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Title: Economic access influences degenerative spine disease outcomes at rural Late Medieval Villamagna (Lazio, IT)

Running Title: Economic access influences spine disease

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Abstract

Objectives: Degenerative joint disease in the spine is heavily influenced by genetic, environmental, and epigenetic factors, as well as exacerbated by physical activity and injury. The objective of this study was to investigate the multivariate relationship between known predictors of degenerative joint disease in the spine, such as age and sex, with mortuary indicators of economic access such as grave inclusions, burial location, and burial type.

Materials & Methods: The presence and severity of vertebral osteophytosis (VO) and vertebral osteoarthritis (VOA) was recorded for the vertebral columns of N=106 adult individuals from the Late Medieval period at the rural monastery of San Pietro at Villamagna in Lazio, Italy (1300-1450 AD). Multiple skeletal indicators of degenerative joint disease, morphological sex, and age were compared with differences in mortuary treatment across four regions of the spine.

Results: There are marked differences in severe joint disease outcome between groups with more and less economic access. Relative risk ratios suggest that males and females with less economic access have elevated risk for VO and VOA in specific spine regions, although this effect is reduced among females.

Discussion: Current research on the consequences of economic and social inequality point to the important role of economic inequality in shaping disease outcomes. Our results suggest that biocultural effects of reduced economic access at the intra-class level may increase vulnerability to the downstream effects of risk exposure (e.g., biomechanical injure, physical activity, biochemical imbalance), and ultimately increase the risk and prevalence for severe degenerative disease outcomes in medieval Italy.

Keywords: *bioarchaeology, osteoarthritis, degenerative joint disease, access, biocultural*

Main Text

1 Introduction

Degenerative Joint Disease (DJD) is common amongst vertebrate organisms (Fox, 1939), and is well documented in New and Old World primates (Jurmain, 2000; Rothschild & Wood, 1992; Rothschild, Hebling, Miles, 2002), *Homo neandertalensis* (Dawson & Trinkaus 1997), and *Homo sapiens* (e.g., Becker & Goldstein, 2018; Bridges, 1991; Schrader, 2012; Walker & Hollimon, 1989). Despite its ubiquity (Bridges, 1991; Jurmain 1977; Jurmain & Kilgore, 1995; Plomp, 2017; Weiss, 2006), the specific etiology of degenerative joint diseases in the spine remains unclear (Weiss, 2006; Weiss & Jurmain, 2007). Progressive degeneration in the many fibro-cartilaginous and synovial joints has a positive relationship

with increasing age (Calce, Kurki, Weston & Gould, 2018; Snodgrass, 2004; Weiss, 2006, Zampetti, Mariotti, Radi, & Belcastro, 2016), however it is increasingly clear that its pathogenesis is non-linear and modulated by multiple factors across the life course (Risbud & Shapiro, 2014; Wang, Cai, Shi, Wang, & Wu, 2016). Epidemiological research suggests that risk for general arthritis is elevated based on social inequality, which is bioculturally entangled with occupation and social status in modern populations due to various epigenetic, genetic, and environmental covariates (Brennan-Olsen et al., 2018; Brennan-Olsen et al., 2019; Rubin, 2007). Bioarchaeological studies of DJD have examined its expression as a possible marker for activity-related stress with varying conclusions and no overall consensus, likely due to the specific pathophysiology of the disease in different joints (e.g., Klaus, Larsen, & Tam, 2009; Larsen, Ruff, & Kelly, 1995; Novak & Šlaus, 2011; Sofaer Derevenski 2001; Weiss & Jurmain, 2007; Woo & Pak, 2014; Zampetti et al., 2016). Recent work by Zampetti et al., (2016) found that there was no association between occupation type and degenerative joint disease expression across the body in a historic (19th and 20th century) Italian sample, suggesting that other interacting factors, beyond activity alone, produce differential disease outcomes in degenerative joint disease. The relationship between physical activity and DJD is certainly multifactorial, joint-specific, and contingent on the specific mechanics of a given activity and certainly has a relationship with biocultural experiences that modulate immune function, aging, and bodily biochemistry. In this study we focus on the vertebral degenerative joint diseases: vertebral osteophytosis and vertebral osteoarthritis.

1.1 Vertebral Degenerative Joint Diseases

The distribution of static (weight-bearing) and dynamic (movement) loading across the skeleton plays an important role in the differential expression and pathophysiology of DJD (Bogduk & Mercer, 2000; Klaus et al., 2009; Zampetti et al., 2016). The bipedal spine is a unique biomechanical system, in humans it is composed of 25 consecutive amphiarthrodial (fibrocartilaginous) joints between the

vertebral bodies, 4 zygapophyseal (synovial) joints between the articular facets of each vertebrae, and a mix of synovial and fibrocartilaginous costovertebral joints in the thoracic region. In *H. sapiens* loadings in the axial skeleton during bipedal posture and locomotion are passed through the vertebral bodies and discs, zygapophyseal joints and posterior elements, and the lateral pedicles (Shapiro, 1993; Bogduk & Endres, 2005). Disturbances in the metabolic balance of the joint matrices of the intervertebral and zygapophyseal joints due to the compounding effects of aging, mechanical loading, epigenetic, and genetic factors ultimately cause morphological changes and remodeling of vertebral centra and articular facet joints' margins and surfaces (Bogduk, 2012; Klaus et al., 2009; Risbud & Shapiro, 2014; Shen et al., 2012). In contemporary populations the prevalence of degenerative joint disease in the lumbar region of the spine ranges from 40-85% (Goode, Carey, & Jordan, 2013). Generalized low back pain (LBP) is a common symptom of spinal degenerative joint disease and affects a large proportion of the US American population: 80% of adults in the United States experience at least one episode of LBP in their lifetime (Goode et al., 2013; Rubin, 2007).

1.2 Vertebral Osteophytosis

The pathophysiology and expression of vertebral osteophytosis (VO) has been well documented in the bioarchaeological and clinical record (e.g., Nathans, 1962; Snodgrass, 2004; van der Merwe, İşcan, & L'Abbè, 2006; Wang et al., 2016; Weiss, 2006). Vertebral osteophytes are the result of localized and progressive hyperostoses that develop at the attachment sites of the annulus fibrosa at the margins of the amphiarthrodial joints of the vertebral centra. Early stages in the pathogenesis of vertebral osteophytosis are marked by horizontally oriented osteophytes on the anterior margin of the vertebral body, which expand to stabilize the compromised disc joint. Severe cases of VO are marked by vertically oriented osteophytes, which may eventually articulate or fuse to form a bony bridge with adjacent vertebral elements. Intervertebral disc degeneration involves age-related changes in disc composition

and biochemistry, as well as accumulated tissue damage due to multiple age progressive stressors, including avascularity resulting in oxidative injure, high magnitude mechanical compression at high frequencies or for prolonged duration, and depleted cellular waste disposal due to acidic, hypertonic, and/or oxidative joint microenvironment (Wang et al., 2016; Risbud & Shapiro, 2014). Recent research from immunology suggests there is a complex series of cellular mechanisms central to a cycle of phenotypic change in the disc and centra, affecting and affected by the amplification of inflammatory pathways and sensitization via neutrophils and other inflammatory mediators (Risbud & Shapiro, 2014). The initiation of degenerative changes in the spine likely occurs due to a combination of these stressors and progresses in a positive feedback system. Previous research suggests that the pattern of osteophyte expression is also related to the curvature of the spine and biomechanical use during load-bearing activities, which result in differentially patterned osteophyte development (Sofaer Derevenski, 2000; Merbs, 1983). These biomechanical and degenerative changes in the vertebral bodies are hypothesized to impact loading and degeneration in the posterior portion of the vertebrae thereby effecting the vertebral articular facets (Shapiro, 1993; Bogduk, 2012). However, previous bioarchaeological finds that VO and VOA (vertebral osteoarthritis) have different patterning in the spine and sometimes an inverse relationship (Bridges, 1994; Knüsel et al., 1997). Overall, bioarchaeological studies of osteophytosis demonstrate a correlation between known activities and disease prevalence (Merbs, 1983); and differential distributions of VO based on sex, physical activity, and/or spine region (Dawson & Trinkaus, 1997; Lieverse, Weber, Bazaliiskiy, Goriunova & Savel'ev, 2007; Lovell, 1994; Maat, Mastwijk, & Van Der Velde, 1995; Sofaer Derevenski, 2000).

1.3 Vertebral Osteoarthritis

Vertebral Osteoarthritis (VOA) involves the vertebral articular facets, or zygapophyseal joints; these are synovial joints and therefore their degeneration and morphological change are a true arthrosis

of the spine (Gellhorn, Katz, & Suri, 2013). Like VO, VOA is a dynamic process of whole-joint failure, on mechanical, metabolic, and cellular levels, although OA in the facet joints remains one of the most understudied phenotypes of osteoarthritis in the skeleton. VOA is a positive feedback phenomenon, whereby a cycle of degenerative and proliferative bone changes (i.e., narrowing of joint space, subarticular bone erosion, hypertrophy, and osteophyte formation) modulated by pro-inflammatory pathways, metainflammation, and toxic internal joint microenvironment lead to disease progression (Gellhorn et al., 2013; Kalichman et al., 2008; Risbud & Shapiro, 2014; Wang et al., 2015). Previous bioarchaeological studies of VOA have shown a relationship between weight-bearing activities and VOA prevalence (Novak & Slaus, 2007), however the results of bioarchaeological analyses of VOA have largely been inconclusive with regard to physical activity, highlighting the confounding effects of epigenetic and environmental factors. Larsen (2003) argues that articular pathology like VOA is more indicative of general physical injury and stress, rather than particular to specific occupational activities. Prevalence of VOA in the bioarchaeological record is often associated with biomechanical overuse, or injure of the spinal column, and results in differential patterning across regions of the spine (Knüsel et al., 1997; Merbs, 1983; Stirland & Waldron, 1997).

2 Medieval Context

Medieval Europe is broadly characterized by its increasing urbanization, migration, regional conquest, and socio-cultural differentiation. Historians postulate that the majority of medieval people lived and worked in the countryside (Kowaleski, 2014), and attention to the bioarchaeological records of rural medieval sites has grown in recent years (e.g., Reitsema & Vercellotti, 2012; Reitsema et al., 2017; Stewart, 2017; Veselka, Hoogland & Waters-Rist, 2015; Walter & DeWitte, 2017). Rural economies were shaped by experiences of difference along multiple lines of identity, especially gender, religious, social, economic, and ethnic status (Whittle, 2013; Moore, 2007; Kent 2009). Based on previous bioarchaeological studies, we are cautious to use urban models of health and disease to predict

outcomes for rural populations. Lewis et al., (1995) showed marked differences in prevalence of maxillary sinusitis between urban and rural populations in England, and more recent work by Veselka et al., (2015) suggests that disease outcomes are variable between rural and urban populations in the Netherlands.

Several bioarchaeological studies have examined the consequences of social and status differences in medieval Europe (e.g., Stewart & Vercellotti, 2017; Trautmann, Wißing, Díaz-Zorita, & Bonilla, 2017; Vercellotti, Stout, Boano, & Sciulli, 2011; Watts, 2015). This research has demonstrated the impact of status differences on health, stress, diet, and disease. For example, differences in economic and religious status have marked variations in diet (Reitsema & Vercellotti, 2012), reduced stature for males, and elevated linear enamel hypoplasia for females (Vercellotti et al., 2014). Positive associations between increased growth outcomes and socioeconomic status have been found in northern Italy (Stewart & Vercellotti, 2017; Vercellotti et al., 2011); and more broadly, research has documented the dynamic and synergistic effects of social differences on diet and foodways in the medieval period at the local, regional, and continental scale (Müldner et al., 2009; Reitsema, Crews, & Polcyn, 2010; Reitsema & Vercellotti, 2012; Salamon, Coppa, McCormick, Rubini, Vargiu & Tuross, 2007; Smith, Reitsema, Williams, Boano, & Vercellotti, 2019).

Social status in medieval contexts has been examined using multiple lines of mortuary evidence, especially burial location, burial typology, and grave good inclusions (Vercellotti et al., 2011). From the Early Medieval period onward, it was common for clergy, privileged families, and patrons to be buried inside the church structures, while the general population was buried outside the church (Goodson, 2016; Vercellotti et al., 2011). Burial typology also reveals much about the status of the interred individuals in the Medieval period. In Italy it is typical for burials at the periphery of the churchyard to be earthen, while many of the burials in or along the church structure are tombs, and proximity to the sanctuary of the church is more desirable (Goodson, 2016). Although the inclusion of grave goods is

complicated by social mores, cultural ideology, and spatiotemporal variation, the presence and typology of grave goods can yield information about how an individual was considered by others in their death, and about the overall wealth of an individual and/or their familial network. In the context of Medieval Christianity, where grave goods are typically rare (O'Sullivan, 2013), the presence of any object, including clothing notions, jewelry, or ceramic offerings provides information on individual status (Vercellotti et al., 2011).

We frame burial differentiation in terms of individual, familial, and/or collective access to wealth and economic privilege. Framing this phenomenon of economic differences in terms of *access* highlights the actual intra-class differences between and amongst peasants in the rural medieval landscape, instead of as compared to elite or noble people (rural or urban). In this paper, we consider how these intra-class differences (i.e., amongst peasant farmers) may affect health outcomes and how increased access to modest economic privileges might impact spine disease risk and vulnerability, patterns that have been observed in contemporary human populations (e.g., Brennan-Olsen et al. 2019; Miszkiewicz et al. 2019). We hypothesize that less access to economic resources produces higher prevalence of severe VO and VOA due to increased risk exposure and increased vulnerability to labor-related wear-and-tear changes to the joints.

3 Materials

The study site, Villamagna, represents a cross-section of everyday people from the rural medieval countryside of Central Italy (Fentress & Maiuro, 2011; Fentress, Goodson, & Maiuro, 2016). The site was excavated between 2006 and 2010 and is located nearly 65 km southeast of Rome in Lazio (Fentress & Maiuro, 2011), and is one of the largest stratigraphically excavated medieval cemeteries in Europe. It is in close visual and political proximity to the city of Anagni in the Sacco Valley (see Figure 1), an active site of much political power throughout the Medieval Period due to its associations with Rome and the papacy.

[Figure 1. Map of Villamagna, Lazio, Italy]

The skeletal assemblage excavated from Villamagna includes individuals from the Early (800-1000 AD), Central (1000-1300 AD), and Late Medieval (1300-1450AD) periods based on 23 radiocarbon dates (Fenwick, 2016). The site was dominated in the second century by a villa, probably constructed by the emperor Antoninus Pius (Fentress & Maiuro, 2011). Later in the sixth century, the church San Pietro was constructed 150m northwest of the Roman Villa; and during the ninth century the villa was reconfigured as an elite residence and costly architectural interventions were made at the church (Goodson, 2016). The Benedictine monastery was formed in 976 AD and suppressed in 1297 AD (Goodson, 2016; Carrocci, 2016). By the Late Medieval Period (c. 1300 AD), Villamagna had been restructured as a fortified village, or *castrum*, which produces a variety of crops and produce for the local diocese. During the 14th century, ownership of the site was contested between the church of Anagni and local noble families with ties to the papacy, and archaeological evidence suggests that the residents of Villamagna were ordinary rural farmers. Extensive archaeological studies have been completed at Villamagna (Fentress et al., 2016), providing rich contextual information and multiple lines of evidence to support the interpretation of bioarchaeological and skeletal indicators of life experience. Archaeological evidence of privileged tombs, military personnel, and rare glassware demonstrate the presence of people with elevated economic access to resources (Rascaglia, 2016).

Evidence from the fortified occupation in the Late Medieval Period is markedly characterized by material culture of military and equestrian uses, suggesting that the defunct monastery then operated as a fortified military center in the Late Medieval period (Franconi, 2016). In the churchyard, tomb burials have been interpreted as family plots, a privilege associated with economic access to more prestigious burial, while earthen graves are generally undifferentiated (Fenwick, 2016). Burials inside the church likely belonged to a wealthy family (Fenwick, 2016). While the inclusion of grave goods is interpreted as a sign of (albeit limited) access to disposable or replaceable material resources. These

mortuary treatments and interpretations are typical of medieval Christian cemeteries (Fenwick, 2016; Gilchrist & Sloane, 2005). Unlike many other published sites from this period, there is no evidence that an epidemic of *Yersinia* (Black Death) affected the site (Agarwal et al., 2015; Goodson, 2016). Recent bioarchaeological research at Villamagna suggests that oral health indicators had complex patterning with relation to age and sex (Trombley et al., 2019).

In order to investigate the role of economic experience and sex in determining disease outcomes, we examined the spines of N=106 individuals (Male n= 60, Female n= 46) from the Late Medieval Period at Villamagna (Table 1). We analyzed the spine elements for all excavated adult individuals with good to excellent preservation from the site from the Late period.

[Table 1. Spine observations at Villamagna by sex and age]

Late Medieval burials are distributed across the church and churchyard, where individuals were buried in earthen graves or subterranean tombs and were buried in three different directions: east-west, north-south, or southwest-northeast. Individuals at the site were buried with and without grave inclusions, such as rings, rosaries, lamps, coins, and clothing notions (Goodson, 2016); fill inclusions such as nails or nonspecific iron or unidentified ceramics sherds were not counted as grave goods. For our analyses, we pooled grave goods as present (1) or absent (0) due to the relatively small proportions for sub-categories of grave goods.

4 Methods

4.1 Biological Profile

Morphological sex was estimated based on observation of the *os coxae* and cranial morphology (Ascàdi & Nemeskèri, 1970; Brothwell, 1981; Buikstra & Ubelaker, 1994; see Trombley et al., 2019 for further discussion of sex estimation at Villamagna). Adult age was estimated using multiple standard morphological indicators from the pubic symphysis (Brooks & Suchey, 1990) and auricular surface (Lovejoy, Meindl, Pryzbeck, & Mensforth, 1985); these were corroborated by examination of the sternal

end of the rib when possible (İşcan, Loth & Wright, 1984; 1985). We categorized individuals using three conservative age groups: 18-29 years (young adult), 30-49 years (middle adult), and 50+ years (older adult) to remedy the issue of precise aging in skeletal assemblages without documentary records of age (Jackes, 2000). Four individuals (VO n=19, VOA n= 18) could not be classed into an age group and were included in our analyses (excepting age-based analyses) as 18+ years (indeterminate age adult).

We observed the vertebral body, articular facets, intervertebral disc surfaces of each element of the spine, and scored the degree of morphological change. Occasionally vertebral bodies had been somewhat damaged post-mortem and one or more articular facets were missing or disarticulated; where possible and in most cases, individual vertebrae were reconstructed, and articular facets were refit with their corresponding vertebra.

4.2 Spine Observation

We scored Vertebral Osteophytosis (VO) according to standard procedures for recording presence and severity of osteophytosis on an ordinal scale of 0 to 5 (Table 2, Kinkopf, 2020; adapted from Agarwal, 2001; see also Buikstra & Ubelaker, 1994; Sofaer Derevenski, 2000). Vertically oriented enthesophytes that are associated with spondyloarthropathies (such as ankylosing spondylitis), and diffuse idiopathic skeletal hyperostosis (DISH) were scored as 6.1-6.4 but were not included in our analysis.

[Table 2. Vertebral Osteophytosis scoring system]

Vertebral Osteoarthritis (VOA) was scored according to standard procedures for recording presence and severity of zygapophyseal osteoarthritis (Table 3, Kinkopf, 2020; adapted from Agarwal, 2001; see also Sofaer Derevenski, 2000; Klaus et al., 2009). Where possible all four articular facets were observed and scored during data collection.

[Table 3. Vertebral Osteoarthritis scoring system]

4.3 Data Analysis

Data were prepared for analysis according to tidyr protocols in RStudio Cloud (Wickham, 2014; R Studio Team, 2019). Completely missing observations (i.e., all 4 facets missing due to preservation) were removed from the dataset using a list-wise deletion method. Vertebral "regions" were assigned by reducing vertebral elements (1-24) into functional anatomical region: cervical (C1-C7), upper thoracic (T1-T7), lower thoracic (T8-T12), lumbar (L1-L5). The separation of the thoracic segment into upper and lower regions has been shown to be efficacious in differentiating biomechanical and physiological variation in degenerative processes by bioarchaeologists and clinicians and reflects the usual curvature of the spine (e.g., Sofaer Derevenski, 2000; Klaus et al., 2009; Larsen et al., 1995), as well as the biomechanical difference between the region of the thoracic spine (upper) with less rotational capacity due to the articulation of the spine with the ribs and sternum (Watkins et al., 2005).

To increase our statistical power, vertebral body osteophytosis (VO) and vertebral articular facet osteoarthritis (VOA) raw scores were reduced to a binomial variable: low severity (0) or high severity (1). We re-classed these observations based on morphological changes to the joints and known clinical symptomology of those associated changes. Low severity VO includes scores of 0 to 3 (Figure 2), where there would be little to no pain or nerve involvement, minimal joint involvement, and individuals would likely be asymptomatic (Risbud & Shapiro, 2014); high severity VO includes scores of 3.5 to 5 (Figure 3), where there would be marked involvement of the joint, dramatic changes to the biochemical and biomechanical functionality of the disc, and restriction of movement resulting from morphological limitations or nerve pain (Risbud & Shapiro, 2014; Wang et al., 2016). These designations are based on pathophysiology known in clinical studies of VO and VOA (e.g., Risbud & Shapiro, 2014; Wang et al., 2016), however these studies are limited regarding low severity changes by a general bias in clinical literature against asymptomatic patients, who are rarely represented in these clinical studies. For the vertebral articular facets (VOA), the outcomes were reduced to a single high severity or low severity

outcome for each vertebral element based on the median. Low severity VOA included any score between 0 to 3.5 (Figure 4), and high severity VOA was any score 4 to 7 (Figure 5), where there was involvement of more than 25% of the articular surface, macroporosity, pitting, and most often eburnation and partial or complete immobility of the joint (Table 3).

4.4 Statistical Analyses

Multiple correspondence analysis (MCA) was conducted as an exploratory analysis in order to assess associations between explanatory mortuary treatment variables that may be associated with a latent variable, such as economic access during life, using the FactoMineR package (Abdi, Williams, Valentin, 2013; Abdi & Valentin, 2007; Lê, Josse, Rennes, & Husson, 2008). MCA is an extension of correspondence analysis and does not make any distributional assumptions about the data and provides a more precise measure of associations between variables because it does not allow large proportions of one outcome to dominate the distance calculation (Sourial et al., 2010).

Spearman's Rank correlation coefficients were computed to assess the relationship between VO and VOA disease outcomes. To test our hypotheses about the relationship between sex, age, and disease outcome in the population, and to understand that relationship across the spine, we used Pearson's chi-squared test of homogeneity (with Yates correction for continuity, where $df = 1$), and a Fisher's Exact test where expected counts were less than five.

In order to assess the probability of severe disease outcome after exposure to the effects of a given risk variable (i.e., less economic access) compared to the probability of severe disease outcome in our unexposed group (i.e., more economic access) we employed relative risk ratios (Andrade, 2015; see also Trombley et al., 2019 for further discussion of relative risk ratios in bioarchaeology). Relative risk is expressed as a ratio value and is estimated based on the absolute risk given exposure divided by the absolute risk in the unexposed (control) group. The relative risk ratio is similar to the odds ratio (OR);

however, the relative risk ratio considers the probability of an event (i.e., "how likely") whereas the odds ratio examines the odds of an event (i.e., "odds likely") (Ranganathan et al., 2015; Andrade, 2015). In our results, $\widehat{RR}$ values greater than 1.01 indicate an increased risk for severe disease outcome in the exposed group (less economic access), while $\widehat{RR}$ values less than 0.99 indicate greater risk for severe disease outcome in the unexposed group (more economic access).

In addition to the $\widehat{RR}$ point estimate, we report the 95% confidence interval so that the precision of the effect can be understood; if the range given by the confidence interval includes 1.0, that variable may not be significant as it encompasses both probabilities. All statistical analyses were completed in R-Studio Cloud v.1.2 (RStudio Team, 2019); statistical tests and relative risk ratios were computed using the mosaic package (Pruim, Kaplan, & Horton, 2019).

5 Results

5.1 Multiple Correspondence Analysis

Multiple correspondence analysis (MCA) provided four significant dimensions, which together retain 92.8% of the variance for the categorical data (see Supplement 1.1 for inertia decomposition). The first dimension, primarily based on burial location and burial direction, explains 32.3% of the variance in the data; the second dimension, based on grave good inclusion and burial type, explains 23.9% of the variance for the data (Supplement 1.1).

Access to economic privilege can be expressed through multiple types of mortuary treatment; burial inside the church may be indicative of economic access to family plots and an expression of intergenerational privilege and piety. Inclusion of grave goods, particularly of gold coins, rings, and clothing notions—the most common burial inclusions at Villamagna—may be indicative of increased economic access without the benefit of intergenerational economic or spiritual privilege. We interpret the significant dimensions of our eMCA as indicative of expected trends in mortuary practice, reflecting

differences in economic privilege and access amongst the people of Villamagna. Each dimension has two observation groups based on positive and negative loading values for each latent variable.

We supplemented our relative risk analyses with these compromise variables as a way to test for differences in disease outcome risk based on economic experience and difference. Further, these latent variables are commensurate with the findings from Stewart and Vercellotti's (2017) comprehensive examination of mortuary factors and social status from the Piedmont region of Italy, also in the Medieval period and align with historical and archaeological evidence from Villamagna itself (Fentress et al., 2016). Due to the very small number of burials inside the church, we include comparisons between burial location in the supplementary materials (Supplement 2).

5.2 Vertebral Osteophytosis Results

Overall, there is a moderate positive correlation between VO and VOA outcome for the cervical (ρ=0.61, p<.001) and lumbar(ρ=0.55, p<.001) regions, and a small positive correlation effect for the upper thoracic (ρ=0.45, p<.001) and lower thoracic (ρ=0.41, p<.001) regions. There are no overall sex differences in the prevalence of VO in any region of the spine when pooled by age (Table 4).

[Table 4. Comparison of sex differences in severe VO outcome by region of spine]

Young males and females have significantly lower than expected prevalence of severe VO, and middle and older age adults have higher than expected prevalence of severe VO overall (Table 5). Amongst males, the cervical and lumbar spine regions demonstrate a clear increase in prevalence of severe VO in middle and older age groups. The thoracic regions have greater prevalence in young and middle age, and a lesser prevalence in older age, although this trend may be due to the small sample size for older age males (Table 5). In females there is a clear trend of greater prevalence of severe VO in all spine regions in increased age groups (Table 5).

[Table 5. Age comparisons of VO across spine region stratified by sex]

Individuals with less economic access (no grave goods, earthen burial) have increased risk for severe VO (Table 6, Figure 6): Males have significantly increased risk in the lower thoracic and lumbar regions; and females have increased risk in the lower thoracic region only. There is a significant increased risk in middle age males for the lumbar region (Table 7), and a significant increased risk for middle age females in the cervical and lower thoracic regions (Table 7).

[Table 6. Relative risk for severe VO outcome by sex and spine region based on economic access]

[Table 7. Relative risk for severe VO outcome by sex, age, and spine region based on economic access]

[*Figure 6. Spine disease by economic access*]

5.3 Vertebral Osteoarthritis Results

The prevalence of severe VOA outcomes was significantly higher in females compared to males in the lumbar region of the spine; while males have significantly higher prevalence of severe VOA in the upper thoracic region (Table 8).

[Table 8. Comparison of sex differences in severe VOA outcome by region of spine]

There is a significant difference in VOA severity based on age. When compare prevalence across age groups within each sex group, there are sex-based differences in which regions have greater severe VOA prevalence. For males, there is a positive relationship between increasing age and increasing prevalence of VOA for all regions except the lower thoracic, which is likely due to the small number of observations for males in the 50+ years cohort (n=8). However, males attain a 23.9% prevalence of severe VOA in the lower thoracic region, the highest of any region, in young age and maintain that level of prevalence through middle age (25%) (Table 9).

[Table 9. Age comparisons of severe VOA across spine region stratified by sex*]*

Females have a significant difference in the distribution of severe VOA across age groups for the cervical and upper thoracic regions (Table 9). Although females do not have a significant increase in

lumbar VOA across age groups, young age females have the highest prevalence of severe VOA in that region with slight increases in prevalence in middle and old age (Table 9).

[Table 10. Relative risk for severe VOA outcome by sex and spine region based on economic access]

[Table 11. Relative risk for severe VOA outcome by sex, age, and spine region based on economic access]

Males with less economic access have significantly increased risk for severe VOA in each spine region, except the lumbar (Table 10, Figure 6). Young age males in particular have increased risk in the thoracic regions, and middle age males in the cervical and lower thoracic regions (Table 11). Females with less economic access have significantly increased risk ($\widehat{RR}$ = 2.60) in the upper thoracic region and in the full spine, with all regions pooled (Table 10). Amongst females with less economic access, young age females have a general increased risk (full spine), particularly in the lower spine; middle age females have increased risk in the cervical and upper thoracic regions (Table 11). In contrast, older age females with less economic access have decreased risk ($\widehat{RR}$ = 0.50) for VOA in the lumbar region (Table 11).

6 Discussion

We found that less economic access was associated with elevated risk for VO and VOA across the population in multiple regions of the spine. These results demonstrate the important influence of intra-class differences in disease outcomes, and point towards differential risks and vulnerabilities that shape the biocultural experience of economic inequalities. Our results suggest that the effects of intra-class differences intersect with age and sex differences, while also cutting across these boundaries.

6.1 Vertebral Osteophytosis

Across the population, there is a significant increase in the prevalence of severe VO with age in the cervical and lumbar regions of the spine in particular (Table 5). Due to the morphology, physiology, and biochemistry of the cervical and lumbar segments of the spine, these regions are particularly

sensitive to age-related changes in the biochemical and structural changes to the joint environment. The intervertebral disc functions to transmit, absorb, and diffuse mechanical loads/strains in the spine (Risbud & Shapiro, 2014), and the degeneration of disc with senescence is responsible for loss of joint stability, stenosis, and reduction of movement in the spine, usually resulting from a combination of morphological changes to the bone and inflammatory internal joint microenvironment. The cervical disc lacks a concentric anulus fibrosus, and therefore the anulus functions more akin to an interosseous ligament (Bogduk, 2012; Mercer & Bogduk, 1999; Oda, Tanaka, Tsuzuki, 1988); additionally, the nucleus pulposus only persists for approximately 20 years, when it disappears and leaves a fibrocartilaginous plate in its stead (Bland & Boushey, 1990; Bogduk 2012). In contrast, the lumbar disc has a robust concentric anulus fibrosus, supporting its robust weight-bearing capabilities, and degenerative changes to the disc are related to the dehydration of the nucleus and changes in the concentration and nature of proteoglycans, which shift dramatically across the life course, especially in older age (Oda et al., 1988; Risbud & Shapiro, 2014; Shen et al., 2012; Taylor & Twomey, 1986).

Compressive loadbearing in the thoracic spine ranges from 9%-47% of body mass between T1-T12 (White, 1969), and overall the stability of the thoracic spine benefits from the structure of the ribcage and accompanying fascia and ligaments (Edmondston & Singer, 1997). Higher prevalence of severe VO in the lower thoracic regions in middle age for males and females may be a consequence of loadbearing physical labor resulting in mechanical strain and injure to that region (Jurmain, 1999; Klaus et al., 2009). The lack of older males with severe VO in the thoracic regions may be due in part to confounding factors relating to the osteological paradox, whereby males with severe thoracic VO are less likely to live to old age, and older age individuals therefore were the least vulnerable to VO from their cohort; or merely due to the small sample size for older age males in the population.

We found that individuals with less economic access were at higher risk for VO in the thoracic and lumbar regions of the spine; although when we controlled for age and sex, we saw a more nuanced

pattern. Less economic access is associated with an 83% increase in risk for severe VO across all sex groups ($\widehat{RR}$=1.83, Table 6). Additionally, although males and females had elevated risk for severe disease outcome when we sex-stratified our analyses, females had significantly increased risk in the lower thoracic region and males had significantly increased risk in lower thoracic and lumbar regions (see Table 6). The possible causes of economic-based differences in disease outcome may be attributed to the complex environmental (i.e., activity-related) and epigenetic consequences of inequality (e.g., Brennan-Olsen et al., 2019; Dressler, Oths & Gravlee, 2005).

6.2 Vertebral Osteoarthritis

At Villamagna, significant differences in severe VOA outcome are seen between sex groups, but these differences were only observed in the upper thoracic and lumbar regions of the spine. This difference may be due in part to different modes of weight-bearing and movement, differential divisions of labor, and/or reproductive life history, especially given the particularly low prevalence of severe VO in the upper thoracic region, and the role movement, physical activity, and load-bearing play in spine disease in the lumbar region. It is also significant that the age-distribution of the sample is not uniform: 70% of males are in the middle age group, while 30% of females are in the older age group, which likely accounts for some of the differences between males and females in this sample (Table 1). The prevalence of lumbar VOA among females at Villamagna is 11% higher than the prevalence for males (Table 8), indicating that females either were more vulnerable to severe VOA in the lumbar region, or were differentially affected by or participating in weight-bearing physical activities. It is also possible that this higher prevalence reflects the larger proportion of older age females in our sample. However, similar trends in elevated lumbar spine disease have been observed amongst females in the Medieval English population at Wharram Percy (Sofaer Derevenski, 2000), and results from other parts of the world suggest the lumbar region is particularly affected by DJD (Klaus et al., 2009).

Documentary sources from the medieval period in Italy suggest that non-elite women were likely involved in a range of general activities of the home, farm, and village, and overall occupational experiences were more homogenous, therefore we expect less differentiation amongst females. Clinical research on postural changes during pregnancy have found flattening of the lumbar spine during pregnancy, however the long-term consequences of such changes remain unstudied so it is difficult to fully contextualize these changes in terms of reproductive life history (Moore, Dumas & Reid, 1990; Gutke, Östgaard & Öberg, 2006). We suggest that heterogeneity in severe spine disease outcomes for males may be due to the wide array of known occupations available to men in rural contexts (e.g., military service, various agricultural activities), which make it possible for men to have variable life experiences, occupations, and therefore also to differentially embody their lived experience (Goodson, 2016; Whittle, 2013).

Significant age differences in severe VOA prevalence are expected due to the pathophysiology of VOA, where severe disease results from an accumulation of changes to joint biochemistry and biomechanics. For both males and females there were significant difference in the distribution of severe VOA by age in the cervical and upper thoracic regions (Table 9). Although males had a significant difference in the lumbar region, this is based on a small sample size and is likely not representative of the population overall (Table 9). Across the population, the prevalence of severe VOA is 2-4 times higher in middle versus young age in the cervical and upper thoracic regions (Table 9), so although the 4 older males in the population had an even higher prevalence of severe VOA we see that age is related to disease outcome even in middle age (30-49 years). Age-related increases in the cervical region likely reflect the aging and continued use of the neck for weight-bearing activities, as the articular facets of the cervical spine face superior-posteriorly and therefore share in the axial and compression loading and weight bearing function of the cervical centra (Bland & Boushey, 1990; Bogduk & Mercer, 2000). In contrast, thoracic articular facets have limited flexion and anterior translation due to the configuration

of their lamellae, and primarily provide rotation in the upper back (White, 1969). We expect then, that differences in thoracic region VOA are related also to occupational-labor stress, and degenerative changes are exacerbated by these activities, if not a direct consequence.

We know from historical documents (Carocci, 2016, Goodson, 2016) that the annual grape harvest and regular agricultural work at Villamagna were a foundation to everyday life at Villamagna and are possible causes of severe cervical VOA (Kinkopf, 2020). Therefore, it is possible that grape and agricultural harvesting contributed to the elevated levels of cervical VOA in middle age adults. Lovell (1994) and Bridges (1994) have suggested that a higher prevalence of VOA in the cervical spine region may reflect activity-related stresses, such as carrying heavy loads on top of the head, or the use of tumplines.

Males with less economic access were at higher risk for VOA in every region of the spine, except the lumbar region ($\widehat{RR}$=1.70, 95% CI 0.98-2.64). Females, by comparison only have elevated risk for the upper thoracic region and generally are more homogeneous. For example, all females have elevated lumbar VOA (32.3% prevalence for all females; Table 8) and there is no significant difference in lumbar VOA risk between females with less (30.9%) or more (34.2%) economic access (Table 10).

Although it is expected that activity and labor differences influenced the expression and severity of spine disease in the population (Bridges, 1994; Kiorpe, 2014; Rojas-Sepúlveda et al., 2008; Sofaer Derevenski, 2001; Zhang et al., 2017), there were possibly other epigenetic and environmental factors that contributed to the differential prevalence of disease severity amongst lower and higher status individuals, as the primacy of biochemical components of VO and VOA has been established in recent years (Gellhorn et al., 2013; Kalichman et al., 2008; Risbud & Shapiro, 2014; Wang et al., 2016) and further research has demonstrated the role of epigenetic modifications in the pathogenesis of VO and VOA in clinical populations (e.g., Barter, Bui, & Young, 2012; Shen et al., 2017). Individuals with less access to economic privilege may have increased risk for VO and VOA because of epigenetic and

environmental risk factors, such as high pathogen load, nutrition quality, infection/adaptive immune response, mechanical stress and trauma, toxin exposure, and maternal stress, which may be differentially incorporated into the skeletal system across the life course (e.g., Thayer & Kuzawa, 2011; Gowland, 2015), and may lead to increased vulnerability to chronic disease. McDade et al., (2019) suggest that socio-economic status plays a role in the enrichment of genes related to the regulation of T-cell mediated cytotoxicity, which has been hypothesized by Risbud & Shapiro (2014) to play a role in the proinflammatory response and resulting phenotypic changes in disc degeneration associated with VO. The role of epigenetic modifications in so-called non-inflammatory arthroses, such as osteoarthritis, is well established (Barter et al., 2012; Barter & Young, 2013; Shen et al., 2017), although the role of socio-economic status, or social inequality in these epigenetic modifications remains unstudied. Future studies on the epigenetic regulators of osteoarthritis and osteophytosis are needed to better understand the role of immune function in osteoarthritis, as well as the role of biocultural factors in degenerative joint disease pathogenesis. Future bioarchaeological work should consider the patterning and prevalence of severe VOA and VO alongside other skeletal indicators of generalized physiological stress, although these are also often entangled with biocultural and developmental processes.

7 Conclusion

Socioeconomic status (SES) is an important determinant of health and disease outcomes in modern human populations. Bioarcheologists offer unique insights into pre-industrial, pre-globalization populations, with varying implementations and configurations of status differentiation, which allow us to test hypotheses not possible due to medical interventions in the post-industrial era. Bioarchaeological approaches have considered the complex relationship between occupation, physical activity, and disease outcome, but few studies consider the downstream effects of status on the molecular and cellular systems that regulate disease pathogenesis and physiology. Future bioarchaeological research

might implement immunoassays or assess other biochemical, microbiome, isotopic, or genomic data into studies of social inequality and health disparities in past societies. One difficulty in this research remains the variable taphonomic preservation of skeletal remains that often intersects with other biocultural experiences of inequality and social-mortuary difference.

Anthropological research has highlighted the consequences of social inequality in producing human health disparities for decades (Gravlee, 2009; Nguyen & Peschard, 2003; McDade 2008), and the development of a biocultural approach to disease ecology and health disparities in the past and present has demonstrated the complexity of intra-actions between social life, health, and disease in multiple contexts (e.g., Buikstra & Beck, 2006; Cohen & Armelagos, 1984; Klaus, 2014). Socio-economic status, synonymous with social inequality or difference in many studies, is a key predictor of health and disease outcomes in our contemporary world, and typically access to economic resources and privileges are encompassed in SES. The relationship between health outcomes, physical and occupational activities, and access to economic resources is multifactorial and intersectional. If we understand occupational activities as situated and socially contextual experiences, we begin to see that occupation or "activity" is not straightforward as a singular variable for analysis. Occupational activities and various types of manual labor are situated in broader political and cultural landscapes of inequality, such as gendered labor practices, in/accessibility to jobs, differential access to quality nutrition, and health maintenance to name a few. We suggest that occupational activity, as a variable of analysis, is confounded by the interaction effects of systemic institutional inequality and hierarchical social structures. Where physiological stress, social status, and labor occupation are typically analyzed as discrete effects, we argue for a more intersectional view of these influences. Attention to how inequality shapes life history and differentially produces occupational risk and vulnerability to that risk is crucial for understanding the multiple, cofounding, and inter-related effects of social inequalities on disease outcomes.

Our results suggest that more subtle differences in economic experience, an order of magnitude smaller than the traditional "socio-economic status" scale may influence and affect disease outcomes and should be considered as possible confounding factors for understanding epidemiological, or population-wide trends. In our context, subtle "intra-class" differences in lifestyle including occupational hazards, pathogen-load, access to clean water/foods, nutrition quality and variation due to cultural or practical mores, biological ancestry, and/or environmental exposure to toxins may affect the differential vulnerability to and effects of regulatory and biochemical mechanisms that influence degenerative spine disease pathogenesis and pathophysiology. Much research focuses on the differences *between* economic class groups; however, we suggest that intra-class differences in lived experience, and the ways in which more subtle forms of inequality operate may be meaningful in terms of understanding disease experience and outcome.

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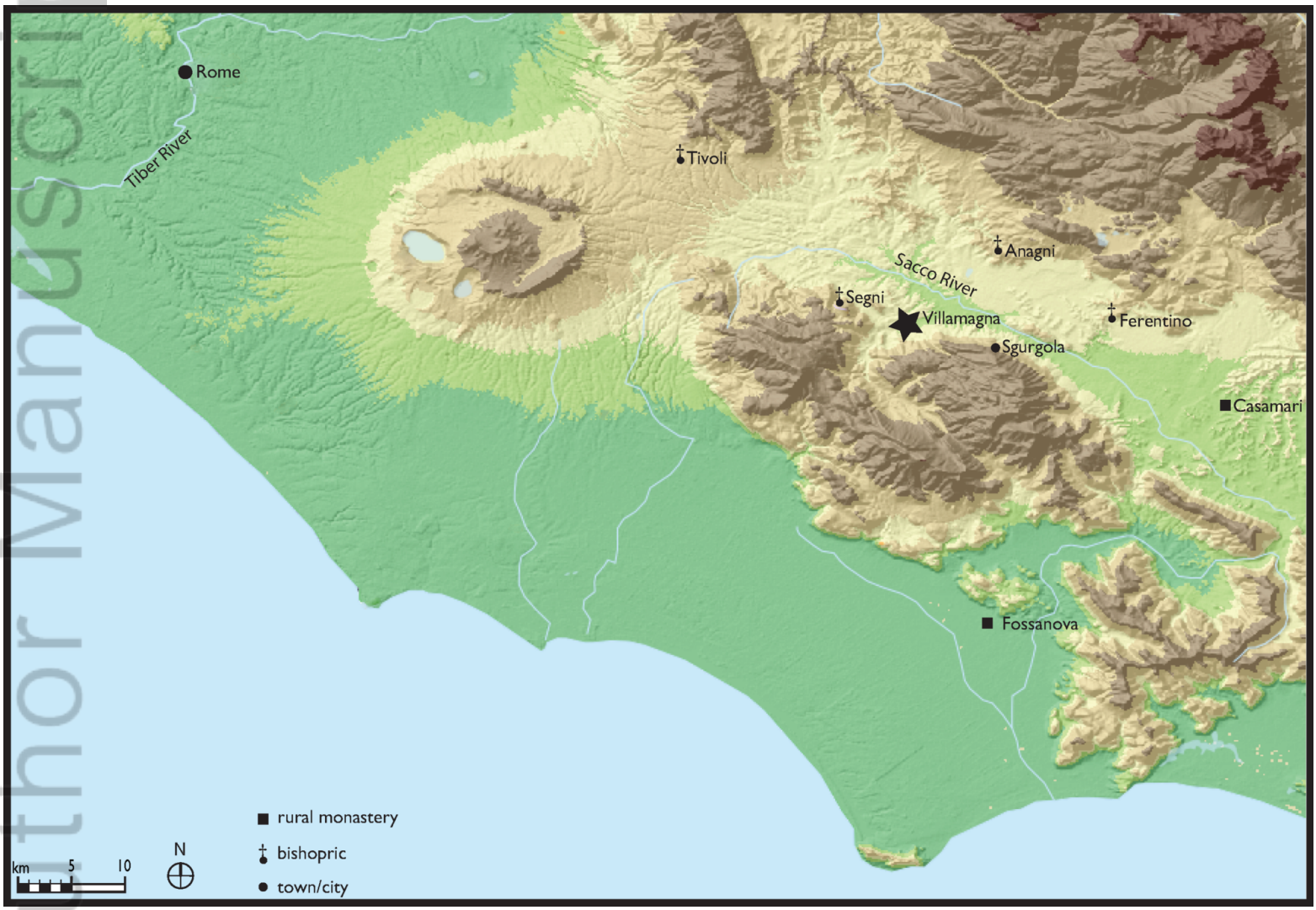

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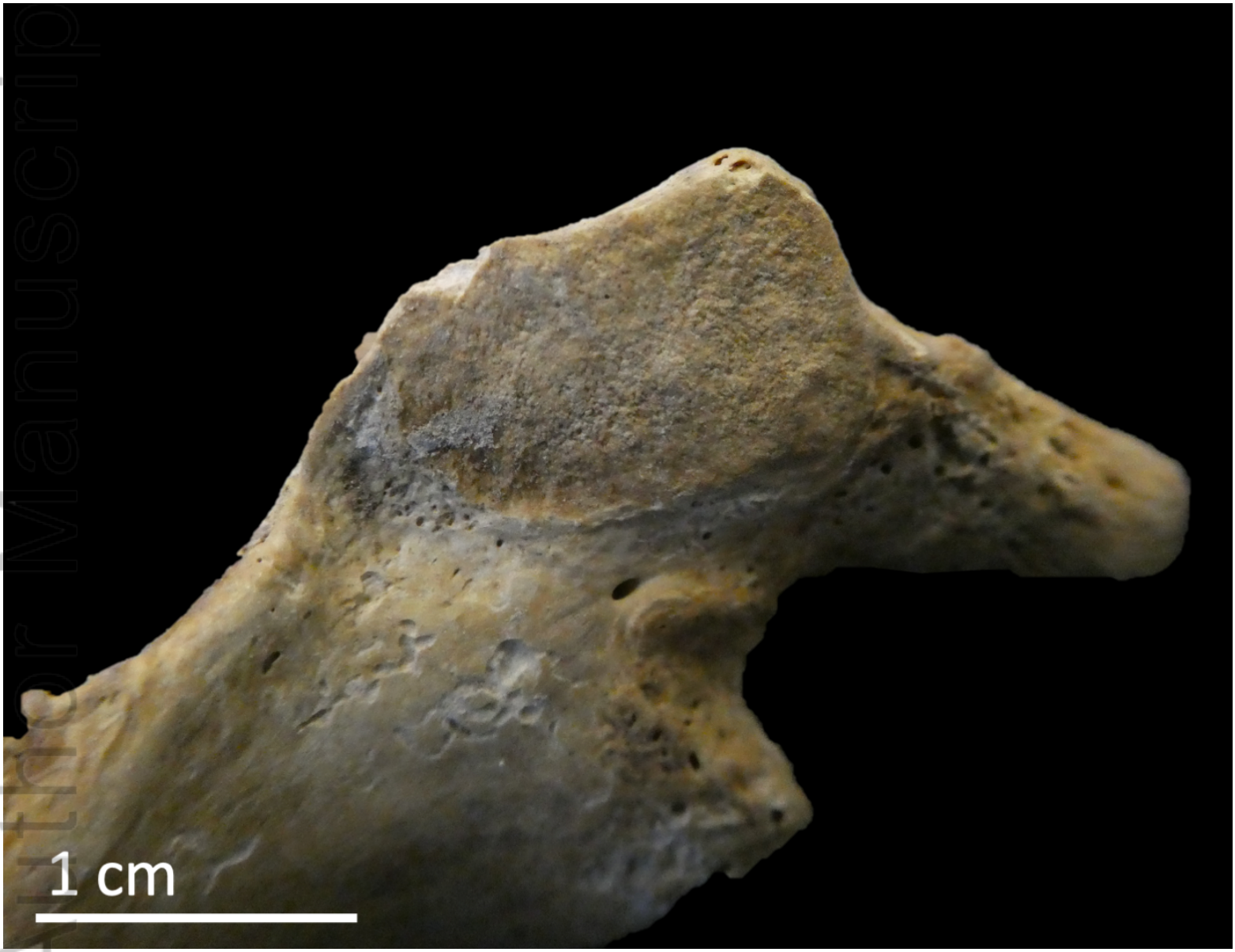

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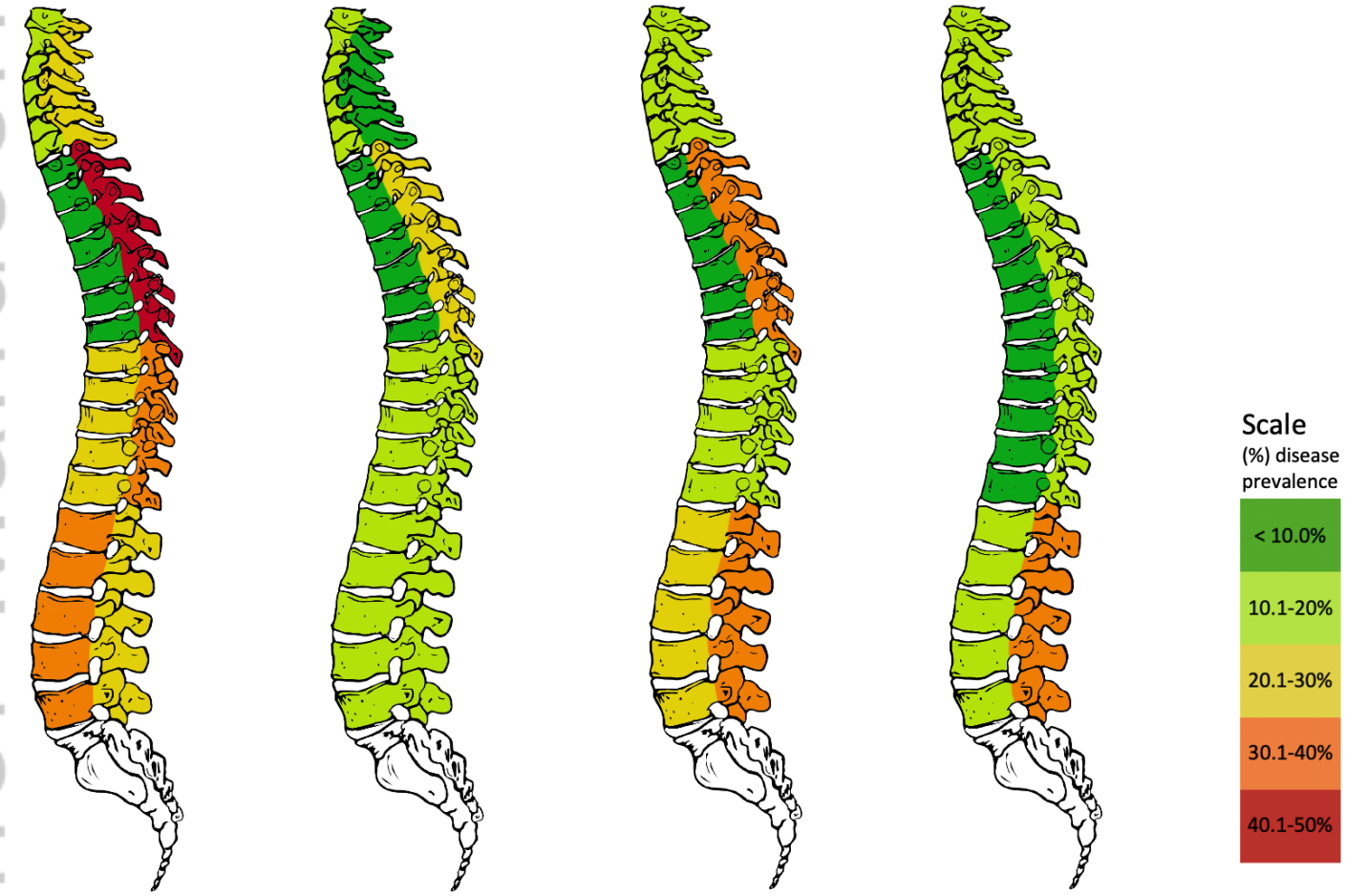

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Figure Legends

Figure 1
Location of Villamagna (star) in Lazio, Italy (adapted from Trombley et al. 2019; Goodson based on Ancient World Mapping Center, http://awmc.unc.edu/awmc/applications/alacarte/)

Figure 2
Low severity vertebral osteophytosis (VO) observed in a typical lumbar vertebra; stage 2.5, based on Table 2 (Photo by KM Kinkopf)

Figure 3
High severity vertebral osteophytosis (VO) observed in a lumbar vertebra; stage 4 based on Table 2 (Photo by KM Kinkopf)

Figure 4
Low severity vertebral osteoarthritis (VOA) observed in the superior right articular facet of a cervical vertebra; stage 2 based on Table 3. (Photo by KM Kinkopf)

Figure 5
High severity vertebral osteoarthritis (VOA) observed in the superior left articular facet of a thoracic vertebra; stage 5 based on Table 3. (Photo by KM Kinkopf)

Figure 6
Heat map of severe spine disease observations aggregated by region (anterior aspect of spine is VO prevalence, posterior aspect of spine is VOA prevalence, see numeric data in Tables 6, 8): in males less access to economic resources increases risk for lower spine VO, and full spine VOA; in females less access increases risk for lumbar VO and upper thoracic VOA.

Table 1 Spine observations at Villamagna by sex and age

Time Period	Individuals	Spine observations	
		VOA (facet)	**VO** (body)
Late Medieval (1300-1450 AD)	n = 106	n = 1823	n = 1909
Male	n = 60	n = 1064	n = 1092
Young (18-29 years)	n = 13	n = 217	n = 223
Middle (30-49 years)	n = 42	n = 793	n = 804
Older (50 years)	n = 4	n = 42	n = 54
Adult (indeterminate age)	n = 1	n = 12	n = 11
Female	n = 46	n = 759	n = 817
Young (18-29 years)	n = 13	n = 201	n = 215
Middle (30-49 years)	n = 18	n = 315	n = 329
Older (50 years)	n = 14	n = 236	n = 266
Adult (indeterminate age)	n = 1	n = 7	n = 7

Table 2 Vertebral osteophytosis (VO) ordinal scoring system

VO Score	Description	Analysis Category
0.0	No degenerative changes present; smooth body margin	Low
1.0	Initial localized bony deposition on the joint margin; <3 mm discontinuous traction spurs at the superior or inferior margin	
2.0	Osteophytes generally present on less than 50% of the margin with vertical deposition across the joint space <5mm; occasional minor pitting adjacent to the centrum at the base of the traction spurs	
3.0	Pronounced osteophyte deposition on >50% of the margin with marked vertical deposition across the joint space; early claw formation; subperiosteal bone deposition on the antero-lateral aspect of the vertebral body cortex; Mild to moderate expansion and distortion of the centrum	
3.5	More developed osteophytosis than seen in stage 3, marked by involvement of the articular surface, but no eburnation present	High
4.0	Severe osteophytosis and claw formation extending across the IVD; osteophytes articulate with adjacent vertebrae; large claw formations give centrum a pinched appearance; severe subperiosteal ossification of the antero-lateral cortex; severe expansion and distortion of the centrum morphology; eburnation on articular surface or on claw(s)	
5.0	All of Grade 4, with ankylosis of claw osteophyte formation	

Table 3 Vertebral osteoarthritis (VOA) scoring system

VOA Score	Description	Analysis Category
0.0	Smooth joint margin and surface; no evidence of remodeling or degenerative changes	Low
1.0	Incipient changes and remodeling of the facet margins	
2.0	Slight lipping of the facet rim; deposition at the facet margins; articular surface unaffected	
3.0	Joint enlargement and lipping; deposition at facet margins	
3.5	Pronounced joint enlargement and lipping; deposition at facet margins accompanied by surface pitting $\leq$10%	
4.0	Pronounced lipping and pitting of <25% of the articular surface; enlargement of articular surface	High
4.5	Pronounced lipping and pitting of >25% of the articular surface; marked joint enlargement; no eburnation	
5.0	Involvement of entire joint surface: enlargement, pitting, porosity of most of the surface; eburnation and polishing of the articular facet surface	
6.0	Stage 5 with partial segmental immobility	
7.0	Complete ankylosis of the joint; complete immobility	

Table 4 Sex comparisons of severe VO by spine region

	Female		Male			
Spine Region	**n/total n**	**%**	**n /total n**	**%**	***X²** (df=1)*	***p***
Full Spine	116/817	14.2	166/1092	15.2	0.30	.585
Cervical	34/204	16.7	32/285	11.2	2.56	.109
Upper Thoracic	13/217	6.0	16/292	5.5	0.00	.958
Lower Thoracic	34/218	15.6	65/285	22.8	3.62	.057
Lumbar	35/178	19.7	53/230	23.0	0.49	.483

* significant at .05, ** significant at .01, *** significant at .001, α = .05, *df = 1*
Pearson's chi-squared test with Yates continuity correction

Table 5 Age comparisons of severe VO by spine region

Sex	Spine Region	Young (18-29 years) n/total n	%	Middle (30-49 years) n/total n	%	Old (50+ years) n/total n	%	χ^2 (df =2)	p
Pooled									
	Full Spine	6/438	1.4	210/1133	18.5	66/320	20.6	83.25	<.001 ***
	Cervical	1/116	0.9	44/283	15.5	21/79	26.6	27.89	<.001 ***
	Upper Thoracic	2/120	1.7	19/292	6.5	8/90	8.9	5.61	.060
	Lower Thoracic	2/114	1.8	82/305	26.9	15/84	17.9	33.37	<.001 ***
	Lumbar	1/88	1.1	65/253	25.7	22/67	32.8	29.29	<.001 ***
Male									
	Full Spine	3/223	1.3	150/804	18.7	13/54	24.1	43.58	<.001 ***
	Cervical	1/64	1.6	26/199	13.1	5/16	31.2	-	<.001 ***
	Upper Thoracic	2/63	3.2	14/210	6.7	0/14	0.0	-	.548
	Lower Thoracic	0/57	0.0	63/214	29.4	2/14	14.3	-	<.001 ***
	Lumbar	0/39	0.0	47/181	26.0	6/10	60.0	-	<.001 ***
Female									
	Full Spine	3/215	1.4	60/329	18.2	53/266	19.9	40.20	<.001 ***
	Cervical	0/52	0.0	18/84	21.4	16/63	25.4	14.91	<.001 ***
	Upper Thoracic	0/57	0.0	5/82	6.1	8/76	10.5	-	.024 *
	Lower Thoracic	2/57	3.5	19/91	20.9	13/70	18.6	8.73	.013 *
	Lumbar	1/49	2.0	18/72	25.0	16/57	28.1	13.48	.001 ***

* significant at .05, ** significant at .01, *** significant at .001, $\alpha = .05$, $df = 2$

Pearson's chi-squared test with Yates continuity correction

- Indicates Fisher's exact test performed due to small expected counts

Does not include observations where Age could not be accurately estimated (n=18)

Table 6 Relative risk for severe VO outcome by sex and spine region based on economic access

Sex	Spine Region	**Less Economic Access** (earthen grave and no grave goods) n/total n	%	**More Economic Access** (tomb or grave goods) n/total n	%	$\widehat{RR}$	95% CI
Pooled							
	Full Spine	201/1099	18.3	81/810	10.0	1.83	1.44 - 2.33*
	Cervical	42/279	15.1	24/210	11.4	1.32	0.82 - 2.10
	Upper Thoracic	23/296	7.8	6/213	2.8	2.76	1.14 - 6.66*
	Lower Thoracic	72/290	24.8	27/213	12.7	1.96	1.31 - 2.94*
	Lumbar	64/234	27.4	24/174	13.8	1.98	1.30 - 3.04*
Males							
	Full Spine	120/624	19.2	46/468	9.8	1.96	1.42 - 2.69*
	Cervical	20/169	11.8	12/116	10.3	1.14	0.58 - 2.25
	Upper Thoracic	13/165	7.9	3/127	2.4	3.33	0.97 - 11.46
	Lower Thoracic	46/159	28.9	19/126	15.1	1.92	1.19 - 3.10*
	Lumbar	41/131	31.3	12/99	12.1	2.58	1.43 - 4.65*
Females							
	Full Spine	81/475	17.1	35/342	10.2	1.67	1.15 - 2.42*
	Cervical	22/110	20.0	12/94	12.8	1.57	0.82 - 2.99
	Upper Thoracic	10/131	7.6	3/86	3.5	2.19	0.62 - 7.72
	Lower Thoracic	26/131	19.8	8/87	9.2	2.16	1.03 - 4.55*
	Lumbar	23/103	22.3	12/75	16.0	1.40	0.74 - 2.62

Relative Risk ratio results, RR values ≥ 1.01 indicate higher risk of severe VO in individuals in Group 1 (less economic access) and are considered statistically significant (*) if the 95% confidence interval does not include 1.0

Table 7 Relative risk for severe VO outcome by sex, age, and spine region based on economic access

Sex	Spine Region	Less Economic Access (earthen grave & no grave goods) n/ total n	%	More Economic Access (tomb and/or grave goods) n/total n	%	$\widehat{RR}$	95% CI
Male							
Young (18-29 years)							
	Full Spine	2/71	2.8	1/152	0.7	4.28	0.39 - 46.44
	Cervical	0/22	0.0	1/42	2.4	-	
	Upper Thoracic	2/13	13.3	0/48	0.0	-	
	Lower Thoracic	0/20	0.0	0/37	0.0	-	
	Lumbar	0/14	0.0	0/25	0.0	-	
Middle (30-49 years)							
	Full Spine	109/504	21.6	41/300	13.7	1.58	1.14 - 2.20*
	Cervical	18/130	13.9	8/69	11.6	1.19	0.55 - 2.61
	Upper Thoracic	11/136	8.1	3/74	4.1	2.00	0.57 - 6.93
	Lower Thoracic	44/130	33.9	19/84	22.6	1.50	0.94 - 2.38
	Lumbar	36/108	33.3	11/73	15.1	2.21	1.21 - 4.06*
Older (50+ years)							
	Full Spine	9/29	23.7	4/16	25.0	0.95	0.34 - 2.63
	Cervical	2/11	18.2	3/5	30.3	0.30	0.07 - 1.28
	Upper Thoracic	0/9	0.0	0/5	0.0	-	
	Lower Thoracic	2/9	22.2	0/5	0.0	-	
	Lumbar	5/9	55.6	1/1	100.0	0.30	0.07 - 1.28
Female							
Young (18-29 years)							
	Full Spine	3/116	2.6	0/99	0.0	-	
	Cervical	0/27	0.0	0/25	0.0	-	
	Upper Thoracic	0/33	0.0	0/24	0.0	-	
	Lower Thoracic	2/31	6.4	0/26	0.0	-	
	Lumbar	1/25	4.0	0/24	0.0	-	
Middle (30-49 years)							
	Full Spine	39/150	26.0	21/179	11.7	2.22	1.37 - 3.60*
	Cervical	11/29	37.9	7/55	12.7	2.98	1.29 - 6.86*
	Upper Thoracic	2/38	5.3	3/44	6.8	0.77	0.14 - 4.38
	Lower Thoracic	14/47	29.8	5/44	11.4	2.62	1.03 - 6.68*
	Lumbar	12/36	16.7	6/36	33.3	2.00	0.84 - 4.75
Older (50+ years)							
	Full Spine	39/202	19.3	14/64	21.9	0.88	0.51 - 1.52
	Cervical	11/49	22.5	5/14	35.7	0.63	0.26 - 1.51
	Upper Thoracic	8/58	13.8	0/18	0.0	-	
	Lower Thoracic	10/53	18.9	3/17	17.7	1.07	0.33 - 3.44
	Lumbar	10/42	23.8	6/15	40.0	0.60	0.26 - 1.36

Relative Risk ratio results, RR values ≥ 1.01 indicate higher risk of severe VO in individuals in Group 1 (Less Economic Access) and are considered statistically significant (*) if the 95% confidence interval does not include 1.0

Table 8 Comparison of sex differences in severe VOA outcome by region of spine

	Female		Male		X^2	
Spine Region	**n/N**	%	**n/N**	%	*(df=1)*	***p***
Full Spine	165/759	21.7	260/1064	24.4	1.65	.198
Cervical	33/230	14.3	56/315	17.8	0.91	.341
Upper Thoracic	48/188	25.5	95/270	35.2	4.37	.037 *
Lower Thoracic	30/174	17.2	61/254	24.0	2.44	.118
Lumbar	54/167	32.3	48/225	21.3	5.47	.019 *

* significant at .05, α = .05, *df = 1*

Pearson's chi-squared test with Yates continuity correction

Table 9 Age comparisons of severe VOA across spine region stratified by sex

		Young (18-29 years)		Middle (30-49 years)		Old (50+ years)			
Sex	**Spine Region**	**n/N**	***%***	**n/N**	***%***	**n/N**	***%***	χ^2 *(df = 2)*	***p***
Pooled									
	Full Spine	57/418	13.6	277/1108	25.0	91/278	32.7	37.13	<.001 ***
	Cervical	6/134	4.5	56/313	17.9	27/86	31.4	30.57	<.001 ***
	Upper Thoracic	14/103	13.6	102/279	36.6	27/69	39.1	20.40	<.001 ***
	Lower Thoracic	19/95	20.0	61/271	22.5	11/62	17.7	0.80	.670
	Lumbar	18/86	20.9	58/245	23.7	26/61	42.6	10.59	.005 **
Male									
	Full Spine	32/217	14.7	203/793	25.6	25/42	59.5	39.272	<.001 ***
	Cervical	3/73	4.1	41/221	18.6	12/14	85.7	-	<.001 ***
	Upper Thoracic	10/56	17.9	78/198	39.4	7/11	63.6	-	.001 ***
	Lower Thoracic	11/46	23.9	50/200	25.0	0/8	0.0	-	.362
	Lumbar	8/42	19.0	34/174	19.5	6/9	66.7	-	.009 **
Female									
	Full spine	25/201	12.4	74/315	23.5	66/236	28.0	16.04	.001 ***
	Cervical	3/61	4.9	15/92	16.3	15/72	20.8	7.02	.030 *
	Upper Thoracic	4/47	8.5	24/81	29.6	20/58	24.5	10.24	.006 **
	Lower Thoracic	8/47	17.0	11/71	15.5	11/53	20.8	0.55	.759
	Lumbar	10/44	22.7	24/71	33.8	20/52	38.5	2.82	.244

* significant at .05, ** significant at .01, *** significant at .001*, $\alpha = .05$, $df=2$*

Pearson's chi-squared test with Yates continuity correction

- Indicates Fisher's exact test performed due to small expected counts

Table does not include observations where age could not be accurately estimated (n=19)

Table 10 Relative risk for severe VOA outcome by sex and spine region based on economic access

Sex	Spine Region	**Less Economic Access** (earthen grave & no grave goods) n/ total n	%	**More Economic Access** (tomb and/or grave goods) n/total n	%	$\widehat{RR}$	95% CI
Pooled							
	All	291/1023	28.4	134/800	16.8	1.70	1.42 - 2.04*
	Cervical	69/313	22.0	20/232	8.6	2.56	1.60 - 4.08*
	Upper Thoracic	99/255	38.8	44/203	21.7	1.79	1.32 - 2.43*
	Lower Thoracic	61/234	26.1	30/194	15.5	1.69	1.14 - 2.50*
	Lumbar	62/221	28.1	40/171	23.4	1.20	0.85 - 1.69
Male							
	All	186/609	30.5	74/455	16.3	1.88	1.48 - 2.39*
	Cervical	48/192	25.0	8/123	6.5	3.84	1.88 - 7.85*
	Upper Thoracic	62/149	41.6	33/121	27.3	1.53	1.08 - 2.16*
	Lower Thoracic	43/141	30.5	18/113	15.9	1.91	1.17 - 3.12*
	Lumbar	33/127	26.0	15/98	15.3	1.70	0.98 - 2.94
Female							
	All	105/414	25.4	60/345	17.4	1.46	1.10 - 1.94*
	Cervical	21/121	17.4	12/109	11.0	1.58	0.81 - 3.05
	Upper Thoracic	37/106	34.9	11/82	13.4	2.60	1.42 - 4.78*
	Lower Thoracic	18/93	19.4	12/81	14.8	1.31	0.67 - 2.55
	Lumbar	29/94	30.9	25/73	34.2	0.90	0.58 - 1.40

Relative Risk ratio results, RR values ≥ 1.01 indicate higher risk of severe VO in individuals in Group 1 (Less Economic Access) and are considered statistically significant (*) if the 95% confidence interval does not include 1.0

Table 11 Relative risk for severe VOA outcome by sex, age, and spine region based on economic access

Sex	Spine Region	Less Economic Access (earthen grave & no grave goods) n/ total n	%	More Economic Access (tomb and/or grave goods) n/total n	%	$\widehat{RR}$	95% CI
Male							
Young (18-29 years)							
	Full Spine	21/76	27.6	11/141	7.8	3.54	1.81 - 6.95*
	Cervical	3/28	10.7	0/45	0.0	-	
	Upper Thoracic	7/15	46.7	3/41	7.3	6.38	1.89 - 21.52*
	Lower Thoracic	7/16	43.8	4/30	13.3	3.28	1.13 - 9.55*
	Lumbar	4/17	23.5	4/25	16.0	1.47	0.43 - 5.09
Middle (30-49 years)							
	Full Spine	145/487	29.8	58/306	19.0	1.57	1.20 - 2.06*
	Cervical	34/144	23.6	7/77	9.1	2.60	1.21 - 5.58*
	Upper Thoracic	51/123	41.5	27/75	36.0	1.15	0.80 - 1.66
	Lower Thoracic	36/118	30.5	14/82	17.1	1.79	1.03 - 3.10*
	Lumbar	24/102	23.5	10/72	13.9	1.69	0.86 - 3.32
Older (50+ years)							
	Full Spine	20/34	58.8	5/8	62.5	0.94	0.51 - 1.73
	Cervical	11/13	84.6	1/1	100.0	0.85	0.67 - 1.07
	Upper Thoracic	4/6	66.7	3/5	60.0	1.11	0.45 - 2.77
	Lower Thoracic	0/7	0.0	0/1	0.0	-	
	Lumbar	5/8	62.5	1/1	100.0	0.63	0.37 - 1.07
Female							
Young (18-29 years)							
	Full Spine	19/111	17.1	6/90	6.7	2.57	1.07 - 6.16*
	Cervical	2/32	6.3	1/29	3.4	1.81	0.17 - 18.95
	Upper Thoracic	0/20	0	4/27	14.8	-	
	Lower Thoracic	6/28	21.4	2/21	9.5	2.25	0.50 - 10.05
	Lumbar	3/20	29.2	7/24	15.0	1.94	0.58 - 6.56
Middle (30-49 years)							
	Full Spine	43/126	34.1	31/189	16.4	2.08	1.39 - 3.11*
	Cervical	10/28	35.7	5/64	7.8	4.57	1.72 - 12.15*
	Upper Thoracic	16/37	43.2	8/44	18.2	2.38	1.15 - 4.92*
	Lower Thoracic	6/28	21.4	5/43	11.6	1.84	0.62 - 5.47
	Lumbar	11/33	33.3	13/38	34.2	0.97	0.51 - 1.87
Older (50+ years)							
	Full Spine	43/170	25.3	23/66	34.9	0.73	0.48 - 1.10
	Cervical	9/56	16.1	6/16	37.5	0.43	0.18 - 1.02
	Upper Thoracic	17/40	42.5	3/18	16.7	2.55	0.85 - 7.62
	Lower Thoracic	6/37	16.2	5/17	29.4	0.55	0.20 - 1.56
	Lumbar	11/37	29.7	9/15	60.0	0.50	0.26 - 0.94*

Relative Risk ratio results, RR values ≥ 1.01 indicate higher risk of severe VO in individuals in Group 1 (Less Economic Access) and are considered statistically significant (*) if the 95% confidence interval does not include 1.0