M., Schuplerová, E., & Hora, M. (2016). The impact of subsistence changes on humeral bilateral asymmetry in terminal Pleistocene and Holocene Europe. *Journal of Human Evolution*, *92*, 37–49. https://doi.org/10.1016/j.jhevol.2015.12.001

Sode, M., Burghardt, A. J., Kazakia, G. J., Link, T. M., & Majumdar, S. (2010). Regional variations of gender-specific and age-related differences in trabecular bone structure of the distal radius and tibia. *Bone*, *46*, 1652–1660. https://doi.org/10.1016/j.bone.2010.02.021

Stephens, N. B., Kivell, T. L., Pahr, D. H., Hublin, J. J., & Skinner, M. M. (2018). Trabecular bone patterning across the human hand. *Journal of Human Evolution*, *123*, 1–23. https://doi.org/10.1016/j.jhevol.2018.05.004

Stock, J. T. (2006). Hunter-gatherer postcranial robusticity relative to patterns of mobility, climatic adaptation, and selection for tissue economy. *American Journal of Physical Anthropology*, *131*, 194–204. https://doi.org/10.1002/ajpa.20398

Stock, J. T., O'Neill, M. C., Ruff, C. B., Zabecki, M., Shackelford, L., & Rose, J. C. (2011). Body size, skeletal biomechanics, mobility and habitual activity from the late palaeolithic to the mid-dynastic Nile Valley. In R. Pinhasi & J. T. Stock (Eds.), *Human bioarchaeology of the transition to agriculture* (pp. 347–367). Chichester: John Wiley & Sons, Ltd. https://doi.org/10.1002/9780470670170.ch14

Stock, J. T., & Pfeiffer, S. (2001). Linking structural variability in long bone diaphyses to habitual behaviors: Foragers from the southern African later stone age and the Andaman Islands. *American Journal of Physical Anthropology*, *115*, 337–348. https://doi.org/10.1002/ajpa.1090

Su, A., & Carlson, K. J. (2017). Comparative analysis of trabecular bone structure and orientation in south African hominin tali. *Journal of Human Evolution*, *106*, 1–18. https://doi.org/10.1016/j.jhevol.2016.12.006

Sugiyama, T., Meakin, L. B., Browne, W. J., Galea, G. L., Price, J. S., & Lanyon, L. E. (2012). Bones' adaptive response to mechanical loading is essentially linear between the low strains associated with disuse and the high strains associated with the lamellar/woven bone transition. *Journal of Bone and Mineral Research*, *27*, 1784–1793. https://doi.org/10.1002/jbmr.1599

Temple, D. H., Auerbach, B. M., Nakatsukasa, M., Sciulli, P. W., & Larsen, C. S. (2008). Variation in limb proportions between Jomon foragers and Yayoi agriculturalists from prehistoric Japan. *American*

Journal of Physical Anthropology, *137*, 164–174. https://doi.org/10.1002/ajpa.20853

Trinkaus, E., Churchill, S. E., & Ruff, C. B. (1994). Postcranial robusticity in *Homo*. II: Humeral bilateral asymmetry and bone plasticity. *American Journal of Physical Anthropology*, *93*, 1–34. https://doi.org/10.1002/ajpa.1330930102

Tsegai, Z. J., Kivell, T. L., Gross, T., Nguyen, N. H., Pahr, D. H., Smaers, J. B., & Skinner, M. M. (2013). Trabecular bone structure correlates with hand posture and use in hominoids. *PLoS One*, *8*, e78781. https://doi.org/10.1371/journal.pone.0078781

Tsubota, K., Adachi, T., & Tomita, Y. (2002). Functional adaptation of cancellous bone in human proximal femur predicted by trabecular surface remodeling simulation toward uniform stress state. *Journal of Biomechanics*, *35*, 1541–1551. https://doi.org/10.1016/s0021-9290(02)00173-2

Turner, C. H., Owan, I., & Takano, Y. (1995). Mechanotransduction in bone: Role of strain rate. *American Journal of Physiology*, *269*, E438–E442. https://doi.org/10.1152/ajpendo.1995.269.3.E438

Turner, C. H., & Robling, A. G. (2003). Designing exercise regimens to increase bone strength. *Exercise and Sport Sciences Reviews*, *31*, 45–50. https://doi.org/10.1097/00003677-200301000-00009

van der Meulen, M. C., Morgan, T. G., Yang, X., Baldini, T. H., Myers, E. R., Wright, T. M., & Bostrom, M. P. (2006). Cancellous bone adaptation to in vivo loading in a rabbit model. *Bone*, *38*, 871–877. https://doi.org/10.1016/j.bone.2005.11.026

van der Meulen, M. C., Yang, X., Morgan, T. G., & Bostrom, M. P. (2009). The effects of loading on cancellous bone in the rabbit. *Clinical Orthopaedics and Related Research*, *467*, 2000–2006. https://doi.org/10.1007/s11999-009-0897-4

Wallace, I. J., Demes, B., & Judex, S. (2017). Ontogenetic and genetic influences on bone's responsiveness to mechanical signals. In C. J. Percival & J. T. Richtsmeier (Eds.), *Building bones: Bone formation and development in anthropology* (pp. 205–232). Cambridge: Cambridge University Press. https://doi.org/10.1017/9781316388907.011

Wallace, I. J., Demes, B., Mongle, C., Pearson, O. M., Polk, J. D., & Lieberman, D. E. (2014). Exercise-induced bone formation is poorly linked to local strain magnitude in the sheep tibia. *PLoS One*, *9*, e99108. https://doi.org/10.1371/journal.pone.0099108

Wallace, I. J., Judex, S., & Demes, B. (2015). Effects of load-bearing exercise on skeletal structure and mechanics differ between outbred populations of mice. *Bone*, *72*, 1–8. https://doi.org/10.1016/j.bone.2014.11.013

Wallace, I. J., Tommasini, S. M., Judex, S., Garland, T., Jr., & Demes, B. (2012). Genetic variations and physical activity as determinants of limb bone morphology: An experimental approach using a mouse model. *American Journal of Physical Anthropology*, *148*, 24–35. https://doi.org/10.1002/ajpa.22028

Watson, S. (2006). The origins of the English hospital. *Transactions of the Royal Historical Society*, *16*, 75–94. https://doi.org/10.1017/S0080440106000466

Wells, J. C. (2012). Ecogeographical associations between climate and human body composition: Analyses based on anthropometry and skinfolds. *American Journal of Physical Anthropology*, *147*, 169–186. https://doi.org/10.1002/ajpa.21591

Wescott, D. J. (2006). Effect of mobility on femur midshaft external shape and robusticity. *American Journal of Physical Anthropology*, *130*, 201–213. https://doi.org/10.1002/ajpa.20316

Willie, B. M., Birkhold, A. I., Razi, H., Thiele, T., Aido, M., Kruck, B., … Duda, G. N. (2013). Diminished response to in vivo mechanical loading in trabecular and not cortical bone in adulthood of female C57Bl/6 mice coincides with a reduction in deformation to load. *Bone*, *55*, 335–346. https://doi.org/10.1016/j.bone.2013.04.023

SUPPORTING INFORMATION

Additional supporting information may be found online in the Supporting Information section at the end of this article.

How to cite this article: Mulder B, Stock JT, Saers JPP, Inskip SA, Cessford C, Robb JE. Intrapopulation variation in lower limb trabecular architecture. *Am J Phys Anthropol*. 2020; 1–18. https://doi.org/10.1002/ajpa.24058