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Rickets, resorption and revolution: An investigation into the relationship between vitamin D deficiency in childhood and osteoporosis in adulthood in an 18th-19th century population

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ABSTRACT

Objective: This study employs a Developmental Origins of Health and Disease (DOHaD) approach to assess the effect of vitamin D deficiency (VDD) in childhood on the risk of osteoporosis in adulthood in an archaeological sample of skeletons dating from the 18th to 19th centuries.
Materials: Femora and lumbar vertebrae of 65 adults aged 18+ years (26 diagnosed with residual rickets and 39 without) from an 18th-19th century Quaker burial ground at Coach Lane, North Shields, England.
Methods: Bone mineral density (BMD) was measured for the femoral neck and first four lumbar vertebrae of each individual using a dual energy X-ray absorptiometry (DXA) scanner as a proxy for assessing osteoporotic fracture risk.
Results: 3-way ANOVA revealed no statistically significant differences in BMD between individuals with and without residual rickets across age and sex.
Conclusions: A combination of lifestyle and environmental factors likely influenced the BMD of people buried at Coach Lane across the life course. The impact of childhood VDD on BMD later in life can be mitigated through other factors such as physical activity and diet.
Significance: This is one of the first bioarchaeological studies to take a DOHaD approach to understand osteoporosis risk in 18th-19th century England. It highlights the complexity of aetiological factors for osteoporosis and that VDD in early life does not necessarily predispose a person to osteoporosis in adulthood.
Limitations: BMD is not the only indicator of osteoporosis. Microscopic methods for the assessment of childhood vitamin D deficiency, such as inter-globular dentine analysis, were not applied.

1. Introduction

1.1. Osteoporosis and bone mineral density

The bone remodelling cycle is controlled by a complex system of osteoblastic (modelling cell) and osteoclastic (resorbing cell) mechanisms (Kenkre and Bassett, 2018). Interruption to this normal remodelling cycle can cause greater absorption of calcium from bone into the blood and body fluids, resulting in general deterioration of bone structure and strength, commonly diagnosed as osteoporosis (WHO, 1994; Khosla and Riggs, 2005; Kenkre and Bassett, 2018). Osteoporosis is a metabolic bone disease in which there is greater bone resorption than formation, leading to loss of bone quantity and quality to the point of high fracture risk (WHO, 1994; Kanis and Glüer, 2000; Khosla and Riggs, 2005; Brickley et al,. 2020). Primary osteoporosis is caused mainly by hormone sex steroid influences, where reduction in oestrogen levels over time decreases osteoblastic ability to remodel bone, resulting in greater bone resorption over time (see Kenkre and Bassett, 2018, Table 2, p.318 for more information on the causes at a cellular level). Loss of structure, strength and mass increases risk of fracture, as bone can no longer withstand external mechanical forces (WHO, 1994; Khosla and Riggs, 2005; Li and Xu, 2020). This means that minor accidents can result in serious injury (Cooper, 1997; Cauley et al., 2000; Kanis et al., 2003; MacLaughlin et al., 2006). As osteoporosis is clinically silent until

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fracture occurs (Brickley and Mays, 2019), Bone Mineral Density (BMD) acts as a proxy for relative osteoporotic fracture risk (Kelsey et al., 1992; WHO, 1994). One factor influencing BMD that has received particular attention in recent years is vitamin D deficiency (VDD), which affects a large range of bodily and skeletal processes.

1.2. Vitamin D deficiency

Vitamin D is a pro-hormone recognised as a key component of many homeostatic processes (Brickley and Ives, 2008, p.79, Figure 5.3; Snoddy et al., 2016; Lockau and Atkinson, 2018; Brickley et al., 2020). Vitamin D works alongside other hormones to regulate bone resorption and formation (Vieth, 2003; Fausto-Sterling, 2005; Lockau and Atkinson, 2018). Disruption to this regulation results in poor osteoid mineralisation (Vieth, 2003; Brickley et al., 2018).

During growth, VDD prevents proper calcification and mineralisation of the cartilaginous growth plates (Pettifor, 2003; Donnelly and Boskey, 2011; Brickley et al,. 2020). This can cause areas of weakness and stress in the growing skeleton which, in combination with mechanical loading from crawling and walking, leads to the characteristic bowing of long bones, tibial twisting, and metaphyseal flaring known as rickets (Parfitt, 1997; Pettifor, 2003; Brickley et al., 2018; Lewis, 2018; Brickley et al., 2020; Tschinkel and Gowland, 2020). Permanent changes retained in the adult skeleton resulting from VDD during growth are known as residual rickets (Brickley et al., 2018). Disruption to bone formation and osteoid mineralisation due to lack of vitamin D in adulthood is known as osteomalacia (Brickley et al., 2020). Osteomalacia differs to rickets in that it affects the formation and mineralisation of pre-existing, fully ossified bone, not the endochondral bone laid down during growth. (Pettifor, 2003; Kuhn, 2014; Brickley et al., 2020). Slower adult bone turnover and cell regeneration often results in relatively subtle skeletal expressions of osteomalacia, including porosity and pseudofractures, although more severe bending deformities in the vertebrae and os coxa have also been reported (Bhan et al., 2010; Kuhn, 2014; Brickley et al., 2018).

1.3. Theoretical framework

The DOHaD theory argues that adverse circumstances during early life can increase the risk of chronic disease in adulthood (Fig. 1) (Gluckman and Hanson, 2006; Barker, 2012). Biographical narratives constructed from skeletal remains adopt the DOHaD approach to aid understandings of underlying risks of mortality, illness and injury during specific stages of the life course (Robb, 2002; Grauer and Buikstra, 2019; Brickley et al., 2020; Gowland and Caldwell, 2022; Swan et al., 2023).

This research adopts a DOHaD perspective by assessing VDD during childhood and BMD in adulthood to determine how environmental and social conditions during growth may have impacted the development of peak bone mass and consequent risk of developing osteoporosis. Peak bone mass is the point at which bone achieves its maximum structural strength, usually around full long bone epiphyseal fusion, c.25yrs, when bone development starts to plateau (Fausto-Sterling, 2005; Weaver et al., 2016). The acquisition of peak bone mass during growth greatly reduces osteoporotic fracture risk, as the more bone developed earlier in

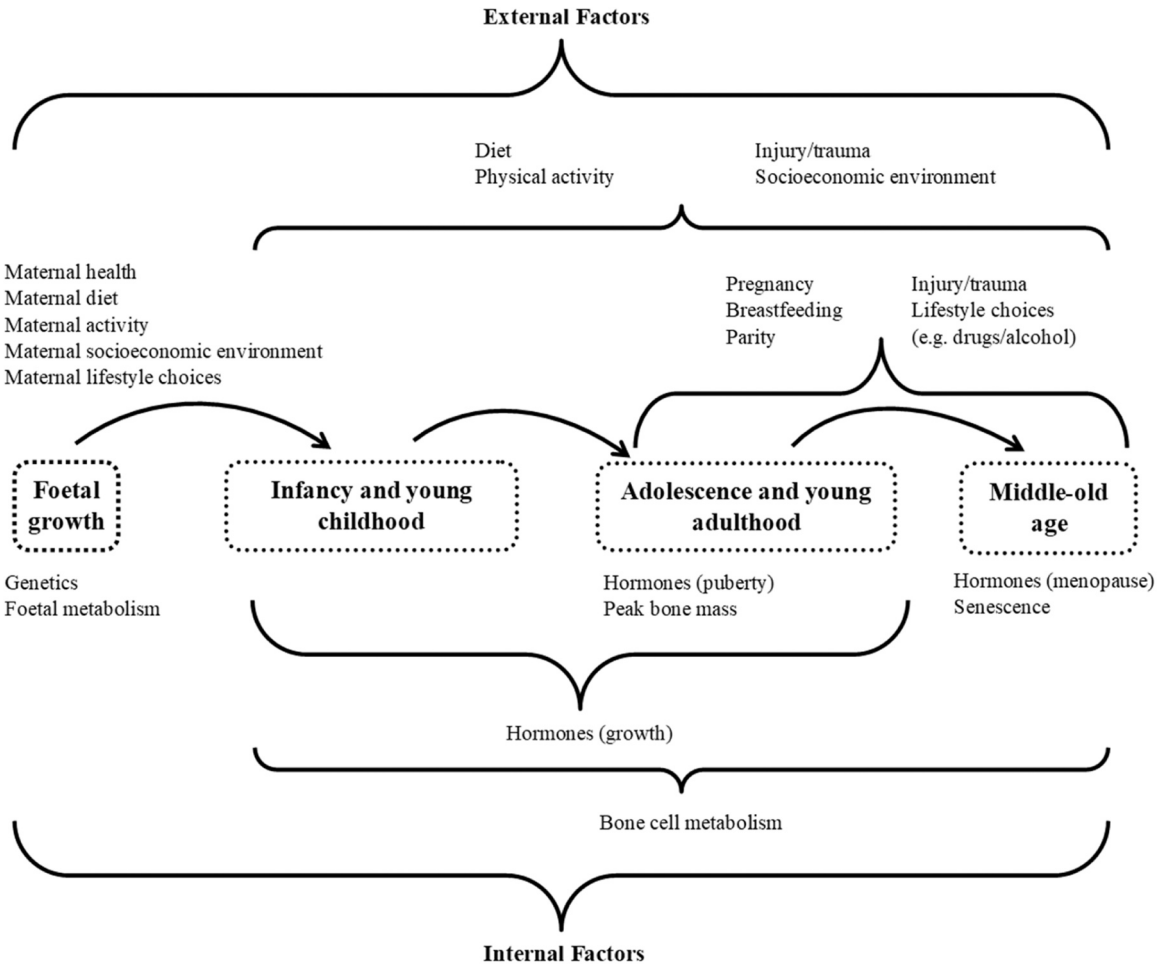

Fig. 1. Diagram showing all the interrelating factors affecting bone development, growth and change at particular stages of the life course. See also Fausto-Sterling (2005), Agarwal and Beauchesne (2011).

life, the more can be lost later in life before reaching a fracture risk level (Fig. 2) (Cooper et al., 2005; Cooper et al., 2006; Fausto-Sterling, 2005).

Rickets in childhood affects bone mineralisation during growth, modelling, and remodelling (Vieth, 2003; Fausto-Sterling, 2005), and osteoporosis is a result of poor mineralisation and low bone quality and mass in adulthood (Grynpas, 2003). Therefore, it can be inferred that rickets in childhood could lead to poor bone quality and/or quantity development, decreasing BMD and increasing the risk of osteoporosis in adulthood (Holick, 2004; Thacher et al., 2014; Zerofsky et al., 2016). We hypothesise that individuals with residual rickets will have significantly lower BMD levels than those without residual rickets.

2. Materials

The skeletal individuals examined in this study were excavated in 2010 by Pre-Construct Archaeology Limited from the 18th-19th century Quaker burial ground located at Coach Lane, North Shields, Northeast England (Fig. 3); and are currently curated at the Department of Archaeology, Durham University. A total of 236 skeletal individuals of varying ages were excavated from the site with generally good preservation and completeness averaging more than 50 % per individual (Goode et al., 2012).

The burial site was owned and used by The Society of Friends (Quakers) c.1710–1853 (Cherryson et al., 2012; Proctor et al., 2016; Goode et al., 2012). North Shields became a heavily industrialised urban area in the 18th century with particular focus on quayside industries (Cherryson et al., 2012; Hudson, 1992; Proctor et al., 2016). The area descended into slums for the poorest of the working class in the 19th century after the wealthier inhabitants moved to more 'favourable' housing further away and the demand for low-paid manual labour increased (Barke, 2001; Proctor et al., 2016). The Northeast was an economic powerhouse during this period of industrialisation, but with considerable wealth inequality. Many poorer people were drawn to non-conformist communities during this period who were more sympathetic to their circumstances than the Church of England (Barke, 2001; Cherryson et al., 2012; Proctor et al., 2016; Gowland et al., 2018). Therefore, many buried in this cemetery were likely from a working-class background and experienced the difficulties associated with the poorer or lower-middling classes during the Industrial Revolution (Gowland et al., 2018).

VDD was endemic during the British Industrial Revolution and has already been reported as prevalent in the Coach Lane population in studies of rickets in non-adults (Goode et al., 2012; Gowland et al., 2018; Newman et al., 2019) and residual rickets in adults (Tschinkel and Gowland, 2020). High levels of VDD were likely caused by environmental factors such as polluted atmosphere, reduced sunlight hours of a northerly latitude; and social factors such as remaining indoors to avoid atmospheric pollution and work within factories and mines during daylight hours (Holick, 2004; Brickley et al., 2007; Macdonald et al., 2011; Gowland et al., 2018; Newman et al., 2019; Tschinkel and Gowland, 2020; Snoddy et al., 2024). There have been no previous studies of osteoporosis in the sample, so this research assesses osteoporosis risk through measurement of BMD and the hypothesis explores if these circumstantial factors may have led to low BMD in adults (Fig. 4).

3. Methods

3.1. Assessing childhood vitamin D deficiency

VDD during childhood was diagnosed using the most frequently identifiable traits for residual rickets in adult archaeological remains, which included: bowing, torsion and thickening of the long bones; flared metaphyses; and genu valgum (Fig. 5) (Roberts and Manchester, 2010; Brickley et al., 2018; Tschinkel and Gowland, 2020; Brickley et al., 2020; Zedda et al., 2021). Porosity and new bone formation on their own were not enough to diagnose residual rickets, as both are associated with a range of metabolic diseases and other pathological conditions (Brickley et al., 2018). All long bones were assessed for signs of macroscopic rickets and were recorded on a presence or absence basis according to guidelines by Zedda et al. (2021). Presence was recorded where the palaeopathological traits outlined above were observed, past normal expected expression for this population. It was not necessary for residual rickets to be present in the sampled bones, only within the whole individual. For example, in the cases where the femora did not show signs of bowing or torsion, but the tibiae or humeri did, they were catagorized as individuals with residual rickets (Fig. 5). At least one lower leg bone needed to be present in order to assign absence of rickets as these are weight-bearing long bones and most likely to manifest macroscopically visible bone deformities (Waldron, 2020; Zedda et al., 2021). New methods of analysis provide histological assessments of rickets through the identification of inter-globular dentine of teeth. It was not possible to conduct such histological analysis for the purposes of this study due to the destructive nature of the method, and it is recognised as a limitation of the current study (see Section 6.3).

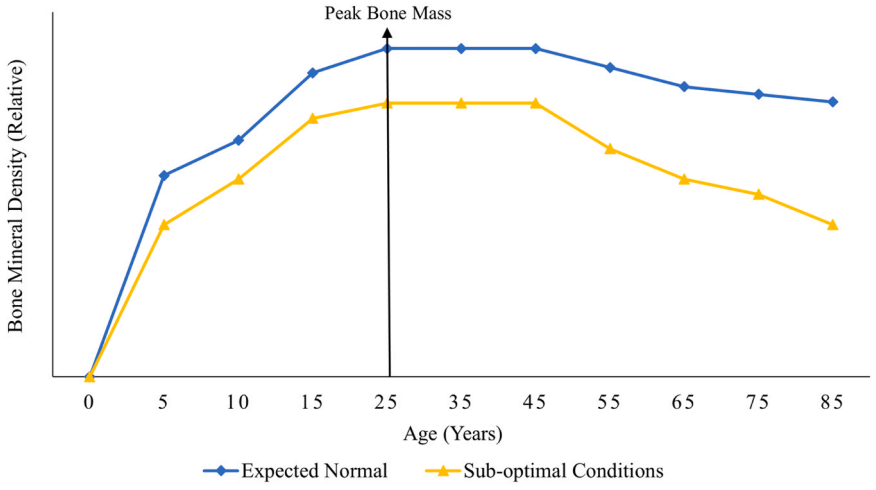

Fig. 2. Line graph showing general bone mineral density changes across a lifetime. Anything which inhibits bone development and an individual's ability to reach peak bone mass (such as vitamin D deficiency) could result in low bone mineral density across the life course, greatly impacting their susceptibility to osteoporotic fracture at an older age. See also Weaver et al. (2016); GE Healthcare (2020).

Fig. 3. Map of Coach Lane, North Shields, Tyneside, England archaeological site, located slightly north-east of Newcastle-upon-Tyne in the Northeast of England (UK Grid Reference Finder, 2013; National Grid Reference code provided by Goode et al. 2012, p.4).

3.2. Measuring bone mineral density

BMD was measured in the archaeological remains using a dual energy X-ray absorptiometry (DXA) scanner (Cooper et al., 2006). The skeletal sites most vulnerable to fracture and commonly measured in clinical studies are the femoral neck and lumbar vertebrae as the most weight-bearing regions (Table 1) (Masud et al., 1993; Kröger et al., 1999; Kanis and Glüer, 2000; Bousson et al., 2004; Khoo et al., 2009). It was a requirement for individuals to have at least the femoral neck or lumbar vertebrae preserved for inclusion in this study. For consistency,

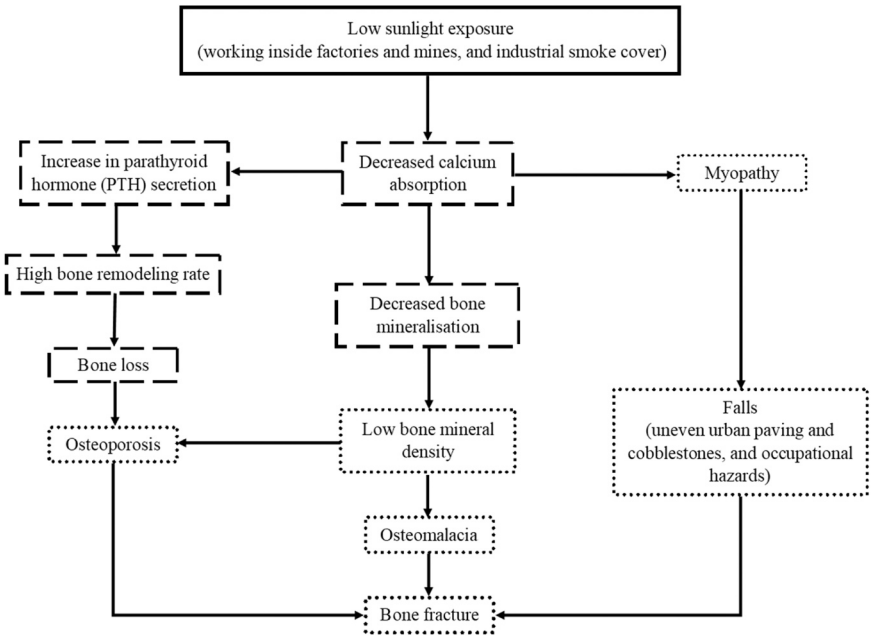

Fig. 4. Diagram showing the relationship between vitamin D deficiency, osteoporosis and fracture risk specific to the Coach Lane population dating to the British Industrial Revolution (adapted from Lips, 1994, Fig.3 , p.158). Dashed outlines (- - -) relate to bodily processes; dotted outlines (...) relate to consequences.

Fig. 5. Photographs of anterior view of left tibia from B035 showing residual bowing next to no visible changes in the left femur (left); and anterior view of the humeri from B137 subtle residual bowing of the diaphysis (right).

the left femur was preferentially selected following clinical practice (GE Healthcare, 2020). Where the left femoral neck was not preserved, the right femur was substituted. Complete lumbar vertebrae from L1-L5 were selected when preserved but where this was not possible, the lumbar vertebrae in the best condition were selected.

3.2.1. *Age and sex estimates*

As the software for the DXA scanner required age and sex input, only individuals for which age and sex had been recorded could be used. Age-at-death and sex estimations for the Coach Lane population had been previously carried out by Gowland (2012) using standard methods (Buikstra and Ubelaker, 1994) and are provided in the records

Table 1
Comparisons of the use of cortical vs trabecular bone in DXA BMD studies.

Type of Bone	Characteristic	Reason for Use in this Study
Trabecular – lumbar vertebrae	More longitudinal loss of trabecular bone in both sexes at younger ages (Lauretani et al., 2008; Riggs et al., 2008; Agarwal and Grynpas, 2009)	May be more beneficial for observing BMD loss not influenced by sex hormones in pre-menopausal adults (Lauretani et al., 2008; Riggs et al., 2008; Agarwal and Grynpas, 2009)
	Periods of stress affecting BMD are more observable in trabecular bone in both sexes (McEwan et al., 2005; Agarwal and Grynpas, 2009)	May be more reflective of environmental stresses than cortical bone (McEwan et al., 2005; Agarwal and Grynpas, 2009)
	More reflective of metabolic changes and stresses (Agarwal and Grynpas,2009; Kenkre and Bassett, 2018)	May be the better candidate for assessment of the effects of vitamin D deficiency on BMD loss
	Faster remodeling rate than cortical bone (Agarwal and Grynpas, 2009; Kenkre and Bassett, 2018)	Reflects bone composition closer to the age at death of the individual (Agarwal and Grynpas, 2009; Kenkre and Bassett, 2018)
Cortical – femoral neck	Vertebrae are used in clinical studies as the most susceptible to fracture from BMD loss relating to menopausal hormonal changes (Cauley et al., 2007)	Areas of high cortical bone concentration accounts for bone loss due to menopausal changes and assesses bone loss more likely due to environmental factors (Beauchesne and Agarwal, 2017)
	Compared to the vertebrae, the femoral neck contains fewer major foramina and canals and so likely undergoes less diagenetic alteration relating to hormonal changes (Agarwal and Grynpas, 2009)	
	DXA scanning of the femoral neck has been found to be as sensitive to BMD and osteoporotic changes as the lumbar vertebrae (Jergas and Genant, 1997)	The femoral neck is the preferred site if multiple sites cannot be measured(Jergas and Genant, 1997)

associated with the collection. As this study investigates osteoporosis in adulthood, only individuals aged over 18yrs were selected.

Sex estimation in bioarchaeology includes the categories of 'probable male' and 'probable female'(Buikstra and Ubelaker, 1994). However, as these are not recognised biological clinical categories by the DXA, individuals assigned as 'probable' in the records were re-assigned as 'male' and 'female', respectively. Individuals were grouped into broad age categories for analysis roughly corresponding with critical transitional stages of bone growth, development and loss (Table 2) (Beauchesne and Agarwal, 2017). Where age ranges overlapped with multiple age categories, the age category which encompassed the larger range was chosen (e.g., 20–29yrs is covered more by the 18–25yrs range than the 25–30yrs range, 6 vs 5yrs). The software for the DXA scanner required a specific age input so the median age range for each individual was entered.

Table 2
Age categories assigned for different age ranges by the authors and the corresponding critical transitional stages of bone growth, development and loss (information from Szulc et al., 2000; Baxter-Jones et al., 2011; Weaver et al., 2016; Beauchesne and Agarwal, 2017).

Age Range (yrs)	Age Category	Transitional Stage
18–25	Young adult	Fast remodelling and development of peak bone mass
25–30	Young-middle adult	Peak bone mass attainment and slowing of remodelling
35–45	Old-middle adult	Pre-menopausal stages in females and the start of age-related bone loss in both sexes
45+	Mature adult	Post-menopausal stage in females and accelerated age-related bone loss in both sexes

3.2.2. Height and weight estimates

BMD varies with vertebral body widths, meaning measurements can be underestimated in larger individuals simply due to body size variation (Kanis and Adami, 1994; Dennison et al., 2005). These issues are addressed clinically by inputting height and weight estimates into the DXA scanner. Stature estimations were calculated using Trotter (1970) for white males and females (Supplementary Material, Table A.1). Where stature could not be calculated, the average height from the Coach Lane population for specific age and sex was used. For weight estimation, the Broca Index was used, which provides an estimation of the 'ideal' body weight of an individual based on height (Shah et al., 2006; Weber-Sanchez et al., 2018; Irakoze et al., 2020). This may lead to inaccuracies; however, as of yet, there is no universally agreed method for calculating body mass from archaeological human remains.

3.2.3. DXA scanning process

Trial scanning was undertaken to optimise the process. A container of rice large enough to fit complete bones (c.15cm depth in total) was used to simulate soft tissue, following guidance from Mays et al. (1998), McEwan et al. (2005), and Agarwal and Grynpas (2009). Scanning was set to mode 'thin' as dry rice is less dense than human soft tissue. First, skeletal elements were arranged anatomically in the rice (Fig. 6). Trials revealed it was necessary to leave gaps in between each vertebral body to simulate the intervertebral discs. Without gaps, the vertebrae were treated by the scanner as one entity and could not identify the individual features necessary for calculating an accurate BMD measurement. A single vertebra or sequential vertebrae (e.g., L3-L4) could be scanned. Missing vertebrae in the middle of a sequence disrupted the scan, creating an invalid measurement. Next, the DXA laser was positioned for scanning. For the femora, this is c.7–8cm below the greater trochanter where the scanner moves from the proximal end of the diaphysis cranially, scanning the region of the femoral neck and taking multiple measurements (GE Healthcare, 2020). For the lumbar vertebrae, this is the mid-point of L5 upwards to L1 (GE Healthcare, 2020). Then, the skeletal element was completely covered in the dry rice. Finally, the focal areas for scanning were highlighted on the initial radiograph to ensure measurements were taken only from those areas (Fig. 7).

3.3. Assessing osteoporosis

The DXA scanner uses x-rays to produce body composition measurements in g/cm^2 and compares bone density of the sample measured to a database of density values of a healthy modern population – UK (GE Healthcare, 2020). Data is given as absolute BMD measurements and as Z-scores for each bone scanned. The Z-score is the number of standard deviations an individual varies from the expected BMD of a healthy individual of similar age and sex (Kanis et al., 2000; Shenoy et al., 2014). Z-scores greater than −1 are considered normal BMD levels; scores between −1 and −2.5 are indicative of some bone loss but with no risk of fracture known as osteopenia; and scores lower than −2.5 are diagnostic of osteoporosis (WHO, 1994; NHS, 2019). The lowest Z-score of the two skeletal elements (femoral neck and lumbar) was used for diagnosis (GE Healthcare, 2020). The femoral neck and lumbar vertebrae were also macroscopically assessed for fractures, noting presence and absence.

3.4. Data analysis

Different populations express different levels of 'normal' BMD, and therefore varying predispositions to developing osteoporosis (Kanis and Glüer, 2000; Agarwal et al. 2004; Mohamed et al. 2019). Archaeological populations may not have the same fracture risks as modern Europeans (Brickley and Mays, 2019), meaning BMD results in relation to modern thresholds may be inaccurately estimated. Therefore, while Z-scores

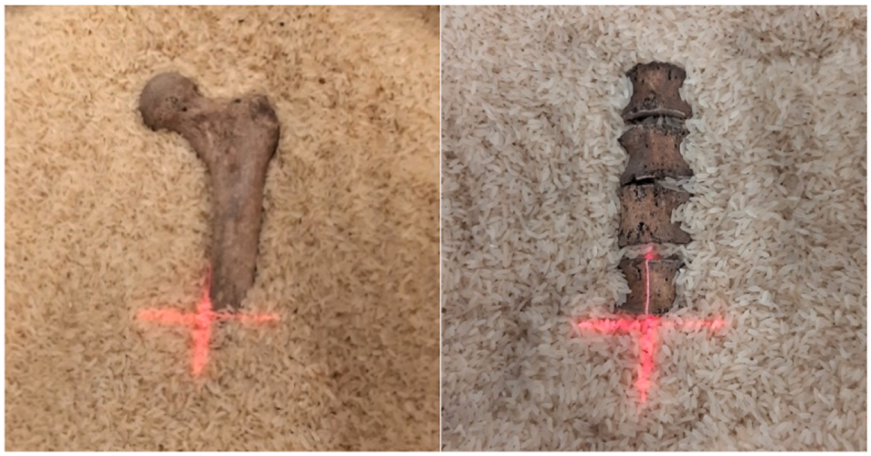

Fig. 6. Photograph showing the positioning of the laser (red cross) when scanning the femur (left) and lumbar vertebrae (right).

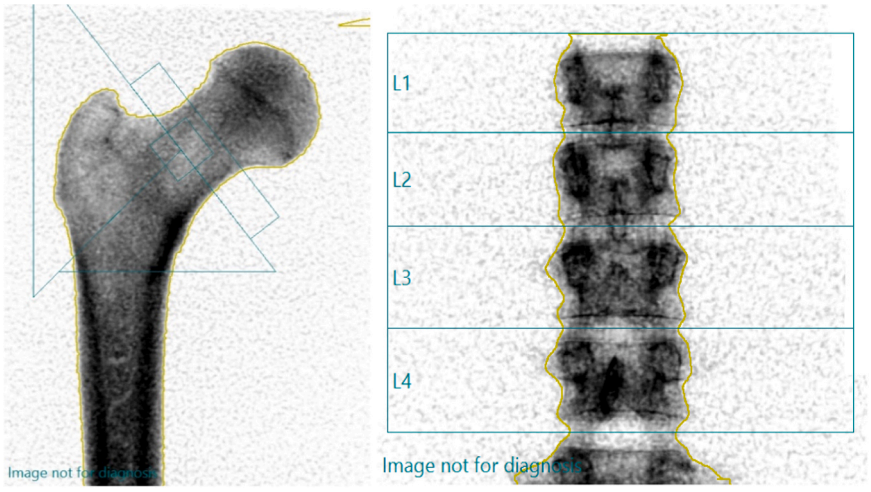

Fig. 7. Radiograph of the femur (left) and lumbar vertebrae (right). The green rectangles were centred at the focal areas for measurement before final scans.

have been commented on for the diagnosis of osteoporosis, statistical analyses were carried out using absolute BMD values. In this way, BMD could be compared within the population rather than in relation to a modern reference sample. Analyses compared values within Coach Lane to keep the variables affected by time and space as consistent as possible.

Data was analysed using a combination of Microsoft Excel and R-studio software. Shapiro-wilk residuals model showed the data was normally distributed and Levene's test for homogeneity of variance indicated spreads of the samples were approximately equal (Supplementary Material, Table A.2; Figures B.1-B.4), meaning the data met assumptions for 3-way ANOVA statistical testing (Drennan, 2009). Four outliers were detected for femoral neck BMD and two outliers for lumbar BMD. These were included in analysis as small standard deviations (<1) as well as similar mean and median values (Supplementary Material, Figures B.3-B.4) indicated statistical analysis was unlikely to be affected by outliers (Drennan, 2009).

Statistical analysis was performed using 3-way ANOVA to test for the relationship between three categorical independent variables – age, sex, and residual rickets (presence vs absence) and a continuous dependent variable – BMD. If any of the ANOVA tests were significant, they were followed by a post-hoc test (Tukey HSD) to further define the group interactions. Femoral neck and lumbar BMD were analysed separately as they are treated as independent skeletal elements (GE Healthcare, 2020).

4. Results

4.1. Bone mineral density measurements

A total of 65 individuals met the criteria outlined in Section 3 above (Table 3), of which 62 produced viable BMD results from femoral neck scanning and 53 from lumbar vertebrae scanning (see Supplementary Material, Tables A.3-A.4 for details). A total of 50 individuals produced BMD measurements for both femoral neck and lumbar vertebrae, 19 with residual rickets and 31 without residual rickets.

When BMD measurements were compared between categories there

Table 3
Demography of the 65 individuals which produce viable results from scanning.

Sex	Pathology	Young Adult	Young-middle Adult	Old-middle Adult	Mature Adult	Total
Female	Residual Rickets	2	3	2	0	7
	No Residual Rickets	3	10	4	1	18
Male	Residual Rickets	2	10	5	2	19
	No Residual Rickets	2	6	9	4	21
Total		9	29	20	7	65

was no clear differentiation between those with or without residual rickets across age and sex (Figs. 8–10).

4.2. Osteoporosis

No ante-mortem fractures were found at the femoral neck or lumbar vertebrae. Some elements were fragmented post-mortem (see Supplementary Material Table A.3 for details), which may have obscured ante-mortem fracture observation. Only 12 % of all individuals showed BMD levels indicative of osteoporosis (Fig. 11). Lack of fracture at these skeletal sites and low frequency of low BMD suggests osteoporosis risk was small with no identifying correlation between those with and without residual rickets.

4.3. Statistical analyses

3-way ANOVA statistical testing revealed a slightly statistically significant three-way interaction between sex, age, and residual rickets (presence vs absence) in relation to femoral neck BMD (Table 4). However, the p-value is close to the threshold of significance at $p<0.05$, implying the correlation may not be statistically strong. Post-hoc tests (Tukey HSD) revealed statistical significance only between males (residual rickets):females (no residual rickets) (P=0.003–3 sf). Lack of statistical significance interaction between any other groups from post-hoc tests supports low statistical strength of a 3-way interaction. Statistical significance was found between males and females suggesting males had significantly higher femoral neck BMD than females independent of age and residual rickets.

There was no statistically significant three-way interaction between age, sex and residual rickets for lumbar BMD (Table 5). Statistical significance was found between males and females suggesting males had significantly higher lumbar BMD than females independent of age and residual rickets.

These results fail to reject the Null hypothesis, implying residual rickets does not have a meaningful impact on adult femoral neck or lumbar BMD.

5. Discussion

5.1. Statistical significance

The discrepancy between the significant result in the ANOVA for the Age:Sex:RR interaction and the lack of significant pairwise comparisons in Tukey post-hoc tests may be attributed to various factors including test power, sample size, and group mean distribution (for in-depth discussions, see Mchugh, 2011; Carlson, 2017; Montgomery, 2019). The most likely factor here is the small sample size. The interaction term in the ANOVA might have had a small effect size that was detectable when considering the overall model but not large enough to show up in post-hoc comparisons (Mchugh, 2011; Kim, 2015). Smaller sample sizes can make it harder for the post-hoc test to detect significant differences between individual groups, even if an overall interaction effect is present (Mchugh, 2011; Kim, 2015).

The significant ANOVA result for Age:Sex:RR suggests there may be some combined effect of these three factors relating to BMD. The one significance found at males (rickets):females (no rickets) (P=0.003–3 sf) more likely relates to the strength of sex differences rather than differences between residual rickets and no residual rickets, especially as significance was not found in the reverse (i.e., females with no rickets: males with rickets, P=0.782–3 sf). Tukey post-hoc test did not find any other significant pairwise differences, which means the interaction might not have manifested as large differences between specific group pairs but rather as a subtle combined effect across multiple groups, where sex differences were the leading factor.

5.2. Sex differences

Females had statistically significant lower BMD than their male counterparts independent of age and residual rickets. These differences have been suggested to relate to female reproduction where dietary calcium and fluctuations from nutritional absorption during pregnancy and lactation could cause a reduction in BMD (Agarwal and Grynpas, 1996; Agarwal and Stuart-Macadam, 2003; Wierzbicka and Oczkowicz, 2022). However, studies have suggested these changes may be

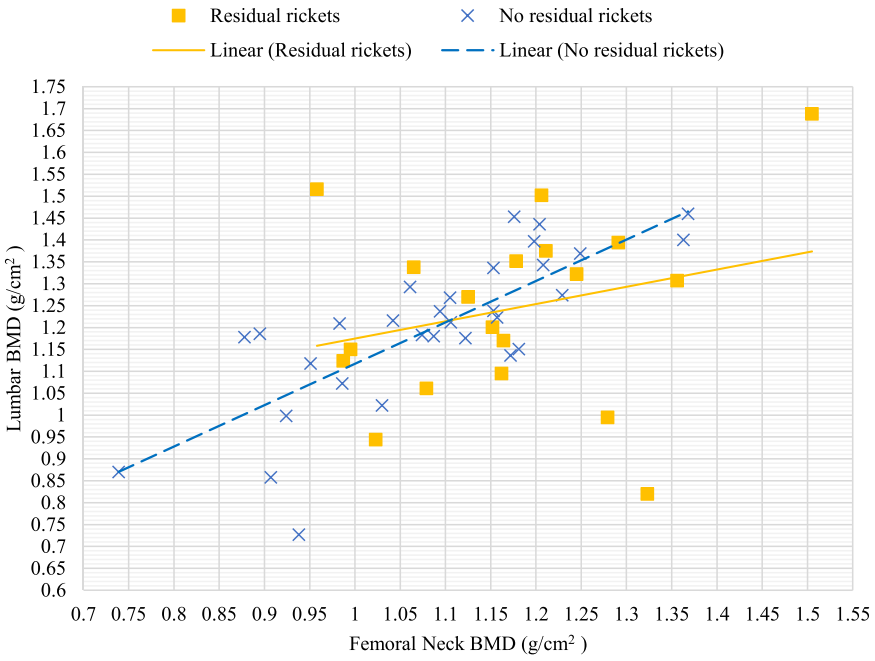

Fig. 8. Scatterplot showing each BMD value where both femoral neck and vertebrae were measured in individuals with and without rickets. There are fewer data points than total sample size as BMD for both femoral neck and lumbar vertebrae were needed for this plot, meaning individuals for which only one skeletal element was scanned could not be plotted. As femoral neck BMD increases so does lumbar BMD, signifying a positive relationship between the two skeletal elements, as would be expected.

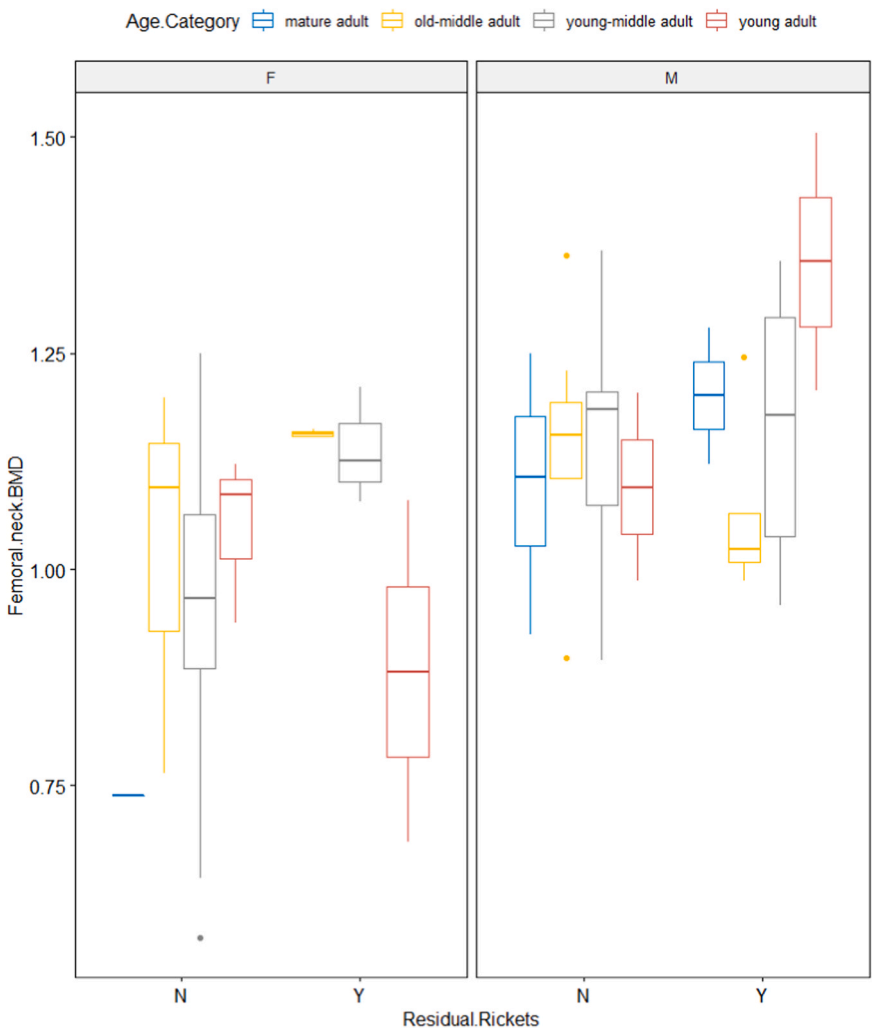

Fig. 9. Boxplot showing the results of femoral neck BMD in relation to sex, age and residual rickets. 'N' represents those without residual rickets and 'Y' represents those with residual rickets. Colours correspond to age categories. The boxes show the interquartile range, the median is indicated by the central horizontal line and the vertical lines from the central box represent the maximum and minimum points of the data. Outliers are identified by the single dots.

short-term and unlikely to significantly affect bone density (Agarwal and Stuart-Macadam, 2003; Agarwal, 2016). Therefore, the BMD sex differences seen here are more likely related to biological bone differences between males and females rather than the specifics of reproduction. The results here follow expected patterns due to hormonal influences on bone mass and structure (Aaron et al., 1987; Weaver et al., 2016). Females have different bone mass and structure to males – which becomes pronounced during puberty (Leonard et al., 2010). Male bone densities can reach higher values than females at peak development in prime adulthood (Weaver et al., 2016; Rogucka et al., 2000). Furthermore, loss of cortical bone can occur in adults after peak bone development phase (Riggs et al., 1986; Nordström et al., 2007), but this loss is more severe around the mid-life phase in females than in males, with males experiencing a more constant rate of loss over time (Riggs et al., 2008). This evidence supports known and expected trends, showing that BMD patterns are identifiable within archaeological populations using this method.

5.3. Osteoporosis and post-medieval Britian

Studies of post-medieval British populations found low osteoporotic fracture risk compared to modern populations (Lees et al., 1993; Mays, 2000; Ives et al., 2017), aligning with the results from Coach Lane, and suggesting low osteoporosis risks are normal for the time. However, the nuances of the interaction between VDD and osteoporosis are widely debated in literature. The complex environment of the industrial revolution meant VDD was not the only influencing factor on osteoporotic fracture risk.

5.3.1. Calcium and vitamin D

The active vitamin D hormone in the body, $1,25(OH)_2D$, aids regulation of calcium levels and bone metabolism; hence, calcium and vitamin D work together for healthy bone maintenance (Vieth, 2003; Fausto-Sterling, 2005; Mays and Brickley, 2022). Inadequate vitamin D absorption means the body cannot properly process calcium for sufficient bone mineralisation. Inadequate calcium can cause $1,25(OH)_2D$ to increase resorption of calcium from bone to make-up for the shortfall in important body fluids (Holick, 2004; Mason et al., 2011; Roth et al., 2018). Both can result in poor bone quality and reduced bone mass. Therefore, when assessing the relationship between VDD and BMD in archaeological populations, diet may be an influencing factor. Black and Cooper (2000) suggest calcium intake can have a positive effect on BMD, and studies have shown a reduction in adult BMD loss associated with high calcium consumption from childhood. Longitudinal studies found that calcium supplements had the greatest influence on BMD and bone structure when taken long-term (Dibba et al., 2000; Cameron et al., 2004).

Reliance on staples such as bread, potatoes, basic dairy products like

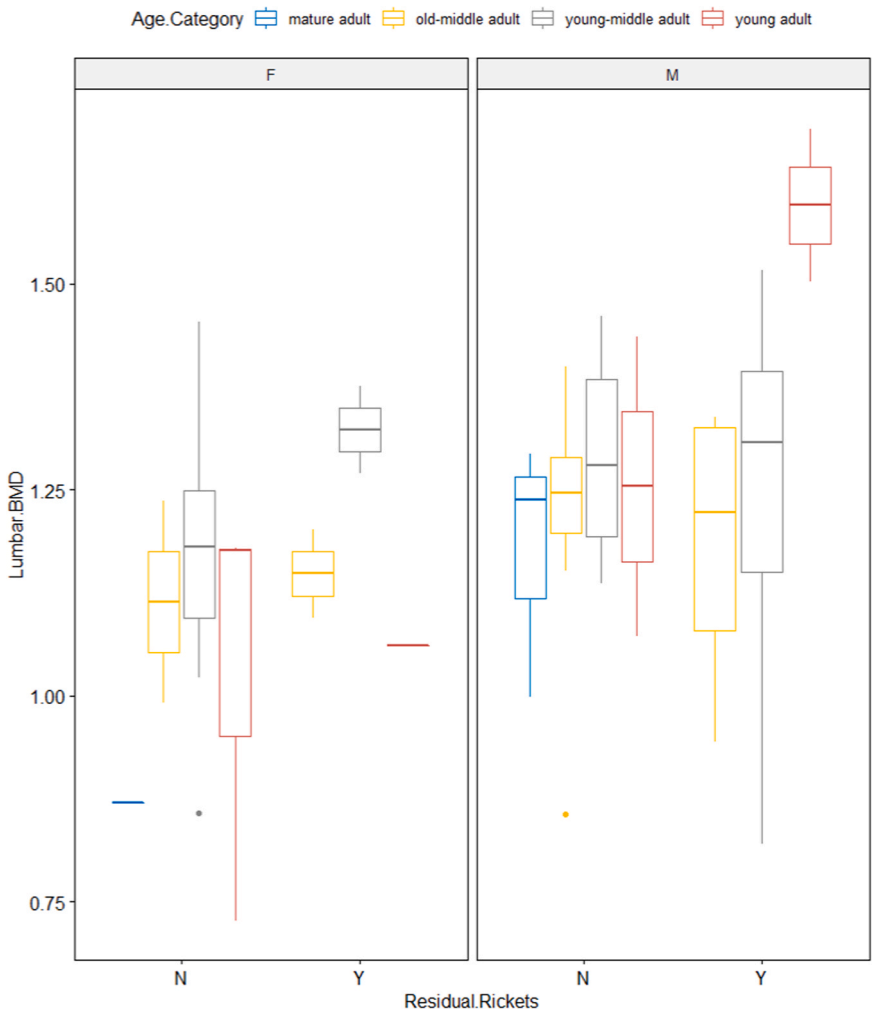

Fig. 10. Boxplot showing the results of lumbar BMD in relation to sex, age and residual rickets. 'N' represents those without residual rickets and 'Y' represents those with residual rickets. Colours correspond to age categories. The boxes show the interquartile range, the median is indicated by the central horizontal line and the vertical lines from the central box represent the maximum and minimum points of the data. Outliers are identified by single dots.

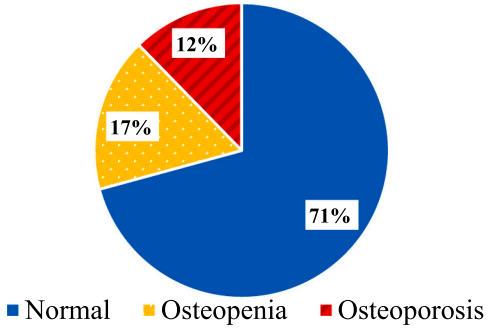

Fig. 11. Pie chart showing the percentages of individuals from Coach Lane having evidence for low BMD according to clinical diagnosis based on Z-scores from DXA scanning.

Table 4
Results of a 3-way ANOVA test for femoral neck BMD at a significance threshold of $p < 0.05$. Residual rickets (RR) is reported as present/absent. A significant result implies a relationship between categories and femoral neck BMD. A non-significant result indicates no relationship between categories and femoral neck BMD. P-values are reported to 3 significant figures.

Category	Statistic	Significance
Age	$F(3, 47) = 0.085$, $p = 0.968$	Not significant
Sex	$F(1, 47) = 0.085$, $p = 0.000$	Significant
RR	$F(1, 47) = 1.597$ $p = 0.213$	Not significant
Age:Sex	$F(3, 47) = 1.300$, $p = 0.285$	Not significant
Age:RR	$F(3, 47) = 0.475$, $p = 0.701$	Not significant
Sex:RR	$F(1, 47) = 0.478$, $p = 0.493$	Not significant
Age:Sex:RR	$F(2, 47) = 3.209$, $p = 0.049$	Significant

cheese, milk and butter, with occasional meat (Horrell and Oxley, 2012; Griffin, 2018), by the people from Coach Lane over a lifetime may have provided enough calcium to offset some of the impact of VDD on BMD later in life. Oatmeal, barley and rye are also considered sources of calcium and vitamins important for growth and in many counties across Britain, variations of all three were used for broths, soups, puddings and breads. The North Shields population was a coastal one, and while fish was only a small part of most people's diet, they were likely to have consumed some, which may also have contributed to high calcium intake (Roth et al., 2018).

As long as there is sufficient calcium intake over the life course, peak bone mass can be maintained in adulthood despite VDD in childhood (Holick, 2009; Roth et al., 2018). Calcium supplementation in clinical research has shown positive effects on bone mineralisation in children who were vitamin D deficient at younger ages (Dibba et al., 2000; Ward et al., 2014). This is shown to be particularly effective during the adolescent growth spurt when dietary-energy deficiency delays skeletal growth and peak bone mass accruement much more than VDD (Parfitt,

Table 5
Results of a 3-way ANOVA test for lumbar BMD at a significance threshold of $p < 0.05$. Residual rickets (RR) is reported on as present/absent. A significant result implies a relationship between categories and lumbar BMD. A non-significant result indicates no relationship between categories and lumbar BMD. P-values are reported to 3 significant figures.

Category	Statistic	Significance
Age	$F(3, 39) = 0.781$, $p = 0.512$	Not significant
Sex	$F(1, 39) = 6.077$, $p = 0.018$	Significant
RR	$F(1, 39) = 0.323$, $p = 0.573$	Not significant
Age:Sex	$F(3, 39) = 1.925$, $p = 0.142$	Not significant
Age:RR	$F(2, 39) = 0.932$, $p = 0.402$	Not significant
Sex:RR	$F(1, 39) = 0.228$, $p = 0.636$	Not significant
Age:Sex:RR	$F(2, 39) = 1.131$, $p = 0.333$	Not significant

1994; Wharton and Bishop, 2003). Thus, the high calcium sources of children's diets at Coach Lane may have outweighed the negative impacts of VDD on bone mineral development enough to normalise BMD levels, although not enough to overcome skeletal deformities. In the 19th century rural community of Beemster, The Netherlands, high levels of VDD were found amongst subadults and residual rickets amongst adults (Waters-Rist and Hoogland, 2018). Similar to Coach Lane, diets consisted predominantly of dairy products such as milk, butter, and cheese, potatoes, wheat and rye bread, and eggs. Isotopic analysis revealed there was no significant difference in $\delta^{15}N$ or $\delta^{13}C$ levels between juveniles, adolescents and adults with and without residual rickets, but there was significance at infancy and childhood ages. This suggests that calcium interactions with bone development might be most influential at the critical growth periods of younger ages (i.e., breastfeeding and weaning). In their study of 138 children aged 0–8.5yrs from 18th-19th century London sites, Swan et al. (2023) observed significantly greater cortical bone porosity in children with active rickets than in those without during periods of rapid growth. They attribute this difference to the high calcium demands during growth spurts. VDD reduces calcium absorption during normal bodily functions, creating regulation imbalances (Pettifor, 2004; Mays and Brickley, 2022; Vlok et al., 2023). During growth-demands for calcium, hypomineralisation is exacerbated in those with VDD as the body requires more in a shorter period (Parfitt, 1994; Swan et al., 2023).

It may be that there was not enough calcium in the Coach Lane diet during young childhood development to mitigate for the lack of vitamin D and prevent the skeletal deformities of rickets (Pettifor, 2004; Waters-Rist and Hoogland, 2018; Vlok et al., 2023; Mays and Brickley, 2022), which became 'locked-in' in the form of residual rickets once fusion was complete. However, after fusion, there are lower nutritional demands due to slower bone turnover and lack of growth (Bhan et al., 2010; Kuhn, 2014; Brickley et al., 2018), suggesting continued consumption of calcium throughout adulthood may have been adequate to compensate for VDD and maintain normal metabolic processes and BMD (Flynn, 2003; Pettifor, 2004; Roth et al., 2018; Vlok et al., 2023).

Isotopic analyses of Industrial British populations suggest there may have been dietary shifts over the life course with potential consumption differences between infants, children and adults (Nitsch et al., 2011; Henderson et al., 2014) which may have caused varying effects on BMD during growth and development. An isotopic study of children and adults from 19th century Fewston, North Yorkshire found variations in $\delta^{15}N$ and $\delta^{13}C$ values between children aged 8–20yrs and adults aged 20+yrs (Gowland et al., 2023). Although the focus of this study was to assess health of 'pauper apprentices' and highlight differences according to social status, it particularly illustrates that dietary differences did exist between children and adults, and that children may have received poorer quality foods with less nutritional value due to social perception of being 'lesser'. In this way, dietary shifts over the life course may have been associated with shifting social status as even for the poorest working class, adults were perceived as socially higher than children of the same status. Low calcium consumption combined with VDD and higher metabolic demands in younger years followed by a change in diet, greater calcium intake and reduced metabolic demands into adulthood might explain the presence of residual rickets in the adult skeleton but with 'normal' BMD levels. Isotopic analysis of both subadults and adults from Coach Lane will help expand understandings of dietary influences on VDD and if dietary shifts over the life course affected bone mineral development.

5.3.2. *Physical activity*

Physical activity has been identified as a significant influencer on BMD across multiple studies (Weaver et al., 2016). Lees et al., (1993) use DXA to compare the BMD of females from 18th-19th century Spitalfields, London to modern women. They found women had greater fracture risk in modern day than in the past. One suggestion for this lower risk was greater and more regular physical activity, reinforcing bone structure. Greater mechanical loading stress and compression forces on bone increases osteoblastic activity which can lead to increased peak bone mass acquirement and BMD (Black and Cooper, 2000; Janz et al., 2014; Martin, 2003; O'Rourke et al., 2021).

Studies of children and adolescents found significantly greater peak bone mass attainment in those who performed regular physical exercise than those who did not (Bailey et al., 1999; Baxter-Jones et al., 2008; Black and Cooper, 2000; Janz et al., 2014; Nelson et al., 2003; O'Rourke et al., 2021). Bone is particularly sensitive and vulnerable before peak bone mass is achieved as development is ongoing and BMD is not yet stabilised (Berger et al., 2010; Weaver et al., 2016). The study by Swan et al., (2023) mentioned in Section 5.3.1. found an increase in cortical bone area in children with healed rickets compared to those without rickets. They suggest this relates to the bending deformity from VDD resulting in increased cortical thickness from locomotor mechanical loading during walking (Swan et al, 2023, Fig.5, p.291). Thickening during recovery may be a result of new bone mineralisation on top of excess osteoid formed from bowing, which in combination with mechanical loading from walking increases overall cortical bone area (Mays et al., 2006; Brickley et al., 2018; Swan et al., 2020).

Industrialisation of Britain marked a sharp increase in workforce labour, particularly in areas of focused industry like the Northeast, and the nature of society often required children to work from a young age to contribute to their families' incomes (Griffin, 2018). Therefore, it is almost certain that the working classes of Coach Lane were involved in intense physical activity, especially as businesses consisted of ship building, engineering, coal, and iron working (Cherryson et al., 2012; Hudson, 1992; Proctor et al., 2016), all of which required heavy lifting and weight bearing. Even domestic activities such as food preparation, cleaning and laundry would also have been much more physical in the past compared to the present. Constant mechanical loading and stresses on bone from youth culminating from physical activity relating to these occupations could have resulted in high peak bone mass attainment. The reinforcement of bone structure from years of mechanical loading and physical activity may have meant there was a greater peak bone mass attainment on reaching maturity. This then means much more bone had to be lost in adulthood to reach the dangerous BMD levels associated with osteoporosis. It may be that VDD did affect BMD but that this was mitigated in the past due to heightened physical demands throughout the life course.

5.3.3. *DOHaD – growth, environment and consequence*

McEwan et al. (2005) used DXA in their study of juvenile skeletons from Medieval Wharram Percy and found no significant relationship between cortical BMD and stress indicators. The authors propose that poorer individuals likely suffered seasonal deficiency and it was because this malnourishment was not chronic that 'catch-up' growth could have occurred, meaning there was no lasting effect on BMD by the time they reached maturity (Tanner, 1986; Branca et al., 1992). However, the residual rickets seen in Coach Lane is considered indicative of prolonged chronic VDD at critical points during childhood, enough to leave

indicators on the bone in adulthood (Cooper et al., 2006; Brickley et al., 2018). 'Catch-up' growth requires the bone to develop and mineralise in a shorter amount of time than normal, resulting in hypomineralisation and reduced capacity to reach peak bone mass (Cooper et al., 2001, 2006). This relates to McPherson's (2021) sensitive developmental windows (SDW) theory which proposes that short-term plastic changes to bone in response to adverse conditions earlier in life also create developmental disruptions which have a cumulative impact on long-term health trajectories.

The non-significant difference in BMD between those with and without residual rickets could relate to the absence of these short-term plastic changes. Constant malnutrition throughout childhood and potentially into adulthood from poor living conditions at Coach Lane would have restricted, to some degree, the opportunity for 'catch-up' growth. Evidence for stunted growth from 18th-19th century Britain reinforces this theory, as lack of catch-up growth stemming from insufficient vitamin D and inadequate recovery from periodic stress may be the reason why children did not grow to their full height potential (Mays et al., 2006; 2009; Ives and Humphrey, 2018; Newman et al., 2019; Reedy, 2020). Furthermore, there is evidence to suggest there was delayed onset of puberty and an extended growth period into adulthood (Papadimitriou, 2016; Ives and Humphrey, 2017; Gowland et al., 2018) meaning growth could have been more evenly spaced and drawn out, limiting the potential impacts of growth spurts on BMD.

6. Methodological considerations

6.1. Residual rickets and active osteomalacia

Studies have found a relationship between osteomalacia in adults and osteoporotic fracture risk (Bhan et al., 2010; Charoenngam et al., 2019; Morgan et al., 2020). A study by Ives et al. (2017) of post-medieval skeletons across eight urban sites from England attributes one fracture found in an individual to both osteoporosis and osteomalacia increasing bone weakness and predisposition to breakage. Chronic osteomalacia can result in low BMD and eventually loss of bone mass, associated with osteoporosis and fracture (Charoenngam et al., 2019; Jha et al., 2019; Lips, 1994). It is plausible that the individuals from Coach Lane suffered from osteomalacia in adulthood. These effects could have masked the impact of residual rickets on BMD levels as those without signs of residual rickets could still have been experiencing VDD as adults, giving lower BMD values than expected in comparison to those with residual rickets. Measurements of BMD as a proxy for osteoporosis may have been influenced by the presence of osteomalacia across both sample groups. However, investigations into vitamin D supplements on improving BMD are contradictory, with many suggesting vitamin D supplements and treatment of osteomalacia have little to no effect on reducing fracture risk depending on the population sample (Charoenngam et al., 2019; Lips, 1994; Parfitt et al., 1985). It is therefore unlikely that osteomalacia would have overshadowed any impact childhood VDD could have had on BMD during growth and development. Furthermore, osteomalacia has a more profound effect on mineralisation of cortical bone with osteoporosis mainly impacting loss of trabecular bone (Bhan et al., 2010). Consequently, osteomalacia most commonly manifests as pseudofractures – disruptions to metabolic processes resulting in bony spicule, woven bone, and poor mineral formation (Brickley et al., 2018) – in the subtrochanteric region of the femur, metatarsals, ribs and sternum (Bhan et al., 2010; Van der Merwe et al., 2018). However, considering both the femoral neck and lumbar BMD show the same patterns between both sample groups, and a lack of evidence for ante-mortem fracture, it is unlikely that osteomalacia has played a significant role in influencing the results.

6.2. Measuring osteoporosis

Jha et al. (2019) emphasise the importance of being aware that osteoporosis is not the only factor contributing towards low BMD and that low BMD is not always a direct indicator of osteoporotic fracture risk. Clinically, BMD is the most commonly used indicator of osteoporotic fracture risk but it only accounts for around 70 % of total bone strength, with the other 30 % consisting of bone quality, bone microarchitecture and general bone size (Fausto-Sterling, 2005; Rauch and Schoenau, 2001; Rubin, 2005; Leonard et al., 2010; Weaver et al., 2016). Therefore, there can be instances where people have high fracture risks but with normal BMD levels due to factors such as bone mineral content (BMC), microgeometric structure, and peak bone mass potential (Dennison et al., 2005; Agarwal, 2016). Bone microarchitecture can be measured by trabecular bone score on lumbar spine, femur, or radius DXA (GE Healthcare, 2020); by pQCT imaging of the tibia and fibula (Riggs et al., 2008); or by Quantitative Ultrasound (QUS) of the calcaneus (Schraders et al., 2019). Different bone locations and types of measurement can result in varying interpretations. For example, a study by Leonard et al. (2010) found that girls generally have lower tibial cortical BMC than boys during all stages of growth but higher tibial cortical BMD around puberty. This shows varying sex differences in bone strength according to the type of measurement used. Ideally studies should use several different methods of assessing bone loss including quantity and quality to reveal more accurate representations of patterns of skeletal health (Felsenberg and Boonen, 2005; Brickley and Mays, 2019), but this is often not possible due to financial and time constraints. Investigating these elements in future studies could further understandings of how exactly osteoporosis develops from a holistic perspective of bone strength and how each of these elements are impacted by conditions throughout the life course in a particular population.

6.3. Assessment of vitamin D deficiency

Snoddy et al. (2024) found that of the 76.1 % (16/21) individuals from Coach Lane who exhibited at least one seasonal occurrence of interglobular dentin (a proxy for VDD) during their lifetime, only 37.5 % (6/21) also exhibited macroscopic rickets. This suggests VDD was experienced by more people than could be detected macroscopically. Macroscopic features of residual rickets were used in this study as they provided non-destructive indicators of VDD affecting the bone which directly relate to BMD. However, it is clear from Snoddy et al (2024) that these results provide only a partial window into the extent and nature of VDD within skeletal samples. Macroscopic studies of pathological features will always provide a limited view into the realities of disease in the past: however, as palaeopathologists we must consider the ethical issues concerned with destructive analysis. While this study may only provide partial insights into the association, or lack thereof, between childhood VDD and BMD in later life, during this period and place, the results are still valid and of significance. Future studies could test if the other individuals from Coach Lane, who showed microscopic indicators of seasonal VDD, also exhibit any adverse impact on BMD. These individuals would then fall into the category of 'experienced VDD during childhood' which might influence the results of statistical comparisons. If differences in BMD levels are found between individuals based on these subtler indicators, it poses considerations of the long-term impacts even slight changes in vitamin D intakes can have over the life course (see also Ives, 2018). Our sense, based on this evidence, however, is that individuals buried in Coach Lane showed relatively robust BMD in adulthood despite earlier tribulations. We believe that this is likely due to more physical lifestyles than typically seen in the present, in conjunction with an adequate diet.

7. Conclusion

The results of this study suggest the link between macroscopic VDD and osteoporosis is not detectable from a DOHaD perspective, at least amongst the Coach Lane population. There are many health risks

associated with the British Industrial Revolution, but it appears that low BMD was not one of them. This may be due to other influencing factors overshadowing the impact of childhood VDD on BMD in adulthood. The culmination of shifts in calcium intake across the life course and high physical activity from a young age may have played a role in increasing, or at least stabilising, peak bone mass development and reducing BMD related osteoporotic risk fracture. The impact might also be more apparent with further bone microarchitecture studies (including micro-CT of the vertebrae), analysis of the cross-sectional geometry of the femora, and investigations into microscopic indicators of VDD. More multi-method assessments of VDD in skeletal populations from various 18th-19th century sites across Britain will help clarify the environmental and social circumstances of this period which resulted in a reduced risk of osteoporotic fracture. Future work could involve scaling-up sample sizes to make results more comparable to other studies such as Ives et al. (2017). This way, patterns and trends may be more evident and may provide a more accurate reflection of skeletal health during 18th-19th century Britain.

CRediT authorship contribution statement

Alexandra Bowers: Writing – review & editing, Writing – original draft, Software, Resources, Project administration, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Rebecca Gowland:** Writing – review & editing, Validation, Supervision, Resources, Conceptualization. **Karen Hind:** Writing – review & editing, Validation, Software, Resources, Methodology, Formal analysis, Data curation.

Declaration of Competing Interest

None.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ijpp.2024.09.002.

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