ROMAN VITAMIN D DEFICIENCY AND RESPIRATORY INFECTIONS

SKELETAL EVIDENCE FOR VITAMIN D DEFICIENCY AND CHRONIC RESPIRATORY INFECTIONS ACROSS THE LIFE COURSE AT TWO ROMAN PERIOD SITES

By LAURA LOCKAU, M.A.

A Thesis Submitted to the School of Graduate Studies in Partial Fulfilment of the Requirements for the Degree Doctor of Philosophy

McMaster University DOCTOR OF PHILOSOPHY (2017) Hamilton, Ontario (Anthropology)

TITLE: Skeletal evidence for vitamin D deficiency and chronic respiratory infections across the life course at two Roman period sites

AUTHOR: Laura Lockau, M.A. (McMaster University)

SUPERVISOR: Professor Megan Brickley

PAGES: xvi, 444

ABSTRACT

This research contributes to understandings of the occurrence of and associations between skeletal evidence of vitamin D deficiency and chronic respiratory infections across the life course based on human skeletal material from the Roman period sites of Isola Sacra in Italy (1st-3rd centuries AD) and Ancaster in the United Kingdom (3rd-4th centuries AD). Modern clinical data demonstrate a positive association between these two conditions that affects the ways in which they are experienced today, and may extend into the past. Macroscopic, radiographic, and histological evidence for skeletal manifestations of vitamin D deficiency and chronic respiratory infections were considered in the context of archaeological and historical evidence available for the Roman period in order to elucidate patterns in disease occurrence that reflect the unique local biologies of these two assemblages. Differing prevalence values for active and healed lesions caused by both conditions, as well as variation in age at death distributions and the relationship of lesions associated with vitamin D deficiency and chronic respiratory infections with one another and with age at death, provide information on the experience of both conditions and the potential interactions between them. Skeletal lesions caused by both conditions are present in individuals throughout the life course at Ancaster and Isola Sacra, with particular implications for disease experiences during infancy, adolescence, and pregnancy in the Roman period. These results point to a picture of morbidity and mortality at Ancaster that involves longer term survival of and more efficient immune responses to chronic disease processes, with higher levels of skeletal lesions indicating the presence of more "survivors" at this site. The combination of lower frequencies of skeletal lesions and higher mortality at Isola Sacra, on the other hand, suggests that fewer individuals may have survived to the point where they were able to mount a skeletal response to disease.

ACKNOWLEDGEMENTS

I would most of all like to thank my supervisor, Dr. Megan Brickley, and committee members Dr. Ann Herring and Dr. Stephanie Atkinson, for their helpful comments and support. I could not possibly have had more knowledgeable, accomplished, and inspirational examples of academic research and mentorship.

Thanks are due to the principal investigators of the SSHRC vitamin D project, Dr. Megan Brickley, Dr. Simon Mays, Dr. Tracy Prowse, and Dr. Michele George. Thank you to Dr. Luca Bondioli and Dr. Simon Mays for providing access to the human skeletal remains analyzed in this dissertation, and to others at the English Heritage Centre for Archaeology in Portsmouth and the Museo Nazionale Preistorico Etnografico "L. Pigorini" in Rome, particularly Dr. Alessandra Sperduti, for their invaluable assistance. I would like to thank Annabelle Schattmann and Marissa Ledger for their help with data collection, and for all of the adventures in Portsmouth, Rome, and beyond.

I am grateful for the assistance of Dr. Glynis de Silveira and others at the Canadian Centre for Electron Microscopy at McMaster University. Thank you to Bonnie Kahlon, and to Sarah Timmins for many early mornings spent in the SEM.

Last but far from least, I would like to acknowledge the friends and family without whose support this dissertation would not exist. Thank you to Lori D'Ortenzio, Maddy Mant, and especially Alyson Holland for being my people, hating my enemies, and always being up for cake. To Erin Hamilton for the endless friendship, unequivocal support, and visits to the other side of the country and across the ocean. I am so grateful to my ballet family, especially to Irina and Evguenia, for saving my sanity and my timbits and for making Hamilton feel like home. Thank you to several summers' worth of fellow "Thesis Jail" inmates for their encouragement and commiseration during the difficult stages of writing, especially to Kandace Bogaert, Robert Stark, Lisa Semchuk, Daiana Rivas-Tello, Katie East, Samantha Price, and Sophie Reilly. Thanks also to Rebecca Psutka, Dorian Juríc, Kyle Freund, and Amy Hirshkowitz for the many adventures. I would like to thank my family, particularly my parents, for their support and encouragement. Special thanks to Jesse Cooper for being there, appreciating my oddities, and keeping me from starving. Thanks also go to Isabelle, Heidi, and Hobo, and to Allee for revealing to me my true cat lady nature.

This research was supported by a SSHRC Canadian Graduate Scholarship award, an Ontario Graduate Scholarship, and the Shelley Saunders Memorial Scholarship in Anthropology.

TABLE OF CONTENTS

LIST OF FIGURES

LIST OF TABLES

LIST OF ALL ABBREVIATIONS AND SYMBOLS

25-OHD	25-hydroxyvitamin D
1,25-$(OH)_2$D	1,25-dihydroxyvitamin D
AMP	Antimicrobial peptide
ANC	Ancaster
APC	Antigen presenting cells
BSEM	Backscattered scanning electron microscopy
CCEM	Canadian Center for Electron Microscopy
CRI	Chronic respiratory infection
DC	Dendritic cells
EtOH	Ethyl alcohol
HOA	Hypertrophic osteoarthropathy
HPO	Hypertrophic pulmonary osteoarthropathy
IL-1B	Interleukin 1 beta
MM	Methyl methacrylate
MTB	*Mycobacterium tuberculosis*
MTBC	*Mycobacterium tuberculosis* complex
PTH	Parathyroid hormone
RANK	Receptor activator of NF-κB
SCR	Isola Sacra
SEM	Scanning electron microscope
TB	Tuberculosis
Th1	Type one helper T cells
Th2	Type two helper T cells
TNF-α	Tumor necrosis factor alpha
UK	United Kingdom
VDR	Vitamin D receptor

DECLARATION OF ACADEMIC ACHIEVEMENT

I declare that the content of the research in this document has been completed by myself, Laura Lockau, with recognition of the contributions of Dr. Megan Brickley, Dr. D. Ann Herring, and Dr. Stephanie Atkinson in both the research process and the completion of the thesis.

CHAPTER 1 – Introduction

1.0. Introduction

This research investigates the occurrence of and associations between vitamin D deficiency and chronic respiratory infections across the life course at the Roman period sites of Isola Sacra in Italy (1st-3rd centuries AD) and Ancaster in the United Kingdom (3rd-4th centuries AD). It is based on the hypothesis, gleaned from modern clinical data, that a positive association exists between the occurrence of these two disease processes that has the potential to significantly affect the ways in which these conditions are experienced today as well as in the past. This project gathers evidence for disease experience by evaluating the presence of macroscopic, radiographic, and histological evidence for skeletal manifestations of vitamin D deficiency and chronic respiratory infections in human skeletal remains from the Roman period, and considers this evidence in the context of archaeological and historical evidence available for the Roman empire. Disease experience varies over the life course, affected by collective identities related to age and gender as well as by societal behavioral expectations tied to various life stages and population groups. Variation in the experience of disease and other aspects of the natural and social environment can also be geographically and temporally situated, leading to the development of unique local biologies. This examination of qualitative and quantitative data related to skeletal expressions of vitamin D deficiency and chronic respiratory infections in juvenile and adult human skeletal remains from two Roman period assemblages provides information related to disease occurrence and experience

across the life course at these two sites, revealing meaningful variation on individual and population levels based on age at death, sex, and geographic location.

Paleopathology contributes to understanding disease in the past by integrating medicine and anthropology, contextualizing clinical data with anthropological perspectives. Vitamin D deficiency and chronic respiratory infections represent two conditions that affect the skeleton, and can therefore be investigated in ancient human skeletal material. Recent research into the biological functions of vitamin D has implicated this molecule in actions of the immune, cardiovascular, and neurological systems, in addition to its primary role in mineral metabolism. As a result of the involvement of vitamin D in immune actions, clinical associations have been detected between serum levels of vitamin D and multiple specific health outcomes, as well as all-cause mortality. A putative association between vitamin D deficiency and infectious diseases, including respiratory infections, has been observed in modern populations. Clinical and epidemiological studies have found a higher incidence of respiratory infections in vitamin D deficient individuals (Wilkinson et al., 2000) and in populations at high risk of deficiency (Douglas et al., 1996), as well as lower vitamin D levels in respiratory infection patients (Gibney et al., 2008). The visibility of both conditions in the skeleton makes this association well suited to the paleopathological examination of clinically demonstrated relationships, linking paleopathological research with topics of current interest to clinicians and epidemiologists regarding broader biological roles of vitamin D. Previous paleopathological investigations (e.g., Canci et al., 2005; Cox, 1993; Lewis, 2011a; Minozzi et al., 2012; Rohnbogner & Lewis, 2017), as well as significant

documentary evidence (e.g., Dormandy, 1999; Findlay, 1919; Foote, 1927; Grmek, 1989; Keers, 1978; Meinecke, 1927; Nutton, 2004; Rajakumar, 2003; Webb, 1936), support the occurrence of both vitamin D deficiency and chronic respiratory infections in the Roman world, making the Roman period an appropriate one for this type of paleopathological examination.

Juvenile vitamin D deficiency has been extensively studied within paleopathology (e.g., Capasso et al., 1995; Formicola, 1995; Giuffra et al., 2015; Littleton, 1998; Mays et al., 2006; Ortner & Mays, 1998), but subtle skeletal changes resulting from active deficiency in adulthood have received far less attention (e.g., Brickley et al., 2005, 2007; Haduch et al., 2009; Ives, 2005; Ives & Brickley, 2014). Bioarchaeologists have begun to recognize the value of recent clinical research on the developmental origins of health and disease (Gowland, 2015) and the broad actions of vitamin D (Snoddy et al., 2016) for paleopathology, and specifically for the study of vitamin D deficiency in the past. However, the only practical application of these data to date has investigated relationships between vitamin D deficiency and the problematic category of "nonspecific infection" (Snoddy et al., 2016). Paleopathological studies of specific skeletal evidence for respiratory infections have largely focused on the examination of tuberculosis (TB; e.g., Arriaza et al., 1995; Canci et al., 2005; Dabbs, 2009; Évinger et al., 2011; Lambert, 2002; Matos et al., 2011; Mays et al., 2001; Nicklisch et al., 2012; Pálfi et al., 1999; Suzuki & Inoue, 2007; Ubelaker et al., 2000). Beyond spinal and joint lesions associated specifically with skeletal TB, periosteal new bone formation on the visceral surfaces of the ribs has been examined as an indicator of pulmonary infection (e.g., Kelley & Micozzi,

1984; Matos & Santos, 2006; Mays et al., 2002; Lewis, 2011a; Raff et al., 2006; Roberts et al., 1994; Santos & Roberts, 2001, 2006). New bone formation on the long bones characteristic of hypertrophic osteoarthropathy (HOA) has also been identified paleopathologically (e.g., Anselmo et al., 2016; Blondiaux et al., 1992; Fennel & Trinkaus, 1997; Gladykowska-Rzeczycha & Prejzner, 1993; González-Reimers et al., 2015; Hershkovitz et al., 2008; Martinez-Lavin et al, 1994; Masson et al., 2013; Mays & Taylor, 2002). However, while respiratory infections are likely to have been an important cause of HOA in the past (Locke, 1915; Webb & Thomas, 1986), evidence for this condition has not previously been integrated into population-level bioarchaeological studies of respiratory disease.

By integrating concepts recently developed in clinical medicine that have had limited application within paleopathology (e.g., Snoddy et al., 2016; Wilbur et al., 2008), this research contributes to the paleopathological literature on the bioarchaeological construction of disease experience, interactions between metabolic and infectious disease occurrence, and the intersection of disease experience and social identity within the Roman world. The novel approach used in this research, which combines evidence for active and healed vitamin D deficiency in juveniles and adults, contributes valuable data on deficiency in adults. This thesis therefore builds a more representative view of disease experience by accessing information on individuals who experienced active disease as adults, and those who experienced deficiency in childhood and survived to adulthood. This analysis also reveals meaningful variation in experiences of chronic respiratory infections over the life course by analyzing multiple types of active and healed lesions

indicative of respiratory disease, and using qualitative and quantitative features of proliferative lesions to represent the extent of infection. Evaluating mortality along with the presence of skeletal lesions in the context of information on the natural, constructed, and social environments experienced by ancient individuals reveals features of the unique local biologies that developed at these two Roman period sites. This evidence indicates longer term survival of and more efficient immune responses to chronic disease processes at Ancaster than at Isola Sacra, representing a higher number of "survivors" in this assemblage. It also reveals a significant relationship between vitamin D deficiency and chronic respiratory infections at Isola Sacra, along with a lower number of "survivors" at this site.

1.1. Research Questions

This research aims to reveal meaningful variation in the occurrence and experiences of vitamin D deficiency and chronic respiratory infections at the Roman period sites of Ancaster and Isola Sacra by asking several research questions. Demographic differences between the two sites are evaluated, including mean age at death, age at death distributions, and numbers of individuals surviving to old adulthood. For both vitamin D deficiency and chronic respiratory infections, this project evaluates how evidence for active and healed disease varies based on age at death. For vitamin D deficiency specifically, it asks whether any individuals display evidence for multiple episodes of deficiency, and whether there are any lesions that can be associated with the experience of deficiency at a specific age. Additionally, this research evaluates the

relationship between lesions associated with vitamin D deficiency and chronic respiratory infections and age at death distributions, examining whether having evidence for either condition has an effect on survival in either sample. For individuals over the age of 16, evidence for active and healed vitamin D deficiency and chronic respiratory infections is evaluated for variation based on sex. In order to evaluate the relationship between vitamin D deficiency and chronic respiratory infections, both assemblages were investigated for the presence of individuals displaying evidence for both conditions, and statistical analyses were used to test for an association between the prevalence values of these conditions in either population. For both conditions, this research also investigates whether evidence for active or healed disease varies between Ancaster and Isola Sacra, and how this may be affected by associated differences in the natural, constructed, and social environments experienced by individuals at these two sites.

1.2. Thesis Chapters

This thesis is organized into five chapters. Following the introduction in Chapter One, Chapter Two discusses the pathophysiology, clinical features, and patterns of occurrence of vitamin D deficiency and chronic respiratory infections, based on modern and historical evidence from clinical and epidemiological research. On the basis of clinical data demonstrating the breadth of actions vitamin D has within the body, this chapter suggests ways in which vitamin D deficiency may interact with respiratory infections in order to modify disease experience and skeletal lesion formation. Chapter Three outlines the materials and methods used in this analysis, including archaeological

and historical information regarding the Roman period sites of Ancaster and Isola Sacra. It also details how information on demographic variables and lesions associated with vitamin D deficiency and chronic respiratory infections was collected and analyzed, including paleopathological precedents for methodological decisions made and a clear explanation of how paleopathological criteria relate to clinical signs of disease. Chapter Four communicates the results of these analyses, looking at how prevalence values of skeletal lesions associated with vitamin D deficiency and chronic respiratory infections vary based on age at death, sex, and archaeological site, investigating statistical relationships between skeletal lesions for the two conditions and survival, examining how aspects of proliferative rib lesions relate to the severity of disease, and detailing features of individual skeletons with evidence for both conditions. Chapter Five discusses the relevance and meaning of these results by contextualizing the patterns observed using data from modern clinical and epidemiological research, other paleopathological studies of vitamin D deficiency and respiratory infections, and information from other skeletal analyses at Isola Sacra and Ancaster. Implications for the survival of disease episodes and formation of skeletal lesions at these two sites are explored by combining evidence for the overall patterns of occurrence of vitamin D deficiency and chronic respiratory infections with mean age at death and statistical relationships between skeletal lesions and survival. Chapter Five concludes with a summary of the findings of this research, a discussion of what it contributes to the paleopathological literature, and suggestions for future research directions based on the results obtained and approaches used in this project.

CHAPTER 2 – Background
Vitamin D Deficiency and Chronic Respiratory Infections: Pathophysiology, Clinical Features, and Interactions

2.0. Introduction

Metabolic and infectious diseases represent two major categories of pathological conditions investigated both clinically and paleopathologically. The term metabolic bone disease can refer to any condition that interferes with normal skeletal metabolism by disrupting normal bone formation, mineralization, remodeling, or a combination of these processes, (Albright & Reifenstein, 1948), which includes rickets and osteomalacia related to vitamin D deficiency. Infectious diseases are those caused by pathogenic micro-organisms, including bacteria, viruses, fungi, and parasites; pathogens infecting the lungs can cause chronic respiratory infections, including tuberculosis (TB). Both vitamin D deficiency and chronic respiratory infections affect the skeleton, and both can therefore be investigated in archaeological skeletal material.

Investigations of metabolic and infectious conditions in the past, as in the present, are complicated by the fact that disease development most often involves multiple causal and predisposing factors, and that these conditions rarely exist in isolation. The complex interplay between environmental, nutritional, and genetic influences on an individual as well as on characteristics of pathogenic organisms can influence the incidence, severity, progression, and course of disease. The possibility for co-occurrence of metabolic bone disease with other metabolic conditions as well as with infectious disease has been noted by many paleopathologists (e.g. Stuart-Macadam, 1989; Lewis, 2000; Rose, 1985; Saul, 1973; Stirland, 2000), but few have attempted to deal with these issues in depth (e.g.,

Schattmann et al., 2016; see discussion in Wilbur et al., 2008). Vitamin D deficiency and chronic respiratory infections represent two conditions for which a potential correlation is supported by significant clinical evidence. Skeletal involvement in both conditions is complex; however, examining clinical data regarding how each affects the skeleton and how they likely affect one another is important in order to elucidate how this interaction may be reflected in human remains from past populations.

Clinical data provide a primary source of evidence on the pathophysiology of metabolic and infectious disease processes and on interactions between them, and are necessary for their investigation in the past. This chapter will outline clinical evidence for pathophysiological processes underlying the development of vitamin D deficiency rickets and osteomalacia and chronic respiratory infections including TB, as well as experimental and clinical data on the potential correlations and interactions between the two. These clinical features provide information on manifestations of disease that may be identifiable in archaeological skeletal material, as well as insight into the symptoms and outcomes that may have shaped the disease experiences of individuals who lived with these conditions in the past.

2.1. Vitamin D Deficiency: Rickets and Osteomalacia

2.1.1. Vitamin D

Vitamin D is a pro-hormone mainly derived from cutaneous synthesis upon exposure to ultraviolet B radiation, or through dietary intake. Vitamin D from the skin or the digestive tract must undergo two hydroxylation steps: the first at position 25 in the

liver to form 25-hydroxyvitamin D (25-OHD) and the second at position one in the kidney to form the active vitamin D metabolite 1,25-dihydroxyvitamin D (1,25-$(OH)_2D$) (Figure 2.1). The major physiological function of this molecule is generally considered to be the regulation of calcium and phosphorous metabolism and maintenance of homeostasis of these minerals, through regulation of the efficiency of intestinal absorption as well as through release from reservoirs in the skeleton (Favus, 1999; Heaney, 2005; Holick, 2003). Primary target organs of vitamin D are therefore intestine, bone, and the kidney in order to regulate production of its own active metabolite (Holick, 2006a). The major skeletal actions of vitamin D are mobilization of calcium and

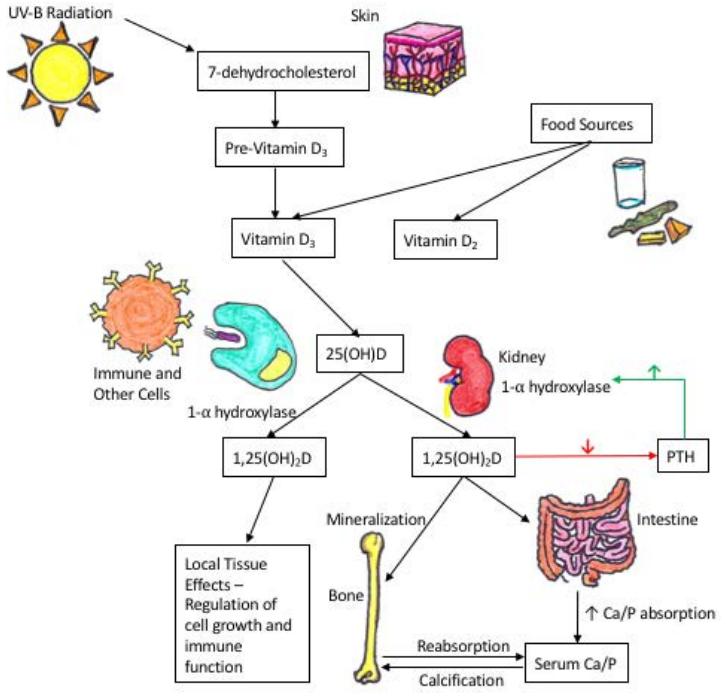


Figure 2.1. Vitamin D metabolism and actions on major target organs. Vitamin D influences the efficiency of calcium (Ca) absorption in the intestine, and regulates calcium and phosphorous (P) mobilization from the skeleton. PTH acts to increase renal hydroxylation of 25-OHD to 1,25-$(OH)_2D$ when calcium is low, and 1,25-$(OH)_2D$ feeds back to decrease production of PTH.

phosphorous from bone as well as promotion of bone matrix maturation and mineralization (Pitt, 2002). Vitamin D acts systemically through the regulation of mineral metabolism and skeletal homeostasis, as well as locally through the regulation of cellular differentiation (Pitt, 2002; St-Arnaud & Demay, 2003). The 'non-classic' actions of vitamin D that operate outside of its role in mineral homeostasis are cell-specific, but generally involve promotion of cellular differentiation and inhibition of cellular proliferation (Holick, 2002a). They operate outside of the main feedback loop controlling mineral balance, and so remain limited by the primary effects of 1,25-$(OH)_2$D on calcium and phosphorous metabolism (Bikle, 2009; Chesney, 2010).

The role of vitamin D in mineral and skeletal homeostasis has long been recognized; more recently, discovery of the expression of both the vitamin D receptor (VDR) and the hydroxylase enzyme needed to produce the active metabolite of vitamin D in many cell types throughout the body has alerted researchers to many other potential functions of this molecule, indicating its likely importance for overall health and wellbeing (Cantorna et al., 2004; Holick, 2003, 2005, 2008). Any cell that expresses the VDR is a potential target of 1,25-$(OH)_2$D, and the presence of both systemic and local production of and response to 1,25-$(OH)_2$D indicates that this molecule has both endocrine and autocrine or paracrine effects (Heaney, 2003). Binding of 1,25-$(OH)_2$D to its receptor is followed by conformational changes promoting heterodimerization of this complex with the retinoid X receptor (RXR); interaction with vitamin D responsive elements in the cell's nuclear DNA then modulates transcriptional activity (Adorini, 2005; St-Arnaud & Demay, 2003; White, 2008). Severe and longstanding defects in

growth and skeletal mineralization associated with inadequate vitamin D metabolism lead to the development of rickets and osteomalacia. However, while these conditions most commonly involve a deficiency of vitamin D, there is increasing recognition that they can develop from the disruption of any part of the calcium, phosphorous, and vitamin D system (Pitt, 2002; Prentice, 2008; Reginato & Coquia, 2003).

2.1.1.1. Vitamin D: Classic actions on mineral metabolism

Vitamin D exerts its major actions on mineral metabolism primarily by regulating the efficiency of calcium and phosphorous absorption in the small intestine (Pitt, 2002). Mineral homeostasis is important to support metabolic functions, bone mineralization, and neuromuscular transmission (Holick, 2006a,b). Extracellular calcium homeostasis is determined by the balance between movement of calcium out of the extracellular fluid via unregulated processes of mineralization and excretion in bodily fluids and its movement into the extracellular fluid via vitamin D-regulated processes of absorption from ingested food and resorption from skeletal reservoirs (Heaney, 2005) (Figure 2.1). The efficiency of intestinal calcium absorption varies with intake (Heaney, 2005); at higher intakes passive absorption predominates, while at lower intakes vitamin D induces an increase in the number of calcium channels for active absorption at the intestinal enterocyte brush border (Favus, 1999; Holick, 2006b; Prentice, 2003). Vitamin D-induced active transport is able to increase absorption of calcium from about 10-15% of that present in ingested food to about 30-40% (Heaney, 2005; Holick, 2006a). Vitamin D deficiency will therefore be most evident at low calcium intakes, as this is when its intestinal actions are most crucial (Favus, 1999).

Vitamin D also regulates calcium and phosphorous mobilization from the skeleton, which acts as a reservoir from which these minerals can be released if necessary. When dietary intake of calcium is low and serum calcium and phosphorous are insufficient even with vitamin D-induced increases in absorption efficiency, vitamin D acts to mobilize these minerals from skeletal reserves. Vitamin D is able to mitigate problems created by low calcium intake but not to counterbalance them completely, meaning that at high intakes vitamin D is able to protect calcium in both extracellular fluid and in body stores such as the skeleton by increasing intestinal absorption (Priemel et al., 2010). However, at low intakes homeostasis is protected in extracellular fluid at the expense of skeletal stores (Heaney, 2005).

Calcium is also regulated by parathyroid hormone (PTH), which displays significant involvement in the calcium, phosphorous, and vitamin D system (Figure 2.1). In response to low levels of calcium, PTH increases renal hydroxylation of 25-OHD to 1,25-$(OH)_2$D. In a classic hormonal loop, 1,25-$(OH)_2$D then feeds back on the parathyroid gland to decrease both proliferation of parathyroid cells and synthesis and release of PTH (Clements et al., 1987; St-Arnaud & Demay, 2003). 1,25-$(OH)_2$D also feeds back on its own production, decreasing expression of renal hydroxylase, inducing expression of the enzyme needed for its catabolism, and preventing hypercalcemia (St-Arnaud & Demay, 2003). 1,25-$(OH)_2$D therefore acts to close regulatory loops initiated by calcium, phosphorous, and PTH (Pitt, 2002).

In addition to its effects on mineral homeostasis, vitamin D may regulate skeletal remodeling via direct effects on bone cells (Figure 2.2). At physiological concentrations,

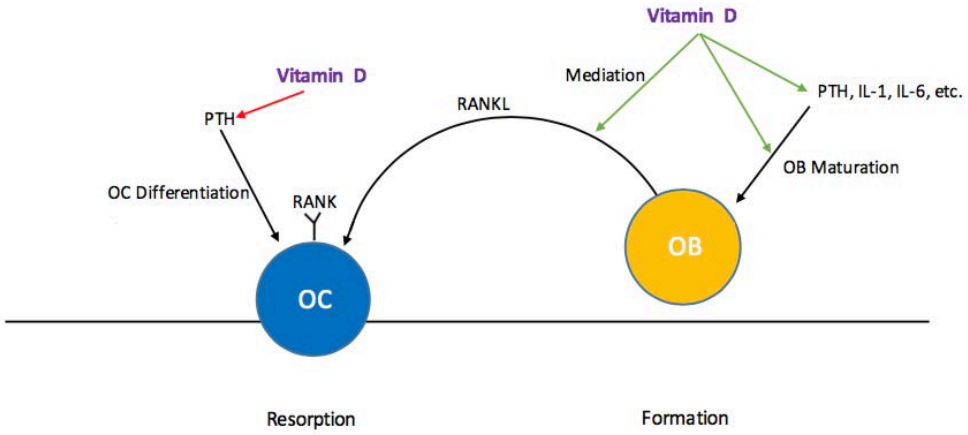


Figure 2.2. Vitamin D-mediated actions on bone cells for regulation of remodeling (after Rosen & Bilezekian, 2001). Vitamin D acts to promote the development of mature osteoblasts and increase their secretory functions, as well as to modify osteoblast responsiveness to other regulators indirectly through actions on hormones and growth factors. Vitamin D mediates osteoblasts` regulation of osteoclast differentiation (through pathways involving RANK and RANK-ligand). It can also inhibit resorption through inhibition of PTH. Adequate vitamin D most likely results in properly coupled actions of osteoblasts and osteoclasts in bone remodeling.

1,25-$(OH)_2$D enhances bone formation and coordinates the sequence of development and function of osteoblasts, or bone-forming cells, promoting the development of mature osteoblasts and increasing their secretory functions (Hurley & Lorenzo, 2004; Peterlik, 2004; Stern, 2005). Osteoblasts have an important role in regulating differentiation of osteoclasts, or bone-resorbing cells, and this role is suggested to be mediated by both PTH and 1,25-$(OH)_2$D through pathways involving the receptor activator of NF-κB (RANK) (Peterlik, 2004; St-Arnaud & Demay, 2003). There is also evidence that vitamin D may inhibit resorption, potentially through its inhibition of PTH (Stern, 2005). *In vivo* effects of vitamin D on resorption are therefore suggested to be biphasic (Stern, 2005), and adequate vitamin D is likely to result in properly coupled actions of osteoblasts and osteoclasts in bone remodeling (Favus, 1999). Vitamin D-induced promotion of osteoblast maturation and secretory function may result in preparation of bone surfaces

for resorption by osteoclasts, which require bone matrix to be mineralized before resorption can occur (Aubin & Heersche, 2005). Vitamin D is also suggested to have protective actions promoting maintenance of skeletal integrity by both preventing excessive remodeling that might increase skeletal fragility and improving neuromuscular function to prevent falls (Priemel et al., 2010). This concept of 1,25-$(OH)_2$D as a promoter of properly coupled remodeling is consistent with the suggestion that vitamin D deficiency and resultant low calcium places individuals at greater risk of imbalance between processes of bone formation and resorption (Bilezikian & Silverberg, 2001).

Vitamin D also indirectly affects mineralization of bone during skeletal growth and remodeling. Mineralization is a passive, unregulated process that lags behind osteoblast-initiated bone formation (Heaney, 2005). The primary actions of vitamin D on absorption and therefore on serum concentrations of calcium and phosphorous affect mineralization, which depends upon maintenance of adequate levels of these minerals (Holick, 2005, 2006b; Oginni et al., 1996). Mineralization is suggested to depend on the availability of calcium and phosphorous ions and on the activity of osteoblasts and chondrocytes, with a potential role for 1,25-$(OH)_2$D in the regulation of both (Parfitt, 2005). Mineralization effects of vitamin D have been suggested to modulate some of its other actions; this is relevant in deficiency states, where impaired mineralization may interfere with resorption (Stern, 2005) and therefore prevent normal adaptive mechanisms for dealing with low extracellular calcium by mobilizing skeletal stores (Jaffe, 1975).

2.1.1.2. Vitamin D: Non-classic immune actions

Vitamin D has been characterized as a potent immunomodulator due to its regulatory actions on both innate and adaptive immune responses (Figure 2.3). Vitamin D exerts important effects on the growth and differentiation of many cell types (Adorini, 2005), and its effects on cells of the immune system are thought to impact the development and course of neoplastic, autoimmune, and infectious conditions (Bikle, 2009; Grant, 2006; Prentice, 2008). As in all other cell types, vitamin D acts to encourage cellular maturation and differentiation, and to inhibit cellular proliferation (Davies, 1985). Within the immune system, 1,25-$(OH)_2$D is generally considered to inhibit adaptive immune responses and promote innate immunity (Bikle, 2009). In general, the effect of vitamin D is to promote antigen processing, phagocytosis, and the production of

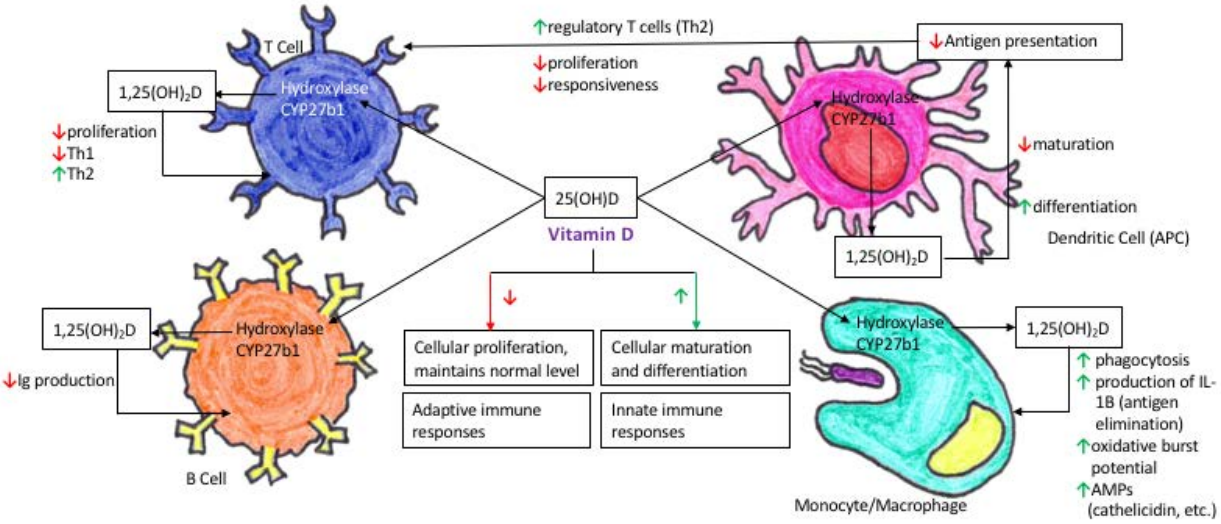


Figure 2.3. Immune actions of vitamin D. Generally, vitamin D, acting both through endocrine and through paracrine and autocrine actions, encourages cellular maturation and differentiation, modulates inflammation, and inhibits cellular proliferation. It promotes innate immunity and inhibits adaptive immune responses, both through direct effects on T and B cells and through regulating APCs. Abbreviations are Th1 (Type 1 helper T cells), Th2 (Type 2 helper T cells, or regulatory T cells), Ig (immunoglobulin), APC (antigen presenting cell), IL-1B (interleukin 1-beta), AMP (antimicrobial peptide).

interleukin 1 beta (IL-1B) to encourage the elimination of foreign antigens (Chesney, 2010), potently stimulating mechanisms associated with pathogen elimination (Hewison, 2012).

Immune actions of vitamin D are thought to be mediated mainly through local expression of the relevant hydroxylase (CYP27b1) and the VDR in immune cells, and therefore by local production of and autocrine or paracrine response to 1,25-$(OH)_2$D from circulating 25-OHD (Adams et al., 2007; White, 2008). Local 1,25-$(OH)_2$D synthesis is thought to be largely independent from regulation by PTH and calcium signals, and therefore to be much more substrate-dependent than renal production (Adams et al., 2007; Bikle, 2009; Heaney, 2003). As a result, local functions may be impaired sooner by a fall in serum 25-OHD than the systemic production of 1,25-$(OH)_2$D as regulated by PTH (Cianferotti & Marcocci, 2012; Parfitt, 2005). It has also been suggested that the negative feedback loop may be reduced in macrophages due to defective production of the enzyme necessary for 1,25-$(OH)_2$D catabolism, resulting in maintenance of 1,25-$(OH)_2$D signaling over an extended period of time and therefore increased vitamin D-induced immune processes in these cells (Bikle, 2009; White, 2008).

Vitamin D exerts direct effects on the adaptive immune response, generally suppressing adaptive immunity by inhibiting T cell proliferation and suppressing B cell immunoglobin production (Bikle, 2009). 1,25-$(OH)_2$D also modulates the phenotype and function of antigen presenting cells (APCs) such as dendritic cells (DCs) (Adorini, 2005), which are important in initiating T cell responses. 1,25-$(OH)_2$D promotes DC differentiation and stalls their maturation, which results in suppression of antigen

presentation and attenuation of T cell proliferation (Adams et al., 2007; White, 2008). Vitamin D therefore inhibits DC maturation and modulates their activation and survival, ultimately affecting T cell phenotype and function, and resulting in T cell hyporesponsiveness (Penna & Adorini, 2000).

The effect of 1,25-$(OH)_2$D is to inhibit type one helper T cells (Th1) and encourage development of type two helper T cells (Th2), shifting the balance of the T cell response away from type one and toward a more regulatory type two response (Adorini, 2005; Bikle, 2009; White, 2008). This occurs through direct actions of 1,25-$(OH)_2$D on T cells (Bhalla et al., 1984) as well as through its effect on the developmental microenvironment of T cells via DC maturation and function (Adorini, 2005; Cantorna et al., 2004; Hewison, 2012). Vitamin D-induced promotion of regulatory T cell responses may allow normal activity while suppressing excessive immune reactions (Adams et al., 2007; White, 2008), possibly relating to a role for vitamin D in preventing autoimmune diseases.

Vitamin D has also been found to directly affect the innate immune response, increasing the oxidative burst potential of macrophages and stimulating expression of specific antimicrobial peptides (AMPs) involved in the direct killing of microbes (Cannell et al., 2006). Immune roles of vitamin D may appear contradictory, as it tends to enhance some immune responses and impair others. However, the overall effect of this molecule is suggested to be protective, with stimulation of innate immunity complemented by modulation of inflammation and prevention of over-exuberant immune responses (Hewison, 2012).

2.1.2. Vitamin D deficiency

There has been some disagreement within the clinical literature regarding what constitutes a deficiency or insufficiency of vitamin D (Pettifor, 2003), and there is as yet no standard definition of optimal vitamin D status based on measurements of serum levels of 25-OHD (Mithal et al., 2009). Functional outcomes used to indicate sufficient 25-OHD levels vary. However, agreement is lacking even among those basing the definition of sufficiency on maximal suppression of PTH and optimal absorption of calcium, with some suggesting deficiency between 0-10 nmol/L and insufficiency between 10-50 nmol/L and others extending the lower border of sufficiency to 75 nmol/L or even higher (Ross et al., 2011a; Yetley et al., 2009). Durazo-Arvizu et al. (2010) suggest that some of these differences may relate to statistical method choice, as well as to differing study populations and definitions of maximal suppression of PTH, while Yetley et al. (2009) caution that different assays can result in different serum 25-OHD measurements, creating difficulties with inter-study comparisons. Severe clinical deficiency is commonly associated with 25-OHD levels below around 12.5 nmol/L (Docio et al., 1998), although it has been suggested that skeletal defects can develop if 25-OHD levels remain below 25 nmol/L for a prolonged period of time (Cianferotti & Marcocci, 2012; Pearce & Cheetham, 2010). Cianferotti and Marcocci (2012) indicate that compromised bone histology and muscle function can be found even with subclinical deficiency, associated with 25-OHD levels of 25-75 nmol/L. Histomorphometric measures have been proposed as a direct way to determine vitamin D adequacy; Priemel et al. (2010) investigated histomorphometric correlates of 25-OHD serum levels and suggested that 75 nmol/L be

considered a minimum threshold for adequacy as no individuals with serum 25-OHD above this level exhibited evidence of mineralization defects. Other functional outcome measures, such as maximal neuromuscular performance in elderly individuals, may be associated with even higher serum 25-OHD concentrations around 100 nmol/L (Cannell et al., 2006). The term 'deficiency' is therefore heterogeneous, and attention must be paid to the definition of various vitamin D states used by researchers in order to interpret their results meaningfully (Meunier & Chapuy, 2005).

2.1.2.1. Vitamin D deficiency: Pathology, pathophysiology, and clinical presentation

Vitamin D deficiency is characterized by increased bone resorption and prevented or delayed mineralization (Holick, 2003; Parfitt, 2005; Pitt, 2002; Prentice, 2008), resulting in abnormal quantities of osteoid or unmineralized organic bone matrix in areas of bone formation (Jaffe, 1972, p. 381). Clinically, low serum calcium and increased PTH often lead to the development of secondary hyperparathyroidism (Meunier & Chapuy, 2005), which stimulates increased osteoclastic resorption and is therefore associated with generalized bone loss (Gloth III, 1999; Holick, 2006a; Peterlik, 2004; Pettifor, 2003). Increased PTH also enhances renal clearance of phosphorous, resulting in hypophosphatemia (Holick, 2002b, 2006a). This phase of vitamin D deficiency, associated mainly with secondary hyperparathyroidism, may be clinically silent until further osseous complications, including mineralization defects, develop (Parfitt, 2005). Defective mineralization, and potentially increased bone turnover and resorption as a result of secondary hyperparathyroidism, result in reduced bone strength (Jaffe, 1975;

Meunier & Chapuy, 2005), contributing to the gross manifestations seen in rickets and osteomalacia.

Severe or longstanding deficiency of vitamin D can lead to the clinically recognizable syndromes of rickets and osteomalacia. These two conditions share a common pathophysiological mechanism, and therefore display similar histological features, although their gross effects differ by age based on where growth is occurring (Pitt, 2002; Reginato & Coquia, 2003). Osteomalacia is characterized by an increased delay between osteoid synthesis and mineralization, resulting in the deposition of abnormally high quantities of unmineralized osteoid on both trabecular and cortical bone surfaces (Heaney, 2005). Features of this condition therefore include increased osteoid seam thickness and number, some of which may be preserved as buried osteoid seams once normal mineralization resumes, as well as decreased numbers of trabeculae that may also be thinner than normal, irregular Haversian systems with larger than normal channels, and often generalized bone loss related to secondary hyperparathyroidism (Pitt, 2002). Since the development of skeletal changes requires deficiency that is severe and longstanding, skeletal manifestations of vitamin D deficiency can be regarded as the extreme end of the spectrum of morbidity associated with negative health outcomes in this condition (Snoddy et al., 2016).

Vitamin D deficiency has been described as threatening rather than fatal per se, because it adds to danger and mortality from all acute diseases, particularly in infancy but also in later life (Banajeh et al., 1997; Holt, 1908, p. 269). Rickets in young children has been associated with an increased risk of respiratory and gastrointestinal infections, and

often co-occurs with anemia and malnutrition (Pettifor, 2003). By the early 20th century, clinicians noted a susceptibility to other acute illnesses in children with rickets, especially with conditions in the lungs; rickets was therefore considered to be a factor in mortality in the first two years of life through predisposition to other acute diseases, particularly respiratory disease (Holt, 1908, p. 269). The mechanism for this predisposition is thought to relate to a combination of structural and immunological factors (Pettifor, 2003), as well as broader effects of vitamin D deficiency on the immune system (Banajeh et al., 1997). Muscle weakness, a pliable rib cage, and thoracic deformities, including bending in the spine and movement of the sternum and flaring of the ribs to form a 'pigeon-breast' (Holick, 2006a; Holt, 1908, p. 261; Pearce & Cheetham, 2010), can lead to an inability to clear the lungs of pathogens and mucus.

2.1.2.1.1. Juvenile vitamin D deficiency

In rickets, proper organization and ossification of cartilage at the growth plate is impaired (Pettifor, 2003). Developing cartilage shows severe abnormalities in the zone of maturation, leading to structural disorganization (Pitt, 2002), and ultimately to expansions in length and width of the growth plate that are detected clinically using radiographic methods (Parfitt, 2005; Pitt, 2002) and can be observed in dry bone following mineralization (Brickley & Ives, 2008, p. 90). Other clinical features of rickets include frontal bossing, thickened long bone ends, bowing of the long bones especially in the legs, delayed dental eruption, wide anterior fontanelle, rachitic rosary, and chest deformity (Holt, 1908, p. 258-266). In the past, clinically flagrant rickets was typically seen between eight and 18 months of age (Jaffe, 1972, p. 383), and modern studies have estimated peak

incidence before 18 months (Holick, 2006a; Pettifor, 2003). In some cases, rickets can be congenital; this is typically seen when the mother has severe deficiency, with or without clinical signs of osteomalacia (Lubani et al., 1989; Paterson & Ayoub, 2014), or with hereditary forms such as vitamin D-dependent rickets or hypophosphatemic rickets (Reginato & Coquia, 2003).

Jaffe (1972, p. 383-6) outlines symptoms experienced over the natural course of rickets, tracing development of the disease if it began in early infancy and was allowed to continue without treatment or remission for a period of two years. Rickets often has an insidious onset, so it is not usually diagnosed until characteristic skeletal changes have developed. At the age of three or four months, the infant may have some widening of the cranial sutures and anterior fontanel, some slight beading at the costochondral junctions, and slight enlargement of the distal radius and ulna. Changes at this early stage correspond with the development of hypocalcemia (Pettifor, 2003). By six to nine months, there may be extensive craniotabes and the development of bossing in the frontal bone. The rachitic rosary is developing, potentially with some associated deformation of the rib cage. In active infants, deformities may be developing in the extremities, with enlargement of the wrists and ankles and potentially slight curvature in the long bones, and even exaggerated curvature in the clavicles (Holt, 1908, p. 259-264). With loss of muscle tone, the infant often develops a ‘potbelly’, and may even be unable to sit up without support. By 15 to 24 months, skeletal manifestations will be exaggerated, with the development of a flattened and squared off cranial shape. Dental eruption is often delayed (Pettifor, 2003), and when teeth do erupt the order of appearance may be

abnormal. Thoracic deformation involves protrusion of the sternum, indentation of the chest wall along the lines of the costochondral junctions, and retraction of the sides of the chest at the attachments of the diaphragm. There may be gradual curvature in the thoracic spine, or exaggerated lordosis in the lumbar spine, resulting from loss of muscle tone as well as collapse of vertebral bodies (Pettifor, 2003). Long bone ends are typically enlarged, particularly at the wrists and ankles but also potentially in the knees and elbows. The finger phalanges may also be thickened. Poor muscular development affects the child's ability to stay sitting, pull to standing, stand, and walk. Functional stresses on the long bone diaphyses due to muscular pulls increase the likelihood and severity of lateral and anteroposterior bowing deformities that develop due to deformation of relatively undermineralized elements (Pettifor, 2003); deformities are generally more severe in the lower limb, typically including bowlegs (*genu varum*) or knock knees (*genu valgum*). Complete fractures or pseudofractures may also occur in the diaphyses or more commonly in the ribs, and are usually multiple and often bilateral and symmetrical (Jaffe, 1972, p. 401). If the disease continues to be active into later childhood, the child is likely to show striking deformities and significantly stunted height (Holick, 2005). If the deficiency is severe and longstanding, extending into childhood, there may also be deformation of other elements such as the pelvis (Holt, 1908, p. 263; Jaffe, 1972, p. 390), which can have severe consequences in adult life for women who retain these deformities and then give birth (Hill, 2005). Generally, the extent of the lesions seen will vary with the severity and duration of deficiency (Holt, 1908, p. 254).

Radiographically, defective mineralization at the growth plate blurs the distinction between the growth plate and the calcified metaphysis (Pettifor, 2003). Changes are typically visible at long bone metaphyses, including cupping and flaring of the epiphyseal junction, and a fuzzy or frayed texture of the growth plate (Pitt, 2002). Fractures in the long bones and ribs can also be detected on x-ray, with pseudofractures presenting in living patients as a perpendicular translucent strip of unmineralized osteoid in cortical bone (Pettifor, 2003). Microscopically, the changes that can be seen in rickets reflect disorganization of normal endochondral bone formation (Pitt, 2002), and failure or delay of endochondral calcification at the growth plates (Pettifor, 2003). Impaired mineralization and abnormal cartilage organization result in abnormal buildup of osteoid at the growing long bone ends, where softened tissue can cause the development of deformities with functional stress, including displacement and angulation of the epiphyses. Diaphyses may be thickened with periosteal deposition of poorly mineralized or unmineralized osteoid (Jaffe, 1972, p. 393), resulting in cortices that are thick but weak.

Gross, radiographic, and microscopic changes are all most pronounced in areas of the skeleton where growth is normally most rapid (Pitt, 2002). In childhood, this is generally the middle six ribs and metaphyses at the distal femur and proximal tibia (Jaffe, 1972, p. 392), but the pattern will also differ significantly by age and the bones subjected to weight bearing or bending stresses (Pettifor, 2003). With healing, deposited osteoid begins to be mineralized normally again, but remodeling of deformities may take months or years.

2.1.2.1.2. Adult vitamin D deficiency

In adults, since skeletal growth is complete, vitamin D deficiency results only in osteomalacia. In most patients, clinically evident osteomalacia is preceded for many years by undetected secondary hyperparathyroidism as bone weakens and age-related bone loss is accelerated (Parfitt, 2005). Clinically, symptoms are often very subtle and nonspecific, including generalized bone loss, muscle weakness, muscle pains or aches, and diffuse bone pain (Holick, 2002a; Holick & Chen, 2008; Reginato & Coquia, 2003). Skeletal involvement is systemic, and impaired mineralization can be seen wherever remodeling is taking place; histological changes can be seen even in bones that look superficially normal (Jaffe, 1972, p. 400).

Microscopically, osteomalacia causes resorption and replacement with unmineralized osteoid, resulting in large areas of poorly mineralized bone (Bonucci et al., 1969) that make skeletal elements, pliable, fragile, and susceptible to deformation and fracture. The most common locations of deformity noted historically are the spine, the ribs or sternum, the pelvis, and possibly some bowing in the long bones, although this requires very severe deficiency that likely develops at a younger age (Jaffe, 1972, p. 400-1), and so these deformities typically develop late in the course of disease (Reginato & Coquia, 2003). Pseudofractures or translucent strips of unmineralized osteoid are often detected in the ribs, diaphyses of the long bones, femoral necks, ischia, pubic rami, or axillary margins of the scapulae (Pettifor, 2003; Schamall et al., 2003). They may be multiple, and it is not uncommon, especially in the ribs, to see multiple infractions at different stages of healing; they are often bilateral and symmetrical (Jaffe, 1972, p. 401).

Some describe pseudofractures as the most characteristic indicator (Reginato & Coquia, 2003) or even as a pathognomonic feature of osteomalacia (Pettifor, 2003). However, clinical findings are variable, and typical pseudofractures may not be present even in very severe cases exhibiting marked deformities (e.g., Watanabe et al., 2015). Bone loss often accompanies, and may be exacerbated by, vitamin D deficiency (Bilezikian & Silverberg, 2001; Favus, 1999; Gloth III, 1999; Halloran & Portale, 2005; Holick & Chen, 2008). This may also result in a predisposition to fragility fractures. Soft tissue features of osteomalacia, including muscle weakness, limb pain, and impaired muscle function, can also lead to functional disability, which may increase the risk of falls and therefore of fractures (Priemel et al., 2010), and may also keep individuals indoors and thereby exacerbate vitamin D deficiency (Meunier & Chapuy, 2005).

Osteomalacia was described as common in young women in the past, often setting in during adolescence or young adulthood (Jaffe, 1972, p. 399). Confinement indoors and dietary deficiencies are considered to be etiological factors; past studies suggested that increased demands were also associated with repeated pregnancies (Pearce & Cheetham, 2010) and pregnancy during adolescence (Jaffe, 1972, p. 399), although this has not been borne out by more recent research which has failed to demonstrate sufficient evidence supporting an association between 25(OH)D concentration and changes in bone density during pregnancy (Ross et al., 2011a). It is well established that low maternal vitamin D is a risk factor for poor vitamin D status in infants (Delvin et al., 1986; Nesby-O'Dell et al., 2002; Pearce & Cheetham, 2010; Sachan et al., 2005; Specker, 1994). If severe osteomalacia is present, it may lead to congenital rickets in the infant.

2.1.2.2. Vitamin D deficiency: Etiological factors

Rickets and osteomalacia can be caused solely by a deficiency of calcium (Pfitzner et al., 1998), but more often result from a deficiency of vitamin D due to insufficient exposure to UV and insufficient dietary intake. The importance of cod liver oil and UV light, and therefore of the crucial role of a substance in sunlight and some dietary components, was recognized as early as 1919 (Lubani et al., 1989). More recent examinations have determined that production and absorption of vitamin D are affected by many factors that in turn impact susceptibility to deficiency. Vitamin D status can be affected by physical variables, including impaired production and possibly absorption of vitamin D with increasing age (Favus, 1999; Gloth III, 1999; Halloran & Portale, 2005; Lips, 2007; Reginato & Coquia, 2003), reduced synthesis with increased skin pigmentation, or states of increased clearance such as diarrheal disease resulting in nutrient malabsorption (Brickley & Ives, 2008, p. 93). Older studies suggested that increased demand for vitamin D was associated with puberty (Tylavsky et al., 2005) or pregnancy (Delvin et al., 1986; Pearce & Cheetham, 2010; Prentice, 2003; Purdie et al., 1988); however, this is not supported by recent studies which have failed to demonstrate increased vitamin D requirements in teenagers or pregnant women (Ross et al., 2011a).

While pregnancy has not consistently been shown to correlate with increased demands for vitamin D (Ross et al., 2011a), maternal vitamin D levels have been found to correlate strongly with those of newborns (Hollis & Pittard III, 1984; Karatekin et al., 2009; Okonofua et al., 1986; Sachan et al., 2005; Specker, 1994), and maternal deficiency has been identified as a risk factor for adverse outcomes such as decreased growth,

impaired ossification, and rickets in infants (Cockburn et al., 1980; Morley et al., 2006; Mughal et al., 1999; Nesby-O'Dell et al., 2002; Pearce & Cheetham, 2010; Prentice, 2003; Shaw & Pal, 2002). In addition to biological factors, maternal-infant relationships provide a social pathway that influences vitamin D status, as the mother is typically an important caregiver who will provide food and may determine UV exposure in early life (Brickley et al., 2014). Environmental factors are also relevant. Sunlight exposure is affected by seasonality, latitude, architecture, clothing customs, and time spent outside (Holick, 2002, 2005; Okonofua et al., 1986; Prentice, 2008). Vegetarian diets, or those high in phytates that bind and sequester calcium, have also been identified as possible risk factors for deficiency (Holick, 2006b; Pettifor, 2003; Pettifor et al., 1978). These factors must be considered when attempting to interpret paleopathological evidence for the past occurrence of rickets and osteomalacia (Brickley et al., 2014); studies in modern populations have suggested that factors such as skin pigment and cultural practices seem to override the effect of physical environmental variables, like geography and climate (e.g. Mithal et al., 2009). It is also important to consider interactions between different types of variables, as human biocultural adaptation to environments with low UV exposure or a lack of vitamin D-containing foods may involve the formation of an adaptive complex comprised of both biological and cultural traits (Chaplin & Jablonski, 2013).

In some populations, rickets has been found to occur in the absence of vitamin D deficiency, and has instead been attributed to low levels of calcium (Oginni et al., 1996; Pettifor et al., 1978; Pfitzner et al., 1998). Ages of onset associated with calcium and vitamin D deficiency rickets were found to differ, with cases relating to low calcium

occurring slightly later (Pettifor, 2003); however, all clinical manifestations were indistinguishable. The potential causative role of deficiencies of nutrients other than vitamin D in the pathogenesis of rickets has as yet been given insufficient attention by paleopathologists. Clinically, it has been suggested that rickets causation should realistically be viewed as occurring along a spectrum, with isolated vitamin D deficiency at one end, isolated calcium deficiency at the other, and the majority of cases in the middle comprising some combination of the two (Pettifor, 2003). This is also relevant to osteomalacia, as increased importance of vitamin D-induced calcium absorption at low intake levels means that vitamin D deficiency is likely to be most evident or most severe when accompanied by insufficient calcium ingestion (Favus, 1999; Holick, 2006b; Lips, 2007; Parfitt, 2005). Additionally, manifestations of vitamin D deficiency may be masked by general malnutrition with reduced bone matrix formation (Pitt, 2002). The importance of calcium and other dietary factors in this process therefore warrant greater consideration in paleopathological interpretations.

2.1.2.3. Vitamin D deficiency: Paleopathological diagnosis

Paleopathological diagnoses of vitamin D deficiency involve detecting evidence for gross, radiographic, and histological features of these conditions. Bending deformities in long bones and other areas of the skeleton, widened metaphyses, changes to the surface of the growth plate, particularly in the distal ends of the long bones, folding or collapse of vertebral bodies, and the presence of pseudofractures, particularly those that have developed into full fractures, can be visualized in archaeological skeletal remains (Ives & Brickley, 2014; Mays et al., 2006; Ortner & Mays, 1998). Histological evidence for

defective mineralization, including buried osteoid seams and abnormal resorption, also assists in detecting these conditions paleopathologically when bone microstructure is sufficiently preserved (Brickley & Ives, 2008, p. 108). Evidence available for rickets and osteomalacia in the past is typically related to lesions that are preserved in skeletal material; however, the inaccessibility of biochemical and soft tissue evidence available to clinicians often makes paleopathological diagnosis more difficult.

2.2. Chronic Respiratory Infections

Respiratory infections refer to infectious diseases involving the respiratory tract, including both bacterial and viral diseases, such as pneumonia, bronchitis, emphysema, pleurisy, influenza, and TB. While acute respiratory diseases represent a major source of morbidity in modern and likely also in past populations, conditions must be chronic in order to have effects longstanding enough to manifest in the skeleton, and therefore to be detectable in archaeological material (Ortner, 2003, p. 110). As very few chronic respiratory infections cause skeletal lesions that can be specifically identified and differentiated from manifestations of other respiratory pathologies, the identification of chronic respiratory infections as a general category relies on evaluation of non-specific skeletal lesions such as new bone formation on the ribs and evidence for hypertrophic pulmonary osteoarthropathy (HPO). Discussion of chronic respiratory infection in the paleopathological literature typically focuses on TB, as this condition results in characteristic manifestations in the skeleton that may lead to specific diagnoses. However, there is also significant discussion of proliferative lesions on the visceral surface of the

ribs (e.g., Mays et al., 2002; Roberts et al., 1994, 1998; Santos & Roberts, 2001, 2006), which appear most likely to be caused by chronic pulmonary infection through direct spread from inflamed pleura (Roberts et al., 1994). Differential diagnoses for these lesions typically include pulmonary TB, pneumonia, bronchiectasis, bronchitis, emphysema, and pleurisy (Kelley et al., 1994; Mays et al., 2002; Nicklisch et al., 2012; Raff et al., 2006; Roberts et al., 1994, 1998), with the most focus placed on TB and pneumonia as diagnostic possibilities. Other conditions, such as neoplastic disease, actinomycosis, treponemal disease, and nonspecific osteomyelitis, should also be considered (Lambert, 2002; Matos & Santos, 2006; Nicklisch et al., 2012; Roberts et al., 1994, 1998; Santos & Roberts, 2006), but are usually eliminated as probable diagnoses due to differential lesion patterning and appearance.

2.2.1. Chronic respiratory infections: Pneumonia

Pneumonia is a lower respiratory tract illness resulting from infection with one of a variety of species of bacteria, fungi, viruses, or protozoa, as well as atypical infections or other causes (Leach, 2009). It therefore encompasses several clinical entities, and clinical classification is usually based on where or how the infection was acquired, for example in the community, in the hospital, through aspiration, or via an opportunistic pathogen (Leach, 2009). Pneumonia is typically acute, but the course of disease is greatly affected in modern populations by the availability of antibiotics, and even with effective treatment disease can be recurrent (Leach, 2009). In community acquired pneumonia, the form that is likely to be most relevant to past populations, the organism most frequently identified in affected individuals is *Streptococcus pneumoniae* (Marrie, 1999; Michelow

et al., 2004). Michelow et al. (2004) suggest that viral causes may be more relevant in very young children, and that in a significant proportion of cases of lower respiratory infection in hospitalized children multiple bacteria, viruses, or a combination of the two can be identified. Brucellosis is also rarely identified as the cause of pneumonia, with the reported incidence of respiratory complications ranging from less than one to as high as seven percent (Pappas et al., 2003). This condition is commonly considered in paleopathological differential diagnoses of spinal pathology and has been suggested as the probable cause of lesions in archaeological human skeletal remains (e.g., Anderson, 2003; Curate, 2006), including those from the Roman period (e.g., Capasso, 1999).

Epidemiological features of pneumonia vary along with its diverse causes. Risk factors for community acquired pneumonia can be related to occupation, environment, geography, and the presence and severity of co-morbid conditions (Leach, 2009). Age is also a very important factor, with the highest incidence in modern populations occurring in the very young and the elderly (Marrie, 1999). Determining the epidemiology of pneumonia is complicated by the fact that identifying the causative organism is often very difficult, and few clinical or radiographic features adequately differentiate various forms of infection. Michelow et al. (2004) identify the presence of pleural effusion as one of only two features significantly associated with bacterial pneumonia in children, in comparison with pneumonia caused by a virus or a combination of bacterial and viral pathogens.

Clinical features of pneumonia include general symptoms like malaise, fever, and myalgia, as well as chest-specific symptoms including pleurisy, cough, and even

hemoptysis. The signs and symptoms of pneumonia are relatively non-specific, and Leach (2009) asserts that clinical diagnosis is inaccurate without a chest radiograph. The mortality rate of pneumonia is variable and highly dependent on the causative organism, with reported modern mortality in pneumococcal pneumonia ranging from seven to 36% (Marrie, 1999). Since modern pneumonia often responds well to antibiotic treatment, this figure is likely to have been significantly higher in ancient populations, and pneumonia probably represented an important cause of morbidity and mortality in the pre-antibiotic era (Lambert, 2002). In bacterial pneumococcal pneumonia, the course of disease may be complicated, often including features like respiratory failure, empyema, and meningitis (Marrie, 1999), as well as pleural effusion, or extra fluid surrounding the lung, as a result of inflammation. Widespread pleural inflammation is a feature of acute lobar pneumonia that has progressed to the stage of red hepatization of the lung (Ogilvie, 1957).

Cases of pneumonia that have progressed to the stage where significant inflammation occurs in the pleura, often resulting in the clinical symptom of effusion, could result in an inflammatory reaction on the ribs in the form of periosteal new bone formation. Such rib lesions have been observed in individuals with a diagnosis of pneumonia in documented skeletal collections (Roberts et al., 1994). Additionally, there are modern clinical cases in which bacteria associated with community acquired pneumonia have caused primary or secondary infection of the bone. For example, *Klebsiella pneumoniae* has been associated with invasive infections including osteomyelitis (Prokesch et al., 2016) as well as meningitis and pleural empyema (Lee et al., 2006). While the hypervirulent strain most often associated with invasive infections

has become important only within the last few decades (Prokesch et al., 2016), the potential for other strains and other pneumonia-related pathogens to cause invasive infections in the bone would also have existed in the past.

2.2.2. Chronic respiratory infections: Bronchitis

Bronchitis is an inflammation of the bronchi in the lungs which, like pneumonia, has a variety of causes including bacterial and viral infections as well as irritants or pollutants in the air. The condition can be acute or chronic, with the majority of chronic bronchitis patients in modern populations also suffering from chronic obstructive pulmonary disease. Chronic bronchitis is commonly defined by a chronic, recurrent, productive cough that persists for at least three months during each of two consecutive years (Gump et al., 1976). In modern populations it is most commonly caused by smoking, with the role of bacterial and viral agents usually discussed in relation to exacerbation of an existing condition (Gump et al., 1976). However, protracted bacterial bronchitis is re-emerging as an important cause of chronic morbidity, particularly in children, and represents a condition that was probably prevalent in the pre-antibiotic era. Craven and Everard (2013) suggest that it would frequently have led to bronchiectasis if it progressed untreated, through the impact of impaired mucociliary clearance and chronic endobronchial infection leading to inflammation and damage to the walls of the bronchi. This deterioration may take years to decades to develop, and its rate is thought to have been determined by the type and extent of causative infection, the frequency of exacerbations of the condition by other respiratory infections, and the nature of any conditions underlying bronchitis, in addition to factors related to treatment (Craven &

Everard, 2013). Chronic bronchitis associated with inflammation and potentially with bronchiectasis may also lead to the development of an inflammatory reaction in the form of periosteal new bone formation on the visceral surfaces of the ribs.

2.2.3. Chronic respiratory infections: Tuberculosis

TB is a disease state caused by infection with members of the *Mycobacterium tuberculosis* complex (MTBC), typically by *Mycobacterium tuberculosis* (MTB), a facultative intracellular pathogen primarily spread through the inhalation of infected droplets. More rarely, disease in humans can be caused by other members of the MTBC, including *Mycobacterium bovis* which has a much wider host range and most often infects cattle, as well as non-typical species such as *Mycobacterium fortuitum* (Vijaya Bhanu et al., 2004). The majority of modern cases of TB involve pulmonary infection (Davidson & Horowitz, 1970); this is also likely to have been the case in the past, although there has been some suggestion that patterns of MTB infection have changed over time (Resnick, 2002; Santos & Roberts, 2001; Stirland & Waldron, 1990). With the eradication of TB in cattle and the introduction of pasteurization processes for dairy products, rates of TB caused by *Mycobacterium bovis* have decreased (Davies et al., 1984; Grange, 1995). Infection caused by other members of the MTBC may have alternative localizations in the body due to variation in routes of transmission; for example, infection with *Mycobacterium bovis* often resulted from the ingestion of infected meat or dairy products and therefore was likely to result in TB in the abdomen or gastrointestinal system (Grange, 1995; Ritacco et al., 2006). In terms of symptomatology,

disease caused by *Mycobacterium bovis* is clinically indistinguishable from that caused by MTB (Jaffe, 1972, p. 952-3).

Despite the primacy of pulmonary infection, TB can infect any part of the body. Rates of extrapulmonary infection vary; it is estimated that between nine and 23% of pediatric cases are extrapulmonary (Feja & Saiman, 2005). MTB primarily infects soft tissue, but can disseminate to bone through blood or lymph. Skeletal involvement is estimated to occur in about three to five percent of untreated tuberculous individuals (Resnick, 2002), although some estimate its incidence as low as one percent (Davidson & Horowitz, 1970), and to represent up to 30% of extrapulmonary TB (Resnick, 2002; Roberts & Buikstra, 2003a, b). Migration to the skeleton primarily occurs via hematogenous dissemination (Resnick, 2002), is typically secondary to a primary pulmonary lesion (Martini, 1988b), and is estimated to occur about one to five years after primary soft tissue infection (Anderson, 2001).

Only a fraction of individuals exposed to MTB contract the disease, with about one third of immunocompetent individuals who are exposed to an active case becoming infected (Garay, 2004). Of those who are infected, without treatment only five to 10% of immunocompetent adults develop active disease over their lifetime (Elkington & Friedland, 2015; Gao et al., 2010), with three to five percent developing disease within the first year and another three to five percent developing disease in later life (Garay, 2004). In more vulnerable groups, such as older adults, this figure may be higher (Stead, 2001). Risk of progression to active disease is also greater in children, increasing to up to 43% for infants, 24% for children one to five years, and 15% for adolescents 11-15 years

(Eamranond & Jaramillo, 2001; Feja & Saiman, 2005). An even smaller fraction of individuals with active TB display skeletal symptoms, so those with skeletal involvement represent a very small sample of those initially exposed to TB infection. However, while bone and joint TB is very rare in industrialized countries, it is still relatively frequent in developing countries where TB is still more prevalent (Martini, 1988a).

Skeletal TB is both an infectious disease and an orthopedic condition, and this unique combination influences its natural history and clinical features. Any element can be infected, but most cases of skeletal TB involve the spine, followed by major weight-bearing joints such as the hip and knee. The spine is estimated to be affected in anywhere from 25-50% (Resnick, 2002) to 50-70% (Hugosson et al., 1996) of cases of skeletal TB. Concomitant pulmonary TB is reported to occur in 12-50% of cases of skeletal TB (Hugosson et al., 1996), and pulmonary disease is most clearly associated with spinal involvement (Resnick, 2002), but this will vary by population. Dissemination of MTB to the skeleton indicates a chronic and long-term infectious process and a relatively competent immune response (Roberts & Buikstra, 2003b; Santos & Roberts, 2001), as individuals whose immune reactions are insufficient to deal with TB infection will die before skeletal lesions can develop. Conversely, individuals whose immune systems react very strongly to MTB will also fail to develop skeletal lesions, as they may either not become infected upon exposure, or may maintain the infection in latent form without developing active disease.

Tuberculosis can cause epidemic disease, as was the case in Europe in the 16th-19th centuries and North America in the early 20th century, with European epidemics

running their full course in around 300 years (Hurtado et al., 2003). In much of the developing world, TB is currently considered to be endemic, although exact trends often remain undocumented in these populations (Hurtado et al., 2003). As with many other infectious diseases, TB behaves differently in populations and hosts that have a long history of exposure to the pathogen than in those that are considered to be epidemiologically naïve. Naïve hosts are highly susceptible to MTB, meaning that higher proportions of exposed individuals become infected and develop clinical disease; over time, this influences immune evolution to favor a more efficient response to MTB (Hurtado et al., 2003). TB is considered to be a re-emerging infectious disease in many modern populations, due to decreased immunocompetence associated with HIV infection as well as immigration from countries in which the disease is endemic (Nyman et al., 1996).

2.2.3.1. Tuberculosis: Pathology and pathophysiology

Most cases of pulmonary TB result from MTB entering the lungs in aerosolized droplets. A single organism can potentially cause disease, but normally between five and 200 bacilli are necessary to establish an infection (Garay, 2004). Bacilli encounter and multiply within alveolar macrophages, creating a small area of nonspecific inflammation called the primary focus (Feja & Saiman, 2005). At this point, bacilli may also spread to regional lymph nodes or disseminate in the bloodstream, with the primary focus and affected regional lymph nodes forming the primary TB complex (Jaffe, 1972, p. 954). Immune cells involved in the inflammatory reaction to bacilli gather in nodules, in which phagocytes mature and are transformed into epithelioid cells. These cells form a hard

tubercle consisting of epithelioid cells and lymphocytes (Lahreche, 1988). The tubercle represents the local defense reaction, which persists as long as any live bacilli are in the tissues, and may undergo central necrosis and caseation to become a soft tubercle, which is characteristic of TB (Jaffe, 1972, p. 970; Lahreche, 1988).

At the site of disease and then within the regional lymph nodes, bacilli encounter alveolar macrophages and monocytes such as DCs. These innate immune cells bind to and engulf bacilli, which are then transported to the phagosome to be destroyed through autophagy (Bruns & Stenger, 2014). Phagosomes fuse with lysosomes to form the autolysosome, where bacilli are degraded by lysosomal enzymes including reactive oxygen species (Bruns & Stenger, 2014); following this, these APCs present MTB antigens on their cell membranes and release cytokines that recruit T cells (Wilbur et al., 2008). T cell-produced cytokines activate macrophages, which then have enhanced abilities to both present antigens for further induction of the adaptive immune response as well as to directly kill bacilli through production of AMPs such as cathelicidin (Wilbur et al., 2008). Cathelicidin is also required for MTB-mediated macrophage production of reactive oxygen species and the production of other pro-inflammatory cytokines (Bruns & Stenger, 2014). An alternative macrophage strategy to both autophagy and AMP production is efferocytosis; this involves the induction of apoptosis in MTB-infected macrophages, followed by engulfment and lysosomal clearance of these cells by bystander macrophages (Bruns & Stenger, 2014). Anti-MTB strategies are interrelated in a positive loop of inflammation initiated in response to MTB (Bruns & Stenger, 2014). As an intracellular pathogen, MTB is most effectively combated with a cell-mediated Th1

type response (Rook & Hernandez-Pando, 1996), and DCs presenting MTB antigens therefore stimulate T cell development toward the Th1 pathway. Th1-mediated activation of macrophages is particularly important in MTB infection because bacilli preferentially live in these cells, and activated macrophages demonstrate much more effective MTB killing (Wilbur et al., 2008). The outcome of MTB infection is therefore determined by multiple interactions between bacilli and the immune system, including the initial innate immune response as well as later actions of the adaptive immune system (Bruns & Stenger, 2014).

If the development of cellular immunity over the first two to six weeks following exposure to MTB is effective, as in 95% of normal adults (Ellner, 1997; McGuinness & Rubinowitz, 2004), the spread of infection will be controlled. An effective inflammatory response to bacterial infection involves containment of bacilli within a granuloma formed by activated macrophages (Garay, 2004). The primary focus becomes encapsulated, perifocal inflammation increases, and the lesion manifests as a granuloma (Feja & Saiman, 2005). This granuloma serves to create an environment that restricts MTB growth and prevents dissemination, maintaining disease in a latent state (Wilbur et al., 2008). The formation of the granuloma includes caseous necrosis, fibrosis, and healing of the primary complex components with or without calcification of the lesion (Feja & Saiman, 2005). Maximal immune competence is necessary to contain bacilli and prevent development of active disease. If the immune response is compromised and bacilli are allowed to replicate, they may destroy infected tissue and cause granuloma expansion and breakdown, allowing bacteria access to blood, lymph, or the airway and facilitating

spread (Resnick, 2002). In latent disease, the granuloma is formed but healing of the infection will not be complete, allowing viable bacilli to persist for many years (Feja & Saiman, 2005). Helper T cells maintain the inactivity of latent foci through active surveillance (Ellner, 1997). However, bacilli can reactivate and cause active disease at any time if the immune system no longer functions efficiently enough to control the infection; acquired resistance therefore does not necessarily persist for life (Ellner, 1997).

MTB has evolved mechanisms to evade host defenses, including manipulation of phagosome membranes to prevent phagolysosomal fusion (Armstrong & Hart, 1975) or inhibit the production of reactive oxygen species or apoptosis of infected cells (Bruns & Stenger, 2014), and therefore decrease effective antigen presentation and subsequent macrophage activation, T cell responses, and MTB killing (Chocano-Bedoya & Ronnenberg, 2009). If the cellular immune response is unable to contain the infection, either primary TB or disease progression of any part of the primary complex will develop (Feja & Saiman, 2005). This occurs most commonly in younger children. The most common form of primary TB is pulmonary, from disease progression within the lung (Feja & Saiman, 2005). If the primary focus caseates and liquefies, it may spread through the bronchi, causing progressive pulmonary primary TB (Feja & Saiman, 2005). In cases where disease is initially controlled, with incomplete healing of the primary focus, later re-exposure or depression of the immune system can cause postprimary reinfection (Jaffe, 1972, p. 955). If bacilli are either allowed to escape the granuloma or are never fully contained within it, they will undergo uncontrolled replication and can disseminate to any other site in the body. Other organs, including bones and joints, are

therefore infected secondarily. This means that if skeletal symptoms are present, another focus of disease is generally present in the body. Individuals do not typically have two fully evolved clinical forms of TB simultaneously, but will often show active disease in one location and a non-clinical primary focus elsewhere in the body (Jaffe, 1972, p. 1001-2). Progression beyond the lungs occurs more frequently and earlier in the course of disease in younger children (Feja & Saiman, 2005).

With hematogenous dissemination, bacilli seed to areas of high oxygen tension (Garay, 2004). In the skeleton, they therefore focus on the myeloid (red) bone marrow. Primary tubercle formation in marrow then leads to secondary infection and progressive resorption of trabeculae (Jaffe, 1972, p. 972; Resnick, 2002). The first stage in the natural course of skeletal TB corresponds to onset, in which lesions form in the bone or, in the case of joints, in either the synovial membrane or juxta-articular bone (Martini, 1988b). This stage, consisting of small lesions with a limited zone of destruction surrounded by diffuse decalcification, lasts a few weeks or months (Martini, 1988b). The development of skeletal lesions involves gradual destruction of bony tissue (Ortner, 2003; Roberts & Buikstra, 2003b); the second stage of disease is therefore one of destruction. Once bacilli are established in the skeleton, they stimulate the formation of tubercles characterized by caseating necrosis in a central mass of multinucleated giant cells surrounded by lymphocytes (Roberts & Buikstra, 2003a). As granulation tissue forms within a lesion, the mass of tissue begins to erode and destroy cartilage and bone, ultimately resulting in progressive demineralization and necrosis (Davidson & Horowitz, 1970). In the joints, granulation tissue forms at the margins of articular cartilage and spreads over the surface,

eroding the cartilage and detaching it from subchondral bone as well as eroding the bone itself (Daoud, 1988). Without treatment, disease in the joint progresses until the entire joint is involved and destroyed, including the articular cartilage, with resulting deformities (Martini, 1988b). There may also be soft tissue complications of skeletal lesions, including cold abscesses and frequently secondary pyogenic infections that may lead to other consequences, including death (Martini, 1988b). With skeletal TB, aside from other complications of disease, death is frequently caused by the development of other forms of TB including tuberculous meningitis, miliary TB, or chronic pulmonary TB (Jaffe, 1972, p. 1003).

While bone resorption typically predominates in the formation of bony lesions (Roberts et al., 1998), new bone formation may be observed on visceral surfaces of the ribs. In some cases, secondary proliferation or periostitis may accompany primary resorptive lesions so that both processes are seen in concert with one another (Resnick, 2002; Roberts & Buikstra, 2003a), although this is more commonly seen with primary bone tumors and other infectious diseases such as brucellosis (Curate, 2006; Hugosson et al., 1996). With an effective immune response and containment of infection, necrotic lesions may eventually ossify. The final stage in the natural course of an untreated infection is therefore repair, which generally occurs spontaneously after two to three years of disease development (Martini, 1988b). Healing typically takes place during the fourth year, with resorption of abscesses and either bony fusion or fibrous stiffness developing in the joints (Martini, 1988b). If allowed to run its natural course, then, skeletal TB develops over a total duration of about three to five years; this course of

disease is most common in children (Martini, 1988b). The course of disease generally differs based on the age of the patient, as the evolution of disease is less clear cut in adults, with more frequent and earlier formation of abscesses but also less severe development of deformities due to the absence of issues that occur in children with continued growth (Martini, 1988b).

The pathogenesis of different forms of active disease can be conceptualized as a continuum, in which host immune factors are important in controlling the extent and manifestations of disease (Feja & Saiman, 2005). Generally, an efficient immune response will result in the prevention of infection or development of active disease. However, paradoxically, part of the immune response to MTB may also contribute to TB pathophysiology. The release of tumor necrosis factor alpha (TNF-α) from activated macrophages has been proposed to partially explain the weight loss and necrotic tissue damage associated with MTB infection (Rook et al., 1987), and may be modulated by Th1/Th2 balance and disease severity (Rook & Hernandez-Pando, 1996). Pathogenesis of TB infection may also relate to enhanced T cell apoptosis and cytokine-mediated T cell hyporesponsiveness accompanying inflammation and an over-active immune response (Hirsch et al., 1999). Although causal relationships have not been elucidated, the systemic expression of immunosuppressive cytokines is seen with advanced disease, potentially contributing to the vicious cycle of immune suppression, deactivation of macrophage functions, and progression of disease (Ellner, 1997). These proposed mechanisms implicate involvement of immune malfunction in the development of active disease.

2.2.3.2. Tuberculosis: Clinical presentation

Clinical manifestations of pulmonary TB appear gradually over months to years (Hurtado et al., 2003). Symptoms can include malaise, anorexia, weight loss, fever, night sweats, and cough. In the pre-antibiotic era, pulmonary TB was one of the leading causes of hemoptysis (Garay, 2004). However, disease can also be asymptomatic, or physical manifestations may be relatively mild (Feja & Saiman, 2005). When symptoms do develop, clinical investigation reveals destructive and inflammatory processes within the lung (Garay, 2004). The type of disease that develops and natural history of infection vary depending on the tissues of the body that are affected as well as the number of bacilli, duration of infection, and host age, sex, genetic factors, and immune function (Feja & Saiman, 2005). Diagnosing TB is often difficult as clinical symptoms are often minimal or absent, those present are frequently nonspecific (Nyman et al., 1996), and clinical presentation can vary widely (Hugosson et al., 1996; Nussbaum et al., 1995). This may be even more difficult in children, as characteristics of disease tend to be even less distinctive than in adults (Eamranond & Jaramillo, 2001; Feja & Saiman, 2005).

Skeletal TB often appears in children six to 18 months after primary infection. With spread of infection to the skeleton, clinical symptoms can include localized inflammation, pain, swelling, and fever, as well as decreased range of motion in the affected area (Feja & Saiman, 2005). However, the clinical course of disease in the skeleton may be ambiguous and slow to develop, leading to difficulties in diagnosis (Jaffe, 1972, p. 960). Other symptoms of skeletal TB generally include the development of abscesses, sometimes with sinuses or secondary pyogenic infections, and deformities

including dislocation, spinal kyphosis, permanent flexure of the knee, or deformity of the hip leading to a limp (Martini, 1988c). Radiographically, TB demonstrates features of inflammation and bone destruction (Martini, 1988c).

In the skeleton, TB most commonly localizes in the spine, followed by the hip and then the knee. Spinal disease is associated with the highest morbidity and mortality of any form of skeletal TB (Jaffe, 1972, p. 958-60). In the spine, TB generally affects the thoracic or thoracolumbar regions, most often occurring in two or three, or as many as seven, vertebrae between the eighth thoracic and third lumbar (Ouahes & Martini, 1988a). Destructive osteomyelitic lesions typically develop in the anterior vertebral body, rupturing the vertebral cortex and progressing toward the disc, which may be affected as well. Infection can spread between adjacent vertebrae through the disc, or it can travel beneath the anterior or posterior longitudinal ligaments (Jaffe, 1972, p. 957, 983; Ouahes & Martini, 1988a). Vertebral destruction due to the expansion of caseous lesions eventually leads to collapse, generally more marked in the anterior bodies, and development of a characteristic sharp angular kyphosis. Uncommonly, posterior spinal elements can be involved (Kumar, 1985; Martini & Ouahes, 1988), or unaffected vertebrae may separate multiple foci of disease. Abscesses are a common complication, and can result in large areas of soft tissue destruction, occasionally also developing sinuses and superadded pyogenic infections (Ouahes & Martini, 1988a). Sometimes patients also develop neurological deficits (Kumar, 1985). With healing, affected vertebrae may fuse (Leibert & Haralambou, 2004). In children in the pre-antibiotic era, this generally occurred spontaneously after three to four years (Ouahes & Martini, 1988a).

Radiological features of spinal TB include disruption of the vertebral endplates with erosion of the margins, narrowing of the disc-space, localized bone loss, and anterior wedging and collapse of the vertebral bodies, as well as destructive lesions in the bone (Nussbaum et al., 1995; Tuli, 1995). With collapse, the angle of the resulting kyphosis relates to the number of vertebral bodies affected, as well as the natural curvature of the location of disease within the spine (Jaffe, 1972, p. 983). Almost three percent of cases of tuberculous spondylitis are estimated to develop a severe kyphosis, with the highest risk of severe deformity in those who developed active disease before the age of ten, in whom disease affected three or more vertebral bodies, and who developed lesions in the thoracic vertebrae which undergo the greatest amount of pressure stress (Tuli, 1995). This is particularly dangerous in childhood because the deformity can be unstable and progressive, deteriorating with continued growth of the posterior elements when damage to the vertebral endplates has halted anterior growth (Daoud, 1988; Ouahes & Martini, 1988b; Tuli, 1995). With healing, fibrous ankylosis or bony fusion can develop (Jaffe, 1972, p. 999).

Among the most serious complications of skeletal TB, and particularly of spinal TB, is the development of neurologic symptoms such as paraplegia (Martin, 1971). Neurologic complications can develop during the active stage of disease or after healing. They are associated with pressure on the spinal cord from soft tissue masses, compromise of the spinal canal from collapse of the vertebral bodies, or stretching of the cord over a gibbus or spinal deformity (Jain, 2002; Nussbaum et al., 1995; Ouahes & Martini, 1988b). Most patients, even with severe kyphosis, tend to retain their ability to walk for many

years because of the slow development of the deformity; however, neurological symptoms may eventually develop due to prolonged stretching of the cord, resulting in atrophy or ischemic changes (Tuli, 1995). Patients with severe kyphotic deformity often develop compression of the spinal cord with associated paraplegia, as well as serious symptoms such as cardiopulmonary dysfunction and pain (Tuli, 1995). Even in the absence of neurological symptoms, severe kyphosis can affect the lungs, even contributing to respiratory failure (Garay, 2004).

TB can also manifest in the skeleton in the form of inflammatory arthritis. This is typically characterized by pain and tenderness, diminished range of motion, and atrophy of the muscles (Martini, 1988c). Radiologically, osteoarticular TB classically manifests as solitary metaphyseal or epiphyseal lesions without sclerosis, sequestration, or periosteal reactions (Hugosson et al., 1996). However, the lesion may present with any of these uncharacteristic features, or may not be visible radiographically at all (Phemister & Hatcher, 1933). With extensive involvement of the epiphyseal ends of the bones, cone-shaped areas of destruction may develop symmetrically on both sides of the joint as "kissing sequestra" (Jaffe, 1972, p. 965; Phemister & Hatcher, 1933). Pediatric manifestations of disease differ because of the relative amounts of cartilage and bone present; in children, cartilage is often affected to a greater extent than bone, which may have significant effects on growth that will be more severe if disease develops at a young age (Daoud, 1988; Phemister & Hatcher, 1933). Clinically, childhood lesions typically appear in the metaphyses, and children one to two years old often have epiphyseal involvement and metaphyseal new bone formation (Hugosson et al., 1996).

The most common locations for tuberculous arthritis are the hip and the knee, both of which were more commonly affected in children in the pre-antibiotic era (Martini & Adjrad, 1998; Martini & Kerri, 1988). The destruction and deformity that can occur at these sites as a result of tuberculous arthritis can be very disabling, with particularly serious consequences associated with continued growth (Martini & Adjrad, 1988). Symptoms associated with hip TB include pain and stiffness in the joint, muscular atrophy, and often a limp, with significant restriction of hip movement associated with considerable destruction of the femoral head and widening of the acetabulum in cases of advanced disease (Martini & Adjrad, 1988). Hip TB can be very difficult to differentiate from other sources of destruction in this joint, including pyogenic arthritis, rheumatoid arthritis, or Perthes-Calve disease (Martini & Adjrad, 1988), although diagnostic issues in clinical cases may relate to the difficulty of visualizing this area of the skeleton on radiographs.

In cases of tubercular arthritis affecting the knee joint, early symptoms include pain and swelling, muscle atrophy, restriction of movement, and often a limp. Radiographic signs, developing slightly later on in the course of disease, include bone loss, erosion of the patella or tibial condyles, and, in advanced disease, considerable destruction of the joint and deformity (Martini & Kerri, 1988). TB can less commonly manifest in any other joint in the body, with lower limb joints more commonly affected than upper limb joints. TB of the sacroiliac joint was common and relatively dangerous before the introduction of antibiotic therapy (Martini, 1988d), especially in young adults (Jaffe, 1972, p. 989). TB in this location can be very serious, with frequent formation of

abscesses, sinuses, and superadded pyogenic infections, and it had one of the highest mortality rates in the pre-chemotherapy era (Martini, 1988d).

TB can also cause osteomyelitis in any bone, but most commonly in the long bones or as spina ventosa in the metatarsals and metacarpals (Martini & Boudjemaa, 1988). Radiographically, spina ventosa manifests as expansion and thickening of the cortical bone, surrounded by subperiosteal new bone formation, while osteomyelitis typically appears as a cavity delineated by a thin layer of sclerosis. However, radiographs may show no features other than localized bone loss, and tuberculous osteomyelitis can be very difficult to diagnose (Martini & Boudjemaa, 1988).

Ultimately, TB can have serious consequences for affected individuals, particularly for children under six years in whom MTB has a very short incubation period. Young children can have a very rapid course of disease (Starke, 2003), and are at greater risk for more severe and extrapulmonary forms of TB, with a higher risk of developing active disease (Eamranond & Jaramillo, 2001). Modern disease outcomes have been greatly impacted by the development of effective antibiotics in the 1940s. However, studies of epidemiologically naïve populations suggest that mortality from TB can be very high, estimating that without chemotherapy up to 18% of one population would have died of the infection within the first decade of exposure (Hurtado et al., 2003). Prior to the development of antibiotics, and during the early years after the development of chemotherapy, TB mortality was high, with only 35% survival after 10 years in 1947 (Springett, 1971). The highest mortality was seen in the first few years after the development of disease, with the mortality curve slowly leveling off after this (Springett,

1971). Over time, with the development of increasingly effective anti-TB treatments, substantial improvements in survival were achieved, and the mortality pattern changed to a more gradual curve (Springett, 1971). Patterns of healing also underwent changes; spontaneous bony fusion increased in adults and decreased in children, a reversal of the natural pattern, after the development of antibiotics (Martini, 1988b; Ouahes & Martini, 1988a, b, c). Chemotherapy has modified the course of disease, including aspects such as duration, progression of damage to bones and joints, healing, and the danger of dissemination (Martini, 1988e).

The clinical presentation of TB has shifted over time, along with changes in the age structure of TB incidence, resulting in more uncharacteristic, and therefore difficult to diagnose, presentations of TB in modern cases (Martin, 1971; Nyman et al., 1996). In the past, infection and development of the primary complex typically developed in childhood or adolescence, and the incidence of primary TB in children between one and five years was very high (Jaffe, 1972, p. 954). In both modern and past cases, children with latent infection represent a reservoir for future disease, as latent foci can activate at any time either from exogenous reinfection or endogenous reactivation (Feja & Saiman, 2005; Starke, 2003). More recent studies reveal that, in Western countries, this process has predominantly shifted to later stages of life (Garay, 2004).

Clinically, as well as paleopathologically, differential diagnosis of TB may be difficult. Features of TB can mimic many other conditions, including malignant disease as well as other respiratory infections (Nyman et al., 1996). No clinical findings of skeletal TB are considered to be specific for the disease. Therefore, the detection of MTB is

necessary for a definitive clinical diagnosis (Leibert & Haralambou, 2004; Martini, 1988c). Bacteriological confirmation of bone and joint TB is also challenging to accomplish, since bacilli tend to be scarce in these lesions due to low oxygen tension (Boulahbal, 1988). Radiographic features are also never typical, although there is a much lower chance for error in identifying destructive lesions than other types of abnormalities (Martini, 1988c). Some lesions are therefore more specific and have less need for confirmation from other sources of evidence, which likely also holds true for paleopathological diagnoses. There is no known difference in appearance between tuberculous arthritis and arthritis caused by any other pyogenic infection or inflammatory joint disease (Hugosson et al., 1996), and spinal lesions may be impossible to differentiate from vertebral osteomyelitis caused by pyogenic or fungal infection or by primary or metastatic bone tumors (Nussbaum et al., 1995). This is further complicated by the fact that TB can also co-occur with these conditions: cancer may result in declining immunocompetence, and therefore increased susceptibility to infection or reactivation of a latent TB focus (Nyman et al., 1996). TB infection can also result in immunosuppression and physical damage to the lung, and may therefore also increase mortality from other infectious and neoplastic pulmonary diseases (Springett, 1971).

2.2.3.3. Tuberculosis: Transmission

The age structure associated with TB infection varies by population. Generally, there has been a shift over time with an increase in the age of those most affected, in association with increases in socioeconomic status and other lifestyle changes (Nyman et al., 1996). These patterns may also differ geographically. In less developed countries, 15-

40% of cases occur in children, whereas in industrialized countries pediatric cases represent only two to seven percent of the TB case load (Feja & Saiman, 2005), potentially relating to differences in population age structure and socioeconomic factors affecting TB transmission (Eamranond & Jaramillo, 2001). In the early 20th century, TB was a prime killer of young adults (McFarlane, 1989), while in many modern populations older adults have the highest rates of infection and clinical disease. This is likely partly because the probability of being diagnosed with TB increases cumulatively over the life course (Hurtado et al., 2003). Since children with TB are less likely to have a productive cough, to develop pulmonary cavitations, or to have detectable numbers of bacilli in their sputum, it is generally held that childhood disease is not contagious (Starke, 2003) and that childhood cases are transmitted from infected adults (Feja & Saiman, 2005). As such, the incidence of TB in children is considered to be a sentinel event for ongoing or recent transmission of the disease within a community (Walls & Shingadia, 2004).

Susceptibility and resistance to TB infection and disease are affected by a variety of behavioral, social, and physiological factors (Farer et al., 1979; Hurtado et al., 2003). Factors that increase the risk of progression to active disease usually act through their effects on the immune response to MTB (Feja & Saiman, 2005). Many studies, particularly those examining twins, indicate that genetic factors play a significant role in influencing susceptibility to or outcomes of infectious diseases including TB, by determining phenotypic variation in innate immunity (Bellamy, 2005; Ellner, 1997). Variation in innate resistance to MTB infection and the development of active disease was dramatically demonstrated by a German vaccination accident in 1930, in which

hundreds of infants were accidentally given fully virulent MTB rather than an attenuated virus (Stead, 2001). Several specific genes have since been identified, and there are likely many others that significantly influence one of the many steps in the complex interactions between host, pathogen, and environment in the development of TB (Bellamy, 2005).

TB has classically been associated with poverty and malnutrition (Jaffe, 1972, p. 953; McFarlane, 1989; Starke, 2003). It is often difficult to separate components of the poverty complex, which includes overcrowding both within rooms and within houses, undernourishment, low income, long work hours, heavy labor, large families, and the presence of other infections (McFarlane, 1989). Observational studies in humans, supported by research in animal models, have noted an increased prevalence, worse and more frequent complications in children, and increased mortality with the co-occurrence of TB and malnutrition (Cegielski & McMurray, 2004). However, this association is not stable across all populations. In indigenous communities in Paraguay, Hurtado et al. (2003) found a higher risk of both TB infection and active disease in better nourished and wealthier individuals. Nutrition is particularly important for immune responses to MTB infection, and adequate calcium is required for maintenance of the granulomas that represent the primary response to TB (Wilbur et al., 2008). Additionally, inadequate protein results in decreased antimicrobial activity in macrophages, ill-formed granulomas that fail to prevent dissemination, decreased T cell maturation, and decreased induction of the Th1 response (Wilbur et al., 2008). Physiological factors may also modify the effects of various environmental conditions on TB susceptibility. In Saudi Arabia, it has been suggested that living conditions are more closely tied to TB incidence in children than in

adults (Nyman et al., 1996). The importance of various factors in TB mortality has also shifted over time, with severity being more important as a prognostic factor than age in pre-antibiotic populations, and age being more predictive of prognosis in modern TB cases (Springett, 1971).

When examining potential causal factors for TB incidence within or among members of a population, it is also important to consider selective pressures that may result from intergroup interactions. Factors like social domination can cause stress, leading to increased disease burden, or may buffer from disease effects (Hurtado et al., 2003). This can combine with differences in genetic factors influencing immune responsiveness (Hurtado et al., 2003) to influence the burden of infection and active disease in different groups within a population. TB has a huge physical, economic, and social burden for those who develop active disease (Starke, 2003). In observational studies, which form the majority of data supporting these links in humans, timing of various factors in relation to disease development is unknown, and the direction of associations cannot be confirmed (Cegielski & McMurray, 2004).

2.2.4. Chronic respiratory infections: Paleopathological diagnosis

Diagnoses of chronic respiratory infections in archaeological skeletal material typically involve the examination of lytic lesions in the spine and joints characteristic of TB, as well as visceral new bone formation on the ribs, and possibly also proliferative lesions on the long bones attributed to hypertrophic osteoarthropathy (HOA) (Table 3.5). Investigations of paleopathological evidence for chronic respiratory infections, including TB, have suggested a role for proliferative lesions on the visceral surfaces of the ribs,

which are not generally noted in the clinical literature but may be of value for diagnosing respiratory infections in past populations (Roberts et al., 1998). Investigations of new bone formation on ribs and long bones of individuals from documented skeletal collections indicate that periosteal reactions in these two areas of the skeleton are significantly more common in both children and adults who died of TB than those who died of non-tuberculous causes (Santos & Roberts, 2001, 2006). Dissemination of MTB to the ribs is suggested to occur either through spread from spinal lesions, or directly from infection in lung tissue via inflammation of the pleura (Roberts & Buikstra, 2003a), and although clinical disease in the ribs is rare it often occurs secondary to pleurisy (Leader, 1950). Like other forms of skeletal involvement in infectious disease, this would require a chronic and long-standing disease process with at least partially adequate host resistance (Roberts et al., 1998; Santos & Roberts, 2006). While rib involvement is categorized as an uncommon form of osteoarticular TB, TB is suggested to be the most common cause of inflammation in the ribs (Davidson & Horowitz, 1970; Lee et al., 1993). Clinically, rib enlargement is occasionally noted on radiographs in association with chronic pulmonary disease (Eyler et al., 1996); Roberts et al. (1998) suggest that this likely corresponds to new bone formation, although in living patients this new bone cannot be directly visualized. Guttentag and Salwen (1999) suggest that acute rib infections are seen as focal areas of bone destruction, whereas chronic infections may result in a periosteal reaction or sequestrum. Clinical reports estimate destructive lesions of ribs to be involved in one to 16% of cases (Roberts et al. 1998), although even destructive lesions of the rib are not always visible radiographically (Lee et al., 1993). Lack of clinical recognition of

periosteal reactions of the ribs in living patients has been seen as a serious limitation for its use in paleopathological diagnoses. However, this appears to represent a situation in which clinical diagnostic criteria may not be the most appropriate for application to archaeological skeletal material, due to significant differences in the types of evidence available to clinicians and to paleopathologists (Santos & Roberts, 2001, 2006). Clinical evidence for orthopedic diseases is restricted to radiography and autopsy, which often does not directly examine the ribs (Guttentag & Salwen, 1999), and therefore the full pattern of skeletal involvement may not be well known (Santos & Roberts, 2006). However, a close understanding of the pathophysiology of respiratory infections and associated pleural inflammation provides convincing support for an association between these infections and new bone formation on the visceral surfaces of the ribs.

Identification of possible chronic respiratory infections in the past may also consider skeletal evidence for HPO. This form of HOA involves the presence of symmetrical, bilateral deposits of periosteal new bone formation on the mid- to distal-diaphyses of the tubular bones, particularly those of the lower leg and forearm (Assis et al., 2011); clinically, this is associated with painful swelling of the distal limbs (Anselmo et al., 2016). Clinical radiographic observation of these lesions has been corroborated by studies in documented skeletal collections (Assis et al., 2011). Chronic pulmonary disease is generally considered to be the primary cause of HOA. While in clinical cases this is typically due to neoplastic conditions, in the pre-antibiotic era respiratory infections are likely to have been a prominent cause (Locke, 1915; Webb & Thomas, 1986). HOA has been diagnosed secondary to pulmonary TB (e.g., Kelly et al., 1991), and this association

may have been more common in the past (Mays & Taylor, 2002). A limited number of paleopathological cases of HOA have been identified based on skeletal lesions (e.g. Anselmo et al., 2016; Blondiaux et al., 1992; Fennel & Trinkaus, 1997; Gladykowska-Rzeczycha & Prejzner, 1993; González-Reimers et al., 2015; Martinez-Lavin et al., 1994), and in a few cases macroscopic lesions have been found to correlate with biomolecular evidence for MTBC DNA and lipid biomarkers (Hershkovitz et al., 2008; Masson et al., 2013; Mays & Taylor, 2002).

In addition to evidence for chronic respiratory infections more generally, skeletal TB takes three forms that can be specifically identified in archaeological skeletal material: spondylitis, arthritis, and osteomyelitis. Paleopathological identification of TB relies mainly on identification of tuberculous spondylitis, which causes destructive lesions in the spine, referred to as Pott's disease (Roberts & Buikstra, 2003a). Skeletal lesions of tuberculous spondylitis, arthritis, and osteomyelitis identified by paleopathologists correspond to the skeletal manifestations documented by clinicians (Section 2.2.3.2). This primarily involves the identification of destructive lesions with minimal formation of reactive bone.

2.3. Vitamin D Deficiency and Chronic Respiratory Infections: Correlation and Interaction

Significant epidemiological evidence exists to support a correlation between the occurrence of vitamin D deficiency and insufficiency and TB susceptibility and progression (Adams et al., 2007; Holick & Chen, 2008). These data support longstanding observations of the benefits of sunlight and cod liver oil, and therefore vitamin D, for TB

treatment (Crowle et al., 1987; Rook et al., 1986; Salahuddin et al., 2013). More recently, molecular evidence has provided a plausible mechanism for the correspondence of these two conditions (Figure 2.4). Inadequate vitamin D has been implicated as a risk factor for the occurrence and severity of respiratory infections in children (Banajeh et al., 1997; Cannell et al., 2006; Fleming et al., 2007; Karatekin et al., 2009; McNally et al., 2009; Muhe et al., 1997; Pettifor, 2003; Roth et al., 2010; Sachan et al., 2005; Wayse et al., 2003) and more recently in adults as well (Ginde et al., 2009; Laaksi et al., 2007). Although some studies have failed to find an association between the two (e.g., Roth et al., 2009), the majority demonstrate a clear link. In children under five years of age in Yemen, 50% of those with severe pneumonia showed symptoms of clinical rickets, and rickets

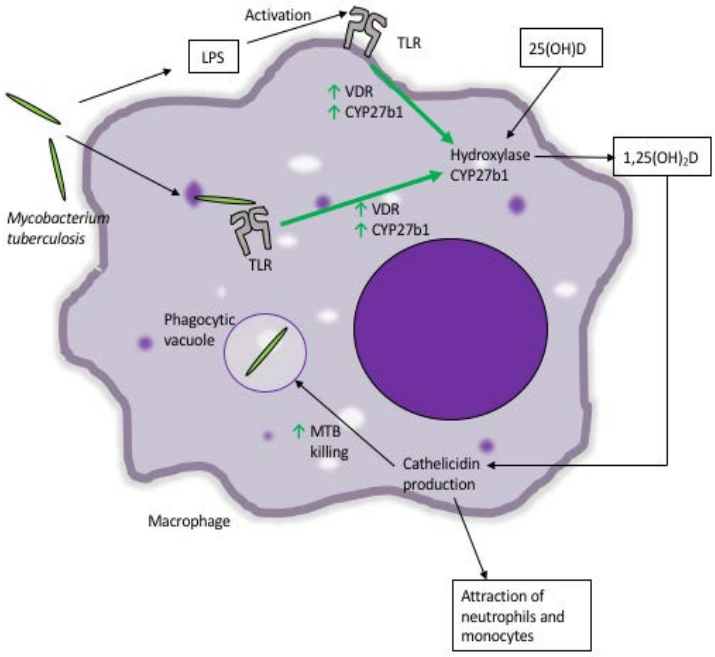


Figure 2.4. Mechanism of vitamin D-mediated potentiation of MTB killing in immune cells. As demonstrated by Liu et al. (2006), vitamin D produced by macrophages is necessary for the production of cathelicidin, an AMP involved in killing intracellular MTB. Cathelicidin enhances killing of MTB in the phagocytic vacuoles, and attracts neutrophils and monocytes to the site of infection. MTB-induced TLR activation (both by the bacterium itself and by lipopolysaccharides or LPS it produces) also upregulates both the VDR and the CYP23b1 hydroxylase, increasing vitamin D responsiveness and production, respectively.

was found to be associated with an increased risk of dying from this respiratory infection (Banajeh et al., 1997). In adults, vitamin D status has been shown to impact lung function (Holick, 2006b; Karatekin et al., 2009), which could potentially affect the risk of or response to respiratory infections.

Observation of the unusual summer notification peak of TB in the United Kingdom (UK) led to propositions of a relationship with low post-winter trough levels of vitamin D, which may affect macrophage function and cell-mediated immunity and promote reactivation of latent TB infection (Douglas et al., 1996). A higher incidence of TB has also been found to occur in populations at high risk of vitamin D deficiency, including Asian immigrants in the UK (Davies, 1985). Children with rickets are abnormally prone to TB infection, and several studies have demonstrated that serum 25-OHD is significantly lowered in TB patients (Chan, 2000; Davies, 1985; Sita-Lumsden et al., 2007; Ustianowski et al., 2005; Wilkinson et al., 2000; Williams et al., 2008). There is some indication that vitamin D levels may be higher in patients with latent infection than those with active or past TB infection, although these patients' serum 25-OHD concentrations are still lower than those with no TB infection (Gibney et al., 2008). Wilkinson et al. (2000) found the greatest risk of TB infection to be associated with undetectable serum levels of 25-OHD. However, there has been some suggestion that active TB can also decrease serum levels of 25-OHD, so these results should be interpreted cautiously (Cegielski & McMurray, 2004).

Vitamin D deficiency has been suggested to increase the risk of developing overt disease, as well as extra-pulmonary forms (Chan, 2000; Davies, 1985; Nnoaham &

Clarke, 2008; Talat et al., 2010; Wilkinson et al., 2000), and has been associated with more severe and invasive TB and lower respiratory infections (Holick, 2008; Snoddy et al., 2016). However, more prospective studies are needed to confirm the directionality of this association (Nnoaham & Clarke, 2008). Some vitamin D supplementation trials indicate improved measures of TB treatment outcome (Coussens et al., 2012; Martineau et al., 2007a; Nursyam et al., 2006; Salahuddin et al., 2013), but these results are not consistent (Wejse et al., 2009). Recent positive results in supplementation trials have suggested a role for vitamin D in accelerating the resolution of inflammatory responses associated with an increased risk of TB-related mortality (Coussens et al., 2012; Salahuddin et al., 2013). Inconsistent findings of improvements in outcome measures may relate to inconsistencies between major mechanisms of action of vitamin D in the immune response to TB and the outcomes being tested; Cegielski and Vernon (2015) suggest that, if the major action of vitamin D is to mitigate inflammation and the immune response, the benefits of supplementation would be better assessed by measuring restriction of tissue damage or prevention of relapse. Responses to vitamin D inclusion in TB therapy may also vary by individual based on genetic factors, as some VDR polymorphisms have been associated with differences in the relation of vitamin D deficiency and TB risk (Gao et al., 2010) as well as with alterations in responsiveness to supplementation (Martineau et al., 2011).

Vitamin D enhances and activates the ability of macrophages to limit intracellular growth and replication of MTB (Chan, 2000; Crowle et al., 1987; Martineau et al., 2007b; Rook, 1988; Rook et al., 1986; Williams et al., 2008), and has been found to enhance

phagocytosis and granuloma formation (Figure 2.3; Sita-Lumsden et al., 2007). These are paracrine and autocrine actions of vitamin D, accomplished by local production of 1,25-$(OH)_2$D by immune cells which express the VDR and CYP27b1 hydroxylase (Biyoudi-Vouenze et al., 1991). Vitamin D deficiency is associated with decreased proliferation of lymphocytes, impaired cell-mediated immunity (Figure 2.3), and a subsequent loss of the ability to control and contain MTB infection (McMurray et al., 1990; Ustianowski et al., 2005). Vitamin D is a vital mediator of macrophage and T cell functions and interactions in the successful immune response against TB (Cadranel et al., 1990), and deficiency negatively impacts both susceptibility to and outcome of infection.

Investigation of vitamin D actions in an *in vitro* model elucidated a physiologically relevant mechanism of the innate immune system in which 1,25-$(OH)_2$D produced locally by macrophages induced production of an AMP (cathelicidin) directly involved in MTB killing, the production of which has also been demonstrated to be dependent upon local levels of 25-OHD (Figure 2.4; Adams et al., 2007). This is most likely complemented by adaptive immune mechanisms related to Th1 actions. Liu et al. (2006) demonstrated that low serum 25-OHD resulted in an inefficient response to MTB, and the response was restored with supplementation to normal serum 25-OHD levels. Cathelicidin also co-localized with MTB in the phagosome, where microbial killing takes place (Liu et al., 2006; White, 2008). The link between toll-like receptor activation and vitamin D-mediated innate immunity suggests that TB susceptibility is likely related to immune cells' ability to locally produce 1,25-$(OH)_2$D (Liu et al., 2006), which is substrate-dependent and therefore closely linked to host vitamin D status.

Some immunomodulatory effects of vitamin D appear to have a contradictory effect on development of TB infection, as vitamin D promotes Th2 over Th1 development, can induce TNF-α production, and generally suppresses adaptive immune responses. However, demonstration of direct vitamin D-mediated potentiation of MTB killing by cells of the innate immune system, and the relatively well established observational association between vitamin D deficiency and increased TB risk, imply that the overall impact of vitamin D is to increase effectiveness of the immune response to MTB infection. Mechanisms responsible for these effects have yet to be investigated *in vivo*, and it is likely that with further investigation some of these apparent contradictions will be resolved.

2.4. Conclusions

Clinical data provide a primary source of evidence on metabolic and infectious disease processes, and are necessary for their investigation in the past. Paleopathological investigations of metabolic and infectious bone disease use clinical data to elucidate pathophysiology and skeletal manifestations, to discuss etiological factors related to disease occurrence in the present and the past, to discuss functional outcomes, consequences, and disease experiences, and to impart a dimension of time to the static skeletal picture of disease. Time is accessed through clinical evidence for dynamic aspects of disease expression, including severity, manifestations of different disease stages, and differences between active and healed disease (Brickley et al., 2010). For vitamin D deficiency and chronic respiratory infections, clinical evidence for these aspects of disease expression and

experience allow paleopathologists to determine not only how these conditions may manifest in the skeleton and be recognized in archaeological skeletal material, but also how they may interact, and how these interactions could affect the skeletal expression of both diseases.

In paleopathological investigations of infectious and metabolic bone disease in the past, detailed understandings of pathological processes at cellular, tissue, and organ levels are important in order to adequately interpret skeletal evidence. This can facilitate the investigation of complex relationships and interactions between metabolic conditions and exposure to infectious conditions, development of disease, and expression of lesions in the skeleton. An increased understanding of the complex interplay between infectious disease, nutritional factors, and immune competence can lead to a more nuanced conceptualization and interpretation of disease occurrence and manifestation in past populations.

Effects of vitamin D on mineral homeostasis, skeletal remodeling, and immune responses are complex and difficult to relate to the archaeological appearance of interactions between vitamin D deficiency states and TB in past populations. The development of a predictive model similar to that formulated by Wilbur et al. (2008) is not possible for vitamin D at this time. However, it is important for paleopathologists to consider how vitamin D and calcium status may have affected chronic respiratory infections in terms of transmission, lesion development, and skeletal involvement. Recognition of these and other nutritional factors as potential modulators of chronic respiratory infection prevalence and pathophysiology through consideration of relevant

clinical evidence has the potential to increase the interpretive power of paleopathological examinations of infectious and metabolic bone disease experience in the past.

CHAPTER 3 - Materials and Methods

3.0. Introduction

In order to address questions surrounding the experience of vitamin D deficiency and chronic respiratory infections over the life course during the Roman period at Ancaster and Isola Sacra, features associated with these pathological conditions were evaluated in individuals from these two collections. Features associated with age and sex estimation were also evaluated in order to standardize methods used at the two sites. Patterns in the occurrence of vitamin D deficiency and chronic respiratory infections were evaluated and compared between Ancaster and Isola Sacra based on age at death, evidence for active or healed lesions, and sex. Non-parametric statistical analyses were used to address how the occurrence of these two conditions may be associated with one another, as well as how each may relate to survival based on age at death distributions.

3.1. Materials

3.1.1. Ancaster

The Ancaster collection encompasses human skeletal material from 276 individuals (182 adults and 94 juveniles) from a small defended settlement in Lincolnshire, England (Figure 3.1), buried between the third and fourth centuries AD (Cox, 1993; Wilson, n.d.). The burials were excavated between 1964 and 1973 by Nottingham University; the Ancaster sample contains only the remains of individuals excavated from the cemetery, and does not include any human remains found in other

Figure 3.1. Map of the Roman Empire (light green), showing the locations of both Ancaster and Isola Sacra (red stars). After Mattingly (2006).

parts of the archaeological site (Cox, 1993). Initial analyses of age and sex indicators, stature calculations, and evaluation of nonmetric and pathological features were undertaken by Dr. Margaret Cox (1993). The collection is now housed at the English Heritage offices at Fort Cumberland in Portsmouth, UK. Due to the loss of notes associated with the excavation, as well as the loss of some labels in transit between the excavation and the museum, there is confusion surrounding the correspondence of excavation numbers with the current skeleton numbering system. As a result, contextual evidence regarding burial position, orientation, and associated grave goods is not available for all individuals. In addition, not all of the cranial and postcranial human

remains that were separated from one another during transport can be reunited based on the evidence available. Wilson (n.d.) suggests that a number of specimens exhibiting striking evidence of pathological lesions have been removed, presumably for study elsewhere, and there is no indication that these have been reincorporated into the collection.

The cemetery at Ancaster is located just outside of the west defenses of the Roman walled settlement of *Causennae* (Wilson, n.d.). This location corresponds with that of a modern cemetery, and the burials were discovered while digging modern graves. Excavations revealed a history of occupation at the site stretching back to the Iron Age, with late Iron Age settlement followed by an early Roman military occupation and subsequent Roman town (Wilson, n.d.). Relating to the Roman occupation of the site, excavations uncovered 238 Roman burials, of which 167 were more or less complete, as well as defensive ditches belonging to the Roman fort and potentially contemporary gravel-workings (Wilson, n.d.). Fragments of minor buildings associated with the Roman town were also uncovered (Wilson, 2006).

The town of Ancaster was a small defended settlement situated along Ermine Street, a great ancient road and major travel route during the Roman period leading from London to Lincoln (Wilson, 1968). Previous archaeological analyses focused on the defense system of rampart, wall, and ditches that made up the military fort associated with earlier phases of occupation at the site (Marsden, 1863; Trollope, 1870; Wilson, 1968) at the expense of focus on the layout of the settlement (Mays et al., 2006a), which is suggested to have replaced the fort around the beginning of the third century AD

(Wilson, 1968). While defensive structures in smaller settlements like Ancaster are often assumed to relate to phases of military occupation, Mattingly (2006) suggests that some of the smaller defended sites located along main roads may also have had defenses constructed by the state to protect parts of the Roman supply and communications system. Small towns around the same size as Ancaster generally lacked public buildings or administrative functions, instead acting as a focus of trade and craft activities for the surrounding rural area (Mays et al., 2006a). Todd (1970) suggests that the Roman town of Ancaster had connections with agriculture, as well as with quarrying of nearby limestone deposits. There is evidence for substantial villas adjacent to the settlement, and agricultural activities at these private or imperial estates may have been bound up in the growth of the town (Mattingly, 2006). There is also archaeological evidence to support the possibility of quarrying, stoneworking, ironworking, and pottery manufacture at the site (Burnham & Wacher, 1990).

The cemetery at Ancaster is a "managed" cemetery, with some indication of planning in the layout of graves in relatively tidy rows (Wilson, 2006). However, in some cases later burials have disturbed earlier ones. The excavation report points to grave robbing, animal activity, the encroachment of the modern cemetery, and archaeological excavation itself as potential sources of disturbance of and damage to the human remains (Wilson, n.d.). Earthmoving machinery was used in some areas to remove the topsoil, potentially damaging some of the skeletons that were in shallower graves (Wilson, n.d.).

The majority of individuals at Ancaster were buried in a supine extended position, with the head facing to the west (Wilson, 1968). Based on the orientation of the graves,

Wilson (1968, 2006) suggests that there is some indication of Christian burial rites. There was apparently a tendency to bury infants and juveniles in groups, and, while most individuals in the cemetery were interred separately, all burials in which multiple individuals were buried together include at least one juvenile (Cox, 1993). The reasoning behind the layout of the cemetery is unknown, but based on nonmetric traits Cox (1993) concludes that there is no evidence here for burial in family groups. Many burials were associated with stonework, in the form of coffins, linings for the grave pit, or markers. Thirteen burials contained stone coffins, which are described as generally poorer quality models or manufacturers' seconds that are likely to have been unsuitable for sale in major centers, but could probably have been purchased at a lower price in areas local to the quarry (Wilson, 1968). The coffins found at Ancaster were made of local limestone, and were very heavy with tapering shapes and coverings made of heavy stone slabs. There are also slab-lined graves, either covered with stone slabs or uncovered. Some of the stones used to line these graves and to cover both slab-lined graves and stone coffins may have been originally meant for other purposes, as some of them appear to have been partially prepared for masonry or as building stones before they were put to funerary uses. Some graves also contain stone markers placed at the head, foot, or both. Wilson (n.d.) also mentions evidence present in 49 burials that wooden coffins were used, based on differences in the grave fill, or the presence of putative coffin nails based on location or oxidation thought to relate to decayed wood.

There were some objects present in the burials. These mainly consist of iron objects, nails, coins, some fragmented pottery vessels, a bone spindle whorl and pin, and

some personal decorations including brooches, bangles made of copper-alloy and of bone, and beads made of amber, jet, and glass (Wilson, n.d.). Despite the presence of objects in 84 burials, Wilson (n.d.) concludes that there are few items present that have obvious ritual connotations, which might have included things like food offerings, or items related to the journey into the afterlife such as boots or a coin placed in the mouth. Dates on the coins found range from 268 to 364 AD, and the types of beads found in one burial suggest a date in the later third to fourth century AD. Not many datable objects were associated with the burials (Wilson, 2006).

Initial osteological analysis of the Ancaster skeletal material indicated that the collection contained 243 adults and 84 juveniles, of which 29% were infants (Cox, 1993). Cox (1993) suggests that there are two cases of TB in the collection, one (ANC 1) involving multifocal involvement of the right foot and right hip and sacroiliac joint, and the other (ANC 11) displaying classic signs of tuberculous spondylitis, or "Pott's spine". In her report, Cox (1993) identifies the presence of abnormal curvature in the sacrum of one individual (ANC 112), but concludes that there is no other evidence to indicate that either rickets or osteomalacia were present in the collection. Metabolic bone disease is also suggested to be present in the form of osteoporosis, particularly for older female adults (Mays, 2006a,b). Mays (2006a) connects evidence for fragility fractures in several middle and older adult females, including a fracture of the femoral neck, with poor anatomical and functional outcomes associated with osteoporosis within this collection.

3.1.2. Isola Sacra

Initial excavations at the site of Isola Sacra in the 1920s and 1940s by Calza uncovered evidence for major monumental tombs; more recent work undertaken in 1988-1989 excavated more than 600 single and multiple burials (Baldassarre, 1978, 1990). The total number of individuals is estimated at around 2000 (Sperduti, 1995), however many of these are commingled human remains with limited contextual evidence recorded during early stages of excavation. Over 800 skeletons, mainly from later excavations of burials between the monumental tombs, have been catalogued individually. These individuals form the sample of 447 juveniles and 376 adults (823 individuals in total) considered in the current analysis. The human remains are curated at the L. Pigorini National Museum of Prehistory and Ethnography in Rome.

The necropolis of Isola Sacra was associated with *Portus Romae*, the port of the city of Rome located on the western coast of Italy (Figure 3.1), and was used by the inhabitants of this city between the first and third centuries AD (Prowse et al., 2004). It is located about 23 kilometers west of Rome, between Ostia and Fiumicino (Pavolini, 1996), and was built on an artificial island that was created by dredging a canal connecting the river with the coast in 103 AD (Mannucci & Verduchi, 1996). *Portus Romae* was a key maritime trading center during the height of the Roman Empire that was connected to Rome by the Tiber River. This city grew during the mid to late first century and early second century AD around the harbors built during the reigns of emperors Claudius (41-54 AD) and Trajan (98-117 AD) (Baldassarre, 1978). The harbors acted as major Mediterranean ports holding an important commercial role as the trading entry point to

the Imperial city of Rome, and the individuals who lived there were likely to be middle-class traders, administrators, and merchants involved in economic activities at the port (Mannucci & Verduchi, 1996). Inscriptional evidence from the site provides no reference to a local aristocracy, which is considered to be unusual for Roman towns from the Imperial period (Garnsey, 1998). While trade in the city began to decline by the end of the fourth century AD, it continued to be used for military activities until the sixth century AD. Archaeological investigation of the site has focused on the harbor and structures associated with it, rather than on details of daily life for its inhabitants; the site is privately owned, and further excavation is not currently possible. Some studies have utilized archaeological evidence from the nearby contemporaneous site of Ostia to provide relevant information on aspects of daily life, for example faunal remains relevant to dietary practices (Prowse et al., 2005).

A variety of burial structures were utilized at Isola Sacra, including simple interments and monumental multiple tombs (Wood, 2003). Individuals were placed in single and multiple burials, either directly in the ground, within coffins of wood or brick, in '*cappuccina*' burials covered by tiles, within storage vessels called *amphorae*, or within tomb chambers (Angelucci et al., 1990). Limited contextual information is available for many of the burials, as archaeological reports generally focus on the architectural features of the monumental tombs rather than other secondary burial structures (Prowse, 2001). According to Baldassarre (1984), older tombs dating to the first century AD were constructed closer to the road, with successive phases of cemetery use moving further from the road. However, in later periods of use there is some

indication that earlier structures were reused. The majority of inhumations at the site did not contain associated grave goods (Sperduti, 1995).

Information on diet and migration at Isola Sacra has been accessed through analyses of stable isotope values in bones and teeth. Dietary analyses using collagen and bone apatite from individuals five years of age and older indicated that a mixture of marine and terrestrial resources were exploited (Prowse et al., 2004). Further analyses indicate that dietary status varied based on age at death, suggesting that females may have had less access to marine foods, historically considered to be higher-status foods, and that juveniles may have been nutritionally disadvantaged compared to adults (Prowse et al., 2005). Prowse et al. (2008) employed stable isotope analysis of nitrogen and carbon from bone collagen in Isola Sacra juveniles, in combination with data on dental pathology, to determine that transitional feeding began from the end of the first year of life, with weaning occurring by two to two and a half years of age. A study of oxygen isotope ratios in carbonate from adult teeth by Prowse et al. (2007) found that about one third had values outside of the range associated with modern inhabitants of the area, implying a high rate of population turnover. As such, there is evidence for movement of individuals into the population from other areas of Italy and Europe, with one individual displaying values possibly consistent with Northern Africa, and this migration possibly involved younger individuals and families (Prowse et al., 2007).

A limited number of published studies have also considered health in this population, focusing mainly on juveniles. FitzGerald et al. (2006) examined dental microstructure, or evidence for Wilson bands, as a marker of health in the first year of life,

finding two periods of high prevalence indicating elevated risk for growth disruption at two to five months and six to nine months of age. Initial analyses of evidence for rickets by Wood (2003) found a high prevalence of rickets among juvenile individuals at Isola Sacra, with 15% of individuals 15 years of age and younger displaying evidence for vitamin D deficiency, spanning all age categories and burial types. No previous analyses have considered evidence for chronic respiratory infections at Isola Sacra.

3.2. Methods

3.2.1. Methods: Data collection

In order to address questions surrounding the experience of vitamin D deficiency and chronic respiratory infections over the life course during the Roman period at Ancaster and Isola Sacra, features associated with these pathological conditions were evaluated in adult and juvenile individuals from these two collections. Collection of data on age and sex as well as features of vitamin D deficiency rickets and osteomalacia was done in collaboration with a SSHRC funded project on vitamin D deficiency in the Roman world led by Drs. Megan Brickley, Tracy Prowse, Michele George, and Simon Mays. All data were collected between January 2014 and January 2015. Vitamin D deficiency features and age and sex data were recorded with the assistance of research assistants associated with the SSHRC project, Annabelle Schattmann for Ancaster and Marissa Ledger for Isola Sacra. For each collection, the author worked along with one research assistant; training was completed together, skeletal individuals were split relatively evenly, and any features for age and sex estimation or pathological features

around which there was any uncertainty were discussed and a score agreed upon together. Every skeleton was then examined by the author for features associated with chronic respiratory infections. This analysis considers 94 juveniles and 182 adults from Ancaster (276 individuals total) and 447 juveniles and 376 adults from Isola Sacra (823 individuals total), for a total sample size of 1099 skeletons. Adult individuals represented by only a cranium and/or hand and foot bones, as well as juveniles represented only by hand or foot bones, were excluded.

Data collected were recorded using fillable PDF forms created for the evaluation of age and sex (Appendix A.1), juvenile vitamin D deficiency (Appendix A.2), adult vitamin D deficiency (Appendix A.3), juvenile chronic respiratory infection (Appendix A.4), and adult chronic respiratory infection (Appendix A.5). Information from these forms was exported into Microsoft Excel software for further analysis. Photographs were taken of each auricular surface used for age estimation, as well as of all potential lesions identified, using a Nikon Coolpix P7800 under artificial light on a background of black velvet. Each photograph included a scale and a paper label indicating the individual skeleton number, element, and date.

3.2.1.1. Age estimation: Juveniles

Several methods were employed to produce data on juvenile age, and the results were evaluated based on a hierarchy of reliability of the various techniques used. Decisions on methods used were made as part of the SSHRC project, and were also considered to be most suitable for the current analysis. Dental development was assessed based on macroscopic observation, and age was estimated following standards developed

by Gustafson and Koch (1974). Each deciduous and permanent tooth present was scored based on specific dental development stages, including tooth mineralization, eruption, and the completion of the crown and root (Gustafson & Koch, 1974); additional stages were added to indicate intermediate development, in which a tooth had surpassed one full stage but not quite reached the next. The standards used were developed by Gustafson and Koch (1974) based on data from multiple modern clinical and developmental studies done on European samples, utilizing both radiographic and histological data.

Long bone length was recorded to the nearest tenth of a mm for all elements for which complete growth plates were present at both the proximal and distal ends, as set out in Buikstra and Ubelaker (1994, p. 44). Measurements were taken using sliding calipers for long bones up to 18 cm long, and using a long ruler for elements which exceeded the maximum length measured by the calipers. Age ranges were estimated based on standards developed by Fazekas and Kósa (1978) for prenatal individuals and Maresh (1970) for postnatal individuals, as collated by Scheuer and Black (2000); both of these techniques are commonly employed, and can be considered standard practice within biological anthropology.

Epiphyseal fusion was scored for all epiphyses of the femur, tibia, humerus, and radius, the iliac crest and ischium on the pelvis, and the sternal end of the clavicle. The union of each epiphysis was scored as complete (3), partial (2), or non-union (1) as set out by Cardoso (2008a, b; see also Buikstra & Ubelaker, 1994). In all cases, fusion was scored preferentially on the left sided element, and a score for the right sided element was recorded only when the left was not present. From these scores, age estimates were

generated following Cardoso (2008a, b). Data presented by Cardoso (2008a, b) were generated from European skeletal material based on observations in dry bone, making them more applicable to the current study than clinical observations based only on radiographs.

For juveniles whose permanent molars were erupted and in occlusion, wear was scored on a modified scale in which the seven groupings depicted by Brothwell (1965) were split into 13 stages (Appendix B). A category was also added to indicate antemortem tooth loss, which may be an important factor for contextualizing the absence of tooth wear scores, particularly in older adults. Dental wear on the molar teeth, at least in high dental wear populations in antiquity, has been lauded as a valuable indicator of age; teeth are more likely to preserve archaeologically than many more fragile elements of the skeleton, and changes to the dentition occur independently of skeletal degenerative changes, which may become increasingly unreliable in older age categories (Mays, 2014).

Final age estimates were generated for each juvenile individual, with preference given to information on dental development, followed by epiphyseal fusion, long bone length, and finally dental wear, according to the relative reliability of estimations based on these techniques. For each individual, age is reported as a point estimate or range, as well as the general category into which this age estimate fits, following Buikstra and Ubelaker (1994). Categories include fetal/neonate (before birth to under 0.125 years), infant/younger child (0.125 to three years, with infants being 0.125 to one and younger children being over one to three years), middle child (four to seven years), older child (eight to 11 years), younger adolescent (12-15 years), older adolescent (16-19 years), and

undetermined juvenile (individuals lacking features needed to produce a specific age estimate). Many of the individuals in the older adolescent category were recorded using both adult and juvenile forms, or were recorded as adults.

A large number of individuals from Isola Sacra lacked specific age information and could be classified only as juveniles. Additional information was collected for the majority of these individuals that allowed them to be classified into the broad categories above (fetal/neonate, infant/younger child, middle child, older child, younger adolescent, older adolescent) without generating a point estimate or range. Information used to generate these estimates included the measurement of long bones that were at least 75% complete, which were then evaluated based on the standards of Maresh (1970). Individuals at the upper end of the range for a category were pushed into the next category to account for the missing portion of the bone. For individuals lacking nearly complete long bones, long bone thickness was evaluated in comparison to other individuals from the same sample for whom a more precise age estimate had been established; in a few cases, the size of the ilium was evaluated comparatively in the same fashion. Some individuals were assigned to a broad age category based on the fusion of the second cervical vertebra, given that the arches fuse between around four to six years, with complete fusion of the dens around the age of 12 years (Schaefer et al., 2009).

3.2.1.2. Age estimation: Adults

For any adults young enough to have epiphyses that were not fully united, epiphyseal union was scored and evaluated (see Section 3.2.1.1). Past the point of complete fusion of skeletal epiphyses, adult age estimation relies on the identification of

progressive degenerative changes in the skeleton, which have best been characterized for features of the pelvis and dentition. Tooth wear was evaluated (see Section 3.2.1.1, Appendix B) for any molars that were fully erupted and in occlusion, or which displayed clear evidence of antemortem loss.

Morphological changes to the face of the pubic symphysis are typically viewed as one of the most reliable criteria for estimating adult age at death from the skeleton (Garvin & Passalacqua, 2012; Milner & Boldsen, 2012). Changes to the surface of the pubic symphysis were scored using the Suchey-Brooks method, following phases outlined by Brooks and Suchey (1990) and Katz and Suchey (1986). This is one of the methods recommended by Buikstra and Ubelaker (1994), and its use is standard within biological anthropology. All features of the pelvis (including the pubic symphysis and the auricular surface) were preferentially scored on the left side, with the right element being scored only if the left was missing.

Age-related changes to the auricular surface are more complex and are often considered to be less reliable than alterations of the pubic symphysis, but this area is more frequently preserved in archaeological skeletons (Buikstra & Ubelaker, 1994); as such, the evaluation of the auricular surface is very useful in cases where the pubic symphysis is insufficiently preserved in order to generate age estimates for a larger number of individuals. The auricular surface is often present, but not often well preserved, precluding the application of many standard methods for scoring alterations. Changes at the auricular surface were scored using transition analysis, a technique that allows scores to be assigned separately for individual areas within the auricular surface, enabling the

estimation of age from elements that are incomplete and giving increased resolution from fragmentary archaeological skeletal remains (Milner & Boldsen, 2012). Following Boldsen et al. (2002), minimum and maximum scores were assigned for the topography of the superior and inferior auricular surface, characteristics of the superior, apical, and inferior surface, texture of the inferior surface, and exostoses on the superior and inferior posterior iliac crest, as well as on the surface posterior to the sacroiliac joint. Age estimates, consisting of both point estimates and age ranges, were generated from these scores using ADBOU (Anthropological Database, Odense University, version 2.1.045, developed by Milner and Boldsen) age estimation software.

A final age estimate was generated for each adult individual, with preference generally given to information on epiphyseal fusion when available, followed by dental wear, pubic symphysis, and finally auricular surface (transition analysis) data, according to the relative reliability of estimations based on these techniques. For each individual, age is reported as a point estimate or range, as well as the general category into which this estimate fits. Categories included young (20-34 years), middle (35-49 years), and old adult (50 years and over) following Buikstra and Ubelaker (1994), as well as a general category of undetermined adult (individuals lacking features necessary to produce a specific age estimate).

3.2.1.3. Sex estimation

Sex was estimated for individuals aged at least sixteen years. In the adult skeleton, estimation of sex relies on the evaluation of sexually dimorphic features that develop based on growth changes during adolescence leading to distinctive differences in the male

and female pelvis and cranium (Buikstra & Ubelaker, 1994). Features of the skull, mandible, and pelvis were evaluated for sex estimation as set out by Buikstra and Ubelaker (1994). Using the scores developed by Buikstra and Ubelaker (1994), features of the ventral arc, subpubic concavity, pubic ramus ridge, greater sciatic notch, and preauricular sulcus in the pelvis, and of the nuchal crest, mastoid process, supraorbital margin, glabella, and mental eminence of the skull were evaluated. As described for age estimation techniques (see Sections 3.2.1.1 and 3.2.1.2), the left side was preferentially scored, with the right being scored if the left was absent. Scores for the pelvis were accorded more weight than cranial features, as sex-based differences in the pelvis correspond to functional differences related to giving birth, and pelvic differences are considered to be the most reliable skeletal indicators of sex (Buikstra & Ubelaker, 1994). Based on the scoring of these features, sex was estimated for each individual as female, probable female, ambiguous, probable male, male, or undetermined (individuals lacking any features needed to estimate sex).

3.2.1.4. Vitamin D deficiency: Juveniles

For each juvenile individual, macroscopic pathological features potentially relating to vitamin D deficiency were evaluated for the cranium, ribs, long bones, ilium, and sacrum. Recording forms were developed for use in the SSHRC project by Drs. Brickley and Mays (Appendices A.2 and A.3); given their extensive past experience investigating vitamin D pathology (e.g., Brickley et al., 2005, 2007, 2010; Ives & Brickley, 2014; Mays et al., 2006; Ortner & Mays, 1998), as well as the ability to facilitate cross-comparison with other studies, these forms were deemed most appropriate

for use in the current project as well. Macroscopic data were supplemented by radiographic evaluation of those individuals displaying possible evidence of deficiency. Rib samples were collected for histological analysis from all individuals in the Ancaster collection and those individuals in the Isola Sacra collection displaying possible evidence of deficiency.

Criteria for the diagnosis of vitamin D deficiency in juvenile material were based primarily on methods set out by Mays et al. (2006), who expanded upon and refined the ten principal features elucidated by Ortner and Mays (1998). These seminal studies systematically developed a set of criteria that can be used to identify vitamin D deficiency in juvenile skeletal material (Table 3.1), which have subsequently been applied or adapted by other researchers (e.g., Ellis, 2010; Giuffra et al., 2013; Mays et al., 2007; Pfeiffer & Crowder, 2004; Pinhasi et al., 2006; Veselka et al, 2015). Radiographic features can confirm the presence of biomechanical alterations also observed macroscopically (Mays et al., 2006). Cortical bone porosity and porosity or roughening of bone beneath the growth plates, which would have been filled with unmineralized osteoid during life, is only present in active deficiency (Ortner & Mays, 1998). Active and healed cases can therefore be differentiated based on the presence or absence of these features.

Table 3.1. Criteria used to identify vitamin D deficiency in juvenile skeletal material

Diagnostic Criterion		Seminal Study
General macroscopic features	Porosity of the cranial vault	Ortner & Mays, 1998
	Porosity of the orbital roof	
	Ilium concavity	
	Deformation of the leg and arm bones	
	Porosity on the concave surfaces of long bone curvature	
	Long bone metaphyseal flaring	
	Long bone metaphyseal porosity	
	Long bone general thickening	
	Porosity or roughening of the bone underlying the growth plates (especially distal)	
	Coxa vara, superior flattening of the proximal femoral metaphysis	Mays et al., 2006
	Medial tilting of the distal epiphysis (especially tibia)	
Radiographic features	General osteopenia	
	Thinning or coarsening of trabeculae	
	Loss of cortico-medullary distinction	
	Cortical tunneling	

In the current study, data were collected on the completeness of elements present as well as on the presence or absence of pathological features associated with vitamin D deficiency (Appendix A.2). In order to evaluate completeness of the cranium, each element was scored as either present or absent. Cranial features of juvenile deficiency can include abnormal porosity or the deformation of cranial elements, resulting in abnormal shape, particularly deformation of the mandibular ramus (Mays et al., 2006) or bossing of the cranial vault. The presence or absence of abnormal porosity and abnormal shape were scored for the left and right frontal, orbital roof, parietal, temporal, and mandibular ramus, and for the occipital. The left and right maxillae were scored only for the presence or absence of abnormal shape. For all cranial and postcranial elements evaluated, space was

provided for detailed notes on any features identified as well as any aspects that might affect or qualify how these features should be interpreted.

Completeness of the ribs was evaluated by recording the number of left and right ribs as represented by the number of vertebral ends, as well as the number of unsided costochondral rib ends present. Documented features of rickets in the rib cage include flaring, cupping, and abnormal porosity at the costochondral ends of the ribs associated with the development of a rachitic rosary, as well as changes in the shape of the ribs accompanying the typical "pigeon breast" deformity associated with rachitic children (Mays et al., 2006). The number of costochondral rib ends displaying evidence of abnormal porosity, flaring, cupping, or fractures were recorded. Abnormal curvature was evaluated only for complete ribs.

In order to evaluate completeness of the long bones, scores indicating the amount of bone preserved in 25% increments were assigned for the proximal and distal epiphyses as well as the proximal, middle, and distal thirds of the diaphysis for each element of the arm and leg, as well as the clavicles. Improper mineralization of bone in rachitic individuals can result in abnormalities of the shape of long bone metaphyses, including flaring and tilting, as well as bending deformities of the diaphyses, generalized thickening of the diaphyses, and porosity of the metaphyses or diaphyses, especially in association with bending deformities (Mays et al., 2006). In active cases of rickets, alterations can also be seen in the bone underlying the growth plate, particularly at the distal metaphysis (Mays et al., 2006). The distal growth plate of each long bone, with the exception of the clavicle, was scored as normal (0) or abnormal (1-4), with epiphyses that had already

begun to fuse given a score of not applicable. The majority of these stages (0 and 2-4) follow those outlined by Ortner and Mays (1998), while a score of one was added to account for the subtle changes indicated by the "velvety" texture identified by Mays et al. (2006). Each long bone was evaluated for the presence or absence of thickening, abnormal shape of the diaphysis or metaphysis, and other features such as evidence for fractures.

Completeness of the ilium was evaluated in increments of 25%. Abnormal lateral curvature of the ilium, associated with deformation related to improper mineralization in rachitic individuals, was evaluated following Ortner and Mays (1998), and was scored as present or absent for the right and left sides. Similarly, the sacrum was scored for completeness in 25% increments, and abnormal curvature was scored as present or absent.

For each individual, a determination was made of whether or not radiographs were required. This imaging technique is primarily useful for visualizing changes beneath the growth plate associated with active deficiency, differentiating these from features associated with healed deficiency, and potentially identifying recurrent episodes of disease (Mays et al., 2006), and so its application was restricted to individuals most likely to represent possible active cases. Radiographs were taken of individuals with evidence for rickets who were less than four years of age, or those who were older but with changes to the growth plate indicating that the condition might be active. For these individuals, the long bones present from the left side, or those from the right if the left sided elements were absent, were radiographed. Preliminary notes were made at this point

regarding whether potential vitamin D deficiency was suspected, with final diagnostic categories being assigned during data analysis (see Section 3.2.2.1).

3.2.1.5. Vitamin D deficiency: Adults

For each adult individual, macroscopic pathological features potentially relating to vitamin D deficiency were evaluated for the ribs, sternum, scapulae, vertebrae, innominates, sacrum, and long bones (Appendix A.3). Macroscopic data were supplemented by radiographic evaluation of some individuals displaying possible pseudofractures. Rib samples were collected for histological analysis from all individuals in the Ancaster collection and those individuals in the Isola Sacra collection displaying possible evidence of deficiency.

Criteria for the diagnosis of adult vitamin D deficiency were based primarily on methods set out by Ives and Brickley (2014), expanding upon criteria developed by Brickley et al. (2005) (Table 3.2). Skeletal features of adult deficiency were set out by Brickley et al. (2005) based on those seen in documented historical collections. Due to their recent development, these features have subsequently been applied to archaeological human skeletal material by very few studies to date (e.g., Brickley et al., 2007; Haduch et al., 2009; Ives & Brickley, 2014). Subtle features associated with adult vitamin D deficiency are likely to go unnoticed by researchers who are not directly looking for them. Ives and Brickley (2014) base the diagnosis of adult vitamin D deficiency mainly upon the identification of pseudofractures in characteristic locations of the skeleton. These fractures are typically incomplete, and are sometimes associated with irregular ossification of the fracture callus and excess osteoid, resulting in the presence of

characteristic spiculated bone (Ives & Brickley, 2014). Inadequate vitamin D deficiency can also cause deformation of many elements (Brickley et al., 2005); Ives and Brickley (2014) observed bending of the sternum, compression or folding of the vertebral bodies, and anterolateral bending of the proximal femora for the diagnosis of deficiency in archaeological individuals with vitamin D deficiency. Ives and Brickley (2014), following Brickley et al. (2005, 2007), also use microscopic evidence to confirm the presence of adult deficiency.

Table 3.2. Criteria used to identify vitamin D deficiency in adult skeletal material, identifying features relevant to active adult deficiency and those relevant to healed deficiency in adulthood or childhood

Diagnostic Criterion		**Relevant Studies**
General macroscopic features – adult deficiency	Pseudofractures (scapula, ribs, pelvis, vertebral lamina, femoral neck, distal ulna)	Ives & Brickley, 2014, Brickley et al., 2007
	Deformation of thoracic elements (sternum, scapulae, ribs)	
	Folding and collapse of vertebral bodies	
General macroscopic features – adult or residual deficiency	Deformation of long bones (especially proximal femora)	
	Deformation of pelvis	Brickley et al., 2005
Microscopic features – adult deficiency	Patchy and incomplete mineralization	Ives & Brickley, 2014, Brickley et al., 2007
	Mineralization defects adjacent to cement lines	

As set out by Brickley et al. (2005, 2007) and Ives and Brickley (2014), adult individuals were examined for evidence of pseudofractures, in all elements but particularly those identified as characteristic locations for vitamin D deficiency, and deformation of elements of the axial and appendicular skeletons. Features were separated into those associated with deficiency in adulthood and those associated with a previous episode of deficiency, possibly in childhood or adolescence. Adult deficiency was indicated by the presence of characteristic fractures, including pseudofractures as well as

compression fractures and folding in the vertebral bodies (Brickley et al., 2005; Ives & Brickley, 2014). Residual evidence of past deficiency was indicated by deformation of the skeleton, mainly of the sternum, pelvis, and long bones (Brickley et al., 2010; Ives & Brickley, 2014), similar to those seen in healed cases of childhood deficiency.

The ribs were sided and counted using the vertebral ends, and these numbers were recorded for both left and right. For left, right, and unsided pieces of rib, the number of rib fragments displaying evidence of single fractures and multiple fractures were recorded, along with a count of the total number of fractures in the left, right, and unsided fragments. For complete left and right ribs only, the numbers of ribs displaying evidence of abnormal curvature were recorded. Additional information was recorded for each fracture identified, specifying the side of the fragment, the type of new bone formed (woven, lamellar, or spiculated), fracture union (united, un-united, or pseudofracture), and the location of the fracture (angle or shaft). For all cranial and postcranial elements evaluated, space was provided for detailed notes on any features identified as well as any aspects that might affect or qualify how these features should be interpreted.

Completeness of the sternum was classified in increments of 25% for both the manubrium and the sternal body. For each component, the presence or absence of abnormal curvature was evaluated and recorded. For the scapulae, completeness was evaluated in 25% increments for the element as a whole as well as for the spinous process, coracoid process, and lateral border individually. It was noted for each side whether or not the curvature of the body of the scapula could be assessed, and if so whether abnormal curvature was present or absent. Evidence of fractures was scored as present,

absent, or pseudofracture for each spinous process, coracoid process, and lateral border, as well as the presence or absence of fracture or new bone formation at alternate locations on the scapula. For any fractures scored as present, further information was recorded on the state of bone formed (woven, lamellar, or spiculated).

Counts of the vertebrae were recorded as numbers of vertebral bodies and arches for the cervical, thoracic, and lumbar vertebrae. For each category, the number of elements with evidence for collapse or buckling of the vertebral body or fractures in the laminae of the arches was recorded. For the spine as a whole, the presence or absence of kyphosis or posterior thoracic curvature, lordosis or anterior lumbar curvature, and scoliosis or lateral curvature was recorded when possible. Completeness of the innominates was estimated in 25% increments for the innominate as a whole, the iliac crest, the ascending pubic ramus, and the pubis. For each of these components, the presence or absence of evidence for folding, fracture, and other features was recorded. For the sacrum, completeness was recorded in 25% increments. It was noted whether or not sacral curvature could be evaluated, and if so whether abnormal curvature was present or absent, keeping in mind normal variation in curvature between male and female sacra.

For the long bones, scores indicating the amount of bone preserved in 25% increments were assigned for the proximal and distal epiphyses as well as the proximal, middle, and distal thirds of the diaphysis for each element of the arm and leg, as well as the clavicles. For each element, the presence or absence of fractures, bending deformities, and other features was recorded. Additional information was recorded for any fractures present, to indicate the type of new bone formed (woven, lamellar, or spiculated) the state

of fracture union (united, un-united, or pseudofracture), and the location (proximal or distal epiphysis, or proximal, middle, or distal third of the diaphysis).

For each individual, a determination was made of whether or not radiographs were required to look for further evidence of pseudofractures (Brickley et al., 2007). Radiographs were taken of individuals with evidence of a possible pseudofracture, particularly when this evidence was not clear, may have been partially obscured by remodeling, or represented a possible pseudofracture in an uncommon location. Preliminary notes were made at this point regarding whether potential vitamin D deficiency was suspected, with final diagnostic categories being assigned during data analysis (see Section 3.2.2.1).

3.2.1.6. Vitamin D deficiency: Microscopic analysis

Samples of rib were collected from all Ancaster individuals and from Isola Sacra individuals who demonstrated some macroscopic evidence that may be associated with vitamin D deficiency, but for whom macroscopic features alone did not provide a completely clear diagnosis. In these cases, it was thought that microscopic evidence may help to clarify whether vitamin D deficiency was present. More comprehensive sampling of the Ancaster collection was undertaken to elucidate how many individuals who did not display macroscopic evidence of vitamin D deficiency showed microscopic features associated with this condition. The smaller size of this collection and greater ease of acquiring the necessary permissions for destructive analyses made this type of investigation possible. Ribs are considered to be an appropriate element for histological analysis due to their high rate of growth and rapid turnover rates related to high trabecular

bone content (Epker & Frost, 1965), meaning that mineralization defects are likely to develop more quickly in the ribs than in many other elements in response to vitamin D deficiency. Ribs are present in a high number in the skeleton, are often already fragmented in archaeological contexts, and are not often used for other skeletal assessments. For individuals at Ancaster who had no fragments of rib available for sampling, a small portion of another element with high trabecular bone content, such as a vertebral body or fragment of iliac crest, was taken instead. In all cases, sampling was preferentially conducted on elements that were already damaged, in order to reduce the destructive impact of analysis on these collections.

Small sections of rib were cut from larger samples using a hacksaw blade (Ancaster females) or bandsaw (all other samples). Samples were embedded into resin blocks using a methyl methacrylate (MM) resin, with styrene as a stabilizer, and an accelerator or reactive agent. Each sample was placed in an individual glass vial. The bones were dried for a period of 72 hours, using washes of ethyl alcohol (EtOH) changed every 24 hours, in a vacuum dessicator. Following this, the EtOH wash was replaced with a 1:1 solution of EtOH combined with MM, and the samples were allowed to sit in the vacuum dessicator for a further 24 hours. This process was repeated with a solution containing only MM. The MM solution was then replaced by resin.

The resin mixture was prepared by first 'washing' the MM using a separate funnel, rinsing the MM with two successive washes of 5% sodium hydroxide solution, followed by three washes of distilled water, in order to remove any stabilizer. The pH of the MM was then measured, and, if higher than seven (basic), additional washes with distilled

water were performed as needed to lower the pH to seven or below. The MM was then drained through calcium chloride in order to remove any residual water. The final step involved mixing a solution of 95% MM, 5% styrene, and 0.2% accelerator, which was then poured over each sample. The vials were capped and placed in a water bath at 37 degrees C until the resin had set. The hardened embedded blocks of bone were removed by smashing the glass vials.

Sections 3mm in height were cut from each embedded sample using a diamond blade Buehler Isomet 1000 precision saw (Figure 3.2). Parallel and smooth surfaces were created on each sample by polishing the cut surface. Polishing was accomplished by grinding the blocks down in a "figure 8" motion against Buehler Carbimet Paper Discs of

Figure 3.2. Diamond blade Buehler Isomet 1000 precision saw, used to cut sections of embedded rib bone samples for viewing in the SEM.

different grits, in order to remove surface imperfections and remnant grooves from the saw. Samples were polished for three minute intervals using 600 grit pads, followed by 1200 grit pads, and finally 1500 grit pads in combination with diamond polish (Buehler Matadi diamond polishing compound for metallography, 3 microns) and Buehler Metadi Fluid (extender for diamond abrasives). Between steps, the blocks were placed in a sonicator with distilled water in order to clean the surface. Embedding was completed as part of graduate courses in the bioarchaeology of metabolic bone disease run by Dr. Brickley at McMaster in 2013 and 2015. Some samples were polished and underwent scanning electron microscope (SEM) analysis as part of these courses, and others were processed by research assistant Xuan Wei, but the majority were polished and analyzed by the author and research assistant Sarah Timmins.

Many of the samples were affected by taphonomic alteration that was visible microscopically. Pre-screening prior to SEM analysis using a light microscope allowed for the exclusion of any samples from Ancaster with no unaltered bone preserved. Since all of the Isola Sacra individuals sampled displayed some evidence that may be associated with vitamin D deficiency, all samples were analyzed.

Scanning electron microscope analysis was undertaken at the Canadian Center for Electron Microscopy (CCEM) at McMaster University. Each sample surface was coated with carbon to provide a conductive surface. The samples were then affixed to a small strip of metal using double sided tape, and a stripe of nickel paint provided a path from the metal surface to the top of each sample. Each strip of metal was then attached to a metal stub using double sided tape; metal stubs could then be screwed onto the plate on

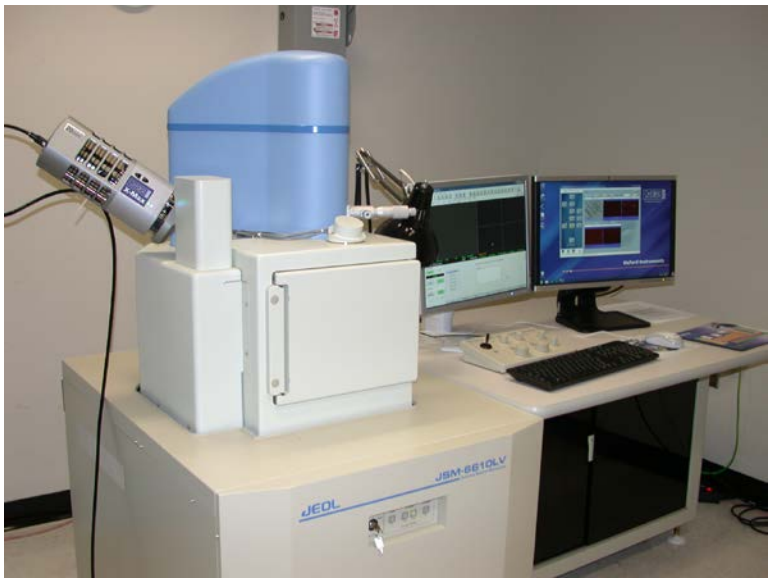


Figure 3.3. JEOL JSM-6610 LV tungsten filament equipped SEM at the CCEM at McMaster University, used in the analysis of embedded samples of rib bone for histological features associated with vitamin D deficiency. Image from https://ccem.mcmaster.ca/.

the SEM stage. Samples were visualized using a JEOL SEM (JEOL JSM-6610LV tungsten filament equipped SEM; Figure 3.3) on backscatter imaging at 15 or 20kV, with a working distance of 11-12mm. Digital backscattered SEM (BSEM) images were collected during examination of each sample at varying magnifications to provide overview images as well as more detailed depictions of any features observed. The preservation of each sample was classified in 25 percent increments based on the amount of unaltered bone present.

Samples were examined for evidence of pathological alterations, including features of abnormal bone resorption, formation, and mineralization. These include large areas of poorly mineralized bone, mineralization defects at cement lines, scalloped edges of bone indicating increased resorption, enlarged osteocyte lacunae, and irregular Haversian systems (Brickley & Ives, 2008). In living patients and therefore in clinical studies, deficiency is indicated microscopically by thick osteoid seams at the mineralization front, as well as buried areas of osteoid or poorly mineralized bone that are

trapped once mineralization resumes, indicating a previous disruption in bone formation. Due to the lack of preservation of osteoid in archaeological bone, thickened osteoid seams can only be detected archaeologically if they are represented by gaps within mineralized bone that would have been filled with osteoid in life. Histological analyses have fallen out of favor with many medical researchers, as sampling bone from living individuals is painful and invasive (Mays, 2012), and may be considered unnecessary due to the availability of biochemical testing for diagnosis. When histological techniques are incorporated, clinical research routinely uses histomorphometry, which allows the quantitative evaluation of bone amounts and ratios of the volume or surface of osteoid to bone (Priemel et al., 2010). Again, due to the lack of preservation of osteoid in archaeological samples, these types of analyses are inaccessible to paleopathologists.

Based on the presence of histological features associated with vitamin D deficiency, samples with sufficient unaltered bone present to evaluate were assigned a classification of probable, possible, or no evidence for deficiency. A designation of probable or possible deficiency typically required multiple features, including consideration of how widespread pathological changes were throughout the sample. Buried mineralization defects in the form of osteoid seams were given increased weight for diagnosis, because thick osteoid seams are considered to be highly suggestive of vitamin D deficiency (Mankin, 1974).

3.2.1.7. Chronic respiratory infections

Features recorded in order to evaluate chronic respiratory infections were limited to those visible macroscopically, and were the same for juvenile and adult individuals

(Appendices A.4 and A.5). For juveniles, additional information was recorded regarding the completeness of the vertebrae, ischium, and pubis, as these elements were not evaluated during the examination of rickets. For the vertebrae, counts were recorded as numbers of vertebral bodies and arches for the cervical, thoracic, and lumbar vertebrae. Completeness of the ischium and pubis were evaluated for each side in increments of 25%.

The current analysis investigated evidence for chronic respiratory infections by evaluating the presence of new bone formation on the visceral surfaces of the ribs. This feature has been correlated with chronic respiratory infections, particularly TB, in documented skeletal collections (Kelley & Micozzi, 1984; Matos & Santos, 2006; Roberts et al., 1994, 1998; Santos & Roberts, 2001, 2006; see Section 2.2.4), typically appearing toward the vertebral end of the upper and middle ribs. Following the establishment of this correlation in documented collections, proliferative lesions on the ribs have been investigated as a criterion of chronic respiratory infection in several archaeological studies (e.g., Baker, 1999; Kelley et al., 1994; Lambert, 2002; Lewis, 2011a; Mays et al., 2002; Nicklisch et al., 2012; Pfeiffer, 1991; Raff et al., 2006; Sledzik & Bellantoni, 1994; Wakely et al., 1991; Wiltschke-Schrotta & Berner, 1999). The presence, quality, and location of new bone formation on the rest of the skeleton was also recorded, due to the potential association of HPO with chronic respiratory disease (Section 2.2.4); this condition is indicated by symmetrical, bilateral deposition of periosteal new bone formation on the mid to distal diaphyses of the tubular bones, especially the lower leg and forearm (Assis et al., 2011). Several paleopathological

studies have considered HPO as a potential indicator of chronic respiratory infection (e.g., Anselmo et al., 2016; Christensen et al., 2013; González-Reimers et al., 2015; Masson et al., 2013; Mays & Taylor, 2002). Additionally, features were chosen to identify changes associated with tuberculosis as a specific chronic respiratory infection likely to have been experienced during this time period, including primarily destructive changes in the vertebrae and major joints of the lower body such as the hip and the knee (Waldron, 2009). More recently identified features, such as more widespread new bone formation in juveniles associated with putative cases of tuberculosis by Lewis (2011a), were also considered.

The numbers of ribs with evidence of new bone formation and abnormal porosity were recorded for left, right, and unsided fragments. Additional information was recorded for any ribs with evidence of new bone formation, indicating the side, type of bone formed (woven, lamellar, or mixed), and the location, both in terms of which surface was affected (visceral or exterior) and the area of the rib affected (angle or shaft). For all cranial and postcranial elements evaluated, space was provided for detailed notes on any features identified as well as any aspects that might affect or qualify how these features should be interpreted.

The numbers of cervical, thoracic, and lumbar vertebrae with evidence for lytic lesions and new bone formation were recorded. If present, the type, location, and features of lesions were recorded. For the spine as a whole, features typical of advanced cases of spinal tuberculosis including kyphosis or posterior thoracic curvature, the collapse of vertebral bodies, and ankylosis or fusion were scored as present or absent. The presence

or absence of lytic lesions, new bone formation, and fusion was also recorded for the left and right innominate.

The long bones were evaluated for the presence or absence of lytic lesions, new bone formation, and ankylosis or fusion, and space was given to indicate any other pathological features that were present. If any of these features were scored as present, additional information was recorded on lesion location (including which element was affected, the location on the element, for example proximal or distal epiphysis and proximal, middle, or distal diaphysis, and the aspect of the bone, for example anterior or posterior and medial or lateral), and for any new bone formation information on the type of bone formed (woven, lamellar, or mixed), indicating whether remodeling had occurred, as well as any observations on the appearance of the new bone formation, was also recorded. Preliminary notes were made at this point regarding whether potential chronic respiratory infection was suspected, with final diagnostic categories being assigned during data analysis (see Section 3.2.2.2).

3.2.2. Methods: Data analysis

Following data collection, each individual was assigned to categories based on age (Sections 3.2.1.1-3.2.1.2), sex (for individuals 16 years and over, see Section 3.2.1.3), and pathological diagnosis for vitamin D deficiency (Sections 3.2.1.4-3.2.1.6) and chronic respiratory infection (Section 3.2.1.7). Criteria for diagnosis were determined based on a consideration of clinical evidence for the skeletal manifestations of these conditions, as well as how these clinically identified features have been utilized in previous paleopathological investigations. Patterns within the data based on differences in age, sex,

and archaeological site between various pathological diagnostic categories were then identified and interpreted.

3.2.2.1. Data analysis: Vitamin D deficiency

For the diagnosis of rickets, criteria used by Mays et al. (2006) were classified into groups based on the strength of evidence they provided for the presence of vitamin D deficiency based on the analysis of Schattmann et al. (2016). Macroscopic criteria were determined to represent probable, possible, or non-diagnostic features of vitamin D deficiency (Table 3.3). Spreadsheets were compiled based on the presence of these criteria, with each criterion scored as present, absent, or unable to evaluate for each individual. Based on these scores, individuals were categorized in terms of the strength of evidence present for possible rickets, with the categories being probable case (1), possible case (2), insufficient data to confirm a diagnosis (3), no evidence for deficiency because features are normal (4), and no evidence for deficiency due to insufficient features present to score (5). Diagnosis of a probable case required at least one probable feature, along with possible and non-diagnostic features. Diagnosis of a possible case generally required multiple possible features, or possible and non-diagnostic features. Cases categorized as having insufficient data generally had only one specific feature associated with vitamin D deficiency, combined in some cases with the presence of non-diagnostic features. This provided a clear category for cases about which there was considerable uncertainty, but still recognizing that pathological changes that may relate to a period of vitamin D deficiency were present. In all cases, the specific combination of features present as well as the severity of the features were very important in determining the strength of the

evidence available for diagnosis, so there were no unalterable rules for determining the diagnostic category to which an individual belonged.

Table 3.3. Macroscopic criteria considered to be probable, possible, and non-diagnostic features for the evaluation of juvenile vitamin D deficiency

Classification	Feature
Probable	Deformed leg bones
	Deformed arm bones
	Long bone general thickening
	Costochondral rib flaring with cupping
	Superior flattening of the femoral metaphysis
	Coxa vara
	Porosis/roughening of bone underlying the growth plates, score of 2+
Possible	Deformed mandibular ramus
	Rib deformity
	Costochondral rib flaring
	Costochondral rib porosity
	Ilium concavity
	Long bone metaphyseal flaring
	Long bone concave curvature porosity
	Porosis/roughening of bone underlying growth plates, score of 1
Non-diagnostic	Cranial vault porosity
	Orbital roof porosity
	Long bone metaphyseal porosity

Individuals placed in categories one and two almost certainly experienced vitamin D deficiency, so probable and possible cases were considered together in all analyses. Slightly greater confidence can be placed in the diagnoses of category one individuals, but the key feature of these cases is more marked skeletal expression of deficiency-associated features. This could be linked to many factors, including the age at which deficiency occurred and the length of time that has passed since the deficiency healed, as well as the severity or duration of deficiency. Individuals in category two had fewer or less well developed lesions, and, despite a slightly lower level of confidence than

category one cases, greater confidence can be placed in these diagnoses than may be implied by the term “possible”.

For individuals displaying no evidence of deficiency, differentiation between categories four and five was based on skeletal completeness. Key areas considered for juveniles were sternal rib ends, growth plates of long bones, and whether enough of long bone diaphyses were present to properly evaluate shape. If one of these areas was absent and the other two were partial or difficult to assess, individuals were placed in category five. For adults, any bone of the skeleton can show pathological changes associated with osteomalacia, so category five was applied only to individuals with only the skull or a few fragments of long bone present. In the consideration of skeletal features in adults that possibly indicate past deficiency, deformity of long bones is a key feature, and the legs are more commonly affected than the arms. As such, individuals were only placed into category five if they did not have two leg bones present that could be assessed for deformity.

Radiographic evidence was also evaluated for some individuals, based on features outlined by Mays et al. (2006). These radiographic criteria were used to support the diagnoses made based on macroscopic evidence, and to evaluate features of the growth plate and metaphysis not visible using other techniques in order to evaluate whether the condition was likely to have been active or healed at the time of death. Similarly, data from SEM analysis of rib samples embedded in methyl methacrylate resin (Section 3.2.1.6) were complementary to the macroscopic evidence primarily used to determine diagnoses. Generally, the presence of histological evidence for vitamin D deficiency was

used to strengthen the certainty of a diagnosis based on macroscopic features. In cases where microscopic features were particularly clear and were present throughout the sample (weighted similarly to a 'probable' macroscopic trait), microscopic evidence alone could support a diagnosis of deficiency.

For individuals in categories one and two, a determination was then made as to whether the condition was likely to have been active or healed at the time of death. Active deficiency was indicated by fraying, roughening, or porosity of the bone underlying the growth plate, visualized either radiographically or through macroscopic observation (Mays et al., 2006). Histological evidence for features of deficiency such as immature or woven bone that is separated from well formed bone, or large areas of incomplete mineralization or resorption, were also considered to indicate active deficiency. Individuals who did not display any indicators of active disease were considered to represent healed cases of deficiency.

For adults, it was necessary to consider vitamin D deficiency that may have been experienced during adulthood, but also evidence that could represent deficiency experienced during childhood. Diagnoses of adult osteomalacia were based upon criteria discussed by Ives and Brickley (2014), while diagnoses of residual childhood deficiency relied on the identification of bending deformities in the long bones and axial skeleton (Brickley & Ives, 2008, p. 110-111). Macroscopic criteria were classified similarly to those evaluated for juveniles (Table 3.4), and the same diagnostic categories were applied for both adult deficiency and residual childhood deficiency. Probable cases of adult deficiency required a clear pseudofracture, while a possible case could be diagnosed

based on possible pseudofractures that are less clear, possibly combined with a lighter or poorer quality of the skeletal material. Probable cases of childhood deficiency in adults could be diagnosed based on clear and marked evidence for bending deformities, especially those in typical areas of the skeleton such as the proximal femoral diaphyses, whereas possible cases were generally diagnosed based on less severe bending deformities, or those that are considered to be less specific to vitamin D deficiency such as bending in the sternum or sacrum. As with juvenile cases of deficiency, the presence of histological evidence for vitamin D deficiency was typically used to strengthen the certainty of a diagnosis based on macroscopic features, but in cases where microscopic features were particularly clear, microscopic evidence alone could support a diagnosis of deficiency.

Table 3.4. Macroscopic criteria considered to be probable, possible, and non-diagnostic features for the evaluation of active and healed vitamin D deficiency in adults

Classification	Feature
Probable (Adult)	Rib fracture with spiculated bone
	Scapula spinous process pseudofracture
	Scapula coracoid process pseudofracture
	Scapula lateral border pseudofracture
	Vertebral body compression fracture (folding, collapse)
	Vertebral lamina pseudofracture
	Inferior pubic rami pseudofracture
	Iliac crest pseudofracture
	Ilium pseudofracture
	Pubic symphysis angulation
	Pseudofracture of the clavicle
	Distal ulna unhealed fracture
	Proximal femur pseudofracture
Possible (Adult)	Healing or unhealed rib fracture
Non-diagnostic (Adult)	Healed rib fractures
	Healed vertebral lamina fracture
	Healed fracture, suspicious area (scapula, pelvis, distal ulna, proximal femur)
Probable/Possible (Childhood - certainty dependent on severity and location)	Sternum bending
	Scapula lateral border curvature
	Anterolateral bending, proximal femur
	Residual bending of long bones

3.2.2.2. Data analysis: Chronic respiratory infections

For the diagnosis of chronic respiratory infections, criteria considered by other paleopathological studies (Sections 2.2.4, 3.2.1.7) were categorized as probable, possible, or non-diagnostic traits based on their diagnostic value (Table 3.5).

Table 3.5. Macroscopic criteria considered to be probable, possible, and non-diagnostic features for the evaluation of chronic respiratory infections

Feature	Classification
Probable	Visceral rib new bone formation – clear, on the vertebral ends
	Vertebral body collapse, with kyphosis and/or ankylosis (classic Pott's spine)
	Vertebral lytic lesions in the anterior thoracic and lumbar vertebral bodies, no new bone formation
	Lytic lesions of the major joints (hip, knee), typical appearance
	New bone formation that is bilateral and symmetrical, localized to the forearm and lower leg (HPO)
Possible	Visceral rib new bone formation that is not completely typical (sternal end, not clear, etc.)
	Vertebral lytic lesions that are not completely typical (some new bone formation, cervical vertebrae or posterior elements, etc.)
	Lytic lesions of the joints that are not completely typical (not in the hip or knee, some new bone formation, etc.)
	New bone formation with some characteristics of HPO, but not completely typical (not symmetrical, not completely bilateral, in locations other than the forearm or lower leg, etc.)
Non-diagnostic	Rib new bone formation that is not localized to the visceral surface, has a different appearance, etc.
	Periosteal new bone formation that does not resemble HPO
	Lytic lesions that are not typical in location or appearance for TB

Based on the presence or absence of these features, individuals were classified as having evidence for probable (1) or possible (2) chronic respiratory infection, insufficient evidence to confirm a diagnosis (3), no evidence because features are normal (4), or no evidence due to insufficient features present to score (5). The primary evidence considered was the presence of new bone formation on the visceral surfaces of the ribs (conditions considered for differential diagnosis in Table 3.6). The presence or absence of

Table 3.6. Conditions considered in the differential diagnosis of proliferative rib lesions

Condition	Lesion Characteristics			
	Location in the Rib Cage	**Location on the Rib**	**Type of New Bone Formation**	**Other Features**
Tuberculosis	Bilateral or unilateral; some studies have noted more common toward the middle of the rib cage	Visceral surface; several studies have noted most common toward the vertebral end	Woven, lamellar, or mixed	In several documented skeletal collections, rib lesions found to be significantly more common in individuals who died of TB; included in general category of chronic respiratory infection
Pneumonia	No noted predilection	Visceral surface; some studies suggest more common toward the sternal end	Some suggestion that bone is more likely to be woven, in accordance with more acute condition	Noted as less likely to impact the skeleton; included in general category of chronic respiratory infection
Bronchitis	No noted predilection	Visceral surface; some studies suggest more common toward the sternal end	Some suggestion that bone is more likely to be woven, in accordance with more acute condition	Included in general category of chronic respiratory infection
Emphysema	No noted predilection	Visceral surface	No noted predilection	Included in general category of chronic respiratory infection
Neoplastic Disease	Widespread in thorax; some studies also note in pelvis	No noted predilection	Some studies document distinct texture of new bone formation, described as “hair-on-end”, “coral-like”, exuberant	
Fungal Infection (Blastomycosis, Pulmonary Aspergillosis, Actinomycosis)	No noted predilection	No noted predilection	May be primarily lytic or mixed osteolytic and osteoblastic lesions	Consider regional factors impacting exposure; ribs can be involved if disease is pulmonary
Treponemal Disease	Ribs as an uncommon site of skeletal involvement	Absence of predilection for visceral surface	Predominantly destructive changes	

Bolded conditions indicate those that are frequently considered in paleopathological differential diagnoses for destructive lesions in the spine.

new bone formation was considered along with other quantitative and qualitative features, including the number of ribs affected, the amount of new bone present, and the type of bone formed, in order to classify each individual. As secondary HOA or HPO can also be

Table 3.7. Conditions considered in the differential diagnosis of proliferative long bone lesions

Condition	Lesion Characteristics			
	Location in the Skeleton	**Location in the Long Bone**	**Type**	**Other Features**
Hypertrophic Osteoarthropathy (Secondary)	Bilaterally symmetrical; diffuse; appendicular tubular bones (long and short); most pronounced distal to the elbow and knee	Several studies suggest most common on mid to distal diaphyses; no involvement of the joints	Single or multiple layers of new bone formation; advanced changes may develop irregular texture or "tree bark" configuration; lack of endosteal changes	Limited or no involvement of axial skeleton
Tuberculosis	Appendicular tubular bones (long and short); suggested as more likely to be unilateral and non-symmetrical	Diaphyses	In hand and foot bones (tuberculous dactylitis), see mixed lytic and blastic changes	Proliferative lesions on the long bones less common than other types of skeletal involvement; more frequent in juveniles
Neoplastic Disease (Metastatic Carcinoma)	Can be widespread; some suggestion that metastases do not generally affect bones distal to the elbow or knee (more commonly axial and proximal appendicular elements)	No noted predilection	Can be widespread new bone formation; may also be lytic or sclerotic lesions; endosteal new bone formation as a common feature	
Hyperparathyroidism (Thyroid Acropachy)	Most commonly confined to the hand and foot bones	No noted predilection	Exuberant proliferative lesions	
Treponemal Disease (Non-gummatous Lesions)	Tubular bones; tibiae as common location; unusual to see marked symmetry or diffuse involvement	Some studies suggest that diaphysis, potentially distal diaphysis, is most commonly affected	New bone formation; associated with endosteal bone formation, obliteration of medullary cavity; may be accompanied by focal areas of necrosis	
Melorheostosis	Long bones, but often also involves pelvis and cranium; usually affects only one element or one limb	No noted predilection	New bone formation can be exuberant; cortical and endosteal involvement	
Hypervitaminosis A, Fluorosis	Long bones, but also affect axial skeleton	No noted predilection	Cortical and endosteal involvement	
Chronic Venous Stasis	Limited to lower extremities (lower legs)	No noted predilection	New bone formation	Most common in older adults

Bolded conditions indicate those that are frequently considered in paleopathological differential diagnoses for destructive lesions in the spine. Other conditions, mentioned by only one or two studies, demonstrate substantial differences from and are unlikely to represent the etiology of lesions examined here (e.g., osteopoikilosis and osteopathia striata, endocrine disturbances such as pituitary tumors, scurvy, and endosteal hyperostosis).

caused by chronic respiratory infections, and paleopathological cases of this condition have previously been associated with biomolecular evidence for chronic respiratory diseases (Section 2.2.4), evidence for HOA in the form of proliferative lesions on the long bones was also considered to represent likely evidence of a chronic respiratory infection (conditions considered for differential diagnosis in Table 3.7).

In diagnosing chronic respiratory infections, analyses considered evidence for specific conditions, primarily TB, as well as evidence for the presence of a chronic infectious process in the lungs more generally. Features associated specifically with the manifestation of skeletal TB were evaluated for adults in the spine (resorptive lesions with minimal bone formation on the anterior thoracic and lumbar bodies, vertebral body collapse and resulting angular kyphosis, possible ankylosis in cases where healing has occurred; conditions considered for differential diagnosis in Table 3.8) and in the major weight-bearing joints (destructive lesions with minimal bone formation, possible ankylosis in cases where healing has occurred, primarily in large weight-bearing joints of the lower body such as the hip and knee; conditions considered for differential diagnosis in Table 3.9), as well as lytic lesions with minimal bone formation in other skeletal elements. For juveniles, widespread new bone formation on the ribs, long bones, bones of the hands and feet (dactylitis), and other elements was considered to be possible evidence for TB, as discussed by Lewis (2011a), in addition to the same types of lytic lesions evaluated for adults.

Table 3.8. Conditions considered in the differential diagnosis of spinal lesions

Condition	Lesion Characteristics			
	Location in Spine	**Location in Vertebra**	**Lesion Type**	**Other Features**
Tuberculosis	Most often mid-lower thoracic and lumbar	Typically anterior vertebral body; involvement of posterior spinal elements uncommon; classically involves 1-4 contiguous vertebrae	Lytic; new bone formation characteristically minimal or absent	More commonly associated with vertebral body collapse, angular kyphosis or gibbus, and ankylosis; frequent extension beneath anterior or posterior longitudinal ligaments
Pyogenic Vertebral Osteomyelitis	Generally lumbar, also thoracic, sacral	Most frequently in vertebral bodies, but also often involves posterior elements; usually single vertebra or two adjacent vertebrae and intervertebral disc	Lytic; often have marked new bone formation as well	Can have anterior wedging and kyphosis, but uncommon that it leads to gibbus formation; some bone loss and localized osteoporosis; more common in adults
Brucellosis	Most often in lumbar	Begins in anterior portions of vertebral bodies at the growth plate; can have simultaneous involvement of several different sites in the spine (non-contiguous vertebrae)	Lytic (Pedro-Pons sign characteristic, erosion at anterosuperior angle of vertebral body with marginal sclerosis); proliferative and reparative changes common and occur simultaneously to destructive changes, often with formation of osteophytes (anterior "parrot's beak" osteophyte characteristic)	Less frequently see vertebral collapse and deformation, but do see ankylosis; spinal involvement most common in older males
Fungal Infections (Aspergillosis, Coccidioidomycosis, Blastomycosis)	Typically favor thoracic, coccidioidomycosis in cervical	Frequent involvement of posterior elements; often in non-contiguous vertebrae	Well-defined lytic lesions, often with marginal sclerosis	Can lead to vertebral collapse, but less common; consider regional and occupational factors affecting exposure (especially for blastomycosis)
Actinomycosis	Most frequently in cervical, can affect any spinal level	Begins on anterior vertebral body, but often involves posterior vertebral elements	Lytic and sclerotic processes; often have new bone formation which can be substantial	Infrequently leads to vertebral body collapse
Echinococcus	No predilection indicated in the literature	Often involves posterior vertebral elements as well as vertebral body; usually limited to a single element	Well-circumscribed lytic lesions	Osseous involvement relatively rare
Neoplastic Disease (Metastatic, Multiple Myeloma, Lymphoma)	Often in thoracic and lumbar	Can affect vertebral bodies; commonly affect posterior elements; multifocal skeletal involvement common	Lytic foci, often associated with sclerosis	
Sarcoidosis	No predilection indicated in the literature	Often multifocal lesions	Lytic	Rare in the vertebrae, more commonly seen in the hands and feet
Scheuermann's Disease	No predilection indicated in the literature	Often involves a larger number of vertebrae	Lytic, no proliferative marginal reaction	

Bolded conditions indicate those that are frequently considered in paleopathological differential diagnoses for destructive lesions in the spine. Other conditions, mentioned by only one or two studies, demonstrate substantial differences from and are unlikely to represent the etiology of lesions examined here (e.g., typhoid spine, histiocytosis, and Paget's disease of bone).

Table 3.9. Conditions considered in the differential diagnosis of joint lesions

Condition	**Lesion Characteristics**		
	Location	**Type**	**Other Features**
Tuberculosis	Most commonly larger weight-bearing joints; typically monoarticular; may affect metaphyses in children	Lytic; no sclerosis or periosteal reaction; often marked destruction of cartilage and articular surface	Characteristically see juxta-articular osteoporosis and narrowing of the articular space; can have ankylosis but with minimal bone formation; deformity frequent; can be associated with secondary pyogenic infection
Pyogenic Osteomyelitis	Sites of residual red marrow; typically single focus		Ankylosis more common
Brucellosis	Larger peripheral joints	Lytic (but relatively rare)	Destructive lesions less common in joints than in the spine
Degenerative Osteoarthritis	Peripheral joints	Lytic aspects less marked, more commonly sclerosis and new bone formation	See subchondral sclerosis, cysts, and bone spurs; do not typically see bone loss or marked destruction of the cartilage or articular surface
Neoplastic Disease (Sarcoma, Adult Leukemia)	Peripheral joints; some studies suggest more common in knees, ankles, and wrists (particularly with leukemia)	Typically both destruction and new bone formation	Not commonly considered

Bolded conditions indicate those that are frequently considered in paleopathological differential diagnoses for destructive lesions in the spine.

3.2.2.3. Data analysis: Quantitative analyses

Mean ages at death were calculated for each site as a whole, as well as for subsets composed of individuals who survived past infancy, individuals who survived past the age of five years, individuals with and without evidence for vitamin D deficiency and

chronic respiratory infections, individuals with active or healed lesions, and male and female adults. Since point estimates of age were required for this calculation, individuals who lacked specific information for age estimation were excluded from this portion of the analysis. T-tests were used to make comparisons between the mean ages at death for these groups, overall age at death distributions were compared using Kolmogorov-Smirnov tests, and age at death distributions for individuals with and without lesions and with active or healed lesions were mapped out using Kaplan-Meier survival curves and compared using Mantel-Cox log rank tests, following DeWitte (2014). These and all other statistical tests were performed using Graphpad Prism 7 software.

In addition to looking at age at death means and distributions in various groups within and between the two sites, the number of individuals surviving to older adulthood was evaluated for the two samples. The proportion of individuals who survived to older adulthood was calculated in relation to the number of individuals in the total population, the number of individuals surviving past infancy, and the number of individuals surviving to adulthood. Differences in each of these proportions between populations were evaluated for statistical significance using chi-square tests.

Crude prevalence rates were calculated for both active and healed vitamin D deficiency and chronic respiratory infections at Ancaster and Isola Sacra. Comparisons were made between the two sites for overall prevalence, prevalence of active and healed lesions, prevalence for male and female adults, and prevalence for juvenile and adult individuals. For all differences observed, statistical significance was evaluated using chi-square tests. To test for associations between the prevalence of cases of vitamin D

deficiency and chronic respiratory infections in each of the two collections, odds ratios were calculated, following Snoddy et al. (2016). Odds ratios can be used as an epidemiological tool to describe the strength of the relationship or non-independence between binary data points (Klaus, 2014), and have recently been used in bioarchaeology as a method for comparing disease prevalence values (Klaus & Tam, 2009).

Crude prevalence values were also calculated for individuals displaying proliferative lesions on the visceral surfaces of the ribs at Ancaster and Isola Sacra. For individuals with evidence for these lesions, the mean number of ribs affected was calculated for each site as a whole and for those with active, healing, and healed lesions in each collection. T-tests were used to compare the means between sites (overall, active, healing, and healed) as well as for individuals with active, healing, and healed lesions within each site. The distributions of the number of ribs affected for each individual with rib lesions were compared between sites using a Kolmogorov-Smirnov test. Mean age at death was also calculated for each of the above groups; means were compared using t-tests, and age at death distributions were compared using Kolmogorov-Smirnov tests, following DeWitte (2014).

3.3. Addressing Limitations in Skeletal Evidence for Disease

Extrapolating from skeletal evidence for pathological conditions to experiences of disease in the population as a whole can be problematic, given significant problems with the representativeness of skeletal samples. These issues range from specific biases toward recognition of conditions that are chronic, longstanding, or severe, and those that affect

the skeleton rather than only soft tissue (Schultz, 2012), to the overall nature of these assemblages, which are made up of dead individuals (Wood et al., 1992). These limitations make it clear that absence of evidence cannot be assumed to indicate evidence of absence, and there will be no difference in appearance between individuals who do not display evidence for lesions because they died of an acute illness before a skeletal response could be mounted and those who did not experience disease (Wood et al., 1992). Snoddy et al. (2016) conceptualize skeletal cases of vitamin D deficiency as the "extreme end of a spectrum of morbidity associated with negative health outcomes" (p. 1), acknowledging that there will have been many other individuals in the population with less severe states of deficiency or insufficiency, who may have experienced negative health effects associated with this, but who are also likely to be invisible archaeologically. However, they do not appear to consider issues of representation. If individuals who display skeletal manifestations of vitamin D deficiency are experiencing disease that is more severe, chronic, or longstanding, or occurred during a period of more rapid growth, than individuals who may have had low serum vitamin D without developing skeletal lesions, then can they be considered representative of all vitamin D deficient individuals in the population? Similarly, can individuals with skeletal evidence for chronic respiratory infections be considered representative of the larger group of individuals experiencing these conditions in the living population? One way to access information on subtler evidence for vitamin D deficiency that has not yet manifested macroscopically in the skeleton may be through the use of histological investigation. This analysis attempted to evaluate subtle microscopic evidence for vitamin D deficiency at Ancaster by sampling

ribs from all individuals in the assemblage for investigation using SEM. However, the usefulness of this technique was greatly impacted by poor microscopic preservation in the ribs of many individuals; while additional information on possible vitamin D deficiency could be gleaned for some individuals from this site, the majority could not be properly evaluated. At sites with excellent microscopic preservation, SEM analysis can provide a more comprehensive picture of sub-macroscopic changes associated with vitamin D deficiency. Examination of teeth for interglobular dentine represents another technique for detecting cases of childhood deficiency when skeletal indicators are not clear or have remodeled, and has recently been applied to archaeological skeletal material (D'Ortenzio et al., 2016).

The elucidation of disease interactions and relationships based on paleopathological evidence is necessarily restricted to individuals who have developed skeletal lesions that remain visible at the time of death. Individuals with skeletal involvement represent severe and longstanding cases of both vitamin D deficiency and chronic respiratory infections, and many other individuals in both samples would have experienced either or both conditions without developing skeletal manifestations, remaining archaeologically invisible. Additionally, deformities that develop as a result of vitamin D deficiency can remodel; based on a number of German studies in the late 19th and early 20th centuries, Hess (1929) estimates that bowing deformities resolved in roughly 75% of children, usually by the age of five or six years. Similar to the suggestion made by Snoddy et al. (2016) that subadult vitamin D deficiency is representative of deficiency levels in the population as a whole, Gokhale et al. (2003) have suggested that

the presence of infectious disease in children within modern populations suggests that these diseases are endemic. This also relates to the TB-specific assertion that pediatric disease can be conceptualized as a sentinel event reflecting recent transmission within the community, with those children in whom disease becomes latent representing an important reservoir for future fulminant disease (Feja & Saiman, 2005). The importance of childhood cases of disease is acknowledged within both modern and paleopathological studies. In the case of vitamin D deficiency, Snoddy et al. (2016) go so far as to suggest that considering subadult disease can partially compensate for the large proportion of paleopathologically invisible individuals who may still have experienced vitamin D deficiency. Since the majority of evidence for healed vitamin D deficiency relates to deformities that are most likely to represent childhood disease, prevalence values for healed vitamin D deficiency do reflect the occurrence of childhood skeletal involvement in this condition. In addition to individuals who experienced only vitamin D deficiency or chronic respiratory infections in such a way that skeletal lesions did not develop, there are probably also individuals who did not develop skeletal lesions associated with chronic respiratory infections because of vitamin D deficiency (Section 5.1).

Several recent publications have critiqued traditional approaches to quantitative analysis in paleopathology. Authors have suggested that bioarchaeologists need to go beyond simple counts of pathologies (DeWitte, 2014), and have stressed the importance of considering age-at-death distributions and their influence on disease prevalence (Klaus, 2014). In contrast to approaches that detect and analyze differences in the presence and frequency of lesions, Wilson (2014) advocates for approaches that aim to model

individuals' entry into the death assemblage, framing skeletal lesions as possible covariates of mortality and attempting to understand whether and how the etiologies of these lesions may have influenced individuals' deaths at particular ages. Traditional approaches that assess the frequency of pathological lesions and test for significant differences within and between skeletal samples are suggested to possibly conflate the effects of demographic and epidemiological processes, which can be more meaningfully assessed using statistical approaches that evaluate the relationship between age at death and the presence of skeletal lesions (Wilson, 2014).

In the analysis of evidence for disease in the past, many studies focus on the assessment of quantitative data, whether this is a traditional "frequentist" (Wilson, 2014, p. 272) approach to counting lesions and calculating disease prevalence or more sophisticated statistical analyses of lesion patterns according to variables such as age and sex. Fewer studies discuss variation in qualitative features of skeletal lesions between or within skeletal assemblages. While both types of data are important, it is crucial to differentiate what each can be taken to represent, and what types of questions each can therefore be used to address. Quantitative data speak to disease occurrence within and between populations, and statistical analyses of the presence or absence of skeletal lesions can be used to address disease occurrence and potential variation in disease risk based on factors like sex or age at death. Qualitative results, on the other hand, speak more to the consequences of disease experienced by individuals, and can therefore be used to address not just whether or not disease occurred, but how it was actually experienced by individuals living in past populations. Considering evidence for disease in the past as

more complex than simply presence or absence can reveal variation in lesion expression that may relate to important differences in disease experience for past individuals.

The results of both traditional "frequentist" and likelihood approaches to the quantitative evaluation of skeletal lesions associated with vitamin D deficiency and chronic respiratory infections at Isola Sacra and Ancaster demonstrate the degree to which method choice can influence data interpretations. Critics of frequency-based approaches in paleopathology have correctly identified that these methods can essentialize differences between samples, potentially conflating the effects of demographic processes, and missing variation in disease experience that may relate to the presence of subgroups within the sample that exhibit heterogeneity in frailty as outlined by Wood et al. (1992). More sophisticated statistical methods that aim to evaluate the relationship between pathological lesions and survival or longevity can add depth to interpretations by considering how apparent differences in lesion frequency may be affected by variation in the age structure of the samples being considered. However, these methods are more easily and usefully applied to some types of samples than others. The use of methods that account for age at death require the generation of a point estimate for age at death for each individual. In poorly preserved skeletal samples, such analyses may necessarily exclude a large number of individuals. This can be particularly problematic given that certain individuals, including those in the oldest age categories and those with pathological conditions that impact skeletal strength, like vitamin D deficiency, are more likely to be poorly preserved, and therefore to be missing features required for age estimation. Analyses that exclude these individuals may therefore be cutting out valuable

information related to disease experience within the population. This suggests that the correct response may not be to reject "frequentist" approaches altogether, but rather to acknowledge that there is value in both types of analyses, that both are limited in different ways, and that interpretations made using each should reflect this. At Ancaster and Isola Sacra, consideration and analysis of overall lesion frequencies, age-at-death distributions, qualitative differences in lesion appearance, and statistical measurements of the impact of skeletal lesions on survival and relationships between different types of lesions for vitamin D deficiency and chronic respiratory infections are combined to yield meaningful information on the occurrence and experience of both conditions, as well as potential interactions between the two, in these samples.

CHAPTER 4 – Results

4.0. Introduction

Skeletal features associated with age and sex estimation, as well as with the evaluation of vitamin D deficiency and chronic respiratory infections, were assessed for human skeletal material from Isola Sacra and Ancaster (as outlined in Chapter 3). After excluding individuals represented by only a cranium (adults) or hand and foot bones (juveniles and adults; Section 3.2.1), the analyzable Isola Sacra assemblage consisted of 823 individuals (447 juveniles and 376 adults; Table 4.1), and the analyzable Ancaster assemblage consisted of 276 individuals (94 juveniles and 182 adults; Table 4.1). This chapter outlines the results of this analysis, including age at death estimation, sex estimation, patterns in the occurrence of vitamin D deficiency and chronic respiratory infections, and relationships between skeletal features associated with the two conditions.

4.1. Age and Sex

Features related to aging and sexual dimorphism in the skeleton were evaluated (as outlined in Sections 3.2.1.1 to 3.2.1.3) in order to estimate age for all individuals and sex for individuals over the age of 16 in the Ancaster and Isola Sacra collections. The age and sex estimates generated provide basic demographic information for both assemblages, and contextualize observations made for skeletal evidence of vitamin D deficiency and chronic respiratory infections.

4.1.1. Age at death distribution

Following the assessment of features relevant to skeletal age estimation (Sections 3.2.1.1 and 3.2.1.2), age categories were assigned for 823 individuals from Isola Sacra, and for 276 individuals from Ancaster (Table 4.1).

Table 4.1. Age category designations for Isola Sacra and Ancaster juveniles and adults

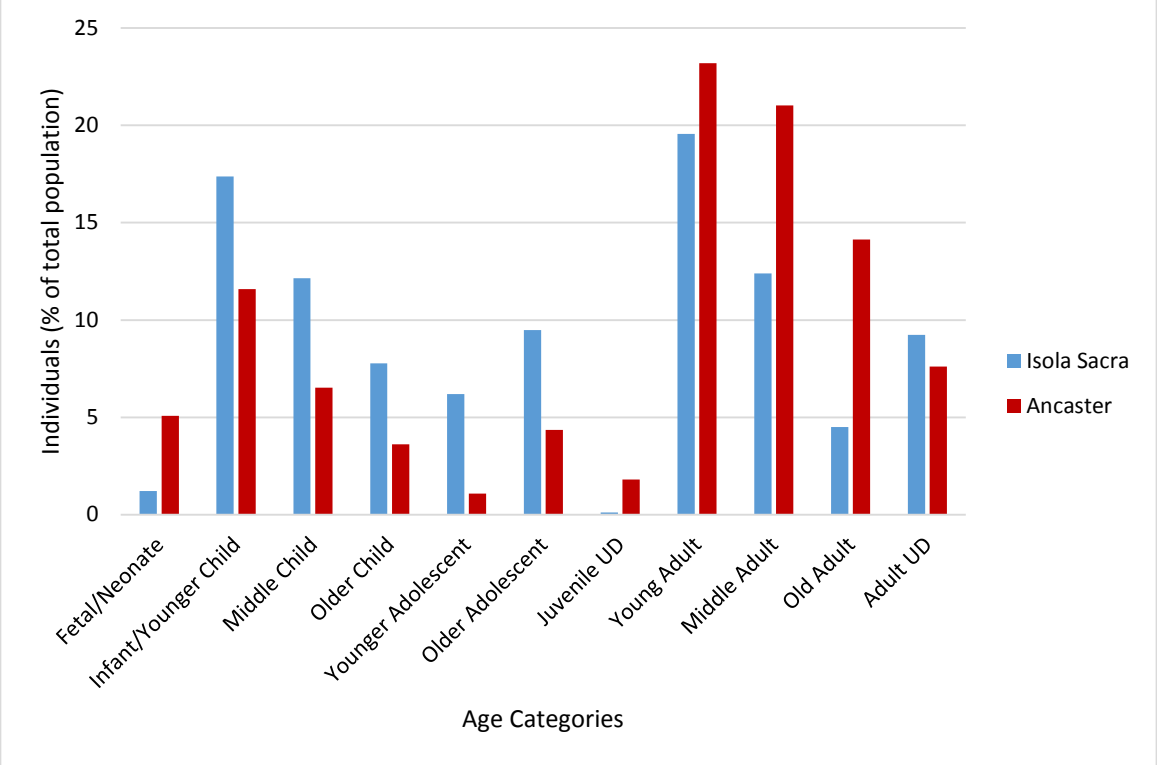
Age Category		**Individuals (Isola Sacra)**	**Individuals (Ancaster)**
Juvenile	Fetal/Neonate	10 (1.22%)	14 (5.07%)
	Infant/Younger child	143 (17.38%)	32 (11.59%)
	Middle Child	100 (12.15%)	18 (6.52%)
	Older Child	64 (7.78%)	10 (3.62%)
	Younger Adolescent	51 (6.20%)	3 (1.09%)
	Older Adolescent	78 (9.48%)	12 (4.35%)
	Juvenile (Undetermined)	1 (0.12%)	5 (1.81%)
	Juvenile Total	**447 (57.96%)**	**94 (34.06%)**
Adult	Young Adult	161 (19.56%)	64 (23.19%)
	Middle Adult	102 (12.39%)	58 (21.01%)
	Old Adult	37 (4.50%)	39 (14.13%)
	Adult (Undetermined)	76 (9.23%)	21 (7.61%)
	Adult Total	**376 (45.69%)**	**182 (65.94%)**
	TOTAL	**823**	**276**

Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years). Percentages listed after counts are expressed as a fraction of the sample as a whole.

Age at death distributions for Isola Sacra and Ancaster are significantly different (Kolmogorov-Smirnov D 0.2884, $p < 0.0001$). A significantly greater ($p < 0.0001$) proportion of individuals at Isola Sacra can be placed in juvenile than in adult age categories (Figure 4.1), while a significantly greater ($p < 0.0001$) proportion of Ancaster individuals are aged as adults than as juveniles. The proportion of individuals who survived to older adulthood is significantly smaller at Isola Sacra than at Ancaster. This holds true if the number of individuals who died as old adults is examined in relation to

the number of individuals in the total sample ($p < 0.0001$; Table 4.1), the number of individuals surviving past the age of three (5.52% at Isola Sacra vs. 14.50% at Ancaster, $p < 0.0001$), or the number of individuals surviving to adulthood (9.84% at Isola Sacra vs. 21.43% at Ancaster, p 0.0003). Mean age at death is lower overall at Isola Sacra than at Ancaster; this holds true for the sample as a whole, for individuals who survived past the age of five years, and for males and females (Table 4.2).

Figure 4.1. Distribution of individuals by estimated age at death



Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Juvenile UD (juvenile of undetermined age), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years), Adult UD (adult of undetermined age).

Table 4.2. Age at death population means, standard deviations, and sample sizes

Sample	Mean Age at Death ± SD (N), years		Mean Difference P Value
	Isola Sacra	Ancaster	
Total Sample	23.07 ± 16.86 (581)	30.12 ± 21.77 (239)	**< 0.0001**
Individuals > 5	27.30 ± 15.35 (482)	37.54 ± 18.06 (190)	**< 0.0001**
Males	33.08 ± 14.69 (146)	40.39 ± 15.90 (98)	**0.0003**
Females	32.00 ± 13.00 (161)	40.23 ± 17.40 (74)	**<0.0001**

Abbreviations used are SD (standard deviation), N (number of individuals). Individuals included in these calculations are those for whom a point estimate could be generated for age at death. Males include individuals identified as male and probable male, and females include individuals identified as female and probable female. P values given are for comparisons between the two sites. Statistically significant values are bolded.

In both samples, infants are the best represented juvenile age group, and young adults are the best represented adult age group. Specific age estimates could be generated for a higher proportion of juveniles than adults in both samples, so individuals categorized as undetermined represent a smaller percentage of juveniles, for whom multiple lines of specific evidence related to skeletal development and growth are potentially available, than of adults. Despite generally better preservation at Ancaster, the number of individuals for whom age at death could not be estimated (undetermined categories) is similar as a proportion of the total sample for both Isola Sacra and Ancaster (Table 4.1).

4.1.2. Sex Estimation

Following the assessment of skeletal features relevant to sex estimation (Section 3.2.1.3), sex could be estimated for 325 individuals from Isola Sacra and 183 individuals from Ancaster (Table 4.3).

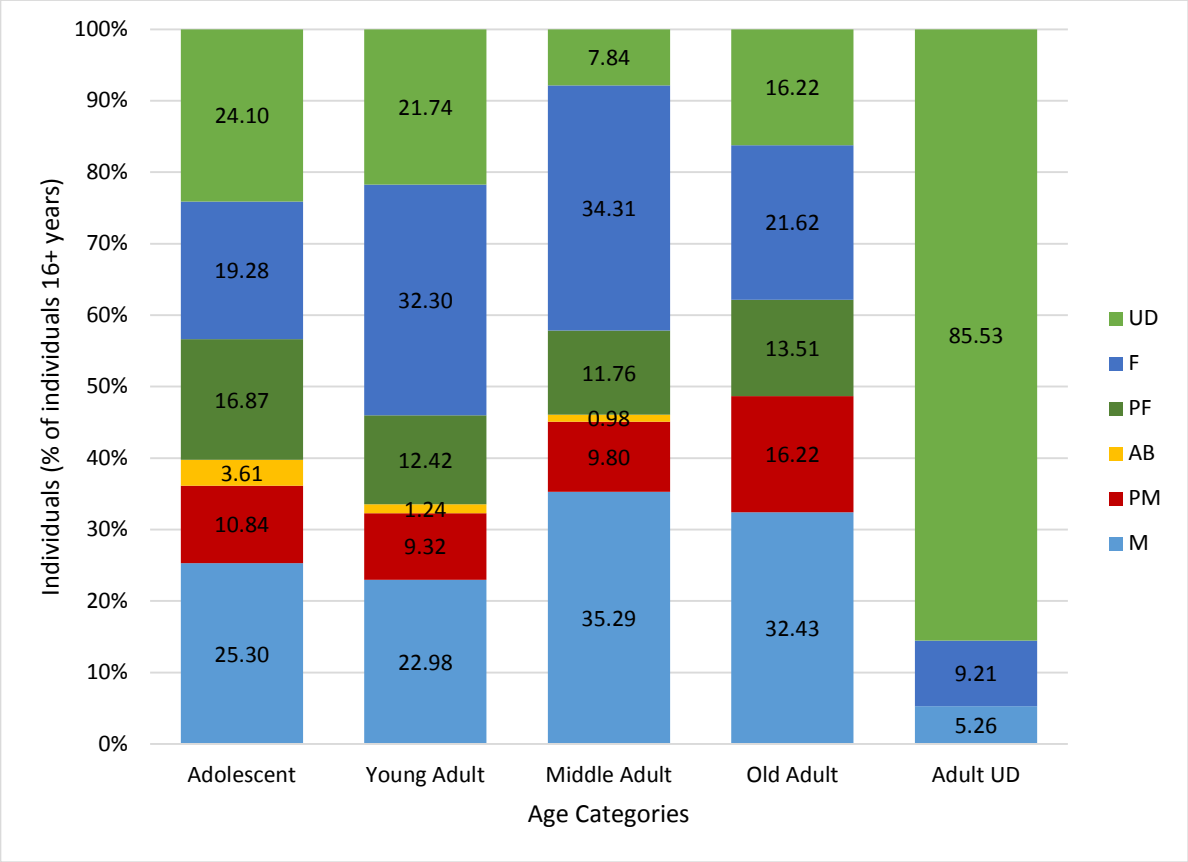
Table 4.3. Sex estimations for individuals 16 years and over from Isola Sacra and Ancaster

Sex Category	Individuals (Isola Sacra)	Individuals (Ancaster)
Male	110 (23.97%)	65 (33.33%)
Probable Male	40 (8.71%)	38 (19.49%)
Ambiguous	6 (1.31%)	1 (0.51%)
Probable Female	51 (11.11%)	26 (13.33%)
Female	118 (25.71%)	53 (27.18%)
Total for Sexed Skeletal Sample	**325 (70.81%)**	**183 (93.85%)**
Undetermined	134 (29.19%)	12 (6.15%)

Percentages listed after counts are expressed as a fraction of the total number of individuals 16 years and over (n = 459 for Isola Sacra and 195 for Ancaster).

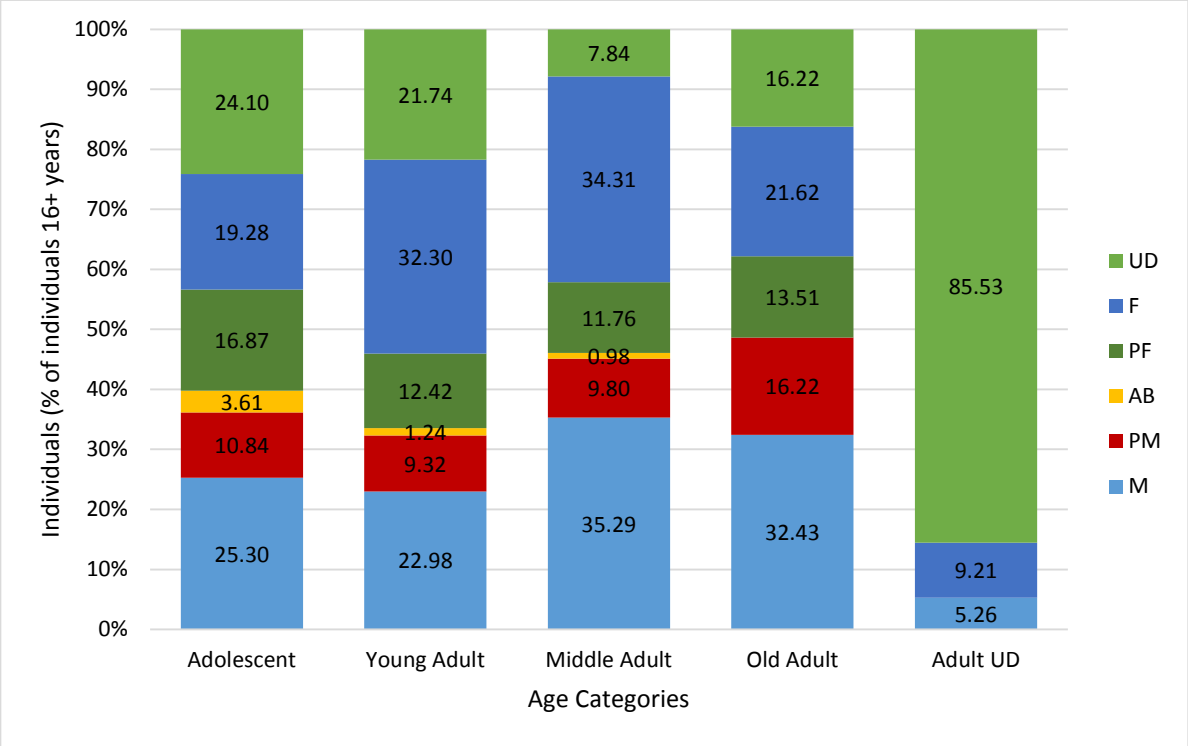
A greater percentage of individuals in all age categories are classified as undetermined at Isola Sacra (Figure 4.2) than at Ancaster (Figure 4.3), indicating that sex could not be reliably estimated for these individuals; this difference is significant ($p < 0.05$) for all age categories except older adolescents, and is most likely a reflection of poorer preservation at this site compared to Ancaster. The overall numbers of individuals sexed as male and female do not differ significantly between the two samples, although a significantly greater percentage of young adults are identified as male at Ancaster than at Isola Sacra ($p < 0.01$). In both samples, the mean ages at death for males and females are similar (Table 4.2).

Figure 4.2. Distribution of Isola Sacra individuals 16 years and older by estimated age at death and sex



Older adolescent (16-19 years), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years), Adult UD (adult of undetermined age). Sex categories are abbreviated as UD (undetermined), F (female), PF (probable female), AB (ambiguous), PM (probable male), M (male). Exact values for the percentage of individuals in each sex category are represented by the numbers within each section of each column.

Figure 4.3. Distribution of Ancaster individuals 16 years and older by estimated age at death and sex



Older adolescent (16-19 years), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years), Adult UD (adult of undetermined age). Sex categories are abbreviated as UD (undetermined), F (female), PF (probable female), AB (ambiguous), PM (probable male), M (male). Exact values for the percentage of individuals in each sex category are represented by the numbers within each section of each column.

4.2. Vitamin D Deficiency

The evaluation of macroscopic, radiographic, and microscopic features as outlined in Sections 3.2.1.4 and 3.2.1.5 enabled the assignation of a vitamin D deficiency diagnosis (Categories 1-4; Section 3.2.2.1) for 307 juveniles and 370 adults from Isola Sacra (n = 656) and for 83 juveniles and 182 adults from Ancaster (n = 265). Patterns of occurrence were analyzed based on age at death, sex, and archaeological site.

4.2.1. Vitamin D deficiency: Patterns based on age at death

Overall prevalence values for evidence of vitamin D deficiency are similar between the two sites (Table 4.4), but the value for juveniles is significantly higher at Ancaster than at Isola Sacra (p 0.018). The prevalence of lesions is significantly higher in juveniles than in adults at Ancaster (p 0.01), while at Isola Sacra the prevalence of lesions is similar in juveniles and adults.

Table 4.4. Prevalence of skeletal evidence for active and healed vitamin D deficiency

Age Category		**Active Deficiency**	**Healed Deficiency**	**Total**
Isola Sacra	Fetal/Neonate	0/1 (0.00%)	0/1 (0.00%)	0/1 (0.00%)
	Infant/Younger Child	4/76 (5.26%)	6/76 (7.89%)	10/76 (13.16%)
	Middle Child	0/64 (0.00%)	2/64 (3.13%)	2/64 (3.13%)
	Older Child	0/47 (0.00%)	6/47 (12.77%)	6/47 (12.77%)
	Younger Adolescent	0/42 (0.00%)	1/42 (2.38%)	1/42 (2.38%)
	Older Adolescent	0/77 (0.00%)	4/77 (5.19%)	4/77 (5.19%)
	Juvenile UD	0/0 (0.00%)	0/0 (0.00%)	0/0 (0.00%)
	Juvenile Total	**4/307 (1.30%)**	**19/307 (6.19%)**	**23/307 (7.49%)**
	Young Adult	3/160 (1.88%)	11/154 (7.14%)	14/160 (8.75%)
	Middle Adult	2/101 (1.98%)	3/100 (3.00%)	5/101 (4.95%)
	Old Adult	0/37 (0.00%)	1/37 (2.70%)	1/37 (2.70%)
	Adult UD	0/72 (0.00%)	1/58 (1.72%)	1/72 (1.39%)
	Adult Total	**5/370 (1.35%)**	**16/349 (4.58%)**	**21/370 (5.68%)**
	TOTAL	**9/677 (1.33%)**	**35/656 (5.34%)**	**44/677 (6.50%)**
Ancaster	Fetal/Neonate	2/14 (14.29%)	0/14 (0.00%)	2/14 (14.29%)
	Infant	5/28 (17.86%)	4/28 (14.29%)	9/28 (32.14%)
	Younger Child	0/15 (0.00%)	2.15 (13.33%)	2/15 (13.33%)
	Older Child	0/8 (0.00%)	1/8 (12.5%)	1/8 (12.5%)
	Adolescents	0/15 (0.00%)	0/15 (0.00%)	0/15 (0.00%)
	Juvenile UD	0/3 (0.00%)	0/3 (0.00%)	0/3 (0.00%)
	Juvenile Total	**7/83 (8.43%)**	**8/83 (9.64%)**	**14/83 (16.87%)**
	Young Adult	0/64 (0.00%)	1/62 (1.61%)	1/64 (1.56%)
	Middle Adult	1/58 (1.72%)	6/56 (10.71%)	7/58 (12.07%)
	Old Adult	1/39 (2.56%)	1/38 (2.63%)	2/39 (5.13%)
	Adult UD	0/21 (0.00%)	1/20 (5.00%)	1/21 (4.76%)
	Adult Total	**2/182 (1.10%)**	**9/176 (5.11%)**	**11/182 (6.04%)**
	TOTAL	**8/265 (3.02%)**	**17/259 (6.56%)**	**25/265 (8.30%)**

Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years). The numbers in each cell indicate the number of individuals, withthe values in parentheses representing these values as a percentage of observable individuals

A greater proportion of individuals were placed into category five at Isola Sacra than at Ancaster (Table 4.5), indicating that they could not be evaluated for skeletal features of vitamin D deficiency. This difference is significant for the evaluation of deficiency in children and the evaluation of healed deficiency in adults ($p < 0.0001$), and likely relates to poorer preservation at this site. A significantly greater number of individuals were placed into category three at Ancaster than at Isola Sacra (p 0.0001), indicating that there was some evidence of deficiency that was insufficient to support a diagnosis.

At Isola Sacra, the total number of healed cases of vitamin D deficiency was significantly higher than the number of active cases (Figure 4.4; p 0.0003), whereas at Ancaster (Figure 4.5) there was no significant difference between the numbers of healed and active cases of deficiency. At Isola Sacra, the prevalence of healed deficiency is also significantly higher than active deficiency in older children (p 0.03). No significant differences exist between Ancaster and Isola Sacra for the prevalence values of healed or active disease in any age category, although the higher prevalence value for healed deficiency in middle adults at Ancaster in comparison to Isola Sacra approaches significance (p 0.07).

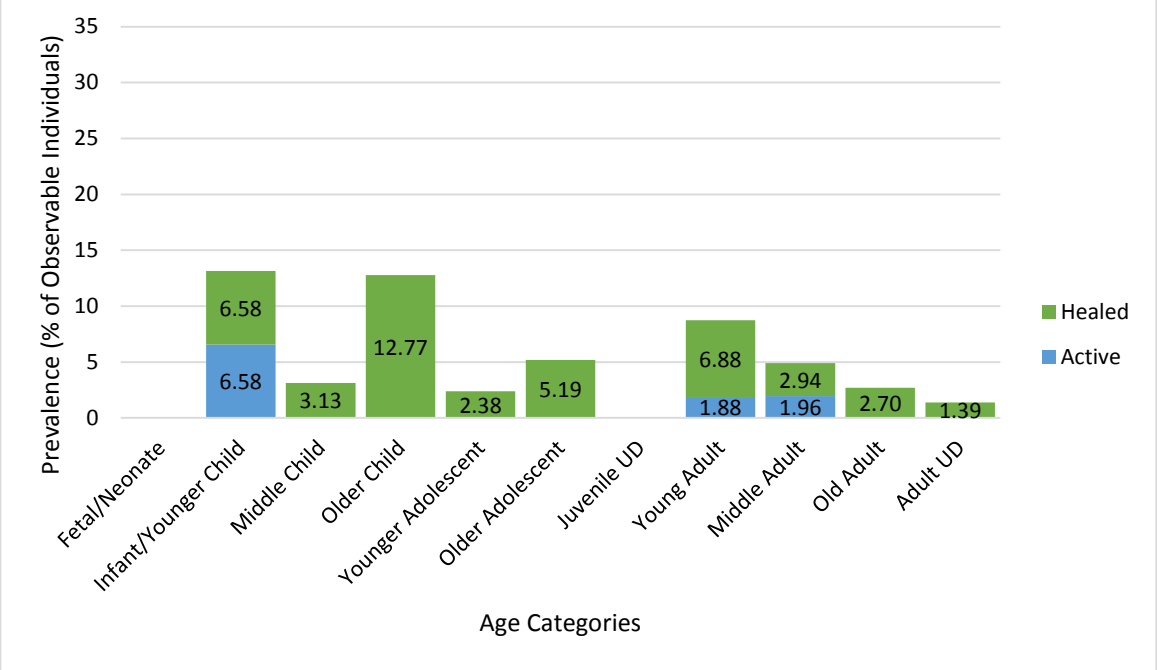
Table 4.5. Vitamin D deficiency diagnostic category breakdown by age for juvenile and adult individuals from Isola Sacra and Ancaster

Age Category		Total	Category 5	Observable	Diagnosis			
					1	2	3	4
Isola Sacra	Fetal/Neonate	10	9/10 (90.00%)	1	0/1 (0.00%)	0/1 (0.00%)	0/1 (0.00%)	1/1 (100.00%)
	Infant/Younger Child	143	67/143 (46.85%)	76	4/76 (5.26%)	6/76 (7.89%)	16/76 (21.05%)	50/76 (65.79%)
	Middle Child	100	36/100 (36.00%)	64	2/64 (3.12%)	0/64 (0.00%)	4/64 (6.25%)	58/64 (90.63%)
	Older Child	64	17/64 (26.56%)	47	3/47 (6.38%)	3/47 (6.38%)	2/47 (4.26%)	39/47 (82.98%)
	Younger Adolescent	51	9/51 (17.65%)	42	0/42 (0.00%)	1/42 (2.38%)	0/42 (0.00%)	41/42 (97.62%)
	Older Adolescent	78	1/78 (1.28%)	77	2/77 (2.60%)	2/77 (2.60%)	1/77 (1.30%)	72/77 (93.51%)
	Juvenile UD	1	1/1 (100.00%)	0	0/0 (0.00%)	0/0 (0.00%)	0/0 (0.00%)	0/0 (0.00%)
	Young Adult	161	1/161 (0.62%)	160	2/160 (1.25%)	12/160 (7.50%)	1/160 (0.63%)	145/160 (96.25%)
	Middle Adult	102	0/102 (0.00%)	102	1/102 (0.98%)	4/102 (3.92%)	5/102 (4.90%)	92/102 (90.20%)
	Old Adult	37	0/37 (0.00%)	37	0/37 (0.00%)	1/37 (2.70%)	1/37 (2.70%)	35/37 (94.59%)
	Adult UD	76	4/76 (5.26%)	72	1/72 (1.39%)	0/72 (0.00%)	0/72 (0.00%)	71/72 (98.61%)
	TOTAL	**823**	**145/823 (17.62%)**	**678**	**15/678 (2.21%)**	**29/678 (4.28%)**	**30/678 (4.42%)**	**604/678 (89.09%)**
Ancaster	Fetal/Neonate	14	0/14 (0.00%)	14	1/14 (7.14%)	1/14 (7.14%)	5/14 (35.7%)	7/14 (50.00%)
	Infant/Younger Child	31	3/31 (9.68%)	28	4/28 (14.29%)	5/28 (17.86%)	7/28 (25.00%)	12/28 (42.86%)
	Middle Child	18	3/18 (16.67%)	15	1/15 (6.67%)	1/15 (6.67%)	3/15 (20.00%)	10/15 (66.67%)
	Older Child	10	2/10 (20.00%)	8	0/8 (0.00%)	1/8 (12.50%)	0/8 (0.00%)	7/8 (87.50%)
	Younger Adolescent	3	0/3 (0.00%)	3	0/3 (0.00%)	0/3 (0.00%)	1/3 (33.33%)	2/3 (66.67%)
	Older Adolescent	12	0/12 (0.00%)	12	0/12 (0.00%)	0/12 (0.00%)	1/12 (8.33%)	11/12 (91.67%)
	Juvenile UD	5	2/5 (40.00%)	3	0/3 (0.00%)	0/3 (0.00%)	0/3 (0.00%)	3/3 (100.00%)
	Young Adult	64	0/64 (0.00%)	64	0/64 (0.00%)	1/64 (1.56%)	3/64 (4.69%)	60/64 (93.75%)
	Middle Adult	58	0/58 (0.00%)	58	3/58 (5.17%)	4/58 (6.90%)	7/58 (12.07%)	44/58 (75.86%)
	Old Adult	39	0/39 (0.00%)	39	1/39 (2.56%)	1/39 (2.56%)	7/39 (17.95%)	30/39 (76.92%)
	Adult UD	21	0/21 (0.00%)	21	1/21 (4.76%)	0/21 (0.00%)	2/21 (9.52%)	18/21 (85.71%)
	TOTAL	**275**	**10/275 (3.64%)**	**265**	**11/265 (4.15%)**	**14/265 (5.28%)**	**36/265 (13.58%)**	**204/265 (76.98%)**

Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years). Diagnostic categories are outlined in 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate). The numbers in each cell indicate the number of individuals, with the values in parentheses representing these values as a percentage of observable individuals (diagnostic categories 1-4) or of all individuals present (category 5).

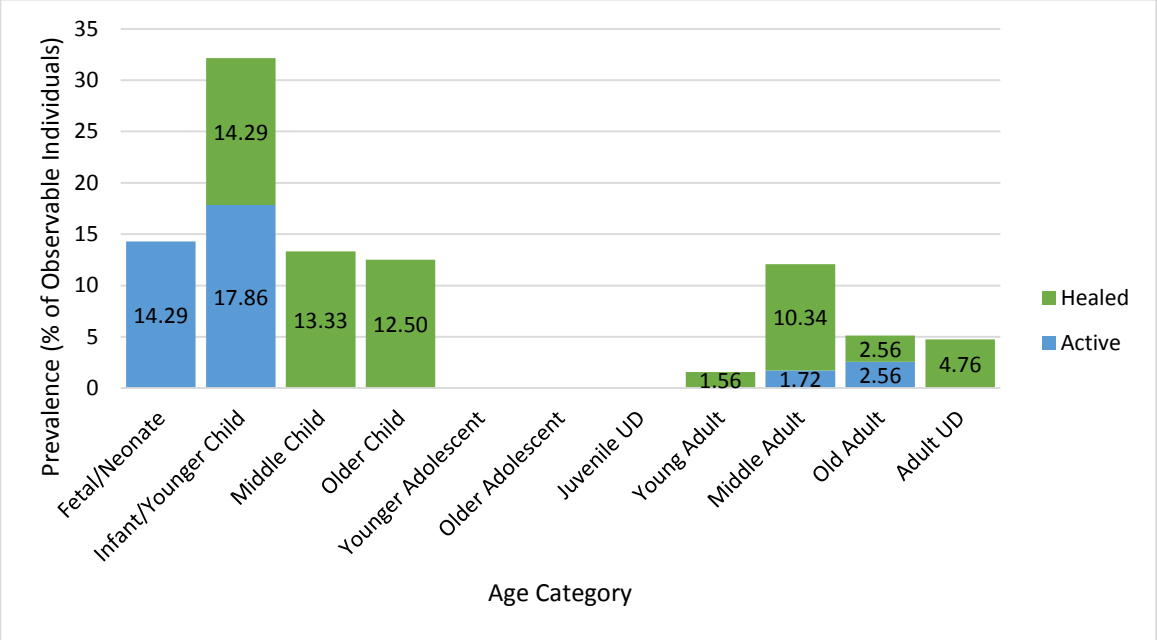
The prevalence of active cases of juvenile vitamin D deficiency is significantly higher at Ancaster than at Isola Sacra (p 0.005). It is most important to consider active juvenile deficiency in the subset of each sample aged as neonates, infants, and younger children, who are growing quickly and are most likely to experience active deficiency that manifests in the skeleton. At Ancaster, seven of the 57 individuals (12.28%) in these categories display evidence for active deficiency, while at Isola Sacra only five of the 141 individuals (3.55%) in these categories represent active cases. The prevalence of active juvenile vitamin D deficiency in the age categories in which active deficiency would be expected is therefore significantly higher at Ancaster (p 0.042).

Figure 4.4. Prevalence of active and healed vitamin D deficiency by estimated age at death for Isola Sacra



Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Juvenile UD (juvenile of undetermined age), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years), Adult UD (adult of undetermined age). Exact values for the percentage of individuals in each age category are represented by the numbers within each section of each column.

Figure 4.5. Prevalence of active and healed vitamin D deficiency by estimated age at death for Ancaster



Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years), UD (undetermined). Exact values for the percentage of individuals in each age category are represented by the numbers within each section of each column.

At both sites, the highest prevalence of evidence for vitamin D deficiency is found in individuals who died as infants and younger children (Figures 4.4 and 4.5). Active childhood deficiency is seen in the infant or younger child (both sites) and fetal or neonatal categories (Ancaster), with middle and older children (both sites) and adolescents (Isola Sacra; there are no cases in the small number of individuals who died as adolescents at Ancaster) only displaying evidence of healed deficiency. For individuals who survived to adulthood, healed deficiency is most often seen in young adults at Isola Sacra, but in middle adults at Ancaster. The pattern of adult deficiency also differs

between the two sites, with evidence for active deficiency present in those who died during young and middle adulthood at Isola Sacra, but in individuals who died during middle and old adulthood at Ancaster.

Within the group of individuals who could be assessed for the presence of active and healed vitamin D deficiency in each sample, mean age at death is significantly lower in individuals with deficiency than those without deficiency at Ancaster (Table 4.6). At this site there is also a significant difference between the age at death distributions of individuals with and without vitamin D deficiency lesions (active and healed), as indicated by Kaplan-Meier survival analysis (Mantel-Cox p 0.03), indicating that the presence of lesions has a negative effect on survival in this sample. At Isola Sacra, there are no significant differences in mean age at death between individuals with category one and two diagnoses and those without evidence for deficiency; age at death differences only become significant if individuals in category three are included (Table 4.6). Within the group of individuals who can be diagnosed as representing cases of vitamin D deficiency at Isola Sacra, there is a significant difference in mean age at death between those placed in categories one and two (Table 4.6).

Table 4.6. Age at death for individuals with and without evidence for healed vitamin D deficiency

Characteristic (N)		Mean Age at Death ± SD, years	Mean Difference P
Isola Sacra	Vitamin D Deficiency (42)	20.01 ± 16.61	0.224
	No Vitamin D Deficiency (539)	23.30 ± 16.87	
	Healed Deficiency (32)	20.62 ± 16.15	0.399
	No Healed Deficiency (549)	23.21 ± 16.90	
	Healed Deficiency, Category 1 (12)	12.84 ± 11.13	**0.014**
	Healed Deficiency, Category 2 (19)	26.93 ± 16.47	
	Healed Categories 1-3 (51)	17.40 ± 16.79	**0.012**
	No Healed Categories 1-3 (530)	23.61 ± 16.78	
	Healed Deficiency > 5 years (27)	23.54 ± 15.24	0.191
	No Healed Deficiency > 5 years (455)	27.52 ± 15.34	
Ancaster	Vitamin D Deficiency (24)	19.43 ± 22.33	**0.011**
	No Vitamin D Deficiency (223)	31.36 ± 21.40	
	Healed Deficiency (16)	20.83 ± 19.94	0.077
	No Healed Deficiency (223)	30.78 ± 21.78	
	Healed Deficiency, Category 1 (7)	16.69 ± 17.83	0.337
	Healed Deficiency, Category 2 (8)	26.95 ± 21.49	
	Healed Categories 1-3 (39)	23.75 ± 22.43	0.084
	No Healed Categories 1-3 (208)	30.34 ± 21.68	
	Healed Deficiency > 5 years (9)	35.36 ± 14.15	0.711
	No Healed Deficiency > 5 years (181)	37.65 ± 18.25	

Abbreviated terms are SD (standard deviation), P (p value), N (number of individuals). P values given are for comparisons between the two characteristics in the relevant rows. Significant values are bolded.

4.2.2. Vitamin D deficiency: Patterns based on sex

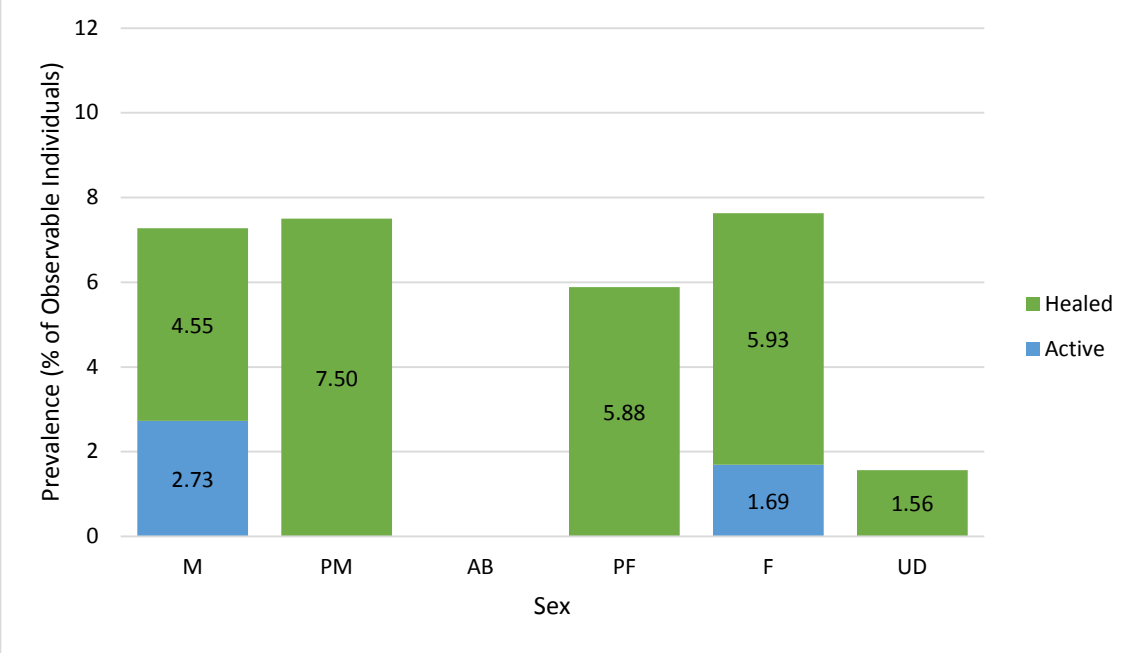
Prevalence values for features associated with vitamin D deficiency in individuals 16 years of age and older (Table 4.7) do not show statistically significant differences based on sex at either Isola Sacra (Figure 4.6) or Ancaster (Figure 4.7). No cases of either active or healed deficiency are observed in any of the small number of individuals classified as ambiguous at either site.

Table 4.7. Prevalence values by sex for skeletal evidence of active and healed vitamin D deficiency in individuals aged at least 16 years

Sex		Active Deficiency	Healed Deficiency	Total
Isola Sacra	Male	3/150 (2.00%)	8/148 (5.41%)	11/150 (7.33%)
	Ambiguous	0/6 (0.00%)	0/6 (0.00%)	0/6 (0.00%)
	Female	2/169 (1.18%)	10/168 (5.95%)	12/169 (7.10%)
	Undetermined	0/128 (0.00%)	2/102 (1.96%)	2/128 (1.56%)
	TOTAL	**5/453 (1.11%)**	**20/424 (4.72%)**	**25/453 (5.52%)**
Ancaster	Male	0/103 (0.00%)	4/99 (4.04%)	4/103 (3.88%)
	Ambiguous	0/1 (0.00%)	0/1 (0.00%)	0/1 (0.00%)
	Female	2/79 (2.53%)	5/77 (6.49%)	7/79 (8.86%)
	Undetermined	0/12 (0.00%)	0/11 (0.00%)	0/12 (0.00%)
	TOTAL	**2/195 (1.03%)**	**9/188 (4.79%)**	**11/195 (5.64%)**

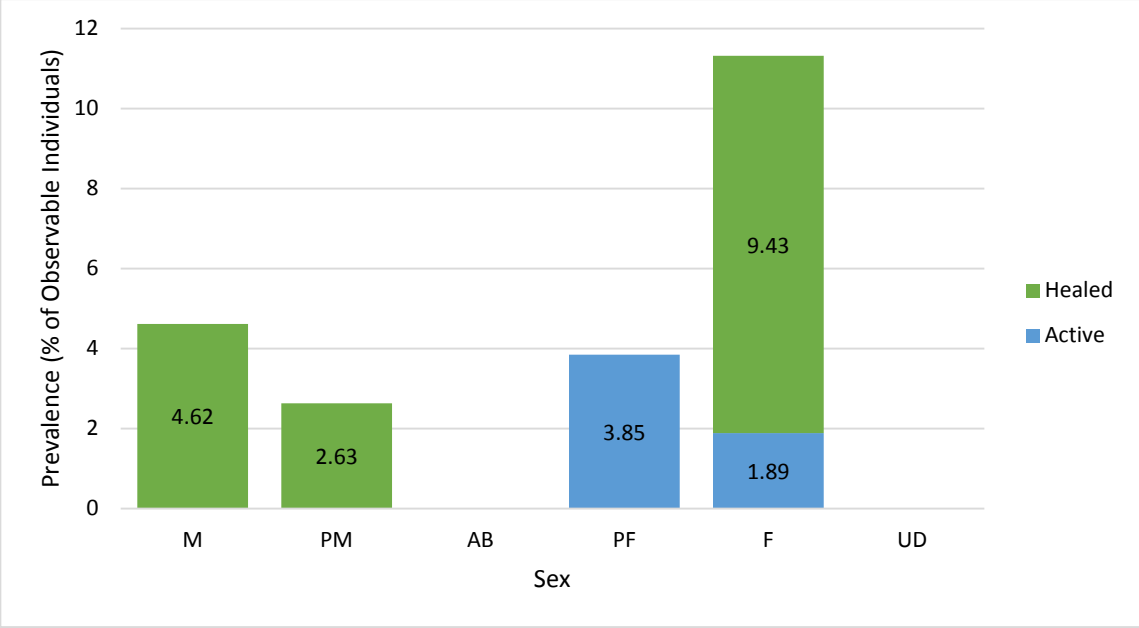
The male category includes individuals scored as male or probable male, and the female category includes individuals scored as female or probable female. The denominator indicates the number of individuals who could be evaluated for vitamin D deficiency in each sex category (diagnostic categories 1-4), which may differ between active and healed deficiency as different features were evaluated for each.

Figure 4.6. Prevalence of active and healed vitamin D deficiency cases by sex at Isola Sacra



Sex abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), UD (undetermined). Exact values for the percentage of individuals in each sex category are represented by the numbers within each section of each column.

Figure 4.7. Prevalence of active and healed vitamin D deficiency cases by sex at Ancaster



Sex abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), UD (undetermined). Exact values for the percentage of individuals in each age category are represented by the numbers within each section of each column.

4.2.3. Vitamin D deficiency: Skeletal features for diagnosis

Each individual skeleton from both assemblages was evaluated for the presence or absence of features associated with active and healed vitamin D deficiency (Tables 3.3, 3.4, and C.1-C.4). In juvenile individuals, the most common features in category one cases were deformed leg bones at Isola Sacra (Figure 4.8) and long bone general thickening at Ancaster (Figure 4.8; Tables 4.8 and 4.9). These features were seen in both active and healed deficiency. In category two cases, the most commonly observed feature at Isola Sacra was deformed leg bones, while at Ancaster costochondral rib flaring (Figure 4.10) was most common. Costochondral rib porosity (Figure 4.10) was also a relevant feature of deficiency at both sites, particularly for category three individuals at Ancaster (Tables C.2, C.4). Overall, the strongest and most commonly observed evidence for juvenile

Figure 4.8. Deformation of the leg bones in juvenile individuals from Isola Sacra. A) Medial tilting of the epiphyses in the tibiae of SCR 92; B) Anteroposterior bowing of the diaphysis in the right and left tibiae and fibulae of SCR 62; C) Anteroposterior bending in the proximal femur of SCR 530 (similar to deformation seen in some adult individuals from this site; see Figure 4.19)

Figure 4.9. Thickening of the long bones in juvenile individuals from Ancaster. A) Thickening of the diaphysis, particularly in the distal segment, of the left ulna in ANC 124A; B) Thickening of the distal femoral diaphysis in ANC 164, also note superior flattening of the proximal femoral metaphyses, deformation of the angle of the femoral neck, and some mediolateral deformation of the diaphyses.

Table 4.8. Active cases of vitamin D deficiency in juveniles

Feature	Isola Sacra					Ancaster						
	SCR 3	SCR 33	SCR 92	SCR 110	SCR 653	ANC 95	ANC 124A	ANC 180	ANC 192	ANC 207	ANC 249	ANC 265
Age Category	I	YC	I	YC	I	I/YC	I	YC	F	I	I	N
Cranial vault porosity	A	A	**P**	A	-	A	A	A	**P**	A	A	A
Orbital roof porosity	A	A	A	A	-	-	A	A	A	-	A	A
Long bone metaphyseal porosity	A	A	A	**P**	A	A	A	A	A	A	A	A
Deformed mandibular ramus	A	-	-	A	-	-	A	A	A	-	-	A
Rib deformity	A	-	-	A	-	A	A	A	A	-	-	A
Costochondral rib porosity	A	A	**P**	**P**	-	**P**	**P**	A	**P**	A	A	**P**
Ilium concavity	A	-	A	A	-	A	A	A	A	A	A	-
Long bone metaphyseal flaring	A	A	A	A	**P**	**P**	A	**P**	A	A	A	A
Long bone concave curvature porosity	A	A	A	A	A	A	A	A	A	A	A	A
Costochondral rib flaring	A	A	-	A	-	**P**	A	A	**P**	**P**	A	**P**
Deformed leg bones	**P**	A	**P**	**P**	**P**	A	A	**P**	A	A	A	A
Deformed arm bones	A	-	A	A	A	A	A	A	A	A	A	A
Long bone general thickening	**P**	A	A	A	A	**P**	**P**	**P**	A	A	A	A
Superior flattening of femoral metaphysis	A	A	A	A	A	-	A	A	A	A	A	A
Coxa vara	A	-	A	A	A	-	A	A	A	A	A	A
Porosis/roughening of bone underlying growth plate	**P**	-	**P**	**P**	**P**	**P**	**P**	**P**	A	-	-	**P**
Histological features on SEM	A	**P**	-	A	-	-	-	A	A	**P**	**P**	-
Diagnosis	2	2	2	1	2	1	2	2	2	2	2	1

Non-diagnostic features are highlighted in red, possible features in green, and probable features in blue. Features are classified as absent (A), present (P), or not observable (-). Age categories abbreviated as F (Fetal), N (Neonate), I (Infant), YC (Younger child). Diagnostic categories are outlined in 3.2.2.1 (1 probable, 2 possible).

Table 4.9. Healed cases of vitamin D deficiency in juveniles

Feature	**Isola Sacra**														
	SCR 1	SCR 22	SCR 62	SCR 103	SCR 175	SCR 244	SCR 290	SCR 333	SCR 393	SCR 522	SCR 530	SCR 542	SCR 594	SCR 663	SCR 721
Age Category	YC	I	I	OC	OC	MC	OC	OC	YAL	MC	OC	YC	YC	OAL	OC
Cranial vault porosity	A	A	**P**	A	A	A	A	A	A	**P**	A	A	-	-	-
Orbital roof porosity	A	**P**	A	**P**	A	A	**P**	A	A	A	**P**	**P**	-	-	-
Long bone metaphyseal porosity	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A
Deformed mandibular ramus	A	-	A	A	A	A	-	A	A	A	A	A	-	-	-
Rib deformity	A	-	A	-	A	A	A	A	-	A	-	A	-	-	-
Costochondral rib porosity	A	-	A	A	A	A	A	A	-	A	-	A	-	A	-
Ilium concavity	A	-	A	A	A	**P**	A	A	A	A	-		A	A	-
Long bone metaphyseal flaring	A	**P**	A	A	A	**P**	A	A	A	A	A	**P**	**P**	A	A
Long bone concave curvature porosity	A	A	A	A	A	**P**	A	A	A	A	A	A	A	A	A
Costochondral rib flaring	A	-	A	A	**P**	**P**	**P**	A	-	A	-	A	-	A	-
Deformed leg bones	**P**	**P**	**P**	**P**	**P**	**P**	**P**	**P**	**P**	A	**P**	**P**	**P**	**P**	**P**
Deformed arm bones	A	A	A	A	A	**P**	A	A	A	**P**	**P**	A	A	A	A
Long bone general thickening	A	**P**	A	**P**	A	A	A	A	A	A	A	**P**	**P**	A	**P**
Superior flattening of femoral metaphysis	A	A	A	A	**P**	A	A	A	A	A	A	A	-	A	A
Coxa vara	A	A	A	A	A	A	A	A	A	A	A	A	-	A	A
Porosis/roughening of bone underlying growth plate	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Histological features on SEM	-	-	A	-	A	-	-	-	-	-	A	-	-	A	-
Diagnosis	2	2	1	2	1	1	2	2	2	1	1	1	1	2	1

Feature	Ancaster						
	ANC 138	ANC 146	ANC 164	ANC 181	ANC 208	ANC 219	ANC 260
Age Category	YC	MC	YC	MC	I	OC	YC
Cranial vault porosity	A	A	A	A	A	A	**P**
Orbital roof porosity	A	A	A	**P**	A	**P**	**P**
Long bone metaphyseal porosity	A	A	A	A	A	A	A
Deformed mandibular ramus	A	A	A	A	A	A	A
Rib deformity	A	A	A	-	**P**	A	A
Costochondral rib porosity	A	A	A	A	A	A	**P**
Ilium concavity	A	A	A	A	A	A	A
Long bone metaphyseal flaring	A	A	A	A	A	A	A
Long bone concave curvature porosity	A	A	A	A	A	A	A
Costochondral rib flaring	A	**P**	**P**	A	A	**P**	A
Deformed leg bones	**P**	**P**	**P**	A	**P**	A	**P**
Deformed arm bones	A	A	A	A	A	A	A
Long bone general thickening	**P**	**P**	**P**	A	A	A	**P**
Superior flattening of femoral metaphysis	A	A	**P**	**P**	A	A	A
Coxa vara	A	A	A	A	A	A	A
Porosis/roughening of bone underlying growth plate	A	A	A	A	A	A	A
Histological features on SEM	A	A	A	A	A	A	A
Diagnosis	1	1	1	2	2	2	1

Non-diagnostic features are highlighted in red, possible features in green, and probable features in blue. Features are classified as absent (A), present (P), or not observable (-). Age categories abbreviated to I (Infant), YC (Younger child), MC (Middle child), OC (Older child), YAL (Younger adolescent), OAL (Older adolescent). Diagnostic categories are outlined in 3.2.2.1 (1 probable, 2 possible).

Figure 4.10. Costochondral rib flaring (A, B) and porosity (C) in juvenile individuals from Ancaster. A) Costochondral ends of four ribs from ANC 192 demonstrating flaring; B) Costochondral ends of four ribs from ANC 219 demonstrating flaring, also note clear cupping in one rib end (arrow); C) Costochondral ends of eight ribs from ANC 265 demonstrating abnormal porosity, with pores that are large and extend further than normal from the sternal end of the rib.

deficiency at these two sites is represented by changes in the long bones, including deformation and thickening of the long bone diaphyses. Features in the ribs, namely costochondral flaring and porosity, were also present in a number of individuals placed in categories one and two. The strongest case can be made for the presence of deficiency in individuals who display multiple probable features with a marked expression (Figure

Figure 4.11. Multiple features present to support a diagnosis of vitamin D deficiency in individual SCR 244. A) Deformation of the leg bones, showing bending in the diaphyses of the femora, tibiae, and fibulae; B) Medial view of the femora, showing both anteroposterior and mediolateral deformation; C) Ilium of SCR 244 (left) in comparison with normal ilium of SCR 168 (right), showing abnormal curvature of the iliac blade; D) Clear flaring of one costochondral rib end in SCR 244 (top) compared with a normal rib end (bottom). Apparent porosity at the costochondral rib end of SCR 244 represents post-mortem damage rather than a pathological feature.

4.11). In accordance with diagnostic criteria (Section 3.2.2.1), some individuals were placed in category two based on only one very clear probable feature (e.g., SCR 1, 33, 333, and 393; Figure 4.12). Cases that were deemed to represent active deficiency displayed either porosity or roughening of the bone underlying the growth plate (Figure 4.13) or histological features of deficiency (Figure 4.14; Table 4.9). Cases that were determined to represent healed deficiency had features of deficiency along with normal bone underlying the growth plates and/or the absence of histological signs of deficiency. When radiographs were available, the appearance of the growth plate was evaluated on x-ray for additional clues as to whether normal growth had resumed (Figure 4.15). No cases were determined to have been active at the time of death based on radiographic evidence.

Figure 4.12. Proximal femur of SCR 393 (right) compared with normal proximal femur of SCR 309 (left), showing thickening of the metaphysis and proximal diaphysis as well as superior flattening of the proximal metaphysis. This represents an example of a single feature considered to be clear enough to support a category two diagnosis despite the absence of other affected elements in this individual.

Figure 4.13. Bone underlying the growth plate of the distal tibia of SCR 92, demonstrating the velvety texture associated with a score of one for porosity and roughening of this surface. This feature provides evidence that vitamin D deficiency was active at the time of death in this individual.

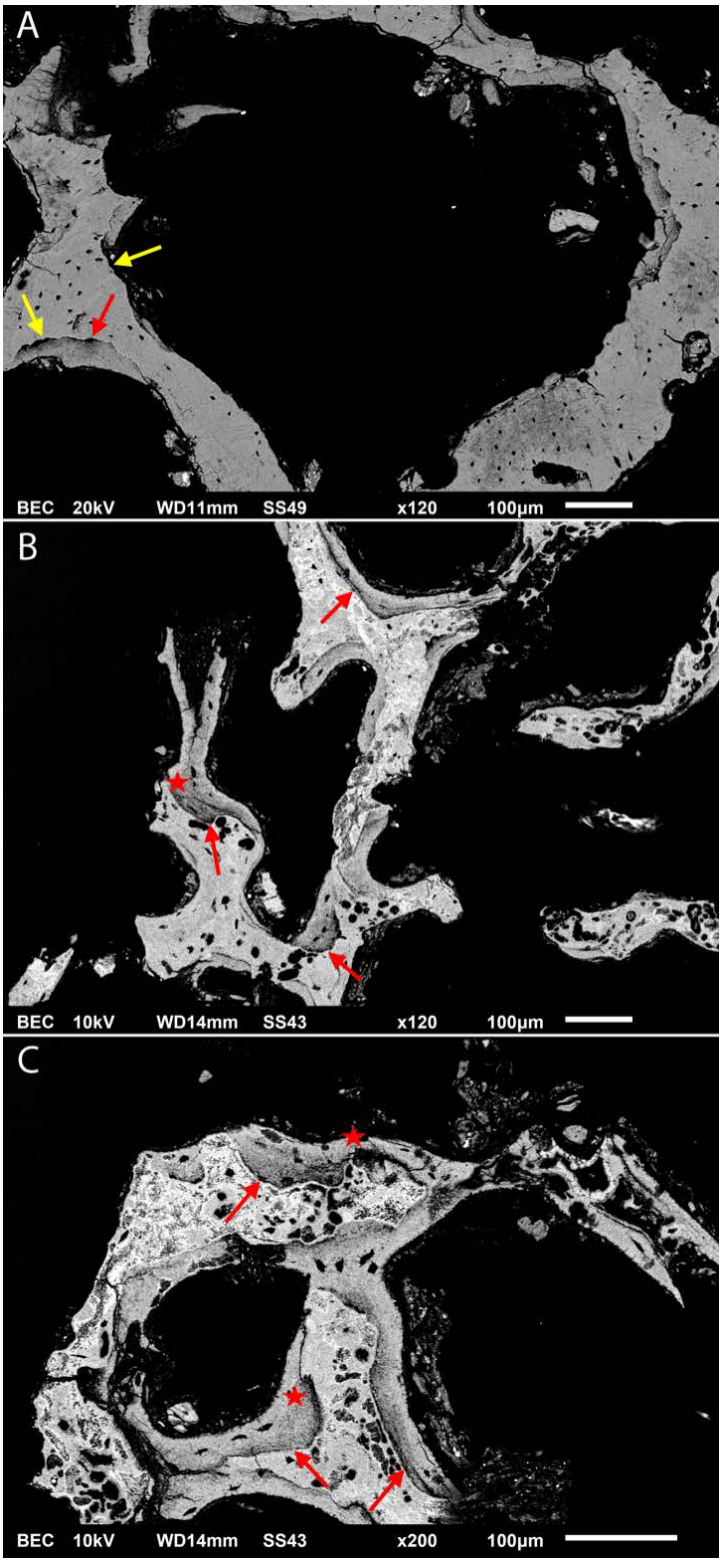


Figure 4.14. Histological features of vitamin D deficiency in BSEM images of sections of rib from ANC 249 (A) and SCR 33 (B, C), showing large areas of poorly mineralized bone (red stars), mineralization defects at cement lines (red arrows), and scalloped edges of bone indicating increased resorption (yellow arrows).

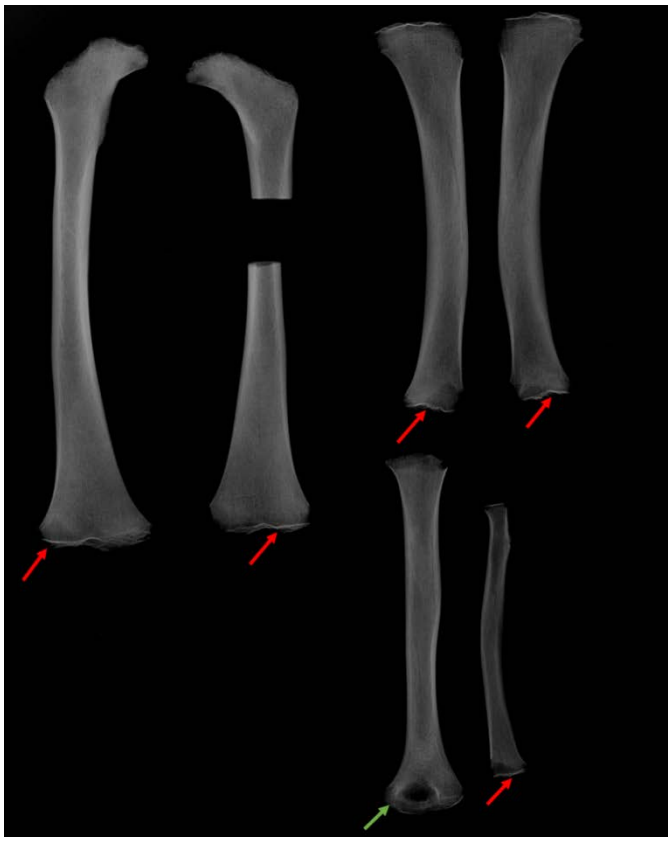


Figure 4.15. Radiograph of long bones from SCR 175 (femora, tibiae, left humerus, and left radius), showing radiographic features evaluated to determine whether vitamin D deficiency was active or healed. Deficiency in this individual is healed, based on features of the bone underlying the growth plates which has regained definition (indicated by the solid white lines, marked with red arrows), and do not show any of the fraying or lack of definition associated with active deficiency. The distal humerus has a less defined growth plate as a result of postmortem damage (green arrow).

No adult individuals were identified as category one cases of adult deficiency at Isola Sacra (Table 4.10). At Ancaster, the features observed in the single probable case of active deficiency were histological features on SEM (Figure 4.16), rib fractures with spiculated bone (Figure 4.17), and vertebral body compression fracture. The most common feature specific to active vitamin D deficiency in category two cases at Isola Sacra was rib fractures with spiculated bone (Table 4.10). At Ancaster, category two cases most frequently displayed healing or unhealed rib fractures and proximal femoral pseudofracture (Figure 4.18; Table 4.10). Several individuals from Ancaster were placed in category three for active vitamin D deficiency based on histological features on SEM (Figure 4.19; Table 4.10), making this an important type of evidence for identifying

Table 4.10. Active cases of vitamin D deficiency in adults.

Feature	Isola Sacra					Ancaster		
	SCR 44	SCR 69	SCR 181	SCR 323	SCR 590	ANC 113	ANC 212	ANC 263
Age Category	MA	YA	YA	MA	YA	MA	MA	OA
Sex	M	F	M	F	M	F	F	PF
Healing/unhealed rib fracture	**P**	A	A	**P**	A	A	**P**	A
Healed rib fracture	**P**	A	A	**P**	**P**	A	A	A
Healed vertebral lamina fracture	A	A	A	A	A	A	A	A
Vertebral curvature	A	**P**	A	A	-	**P**	-	A
Scapula lateral border curvature	-	A	A	A	A	A	A	A
Pubic symphysis angulation	A	A	A	A	-	A	A	-
Rib pseudofracture	A	A	**P**	**P**	**P**	A	**P**	**P**
Scapula spinous process pseudofracture	A	A	A	A	A	A	A	A
Scapula coracoid process pseudofracture	-	A	-	A	A	A	A	A
Scapula lateral border pseudofracture	A	A	A	A	A	A	A	A
Vertebral body compression fracture	A	A	A	A	A	A	A	**P**
Vertebral lamina pseudofracture	A	A	A	A	A	A	A	A
Inferior pubic rami pseudofracture	-	A	A	A	-	A	-	-
Iliac crest fracture	A	A	A	A	A	A	A	-
Ilium pseudofracture	A	A	A	A	A	A	A	A
Healing/unhealed long bone fracture	-	**P**	A	A	A	A	-	A
Distal ulna pseudofracture	A	A	-	A	A	A	A	A
Proximal femur pseudofracture	A	A	-	A	A	**P**	A	A
Histological features on SEM	-	-	A	A	**P?**	-	A	**P**
Diagnosis	2	2	2	2	2	2	2	1

Non-diagnostic features are highlighted in red, possible features in green, and probable features in blue. Features are classified as absent (A), present (P), or not observable (-). Age categories abbreviated to YA (Young adult), MA (Middle adult), OA (Old adult). Sex categories abbreviated to F (Female), PF (Probable female), M (Male), UD (Undetermined). Diagnostic categories are outlined in 3.2.2.1 (1 probable, 2 possible).

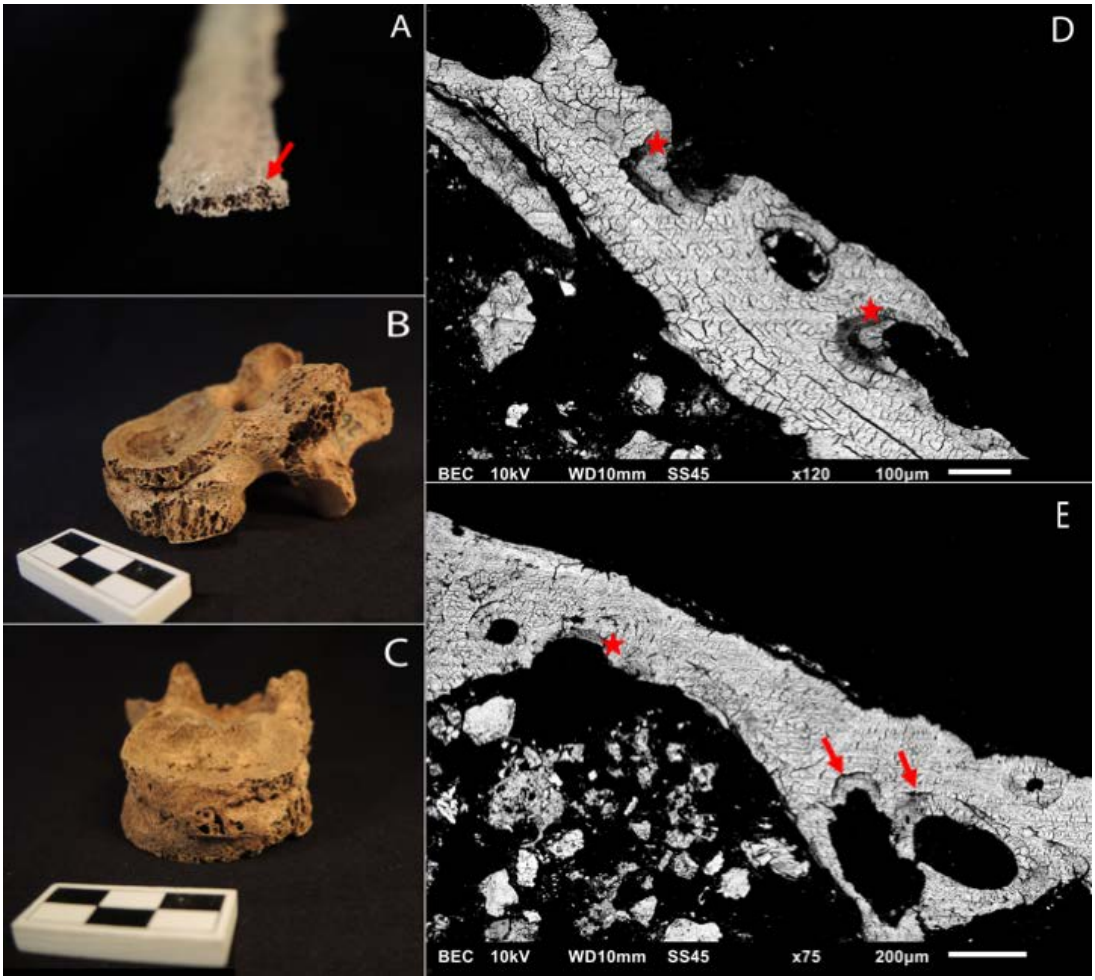


Figure 4.16. Features of active vitamin D deficiency in adulthood in a category one case from Ancaster (ANC 263). A) Incomplete rib fracture (pseudofracture) with spiculated bone (arrow); B, C) Compression fracture in the body of a lumbar vertebra, showing folding of the body from lateral (B) and anterior (C) views; D, E) BSEM images of a section of rib showing areas of poorly mineralized bone (stars) and possible mineralization defects at cement lines (arrows).

Figure 4.17. Incomplete rib fracture associated with some slightly spiculated bone (arrow) in individual SCR 181. The fractured edge of the bone represents postmortem damage.

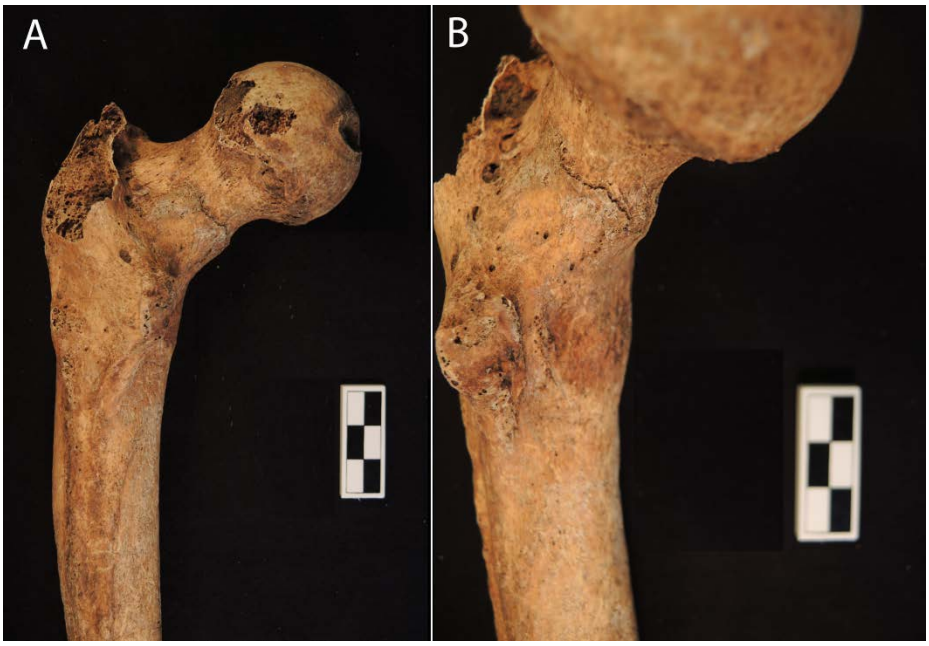


Figure 4.18. Incomplete fracture (pseudofracture) in the proximal femur of individual ANC 113, in posterior (A) view and medial (B) view with a more detailed depiction of the small amounts of bone beginning to form at the edges of the fracture.

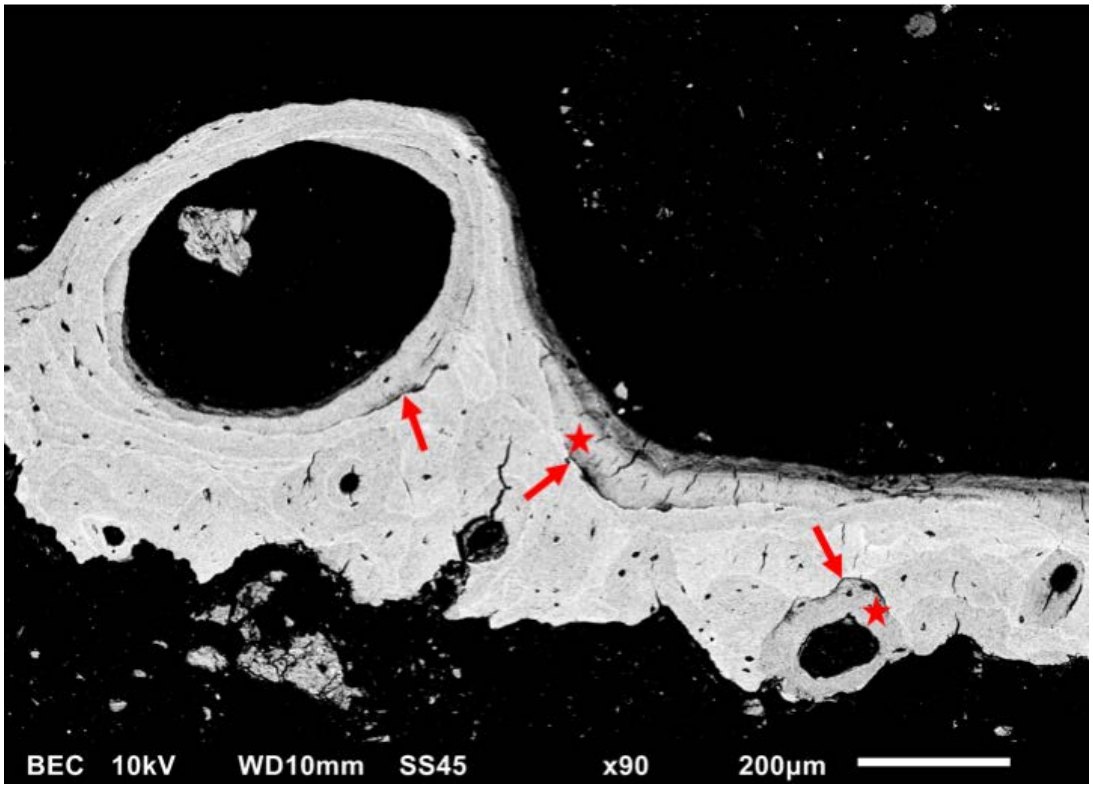


Figure 4.19. Histological features of vitamin D deficiency in BSEM images of a section of rib from category three individual ANC 220, showing possible poorly mineralized bone (red stars) and possible mineralization defects at cement lines (red arrows). Features in individuals placed in category three are less clear or less widespread throughout the sample than in category one and two individuals (e.g., Figures 4.14 and 4.16).

Figure 4.20. Deformation of the long bones associated with healed vitamin D deficiency in adult individuals from Isola Sacra and Ancaster. A) Anterior view of the humeri of SCR 159, showing mediolateral bending of the diaphyses; B) Medial view of the right femur of SCR 838, showing anteroposterior bending of the proximal diaphysis (similar to deformation seen in some juvenile individuals from this site; see Figure 4.8); C) Anterior view of the left tibia and fibula of ANC Uncatalogued F, showing mediolateral deformation of the tibial diaphysis.

category three cases at this site. Some of the strongest and most commonly observed evidence for active deficiency in adults at these two sites is represented by pseudofractures in the ribs and in the femoral neck, with the majority of category one and two cases having at least one fracture that could either be identified as a pseudofracture or had suspicious features typically associated with pseudofractures. However, pseudofractures in the scapulae, pelvis, clavicles, and ulnae were not observed in either collection. Bending in the long bones was the primary feature used to evaluate healed vitamin D deficiency in adults (Figure 4.20; Table 4.11). This feature was marked enough to support a category one diagnosis of healed deficiency in several individuals (Figure 4.21; Table 4.11; e.g., SCR 220 and 563, ANC 93, 122, 161A, and 212). In category three

individuals, features such as vertebral curvature (Figure 4.22) were also observed (Appendix C).

Figure 4.21. Deformation in the long bones representing healed vitamin D deficiency in adults from Isola Sacra and Ancaster, representing examples of single features considered to be clear enough to support a category one diagnosis despite the absence of other features in these individuals. A) Anterior view of the tibiae of SCR 220, demonstrating medial bending of the proximal metaphyses; B) Fibulae of ANC 93, demonstrating anterior bending of the proximal metaphyses (plastic model in the middle for comparison).

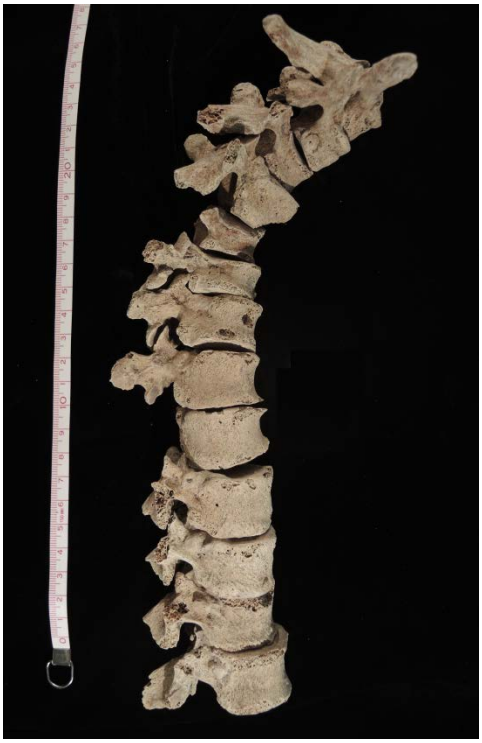


Figure 4.22. Vertebral column of SCR 269 showing lateral and anteroposterior curvature in the thoracic vertebrae, due to wedging of eight vertebral bodies.

Table 4.11. Healed cases of vitamin D deficiency in adults.

Feature	**Isola Sacra**													
	SCR 18	SCR 27	SCR 159	SCR 161	SCR 170	SCR 190	SCR 197	SCR 220	SCR 409	SCR 416	SCR 457	SCR 458	SCR 550	SCR 563
Age Category	YA	YA	UD	YA	YA	YA	YA	OAL	YA	OAL	OA	YA	YA	OAL
Sex	PF	PF	F	PF	PM	F	F	M	F	F	PM	M	UD	PM
Vertebral curvature	A	A	A	A	A	A	A	A	-	A	A	-	-	A
Sternum bending	**P**	A	-	-	-	A	-	A	**P**	A	-	-	-	A
Scapula lateral border curvature	A	A	-	-	-	A	A	A	A	A	-	A	-	A
Pubic symphysis angulation	A	A	-	A	A	A	A	A	A	A	-	-	-	A
Sacral curvature	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Anterolateral bending proximal femur	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Residual bending of long bones	A	**P**	**P**	**P**	**P**	**P**	**P**	**P**	A	**P**	**P**	**P**	**P**	**P**
Diagnosis	2	1	1	2	2	2	2	1	2	2	2	2	2	1

Feature	Isola Sacra					Ancaster								
	SCR 652	SCR 691	SCR 806	SCR 837	SCR 838	ANC 45	ANC 62	ANC 93	ANC 122	ANC 161A	ANC 212	ANC 247	ANC 262A	ANC Uncat F
Age Category	MA	YA	MA	MA	YA	OA	YA	MA	MA	UD	MA	MA	MA	MA
Sex	F	F	M	M	M	F	F	PM	M	M	F	F	F	M
Vertebral curvature	-	A	A	-	A	A	A	A	A	-	-	-	**P**	A
Sternum bending	-	-	A	-	-	**P**	A	A	A	-	-	-	A	A
Scapula lateral border curvature	-	A	A	-	A	A	A	A	A	-	A	A	A	A
Pubic symphysis angulation	A	A	A	A	A	A	A	A	A	-	A	-	A	A
Sacral curvature	A	A	A	A	A	A	A	A	A	A	A	A	**P**	A
Anterolateral bending proximal femur	A	A	**P**	A	**P**	-	A	A	A	A	A	A	A	A
Residual bending of long bones	**P**	**P**	**P**	**P**	A	A	**P**	**P**	**P**	**P**	**P**	**P**	A	**P**
Diagnosis	2	2	1	2	1	2	2	1	1	1	1	2	2	2

Non-diagnostic features are highlighted in red, possible features in green, and probable features in blue. Features are classified as absent (A), present (P), or not observable (-). Age categories abbreviated to OAL (Older adolescent), YA (Young adult), MA (Middle adult), OA (Old adult). Sex categories abbreviated to F (Female), PF (Probable female), M (Male), PM (Probable male), UD (Undetermined). Diagnostic categories are outlined in 3.2.2.1 (1 probable, 2 possible).

4.3. Chronic Respiratory Infections

The evaluation of macroscopic skeletal features, as outlined in Section 3.2.1.7, enabled the assignation of a chronic respiratory infection diagnosis (Categories 1-4; Section 3.2.2.2) for 356 juveniles and 334 adults from Isola Sacra (n = 690) and 82 juveniles and 174 adults from Ancaster (n = 256). Patterns of occurrence were analyzed based on age at death, sex, and archaeological site.

4.3.1. Chronic respiratory infections: Differential diagnoses

Differential diagnoses of pathological features of the ribs, long bones, vertebrae, and joints considered multiple possible etiologies. Diagnoses evaluated the likelihood of an association with the category of chronic respiratory infection, which includes conditions such as tuberculosis, pneumonia, bronchitis, and emphysema, against the possibility of an etiological association with other infectious, neoplastic, nutritional, and endocrine disorders, based on features outlined in Tables 3.6 to 3.9.

4.3.1.1. Differential diagnosis: Rib lesions

The most commonly observed evidence consistent with chronic respiratory infections at both Isola Sacra and Ancaster is the presence of new bone formation on the visceral surfaces of the ribs (Figure 4.23; Section 3.2.1.7). The type of new bone formation observed on the visceral surfaces of the ribs in eight juveniles and 12 adults from Isola Sacra, as well as in five juveniles and 18 adults from Ancaster, is consistent with proliferative lesions associated with an infectious rather than a neoplastic etiology in studies done on individuals with known causes of death (Table 3.6). The protected location of the visceral surfaces of the ribs mean that this area is not affected by changes

Figure 4.23. New bone formation on the visceral surface at the vertebral end of a rib from SCR 272.

associated with joint disease, and is unlikely to be affected by trauma without other evidence of extensive injury, lending support to the idea that chronic respiratory infections are the primary cause of proliferative lesions in this region of the ribs.

4.3.1.2. Differential diagnosis: Long bone lesions

Four individuals from Isola Sacra display a distinctive pattern of proliferative lesions on the diaphyses of the long bones. New bone formation in these individuals was extensive, markedly bilaterally symmetrical, and present on several pairs of long bones, including those of the forearms and lower legs (Figure 4.24). Some of these lesions in individuals SCR 221, 390, 706, and 729 have a distinctive irregular configuration of the cortex that resembles tree bark (Figure 4.25). New bone formation on the long bones can be caused by many pathological conditions; however, the pattern and distribution of new bone in these four individuals does not correspond well with clinical features of new bone

Figure 4.24. New bone formation in the long bones of individual SCR 706 illustrating a distribution consistent with HPO/HOA. New bone is bilaterally symmetrical, and present on the bones of the lower legs and the forearms, including the tibiae (A), fibulae (B), and distal ulnae (C). Close-up views of the distal right fibula (D) and right tibial diaphysis (E) demonstrate the appearance of the new bone formed on these elements.

formed as a result of neoplastic conditions like metastatic carcinoma, hyperparathyroidism, treponemal disease, melorheostosis, or metabolic conditions like hypervitaminosis A and fluorosis (Table 3.7).

In all four of the individuals described, new bone formation is diffuse, is present on many appendicular tubular bones, demonstrates marked bilateral symmetry, and is most pronounced distal to the elbow and the knee. The patterning of these lesions within the skeleton, as well as the presence of new bone formation with a characteristic texture

Figure 4.25. Exuberant new bone formation on the distal right fibula of SCR 729 illustrating the "tree bark-like" formation observed in this and other skeletal cases of HPO/HOA.

resembling tree bark, is most consistent with a diagnosis of hypertrophic osteoarthropathy (HOA; Table 3.7). Poorer preservation of individual SCR 399 precluded observation of the right radius and left tibia, and therefore the evaluation of whether or not new bone formation was fully bilaterally symmetrical. However, marked symmetry in proliferative lesions on the femora and fibulae, as well as the characteristic tree bark-like texture of new bone formation in the fibulae and the right tibia, indicate close correspondence with features of HOA (Table 3.7) sufficient to conclude that this is the most likely diagnosis for the lesions observed in this individual.

4.3.1.3. Differential diagnosis: Vertebral lesions

Vertebral lesions were observed in two individuals, one from Isola Sacra and one from Ancaster. Individual SCR 462 displayed well-circumscribed lytic lesions in the bodies of two contiguous thoracic vertebrae (Figure 4.26); these lesions affect large areas of the anterior, central, and posterior vertebral bodies, but do not show any involvement of the posterior vertebral elements. There is no associated reactive bone formation. Features such as localization in the thoracic vertebral bodies, lack of posterior vertebral

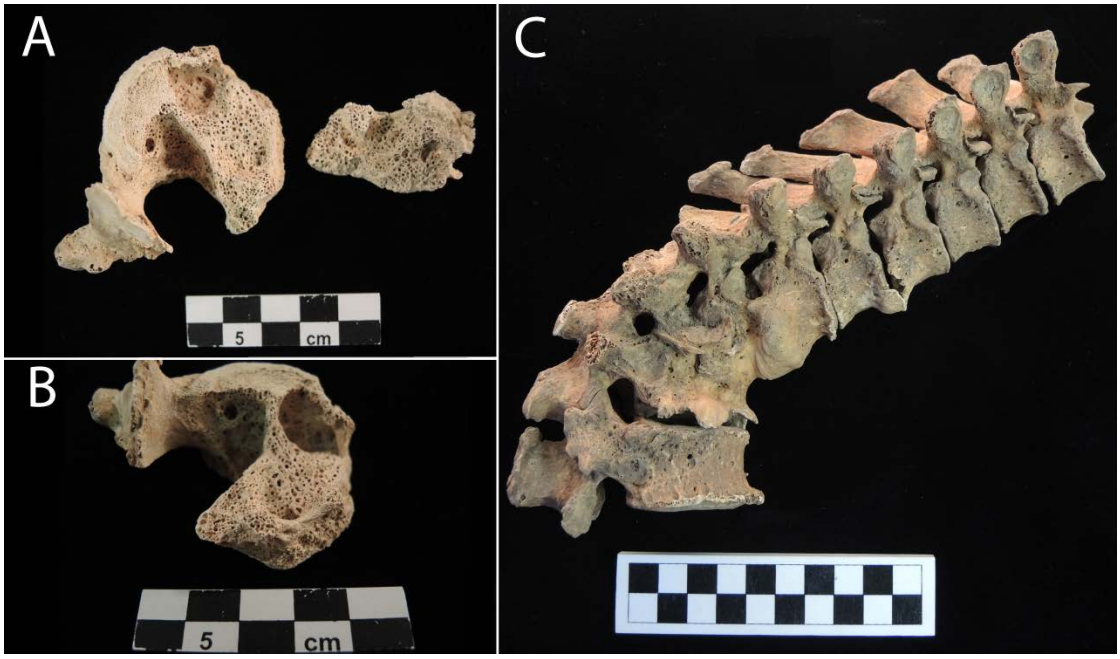


Figure 4.26. Vertebral lesions identified as potentially related to a diagnosis of tuberculous spondylitis. A, B) Lytic lesions in two thoracic vertebral bodies from SCR 462; C) Spinal column of ANC 11, showing destruction and collapse of thoracic vertebral bodies (T9-T11) resulting in angular kyphosis that resembles a classic Pott's spine.

involvement, and absence of sclerosis and new bone formation suggest that these lesions most likely represent an early manifestation of spinal TB (Table 3.8).

More typical features of tuberculous spondylitis are observed in individual ANC 11. In this individual, destruction and collapse of three thoracic vertebral bodies (T9-T11) resulted in angular kyphosis that resembles a classic Pott's spine (Figure 4.26). In this case, healing resulted in ankylosis, with bony fusion of anterior and posterior elements of T8 through T11. Severe vertebral body destruction, resulting in collapse and kyphosis, is more commonly seen in TB than in other forms of infectious spondylitis considered (Table 3.8), and the features observed in this individual are most consistent with a diagnosis of tuberculosis.

4.3.1.4. Differential diagnosis: Joint lesions

Joint lesions were observed in one individual from Ancaster. Individual ANC 1 displays lytic lesions in the right hip joint that involve both the acetabulum and the femoral proximal epiphysis, resulting in extensive destruction of the femoral head and widening of the acetabulum (Figure 4.27). These lesions are associated with a very small amount of reactive new bone formation. While it is difficult to differentiate lesions associated with TB from those caused by pyogenic infections in the joints (Table 3.9), potentially more so than in other locations in the skeleton such as the spine, the lesions observed in this individual correspond well with Waldron's (2009) operational definition of skeletal tuberculosis as a unifocal lytic lesion with little or no new bone formation.

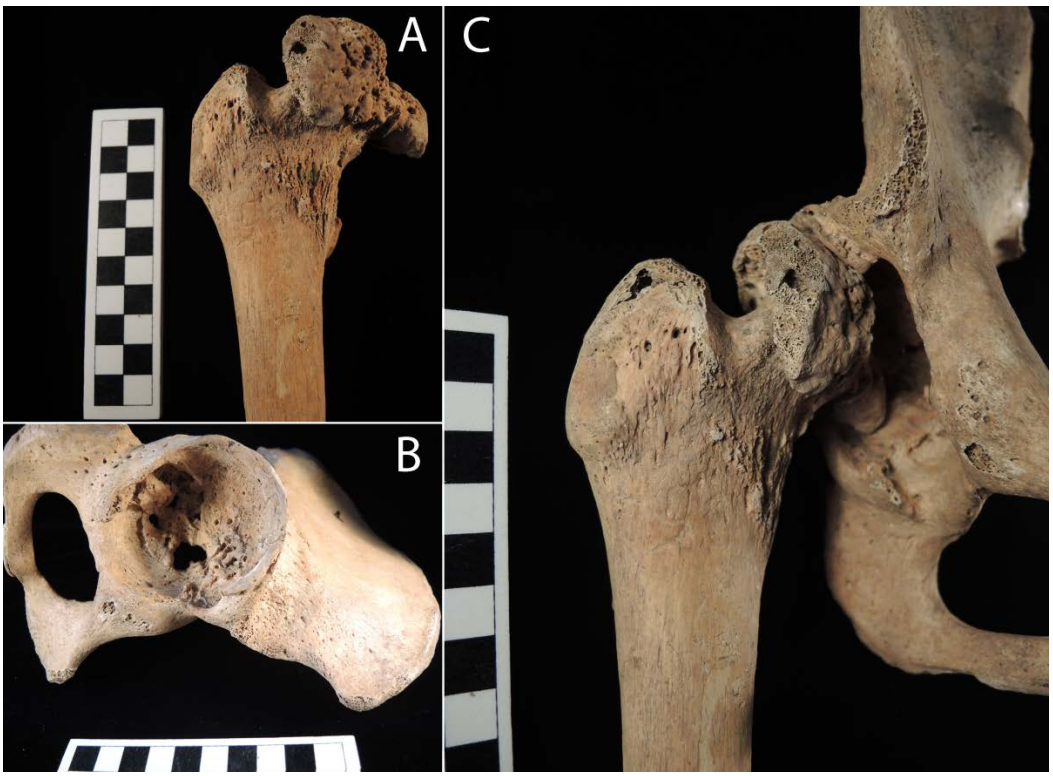


Figure 4.27. Destruction of the right femoral head (A) and acetabulum (B) of individual ANC 1 identified as potentially related to a diagnosis of skeletal TB in the hip joint, showing the surface of each element as well as how the two articulate with one another (C).

4.3.2. Chronic respiratory infection: Patterns based on age at death

The overall prevalence of chronic respiratory infection lesions is significantly higher at Ancaster than at Isola Sacra (Table 4.12; p 0.0004). This is true both for active lesions (p 0.045) and for those with some evidence of healing (p 0.005). The overall prevalence of lesions associated with chronic respiratory infection does not differ significantly between juveniles and adults at either site.

Table 4.12. Prevalence values by age for skeletal evidence of active and healing/healed chronic respiratory infections

Age Category		**Active Lesions**	**Healing/Healed Lesions**	**Total**
Isola Sacra	Fetal/Neonate	0/6 (0.00%)	0/6 (0.00%)	0/6 (0.00%)
	Infant/Younger Child	2/92 (2.17%)	3/92 (3.26%)	5/92 (5.43%)
	Middle Child	1/84 (1.19%)	2/84 (2.38%)	3/84 (3.57%)
	Older Child	0/53 (0.00%)	0/53 (0.00%)	0/53 (0.00%)
	Younger Adolescent	0/47 (0.00%)	0/47 (0.00%)	0/47 (0.00%)
	Older Adolescent	2/74 (2.70%)	2/74 (2.70%)	4/74 (5.41%)
	Juvenile UD	0/0 (0.00%)	0/0 (0.00%)	0/0 (0.00%)
	Juvenile Total	**5/356 (1.40%)**	**7/356 (1.97%)**	**12/356 (3.37%)**
	Young Adult	2/152 (1.32%)	5/152 (3.29%)	7/152 (4.61%)
	Middle Adult	3/100 (3.00%)	1/100 (1.00%)	4/100 (4.00%)
	Old Adult	0/37 (0.00%)	1/37 (2.70%)	1/37 (2.70%)
	Adult UD	1/45 (2.22%)	0/45 (0.00%)	1/45 (2.22%)
	Adult Total	**6/334 (1.80%)**	**7/334 (2.10%)**	**13/334 (3.89%)**
	TOTAL	**11/690 (1.59%)**	**14/690 (2.03%)**	**25/690 (3.62%)**
Ancaster	Fetal/Neonate	0/14 (0.00%)	0/14 (0.00%)	0/14 (0.00%)
	Infant/Younger Child	0/29 (0.00%)	0/29 (0.00%)	0/29 (0.00%)
	Middle Child	2/15 (13.33%)	1/15 (6.67%)	3/15 (20.00%)
	Older Child	1/8 (12.50%)	1/8 (12.50%)	2/8 (25.00%)
	Younger Adolescent	0/3 (0.00%)	0/3 (0.00%)	0/3 (0.00%)
	Older Adolescent	1/12 (8.33%)	2/12 (6.67%)	3/12 (25.00%)
	Juvenile UD	0/1 (0.00%)	0/1 (0.00%)	0/1 (0.00%)
	Juvenile Total	**4/82 (4.88%)**	**4/82 (4.88%)**	**8/82 (9.76%)**
	Young Adult	2/62 (3.23%)	5/62 (8.06%)	7/62 (11.29%)
	Middle Adult	2/58 (3.45%)	4/58 (6.90%)	6/58 (10.34%)
	Old Adult	2/38 (5.26%)	0/38 (0.00%)	2/38 (5.26%)
	Adult UD	0/16 (0.00%)	2/16 (12.50%)	2/16 (12.50%)
	Adult Total	**6/174 (3.45%)**	**11/174 (6.32%)**	**17/174 (9.77%)**
	TOTAL	**10/256 (3.91%)**	**15/256 (5.86%)**	**25/256 (9.77%)**

Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years). Diagnostic categories are outlined in 3.2.2.2 (1 probable, 2 possible). The numbers in each cell indicate the number of individuals, withthe values in parentheses representing these values as a percentage of observable individuals

As is the case for vitamin D deficiency, a significantly higher proportion of individuals were placed in category five at Isola Sacra compared with Ancaster (Table 4.13; p 0.0001). There are no significant differences between the numbers of individuals placed in category three at Isola Sacra and Ancaster.

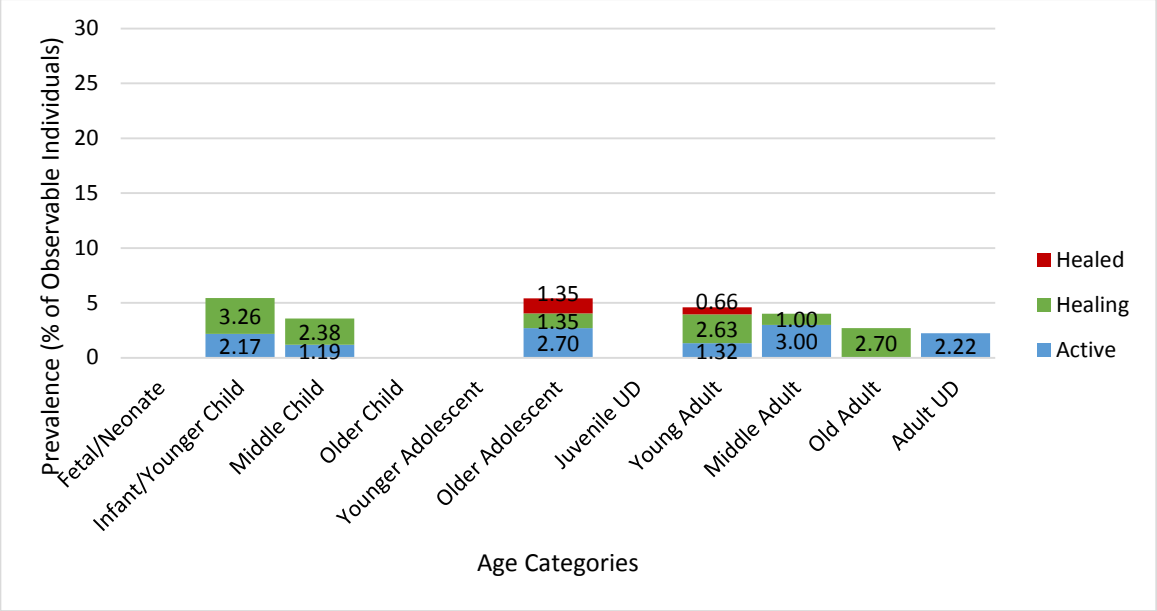
At both sites, most cases of chronic respiratory infections involve skeletal lesions that display some evidence of healing (Figures 4.28 and 4.29), but there are no significant differences between prevalence values for active and healing or healed lesions in any age category or in either sample as a whole. Between the two sites, prevalence values differed significantly for all lesions in adults (p 0.01), all lesions in juveniles (p 0.034), and healing or healed lesions in adults (p 0.021). The prevalence values for evidence of both active (p 0.04) and healing or healed (p 0.005) lesions associated with respiratory infections are significantly higher at Ancaster than at Isola Sacra. Skeletal evidence for chronic respiratory infections is present in individuals who died as infants or younger children at Isola Sacra (Figure 4.28) but not at Ancaster (Figure 4.29), and in individuals who died as older children at Ancaster but not at Isola Sacra. At both sites, there are no significant differences between juveniles and adults for the prevalence values of active, healing or healed, or all lesions associated with chronic respiratory infection.

Table 4.13. Chronic respiratory infection diagnostic category breakdown for juvenile and adult individuals from Isola Sacra and Ancaster

Age Category		Total	Category 5	Total Observable	Diagnosis			
					1	2	3	4
Isola Sacra	Fetal/Neonate	10	4/10 (40.00%)	6	0/6 (0.00%)	0/6 (0.00%)	0/6 (0.00%)	6/6 (100.00%)
	Infant/Younger Child	143	51/143 (35.66%)	92	4/92 (4.35%)	1/92 (1.09%)	1/92 (10.09%)	86/92 (93.48%)
	Middle Child	100	16/100 (16.00%)	84	2/84 (2.38%)	1/84 (1.19%)	0/84 (0.00%)	81/84 (96.43%)
	Older Child	64	11/64 (17.19%)	53	0/53 (0.00%)	0/53 (0.00%)	0/53 (0.00%)	53/53 (100.00%)
	Younger Adolescent	51	4/51 (7.84%)	47	0/47 (0.00%)	0/47 (0.00%)	1/47 (2.13%)	46/47 (97.87%)
	Older Adolescent	78	4/78 (5.13%)	74	2/74 (2.70%)	2/74 (2.70%)	1/74 (1.35%)	69/74 (93.24%)
	Juvenile UD	1	1/1 (100.00%)	0	0/0 (0.00%)	0/0 (0.00%)	0/0 (0.00%)	0/0 (0.00%)
	Young Adult	162	10/162 (6.17%)	152	5/152 (3.29%)	2/152 (1.32%)	3/152 (1.97%)	142/152 (93.42%)
	Middle Adult	102	2/102 (1.96%)	100	3/100 (3.00%)	1/100 (1.00%)	0/100 (0.00%)	96/100 (96.00%)
	Old Adult	37	0/37 (0.00%)	37	0/37 (0.00%)	1/37 (2.70%)	0/37 (0.00%)	36/37 (97.30%)
	Adult UD	78	30/75 (40.00%)	45	1/45 (2.22%)	0/45 (0.00%)	0/45 (0.00%)	44/45 (97.78%)
	TOTAL	**823**	**133/823 (16.16%)**	**690**	**17/690 (2.46%)**	**8/690 (1.16%)**	**6/690 (0.87%)**	**659/690 (95.51%)**
Ancaster	Fetal/Neonate	14	0/14 (0.00%)	14	0/14 (0.00%)	0/14 (0.00%)	0/14 (0.00%)	14/14 (100.00%)
	Infant/Younger Child	32	3/32 (9.38%)	29	0/29 (0.00%)	0/29 (0.00%)	0/29 (0.00%)	29/29 (100.00%)
	Middle Child	18	3/18 (16.67%)	15	2/15 (13.33%)	1/15 (6.67%)	0/15 (0.00%)	12/15 (80.00%)
	Older Child	10	2/10 (20.00%)	8	1/8 (12.50%)	1/8 (12.50%)	0/8 (0.00%)	6/8 (75.00%)
	Younger Adolescent	3	0/3 (0.00%)	3	0/3 (0.00%)	0/3 (0.00%)	0/3 (0.00%)	3/3 (100.00%)
	Older Adolescent	12	0/12 (0.00%)	12	3/12 (25.00%)	0/12 (0.00%)	0/12 (0.00%)	9/12 (75.00%)
	Juvenile UD	5	4/5 (80.00%)	1	0/1 (0.00%)	0/1 (0.00%)	0/1 (0.00%)	1/1 (100.00%)
	Young Adult	64	2/64 (3.13%)	62	6/62 (9.68%)	1/62 (1.61%)	1/62 (1.61%)	54/62 (87.10%)
	Middle Adult	58	0/58 (0.00%)	58	5/58 (8.62%)	1/58 (1.72%)	2/58 (3.45%)	50/58 (86.21%)
	Old Adult	39	1/39 (2.56%)	38	2/38 (5.26%)	0/38 (0.00%)	0/38 (0.00%)	36/38 (94.74%)
	Adult UD	21	5/21 (23.81%)	16	2/16 (12.50%)	0/16 (0.00%)	0/16 (0.00%)	14/16 (87.50%)
	TOTAL	**276**	**20/276 (7.25%)**	**256**	**21/256 (8.20%)**	**4/256 (1.56%)**	**3/256 (1.17%)**	**228/256 (89.06%)**

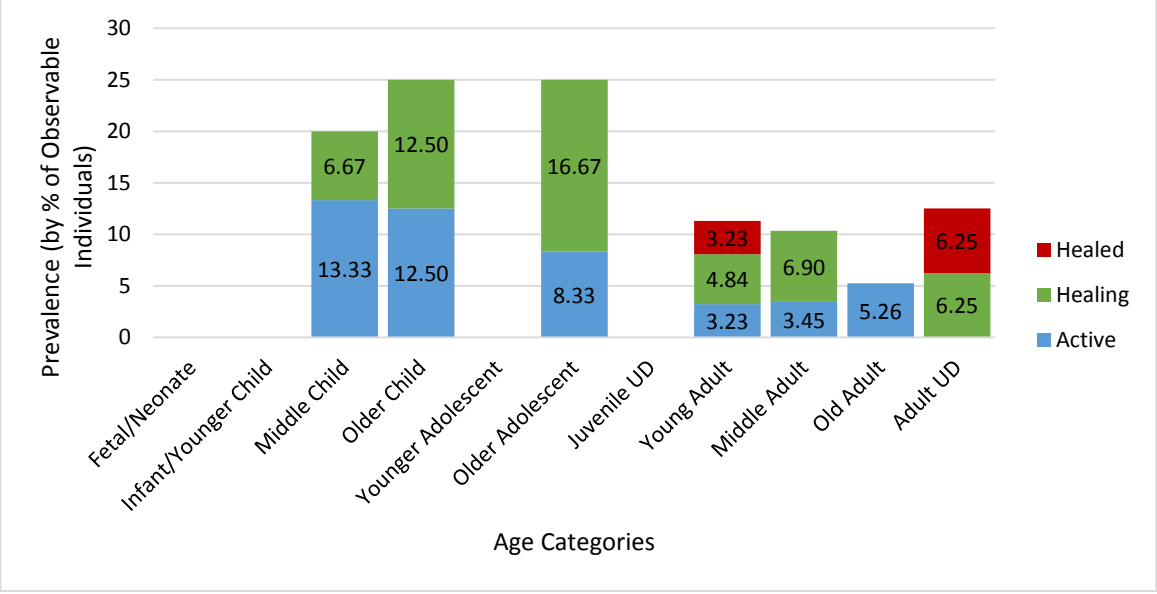
Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years). Diagnostic categories are outlined in 3.2.2.2 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate). The numbers in each cell indicate the number of individuals, with the values in parentheses representing these values as a percentage of observable individuals (diagnostic categories 1-4) or of all individuals present (category 5).

Figure 4.28. Prevalence of chronic respiratory infections by age at death for Isola Sacra



Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Juvenile UD (juvenile of undetermined age), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years), Adult UD (adult of undetermined age). Exact values for the percentage of individuals in each age category are represented by the numbers within or above each section of each column.

Figure 4.29. Prevalence of chronic respiratory infections by age at death for Ancaster



Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Juvenile UD (juvenile of undetermined age), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years), Adult UD (adult of undetermined age). Exact values for the percentage of individuals in each age category are represented by the numbers within each section of each column.

Within each sample, there are no significant differences between the mean ages at death of individuals in categories one and two and those without evidence for chronic respiratory infections (Table 4.14). As is the case for lesions associated with vitamin D deficiency, there is a significant difference between the age at death distributions of individuals with and without chronic respiratory infection lesions only in the group of individuals who survived past the age of three at Ancaster (Mantel-Cox p 0.03). This indicates that the presence of lesions had an effect on survival in this sample.

Table 4.14. Age at death for individuals with and without evidence for chronic respiratory infections

Characteristic (N)		**Mean Age at Death ± SD, years**	**Mean Difference P**
Isola Sacra	CRI (24)	20.15 ± 15.68 (24)	0.574
	No CRI (574)	22.16 ± 17.20 (574)	
	Active CRI (10)	19.76 ± 13.82 (10)	0.666
	No Active CRI (588)	22.12 ± 17.19 (588)	
Ancaster	CRI (23)	27.92 ± 17.36 (23)	0.665
	No CRI (214)	30.01 ± 22.36 (214)	
	Active CRI (10)	28.24 ± 20.38 (10)	0.817
	No Active CRI (227)	29.88 ± 22.01 (227)	

Abbreviated terms are SD (standard deviation), P (p value), N (number of individuals), CRI (chronic respiratory infections, includes individuals in categories one and two). P values given are for comparisons between the two characteristics in relevant rows. Significant values are bolded.

4.3.3. Chronic respiratory infections: Patterns based on sex

Prevalence values for features associated with chronic respiratory infections in individuals 16 years of age and older (Table 4.15) do not differ significantly based on sex at either Isola Sacra (Figure 4.30) or Ancaster (Figure 4.31), although a higher percentage of cases of chronic respiratory infection are observed in males than in females at both sites. Prevalence values for females and for males also do not differ significantly between the two samples. The highest prevalence values in each sample, for individuals sexed as ambiguous at Isola Sacra (Figure 4.30) and those of undetermined sex at Ancaster (Figure

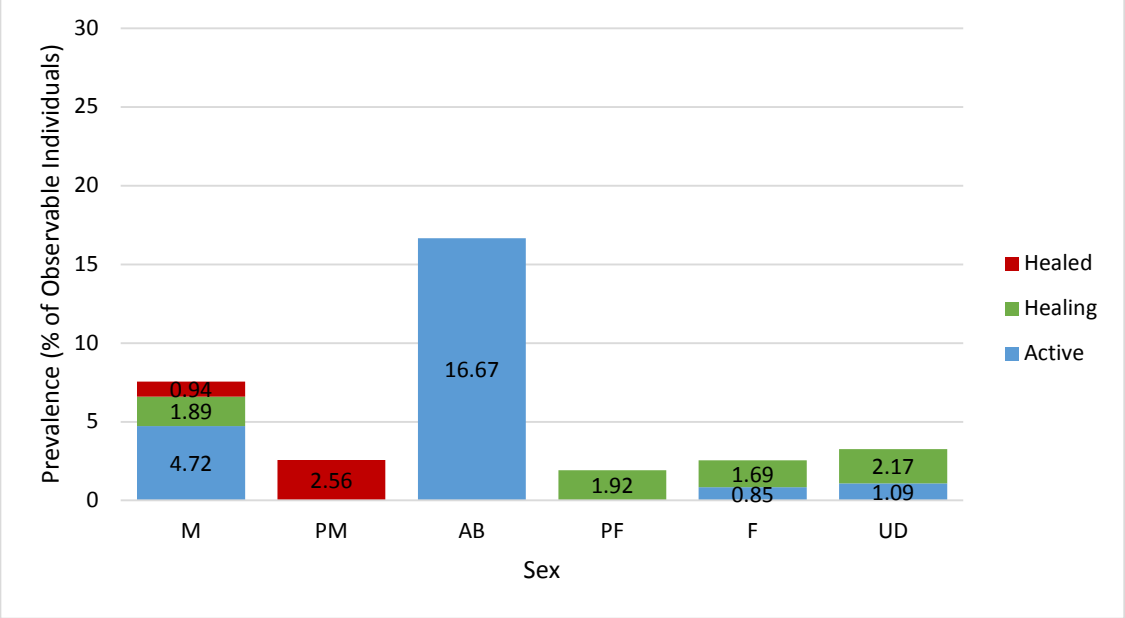
4.31), reflect the small numbers of individuals placed in these categories rather than a large number of individuals with evidence for chronic respiratory infections.

Table 4.15. Prevalence values by sex for skeletal evidence of active and healing/healed chronic respiratory infections for individuals aged at least 16 years

Sex		Active Lesions	Healing/Healed Lesions	Total
Isola Sacra	Male	5/145 (3.45%)	4/145 (2.76%)	9/145 (6.21%)
	Ambiguous	1/6 (16.67%)	0/6 (0.00%)	1/6 (16.67%)
	Female	1/170 (0.59%)	3/170 (1.76%)	4/170 (2.35%)
	Undetermined	1/92 (1.09%)	2/92 (2.17%)	3/92 (3.26%)
	TOTAL	**8/413 (1.94%)**	**9/413 (2.18%)**	**17/413 (4.12%)**
Ancaster	Male	5/100 (5.00%)	7/100 (7.00%)	12/100 (12.00%)
	Ambiguous	0/1 (0.00%)	0/1 (0.00%)	0/1 (0.00%)
	Female	2/78 (2.56%)	4/78 (5.13%)	6/78 (7.69%)
	Undetermined	0/8 (0.00%)	2/8 (25.00%)	2/8 (25.00%)
	TOTAL	**7/187 (3.74%)**	**13/187 (6.95%)**	**20/187 (10.70%)**

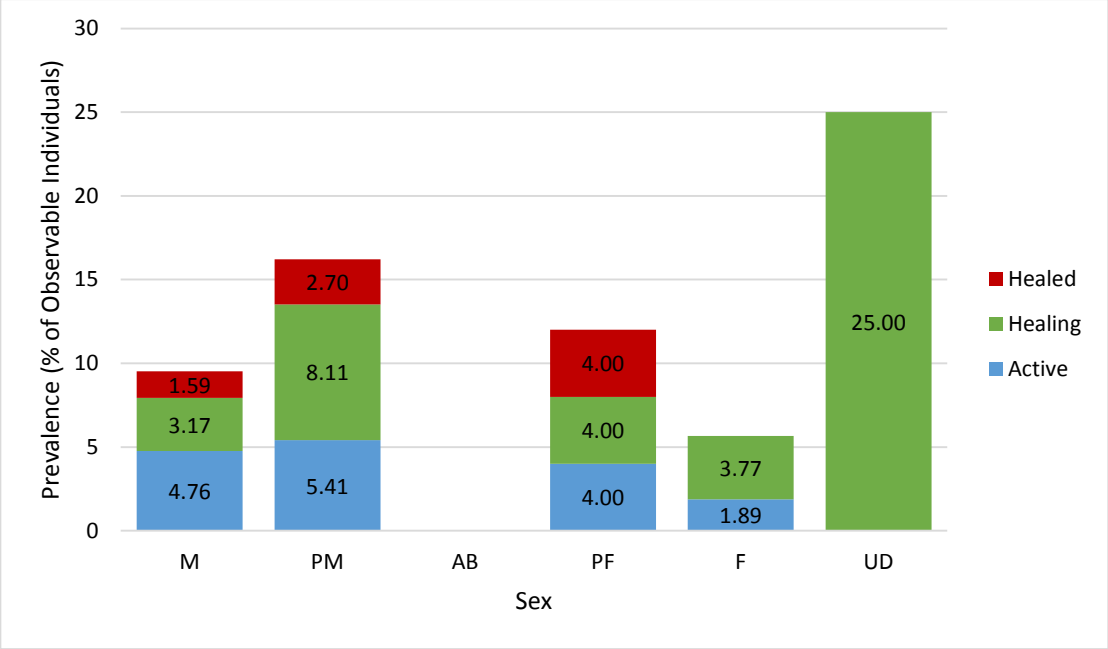
The male category includes individuals scored as male or probable male, and the female category includes individuals scored as female or probable female. The denominator indicates the number of individuals who could be evaluated for chronic respiratory infections in each sex category (diagnostic categories 1-4).

Figure 4.30. Prevalence of chronic respiratory infections by sex for Isola Sacra



Sex categories abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), UD (undetermined). Exact values for the percentage of individuals in each age category are represented by the numbers within each section of each column.

Figure 4.31. Prevalence of chronic respiratory infections by sex for Ancaster



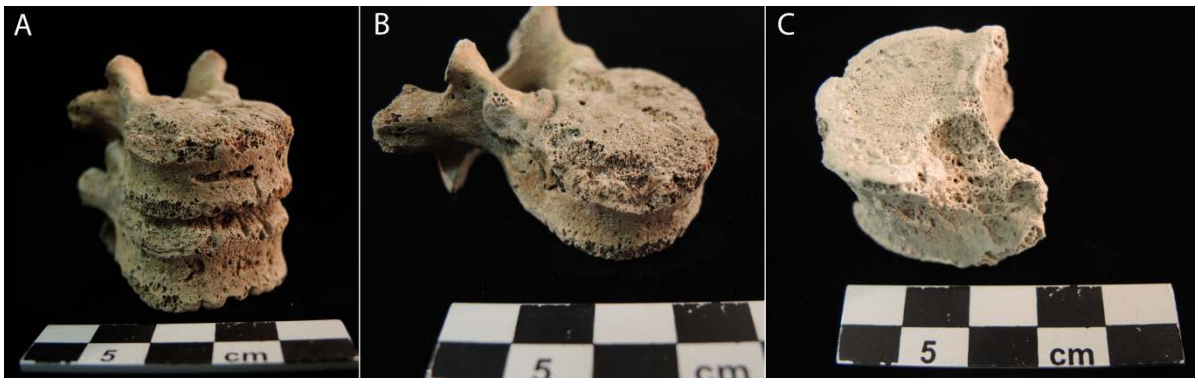
Sex categories abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), UD (undetermined). Exact values for the percentage of individuals in each age category are represented by the numbers within each section of each column.

4.3.4. Chronic respiratory infections: Skeletal features for diagnosis

Each individual skeleton from both assemblages was evaluated for the presence or absence of features associated with active, healing, and healed chronic respiratory infections (Table 3.5; Tables D.1-D.4). In juvenile cases, at both Isola Sacra and Ancaster, the most common feature in category one cases was clear new bone formation on the visceral aspect of the ribs at the vertebral ends (Figure 4.32), representing inflammation of the periosteum that has been argued to correspond directly with inflammation of the underlying pleura (Section 2.2.4). In category two cases, the most commonly observed feature was atypical new bone formation on the ribs, which was patchy, less clear, or spread along the rib shaft (Figure 4.32). The new bone formation observed in category one cases was typically more widespread than in category two cases; it often affected a

Figure 4.32 (Left). New bone formation on the visceral surfaces of the ribs associated with chronic respiratory infections in juveniles, demonstrating clear new bone formation at the vertebral end in SCR 319 (A) and less typical new bone formation along the rib shaft in SCR 95 (B).

Figure 4.33 (Below). Atypical lytic lesions in the vertebral bodies of juvenile (A, B) and adult (C) individuals from Isola Sacra. Lytic lesions are located at the superior anterolateral edge of two thoracic vertebral bodies in juvenile individual SCR 474 (A), showing a lack of smooth resorption and a small amount of reactive new bone formation (B). A larger lytic lesion is present on the inferior surface of one thoracic vertebral body in adult individual SCR 174, at the posterolateral corner (C), and although the resorbed surface is smoother, the location is not typical for a respiratory condition like TB.



larger number of ribs and was present in greater amounts or in plaques that were thicker or larger. Category three individuals were only present at Isola Sacra, and displayed evidence for widespread new bone formation and lytic lesions in the vertebral bodies

(Figure 4.33) that do not have features considered to be typical of TB (Table 3.8). Overall, the strongest and most commonly observed evidence for juvenile respiratory infection at these two sites is represented by clear new bone formation on the visceral surfaces of the ribs.

In adult individuals, at both sites, the most common feature in category one cases was also clear new bone formation on the visceral aspect of the vertebral ends of the ribs (Figure 4.34; Tables 4.16 and 4.17). In category two cases, the most commonly observed feature at Isola Sacra was atypical new bone formation on the ribs (Figure 4.34), whereas at Ancaster this feature co-occurred with new bone formation on other skeletal elements in the small number of cases present. Category one cases displayed new bone formation that was clearer, more widespread, and more likely to be located at the vertebral end of the rib than the new bone formation observed in category two cases. Individuals placed in category three often displayed evidence for atypical new bone formation on the ribs, and some individuals also

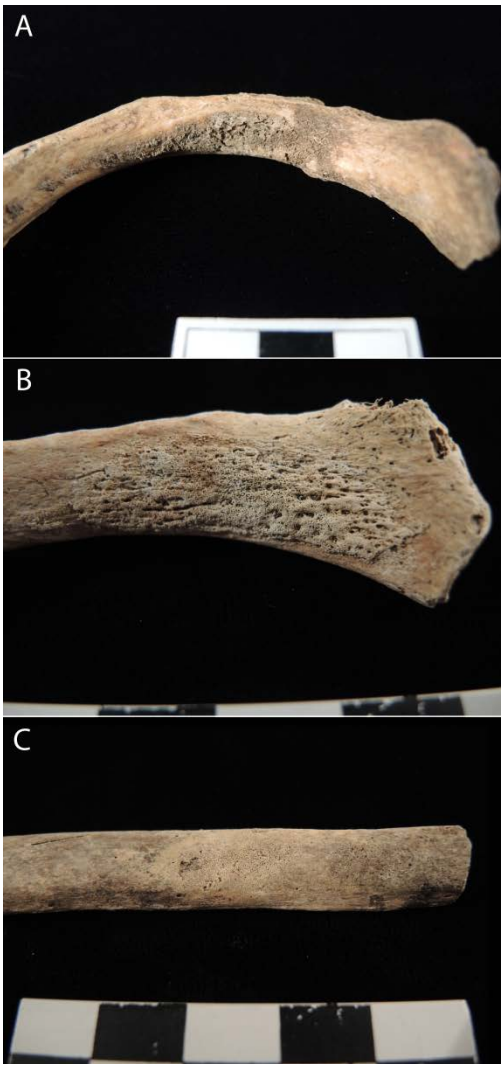


Figure 4.34. New bone formation on the visceral surfaces of the ribs associated with chronic respiratory infections in adults, demonstrating clear new bone formation at the vertebral rib end in ANC 47 (A) and SCR 272 (B), and less typical new bone formation along the rib shaft in SCR 434 (C).

Table 4.16. Active cases of chronic respiratory infection

Feature	Isola Sacra										
	SCR 95	SCR 136	SCR 168	SCR 221	SCR 319	SCR 343	SCR 390	SCR 434	SCR 462	SCR 706	SCR 804
Age Category	MC	I	YC	MA	OAL	OAL	AUD	MA	MA	YA	YA
Sex	-	-	-	M	M	AM	UD	F	M	M	M
Other rib new bone formation	A	A	A	A	A	A	**P**	A	A	-	A
Other lytic lesions	A	A	A	A	A	A	A	A	A	A	A
Periosteal new bone formation	A	**P**	A	A	A	A	A	**P**	A	**P**	A
Less typical rib new bone formation	**P**	**P**	**P**	**P**	A	**P**	A	**P**	A	-	**P**
Atypical vertebral lytic lesions	A	A	A	A	A	A	-	A	A	-	A
Lytic lesions of other joints	A	-	A	A	A	A	A	A	A	A	A
Widespread new bone formation	A	A	A	A	A	A	A	A	A	A	A
Atypical new bone formation	A	A	A	**P**	A	A	A	A	A	A	A
Typical rib new bone formation	**P**	**P**	**P**	A	**P**	**P**	**P**	**P**	A	-	**P**
Vertebral body collapse	-	A	A	A	A	A	-	A	A	-	A
Typical vertebral lytic lesions	-	A	A	A	A	A	-	A	**P**	-	A
Lytic lesions of major weight-bearing joints	-	-	A	A	A	A	-	A	A	-	-
Bilateral symmetrical new bone formation	A	-	A	**P**	A	A	**P**	A	A	**P**	A
Diagnosis	1	1	1	1	1	1	1	1	2	1	1

Feature	Ancaster									
	ANC 1	ANC 47	ANC 55	ANC 143	ANC 146	ANC 206	ANC 240	ANC 241	ANC Uncat C	ANC Uncat F
Age Category	OAL	OA	OC	MA	MC	MC	YA	OA	YA	MA
Sex	F	M	-	PM	-	-	PM	PF	M	M
Other rib new bone formation	A	A	A	**P**	A	A	**P**	**P**	A	A
Other lytic lesions	A	A	A	A	A	A	A	A	-	A
Periosteal new bone formation	A	A	A	A	**P**	A	**P**	A	-	A
Less typical rib new bone formation	A	A	**P**	A	**P**	A	**P**	A	A	A
Atypical vertebral lytic lesions	A	A	A	A	A	A	A	A	A	A
Lytic lesions of other joints	A	A	A	A	-	-	A	A	-	A
Widespread new bone formation	A	A	**P**	A	A	A	A	A	-	A
Atypical new bone formation	A	A	A	A	A	A	A	A	-	A
Typical rib new bone formation	A	**P**	**P**	**P**	**P**	**P**	**P**	**P**	**P**	**P**
Vertebral body collapse	A	A	A	A	A	A	A	A	A	A
Typical vertebral lytic lesions	**P**	A	A	A	A	A	A	A	A	A
Lytic lesions of major weight-bearing joints	**P**	A	A	A	-	-	A	A	A	A
Bilateral symmetrical new bone formation	A	A	A	A	A	A	A	A	-	A
Diagnosis	1	1	1	1	1	1	1	1	1	1

Non-diagnostic features are highlighted in red, possible features in green, and probable features in blue. Features are classified as absent (A), present (P), or not observable (-). Age categories abbreviated to I (Infant), YC (Younger child), MC (Middle child), OAL (Older adolescent), YA (Young adult), MA (Middle adult), OA (Old adult) AUD (Adult undetermined). Sex categories abbreviated as M (Male), PM (Probable male), AM (Ambiguous), PF (Probable female), F (Female), UD (Undetermined). Diagnostic categories are outlined in 3.2.2.2 (1 probable, 2 possible).

Table 4.17. Cases of chronic respiratory infection that are healing or healed.

Feature	Isola Sacra													
	SCR 36	SCR 120	SCR 248	SCR 272	SCR 276	SCR 297	SCR 399	SCR 411	SCR 531	SCR 676	SCR 729	SCR 761	SCR 791	SCR 830
Age Category	OAL	YA	YC	YA	YC	YA	YA	OAL	I	OA	MA	MC	MC	YA
Sex	PM	M	-	F	-	M	UD	F	-	M	UD	-	-	PF
Other rib new bone formation	A	A	A	A	A	A	-	A	A	A	A	A	A	A
Other lytic lesions	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Periosteal new bone formation	**P**	A	A	A	A	A	A	**P**	A	**P**	**P**	**P**	A	A
Less typical rib new bone formation	**P**	**P**	A	**P**	A	**P**	-	**P**	**P**	**P**	A	**P**	**P**	A
Atypical vertebral lytic lesions	A	A	A	A	A	**P**	-	A	A	-	A	-	A	-
Lytic lesions of other joints	A	-	A	A	A	A	A	A	-	A	A	-	-	-
Widespread new bone formation	A	A	A	A	A	A	A	A	A	A	A		A	A
Atypical new bone formation	A	A	A	A	A	A	**P**	A	A	A	A	A	A	A
Typical rib new bone formation	A	A	**P**	**P**	**P**	**P**	-	A	A	A	A	A	A	**P**
Vertebral body collapse	A	A	A	A	A	A	-	A	A	-	A	-	-	-
Typical vertebral lytic lesions	A	A	A	A	A	A	-	A	A	-	A	-	A	-
Lytic lesions of major weight-bearing joints	A	-	A	A	A	A	-	A	-	-	-	-	-	-
Bilateral symmetrical new bone formation	A	A	A	A	A	A	**P**	A	A	A	**P**	-	-	A
Diagnosis	2	2	1	1	1	1	2	2	2	2	1	1	2	1
Healing	H	H	HL	HL	HL	HL	HL	HL	HL	HL	HL	HL	HL	HL

Feature	Ancaster														
	ANC 11	ANC 14	ANC 48B	ANC 65	ANC 69	ANC 75	ANC 78	ANC 105	ANC 109	ANC 140	ANC 148A	ANC 167	ANC 235	ANC 244	ANC 261
Age Category	YA	OA	OAL	MA	AUD	AUD	MA	OC	MA	YA	MA	OAL	YA	YA	MC
Sex	M	PM	M	PM	PF	UD	F	-	F	PM	PF	M	UD	PM	-
Other rib new bone formation	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A
Other lytic lesions	A	A	A	A	A	A	A	A	A	A	-	A	A	A	A
Periosteal new bone formation	**P**	A	**P**	**P**	A	A	A	A	**P**	**P**	-	A	A	**P**	A
Less typical rib new bone formation	A	A	A	**P**	**P**	A	A	**P**	**P**	A	A	A	**P**	**P**	**P**
Atypical vertebral lytic lesions	A	**P**	A	A	A	-	A	A	A	A	A	A	A	A	A
Lytic lesions of other joints	A	A	A	A	A	A	A	-	A	A	-	A	A	A	-
Widespread new bone formation	A	A	A	A	A	-	A	A	A	A	-	A	A	A	A
Atypical new bone formation	A	A	A	A	A	A	A	A	A	A	-	A	A	A	A
Typical rib new bone formation	A	**P**	**P**	**P**	**P**	**P**	**P**	A	**P**	**P**	**P**	**P**	**P**	A	A
Vertebral body collapse	**P**	A	A	A	A	-	A	A	A	A	A	A	A	A	A
Typical vertebral lytic lesions	A	A	A	A	A	-	A	A	A	A	A	A	A	A	A
Lytic lesions of major weight-bearing joints	A	A	A	A	-	-	A	A	A	A	-	A	A	A	A
Bilateral symmetrical new bone formation	A	A	A	A	-	-	A	A	A	A	-	A	A	A	A
Diagnosis	1	1	1	2	1	1	1	2	1	1	1	1	1	2	2
Healing	H	HL	HL	HL	H	HL	HL	HL	HL	HL	HL	HL	HL	H	HL

Non-diagnostic features are highlighted in red, possible features in green, and probable features in blue. Features are classified as absent (A), present (P), or not observable (-). Age categories abbreviated to I (Infant), YC (Younger child), MC (Middle child), OC (Older child), OAL (Older adolescent), YA (Young adult), MA (Middle adult), OA (Old adult), AUD (Adult undetermined). Sex categories abbreviated as M (Male), PM (Probable male), AM (Ambiguous), PF (Probable female), F (Female), UD (Undetermined). Diagnostic categories are outlined in 3.2.2.2 (1 probable, 2 possible). Healing categorized as H (healed), HL (healing).

showed evidence for atypical vertebral lytic lesions (Figure 4.33). The strongest and most commonly observed evidence for chronic respiratory infections in both adult and juvenile individuals in both assemblages is represented by new bone formation on the ribs, with the location and appearance of this new bone formation impacting the strength and specificity of the evidence it provides.

New bone formation on the ribs was the most commonly observed evidence for chronic respiratory infections in both active (Table 4.16) and healing or healed cases (Table 4.17). All juvenile individuals and the majority of adult individuals with evidence for chronic respiratory infections displayed some evidence of new bone formation on the visceral aspects of the ribs, in many cases co-occurring with new bone formation on other elements, particularly the long bones or hand and foot bones. Several adult individuals also displayed other types of evidence for respiratory conditions (Tables 4.16 and 4.17). At Isola Sacra, lesions in the vertebrae (Figure 4.26) and patterns of bilaterally symmetrical new bone formation in the long bones characteristic of HOA (Figures 4.24 and 4.25) were also observed; at Ancaster, lesions were also present in the vertebrae (Figure 4.26) and hip joint (Figure 4.27). Due to the strength of associations between new bone formation in the ribs and chronic respiratory infections, new bone formation with a specific distribution and appearance in the long bones with HOA, and lytic lesions in the vertebral bodies and joints with skeletal TB, diagnoses could be made based on only one of these features. In many individuals, characteristic new bone formation on the visceral surfaces of the ribs co-occurred with other rib lesions that were less clear or were located further toward the sternal end of the rib. Differences between active (Table 4.16) and

healing or healed cases (Table 4.17) of chronic respiratory infection were determined based on the state of remodeling of new bone formation on the ribs or long bones (Figure 4.35), as well as the presence or absence of collapse and fusion in the vertebrae and joints.

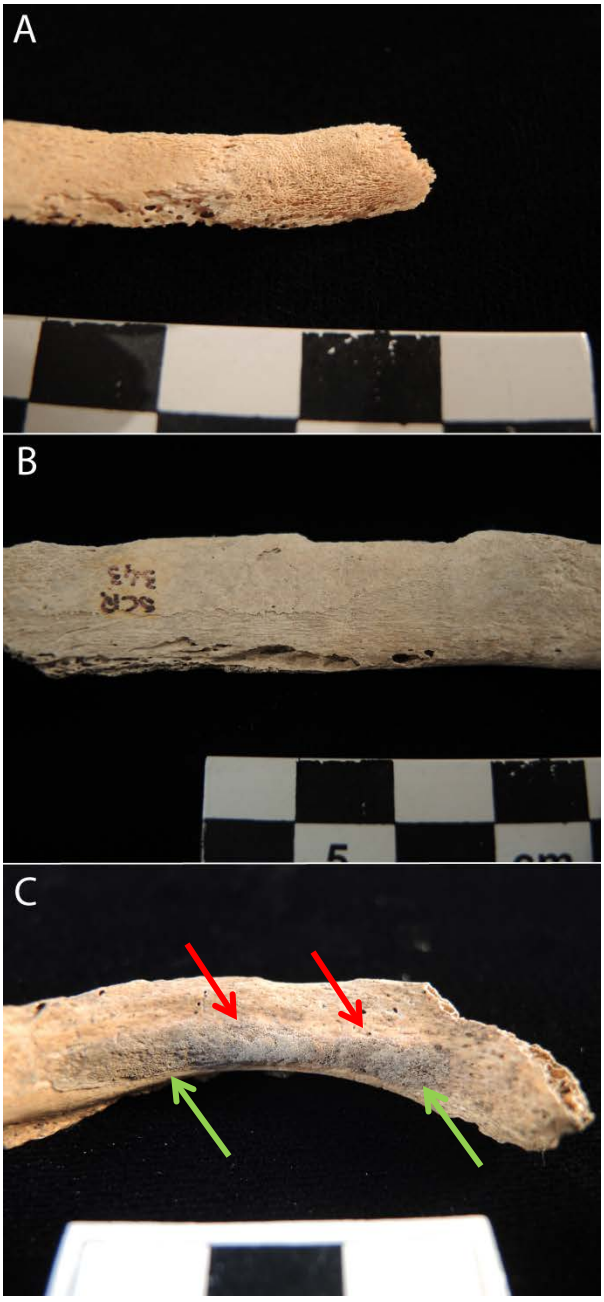


Figure 4.35. New bone formation on the visceral surfaces of the ribs demonstrating the appearance of active lesions in SCR 136 (A), healed lesions in SCR 343 (B), and a mix of active (green arrows) and healed (red arrows) lesions classified as healing in ANC 109 (C).

4.3.5. Chronic respiratory infections: Rib lesions

A significantly greater number of individuals displayed proliferative lesions on the visceral surfaces of the ribs at Ancaster than at Isola Sacra (p 0.0004). This may be affected by better general preservation of the ribs at this site, given that 81.7% of Ancaster individuals had observable ribs while only 66.5% of individuals from Isola Sacra had ribs preserved. However, if only individuals with observable ribs are considered, the prevalence of proliferative lesions on the ribs remains significantly higher at Ancaster (p 0.0007). The average number of ribs preserved per individual is also higher at Ancaster (13.57) than at Isola Sacra (8.29); this difference is maintained if the number of identifiable ribs is considered only for individuals with some ribs preserved, with Ancaster individuals having an average of 16.57 ribs preserved and Isola Sacra individuals having 12.34. Despite poorer general preservation of the ribs and a lower prevalence of proliferative rib lesions at Isola Sacra, the extent of active respiratory disease, as indicated by the mean number of ribs affected, is significantly higher at this site than at Ancaster (Tables 4.18 and 4.19). At Isola Sacra, the number of ribs affected is higher for individuals with active lesions than for those with healing or healed lesions, which is significant both in terms of the mean number of ribs affected (Table 4.19) and the distribution of the two groups (two sample Kolmogorov-Smirnov D 0.67, p 0.02). No significant differences exist between the numbers of ribs affected in individuals with active and healing or healed lesions at Ancaster. In comparisons between the two sites, the mean number of ribs affected in individuals with lesions that were active at the time of death is significantly greater at Isola Sacra than at Ancaster (Table 4.19). There were

Table 4.18. Individuals with proliferative lesions on the visceral surfaces of the ribs

Site	Individual	Age Category	Sex	Diagnosis	Active/Healed	# Ribs
Isola Sacra	SCR 095	Middle Child	-	1	Active	12
	SCR 136	Infant/Younger Child	-	1	Active	15
	SCR 168	Infant/Younger Child	-	1	Active	3
	SCR 221	Middle Adult	M	1	Active	4
	SCR 319	Older Adolescent	M	1	Active	3
	SCR 343	Older Adolescent	AB	1	Active	24
	SCR 390	Adult UD	UD	1	Active	4
	SCR 434	Middle Adult	F	1	Active	9
	SCR 804	Young Adult	M	1	Active	12
	SCR 036	Older Adolescent	PM	2	Healed	1
	SCR 120	Young Adult	M	2	Healed	1
	SCR 248	Infant/Younger Child	-	1	Healing	6
	SCR 272	Young Adult	F	1	Healing	12
	SCR 276	Infant/Younger Child	-	1	Healing	1
	SCR 297	Young Adult	M	1	Healing	4
	SCR 411	Older Adolescent	F	2	Healing	1
	SCR 531	Infant/Younger Child	-	2	Healing	2
	SCR 676	Old Adult	M	2	Healing	1
	SCR 761	Middle Child	-	1	Healing	4
	SCR 791	Middle Child	-	2	Healing	1
	SCR 830	Young Adult	PF	1	Healing	2
Ancaster	ANC 047	Old Adult	M	1	Active	3
	ANC 055	Older Child	-	1	Active	8
	ANC 143	Middle Adult	PM	1	Active	2
	ANC 146	Middle Child	-	1	Active	9
	ANC 206	Middle Child	-	1	Active	3
	ANC 240	Young Adult	PM	1	Active	3
	ANC 241	Old Adult	PF	1	Active	3
	ANC Uncat C	Young Adult	M	1	Active	4
	ANC Uncat F	Middle Adult	M	1	Active	1
	ANC 014	Young Adult	PM	1	Healing	5
	ANC 048B	Older Adolescent	M	1	Healing	3
	ANC 065	Middle Adult	PM	2	Healing	2
	ANC 069	Adult UD	PF	1	Healed	4
	ANC 075	Adult UD	UD	1	Healing	2
	ANC 078	Middle Adult	F	1	Healing	2
	ANC 105	Older Child	-	2	Healing	3
	ANC 109	Middle Adult	F	1	Healing	8
	ANC 140	Young Adult	PM	1	Healing	3
	ANC 148A	Middle Adult	PF	1	Healing	1
	ANC 167	Older Adolescent	M	1	Healing	2
	ANC 235	Young Adult	UD	1	Healing	12
	ANC 244	Young Adult	PM	2	Healed	9
	ANC 261	Middle Child	-	2	Healing	1

Diagnostic categories are outlined in 3.2.2.2 (1 probable, 2 possible). Sex categories abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), and Sex/Age categories abbreviated as UD (undetermined). Age categories are Fetal/Neonate (< 0.125 years), Infant (0.125-1 year), Younger child (1.1-3 years), Middle child (4-7 years), Older child (8-11 years), Younger adolescent (12-15 years), Older adolescent (16-19 years), Juvenile UD (juvenile of undetermined age), Young adult (20-34 years), Middle adult (35-49 years), Older adult (50+ years), Adult UD (adult of undetermined age). The number of ribs given identifies the number of ris affected in each individual.

no significant differences between Isola Sacra and Ancaster individuals with healed or healing lesions, or for all individuals with lesions as a group.

The significant relationship observed at Isola Sacra between the extent of disease, as measured by the number of ribs affected, and recovery is not associated with any significant differences in age at death between individuals with active and healed rib lesions, either in terms of differences between the means (Table 4.19) or between age distributions (p 0.93). Differences in average age at death (Table 4.19) and age distribution (p 0.96) also do not differ significantly between individuals with active and healing or healed lesions at Ancaster. Significant differences between the extent of respiratory disease at Isola Sacra and Ancaster do not correspond with any significant differences in age at death between the two sites.

Table 4.19. Summary statistics for individuals with proliferative rib lesions

Characteristic		**Mean # Ribs ± SD (N)**	**Mean Difference P**	**Mean Age at Death ± SD (N), years**	**Mean Difference P**
Isola Sacra	Active	9.60 ± 7.06 (9)	**0.01**	16.71 ± 13.77 (8)	0.87
	Healing/Healed	3.00 ± 3.28 (12)		17.95 ± 17.13 (12)	
	Total	5.81 ± 6.07 (21)	**0.04**	17.45 ± 15.49 (20)	0.06
Ancaster	Active	4.00 ± 2.69 (9)	0.96	29.21 ± 21.36 (9)	0.69
	Healing/Healed	4.07 ± 3.32 (14)		25.97 ± 14.90 (12)	
	Total	4.04 ± 3.02 (23)	**0.04**	27.36 ± 17.53 (21)	0.06

Abbreviations used are SD (standard deviation), N (number of individuals), P (p value). P values given are for the comparison between active and healing/healed lesions, and P values in the 'Total' row are for the comparison in total lesions between the two sites. Statistically significant values are bolded.

4.4. Vitamin D Deficiency and Chronic Respiratory Infections

Following the observation of a relationship between vitamin D deficiency and respiratory infections based on clinical data from modern populations (Section 2.3), potential associations between these two conditions were investigated in the Isola Sacra and Ancaster assemblages. Possible links between vitamin D deficiency and chronic respiratory infections were evaluated by considering individuals who displayed skeletal evidence for both conditions. This association was also tested quantitatively through the use of odds ratios.

4.4.1. Vitamin D deficiency and chronic respiratory infections: Possible co-occurrence

Two individuals from Ancaster display evidence for both vitamin D deficiency and a chronic respiratory infection, representing possible cases of co-occurrence. Individual ANC 146 (Figure 4.36), a middle child, is classified as a category one case of healed vitamin D deficiency (Table 4.9) based on thickening of the fibular diaphyses, flaring of one sternal rib end, and tilting of the left distal femoral metaphysis. This individual is also classified as a category one case of chronic respiratory infection (Table 4.17) based on the presence of both characteristic and less typical visceral rib new bone formation. Individual ANC Uncatalogued F (Figure 4.37), a male middle adult, is classified as a category two case of healed vitamin D deficiency (Table 4.11) based on clear bending of the left tibia (Figures 4.20 and 4.37). The deformity appears to be unilateral, but there is a healed fracture of the distal right tibia and fibula which prevent the proper evaluation of bending on this side. This individual is also classified as a category one case of chronic respiratory infection (Table 4.16) based on the presence of

Figure 4.36. Features of healed vitamin D deficiency (A, B) and chronic respiratory infection (C, D) present in ANC 146. A) Femora, particularly showing tilting of the distal left femoral metaphysis; B) Fibulae, showing thickening of the diaphyses; C, D) Clear new bone formation on the visceral surfaces of the ribs at the vertebral ends, present on nine rib fragments. Many of the lesions show a mixture of woven and lamellar bone.

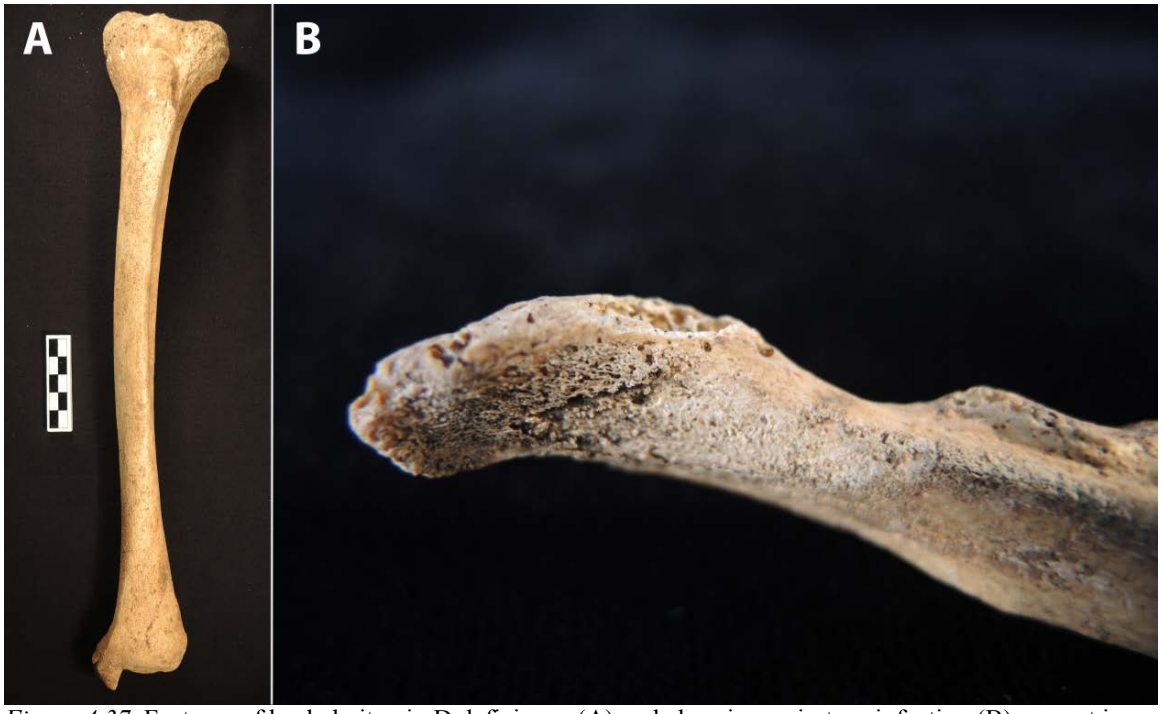


Figure 4.37. Features of healed vitamin D deficiency (A) and chronic respiratory infection (B) present in ANC Uncatalogued F. A) Mediolateral deformation of the left tibia (also pictured with the fibula in Figure 4.20); B) Clear woven new bone formation on the visceral aspect of the vertebral end of a rib.

clear active visceral rib new bone formation. These represent the only instances in which clear skeletal features of both vitamin D deficiency and chronic respiratory infections are present in the same individual.

One additional individual from Ancaster displays evidence for a chronic respiratory infection in combination with some histological evidence for vitamin D deficiency. Individual ANC 78, a female middle adult, is classified as a category three case of vitamin D deficiency (Table C.4) based on histological evidence for mineralization defects in the absence of macroscopic evidence for deficiency. This individual is also classified as a category one case of chronic respiratory infection (Table 4.17) based on the presence of clear visceral rib new bone formation.

There are a small number of other individuals from both sites who display evidence for chronic respiratory infections (Tables 4.16 and 4.17) and have also been placed in category three for vitamin D deficiency (Tables C.1, C.3, and C.4). However, none of these individuals can be securely diagnosed as representing cases of vitamin D deficiency. Individual SCR 136, an infant, has a combination of non-diagnostic features which may result from vitamin D deficiency or from a number of other pathological conditions, as well as both clear and less typical new bone formation on the visceral surfaces of the ribs, scapulae, and some of the long bones. Individual SCR 221, a male middle adult, displays a slight possible deformity in the femora, as well as new bone formation consistent with HOA and some slight new bone formation on the visceral ribs. Individual ANC 1, an older adolescent female, displays slight mediolateral bending of only the left tibia, as well as evidence for TB in the hip (Section 4.3.1.4). Individual ANC 69, a female adult, displays slight abnormal curvature of the clavicles, as well as both characteristic and less typical new bone formation on the visceral ribs. Individual ANC 109, a female middle adult, displays a slight deformation of only the right tibia, as well as both characteristic and less typical new bone formation on the visceral ribs. All of these individuals have clear features of chronic respiratory infections, but the evidence present for possible vitamin D deficiency is not sufficient to support a diagnosis. Interpretations are limited by the lack of confidence in identifying vitamin D deficiency in these cases; as a result, a connection between possible deficiency and respiratory infection in these individuals cannot be established.

4.4.2. Vitamin D deficiency and chronic respiratory infections: Quantitative associations

Following Snoddy et al. (2016), odds ratios were calculated to test for associations between the prevalence of evidence for vitamin D deficiency (Table 4.4) and chronic respiratory infections (Table 4.12) in each collection. In this scenario, following the demonstrated clinical association between the two conditions, as well as the plausible mechanism provided by molecular evidence (Section 2.3), vitamin D deficiency represents a possible risk factor for the outcome of chronic respiratory infection. At Isola Sacra, there was a significant association between the point prevalence values for these two conditions (OR 1.85, 95% CI 1.12-3.05, p [Fisher's exact] 0.019). However, at Ancaster, there was no significant association between skeletal evidence for vitamin D deficiency and chronic respiratory infections (OR 0.96, 95% CI 0.53-1.74, p [Fisher's exact] >0.99).

CHAPTER 5: Discussion

5.0. Introduction: Disease Occurrence and Experience at Ancaster and Isola Sacra

This comparative paleopathological analysis identified substantial quantitative and individual qualitative differences in skeletal lesions associated with vitamin D deficiency and chronic respiratory infections at two Roman period sites, reflecting considerable variation in the occurrence and experience of disease. A significant relationship between lesions associated with vitamin D deficiency and chronic respiratory infections can be demonstrated quantitatively at Isola Sacra. The Ancaster collection demonstrated a significantly higher prevalence of chronic respiratory infection lesions, a higher number of individuals identified as older adults, and a higher mean age at death than the Isola Sacra assemblage, along with demonstrably significant effects on survival associated with lesions related to vitamin D deficiency and chronic respiratory infection, and two individuals displaying skeletal features associated with both conditions. The higher number of individuals with skeletal evidence for disease in this assemblage is suggested to represent a higher number of "survivors", who lived with disease long enough for skeletal manifestations to form. Variations in the occurrence of and association between lesions caused by vitamin D deficiency and chronic respiratory infections can be productively conceptualized using the concept of local biologies, which highlights the importance of individual experience and the influence of geographic patterns of disease that form through interactions with external environmental factors (Lock & Nguyen, 2010). Local biologies develop from the combination of differential experiences of

vitamin D deficiency, chronic respiratory infections, and longevity, and from the varying ways in which these conditions interact over the life course.

5.1. Vitamin D Deficiency and Chronic Respiratory Infections: Interactions

The prevalence of skeletal lesions associated with vitamin D deficiency is higher at Ancaster than at Isola Sacra, corresponding with a significantly higher prevalence of proliferative rib lesions. Destructive lesions associated with chronic respiratory infections are also more commonly observed at this site, and are more severe in terms of progression. In evaluating whether these patterns of occurrence may relate to an association between the two conditions, it is necessary to examine specific ways in which the interaction of vitamin D deficiency and chronic respiratory infections may affect the appearance or development of skeletal lesions, a consideration which has not been previously explored.

The investigation of potential interactions between vitamin D deficiency and respiratory infections in the past is predicated upon specific clinical evidence that supports an association between the two conditions in modern populations (e.g., Fleming et al., 2007; Laaksi et al., 2007; McNally et al., 2009; Pettifor, 2003; Wayse et al., 2003). In order to elucidate the nature of the potential relationship between vitamin D deficiency and chronic respiratory infections, it is necessary to consider how these conditions develop and interact throughout the life course. This is particularly relevant for chronic respiratory infections like TB, which may have multiple active episodes separated by long latency periods (Ellner, 1997; Feja & Saiman, 2005). Similarly, vitamin D

deficiency is often episodic; as a condition that is reversible with repletion, it is likely to recur (Brickley et al., 2014; D'Ortenzio et al., 2016).

A model examining interactions between dietary protein and iron adequacy with tuberculosis was developed by Wilbur et al. (2008), based on the fact that inadequate protein impairs the immune response to *Mycobacterium tuberculosis* (MTB), as well as on the slight protective advantage given by mild iron deficiency. In this model, various outcomes, ranging from fulminant disease with rapid host death to slow growth of MTB with increased likelihood of skeletal dissemination, are connected with specific combinations of iron and protein intake (Wilbur et al., 2008). Unfortunately, the authors dismiss the possibility of creating a similar model for vitamin D given the current state of knowledge and the complexities of skeletal and immune actions of this molecule (Wilbur et al., 2008). While the intricacies of vitamin D function make it imperfectly suited to the type of simple model developed by Wilbur et al. (2008), there is value in attempting to synthesize epidemiological and molecular evidence from current clinical research in order to better understand interactions between vitamin D deficiency and chronic respiratory infections in past populations. Understanding processes by which vitamin D deficiency impacts the skeleton and the immune response to infection will assist in elucidating factors that affect which individuals are likely to exhibit skeletal involvement, as well as how the appearance and development of lesions could be altered if these conditions co-occur.

Vitamin D deficiency is likely to modulate the appearance of chronic respiratory infection lesions in archaeological skeletal remains through two main pathways. First,

vitamin D status may modify the effectiveness of the immune response to infection, and therefore the likelihood of pathogen containment versus dissemination (McMurray et al., 1990; Ustianowski et al., 2005). Second, actions of vitamin D in skeletal homeostasis and processes of bone formation, resorption, and mineralization (Stern, 2005) may affect the formation of skeletal lesions associated with respiratory infections in deficiency states. In terms of the first proposed pathway, vitamin D deficiency decreases the efficacy of the immune response to infection by impairing the potentiating effects of vitamin D on macrophage functions (Cannell et al., 2006). For MTB specifically, these effects include inhibition of pathogens' growth as well as promotion of their direct killing, through increased production of antimicrobial peptides (AMPs) such as cathelicidin and increased macrophage activation, among other mechanisms (Adams et al., 2007; Liu et al., 2006). In the case of TB, vitamin D enhances granuloma formation and control of MTB infection (Sita-Lumsden et al., 2007), and calcium is required for granuloma maintenance (Wilbur et al., 2008). As a result, vitamin D deficiency is likely to impair effective MTB containment. Bacilli may be more likely to escape from or never adequately be contained within a granuloma, making dissemination more probable and possibly leading to a higher incidence of skeletal involvement in TB infection in the presence of concomitant vitamin D deficiency. This scenario is supported by epidemiological evidence, as an increased risk of non-pulmonary infection, which could include skeletal involvement, has been observed in association with vitamin D deficiency (e.g., Chan, 2000; Davies, 1985; Wilkinson et al., 2000). In combination with other factors increasing the likelihood of more severe respiratory infection, increased dissemination may result in fulminant disease

and rapid host death, as proposed by the model developed by Wilbur et al. (2008) for the combination of protein and iron deficiencies with TB. In this case, a reduced prevalence of skeletal involvement may be observed. The likelihood of skeletal involvement may therefore also depend on whether increased dissemination of MTB is associated with severe infection and rapid death, or only with the development of extrapulmonary lesions.

The effects of co-occurrence in the case of vitamin D deficiency and TB are further complicated by the fact that the majority of tuberculous skeletal lesions, such as those observed in the vertebrae of individuals at both Isola Sacra and Ancaster and in the hip of one individual at Ancaster (Figures 4.26 and 4.27), are resorptive and destructive (Resnick, 2002). Vitamin D status can have varying effects on bone resorption processes over the course of deficiency (Stern, 2005), and therefore the appearance of skeletal lesions with concomitant TB infection may vary according to the phase of vitamin D deficiency. Early stages of deficiency are associated with secondary hyperparathyroidism, which has potentiating effects on osteoclastogenesis and bone resorption in order to correct low serum calcium (Pettifor, 2003). As a result, if tuberculous lesions developed in the skeleton during this stage, destruction may be much more severe. In the spine, this could lead to the involvement of a higher number of vertebrae, more rapid development of vertebral collapse, and potentially more severe angular kyphosis and other deformities. However, in the later stages of vitamin D deficiency, depressed extracellular levels of calcium and phosphorous cause newly formed bone to be improperly or unevenly mineralized (Bonucci et al., 1969), and result in the deposition of abnormally high numbers of pathologically thickened osteoid seams (Pitt, 2002). Given the fact that

osteoclasts require bone matrix to be mineralized before resorption can occur (Aubin & Heersche, 2005), impaired mineralization could interfere with resorption (Jaffe, 1975; Stern, 2005); since 1,25-$(OH)_2$D also stimulates normal osteoclast activity (Atkins et al., 2007), a deficiency of vitamin D may also directly impair osteoclast-mediated resorption. The development of destructive lesions in the skeleton during later phases of vitamin D deficiency may therefore occur more slowly due to the inhibition of osteoclastic resorption. However, given the negative effect of mineralization defects on skeletal strength, once destructive lesions did develop they may more easily lead to the collapse of weakened and structurally compromised skeletal elements.

The production of 1,25-$(OH)_2$D in granulomas is suggested to favor MTB dissemination and subsequent tissue destruction (Wilbur et al., 2008). However, 1,25-$(OH)_2$D produced locally at granuloma sites is likely to relate primarily to peripheral hydroxylation of 25-OHD by immune cells (Adams et al., 2007; White, 2008) as part of an effective local response to MTB, rather than to systemic effects of vitamin D on mineral or skeletal homeostasis. Given that the effects of local production of 1,25-$(OH)_2$D are normally not related to calcium balance (Rook, 1988), and quantities large enough to affect circulating hormone levels and relate to systemic effects are not commonly observed, it is difficult to accept that 'overspill' at lesion sites would have a significant effect on skeletal homeostasis. Wilbur et al. (2008) also point to systemic vitamin D-induced upregulation of skeletal resorption; however, this effect is dependent on available calcium, with vitamin D only acting to promote calcium release from the skeleton when intestinal absorption is insufficient to maintain mineral homeostasis. The relationship of vitamin D

to systemic effects on resorption is therefore complicated by dietary intake of calcium. Parathyroid hormone (PTH) may potentiate resorption, but this process only operates when serum calcium is insufficient. Immune effects of vitamin D and local production of 1,25-$(OH)_2$D by immune cells will also depend on calcium status, as 25-OHD is preferentially used for renal production of 1,25-$(OH)_2$D to facilitate systemic effects on mineral homeostasis (Holick, 2008). Given primary regulation of local 1,25-$(OH)_2$D synthesis by substrate availability, reduced serum 25-OHD as a result of increased 1,25-$(OH)_2$D production for mineral homeostasis may significantly affect the ability of macrophages to initiate or increase antimicrobial activity. This clearly illustrates that that all non-classic actions of vitamin D, including its immunomodulatory effects, are necessarily limited by its primary classic function in mineral homeostasis (Bikle, 2009). Calcium status is therefore an important modulator of the physiological manifestations of vitamin D status, and attempts to elucidate the effects of vitamin D status on the immunological response to MTB and other respiratory pathogens must take this into account.

Proliferative lesions associated with chronic respiratory infections, including periosteal reactions on the visceral surfaces of the ribs and in the long bones, involve the formation of new bone (Roberts & Buikstra, 2003a). New bone formation on the visceral surfaces of the ribs was the most commonly observed type of evidence for chronic respiratory infections at both Isola Sacra and Ancaster (Section 4.3.4), and the presence of proliferative lesions on the long bones provided evidence consistent with hypertrophic osteoarthropathy (HOA) for several individuals at Isola Sacra (Figures 4.24 and 4.25). It

is therefore important to consider the fact that vitamin D deficiency-induced defects in mineralization (Pitt, 2002) may impair the formation of proliferative lesions. Despite the production of organic matrix, vitamin D deficiency would result in the delay or failure of mineralization such that, if the individual died while deficiency was still active, lesions may remain unmineralized. Poorly mineralized bone is more likely to undergo postmortem destruction, and is less likely to preserve in archaeological remains (Brickley & Ives, 2008, p. 13; Brickley et al., 2014). This could result in a lack of paleopathological evidence for chronic respiratory infections in vitamin D deficient individuals.

If the effect of vitamin D deficiency on chronic respiratory infection manifestation is considered independently of other factors, it appears most likely to result in increased rates of infection and pathogen dissemination. This could lead to an increase in either the number or severity of destructive skeletal lesions, in which weakened bone would collapse and deform more rapidly. Destructive lesions are both more commonly observed and more severe in terms of progression at Ancaster compared to Isola Sacra, and it is possible that this could be related to the slightly higher prevalence of evidence for vitamin D deficiency overall and the significantly higher prevalence of deficiency in juveniles at this site. In combination with this effect on destructive lesions, vitamin D deficiency may cause proliferative lesions to occur less often as a result of decreased bone formation and mineralization. Deficiency also has negative effects on bone strength that could affect the preservation and subsequent observation of these lesions. The prevalence of proliferative rib lesions is significantly greater at Ancaster than at Isola Sacra. However, given the relatively high prevalence of evidence for vitamin D deficiency at this site,

there may have been more individuals who experienced a respiratory infection but were unable to form proliferative lesions as a result of vitamin D deficiency-related impairment of normal mineralization.

Relationships between nutritional or hormonal factors and infection are rarely straightforward, due to multifactorial influences on disease susceptibility and development. The complexity of vitamin D's actions, as well as unanswered questions regarding apparent inconsistencies between *in vitro* actions of this molecule and *in vivo* function (Cantorna et al., 2004), further complicate the situation. The majority of evidence for chronic respiratory infections in the past, including features observed at both sites examined here, relates to proliferative skeletal changes. Given this fact, the potential for vitamin D deficiency to co-occur with respiratory infections, and also to decrease the development or preservation of associated lesions, is a particularly important factor to consider in the interpretation of paleopathological cases of these conditions.

5.1.1. Vitamin D deficiency and chronic respiratory infections: Bioarchaeological considerations

This analysis investigates vitamin D deficiency and chronic respiratory infection lesions using an approach that differs in two important ways from previous studies. The approach taken addresses difficulties faced by other researchers by considering the potential effects of co-occurrence on the appearance and presence of skeletal lesions and examining chronic respiratory infections as a general category represented by several different types of skeletal evidence. These go part of the way toward accommodating some of the limitations associated with paleopathological evidence for disease.

Paleopathological investigations, including the current analysis, rely on counting individuals with vitamin D deficiency and chronic respiratory infections who can be detected based only on the presence of skeletal lesions. As a result, it is particularly important to consider how vitamin D deficiency, as the potential "risk factor" condition, may impact the development and skeletal expression of features of chronic respiratory infection as the potential "outcome" condition. This applies especially to the most severe forms of vitamin D deficiency, which are likely to have the largest effect on the expression of lesions associated with other pathological processes. Beyond the low prevalence of skeletal involvement on a macroscopic level in both conditions, interpretations of the occurrence of vitamin D deficiency and chronic respiratory infections in the past are affected by, and must therefore account for, several other important limitations that decrease their visibility in archaeological skeletal material (Section 3.3). These include limited preservation of pathological bone, as well as variability in the potential effects of vitamin D status on the development and expression of skeletal lesions related to both conditions. It is difficult or impossible to estimate the effect of archaeologically invisible cases of respiratory infection or vitamin D deficiency on mortality, or on each other, within an archaeological sample. This includes cases of infection that were acute or that did not stimulate a bony reaction in the ribs or spread hematogenously to the skeleton, or cases of deficiency that did not lead to significant skeletal changes or caused lesions that occurred long enough before death to have completely remodeled.

Since skeletal reactions to metabolic disturbances and infections are limited, it is often difficult to diagnose a specific pathological condition based on archaeological evidence (Grauer, 2008; Rothschild & Martin, 1993; Waldron, 2009), and it may be more appropriate in some cases to use broader diagnostic categories (Ubelaker, 1982; Ragsdale, 1997). The approach taken here, which examines relationships between vitamin D deficiency and chronic respiratory infections as a category, therefore addresses some of the difficulties associated with previous approaches. Snoddy et al. (2016) examine vitamin D deficiency along with the extremely problematic category of "nonspecific infection" (Weston, 2012), justifying their use of this category by pointing to the prohibitively small number of cases that can be diagnosed specifically as skeletal TB. The category of chronic respiratory infection, as employed in the current analysis, is general enough to encompass several types of lesions, and therefore to increase the number of cases likely to be observed within a sample, but is also specific enough to allow meaningful interpretations. Examining relationships between vitamin D deficiency and chronic respiratory infections is a more valuable approach than drawing a vague connection with lesions that may be related to generalized "chronic infection" based on the immunomodulatory actions of vitamin D, which are in themselves complex and context-dependent. Using the category of chronic respiratory infection therefore represents a way forward that could make examining potential correlations between vitamin D deficiency and respiratory disease in the past more achievable, something which many researchers have identified as a desirable goal (e.g., Roberts & Buikstra, 2003a; Snoddy et al., 2016; Wilbur et al., 2008).

The suggestion made here, that the co-occurrence of conditions could impact not only the appearance but also the presence of lesions, has not previously been widely considered. The fact that prior or contemporaneous experience of one condition could influence whether lesions associated with another condition develop at all could be crucially important in the consideration of hidden heterogeneity in frailty as put forward by Wood et al. (1992). Considering the occurrence and expression of a condition like vitamin D deficiency, which has extensive effects beyond its main role in calcium homeostasis, could represent a valuable way to begin unraveling some potential explanations for the presence, absence, and expression of lesions associated with other disease states. This is especially relevant to conditions that have clinically-documented associations with vitamin D deficiency in modern populations, as well as to the experience of overall mortality. Paleopathological approaches, particularly those relating to the examination of skeletal evidence for nonspecific "stress", have grown from solely considering the presence or absence of lesions to evaluating multiple indicators, albeit often subsuming lesions with heterogeneous causes under the same nonspecific process or generalized experience of stress (Mays, 2012). From there, approaches have begun to use paleodemographic indicators to account for differences in experience based on age and variation in age at death distributions (e.g., DeWitte, 2014; Klaus, 2014). However, these approaches still generally do not consider the impact of interactions between different specific pathological conditions. Vitamin D deficiency represents an excellent place to begin exploring some of these interactions; the more that new research reveals about the wide-reaching effects of vitamin D deficiency, the more importance this condition stands

to gain in the consideration of both disease-specific morbidity and overall mortality in populations in which vitamin D deficiency has a notable presence.

5.1.2. Vitamin D deficiency and chronic respiratory infections: Isola Sacra and Ancaster

The significant relationship demonstrated to exist between vitamin D deficiency and chronic respiratory infections at Isola Sacra (Section 4.4.2), as well as the presence of evidence for both conditions in two individuals from Ancaster (Section 4.4.1), indicate that the association between the two conditions noted in modern populations (e.g., Adams et al., 2007; Banajeh et al., 1997; Holick & Chen, 2008; Karatekin et al., 2009; Section 2.3) may also have extended into the past. Using the same statistical methods as those used here on data from the WORD database, Snoddy et al. (2016) found a significant association in two medieval British samples between point prevalence values for vitamin D deficiency and "chronic infection". However, they were unable to demonstrate a positive relationship between vitamin D deficiency and cases of TB more specifically (Snoddy et al., 2016). At Isola Sacra there are no classic cases of skeletal TB, but there is considerable and convincing evidence for the presence of chronic respiratory infections more generally, and the presence of these lesions is significantly associated with skeletal cases of vitamin D deficiency. The absence of a significant association between vitamin D deficiency and chronic respiratory infections at Ancaster, despite higher prevalence values for lesions associated with both conditions, could indicate a genuine lack of association between the two conditions in this population. Alternatively, it could indicate a difference in the effect that vitamin D deficiency has on skeletal manifestations of chronic respiratory infections in these individuals, either based on the experience of

vitamin D deficiency itself or the timing of deficiency in relation to the contraction and progression of infection, or the effects of other co-occurring pathological conditions. The presence of two individuals with skeletal evidence associated with both conditions at this site suggests that the latter explanation may be more likely.

The theoretical relationship between vitamin D deficiency and skeletal manifestations of chronic respiratory infections (Section 5.1) suggests one potential interpretation for the relationships observed based on skeletal evidence for these two conditions at Isola Sacra and Ancaster. Odds ratios indicate that the association between skeletal vitamin D deficiency and chronic respiratory infections is statistically significant at Isola Sacra (Section 4.4). Prevalence values for chronic respiratory infections are significantly higher at Ancaster (Table 4.12). There are also qualitative differences in the type and extent of lesions observed between the two collections. More evidence for typical cases of skeletal TB is present at Ancaster, including Pott's spine and a destructive lesion in the hip joint. At Isola Sacra, specific evidence for TB consists only of destructive spinal lesions that have not yet led to collapse or kyphosis, and probably represent an earlier or less advanced stage of disease. Four individuals at Isola Sacra display periosteal new bone formation typical of HOA, while no Ancaster individuals have these lesions. A significantly greater number of Ancaster individuals have proliferative rib lesions, but Isola Sacra individuals who do have proliferative lesions associated with active disease show significantly more extensive involvement of the ribs (Table 4.18).

At Isola Sacra, the crude prevalence value for vitamin D deficiency lesions is almost twice as high as the value for chronic respiratory infection lesions (6.5% vs. 3.6%; Tables 4.4 and 4.12). This lends support to the possibility that the manifestation or timing of vitamin D deficiency may have been such that having a deficiency decreased the formation or preservation of skeletal lesions in response to chronic respiratory infections. This could happen if deficiency were more frequent or longstanding in this collection, preventing or limiting lesion formation for a longer period of time. Cases of flagrant osteomalacia in adults take longer to develop than those in children, and therefore reflect more longstanding cases of deficiency; prevalence values for active cases of vitamin D deficiency in adults are similar at Isola Sacra (1.33%) and Ancaster (1.10%). Vitamin D deficiency could also reduce the formation or preservation of respiratory infection lesions if the deficiency remained active until death, rather than abating and allowing a period of normal mineralization of the new bone formed before the individual died. Since vitamin D deficiency has been shown to affect immune function at levels of severity that will not necessarily manifest macroscopically in the skeleton, immunologically relevant cases may also remain archaeological invisible.

In the case of vitamin D deficiency, Snoddy et al. (2016) propose that juvenile disease can be used as a proxy for the health status of past populations, as rapidly developing and immunologically more immature young individuals are more sensitive to changes in the environment. This is consistent with the more general suggestion that the health and survival of juveniles, especially infants, can be used as a sensitive measure for the impact of social and environmental conditions on mortality and morbidity (e.g.,

Lewis, 2011b; Redfern & Roberts, 2005). Following this, estimating how many deficient individuals may have existed in a population relies on the use of skeletal evidence for childhood vitamin D deficiency as a proxy for less visible levels of adult deficiency. The majority of evidence for vitamin D deficiency at Ancaster and Isola Sacra represents cases that have healed before the time of death. The episodic and often seasonal nature of this condition also suggests the strong possibility of additional recurrent episodes of deficiency closer to the time of death that would not manifest in the skeleton. Since the majority of putative cases of chronic respiratory infection are represented by proliferative lesions rather than destructive ones, the appearance of skeletal manifestations of respiratory disease at both Isola Sacra and Ancaster would be sensitive to these types of effects. This may be particularly relevant at Isola Sacra, based on the demonstrated significant relationship between the two conditions. Therefore, the relationship between vitamin D deficiency and infectious disease might be the reason for the invisibility of respiratory infection in some archaeological individuals, where mineralization defects may have prevented the formation or preservation of proliferative lesions. While many paleopathological studies have recognized the co-occurrence between metabolic and infectious disease, and the potential for their interaction in past populations (e.g., Lewis, 2000; Roberts & Buikstra, 2003a; Roberts & Manchester, 2005; Snoddy et al., 2016; Stuart-Macadam, 1989), few researchers have considered the effects of the co-occurrence of these conditions directly on the skeletal lesions formed (Wilbur et al., 2008).

The presence of vitamin D deficiency may also impact the development of destructive lesions in the skeleton, increasing their severity due to potentiating effects on

resorption at some points during deficiency as well as through the general weakening of the skeleton that occurs as a result of defective mineralization (Section 5.1). At Ancaster, there are a greater number of individuals who display evidence of destructive lesions specifically associated with TB, including those with lesions in the spine and in the hip. A higher prevalence of evidence for vitamin D deficiency at this site as well, particularly in juveniles, raises the possibility that vitamin D deficiency may have been a factor in increasing the severity or hastening the progression of destructive lesions in the skeleton. Individual ANC 1, who displays evidence for a destructive lesion in the hip that may be associated with skeletal TB, was also placed in category three for healed vitamin D deficiency based on a long bone bending deformity (Section 4.4.1). In this individual in particular, a deficiency of vitamin D may have been one of the factors that influenced the dissemination of TB to the skeleton and the development of a destructive lesion in the hip joint.

5.1.3. Vitamin D deficiency and chronic respiratory infections: Effects on survival

The demonstration that both vitamin D deficiency and chronic respiratory infection lesions have a significant effect on survival at Ancaster (Sections 4.2.1 and 4.3.2) bolsters the proposition that an increased susceptibility to chronic respiratory infections may have been one of the ways through which vitamin D deficiency affected longevity at this site. This effect was observed for vitamin D deficiency lesions at all stages of healing in the total sample, but for chronic respiratory infections only in the group of individuals who survived to the age of three. This seems to run counter to clinical data for TB specifically, which show that infants who contract TB tend to

experience more rapid progression and a poorer disease outcome than older children with this disease (Feja & Saiman, 2005). For example, TB mortality rates in the late 19th and early 20th centuries in the United States were higher for infants than all other age categories, with mortality declining in childhood and then increasing into adolescence and adulthood (Frost, 1939). Mortality from acute respiratory infections has been categorized as the first cause of death outside of the neonatal period for infants and children in developed countries over the last century, as well as accounting for about one third of deaths of children under the age of five in developing countries in the later 20th century (Garenne et al., 1992). Based on global estimates from WHO data in the mid-20th century, Leowski (1986) reports that two thirds of deaths due to acute respiratory infections during childhood occur during the first year of life, with the majority of these deaths occurring in developing countries. A review of community-based longitudinal studies from developing countries found that acute respiratory infection deaths were typically concentrated between one and 11 months of age (Garenne et al., 1992).

The importance of acute respiratory infections as a cause of death in infants and younger children, as well as high TB mortality and rapid disease progression in the first year of life, indicates that any effect of respiratory infections on survival in this age group may not be detectable based on skeletal evidence. It is therefore possible that infants dying from respiratory infections at Ancaster experienced disease that progressed rapidly, and these individuals entered the mortality sample before developing skeletal lesions associated with the infection. In this case, the effect of respiratory infections, as detected

using skeletal evidence for disease, may only become evident in individuals who survived past infancy and experienced a more chronic and slowly progressing form of infection.

Vitamin D deficiency lesions were found to have a significant effect on survival at Ancaster in the total sample, including individuals who died during infancy and younger childhood. This is consistent with recent clinical studies that have demonstrated a significant inverse association between vitamin D status and all-cause mortality, which considers death of study participants from any cause, based on the results of both observational studies (Khaw et al., 2014; Schöttker et al., 2013) and randomized controlled trials in mainly elderly individuals (Autier & Gandini, 2007; Bjelakovic et al., 2011, 2014). Skeletal evidence for active deficiency was also observed in the youngest age categories at Ancaster, including infants and those aged as fetal or neonatal (Sections 4.2.1 and 5.3.1.1.1; Table 4.8). If acute respiratory infections were an important cause of death in neonates and infants at this site, vitamin D deficiency in these age groups may have impacted immune function in a way that led to increased infection rates or rapid disease progression and poorer outcomes. This is particularly relevant at this developmental stage because the immune system is relatively immature, and thus more sensitive to disturbances, in young infants (McDade, 2003). Infections that run an acute course or rapidly progress to cause severe disease and death do not allow for the development of skeletal lesions, and would not be detectable by examining skeletal evidence for respiratory infection. Co-occurring vitamin D deficiency may increase the severity or hasten the progression of infection, thereby making this situation more likely. This is one possible scenario which corresponds well with clinical evidence for the age-

specific mortality of and relationship between vitamin D deficiency and chronic respiratory infections, and would account for the observation of a significant effect of skeletal lesions on mortality for vitamin D deficiency in the total sample and chronic respiratory infections only in individuals surviving past infancy.

While a significant association between the prevalence values for vitamin D deficiency and chronic respiratory infection lesions could be demonstrated at Isola Sacra (Section 4.4.2), skeletal evidence for neither condition demonstrated a significant effect on survival in this sample. The relationship detected here necessarily only relates to deficiency and infection that resulted in skeletal lesions. However, cases of either condition that did not result in skeletal disease could still have a major impact on longevity, particularly through indirect effects of deficiency on other pathological conditions and on overall mortality. The lack of a significant association between evidence for either vitamin D deficiency or chronic respiratory infections and survival at Isola Sacra could indicate that neither condition had an impact on longevity for individuals at this site. Alternatively, the effect of respiratory infections on mortality may be obscured by the contribution of cases of disease that did not leave skeletal evidence, as suggested above for infants at Ancaster. Similarly, the impact of vitamin D deficiency on survival may be mediated through its effects on diverse target organs, including the immune system, many of which are likely to be invisible in the skeleton. Experiences of vitamin D deficiency and chronic respiratory infections at Isola Sacra may therefore have occurred in such a way as to have less of an effect on survival at

this site than at Ancaster, or these conditions may have affected longevity primarily through processes that did not produce skeletal evidence.

5.1.4. Vitamin D deficiency and chronic respiratory infections: The osteological paradox

Stronger evidence for both conditions at Ancaster, particularly chronic respiratory infections, may indicate that individuals in this sample correspond more closely to the scenario posited by Wood et al. (1992) in their seminal article on the Osteological Paradox. These authors suggested that a higher frequency of skeletal lesions could be interpreted as representing the result of a significant health advantage, with higher lesion frequencies reflecting an enhanced ability to survive disease episodes. This is often discussed within paleopathology in relation to nonspecific stress markers (DeWitte & Stojanowski, 2015); many studies have focused on the relationship between stress markers and survival (e.g., Bennike et al., 2005; Cucina, 2011; Littleton, 2011; Wright & Chew, 1998).

Such a proposition may have different implications for the interpretation of lesions associated with vitamin D deficiency and chronic respiratory infections than for nonspecific stress markers, based on the way that relevant lesions develop. The majority of evidence for chronic respiratory infections observed at Ancaster and Isola Sacra consists of proliferative lesions that develop over time in association with pleural inflammation. As a result, the formation of an osseous reaction requires disease that is sufficiently longstanding to stimulate an inflammatory response in the periosteum and form a large enough amount of bone to be macroscopically visible and to preserve archaeologically. Individuals who may have contracted respiratory infections without

manifesting skeletal evidence are likely to have experienced an acute course of infection, and may have died before lesions could form. This condition behaves in the manner envisaged by Wood et al. (1992).

Vitamin D deficiency lesions, on the other hand, are primarily associated with improper mineralization and resultant weakness and deformity. While this also takes time to progress to an extent that is macroscopically visible in the skeleton, the development of bone disease is affected by the severity and length of the deficiency as well as by growth rates, calcium intake, and potentially also genetic variation in proteins and receptors necessary for vitamin D metabolism and signalling (Paterson & Ayoub, 2014). Vitamin D deficiency is more likely to represent a chronic process which, while it may eventually contribute to death, is unlikely to directly and acutely cause the death of an individual (Comacchio, 1998; Tisdall, 1921). Longstanding but mild deficiency, or subclinical deficiency, can have significant effects on the body, particularly in terms of calcium homeostasis and immune function (Cianferotti & Marcocci, 2012; Wayse et al., 2003), without being severe enough to cause flagrant rickets or osteomalacia. This condition does not, therefore, behave in the manner proposed by Wood et al. (1992). Consideration of potential interpretations outlined in the Osteological Paradox raises the issue of which individuals may appear "healthy" if only skeletal evidence for a condition can be evaluated, revealing that this may differ for various types of metabolic and infectious disease. Restricting analysis to skeletally manifested cases of vitamin D deficiency and chronic respiratory infections is likely to miss, respectively, individuals who have experienced mild disease episodes, or those that occurred during periods of slower growth

and lower susceptibility, and those who have experienced acute disease. As a result, it is necessary to take different approaches to the interpretation of these two conditions and their interactions.

At Ancaster, the higher frequency of individuals with lesions associated with these conditions, and particularly with chronic respiratory infections, could indicate a greater number of individuals who were surviving long enough to form lesions, or, in other words, an increased number of survivors. A greater mean age at death in this population, as well as a greater number of old adults and a different age at death distribution compared to Isola Sacra, could also indicate improved "health". Mean age at death has been criticized in terms of the usefulness of its application to bioarchaeological samples, as well as its accuracy as a statistic measuring health (Hoppa & Saunders, 1998). However, several features of both the Isola Sacra and Ancaster samples, including a number of analyzable individuals greater than 100 and accumulation over a longer period of time than one human lifespan, indicate that they may be less susceptible to representation biases (Hoppa & Saunders, 1998). Considering mean age at death as one small part of a complex of features, including age at death distributions and evidence for specific pathological conditions, provides more information about morbidity and mortality at these sites than would relying on mean age at death alone.

Examining skeletal evidence for vitamin D deficiency, chronic respiratory infections, and age at death at Ancaster and Isola Sacra in light of the considerations outlined by Wood et al. (1992) suggests one possible interpretation for the observations made in both samples. At Ancaster, a greater number of individuals with lesions might

actually indicate a population with more robust immune responses, who were able to survive infection long enough to form lesions. Conversely, at Isola Sacra, a lower number of individuals with lesions could indicate reduced survival of disease conditions. The stronger relationship between vitamin D deficiency and chronic respiratory infection at Isola Sacra raises the possibility that vitamin D deficiency could be a factor in the reduced efficacy of immune responses at this site, leading to a lower mean age at death as well as to decreased survival of deficiency itself, associated chronic respiratory infections, and other conditions that cannot be detected paleopathologically. The lower prevalence of skeletal lesions associated with vitamin D deficiency at Isola Sacra could indicate that episodes of deficiency were less severe. However, frequent or long-lasting episodes of deficiency that were not severe enough, or did not occur during a period of rapid growth and heightened susceptibility such as infancy (Creo et al., 2017) or adolescence (Pearce & Cheetham, 2010), may have impacted immune function without being visible in the skeleton. Immunologically relevant but skeletally invisible episodes of vitamin D deficiency could negatively affect an individual's ability to mount an effective response to respiratory infections. The recent development of paleopathological applications for histological techniques using interglobular dentine (D'Ortenzio et al., 2016) raises the possibility of detecting such episodes in future studies through the examination of archaeological teeth.

Considering patterns of vitamin D deficiency and respiratory infection-related lesions and mortality within each population in relation to the models set out by Goodman (1993) and Wood et al. (1992) may broadly indicate some of the implications for overall

"morbidity" in these two samples. At Isola Sara, the data appear to reflect a higher "stress" profile (Goodman, 2003), with a lower prevalence of skeletal lesions corresponding with lower "morbidity" and a higher mortality represented by a lower mean age at death and different age at death distribution. In contrast, at Ancaster, higher metabolic and infectious disease morbidity combined with lower mortality may reflect a "low stress" group (Goodman, 1993). In both cases, "morbidity" refers to a very specific complex of pathological conditions related to vitamin D deficiency, chronic respiratory infections, and other paleopathologically invisible processes associated with these conditions through their effects on the immune response. Skeletal differences between Ancaster and Isola Sacra suggest that the local biologies associated with this complex differ at these two sites, leading to variation in disease experience for individuals at these two sites. At Isola Sacra, with the demonstration of a significant relationship between the two conditions, this complex may particularly involve vitamin D deficiency and associated decreases in immune response indicated by morbidity associated with chronic respiratory infections as well as overall mortality.

A similar pattern of higher "morbidity" combined with lower mortality was noted by Redfern et al. (2015) in their investigation of variation in frailty and mortality risk between urban and rural sites in Roman Britain. While urban sites demonstrated higher frequencies of poor health indicators, they also showed higher survival and a greater presence of older adults. Redfern et al. (2015) relate these patterns to a less hazardous urban living environment in Roman Britain compared with other areas of the Roman empire and later periods in British history, as well as to a greater degree of social

inequality in rural contexts (Pitts & Griffin, 2012); a link to the models set out by Wood et al. (1992) and Goodman (1993), while not invoked by the authors, seems plausible.

In considering vitamin D deficiency lesions as indicators of a chronic disease process, a distinction should be drawn between skeletal features associated with active disease in juveniles and those associated with healed deficiency. In neonates and infants, who are particularly vulnerable to vitamin D deficiency (Creo et al., 2017) since mineral requirements increase in this period to support rapid growth, hypocalcemia associated with vitamin D deficiency can lead to hypocalcemic dilated cardiomyopathy. This is considered to be the most serious complication of vitamin D deficiency, and can cause death by leading to heart failure or cardiogenic shock (Högler, 2015). Högler (2015) proposes that the association between hypocalcemic cardiomyopathy and vitamin D deficiency may often be missed in modern clinical contexts because the two conditions are examined by different specialists who may not be looking for subtle symptoms of one or the other. Clinically, the majority of infants with this type of cardiomyopathy as a result of vitamin D deficiency present between three weeks and 10 months of age (Högler, 2015). This association would almost certainly have been missed in historical contexts as well as modern ones. For individuals who display skeletal evidence of vitamin D deficiency and who died as neonates or infants with active lesions, the possibility of death as a result of cardiac complications directly associated with deficiency must be considered.

5.2. Vitamin D Deficiency and Chronic Respiratory Infections: Skeletal Evidence

Given limited skeletal reactions to metabolic disturbance or infection and the general inaccessibility of soft tissue evidence available to researchers of disease in modern populations (Grauer, 2008; Waldron, 2009), paleopathological diagnoses of vitamin D deficiency and chronic respiratory infections must carefully consider skeletal features in the context of evidence from clinical and other paleopathological studies. The skeletal evidence for these two conditions observed at Isola Sacra and Ancaster displays important similarities to and differences from skeletal features described in the clinical and paleopathological literature that assist in developing a thorough differential diagnosis and provide information on the experience of vitamin D deficiency and chronic respiratory infections at these two sites.

5.2.1. Skeletal evidence: Vitamin D deficiency

In diagnosing adult vitamin D deficiency using skeletal evidence, the most characteristic manifestations of fragility associated with osteomalacia in the skeleton are pseudofractures (Brickley et al., 2005). However, the evidence observed at Ancaster and Isola Sacra differs from other studies of archaeological human skeletal material that have found evidence for pseudofractures in the scapula, ribs, and clavicle (Brickley et al., 2007; Ives & Brickley, 2014), as well as in the distal ulna, transverse processes of the vertebrae, and proximal femur (Ives & Brickley, 2014). At Ancaster and Isola Sacra, while several individuals displayed possible pseudofractures in the ribs, no typical pseudofractures were observed in the scapulae, clavicles, ulnae, or vertebrae. The possible pseudofracture observed in the medial proximal femur of one Ancaster

individual (Figure 4.18) is, however, similar in appearance and location to that observed by Ives and Brickley (2014, p. 51) in an individual from Christ Church, Spitalfields. The incomplete hip fracture in ANC 113 was previously identified as a fragility fracture related to osteoporosis (Mays, 2006a). Pseudofractures associated with adult vitamin D deficiency are observed clinically in the proximal femur (e.g., Gallagher et al., 1980; Kanberoglu et al., 2005). In two studies in England, histological evidence for osteomalacia was found in around 40% of individuals with proximal femoral fractures, with osteomalacia often being superimposed on osteopenia (Aaron et al., 1974a,b). Aaron et al. (1974b) hypothesize that some osteoporotic individuals who did not show histological evidence for osteomalacia may also have experienced a low level vitamin D deficiency which would affect calcium absorption and cause bone loss without producing specific signs of osteomalacia. Similarly, Ross et al. (2011a) suggest that osteomalacia is likely to be more important in hip fractures than previously thought, either on its own or in combination with osteoporosis. While the proximal femoral fracture observed in ANC 113 may have been caused by vitamin D deficiency, osteoporosis, or a combination of the two, the presence of a small amount of poorly formed bone at the fracture edges lends support to the idea that a deficiency of vitamin D was involved in the underlying process that led to skeletal fragility in this individual.

Two individuals from Ancaster (ANC 98 and 220) do not have clear and unambiguous evidence for vitamin D deficiency, but display some relevant features and are scored in category three for both childhood and adult deficiency. These two individuals illustrate the importance of category three in drawing attention to the possible

existence of individuals within the population who may have experienced vitamin D deficiency, but cannot necessarily be securely diagnosed as such. Five Ancaster adults (ANC 23, 78, 135, 202, and 220) could be placed in category three based on histological features despite showing no macroscopic evidence for active adult deficiency; these individuals may represent cases in which deficiency was either insufficiently severe, or not yet longstanding enough given the rate of growth the individual was experiencing at the time of deficiency, to lead to the development of macroscopic features. The significantly greater number of category three individuals at Ancaster (Table 4.5) could indicate a higher occurrence of low-level deficiency at this site, which may have affected immune function, and could be a contributing factor in the significantly higher prevalence of evidence for chronic respiratory infections at this site. The presence of skeletal evidence for chronic respiratory infection in ANC 78 lends support to the idea that low-level deficiency in category three individuals may have negatively impacted immune function.

Histological evidence was important, particularly at Ancaster, in providing evidence that led to category three (ANC 23, 78, 135, 202, and 220) or even category two (ANC 249 and SCR 33) diagnoses, or allowed a diagnosis that would have been considered category three based on macroscopic evidence to be increased to category two (ANC 207). Apart from vitamin D deficiency, defects in mineralization can also be associated with renal osteodystrophy, which encompasses the spectrum of bone disorders that develop as a result of chronic renal failure or end-stage renal disease. Skeletal changes can develop quite early on in the progression of chronic kidney disease

(Spasovski et al., 2003), at a stage to which individuals could most likely easily survive in the past in the absence of medical treatment. Renal osteodystrophy is common in developing countries, where, despite diminished access to treatment, patients survive long past the development of skeletal changes (Afifi, 2002). However, this condition is much more common in elderly individuals above the age of 70 or 80 (Feest et al., 1990), and is unlikely to represent the cause of mineralization defects observed in the majority of these individuals from Ancaster and Isola Sacra, who are aged as juveniles, young adults, or middle adults. Renal osteodystrophy should be considered as a possible differential diagnosis for the mineralization defects observed in ANC 135, aged as an old adult.

Better microscopic preservation at Ancaster than at Isola Sacra allowed for a multi-scalar approach considering both microscopic and macroscopic evidence to be applied to many more individuals at this site, although histological analyses could be performed for a number of samples from both assemblages. The consideration of both macroscopic and microscopic evidence for vitamin D deficiency in these individuals allowed for the examination of features occurring on different time scales, and at different points throughout the life course. Macroscopic features represent deficiency that was not only severe enough to significantly weaken the bone, but also occurred over a long enough period of time for noticeable changes to develop, and therefore likely began a greater amount of time prior to death. This is especially true for healed cases of deficiency, particularly those in which evidence of long bone deformity persists into adulthood. Conversely, microscopic features represent manifestations of deficiency that developed more recently in relation to the time of death, and may also have been subtler

or less severe. Examining both types of evidence for deficiency, as well as evidence for both healed and active deficiency in juveniles and adults, allows the evaluation of disease experience at different periods over the life course, on both individual and population levels.

Ancaster individuals ANC 98 and ANC 220, both placed in category three, died during adulthood and display some evidence for both active and healed vitamin D deficiency. One individual (ANC 98) has a number of fractures in the ribs at different stages of healing, some of which have slightly strange, although not clearly spiculated, bone associated with them, as well as abnormal curvature of the sacrum. Poor microscopic preservation precluded histological analysis for this individual. Individual ANC 220 also displays evidence of abnormal sacral curvature, along with some histological features of deficiency. While no features are particularly clear, and the evidence present was not convincing enough to securely diagnose cases of deficiency in these individuals, they display some features associated with deficiency experienced in both childhood and adulthood. The presence of evidence for both healed deficiency, possibly during adolescence (Section 5.3.1.1.2), and features that relate to active deficiency in adulthood raises the possibility that these individuals experienced deficiency at multiple periods during their lives, but never at a level of seriousness sufficient to develop unambiguous skeletal signs that remained present until death. This pattern of occurrence aligns well with the episodic and often seasonal nature of vitamin D deficiency in modern populations (Brickley et al., 2010; Mays et al., 2006).

5.2.2. Skeletal evidence: Chronic respiratory infections

Skeletal evidence for chronic respiratory infections at both Ancaster and Isola Sacra demonstrates a range of expression, including proliferative lesions in the ribs and in the long bones, and destructive lesions in the vertebrae and the joints. Mays (2007) suggests that this corresponds well with expectations for the skeletal expression of a systemic infectious disease, where individual disease experience, including the effects of disease on the skeleton, varies based on individual features. Individual responses to disease would depend on interactions between pathogen and host, as well as on immune function more generally, which is likely to have been affected by diet (Klaus et al., 2010). Given this variation, considering multiple types and expressions of skeletal lesions as potential indicators of the general category of chronic respiratory infections allows for the identification of a greater proportion of the range of variation that is likely to exist within each sample. Based on paleopathological reports, the prevalence of skeletal TB in ancient Rome seems low despite the fact that Roman writers like Pliny the younger describe *phthisis*, the ancient Greek and Roman term for a disease entity generally accepted to represent pulmonary TB (Keers, 1978; Grmek, 1989), as widespread (Canci et al., 2005). Including evidence specifically connected to skeletal TB as well as proliferative rib and long bone lesions connected to TB and other chronic respiratory infections provides more evidence on Roman experiences of respiratory infection that can help to build a more complete picture of disease experience in this time period.

5.2.2.1. Skeletal evidence of chronic respiratory infections: Rib lesions

The significantly higher number of ribs affected in Isola Sacra individuals with proliferative lesions that were active at the time of death (Table 4.18) may represent information on aspects of infectious disease experience that go beyond occurrence, such as the extent and possibly the severity of disease in these individuals. Accepting the predominant etiological explanation of proliferative rib lesions as the result of an inflammatory reaction to infection in the adjacent pleura (e.g., Kelley & Micozzi, 1984; Nicklisch et al., 2012; Roberts et al., 1998; Roberts & Buikstra, 2003a), the direct relationship between inflammation in the pleura and inflammation in the periosteum means that the ribs affected will correspond with the areas of the pleura that are inflamed. The involvement of multiple ribs in this inflammatory process would therefore indicate that pleural inflammation is also widespread (Roberts et al., 1994). Close correspondence between the areas of pleura and rib affected suggests that the number of ribs affected by new bone formation could be considered as an indication of the extent of inflammation in the pleura and lungs, and therefore of the extent of disease. This provides a novel and concrete approach to comparing some aspects of disease experience between groups that has not previously been applied.

Considering the stage of disease at the time of death, along with the extent of disease, highlights interesting differences between individuals with evidence for chronic respiratory infections at Ancaster and Isola Sacra. In comparisons between the two sites, Isola Sacra individuals with active lesions have a significantly greater number of ribs affected. Therefore, the extent of disease in Isola Sacra individuals who died with active

lesions was significantly greater than for individuals at the same site who died with healed or healing lesions. These individuals also showed more extensive evidence for disease than Ancaster individuals who died with active lesions. It seems likely that something distinct was occurring in terms of disease experience for these individuals at Isola Sacra.

The presence of active new bone formation in the ribs has been taken to indicate that the disease process itself was active at the time of death (Mays et al., 2002; Nicklisch et al., 2012). Following this reasoning, individuals who died with active lesions can be conceptualized as non-survivors who were unable to combat and recover from respiratory infections. However, an osseous response to infection also takes time to form, meaning that individuals who manifest an inflammatory response that was still active at the time of death must have survived long enough to develop lesions in the first place. The group of individuals with active proliferative rib lesions therefore represents those who were able to mount a strong enough immune response to survive with the infection long enough to develop bony lesions, but who were unable to initiate the process of healing or recovery from this infection prior to their death.

There is no way of determining how long respiratory infections experienced by these individuals persisted before their deaths, or whether individuals died due to the infections themselves or from some other related or unrelated cause. However, if the extent of disease is roughly proportional to the length of disease progression, as proposed for other proliferative lesions associated with respiratory infections (Assis et al., 2011), then individuals at Isola Sacra appear to have been surviving longer with the infection

prior to death, compared to their counterparts at Ancaster. This also implies that individuals who died while chronic respiratory infection lesions were still active at Isola Sacra experienced more extensive and severe disease than their counterparts at Ancaster, which may lend some support to the idea that a higher prevalence of lesions at Ancaster actually indicates longer survival. Similarly, Steyn et al. (2013) interpreted an increase in the number of individuals with rib lesions after the introduction of antibiotics in a South African documented skeletal collection as an indication that individuals were living longer, and therefore had more opportunity to develop skeletal signs of disease.

The extent of disease appears to be very similar, if not slightly lower, in Isola Sacra individuals with healing or healed lesions compared to those at Ancaster. This suggests that individuals whose immune response was strong enough to initiate the healing process and partially or fully recover from disease were more similar between the two samples in terms of the extent of disease that was still evident at the time of death. Prior to the advent of antibiotics, disease severity was a more important prognostic factor than age in cases of TB, in opposition to the pattern observed in modern populations (Springett, 1971). Increased severity of disease in Isola Sacra individuals who do not appear to have been able to mount an effective immune response to infection may indicate a worse prognosis in these individuals compared with those at Ancaster. This is interesting to consider in light of the significantly lower age at death for the Isola Sacra sample (Table 4.2), although it must be noted that the significant relationship between the extent of disease and recovery observed at Isola Sacra is not associated with any

significant differences in age at death between individuals with active and healed rib lesions.

The relationship between lesion healing stage and immune response is complicated by the chronic and sometimes episodic nature of respiratory infections, especially TB. Multiple layers of new bone formation are proposed to represent clear evidence for chronic and likely longstanding inflammation (Nicklisch et al., 2012), and chronicity of the infectious process is also identified as a factor that may lead to the presence of new bone formation at different stages of remodeling (Assis et al., 2016). In a disease like TB, where an adequate immune response can contain infection successfully for long periods of time, but a latent infection can also reactivate if the immune system becomes compromised (Ellner, 1997), the presence of new bone at multiple stages of remodeling could indicate multiple episodes of disease with partial or even complete recovery between them. In this analysis, proliferative lesions were scored as "active" only if there was no significant evidence of remodeling, and the new bone formation present consisted of woven bone. Therefore, individuals in this category represent either those in whom respiratory infection had not undergone any healing prior to death, or in whom a previous episode of infection had completely healed sufficiently long before to allow full remodeling and obliteration of evidence of any associated lesions. The different degrees of remodeling displayed by individuals in the "healing" category indicate that this is a much more heterogeneous group, and very few individuals could be fully placed within the "healed" category (two at Isola Sacra and one at Ancaster). It is likely that many individuals who had fully recovered from infection and completely remodeled any new

bone deposited on the rib surfaces cannot be identified, as these lesions are no longer visible.

5.2.2.2. Skeletal evidence of chronic respiratory infections: Hypertrophic osteoarthropathy (HOA)

A distinctive pattern of diffuse and bilaterally symmetrical new bone formation consistent with HOA observed on the appendicular skeletons of four individuals from Isola Sacra represents additional evidence for longstanding chronic respiratory infection at this site. A limited number of paleopathological cases of HOA have previously been identified based on skeletal lesions, in a few cases correlating with biomolecular evidence for TB (e.g., Hershkovitz et al., 2008; Masson et al., 2013; Mays & Taylor, 2002); however, evidence for HOA has typically been presented as case studies or as detailed discussions of the lesions present in one or two individuals from a skeletal sample (e.g., Christensen et al., 2013; Gladykowska-Rzeczycka & Prejzner, 1993; González-Reimers et al., 2015; Mays & Taylor, 2002; Masson et al., 2013). Part of the reason for this is that the low number of individuals in each population with evidence for this condition precludes larger-scale population analyses. The type of multi-scalar approach promoted by Agarwal (2016) can be incorporated here by considering lesions associated with HOA in the small group of individuals in whom they occur as well as within the context of all types of lesions associated with chronic respiratory infections in these two samples. This approach investigates infectious disease experience on two levels, considering both an individual and a population scale.

Given the importance of evaluating the patterning of lesions within the skeleton to accurately identifying HOA, visibility of this condition is likely to be greatly affected by

preservation issues commonly associated with ancient human skeletal remains. As Mays and Taylor (2002) suggest, HOA is likely to be under-recognized in archaeological samples. Despite general acknowledgement that respiratory infections were probably the most important cause of this condition in the past (Locke, 1915; Webb & Thomas, 1986), and recognition of the potential value of HOA as a general indicator of pulmonary infection (Mays et al., 2002; Mays & Taylor, 2002), previous analyses have not considered it in the context of other skeletal evidence for chronic respiratory infections. In populations containing additional evidence for respiratory infections, combining individuals with different types of lesions under the general category of chronic respiratory infections provides a way in which putative cases of HOA can be considered using a population approach, despite the low frequency of this condition in archaeological assemblages.

The four Isola Sacra individuals with lesion patterning consistent with HOA all display evidence for exuberant new bone formation on affected elements (Section 4.3.1.2), some of which has developed a distinctive "tree-bark" texture described as characteristic of HOA (Anselmo et al., 2016; Christensen et al., 2013; Fennel & Trinkaus, 1997; Gladykowski-Rzeczycka & Prejzner, 1993; Martinez-Lavin et al., 1994). Clinical evidence indicates that the shape and extent of the new bone formed is related to disease duration (Assis et al., 2011; González-Reimers et al., 2015), and that thicker, more extensive, and more advanced changes indicate that disease was longstanding (Christensen et al., 2013; Martinez-Lavin et al., 1994). The lesions observed in these four individuals are therefore most likely to represent longstanding pulmonary disease, with

the presence of both woven bone and some remodeled or remodeling bone corroborating the suggestion that the disease process was chronic (Assis et al., 2011). This presents additional evidence to support the idea that individuals at Isola Sacra experienced particularly severe or extensive disease, echoing interpretations for the greater involvement of ribs in individuals with active proliferative lesions in this collection (Section 5.2.2.1).

5.2.2.3. Skeletal evidence of chronic respiratory infections: Vertebral lesions

At Isola Sacra, lytic lesions in the vertebrae of individual SCR 462 are consistent with an early manifestation of spinal TB, but do not resemble more characteristic tuberculous spondylitis lesions like those observed in individual ANC 11 from Ancaster. The lytic lesions observed in the vertebrae of SCR 462 are similar in appearance to those observed by Pfeiffer (1984, p. 185) in an individual from the Uxbridge Ossuary. Pfeiffer (1984) describes these lesions as representative of the lower end of the range of severity observed at this site, with shallow resorptions present on the vertebral bodies adjacent to normal bone, and concludes that the most likely diagnosis for this and other spinal lesions in the assemblage is TB. Therefore, while lesions observed in individual SCR 462 do not correspond to the classic picture of vertebral body destruction and collapse, with resulting angular kyphosis, considered to be most specific to tuberculous spondylitis, there is precedent within the paleopathological literature for associating less extensive or severe destructive lesions in the spine with a likely tuberculous etiology (Pfeiffer, 1984; see also Baker, 1999).

5.2.2.4. Skeletal evidence of chronic respiratory infections: Joint lesions

Specific evidence for TB affecting the joints of the appendicular skeleton is present in one individual at Ancaster (ANC 1), who displays lytic lesions in the hip, resulting in extensive destruction of the femoral head and acetabulum (Section 4.3.1.4). The joints, particularly the weight-bearing joints of the lower body, are the second most common site for skeletal dissemination of TB after the vertebral bodies (Davidson & Horowitz, 1970; Resnick, 2002). For ANC 1, additional evidence is present to support the idea that these lesions may be related specifically to a TB infection. Müller et al. (2014) analyzed a sample taken from the femur of this individual for MTBC DNA, and identified ANC 1 as a possible case of TB based on the presence of a signal for IS1081 but not for IS6110 (Müller et al., 2014). This must be interpreted cautiously, given that IS6110 could not be amplified in the sample, as well as the fact that the presence of MTBC DNA does not prove that the specific lesions observed were actually caused by TB infection (Haas et al., 2000; Müller et al., 2014). However, the presence of an ancient DNA sequence associated with MTB is encouraging in terms of demonstrating that TB was likely to have been present at this site, and additional evidence for a TB infection in this individual specifically supports the idea that the lesions observed might be related to TB.

5.2.3. Skeletal evidence: Co-occurrence of vitamin D deficiency and chronic respiratory infections

Possible evidence for the co-occurrence of vitamin D deficiency and chronic respiratory infections is present in three Ancaster individuals who display skeletal lesions associated with both conditions. One middle child (ANC 146) and one middle adult (ANC Uncatalogued F) from Ancaster display features of healed vitamin D deficiency

along with evidence for a chronic respiratory infection. Another middle adult (ANC 78) displays skeletal features associated with a chronic respiratory infection, as well as some histological evidence for mineralization defects associated with vitamin D deficiency. No cases in which evidence for both of these conditions co-exists in the same individual have been published previously, despite recognition by paleopathologists that these conditions co-occur in modern populations and are likely to have been related in the past as well (e.g., Roberts & Buikstra, 2003a, b; Snoddy et al., 2016). Snoddy et al. (2016) point to the small number of individuals with vitamin D deficiency and TB that develop skeletal lesions, and can therefore be identified paleopathologically, to account at least partially for the difficulties in detecting a specific relationship between these two conditions in the past based on skeletal evidence.

New bone formation on the visceral surfaces of the ribs provides evidence for the presence of chronic respiratory infections in ANC 78, ANC 146, and ANC Uncatalogued F. In all three individuals, at least some of this new bone is woven, indicating that the infection may have been active close to the time of death. Proliferative lesions on the ribs of ANC 78 and ANC 146 also display some evidence of remodeling, indicating either that the infection had begun to heal, or possibly that these individuals had also experienced previous episodes of infection. In all three cases, the presence of unremodeled woven new bone formation on the ribs suggests that these individuals experienced an active respiratory infection not long before they died. However, the evidence present for vitamin D deficiency in ANC 146 and ANC Uncatalogued F indicates that the deficiency had healed before the time of death; based on the evidence available in these two cases, it is

not possible to establish the timing of the deficiency, either on its own or in relation to the respiratory infection.

Individual ANC 146, as a middle child aged at four and a half to five and a half years, is most likely to have experienced vitamin D deficiency as an infant or younger child leading to skeletal signs of rickets (Creo et al., 2017), as was the case for all juvenile individuals who died with active deficiency at both Ancaster and Isola Sacra (Table 4.4). The presence of nine ribs with new bone formation (Table 4.18) in various stages of remodeling indicates that the respiratory infection experienced by this individual was likely to have been extensive and chronic (Section 5.2.2.1), and may have involved a recurring infection. This individual also displays evidence for new bone formation on the diaphyses of the fibulae and the left tibia, in addition to smaller amounts of new bone formation on the diaphyses of other long bones that look typical for a young child undergoing rapid growth. The connection of these features with TB infection is supported by previous reports that identified widespread new bone formation in the skeleton as a feature associated with TB in a study of seven to 21 year olds from a documented skeletal collection (Santos & Roberts, 2001). In studies of juvenile human skeletal remains from the Roman site of Poundbury in the United Kingdom (Lewis, 2011a) and a number of other Romano-British sites (Rohnbogner & Lewis, 2017), new bone formation on the long bones as well as the visceral surfaces of the ribs is also proposed to indicate a diagnosis of possible TB, rather than a more general diagnosis of pulmonary infection. Given the presence of new bone formation in the ribs as well as on the long bones of ANC 146, it is possible that this individual experienced a TB infection, and they would

have had to survive the infection for quite some time in order to form such widespread new bone in various stages of remodeling. The state of skeletal changes associated with vitamin D deficiency in this individual indicates that the deficiency had healed prior to death. It is possible that this individual experienced additional episodes of deficiency closer to the time of their death that were not severe, longstanding, or associated with a period of growth rapid enough to lead to the development of skeletal lesions. Alternatively, based on the relationship between vitamin D deficiency and TB susceptibility and progression in modern populations (e.g., Adams et al., 2007; Holick & Chen, 2008), and the demonstration by Liu et al. (2006) of a molecular mechanism for vitamin D in immune cell-mediated killing of *Mycobacterium tuberculosis*, an earlier episode of vitamin D deficiency in this individual may have made them more susceptible to contracting a TB infection. If the deficiency then healed, new bone could form normally in reaction to a subsequent activation or reactivation of TB, creating lesions that preserved in the skeleton following death. This scenario corresponds well with observed relationships between vitamin D deficiency and TB infection in modern populations (e.g., Chan, 2000; Davies, 1985; Ustianowski et al., 2005; Wilkinson et al., 2008). It remains speculative, however, as the precise timing of the development of the two conditions, and therefore the exact relationship between them, cannot be determined based on skeletal evidence alone.

Evidence for healed vitamin D deficiency in individual ANC Uncatalogued F consists of a bending deformity in the tibia, which has preserved until the time of death in one leg and cannot be properly evaluated in the other due to the presence of a healed

fracture. Bending deformities in the long bones are most likely to be associated with a deficiency experienced during rapid skeletal growth in childhood, although severe cases of osteomalacia can cause similar lesions (Brickley et al., 2005); this individual is therefore most likely to have experienced vitamin D deficiency as a child, long before the respiratory infection that led to the development of proliferative rib lesions soon before their death in middle adulthood. This respiratory infection may have been contracted at any point during the lifetime of individual ANC Uncatalogued F, and may represent one of several different types of chronic pulmonary infections, including pneumonia and bronchitis as well as TB. Given the propensity for TB to remain latent for long periods of time (Ellner, 1997), and the possibility of contracting a TB infection in childhood that activates and creates fulminant disease only in adulthood (Feja & Saiman, 2005), it is possible that the two conditions were associated in this individual despite the length of time between skeletally evident disease episodes. However, interpretations are limited in this case by the imprecision of the skeletal evidence available in terms of indicating the timing of disease onset and development, as well as by the impossibility of reaching a diagnosis more specific than the category of chronic respiratory infection.

Individual ANC 78 was placed in category three for vitamin D deficiency based solely on histological features, as no macroscopic evidence for deficiency is present. This individual therefore could not be securely diagnosed as a case of vitamin D deficiency. However, given the presence of microscopic evidence for mineralization defects, it is likely that they experienced a low level of deficiency that was not severe or longstanding enough to lead to pseudofractures or deformation of the skeleton, but evidently still had

some effect on bone mineralization. Given epidemiological evidence showing that low vitamin D levels in adults, even in the absence of gross skeletal manifestations of osteomalacia, co-occur with respiratory infections in some modern populations (e.g., Ginde et al., 2009; Laaksi et al., 2007), this low-level deficiency may have had an impact on immune function. The presence of microscopic features in ANC 78 indicates that vitamin D deficiency occurred much closer to the time of death of this individual, before the affected bone had time to remodel. While a direct association between vitamin D deficiency and chronic respiratory infection cannot be identified in this individual, there is evidence to support the idea that the timing of the two conditions corresponded more closely than in other individuals in this collection, as both display signs of having been active relatively recently prior to death. This raises the possibility that vitamin D deficiency may have played a role in the reactivation of a latent infection, or in decreasing the efficiency of the response to infection in this individual, by affecting the actions of vitamin D either on immune cells (Section 2.1.1.2) or on lung function (Holick, 2006b; Karatekin et al., 2009). It is also possible that vitamin D deficiency, by disrupting the role of vitamin D in normal bone remodeling (Peterlik, 2004; Stern, 2005), negatively impacted the formation or remodeling of rib lesions associated with chronic respiratory infection in this individual (Section 5.1). However, the presence of mineralization defects along cement lines encased within normally formed bone, as well as the presence of some lamellar bone in the proliferative rib lesions, indicate that vitamin D status did return to a level sufficient to allow normal bone formation for a period prior to the death of this individual.

In both ANC 146 and ANC Uncatalogued F, the presence of features of vitamin D deficiency that healed before the time of death, in combination with evidence for a chronic respiratory infection that was likely to have been active not long before these individuals died, leaves some ambiguity in terms of the timing of the two conditions in relation to one another, and the relationship between them. While the timing of a possible vitamin D deficiency can be more precisely established for ANC 78, evidence for deficiency in this individual is not as strong. The situation is further complicated by the possibility that vitamin D deficiency may affect the development of skeletal lesions associated with chronic respiratory infections, particularly proliferative lesions (Section 5.1). However, features observed in ANC 78 and ANC 146, for whom much less time is likely to have elapsed between skeletally evident episodes of deficiency and infection, raise the strong possibility that vitamin D deficiency played a role in the contraction or development of respiratory infection in these two individuals. This suggests that the epidemiological association between these two conditions in modern populations may extend into the past, and raises the possibility that a relationship did exist between vitamin D deficiency and chronic respiratory infections at Ancaster, despite the lack of a statistically significant association based on prevalence data.

5.3. Vitamin D Deficiency and Chronic Respiratory Infections: Variation in Occurrence

At Isola Sacra and Ancaster, the occurrence of skeletal features associated with vitamin D deficiency and chronic respiratory infections varies in accordance with age at death, sex, and archaeological site. Considering this variation in the context of other

sources of information about life in the Roman world, including historical, archaeological, and other bioarchaeological evidence, allows for the interpretation of how such differences may have related to meaningful variation in disease occurrence. Features of the natural, built, and social environments at Isola Sacra and Ancaster interacted to influence experiences of vitamin D deficiency and chronic respiratory infections as part of the milieu of factors that combined to create unique local biologies at each of these two sites.

5.3.1. Variation in disease occurrence: Vitamin D deficiency

The higher frequency of evidence for vitamin D deficiency at Ancaster in comparison to Isola Sacra corresponds well with latitudinal differences between the two sites, given that Ancaster is located over ten degrees further north. With higher latitude, the increased zenith angle of the sun causes ultraviolet B rays of the wavelength needed for vitamin D production to travel further through the ozone layer, causing more of them to be absorbed and decreasing the amount of radiation available for cutaneous vitamin D synthesis (Holick, 2003; Mithal et al., 2009; White, 2008); as distance from the equator increases, the required wavelengths of light are accessible for a smaller amount of time each year, and may be completely absent during the winter months (Prentice, 2008). However, features associated with the built environments in which these individuals most likely lived are less intuitively connected with observed differences in lesion frequency between the two collections. Ancaster is thought to have been a smaller settlement with agricultural connections (Todd, 1970; Wilson, 1968), while *Portus Romae* was a key maritime trading center close to the major city of Rome (Mannucci & Verduchi, 1996).

Both the smaller size and less crowded design of a defended settlement, and the potentially more agricultural or craft-related occupations of individuals living at Ancaster, suggest that, despite higher latitudes, individuals at this site were more likely to have regular access and exposure to sunlight. Ancaster is a community with some industrial and craft work, in which individuals are likely to have had easy access to unshaded outdoor spaces and non-built landscapes. Residents of this community would have had access to outdoor space, and the settlement is unlikely to have had high density housing or working spaces. Other analyses have classified Ancaster as a minor urban site (Rohnbogner & Lewis, 2017) or as a nucleated settlement (Pitts & Griffin, 2012), placing it between fully urban and rural contexts. Isola Sacra, on the other hand, had significant infrastructure, and the density of buildings was most likely to have been relatively high. Individuals would not have had to engage in household-level food production, and many are more likely to have worked at indoor occupations. However, in both communities, people are still likely to have had to go outside regularly, evidently maintaining the importance of latitude as a factor in levels of vitamin D deficiency. The longer period of time every winter in which vitamin D cannot be produced upon exposure to sunlight in Britain compared with Italy may also have caused a more significant seasonality for deficiency at Ancaster. Colder winter temperatures in Britain would require individuals to cover themselves with greater amounts of clothing for warmth, or to spend more time indoors during the colder months. These factors may have led to a buildup of severity, and a resultant increase in skeletally manifested cases of deficiency, in individuals at Ancaster compared to Isola Sacra.

Dietary factors should also be considered in the etiology of vitamin D deficiency, including dietary sources of both vitamin D and calcium. Vitamin D is typically obtained from cutaneous synthesis and very little vitamin D is present naturally in most foods (Holick, 2002a); dietary sources of vitamin D include oily fish and egg yolk (Prentice, 2008). During the Roman period, fish and meat were relatively expensive resources that were probably less accessible to ordinary people for regular consumption (Waterlow, 1989). Fish were consumed in ancient Rome in various forms, including salted (*salsamenta*) and as fish sauces (for example, *garum*) which were used in food as well as medicinally (Curtis, 1991). Prowse et al. (2004) argue that fish consumption may have been higher in coastal regions, including at *Portus Romae*, and isotopic evidence from Isola Sacra indicates that individuals at this site ate a mixture of marine and terrestrial foods. There is no direct evidence to indicate whether individuals at Ancaster were consuming fish. If, as Prowse et al. (2004) propose, marine resources were more accessible to Isola Sacra individuals than is typical for this period, then lower levels of vitamin D lesions at this site may indicate increased exposure to sunlight as well as enhanced access to dietary sources which could compensate for lower sun exposure in some individuals.

Calcium intake is important in mineral homeostasis, and, while vitamin D can compensate for low calcium intake to some extent (Ross et al., 2011a), skeletal aspects of vitamin D deficiency become most evident when calcium intake is low (Favus, 1999). Food sources of calcium include dairy products, certain low-oxalate vegetables, legumes, and nuts (Ross et al., 2011b). In addition to calcium present in the small fish bones that

may have been consumed along with fish, which would have been accessed by individuals at Isola Sacra (Prowse et al., 2004), the easiest dietary sources of calcium to discuss based on the evidence available for the Roman period are dairy products. Due to a lack of refrigeration techniques it is doubtful whether liquid milk would have formed a large part of the regular diet, although it is mentioned by Roman medical writers like Galen and Soranus (Garnsey, 1991; Temkin, 1956). Descriptions in literary sources and archaeological evidence for cheese presses indicate that cheese could have provided a source of calcium for Roman individuals (Cool, 2006). Cheese consumption was well established in classical Rome, and its use and production were described by many Roman writers, including Columella, Cato the Elder, and Pliny the Elder (Fox et al., 2017, p. 4). Waterlow (1989) indicates that cheese would have been part of the diet of ordinary Romans, and it was included in the rations of Roman soldiers (Fox et al., 2017, p. 4).

While it is not possible to definitively determine the adequacy of individuals' diets at either Isola Sacra or Ancaster in terms of calcium consumption, historical evidence indicates that food sources of calcium were commonly available during this period, and there is no reason to suspect that the average Roman diet would be deficient in calcium. This is particularly true for Ancaster, which is located on limestone geology that would have caused calcium to be plentiful in both the water supply and local produce (Mays, 2006a). However, it is also important to consider factors that might decrease the absorption of nutrients, which may impact individuals' access to calcium, even if intake is adequate. This could include parasitic infections or gastrointestinal maladies like diarrhea

(Rohnbogner & Lewis, 2017), which is particularly relevant to infants and younger children who are vulnerable to developing weanling's diarrhea.

5.3.1.1. Vitamin D deficiency: Variation in disease occurrence based on age

There is a trend within both samples for individuals who display evidence of healed vitamin D deficiency to have a lower average age at death (Table 4.6). The only difference in mean age at death that reaches statistical significance is that between all individuals with evidence for vitamin D deficiency and those with no evidence of deficiency at Ancaster. Accordingly, age at death distributions also differ significantly between these groups at Ancaster (Section 4.2.1), indicating that skeletal vitamin D deficiency has a significant effect on survival at this site. The significantly higher prevalence value for skeletal evidence of vitamin D deficiency in juveniles compared with adults at Ancaster may affect this relationship, since significantly more individuals who experienced vitamin D deficiency that manifested in the skeleton died before reaching adulthood. Since the majority of cases of deficiency do not appear to be active at the time of death (Table 4.4), this is unlikely to reflect a direct contribution of vitamin D deficiency to the death of these individuals. The existence of a significant relationship does, however, suggest the strong possibility of an indirect contribution of deficiency to the eventual death of these individuals. Recent work on the importance of early life adversity, particularly in critical periods in utero and during early infancy (Barker, 1992; Cooper et al., 2002, 2005; Gluckman & Hanson, 2006; Gowland, 2015), highlights the importance of these periods of life for later health. These critical periods are also times of high susceptibility to vitamin D deficiency (Creo et al., 2017). The long-term effects of

deficiency could work either through a correlation with or predisposition to the development of another condition or disease that then directly contributes to death, or through a more general effect of deficiency on immune function. Given the widespread presence of the vitamin D receptor on many cell types throughout the body, including many immune cells, it is extremely likely that vitamin D deficiency could have long-lasting effects on the function of many organs and systems (Cantorna et al., 2004; Holick, 2003, 2005, 2008). This could be particularly relevant to deficiency experienced during early childhood, the period of life when many body systems are developing, and also when severe deformity associated with lasting visible evidence for deficiency occurs most easily (Lewis, 2007). In the specific case of TB, early life vitamin D deficiency could increase susceptibility to contracting an infection (Adams et al., 2007; Liu et al., 2006) which may remain latent for long periods of time before ultimately activating, and potentially contributing to death, years later.

The relationship between age at death and the presence of evidence for vitamin D deficiency is complex; it is not enough to assume that vitamin D deficiency has no effect on longevity just because the sample with higher frequencies of skeletal evidence for deficiency does not also have a lower mean age at death. While mean age at death is significantly higher at Ancaster than at Isola Sacra (Table 4.2), the frequencies of both vitamin D deficiency (Table 4.4) and chronic respiratory infections (Table 4.12) are higher in the Ancaster sample. At Ancaster, prevalence values for both healed and especially active vitamin D deficiency lesions are higher than at Isola Sacra in many age categories, with significant differences in the prevalence of active disease in juveniles and

the total prevalence in juveniles (Section 4.2.1). One possible confounding factor in the relationship between vitamin D deficiency and age at death is the group of adult individuals excluded from the calculation of mean age at death due to the absence of available features for age estimation. More individuals are present in this undetermined adult category at Isola Sacra (Table 4.1), and it is possible that their exclusion may lower the mean age at death for Isola Sacra. However, the proportion of the total sample represented by this category is similar at both sites, and the trend for frequencies of deficiency to be higher at Ancaster is reflected in the results for this category as well (Table 4.4). This suggests that the effect of excluding these individuals on the relationship between evidence for vitamin D deficiency and mean age at death in these two samples is likely to be small.

At Isola Sacra, there is also a significant difference in mean age at death between individuals placed in categories one and two for healed vitamin D deficiency, with category one individuals having a lower mean age at death than category two individuals (Table 4.6). The slightly stronger evidence present in category one cases indicates that the deficiency experienced by these individuals may have been more severe, more longstanding, may have corresponded with a period of rapid growth, or may have occurred closer to the time of death. The difference in mean age at death between individuals placed in these categories may therefore reflect a greater impact of more severe or longstanding cases of deficiency, or those occurring in certain critical periods, on survival and longevity, with these individuals surviving deficiency but dying sooner than individuals who experienced less severe or longstanding cases. Alternatively, the

presence of less marked skeletal features in individuals who tend to be older may indicate that bone remodeling processes gradually erase evidence for deformities. In this case, more features would be expected to preserve in individuals who died at younger ages, and presumably also sooner after experiencing deficiency, and it would most likely be easier to identify category one cases in these individuals. However, following the cessation of growth, changes in the shape of the long bones are caused primarily by changes in habitual patterns of biomechanical forces (Trinkaus et al., 1991). In adulthood, remodeling may only work to erase evidence for deformities caused by vitamin D deficiency if encouraged to do so by habitual activity patterns, implying that, past adolescence, age may not be the primary factor in the weakening of evidence for deformation of the long bones. In the absence of other evidence, neither of these scenarios can be ruled out, but the patterns observed seem more likely to relate to a difference in the long-term survival of individuals with severe or longstanding cases of deficiency.

It is also possible that the strength of evidence for deficiency that is observable in an individual may be affected by preservation, with better preserved individuals having more features that can be evaluated for signs of deficiency. However, there are no significant differences between category one and category two cases of vitamin D deficiency in terms of the percentage of features that can be evaluated for each individual (Tables 4.9 and 4.11). At Ancaster, category two individuals actually have a higher average percentage of features present for evaluation than category one individuals. Differences in preservation are therefore unlikely to explain the majority of the variation observed between category one and two cases of deficiency in these two samples.

5.3.1.1.1. Age-related variation in vitamin D deficiency: Infancy and childhood

While differences in the prevalence of vitamin D deficiency are not significant when comparing either the samples as a whole or healed deficiency between the two sites, juveniles at Ancaster do have a significantly higher prevalence of active vitamin D deficiency compared to Isola Sacra juveniles (Section 4.2.1). This indicates that climatic and latitudinal differences between the two sites may have had a greater impact on juveniles. Since active disease in juveniles is only seen in the youngest age categories, this is particularly relevant to neonates, infants, and very young children, who are generally dependent on caregivers.

Issues with the accuracy of skeletal age estimation techniques must be kept in mind when interpreting these results. Liversidge (1994) evaluated the dental development method used in this analysis (Gustafson & Koch, 1974) on known age individuals from Spitalfields, finding it to have a high accuracy in determining the age of individuals between zero and 5.4 years of age (0.10 ± 0.37 years' difference between estimated and known chronological age). Clinical evidence indicates that rickets can cause developmental delays which could affect dental and skeletal features used for age estimation (Pitt, 2002). However, Ives (2015) showed that, in a 19th century child of known age who experienced active rickets either at or shortly before death, dental techniques underestimated age by only one month, but measurements of long bone length underestimated the age of the individual by over a year. Dental development data were available to generate reliable age estimates for all but two of the young infants and neonates with evidence for active deficiency, meaning that age estimates for only two

individuals (SCR 594 and SCR 653) depended on less reliable measurements of long bone length. While the possibility that some of these individuals, particularly those aged using long bone data, are older than suggested based on skeletal evidence cannot be excluded, the dental age estimation methods applied have been found to have relatively high accuracy (Liversidge, 1994), and an age difference of a few months is unlikely to invalidate the interpretations made.

Higher levels of active disease in infants at Ancaster could indicate that individuals at this site were practicing Roman childcare behaviors described in medical texts from this period (Temkin, 1956) that have been identified as potential contributors to the risk of developing vitamin D deficiency, including swaddling or the use of nutrient deficient weaning foods such as bread and honey or animal milk (Garnsey, 1991). Swaddling involves covering the skin of the infant with wrappings, and there is some modern clinical evidence that this practice increases the risk of subclinical vitamin D deficiency, based on a case control study in India (Wayse et al., 2003), as well as research in Mongolia (Manaseki, 1993). Swaddling could also compromise cardiorespiratory abilities, especially if it is tight around the chest (Gerard et al., 2002), and this could increase susceptibility to respiratory infection (Van Sleuwen et al., 2007). In Turkey, a country in which swaddling was commonly practiced, Yurdakok et al. (1990) found that rickets was more common in swaddled than unswaddled infants. This study also found that pneumonia and a history of frequent respiratory infections were four times more common in infants who were either completely or partially swaddled (Yurdakok et al., 1990). Swaddling therefore has the potential to increase the risk of respiratory infections

both through direct effects on the lungs and also indirectly by increasing the risk of vitamin D deficiency (Van Sleuwen et al., 2007). In a location like Roman Britain, where the amount of ultraviolet B radiation available is already relatively low, decreasing an infant's access to sunlight further through swaddling may have a major effect on their susceptibility to vitamin D deficiency.

Roman physicians like Galen and Soranus recommended gradually weaning infants onto foods such as milk and cereals. Soranus of Ephesus advocated using pieces of bread softened with milk, sweet wine, or honey wine, followed later by soup made of spelt, or porridge (Temkin, 1956). Similarly, Galen recommended feeding infants milk, followed by bread, and then by more solid foods including vegetables and meats (Garnsey, 1991). Access to these foods would most likely have varied based on socioeconomic status, with poorer families being dependent on relatively nutrient-poor cereal foods for infant feeding (Garnsey, 1991). This may be the case even in a small settlement with agricultural connections like Ancaster, where there is evidence for a local elite (Mattingly, 2006); based on an archaeological study of Romano-British sites, Pitts and Griffin (2012) actually found higher levels of social inequality to exist in rural than in urban settlements.

In modern populations, rickets can also be associated with prolonged breastfeeding without supplementation (Mithal et al., 2009). The relatively low amount of vitamin D in breast milk is not sufficient to sustain rapid growth; Danish food composition data indicate that the vitamin D content of human breast milk varies from 0.066 µg/100g in colostrum to 0.085 µg/100g in mature milk (DTU Fødevareinstituttet,

2016). It is necessary to supplement infants' vitamin D intake through either the diet or exposure to ultraviolet radiation (Thandrayen & Pettifor, 2010). The calcium content of the diet may also be an important factor, as weaning diets that are low in calcium can contribute to the development of rickets (DeLucia, Mitnick, & Carpenter, 2003).

At Isola Sacra, isotopic evidence indicates that transitional feeding began from the end of the first year of life, and weaning had occurred by two to two and a half years of age (Prowse et al., 2008). Individuals as young as one and a half years also showed dental wear on the deciduous incisors, providing additional evidence for transitional feeding between one and two years of age (Prowse et al., 2008). Two cases of active juvenile deficiency at Isola Sacra occur in individuals whose ages at death fit within this period (SCR 33 and 110). While equivalent information on weaning age based on isotopic evidence or juvenile dental wear is not currently available for Ancaster, one individual (ANC 180) died at an age within this period as well. One of the difficulties with evaluating the impact of proscriptions made by physicians in the Roman world is the inability to determine how far recommendations correspond with actual practice (Nutton, 2004), particularly in communities located further from the center of the empire; there are also issues with determining whether what is being depicted represents societal ideals, norms, and attitudes, or actual behavior (Saller & Kertzer, 1991; Garnsey, 1998). Prowse et al. (2008) argue that isotopic and dental data from Isola Sacra are generally consistent with historical evidence from the Roman Empire with respect to the types of complementary foods given to children during weaning, which would include cereal foods. It cannot be determined based on this evidence whether weaning foods were

inadequate, but only that the pattern of breastfeeding and weaning seen at this site is consistent with the descriptions present in proscriptive ancient medical texts (Prowse et al., 2008). The high prevalence of evidence for vitamin D deficiency observed in juveniles at Ancaster implies that, in addition to geographic factors, some of these recommendations for infant feeding and other childcare practices may have been followed here, to the detriment of children's health.

Several juvenile individuals with evidence for active deficiency (Table 4.8) are aged as fetal or neonatal (ANC 192 and 265), or as infants under six months of age (SCR 92 and 653, ANC 124A). A number of infants and very young children, some aged at less than one and a half years (SCR 594 and ANC 138) and others at less than one year of age (SCR 22 and 62, ANC 208), also show evidence for healed deficiency (Table 4.9), meaning that active deficiency would have occurred early in infancy. Other than SCR 594 and SCR 653, all of these individuals' ages were estimated based on dental development, a technique which provides reasonably accurate age at death estimates. As newborn vitamin D levels have been found to correlate strongly with maternal vitamin D status (Karatekin et al., 2009; Sachan et al., 2005), it is possible that many of these individuals' mothers were deficient during pregnancy or lactation. The two fetal or neonatal individuals in particular may represent cases of congenital rickets.

Maternal vitamin D deficiency can lead to overt bone disease in the fetus as early as 30 weeks' gestation (Paterson & Ayoub, 2014), with dental evidence indicating that the effect on calcified tissues in the fetus may begin as early as 20 weeks. The newborn is dependent on the maternal supply of 25-OHD transferred through the placenta to ensure

adequate vitamin D status at birth, and, due to the short three-week half-life of 25-OHD, in early infancy (Thandrayen & Pettifor, 2010). The amount of vitamin D in breast milk is relatively small, and is even less if maternal vitamin D status is low (Thandrayen & Pettifor, 2010), meaning that optimal vitamin D status at birth is extremely important for preventing the development of infantile rickets. The presence of active vitamin D deficiency in neonates and/or young infants at both sites therefore not only indicates that deficiency was present in these age groups, but also suggests that women are likely to have experienced vitamin D deficiency during pregnancy. Of the 24 cases of congenital rickets reviewed by Paterson and Ayoub (2014), 21 mothers experienced symptoms of osteomalacia, and in 18 of these cases the symptoms described involved the skeleton. Skeletal symptoms included bone pain as well as many cases where pelvic deformity and obstructed labour are described. One individual experienced spontaneous fractures, another is described as having a waddling gait, which may indicate deformities in the long bones of the legs or the pelvis, and two others are described as having radiological signs of osteomalacia (Paterson & Ayoub, 2014), which most likely refers to the presence of pseudofractures. While only one case of active deficiency was observed in a female of childbearing age at Isola Sacra (SCR 69), one of the individuals placed into category three at Ancaster also fits into this age group (ANC 202). Although vitamin D deficiency is not particularly visible in this group based on paleopathological evidence, the presence of multiple possible cases of congenital or infantile rickets indicates that some women at both sites probably did experience deficiency during pregnancy that affected bone quality in their infants.

Active cases of vitamin D deficiency in juveniles are only seen in the neonate, infant, and younger child categories at both Ancaster and Isola Sacra; it is expected that these groups would be most susceptible to developing flagrant rickets given their rapid rate of growth (Holick & Chen, 2008). Although severity and length of deficiency are likely to play a role in the formation of skeletal lesions, other factors are also important, including the speed of growth. Paterson and Ayoub (2014) argue that, in the case of congenital rickets, there is no consistent relationship between the severity of deficiency and the presence or absence of bone disease. Creo et al. (2017) identify infants and toddlers as the group at highest risk of nutritional rickets worldwide, finding that this is often related to low vitamin D status in women of childbearing age.

5.3.1.1.2. Age-related variation in vitamin D deficiency: Adolescence

In addition to infancy, the adolescent growth spurt has also been identified as a period of higher risk of vitamin D deficiency (Pearce & Cheetham, 2010), and evidence that several individuals at Isola Sacra and Ancaster may have experienced deficiency during this period is present in the form of deformation of the sacrum and sternum. However, biochemical vitamin D deficiency in this age group does not always lead to skeletal disease. A study in Iran found the prevalence of asymptomatic nutritional rickets in adolescent girls, diagnosed biochemically, to be as high as 10.6% (Dahifar et al., 2007). Creo et al. (2017) found that, while girls in the Middle East appeared to have the highest rates of vitamin D deficiency of any juvenile group worldwide, they did not also show the highest frequency of overt nutritional rickets. Similarly, Spiro and Buttriss (2014) demonstrated a high prevalence of low serum vitamin D among older children and

adolescents from European populations in combination with a very low prevalence of clinical symptoms, including overt bone disease. Whether or not an individual shows skeletal evidence of juvenile vitamin D deficiency is therefore likely to relate to the speed of growth, as well as to the severity and length of deficiency, and possibly to factors such as calcium intake and genetic variation in the vitamin D receptor or binding proteins (Paterson & Ayoub, 2014), with the interaction between these factors being important in determining whether and how deficiency manifests in the skeleton.

Beyond identifying juveniles as most susceptible to developing skeletal deformity in response to vitamin D deficiency, the timing of deficiency leading to certain residual bending deformities might be more precisely estimated based on the timing of fusion of the elements involved. Deformation in the sacrum has been documented in clinical or historical cases of osteomalacia in adults (e.g., Brickley et al., 2005; Ortner, 2003, p. 400). The sacrum and ilia are frequently involved in osteomalacia in modern cases as well, but this most often involves less severe changes like insufficiency fractures in these bones rather than overt deformation (Kanberoglu et al., 2005). Although the timing of skeletal fusion can be variable, the sacral vertebrae typically fuse during adolescence (Schaefer et al., 2008); lower components of the sternal body also most often fuse soon after puberty, with the entire sternal body united by early adulthood. Deformities may develop more easily between the sacral or sternal segments, or may be most likely to preserve in the resultant shape of the sternum or sacrum, if mineralization defects associated with vitamin D deficiency developed while the element was fusing: during adolescence. Molleson and Cox (1993, p. 138-139) propose that sacra displaying

angulation between sacral segments observed in several individuals from Christ Church, Spitalfields in the United Kingdom may be associated with adolescent vitamin D deficiency. One individual studied by D'Ortenzio et al. (2016) displayed both dental evidence for four separate episodes of deficiency, including one episode estimated to have occurred around 12.5 years of age, and angulation of the sacrum suggested to relate to the episode occurring during adolescence.

Abnormal sacral curvature is observed in one case of deficiency at Ancaster (ANC 262A; Figure 5.1), and deformation of the sternum is observed in two cases of deficiency

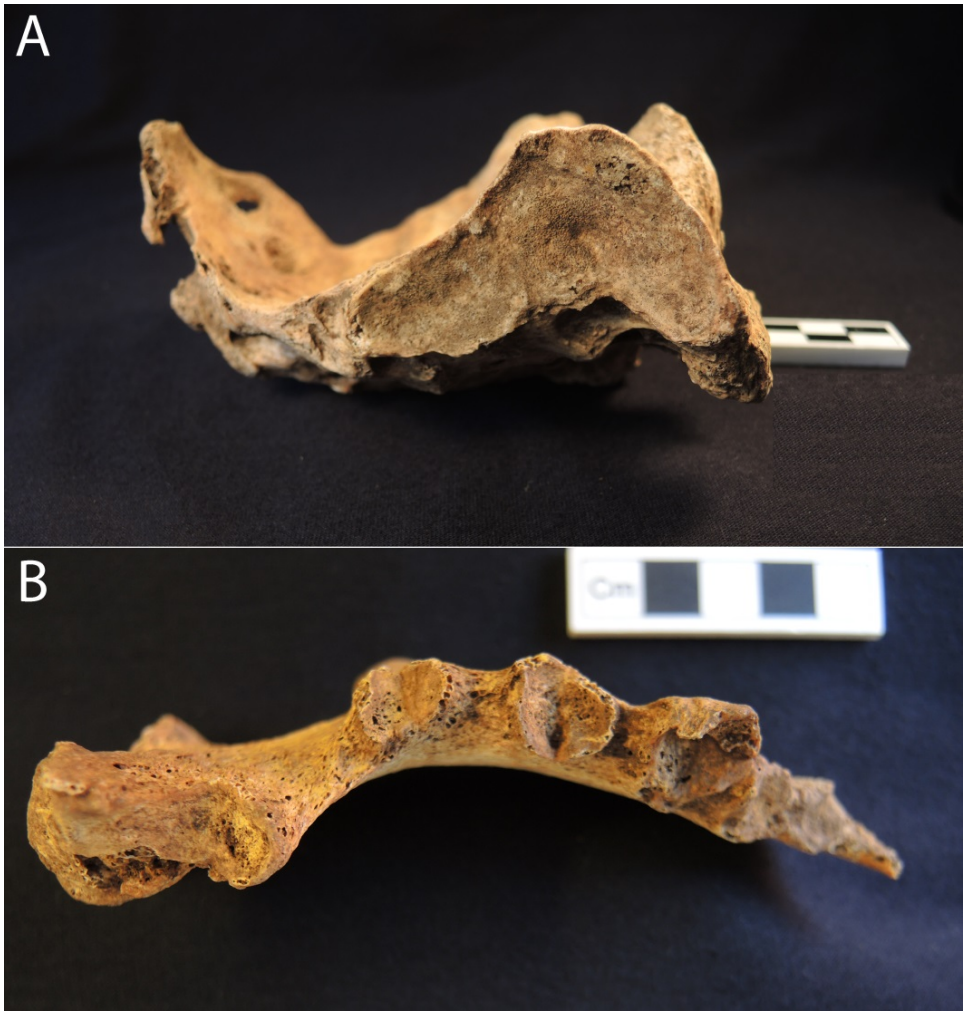


Figure 5.1. Deformation of elements of the axial skeleton associated with vitamin D deficiency, potentially relating to episodes of deficiency experienced in adolescence. A) Angulation of the distal portion of the sacrum, between the third and fourth segments, in individual ANC 262A; B) Anteroposterior curvature of the sternum in individual ANC 45.

at Isola Sacra (SCR 18 and 409) and one case at Ancaster (ANC 45; Figure 5.1). Subtler curvature in the sacrum, considered insufficient on its own to support a diagnosis of vitamin D deficiency, was observed in three additional category three individuals at Ancaster (ANC 98, 220, and 276). Individuals displaying evidence for abnormal curvature in the sacrum and sternum are sexed as female (ANC 45, 220, 262A, and 276, SCR 409) or probable female (SCR 18), with only one displaying male skeletal characteristics (ANC 98). The fact that these features are more common in females than in males supports the idea that the period surrounding puberty and adolescence may have been a time of increased restriction for young women in comparison with males of the same age. Historical descriptions of behavioural expectations for female Romans during this stage in the life course suggest that this could have involved restriction in terms of nutrition or permitted activity outside of the home, as well as the possibility of marriage and pregnancy during adolescence or very early adulthood. Cultural factors affecting behaviour at this age may then have compounded the effect of biological factors of increased risk associated with adolescence as a period of rapid growth (Pearce & Cheetham, 2010). Deformation of the sacrum in particular has different implications for females and males, because severe curvature can reduce the anteroposterior diameter of the pelvic outlet, leading to pelvic obstruction that can cause serious complications during childbirth (Hill, 2005).

5.3.1.1.3. Age-related variation in vitamin D deficiency: Adulthood

The prevalence value for healed vitamin D deficiency is highest in young adults at Isola Sacra and in middle adults at Ancaster. While there is no significant difference

between the mean ages at death for individuals with evidence for healed vitamin D deficiency at these two sites (Table 4.6), the fact that healed deficiency in adults is more common in an older age group at Ancaster than at Isola Sacra does provide some support for the idea that individuals with deficiency at this site may have been living longer into adulthood following disease in childhood. This corresponds well with the idea of Ancaster as a "lower stress" group (Goodman, 1993) with higher skeletal evidence for metabolic and infectious disease morbidity and lower mortality, possibly indicating that individuals at Ancaster were better able to survive disease episodes and live into older adulthood.

No evidence for adult osteomalacia was observed in older adults at Isola Sacra (Figure 4.4). This runs counter to the trend noted at Ancaster (Figure 4.5), as well as in modern populations (e.g., Chapuy & Meunier, 1997; Halloran & Portale, 2005) and other archaeological samples (Ives & Brickley, 2014), where the risk and prevalence of active adult deficiency are often highest in the oldest age groups. In a study of individuals over five years of age at Isola Sacra, Prowse et al. (2005) found significant isotopic differences in older adults that were indicative of variations in diet and access to food resources. With older age, adults at Isola Sacra appear to have been consuming a more varied diet that included more prestige foods such as marine resources and olive oil; alternatively, individuals who had increased access to these foods survived to older ages (Prowse et al., 2005). This could occur either through a direct effect of improved diet on longevity, or through a correlation with another factor, like socioeconomic status, that contributed to both access to prestigious resources and increased survival into old age. It is possible that

a higher quality diet, and any other lifestyle features correlated with this, in individuals surviving to older adulthood at Isola Sacra may have contributed to lower susceptibility to vitamin D deficiency, or maintenance of any deficiency that was experienced at a low enough level so as not to manifest as skeletally recognizable lesions. While evidence for adult osteomalacia is absent in old adults at Isola Sacra, evidence for healing lesions associated with chronic respiratory infections is higher in this group than in any other category of adults at this site (Table 4.12). If, as proposed by Wood et al. (1992), individuals with lesions represent those who survived long enough to mount an immune response to chronic respiratory infections, then a lower prevalence or less severe course of vitamin D deficiency in this group may have contributed to better immune function, and consequently to longer survival with respiratory infections. The opposite pattern is observed at Ancaster (Figure 4.5), with evidence for active vitamin D deficiency in adulthood being highest in old adults. Older adults, or individuals surviving to older adulthood, at Ancaster may have been more susceptible to developing or experiencing more severe forms of active adult vitamin D deficiency. In modern populations, vitamin D deficiency in the elderly is often related to a congruence of factors, including age-related physiological decreases in the capacity to synthesize vitamin D in the skin, reduced physical activity and less time spent outside leading to reduced skin exposure to ultraviolet radiation, and a loss of appetite or changes in dietary habits resulting in reduced dietary intake of vitamin D and calcium (Autier et al., 2014). Some of these behavioral changes also apply to individuals who are institutionalized, and may be relevant for past individuals who were incapacitated by or undergoing treatment for

various illnesses. A combination of these factors at Ancaster may have affected older adults' vitamin D status, and consequently their immune function and ability to deal with other pathological conditions, including respiratory infections (Section 5.3.2.1).

5.3.1.2. Vitamin D deficiency: Variation in disease occurrence based on sex

At Ancaster, lesions associated with vitamin D deficiency are more commonly observed in females than in males (Table 4.7). A higher prevalence value for vitamin D deficiency features in women corresponds well with historical clinical descriptions indicating that deficiency was common in women in the past (Jaffe, 1972, p. 399). While recent studies have not found that vitamin D requirements are higher during pregnancy (Ross et al., 2011a), deficiency in the past was described as being common in women, with confinement indoors and the demands of repeated pregnancies and those occurring during adolescence cited as possible etiological factors (Jaffe, 1972, p. 399). Some clinical data indicate that numerous closely spaced pregnancies may be a risk factor for low vitamin D status (Pearce & Cheetham, 2010), and that prolonged lactation can result in a higher demand for calcium and phosphorous (Prentice, 2003), both of which may be relevant for women of reproductive age in the past. While the frequency of active adult deficiency is not higher in females of reproductive age than in other adult age categories in either sample, the presence of several cases of juvenile deficiency in neonates or very young infants (Tables 4.8 and 4.9) indicates that some women at both Ancaster and Isola Sacra are likely to have experienced low vitamin D status during pregnancy that affected their offspring (Section 5.3.1.1.1).

Since the majority of cases of deficiency observed at both sites are classified as healed and are represented by evidence for deformities probably associated with deficiency experienced during childhood, it is possible that the female experience of childhood at Ancaster differed from that of males in a way that contributed to a greater prevalence of vitamin D deficiency in female juveniles. Historical evidence indicates that Roman experiences of childhood differed significantly for males and females in many ways, including expectations for behavior during childhood itself as well as the timing and events associated with the transition to adulthood. Scenes from children's sarcophagi in the second to third century AD show boys playing outside while girls play inside (Harlow & Laurence, 2002), representing possible differences in exposure to sunlight. Female children transitioned to adulthood at marriage, which has been estimated to occur at any time from the early teens, around the time of menarche (based on legal texts) to the late teens or early twenties (Harlow & Laurence, 2002; Jackson, 1988). Harlow and Laurence (2002) argue that puberty was a time of strict control for young women, in which diet and activities were restricted in preparation for marriage and motherhood. Male children underwent a transitional "youth" period lasting from their mid-teens until they became full adults with marriage and entry into public life in their mid-twenties (Harlow & Laurence, 2002). Male youths were accorded a much greater degree of freedom (Harlow & Laurence, 2002), highlighting the fact that the stage of adolescence in particular held very different expectations for males and females during the Roman period. Differences in expectations for male and female adolescents may also be reflected in evidence for vitamin D deficiency that could relate to episodes experienced in

adolescence, given that almost all individuals in these two samples who exhibit evidence for these features are female (Section 5.3.1.1.2). Differences observed between Ancaster and Isola Sacra may also relate to cultural differences between the central Roman empire and the provinces, particularly given the "middle ground" colonialism often ascribed to Roman imperialism, with its focus on accommodating between typically "Roman" and local cultures (Mattingly, 2006).

At Isola Sacra, differences in the prevalence values for vitamin D deficiency between males and females are smaller than at Ancaster. This suggests that male and female experiences of childhood may have differed less at Isola Sacra than at Ancaster, or that the specific factors leading to the development of vitamin D deficiency at this site were experienced more equally between males and females. Given the presence of a more densely built environment, larger settlement size, potential for indoor occupations, and likely lower access to open areas with large amounts of sunlight at Isola Sacra (Section 5.3.1), it is possible that male children and adolescents at this site may not have had easy access to sunlight even if they were given more freedom than females of the same age.

5.3.2. Variation in disease occurrence: Chronic respiratory infections

As observed for vitamin D deficiency lesions, particularly in juveniles, the number of individuals with evidence for chronic respiratory infections is greater at Ancaster (Table 4.12). While placement of both sites along major travel routes represents a possible mechanism for the introduction of respiratory pathogens into these populations, the smaller settlement size and agricultural connections at Ancaster make it appear to lack the complex of features typically associated with high mortality from respiratory

infections, including overcrowded living conditions and poor nutrition and sanitation (McFarlane, 1989; Scheidel, 2003; Stead, 1997; Stone et al., 2009). It is possible that, in a small town setting with a strong agricultural base (Mays, 2006a), close contact with livestock, potentially including infected cattle, could be a factor in the transmission of infections like TB or brucellosis (Wiltschke-Schrotta & Berner, 1999). Occupations like mining that involve exposure to particulates which might cause respiratory infections may also be a contributing factor at Ancaster, given the occurrence of quarrying and other industrial activities near this site (Mays, 2006a; Wilson, n. d.). It is also possible that occupation, especially participation in manual labor such as mining, quarrying, or agricultural activities, could have an effect on nutritional requirements, which could in turn impact immune function if increased needs are not being met (Lewis, 2003).

Based on data from later historic and modern populations, while urban and rural settlements are likely to have similar types of disease, including respiratory infections, the prevalence of these conditions should be higher in more urbanized centers as a result of higher population densities and poorer living conditions (Redfern & Gowland, 2011), particularly for individuals in the lower social classes. There has been some suggestion, however, that urbanization alone may not have the same detrimental effects on health when not also combined with industrialization (Lewis, 2003). In a study of skeletal evidence pertaining to health and diet for Romano-British samples from the third to fifth centuries AD, Pitts and Griffin (2012) found that individuals from urban sites actually exhibited evidence for better "health" than those from rural sites, with small towns or nucleated settlements (including Ancaster) falling in between these two extremes. They

suggest that both settlement size and connectivity by road were important factors in determining patterns of disease during this period, and relate the presence of higher levels of social inequality in rural samples, as measured by archaeological evidence for burial type and grave inclusions, to poorer health in these populations (Pitts & Griffin, 2012). The presence of large villas in the vicinity of Ancaster (Mattingly, 2006) may provide evidence for the existence of higher levels of social inequality between local elites and the general population that could be reflected in higher levels of respiratory disease at this site, in comparison with Isola Sacra where the lack of mention of a local aristocracy (Prowse et al., 2005) and the suggestion that the majority of inhabitants were moderately well off (Gowland & Redfern, 2010) may indicate a more homogeneous group.

In addition to settlement size, environmental factors related to individuals' living conditions are likely to be affected by socioeconomic status. Wealthy Romans could afford to have spacious homes organized around inner courtyards, while most of the population would have been restricted to much smaller quarters. Artisans usually lived in a few rooms behind or above their workshops, and agricultural workers often lived in very basic quarters in the villages (Jackson, 1988). These conditions seem more likely to have existed at Isola Sacra, especially given that the two nearby cities of Rome and Ostia have been specifically identified as places where apartment blocks of several stories were common in order to accommodate dense occupation (Jackson, 1988). Based on a study of nutritional and nonspecific stress indicators in human skeletal remains, Canci et al. (2005) argue that the quality of life in the Roman suburbs was relatively poor. Less is known about settlement morphology at Ancaster. However, towns of comparable size in Roman

Britain generally lacked larger public buildings (Mays, 2006a), had buildings that were more likely to be used for humble domestic or artisanal functions, including structures that were more similar to those found in rural contexts (Mattingly, 2006), and were more likely to provide residents with a less built environment and greater access to open spaces. Also relevant for Isola Sacra are the potentially high rates of population turnover and migration based on isotopic evidence from this site (Prowse et al., 2007), which could have led to the introduction of new pathogens into the population.

At other sites in Roman Britain, Redfern and Gowland (2011) found that urban settlements displayed higher levels of infectious disease, accompanied by a higher mortality risk, than more rural sites, due to increased density of housing, poor sanitation, a reliance on being able to access imported foods, and higher migration and population turnover. Similarly, Redfern and colleagues (2015) found that Romano-British urban cemeteries had significantly higher frequencies of enamel hypoplasias, caries, and skeletal features of rickets than those from rural contexts. Based on these results, a smaller settlement like Ancaster would be expected to show lower frequencies of lesions associated with chronic respiratory infections. However, prevalence values for lesions associated with pulmonary infections for adults and juveniles at this site are higher than those for more urban samples, including Isola Sacra and the Romano-British site of Poundbury Camp (Lewis, 2011a). The prevalence of pulmonary disease in juveniles at Poundbury was 6.1% (vs. 9.76% at Ancaster), with 4.2% of these considered likely to represent TB more specifically; these figures are said to represent a higher level of

infection than previous (although probably less comprehensive) studies of Romano-British samples (Lewis, 2011a).

Higher levels of skeletal lesions associated with chronic respiratory infections at Ancaster are more consistent with the results of Pitts and Griffin (2012), who found that individuals from rural sites and small towns generally exhibited poorer "health" than those from urban contexts, and attributed this to greater levels of social inequality. Alternatively, if the greater prevalence of skeletal markers at Ancaster is interpreted as representing an increased number of individuals surviving infection long enough to produce skeletal evidence (as put forth by Wood et al., 1992), then the higher prevalence of chronic respiratory infection lesions at Ancaster may actually indicate that people were surviving longer and mounting a more effective immune response to infection. There may be a greater number of individuals at Isola Sacra who experienced acute respiratory infections, but failed to survive long enough to mount a skeletal response that would preserve archaeologically. However, in the absence of other evidence for respiratory infections at these two sites, it is unclear whether this may have been the case. The inter-cemetery analysis completed by Pitts and Griffin (2012) examined published evidence for lesions associated with specific skeletal and dental diseases as well as several nonspecific stress indicators. While these authors did consider the possibility that a higher frequency of skeletal lesions could indicate improved survival as suggested by Wood et al. (1992), they concluded that consistency of this relationship across multiple health indicators supported an association between skeletal lesions and poor health. However, Pitts and Griffin (2012) did not account for possible differences in the relationship between

survival with each pathological condition and skeletal lesion formation (Section 5.1.4), which may have affected their evaluation of this relationship.

5.3.2.1. Chronic respiratory infections: Variation in disease occurrence based on age

Similar to the results for vitamin D deficiency and age (Section 5.3.1.1), there is a general trend in both samples for individuals who display evidence for chronic respiratory infections to have a lower average age at death (Table 4.14). No significant differences between the mean ages at death of individuals with and without evidence for chronic respiratory infections are observed at either site (Section 4.3.2). However, at Ancaster, the age at death distributions of individuals with and without evidence for chronic respiratory infections are significantly different for individuals who survived past the age of three, indicating that the presence of lesions has an effect on individuals' survival after this age. If Ancaster individuals lived past the first three years of life, including the dangerous period of infancy and young childhood, their survival could be significantly impacted by experiencing a chronic respiratory infection that manifested in the skeleton. The majority of lesions observed in these individuals do show some evidence of healing. However, this does not rule out the possibility that infection directly contributed to their deaths, particularly given the episodic nature of many such infections and the tendency of infections like TB to reactivate after periods of latency (Ellner, 1997; Feja & Saiman, 2005).

As is the case for vitamin D deficiency, the relationship between lesions of chronic respiratory infection and longevity is likely to have been complex. A significantly higher mean age at death at Ancaster (Table 4.2) corresponds with a significantly higher

prevalence of both active and healing or healed lesions at this site compared with Isola Sacra. The prevalence values for all lesions in adults, all lesions in juveniles, and healing or healed lesions in adults and middle adults are also significantly higher at Ancaster compared with Isola Sacra (Section 4.3.2). The significantly higher proportion of individuals at this site displaying healed lesions associated with respiratory infections, especially in adults, may indicate a greater number of "survivors" who lived with a respiratory disease long enough to form and at least partially heal skeletal lesions. This situation would correspond more closely with the picture created by increased longevity at Ancaster, despite increased skeletal expression of disease, that is consistent with a higher prevalence of vitamin D deficiency and chronic respiratory lesions and a higher mean age at death.

Among juvenile individuals at Isola Sacra, the highest prevalence value for chronic respiratory infection lesions occurs in infants and younger children (Table 4.12; Figure 4.28). Gowland (2015) argues that lesions in infants can be considered as an important proxy for maternal health, due to close links between maternal and infant health and the accumulation of risk across and potentially between life courses due to the developmental origins of health and disease (Barker, 1992; Gluckman & Hanson, 2006). Close correspondence between the health of mothers and their infants relates to heritable factors that can affect immune status and disease susceptibility (Gowland, 2015), as well as to similarities in the social and environmental factors that act to cause or increase vulnerability to disease (Thandrayen & Pettifor, 2010). Infants and young children, who are typically dependent on caregivers, most often contract disease from the adults with

whom they have close contact, and inhabit the same environments which are conducive to the development of respiratory infections in adult individuals. The prevalence of skeletal lesions in infants and younger children is higher at Isola Sacra than at Ancaster, where no lesions are seen in individuals who died during this period (Figure 4.29), but the prevalence values of lesions in older adolescents and adults, specifically in individuals of reproductive age, are higher at Ancaster. The presence of chronic respiratory infection lesions in Isola Sacra infants may indicate the presence of disease in mothers or other caregivers that did not manifest in the skeleton; alternatively, infants and younger children at Ancaster may have experienced acute respiratory infections and entered the mortality sample before forming a skeletal response.

At Ancaster, evidence for active vitamin D deficiency in adulthood is highest in old adults (Section 5.3.1.1.3). However, the prevalence of evidence for healing or healed lesions associated with chronic respiratory infections is lowest, and the prevalence of active lesions associated with chronic respiratory infection with no signs of healing is highest, in this group compared to all other adult age categories (Table 4.12). Increased susceptibility to more severe forms of active vitamin D deficiency in older adults at Ancaster (Section 5.3.1.1.3) may have led to a less successful immune response to chronic respiratory infections in this group, such that individuals who contracted these infections died of acute disease either before lesions could form, or before lesions had time to begin to remodel.

McGuinness and Rubinowitz (2004) outline two predominant patterns of occurrence specifically for TB, in which the majority of cases are seen in the elderly as a

result of reactivation of previously latent disease, or in people of working age as a result of recent infection. These patterns correspond with economically developed and less developed countries, respectively, an observation which is echoed by the findings of Leibert and Haralambou (2004) that individuals with TB in developing countries are more likely to be younger, and to have contracted the infection more recently. Patterns of disease in the Roman period would be expected to align more closely with those seen in economically less developed countries, where individuals are likely to have lower access to health care, including modern antibiotic treatments. Higher levels of skeletal evidence for chronic respiratory infections in individuals aged between 16 and 49 years (older adolescents, young adults, and middle adults; Figure 4.29) at Ancaster may therefore reflect this pattern. Since this is typically the most productive group within a society, and infection may negatively impact an individual's ability to work or perform necessary household tasks, a high prevalence of respiratory infections in these age categories has implications for the socioeconomic and cultural impact of disease at this site (Geyik et al., 2002).

5.3.2.2. Chronic respiratory infections: Variation in disease occurrence based on sex

In opposition to the trends observed for vitamin D deficiency at Ancaster, both samples show a higher prevalence of evidence for chronic respiratory infections in males than in females (Table 4.15). Globally, the male to female ratio of the case notification rate for pulmonary TB was 1.9 ± 0.6 in 2009 (Neyrolles & Quintana-Murci, 2009), with almost twice as many males as females being diagnosed. While the case notification rate reflects a combination of factors, including variation in access to health care as well as

differences in actual exposure and susceptibility to TB infection (Neyrolles & Quintana-Murci, 2009), other research, including a large case-control study in West Africa, has shown that male sex is an independent risk factor for pulmonary TB after accounting for confounding factors (Lienhardt et al., 2005). Epidemiological surveys have also found differences in susceptibility to pulmonary TB between men and women; in a large survey in Bangladesh, Hamid Salim et al. (2004) report a male to female ratio of three to one even after controlling for potential confounding factors, and conclude that the sex difference in this case is not related to variability in access to health care. This phenomenon is not restricted to TB specifically, as sex differences have been observed in the incidence of a number of bacterial respiratory tract infections (Falagas et al., 2007). Based on a review of evidence from animal and human studies, Neyrolles and Quintana-Murci (2009) suggest that part of the apparent increase in susceptibility experienced by men may relate to biological factors, including those related to sex hormones, genetic variation both in sex chromosomes and in sex-related autosomal gene regulation, and sex-specific differences in nutrition and metabolic processes. A higher prevalence of skeletal evidence for chronic pulmonary conditions in men at both Ancaster and Isola Sacra aligns well with the overall trends observed in modern clinical studies on a global scale.

While TB is more common in men overall, women of reproductive age also experience heightened TB risk (Lambert, 2002). In modern developing countries, TB is one of the leading non-obstetric causes of maternal mortality, and can be an important cause of infertility if it spreads to the genitourinary tract (Molina et al., 2013). A few cases of chronic respiratory infection at Isola Sacra are present in females of reproductive

age (e.g., SCR 272, 411, and 830); for these individuals, possible obstetric complications, as well as the possibility of respiratory spread to any children they may have been actively caring for, should be considered.

A limited number of other bioarchaeological studies have broadly considered evidence for chronic respiratory infections represented by different types of skeletal lesions. Nicklisch et al. (2012) found no significant differences in the distribution of rib lesions based on age and sex, and other studies have either focused on juvenile remains (e.g., Lewis, 2011a) or have not discussed the distribution of lesions based on sex (e.g., Pfeiffer, 1991; Raff et al., 2006). Lambert (2002) found that rib lesions were more common in females than in males in samples from the American Southwest, as well as being more common in juveniles than in adults, and argued that sex-based differences may relate to the younger age of the female sample. Lambert (2002) specifically proposes that this pattern, in which the very young, very old, and women of reproductive age are affected in higher numbers, is consistent with pulmonary TB. This differs from the pattern seen at Ancaster and Isola Sacra in all respects, as neither collection has a significantly different prevalence of chronic respiratory infection lesions between juveniles and adults, and the difference between mean ages at death for females and males are not significant for either site (Sections 4.3.2 and 4.3.3). Any observed sex-based differences in the occurrence of chronic respiratory infection lesions at these two sites are therefore not likely to be explained by variation in age at death.

In specifically considering TB and other pulmonary diseases that may have been encompassed within the Roman disease entity of *phthisis*, Roman ideas about the type of

person most susceptible to these conditions do seem to include sex as a predisposing factor. The notion of *habitus phthisicus*, as outlined by Hippocrates and copied by later Roman medical writers including Celsus and Aretaeus, characterizes *phthisis* as most common in younger adults, with women in particular being at risk, especially during pregnancy (Grmek, 1989). This runs counter to the overall modern pattern of TB occurrence where males are more often affected (e.g., Hamid Salim et al., 2004; Lienhardt et al., 2005; Neyrolles & Quintana-Murci, 2009), but corresponds well with higher TB risk specifically in females of reproductive age (Lambert, 2002; Molina et al., 2013). It is unclear whether this represents an actual difference in who most commonly experienced disease in the past, with males experiencing a lower risk of TB overall, or simply Roman writers' ideas about vulnerability to disease. Increased risk of disease for women is also not reflected in the distribution of lesions associated with chronic respiratory infection at Ancaster and Isola Sacra, although if younger adults and especially women of reproductive age were at risk of experiencing more serious disease, it is possible that they developed acute infections and died before they were able to produce an osseous reaction. In terms of behavioral factors, it is difficult to speculate about how opportunities for exposure to infectious disease may have differed for Roman men and women, as much less has been written about specifically female activities and occupations in the Roman world (Harlow & Laurence, 2002). Given that men were expected to be much more active in public life, with women's work generally being more relegated to the domestic sphere (Harlow & Laurence, 2002), it is possible that men experienced higher degrees of interaction with others, and resultant higher exposure to a

greater number and variety of pathogens in the environment. Conditions within the home may not have been optimal in terms of respiratory health, however, particularly for lower class individuals in crowded apartments. In addition to increased opportunities for pathogen transmission in cramped environments, cooking and heating fires or braziers, as well as oil lamps, may have led to high levels of smoke and other respiratory irritants by creating internal air pollution in poorly ventilated dwellings (Jackson, 1988; Lewis, 2003; Rohnbogner & Lewis, 2017) which could have contributed to the development of chronic bronchitis.

5.4. Conclusions

Considering evidence for skeletal lesions associated with vitamin D deficiency and chronic respiratory infections reveals patterns in disease occurrence at Isola Sacra and Ancaster that reflect the development of unique local biologies, and suggest that individuals at Ancaster may have been surviving longer with these conditions in order to form skeletal lesions. This analysis considered potential relationships between vitamin D deficiency and chronic respiratory infections, finding that the higher prevalence and greater severity of destructive lesions associated with respiratory infections at Ancaster correlates with a higher prevalence of vitamin D deficiency lesions at this site. This raises the possibility that vitamin D deficiency could have been a factor in increasing the severity or hastening the progression of destructive lesions in this sample. Clinical evidence suggests that, independent of other factors, vitamin D deficiency appears most likely to contribute to increased rates of infection and pathogen dissemination, potentially causing an increase in destructive lesions as well as more rapid collapse and deformity of

weakened bone. Deficiency could also cause proliferative lesions to occur less often, and might negatively affect bone strength in a way that affects lesion preservation. The significant relationship between vitamin D deficiency and chronic respiratory infection lesions at Isola Sacra, as well as the presence of evidence for both conditions in two individuals from Ancaster, indicate that the modern association between these conditions may also have extended into the past. Both of these Ancaster individuals display skeletal features associated with healed vitamin D deficiency as well as evidence for a chronic respiratory infection that was active close to the time of death. Earlier episodes of deficiency in these individuals may have made them more susceptible to contracting an infection, although interpretations are limited by the inability to determine the precise timing of development of both conditions.

At Ancaster, both vitamin D deficiency and chronic respiratory infection lesions are shown to have had a significant effect on survival. In the case of vitamin D deficiency, this corresponds well with recent clinical studies that have demonstrated a significant inverse association between vitamin D status and all-cause mortality. For chronic respiratory infections, the effect is only observed in individuals over the age of three. This suggests that infants and young children may have been more likely to experience acute respiratory infections, which are an important cause of death in these age groups in modern contexts. Vitamin D deficiency in infancy may also have impacted immune function, leading to enhanced mortality from respiratory and other infectious causes in the youngest age groups.

A higher prevalence of lesions associated with both vitamin D deficiency and chronic respiratory infections at Ancaster is argued to represent a greater number of "survivors" in this assemblage who were able to live with disease long enough to form a skeletal response; this interpretation is supported by a higher mean age at death, a greater number of old adults, and a different age at death distribution in this sample compared to Isola Sacra. A greater number of Isola Sacra individuals may have experienced acute episodes of disease and died before skeletal lesions could form. The stronger relationship between vitamin D deficiency and chronic respiratory infections at Isola Sacra also raises the possibility that deficiency could be a factor in the reduced efficacy of immune responses at this site, leading to reduced survival of disease and a lower mean age at death. Differences in the ways that lesions associated with vitamin D deficiency and chronic respiratory infections form mean that individuals who do not show skeletal evidence for disease are likely to represent, respectively, those who experienced acute disease and those who experienced episodes that were mild or occurred during periods of slower growth and lower susceptibility.

Several features of the skeletal evidence present in these two assemblages are informative regarding experiences of disease at Ancaster and Isola Sacra. The presence of some macroscopic and especially microscopic features associated with vitamin D deficiency, corresponding with a category three diagnosis, in a significantly greater number of individuals from Ancaster compared to Isola Sacra, could indicate a higher occurrence of low-level deficiency at this site. This might have affected immune function and contributed to the significantly higher prevalence of evidence for chronic respiratory

infections in this collection. While the prevalence of proliferative rib lesions is higher at Ancaster than at Isola Sacra, individuals from Isola Sacra with lesions that were active at the time of death have a significantly higher number of ribs affected, representing the presence of more extensive disease, compared both to individuals from the same site with healed or healing lesions and to Ancaster individuals with active lesions. If the extent of disease is roughly proportional to the length of disease progression, then individuals with active lesions at Isola Sacra appear to have experienced more extensive and severe disease than those at Ancaster, which is also consistent with the presence of evidence for extensive lesions associated with HOA only at Isola Sacra. This supports the idea that a higher prevalence of chronic respiratory infection lesions at Ancaster actually indicates longer survival with disease.

The higher prevalence value for lesions associated with vitamin D deficiency at Ancaster compared with Isola Sacra corresponds well with the higher latitude of this site, indicating that climate may have been an important factor in the occurrence of deficiency despite Ancaster's smaller settlement size and less built environment. Individuals at Isola Sacra are also likely to have had greater access to dietary sources of vitamin D, including fish. Juveniles at Ancaster have a significantly higher prevalence of active deficiency compared to those at Isola Sacra, and higher levels of active disease in infants could indicate the practice of Roman childcare behaviours at this site that may have contributed to the risk of developing a deficiency, such as swaddling or reliance on nutrient deficient weaning foods such as cereals. The presence of active deficiency in several Isola Sacra individuals at an age identified based on isotopic evidence as the period during which

weaning occurred here also raises the possibility that childcare practices associated with weaning may have contributed to the vulnerability of children in this age group to developing vitamin D deficiency. The significant effect of skeletal evidence for vitamin D deficiency on survival at Ancaster could be particularly relevant to deficiency experienced in utero or during infancy and early childhood, especially given evidence for deficiency in several individuals from both sites aged as neonates and young infants. This also raises the strong possibility of maternal deficiency during pregnancy, given established clinical correlations between newborn and maternal vitamin D status. The presence of evidence for deformation in elements that fuse during adolescence, including the sternum and the sacrum, suggests that individuals at both sites experienced deficiency during the adolescent growth spurt. Evidence for vitamin D deficiency that was active in the neonatal period, infancy, young childhood, adolescence, and adulthood, as well as indirect evidence for deficiency during pregnancy, provides data to support the occurrence of vitamin D deficiency across the life course at both sites, especially during periods that have been identified as carrying a high risk of deficiency based on modern clinical studies.

Healed vitamin D deficiency in adults is more common in young adults at Isola Sacra and in middle adults at Ancaster, supporting the idea that individuals who experienced deficiency at Ancaster may have been living longer into adulthood following a childhood deficiency. No evidence for active deficiency was observed in older adults at Isola Sacra, which runs counter to the trends observed in modern populations, other archaeological samples, and at Ancaster, and may relate to isotopic differences in older

adults at this site indicative of higher variation in diet and increased access to food resources. The presence of more individuals in this age group with evidence for chronic respiratory infections also supports the idea that older adults at Isola Sacra may have been better able to survive long enough to form skeletal lesions associated with infectious disease. Isola Sacra individuals placed in category one for healed vitamin D deficiency have a significantly lower mean age at death than those placed in category two, which may reflect a greater impact of more severe or longstanding cases of deficiency, or those occurring in certain critical periods, on survival and longevity.

The prevalence of lesions associated with chronic respiratory infections is significantly higher at Ancaster than at Isola Sacra, which could relate to close contact with livestock or trade and craft occupations in a smaller town setting with a strong agricultural and craft base. If a lower prevalence of lesions at Isola Sacra is related to a greater presence of acute disease and death before a skeletal reaction could be formed, then more crowded settlement and living conditions at Isola Sacra may have been a factor. At Ancaster, the presence of lesions associated with chronic respiratory infections is significantly associated with survival in individuals over the age of three. Lower prevalence values for lesions in very young and old individuals may reflect reduced survival of individuals in these age groups to the point where a skeletal response could form.

Patterns in the occurrence of skeletal lesions based on sex can also be connected to historical information related to expectations for behaviour during the Roman period. Lesions associated with healed vitamin D deficiency at Ancaster, as well as deformation

associated with deficiency in adolescence, are more common in females than in males. Female experiences of childhood and adolescence, especially at Ancaster, may have differed from male experiences in ways that affected the occurrence of vitamin D deficiency, with female adolescence particularly identified as a time of comparative restriction for young women during the Roman period. Prevalence values for chronic respiratory infection lesions are higher in males than in females in both assemblages. This corresponds well with a higher incidence of these infections in males in clinical studies, as well as with Roman expectations that males be much more active in public life.

Taken together, a higher prevalence for evidence of vitamin D deficiency, particularly in juveniles, a significantly higher prevalence of chronic respiratory infection lesions, a significantly higher mean age at death, and a higher number of older adults at Ancaster compared to Isola Sacra may indicate a population with a higher number of "survivors". Both vitamin D deficiency and chronic respiratory infection lesions are also demonstrated to have a significant effect on survival at Ancaster, suggesting that an increased susceptibility to chronic respiratory infections may have been one of the ways through which vitamin D deficiency affected longevity at this site. At Isola Sacra, a lower prevalence of evidence for vitamin D deficiency, particularly in juveniles, a significantly lower prevalence of chronic respiratory infection lesions, a significantly lower mean age at death, and a significantly smaller number of old adults may indicate a population in which fewer individuals survived long enough to develop skeletal reactions to disease. A significant relationship can be demonstrated between prevalence values for vitamin D deficiency and chronic respiratory infection lesions at this site, indicating that vitamin D

deficiency may have influenced the experience of respiratory infections for Isola Sacra individuals; differences in the mean age at death of individuals with category one and two diagnoses of deficiency at this site also imply that those who experienced more severe or longstanding cases of deficiency did not live as long after the condition healed due to long-term effects on health and longevity, which could be mediated through the effects of deficiency on immune function.

At both Ancaster and Isola Sacra, features of the natural, constructed, and social environments therefore represent important influences on the age-, sex-, and site-specific patterning of occurrence of skeletal lesions associated with vitamin D deficiency and chronic respiratory infections. Interactions between these factors led to a picture of morbidity and mortality at these two sites that involves longer term survival of and more efficient immune responses to chronic disease processes at Ancaster, with higher levels of skeletal lesions indicating the presence of more "survivors" at this site (Wood et al., 1992). The combination of lower frequencies of skeletal lesions and higher mortality at Isola Sacra, on the other hand, introduces the possibility that fewer individuals survived to the point where they were able to mount a skeletal response to disease, possibly indicating a greater importance of acute conditions including respiratory infections in this assemblage.

5.4.1. Disease experience in context: Contributions to the paleopathological literature

As part of this analysis, information on the occurrence of vitamin D deficiency and chronic respiratory infections at Isola Sacra and Ancaster is considered in the context of clinical and paleopathological data on experiences of these conditions in both modern

populations and other archaeological samples. While clinical data represent an important source of evidence used to contextualize the occurrence of disease in the past, recent developments in clinical medicine regarding the occurrence and experience of vitamin D deficiency, particularly in terms of its potential correlation with chronic respiratory infections, have yet to be fully integrated into paleopathological analyses. Previous paleopathological studies have recognized the co-occurrence and potential synergistic interactions between metabolic and infectious diseases (e.g., Lewis, 2000; Snoddy et al., 2016; Wilbur et al., 2008), but the idea that co-occurrence could impact not only the appearance but also the presence of lesions has not been widely considered. Here, clinical data on vitamin D deficiency, chronic respiratory infections, and their interactions are considered in order to develop a novel model proposing that concurrent vitamin D deficiency may potentiate the formation of destructive lesions in its early stages, increase their severity in its later stages, and may prevent the formation of proliferative lesions on the visceral surfaces of the ribs and on the long bones.

In examining experiences of vitamin D deficiency in the past, paleopathologists have extensively studied evidence for deficiency in juveniles (e.g., Capasso et al., 1995; Formicola, 1995; Littleton, 1998; Mays et al., 2006; Ortner, 2003; Ortner & Mays, 1998). However, pathological skeletal changes associated with active deficiency in adults are subtle and have only relatively recently been described (Brickley et al., 2005), and a limited number of studies have considered skeletal evidence for either active (Brickley et al., 2007; Haduch et al., 2009; Ives, 2005; Ives & Brickley, 2014) or healed (Brickley et al., 2010) deficiency in adults. This study adds to the considerable body of

paleopathological work on vitamin D deficiency, and contributes a novel approach that considers active and healed vitamin D deficiency throughout the life course. Given that evidence for healed deficiency in adults most often results from deficiency experienced in childhood, separating analyses of deficiency in juveniles and adults excludes valuable information on individuals who experienced childhood deficiency but survived into adulthood. The analysis of paleopathological lesions only in juveniles must also contend with the issue of representation; the frequency of lesions in individuals who died during childhood may not reflect the disease experience of juveniles who survived into adulthood (Lewis, 2011b). Considering evidence for healed vitamin D deficiency in adults along with evidence for deficiency in juveniles therefore accesses information on individuals who experienced deficiency in childhood and survived to adulthood, building a more representative view of disease experience in ancient populations. By examining evidence for active vitamin D deficiency in adults, considering healed deficiency in adults along with deficiency in juveniles, and using both macroscopic and microscopic analytical techniques, this analysis develops a new perspective that provides a more comprehensive picture of the number of individuals who experienced vitamin D deficiency and enables the evaluation of how deficiency impacted survival at these sites. Considering potential relationships between vitamin D deficiency, chronic respiratory infections, and mean age at death also integrates statistical analytical methods that are most often applied to the analysis of stress indicators in paleopathology, and have not been widely used in combination with lesions associated with specific metabolic or infectious diseases.

Most paleopathological evaluations of respiratory disease either focus specifically on TB or discuss proliferative lesions on the visceral surfaces of the ribs, although some analyses have also considered skeletal evidence for HOA, typically as a case study or discussion of a limited number of cases in isolation. In this study, including a wider range of expression of skeletal lesions in the consideration of evidence for respiratory infections identifies a higher number of individuals who may have experienced such conditions in these two samples. Chronic respiratory infection as a category is broad enough to compensate for the very small number of cases that can be specifically diagnosed as TB, while being specific enough to allow for meaningful interpretations. This is the first paleopathological analysis to consider all three of these types of evidence together as indicators for a general category of chronic respiratory infection, and to integrate evidence for HOA into a study at the population level. This analysis also proposes a new approach to evaluating the extent and severity of chronic respiratory infections by considering the number of ribs affected by proliferative lesions, along with the stage of healing of the lesions themselves.

The approach to examining skeletal evidence for vitamin D deficiency and chronic respiratory infections taken in this analysis allowed for the construction of a comprehensive picture of mortality and skeletal markers of morbidity related to these two conditions at Isola Sacra and Ancaster. This approach combined evidence available in the skeletons of the individuals represented within these collections with information on cultural and historical context from Roman literary sources. As a result, features of the natural, constructed, and social environments that might have impacted the development

of disease at Isola Sacra and Ancaster, and their implications for individuals' experiences of disease at these sites, can be elucidated. Quantitative and qualitative differences in the occurrence of vitamin D deficiency and respiratory infections, as well as variation in age at death and the effects of deficiency and respiratory infections on survival and on one another, reflect features of the unique local biologies that developed at these two Roman period sites.

5.4.2. Future research directions

This study represents one of the first attempts at investigating a clinically-noted association between vitamin D and a specific health outcome in the past. Recent clinical and epidemiological research provides some evidence for associations between vitamin D deficiency and several pathological conditions that affect the skeleton, affording opportunities for the examination of these links in paleopathological analyses. For example, potential links between vitamin D deficiency and certain neoplastic conditions or rheumatoid arthritis could be investigated paleopathologically. Future studies of associations between vitamin D deficiency and chronic respiratory infections, as well as other health outcomes, are needed in which examining co-occurrence is built into the study design as a main defining question during data collection, rather than being applied to previously collected data. Additional work in this area will more fully elucidate how ancient individuals experienced vitamin D deficiency, as well as the nature of the relationship between vitamin D deficiency and associated comorbidities in the past.

Further work on the relationship between vitamin D deficiency and respiratory infection in the past would also be valuable for comparative purposes, in order to

determine what geographic, temporal, and cultural factors at Ancaster and Isola Sacra uniquely affect the experience of both conditions and the relationship between them. Within the Roman period, there has been some comparison of pathological lesions between sites of different sizes and settlement types, particularly within Roman Britain (e.g., Pitts & Griffin, 2012; Redfern et al., 2015; Rohnbogner & Lewis, 2017). As both vitamin D deficiency and chronic respiratory infections can be greatly affected by living environment, the examination of associations between these two conditions within assemblages from a greater range of settlement types in the Roman period would be useful in determining what features of urban, smaller town, and rural life may affect the occurrence or experience of, and relationship between, these conditions. One of these previous studies broadly considered evidence for a number of pathological conditions, including lesions linked with vitamin D deficiency and with TB (Rohnbogner & Lewis, 2017). However, a more in depth analysis of lesions at relevant sites that focuses specifically on examining relationships between a few conditions and takes into account whether lesions represent healed or active disease would be most useful for the purposes of comparison with the results of this analysis.

Further examination of the human skeletal remains considered as a part of this study using recently developed techniques would also be helpful in order to evaluate additional evidence for vitamin D deficiency at Ancaster and Isola Sacra. Recently developed applications of histological techniques using interglobular dentine (D'Ortenzio et al., 2016) could allow for the detection of immunologically relevant but skeletally invisible episodes of vitamin D deficiency. Identifying such individuals would provide

further insight into cases of deficiency that did not manifest in the skeleton, and allow the detection of those who experienced multiple episodes of deficiency. This would be especially useful for the further examination of deficiency in individuals who display macroscopic and/or microscopic evidence for deficiency that occurred in both childhood and adulthood. Examining interglobular dentine would also allow a more precise determination of when episodes of deficiency occurred, which would be particularly valuable for confirming the timing of changes like deformation in the sacrum and sternum hypothesized to occur during adolescence.

In this analysis, statistical methods that have previously been used largely to examine interactions between nonspecific stress indicators and demographic features were applied to an investigation of lesions associated with specific pathological conditions. In particular, this involved evaluating age at death distributions and determining whether vitamin D deficiency or chronic respiratory infections had an impact on survival. Given the existence of clinical evidence from both observational studies (Khaw et al., 2014; Schöttker et al., 2013) and randomized controlled trials (Autier & Gandini, 2007; Bjelakovic et al., 2011, 2014) that supports an association between low vitamin D status and increases in all-cause mortality, particularly in older adults, future paleopathological studies should further examine these and other methods of evaluating the impact of vitamin D deficiency on mortality in the past. Because vitamin D deficiency does not typically directly and acutely lead to death (Comacchio, 1998), the effects of deficiency are most often considered in terms of its associated skeletal manifestations, or in terms of associations with specific comorbid conditions. However, clinical support for

a relationship between vitamin D deficiency and all-cause mortality implies that vitamin D has a broader role in the deaths of individuals from diverse causes, and should be considered as a potential contributor to mortality in future paleopathological research.

The results of the current study demonstrate the value of combining diverse qualitative and quantitative analytical techniques in order to provide a more nuanced view of disease experience in the past. Considering a broad range of lesion types in the examination of chronic respiratory infection as a general category, including specific evidence for TB as well as proliferative lesions on the visceral surfaces of the ribs and evidence in the long bones linked to HOA, allows the detection of a higher number of cases with a greater range of expression, and could be implemented by other researchers when evidence for these types of lesions is observed in skeletal assemblages. This analysis also demonstrates the value of using clinical reasoning to develop new ways to quantify aspects of disease experience, including the extent or severity of infection, which could be applied to lesions in other areas of the skeleton as it was here to the ribs. Future analyses in which multiple analytical and statistical techniques are used to elucidate different aspects of disease occurrence, experience, and interaction, interpreted using contextual information from historical, clinical, and other sources, are desirable in order to construct more detailed pictures of the local biologies associated with health in past populations, in the Roman period and beyond.

CHAPTER 6 - References Cited

Aaron, J. E., Gallagher, J. C., & Nordin, B. E C. (1974a). Seasonal variation of histological osteomalacia in femoral-neck fractures. *The Lancet, 304*, 84-85.

Aaron, J. E., Stasiak, L., Gallagher, J. C., Longton, E. B., Nicholson, M., Anderson, J., & Nordin, B. E. C. (1974b). Frequency of osteomalacia and osteoporosis in fractures of the proximal femur. *The Lancet*, *303*, 229-233.

Adams, J. S., Liu, P. T., Chun, R., Modlin, R. L., & Hewison, M. (2007). Vitamin D in defense of the human immune response. *Annals of the New York Academy of Sciences*, *1117*, 94-105.

Adorini, L. (2005). Regulation of immune responses by vitamin D receptor ligands. In D. Feldman, J. W. Pike, & F. H. Glorieux (Eds.), *Vitamin D* (2nd ed., pp. 631-648). San Diego: Elsevier Academic Press.

Afifi, A. (2002). Renal osteodystrophy in developing countries. *Artificial Organs*, *26*, 767-769.

Agarwal, S. C. (2016). Bone morphologies and histories: Life course approaches in bioarchaeology. *Yearbook of Physical Anthropology*, *159*, S130-S149.

Albright, F., & Reifenstein, E. C. (1948). *The Parathyroid Glands and Metabolic Bone Disease*. Baltimore: The Williams and Wilkins Co.

Anderson, T. (2001). A case of skeletal tuberculosis from Roman Towcester. *International Journal of Osteoarchaeology*, *11*, 444-446.

Anderson, T. (2003). The first evidence of brucellosis from British skeletal material. *Journal of Paleopathology*, *15*, 153-158.

Angelucci, S., Baldassarre, I., Bragantini, I., Lauro, M. G., Mannucci, V., Mazzoleni, A., Morselli, C., & Taglietti, F. (1990). Sepolture e riti nella necropolis dell'Isola Sacra. *Bollettino di Archeologia*, *5-6*, 50-113.

Anselmo, D., Capela e Silva, F., & Fernandes, T. (2016). Characterization of hypertrophic osteoarthropathy in an identified skeleton from Évora, Portugal, using combined and comparative morphology and microscopy. *International Journal of Paleopathology*, *12*, 11-16.

Armstrong, J. A., & Hart, P. D. (1975). Phagosome-lysosome interactions in cultured macrophages infected with virulent tubercle bacilli. *The Journal of Experimental Medicine*, *142*, 1-16.

Arriaza, B. T., Salo, W., Aufderheide, A. C., & Holcomb, T. A. (1995). Pre-columbian tuberculosis in northern Chile: Molecular and skeletal evidence. *American Journal of Physical Anthropology*, *98*, 37-45.

Assis, S., Santos, A. L., & Roberts, C. A. (2011). Evidence of hypertrophic osteoarthropathy in individuals from the Coimbra skeletal identified collection (Portugal). *International Journal of Paleopathology*, *1*, 155-163.

Atkins, G. J., Anderson, P. H., Findlay, D. M., Welldon, K. J., Vincent, C., Zannettino, A. C. W., O'Loughlin, P. D., & Morris, H. A. (2007). Metabolism of vitamin D_3 in human osteoblasts: Evidence for autocrine and paracrine activities of 1α,25-dihydroxyvitamin D_3. *Bone, 40,* 1517-1528.

Aubin, J. E., & Heersche, J. N. M. (2005). Vitamin D and osteoblasts. In D. Feldman, J. W. Pike, & F. H. Glorieux (Eds.), *Vitamin D* (2nd ed., pp. 649-663). San Diego: Elsevier Academic Press.

Autier, P., & Gandini, S. (2007). Vitamin D supplementation and total mortality: A meta-analysis of randomized controlled trials. *Archives of Internal Medicine*, *167*, 1730-1737.

Autier, P., Boniol, M., Pizot, C., & Mullie, P. (2014). Vitamin D status and ill health: A systematic review. *Lancet Diabetes and Endocrinology*, *2*, 76-89.

Baker, B. J. (1999). Early manifestations of tuberculosis in the skeleton. In G. Y. Pálfi, O. Dutour, J. Deák, & I. Hutás (Eds.). *Tuberculosis: Past and Present* (pp. 301-307). Budapest-Szeged: Golden Book – TB Foundation.

Baldassarre, I. (1978). La necropolis dell'Isola Sacra. *Quaderni de 'La Ricerca Scientifica'*, *100*, 3-20.

Baldassarre, I. (1984). Una necropolis imperiale Romana: proposte di lettura. *Annali di Archeologia e Storia Antica*, *IV*, 141-149.

Baldassarre, I. (1990). Nuove ricerche nella necropolis dell'Isola Sacra. *Quaderni di Archeologia Etrusco-Italica*, *19*, 164-172.

Banajeh, S. M., Al-Sunbali, N. N., & Al-Sanahani, S. H. (1997). Clinical characteristics and outcome of children aged under 5 years hospitalized with severe pneumonia in Yemen. *Annals of Tropical Paediatrics*, *17*, 321-326.

Barker, D. J. P. (1992). *Fetal and Infant Origins of Adult Disease*. London: BMJ Publishing Group.

Bellamy, R. (2005). Genetic susceptibility to tuberculosis. *Clinics in Chest Medicine*, *26*, 233-246.

Bennike, P., Lewis, M. E., Schutkowski, H., & Valentin, F. (2005). Comparison of child morbidity in two contrasting medieval cemeteries from Denmark. *American Journal of Physical Anthropology*, *128*, 734-746.

Bhalla, A. K., Amento, E. P., Serog, B., & Glimcher, L. H. (1984). 1,25-dihydroxyvitamin D_3 inhibits antigen-induced T cell activation. *The Journal of Immunology*, *133*, 1748-1754.

Bikle, D. (2009). Nonclassic actions of vitamin D. *Journal of Clinical Endocrinology and Metabolism*, *94*, 26-34.

Bilezikian, J. P., & Silverberg, S. J. (2001). The role of parathyroid hormone and vitamin D in the pathogenesis of osteoporosis. In R. Marcus, D. Feldman, & J. Kelsey (Eds.), *Osteoporosis* (Vol. 2, pp. 71-84). San Diego: Academic Press.

Biyoudi-Vouenze, R., Cadranel, J., Valeyre, D., Milleron, B., Hance, A. J., & Soler, P. (1991). Expression of $1,25(OH)_2D_3$ receptors on alveolar lymphocytes from patients with pulmonary granulomatous diseases. *American Review of Respiratory Disease*, *143*, 1376-1380.

Bjelakovic, G., Gluud, L. L., Nikolova, D., Whitfield, K., Wetterslev, J., Simonetti, R. G.,… ,& Gluud, C. (2011). Vitamin D supplementation for prevention of mortality in adults. *Cochrane Database of Systematic Reviews*.

Bjelakovic, G., Gluud, L. L., Nikolova, D., Whitfield, K., Wetterslev, J., Simonetti, R. G.,… , & Gluud, C. (2014). Vitamin D supplementation for prevention of mortality in adults. *Cochrane Database of Systematic Reviews*.

Blondiaux, J., Baud, C. A., Boscher-Barré, N., Dardenne, C., Deschamps, N., Trocellier, P., & Buchet, L. (1992). Trace elements in palaeopathology: Quantitative analysis of a case of hypertrophic osteoarthropathy by instrumental neutron activation analysis. *International Journal of Osteoarchaeology*, *2*, 241-244.

Boldsen, J. L., Milner, G. R., Konigsberg, L. W., & Wood, J. W. (2002). Transition analysis: A new method for estimating age from skeletons. *Cambridge Studies in Biological and Evolutionary Anthropology*, 73-106.

Bonucci, E., Denys-Matrajt, H., Tun-Chot, S., & Hioco, D. J. (1969). Bone structure in osteomalacia, with special reference to ultrastructure. *Journal of Bone and Joint Surgery*, *51*, 511—528.

Boulahbal, F. (1988). Bacteriology. In M. Martini M (Ed.), *Tuberculosis of the Bones and Joints* (pp. 23-27). Berlin: Springer-Verlag.

Brickley, M., Mays, S., & Ives, R. (2005). Skeletal manifestations of vitamin D deficiency osteomalacia in documented historical collections. *International Journal of Osteoarchaeology*, *15*, 389-403.

Brickley, M., Mays, S., & Ives, R. (2007). An investigation of skeletal indicators of vitamin D deficiency in adults: Effective markers for interpreting past living conditions and pollution levels in 18th and 19th century Birmingham, England. *American Journal of Physical Anthropology*, *132*, 67-79.

Brickley, M., & Ives, R. (2008). *The Bioarchaeology of Metabolic Bone Disease*. Oxford: Academic Press.

Brickley, M., Mays, S., & Ives, R. (2010). Evaluation and interpretation of residual rickets deformities in adults. *International Journal of Osteoarchaeology*, *20*, 54-66.

Brickley, M. B., Moffat, T., & Watamaniuk, L. (2014). Biocultural perspectives of vitamin D deficiency in the past. *Journal of Anthropological Archaeology*, *36*, 48-59.

Brooks, S., & Suchey, J. M. (1990). Skeletal age determination based on the os pubis: A comparison of the Acádi-Nemeskéri and Suchey-Brooks methods. *Human Evolution*, *5*, 227-238.

Brothwell, D. (1965). Dental wear patterns in the Libben population. *American Journal of Physical Anthropology*, *68*, 47-56.

Bruns, H., & Stenger, S. (2014). New insights into the interaction of *Mycobacterium tuberculosis* and human macrophages. *Future Microbiology*, *9*, 327-341.

Buikstra, J. E., & Ubelaker, D. H. (Eds.). (1994). *Standards for Data Collection from Human Skeletal Remains*. Arkansas Archaeological Survey Research Series No. 44. Fayetteville: Arkansas Archaeological Society.

Burnham, B. C., & Wacher, J. (1990). *The Small Towns of Roman Britain*. London: Batsford.

Cadranel, J., Garabedian, M., Milleron, B., Guillozo, H., Akoun, G., & Hance, A. J. (1990). $1,25(OH)_2D_3$ production by T lymphocytes and alveolar macrophages recovered by lavage from normocalcemic patients with tuberculosis. *Journal of Clinical Investigation*, *85*, 1588-1593.

Canci, A., Nencioni, L., Minozzi, S., Catalano, P., Caramella, D., & Fornaciari, G. (2005). A case of healing spinal infection from classical Rome. *International Journal of Osteoarchaeology*, *15*, 77-83.

Cannell, J. J., Vieth, R., Umhau, J. C., Holick, M. F., Grant, W. B., Madronich, S., Garland, C. F., & Giovannucci, E. (2006). Epidemic influenza and vitamin D. *Epidemiology and Infection*, *134*, 1129-1140.

Cantorna, M. T., Zhu, Y., Froicu, M., & Wittke, A. (2004). Vitamin D status, 1,25-dihydroxyvitamin D_3, and the immune system. *American Journal of Clinical Nutrition*, *80*, 1717S-1720S.

Capasso, L., Metoni, C., & Di Tota, G. (1995). Bone changes due to rickets: Preliminary histological observations on paleopathological samples. *Gazzette medica italiana, archivio per le scienze mediche*, *154*, 91-95.

Capasso, L. (1999). Brucellosis at Herculaneum (79 AD). *International Journal of Osteoarchaeology*, *9*, 277-288.

Cardoso, H. F. V. (2008a). Epiphyseal union at the innominate and lower limb in a modern Portuguese skeletal sample, and age estimation in adolescent and young adult male and female skeletons. *American Journal of Physical Anthropology*, *135*, 161-170.

Cardoso, H. F. V. (2008b). Age estimation of adolescent and young adult male and female skeletons II, epiphyseal union at the upper limb and scapular girdle in a modern Portuguese skeletal sample. *American Journal of Physical Anthropology*, *137*, 97-105.

Cegielski, J. P., & McMurray, D. N. (2004). The relationship between malnutrition and tuberculosis: Evidence from studies in humans and experimental animals. *International Journal of Tubercular Lung Disease*, *8*, 286-298.

Cegielski, P., & Vernon, A. (2015). Tuberculosis and vitamin D: What's the rest of the story? *The Lancet Infectious Diseases*, *15*, 489-490.

Chan, T. Y. K. (2000). Vitamin D deficiency and susceptibility to tuberculosis. *Calcified Tissue International*, *66*, 476-478.

Chaplin, G., & Jablonski, N. G. (2013). The human environment and the vitamin D compromise: Scotland as a case study in human biocultural adaptation and disease susceptibility. *Human Biology*, *85*, 529-552.

Chapuy, M. C., & Meunier, P. J. (1997). Vitamin D insufficiency in adults and the elderly. *Vitamin D*, *2*, 679-693.

Chesney, R. W. (2010). Vitamin D and the magic mountain: The anti-infectious role of the vitamin. *The Journal of Pediatrics*, *156*, 698-703.

Chocano-Bedoya, P., & Ronnenberg, A. G. (2009). Vitamin D and tuberculosis. *Nutrition Review*, *67*, 289S-293S.

Christensen, T., Martínez-Lavín, M., & Pineda, C. (2013). Periostitis and osteolysis in a medieval skleton from south-west Hungary: (Leprosy, treponematosis, tuberculosis or hypertrophic osteoarthropathy) a diagnostic challenge! *International Journal of Osteoarchaeology*, *23*, 69-82.

Cianferotti, L., & Marcocci, C. (2012). Subclinical vitamin D deficiency. *Best Practice & Research Clinical Endocrinology & Metabolism*, *26*, 523-537.

Clements, M. R., Johnson, L., & Fraser, D. R. (1987). A new mechanism for induced vitamin D deficiency in calcium deprivation. *Nature*, *325*, 62-65.

Cockburn, F., Belton, N. R., Purvis, R. J., Giles, M. M., Brown, J. K., Turner, T. L., Wilkinson, E. M., Forfar, J. O., Barrie, W. J. M., McKay, G. S., & Pocock, S. J. (1980). Maternal vitamin D intake and mineral metabolism in mothers and their newborn infants. *British Medical Journal*, *281*, 11-14.

Comacchio, C. R. (1998). *Nations are Built of Babies: Saving Ontario's Mothers and Children, 1900-1940*. Montreal: McGill-Queen's University Press.

Cool, H. E. M. (2006). *Eating and Drinking in Roman Britain*. Cambridge: Cambridge University Press.

Cooper, C., Javaid, M. K., Taylor, P., Walker-Bone, K., Dennison, E., & Arden, N. (2002). The fetal origins of osteoporotic fracture. *Calcified Tissue International*, *70*, 391-394.

Cooper, C., Javaid, K., Westlake, S., Harvey, N., & Dennison, E. (2005). Developmental origins of osteoporotic fracture: The role of maternal vitamin D insufficiency. *Journal of Nutrition*, *135S*, 2728-2734.

Coussens, A. K., Wilkinson, R. J., Hanifa, Y., Nikolayevskyy, V., Elkington, P. T., Islam, K., Timms, P. M., Venton, T. R., Bothamley, G. H., Packe, G. E., Darmalingam, M., Davidson, R. N., Milburn, J., Baker, L. V., Barker, R. D., Mein, C. A., Bhaw-Rosun, L., Nuamah, R., Young, D. B., Drobniewski, F. A., Griffiths, C. J., & Martineau, A.

R. (2012). Vitamin D accelerates resolution of inflammatory responses during tuberculosis treatment. *PNAS*, *109*, 15449-15454.

Cox, M. (1993). *The Human Bones from Ancaster: Ancient Monuments Laboratory Report 93/89*. Historic Buildings and Monuments Commission for England.

Craven, V., & Everard, M. L. (2013). Protracted bacterial bronchitis: Reinventing an old disease. *Archives of Disease in Childhood*, *98*, 72-76.

Creo, A. L., Thacher, T. D., Pettifor, J. M., Strand, M. A., & Fischer, P. R. (2017). Nutritional rickets around the world: An update. *Paediatrics and International Child Health*, *37*, 84-98.

Crowle, A. J., Ross, E. J., & May, M. H. (1987). Inhibition by $1,25(OH)_2$-vitamin D_3 of the multiplication of virulent tubercle bacilli in cultured human macrophages. *Infection and Immunity*, *55*, 2945-2950.

Cucina, A. (2011). Maya sub adult mortality and individual physiological frailty: An analysis of infant stress by means of linear enamel hypoplasia. *Childhood in the Past*, *4*, 105-116.

Curate, F. (2006). Two possible cases of brucellosis from a Clarist monastery in Alcácer do Sal, southern Portugal. *International Journal of Osteoarchaeology*, *16*, 453-458.

Curtis, R. I. (1991). *Garum and Salsamenta: Production and Commerce in Materia Medica*. Leiden: Brill Academic Publishers.

Dabbs, G. R. (2009). Resuscitating the epidemiological model of differential diagnosis: Tuberculosis at prehistoric Point Hope, Alaska. *Paleopathology Newsletter*, *148*, 11-24.

Dahifar, H., Faraji, A., Yassobi, S., & Ghorbani, A. (2007). Asymptomatic rickets in adolescent girls. *The Indian Journal of Pediatrics*, *74*, 571-575.

Daoud, A. (1988). Bone and joint tuberculosis in the child. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 34-38). Berlin: Springer-Verlag.

Davidson, P. T., & Horowitz, I. (1970). Skeletal tuberculosis: A review with patient presentations and discussion. *American Journal of Medicine*, *48*, 77-84.

Davies, P. D. O., Humphries, M. J., Byfield, S. P., Nunn, A. J., Darbyshire, H., Citron, K. M., & Fox, W. (1984). Bone and joint tuberculosis: A survey of notifications in England and Wales. *Journal of Bone and Joint Surgery*, *66*, 326-330.

Davies, P. D. O. (1985). A possible link between vitamin D deficiency and impaired host defence to *Mycobacterium tuberculosis*. *Tubercle*, *66*, 301-306.

DeLucia, M. C., Mitnick, M. E., & Carpenter, T. O. (2003). Nutritional rickets with normal circulating 25-hydroxyvitamin D: A call for reexamining the role of dietary calcium intake in North American infants. *The Journal of Clinical Endocrinology & Metabolism*, *88*, 3539-3545.

Delvin, E. E., Salle, B. L., Glorieux, F. H., Adeleine, P., & David, L. S. (1986). Vitamin D supplementation during pregnancy: Effect on neonatal calcium homeostasis. *Journal of Pediatrics*, *109*, 328-334.

DeWitte, S. N. (2014). Health in post-Black Death London (1350-1538): Age patterns of periosteal new bone formation in a post-epidemic population. *American Journal of Physical Anthropology*, *155*, 260-267.

DeWitte, S. N., & Stojanowski, C. M. (2015). The osteological paradox 20 years later: Past perspectives, future directions. *Journal of Archaeological Research*, *23*, 397-450.

Docio, S., Riancho, J. A., Pérez, A., Olmos, J. M., Amado, J. A., & González-Macías, J. (1998). Seasonal deficiency of vitamin D in children: A potential target for osteoporosis-preventing strategies. *Journal of Bone and Mineral Research*, *13*, 544-548.

Dormandy, T. (1999). *The white death: A history of tuberculosis*. New York: New York University Press.

D'Ortenzio, L., Ribot, I., Raguin, E., Schattmann, A., Bertrand, B., Kahlon, B., & Brickley, M. (2016). The rachitic tooth: A histological examination. *Journal of Archaeological Science*, *74*, 152-163.

Douglas, A. S., Strachan, D. P., & Maxwell, J. D. (1996). Seasonality of tuberculosis: The reverse of other respiratory diseases in the UK. *Thorax*, *51*, 944-946.

DTU Fødevareinstituttet. (2016). *Documentation of food composition data*. Retrieved from Frida.fooddata.dk.

Durazo-Arvizu, R. A., Dawson-Hughes, B., Sempose, C. T., Yetley, E. A., Looker, A. C., Cao, G., Harris, S. S., Burt, V. L., Carriquiry, A. L., & Picciano, M. F. (2010). Three-phase model harmonizes estimates of the maximal suppression of parathyroid hormone by 25-hydroxyvitamin D in persons 65 years of age or older. *The Journal of Nutrition*, *140*, 595-599.

Eamranond, P., & Jaramillo, E. (2001). Tuberculosis in children: Reassessing the need for improved diagnosis in global control strategies. *International Journal Tubercular Lung Disease*, *5*, 594-603.

Elkington, P. T., & Friedland, J. S. (2015). Permutations of time and place in tuberculosis. *The Lancet Infectious Diseases*, *15*, 1357-1360.

Ellis, M. A. B. (2010). The children of Spring Street: Rickets in an early nineteenth-century congregation. *Northeast Historical Archaeology*, *39*, 120-133.

Ellner, J. J. (1997). The immune response in human tuberculosis: Implications for tuberculosis control. *The Journal of Infectious Diseases*, *176*, 1351-1359.

Epker, B. N., & Frost, H. M. (1965). A histological study of remodeling at the periosteal, Haversian canal, cortical endosteal, and trabecular endosteal surfaces in human rib. *The Anatomical Record*, *152*, 129-136.

Évinger, S., Bernert, Z., Fóthi, E., Wolff, K., Kövári, I., Marcsik, A., Donoghue, H. D., O'Grady, J., Kiss, K. K., & Hajdu, T. (2011). New skeletal tuberculosis cases in past populations from Western Hungary (Transdanubia). *HOMO – Journal of Comparative Human Biology*, *62*, 165-183.

Eyler, W. R., Monsein, L. H., Beute, G. H., Tilley, B., Schultz, L. R., & Schmitt, W. G. H. (1996). Rib enlargement in patients with chronic pleural disease. *American Journal of Roentgenology*, *167*, 921-926.

Falagas, M. E., Mourtzoukou, E. G., & Vardakas, K. Z. (2007). Sex differences in the incidence and severity of respiratory tract infections. *Respiratory Medicine*, *101*, 1845-1863.

Farer, L. S., Lowell, A. M., & Meador, M. P. (1979). Extrapulmonary tuberculosis in the United States. *American Journal of Epidemiology*, *109*, 205-217.

Favus, M. J. (1999). Vitamin D. In C. J. Rosen, J. Glowachi, & J. P. Bilezikian (Eds.), *The Aging Skeleton* (pp. 613-622). San Diego: Academic Press.

Fazekas, I. G., & Kósa, F. (1978). *Forensic fetal osteology*. Budapest: Akademiai Kiado.

Feest, T. G., Mistry, C. D., Grimes, D. S. & Mallick, N. P. (1990). Incidence of advanced chronic renal failure and the need for end stage renal replacement treatment. *British Medical Journal*, *301*, 897-900.

Feja, K., & Saiman, L. (2005). Tuberculosis in children. *Clinics in Chest Medicine*, *26*, 295-312.

Fennell, K. J., & Trinkaus, E. (1997). Bilateral femoral and tibial periostitis in the La Ferrassie 1 Neanderthal. *Journal of Archaeological Science*, *24*, 985-995.

Findlay, L. (1919). Rickets: A historical note. *Glasgow Medical Journal*, *91*, 147-155.

FitzGerald, C., Saunders, S., Bondioli, L., & Macchiarelli, R. (2006). Health of infants in an Imperial Roman skeletal sample: Perspective from dental microstructure. *American Journal of Physical Anthropology*, *130*, 179-189.

Fleming, D. M., Elliot, A. J., Cannell, J. J., Vieth, R., Umhau, J. C., Holick, M. F., Grant, W. B., Madronich, S., Garland, C. F., Giovannucci, E., Aloia, J. F., & Li-Ng, M. (2007). Epidemic influenza and vitamin D. *Epidemiology and Infection*, *135*, 1091-1098.

Foote, J. A. (1927). Evidence of rickets prior to 1650. *American Journal of Diseases of Children*, *34*, 443-452.

Formicola, V. (1995). X-linked hypophosphatemic rickets: A probable Upper Paleolithic case. *American Journal of Physical Anthropology*, *98*, 403-409.

Fox, P. F., Guinee, T. P., Cogan, T. M., & McSweeney, P. L. H. (2017). *Fundamentals of Cheese Science* (2nd ed.). New York NY: Springer US.

Frost, W. H. (1939). The age selection of mortality from tuberculosis in successive decades. *American Journal of Epidemiology*, *30*, 91-96.

Gallagher, J. C., Melton, L. J., Riggs, B. L., & Bergstrath, E. (1980). Epidemiology of fractures of the proximal femur in Rochester, Minnesota. *Clinical Orthopaedics and Related Research*, *150*, 163-171.

Gao, L., Tao, Y., Zhang, L., & Jin, Q. (2010). Vitamin D receptor genetic polymorphisms and tuberculosis: Updated systematic review and meta-analysis. *International Journal of Tuberculosis and Lung Disease*, *14*, 15-23.

Garay, S. M. (2004). Pulmonary tuberculosis. In W. N. Rom & S. M. Garay (Eds.), *Tuberculosis* (2nd ed., pp. 345-394). Philadelphia: Lippincott Williams & Wilkins.

Garenne, M., Ronsmans, C., & Campbell, H. (1992). The magnitude of mortality from acute respiratory infections in children under 5 years in developing countries. *World Health Statistics Quarterly*, *45*, 180-191.

Garnsey, P. (1991). Child rearing in ancient Italy. In D. I. Kertzer & R. P. Saller (Eds.), *The Family in Italy from Antiquity to the Present* (pp. 48-65). New Haven: Yale University Press.

Garnsey, P. (1998). The people of Isola Sacra. In P. F. Rossi, L. Bondioli, G. Geusa, & R. Macchiarelli (Eds.), *Enamel microstructure and developmental defects of the primary dentition. Osteodental biology of the people of Portus Romae (Necropolis of Isola Sacra, 2nd-3rd cent. AD. I.)* (pp. 1-4) Rome: Soprintendenza speciale al museo nazionale preistorico etnografico "L. Pigorini".

Garvin, H. M., & Passalacqua, N. V. (2012). Current practices by forensic anthropologists in adult skeletal age estimation. *Journal of Forensic Sciences*, *57*, 427-433.

Gerard, C. M., Harris, K. A., & Thach, B. T. (2002). Physiologic studies on swaddling: An ancient child care practice, which may promote the supine position for infant sleep. *Journal of Pediatrics*, *141*, 398-404.

Geyik, M. F., Gür, A., Nas, K., Çevik, R., Saraç, J., Dikici, B., & Ayaz, C. (2002). Musculoskeletal involvement in brucellosis in different age groups: A study of 195 cases. *Swiss Medical Weekly*, *132*, 98-105.

Gibney, K. B., MacGregor, L., Leder, K., Torresi, J., Marshall, C., Ebeling, P. R., & Biggs, B.-A. (2008). Vitamin D deficiency is associated with tuberculosis and latent tuberculosis infection in immigrants from sub-Saharan Africa. *Clinical Infectious Diseases*, *46*, 443-446.

Ginde, A. A., Mansback, J. M., & Camargo, C. A. (2009). Association between serum 25-hydroxyvitamin D level and upper respiratory tract infection in the third national health and nutrition examination survey. *Archives of Internal Medicine*, *169*, 384-390.

Giuffra, V., Vitiello, A., Caramella, D., Fornaciari, A., Giustini, D., & Fornaciari, G. (2015). Rickets in a high social class of Renaissance Italy: The Medici children. *International Journal of Osteoarchaeology*, *5*, 608-624.

Gladykowska-Rzeczycka, J, & Prejzner, W. (1993). A case of probable pulmonary osteoparthropathy from the Polish medieval cemetery of Czarna Wielka, District of Grodzisk. *Journal of Paleopathology*, *5*, 159-165.

Gloth III, F. M. (1999). Vitamin D. In C. J. Rosen, J. Glowachi, & J. P. Bilezikian (Eds.), *The Aging Skeleton* (pp. 185-194). San Diego: Academic Press.

Gluckman, P. D., & Hanson, M. A. (2006). The developmental origins of health and disease. In E. M. Wintour & J. A. Owense (Eds.), *Early Life Origins of Health and Disease* (pp. 1-7). New York NY: Springer US.

Gokhale, Y. A., Ambardekar, A. G., Bhasin, A., Patil, M., Tillu, A., & Kamath, J. (2003). Brucella spondylitis and sacroilitis in the general population in Mumbai. *Journal of the Association of Physicians of India*, *51*, 659-666.

González-Reimers, E., Trujillo-Mederos, A., Machado-Calvo, M., Castañeyra-Ruiz, M., Ordóñez, A. C. &, Arnay-de-la-Rosa, M. (2015). A skeletal case of hypertrophic osteoarthropathy from the Canary Islands dating from 1000 BP. *International Journal of Paleopathology*, *11*, 1-6.

Goodman, A. H. (1993). On the interpretation of health from skeletal remains. *Current Anthropology*, *34*, 281-288.

Gowland, R., & Redfern, R. (2010). Childhood health in the Roman world: Perspectives from the centre and margin of the empire. *Childhood in the Past*, *3*, 15-42.

Gowland, R. L. (2015). Entangled lives: Implications of the developmental origins of health and disease hypothesis for bioarchaeology and the life course. *American Journal of Physical Anthropology*, *158*, 530-540.

Grange, J. M. (1995). Human aspects of *Mycobacterium bovis* infection. In C. O. Thoen & J. H. Steele (Eds.), *Mycobacterium bovis Infection in Animals and Humans* (pp. 29-46). Ames: Iowa State University Press.

Grant, W. B. (2006). Epidemiology of disease risks in relation to vitamin D insufficiency. *Progress in Biophysics and Molecular Biology*, *92*, 65-79.

Grauer, A. L. (2008). Macroscopic analysis and data collection in paleopathology. In R. Pinhasi & S. Mays (Eds.), *Advances in Human Paleopathology* (pp. 57-76). Chichester: John Wiley & Sons.

Grmek, M. D. (1989). *Diseases in the Ancient Greek World*. Baltimore: Johns Hopkins University Press.

Gump, D. W., Phillips, C. A., Forsyth, B. R., McIntosh, K., Lamborn, K. R., & Stouch, W. H. (1976). Role of infection in chronic bronchitis. *American Review of Respiratory Disease*, *113*, 465-474.

Gustafson, G. O. S. T. A., & Koch, G. O. R. A. N. (1974). Age estimation up to 16 years of age based on dental development. *Odontologisk Revy*, *25*, 297-306.

Guttentag, A. R., & Salwen, J. K. (1999). Keep your eyes on the ribs: The spectrum of normal variants and diseases that involve the ribs. *RadioGraphics*, *19*, 1125-1142.

Haas, C. J., Zink, A., Molnar, E., Szeimies, U., Reischl, U., Marcsik, A., Ardagna, Y., Dutour, O., Pálfi, G., & Nerlich, A. G. (2000). Molecular evidence for different stages of tuberculosis in ancient bone samples from Hungary. *American Journal of Physical Anthropology*, *113*, 293-304.

Haduch, E., Szczepanek, A., Skrzat, J., Srodek, R., & Brzegowy, P. (2009). Residual rickets or osteomalacia: A case dating from the 16th-18th centuries from Krosno Odrzanskie, Poland. *International Journal of Osteoarchaeology*, *19*, 593-612.

Halloran, B. P., & Portale, A. A. (2005). Vitamin D metabolism and aging. In D. Feldman, J.W. Pike, & F. H. Glorieux (Eds.), *Vitamin D* (2nd ed., pp. 823-838). San Diego: Elsevier Academic Press.

Hamid Salim, M. A., Declercq, E., Van Deun, A., & Saki, K. A. R. (2004). Gender differences in tuberculosis: A prevalence survey done in Bangladesh. *International Journal of Tubercular Lung Disease*, *8*, 952-957.

Harlow, M., & Laurence, R. (2002). *Growing Up and Growing Old in Ancient Rome: A Life Course Approach*. London: Routledge.

Heaney, R. P. (2003). Long-latency deficiency disease: Insights from calcium and vitamin D. *American Journal of Clinical Nutrition*, *78*, 912-919.

Heaney, R. P. (2005). Vitamin D: Role in the calcium economy. In D. Feldman, J. W. Pike, & F. H. Glorieux (Eds.), *Vitamin D* (2nd ed., pp. 773-787). San Diego: Elsevier Academic Press.

Hershkovitz, I., Donoghue, H. D., Minnikin, D. E., Besra, G. S., Lee, O. Y.-C., Gernaey, A. M., Galili, E., Eshed, V., Greenblatt, C. L., Lemma, E., Bar-Gal, G. K. &, Spigelman, M. (2008). Detection and molecular characterization of 9000-year-old *Mycobacterium tuberculosis* from a Neolithic settlement in the Eastern Mediterranean. *PLoS One*, *3*, e3426.

Hess, A. F. (1929). *Rickets including osteomalacia and tetany*. Philadelphia: Lea & Febiger.

Hewison, M. (2012). Vitamin D and the immune system: New perspectives on an old theme. *Endocrinology Metabolism Clinics of North America*, *39*, 365-379.

Hill, J. C. (2005). Dying to give birth: Obstructed labour in the Hindu Kush. *Global Perspective: The Obstetrician & Gynaecologist*, *7*, 267-270.

Hirsch, C. S., Toossi, Z., Vanham, G., Johnson, J. L., Peters, P., Okwera, A., Mugerwa, R., Mugyenyi, P., & Ellner, J. J. (1999). Apoptosis and T cell hyporesponsiveness in pulmonary tuberculosis. *Journal of Infectious Diseases*, *179*, 945-953.

Högler, W. (2015). Complications of vitamin D deficiency from the foetus to the infant: One cause, one prevention, but who's responsibility? *Best Practice & Research Clinical Endocrinology & Metabolism*, *29*, 385-398.

Holick, M. F. (2002a). Too little vitamin D in premenopausal women: Why should we care? *American Journal of Clinical Nutrition*, *76*, 3-4.

Holick, M. F. (2002b). Sunlight and vitamin D: Both good for cardiovascular health. *Journal of General Internal Medicine*, *17*, 733-735.

Holick, M. F. (2003). Vitamin D: A millennium perspective. *Journal of Cellular Biochemistry*, *88*, 296-307.

Holick, M. F. (2005). The vitamin D epidemic and its health consequences. *Journal of Nutrition*, *135*, 2739S-2748S.

Holick, M. F. (2006a). High prevalence of vitamin D inadequacy and implications for health. *Mayo Clinic Proceedings*, *81*, 353-373.

Holick, M. F. (2006b). Resurrection of vitamin D deficiency and rickets. *Journal of Clinical Investigation*, *116*, 2062-2072.

Holick, M. F. (2008). The vitamin D deficiency pandemic and consequences for nonskeletal health: Mechanisms of action. *Molecular Aspects of Medicine*, *29*, 361-368.

Holick, M. F., & Chen, T. C. (2008). Vitamin D deficiency: A worldwide problem with health consequences. *American Journal of Clinical Nutrition*, *87*, 1080S-1086S.

Hollis, B. W., & Pittard III, W. B. (1984). Evaluation of the total fetomaternal vitamin D relationship at term: Evidence for racial differences. *Journal of Clinical Endocrinology and Metabolism*, *59*, 652-657.

Holt, L. E. (1908). *The Diseases of Infancy and Childhood* (4th ed). New York NY: D Appleton and Company.

Hoppa, R., & Saunders, S. (1998). The MAD legacy: How meaningful is mean age-at-death in skeletal samples. *Human Evolution*, *13*, 1-14.

Hugosson, C., Nyman, R. S., Brismar, J., Larsson, S.-G., Lindahl, S., & Lundstedt, C. (1996). Imaging of tuberculosis V. Peripheral osteoarticular and soft-tissue tuberculosis. *Acta Radiologica*, *37*, 512-516.

Hurley, M. M., & Lorenzo, J. A. (2004). Systemic and local regulators of bone remodeling. In F. Bronner & M. C. Farach-Carson (Eds.), *Bone Formation* (pp. 44-70). London: Springer.

Hurtado, A. M., Hill, K. R., Rosenblatt, W., Bender, J., & Scharmen, T. (2003). Longitudinal study of tuberculosis outcomes among immunologically naïve Aché natives of Paraguay. *American Journal of Physical Anthropology*, *121*, 134-150.

Ives, R. (2005). Vitamin D deficiency osteomalacia in a historic urban collection. An investigation of age, sex and lifestyle-related variables. *Paleopathology Newsletter*, *130*, 6-15.

Ives, R., & Brickley, M. (2014). New findings in the identification of adult vitamin D deficiency osteomalacia: Results from a large-scale study. *International Journal of Paleopathology*, *7*, 45-56.

Ives, R. (2015). Insights into health, life and death in Victorian London's East End. *London Archaeologist*, *14*, 150-154.

Jackson, R. (1988). *Doctors and Diseases in the Roman Empire*. Norman: University of Oklahoma Press.

Jaffe, H. L. (1972). *Metabolic, Degenerative, and Inflammatory Diseases of Bones and Joints*. Philadelphia: Lea & Febiger.

Jaffe, H. L. (1975). Rickets and osteomalacia. In H. L. Jaffe (Ed.), *Metabolic, Degenerative, and Inflammatory Diseases of Bones and Joints* (pp. 381-447). Philadelphia: Lea & Febiger.

Jain, A. K. (2002). Treatment of tuberculosis of the spine with neurologic complications. *Clinical Orthopaedics and Related Research*, *308*, 75-84.

Kanberoglu, K., Kantarci, F., Cebi, D., Yilmaz, M. H., Kurugoglu, S., Bilici, A., & Koyuncu, H. (2005). Magnetic resonance imaging in osteomalacic insufficiency fractures of the pelvis. *Clinical Radiology*, *60*, 105-111.

Karatekin, G., Kaya, A., Salihoglu, O., Balci, H., & Nuhoglu, A. (2009). Association of subclinical vitamin D deficiency in neborns with acute lower respiratory infection and their mothers. *European Journal of Clinical Nutrition*, *63*, 473-477.

Katz, D., & Suchey, J. M. (1986). Age determination of the male os pubis. *American Journal of Physical Anthropology*, *69*, 427-435.

Keers, R. Y. (1978). *Pulmonary tuberculosis: A journey down the centuries*. London: Baillère Tindall.

Kelley, M. A., & Micozzi, M. S. (1984). Rib lesions in chronic pulmonary tuberculosis. *American Journal of Physical Anthropology*, *65*, 381-386.

Kelley, M. A., Murphy, S. P., Levesque, D. R., & Sledzik, P. S. (1994). Respiratory disease among protohistoric and early historic Plains Indians. In D. W. Owsley, & R. L. Jantz (Eds.), *Skeletal biology in the Great Plains: migration, warfare, health, and subsistence* (pp. 123-130). Washington: Smithsonian Institution Press.

Kelly, P., Manning, P., Corcoran, P., & Clancy, L. (1991). Hypertrophic osteoarthropathy in association with pulmonary tuberculosis. *Chest*, *99*, 769-770.

Khaw, K.-T., Luben, R., & Wareham, N. (2014). Serum 25-hydroxyvitamin D, mortality, and incident cardiovascular disease, respiratory disease, cancers, and fractures: A 13-y prospective population study. *American Journal of Clinical Nutrition*, doi: 10.3945/ajcn.114.086413.

Klaus, H. D., & Tam, M. E. (2009). Contact in the Andes: Bioarchaeology of systemic stress in colonial Mórrope, Peru. *American Journal of Physical Anthropology*, *138*, 356-368.

Klaus, H. D., Wilbur, A. K., Temple, D. H., Buikstra, J. E., Stone, A. C., Fernandez, M., Wester, C., & Tam, M. E. (2010). Tuberculosis on the north coast of Peru: Skeletal and molecular paleopathology of late pre-Hispanic and postcontact mycobacterial disease. *Journal of Archaeological Science*, *37*, 2587-2597.

Klaus, H. D. (2014). Frontiers in the bioarchaeology of stress and disease: Cross-disciplinary perspectives from pathophysiology, human biology, and epidemiology. *American Journal of Physical Anthropology*, *155*, 294-308.

Kumar, K. (1985). A clinical study and classification of posterior spinal tuberculosis. *International Orthopaedics*, *9*, 147-152.

Laaksi, I., Ruohola, J.-P., Tuohimaa, P., Auvinen, A., Haataja, R., Pihlajamäki, H., & Ylikomi, T. (2007). An association of serum vitamin D concentrations < 40 nmol/L with acute respiratory tract infection in young Finnish men. *American Journal of Clinical Nutrition*, *86*, 714-717.

Lahreche, H. (1988). Pathology. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 28-33). Berlin: Springer-Verlag.

Lambert, P. M. (2002). Rib lesions in a prehistoric Puebloan sample from southwestern Colorado. *American Journal of Physical Anthropology*, *117*, 281-292.

Leach, R. (2009). Pneumonia. In A. McLuckie (Ed.), *Respiratory Disease and its Management* (pp. 51-60). London: Springer.

Leader, S. A. (1950). Tuberculosis of the ribs. *American Journal of Roentgenology*, *63*, 354-359.

Lee, G., Im, J.-G., Kim, J. S., Kang, H. S., & Han, M. C. (1993). Tuberculosis of the ribs: CT appearance. *Journal of Computer Assisted Tomography*, *17*, 363-366.

Lee, H.-C., Chuang, Y.-C., Yu, W.-L., Lee, N.-Y., Chang, C.-M., Ko, N.-Y., Wang, L.-R., & Ko, W.-C. (2006). Clinical implications of hypermucoviscosity phenotype in *Klebsiella pneumoniae* isolates: Association with invasive syndrome in patients with community-acquired bacteraemia. *Journal of Internal Medicine*, *259*, 606-614.

Leibert, E., & Haralambou, G. (2004). Spinal tuberculosis. In W. N. Rom & S. M. Garay (Eds.), Tuberculosis (2nd ed., pp. 565-576). Philadelphia: Lippincott Williams & Wilkins.

Leowski, J. (1986). Mortality from acute respiratory infections in children under 5 years of age: Global estimates. *World Health Statistics Quarterly*, *39*, 138-144.

Lewis, M. (2000). Non-adult palaeopathology: Current status and future potential. In M. Cox & S. Mays (Eds.), *Human Osteology in Archaeology and Forensic Science* (pp. 39-57). London: Greenwich Medical Media Ltd.

Lewis, M. (2003). A comparison of health in past rural, urban and industrial England. In P. Murphy & P. E. J. Wiltshire (Eds.), *The Environmental Archaeology of Industry* (p. 154-161). Oxford: Oxbow Books.

Lewis, M. (2007). *The Bioarchaeology of Children: Perspectives from Biological and Forensic Anthropology*. Cambridge: Cambridge University Press.

Lewis, M. E. (2011a). Tuberculosis in the non-adults from Romano-British Poundbury Camp, Dorset, England. *International Journal of Paleopathology*, *1*, 12-23.

Lewis, M. E. (2011b). The osteology of infancy and childhood: Misconceptions and potential. In M. Lally & A. Moore (Eds.), *(Re)Thinking the little ancestor: New*

perspectives on the archaeology of infancy and childhood (pp. 1-13). Oxford: Archaeopress.

Lienhardt, C., Fielding, K., Sillah, J. S., Bah, B., Gustafson, P., Warndorff, D., Palayew, M., Lisse, I., Donkor, S., Diallo, S., Manneh, K., Adegbola, R., Aaby, P., Bah-Sow, O., Bennett, S., & McAdam, K. (2005). Investigation of the risk factors for tuberculosis: A case-control study in three countries in West Africa. *International Journal of Epidemiology*, *34*, 914-923.

Lips, P. (2007). Vitamin D status and nutrition in Europe and Asia. *Journal of Steroid Biochemistry & Molecular Biology*, *103*, 620-625.

Littleton, J. (1998). A Middle Eastern paradox: Rickets in skeletons from Bahrain. *Journal of Paleopathology*, *10*, 13-30.

Littleton, J. (2011). Moving from the canary in the coalmine: Modeling childhood in Britain. In S. C. Agarwal & B. A. Glencross (Eds.), *Social Bioarchaeology* (pp. 361-389). Malden MA: Wiley-Blackwell.

Liu, P. T., Stenger, S., Li, H., Wenzel, L., Tan, B. H., Krutzik, S. R., Ochoa, M. T., Schauber, J., Wu, K., Meinken, C., Kamen, D. L., Wagner, M., Bals, R., Steinmeyer, A., Zügel, U., Gallo, R. L., Eisenberg, D., Hewison, M., Hollis, B. W., Adams, J. S., Bloom, B. R., & Modlin, R. L. (2006). Toll-like receptor triggering of a vitamin D-mediated human antimicrobial response. *Science*, *311*, 1770-1773.

Liversidge, H. M. (1994). Accuracy of age estimation from developing teeth of a population of known age (0-5.4 years). *International Journal of Osteoarchaeology*, *4*, 37-45.

Lock, M., & Nguyen, V. (2010). *An Anthropology of Biomedicine*. West Sussex: Wiley Blackwell.

Locke, E. A. (1915). Secondary hypertrophic osteo-arthropathy and its relation to simple club fingers. *Archives of Internal Medicine*, *15*, 659-713.

Lubani, M. M., Al-Shab, T. S., Al-Saleh, Q. A., Sharda, D. C., Quattawi, S. A., Ahmed, S. A. H., Moussa, M. A., & Reavey, P. C. (1989). Vitamin-D-deficiency rickets in Kuwait: The prevalence of a preventable disease. *Annals of Tropical Paediatrics*, *3*, 134-139.

Manaseki, S. (1993). Mongolia: A health system in transition. *British Medical Journal*, *307*, 1609-1611.

Mankin, H. J. (1974). Rickets, osteomalacia, and renal osteodystrophy. *Journal of Bone and Joint Surgery*, *56*,101-128.

Mannucci, I. D., & Verduchi, P. (1996). Il porto imperiale di Roma: Le vicende storiche. In V. Mannucci (Ed.), *Il Parco Archeologico Naturalistico del Porto di Traiano* (pp. 15-28). Roma: Gangemi Editore,

Maresh, M. M. (1970). Measurements from roentgenograms, heart size, long bone lengths, bone, muscles, and fat widths; Skeletal maturation. In R. W. McCammon (Ed.), *Human growth and development* (pp. 155-200). Springfield: Charles C. Thomas.

Marrie, T. J. (1999). Pneumococcal pneumonia: Epidemiology and clinical features. *Seminars in Respiratory Infections*, *14*, 227-236.

Marsden, J. H. (1863). Observations on certain Roman remains at Ancaster. In *Reports and Papers Read at the Meetings of the Architectural Societies of the County of York, Diocese of Lincoln, Archdeaconry of Northampton, County of Bedford, Diocese of Worcester, and County of Leicester During the Year 1863*. Associated Architectural Societies' Reports and Papers VII.

Martin, N. S. (1971). Pott's paraplegia: A report on 120 cases. *The Journal of Bone and Joint Surgery*, *53*, 596-608.

Martineau, A. R., Wilkinson, R. J., Wilkinson, K. A., Newton, S. M., Kampmann, B., Hall, B. M., Packe, G. E., Davidson, R. N., Eldridge, S. M., Maunsell, Z. J., Rainbow, S. J., Berry, J. L., & Griffiths, C. J. (2007a). A single dose of vitamin D enhances immunity to mycobacteria. *American Journal of Respiratory and Critical Care Medicine*, *176*, 208-213.

Martineau, A. R., Honecker, F. U., Wilkinson, R. J., & Griffiths, C. J. (2007b). Vitamin D in the treatment of pulmonary tuberculosis. *Journal of Steroid Biochemistry and Molecular Biology*, *103*, 793-798.

Martineau, A. R., Timms, P. M., Bothamley, G. H., Hanifa, Y., Islam, K., Claxton, A. P., Packe, G. E., Moore-Gillon, J. C., Darmalingam, M., Davidson, R. N., Milburn, H. J., Baker, L. V., Barker, R. D., Woodward, N. J., Venton, T. R., Barnes, K. E., Mullett, C. J., Caussens, A. K., Rutterford, C. M., Mein, C. A., Davies, G. R., Wilkinson, R. J., Nikolayevskyy, V., Drobniewski, F. A., Eldridge, S. M., & Griffiths, C. J. (2011). High-dose vitamin D_3 during intensive-phase antimicrobial treatment of pulmonary tuberculosis: A double-blind randomized controlled trial. *Lancet*, *377*, 242-250.

Martinez-Lavin, M., Mansilla, J., Pineda, C., Pijoán, C., & Ochoa, P. (1994). Evidence of hypertrophic osteoarthropathy in human skeletal remains from pre-Hispanic Mesoamerica. *Annals of Internal Medicine*, *120*, 238-241.

Martini, M. (1988a). Introduction. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 1-2). Berlin: Springer-Verlag.

Martini, M. (1988b). Natural history of bone and joint tuberculosis. In M. Martini M (Ed.), *Tuberculosis of the Bones and Joints* (pp. 5-11). Berlin: Springer-Verlag.

Martini, M. (1988c). Diagnosis. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 12-22). Berlin: Springer-Verlag.

Martini, M. (1988d). Tuberculosis of the girdle joints. In M. Martini (Ed.), Tuberculosis of the Bones and Joints (pp. 149-156). Berlin: Springer-Verlag.

Martini, M. (1988e). Conclusions. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 201-202). Berlin: Springer-Verlag.

Martini, M., & Adjrad, A. (1988). Tuberculosis of the hip joint. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 111-123). Berlin: Springer-Verlag.

Martini, M., & Boudjemaa, A. (1988). Tuberculous osteomyelitis. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 52-79). Berlin: Springer-Verlag.

Martini, M., & Kerri, O. (1988). Tuberculosis of the knee. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 125-138). Berlin: Springer-Verlag.

Martini, M., & Ouahes, M. (1988). Posterior spinal tuberculosis. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 197-200). Berlin: Springer-Verlag.

Masson, M., Molnár, E., Donoghue, H. D., Besra, G. S., Minnikin, D. E., Wu, H. H. T., Lee, O. Y.-C., Bull, I. D., & Pálfi, G. (2013). Osteological and biomolecular evidence of a 7000-year old case of hypertrophic pulmonary osteopathy secondary to tuberculosis from Neolithic Hungary. *PLoS One*, *8*, e78252. doi: 10.1371/journal.pone.0078252

Matos, V., & Santos, A. L. (2006). On the trail of pulmonary tuberculosis based on rib lesions: Results from the human identified skeletal collection from the Museu Bocage (Lisbon, Portugal). *American Journal of Physical Anthropology*, *130*, 190-200.

Matos, V., Marques, C., & Lopes, C. (2011). Severe vertebral collapse in a juvenile from the graveyard (13^{th}/14^{th}-19^{th} centuries) of the São Miguel Church (Castelo Branco,

Portugal): Differential paleopathological diagnosis. *International Journal of Osteoarchaeology*, *21*, 208-217.

Mattingly, D. (2006). An imperial possession: Britain in the Roman empire, 54 BC – AD 409. London: Allen Lane.

Mays, S., Taylor, G. M., Legge, A. J., Young, D. B., & Turner-Walker, G. (2001). Paleopathological and biomolecular study of tuberculosis in a medieval skeletal collection from England. *American Journal of Physical Anthropology*, *114*, 298-311.

Mays, S., Fysh, E., & Taylor, G. M. (2002). Investigation of the link between visceral surface rib lesions and tuberculosis in a medieval skeletal series from England using ancient DNA. *American Journal of Physical Anthropology*, *119*, 27-36.

Mays, S., & Taylor, G. M. (2002). Osteological and biomolecular study of two possible cases of hypertrophic osteoarthropathy from mediaeval England. *Journal of Archaeological Science*, *29*, 1267-1276.

Mays, S. (2006a). Age-related cortical bone loss in women from a 3rd-4th century AD population from England. *American Journal of Physical Anthropology*, *129*, 518-528.

Mays, S. (2006b). A palaeopathological study of Colles' fracture. *International Journal of Osteoarchaeology*, *16*, 415-428.

Mays, S., Brickley, M., & Ives, R. (2006). Skeletal manifestations of rickets in infants and young children in a historic population from England. *American Journal of Physical Anthropology*, *129*, 362-374.

Mays, S. A. (2007). Lysis at the anterior vertebral body margin: Evidence for brucellar spondylitis? *International Journal of Osteoarchaeology*, *17*, 107-118.

Mays, S., Brickley, M., & Ives, R. (2007). Skeletal evidence for hyperparathyroidism in a 19th century child with rickets. *International Journal of Osteoarchaeology*, *17*, 73-81.

Mays, S. (2012). The relationship between paleopathology and the clinical sciences. In A. L. Grauer (Ed.), *A Companion to Paleopathology* (pp. 285-309). Oxford: Wiley-Blackwell.

Mays, S. (2014). Resorption of mandibular alveolar bone following loss of molar teeth and its relationship to age at death in a human skeletal population. *American Journal of Physical Anthropology*, *153*, 643-652.

McDade, T. W. (2003). Life history theory and the immune system: Steps toward a human ecological immunology. *Yearbook of Physical Anthropology*, *46*, 100-125.

McFarlane, N. (1989). Hospitals, housing, and tuberculosis in Glasgow, 1911-51. *Social History of Medicine*, *2*, 59-85.

McGuinness, G., & Rubinowitz, A. N. (2004). Imaging of thoracic tuberculous infections. In W. N. Rom & S. M. Garay (Eds.), *Tuberculosis* (2nd ed., pp. 395-425). Philadelphia: Lippincott Williams & Wilkins.

McMurray, D. N., Bartow, R. A., Mintzer, C. L., & Hernandez-Frontera, E. (1990). Micronutrient status and immune function in tuberculosis. *Annals of the New York Academy of Sciences*, *587*, 59-69.

McNally, J. D., Leis, K., Matheson, L. A., Karuananyake, C., Sankaran, K., & Rosenberg, A. M. (2009). Vitamin D deficiency in young children with severe acute lower respiratory infection. *Pediatric Pulmonology*, *44*, 981-988.

Meinecke, B. (1927). Consumption (tuberculosis) in classical antiquity. *Annals of Medical History*, *9*, 379-402.

Meunier, P. J., & Chapuy, M.-C. (2005). Vitamin D insufficiency in adults and the elderly. In D. Feldman, J. W. Pike, & F. H. Glorieux (Eds.), *Vitamin D* (2nd ed., pp. 1085-1100). San Diego: Elsevier Academic Press.

Michelow, I. C., Olsen, K., Lozano, J., Rollins, N. K., Duffy, L. B., Ziegler, T., Kauppila, J., Leinonen, M., & McCracken, G. H. (2004). Epidemiology and clinical characteristics of community-acquired pneumonia in hospitalized children. *Pediatrics*, *113*, 701-707.

Milner, G., & Boldsen, J. (2012). Transition analysis: A validation study with known-age modern American skeletons. *American Journal of Physical Anthropology*, *148*, 98-110.

Minozzi, S., Catalano, P., Caldarini, C., & Fornaciari, G. (2012). Paleopathology of human remains from the Roman Imperial Age. *Pathobiology*, *79*, 268-283.

Mithal, A., Wahl, A., Bonjour, J.-P., Burckhardt, P., Dawson-Hughes, B., Eisman, J. A., El-Hajj Fuleihan, G., Josse, R. G., Lips, P., Morales-Torres, J., & IOF Committee of Scientific Advisors Nutrition Working Group. (2009). Global vitamin D status and determinants of hypovitaminosis D. *Osteoporosis International*, *20*, 1807-1820.

Molina, R. L., Diouf, K., & Nour, N. M. (2013). Tuberculosis and the obstetrician-gynecologist: A global perspective. *Reviews in Obstetrics & Gynecology*, *6*, 174-181.

Molleson, T., & Cox, M. (1993). *The Spitalfields Project. Volume 2: The Anthropology. The Middling Sort*. York: Council for British Archaeology.

Morley, R., Carlin, J. B., Pasco, J. A., & Wark, J. D. (2006). Maternal 25-hydroxyvitamin D and parathyroid hormone concentrations and offspring birth size. *Journal of Clinical Endocrinology and Metabolism*, *91*, 906-912.

Mughal, M. Z., Salama, H., Greenaway, T., Laing, I., & Mawer, E. B. (1999). Florid rickets associated with prolonged breast feeding without vitamin D supplementation. *British Medical Journal*, *318*, 39-40.

Muhe, L., Lulseged, S., Mason, K. E., & Simoes, E. A. F. (1997). Case-control study of the role of nutritional rickets in the risk of developing pneumonia in Ethiopian children. *The Lancet*, *349*, 1801-1804.

Müller, R., Roberts, C. A., & Brown, T. A. (2014). Biomolecular identification of ancient *Mycobacterium tuberculosis* complex DNA in human remains from Britain and continental Europe. *American Journal of Physical Anthropology*, *153*, 178-189.

Nesby-O'Dell, S., Scanlon, K. S., Cogswell, M. E., Gillespie, C., Hollis, B. W., Looker, A. C., Allen, C., Doughertly, C., Gunter, E. W., & Bowman, B. A. (2002). Hypovitaminosis D prevalence and determinants among African American and white women of reproductive age: Third National Health and Nutrition Examination Survey, 1988-1994. *American Journal of Clinical Nutrition*, *76*, 187-192.

Neyrolles, O., & Quintana-Murci, L. (2009). Sexual inequality in tuberculosis. *PLoS Medicine*, *6*(12), e1000199.

Nicklisch, N., Maixner, F., Ganslmeier, R., Friederich, S., Dresely, V., Meller, H., Zink, A., & Alt, K. W. (2012). Rib lesions in skeletons from early Neolithic sites in central Germany: On the trail of tuberculosis at the onset of agriculture. *American Journal of Physical Anthropology*, *149*, 391-404.

Nnoaham, K. E., & Clarke, A. (2008). Low serum vitamin D levels and tuberculosis: A systematic review and meta-analysis. *International Journal of Epidemiology*, *37*, 113-119.

Nursyam, E. W., Amin, Z., & Rumende, C. M. (2006). The effect of vitamin D as supplementary treatment in patients with moderately advanced pulmonary tuberculous lesion. *Acta Medica Indonesiana – The Indonesian Journal of Internal Medicine*, *38*, 3-5.

Nussbaum, E. S., Rockswold, G. L., Bergman, T. A., Erickson, D. L., & Seljeskog, E. L. (1995). Spinal tuberculosis: A diagnostic and management challenge. *Journal of Neurosurgery*, *83*, 243-247.

Nutton, V. (2004). *Ancient Medicine*. New York NY: Routledge.

Nyman, R. S., Brismar, J., Hugosson, C., Larsson, S.-G., & Lundstedt, C. (1996). Imaging of tuberculosis – Experience from 503 patients. *Acta Radiologica*, *37*, 482-488.

Ogilvie, R. (1957). *Pathological histology* (5th Ed.). Edinburgh: Livingstone.

Oginni, L. M., Worsfold, M., Oyelami, O. A., Sharp, C. A., Powell, D. E., & Davie, M. W. J. (1996). Etiology of rickets in Nigerian children. *Journal of Pediatrics*, *128*, 692-694.

Okonofua, F., Houlder, S., Bell, J., & Dandona, P. (1986). Vitamin D nutrition in pregnant Nigerian women at term and their newborn infants. *Journal of Clinical Pathology*, *39*, 650-653.

Ortner, D. J., & Mays, S. (1998). Dry-bone manifestations of rickets in infancy and early childhood. *International Journal of Osteoarchaeology*, *8*, 45-55.

Ortner, D. J. (2003). *Identification of Pathological Conditions in Human Skeletal Remains* (2nd ed.). San Diego: Academic Press.

Ouahes, M., & Martini, M. (1988a). Tuberculous spondylodiscitis (spinal tuberculosis). In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 157-179). Berlin: Springer-Verlag.

Ouahes, M., & Martini, M. (1988b). Pott's paraplegia. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 179-190). Berlin: Springer-Verlag.

Ouahes, M., & Martini, M. (1988c). Tuberculous kyphosis. In M. Martini (Ed.), *Tuberculosis of the Bones and Joints* (pp. 190-197). Berlin: Springer-Verlag.

Pálfi, G. Y., Dutour, O., Deák, J., & Hutás, I. (1999). *Tuberculosis: Past and Present*. Budapest-Szeged: Golden Book – TB Foundation.

Pappas, G., Bosilkovski, M., Akritidis, N., Mastora, M., Krteva, L., & Tsianos, E. (2003). Brucellosis and the respiratory system. *Clinical Infectious Diseases*, *37*, e95-99.

Parfitt, A. M. (2005). Vitamin D and the pathogenesis of rickets and osteomalacia. In D. Feldman, J. W. Pike, & F. H. Glorieux (Eds.), *Vitamin D* (2nd ed., pp. 1029-1048). San Diego: Elsevier Academic Press.

Paterson, C. R., & Ayoub, D. (2014). Congenital rickets due to vitamin D deficiency in the mothers. *Clinical Nutrition*, *34*, 793-798.

Pavolini, C. (1996). *La Vita Quotidiana a Ostia*. Rome: Gius, Laterza & Figli.

Pearce, S. H. S., & Cheetham, T. D. (2010). Diagnosis and management of vitamin D deficiency. *British Medical Journal*, *340*, 142-147.

Penna, G., & Adorini, L. (2000). 1α,25-Dihydroxyvitamin D_3 inhibits differentiation, maturation, activation, and survival of dendritic cells leading to impaired alloreactive T cell activation. *Journal of Immunology*, *164*, 2405-2411.

Peterlik, M. (2004). Targeting the osteoblast for prevention and treatment of bone diseases. In F. Bronner & M. C. Farach-Carson (Eds.), *Bone Formation* (pp. 138-153). London: Springer.

Pettifor, J. M., Wang, J., & Cooper-Smith, J. (1978). Rickets in children of rural origin in South Africa: Is low dietary calcium a factor? *Journal of Pediatrics*, *92*, 320-324.

Pettifor, J. M. (2003). Nutritional rickets. In F. H. Glorieux, J. M. Pettifor, & H. Jüppner (Eds.), *Pediatric Bone: Biology and Diseases* (pp. 541-566). San Diego: Academic Press.

Pfeiffer, S. (1984). Paleopathology in an Iroquoian ossuary, with special reference to tuberculosis. *American Journal of Physical Anthropology*, *65*, 181-189.

Pfeiffer, S. (1991). Rib lesions and new world tuberculosis. *International Journal of Osteoarchaeology*, *1*, 191-198.

Pfeiffer, S., & Crowder, C. (2004). An ill child among Mid-Holocene foragers of southern Africa. *American Journal of Physical Anthropology*, *123*, 23-29.

Pfitzner, M. A., Thacher, T. D., Pettifor, J. M., Zoakah, A. I., Lawson, J. O., Isichei, C. O., & Fischer, P. R. (1998). Absence of vitamin D deficiency in young Nigerian children. *Journal of Pediatrics*, *133*, 740-744.

Phemister, D. B., & Hatcher, C. H. (1933). Correlation of pathological and roentgenological findings in the diagnosis of tuberculous arthritis. *American Journal of Roentgenology*, *29*, 736-752.

Pinhasi, R., Shaw, P., White, B., & Ogden, A. R. (2006). Morbidity, rickets and long-bone growth in post-medieval Britain – a cross-population analysis. *Annals of Human Biology*, *33*, 372-389.

Pitt, M. J. (2002). Rickets and osteomalacia. In D. Resnick (Ed.), *Diagnosis of Bone and Joint Disorders* (4th ed., pp. 1901-1945). Philadelphia: WB Saunders.

Pitts, M., & Griffin, R. (2012). Exploring health and social well-being in late Roman Britain: An intercemetery approach. *American Journal of Archaeology*, *116*, 253-276.

Prentice, A. (2003). Pregnancy and lactation. In F. H. Glorieux, J. M. Pettifor, & H. Jüppner (Eds.), *Pediatric Bone: Biology and Diseases* (pp. 249-269). San Diego: Academic Press.

Prentice, A. (2008). Vitamin D deficiency: A global perspective. *Nutrition Reviews*, *66*, S153-S164.

Priemel, M., von Domarus, C., Klatte, T. O., Kessler, S., Schlie, J., Meier, S., Proksch, N., Pastor, F., Netter, C., Streichert, T., Püschel, K., & Amling, M. (2010). Bone mineralization defects and vitamin D deficiency: Histomorphometric analysis of iliac crest bone biopsies and circulating 25-hydroxyvitamin D in 675 patients. *Journal of Bone and Mineral Research*, *25*, 305-312.

Prokesch, B. C., TeKippe, M., Kim, J., Raj, P., TeKippe, E. M., & Greenberg, D. E. (2016). Primary osteomyelitis caused by hypervirulent *Klebsiella pneumoniae*. *Lancet Infectious Disease*, *16*, e190-195.

Prowse, T. L. (2001). *Isotopic and Dental Evidence for Diet from the Necropolis of Isola Sacra (1st to 3rd centuries AD), Italy* (Unpublished doctoral dissertation). McMaster University, Hamilton, Ontario, Canada.

Prowse, T., Schwarcz, H. P., Saunders, S., Macchiarelli, R., & Bondioli, L. (2004). Isotopic paleodiet studies of skeletons from the Imperial Roman-age cemetery of Isola Sacra, Rome, Italy. *Journal of Archaeological Science*, *31*, 259-272.

Prowse, T. L., Schwarcz, H. P., Saunders, S. R., Macchiarelli, R., & Bondioli, L. (2005). Isotopic evidence for age-related variation in diet from Isola Sacra, Italy. *American Journal of Physical Anthropology*, *128*, 2-13.

Prowse, T. L., Schwarcz, H. P., Garnsey, P., Knyf, M., Macchiarelli, R., & Bondioli, L. (2007). Isotopic evidence for age-related immigration to Imperial Rome. *American Journal of Physical Anthropology*, *132*, 510-519.

Prowse, T. L., Saunders, S. R., Schwarcz, H. P., Garnsey, P., Macchiarelli, R., & Bondioli, L. (2008). Isotopic and dental evidence for infant and young child feeding practices in an Imperial Roman skeletal sample. *American Journal of Physical Anthropology*, *137*, 294-308.

Purdie, D. W., Aaron, J. E., & Selby, P. L. (1988). Bone histology and mineral homeostasis in human pregnancy. *British Journal of Obstetrics and Gynecology*, *95*, 849-854.

Raff, J., Cook, D. C., & Kaestle, F. (2006). Tuberculosis in the New World: A study of ribs from the Schild Mississippian population, West-Central Illinois. *Memórias do Instituto Oswaldo Cruz, Rio de Janeiro*, *101*(SIII), 25-27.

Ragsdale, B. D. (1997). The irrelevance of contemporary orthopedic pathology to specimens from antiquity (concluded). *Paleopathology Newsletter*, *99*, 5-9.

Rajakumar, K. (2003). Vitamin D, cod-liver oil, sunlight, and rickets: A historical perspective. *Pediatrics*, *112*, e132-e135.

Redfern, R., & Roberts, C. (2005). Health in Romano-British urban communities: Reflections from the cemeteries. In D. N. Smith, M. B. Brickley, & W. Smith (Eds.), *Fertile ground: Papers in honour of Susan Limbrey* (pp. 115-129). Oxford: Oxbow books.

Redfern, R. C., & Gowland, R. L. (2011). A bioarchaeological perspective on the pre-adult stages of the life course: Implications for the care and health of children in the Roman Empire. In M. Harlow & L. Larsson Loven (Eds.), *Families in the Roman and Late Antique Roman World* (pp. 111-140). London: Continuum International Publishing Group.

Redfern, R. C., DeWitte, S. N., Pearce, J., Hamlin, C., & Dinwiddy, K. E. (2015). Urban-rural differences in Roman Dorset, England: A bioarchaeological perspective on Roman settlements. *American Journal of Physical Anthropology*, *157*, 107-120.

Reginato, A. J., & Coquia, J. A. (2003). Musculoskeletal manifestations of osteomalacia and rickets. *Best Practice & Research Clinical Rheumatology*, *17*, 1063-1080.

Resnick, D. (2002). Osteomyelitis, septic arthritis, and soft tissue infection: Organisms. In D. Resnick (Ed.), *Diagnosis of Bone and Joint Disorders* (4th ed., pp. 2510-2624). Philadelphia: WB Saunders.

Ritacco, V., Sequeira, M. D., & de Kantor, I. N. (2006). Human tuberculosis caused by *Mycobacterium bovis* in Latin America and the Caribbean. In C. O. Thoen, J. H.

Steele, & M. J. Gilsdorf (Eds.), *Mycobacterium bovis Infection in Animals and Humans* (2nd ed., pp. 13-17). Oxford: Blackwell Publishing.

Roberts, C., Lucy, D., & Manchester, K. (1994). Inflammatory lesions of ribs: An analysis of the Terry Collection. *American Journal of Physical Anthropology*, *95*, 169-182.

Roberts, C. A., Boylston, A., Buckley, L., Chamberlain, A. C., & Murphy, E. M. (1998). Rib lesions and tuberculosis: The paleopathological evidence. *Tubercular Lung Disease*, *79*, 55-60.

Roberts, C. A., & Buikstra, J. E. (2003a). *The Bioarchaeology of Tuberculosis: A Global View on a Reemerging Disease*. Gainesville: University Press of Florida.

Roberts, C. A., & Buikstra, J. E. (2003b). The history of tuberculosis from earliest times to the development of drugs. In P. O. Davies (Ed.), Clinical Tuberculosis (3rd ed., pp. 3-20). London: Arnold.

Roberts, C., & Manchester, K. (2005). *The Archaeology of Disease*. Ithaca: Cornell University Press.

Rohnbogner, A., & Lewis, M. E. (2017). Poundbury Camp in context: A new perspective on the lives of children from urban and rural Roman England. *American Journal of Physical Anthropology*, *162*, 208-228.

Rook, G. A. W., Steele, J., Fraher, L., Barker, S., Karmali, R., O'Riordan, J., & Stanford, J. (1986). Vitamin D_3, gamma interferon, and control of proliferation of *Mycobacterium tuberculosis* by human monocytes. *Immunology*, *57*, 159-163.

Rook, G. A. W., Taverne, J., Leveton, C., & Steele, J. (1987). The role of gamma-interferon, vitamin D_3 metabolites and tumor necrosis factor in the pathogensis of tuberculosis. *Immunology*, *62*, 229-234.

Rook, G. A. W. (1988). The role of vitamin D in tuberculosis. *American Review of Respiratory Disease*, *138*, 768-770.

Rook, G. A. W., & Hernandez-Pando, R. (1996). The pathogenesis of tuberculosis. *Annual Review of Microbiology*, *50*, 259-284.

Rose, J. C. (1985). Cedar Grove burial interpretation. In J. C. Rose (Ed.), *Gone to a Better Land: A Biohistory of a Rural Black Cemetery in the Post-Reconstruction South*. *Arkansas Archeological Survey Research Series No. 25* (pp. 130-145). Fayetteville: Arkansas Archeological Survey.

Rosen, C. J. & Bilezikian, J. P. (2001). Anabolic therapy for osteoporosis. *The Journal of Clinical Endocrinology & Metabolism*, *86*, 957-964.

Ross, A. C., Taylor, C. L., Yaktine, A. L., Del Valle, H. B., Committee to Review Dietary Reference Intakes for Vitamin D and Calcium, & Institute of Medicine. (2011a). *Dietary Reference Intakes for Calcium and Vitamin D*. Washington: The National Academies Press.

Ross, A. C., Manson, J. E., Abrams, S. A., Aloia, J. F., Brannon, P. M., Clinton, S. K., Durazo-Arvizu, R. A., Gallagher, J. C., Gallo, R. L., Jones, G., Kovacs, C. S., Mayne, S. T., Rosen, C. J., & Shapses, S. A. (2011b). The 2011 report on dietary reference intakes for calcium and vitamin D from the Institute of Medicine: What clinicians need to know. *The Journal of Clinical Endocrinology & Metabolism*, *96*, 53-58.

Roth, D. E., Jones, A. B., Prosser, C., Robinson, J. L., & Vohra, S. (2009). Vitamin D status is not associated with the risk of hospitalization for acute bronchiolitis in early childhood. *European Journal of Clinical Nutrition*, *63*, 297-299.

Roth, D. E., Shah, R., Black, R. E., & Baqui, A. H. (2010). Vitamin D status and acute lower respiratory infection in early childhood in Sylhet, Bangladesh. *Acta Paediatrica*, *99*, 389-393.

Rothschild, B. M., & Martin, L. D. (1993). *Paleopathology: Disease in the Fossil Record*. Boca Raton: CRC Press.

Sachan, A., Gupta, R., Das, V., Agarwal, A., Awasthi, P. K., & Bhatia, V. (2005). High prevalence of vitamin D deficiency among pregnant women and their newborns in northern India. *American Journal of Clinical Nutrition*, *81*, 1060-1064.

Salahuddin, N., Ali, F., Hasan, Z., Rao, N., Aqeel, M., & Mahmood, F. (2013). Vitamin D accelerates clinical recovery from tuberculosis: Results of the SUCCINCT study (Supplementary Cholecalciferol in recovery from Tuberculosis). A randomized, placebo-controlled, clinical trial of vitamin D supplementation in patients with pulmonary tuberculosis. *Infectious Diseases*, *13*, 22.

Saller, R. P., & Kertzer, D. I. (1991). Historical and anthropological perspectives on Italian family life. In D. I. Kertzer & R. P. Saller (Eds.), *The Family in Italy from Antiquity to the Present* (pp. 1-19). New Haven: Yale University Press.

Santos, A. L., & Roberts, C. A. (2001). A picture of tuberculosis in young Portuguese people in the early 20th century: A multidisciplinary study of the skeletal and historical evidence. *American Journal of Physical Anthropology*, *115*, 38-49.

Santos, A. L., & Roberts, C. A. (2006). Anatomy of a serial killer: Differential diagnosis of tuberculosis based on rib lesions of adult individuals from the Coimbra Identified Skeletal Collection, Portugal. *American Journal of Physical Anthropology*, *130*, 38-49.

Saul, F. P. (1973). Disease in the Maya area: The pre-Columbian evidence. In T. P. Culbert (Ed.), *The Classic Maya Collapse* (pp. 301-324). Albuquerque: University of New Mexico Press.

Schamall, D., Teschler-Nicola, M., Kainberger, F., Tangl, S. T., Brandstätter, F., Patzak, B., Muhsil, J., & Plenk Jr, H. (2003). Changes in trabecular bone structure in rickets and osteomalacia: The potential of a medico-historical collection. *International Journal of Osteoarchaeology*, *13*, 283-288.

Schattmann, A., Bertrand, B., Vatteoni, S., & Brickley, M. (2016). Approaches to co-occurrence: Scurvy and rickets in infants and young children of 16-18th century Douai, France. *International Journal of Paleopathology*, *12*, 63-75.

Schaefer, M., Black, S., & Scheuer, L. (2008). *Juvenile Osteology: A Laboratory and Field Manual*. Burlington: Academic Press.

Scheidel, W. (2003). Germs for Rome. In C. Edwards C & G. Woolf (Eds.), *Rome the Cosmopolis* (pp. 158-176). Cambridge: Cambridge University Press.

Scheuer, L., & Black, S. (2000). *Developmental Juvenile Osteology*. San Diego: Academic Press.

Schöttker, B., Ball, D., Gellert, C., & Brenner, H. (2013). Serum 25-hydroxyvitamin D levels and overall mortality. A systematic review and meta-analysis of prospective cohort studies. *Ageing Research Reviews*, *12*, 708-718.

Schultz, M. (2012). A short history of paleohistology. In J. E. Buikstra & C. A. Roberts (Eds.), *The Global History of Paleopathology: Pioneers and Prospects* (pp. 738-750). Oxford: Oxford University Press.

Shaw, N. J., & Pal, B. R. (2002). Vitamin D deficiency in UK Asian families: Activating a new concern. *Archives of Disease in Childhood*, *86*, 147-149.

Sita-Lumsden, A., Lapthorn, G., Swaminathan, R., & Milburn, H. J. (2007). Reactivation of tuberculosis and vitamin D deficiency: The contribution of diet and exposure to sunlight. *Thorax*, *62*, 1003-1007.

Sledzik, P. S., & Bellantoni, N. (1994). Bioarchaeological and biocultural evidence for the New England vampire folk belief. *American Journal of Physical Anthropology*, *94*, 269-274.

Snoddy, A. M. E., Buckley, H. R., & Halcrow, S. E. (2016). More than metabolic: Considering the broader paleoepidemiological impact of vitamin D deficiency in bioarchaeology. *American Journal of Physical Anthropology*, *160*, 183-196.

Spasovski, G. B., Bervoets, A. R. J., Behets, G. J. S., Ivanovski, N., Sikole, A., Dams, G., Couttenye, M.-M., De Broe, M. E., & D'Haese, P. C. (2003). Spectrum of renal bone disease in end-stage renal failure patients not yet on dialysis. *Nephrology Dialysis Transplantation*, *18*, 1159-1166.

Specker, B. L. (1994). Do North American women need supplemental vitamin D during pregnancy or lactation? *American Journal of Clinical Nutrition*, *59*, 484S-491S.

Sperduti, A. (1995). *I resti scheletrici umani della necropolis di età Romano-Imperiale di Isola Sacra (I-II sec. d.C.)* (Unpublished doctoral dissertation). Department of Animal and Human Biology, Universita 'La Sapienza', Rome.

Spiro, A., & Buttriss, J. L. (2014). Vitamin D: An overview of vitamin D status and intake in Europe. *Nutrition Bulletin*, *39*, 322-350.

Springett, V. H. (1971). Ten-year results during the introduction of chemotherapy for tuberculosis. *Tubercle*, *52*, 73-87.

St-Arnaud, R., & Demay, M. B. (2003). Vitamin D biology. In F. H. Glorieux, J. M. Pettifor, & H. Jüppner (Eds.), *Pediatric Bone: Biology and Diseases* (pp. 193-216). San Diego: Academic Press.

Starke, J. R. (2003). Pediatric tuberculosis: Time for a new approach. *Tuberculosis*, *83*, 208-212.

Stead, W. W. (2001). Variation in vulnerability to tuberculosis in America today: Random, or legacies of different ancestral epidemics? *International Journal of Tubercular Lung Disease*, *9*, 807-814.

Stern, P. H. (2005). Bone. In D. Feldman, J. W. Pike, & F. H. Glorieux (Eds.), *Vitamin D* (2nd ed., pp. 565-573). San Diego: Elsevier Academic Press.

Steyn, M., Scholtz, Y., Botha, D., & Pretorius, S. (2013). The changing face of tuberculosis: Trends in tuberculosis-associated skeletal changes. *Tuberculosis*, *93*, 467-474.

Stirland, A., & Waldron, T. (1990). The earliest cases of tuberculosis in Britain. *Journal of Archaeological Science*, *17*, 221-230.

Stirland, A. J. (2000). *Raising the Dead: The Skeleton Crew of King Henry VIII's Great Ship, the Mary Rose*. Chichester: John Wiley & Sons.

Stone, A. C., Wilbur, A. K., Buikstra, J. E., & Roberts, C. A. (2009). Tuberculosis and leprosy in perspective. *Yearbook of Physical Anthropology*, *52*, 66-94.

Stuart-Macadam, P. L. (1989). Nutritional deficiency diseases: A survey of scurvy, rickets, and iron-deficiency anemia. In M. Y. Iscan & K. A. R. Kennedy (Eds.), *Reconstruction of Life from the Skeleton* (pp. 201-222). New York: Alan R. Liss, Inc.

Suzuki, T., & Inoue, T. (2007). Earliest evidence of spinal tuberculosis from the Aneolithic Yayoi period in Japan. *International Journal of Osteoarchaeology*, *17*, 392-402.

Talat, N., Perry, S., Parsonnet, J., Dawood, G., & Hussain, R. (2010). Vitamin D deficiency and tuberculosis progression. *Emerging Infectious Diseases*, *16*, 853-855.

Temkin, O. (Trans.). (1956). *Soranus' Gynecology*. Baltimore: The Johns Hopkins Press.

Thandrayen, K., & Pettifor, J. M. (2010). Maternal vitamin D status: Implications for the development of infantile nutritional rickets. *Endocrinology and Metabolism Clinics of North America*, *39*, 303-320.

Tisdall, F. F. (1921). The etiology of rickets. *The Canadian Medical Association Journal*, *11*, 934-943.

Todd, M. (1970). The small towns of Roman Britain. *Britannia*, *1*, 114-130.

Trinkaus, E., Churchill, S. E., Villemeur, I., Riley, K. G., Heller, J. A., & Ruff, C. B. (1991). Robusticity *versus* shape: The functional interpretation of Neandertal appendicular morphology. *Journal of the Anthropological Society of Nippon*, *99*, 257-278.

Trollope, E. (1870). Ancaster, the Roman Causennae. *The Archaeological Journal*, *27*, 1-15.

Tuli, S. M. (1995). Severe kyphotic deformity in tuberculosis of the spine. *International Orthopaedics*, *19*, 327-331.

Tylavsky, F. A., Ryder, K. A., Lyytikäinen, A., & Cheng, S. (2005). Vitamin D, parathyroid hormone, and bone mass in adolescents. *Journal of Nutrition*, *135*, 2735S-2738S.

Ubelaker, D. H. (1982). The development of American paleopathology. In F. Spencer (Ed.), *A History of American Physical Anthropology 1930-1980* (pp. 337-356). New York NY: Academic Press.

Ubelaker, D. H., Jones, E. B., Donoghue, H. D., & Spigelman, M. (2000). Skeletal and molecular evidence for tuberculosis in a forensic case. *Anthropologie*, *38*, 193-200.

Ustianowski, A., Shaffer, R., Collin, S., Wilkinson, R. J., & Davidson, R. N. (2005). Prevalence and associations of vitamin D deficiency in foreign-born persons with tuberculosis in London. *Journal of Infection*, *50*, 432-437.

Van Sleuwen, B. E., Engelberts, A. C., Boere-Boonekamp, M. M., Kuis, W., Schulpen, T. W. J., & L'Hoir, M. P. (2007). Swaddling: A systematic review. *Pediatrics*, *120*, e1097-e1106.

Veselka, B., Hoogland, M. L. P., & Waters-Rist, A. L. (2015). Rural rickets: Vitamin D deficiency in a post-Medieval farming community from the Netherlands. *International Journal of Osteoarchaeology*, *25*, 665-675.

Vijaya Bhanu, N., van Soolingen, D., van Embden, J. D. A., & Seth, P. (2004). Two *Mycobacterium fortuitum* strains isolated from pulmonary tuberculosis patients in Delhi harbor IS*6110* homologue. *Diagnostic Microbiology and Infectious Disease*, *48*, 107-110.

Wakely, J., Manchester, K., & Roberts, C. (1991). Scanning electron microscopy of rib lesions. *International Journal of Osteoarchaeology*, *1*, 185-189.

Waldron, T. (2009). *Palaeopathology*. New York NY: Cambridge University Press.

Walls, T., & Shingadia, D. (2004). Global epidemiology of paediatric tuberculosis. *Journal of Infection*, *48*, 13-22.

Watanabe, D., Hotta, M., & Ichihara, A. (2015). Osteomalacia, severe thoracic deformities and respiratory failure in a young woman with anorexia nervosa. *Internal Medicine*, *54*, 929-934.

Waterlow, J. C. (1989). Diet of the classical period of Greece and Rome. *European Journal of Clinical Nutrition*, *43*, 3-12.

Wayse, V., Yousafzai, A., Mogale, K., & Filteau, S. (2003). Association of subclinical vitamin D deficiency with severe acute lower respiratory infection in Indian children under 5 years. *European Journal of Clinical Nutrition*, *58*, 563-567.

Webb, G. B. (1936). *Tuberculosis*. New York: Paul B. Hoeber Inc.

Webb, J. G., Thomas, P. (1986). Hypertrophic osteoarthropathy and pulmonary tuberculosis. *Tubercle*, *67*, 225-228.

Wejse, C., Gomes, V. F., Rabna, P., Gustafson, P., Aaby, P., Lisse, I. M., Andersen, P. L., Glerup, H., & Sodemann, M. (2009). Vitamin D as supplementary treatment for tuberculosis: A double-blind, randomized, placebo-controlled trial. *American Journal of Respiratory and Critical Care Medicine*, *179*, 843-850.

Weston, D. A. (2012). Nonspecific infection in paleopathology: Interpreting periosteal reactions. In A. L. Grauer (Ed.), *A Companion to Paleopathology* (pp. 492-512). Oxford: Wiley-Blackwell.

White, J. H. (2008). Vitamin D signaling, infectious diseases, and regulation of innate immunity. *Infection and Immunity*, *76*, 3837-3843.

Wilbur, A. K., Farnback, A. W., Knudson, K. J, & Buikstra, J. E. (2008). Diet, tuberculosis, and the paleopathological record. *Current Anthropology*, *49*, 963-991.

Wilkinson, R. J., Llewelyn, M., Toossi, Z., Patel, P., Pasvol, G., Laivani, A., Wright, D., Latif, M., & Davidson, R. N. (2000). Influence of vitamin D deficiency and vitamin D receptor polymorphisms on tuberculosis among Gujarati Asians in west London: A case-control study. *Lancet*, *355*, 618-621.

Williams, B., Williams, A. J., & Anderson, S. T. (2008). Vitamin D deficiency and insufficiency in children with tuberculosis. *The Pediatric Infectious Disease Journal*, *27*, 941-942.

Wilson, D. R. (No Date). Unfinished report. *Ancaster Excavations* (Vol. 2). Historic Buildings and Monuments Commission for England.

Wilson, D. R. (1968). An early Christian cemetery at Ancaster. In M. W. Barley & R. P. C. Hanson (Eds.), *Christianity in Britain, 300-700* (pp. 197-199). Leicester: Leicester University Press.

Wilson, D. R. (2006). *Ancaster Roman Cemetery: Post-Excavation Progress Report*. Historic Buildings and Monuments Commission for England.

Wilson, J. J. (2014). Paradox and promise: Research on the role of recent advances in paleodemography and paleoepidemiology to the study of "health" in Precolumbian societies. *American Journal of Physical Anthropology*, *155*, 268-290.

Wiltschke-Schrotta, K., & Berner, M. (1999). Distribution of tuberculosis in the skeletal material of Eastern Austrian sites. In G. Y. Pálfi, O. Dutour, J. Deák, & I. Hutás (Eds.). *Tuberculosis: Past and Present* (pp. 543-548). Budapest-Szeged: Golden Book – TB Foundation.

Wood, C. (2003). *An Investigation of the Prevalence of Rickets Among Subadults from the Roman Necropolis of Isola Sacra, Italy* (Unpublished master's thesis). McMaster University, Hamilton, ON, Canada.

Wood, J. W., Milner, G. R., Harpending, H. C., Weiss, K. M., Cohen, M. N., Eisenberg, L. E., Hutchinson, D. L., Jankauskas, R., Cesnys, G., Katzenberg, M. A., Lukacs, J. R., McGrath, J. W., Roth, E. A., Ubelaker, D. H., & Wilkinson, R. G. (1992). The osteological paradox: Problems of inferring prehistoric health from skeletal samples. *Current Anthropology*, *33*, 343-370.

Wright, L. E., & Chew, F. (1998). Porotic hyperostosis and paleoepidemiology: A forensic perspective on anemia among the ancient Maya. *American Anthropologist*, *100*, 924-939.

Yetley, E. A., Brulé, D., Cheney, M. C., Davis, C. D., Esslinger, K. A., Fishcer, P. W. F., Friedl, K. E., Greene-Finestone, L. S., Guenther, P. M., Klurfeld, D. M., L'Abbe, M. R., McMurry, K. Y., Starke-Reed, P. E., & Trumbo, P. R. (2009). Dietary reference intakes for vitamin D: Justification for a review of the 1997 values. *American Journal of Clinical Nutrition*, *89*, 719-727.

Yurdakok, K., Yavuz, T., & Taylor, C. E. (1990). Swaddling and acute respiratory infections. *American Journal of Public Health*, *80*, 873-875.

APPENDIX A – Recording Forms for Skeletal Data Collection

A.1. Recording form: Age and sex

Sex/Age Estimation Date: _____ Site _____

Observer: _____ Sk # _____

Age Estimation – Juvenile

Dental Development (following Gustafson and Koch 1974)

Deciduous Dentition

Maxilla					Mandible				
	Left	Right	Unsided 1	Unsided 2		Left	Right	Unsided 1	Unsided 2
m^2					m_2				
m^1					m_1				
c					c				
i^2					i_2				
i^1					i_1				

Permanent Dentition

Maxilla					Mandible				
	Left	Right	Unsided 1	Unsided 2		Left	Right	Unsided 1	Unsided 2
M^2					M^2				
M^1					M^1				
PM^2					PM^2				
PM^1					PM^1				
C					C				
I^2					I^2				
I^1					I^1				

Scoring: - = could not be assessed; 1 = start of mineralization; 1.5 = past start of mineralization, but not yet at complete crown; 2 = complete crown; 2.5 = crown complete, but not certain if eruption has occurred; 3 = eruption in progress; 3.5 eruption complete (teeth are in occlusion), but not certain if root is fully formed; 4 = eruption and root complete

Long Bone Length
(in mm)

	Left	Right
Femur		
Tibia		
Fibula		
Humerus		
Radius		
Ulna		

Notes:

Epiphyseal Fusion (following Cardoso 2008 a, b) - Fusion should be scored on **left** bone only. If left is not present right should be scored.

Femur: 1 - proximal epiphysis; 2 – greater trochanter; 3 – lesser trochanter; 4 – distal epiphysis
Tibia: 1 – proximal epiphysis; 2 – distal epiphysis
Humerus: 1 – proximal epiphysis; 2 – distal epiphysis; 3 – medial epicondyle
Radius: 1 – proximal epiphysis; 2 – distal epiphysis
Pelvis: 1 – iliac crest; 2 – ischial epiphysis
Clavicle: 1 – sternal epiphysis

	Side	Epiphysis 1	Epiphysis 2	Epiphysis 3	Epiphysis 4
Femur					
Tibia					
Humerus					
Radius					
Pelvis					
Clavicle					
Other					

Scoring: - = could not be assessed; 1 = non-union (epiphysis and diaphysis are completely separate); 2 = partial union; 3 – complete union (all visible aspects of epiphysis are united)

Sex/Age Estimation Date: _____ Site_____

Observer:_____ Sk #_____

Summary Information – Juvenile Age

Dental Dev. Age Estimate	Long Bone Length Age Estimate	Epiphyseal Fusion Age Estimate	Dental Wear Age Estimate (if applicable)
Notes:			

Dental Wear (modified from Brothwell 1965) – for older adolescents and adults (M1 must be erupted and in occlusion)

Maxilla		
	Left	**Right**
M3		
M2		
M1		

Mandible		
	Left	**Right**
M3		
M2		
M1		

Modified scoring: - = could not be assessed; score - 1-13 (refer to diagram)

Notes:

Sex/Age Estimation Date: _____ Site_____

Observer:_____ Sk #_____

Sex Estimation – Adult

Will not be attempted for those <16 years old. For those 16+ years the features of the skull/mandible and pelvis set out in Buikstra and Ubelaker (1994) will be used.

Pelvis		
	Left	Right
Ventral Arc (1-3) *		
Subpubic Concavity (1-3) *		
Ischiopubic Ramus Ridge (1-3) *		
Greater Sciatic Notch (1-5) *		
Preauricular Sulcus (1-4) *		
Estimated Sex		

Skull		
	Left	Right
Nuchal Crest (1-5) *		
Mastoid Process (1-5) *		
Supraorbital Margin (1-5) *		
Glabella (1-5) *		
Mental Eminence (1-5) *		
Estimated Sex		

Notes:

In all cases (skull and pelvis) the left should be preferentially scored. When the left side is absent, the right can be scored.
*** after observations described in Buikstra & Ubelaker 1994 (pp. 16-21):**
0-3 scale: - (blank) = not observable; 1 = female; 2 = ambiguous; 3 = male
0-4 scale: - (blank) = no sulcus; 1 = sulcus is wide (>0.5cm) and deep; 2 = sulcus is wide but shallow; 3 = sulcus is well defined but narrow; 4 = sulcus is a narrow (<0.5cm), shallow, and smooth-walled depression.
0-5 scale: - (blank) = not observable; 1 = female; 2 = probable female; 3 = ambiguous; 4 = probable male; 5 = male

Age Estimation - Adult

Pubic Symphysis Scoring System (following Brooks and Suchey 1990; Suchey and Katz 1986)

	Left	Right
Phase		

Notes:

Scoring: - = could not be assessed; phases 1-6 (see Buikstra and Ubelaker, 1994: 23-24)

Sex/Age Estimation Date: _____ Site_____

Observer:_____ Sk #_____

Auricular Surface Scoring System – Transition Analysis (following Boldsen et al. 2002: 101-103) (can record multiple stages for a single feature)[1]

	Left		Right	
	Min	Max	Min	Max
Superior Topography (1-3)				
Inferior Topography (1-3)				
Superior Characteristics (1-5)				
Apical Characteristics (1-5)				
Inferior Characteristics (1-5)				
Inferior Texture (1-3)				
Superior* Exostoses (1-6)				
Inferior* Exostoses (1-6)				
Posterior Exostoses (1-3)				

Notes:

[1]Record the left auricular surface. When the left is absent, the right can be recorded but do not mix the two sides.
Scoring: - = could not be assessed; see Boldsen et al. 2002
* Superior and Inferior Posterior Iliac Crest

Summary Information – Adult Age and Sex

Age[1]	
Sex[2]	

[1]Young adult (20-34), middle adult (35-49), old adult (50+)
[2]After Buikstra and Ubelaker (1994: 21): undetermined; female; probable female; ambiguous; probable male; male

A.2. Recording form: Juvenile vitamin D deficiency

Date: _____ Site _____

Observer: _____ Sk # _____

Juvenile Pathology Form

Cranium

	Left			Right		
	Present/ Absent	Abnormal Porosity	Abnormal Shape	Present/ Absent	Abnormal Porosity	Abnormal Shape
Frontal						
Orbital roof						
Parietal						
Temporal						
Maxilla						
Mandibular ramus						
Other						

	Unsided			Photo
Occipital				

Notes:

Scoring: - = feature not observable; 0 = feature absent; 1 = feature present

Ribs

	# Left (1-12)	# Right (1-12)	# Unsided (1-24)	Abnormal Porosity[1]	Flaring[1]	Fractures[2]	Cupping[3]
Proximal Ends							
Costochondral Ends							
Abnormal rib curvature*							

Notes:

* can only be assessed on complete ribs

[1] - Only assessed at costochondral ends.

[2] – If fracture is located somewhere other than costochondral end, indicate location and side (if possible in notes section.

[3] – indicates the total number of ribs exhibiting cupping

Scoring: - = not observable; indicate number of ribs with pathology

Photo

Date: _____ Site_____

Observer:_____ Sk #_____

Long Bones – Presence[1]

Element	LEFT					RIGHT				
	Prox epip	Prox 1/3	Mid 1/3	Distal 1/3	Distal epip	Prox epip	Prox 1/3	Mid 1/3	Distal 1/3	Distal epip
Clavicle										
Humerus										
Radius										
Ulna										
Femur										
Tibia										
Fibula										

* segment preservation: - = not present; <25%; 25-50%; 50-75% >75%

Long Bones – Pathology

	Abnormal Growth Plate	Thickening	Abnormal Shaft Shape	Abnormal Metaphysis Shape	Other (features such as fracture)*
LEFT Side					
Clavicle					
Humerus					
Radius					
Ulna					
Femur					
Tibia					
Fibula					
Notes:					

*Provide details about 'other' pathological features in the notes box.

** Indicate which bones/elements photographed in notes box.

[1] n/a is to be used when the growth plate is fused. Only the distal growth plate is scored. Scoring adopted from Mays et al. 2006.

Photo**

Date: _____ Site_____

Observer:_____ Sk #_____

Long Bones (continued)

	Abnormal Growth Plate[1]	Thickening	Abnormal Shaft Shape	Abnormal Metaphysis Shape	Other (features such as fracture)*
RIGHT Side					
Clavicle					
Humerus					
Radius					
Ulna					
Femur					
Tibia					
Fibula					
Notes:					

*Provide details about 'other' pathological features in the notes box.
** Indicate which bones/elements photographed in notes box.
[1] n/a is to be used when the growth plate is fused. Only the distal growth plate is scored. Scoring adopted from Mays et al. 2006.

Photo**

Ilium (following Ortner and Brown 2011)

	Presence (%)	Abnormal Shape
Right ilium		
Left ilium		

Notes:

Photo

- = not present; <25%; 25-50%; 50-75% >75%

Sacrum (only record if sufficiently complete to assess normal curvature)

	Presence (%)	Abnormal Shape
Sacrum		

Notes:

Photo

X-rays required (y/n) (indicate in notes which bones/elements to be radiographed)	
X-rays completed (y/n)	

Summary

Possible Vitamin D deficiency present?	

A.3. Recording form: Adult vitamin D deficiency

Date: _____ Site_____

Observer:_____ Sk #_____

Adult Pathology

Ribs

	Left	Right	Unsided
Number of ribs (count using proximal ends)			
Presence of abnormal curvature*			
Number of ribs with single fracture			
Number of ribs with multiple fractures			
Total number of fractures			
Notes (e.g., indicate any flaring of ribs):			

* can only be assessed on complete ribs; if present - describe curvature in notes section

Ribs – record state of fracture(s) for each rib with one or more fractures

		Fracture 1			Fracture 2			Fracture 3	
Rib*	Side	New Bone	Fracture Union	Location	New Bone	Fracture Union	Location New Bone	Fracture Union	Location
1									
2									
3									
4									
5									
6									
7									
8									
9									
10									
Notes:									

Photo ☐

*indicate approximate location in rib cage (1st, 2nd, upper, middle, lower, 12th) and the location on the rib itself (e.g., head, angle, shaft).

Sternum

	Presence (%)	Abnormal Curvature
Manubrium		
Sternal body		
Notes:		

Photo ☐

- = not present; <25%; 25-50%; 50-75%; >75%

Date: _____ Site_____

Observer: Sk #

Scapulae

	Left	Right
Presence (%)		
Can curvature of body be assessed? (y/n)		
Was curvature present? (y/n)		
Spinous process present		
Fracture (present/absent)		
State of fracture (woven/lamellar/spiculated)		
Coracoid process present		
Fracture (present/absent/pseudofracture)		
State of fracture (woven/lamellar/spiculated)		
Lateral border present (%)		
Fracture (present/absent/pseudofracture)		
State of fracture (woven/lamellar/spiculated)		
Fracture at alternate location*		
Bone formation at alternate location*		

Notes:	Photo ☐

*indicate specific location in notes box

Vertebrae

	Body	Arches
Presence		
Cervical vertebrae (7)		
Thoracic vertebrae (12)		
Lumbar vertebrae (5)		

Pathology	**Collapse/buckling of vertebral body**	**Fractures of laminae**
Cervical vertebrae		
Thoracic vertebrae		
Lumbar vertebrae		

	Present/Absent
Kyphosis (posterior thoracic curvature)	
Lordosis (anterior lumbar curvature)	
Scoliosis (lateral curvature)	

Notes:	Photo ☐

Date: _____ Site _____

Observer: _____ Sk # _____

Innominates

	Presence	Folding	Fracture	Other*
LEFT				
Innominate (% present)				
Iliac crest				
Ascending pubic ramus				
Pubis				

	Presence	Folding	Fracture	Other*
RIGHT				
Innominate (% present)				
Iliac crest				
Ascending pubic ramus				
Pubis				

Photo ☐

Notes**:

*If yes, describe pathology in notes section

**'Other' features to consider include: cortical thinning; decreasing antero-posterior length of the ilium, among other features.

Sacrum (keeping in mind the normal variation in curvature between the male and female sacrum)

Presence (%)	Can curvature of body be assessed? (y/n)	Abnormal Curvature

Notes:

Photo ☐

Long Bones - Presence

Element	LEFT					RIGHT				
	Prox epip	Prox 1/3	Mid 1/3	Distal 1/3	Distal epip	Prox epip	Prox 1/3	Mid 1/3	Distal 1/3	Distal epip
Clavicle										
Humerus										
Radius										
Ulna										
Femur										
Tibia										
Fibula										

* segment preservation : - = not present; <25%; 25-50%; 50-75%; >75%

Date: _____ Site _____

Observer: _____ Sk # _____

Long Bones – Pathology

	Fracture	State of Fracture		Location	Bending Deformity	Other Feature*
LEFT Side		New Bone	Fracture Union			
Clavicle						
Humerus						
Radius						
Ulna						
Femur						
Tibia						
Fibula						

Photo** ☐

Notes:

	Fracture	State of Fracture		Location	Bending Deformity	Other Feature*
RIGHT Side		New Bone	Fracture Union			
Clavicle						
Humerus						
Radius						
Ulna						
Femur						
Tibia						
Fibula						

Photo ☐

Notes:

*Provide details about 'other' pathological features in the notes box.
** Indicate which bones/elements photographed in notes box.

Additional Notes:
X-rays required (y/n) (indicate in 'additional notes' which bones/elements to be radiographed)
X-rays completed (y/n)

Summary

Possible Vitamin D deficiency present?	

A.4. Recording form: Juvenile chronic respiratory infections

Date: _____ Site _____

Sk # _____

Juvenile Pathology

Ribs

	Left	Right	Unsided
Number of ribs with new bone formation			
Number of ribs with porosity			
Notes (describe lesions):			

Ribs – Information about new bone formation

		New Bone Formation		
Rib*	**Side**	State of Healing	Anteroposterior Location	Location
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
Notes:				

Photo ☐

Vertebrae

	Body	Arches
Presence		
Cervical vertebrae (7)		
Thoracic vertebrae (12)		
Lumbar vertebrae (5)		

Pathology	Lytic Lesions	New Bone Formation
Cervical vertebrae		
Thoracic vertebrae		
Lumbar vertebrae		

Date: _____ Site_____

_____ Sk #_____

	Present/Absent
Kyphosis (posterior thoracic curvature)	
Collapse of Bodies	
Ankylosis/Fusion	

Notes:	Photo ☐

Innominates

	Presence		Lytic Lesions	New Bone Formation	Fusion
	Ischium	Pubis			
Left					
Right					

Notes*:

*If yes to any lesions, describe pathology in notes section; Note absence of acetabulum, as this is the most important area to consider

Long Bones

	Lytic Lesions		New Bone Formation			Ankylosis or Fusion		Other Feature
LEFT	P/A	Location	P/A	Location	State of Healing	P/A	Location	
Humerus								
Radius								
Ulna								
Femur								
Tibia								
Fibula								

Photo** ☐

Notes:

Date: _____ Site_____

Sk #_____

	Lytic Lesions		New Bone Formation			Ankylosis or Fusion		Other Feature	
RIGHT	P/A	Location	P/A	Location	State of Healing	P/A	Location		
Humerus									
Radius									Photo ☐
Ulna									
Femur									
Tibia									
Fibula									

Notes:

*Provide details about 'other' pathological features in the notes box.
** Indicate which bones/elements photographed in notes box.

Additional Notes:

Summary

Possible respiratory infection present?	

A.5. Recording form: Adult chronic respiratory infections

Date: _____ Site_____

Sk #_____

Adult Pathology

Ribs

	Left	Right	Unsided
Number of ribs with new bone formation			
Number of ribs with porosity			
Notes (describe lesions):			

Ribs – Information about new bone formation

		New Bone Formation		
Rib*	**Side**	State of Healing	Anteroposterior Location	Location
1				
2				
3				
4				
5				
6				
7				
8				
9				
10				
Notes:				

Photo ☐

Vertebrae

Pathology	**Lytic Lesions**	**New Bone Formation**
Cervical vertebrae		
Thoracic vertebrae		
Lumbar vertebrae		

	Present/Absent
Kyphosis	
Collapse of Bodies	
Ankylosis/Fusion	

Date: _____ Site_____

Sk #_____

Notes:	Photo ☐

Innominates

	Lytic Lesions	New Bone Formation	Fusion
Left			
Right			

Notes*:

*If yes to any, describe pathology in notes section; Note absence of acetabulum as this is the most important area to consider

Long Bones

	Lytic Lesions		New Bone Formation			Ankylosis or Fusion		Other Feature
LEFT	P/A	Location	P/A	Location	State of Healing	P/A	Location	
Humerus								
Radius								
Ulna								
Femur								
Tibia								
Fibula								

Photo ☐

Notes:

Date: _____ Site_____

Sk #_____

	Lytic Lesions		New Bone Formation			Ankylosis or Fusion		Other Feature
RIGHT	P/A	Location	P/A	Location	State of Healing	P/A	Location	
Humerus								
Radius								
Ulna								
Femur								
Tibia								
Fibula								

Photo ☐

Notes:

*Provide details about 'other' pathological features in the notes box.
** Indicate which bones/elements photographed in notes box.

Additional Notes:

Summary

Possible respiratory infection present?	

APPENDIX B - Modified scale for evaluation of dental wear

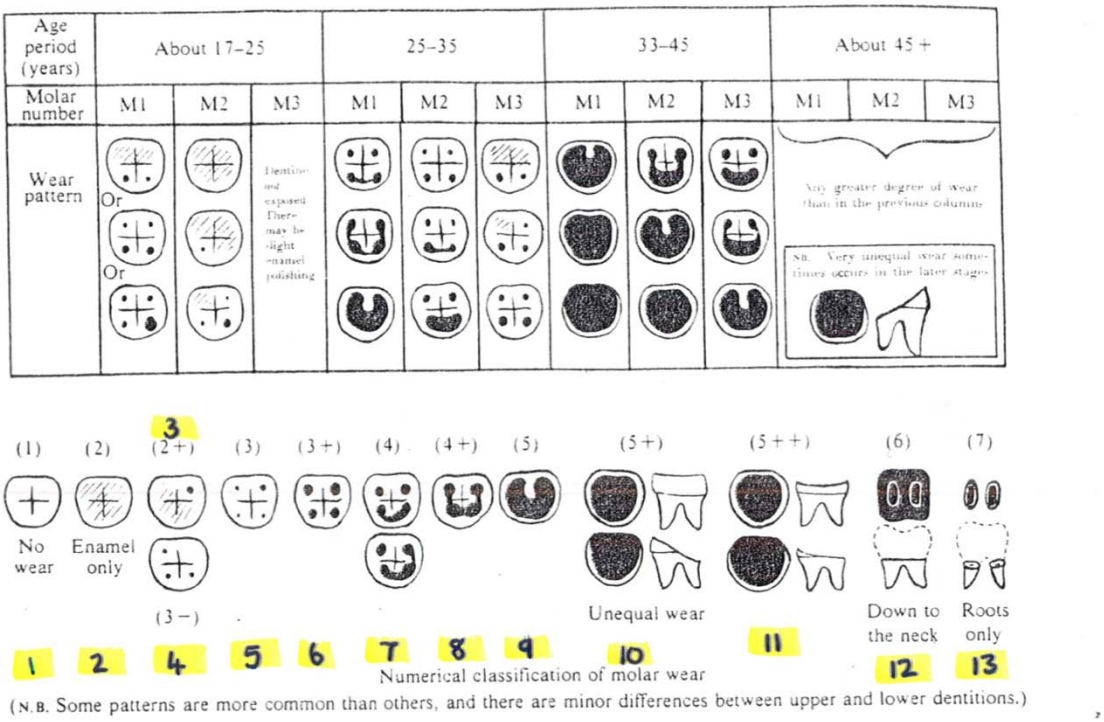


Figure 3.9 A tentative classification of age in Neolithic to Medieval British skulls, based on molar wear.

Stages for recording dental wear for age estimation (highlighted in yellow), modified from Brothwell (1965).

APPENDIX C – Raw Vitamin D Deficiency Data

Table C.1. Features of vitamin D deficiency scored for Isola Sacra juveniles

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 1	YC	1.5-2	A	A	A	A	A	A	A	**P**	A	A	A	A	A	A	A	A	-	**2**
SCR 2	OC	7-9	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 3	I	9-12 M	A	A	A	A	A	A	A	**P**	A	A	**P**	A	A	A	**P**	A	A	**2**
SCR 4	I/YC	UD	-	-	-	-	-	-	-	A	-	-	A	-	-	-	-	A	-	5
SCR 6	MC	4.5-6	**P**	**P**	A	A	**P**	**P**	A	A	A	A	A	A	A	A	A	A	-	**3**
SCR 7	MC	6-8	A	A	A	-	A	A	A	A	A	A	A	A	A	A	**P?**	A	-	4
SCR 8	I/YC	0.5-1.5	A	A	A	-	-	-	-	A	A	A	A	A	A	A	-	A	-	4
SCR 9	OC	8.5-10	-	-	-	-	**P?**	**P**	A	A	A	A	A	A	A	A	A	A	-	**3**
SCR 10	Mc	3-5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 11	YC	1-1.5	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
SCR 12	I	6-8 M	A	-	-	-	-	-	A	A	A	A	A	A	A	A	-	A	-	4
SCR 13	YC	1.5-2	A	-	-	-	-	-	A	-	A	A	A	A	-	-	-	A	-	5
SCR 14	MC	2.5-4.5	A	A	A	A	A	A	-	A	A	A	A	A	A	A	-	A	-	4
SCR 22	I	4-6.5 M	A	**P**	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	**2**
SCR 23	MC	4-5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 24	OC	10-12	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 25	MC	5-7	A	-	A	-	-	-	-	A	A	A	A	A	A	A	-	A	-	4
SCR 26	YC	1.5-2.5	A	A	-	-	A	A	-	-	A	A	A	A	-	-	-	A	-	5
SCR 29	YAL	15-16	-	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 31	MC	5-6.5	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 33	YC	1.25-1.75	A	A	-	-	A	A	-	A	-	A	A	A	-	-	-	A	**P**	**2**

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 40	MC	5-7	A	A	A	-	-	-	-	A	A	-	A	-	-	-	-	A	-	5
SCR 41	I/YC	UD	A	-	A	-	-	-	-	A	A	-	A	-	-	-	-	A	-	5
SCR 42	YC	2.5-3	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 43	MC	4-5	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 45	I	9-12 M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 46	I	7-9 M	A	A	-	-	-	-	-	**P**	A	-	A	-	-	-	-	A	A	**3**
SCR 47	I	5-9 M	A	A	-	A	A	A	A	A	A	A	A	A	-	-	A	A	-	4
SCR 48	I	5-7 M	**P**	A	-	-	-	-	-	-	A	A	A	A	-	-	-	A	A	5
SCR 49	MC	6-7	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 50	YAL	14-15	A	-	-	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 51	MC	6-7.5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 54	YC	1-1.5	A	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 56	YC	1.5-2	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
SCR 58	YAL	14-16	A	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	4
SCR 61	YC	2-3	A	A	A	-	A	A	-	A	A	A	A	A	-	-	-	A	-	4
SCR 62	I	5-7 M	**P**	A	A	A	A	A	A	**P**	A	A	A	A	A	A	A	A	A	**1**
SCR 63	YC	1.5-2.5	A	-	A	A	A	A	-	A	A	-	A	-	-	-	-	A	-	5
SCR 65	YC	1.5-2	A	-	-	-	A	A	-	A	A	A	A	A	-	-	-	A	-	4
SCR 66	MC	2.5-4	A	A	A	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 71	MC	UD	-	-	-	-	-	-	-	A	-	-	A	-	-	-	-	A	-	5
SCR 72	OC	8-10	A	A	-	-	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 74	I	2-6 M	A	-	-	-	-	-	-	A	A	-	A	-	-	-	-	A	-	5
SCR 80	YAL	13-17	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 81	MC	2.5-4	A	**P**	A	-	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 91	I	0-1	A	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 92	I	0-0.125	**P**	A	-	-	-	**P?**	A	**P**	A	A	A	A	A	A	**P**	A	-	**2**
SCR 93	MC	4.5-5	A	A	-	-	-	-	A	A	A	A	A	A	A	A	-	A	-	4
SCR 94	MC	4.5-5	**P**	**P**	-	-	-	-	-	A	A	A	A	A	A	A	-	A	-	4
SCR 95	MC	4-5	A	A	A	-	A	A	A	A	A	A	A	A	-	-	A	A	-	4
SCR 96	MC	4-5	A	-	A	-	-	-	-	A	A	A	A	A	A	A	-	A	-	4
SCR 100	YAL	14-16	**P**	**P**	-	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 101	YC	1.5-2.5	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 102	YC	1.25-1.75	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 103	OC	10-11	A	**P**	A	-	A	A	A	**P**	A	A	**P**	A	A	A	A	A	-	**2**
SCR 104	MC	6-8	A	-	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 107	I/YC	UD	A	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 108	YC	1-1.5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 109	I	0.5-1	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 110	YC	2-3	A	A	A	A	A	**P**	A	**P**	**A**	A	A	**P**	A	A	**P**	A	A	**1**
SCR 111	MC	7-8	A	A	A	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 112	OC	9-11	A	A	A	A	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 114	OC	8-9	A	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 115	MC	6-8	A	A	-	-	A	A	A	A	A	A	A	A	-	-	A	A	-	4
SCR 117	OC	</= 16	A	-	-	-	-	-	-	A	A	-	A	-	-	-	-	A	-	5
SCR 119	I/YC	</= 16	A	-	-	-	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 121	YAL	15-16	A	-	A	-	-	-	-	A	A	A	A	A	A	A	-	A	-	4
SCR 124	OC	</= 16	-	-	-	A	A	A	-	A	A	A	A	A	-	-	A	A	-	4
SCR 131	MC	3-4	A	-	-	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 135	YC	1-1.5	A	A	A	-	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 136	I/YC	0.75-1.25	**P**	**P**	A	-	-	-	-	-	A	A	A	**P?**	-	-	-	A	-	**3**

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 137	YC	1-2	A	A	A	A	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 139	YC	1-1.5	A	A	A	A	A	A	A	**P**	A	A	A	A	A	A	A	A	-	**3**
SCR 140	I	0.5-1	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 141	YC	1.5-2	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 146	YAL	10-14	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 147	OC	8-9	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 149	YAL	16-17.5	A	A	A	-	**P?**	A	-	A	A	A	A	A	A	A	A	A	A	4
SCR 153	YC	1.5-2.5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 154	YC	1-1.75	A	-	-	-	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 162	MC	3-5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 164	MC	3-4.5	A	-	A	-	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 165	MC	5-7	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	4
SCR 166	YAL	13-15	A	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 167	YC	2.5-3	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 168	YC	2.5-3.5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 175	OC	8.5-10	A	A	A	A	**P**	A	A	**P**	A	A	A	A	**P**	A	A	A	A	**1**
SCR 176	OC	7-8	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 182	MC	5-7	A	A	A	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 187	YC	1.5-2.5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 200	MC	6-8	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 202	I/YC	</= 21	A	**P**	-	-	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 204	YC	1.5-2.5	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 206	YC	1-1.5	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
SCR 209	YC	8-9	A	**P**	-	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 214	I/YC	UD	-	-	-	-	-	-	-	A	A	-	A	-	-	-	-	A	-	5

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 218	OC	8-10	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	4
SCR 222	YC	0.5-1	A	A	A	A	A	A	A	A	A	A	A	A	A	A	**P**	A	-	**3**
SCR 225	MC	5.5-8	A	**P**	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	-	**3**
SCR 229	JUD	</= 16	A	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	5
SCR 230	MC	UD	A	A	-	-	-	-	-	A	A	-	A	-	-	-	-	A	-	5
SCR 235	MC	4-5	**P**	A	A	A	A	A	A	**P**	A	A	A	A	A	A	A	A	A	**3**
SCR 237	YAL	14-16	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 238	F/N	<0.125	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 240	OC	9-10	A	-	A	-	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 244	MC	5-7	A	A	A	A	**P**	A	**P**	**P**	A	**P**	**P**	A	A	A	A	**P**	-	**1**
SCR 247	OC	9-11	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 248	YC	1-2	**P**	**P**	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 249	OC	11-12	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 255	YC	1-2	A	-	-	-	-	-	A	A	A	A	A	A	-	-	-	A	-	4
SCR 259	OC	8-9	-	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 268	YAL	14-16	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 270	MC	2.5-4	-	-	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 273	YC	1.5-2.5	A	A	**P**	-	A	A	-	A	A	A	A	A	-	-	-	A	A	**3**
SCR 274	MC	2.5-4	A	-	-	-	-	-	A	A	A	A	A	A	-	-	-	A	-	5
SCR 275	YC	1-1.5	A	A	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 276	YC	1.5-2.5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 277	I/YC	UD	**P**	**P**	-	-	-	-	-	-	-	-	A	-	-	-	-	-	-	5
SCR 278	MC	2.5-4	A	A	A	-	A	A	-	A	A	A	A	A	A	A	-	A	-	4
SCR 279	OC	9-10	A	-	A	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 290	OC	9-11	A	**P**	-	A	**P**	A	A	**P**	A	A	A	A	A	A	A	A	-	**2**

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 309	OC	7-9	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 311	I/YC	UD	-	-	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 313	OC	11-12	A	A	A	-	-	-	-	A	A	A	A	A	A	A	-	A	-	4
SCR 315	MC	7-8.5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 328	YAL	11-14	A	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 333	OC	11-12	A	A	A	A	A	A	A	**P**	A	A	A	A	A	A	A	A	-	**2**
SCR 345	YC	1-2.5	-	-	-	-	-	-	-	-	A	-	A	-	-	-	-	A	-	5
SCR 346	OC	</= 14	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 350	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	-	-	-	-	A	-	5
SCR 351	OC	8-10	A	A	A	A	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 356	OC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 357	OC	9-13	A	-	A	-	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 359	YC	1.5-2.5	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 364	MC	3-5.4	-	-	-	-	-	-	A	A	-	A	A	A	A	A	A	A	-	5
SCR 367	I/YC	</= 18	-	-	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 372	F/N	<0.125	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 373	MC	</= 16	-	-	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 375	I/YC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 378	OC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	A	-	A	A	-	5
SCR 381	MC	7-7.5	-	-	-	-	-	-	A	A	A	A	A	A	A	-	-	A	-	4
SCR 384	I/MC	</= 16	A	-	-	-	-	-	-	A	-	A	A	A	A	A	-	A	-	5
SCR 387	I/YC	</= 18	A	-	-	-	-	-	-	A	-	A	A	A	-	-	A	A	-	5
SCR 388	I	0.5-1	-	-	-	-	-	-	A	-	A	A	A	A	-	-	A	A	-	5
SCR 392	MC	7-9	-	-	A	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 393	YAL	15-16	A	A	A	-	-	-	A	**P**	A	A	A	A	A	A	A	A	-	**2**

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 397	OC	10-11	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 398	YAL	11-16	-	-	-	-	-	-	A	A	A	A	A	A	-	-	A	A	-	4
SCR 400	YC	1-2	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 402	MC	4-5.6	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 408	I	6-10 M	A	-	-	-	-	-	-	A	A	-	A	-	-	-	-	A	-	5
SCR 428	OC	8-10	A	-	A	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 432	YC	1-2	-	-	-	-	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 441	YC	1.5-2	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 446	OC	8-10	A	A	A	A	A	A	-	A	A	A	A	A	-	-	-	A	-	4
SCR 451	YAL	13-15	-	-	A	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 459	I/YC	</= 16	A	-	-	A	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 460A	MC	2.5-4	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 460B	I/YC	</= 21	-	-	-	-	A	A	-	-	-	-	A	-	-	-	-	-	-	5
SCR 471	MC	7-7.5	-	-	-	-	-	-	-	A	-	A	A	A	-	-	A	A	-	5
SCR 473	I	0.75-1	A	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 474	YAL	14-16	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 475	OC	</= 18	A	-	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 477	F/N	32-34 W IU	-	-	-	-	-	-	-	A	A	A	A	A	A	A	-	A	-	5
SCR 478	I	4-7 M	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 483	YC	1.5	A	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	4
SCR 491	I	0.125-0.25	A	-	-	A	A	A	-	-	A	A	A	A	-	-	A	A	-	5
SCR 492	MC	3.5-4	A	-	-	-	-	-	-	**P**	A	A	A	A	-	-	A	A	-	**3**
SCR 496	YC	2-2.5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 506	MC	</= 16	-	-	-	-	-	-	-	A	-	A	A	A	A	A	-	A	-	5
SCR 511	I	8-13 M	A	A	**P**	-	A	A	A	A	A	A	A	A	A	A	A	A	-	**3**

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 512	YAL	16-25	-	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 513	I	0-5 M	**P**	-	-	-	A	A	-	A	A	A	A	A	-	-	-	A	-	**3**
SCR 514	MC	4-5	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 516	I	0-3 M	**P**	-	-	-	-	-	-	A	A	-	A	-	-	-	-	A	-	**3**
SCR 517	YAL	15-24	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 518	MC	2.5-4	A	A	A	-	A	A	-	A	A	A	A	A	-	-	-	A	-	4
SCR 519	OC	10-11	A	-	A	A	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 520	OC	8-10	A	A	-	-	A	A	-	A	A	-	A	-	-	-	-	A	-	5
SCR 522	MC	6-7	**P**	A	A	A	A	A	A	A	**P**	A	A	A	A	A	A	A	-	**1**
SCR 523	MC	5-5.7	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 528	MC	</= 16	-	-	-	-	-	-	-	-	A	A	A	A	-	-	-	-	-	5
SCR 529	YC	2-3	A	-	-	-	-	-	-	A	A	A	A	A	A	A	-	A	-	4
SCR 530	OC	7-10	A	**P**	A	-	-	-	-	**P**	**P**	A	A	A	A	A	A	A	A	**1**
SCR 531	I	5.5-7 M	A	A	-	-	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 532	I	7-11 M	A	-	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 533	YC	1-2	A	A	A	-	A	A	-	A	A	-	A	-	-	-	-	A	-	5
SCR 534	YAL	15-16	A	-	A	-	-	-	-	A	A	-	A	-	-	-	-	A	-	5
SCR 536	MC	3-4	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 537	YAL	14-15	A	-	-	-	A	A	-	A	A	A	A	A	-	-	-	A	-	4
SCR 538	OC	10-12	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 539	OC	11-13	A	A	A	-	-	-	-	A	A	A	A	A	A	A	-	A	-	4
SCR 540	YAL	11.5-15	A	-	-	-	A	A	-	A	A	A	A	A	-	-	A	A	-	4
SCR 541	MC	3-4	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 542	YC	1-2	A	**P**	A	A	A	A	A	**P**	A	**P**	**P**	A	A	A	A	A	-	**1**
SCR 543	I	0-0.5	A	A	A	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 546	MC	4-5	A	A	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 547	MC	3.5-4.5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 548	YC	2	A	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 552	MC	4-5	A	-	A	-	-	-	-	A	A	A	A	A	A	A	A	A	-	5
SCR 554	I/YC	</= 16	A	-	-	-	-	-	-	-	A	A	A	A	-	-	A	A	-	5
SCR 555	MC	6-7	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
SCR 557	YAL	12-14	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 560	MC	</= 16	-	-	-	-	-	-	-	A	-	A	A	A	A	A	-	A	-	5
SCR 564	YC	1.5-3	A	-	-	-	**P?**	A	-	A	A	A	A	A	A	A	A	A	A	**3**
SCR 572	OC	UD	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 579	YAL	15-16	A	-	A	-	-	-	A	A	A	A	A	A	A	A	A	A	-	5
SCR 580	MC	6-8	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 581	MC	</= 16	A	A	-	-	-	-	-	-	A	A	A	A	-	-	-	A	A	5
SCR 582	I/YC	UD	-	-	-	-	-	-	-	A	-	-	A	-	-	-	-	A	-	5
SCR 583	OC	8-9	A	A	-	-	-	-	A	-	-	-	-	-	-	-	-	-	-	5
SCR 584	MC	</= 18	A	-	-	-	-	-	-	A	-	A	A	A	-	-	A	A	-	5
SCR 586	I/YC	</= 16	-	-	-	-	-	-	-	A	-	A	A	A	A	A	-	A	-	5
SCR 587	MC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 588	MC	4-4.5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 589	OC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 593	I/YC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	A	A	-	A	-	5
SCR 594	YC	1-1.5	-	-	-	-	-	-	A	**P**	A	**P**	**P**	A	-	-	A	A	-	**1**
SCR 595	MC	4-4.5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 596	MC	2.5-4	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 597	MC	3.5-4.5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 598	MC	4-4.5	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 599	YC	1-4	**P**	**P**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	**3**
SCR 600	I/YC	</= 18	-	-	-	-	-	-	-	A	-	A	A	A	-	-	-	A	-	5
SCR 606	YAL	14-15	A	A	A	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 610	MC	6.5-8	-	-	A	-	-	-	-	A	A	A	A	A	-	-	-	A	-	4
SCR 612	YC	1.5	-	-	-	-	-	-	-	A	A	**P**	A	A	-	-	A	A	-	**3**
SCR 613	MC	</= 16	-	-	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 614	F/N	<0.125	-	-	-	-	-	-	-	-	A	A	A	A	-	-	A	A	-	5
SCR 615	YAL	15-17	-	-	-	-	-	-	A	-	A	A	A	A	-	-	A	A	-	5
SCR 619	I/YC	</= 16	-	-	-	-	-	-	A	-	A	A	A	A	-	-	-	A	-	5
SCR 620	I	0.5-1	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 621	YC	2-2.5	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 622	OC	7.5-8.5	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 623	OC	9.5-10.5	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 624	OC	7-9	A	**P**	-	-	-	-	-	-	A	A	A	A	-	-	A	A	-	**3**
SCR 625	I/YC	</= 16	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 626	OC	10-11	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 627	F/N	<0.125	-	-	-	-	-	-	-	A	-	A	A	A	A	A	A	A	-	5
SCR 628	I/YC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 629	I	0.25-0.5	-	-	-	-	-	-	-	A	-	A	A	A	A	A	A	A	-	5
SCR 630	YC	1.5-2	-	-	-	-	-	-	-	A	-	A	A	A	A	A	A	A	-	5
SCR 631	YC	2-2.5	-	-	-	-	-	-	-	-	A	A	A	A	-	-	A	A	-	5
SCR 632	MC	5.5-6	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 633	YAL	14-16	-	-	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 634	MC	</= 18	-	-	-	-	-	-	-	A	-	A	A	A	A	A	A	A	-	5

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 635	I	0.125	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	5
SCR 636	YC	1-1.5	-	-	-	-	-	-	-	-	**P**	A	A	A	-	-	A	A	-	**3**
SCR 637	I/YC	</= 16	-	-	-	-	-	-	-	-	A	A	A	A	-	-	A	A	-	5
SCR 639	MC	4-5	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 640	MC	3.5-5	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 641	MC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 642	OC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 643	OC	</= 16	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 644	YC	1-1.5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 646	OC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 647	I/YC	0.5-2	-	-	-	-	-	-	A	-	A	A	A	A	-	-	A	A	-	5
SCR 648	OC	11-13	-	-	-	-	-	-	-	A	-	A	A	A	-	-	A	A	-	4
SCR 649	I/YC	1	A	A	-	-	A	A	A	A	-	A	A	A	A	A	A	A	-	4
SCR 650	MC	4.5-5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 651	OC	9.5-10	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 653	I	0.125-0.25	-	-	-	-	-	-	-	**P**	A	**P**	A	A	A	A	**P**	A	-	**2**
SCR 654	F/N	0	-	-	-	-	-	-	-	A	-	A	A	A	A	A	A	A	-	4
SCR 655	I	0.25-1	-	-	-	-	-	-	-	A	A	**P**	A	A	-	-	A	A	-	4
SCR 656	MC	2.5-3.5	A	-	-	-	-	-	A	A	A	A	A	A	-	-	A	A	-	4
SCR 657	OC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	4
SCR 658	OC	7-9	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 659	I/YC	</= 16	-	-	-	-	-	-	A	A	A	A	A	A	-	-	-	A	-	4
SCR 660	MC	6-8	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 661	YC	1-2	-	-	A	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 662	YAL	12-16	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 663	OAL	16-18	-	-	-	-	A	A	A	**P**	A	A	A	A	A	A	A	A	A	**2**
SCR 664	OC	</= 18	-	-	-	-	A	A	-	-	A	A	A	A	-	-	-	A	-	5
SCR 667	YAL	11-16	A	-	-	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 671	I/YC	</= 18	-	-	-	-	A	A	-	A	A	A	A	A	A	A	-	A	-	4
SCR 672	YC	1.5-2	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 675	I/YC	</= 16	A	-	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 681	YAL	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	A	A	-	A	-	4
SCR 683	YAL	14-15.5	A	-	-	-	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 684	OC	7-9	A	A	-	-	-	-	-	A	-	A	A	A	A	A	-	A	-	5
SCR 685	YAL	</= 18	-	-	-	-	-	-	-	A	-	A	A	A	-	-	A	A	-	5
SCR 687	OC	7-8.5	-	-	A	-	-	-	A	A	A	A	A	A	A	A	-	A	-	4
SCR 693	YAL	14-16	-	-	A	-	-	-	A	A	A	A	A	A	-	-	A	A	-	4
SCR 694	YAL	13-18	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 696	F/N	<0.125	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	5
SCR 700	I/YC	UD	A	-	-	-	-	-	-	A	-	A	A	A	A	A	-	A	-	5
SCR 701	MC	</= 18	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 707	OC	8-10	-	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 716	OC	8-9	-	-	-	-	-	-	-	-	A	A	A	A	-	-	A	A	-	5
SCR 720	MC	6-7	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 721	OC	</= 16	-	-	-	-	-	-	-	**P**	A	A	**P**	A	A	A	A	A	-	**1**
SCR 723	YAL	15-17	A	A	A	-	-	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 725	YAL	13-15	-	-	-	-	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 731	MC	3.5-4	-	-	-	-	-	-	A	-	A	A	A	A	-	-	A	A	-	5
SCR 733	I/YC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 734	I/YC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 735	I/YC	</= 18	-	-	-	-	-	-	-	A	A	A	A	A	A	A	-	A	-	5
SCR 736	MC	3-4	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 737	MC	4-5	A	A	-	-	A	A	A	-	-	-	-	-	-	-	-	-	-	5
SCR 738	MC	</= 16	-	-	-	-	-	-	-	A	-	A	A	A	A	A	-	A	-	5
SCR 739	F/N	<0.125	-	-	-	-	-	-	-	A	A	A	A	A	A	A	-	A	-	5
SCR 740	OC	8.5-9.5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 741	MC	3.5	-	-	-	-	-	-	A	A	-	A	A	A	A	A	A	A	-	4
SCR 742	YAL	</= 18	A	A	A	-	A	A	-	-	-	-	-	-	-	-	-	-	-	5
SCR 743	YAL	</= 16	-	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 744	MC	3.5-4.5	-	-	A	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 745	OC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 746	I/YC	UD	-	-	-	-	-	-	-	A	-	-	A	-	-	-	-	A	-	5
SCR 747	I/YC	UD	-	-	-	-	-	-	-	A	A	-	A	-	-	-	-	A	-	5
SCR 748	MC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 749	MC	3-3.5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 750	MC	7-8	A	-	**P**	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 751	I/YC	</= 18	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 752	MC	</= 16	-	-	-	-	-	-	A	-	A	A	A	A	-	-	A	A	-	5
SCR 753	OAL	16-18	-	-	A	-	-	-	-	A	A	A	A	A	A	A	-	A	-	5
SCR 754	MC	5.5-6	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 755	OC	10.5-11	-	-	-	-	-	-	-	A	-	A	A	A	A	A	A	A	-	4
SCR 756	YC	1.5-2	A	-	-	-	-	-	-	A	-	-	A	-	-	-	-	A	-	5
SCR 757	MC	2.5-4	A	A	A	-	-	-	-	A	-	A	A	A	A	A	A	A	-	5
SCR 758	I/YC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	5
SCR 759	I/YC	</= 16	-	-	-	-	A	A	A	A	A	A	A	A	-	-	-	A	-	5

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 760	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	-	-	-	-	A	-	5
SCR 761	MC	5-7	A	A	-	-	-	-	A	A	A	A	A	A	-	-	A	A	-	5
SCR 762	I/YC	</= 18	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 763	I/YC	</= 16	-	-	-	-	-	-	-	A	A	**P**	**P**	A	A	A	A	A	-	**3**
SCR 764	YAL	14-16	-	-	-	A	A	A	-	A	A	A	A	A	-	-	A	A	-	5
SCR 765	F/N	<0.125	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	5
SCR 766	I/YC	</= 16	-	-	-	-	-	-	A	A	A	A	A	A	-	-	A	A	-	5
SCR 767	YC	1.25-1.75	A	A	-	-	-	-	-	A	-	A	A	A	-	-	A	A	-	5
SCR 768	I/YC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 769	YC	1-1.5	-	-	-	-	-	-	-	-	A	A	A	A	-	-	A	A	-	5
SCR 770	MC	</= 16	-	-	-	-	-	-	-	A	-	A	A	A	A	A	A	A	-	4
SCR 771	MC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 772	MC	2-4	A	-	-	-	-	-	-	A	-	-	A	-	-	-	-	A	-	5
SCR 773	I	7-11 M	-	-	**P**	-	-	-	A	A	A	A	A	A	-	-	A	A	-	**3**
SCR 774	I/YC	</= 16	-	-	-	-	A	A	-	A	A	A	A	A	-	-	A	A	-	4
SCR 775	F/N	<0.125	-	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	5
SCR 776	YC	1-1.5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	5
SCR 777	I/YC	UD	-	-	-	-	-	-	-	A	-	A	A	A	-	-	A	A	-	5
SCR 778	I/YC	</= 16	A	A	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 779	I/YC	</= 16	-	-	-	-	-	-	A	**P**	-	A	A	A	A	A	-	A	-	**3**
SCR 780	YC	1-1.5	A	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 781	MC	4-5	A	-	-	-	A	A	-	A	A	A	A	A	-	-	A	A	-	4
SCR 782	I/YC	</= 16	-	-	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 783	OC	8-9	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
SCR 785	MC	3-5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
SCR 786	MC	</= 18	-	-	-	-	-	-	-	A	A	-	A	-	-	-	A	A	-	5
SCR 788	MC	</= 18	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 789	YAL	15-18	A	-	-	-	-	-	-	-	A	A	A	A	-	-	A	A	-	5
SCR 791	MC	4-5	A	A	A	-	-	-	A	A	A	A	A	A	-	-	A	A	-	5
SCR 792	YAL	14-16	A	-	-	-	-	-	-	A	A	A	A	A	A	**P?**	A	A	-	4
SCR 793	YAL	</= 16	-	-	-	-	-	-	-	A	-	A	A	A	-	-	A	A	-	5
SCR 795	I/YC	UD	-	-	-	-	-	-	-	A	-	-	A	-	-	-	-	A	-	5
SCR 798	I/YC	UD	-	-	-	-	-	-	-	A	-	-	A	-	-	-	-	A	-	5
SCR 799	I/YC	UD	-	-	-	-	-	-	-	-	**P**	A	A	A	-	-	-	A	-	**3**
SCR 800	I/YC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	-	A	-	5
SCR 803	OC	7.5-8.5	A	-	A	-	A	A	-	A	A	A	A	A	A	A	-	A	-	4
SCR 810	YAL	14-16	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 811	MC	3-4.5	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 812	YAL	14-17	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 815	OC	9-10.5	A	A	A	-	-	-	-	A	A	A	A	A	-	-	-	A	-	4
SCR 818	OC	8-11	A	-	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	5
SCR 824	OAL	16-20	-	-	-	-	-	-	-	A	-	A	A	A	-	-	A	A	-	4
SCR 829	MC	</= 16	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	A	-	5
SCR 839	OAL	14-17	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Features scored are cranial vault porosity (1), orbital roof porosity (2), deformed mandibular ramus (3), rib deformity (4), costochondral rib flaring (5), costochondral rib porosity (6), ilium concavity (7), deformed leg bones (8), deformed arm bones (9), long bone metaphyseal flaring (10), long bone general thickening (11), long bone metaphyseal porosity (12), superior flattening of the femoral metaphysis (13), coxa vara (14), porosis/roughening of the bone underlying the growth plate (15), long bone concave curvature porosity (16), and histological features on SEM (17). Nondiagnostic features are highlighted in red, possible features in green, and probable features in blue (with light blue representing features that may be possible or probable based on differential expression). Features scored as present (P), absent (A), or unobservable (-). Ages abbreviated as

F/N (Fetal/Neonate, </= 0.125 years), I (Infant (0.125-1 year), YC (Young child, 1.1-3 years), MC (Middle child, 4-7 years), OC (Older child, 8-11 years), YAL (Younger adolescent, 12-15 years), OAL (Older adolescent, 16-19 years), JUD (Juvenile undetermined). Diagnostic categories are outlined in Section 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate).

Table C.2. Features of vitamin D deficiency scored for Ancaster juveniles

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
ANC 5*	OC	9-10	A	**P**	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
ANC 8	MC	5-7	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
ANC 29	OC	8-9	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 37	I/YC	1	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 40	YC	1-1.5	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 44	N	<0.125	A	A	A	-	A	**P**	-	A	A	A	A	A	A	A	**P**	A	A	**3**
ANC 46B	I	0.125	A	-	-	-	A	**P**	-	A	A	**P**	A	A	-	-	A	A	A	**3**
ANC 48	N	<0.125	A	-	-	A	A	**P**	A	A	**P?**	A	A	A	A	A	A	A	-	**3**
ANC 48 C	YC	1.5-3	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
ANC 51	YC	2.5-3	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	A	4
ANC 53A	OC	9-10	**P**	-	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
ANC 54	F	5-6 M IU	A	-	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 55	OC	8-10	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 59	OC	9-10	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 60	MC	3-5	-	-	A	A	A	A	-	-	A	A	A	A	-	-	A	A	-	4
ANC 66A	MC	3-5	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
ANC 71	YC	1-1.5	-	-	-	A	**P?**	A	A	A	A	A	A	A	A	A	A	A	A	**3**
ANC 72A	YC	2-2.5	A	A	A	A	A	**P**	-	-	A	A	A	A	-	-	A	A	A	**3**
ANC 73	MC	6.5-7.5	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
ANC 78A	N	<0.125	A	-	-	A	**P?**	**P**	-	-	A	A	A	A	-	-	A	A	A	**3**
ANC 89	N	<0.125	A	A	-	-	-	-	-	A	A	A	A	A	-	-	**P?**	A	-	**3**
ANC 90	I	0.125	A	A	-	A	A	A	-	A	A	A	A	A	A	A	**P**	A	A	**3**
ANC 95	I/YC	UD	A	-	-	A	**P**	**P**	A	A	A	**P**	**P**	A	-	-	A	A	-	**1**
ANC 97	F	5 M IU	A	A	A	A	A	A	-	A	A	A	A	A	-	-	A	A	-	4
ANC 99	I/YC	</= 16	**P**	-	-	-	-	-	A	A	A	A	A	A	A	A	-	A	A	4
ANC 101	N	<0.125	**P**	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 105	OC	8.5-9	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 114	N	<0.125	A	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
ANC 124	YC	1-1.5	A	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
ANC 124A	I	2-4 M	A	A	A	A	A	**P**	A	A	A	A	**P**	A	A	A	A	A	-	**2**
ANC 125	YAL	10-14	A	A	-	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 127	JUD	UD	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
ANC 129	YAL	11-16	-	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 130	MC	5.5-6.5	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 131	MC	7-9	A	**P**	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	**3**
ANC 132	YC	1.5-2	**P**	-	-	-	-	-	A	A	-	A	A	A	A	A	-	A	A	4
ANC 138	YC	1-1.5	A	A	A	A	A	A	A	**P?**	A	A	**P?**	A	A	A	A	A	A	**1**
ANC 139	OC	7.5-8	A	A	-	-	-	-	A	A	A	A	A	A	A	A	A	A	A	4
ANC 145	YC	1.5-2	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 145A	I	2-4 M	A	A	A	A	A	A	A	A	A	A	A	A	-	-	A	A	A	4
ANC 146	MC	4.5-5.5	A	A	A	A	**P**	A	A	**P?**	A	A	**P?**	A	A	A	A	A	A	**1**
ANC 147A	MC	3-5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 148	MC	3.5-4.5	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
ANC 150	F	4 M IU	A	A	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	4
ANC 151	MC	5-8	A	A	A	A	A	A	A	A	A	A	**P**	A	A	A	A	A	-	**3**
ANC 153	N	<0.125	A	A	-	-	-	A	A	A	A	A	**A**	A	-	-	A	A	-	4
ANC 161	YC	1.5-2.5	A	A	-	-	A	A	-	-	-	-	-	-	-	-	-	-	A	5
ANC 164	YC	1.5-2	A	A	A	A	**P**	A	A	**P**	A	A	**P**	A	**P**	A	A	A	A	**1**
ANC 166	I	5-7 M	A	A	A	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
ANC 166A	MC	</= 16	A	-	-	-	-	-	-	A	-	-	A	A	-	-	-	A	-	4
ANC 169	MC	3	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 180	YC	1.5-2	A	A	A	A	A	A	A	**P**	A	**P**	**P?**	A	A	A	A	A	A	**2**
ANC 181	MC	3-5	A	**P**	A	-	A	A	A	A	A	A	A	A	**P**	A	A	A	A	**2**
ANC 189	JUD	UD	A	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
ANC 192	F	6IU	**P**	A	A	A	**P**	**P**	A	A	A	A	A	A	A	A	A	A	A	**2**
ANC 194	MC	5-7	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	**P**	A	A	**3**
ANC 195	YC	2.5-3	A	A	A	**P**	**P**	A	A	A	A	A	A	A	A	A	A	A	A	**3**
ANC 197	YC	1.5-2	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 203	I	4-5 M	A	A	A	A	**P**	A	-	-	A	**P?**	A	A	-	-	A	A	A	**3**
ANC 204	MC	3-4.5	A	**P**	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
ANC 206	MC	3-4.5	A	-	A	A	A	A	A	A	A	A	A	A	-	-	A	A	A	4
ANC 207	I	0.5-1	A	-	-	-	**P?**	A	A	A	A	A	A	A	A	A	-	A	**P**	**2**
ANC 208	I	5-7 M	A	A	A	**P**	A	A	A	**P ?**	A	A	A	A	A	A	A	A	A	**2**
ANC 215	JUD	</= 16	A	A	-	-	A	A	A	A	A	A	A	A	-	-	-	A	A	4
ANC 219	OC	7-9	A	**P**	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	**2**
ANC 233	YC	1-3	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 239	I	0.125	**P**	A	-	A	A	**P?**	A	A	A	A	A	A	A	A	A	A	A	**3**

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	Diagnosis
ANC 245	JUD	UD	A	-	-	-	-	-	-	A	-	A	A	A	-	-	-	A	-	4
ANC 246	MC	5-7	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 249	I	10-12 M	A	A	-	-	A	A	A	A	A	A	A	A	A	A	-	A	**P**	**2**
ANC 250	YC	2.5-3	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 251A	JUD	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	-	-	A	A	-	4
ANC 254	N	< 2 M	A	A	A	A	**P**	**P**	A	A	A	A	A	A	A	A	A	A	A	**3**
ANC 255	OC	9-10.5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 258	OC	9.5-10	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 260	YC	1.5-2	**P**	**P**	A	A	A	**P**	A	**P**	A	A	**P**	A	A	A	A	A	A	**1**
ANC 261	MC	3-4.5	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 265	N	< 0.125	A	A	A	A	**P**	**P**	-	A	A	A	A	A	A	A	**P**	A	-	**1**
ANC 268	N	<0.125	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	-	4
ANC Uncat D	I	0.125	A	A	A	A	A	A	-	A	A	A	A	A	A	A	-	A	A	4

Features scored are cranial vault porosity (1), orbital roof porosity (2), deformed mandibular ramus (3), rib deformity (4), costochondral rib flaring (5), costochondral rib porosity (6), ilium concavity (7), deformed leg bones (8), deformed arm bones (9), long bone metaphyseal flaring (10), long bone general thickening (11), long bone metaphyseal porosity (12), superior flattening of the femoral metaphysis (13), coxa vara (14), porosis/roughening of the bone underlying the growth plate (15), long bone concave curvature porosity (16), and histological features on SEM (17). Nondiagnostic features are highlighted in red, possible features in green, and probable features in blue (with light blue representing features that may be possible or probable based on differential expression). Features scored as present (P), absent (A), or unobservable (-). Ages abbreviated as F/N (Fetal/Neonate, </= 0.125 years), I (Infant (0.125-1 year), YC (Young child, 1.1-3 years), MC (Middle child, 4-7 years), OC (Older child, 8-11 years), YAL (Younger adolescent, 12-15 years), OAL (Older adolescent, 16-19 years), JUD (Juvenile undetermined). Diagnostic categories are outlined in Section 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate).

Table C.3. Features of active vitamin D deficiency scored for Isola Sacra adults

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 5	OAL	15-21	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 15	OA	36.9-90.7	PM	A	A	A	A	A	A	A	A	A	A	A	A	-	A	A	-	4
SCR 16	MA	25-45	F	-	-	-	A	-	-	A	A	A	-	A	A	A	A	A	-	4
SCR 17	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	4
SCR 18	YA	25-35	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 19	YA	25-35	UD	A	A	A	-	-	-	A	A	A	-	-	-	A	-	A	-	4
SCR 20	YA	25.7-47.1	F	-	-	-	-	-	-	A	A	A	A	A	A	-	A	A	-	4
SCR 21	YA	16.4-64.6	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 27	YA	17-25	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 30	MA	33-45	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 32	OAL	14-19	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 34	AUD	UD	UD	A	A	A	A	-	A	-	A	A	-	-	-	-	A	-	-	4
SCR 35	OAL	14-21	M	A	A	A	A	-	A	A	A	A	-	-	-	A	A	A	-	4
SCR 36	OAL	16-21	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 37	OA	50-75	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 38	YA	25-35	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 39	OA	34-87	F	A	A	A	A	-	A	A	A	A	A	-	-	A	A	A	-	4
SCR 44	MA	25-45	M	**P**	A	**P**	A	-	A	A	A	A	-	A	A	-	A	A	-	**2**
SCR 52	OAL	15-21	PF	A	A	A	A	-	A	A	A	A	-	A	A	A	A	A	-	4
SCR 53	OA	23.4-88.9	F	A	A	A	A	-	A	-	-	-	-	-	-	A	-	-	-	4
SCR 55	YA	17-35	PF	-	-	-	-	-	-	A	A	A	A	A	A	A	A	A	-	4
SCR 57	YA	26.9-62.4	UD	A	A	A	A	-	A	A	A	A	A	A	A	A	-	A	-	4
SCR 59	YA	17-25	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	-	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 60	OA	34-86	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 64	YA	19-23	UD	A	A	A	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 67	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	-	-	A	-	A	-	4
SCR 68	YA	17-25	PF	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	-	4
SCR 69	YA	17-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	**P**	A	-	**2**
SCR 71	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 73	AUD	UD	UD	A	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 75	OAL	17-21	PM	A	A	A	A	A	A	A	A	**P**	A	A	A	A	A	A	-	4
SCR 76	OA	49.4-91.8	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 77	YA	25-45	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	-	A	-	4
SCR 79	YA	25-35	F	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 82	MA	26-70	F	-	-	-	-	-	A	A	A	A	A	A	A	-	A	A	-	4
SCR 83	MA	26-70	F	-	-	-	-	-	-	A	A	A	A	A	A	-	A	A	-	4
SCR 84	MA	33-45	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 85	YA	21-46	PM	A	A	**P**	A	A	A	A	A	A	A	-	-	A	-	-	A	4
SCR 86	OAL	17-25	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 87	OA	71.3-90.3	UD	A	A	A	-	-	-	A	A	A	A	A	A	-	A	A	-	4
SCR 88	YA	17-35	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	4
SCR 89	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 90	YA	17-25	M	A	A	A	A	A	A	A	A	**P**	A	A	A	A	A	A	-	4
SCR 97	MA	25-75	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 98	OAL	17-21	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 99	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 105	MA	33-45	F	A	A	A	A	A	A	A	A	A	-	-	-	-	-	-	-	4
SCR 106	OAL	15-24	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 113	MA	33-45	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 116	YA	17-25	M	A	A	A	A	A	-	A	A	A	-	-	-	A	A	-	-	4
SCR 120	YA	17-25	M	A	A	A	A	-	A	A	A	A	-	-	-	A	-	-	-	4
SCR 122	AUD	UD	UD	A	A	A	A	A	A	A	A	A	-	-	-	A	A	-	-	4
SCR 123	AUD	UD	UD	A	A	A	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 125	YA	17-25	PF	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	-	4
SCR 126	OAL	15-18	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 127	YA	25-35	M	A	A	A	A		-	A	A	A	-	A	A	A	A	A	-	4
SCR 128	MA	26-70	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 129	YAL	14-16	UD	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	-	4
SCR 130	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 132	YA	17-25	UD	-	-	-	A	A	A	A	A	A	-	-	A	A	A	A	-	4
SCR 133	OAL	17-19	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 134	MA	33-45	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 138	OAL	15-18	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 142	YA	17-25	M	A	A	A	A	-	A	A	A	A	-	A	A	A	A	A	-	4
SCR 143	MA	34-86	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 144	YA	19-25	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 145	MA	33-57	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 148	OA	42-87	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 150	OA	26.2-86.7	PF	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 151	MA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 152	MA	25-83	PF	A	A	**P**	-	-	-	A	A	A	A	A	A	-	A	A	A	4
SCR 155	OAL	17-21	UD	A	A	A	A	-	A	**P?**	A	A	-	A	A	A	-	A	A	4
SCR 156	OA	42-87	PF	A	A	A	A	-	A	**P?**	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 157	OAL	16-21	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 158	MA	25-88.1	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	4
SCR 159	AUD	UD	F	A	A	**P**	A	A	A	A	A	A	-	-	-	A	A	A	-	4
SCR 160	MA	26-70	F	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	**3**
SCR 161	YA	24.3-45	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 163	MA	25-66	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 169	YA	18.3-33.2	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 170	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	-	-	A	A	A	-	4
SCR 171	YA	25-83	F	A	A	A	A	A	-	A	A	A	A	A	A	A	A	A	-	4
SCR 172	MA	33-45	M	A	A	A	-	-	-	A	-	-	-	-	-	-	A	-	-	4
SCR 173	MA	25-83	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 174	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 177	AUD	UD	F	-	-	-	A	-	A	A	A	A	-	-	-	-	A	-	-	4
SCR 178	YA	25-35	M	A	A	A	A	-	A	-	A	A	-	-	-	A	A	-	-	4
SCR 179	MA	33-45	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 180	YA	17-25	UD	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 181	YA	25-35	M	A	**P**	A	A	-	A	A	A	A	A	A	A	A	-	-	A	**2**
SCR 183	MA	42-87	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 184	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 185	OA	69.2-89.7	PF	A	A	**P**	A	A	A	**P?**	A	A	A	A	A	A	A	-	A	4
SCR 186	MA	25-45	M	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	-	4
SCR 188	YA	17-25	AB	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 189	MA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 190	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 191	MA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 192	MA	33-45	UD	A	A	A	A	A	A	A	A	A	-	-	-	A	-	-	-	4
SCR 193	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 194	MA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 196	OAL	17-25	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 197	YA	18-27	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 198	YA	19-34	M	A	A	A	A	-	A	A	A	A	A	A	A	-	A	A	-	4
SCR 199	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 201	MA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 203	OAL	15-18	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 207	YA	17-25	M	-	-	-	-	-	-	A	A	A	-	-	-	-	-	-	-	4
SCR 208	AUD	UD	UD	A	A	A	-	-	-	-	A	A	-	-	-	-	-	-	-	4
SCR 210	MA	25-35	F	A	A	A	A	A	A	A	A	A	A	-	-	A	-	A	-	4
SCR 211	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 212	YA	17-25	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
SCR 213	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 215	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	-	-	A	A	-	-	4
SCR 216	OAL	15-17	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 217	YA	25-35	UD	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 219	YAL	15-16	UD	A	A	A	-	-	-	A	A	A	-	A	-	-	A	-	-	4
SCR 220	OAL	17-20	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 221	MA	23-57	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 223	YA	17-25	UD	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	-	4
SCR 224	YA	17-25	M	A	A	A	A	-	A	A	A	A	-	-	-	A	A	-	-	4
SCR 226	OAL	16-18	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 227	MA	25-35	F	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 228	MA	19.5-79.3	UD	A	A	A	-	-	-	A	A	A	A	A	A	-	A	A	-	4
SCR 231	YA	28.4-63.6	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 232	YA	25-35	M	**P**	A	**P**	A	A	A	A	A	**P**	A	-	-	A	A	-	-	4
SCR 233	MA	25-63.2	F	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 234	MA	25-58.2	UD	A	A	A	A	-	-	A	A	A	A	A	A	-	-	A	-	4
SCR 236	YA	25-35	UD	A	A	**P**	A	A	A	-	A	A	-	-	A	A	A	-	-	4
SCR 239	MA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 241	MA	33-45	F	A	A	A	A	A	A	A	A	A	A	-	-	A	A	A	-	4
SCR 242	YA	25-35	UD	A	A	A	A	-	-	A	A	A	-	-	-	A	-	-	-	4
SCR 243	YA	17-25	UD	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 245	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 246	YA	17-25	PM	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 250	MA	25-35	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 251	YA	17-25	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 252	MA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 253	AUD	UD	M	A	A	A	-	-	-	-	-	-	A	-	-	A	-	-	-	4
SCR 254	AUD	UD	UD	A	A	A	-	A	-	-	-	-	-	-	-	A	-	-	-	4
SCR 256	MA	23-57	M	A	A	A	A	-	-	A	A	A	-	A	A	A	A	A	-	4
SCR 257	AUD	UD	UD	-	-	-	-	-	-	A	A	A	-	-	-	-	-	-	-	4
SCR 258	YA	17-25	F	-	-	-	-	-	-	A	A	A	-	-	-	A	-	A	-	4
SCR 260	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	4
SCR 261	OA	45+	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 262	MA	26-70	PF	-	-	-	-	-	-	-	-	-	A	-	-	-	-	A	-	4
SCR 263	OAL	15-18	F	A	A	A	A	-	A	-	A	A	A	A	A	A	A	A	-	4
SCR 264	OA	67-110	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 265	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 266	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 267	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 269	YA	25-35	PF	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
SCR 271	OAL	18-23	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 272	YA	21-53	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 280	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 281	MA	25-49	PF	A	A	A	A	-	A	-	A	A	-	A	A	A	A	A	-	4
SCR 282	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 283	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 284	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 285	MA	25-45	F	A	A	**P**	A	A	A	A	A	A	-	-	-	A	-	-	-	4
SCR 286	MA	25-35	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 287	MA	26-70	F	A	A	A	A	A	A	A	A	A	A	-	-	A	A	A	-	4
SCR 288	MA	25-45	PM	**P**	**P**	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	**3**
SCR 289	MA	25-73.9	PF	A	A	A	A	A	-	A	A	A	-	-	-	A	A	-	-	4
SCR 291	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SR 292	YA	17-25	PF	A	A	A	A	-	A	A	A	A	-	-	-	A	A	A	-	4
SCR 293	AUD	UD	M	A	A	A	A	-	A	A	A	A	-	-	-	A	-	-	-	4
SCR 294	YA	25-35	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 295	YA	18-27	F	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 296	YA	17-25	PF	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 297	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 298	MA	25-45	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 299	YA	17-25	F	A	A	A	-	-	A	A	A	A	-	-	-	A	A	-	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 301	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 302	MA	25-83	AB	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 303	YA	25-35	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 304	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 305	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 306	OAL	15-25.2	PF	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 307	MA	25-89.5	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 308	OA	44.6-92.1	M	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 310	YAL	14-16	AB	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 312	YA	25-35	F	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 314	YA	17-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 317	OAL	17-18	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 318	MA	19.6-82.9	UD	A	A	A	-	-	-	A	A	A	A	A	A	-	A	-	-	4
SCR 319	OAL	16-18	M	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	-	4
SCR 320	YA	17-21	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 321	YA	17-27	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 322	OAL	14-19	PF	A	A	A	-	-	-	A	A	A	A	A	A	-	A	A	-	4
SCR 323	MA	33-83	F	**P**	**P?**	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	**2**
SCR 324	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 325	OAL	17-21	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 326	YA	17-35	F	A	A	A	A	-	A	A	A	A	-	-	-	A	A	A	-	4
SCR 328A	YA	21-53	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 329	MA	26-70	F	A	A	A	A	A	A	A	A	A	A	-	-	A	A	A	-	4
SCR 330	OAL	18-21	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 331	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 332	OAL	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	-	A	A	-	4
SCR 334	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 335	YA	17-35	PF	A	A	A	A	-	A	A	A	A	A	A	A	-	A	A	-	4
SCR 336	MA	33-45	UD	A	A	A	A	-	-	-	A	A	-	-	-	A	A	-	-	4
SCR 337	OAL	15-17	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 338	MA	33-45	PF	A	A	A	-	A	A	A	A	A	A	-	-	A	A	A	-	4
SCR 339	MA	25-57	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 340	YA	17-25	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 341	MA	25-45	M	**P**	**P?**	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	**3**
SCR 342	YA	25-35	M	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 343	OAL	15-17	AB	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 344	YA	17-25	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 347	YA	17-35	UD	A	A	A	A	-	A	A	A	A	-	-	-	A	A	-	-	4
SCR 350	AUD	UD	UD	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 352	OAL	16-21	PF	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 354	OAL	14-18	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 355A	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 355B	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 358	YA	17-25	F	A	A	A	A	-	A	A	A	A	-	-	-	A	A	-	-	4
SCR 360	OAL	15-18	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 361	OAL	17-18	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 362	YA	17-25	F	-	-	-	-	-	-	-	-	-	A	A	A	-	A	A	-	4
SCR 363	YA	21-53	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 365	OA	72.6-90.7	UD	A	A	A	-	A	A	-	A	A	-	A	A	-	A	-	-	4
SCR 366	OA	45+	M	A	A	A	-	-	-	A	A	A	-	-	-	A	-	A	-	4
SCR 368	OAL	15-17	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 369	OAL	17-21	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 370	YA	20.9-39.1	F	-	-	-	-	-	-	A	A	A	A	A	A	-	-	A	-	4
SCR 371	OA	72.6-90.7	F	A	A	A	A	-	A	A	A	A	-	A	A	A	A	-	-	4
SCR 374	AUD	UD	UD	A	A	A	A	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 376	YA	17-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	4
SCR 377	AUD	UD	UD	A	A	A	A	A	A	A	A	A	-	-	-	A	-	-	-	4
SCR 379	AUD	UD	UD	A	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 380	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 382	OA	74.6-91.3	F	-	-	-	-	-	-	-	-	-	-	-	A	-	-	A	-	4
SCR 383	OAL	17-21	M	-	-	-	-	-	-	A	A	A	A	-	-	A	-	A	-	4
SCR 389	OAL	15-19	M	-	-	-	A	-	A	A	A	A	A	A	A	A	-	-	-	4
SCR 390	AUD	UD	UD	A	A	**P**	-	-	-	-	-	-	-	-	-	-	A	A	-	4
SCR 391	YAL	14-16	M	-	-	-	-	-	-	-	-	-	A	-	A	-	-	-	-	4
SCR 394	OA	72.8-90.7	F	-	-	-	-	-	-	-	-	-	A	-	A	-	A	A	-	4
SCR 395	OAL	16-18	F	-	-	-	-	-	-	-	-	-	A	A	A	-	A	A	-	4
SCR 396	OAL	15-19	M	-	-	-	A	-	A	-	-	-	A	A	A	A	-	A	-	4
SCR 399	YA	25.7-48.9	UD	-	-	-	-	-	-	-	-	-	-	A	A	-	A	-	-	4
SCR 401	YA	17-25	PF	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 403	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 404	OAL	15-18	PF	A	A	A	-	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 405	AUD	UD	F	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	-	4
SCR 406	OAL	15-18	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 407	OA	UD	F	A	A	P	A	A	A	A	A	P	A	A	A	A	A	-	-	4
SCR 409	YA	17-35	F	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 410	AUD	UD	UD	A	A	A	-	-	A	-	A	A	-	-	-	-	A	-	-	4
SCR 411	OAL	16-21	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 412	MA	23-57	PM	A	A	P	-	-	-	-	-	-	A	-	-	A	A	A	-	4
SCR 413	OAL	16-21	UD	A	A	A	A	A	A	A	A	A	-	A	A	A	-	-	-	4
SCR 414	OAL	</= 21	UD	A	A	A	A	-	A	-	-	-	-	-	-	A	-	-	-	4
SCR 415	YA	17-25	UD	A	A	A	-	-	-	-	-	-	-	-	-	A	-		-	4
SCR 416	OAL	16-19	F	A	A	A	A	A	A	A	A	A	A	A	A	-	A	A	-	4
SCR 417	MA	25-38	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 418	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 419	MA	33-45	F	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	-	4
SCR 420	YAL	14-16	PF	A	A	A	A	-	A	A	A	A	-	A	A	A	A	A	-	4
SCR 421	OAL	15.8-30.3	PF	A	A	A	A	-	A	-	-	-	-	A	A	A	A	A	-	4
SCR 422	MA	33-45	F	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 423	MA	33-45	M	A	A	A	A	-	-	-	-	-	-	-	-	A	A	-	-	4
SCR 424	MA	25-38	F	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	-	4
SCR 425	MA	25-45	PM	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 426	YA	17-25	PF	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 427	AUD	UD	UD	A	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	5
SCR 429	OA	38.5-91.6	UD	A	A	A	A	-	-	A	A	A	-	-	-	A	A	-	-	4
SCR 430	OA	32.4-89.9	PM	A	A	P	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 431	AUD	UD	F	A	A	A	A	-	A	A	A	A	-	A	A	-	A	A	-	4
SCR 433	YA	17-25	F	A	A	P	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 434	MA	25-83	F	A	A	P	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 435	YA	25-35	M	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 436	MA	25-45	F	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 437	OA	25-60	PF	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 438	AUD	UD	UD	A	A	A	A	-	A	A	A	A	-	A	A	A	A	-	-	4
SCR 439	MA	23-57	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 440	OA	50-93.4	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 442	OAL	18-19	F	-	-	-	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 443	YA	25-35	F	-	-	-	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 444	OAL	17-21	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 445	YA	17-25	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 447	YA	21-46	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	4
SCR 448	MA	17-38	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 449	OA	33-50+	M	A	A	A	A	-	A	-	A	A	A	-	-	-	A	-	-	4
SCR 450	YA	17-25	UD	-	-	-	-	-	-	A	A	A	A	A	A	-	-	-	-	4
SCR 452	YA	17-25	F	-	-	-	-	-	-	-	-	-	-	A	A	-	A	A	-	4
SCR 453	YA	18.3-33.7	M	A	A	**P**	A	-	A	A	A	A	-	A	A	-	A	-	-	4
SCR 454	YA	25-35	UD	A	A	A	A	-	-	A	-	-	-	A	-	-	A	-	-	4
SCR 455	OAL	17-21	UD	A	A	A	A	A	A	A	A	A	-	-	-	A	A	-	-	4
SCR 456	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 457	OA	55.7-93.2	PM	A	A	A	A	-	-	A	A	**P**	-	-	A	-	A	A	-	4
SCR 458	YA	25.7-47.1	M	-	-	-	A	-	A	A	A	A	-	A	A	A	A	A	-	4
SCR 461	YA	17-35	UD	A	A	A	-	-	-	-	A	A	-	-	-	A	-	-	-	4
SCR 462	MA	23-57	MA	A	A	A	A	A	A	**P?**	A	A	A	A	A	A	A	A	-	4
SCR 463	YA	17-35	PM	A	A	A	A	A	A	A	A	A	-	A	-	A	A	A	-	4
SCR 464	YA	17-29	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 465	AUD	UD	M	A	A	A	A	-	-	-	A	A	-	-	-	-	A	-	-	4
SCR 466	MA	25-75	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 467	MA	25-83	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 468	YA	17-25	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 469	OA	23-83.5	UD	A	A	A	A	-	A	A	A	A	A	A	A	A	A	-	-	4
SCR 470	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 476	AUD	UD	UD	A	A	A	A	A	A	-	A	A	-	-	-	-	-	-	-	4
SCR 479	YA	17-25	PF	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	-	-	4
SCR 480	YA	21-46	M	A	A	A	-	-	-	-	-	-	A	-	A	-	-	A	-	4
SCR 481	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 482	AUD	UD	M	A	A	A	A	A	A	A	A	A	-	-	A	A	A	A	-	4
SCR 484	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 485	YA	17-35	PM	-	-	-	A	A	A	A	A	A	A	-	A	A	A	A	-	4
SCR 486	MA	23-70	UD	-	-	-	A	A	A	-	-	-	A	-	-	A	A	A	-	4
SCR 487	YA	25-35	UD	-	-	-	A	-	-	-	-	-	-	-	-	A	A	-	-	4
SCR 488	AUD	UD	UD	A	A	**P**	A	-	A	-	A	A	A	-	-	A	A	-	-	4
SCR 489	MA	23-70	F	-	-	-	-	-	-	A	-	-	A	A	A	-	A	A	-	4
SCR 490	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
SCR 493	YA	17-25	UD	-	-	-	-	-	A	-	-	-	-	-	-	-	-	-	-	4
SCR 497	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 499	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 500	OAL	15-23	M	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 501	MA	26-70	PF	A	A	A	A	A	A	A	A	A	A	A	A	-	A	A	-	4
SCR 502	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 503	YA	25-35	UD	A	A	A	A	-	-	A	A	A	-	A	A	-	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 504	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	A	-	4
SCR 505	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 507	OAL	</= 21	F	A	A	A	-	-	-	-	-	-	A	A	A	A	-	-	-	4
SCR 508	YA	19-34	M	-	-	-	-	-	-	A	A	A	A	A	A	-	A	A	-	4
SCR 509	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 510	YA	17-38	PF	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 521	YA	17-25	UD	A	A	A	-	-	-	A	A	A	-	-	-	-	A	-	-	4
SCR 524	OA	53.7-92.8	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	A	-	4
SCR 525	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 526	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 527	MA	23-57	M	-	-	-	-	-	-	A	A	A	A	A	A	-	-	-	-	4
SCR 535	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 544	AUD	UD	UD	-	-	-	-	-	-	-	-	-	A	A	A	-	A	A	-	4
SCR 545	YA	18-27	UD	-	-	-	-	-	-	A	A	A	-	A	A	-	A	-	-	4
SCR 549	YA	25-45	F	-	-	-	-	-	-	-	-	-	A	A	A	A	A	A	-	4
SCR 550	YA	27.4-51.1	UD	-	-	-	-	-	-	-	-	-	-	A	A	A	A	A	-	4
SCR 551	YA	19.8-35.1	M	-	-	-	-	-	-	-	-	-	-	A	A	-	A	A	-	4
SCR 553	YA	17-25	UD	-	-	-	-	-	-	-	-	-	-	A	A	-	-	A	-	4
SCR 556	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
SCR 559	AUD	UD	F	-	-	-	A	-	A	A	A	A	-	-	-	A	A	-	-	4
SCR 561	YAL	14-16	UD	-	-	-	A	-	-	A	A	A	-	-	-	A	-	-	-	4
SCR 562	MA	28-45	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	-	-	4
SCR 563	OAL	16-18	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 565	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	5
SCR 566	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 567	YA	25-35	UD	A	A	A	A	-	-	A	-	-	-	-	-	A	A	-	-	4
SCR 568	YA	17-25	F	A	A	A	A	-	A	A	A	A	-	A	-	A	A	A	-	4
SCR 569	YA	17-25	UD	A	A	A	-	-	-	-	-	-	-	-	-	A	A	-	-	4
SCR 570	AUD	UD	UD	A	A	A	-	-	-	-	A	A	-	-	-	-	A	-	-	4
SCR 571	OAL	15-18	UD	-	-	-	-	-	-	-	-	-	A	A	A	-	-	A	-	4
SCR 573	OA	24.2-86.3	M	A	A	A	-	-	-	A	A	A	A	-	-	-	-	-	-	4
SCR 574	OAL	14-18	UD	A	A	A	-	-	-	A	A	A	-	-	-	A	-	-	-	4
SCR 575	OAL	17-21	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 576	MA	23-57	M	A	A	A	A	A	A	A	A	**P?**	A	A	A	A	A	A	-	4
SCR 577	YAL	14-16	M	A	A	A	-	-	-	A	A	A	-	A	A	-	A	A	-	4
SCR 578	YA	22.6-55.2	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	A	-	4
SCR 585	YA	25-35	UD	A	A	A	-	-	A	A	A	A	-	-	-	A	-	-	-	4
SCR 590	YA	25-35	M	A	**P?**	**P**	A	A	A	A	A	A	-	A	A	A	A	A	**P?**	**2**
SCR 591	AUD	UD	UD	A	A	A	A	-	A	A	A	A	-	-	-	A	A	A	-	4
SCR 592	YA	19-34	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 601	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	A	-	4
SCR 602	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	4
SCR 603	YA	30.6-62.7	UD	-	-	-	-	-	-	-	-	-	A	A	A	-	A	A	-	4
SCR 604	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	A	-	4
SCR 605	OAL	14-19	UD	-	-	-	-	-	-	A	A	A	A	A	A	-	-	-	-	4
SCR 607	MA	25-55	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	4
SCR 608	YA	17.7-33.3	PF	-	-	-	-	-	-	A	A	A	A	A	A	-	-	A	-	4
SCR 609	OAL	15-18	M	-	-	-	-	-	-	-	-	-	A	-	-	-	A	-	-	4
SCR 611	OAL	17-19	UD	A	A	A	A	A	A	A	A	A	A	A	A	-	-	A	-	4
SCR 616	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 617	MA	17-75	PM	A	A	A	-	A	A	A	A	A	-	-	A	A	A	A	-	4
SCR 618	OAL	16-21	F	-	-	-	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 638	OAL	14-18	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 645	OAL	15-18	UD	-	-	-	-	-	-	A	A	A	-	A	A	-	A	-	-	4
SCR 652	MA	25-83	F	-	-	-	-	-	-	-	-	-	A	A	A	A	A	A	-	4
SCR 665	OAL	16-18	M	-	-	-	-	-	-	A	A	A	A	-	-	-	A	-	-	4
SCR 666	OAL	14-18	UD	A	A	A	A	A	A	A	A	A	-	-	-	-	A	-	-	4
SCR 668	MA	23-57	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 669	MA	37.4-85.8	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 670	YA	17-35	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 673	MA	18.8-77	F	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	-	-	4
SCR 674	OAL	17-19	UD	-	-	-	-	-	-	-	-	-	-	A	A	-	-	-	-	4
SCR 676	OA	33+	M	A	A	A	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 677	OAL	16-19	F	A	A	A	A	A	A	A	A	A	-	A	-	A	A	A	-	4
SCR 678	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 679	YA	17-27	PF	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 680	AUD	UD	F	-	-	-	-	-	A	-	-	-	-	-	-	-	-	-	-	4
SCR 682	MA	23-57	M	-	-	-	-	-	-	A	A	A	A	A	A	-	A	A	-	4
SCR 686	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 688	AUD	UD	UD	A	A	A	-	-	-	A	A	A	-	-	-	-	-	A	-	4
SCR 689	OAL	15-17	UD	-	-	-	-	-	-	A	A	A	-	A	A	-	-	-	-	4
SCR 690	MA	26-70	F	A	A	A	A	A	-	A	A	A	-	-	-	A	A	A	-	4
SCR 691	YA	18-27	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 692	YA	17-25	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 695	YA	17-38	F	A	A	A	A	-	-	A	A	A	A	A	A	A	-	-	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 697	OAL	17-18	UD	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 698	YA	25-35	AB	A	A	A	A	-	A	A	A	A	-	A	A	A	A	A	-	4
SCR 699	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 702	MA	23-57	M	A	A	A	A	-	A	A	A	A	A	A	A	-	A	A	-	4
SCR 703	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 704	MA	16.2-82.8	UD	-	-	-	A	-	A	-	-	-	-	-	-	-	A	A	-	4
SCR 705	MA	23-57	M	-	-	-	A	A	A	-	-	-	A	A	A	A	-	A	-	4
SCR 706	YA	21-46	M	-	-	-	-	-	-	-	-	-	A	A	A	-	A	A	-	4
SCR 708	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	4
SCR 709	OA	42.4-90.5	F	-	-	-	A	A	A	-	-	-	A	A	A	A	A	A	-	4
SCR 710	OAL	17-21	F	-	-	-	-	-	-	-	-	-	A	A	A	-	A	A	-	4
SCR 711	OA	22.5-88.9	PF	A	A	A	A	-	A	A	A	A	-	-	A	A	A	A	-	4
SCR 712	OAL	15-18	UD	A	A	A	-	-	-	A	A	**P**	A	A	A	-	A	A	-	4
SCR 713	OAL	14-18	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 714	YA	21-53	F	-	-	-	-	-	-	-	-	-	A	A	A	-	A	A	-	4
SCR 715	MA	23-57	M	A	A	A	A	-	A	-	-	-	A	A	A	-	A	A	-	4
SCR 717	YA	16.5-71.9	PF	A	A	A	A	-	A	A	A	A	A	A	-	-	-	-	-	4
SCR 718	AUD	UD	UD	A	A	A	-	A	A	A	A	A	-	A	-	A	A	-	-	4
SCR 719	MA	37-88.8	M	A	A	A	-	-	-	A	A	A	A	A	A	-	A	-	-	4
SCR 722	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	A	A	-	-	4
SCR 724	AUD	UD	UD	A	A	A	A	A	A	A	A	A	A	-	-	A	-	-	-	4
SCR 726	YA	17-25	F	A	A	A	A	A	-	A	A	A	A	A	A	A	A	-	-	4
SCR 727	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 728	YA	25-35	UD	A	A	A	A	-	A	-	A	A	-	-	-	A	-	-	-	4
SCR 729	MA	25-45	UD	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 730	MA	25-45	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 732	YAL	14-16	UD	A	A	A	A	-	-	A	A	A	-	A	-	-	A	A	-	4
SCR 784	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 787	AUD	UD	F	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	-	4
SCR 790	YA	17-25	UD	-	-	-	-	-	-	A	A	A	-	-	-	-	-	-	-	4
SCR 794	OAL	17-25	PF	-	-	-	-	-	-	-	-	-	-	A	A	-	A	A	-	4
SCR 797	YA	17-25	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 801	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
SCR 802	MA	25-37	PF	A	A	A	A	A	A	A	A	A	-	-	-	A	A	-	-	4
SCR 804	YA	19-25	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 805	OA	23-57	M	A	A	**P**	A	A	A	A	A	**P**	A	A	A	A	A	A	-	4
SCR 806	MA	25-57	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 807	YA	22.4-39.4	UD	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	-	-	4
SCR 808	YA	25-35	PM	A	A	A	A	-	A	A	A	A	A	A	-	A	A	A	-	4
SCR 809	OA	72.6-90.7	UD	A	A	A	A	-	A	-	A	A	-	-	A	-	-	-	-	4
SCR 813	OA	18.5-87.3	PM	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	A	-	4
SCR 814	OA	27-66	PM	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 816	MA	25-39	F	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 817	AUD	UD	UD	-	-	-	-	-	-	-	A	A	-	A	-	-	-	-	-	4
SCR 819	MA	33-45	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 820	AUD	UD	UD	-	-	-	A	-	-	-	-	-	-	A	-	-	A	-	-	4
SCR 821	YA	18-27	UD	-	-	-	A	-	-	-	-	-	-	A	A	A	-	-	-	4
SCR 822	MA	25-45	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 823	MA	25-45	PM	-	-	-	-	-	-	A	A	A	-	-	-	-	-	-	-	4
SCR 826	YA	17-35	UD	A	A	A	-	-	-	-	-	-	-	-	-	-	-	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
SCR 827	MA	18.1-81.5	F	A	A	A	A	-	A	A	A	A	A	A	A	A	A	A	-	4
SCR 828	OAL	15-29.6	UD	A	A	A	A	A	A	A	-	-	-	A	A	A	A	-	-	4
SCR 830	YA	17-25	PF	A	A	A	-	-	-	-	-	-	-	-	-	-	A	-	-	4
SCR 831	OAL	15-18	AB	A	A	A	-	-	-	A	A	A	A	A	A	-	A	A	-	4
SCR 833	YA	17-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 834	OA	33-57	M	A	A	**P**	A	A	A	A	A	**P**	A	A	A	A	A	A	-	4
SCR 835	YA	17-25	F	A	A	A	A	-	A	**P?**	A	A	A	A	A	A	A	A	-	4
SCR 836	YA	17-35	PF	**P?**	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 837	MA	33-45	M	A	A	A	A	-	A	A	A	A	A	A	A	A	A	-	-	4
SCR 838	YA	19-25	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 840	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
SCR 841	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Features scored are healing or unhealed rib fractures (1), rib fractures with spiculated bone (2), healed rib fractures (3), scapula spinous process pseudofractures (4), scapula coracoid process pseudofractures (5), scapula lateral border pseudofractures (6), vertebral body compression fractures (7), vertebral lamina pseudofractures (8), healed vertebral lamina fractures (9), inferior pubic ramus pseudofractures (10), iliac crest fractures (11), ilium pseudofractures (12), healing or unhealed clavicle fractures (13), long bone pseudofractures (14), proximal femur pseudofractures (15), and histological features on SEM (16). Nondiagnostic features are highlighted in red, possible features of residual deficiency in green, and probable features of adult deficiency in blue. Features scored as present (P), absent (A), or unobservable (-). Ages abbreviated as YAL (Younger adolescent, 12-15 years), OAL (Older adolescent, 16-19 years), YA (Young adult, 20-34 years), MA (Middle adult, 35-49 years), OA (Older adult, 50+ years), AUD (Adult undetermined). Sex abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), UD (undetermined). Diagnostic categories are outlined in Section 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate).

Table C.4. Features of active vitamin D deficiency scored for Ancaster adults

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
ANC 1	OAL	17-21	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 2	MA	35.2	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 2A	YA	21-53	PM	A	A	A	A	A	A	A	A	A	A	-	-	A	-	-	A	4
ANC 3	MA	25-45	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 3*	MA	48.1	F	A	A	A	-	-	-	A	-	-	A	A	A	-	A	-	-	4
ANC 3A	MA	48.1	F	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 4	OA	45+	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 5	MA	48.1	PM	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 6	OA	77.2	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 10	OA	81.5	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 11	YA	26-34	M	A	A	A	A	A	A	**P**	A	A	A	A	A	A	A	A	**P?**	4
ANC 12	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 12B	OA	82.2	M	A	A	A	A	A	A	A	A	**P**	A	A	A	A	A	A	A	**3**
ANC 13	MA	35.2-38.2	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 14	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	-	A	A	A	-	-	4
ANC 21	OA	60	F	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	-	4
ANC 22	OA	50+	PM	-	-	-	A	-	-	-	-	-	-	A	A	A	A	A	-	4
ANC 23	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	**P**	**3**
ANC 24	MA	35.2	M	A	A	A	A	A	A	A	A	**P**	A	A	A	A	A	A	-	4
ANC 25	OA	75.7	F	A	A	A	A	-	A	-	-	-	-	-	-	-	-	A	-	4
ANC 26	MA	35.2-38.2	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 27	MA	45.6	M	-	-	-	-	-	-	-	-	-	A	-	A	-	A	A	-	4
ANC 28	MA	35.2	M	A	A	**P**	A	A	A	A	A	A	-	A	A	A	-	A	-	4
ANC 32B	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
ANC 34	MA	48.1	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 35	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 38	OA	66.6	PF	A	A	A	A	A	A	-	-	-	-	A	A	-	A	A	-	4
ANC 39	YA	28.7	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 41	MA	35.3-38.3	PF	A	A	A	-	-	-	-	-	-	-	A	A	-	-	A	-	4
ANC 41A Big	AUD	UD	F	A	A	A	A	A	A	-	-	-	-	-	-	-	A	-	-	4
ANC 41A Small	AUD	UD	PF	-	-	-	A	A	A	A	A	A	A	-	-	A	A	-	-	4
ANC 42	OA	73.1	PF	A	A	A	P?	A	A	A	A	A	-	A	A	A	A	A	-	**3**
ANC 43	MA	48.1	M	A	A	A	-	-	-	A	A	A	A	A	A	-	A	A	A	4
ANC 45	OA	60-61.2	F	A	A	A	A	A	A	A	A	A	A	-	-	A	A	-	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
ANC 45A	MA	48.1	F	A	A	A	-	-	-	A	A	A	-	A	A	A	A	-	-	4
ANC 46	YA	17-25	M	A	A	A	-	-	-	A	A	A	-	-	-	A	A	A	A	4
ANC 47	OA	61.2	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 48B	OAL	16-18	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 49	MA	48.9	M	A	A	A	A	-	-	A	A	A	A	A	A	-	-	A	A	4
ANC 50	OA	76.2	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 52	AUD	UD	PF	-	-	-	A	A	A	A	A	A	-	-	-	A	A	-	-	4
ANC 53	OA	79	PF	A	A	A	A	A	A	A	A	A	-	-	A	A	A	A	-	4
ANC 56	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 57	OA	73.8	M	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	A	-	4
ANC 58	OA	79.6	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
ANC 61	MA	48.1	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 62	YA	25	F	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 63	MA	48.1	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	A	4
ANC 64	OA	65.4	M	A	A	A	-	-	-	A	A	A	-	A	A	-	A	-	-	4
ANC 65	MA	45.6	PM	A	A	A	-	-	-	A	A	A	-	A	A	A	A	A	-	4
ANC 66	MA	38.2	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
ANC 67	OA	60	F	-	-	-	-	-	-	A	A	A	A	A	A	-	A	A	-	4
ANC 68	MA	48.1	M	-	-	-	-	-	-	-	-	-	-	A	A	-	A	A	-	4
ANC 69	AUD	UD	PF	A	A	A	A	A	A	A	A	A	-	-	-	A	-	-	A	4
ANC 72	YA	25-35	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	-	A	4
ANC 75	AUD	UD	UD	A	A	A	-	-	-	-	-	-	-	-	-	-	-	-	-	4
ANC 76	OAL	17-21	F	A	A	A	A	A	A	A	A	A	-	-	-	A	-	-	-	4
ANC 77	YA	25-35	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	-	A	4
ANC 78	MA	36.9	F	A	A	A	-	-	-	A	A	A	A	A	A	-	A	A	**P**	**3**
ANC 80	AUD	UD	PM	-	-	-	A	A	A	A	A	A	-	-	A	A	A	-	-	4
ANC 81	MA	48.1	F	A	A	A	-	-	-	A	A	A	A	-	A	-	A	A	A	4
ANC 82	OAL	14-16	PF	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 92	MA	33.2	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 93	MA	35.2	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 94	MA	35.2-38.2	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 96	YA	25-35	PF	-	-	-	-	-	-	A	-	-	-	-	A	A	A	-	**P**	4
ANC 98	OA	60-61.2	M	**P**	**P**	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	**3**
ANC 102	YA	25-35	F	A	A	A	-	-	-	A	A	A	A	A	A	-	-	A	A	4
ANC 104	MA	30.7	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
ANC 106	MA	48.1	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 107A	OAL	16-18	M	A	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 108	OAL	16-21	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 109	MA	36.4	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 110	MA	33-45	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 111	YA	19-25	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 112	YA	30.7	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 112A	AUD	UD	UD	-	-	-	A	A	A	-	A	A	-	-	-	-	A	A	-	4
ANC 113	MA	48.1	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	**P**	-	**2**
ANC 115	MA	35.2-38.2	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 116	OA	50.9	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 117	OA	71.7	M	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	A	-	4
ANC 118	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 119	YA	17-25	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	-	4
ANC 120	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 121	MA	35.2-38.2	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 122	MA	35.2	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 123	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 128	YA	25-35	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 133	YA	17-35	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 134	MA	34.5	F	A	A	A	A	-	A	A	A	A	A	A	A	-	-	A	-	4
ANC 135	OA	45+	M	A	A	A	A	A	A	A	-	-	-	A	A	A	A	A	**P**	**3**
ANC 136	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 137	OA	45+	M	-	-	-	-	-	-	A	A	A	-	-	-	-	-	-	-	4
ANC 140	YA	29.5	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 141	OA	74.4	PM	A	A	A	A	A	A	A	A	A	-	-	A	A	A	A	A	4
ANC 142	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 143	MA	28.7	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 144	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 147	OA	77.5	PM	A	A	A	A	A	A	A	A	P?	-	A	A	A	A	A	-	4
ANC 148A	MA	25+	PF	A	A	A	-	-	-	A	A	A	-	-	-	A	-	-	-	4
ANC 152	YA	15-24	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 154	OA	75	F	A	A	A	A	A	A	A	A	A	-	-	A	A	A	A	-	4
ANC 155	AUD	UD	UD	A	A	A	A	A	A	A	A	A	-	-	A	A	-	A	A	4
ANC 156	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
ANC 157	MA	38.2	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 158	AUD	UD	M	-	-	-	-	-	-	-	-	-	-	-	A	-	A	-	-	4
ANC 159	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
ANC 160	OAL	17-21	F	A	A	A	A	-	A	-	A	A	-	-	-	A	A	A	A	4
ANC 161A	AUD	UD	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
ANC 162	OAL	15-17	F	A	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 165	YA	30.7	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 167	OAL	17-19	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 168	YA	18-27	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 170	MA	48.1	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 171	OAL	15.3	PF	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 172	MA	33-45	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
ANC 173	MA	38.2	PF	A	A	A	A	A	A	A	A	A	A	-	A	A	A	A	-	4
ANC 175	YA	30.7	PM	-	-	-	A	A	-	A	A	A	-	-	-	A	A	-	A	4
ANC 176	MA	33-45	F	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	A	4
ANC 177	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 178	YA	25-35	F	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 179	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 182	YA	17-21	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
ANC 183	OA	50+	PF	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	-	4
ANC 184	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 185	OAL	15-19	F	A	A	A	-	-	A	A	A	A	A	A	A	A	A	A	**P?**	4
ANC 185A	MA	35.2	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 188	YA	17-25	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 190	YA	25-35	PF	A	A	A	A	-	-	A	A	A	A	A	A	A	A	A	A	4
ANC 191	OA	50+	F	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 193	YA	25-35	F	A	A	A	A	A	A	-	A	A	-	-	-	A	-	A	-	4
ANC 198	MA	33-45	M	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	4
ANC 199	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
ANC 200	YA	18-27	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 201	OA	61.2	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 202	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	**P**	**3**
ANC 204A	OA	50+	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 205	OAL	15-21	F	-	-	-	-	-	-	A	A	A	-	A	A	A	A	A	A	4
ANC 209	YA	25-35	PM	-	-	-	A	A	-	-	-	-	-	-	-	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
ANC 210	YA	25-35	PM	A	A	**P**	A	A	A	A	A	A	-	-	-	A	-	A	A	4
ANC 211	YA	25-35	PM	A	A	A	A	A	A	A	A	A	-	-	-	A	A	A	A	4
ANC 212	MA	35.2-38.2	F	**P**	P	A	A	A	A	A	A	A	-	A	A	-	A	A	-	**2**
ANC 213	AUD	UD	M	-	-	-	-	-	-	-	-	-	-	-	-	-	A	A	-	4
ANC 214	MA	33-45	M	A	A	A	-	-	-	A	A	A	-	-	-	A	A	-	-	4
ANC 216	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	**P?**	4
ANC 217	OA	45+	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 217A	MA	42.1	M	A	A	A	A	A	A	A	A	A	-	-	A	A	-	-	A	4
ANC 218	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 220	MA	23-70	F	A	A	**P**	A	A	-	A	A	A	A	A	A	A	A	A	**P**	**3**
ANC 221	YA	30.7	M	-	-	-	-	-	-	A	A	A	A	A	A	-	-	A	-	4
ANC 222	MA	33-45	PM	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	A	4
ANC 223	AUD	UD	UD	-	-	-	A	A	-	-	-	-	-	-	-	-	-	-	-	4
ANC 224	OA	45+	F	A	A	A	A	-	A	A	A	A	-	-	A	A	A	A	-	4
ANC 225	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 226	YA	17-25	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 229	YA	25-35	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 230	YA	18-27	M	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 230A	MA	48.1	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 234	YA	31.3	AB	A	A	A	-	-	-	A	A	A	-	A	A	-	A	A	A	4
ANC 235	YA	25-35	UD	A	A	A	A	-	A	A	A	A	-	A	A	A	A	A	A	4
ANC 237	OA	45+	PM	-	-	-	-	-	-	A	A	A	-	-	-	-	A	-	A	4
ANC 238	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 240	YA	25-35	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 241	OA	50+	PF	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 242	MA	33-45	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 243	YA	23.4-41.4	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 244	YA	17-35	PM	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 247	MA	45.6	F	A	A	A	A	-	A	A	A	A	-	-	A	-	-	A	-	4
ANC 248	YA	25-35	PM	-	-	-	A	-	-	-	-	-	-	-	-	-	-	-	A	4
ANC 252	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	-	A	A	A	A	-	4
ANC 256	AUD	UD	PF	-	-	-	-	-	-	A	A	A	-	-	A	-	-	A	-	4
ANC 257	OA	45-66	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 259	YA	17-25	F	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 262A	MA	35.2-38.2	F	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	Diagnosis
ANC 263	OA	63.2-110	PF	A	**P**	A	A	A	A	**P**	A	A	-	-	A	A	A	A	**P**	**1**
ANC 263A	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	-	-	-	A	-	4
ANC 266	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	-	4
ANC 267	YA	25-35	PF	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-	4
ANC 269	YA	25-45	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 270	YA	17-25	F	A	A	A	A	A	A	A	A	A	-	-	-	A	A	-	**P?**	4
ANC 271	AUD	UD	UD	A	A	A	A	A	A	A	A	A	-	-	-	A	A	-	A	4
ANC 272	AUD	UD	UD	A	A	A	-	-	-	A	A	A	-	-	-	-	-	-	-	4
ANC 274	OAL	18-19	F	-	-	-	-	-	-	-	-	-	A	A	A	-	-	A	-	4
ANC 276	MA	48.1	F	-	-	-	-	-	-	-	-	-	A	A	A	-	-	A	-	4
ANC 277	AUD	UD	PM	-	-	-	A	A	A	A	A	A	-	A	A	A	A	A	**P?**	4
ANC 278	YA	25-35	PM	A	A	A	A	A	A	A	A	A	-	A	A	A	A	-	A	4
ANC 280	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	-	-	A	A	A	-	4
ANC *2	OA	83.4	PF	A	A	**P**	A	A	A	A	A	A	-	A	A	A	A	A	-	4
ANC UNCAT A	OA	76.1	M	-	-	-	A	A	A	A	A	A	-	-	A	A	A	A	-	4
ANC UNCAT B	OA	50+	PM	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC UNCAT C	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	-	-	-	A	4
ANC UNCAT DA	OA	45+	PF	-	-	-	-	-	-	-	-	-	A	A	A	-	A	A	-	4
ANC UNCAT E	AUD	UD	UD	A	A	A	A	A	A	A	A	A	-	-	-	-	A	-	-	4
ANC UNCAT E2	YA	25-35	PM	A	A	A	A	A	A	A	A	A	-	-	-	A	A	-	A	4
ANC UNCAT F	MA	5.2	M	A	A	**P**	A	A	A	A	A	A	A	A	A	A	A	A	A	4

Features scored are healing or unhealed rib fractures (1), rib fractures with spiculated bone (2), healed rib fractures (3), scapula spinous process pseudofractures (4), scapula coracoid process pseudofractures (5), scapula lateral border pseudofractures (6), vertebral body compression fractures (7), vertebral lamina pseudofractures (8), healed vertebral lamina fractures (9), inferior pubic ramus pseudofractures (10), iliac crest fractures (11), ilium pseudofractures (12), healing or unhealed clavicle fractures (13), long bone pseudofractures (14), proximal femur pseudofractures (15), and histological features on SEM (16). Nondiagnostic features are highlighted in red, possible features of residual deficiency in green, and probable features of adult deficiency in blue. Features scored as present (P), absent (A), or unobservable (-). Ages abbreviated as YAL (Younger adolescent, 12-15 years), OAL (Older adolescent, 16-19 years), YA (Young adult, 20-34 years), MA (Middle adult, 35-49 years), OA (Older adult, 50+ years), AUD (Adult undetermined). Sex abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), UD (undetermined). Diagnostic categories are outlined in Section 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate).

Table C.5. Features of healed vitamin D deficiency scored for Isola Sacra adults

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 5	OAL	15-21	F	-	A	A	-	A	A	4
SCR 15	OA	36.9-90.7	PM	-	-	A	A	A	A	4
SCR 16	MA	25-45	F	-	-	-	-	A	A	4
SCR 17	AUD	UD	UD	-	-	-	-	A	A	4
SCR 18	YA	25-35	PF	**P**	A	A	A	A	A	**2**
SCR 19	YA	25-35	UD	-	-	-	-	A	A	4
SCR 20	YA	25.7-47.1	F	-	-	-	A	A	A	4
SCR 21	YA	16.4-64.6	F	A	A	-	A	A	A	4
SCR 27	YA	17-25	PF	A	A	A	A	A	**P**	1
SCR 30	MA	33-45	PM	-	-	-	A	A	A	4
SCR 32	OAL	14-19	PF	A	-	A	A	A	A	4
SCR 34	AUD	UD	UD	A	-	-	-	-	A	4
SCR 35	OAL	14-21	M	-	A	-	-	A	A	4
SCR 36	OAL	16-21	PM	A	A	A	A	A	A	4
SCR 37	OA	50-75	M	A	A	A	A	A	A	**3**
SCR 38	YA	25-35	M	A	A	A	A	A	A	4
SCR 39	OA	34-87	F	-	-	-	A	A	A	4
SCR 44	MA	25-45	M	A	-	A	A	A	A	4
SCR 52	OAL	15-21	PF	-	-	-	-	A	A	4
SCR 53	OA	23.4-88.9	F	-	-	-	-	A	A	4
SCR 55	YA	17-35	PF	-	-	A	A	A	A	4
SCR 57	YA	26.9-62.4	UD	-	A	-	A	A	A	4
SCR 59	YA	17-25	F	-	-	A	A	A	A	4
SCR 60	OA	34-86	PM	-	A	-	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 64	YA	19-23	UD	-	-	-	-	-	A	4
SCR 67	YA	25-35	F	-	A	-	A	A	A	4
SCR 68	YA	17-25	PF	-	-	A	-	A	A	4
SCR 69	YA	17-35	F	A	A	**P**	A	A	A	4
SCR 71	AUD	UD	UD	-	-	-	-	-	A	4
SCR 73	AUD	UD	UD	-	-	-	-	A	A	4
SCR 75	OAL	17-21	PM	A	-	A	A	A	A	**3**
SCR 76	OA	49.4-91.8	M	A	A	A	A	A	A	4
SCR 77	YA	25-45	PM	-	-	-	A	-	A	4
SCR 79	YA	25-35	F	-	-	A	-	A	A	4
SCR 82	MA	26-70	F	A	-	A	A	A	A	4
SCR 83	MA	26-70	F	-	-	A	A	A	A	4
SCR 84	MA	33-45	PF	-	-	A	A	A	A	4
SCR 85	YA	21-46	PM	A	-	-	A	-	A	4
SCR 86	OAL	17-25	M	A	-	A	A	A	A	4
SCR 87	OA	71.3-90.3	UD	-	-	-	A	A	A	4
SCR 88	YA	17-35	M	-	-	-	-	A	A	4
SCR 89	AUD	UD	UD	-	-	-	-	-	A	4
SCR 90	YA	17-25	M	A	A	A	A	A	A	4
SCR 97	MA	25-75	PM	A	A	A	A	A	A	4
SCR 98	OAL	17-21	PF	A	-	-	A	A	A	4
SCR 99	YA	25-35	M	-	-	A	A	A	A	4
SCR 105	MA	33-45	F	-	A	A	-	-	-	5
SCR 106	OAL	15-24	F	A	A	A	A	A	A	4
SCR 113	MA	33-45	F	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 116	YA	17-25	M	-	-	-	-	-	A	4
SCR 120	YA	17-25	M	-	-	-	-	-	A	4
SCR 122	AUD	UD	UD	-	A	-	-	A	A	4
SCR 123	AUD	UD	UD	-	-	-	A	A	A	4
SCR 125	YA	17-25	PF	-	A	-	-	A	A	4
SCR 126	OAL	15-18	PM	A	-	A	-	A	A	4
SCR 127	YA	25-35	M	A	-	-	-	A	A	4
SCR 128	MA	26-70	PF	A	-	A	A	A	A	4
SCR 129	YAL	14-16	UD	-	-	A	-	A	A	4
SCR 130	AUD	UD	UD	-	-	-	-	-	A	4
SCR 132	YA	17-25	UD	-	-	A	-	A	A	4
SCR 133	OAL	17-19	PM	A	A	-	A	A	A	4
SCR 134	MA	33-45	M	A	-	A	A	A	A	4
SCR 138	OAL	15-18	M	-	A	A	A	A	A	4
SCR 142	YA	17-25	M	-	A	-	-	A	A	4
SCR 143	MA	34-86	M	A	A	A	A	A	A	4
SCR 144	YA	19-25	M	-	A	A	A	A	A	4
SCR 145	MA	33-57	M	A	A	**P?**	A	A	A	4
SCR 148	OA	42-87	F	-	A	-	A	A	A	4
SCR 150	OA	26.2-86.7	PF	A	A	-	A	A	A	4
SCR 151	MA	25-35	M	A	A	A	A	A	**P?**	4
SCR 152	MA	25-83	PF	A	-	A	A	A	A	4
SCR 155	OAL	17-21	UD	-	A	-	-	A	A	4
SCR 156	OA	42-87	PF	-	-	A	A	A	A	4
SCR 157	OAL	16-21	PM	-	-	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 158	MA	25-88.1	M	-	-	A	A	A	A	4
SCR 159	AUD	UD	F	-	-	A	-	A	**P**	**1**
SCR 160	MA	26-70	F	A	A	-	A	A	A	4
SCR 161	YA	24.3-45	PF	-	-	A	A	A	**P**	**2**
SCR 163	MA	25-66	M	A	A	A	A	-	A	4
SCR 169	YA	18.3-33.2	F	-	-	A	-	A	A	4
SCR 170	YA	25-35	PM	-	-	A	A	A	**P?**	**2**
SCR 171	YA	25-83	F	-	-	A	A	A	A	4
SCR 172	MA	33-45	M	-	-	-	-	A	A	4
SCR 173	MA	25-83	F	A	A	A	A	A	A	4
SCR 174	YA	17-25	F	A	A	A	A	A	A	4
SCR 177	AUD	UD	F	-	-	-	-	A	A	4
SCR 178	YA	25-35	M	-	-	-	-	A	A	4
SCR 179	MA	33-45	M	A	A	A	A	A	A	4
SCR 180	YA	17-25	UD	A	A	-	-	A	A	4
SCR 181	YA	25-35	M	A	A	A	A	-	A	4
SCR 183	MA	42-87	PF	A	-	A	A	A	A	4
SCR 184	MA	33-45	M	A	A	A	A	A	A	4
SCR 185	OA	69.2-89.7	PF	-	-	A	A	A	A	4
SCR 186	MA	25-45	M	A	A	A	-	-	A	4
SCR 188	YA	17-25	AB	-	A	A	A	A	A	4
SCR 189	MA	25-35	PM	A	A	A	A	A	A	4
SCR 190	YA	17-25	F	A	A	A	A	A	**P?**	**2**
SCR 191	MA	25-35	M	A	A	A	A	A	A	4
SCR 192	MA	33-45	UD	A	A	-	-	-	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 193	YA	17-25	F	A	A	A	A	A	A	4
SCR 194	MA	25-35	F	A	A	A	A	A	A	4
SCR 196	OAL	17-25	M	-	-	-	-	A	A	4
SCR 197	YA	18-27	F	-	A	A	A	A	**P**	**2**
SCR 198	YA	19-34	M	A	A	A	A	A	A	4
SCR 199	YA	17-25	F	-	A	A	A	A	A	4
SCR 201	MA	25-35	F	-	A	A	A	A	A	4
SCR 203	OAL	15-18	PF	-	A	A	A	A	A	4
SCR 207	YA	17-25	M	-	-	-	-	-	-	5
SCR 208	AUD	UD	UD	-	-	-	-	-	-	5
SCR 210	MA	25-35	F	-	-	-	A	A	A	4
SCR 211	AUD	UD	UD	-	-	-	-	-	A	4
SCR 212	YA	17-25	UD	-	-	-	-	-	-	5
SCR 213	AUD	UD	UD	-	-	-	-	A	A	4
SCR 215	YA	25-35	M	-	-	-	A	A	A	4
SCR 216	OAL	15-17	F	A	A	A	A	A	A	4
SCR 217	YA	25-35	UD	A	A	A	-	A	A	4
SCR 219	YAL	15-16	UD	-	-	A	-	-	A	4
SCR 220	OAL	17-20	M	A	A	A	A	A	**P?**	**1**
SCR 221	MA	23-57	M	A	A	A	A	A	A	**3**
SCR 223	YA	17-25	UD	-	-	-	-	A	A	4
SCR 224	YA	17-25	M	-	-	-	-	-	A	4
SCR 226	OAL	16-18	F	A	A	A	A	A	A	4
SCR 227	MA	25-35	F	-	-	-	-	A	A	4
SCR 228	MA	19.5-79.3	UD	A	-	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 231	YA	28.4-63.6	M	A	A	-	-	A	A	4
SCR 232	YA	25-35	M	-	A	-	A	A	A	4
SCR 233	MA	25-63.2	F	-	A	A	-	A	A	4
SCR 234	MA	25-58.2	UD	-	-	A	A	A	A	4
SCR 236	YA	25-35	UD	-	-	-	-	A	A	4
SCR 239	MA	25-35	F	-	A	A	A	-	A	4
SCR 241	MA	33-45	F	-	A	A	A	A	A	4
SCR 242	YA	25-35	UD	-	-	-	-	A	A	4
SCR 243	YA	17-25	UD	A	A	A	A	A	A	4
SCR 245	YA	17-25	F	**P**	A	**P**	A	A	A	4
SCR 246	YA	17-25	PM	-	-	-	A	-	A	4
SCR 250	MA	25-35	M	A	A	A	A	A	A	4
SCR 251	YA	17-25	PM	A	A	A	-	-	A	4
SCR 252	MA	25-35	F	A	A	A	A	A	A	4
SCR 253	AUD	UD	M	-	-	-	A	-	A	4
SCR 254	AUD	UD	UD	-	-	-	-	-	A	5
SCR 256	MA	23-57	M	-	-	-	-	A	A	4
SCR 257	AUD	UD	UD	-	-	-	-	-	A	4
SCR 258	YA	17-25	F	-	-	-	-	A	A	4
SCR 260	AUD	UD	UD	-	-	-	-	A	A	4
SCR 261	OA	45+	M	A	A	A	A	A	A	4
SCR 262	MA	26-70	PF	-	-	-	A	A	A	4
SCR 263	OAL	15-18	F	-	-	-	A	A	A	4
SCR 264	OA	67-110	M	-	-	A	A	A	A	4
SCR 265	AUD	UD	UD	-	-	-	-	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 266	AUD	UD	UD	-	-	-	-	-	A	4
SCR 267	AUD	UD	UD	-	-	-	-	-	A	4
SCR 269	YA	25-35	PF	-	A	**P**	-	A	**P**	**3**
SCR 271	OAL	18-23	PF	A	-	A	A	A	A	4
SCR 272	YA	21-53	F	-	A	A	A	A	A	4
SCR 280	AUD	UD	UD	-	-	-	-	A	A	4
SCR 281	MA	25-49	PF	-	A	-	-	A	A	4
SCR 282	YA	17-25	M	A	A	A	A	A	A	4
SCR 283	AUD	UD	UD	-	-	-	-	-	A	5
SCR 284	AUD	UD	UD	-	-	-	-	-	A	5
SCR 285	MA	25-45	F	A	A	A	-	-	A	4
SCR 286	MA	25-35	PF	-	A	A	A	A	A	4
SCR 287	MA	26-70	F	A	A	A	A	A	A	4
SCR 288	MA	25-45	PM	A	A	A	A	A	A	4
SCR 289	MA	25-73.9	PF	-	-	-	-	-	A	4
SCR 291	YA	25-35	F	-	A	A	A	A	A	4
SR 292	YA	17-25	PF	-	-	A	-	A	A	4
SCR 293	AUD	UD	M	-	A	-	-	-	A	4
SCR 294	YA	25-35	F	-	A	A	-	A	A	4
SCR 295	YA	18-27	F	-	A	A	A	A	A	4
SCR 296	YA	17-25	PF	-	A	**P**	A	A	A	4
SCR 297	YA	25-35	M	-	A	A	A	A	A	4
SCR 298	MA	25-45	M	-	A	A	A	A	A	4
SCR 299	YA	17-25	F	-	-	A	-	A	A	4
SCR 301	MA	33-45	M	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 302	MA	25-83	AB	-	A	A	A	A	A	4
SCR 303	YA	25-35	M	A	A	A	A	A	A	4
SCR 304	AUD	UD	UD	-	-	-	-	-	A	5
SCR 305	YA	17-25	F	-	A	A	A	A	A	4
SCR 306	OAL	15-25.2	PF	A	A	A	-	A	A	4
SCR 307	MA	25-89.5	F	A	A	A	-	A	A	4
SCR 308	OA	44.6-92.1	M	A	A	A	A	A	A	4
SCR 310	YAL	14-16	AB	A	A	A	A	A	A	4
SCR 312	YA	25-35	F	A	A	A	A	A	A	4
SCR 314	YA	17-35	F	-	A	A	A	A	A	4
SCR 317	OAL	17-18	PM	A	A	A	-	A	A	4
SCR 318	MA	19.6-82.9	UD	-	-	-	-	A	A	4
SCR 319	OAL	16-18	M	A	A	A	-	A	A	4
SCR 320	YA	17-21	F	A	A	A	A	A	A	4
SCR 321	YA	17-27	PF	A	A	A	A	A	A	4
SCR 322	OAL	14-19	PF	A	-	A	A	A	A	4
SCR 323	MA	33-83	F	-	A	A	A	A	A	4
SCR 324	YA	17-25	F	-	A	A	A	A	A	4
SCR 325	OAL	17-21	M	A	A	A	A	A	A	4
SCR 326	YA	17-35	F	-	-	-	-	A	A	4
SCR 328A	YA	21-53	F	-	-	A	A	A	A	4
SCR 329	MA	26-70	F	A	-	-	A	A	A	**3**
SCR 330	OAL	18-21	PF	A	A	A	A	A	A	4
SCR 331	YA	17-25	F	A	A	A	A	A	A	4
SCR 332	OAL	17-25	F	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 334	YA	17-25	F	A	A	A	A	A	A	4
SCR 335	YA	17-35	PF	-	-	-	A	A	A	4
SCR 336	MA	33-45	UD	-	-	-	-	-	A	4
SCR 337	OAL	15-17	PM	A	A	A	A	-	A	4
SCR 338	MA	33-45	PF	-	A	-	A	A	A	4
SCR 339	MA	25-57	M	A	A	A	A	A	A	4
SCR 340	YA	17-25	F	A	A	A	-	A	A	4
SCR 341	MA	25-45	M	A	A	A	A	A	A	4
SCR 342	YA	25-35	M	A	A	A	A	A	A	4
SCR 343	OAL	15-17	AB	A	A	A	A	A	A	4
SCR 344	YA	17-25	PM	A	A	A	A	A	A	4
SCR 347	YA	17-35	UD	-	-	-	-	-	A	4
SCR 350	AUD	UD	UD	-	-	A	A	A	A	4
SCR 352	OAL	16-21	PF	-	A	A	A	A	A	4
SCR 354	OAL	14-18	M	-	A	A	A	A	A	4
SCR 355A	YA	25-35	M	A	A	A	A	A	A	4
SCR 355B	AUD	UD	UD	-	-	-	-	-	A	5
SCR 358	YA	17-25	F	-	A	-	-	A	A	4
SCR 360	OAL	15-18	M	-	A	A	A	A	A	4
SCR 361	OAL	17-18	M	A	A	A	A	A	A	4
SCR 362	YA	17-25	F	-	-	-	A	A	A	4
SCR 363	YA	21-53	F	-	A	A	A	A	A	4
SCR 365	OA	72.6-90.7	UD	-	A	-	-	A	A	4
SCR 366	OA	45+	M	-	-	-	-	A	A	4
SCR 368	OAL	15-17	PM	A	-	-	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 369	OAL	17-21	PF	A	A	A	A	A	A	4
SCR 370	YA	20.9-39.1	F	-	-	-	A	A	A	4
SCR 371	OA	72.6-90.7	F	-	A	-	-	A	A	4
SCR 374	AUD	UD	UD	-	-	-	-	A	A	4
SCR 376	YA	17-35	PM	A	A	A	A	A	A	4
SCR 377	AUD	UD	UD	-	-	-	-	-	A	5
SCR 379	AUD	UD	UD	-	-	-	-	A	A	5
SCR 380	AUD	UD	UD	-	-	-	-	A	A	4
SCR 382	OA	74.6-91.3	F	-	-	-	-	A	A	4
SCR 383	OAL	17-21	M	-	-	-	A	A	A	4
SCR 389	OAL	15-19	M	-	A	-	A	A	A	4
SCR 390	AUD	UD	UD	-	-	-	-	A	A	4
SCR 391	YAL	14-16	M	-	-	-	-	A	A	4
SCR 394	OA	72.8-90.7	F	-	-	-	A	A	A	4
SCR 395	OAL	16-18	F	-	-	-	A	A	A	4
SCR 396	OAL	15-19	M	-	-	-	A	-	-	5
SCR 399	YA	25.7-48.9	UD	-	-	-	-	-	A	4
SCR 401	YA	17-25	PF	-	-	-	A	A	A	4
SCR 403	AUD	UD	UD	-	-	-	-	A	A	5
SCR 404	OAL	15-18	PF	-	A	-	A	A	A	4
SCR 405	AUD	UD	F	-	A	A	-	A	A	4
SCR 406	OAL	15-18	F	A	A	A	A	A	A	4
SCR 407	OA	UD	F	-	A	-	A	-	A	4
SCR 409	YA	17-35	F	**P**	A	-	A	A	A	**2**
SCR 410	AUD	UD	UD	-	-	-	-	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 411	OAL	16-21	F	A	**P?**	A	A	A	A	4
SCR 412	MA	23-57	PM	-	-	-	A	A	A	4
SCR 413	OAL	16-21	UD	A	A	A	-	-	-	5
SCR 414	OAL	</= 21	UD	-	A	-	-	-	A	4
SCR 415	YA	17-25	UD	-	-	-	-	A	A	4
SCR 416	OAL	16-19	F	A	A	A	A	A	**P**	**2**
SCR 417	MA	25-38	F	A	A	A	A	A	A	4
SCR 418	AUD	UD	UD	-	-	-	-	A	A	4
SCR 419	MA	33-45	F	-	A	A	-	A	A	4
SCR 420	YAL	14-16	PF	A	A	A	-	A	A	4
SCR 421	OAL	15.8-30.3	PF	-	-	-	-	A	-	4
SCR 422	MA	33-45	F	A	A	A	A	A	A	4
SCR 423	MA	33-45	M	-	-	-	-	A	A	4
SCR 424	MA	25-38	F	-	A	-	A	A	A	4
SCR 425	MA	25-45	PM	-	-	A	A	A	A	4
SCR 426	YA	17-25	PF	A	A	A	-	A	A	4
SCR 427	AUD	UD	UD	-	-	-	-	-	-	5
SCR 429	OA	38.5-91.6	UD	-	-	-	-	A	A	4
SCR 430	OA	32.4-89.9	PM	A	A	A	-	A	A	4
SCR 431	AUD	UD	F	-	A	A	-	A	A	4
SCR 433	YA	17-25	F	A	A	A	-	A	A	4
SCR 434	MA	25-83	F	A	A	A	A	A	A	4
SCR 435	YA	25-35	M	A	-	A	A	A	A	4
SCR 436	MA	25-45	F	-	-	-	A	A	A	4
SCR 437	OA	25-60	PF	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 438	AUD	UD	UD	-	A	-	-	A	A	4
SCR 439	MA	23-57	M	A	A	A	A	A	A	4
SCR 440	OA	50-93.4	M	A	A	A	A	A	A	4
SCR 442	OAL	18-19	F	-	-	-	-	A	A	4
SCR 443	YA	25-35	F	-	A	-	A	A	A	4
SCR 444	OAL	17-21	F	A	A	A	A	A	A	4
SCR 445	YA	17-25	F	-	-	A	A	A	A	4
SCR 447	YA	21-46	M	A	A	A	A	A	A	4
SCR 448	MA	17-38	M	A	-	A	A	A	A	4
SCR 449	OA	33-50+	M	-	A	-	-	A	A	4
SCR 450	YA	17-25	UD	-	-	-	-	-	A	4
SCR 452	YA	17-25	F	-	-	-	-	-	A	4
SCR 453	YA	18.3-33.7	M	-	A	A	-	A	A	4
SCR 454	YA	25-35	UD	-	-	-	-	A	A	4
SCR 455	OAL	17-21	UD	-	A	-	-	A	A	4
SCR 456	AUD	UD	UD	-	-	-	-	A	A	4
SCR 457	OA	55.7-93.2	PM	-	-	A	-	A	**P?**	**2**
SCR 458	YA	25.7-47.1	M	-	A	-	-	A	**P**	**2**
SCR 461	YA	17-35	UD	-	-	-	-	-	-	5
SCR 462	MA	23-57	MA	A	A	-	A	A	A	4
SCR 463	YA	17-35	PM	A	A	A	-	A	A	4
SCR 464	YA	17-29	PM	A	A	A	A	A	A	4
SCR 465	AUD	UD	M	-	-	-	-	A	A	4
SCR 466	MA	25-75	F	-	A	-	A	A	A	4
SCR 467	MA	25-83	F	-	A	-	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 468	YA	17-25	PM	-	A	A	A	A	A	4
SCR 469	OA	23-83.5	UD	-	A	-	-	A	A	4
SCR 470	YA	17-25	F	-	A	-	A	A	A	4
SCR 476	AUD	UD	UD	-	-	-	-	-	A	5
SCR 479	YA	17-25	PF	-	A	**P**	-	-	A	4
SCR 480	YA	21-46	M	-	-	-	A	A	A	4
SCR 481	AUD	UD	UD	-	-	-	-	A	A	4
SCR 482	AUD	UD	M	-	-	A	-	A	A	4
SCR 484	YA	17-25	F	-	A	A	A	A	A	4
SCR 485	YA	17-35	PM	A	A	-	A	A	A	4
SCR 486	MA	23-70	UD	-	-	-	A	A	A	4
SCR 487	YA	25-35	UD	-	-	-	-	-	A	4
SCR 488	AUD	UD	UD	-	-	-	-	-	A	4
SCR 489	MA	23-70	F	-	-	-	A	A	A	4
SCR 490	AUD	UD	UD	-	-	-	-	-	-	5
SCR 493	YA	17-25	UD	-	-	-	-	-	A	4
SCR 497	AUD	UD	UD	-	-	-	-	A	A	4
SCR 499	AUD	UD	UD	-	-	-	-	A	A	4
SCR 500	OAL	15-23	M	-	A	-	A	A	A	4
SCR 501	MA	26-70	PF	-	-	A	A	A	A	4
SCR 502	AUD	UD	UD	-	-	-	-	A	A	4
SCR 503	YA	25-35	UD	-	-	-	-	A	A	4
SCR 504	AUD	UD	UD	-	-	-	-	A	A	4
SCR 505	AUD	UD	UD	-	-	-	-	-	A	5
SCR 507	OAL	</= 21	F	A	-	-	A	-	A	5

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 508	YA	19-34	M	-	-	A	A	A	A	4
SCR 509	AUD	UD	UD	-	-	-	-	-	A	4
SCR 510	YA	17-38	PF	-	A	-	A	A	A	4
SCR 521	YA	17-25	UD	A	-	A	-	-	A	4
SCR 524	OA	53.7-92.8	UD	-	-	-	-	A	A	4
SCR 525	YA	25-35	M	A	A	A	A	A	A	4
SCR 526	YA	25-35	M	A	A	A	A	A	A	4
SCR 527	MA	23-57	M	-	-	-	A	-	-	5
SCR 535	AUD	UD	UD	-	-	-	-	-	A	4
SCR 544	AUD	UD	UD	-	-	-	-	A	A	4
SCR 545	YA	18-27	UD	-	-	-	-	A	A	4
SCR 549	YA	25-45	F	-	-	-	A	A	A	4
SCR 550	YA	27.4-51.1	UD	-	-	-	-	A	**P**	**2**
SCR 551	YA	19.8-35.1	M	-	-	-	-	A	A	4
SCR 553	YA	17-25	UD	-	-	-	-	A	A	4
SCR 556	AUD	UD	UD	-	-	-	-	-	-	5
SCR 559	AUD	UD	F	-	-	A	-	-	A	4
SCR 561	YAL	14-16	UD	-	-	A	-	A	A	4
SCR 562	MA	28-45	M	A	-	A	A	-	A	4
SCR 563	OAL	16-18	PM	A	A	A	A	A	**P**	**1**
SCR 565	AUD	UD	UD	-	-	-	-	-	-	5
SCR 566	AUD	UD	UD	-	-	-	-	A	A	5
SCR 567	YA	25-35	UD	-	-	-	-	-	A	4
SCR 568	YA	17-25	F	A	A	A	A	A	A	4
SCR 569	YA	17-25	UD	-	-	-	-	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 570	AUD	UD	UD	-	-	-	-	-	A	4
SCR 571	OAL	15-18	UD	-	-	-	A	A	-	5
SCR 573	OA	24.2-86.3	M	-	-	-	A	-	A	4
SCR 574	OAL	14-18	UD	-	-	-	-	-	A	4
SCR 575	OAL	17-21	M	-	A	-	A	A	A	4
SCR 576	MA	23-57	M	A	A	A	A	A	A	4
SCR 577	YAL	14-16	M	-	-	-	-	A	A	4
SCR 578	YA	22.6-55.2	UD	-	-	-	-	A	A	4
SCR 585	YA	25-35	UD	-	-	-	-	A	A	4
SCR 590	YA	25-35	M	A	A	-	-	A	A	4
SCR 591	AUD	UD	UD	-	A	-	-	A	A	4
SCR 592	YA	19-34	PM	A	A	A	A	A	A	4
SCR 601	AUD	UD	UD	-	-	-	-	A	A	4
SCR 602	YA	17-25	F	A	-	A	A	-	A	4
SCR 603	YA	30.6-62.7	UD	-	-	-	-	A	A	4
SCR 604	AUD	UD	UD	-	-	-	-	A	A	4
SCR 605	OAL	14-19	UD	-	-	A	A	A	A	4
SCR 607	MA	25-55	PF	-	-	A	-	A	A	4
SCR 608	YA	17.7-33.3	PF	-	-	-	A	A	A	4
SCR 609	OAL	15-18	M	-	-	-	A	-	A	4
SCR 611	OAL	17-19	UD	A	-	A	-	A	A	4
SCR 616	YA	25-35	PM	-	A	-	A	A	A	4
SCR 617	MA	17-75	PM	A	-	-	A	A	A	4
SCR 618	OAL	16-21	F	A	-	-	-	A	A	4
SCR 638	OAL	14-18	UD	-	-	-	-	A	-	5

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 645	OAL	15-18	UD	-	-	A	-	A	A	4
SCR 652	MA	25-83	F	-	-	-	A	A	**P**	**2**
SCR 665	OAL	16-18	M	-	-	-	A	-	A	4
SCR 666	OAL	14-18	UD	-	A	A	-	-	A	4
SCR 668	MA	23-57	PM	-	A	A	A	A	A	4
SCR 669	MA	37.4-85.8	F	-	-	-	A	A	A	4
SCR 670	YA	17-35	PM	A	A	A	-	A	A	4
SCR 673	MA	18.8-77	F	A	A	A	-	-	A	4
SCR 674	OAL	17-19	UD	-	-	-	-	-	A	4
SCR 676	OA	33+	M	-	-	-	-	A	A	4
SCR 677	OAL	16-19	F	-	-	-	A	A	A	4
SCR 678	MA	33-45	M	-	A	A	A	A	A	4
SCR 679	YA	17-27	PF	-	A	-	-	A	A	4
SCR 680	AUD	UD	F	-	A	-	-	-	A	4
SCR 682	MA	23-57	M	A	-	A	A	A	A	4
SCR 686	AUD	UD	UD	-	-	-	-	-	A	4
SCR 688	AUD	UD	UD	-	-	-	-	A	A	4
SCR 689	OAL	15-17	UD	-	-	A	-	-	-	5
SCR 690	MA	26-70	F	-	-	-	A	A	A	4
SCR 691	YA	18-27	F	-	A	A	A	A	**P**	**2**
SCR 692	YA	17-25	M	-	-	-	-	A	A	4
SCR 695	YA	17-38	F	-	-	-	A	A	A	4
SCR 697	OAL	17-18	UD	A	A	A	A	A	**P**	4
SCR 698	YA	25-35	AB	-	-	-	-	A	A	4
SCR 699	YA	17-25	F	-	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 702	MA	23-57	M	-	-	A	A	A	A	4
SCR 703	AUD	UD	UD	-	-	-	-	A	A	4
SCR 704	MA	16.2-82.8	UD	-	-	-	-	A	A	4
SCR 705	MA	23-57	M	-	A	-	A	A	A	4
SCR 706	YA	21-46	M	-	-	-	A	A	A	4
SCR 708	AUD	UD	UD	-	-	-	-	A	A	4
SCR 709	OA	42.4-90.5	F	A	-	-	A	A	A	4
SCR 710	OAL	17-21	F	-	-	-	A	A	A	4
SCR 711	OA	22.5-88.9	PF	A	A	A	A	A	A	4
SCR 712	OAL	15-18	UD	A	-	-	-	A	A	4
SCR 713	OAL	14-18	M	-	A	-	-	A	A	4
SCR 714	YA	21-53	F	-	-	-	A	A	A	4
SCR 715	MA	23-57	M	-	A	-	A	A	A	4
SCR 717	YA	16.5-71.9	PF	A	A	-	-	A	A	4
SCR 718	AUD	UD	UD	-	-	-	-	A	A	4
SCR 719	MA	37-88.8	M	-	-	-	-	A	A	4
SCR 722	AUD	UD	UD	-	-	-	-	-	A	5
SCR 724	AUD	UD	UD	-	A	-	-	-	A	4
SCR 726	YA	17-25	F	-	-	A	A	-	A	4
SCR 727	AUD	UD	UD	-	-	-	-	-	A	4
SCR 728	YA	25-35	UD	-	-	-	-	-	-	5
SCR 729	MA	25-45	UD	-	-	-	-	A	A	4
SCR 730	MA	25-45	PM	A	A	-	-	A	A	4
SCR 732	YAL	14-16	UD	-	-	-	-	A	A	4
SCR 784	AUD	UD	UD	-	-	-	-	-	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 787	AUD	UD	F	A	-	-	A	-	A	4
SCR 790	YA	17-25	UD	-	-	-	-	-	A	4
SCR 794	OAL	17-25	PF	-	-	-	-	A	A	4
SCR 797	YA	17-25	UD	-	-	-	-	-	A	5
SCR 801	AUD	UD	UD	-	-	-	-	-	A	4
SCR 802	MA	25-37	PF	-	A	-	-	-	A	4
SCR 804	YA	19-25	M	-	A	-	A	A	A	4
SCR 805	OA	23-57	M	-	A	A	A	A	A	4
SCR 806	MA	25-57	M	A	A	A	A	**P**	**P**	**1**
SCR 807	YA	22.4-39.4	UD	A	-	-	-	-	A	4
SCR 808	YA	25-35	PM	-	A	-	A	-	A	4
SCR 809	OA	72.6-90.7	UD	-	-	-	-	A	A	4
SCR 813	OA	18.5-87.3	PM	-	A	A	-	A	A	4
SCR 814	OA	27-66	PM	-	**P**	-	A	A	A	4
SCR 816	MA	25-39	F	A	A	-	A	A	A	4
SCR 817	AUD	UD	UD	-	-	-	-	A	A	5
SCR 819	MA	33-45	M	A	A	A	A	A	A	4
SCR 820	AUD	UD	UD	-	-	-	-	A	A	4
SCR 821	YA	18-27	UD	-	-	-	-	-	A	5
SCR 822	MA	25-45	M	A	A	A	A	A	A	4
SCR 823	MA	25-45	PM	-	-	-	-	-	-	5
SCR 826	YA	17-35	UD	-	-	-	-	-	A	5
SCR 827	MA	18.1-81.5	F	-	A	A	A	A	A	4
SCR 828	OAL	15-29.6	UD	-	-	-	-	A	A	4
SCR 830	YA	17-25	PF	-	-	-	-	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
SCR 831	OAL	15-18	AB	A	A	A	A	A	A	4
SCR 833	YA	17-35	F	A	A	A	A	A	**P**	4
SCR 834	OA	33-57	M	-	A	A	A	A	A	4
SCR 835	YA	17-25	F	-	-	**P**	-	A	A	4
SCR 836	YA	17-35	PF	A	A	-	A	A	A	4
SCR 837	MA	33-45	M	-	-	-	A	A	**P**	**2**
SCR 838	YA	19-25	M	-	A	A	A	**P**	A	**1**
SCR 840	YA	17-25	M	A	A	A	A	A	A	4
SCR 841	YA	17-25	F	A	A	A	A	A	A	4

Features scored are sternum bending (1), scapula lateral border curvature (2), vertebral curvature (3), pubic symphysis angulation (4), anterolateral bending of the proximal femur (5), and residual bending of the long bones (6). Nondiagnostic features are highlighted in red, possible features of residual deficiency in green, and probable features of adult deficiency in blue. Features scored as present (P), absent (A), or unobservable (-). Ages abbreviated as YAL (Younger adolescent, 12-15 years), OAL (Older adolescent, 16-19 years), YA (Young adult, 20-34 years), MA (Middle adult, 35-49 years), OA (Older adult, 50+ years), AUD (Adult undetermined). Sex abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), UD (undetermined). Diagnostic categories are outlined in Section 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate).

Table C.6. Features of healed vitamin D deficiency scored for Ancaster adults

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
ANC 1	OAL	17-21	F	-	A	A	A	A	**P**	**3**
ANC 2	MA	35.2	PM	A	A	A	A	A	A	4
ANC 2A	YA	21-53	PM	-	A	A	A	-	-	5
ANC 3	MA	25-45	M	A	A	A	-	A	A	4
ANC 3*	MA	48.1	F	A	-	-	A	-	A	4
ANC 3A	MA	48.1	F	A	A	A	A	A	A	4
ANC 4	OA	45+	M	-	A	A	A	A	A	4
ANC 5	MA	48.1	PM	A	A	A	A	A	A	4
ANC 6	OA	77.2	PM	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
ANC 10	OA	81.5	F	A	A	A	A	A	A	4
ANC 11	YA	26-34	M	A	A	A	A	A	A	4
ANC 12	YA	25-35	M	A	A	A	A	A	A	4
ANC 12B	OA	82.2	M	A	A	A	A	A	A	4
ANC 13	MA	35.2-38.2	M	A	A	A	A	A	A	4
ANC 14	YA	25-35	PM	A	A	A	-	-	A	4
ANC 21	OA	60	F	-	A	A	A	A	A	4
ANC 22	OA	50+	PM	-	-	-	-	A	A	4
ANC 23	MA	33-45	M	A	A	A	A	A	A	4
ANC 24	MA	35.2	M	A	-	-	A	A	A	4
ANC 25	OA	75.7	F	-	-	-	-	A	A	4
ANC 26	MA	35.2-38.2	M	A	A	A	A	A	A	4
ANC 27	MA	45.6	M	-	-	-	A	A	A	4
ANC 28	MA	35.2	M	A	A	A	A	A	**P**	**3**
ANC 32B	AUD	UD	UD	-	-	-	-	-	A	4
ANC 34	MA	48.1	PM	A	A	A	A	A	A	4
ANC 35	YA	25-35	M	A	A	A	A	A	A	4
ANC 38	OA	66.6	PF	-	A	-	-	A	A	4
ANC 39	YA	28.7	M	A	A	A	A	A	A	4
ANC 41	MA	35.3-38.3	PF	-	-	-	-	A	A	4
ANC 41A Big	AUD	UD	F	A	A	-	-	-	A	4
ANC 41A Small	AUD	UD	PF	A	A	A	-	-	A	4
ANC 42	OA	73.1	PF	A	A	A	-	A	A	4
ANC 43	MA	48.1	M	-	-	-	A	A	A	4
ANC 45	OA	60-61.2	F	P	A	A	A	-	A	**2**
ANC 45A	MA	48.1	F	-	-	A	A	A	A	4
ANC 46	YA	17-25	M	A	-	A	-	A	A	4
ANC 47	OA	61.2	M	A	A	A	A	A	A	4
ANC 48B	OAL	16-18	M	A	A	A	A	A	A	4
ANC 49	MA	48.9	M	-	-	-	A	A	A	4
ANC 50	OA	76.2	PM	A	A	A	A	A	A	4
ANC 52	AUD	UD	PF	-	-	A	-	A	P	**3**
ANC 53	OA	79	PF	A	A	A	-	A	A	4
ANC 56	MA	33-45	M	A	A	A	A	A	A	4
ANC 57	OA	73.8	M	A	A	A	-	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
ANC 58	OA	79.6	M	-	A	A	A	A	A	4
ANC 61	MA	48.1	M	A	A	A	A	A	A	4
ANC 62	YA	25	F	A	A	A	A	A	**P**	**2**
ANC 63	MA	48.1	PF	A	A	**P**	A	-	A	**3**
ANC 64	OA	65.4	M	A	-	-	-	A	A	4
ANC 65	MA	45.6	PM	-	-	A	A	A	A	4
ANC 66	MA	38.2	F	A	A	A	A	A	A	4
ANC 67	OA	60	F	-	-	-	A	A	A	4
ANC 68	MA	48.1	M	-	-	-	-	A	A	4
ANC 69	AUD	UD	PF	-	A	-	-	-	**P**	**3**
ANC 72	YA	25-35	F	A	A	A	-	A	A	4
ANC 75	AUD	UD	UD	-	-	-	-	-	-	5
ANC 76	OAL	17-21	F	-	A	A	-	-	A	4
ANC 77	YA	25-35	M	-	A	-	-	A	A	4
ANC 78	MA	36.9	F	-	-	-	A	A	A	4
ANC 80	AUD	UD	PM	-	A	-	-	A	A	4
ANC 81	MA	48.1	F	-	-	A	A	A	A	4
ANC 82	OAL	14-16	PF	-	A	A	-	A	A	4
ANC 92	MA	33.2	M	A	A	A	A	A	A	4
ANC 93	MA	35.2	PM	A	A	A	A	A	**P**	**1**
ANC 94	MA	35.2-38.2	M	-	A	A	A	A	A	4
ANC 96	YA	25-35	PF	-	-	A	-	A	A	4
ANC 98	OA	60-61.2	M	A	A	**P**	A	A	A	**3**
ANC 102	YA	25-35	F	-	-	A	A	A	A	4
ANC 104	MA	30.7	PF	A	A	A	A	A	**P**	4
ANC 106	MA	48.1	PM	A	A	A	A	A	A	4
ANC 107A	OAL	16-18	M	A	A	A	A	A	A	4
ANC 108	OAL	16-21	M	A	A	A	A	A	A	4
ANC 109	MA	36.4	F	A	A	A	A	A	**P**	**3**
ANC 110	MA	33-45	PM	A	A	A	A	A	A	4
ANC 111	YA	19-25	PM	A	A	A	A	A	A	4
ANC 112	YA	30.7	F	-	A	A	A	A	A	4
ANC 112A	AUD	UD	UD	-	A	-	-	A	-	4
ANC 113	MA	48.1	F	A	A	**P**	A	A	A	4
ANC 115	MA	35.2-38.2	F	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
ANC 116	OA	50.9	F	A	A	A	A	A	A	4
ANC 117	OA	71.7	M	-	A	A	-	A	A	4
ANC 118	YA	25-35	M	A	A	A	A	A	A	4
ANC 119	YA	17-25	PF	A	A	A	A	-	A	4
ANC 120	YA	25-35	M	A	A	A	A	A	A	4
ANC 121	MA	35.2-38.2	M	A	A	A	A	A	A	4
ANC 122	MA	35.2	M	A	A	A	A	A	**P**	**1**
ANC 123	YA	25-35	F	A	A	A	A	A	A	4
ANC 128	YA	25-35	PF	A	A	A	A	A	A	4
ANC 133	YA	17-35	PF	-	A	A	A	A	A	4
ANC 134	MA	34.5	F	-	-	A	A	A	A	4
ANC 135	OA	45+	M	A	A	-	-	A	A	4
ANC 136	YA	25-35	M	**P**	A	A	A	A	**P**	**3**
ANC 137	OA	45+	M	-	-	-	-	-	-	5
ANC 140	YA	29.5	PM	A	A	A	-	A	A	4
ANC 141	OA	74.4	PM	A	A	A	-	**P**	A	**3**
ANC 142	YA	25-35	F	A	A	A	A	A	A	4
ANC 143	MA	28.7	PM	A	A	A	A	A	A	4
ANC 144	YA	25-35	PM	A	A	A	A	A	A	4
ANC 147	OA	77.5	PM	-	A	A	-	A	A	4
ANC 148A	MA	25+	PF	-	-	A	-	-	-	5
ANC 152	YA	15-24	F	A	A	A	A	A	A	4
ANC 154	OA	75	F	-	-	-	-	A	A	4
ANC 155	AUD	UD	UD	-	-	-	-	A	A	4
ANC 156	YA	25-35	PM	A	A	A	A	A	A	4
ANC 157	MA	38.2	F	A	A	A	A	A	A	4
ANC 158	AUD	UD	M	-	-	-	-	A	A	4
ANC 159	AUD	UD	UD	-	-	-	-	-	A	4
ANC 160	OAL	17-21	F	-	A	-	-	A	A	4
ANC 161A	AUD	UD	M	-	-	-	-	A	**P**	**1**
ANC 162	OAL	15-17	F	-	A	-	A	A	A	4
ANC 165	YA	30.7	M	A	A	A	A	A	A	4
ANC 167	OAL	17-19	M	A	-	A	-	A	**P**	4
ANC 168	YA	18-27	PF	A	A	A	A	A	A	4
ANC 170	MA	48.1	M	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
ANC 171	OAL	15.3	PF	-	A	A	-	A	**P**	**3**
ANC 172	MA	33-45	F	A	-	A	A	A	A	4
ANC 173	MA	38.2	PF	-	-	A	A	A	A	4
ANC 175	YA	30.7	PM	A	-	-	A	A	A	4
ANC 176	MA	33-45	F	A	A	A	-	A	A	4
ANC 177	YA	25-35	M	A	A	A	A	A	A	4
ANC 178	YA	25-35	F	A	A	A	A	A	A	4
ANC 179	YA	17-25	M	A	A	A	A	A	A	4
ANC 182	YA	17-21	F	A	A	A	-	A	A	4
ANC 183	OA	50+	PF	A	A	A	-	A	A	4
ANC 184	MA	33-45	M	A	A	A	A	A	A	4
ANC 185	OAL	15-19	F	-	A	A	A	A	A	4
ANC 185A	MA	35.2	M	A	A	A	A	A	A	4
ANC 188	YA	17-25	M	-	A	A	-	A	A	4
ANC 190	YA	25-35	PF	-	-	A	A	A	**P?**	4
ANC 191	OA	50+	F	A	A	A	A	A	A	4
ANC 193	YA	25-35	F	-	A	-	A	A	A	4
ANC 198	MA	33-45	M	-	-	-	-	A	A	4
ANC 199	AUD	UD	UD	-	-	-	-	-	A	4
ANC 200	YA	18-27	PM	A	A	A	-	A	A	4
ANC 201	OA	61.2	PM	A	A	A	A	A	A	4
ANC 202	YA	25-35	F	A	A	A	A	A	A	4 (4)
ANC 204A	OA	50+	M	A	A	**P**	A	A	A	**3**
ANC 205	OAL	15-21	F	-	-	-	-	A	A	4
ANC 209	YA	25-35	PM	-	-	-	-	A	A	4
ANC 210	YA	25-35	PM	A	A	A	-	A	A	4
ANC 211	YA	25-35	PM	A	A	A	-	A	A	4
ANC 212	MA	35.2-38.2	F	-	A	-	A	A	**P**	**1**
ANC 213	AUD	UD	M	-	-	-	-	A	A	4
ANC 214	MA	33-45	M	A	-	A	-	A	A	4
ANC 216	YA	17-25	M	A	A	A	A	A	A	4
ANC 217	OA	45+	F	-	A	A	A	A	**P**	**3**
ANC 217A	MA	42.1	M	-	A	-	-	-	-	5
ANC 218	YA	17-25	F	A	A	A	A	A	A	4
ANC 220	MA	23-70	F	A	-	**P**	A	A	A	**3**

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
ANC 221	YA	30.7	M	-	-	-	A	A	A	4
ANC 222	MA	33-45	PM	-	-	-	-	A	A	4
ANC 223	AUD	UD	UD	-	-	-	-	-	A	4
ANC 224	OA	45+	F	-	A	-	-	A	A	4
ANC 225	YA	25-35	PM	A	A	A	A	A	A	4
ANC 226	YA	17-25	F	A	A	A	-	A	A	4
ANC 229	YA	25-35	M	A	A	A	-	A	A	4
ANC 230	YA	18-27	M	A	A	A	A	A	**P**	4
ANC 230A	MA	48.1	M	A	A	A	A	A	A	4
ANC 234	YA	31.3	AB	-	-	-	-	A	A	4
ANC 235	YA	25-35	UD	A	A	A	-	-	A	4
ANC 237	OA	45+	PM	-	-	-	A	A	A	4
ANC 238	YA	25-35	M	A	A	A	A	A	A	4
ANC 240	YA	25-35	PM	A	A	A	-	A	A	4
ANC 241	OA	50+	PF	A	A	A	A	A	A	4
ANC 242	MA	33-45	F	A	A	-	A	A	A	4
ANC 243	YA	23.4-41.4	F	A	A	A	A	A	A	4
ANC 244	YA	17-35	PM	A	A	A	A	A	A	4
ANC 247	MA	45.6	F	-	A	-	-	A	**P**	**2**
ANC 248	YA	25-35	PM	-	-	-	-	-	A	4
ANC 252	YA	25-35	M	-	A	A	A	A	A	4
ANC 256	AUD	UD	PF	-	-	A	-	A	A	4
ANC 257	OA	45-66	PM	A	A	A	A	A	A	4
ANC 259	YA	17-25	F	A	A	-	-	A	**P**	4
ANC 262A	MA	35.2-38.2	F	A	A	**P**	A	A	A	**2**
ANC 263	OA	63.2-110	PF	A	A	A	-	A	A	4
ANC 263A	AUD	UD	UD	-	-	-	-	A	A	4
ANC 266	MA	33-45	M	A	A	A	A	A	A	4
ANC 267	YA	25-35	PF	-	-	-	-	-	A	4
ANC 269	YA	25-45	PM	A	A	A	A	A	A	4
ANC 270	YA	17-25	F	-	A	-	-	A	A	4
ANC 271	AUD	UD	UD	A	A	A	-	-	A	4
ANC 272	AUD	UD	UD	-	-	-	-	A	A	4
ANC 274	OAL	18-19	F	-	-	-	A	A	A	4
ANC 276	MA	48.1	F	-	-	**P**	A	A	A	**3**

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	Diagnosis
ANC 277	AUD	UD	PM	-	A	A	-	A	A	4
ANC 278	YA	25-35	PM	A	**P?**	A	-	-	A	4
ANC 280	YA	17-25	M	-	A	A	A	A	**P**	**3**
ANC *2	OA	83.4	PF	-	A	A	-	A	A	4
ANC UNCAT A	OA	76.1	M	-	-	-	-	A	A	4
ANC UNCAT B	OA	50+	PM	A	A	A	A	A	**P**	4
ANC UNCAT C	YA	25-35	M	-	A	-	A	-	-	5
ANC UNCAT DA	OA	45+	PF	-	-	-	-	A	A	4
ANC UNCAT E	AUD	UD	UD	-	A	A	-	-	A	4
ANC UNCAT E2	YA	25-35	PM	A	A	-	-	-	A	4
ANC UNCAT F	MA	5.2	M	A	A	A	A	A	**P**	**2**

Features scored are sternum bending (1), scapula lateral border curvature (2), vertebral curvature (3), pubic symphysis angulation (4), anterolateral bending of the proximal femur (5), and residual bending of the long bones (6). Nondiagnostic features are highlighted in red, possible features of residual deficiency in green, and probable features of adult deficiency in blue. Features scored as present (P), absent (A), or unobservable (-). Ages abbreviated as YAL (Younger adolescent, 12-15 years), OAL (Older adolescent, 16-19 years), YA (Young adult, 20-34 years), MA (Middle adult, 35-49 years), OA (Older adult, 50+ years), AUD (Adult undetermined). Sex abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), UD (undetermined). Diagnostic categories are outlined in Section 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate).

APPENDIX D – Raw Chronic Respiratory Infection Data

Table D.1. Features of chronic respiratory infections scored for Isola Sacra juveniles.

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 1	YC	1.5-2	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 2	OC	7-9	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 3	I	9-12 M	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 4	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 6	MC	4.5-6	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 7	MC	6-8	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 8	I/YC	0.5-1.5	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 9	OC	8.5-10	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 10	MC	3-5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 11	YC	1-1.5	-	-	-	-	-	A	-	-	-	-	-	-	-	5
SCR 12	I	6-8 M	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 13	YC	1.5-2	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 14	MC	2.5-4.5	A	A	A	A	A	A	-	A	A	A	A	A	A	4
SCR 22	I	4-6.5 M	-	-	-	A	A	A	A	A	A	A	A	A	A	4
SCR 23	MC	4-5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 24	OC	10-12	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 25	MC	5-7	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 26	YC	1.5-2.5	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 29	YAL	15-16	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 31	MC	5-6.5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 33	YC	1.25-1.75	A	A	A	A	A	A	-	-	A	-	A	A	A	4
SCR 40	MC	5-7	-	A	A	-	-	-	-	-	A	A	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 41	I/YC	UD	A	A	A	-	-	-	-	-	A	A	A	A	A	4
SCR 42	YC	2.5-3	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 43	MC	4-5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 45	I	9-12 M	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 46	I	7-9 M	A	A	A	A	A	A	-	-	A	-	A	A	A	4
SCR 47	I	5-9 M	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 48	I	5-7 M	-	A	A	-	-	A	-	-	A	-	A	A	A	5
SCR 49	MC	6-7	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 50	YAL	14-15	-	A	A	-	-	A	-	A	A	A	A	A	**P**	4
SCR 51	MC	6-7.5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 54	YC	1-1.5	-	A	A	A	A	A	-	A	A	-	A	A	A	4
SCR 56	YC	1.5-2	-	A	A	-	-	A	-	-	-	-	-	-	A	5
SCR 58	YAL	16+	-	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 61	YC	2-3	A	A	A	-	-	-	-	A	A	A	A	A	A	4
SCR 62	I	5-7 M	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 63	YC	1.5-2.5	A	A	A	A	A	A	-	-	A	-	A	A	A	4
SCR 65	YC	1.5-2	A	A	A	A	A	A	-	A	A	-	A	A	**P**	4
SCR 66	MC	2.5-4	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 71	MC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 72	IC	8-10	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 74	I	2-6 M	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 80	YAL	13-17	A	A	A	A	A	A	A	A	**P**	A	A	A	A	4
SCR 81	MC	2.5-4	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 91	I	0-1	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 92	I	0-0.125	A	A	A	-	-	A	A	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 93	MC	4.5-5	A	A	A	-	A	A	-	A	A	A	A	A	A	4
SCR 94	MC	4.5-5	A	A	A	-	A	A	-	A	A	A	A	A	**P**	4
SCR 95	MC	4-5	**P**	**P**	A	-	-	A	-	A	A	A	A	A	A	**1**
SCR 96	MC	4-5	A	A	A	-	-	-	-	A	A	A	A	A	**P**	4
SCR 100	YAL	14-16	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 101	YC	1.5-2.5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 102	YC	1.25-1.75	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 103	OC	10-11	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 104	MC	6-8	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 107	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 108	YC	1-1.5	A	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 109	I	0.5-1	A	A	A	A	A	A	-	A	A	A	A	A	A	4
SCR 110	YC	2-3	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 111	MC	7-8	A	A	A	-	-	A	-	A	A	A	A	A	A	4
SCR 112	OC	9-11	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 114	OC	8-9	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 115	MC	6-8	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 117	OC	</= 16	-	A	A	-	-	-	-	A	A	A	A	A	A	4
SCR 119	I/YC	</= 16	A	A	A	A	A	A	-	-	A	-	A	A	A	4
SCR 121	YAL	15-16	A	A	A	A	A	A	-	-	A	-	A	A	A	4
SCR 124	OC	</= 16	-	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 131	MC	3-4	A	A	A	-	-	A	-	A	A	A	A	A	**P**	4
SCR 135	YC	1-1.5	A	A	A	-	-	A	A	A	A	A	A	A	A	4
SCR 136	I/YC	0.75-1.25	**P**	**P**	A	A	A	A	-	-	A	-	A	A	**P**	**1**
SCR 137	YC	1-2	A	A	A	-	A	A	-	-	A	-	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 139	YC	1-1.5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 140	I	0.5-1	A	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 141	YC	1.5-2	A	A	A	A	A	A	-	A	A	A	A	A	A	4
SCR 146	YAL	10-14	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 147	OC	8-9	A	A	A	A	A	A	-	A	A	A	A	A	**P**	4
SCR 149	YAL	16-17.5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 153	YC	1.5-2.5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 154	YC	1-1.75	A	A	A	-	-	A	-	A	A	A	A	A	A	4
SCR 162	MC	3-5	A	A	A	A	A	A	-	A	A	A	A	A	A	4
SCR 164	MC	3-4.5	A	A	A	A	A	A	-	A	A	A	A	A	**P**	4
SCR 165	MC	5-7	-	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 166	YAL	13-15	A	A	A	A	A	A	-	-	A	A	A	A	**P**	4
SCR 167	YC	2.5-3	A	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 168	YC	2.5-3.5	**P**	**P**	A	A	A	A	A	A	A	A	A	A	A	**1**
SCR 175	OC	8.5-10	A	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 176	OC	7-8	A	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 182	MC	5-7	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 187	YC	1.5-2.5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 200	MC	6-8	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 202	I/YC	</= 21	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 204	YC	1.5-2.5	A	A	A	-	-	A	A	A	A	A	A	A	A	4
SCR 206	YC	1-1.5	-	A	A	-	-	A	-	-	-	-	-	-	-	5
SCR 209	OC	8-9	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 214	I/YC	UD	A	A	A	-	-	-	-	-	A	-	A	A	A	5
SCR 218	OC	8-10	-	A	A	-	-	A	-	-	A	A	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 222	I	0.5-1	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 225	MC	5.5-8	A	A	A	A	A	A	-	A	A	A	A	A	A	4
SCR 229	JUD	</= 16	-	A	A	-	-	-	-	-	A	-	A	A	A	5
SCR 230	MC	UD	A	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 235	MC	4-5	A	A	A	-	-	A	-	-	A	A	A	A	A	4
SCR 237	YAL	14-16	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 238	F/N	<0.125	-	-	-	-	-	-	A	A	A	-	A	A	A	4
SCR 240	OC	9-10	A	A	A	A	A	A	-	A	A	A	A	A	**P**	4
SCR 244	MC	5-7	A	A	A	A	A	A	-	A	A	A	A	A	**P**	4
SCR 247	OC	9-11	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 248	YC	1-2	**P**	A	A	A	A	A	A	A	A	A	A	A	A	**1**
SCR 249	OC	11-12	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 255	YC	1-2	-	A	A	-	-	A	-	-	A	A	A	A	A	4
SCR 259	OC	8-9	A	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 268	YAL	14-16	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 270	MC	2.5-4	A	A	A	-	-	-	-	-	A	-	A	A	**P**	4
SCR 273	YC	1.5-2.5	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 274	MC	2.5-4	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 275	YC	1-1.5	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 276	YC	1.5-2.5	**P**	A	A	A	A	A	A	A	A	A	A	A	A	**1**
SCR 277	I/YC	UD	-	A	A	-	-	-	-	-	A	-	A	A	A	5
SCR 278	MC	2.5-4	A	A	A	-	-	A	-	-	A	A	A	A	A	4
SCR 279	OC	9-10	A	A	A	-	A	A	-	-	A	A	A	A	A	4
SCR 290	OC	9-11	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 309	OC	7-9	A	A	A	A	A	A	A	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 311	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 313	OC	11-12	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 315	MC	7-8.5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 328	YAL	11-14	A	A	A	-	-	-	-	A	A	A	A	A	A	4
SCR 333	OC	11-12	A	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 345	YC	1-2.5	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 346	OC	</= 14	-	A	A	-	-	A	-	-	A	A	A	A	A	4
SCR 350	I/YC	UD	A	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 351	OC	8-10	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 356	OC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 357	OC	9-13	A	A	A	-	A	A	-	-	A	A	A	A	A	4
SCR 359	YC	1.5-2.5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 364	MC	3-5.4	-	-	-	-	-	-	A	-	A	-	A	A	A	5
SCR 367	I/YC	</= 18	A	A	A	-	-	-	-	A	A	-	A	A	A	5
SCR 372	F/N	<0.125	A	A	A	-	-	-	-	A	A	-	A	A	A	4
SCR 373	MC	</= 16	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 375	I/YC	</= 16	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 378	OC	</= 16	A	A	A	-	A	A	-	-	A	-	A	A	A	4
SCR 381	MC	7-7.5	-	-	-	-	-	-	-	-	A	-	A	A	**P**	4
SCR 384	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 387	I/YC	</= 18	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 388	I	0.5-1	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 392	MC	7-9	-	-	-	-	-	-	-	A	A	-	A	A	**P**	4
SCR 393	YAL	15-16	-	-	-	A	A	A	-	A	A	-	A	A	A	4
SCR 397	OC	10-11	-	-	-	-	-	-	-	A	A	-	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 398	YAL	11-16	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 400	YC	1-2	A	A	A	-	-	A	A	A	A	A	A	A	A	4
SCR 402	MC	4-5.6	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 408	I	6-10 M	A	A	A	-	-	A	-	-	A	A	A	A	A	4
SCR 428	OC	8-10	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 432	YC	1-2	A	A	A	-	A	A	-	A	A	A	A	A	**P**	4
SCR 441	YC	1.5-2	A	A	A	-	-	A	A	-	A	A	A	A	A	4
SCR 446	OC	8-10	A	A	A	A	A	A	-	A	A	A	A	A	A	4
SCR 451	YAL	13-15	-	-	-	-	-	A	-	-	A	-	A	A	A	4
SCR 459	I/YC	</= 16	A	A	A	-	-	A	-	-	A	-	A	A	**P**	4
SCR 460A	MC	2.5-4	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 460B	I/YC	</= 21	A	A	A	-	-	A	-	-	-	-	-	-	-	4
SCR 471	MC	7-7.5	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 473	I	0.75-1	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 474	YAL	14-16	A	A	A	A	**P?**	A	A	A	A	A	A	A	A	**3**
SCR 475	OC	</= 18	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 477	F/N	32-34 W IU	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 478	I	4-7 M	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 483	YC	1.5	-	A	A	-	-	A	-	A	A	-	A	A	A	4
SCR 491	I	0.125-0.25	A	A	A	-	-	A	-	A	A	-	A	A	A	4
SCR 492	MC	3.5-4	-	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 496	YC	2-2.5	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 506	MC	</= 16	A	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 511	I	8-13 M	A	A	A	-	-	A	-	A	A	A	A	A	**P**	4
SCR 512	YAL	16-25	A	A	A	A	A	A	-	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 513	I	0-5 M	A	A	A	-	-	A	-	A	A	A	A	A	**P**	4
SCR 514	MC	4-5	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 516	I	0-3 M	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 517	YAL	15-24	A	A	A	A	A	A	-	A	A	A	A	A	**P**	4
SCR 518	MC	2.5-4	A	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 519	OC	10-11	A	A	A	A	A	A	-	A	A	A	A	A	A	4
SCR 520	OC	8-10	-	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 522	MC	6-7	A	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 523	MC	5-5.7	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 528	MC	</= 16	-	A	A	-	A	A	-	-	A	-	A	A	A	5
SCR 529	YC	2-3	A	A	A	A	A	A	-	-	A	A	A	A	**P**	4
SCR 530	OC	7-10	A	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 531	I	5.5-7 M	A	**P**	A	A	A	A	-	-	A	A	A	A	A	**2**
SCR 532	I	7-11 M	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 533	YC	1-2	-	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 534	YAL	15-16	-	-	-	-	-	A	-	-	A	-	A	A	A	4
SCR 536	MC	3-4	A	A	A	A	A	A	-	A	A	A	A	A	**P**	4
SCR 537	YAL	14-15	-	A	A	-	-	A	-	-	A	A	A	A	A	4
SCR 538	OC	10-12	A	A	A	A	A	A	A	A	A	A	A	A	**P?**	4
SCR 539	OC	11-13	-	-	-	-	-	A	-	-	A	A	A	A	A	4
SCR 540	YAL	11.5-15	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 541	MC	3-4	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 542	YC	1-2	A	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 543	I	0-0.5	A	A	A	A	A	A	-	-	A	-	A	A	A	4
SCR 546	MC	4-5	-	-	-	-	-	-	-	-	A	A	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 547	MC	3.5-4.5	-	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 548	YC	2	A	A	A	-	-	-	-	A	A	-	A	A	A	4
SCR 552	MC	4-5	-	-	-	-	-	-	-	-	A	-	A	A	**P**	4
SCR 554	I/YC	</= 16	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 555	MC	6-7	-	-	-	-	-	-	-	-	-	-	-	-	-	5
SCR 557	YAL	12-14	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 560	MC	</= 16	-	A	A	-	-	-	-	-	A	-	A	A	A	5
SCR 564	YC	1.5-3	A	A	A	A	A	A	-	A	A	A	A	A	A	4
SCR 572	OC	UD	-	-	-	A	A	A	-	-	A	-	A	A	**P**	4
SCR 579	YAL	15-16	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 580	MC	6-8	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 581	MC	</= 16	A	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 582	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 583	OC	8-9	-	-	-	-	-	A	-	-	-	-	-	-	-	5
SCR 584	MC	</= 18	A	A	A	-	-	-	-	-	A	A	A	A	A	4
SCR 586	I/YC	</= 16	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 587	MC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 588	MC	4-4.5	-	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 589	OC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 593	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 594	YC	1-1.5	A	A	A	-	-	-	-	-	A	A	A	A	A	4
SCR 595	MC	4-4.5	-	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 596	MC	2.5-4	-	-	-	-	-	-	-	-	A	-	A	A	**P**	4
SCR 597	MC	3.5-4.5	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 598	MC	4-4.5	-	-	-	-	-	-	-	-	A	A	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 599	YC	1-4	-	-	-	-	-	-	-	-	-	-	-	-	A	5
SCR 600	I/YC	</= 18	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 606	YAL	14-15	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 610	MC	6.5-8	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 612	YC	1.5	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 613	MC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 614	F/N	<0.125	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 615	YAL	15-17	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 619	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 620	I	0.5-1	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 621	YC	2-2.5	-	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 622	OC	7.5-8.5	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 623	OC	9.5-10.5	-	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 624	OC	7-9	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 625	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 626	OC	10-11	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 627	F/N	<0.125	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 628	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 629	I	0.25-0.5	-	-	-	-	-	-	A	-	A	-	A	A	A	5
SCR 630	YC	1.5-2	-	-	-	-	-	-	A	-	A	-	A	A	A	5
SCR 631	YC	2-2.5	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 632	MC	5.5-6	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 633	YAL	14-16	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 634	MC	</= 18	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 635	I	0.125	-	-	-	-	-	-	-	-	A	-	A	A	A	5

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 636	YC	1-1.5	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 637	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 639	MC	4-5	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 640	MC	3.5-5	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 641	MC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 642	OC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 643	OC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 644	YC	1-1.5	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 646	OC	</= 16	-	-	-	-	-	-	A	-	A	-	A	A	A	4
SCR 647	I/YC	0.5-2	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 648	OC	11-13	A	A	A	A	A	A	-	A	A	-	A	A	A	4
SCR 649	I/YC	1	A	A	A	-	-	-	-	A	A	-	A	A	A	4
SCR 650	MC	4.5-5	-	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 651	OC	9.5-10	-	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 653	I	0.125-0.25	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 654	F/N	0	-	-	-	-	-	-	-	-	A	A	A	A	**P**	4
SCR 655	I	0.25-1	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 656	MC	2.5-3.5	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 657	OC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 658	OC	7-9	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 659	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	**P**	5
SCR 660	MC	6-8	-	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 661	YC	1-2	-	-	-	-	-	-	A	A	A	-	A	A	A	4
SCR 662	YAL	12-16	-	-	-	-	-	-	A	A	A	-	A	A	A	4
SCR 663	OAL	16-18	A	A	A	-	-	-	A	A	A	-	A	A	**P**	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 664	OC	</= 18	A	A	A	A	A	A	-	-	A	-	A	A	A	4
SCR 667	YAL	11-16	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 671	I/YC	</= 18	-	A	A	-	-	-	-	-	A	-	**P?**	A	**P**	**3**
SCR 672	YC	1.5-2	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 675	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 681	YAL	</= 16	-	-	-	A	A	A	-	-	A	-	A	A	A	4
SCR 683	YAL	14-15.5	A	A	A	A	A	A	-	A	A	A	A	A	A	4
SCR 684	OC	7-9	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 685	YAL	</= 18	-	-	-	-	-	-	-	-	A	A	A	A	A	5
SCR 687	OC	7-8.5	A	A	A	-	-	-	-	-	A	A	A	A	A	4
SCR 693	YAL	14-16	-	-	-	A	A	A	-	A	A	-	A	A	A	4
SCR 694	YAL	13-18	-	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 696	F/N	<0.125	-	-	-	-	-	-	-	-	A	-	A	A	**P**	4
SCR 700	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 701	MC	</= 18	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 707	OC	8-10	A	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 716	OC	8-9	-	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 720	MC	6-7	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 721	OC	</= 16	-	-	-	-	-	-	A	-	A	-	A	A	A	4
SCR 723	YAL	15-17	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 725	YAL	13-15	A	A	A	-	A	A	-	A	A	-	A	A	A	4
SCR 731	MC	3.5-4	-	-	-	A	A	A	-	-	A	-	A	A	A	4
SCR 733	I/YC	</= 16	-	-	-	-	-	-	-	-	A	A	A	A	**P**	4
SCR 734	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 735	I/YC	</= 18	-	-	-	-	-	-	-	-	A	-	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 736	MC	3-4	-	-	-	-	A	A	-	-	A	-	A	A	A	4
SCR 737	MC	4-5	A	A	A	-	A	A	-	-	-	-	-	-	-	4
SCR 738	MC	</= 16	A	A	A	-	-	-	-	-	A	-	A	A	A	5
SCR 739	F/N	<0.125	A	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 740	OC	8.5-9.5	-	-	-	A	A	A	-	-	A	-	A	A	A	4
SCR 741	MC	3.5	-	-	-	-	-	-	-	-	A	-	A	A	**P**	4
SCR 742	YAL	</= 18	A	A	A	-	A	A	-	-	A	-	A	A	A	4
SCR 743	YAL	</= 16	A	A	A	A	A	A	-	-	A	-	A	A	A	4
SCR 744	MC	3.5-4.5	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 745	OC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 746	I/YC	UD	-	A	A	-	-	-	-	-	A	-	A	A	A	5
SCR 747	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 748	MC	</= 16	A	A	A	-	-	-	-	-	A	-	A	A	A	5
SCR 749	MC	3-3.5	-	-	-	-	A	A	-	-	A	-	A	A	A	4
SCR 750	MC	7-8	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 751	I/YC	</= 18	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 752	MC	</= 16	A	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 753	OAL	16-18	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 754	MC	5.5-6	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 755	OC	10.5-11	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 756	YC	1.5-2	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 757	MC	2.5-4	A	A	A	-	-	-	-	-	A	-	A	A	A	5
SCR 758	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	**P**	4
SCR 759	I/YC	</= 16	A	A	A	A	A	A	-	-	A	-	A	A	A	4
SCR 760	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 761	MC	5-7	A	**P**	A	-	-	-	-	-	A	-	A	A	**P**	**1**
SCR 762	I/YC	</= 18	-	-	-	-	-	-	-	-	A	-	A	A	**P**	5
SCR 763	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	**P**	4
SCR 764	YAL	14-16	A	A	A	A	A	A	-	A	A	-	A	A	A	4
SCR 765	F/N	<0.125	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 766	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 767	YC	1.25-1.75	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 768	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 769	YC	1-1.5	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 770	MC	</= 16	-	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 771	MC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 772	MC	2-4	A	A	A	-	-	-	-	-	A	-	A	A	A	5
SCR 773	I	7-11 M	A	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 774	I/YC	</= 16	-	A	A	-	-	A	-	-	A	-	A	A	A	4
SCR 775	F/N	<0.125	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 776	YC	1-1.5	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 777	I/YC	UD	-	-	-	-	-	-	-	A	A	-	A	A	A	4
SCR 778	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 779	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	4
SCR 780	YC	1-1.5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 781	MC	4-5	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 782	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 783	OC	8-9	-	-	-	A	A	A	-	-	A	-	A	A	A	4
SCR 785	MC	3-5	-	-	-	-	-	A	-	-	A	-	A	A	**P**	4
SCR 786	MC	</= 18	A	A	A	-	-	A	-	-	A	-	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
SCR 788	MC	</= 18	A	A	A	-	-	-	-	-	A	A	A	A	A	4
SCR 789	YAL	15-18	-	-	-	-	-	-	-	A	A	-	A	A	A	5
SCR 791	MC	4-5	A	**P**	A	-	A	A	-	-	A	-	A	A	A	**2**
SCR 792	YAL	14-16	A	A	A	-	-	A	-	A	A	A	A	A	A	4
SCR 793	YAL	</= 16	-	-	-	-	A	A	-	A	A	-	A	A	A	4
SCR 795	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 798	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 799	I/YC	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 800	I/YC	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
SCR 803	OC	7.5-8.5	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 810	YAL	14-16	A	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 811	MC	3-4.5	A	A	A	A	A	A	-	-	A	-	A	A	A	4
SCR 812	YAL	14-17	A	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 815	OC	9-10.5	A	A	A	A	A	A	-	-	A	A	A	A	A	4
SCR 818	OC	8-11	A	A	A	-	-	-	-	-	A	-	A	A	A	5
SCR 824	OAL	16-20	-	-	-	-	-	-	A	-	A	A	A	A	**P**	4
SCR 829	MC	</= 16	A	A	A	-	-	-	-	-	A	-	A	A	A	4
SCR 839	OAL	14-17	A	A	A	A	A	A	A	A	A	A	A	A	A	4

Features scored are clear rib new bone formation at the visceral end (1), less clear rib new bone formation at the sternal end (2), other rib new bone formation with a different appearance (3), vertebral body collapse (4), vertebral lytic lesions in the anterior thoracic and lumbar bodies (5), vertebral lytic lesions in other locations or with some new bone formation present (6), lytic lesions of the major weight-bearing joints (7), lytic lesions of other joints or with some new bone formation present (8), lytic lesions of other elements or with atypical appearance (9), bilateral symmetrical new bone formation localized to the forearm or lower leg (10), widespread new bone formation (11), new bone formation in atypical locations (12), and other periosteal new bone formation (13). Nondiagnostic features are highlighted in red, possible features in green, and probable features in blue. Features are scored as present (P), absent (A), or unobservable (-). Age categories are abbreviated as F/N (Fetal/Neonate, <

0.125 years), I (Infant, 0.125-1 year), YC (Younger child, 1.1-3 years), MC (Middle child, 4-7 years), OC (Older child, 8-11 years), YAL (Younger adolescent, 12-15 years), OAL (Older adolescent, 16-19 years), JUD (Juvenile undetermined). Ages abbreviated as M (months), W (weeks), IU (intrauterine). Diagnostic categories are outlined in Section 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate).

Table D.2. Features of chronic respiratory infections scored for Ancaster juveniles

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
ANC 5*	OC	9-10	-	-	-	-	-	-	-	-	-	-	-	-	A	5
ANC 8	MC	5-7	-	-	-	-	-	-	-	-	-	-	-	-	A	5
ANC 29	OC	8-9	A	A	A	A	A	A	-	A	A	A	A	A	**P**	4
ANC 37	I/YC	1	A	A	A	A	A	A	-	-	A	A	A	A	**P**	4
ANC 40	YC	1-1.5	A	A	A	A	A	A	-	A	A	A	A	A	A	4
ANC 44	N	<0.125	A	A	A	-	-	-	-	-	A	-	A	A	A	4
ANC 46B	I	0.125	A	A	A	-	-	-	-	-	A	A	A	A	A	4
ANC 48	N	<0.125	A	A	A	-	-	A	A	A	A	A	A	A	A	4
ANC 48 C	YC	1.5-3	-	-	-	-	-	-	-	-	-	-	-	-	A	5
ANC 51	YC	2.5-3	A	A	A	-	-	A	-	-	A	A	A	A	**P**	4
ANC 53A	OC	9-10	-	-	-	-	-	-	-	-	-	-	-	-	A	5
ANC 54	F	5-6IU	A	A	A	A	A	A	-	-	A	-	A	A	A	4
ANC 55	OC	8-10	**P**	**P**	A	A	A	A	A	A	A	A	**P**	A	A	**1**
ANC 59	OC	9-10	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 60	MC	3-5	A	A	A	A	A	A	-	A	A	-	A	A	A	4
ANC 66A	MC	3-5	-	-	-	-	-	-	-	-	-	-	-	-	A	5
ANC 71	YC	1-1.5	A	A	A	A	A	A	-	-	A	A	A	A	A	4
ANC 72A	YC	2-2.5	A	A	A	-	A	A	-	-	A	-	A	A	A	4
ANC 73	MC	6.5-7.5	A	A	A	A	A	A	A	-	A	A	A	A	A	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
ANC 78A	N	<0.125	A	A	A	-	-	-	-	-	A	-	A	A	A	4
ANC 89	N	<0.125	-	-	-	-	-	-	-	-	A	-	A	A	A	4
ANC 90	I	0.125	A	A	A	-	-	-	A	A	A	A	A	A	**P**	4
ANC 95	I/YC	UD	A	A	A	A	A	A	-	-	A	A	A	A	**P**	4
ANC 97	F	5IU	A	A	A	-	-	A	-	-	A	-	A	A	**P**	4
ANC 99	I/YC	</= 16	A	A	A	-	-	-	-	-	A	-	A	A	**P**	4
ANC 101	N	<0.125	A	A	A	-	-	A	-	-	A	-	A	A	A	4
ANC 105	OC	8.5-9	A	**P**	A	A	A	A	A	-	A	A	A	A	A	**2**
ANC 114	N	<0.125	-	A	A	-	-	A	-	-	A	A	A	A	A	4
ANC 124	YC	1-1.5	-	-	-	-	-	-	-	-	-	-	-	-	A	5
ANC 124A	I	2-4 M	A	A	A	A	A	A	-	-	A	A	A	A	A	4
ANC 125	YAL	10-14	A	A	A	A	A	A	-	-	A	A	A	A	**P**	4
ANC 127	JUD	UD	-	-	-	-	-	-	-	-	-	-	-	-	A	5
ANC 129	YAL	11-16	A	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 130	MC	5.5-6.5	A	A	A	A	A	A	-	-	A	-	A	A	A	4
ANC 131	MC	7-9	A	A	A	A	A	A	-	-	A	-	A	A	A	4
ANC 132	YC	1.5-2	A	A	A	-	-	A	-	-	A	-	A	A	A	4
ANC 138	YC	1-1.5	A	A	A	-	-	A	-	-	A	A	A	A	A	4
ANC 139	OC	7.5-8	-	-	-	-	-	-	A	A	A	A	A	A	A	4
ANC 145	YC	1.5-2	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 145A	I	2-4 M	A	A	A	-	-	A	-	-	A	A	A	A	A	4
ANC 146	MC	4.5-5.5	**P**	**P**	A	A	A	A	-	-	A	A	A	A	**P**	**1**
ANC 147A	MC	3-5	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 148	MC	3.5-4.5	-	-	-	A	A	A	A	-	A	A	A	A	**P**	4
ANC 150	F	4 M IU	A	A	A	A	A	A	-	A	A	-	A	A	**P**	4

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
ANC 151	MC	5-8	A	A	A	A	A	A	A	-	A	A	A	A	**P**	4
ANC 153	N	<0.125	A	A	A	A	A	A	-	-	A	A	A	A	A	4
ANC 161	YC	1.5-2.5	A	A	A	-	-	A	-	-	-	-	-	-	-	4
ANC 162A	I/YC	UD	-	-	-	-	A	A	-	-	-	-	-	-	-	5
ANC 164	YC	1.5-2	A	A	A	A	A	A	-	-	A	-	A	A	**P**	4
ANC 166	I	5-7 M	-	-	-	-	-	A	-	-	A	A	A	A	A	4
ANC 166A	MC	</= 16	A	A	A	-	-	A	-	-	A	-	A	A	A	4
ANC 169	MC	3	A	A	A	A	A	A	-	-	A	A	A	A	A	4
ANC 180	YC	1.5-2	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 181	MC	3-5	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 189	JUD	UD	-	-	-	-	-	-	-	-	-	-	-	-	A	5
ANC 192	F	6IU	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 194	MC	5-7	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 195	YC	2.5-3	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 197	YC	1.5-2	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 203	I	4-5 M	A	A	A	-	-	-	-	A	A	-	A	A	A	4
ANC 204	MC	3-4.5	-	-	-	-	A	A	-	-	-	-	-	-	-	5
ANC 206	MC	3-4.5	**P**	A	A	A	A	A	-	-	A	A	A	A	A	**1**
ANC 207	I	0.5-1	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 208	I	5-7 M	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 215	JUD	</= 16	A	A	A	-	-	A	-	-	A	-	A	A	A	4
ANC 219	OC	7-9	A	A	A	A	A	A	-	-	A	A	A	A	A	4
ANC 233	YC	1-3	A	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 239	I	0.125	A	A	A	-	-	A	-	-	A	-	A	A	A	4
ANC 245	JUD	UD	-	-	-	-	-	-	-	-	A	-	A	A	A	5

Individual	Age Category	Age (years)	1	2	3	4	5	6	7	8	9	10	11	12	13	Diagnosis
ANC 246	MC	5-7	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 249	I	10-12 M	A	A	A	-	-	A	-	-	A	A	A	A	**P**	4
ANC 250	YC	2.5-3	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 251A	JUD	</= 16	-	-	-	-	-	-	-	-	A	-	A	A	A	5
ANC 254	N	< 2 M	A	A	A	A	A	A	-	-	A	A	A	A	A	4
ANC 255	OC	9-10.5	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 258	OC	9.5-10	A	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 260	YC	1.5-2	A	A	A	A	A	A	-	A	A	A	A	A	**P**	4
ANC 261	MC	3-4.5	A	**P**	A	A	A	A	A	-	A	A	A	A	A	**2**
ANC 265	N	< 0.125	A	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 268	N	<0.125	A	A	A	A	A	A	-	-	A	A	A	A	**P**	4
ANC Uncat D	I	0.125	A	A	A	A	A	A	-	-	A	-	A	A	A	4

Features scored are clear rib new bone formation at the visceral end (1), less clear rib new bone formation at the sternal end (2), other rib new bone formation with a different appearance (3), vertebral body collapse (4), vertebral lytic lesions in the anterior thoracic and lumbar bodies (5), vertebral lytic lesions in other locations or with some new bone formation present (6), lytic lesions of the major weight-bearing joints (7), lytic lesions of other joints or with some new bone formation present (8), lytic lesions of other elements or with atypical appearance (9), bilateral symmetrical new bone formation localized to the forearm or lower leg (10), widespread new bone formation (11), new bone formation in atypical locations (12), and other periosteal new bone formation (13). Nondiagnostic features are highlighted in red, possible features in green, and probable features in blue. Features are scored as present (P), absent (A), or unobservable (-). Age categories are abbreviated as F/N (Fetal/Neonate, < 0.125 years), I (Infant, 0.125-1 year), YC (Younger child, 1.1-3 years), MC (Middle child, 4-7 years), OC (Older child, 8-11 years), YAL (Younger adolescent, 12-15 years), OAL (Older adolescent, 16-19 years), JUD (Juvenile undetermined). Ages abbreviated as M (months), W (weeks), IU (intrauterine). Diagnostic categories are outlined in Section 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate).

Table D.3. Features of chronic respiratory infections scored for Isola Sacra adults

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 5	OAL	15-21	F	A	A	A	A	A	**P?**	A	A	A	A	A	A	4
SCR 15	OA	36.9-90.7	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 16	MA	25-45	F	-	-	-	A	A	A	A	A	A	A	A	A	4
SCR 17	AUD	UD	UD	-	-	-	-	-	-	A	A	A	A	A	A	5
SCR 18	YA	25-35	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 19	YA	25-35	UD	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 20	YA	25.7-47.1	F	-	-	-	A	A	A	A	A	A	A	A	A	4
SCR 21	YA	16.4-64.6	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 27	YA	17-25	PF	A	A	A	A	A	**P**	A	A	A	A	A	A	4
SCR 30	MA	33-45	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 32	OAL	14-19	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 34	AUD	UD	UD	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 35	OAL	14-21	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 36	OAL	16-21	PM	A	**P**	A	A	A	A	A	A	A	A	A	**P**	**2**
SCR 37	OA	50-75	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 38	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 39	OA	34-87	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 44	MA	25-45	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 52	OAL	15-21	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 53	OA	23.4-88.9	F	A	A	A	-	-	-	A	A	A	A	A	A	4
SCR 55	YA	17-35	PF	-	-	-	A	A	A	A	A	A	A	A	A	4
SCR 57	YA	26.9-62.4	UD	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 59	YA	17-25	F	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 60	OA	34-86	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 64	YA	19-23	UD	A	A	A	-	-	A	-	A	A	A	A	A	4
SCR 67	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 68	YA	17-25	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 69	YA	17-35	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 71	AUD	UD	UD	-	-	-	-	-	-	-	-	-	-	-	A	5
SCR 73	AUD	UD	UD	-	A	A	-	-	-	A	A	A	A	A	A	4
SCR 75	OAL	17-21	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 76	OA	49.4-91.8	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 77	YA	25-45	PM	-	-	-	A	A	A	A	A	A	A	A	A	4
SCR 79	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 82	MA	26-70	F	-	-	-	A	A	A	A	A	A	A	A	A	4
SCR 83	MA	26-70	F	-	-	-	A	A	A	-	A	A	A	A	A	4
SCR 84	MA	33-45	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 85	YA	21-46	PM	A	A	A	A	A	A	-	A	A	-	A	A	4
SCR 86	OAL	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 87	OA	71.3-90.3	UD	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 88	YA	17-35	M	-	-	-	-	-	-	-	A	A	-	A	A	5
SCR 89	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 90	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 97	MA	25-75	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 98	OAL	17-21	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 99	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 105	MA	33-45	F	A	A	A	A	A	A	-	-	-	-	-	-	4
SCR 106	OAL	15-24	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 113	MA	33-45	F	A	A	A	A	A	A	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 116	YA	17-25	M	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 120	YA	17-25	M	A	**P**	A	A	A	A	-	-	A	A	A	A	**2**
SCR 122	AUD	UD	UD	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 123	AUD	UD	UD	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 125	YA	17-25	PF	-	A	A	-	A	A	-	A	A	A	A	A	4
SCR 126	OAL	15-18	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 127	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 128	MA	26-70	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 129	YAL	14-16	UD	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 130	AUD	UD	UD	-	-	-	-	-	-	A	A	A	A	A	A	5
SCR 132	YA	17-25	UD	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 133	OAL	17-19	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 134	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 138	OAL	15-18	M	A	A	**P**	A	A	A	A	A	A	A	A	A	**3**
SCR 142	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 143	MA	34-86	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 144	YA	19-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 145	MA	33-57	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 148	OA	42-87	F	A	A	A	-	A	A	-	A	A	A	A	**P**	4
SCR 150	OA	26.2-86.7	PF	A	A	A	-	A	A	A	A	A	A	A	A	4
SCR 151	MA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 152	MA	25-83	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 155	OAL	17-21	UD	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 156	OA	42-87	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 157	OAL	16-21	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 158	MA	25-88.1	M	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 159	AUD	UD	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 160	MA	26-70	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 161	YA	24.3-45	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 163	MA	25-66	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 169	YA	18.3-33.2	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 170	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 171	YA	25-83	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 172	MA	33-45	M	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 173	MA	25-83	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 174	YA	17-25	F	A	A	A	A	A	**P?**	A	A	A	A	A	A	**3**
SCR 177	AUD	UD	F	-	-	-	A	A	A	-	A	A	A	A	A	4
SCR 178	YA	25-35	M	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 179	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 180	YA	17-25	UD	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 181	YA	25-35	M	A	A	A	A	A	A	-	A	A	-	A	**P**	4
SCR 183	MA	42-87	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 184	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 185	OA	69.2-89.7	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 186	MA	25-45	M	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 188	YA	17-25	AB	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 189	MA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 190	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 191	MA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 192	MA	33-45	UD	A	A	A	A	A	A	-	A	A	A	A	**P**	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 193	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 194	MA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 196	OAL	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 197	YA	18-27	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 198	YA	19-34	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 199	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 201	MA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 203	OAL	15-18	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 207	YA	17-25	M	-	-	-	-	-	A	-	-	-	-	-	-	5
SCR 208	AUD	UD	UD	A	A	A	-	-	A	-	-	-	-	-	A	4
SCR 210	MA	25-35	F	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 211	AUD	UD	UD	-	-	-	-	-	-	-	-	A	A	A	**P**	5
SCR 212	YA	17-25	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 213	AUD	UD	UD	-	-	-	-	-	-	-	A	A	A	A	A	5
SCR 215	YA	25-35	M	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 216	OAL	15-17	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 217	YA	25-35	UD	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 219	YAL	15-16	UD	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 220	OAL	17-20	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 221	MA	23-57	M	A	**P**	A	A	A	A	A	A	A	**P**	**P**	A	**1**
SCR 223	YA	17-25	UD	-	-	-	-	-	-	-	-	A	A	A	A	5
SCR 224	YA	17-25	M	A	A	A	-	-	A		-	A	A	A	A	4
SCR 226	OAL	16-18	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 227	MA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 228	MA	19.5-79.3	UD	A	A	A	A	A	A	A	A	A	A	A	**P**	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 231	YA	28.4-63.6	M	A	A	A	-	A	A	-	A	A	A	A	**P**	4
SCR 232	YA	25-35	M	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 233	MA	25-63.2	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 234	MA	25-58.2	UD	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 236	YA	25-35	UD	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 239	MA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 241	MA	33-45	F	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 242	YA	25-35	UD	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 243	YA	17-25	UD	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 245	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 246	YA	17-25	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 250	MA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 251	YA	17-25	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 252	MA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 253	AUD	UD	M	A	A	A	-	-	-	-	-	A	A	A	A	4
SCR 254	AUD	UD	UD	A	A	A	-	-	-	-	-	A	A	A	A	4
SCR 256	MA	23-57	M	-	-	A	-	-	A	A	A	A	A	A	A	4
SCR 257	AUD	UD	UD	-	-	-	A	A	A	-	A	A	A	A	A	4
SCR 258	YA	17-25	F	-	-	-	-	-	A	-	A	A	A	A	A	4
SCR 260	AUD	UD	UD	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 261	OA	45+	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 262	MA	26-70	PF	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 263	OAL	15-18	F	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 264	OA	67-110	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 265	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	A	5

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 266	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 267	AUD	UD	UD	-	-	-	-	-	-	-	A	A	-	A	A	5
SCR 269	YA	25-35	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 271	OAL	18-23	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 272	YA	21-53	F	**P**	**P**	A	A	A	A	A	A	A	A	A	A	**1**
SCR 280	AUD	UD	UD	-	-	-	-	-	-	-	-	A	A	A	A	5
SCR 281	MA	25-49	PF	A	A	A	-	-	A	A	A	A	A	A	A	4
SCR 282	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 283	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	-	A	5
SCR 284	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 285	MA	25-45	F	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 286	MA	25-35	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 287	MA	26-70	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 288	MA	25-45	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 289	MA	25-73.9	PF	A	A	A	-	-	A	-	A	A	A	A	A	4
SCR 291	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 292	YA	17-25	PF	A	A	A	-	-	A	A	-	A	A	A	A	4
SCR 293	AUD	UD	M	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 294	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 295	YA	18-27	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 296	YA	17-25	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 297	YA	25-35	M	**P**	**P**	A	A	A	**P**	A	A	A	A	A	A	**1**
SCR 298	MA	25-45	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 299	YA	17-25	F	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 301	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 302	MA	25-83	AB	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 303	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 304	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 305	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 306	OAL	15-25.2	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 307	MA	25-89.5	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 308	OA	44.6-92.1	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 310	YAL	14-16	AB	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 312	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 314	YA	17-35	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 317	OAL	17-18	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 318	MA	19.6-82.9	UD	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 319	OAL	16-18	M	**P**	A	A	A	A	A	A	A	A	A	A	A	**1**
SCR 320	YA	17-21	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 321	YA	17-27	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 322	OAL	14-19	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 323	MA	33-83	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 324	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 325	OAL	17-21	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 326	YA	17-35	F	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 328A	YA	21-53	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 329	MA	26-70	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 330	OAL	18-21	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 331	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 332	OAL	17-25	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 334	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 335	YA	17-35	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 336	MA	33-45	UD	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 337	OAL	15-17	PM	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 338	MA	33-45	PF	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 339	MA	25-57	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 340	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 341	MA	25-45	M	A	A	**P**	A	A	A	A	A	A	A	A	**P**	4
SCR 342	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 343	OAL	15-17	AB	**P**	**P**	A	A	A	A	A	A	A	A	A	A	**1**
SCR 344	YA	17-25	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 347	YA	17-35	UD	A	A	A	A	A	A	-	-	A	A	A	A	4
SCR 352	OAL	16-21	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 354	OAL	14-18	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 355A	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 355B	AUD	UD	UD	-	-	-	-	-	-	-	A	A	A	A	A	5
SCR 358	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 360	OAL	15-18	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 361	OAL	17-18	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 362	YA	17-25	F	-	-	-	-	-	-	A	A	A	A	A	**P**	4
SCR 363	YA	21-53	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 365	OA	72.6-90.7	UD	A	A	A	-	-	A	-	A	A	A	A	**P**	4
SCR 366	OA	45+	M	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 368	OAL	15-17	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 369	OAL	17-21	PF	A	A	A	A	A	A	-	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 370	YA	20.9-39.1	F	-	-	-	A	A	A	A	A	A	A	A	A	4
SCR 371	OA	72.6-90.7	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 374	AUD	UD	UD	A	A	A	-	-	-	-	-	A	A	A	A	4
SCR 376	YA	17-35	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 377	AUD	UD	UD	-	A	A	A	A	A	-	-	A	A	A	A	4
SCR 379	AUD	UD	UD	A	A	A	-	-	-	-	-	A	A	A	A	5
SCR 380	AUD	UD	UD	-	-	-	-	-	-	-	-	A	A	A	A	5
SCR 382	OA	74.6-91.3	F	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 383	OAL	17-21	M	-	-	-	A	A	A	-	A	A	A	A	A	4
SCR 389	OAL	15-19	M	-	-	-	A	A	A	A	**P?**	A	A	A	A	4
SCR 390	AUD	UD	UD	**P**	A	**P**	-	-	-	-	A	A	**P?**	A	A	**1**
SCR 391	YAL	14-16	M	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 394	OA	72.8-90.7	F	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 395	OAL	16-18	F	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 396	OAL	15-19	M	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 399	YA	25.7-48.9	UD	-	-	-	-	-	-	-	A	A	**P?**	**P**	A	**2**
SCR 401	YA	17-25	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 403	AUD	UD	UD	-	-	-	-	-	-	-	-	A	A	A	A	5
SCR 404	OAL	15-18	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 405	AUD	UD	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 406	OAL	15-18	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 407	OA	UD	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 409	YA	17-35	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 410	AUD	UD	UD	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 411	OAL	16-21	F	A	**P**	A	A	A	A	A	A	A	A	A	**P**	**2**

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 412	MA	23-57	PM	-	A	A	-	-	-	-	A	A	A	A	A	4
SCR 413	OAL	16-21	UD	A	A	A	A	A	A	-	-	-	-	-	A	4
SCR 414	OAL	</= 21	UD	A	A	A	-	-	-	-	-	A	A	A	A	4
SCR 415	YA	17-25	UD	-	A	A	-	-	-	-	-	A	A	A	A	4
SCR 416	OAL	16-19	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 417	MA	25-38	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 418	AUD	UD	UD	-	-	-	-	-	-	-	-	A	A	A	A	5
SCR 419	MA	33-45	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 420	YAL	14-16	PF	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 421	OAL	15.8-30.3	PF	A	A	A	-	-	-	-	A	A	A	A	A	4
SCR 422	MA	33-45	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 423	MA	33-45	M	-	A	A	-	-	-	-	-	A	A	A	**P**	4
SCR 424	MA	25-38	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 425	MA	25-45	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 426	YA	17-25	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 427	AUD	UD	UD	-	A	A	-	-	-	-	-	-	-	-	-	5
SCR 429	OA	38.5-91.6	UD	-	A	A	A	A	A	-	-	A	A	A	A	4
SCR 430	OA	32.4-89.9	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 431	AUD	UD	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 433	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 434	MA	25-83	F	**P**	**P**	A	A	A	A	A	A	A	A	A	**P**	**1**
SCR 435	YA	25-35	M	-	-	-	A	A	A	A	A	A	A	A	A	4
SCR 436	MA	25-45	F	-	-	-	A	A	A	A	A	A	A	A	**P**	4
SCR 437	OA	25-60	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 438	AUD	UD	UD	A	A	A	A	A	A	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 439	MA	23-57	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 440	OA	50-93.4	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 442	OAL	18-19	F	-	-	-	-	-	A	A	A	A	A	A	A	4
SCR 443	YA	25-35	F	-	-	-	-	-	A	A	A	A	A	A	A	4
SCR 444	OAL	17-21	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 445	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 447	YA	21-46	M	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 448	MA	17-38	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 449	OA	33-50+	M	A	A	A	-	-	A	-	A	A	A	A	**P**	4
SCR 450	YA	17-25	UD	-	-	-	-	A	A	A	A	A	A	A	A	4
SCR 452	YA	17-25	F	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 453	YA	18.3-33.7	M	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 454	YA	25-35	UD	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 455	OAL	17-21	UD	A	A	A	A	A	A	-	-	A	A	A	A	4
SCR 456	AUD	UD	UD	-	-	-	-	-	-	-	-	A	A	A	A	4
SCR 457	OA	55.7-93.2	PM	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 458	YA	25.7-47.1	M	-	-	-	-	A	A	A	A	A	A	A	**P**	4
SCR 461	YA	17-35	UD	A	A	A	-	-	A	-	-	A	-	-	A	5
SCR 462	MA	23-57	M	A	A	A	A	**P**	A	A	A	A	A	A	A	**2**
SCR 463	YA	17-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 464	YA	17-29	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 465	AUD	UD	M	A	A	A	-	-	A	-	-	A	A	A	A	4
SCR 466	MA	25-75	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 467	MA	25-83	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 468	YA	17-25	PM	A	A	A	A	A	A	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 469	OA	23-83.5	UD	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 470	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 476	AUD	UD	UD	A	A	A	-	-	A	-	-	A	-	A	A	4
SCR 479	YA	17-25	PF	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 480	YA	21-46	M	A	A	A	-	-	-	-	-	A	A	A	**P**	4
SCR 481	AUD	UD	UD	-	-	-	-	-	-	-	-	A	A	A	A	4
SCR 482	AUD	UD	M	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 484	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 485	YA	17-35	PM	-	-	-	-	A	A	A	A	A	A	A	A	4
SCR 486	MA	23-70	UD	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 487	YA	25-35	UD	-	-	-	-	-	-	-	A	A	A	A	A	5
SCR 488	AUD	UD	UD	A	A	A	-	-	A	-	A	A	A	A	A	4
SCR 489	MA	23-70	F	-	-	-	-	A	A	A	A	A	A	A	A	4
SCR 490	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 493	YA	17-25	UD	-	-	-	-	-	-	-	A	A	-	A	A	5
SCR 497	AUD	UD	UD	-	-	-	-	-	-	-	A	A	-	A	A	5
SCR 499	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 500	OAL	15-23	M	A	A	A	-	A	A	-	A	A	A	A	A	4
SCR 501	MA	26-70	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 502	AUD	UD	UD	-	-	-	-	-	-	-	-	A	A	A	A	4
SCR 503	YA	25-35	UD	-	A	A	-	A	A	-	A	A	A	A	A	4
SCR 504	AUD	UD	UD	-	-	-	-	-	-	-	A	A	A	A	A	5
SCR 505	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	**P**	5
SCR 507	OAL	</= 21	F	A	A	A	-	-	-	-	A	A	-	A	A	4
SCR 508	YA	19-34	M	-	-	-	A	A	A	A	A	A	A	A	**P**	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 509	AUD	UD	UD	-	-	-	-	-	-	-	A	A	-	A	A	4
SCR 510	YA	17-38	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 521	YA	17-25	UD	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 524	OA	53.7-92.8	UD	-	-	-	-	-	-	A	A	A	A	A	**P**	4
SCR 525	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 526	YA	25-35	M	-	A	A	A	A	A	A	A	A	A	A	A	4
SCR 527	MA	23-57	M	-	-	-	-	A	A	-	-	-	-	-	-	5
SCR 535	AUD	UD	UD	-	-	-	-	-	-	-	A	A	A	A	**P**	4
SCR 544	AUD	UD	UD	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 545	YA	18-27	UD	-	-	-	-	-	A	-	A	A	-	A	A	4
SCR 549	YA	25-45	F	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 550	YA	27.4-51.1	UD	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 551	YA	19.8-35.1	M	-	-	-	-	-	-	A	A	A	A	A	**P**	4
SCR 553	YA	17-25	UD	-	-	-	-	-	-	-	-	A	-	A	**P**	4
SCR 556	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 559	AUD	UD	F	-	-	-	A	A	A	-	-	A	-	A	A	4
SCR 561	YAL	14-16	UD	-	-	-	A	A	A	-	A	A	A	A	A	4
SCR 562	MA	28-45	M	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 563	OAL	16-18	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 565	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 566	AUD	UD	UD	-	-	-	-	-	-	-	-	A	-	A	**P**	5
SCR 567	YA	25-35	UD	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 568	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 569	YA	17-25	UD	-	A	A	-	-	-	-	-	A	A	A	A	4
SCR 570	AUD	UD	UD	A	A	A	-	-	A	-	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 571	OAL	15-18	UD	-	-	-	-	-	-	-	A	A	-	A	A	4
SCR 573	OA	24.2-86.3	M	A	A	A	A	A	A	-	A	A	-	A	A	4
SCR 574	OAL	14-18	UD	A	A	A	A	A	A	-	-	A	-	A	A	4
SCR 575	OAL	17-21	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 576	MA	23-57	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 577	YAL	14-16	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 578	YA	22.6-55.2	UD	-	-	-	-	-	-	A	A	A	-	A	**P**	4
SCR 585	YA	25-35	UD	A	A	A	-	-	A	-	A	A	A	A	A	4
SCR 590	YA	25-35	M	A	A	**P**	A	A	A	A	A	A	A	A	**P**	4
SCR 591	AUD	UD	UD	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 592	YA	19-34	PM	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 601	AUD	UD	UD	-	-	-	-	-	-	-	A	A	A	A	**P**	4
SCR 602	YA	17-25	F	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 603	YA	30.6-62.7	UD	-	-	-	-	-	-	-	A	A	A	A	**P**	4
SCR 604	AUD	UD	UD	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 605	OAL	14-19	UD	-	-	-	A	A	A	-	A	A	A	A	A	4
SCR 607	MA	25-55	PF	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 608	YA	17.7-33.3	PF	-	-	-	-	-	A	-	A	A	A	A	**P**	4
SCR 609	OAL	15-18	M	-	-	-	-	-	-	-	A	A	-	A	A	5
SCR 611	OAL	17-19	UD	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 616	YA	25-35	PM	A	A	A	A	A	A	-	A	A	-	A	A	4
SCR 617	MA	17-75	PM	A	A	A	A	A	A	-	A	A	-	A	A	4
SCR 618	OAL	16-21	F	-	-	-	A	A	A	-	A	A	A	A	**P**	4
SCR 638	OAL	14-18	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 645	OAL	15-18	UD	-	-	-	A	A	A	-	-	A	-	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 652	MA	25-83	F	-	-	-	-	-	-	-	A	A	-	A	A	4
SCR 665	OAL	16-18	M	-	-	-	A	A	A	-	A	A	A	A	A	4
SCR 666	OAL	14-18	UD	A	A	A	A	A	A	-	A	A	-	A	A	4
SCR 668	MA	23-57	PM	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 669	MA	37.4-85.8	F	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 670	YA	17-35	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 673	MA	18.8-77	F	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 674	OAL	17-19	UD	-	-	-	-	-	-	-	-	A	-	A	A	5
SCR 676	OA	33+	M	A	**P**	A	-	-	-	-	A	A	A	A	**P**	**2**
SCR 677	OAL	16-19	F	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 678	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 679	YA	17-27	PF	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 680	AUD	UD	F	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 682	MA	23-57	M	-	-	-	A	A	A	-	A	A	-	A	A	4
SCR 686	AUD	UD	UD	-	-	-	-	-	-	-	A	A	-	A	A	4
SCR 688	AUD	UD	UD	A	A	A	A	A	A	-	A	A	-	A	**P**	4
SCR 689	OAL	15-17	UD	-	-	-	A	A	A	-	-	A	-	-	-	4
SCR 690	MA	26-70	F	-	A	A	A	-	A	-	A	A	A	A	A	4
SCR 691	YA	18-27	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 692	YA	17-25	M	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 695	YA	17-38	F	A	A	A	-	-	A	-	-	A	-	A	A	4
SCR 697	OAL	17-18	UD	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 698	YA	25-35	AB	A	A	A	A	A	A	-	A	A	-	A	**P**	4
SCR 699	YA	17-25	F	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 702	MA	23-57	M	A	A	A	A	A	A	-	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 703	AUD	UD	UD	A	A	A	-	-	-	-	A	A	A	A	A	4
SCR 704	MA	16.2-82.8	UD	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 705	MA	23-57	M	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 706	YA	21-46	M	-	-	-	-	-	-	-	A	A	**P**	A	**P**	**1**
SCR 708	AUD	UD	UD	-	-	-	-	-	-	A	A	A	-	A	**P**	4
SCR 709	OA	42.4-90.5	F	-	-	-	-	-	-	-	A	A	A	A	**P**	4
SCR 710	OAL	17-21	F	-	-	-	-	-	-	-	A	A	A	A	A	4
SCR 711	OA	22.5-88.9	PF	A	A	A	A	A	A	-	A	A	-	A	**P**	4
SCR 712	OAL	15-18	UD	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 713	OAL	14-18	M	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 714	YA	21-53	F	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 715	MA	23-57	M	A	A	A	-	-	-	A	A	A	A	A	A	4
SCR 717	YA	16.5-71.9	PF	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 718	AUD	UD	UD	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 719	MA	37-88.8	M	-	A	A	A	A	A	-	A	A	-	A	A	4
SCR 722	AUD	UD	UD	-	-	-	-	-	-	-	A	A	-	A	A	5
SCR 724	AUD	UD	UD	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 726	YA	17-25	F	A	A	A	A	A	A	-	A	A	-	A	A	4
SCR 727	AUD	UD	UD	-	-	-	-	-	-	-	A	A	-	A	**P**	5
SCR 728	YA	25-35	UD	-	A	A	-	-	A	-	A	A	-	A	A	4
SCR 729	MA	25-45	UD	A	A	A	A	A	A	-	A	A	**P**	A	**P**	**1**
SCR 730	MA	25-45	PM	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 732	YAL	14-16	UD	A	A	A	A	A	A	-	-	A	-	A	A	4
SCR 784	AUD	UD	UD	-	-	-	-	-	A	-	A	A	A	A	**P**	4
SCR 787	AUD	UD	F	A	A	A	-	-	A	-	A	A	-	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 790	YA	17-25	UD	-	-	-	-	-	A	-	A	A	-	A	**P**	4
SCR 794	OAL	17-25	PF	-	-	-	-	-	-	A	A	A	A	A	A	4
SCR 797	YA	17-25	UD	-	-	-	-	-	-	-	A	A	-	A	**P**	5
SCR 801	AUD	UD	UD	-	-	-	-	-	-	-	A	A	-	A	**P**	4
SCR 802	MA	25-37	PF	A	A	A	-	-	A	-	A	A	-	A	A	4
SCR 804	YA	19-25	M	**P**	**P**	A	A	A	A	-	A	A	A	A	A	**1**
SCR 805	OA	23-57	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 806	MA	25-57	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 807	YA	22.4-39.4	UD	A	**P**	**P**	A	A	**P**	-	A	A	A	A	A	**3**
SCR 808	YA	25-35	PM	A	A	A	-	A	A	-	A	A	A	A	**P**	4
SCR 809	OA	72.6-90.7	UD	A	A	A	-	-	A	-	-	A	-	A	A	4
SCR 813	OA	18.5-87.3	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 814	OA	27-66	PM	A	A	A	A	A	**P?**	A	A	A	A	A	**P**	4
SCR 816	MA	25-39	F	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 817	AUD	UD	UD	-	-	-	-	-	A	-	-	A	-	A	**P**	5
SCR 819	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 820	AUD	UD	UD	-	-	-	-	-	-	-	A	A	-	A	**P**	4
SCR 821	YA	18-27	UD	-	-	-	-	-	-	-	A	A	-	A	A	5
SCR 822	MA	25-45	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 823	MA	25-45	PM	-	-	-	-	-	A	-	-	-	-	-	-	5
SCR 826	YA	17-35	UD	-	A	A	-	-	-	-	A	A	-	A	A	5
SCR 827	MA	18.1-81.5	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 828	OAL	15-29.6	UD	A	A	A	A	A	A	-	A	A	A	A	**P**	4
SCR 830	YA	17-25	PF	**P**	A	A	-	-	-	-	-	A	A	A	A	**1**
SCR 831	OAL	15-18	AB	A	A	A	A	A	A	A	A	A	A	A	**P**	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
SCR 833	YA	17-35	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 834	OA	33-57	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 835	YA	17-25	F	A	A	A	**P ?**	A	A	A	A	A	A	A	**P**	**3**
SCR 836	YA	17-35	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 837	MA	33-45	M	A	A	A	A	A	A	-	A	A	A	A	A	4
SCR 838	YA	19-25	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
SCR 840	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
SCR 841	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4

Features scored are clear rib new bone formation at the visceral end (1), less clear rib new bone formation at the sternal end (2), other rib new bone formation with a different appearance (3), vertebral body collapse (4), vertebral lytic lesions in the anterior thoracic and lumbar bodies (5), vertebral lytic lesions in other locations or with some new bone formation present (6), lytic lesions of the major weight-bearing joints (7), lytic lesions of other joints or with some new bone formation present (8), lytic lesions of other elements or with atypical appearance (9), bilateral symmetrical new bone formation localized to the forearm or lower leg (10), new bone formation in atypical locations (11), and other periosteal new bone formation (12). Nondiagnostic features are highlighted in red, possible features in green, and probable features in blue. Features are scored as present (P), absent (A), or unobservable (-). Age categories are abbreviated as YAL (Younger adolescent, 12-15 years), OAL (Older adolescent, 16-19 years), YA (Young adult, 20-34 years), MA (Middle adult, 35-49 years), OA (Older adult, 50+ years), AUD (Adult undetermined). Sex categories abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), UD (undetermined). Diagnostic categories are outlined in Section 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate).

Table D.4. Features of chronic respiratory infections scored for Ancaster adults

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
ANC 1	OAL	17-21	F	A	A	A	A	**P**	A	**P**	A	A	A	A	A	**1**
ANC 2	MA	35.2	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 2*	YA	21-53	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 3	MA	25-45	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 3*	MA	48.1	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 3A	MA	48.1	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 4	OA	45+	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 5	MA	48.1	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 6	OA	77.2	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 10	OA	81.5	F	A	A	**P**	A	A	A	A	A	A	A	A	**P**	4
ANC 11	YA	26-34	M	A	A	A	**P**	A	A	A	A	A	A	A	**P**	**1**
ANC 12	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 12B	OA	82.2	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 13	MA	35.2-38.2	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 14	YA	25-35	PM	**P**	A	A	A	**P?**	A	A	A	A	A	A	A	**1**
ANC 21	OA	60	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 22	OA	50+	PM	-	-	-	-	-	-	A	A	A	A	A	**P**	4
ANC 23	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 24	MA	35.2	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 25	OA	75.7	F	A	A	A	-	-	-	A	A	A	A	A	**P**	4
ANC 26	MA	35.2-38.2	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 27	MA	45.6	M	-	-	-	-	-	-	A	A	A	A	A	A	4
ANC 28	MA	35.2	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 32B	AUD	UD	UD	-	-	-	-	-	-	A	A	A	A	A	**P**	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
ANC 34	MA	48.1	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 35	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 38	OA	66.6	PF	A	A	A	-	-	-	A	A	A	A	A	A	4
ANC 39	YA	28.7	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 41	MA	35.3-38.3	PF	A	A	A	-	-	-	A	A	A	A	A	A	4
ANC 41A Big	AUD	UD	F	A	A	A	-	-	-	-	A	A	A	A	A	4
ANC 41A Small	AUD	UD	PF	-	-	-	A	A	A	A	A	A	A	A	A	4
ANC 42	OA	73.1	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 43	MA	48.1	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 45	OA	60-61.2	F	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 45A	MA	48.1	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 46	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 47	OA	61.2	M	**P**	A	A	A	A	A	A	A	A	A	A	A	**1**
ANC 48B	OAL	16-18	M	**P**	A	A	A	A	A	A	A	A	A	A	**P**	**1**
ANC 49	MA	48.9	M	-	-	-	A	A	A	A	A	A	A	A	A	4
ANC 50	OA	76.2	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 52	AUD	UD	PF	-	-	-	A	A	A	A	A	A	A	A	A	4
ANC 53	OA	79	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 56	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 57	OA	73.8	M	A	A	**P**	A	A	A	A	A	A	A	A	A	4
ANC 58	OA	79.6	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 61	MA	48.1	M	A	**P**	A	A	A	A	A	A	A	A	A	**P**	**3**
ANC 62	YA	25	F	A	**P**	**P**	A	A	A	A	A	A	A	A	**P**	4
ANC 63	MA	48.1	PF	A	A	A	A	A	A	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
ANC 64	OA	65.4	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 65	MA	45.6	PM	**P**	**P**	A	A	A	A	A	A	A	A	A	**P**	**2**
ANC 66	MA	38.2	F	A	**P**	A	A	A	A	A	A	A	A	A	A	**3**
ANC 67	OA	60	F	-	-	-	A	A	A	A	A	A	A	A	**P**	4
ANC 68	MA	48.1	M	-	-	-	-	-	-	A	A	A	A	A	**P**	4
ANC 69	AUD	UD	PF	**P**	**P**	A	A	A	A	-	A	A	-	A	A	**1**
ANC 72	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 75	AUD	UD	UD	**P**	A	A	-	-	-	-	A	A	-	A	A	**1**
ANC 76	OAL	17-21	F	A	A	A	A	A	A	-	A	A	-	A	A	4
ANC 77	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 78	MA	36.9	F	**P**	A	A	A	A	A	A	A	A	A	A	A	**1**
ANC 80	AUD	UD	PM	-	-	-	A	A	A	A	A	A	A	A	**P**	4
ANC 81	MA	48.1	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 82	OAL	14-16	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 92	MA	33.2	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 93	MA	35.2	PM	A	A	A	A	A	A	A	A	**P**	A	A	**P**	4
ANC 94	MA	35.2-38.2	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 96	YA	25-35	PF	-	-	-	A	A	A	A	A	A	A	A	A	4
ANC 98	OA	60-61.2	M	A	A	**P**	A	A	A	A	A	A	A	A	**P**	4
ANC 102	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 104	MA	30.7	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 106	MA	48.1	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 107A	OAL	16-18	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 108	OAL	16-21	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 109	MA	36.4	F	**P**	**P**	A	A	A	A	A	A	A	A	A	**P**	**1**

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
ANC 110	MA	33-45	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 111	YA	19-25	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 112	YA	30.7	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 112A	AUD	UD	UD	-	-	-	A	A	A	-	A	A	-	A	A	5
ANC 113	MA	48.1	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 115	MA	35.2-38.2	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 116	OA	50.9	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 117	OA	71.7	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 118	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 119	YA	17-25	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 120	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 121	MA	35.2-38.2	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 122	MA	35.2	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 123	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 128	YA	25-35	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 133	YA	17-35	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 134	MA	34.5	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 135	OA	45+	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 136	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 137	OA	45+	M	-	-	-	A	A	A	-	-	-	-	-	-	5
ANC 140	YA	29.5	PM	**P**	A	A	A	A	A	A	A	A	A	A	**P**	**1**
ANC 141	OA	74.4	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 142	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 143	MA	28.7	PM	**P**	A	**P**	A	A	A	A	A	A	A	A	A	**1**
ANC 144	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
ANC 147	OA	77.5	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 148A	MA	25+	PF	**P**	A	A	A	A	A	-	-	-	-	-	-	**1**
ANC 152	YA	15-24	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 154	OA	75	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 155	AUD	UD	UD	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 156	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 157	MA	38.2	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 158	AUD	UD	M	-	-	-	-	-	-	A	A	A	A	A	A	4
ANC 159	AUD	UD	UD	-	-	-	-	-	-	A	A	A	A	A	**P**	5
ANC 160	OAL	17-21	F	A	A	A	-	-	A	A	A	A	A	A	**P**	4
ANC 161A	AUD	UD	M	-	-	-	-	-	-	A	A	A	A	A	A	5
ANC 162	OAL	15-17	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 165	YA	30.7	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 167	OAL	17-19	M	**P**	A	A	A	A	A	A	A	A	A	A	A	**1**
ANC 168	YA	18-27	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 170	MA	48.1	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 171	YAL	15.3	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 172	MA	33-45	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 173	MA	38.2	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 175	YA	30.7	PM	-	-	-	A	A	A	A	A	A	A	A	A	4
ANC 176	MA	33-45	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 177	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 178	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 179	YA	17-25	M	A	A	A	A	A	**P**	A	A	A	A	A	A	4
ANC 182	YA	17-21	F	A	A	A	A	A	**P**	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
ANC 183	OA	50+	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 184	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 185	OAL	15-19	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 185A	MA	35.2	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 188	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 190	YA	25-35	PF	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 191	OA	50+	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 193	YA	25-35	F	A	A	A	-	-	A	A	A	A	A	A	**P**	4
ANC 198	MA	33-45	M	-	-	-	-	-	-	A	A	A	A	A	A	4
ANC 199	AUD	UD	UD	-	-	-	-	-	-	A	A	A	A	A	A	5
ANC 200	YA	18-27	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 201	OA	61.2	PM	A	A	A	A	A	**P**	A	A	A	A	A	A	4
ANC 202	YA	25-35	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 204A	OA	50+	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 205	OAL	15-21	F	-	-	-	-	-	A	A	A	A	A	A	A	4
ANC 209	YA	25-35	PM	-	-	-	-	-	-	A	A	A	A	A	A	4
ANC 210	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 211	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 212	MA	35.2-38.2	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 213	AUD	UD	M	-	-	-	-	-	-	A	A	A	A	A	A	4
ANC 214	MA	33-45	M	-	A	A	A	A	A	A	A	A	A	A	A	4
ANC 216	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 217	OA	45+	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 217A	MA	42.1	M	A	A	A	A	A	A	A	-	A	-	-	-	4
ANC 218	YA	17-25	F	A	A	A	A	A	A	A	**P**	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
ANC 220	MA	23-70	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 221	YA	30.7	M	-	-	-	A	A	A	A	A	A	A	A	A	4
ANC 222	MA	33-45	PM	-	-	-	-	-	-	A	A	A	A	A	A	4
ANC 223	AUD	UD	UD	-	-	-	-	-	-	A	A	A	A	A	**P**	5
ANC 224	OA	45+	F	A	A	A	-	-	A	A	A	A	A	A	A	4
ANC 225	YA	25-35	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 226	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 229	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 230	YA	18-27	M	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 230A	MA	48.1	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 234	YA	31.3	AB	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 235	YA	25-35	UD	**P**	**P**	A	A	A	A	A	A	A	A	A	A	**1**
ANC 237	OA	45+	PM	-	-	-	A	A	A	A	A	A	A	A	A	4
ANC 238	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	**3**
ANC 240	YA	25-35	PM	**P**	**P**	**P**	A	A	A	A	A	A	A	A	**P**	**1**
ANC 241	OA	50+	PF	**P**	A	**P**	A	A	A	A	A	A	A	A	A	**1**
ANC 242	MA	33-45	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 243	YA	23.4-41.4	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 244	YA	17-35	PM	A	**P**	A	A	A	A	A	A	A	A	A	**P**	**2**
ANC 247	MA	45.6	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 248	YA	25-35	PM	-	-	-	-	-	-	-	-	A	A	A	A	5
ANC 252	YA	25-35	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 256	AUD	UD	PF	-	-	-	A	A	A	A	A	A	A	A	A	4
ANC 257	OA	45-66	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 259	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4

Individual	Age Category	Age (years)	Sex	1	2	3	4	5	6	7	8	9	10	11	12	Diagnosis
ANC 262A	MA	35.2-38.2	F	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC 263	OA	63.2-110	PF	A	**P**	A	A	A	A	A	A	A	A	A	A	4
ANC 263A	AUD	UD	UD	-	-	-	-	-	-	A	A	A	A	A	A	4
ANC 266	MA	33-45	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 267	YA	25-35	PF	-	-	-	-	-	-	A	A	A	A	A	A	5
ANC 269	YA	25-45	PM	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 270	YA	17-25	F	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 271	AUD	UD	UD	A	A	A	A	A	A	-	A	A	A	A	A	4
ANC 272	AUD	UD	UD	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC 274	OAL	18-19	F	-	-	-	-	-	-	A	A	A	A	A	**P**	4
ANC 276	MA	48.1	F	-	-	-	-	-	-	A	A	A	A	A	A	4
ANC 277	AUD	UD	PM	-	-	-	A	A	A	A	A	A	A	A	**P**	4
ANC 278	YA	25-35	PM	A	A	A	A	A	A	-	A	A	A	A	**P**	4
ANC 280	YA	17-25	M	A	A	A	A	A	A	A	A	A	A	A	A	4
ANC *2	OA	83.4	PF	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC UNCAT A	OA	76.1	M	-	-	-	-	-	A	A	A	A	A	A	A	4
ANC UNCAT B	OA	50+	PM	A	A	A	A	A	A	A	A	A	A	A	**P**	4
ANC UNCAT C	YA	25-35	M	**P**	A	A	A	A	A	A	-	-	-	-	-	**1**
ANC UNCAT DA	OA	45+	PF	-	-	-	-	-	-	A	A	A	A	A	A	4
ANC UNCAT E	AUD	UD	UD	A	A	A	A	A	A	-	A	A	A	-	A	4
ANC UNCAT E2	YA	25-35	PM	A	A	A	A	A	A	-	A	A	A	-	A	4
ANC UNCAT F	MA	5.2	M	**P**	A	A	A	A	A	A	A	A	A	A	A	**1**

Features scored are clear rib new bone formation at the visceral end (1), less clear rib new bone formation at the sternal end (2), other rib new bone formation with a different appearance (3), vertebral body collapse (4), vertebral lytic lesions in the anterior thoracic and lumbar bodies (5), vertebral lytic lesions in other locations or with some new bone formation present (6), lytic lesions of the major weight-bearing joints (7), lytic lesions of other joints or with some new bone formation present (8), lytic lesions of other elements or with atypical appearance (9), bilateral symmetrical new bone formation localized to the forearm or lower leg (10), new bone formation in atypical locations (11), and other periosteal new bone formation (12). Nondiagnostic features are highlighted in red, possible features in green, and probable features in blue. Features are scored as present (P), absent (A), or unobservable (-). Features are scored as present (P), absent (A), or unobservable (-). Age categories are abbreviated as YAL (Younger adolescent, 12-15 years), OAL (Older adolescent, 16-19 years), YA (Young adult, 20-34 years), MA (Middle adult, 35-49 years), OA (Older adult, 50+ years), AUD (Adult undetermined). Sex categories abbreviated as M (male), PM (probable male), AB (ambiguous), PF (probable female), F (female), UD (undetermined). Diagnostic categories are outlined in Section 3.2.2.1 (1 probable, 2 possible, 3 insufficient data, 4 no evidence due to absence of features, 5 no evidence and insufficient preservation to evaluate).