Thesis written by

Emily A. Brahler

B.S., Kent State University, 2015

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Approved by

Linda B. Spurlock, Advisor

Mary Ann Raghanti, Chair, Department of Anthropology

James L. Blank, Dean, College of Arts and Sciences
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CHAPTER I

Introduction

This study aims to examine the skeletal consequences of hypovitaminosis D or vitamin D deficiency in adults, a condition known as osteomalacia (Albright et al., 1946; Albright and Reifenstein, 1948; Magilligan and Dulligan, 1952; Rose, 1964; Chalmers et al., 1967; Holick, 1996; Mensforth, 2002; Rucker et al., 2002; Holick, 2003; Mensforth, 2003; Holick, 2004a; Holick, 2004b; Brickley, Mays, and Ives, 2005; Brickley, Mays, and Ives, 2007; Holick, 2007; Bhan, Rao, and Rao, 2010; Pearce and Cheetham, 2010; Holick, 2012a; DeLuca, 2014; Ives and Brickley, 2014; Treager and Isales, 2017). This pathology has been examined within a historical skeletal collection in order to assess indicators of this condition, explore the demographic distribution of this disease within the specific circumstances of this collection, and assess any additional effects to health and mortality potentially relating to hypovitaminosis D status. In order to fully explore these topics, it is essential to address the specifics of vitamin D synthesis, how osteomalacia is identified, potential nonskeletal ramifications of hypovitaminosis D, and what factors predispose certain groups to risk of deficiency.

Vitamin D Synthesis

Vitamin D primarily functions in stabilizing mineral balance in the body; it works to increase absorption of calcium and phosphate from the intestines, acts in the kidneys to save calcium that could be excreted, and ultimately helps to facilitate hardening or mineralization of bone, with these minerals, during growth and bone turnover (Gloth and Tobin, 1995; Holick,
1996; Haussler et al., 1998; Berry, Davies, and Mee, 2002; Holick, 2003; Holick, 2004a; Holick, 2004b; Jablonski, 2004; Weisberg et al., 2004; Holick, 2007; Holick and Chen, 2008; Chaplin and Jablonski, 2009; Mithal et al., 2009; Holick, 2012a; Genzen et al., 2013; Uday and Högler, 2017). It is acquired by either spending time in the sun, the most significant mode of acquisition, or by intake through diet or specifically designed supplements (Holick, 1989; Holick, 1996; Mensforth, 2002; Holick, 2003; Holick, 2004a; Holick, 2007; Macdonald et al., 2011; Holick, 2012a; Holick et al., 2012; Björk et al., 2013; Vierucci et al., 2013). When the skin is exposed to the sun, UVB rays, rays between 280 and 320 nm in wavelength (Jablonski and Chaplin, 2000 p. 59), interact with a substance naturally in the skin called 7-dehydrocholesterol; the resulting biochemical reactions produce cholecalciferol or vitamin D₃ (Frame and Parfitt, 1978; Holick, 1989; Holick, 1996; Mensforth, 2002; Holick, 2003; Holick, 2004a; Holick, 2004b; Holick, 2007; Holick and Chen, 2008; Macdonald et al., 2011; Holick, 2012a; Björk et al., 2013; Vierucci et al., 2013).

Only vitamin D₃ or cholecalciferol is produced from sun exposure, however, both ergocalciferol or vitamin D₂ and vitamin D₃, both considered precursors for vitamin D, can be obtained from some foods and supplements (Stamp and Round, 1974; Holick, 1996; Heaney et al., 2011; Endres and Rude, 2006 as cited by Genzen et al., 2013). In terms of diet, some foods have been found to naturally bolster vitamin D status, such as certain species of fish and mushrooms (Jablonski and Chaplin, 2000; Lamberg-Allardt et al., 2001; Holick, 2004a; Holick, 2007; Pearce and Cheetham, 2010; Holick, 2012a), whereas other foods in the United States, such as milk, have been fortified with vitamin D since the 1930s (Stamp and Round, 1974; Welch, Bergstrom, and Tsang, 2000; Pearce and Cheetham, 2010).
After reactions in the skin or consumption of vitamin D$_2$ or D$_3$, the substance 25-hydroxycholecalciferol or 25(OH)D is produced through a hydroxylation reaction in the liver (Stamp and Round, 1974; Holick, 1996; Holick, 2004a; Jablonski, 2004; Heaney et al., 2011; Findlay et al., 2012; Endres and Rude, 2006 as cited by Genzen et al., 2013). This substance is often measured to assess poor or appropriate vitamin D status (Heaney, 1999; Chaplin and Jablonski, 2009; Findlay et al., 2012; Endres and Rude, 2006 as cited by Genzen et al., 2013).

Although vitamin D can be saved in different tissues, including fat tissue for future use, its overall longevity has not been agreed upon (Clements et al., 1992; Holick, 2004a; Holick, 2004b; Cannell et al., 2008; Holick and Chen, 2008; Cheng et al., 2014).

Following the hydroxylation in the liver, another reaction is then required in the kidneys, where 25-hydroxycholecalciferol is converted to 1,25-dihydroxycholecalciferol or 1,25(OH)$_2$D, which is the “biologically active form” of vitamin D (Holick, 1996; Holick, 2003; Holick, 2004a; Holick, 2004b p.1678S; Holick, 2007 p. 268; Holick and Chen, 2008; Chaplin and Jablonski, 2009 p. 451; Heaney et al., 2011; Holick, 2012a p. 12S; Jablonksi and Chaplin, 2012 p. 787; Björk et al., 2013). This reaction can also occur in several other tissues including the lungs, breast tissue, several immune system cells, and the skin (Hewison et al., 2004; Holick and Chen, 2008 p. 1083S). In addition, this reaction is influenced by several feedback mechanisms including circulating calcium levels and levels of parathyroid hormone present; parathyroid hormone is secreted in efforts to increase levels of calcium in plasma when they register as too low, in part by taking calcium from bones (Holick, 1996; Holick, 2004a; Holick, 2004b; Kamycheva, Sundsfjord, and Jorde, 2004; Holick, 2007; Holick and Chen, 2008; Holick, 2012a).

Parathyroid hormone is important for increasing the reaction in the kidneys to produce the “active form” of vitamin D; it is involved in a negative feedback loop, inducing synthesis of

Hypovitaminosis D, regardless of cause, can trigger elevated levels of parathyroid hormone, or secondary hyperparathyroidism, that can persist, causing a host of health issues, many of which affect health of the skeleton (Holick, 1996; Mensforth, 2002; Vieth and Fraser, 2002; Bilezikian, 2003; Holick, 2003; Holick, 2004a; Holick, 2004b; Holick, 2007; Lila et al., 2012; Gasser, 2013). Therefore, it is important to recognize that levels of parathyroid hormone can indicate deeper concerns with vitamin D synthesis and metabolism (Szabo et al., 1989; Holick, 2007; Bikle, 2009).

Once 1,25-dihydroxycholecalciferol is produced, this substance goes on to connect with a designated nuclear receptor, referred to as the VDR or vitamin D receptor (Holick, 1996; Haussler et al., 1998; Mughal et al., 1999; Holick, 2003; Holick, 2004a; Holick, 2004b; Holick, 2007; Holick and Chen, 2008; Holick, 2012a; DeLuca, 2014; Kim, 2015). 1,25(OH)₂D affects gene regulation in humans and works in many ways like, and in some ways with, other steroid hormones, such as progesterone (Mughal et al., 1999; Kim, 2015). These receptors are found in a multitude of tissues, well over 30 (Bouillon, Okamura, and Norman, 1995; Norman, 2008a,b) including the intestines, kidneys, bone including the marrow, several immune system cells, breast tissue, uterine tissue, the ovaries and testes, prostate, and some muscle cells (Bouillon, Okamura, and Norman, 1995; Norman, 2008a,b).

The presence of these receptors in many tissues of the body has led to extensive research into potential nonskeletal functions of vitamin D that can even affect mortality (John et al., 1999;
Ahonen et al., 2000; Freedman, Dosemeci, and McGlynn, 2002; Li et al., 2002; Feskanich et al., 2004; Xiang et al., 2005; Garland et al., 2006; Garland et al., 2007; White et al., 2008; Gombart, 2009; Kestenbaum et al., 2011; Ritterhouse et al., 2014; Schmidt et al., 2014; Kim, 2015). For example, vitamin D has been found to specifically affect cells important to immune response such as T and B cells (Ritterhouse et al., 2014; Kim, 2015). Poor vitamin D status has been found to relate to lessened immune responses and in turn a higher likelihood of “bacterial and viral infections” (White et al., 2008; Gombart, 2009 p. 1151). Consequently, vitamin D status has also been considered in risk factors for infectious diseases like tuberculosis (Wilkinson et al., 2000).

In addition to overall immunity, vitamin D is correlated with cardiovascular health (Li et al., 2002; Xiang et al., 2005; Kestenbaum et al., 2011; Schmidt et al., 2014). For example, Kestenbaum et al. (2011), suggests poor vitamin D status is linked with “all-cause mortality and incident myocardial infarction” (Kestenbaum et al., 2011 p. 1436). Additionally, elevated parathyroid hormone secretion was related to “incident heart failure” in this study (Kestenbaum et al., 2011 p. 1436). Vitamin D has also been explored in the renin-angiotensin system (Li et al., 2002; Xiang et al., 2005). A murine model also shows a connection with “vascular and valve calcification” (Schmidt et al., 2014 p. 642).

Vitamin D status has also been linked to several different cancers, including breast, ovarian, and prostate (John et al., 1999; Ahonen et al., 2000; Freedman, Dosemeci, and McGlynn, 2002; Mensforth, 2003; Feskanich et al., 2004; Garland et al., 2006; Garland et al., 2007). Freedman, Dosemeci, and McGlynn (2002), found an association between women with “non-farming outdoor jobs” and a lower risk of both breast and colon cancer (Freedman, Dosemeci, and McGlynn, 2002 p. 259). Similarly, a significant association has been found between higher levels of 25(OH)D and less risk for colorectal cancer in females (Feskanich et
al., 2004). A relationship between risk of prostate cancer in men and lower levels of 25(OH)D has also been suggested (Ahonen et al., 2000).

It is clear that hypovitaminosis D can potentially lead to serious health problems, however there is little agreement on what levels are reflective of definitive deficiency and how supplements should be recommended (Genius et al., 2009; Findlay et al., 2012). According to Pearce and Cheetham (2010), over 75 nmol/L of 25(OH)D is considered “optimal,” between 50-75 nmol/L is “adequate,” 25-50 nmol/L is “associated with disease risk” or “insufficient,” and below 25 nmol/L is “deficient” and accrues risk for “rickets and osteomalacia” (Pearce and Cheetham, 2010 p. 142). In addition, Harris et al. (2000) suggests that levels of “at least 50 nmol/L if not higher” seem to have a positive influence on both “blacks and whites” in terms of decreasing influence of parathyroid hormone (Harris et al., 2000 p. 4129).

Osteomalacia

There are immense impacts of long-standing hypovitaminosis D on the skeleton (Albright et al., 1946; Albright and Reifenstein, 1948; Magilligan and Dulligan, 1952; Rose, 1964; Chalmers et al., 1967; Jaffe, 1972; Ortner and Putschar, 1981; Holick, 1996; Mensforth, 2002; Rucker et al., 2002; Holick, 2003; Mensforth, 2003; Schamall et al., 2003; Holick, 2004a; Holick, 2004b; Weisberg et al., 2004; Brickley, Mays, and Ives, 2005; Holick, 2007; Brickley, Mays, and Ives, 2007; Bhan, Rao, and Rao, 2010; Pearce and Cheetham, 2010; Holick, 2012a; DeLuca, 2014; Ives and Brickley, 2014; Treager and Isales, 2017). Persistent deficiency in children can lead to rickets, a disease in which mineralization does not occur during bone growth (Jaffe, 1972; Ortner and Putschar, 1981; Holick, 1996; Holick, 2003; Mensforth, 2003; Schamall et al., 2003; Holick, 2004a; Holick, 2004b; Weisberg et al., 2004; Brickley, Mays, and Ives,
2005; Holick, 2007; Holick and Chen, 2008; Holick, 2012a). This lack of mineralization leads to specific changes at the “bone-growth cartilage-junction” and overall softened bones that become easily deformed (Ortner and Putschar, 1981; Schamall et al., 2003 p. 284; Weisberg et al., 2004 p. 1697S; Brickley, Mays, and Ives, 2005). Accordingly, rickets causes several distinct deformities including “bowing” of the tibias, which persist into the adult skeleton (Ortner and Putschar, 1981; Schamall et al., 2003 p. 284; Weisberg et al., 2004 p. 1697S; Brickley, Mays, and Ives, 2005).

In adults, osteomalacia can arise (Albright et al., 1946; Albright and Reifenstein, 1948; Magilligan and Dulligan, 1952; Rose, 1964; Chalmers et al., 1967; Holick, 1996; Mensforth, 2002; Rucker et al., 2002; Holick, 2003; Mensforth, 2003; Holick, 2004a; Holick, 2004b; Brickley, Mays, and Ives, 2005; Brickley, Mays, and Ives, 2007; Holick, 2007; Bhan, Rao, and Rao, 2010; Pearce and Cheetham, 2010; Holick, 2012a; DeLuca, 2014; Ives and Brickley, 2014; Treager and Isales, 2017). It is also characterized by a “lack of mineralization” and softened bone tissue due to deficiency, however because growth is no longer occurring, the more “subtle” deformities sustained are different from rickets (Ortner and Putschar, 1981; Brickley, Mays, and Ives, 2005 p. 389; Winzenberg and Jones, 2013 p. 141). It is important to note that “osteomalacia” has been used to describe skeletal alterations caused by hypovitaminosis D in varying age groups; however in this study, this term will be used to refer to this pathology in adults, in accordance with “paleopathological convention,” and in accordance with other recent studies (Brickley, Mays, and Ives, 2007 p. 68).

In osteomalacia, bone remodeling proceeds as normal: old bone is removed by osteoclasts, and new osteoid is laid down by osteoblasts (Albright et al., 1946; Albright and Reifenstein, 1948; White and Folkens, 2005; White, Black, and Folkens, 2012). However,
“calcium salts” do not mineralize the new, and sometimes elevated amounts, of osteoid; this new tissue is therefore “of minor quality” (Albright et al., 1946; Magilligan and Dulligan, 1952 p. 170; Frame and Parfitt, 1978; Schamall et al., 2003 p. 284; White and Folkens, 2005; White, Black, and Folkens, 2012). This key difference in bone turnover results in bone tissue that is “soft,” leading to substantial “weakening,” and more easily susceptible to deformation (Albright et al., 1946; Albright and Reifenstein, 1948; Parfitt, 1998; Mensforth, 2002; Francis and Selby, 1997 as cited by Brickley, Mays, and Ives, 2007 p. 68). Consequently, affected bones often have a “cardboard-like consistency” (Ortner and Pustchar, 1981 p. 280) that “slowly bend rather than fracture” (Rose, 1964 p. 76).

This “softened” texture is characteristic of prolonged hypovitaminosis D, as opposed to other bone pathologies such as osteoporosis (Steinbach, Kolb, and Gilfillian, 1954 p. 394; Rose, 1964; Frame and Parfitt, 1978; Manolagas, 2000; White and Folkens, 2005; Court-Brown and Koval, 2006 as cited by McNulty, 2009; Bhan, Rao, and Rao, 2010; White, Black, and Folkens, 2012). While osteoid is mineralized in osteoporosis, the balance of bone resorption and bone formation is lost, resulting in depleted, “brittle” bones as opposed to “soft” (Rose, 1964 p. 76; Frame and Parfitt, 1978; Manolagas, 2000; White and Folkens, 2005; Rothschild and Martin, 2006; Francis and Selby, 1997 as cited by Brickley, Mays, and Ives, 2007 p. 68; Court-Brown and Koval, 2006 as cited by McNulty, 2009 p. 22; Bhan, Rao, and Rao, 2010; White, Black, and Folkens, 2012). Although both of these pathologies affect bone mineral density and overall strength of the skeleton (Rose, 1964; Frame and Parfitt, 1978; Adams et al., 1999; Manolagas, 2000; White and Folkens, 2005; Court-Brown and Koval, 2006 as cited by McNulty, 2009; Bhan, Rao, and Rao, 2010; White, Black, and Folkens, 2012), these pathologies are not found to commonly present together in the same individual (Nordin et al., 1980).
Osteomalacia leads to characteristic deformations that, as previously mentioned, are more “subtle” than what rickets presents (Ortner and Putschar, 1981; Brickley, Mays, and Ives, 2005 p. 389). These deformations have been faithfully identified using “macroscopic evaluations” and radiographic analysis (Mensforth, 2002; Mensforth, 2003; Schamall et al., 2003; Brickley, Mays, and Ives, 2005; Brickley, Mays, and Ives, 2007; Ives and Brickley, 2014 p. 46). Indications manifest as “ribbon-like zones of decalcification” that are “symmetrical,” and persist (Milkman, 1930; Albright et al., 1946 p. 402; Albright and Reifenstein, 1948 p. 206, 210; Le May and Blunt, 1949; Magilligan and Dulligan, 1952; Steinbach, Kolb, and Gilfillian, 1954; Mankin, 1974; Berry, Davies, and Mee, 2002; Francis and Selby, 1997 as cited by Brickley, Mays, and Ives, 2007). These areas have been commonly deemed “umbauzonen,” “Looser’s zones,” and “pseudofractures,” which were first detailed in the early 20th century (Milkman, 1930; Looser, 1920a,b as cited by Le May and Blunt, 1949 p. 521; Frame and Parfitt, 1978 p. 969; Francis and Selby 1997, as cited by Brickley, Mays, and Ives, 2007 p. 69). These abnormalities differ from “true fractures” which have a “complete separation of bone continuity” (Le May and Blunt, 1949 p. 521; McKenna et al., 1987). Indications of osteomalacia appear in otherwise “normal” bone; tissue not affected by disease or “trauma” (Albright et al., 1946 p. 210; Steinbach, Kolb, and Gilfillian, 1954 p. 388).

These areas of weakness or pseudofractures can lead to visible deformities (Mensforth, 2002; Mensforth, 2003; Brickley, Mays, and Ives, 2005; Brickley, Mays, and Ives, 2007; Brickley and Ives, 2008; Ives and Brickley, 2014). More severe deformities give the appearance of “folding” or buckling of the bone tissue, that differ from fractures caused by typical trauma (Mensforth, 2002; Mensforth, 2003; Brickley, Mays, and Ives, 2005 p. 394; Brickley, Mays, and
Ives, 2007; Brickley and Ives, 2008; Ives and Brickley, 2014). Therefore, the term pseudofractures will refer to these visible buckling deformities in this study.

There are four classifications of osteomalacia; each identified based on specific biochemical characteristics such as calcium and phosphatase serum levels, and whether or not pseudofractures have manifested (Albright and Reifenstein, 1948; Magilligan and Dulligan, 1952). Accordingly, pseudofractures and the observable deformities they can cause are only present in the more severe classifications of the disease; these serious forms are the degrees of osteomalacia that will be explored in this study (Magilligan and Dulligan, 1952; Steinbach, Kolb, and Gilfillian, 1954; Chalmers et al., 1967; Morgan, Hunt, and Paterson, 1970; Nordin et al., 1980; McKenna et al., 1983; Ives and Brickley, 2014).

Another skeletal indication of osteomalacia is the presence of protrusio acetabuli, a condition also called “Otto’s pelvis” (Frame and Parfitt, 1978; Bible et al., 1983 p. 323; Brickley, Mays, and Ives, 2007). This condition is characterized by thinning within the acetabulum, that results in deepening or “protruding” of the acetabulum into the pelvic inlet (Bible et al., 1983 p. 323). Bible et al. (1983), verified this relationship, finding that 50% of their sample of patients with osteomalacia had protrusio acetabuli (Bible et al., 1983).

The exact cause of hypovitaminosis D, whether it be lack of sun exposure, lack of dietary intake of appropriate foods and/or supplements, age related changes in synthesis efficiency, or an underlying health issue (Eisman, 1988; Holick, 1989; Holick, 1996; Mensforth, 2002; Holick, 2004a; Holick, 2007; Macdonald et al., 2011; Holick, 2012a; Holick et al., 2012; Björk et al., 2013; Vierucci et al., 2013) does not affect the characteristics of osteomalacia that present; severe cases will manifest pseudofractures and associated deformities regardless of the root cause of deficiency (Rose, Lumb, and Dent, 1957).
Several key areas of the skeleton demonstrate reliable indicators of osteomalacia. Various areas of the scapula are found to be affected, most notably the “axillary edge” of the scapula (Albright and Reifenstein, 1948 p. 210; Le May and Blunt, 1949; Chalmers et al., 1967; Rothschild and Martin, 2006; Ives and Brickley, 2014), the inferior angle (Rothschild and Martin, 2006), and the “inferior border” of the spinous process (Le May and Blunt, 1949; Brickley, Mays, and Ives, 2007; Ives and Brickley, 2014 p. 53). The ribs are also often cited as a frequently affected region (Albright and Reifenstein, 1948; Le May and Blunt, 1949; Chalmers et al., 1967; Mensforth, 2002; Brickley, Mays, and Ives, 2005; Rothschild and Martin, 2006; Ives and Brickley, 2014). The ilia (Le May and Blunt, 1949), the ischia (Albright and Reifenstein, 1948), and the pubic ramus (Albright and Reifenstein, 1948; Le May and Blunt, 1949; Chalmers et al., 1967; Rothschild and Martin, 2006) are all mentioned as commonly affected areas of the pelvis. The neck of the femur also shows indicators of osteomalacia (Albright and Reifenstein, 1948; Le May and Blunt, 1949; Chalmers et al., 1967; Rothschild and Martin, 2006).

In addition to these more classical areas, characteristic deformities are also identified in the vertebrae (Jaffe, 1972; Mensforth, 2002; Brickley, Mays, and Ives, 2005). However, these deformations differ from what occurs in osteoporosis; osteoporotic vertebrae show “crush” and “wedge” fractures (Rose, 1964; Nordin et al., 1980; Francis and Selby, 1997 as cited by Brickley, Mays, and Ives, 2005; Pitt, 1988 as cited by Brickley, Mays, and Ives, 2005 p. 76; Curate, Silva, and Cunha, 2016 p. 367). Damage to the body of the vertebrae caused by “herniation of the nucleus pulposus of the intervertebral disc,” sometimes result from osteoporotic weakening (Rose, 1964 p. 76; Dar et al., 2010). Referred to as Schmorl’s nodes, this pathology is common among individuals within the Hamann-Todd Collection; however, no
scored vertebrae in this study had Schmorl’s nodes due to their potential connection with osteoporosis and other non-osteomalacic disorders (Rose, 1964; Dar et al., 2010).

Other lesser affected areas that have been mentioned in previous studies include the metatarsals (Chalmers et al., 1967; Rothschild and Martin, 2006), and other long bones, such as the ulna (Chalmers et al., 1967; Rothschild and Martin, 2006), in addition to the sternum (Jaffe, 1972; Mensforth, 2002). According to Molleson et al. (1993), “acutely angled sacra” are also cited as evidence of osteomalacia (Molleson et al., 1993 p. 26). Brickley, Mays, and Ives (2005), found similar results in their survey of osteomalacia within two major historical skeletal collections in Europe: the Galler Collection in Switzerland and the Federal Museum for Pathological Anatomy in Austria (Brickley, Mays, and Ives, 2005).

Individuals suffering from osteomalacia present a variety of symptoms. According to Brickley, Mays, and Ives (2007), symptoms such as “gait disturbance,” in addition to pain and weakness in “the muscles and bones” would be present (Brickley, Mays, and Ives, 2007 p. 76). This weakness can translate into issues standing up from a chair or other “seated position” (Mensforth, 2002 p. 3). Others also detailed the presentation of “pain and weakness” for prolonged periods, in some cases “for months or even years” (Nowell, Evans, and Kurrein, 1951 p. 92, 91; Chalmers et al., 1967). This discomfort is concentrated in “the extremities, pelvis, or chest wall” much in accordance with some of the key areas in which osteomalacia indicators, like pseudofractures, have been found (Albright and Reifenstein, 1948; Le May and Blunt, 1949; Nowell, Evans, and Kurrein, 1951 p. 91; Brickley, Mays, and Ives, 2005; Rothschild and Martin, 2006; Ives and Brickley, 2014). The nature of osteomalacic pain also helps to further distinguish osteomalacia from other bone pathologies such as osteoporosis, in which the experienced pain is more sporadic (Chalmers et al., 1967). In addition to these symptoms, certain levels of calcium,
phosphate, and alkaline phosphatase also biochemically indicate osteomalacia as opposed to other pathologies like osteoporosis (Albright and Reifenstein, 1948; Chalmers et al., 1967).

*Risk Factors of Hypovitaminosis D and Osteomalacia*

Several factors play a role in determining an individual’s vitamin D status, and therefore contribute to the relative risk of complications such as osteomalacia, including biological sex, skin color, latitude, age, presence of other health problems and genetic specificities, and several lifestyle choices (Whitehead et al., 1981; Omdahl et al., 1982; Holick, 1989; Ebeling et al., 1992; Gloth et al., 1995; Holick, 1996; Harris et al., 2000; Jablonski, 2000; Jablonski and Chaplin, 2000; Godar, 2001; Lamberg-Allardt et al., 2001; Mensforth, 2002; Nesby-O’Dell et al., 2002; Rucker et al., 2002; Plotnikoff and Quigley, 2003; Holick, 2004a; Holick, 2004b; Jablonski, 2004; Harkness and Comer, 2005; Herm, Killguss, and Stewart, 2005; Bodnar et al., 2007; Chen et al., 2007; Holick, 2007; Holick and Chen, 2008; Carson, 2009; Chaplin and Jablonski, 2009; Centers for Disease Control and Prevention, 2011; Tsur, Metzger, and Dresner-Pollack, 2011; Jablonski and Chaplin, 2012; Freedman et al., 2013; Holmund-Suila et al., 2013; Vierucci et al., 2013; Wallace, Reider, and Fulgoni, 2013; Bonilla et al., 2014; Larose et al., 2014; Ritterhouse et al., 2014; Ruwanpathirana et al., 2014).

Males and females display differential risk of vitamin D deficiency at varying age levels (Whitehead et al., 1981; Jacques et al., 1997; Jablonski and Chaplin, 2000; Taaffe et al., 2001; Mensforth, 2002; Vieth and Fraser, 2002; Zamboni et al., 2002; Bilezikian, 2003; Plotnikoff and Quigley, 2003; Herm, Killguss, and Stewart, 2005; Chaplin and Jablonski, 2009; Lila et al., 2012; Gasser, 2013; Bonilla et al., 2014). In a recent study in the United Kingdom, female children had an elevated risk of having a poor vitamin D status in comparison to male children
(Bonilla et al., 2014). In addition, Plotnikoff and Quigley (2003), found that many females of “childbearing age” were either “moderately” or “severely” deficient in vitamin D (Plotnikoff and Quigley, 2003 p. 1467). Multiple pregnancies, especially close together, in addition to breastfeeding, can increase risks of deficiency, and in turn osteomalacia, due to higher vitamin D and calcium needs (Whitehead et al., 1981; Jablonski and Chaplin, 2000; Mensforth, 2002; Herm, Killguss, and Stewart, 2005; Chaplin and Jablonski, 2009). Females in older age categories have also been found to exhibit lower levels of vitamin D in comparison to men in their later years (Jacques et al., 1997; Zamboni et al., 2002). Sex differences in parathyroid hormone have also been found; males had lower levels of parathyroid hormone than females (Rucker et al., 2002). This perhaps suggests increased risk of skeletal ramifications in females, considering females are already known to have lower bone mineral density compared to males (Taaffe et al., 2001; Mensforth, 2002; Vieth and Fraser, 2002; Bilezikian, 2003; Lila et al., 2012; Gasser, 2013).

In some populations, sex differences in diet and activities, among other factors, may explain some of the discrepancies in vitamin D status (Godar, 2001; Centers for Disease Control and Prevention, 2011; Wallace, Reider, and Fulgoni, 2013). For example, Wallace, Reider, and Fulgoni (2013), found that males at every age were much more likely to obtain necessary vitamin D from the foods they consumed as opposed to females (Wallace, Reider, and Fulgoni, 2013). In addition, males were more likely than females to drink milk, which in modern times is fortified with vitamin D in the United States (Welch, Bergstrom, and Tsang, 2000; Centers for Disease Control and Prevention, 2011). Adolescent males are also more likely to spend time outside than female adolescents, another potential bolster to their vitamin D levels based on their sex (Godar, 2001).
Skin color, especially in relation to latitude of residence, is another factor that greatly affects vitamin D status (Jablonski and Chaplin, 2000; Jablonski, 2004; Chaplin and Jablonski, 2009; Jablonski and Chaplin, 2012). The immense spectrum of skin tones observed among human populations, is an evolutionary result of adaptations associated with vitamin D and another essential biological substance folate, which has been found to prevent neural tube birth defects; both of these substances have a profound positive effect on “reproductive success” (Medical Research Council Vitamin Study Research Group, 1991; Jablonski and Chaplin, 2000 p. 57, 62; Jablonski, 2004 p. 603; Chaplin and Jablonski, 2009; Jablonski and Chaplin, 2012).

The *Homo* lineage began in “equatorial Africa” with darker skin tones (Jablonski and Chaplin, 2000; Jablonski, 2004; Chaplin and Jablonski, 2009 p. 451; Jablonski and Chaplin, 2012 p. 785). These skin tones allowed folate stores to be shielded from destruction by persistent UVB exposure; the deeper the skin pigmentation, or the more of the “brownish-black” variety of melanin “eumelanin” present, the more “natural protection” is afforded to those in equatorial regions (Jablonski and Chaplin, 2000; Jablonski, 2004 p. 590-591; Chaplin and Jablonski, 2009; Jablonski and Chaplin, 2012). With subsequent “migration” out of Africa, paler skin that allowed ample vitamin D synthesis in locations north and south of the equator, was favored where UVB exposure is lessened and seasonal (Jablonski and Chaplin, 2000; Jablonski, 2004; Chaplin and Jablonski, 2009 p. 456; Jablonski and Chaplin, 2012). Lighter skin pigmentation, skin with less “eumelanin” and more of the “reddish-yellow” variety of melanin “pheomelanin” present, yields more “UVB penetration,” which provides more opportunities for vitamin D synthesis (Jablonski and Chaplin, 2000; Jablonski, 2004 p. 590; Chaplin and Jablonski, 2009 p. 451; Jablonski and Chaplin, 2012). Therefore, individuals with darker skin tones, living in areas farther from the equator inherently have a more difficult time properly synthesizing enough vitamin D due to the

Many studies have been conducted to assess the risks associated with those with darker skin tones living at northern latitudes (Nesby-O’Dell et al., 2002; Gordon et al., 2004; Bodnar et al., 2007; Carson, 2009; Shoben et al., 2011; Freedman et al., 2013; Vierucci et al., 2013; Bonilla et al., 2014). For example, Carson (2009), evaluated records of height for both white and black American male prisoners from the 1800s; records were obtained from prisons in 14 states including Ohio (Carson, 2009). There were noticeable differences in mean height, with white prisoners being taller, suggesting they were more likely to reach their height potential than black prisoners (Carson, 2009). This study went on to assert that black prisoners born outside of Africa were shorter than those born in Africa, indicating that these differences could be due to the difficulty of synthesizing enough vitamin D in a northern latitude (Carson, 2009).

In another study by Nesby-O’Dell et al. (2002), African-American women were much more likely to register as vitamin D deficient than white women, even in those who used supplements (Nesby-O’Dell et al., 2002). A similar result is demonstrated in Bodnar et al. (2007), where both black and white pregnant women in Pittsburgh, Pennsylvania, which has a latitude of 40ºN, were assessed for vitamin D status (Bodnar et al., 2007). Black women were much more likely to have a poor vitamin D status during pregnancy, and their children also had poorer vitamin D status after birth than white mothers and infants (Bodnar et al., 2007). A similar study, Harkness and Cromer (2005), analyzing teenage girls in Cleveland, Ohio, which has a latitude of 41ºN, also found that African-American females had significantly lower levels
of vitamin D than “non-African American girls” (Harkness and Cromer, 2005 p. 75.e3). Secretions of parathyroid hormone are also elevated in black or African-derived individuals (Shoben et al., 2011), within whom it has also been suggested that the parathyroid gland is more robust (Ghandur-Mnaymneh et al., 1986). This suggests increased risk of skeletal ramifications in those with darker skin (Mensforth, 2002; Vieth and Fraser, 2002; Bilezikian, 2003; Lila et al., 2012; Gasser, 2013).

In addition to the difficulties of living in a nonequatorial region, African-derived or black individuals and others with darker complexions are also more at risk of vitamin D deficiency due to aspects of their diet (Wallace, Reider, and Fulgoni, 2013). In Wallace, Reider, and Fulgoni (2013), “black and Mexican subpopulations” were less likely to consume the appropriate amounts of vitamin D and calcium than “white individuals” (Wallace, Reider, and Fulgoni, 2013 p. 328). This may be due in part to the fact that African-derived individuals and other groups with darker skin tones like those of “Hispanic” ancestry have a higher incidence of being lactose intolerant (Nicklas et al., 2009 p. 223). This would consequently restrict some of the fortified food sources available to these groups (Welch, Bergstrom, and Tsang, 2000; Nicklas et al., 2009; Wallace, Reider, and Fulgoni, 2013).

Some populations with lighter skin tones have shown unexpectedly high frequencies of vitamin D deficiency despite having less protective melanin in their skin (Harris et al., 2000; Jablonski and Chaplin, 2000; Lamberg-Allardt et al., 2001; Jablonski, 2004; Chaplin and Jablonski, 2009; Jablonski and Chaplin, 2012; Larose et al., 2014; Ritterhouse et al., 2014). These reports come from populations living at northern latitudes, which constitutes “approximately 30° N to the North Pole” (Harris et al., 2000; Jablonski and Chaplin, 2000 p. 80; Lamberg-Allardt et al., 2001; Larose et al., 2014; Ritterhouse et al., 2014). In these locations,
UVB rays and in turn vitamin D status, show sometimes extreme seasonal variations (Lamberg-Allardt et al., 2001; Rucker et al., 2002; Harkness and Cromer, 2005; Shoben et al., 2011; Vierucci et al., 2013; Larose et al., 2014). In addition, status appears to be at least partially dependent on “the amount of vitamin D produced and stored during the previous summer” (Vierucci et al., 2013 p. 1614). For example, Ritterhouse et al. (2014), found a high degree of “European-American men” as well as “individuals of African-American or Native American descent” from Oklahoma to be deficient (Ritterhouse et al., 2014 p. 9). In another study completed at 64º N in Norway, in a “mostly Caucasian” sample, results also indicated high levels of vitamin D deficiency (Larose et al., 2014 p. 165).

Increasing age is a commonly cited as a factor associated with hypovitaminosis D (Omdahl et al., 1982; Ebeling et al., 1992; Gloth et al., 1995; Jacques et al., 1997; Adams et al., 1999; Mensforth, 2002; Rucker et al., 2002; Shoben et al., 2011; Holmund-Suila et al., 2013). This relationship between vitamin D deficiency and older age holds true for both “homebound” or “confined” older individuals (Gloth et al., 1995 p. 1683, 1686), and populations of “healthy elderly people” (Omdahl et al., 1982 p. 1225). Many studies have also cited a connection between increasing age and indications of osteomalacia specifically (Nowell, Evans, and Kurrein, 1951; Chapuy et al., 1997; Mosekilde, 2005; Ives and Brickley, 2014). Potential reasons for this increased risk include changes with age, such as how the skin reacts to UVB rays and the beginning stages of synthesis (MacLaughlin and Holick, 1985; Holick, 1989; Need et al., 1993; Mosekilde, 2005), lower levels of vitamin D receptors within the intestines (Ebeling et al., 1992), and increases in parathyroid hormone secretions (Harris et al., 2000; Rucker et al., 2002; Kamycheva, Sundsfjord, and Jorde, 2004; Tsur, Metzger, and Dresner-Pollack, 2011; Giusti et al., 2006 as cited by Gorter et al., 2017).
Some genetic specificities also affect vitamin D status (Chen et al., 2005; Wang et al., 2010). For example, specific “genetic variations” found to be associated with increased risk of poor vitamin D status were identified in “individuals of European descent” (Wang et al., 2010 p. 182). Another study found that the genes that code for the vitamin D receptor or VDR “have several polymorphisms” (Chen et al., 2005 p. 2335).

Chronic diseases, and/or health issues associated with the liver and kidneys can also contribute to a poor vitamin D status (Moon, 1994; Jacques et al., 1997; Nesby-O’Dell et al., 2002; Rucker et al., 2002; Gordon et al., 2004; Shoben et al., 2011; Ulitsky et al., 2011; Freedman et al., 2013; Holmund-Suila et al., 2013; Vierucci et al., 2013; Larose et al., 2014; Ritterhouse et al., 2014). According to Holmund-Suila et al. (2013), a high proportion of individuals in Finland suffering from chronic diseases, such as “gastrointestinal diseases, cancer, renal diseases, diabetes and other endocrine diseases” were deficient (Holmund-Suila et al., 2013 p. 2). Similarly, Shoben et al. (2011), reported poorer status for those with diabetes mellitus among other risk factors (Shoben et al., 2011). Another study found vitamin D deficiency in a large proportion of patients with inflammatory bowel disease (Ulitsky et al., 2011). Other issues, such as excessive intake of toxic substances like “lead, cadmium, aluminum, and strontium” also lead to a decrease in synthesis of vitamin D and, in turn, deficiency risk (Moon, 1994 p. 559).

Obesity has also been linked to increase risk of deficiency (Jacques et al., 1997; Nesby-O’Dell et al., 2002; Rucker et al., 2002; Gordon et al., 2004; Shoben et al., 2011; Freedman et al., 2013; Vierucci et al., 2013; Larose et al., 2014; Ritterhouse et al., 2014).

Several aspects of lifestyle also contribute to how well vitamin D is synthesized throughout an individual’s life (Krall and Dawson-Hughes, 1999; Harris et al., 2000; Tsur, Metzger, and Dresner-Pollack, 2011; Cheng et al., 2014; Larose et al., 2014; Ogunsakin et al.,
Smoking has been found to correlate with degraded vitamin D status (Harris et al., 2000; Cheng et al., 2014; Larose et al., 2014), and decreased bone mineral density (Krall and Dawson-Hughes, 1999). In addition to smoking, habitual alcohol use is tied to inefficient vitamin D synthesis (Ogunsakin et al., 2016). According to Ogunsakin et al. (2016), sampled individuals suffering from AUD, or “alcohol use disorder” had lower serum levels of 25(OH)D and the active form of vitamin D (Ogunsakin et al., 2016 p. 191). Individuals in this study who suffered from AUD and were smokers had even lower levels of this substance than those who only smoked (Ogunsakin et al., 2016).

Various clothing styles have also been studied in relation to vitamin D status; lower status has been found in both males and females due to different ways of dress (Plotnikoff and Quigley, 2003; Baroncelli et al., 2008; El-Rassi, Baliki, and El-Hajj Fulheihan, 2009; Tsur, Metzger, and Dresner-Pollack, 2011). For example, a sample of “young, healthy ultra-orthodox men” in Israel was evaluated for vitamin D status (Tsur, Metzger, and Dresner-Pollack, 2011 p. 2897). Many of these young men were afflicted with “severe vitamin D deficiency,” despite being from an otherwise “unrecognized group at high-risk” (Tsur, Metzger, and Dresner-Pollack, 2011 p. 2897). In addition to this study, Plotnikoff and Quigley (2003), found higher levels of vitamin D deficiency among female participants from East Africa who adhere to specific guidelines for clothing modesty, including “covering the head, arms, and legs” than was found in male participants from East Africa (Plotnikoff and Quigley, 2003 p. 1468). Similar deficiencies have also been observed in females in the Middle East due to similar “cultural practices” among other factors (Baroncelli et al., 2008 p. 1743; El-Rassi, Baliki, and El-Hajj Fulheihan, 2009 p. 1).

General practices of avoiding the sun also affect vitamin D status (Jablonski and Chaplin, 2000; Jablonski, 2004; Chaplin and Jablonski, 2009; Jablonski and Chaplin, 2012; Vierucci et
al., 2013). In Vierucci et al. (2013), individuals in Italy ranging in age from 2 to 21 years old were evaluated for vitamin D deficiency (Vierucci et al., 2013). Lower status was associated with habitual use of sunscreen in every season but winter (Vierucci et al., 2013). Overzealous exposure of the skin to the UVB rays is a risk factor for certain skin cancers, however appropriate time spent in the sun is “beneficial” (Holick, 1996; Jablonski and Chaplin, 2000 p. 61; Jablonski, 2004; Holick, 2007; Holick and Chen, 2008; Chaplin and Jablonski, 2009; Genius et al., 2009; Holick, 2012b; Jablonski and Chaplin, 2012).

This study ultimately expects to expand upon previous literature in terms of what osteomalacia may look like in skeletal remains. We will explore how this disease distributes in relation to several of the demographic factors that predispose certain groups to deficiency, including biological sex, ancestry, and age in the context of this specific, past population living at a northern latitude. Through the use of associated records, any connections between hypovitaminosis D status and cause of death will also be evaluated, in accordance with the abundance of nonskeletal roles of vitamin D (John et al., 1999; Ahonen et al., 2000; Wilkinson et al., 2000; Freedman, Dosemeci, and McGlynn, 2002; Li et al., 2002; Feskanich et al., 2004; Xiang et al., 2005; Garland et al., 2006; Garland et al., 2007; White et al., 2008; Gombart, 2009; Kestenbaum et al., 2011; Ritterhouse et al., 2014; Schmidt et al., 2014; Kim, 2015).

**Hypotheses**

We posit that indicators of osteomalacia within the Hamann-Todd Osteological Collection, a historical skeletal collection representative of individuals from the late 19th and early 20th centuries in Cleveland, Ohio, will distribute the same demographically as is demonstrated in modern, living populations and archaeological remains. If correct, we expect to
find higher frequencies of osteomalacia indicators in females over males, those with darker skin
tones, or African-derived ancestry over European-derived ancestry, and in older individuals over
younger individuals.

We posit that osteomalacia causes skeletal changes to only certain bones. If correct, indicators of osteomalacia should be found in higher frequencies in the scapulae, ribs, areas of the pelvis, and the femur within this skeletal collection as has been demonstrated in previous clinical and archaeological studies.

We posit that established relationships between hypovitaminosis D and nonskeletal pathologies, such as infectious diseases, cardiovascular complications, and cancer, will hold true for the Hamann-Todd Osteological Collection. If correct, significant variation in frequency of osteomalacia indicators will be present when these individuals are evaluated based on reported cause of death.
CHAPTER II
Materials and Methods

Sampling and Methodology

Individuals from the Hamann-Todd Osteological Collection, currently housed at the Cleveland Museum of Natural History in Cleveland, Ohio were examined for gross evidence of osteomalacia, namely indications of pseudofractures. Osteomalacic pseudofractures are caused by sustained inadequate vitamin D metabolism (Albright et al., 1946; Albright and Reifenstein, 1948; Le May and Blunt, 1949; Mensforth, 2002; Mensforth, 2003; Brickley, Mays, and Ives, 2005; Brickley, Mays, and Ives, 2007; Brickley and Ives, 2008; Ives and Brickley, 2014). These pseudofractures are vulnerabilities in bone tissue that in severe cases can lead to “macroscopic” deformities that differ in cause and pattern from “true fractures” sustained from typical trauma; they manifest as “‘folding’” or collapse in the bone tissue (Le May and Blunt, 1949 p. 521, 524; McKenna et al., 1987; Mensforth, 2002; Mensforth, 2003; Brickley, Mays, and Ives, 2005 p. 394; Brickley, Mays, and Ives, 2007; Brickley and Ives, 2008; Ives and Brickley, 2014 p. 46).

This study aims to view osteomalacia within this historical skeletal collection by combining two separate samples of data collected using the same methodology. Dr. Robert Mensforth of Cleveland State University collected the first sample between 2001 and 2005. This sample yielded 1,132 individuals of both sexes and representatives of both European-derived or white, and African-derived ancestry, or black individuals. All individuals were adults with ages ranging from 18 years old to 99 years old.
The second sample was collected in 2016 by Emily A. Brahler of Kent State University, and served to supplement the original sample by increasing the proportion of older adult male individuals to accurately reflect the demographic distribution present in the Hamann-Todd Human Osteological Collection. This sample yielded 163 additional male individuals who were all 50 years old or older and representative of both European-derived and African-derived ancestry. Due to the supplementary nature of this second sample, not previously sampled European-derived males aged 50 years old or older housed in the lower twelve rows of organization within the collection were selected. African-derived males estimated to be 50 years old or older, and not previously sampled, were selected regardless of location due to the relative scarcity of this group within the collection as a whole. These two samples yielded a total of 1,295 individuals that are statistically represented in this study. The combination of these two samples provides a means of examining the frequency and distributions of osteomalacia among adult individuals in this collection for the first time on such a large-scale.

Throughout both samples individuals were also chosen for sampling if remains were relatively complete: the sternum, pelvis, and sacrum had to be present, along with some representative material from the vertebral column, ribs, at least one or both of the hands, feet, clavicles, and scapulae, and representative long bone material from one or both sides of the body. In addition, data such as sex, age, ancestry, and listed cause of death were also collected and used for all individuals from associated collection records.

Only postcrania were examined in this study, since deformations in the skull have mostly been attributed to complications of rickets found in children as opposed to osteomalacia in adults (Mankin, 1974; Eisman, 1988; Berry, Davies, and Mee, 2002; Pearce and Cheetham, 2010). In addition, several osteomalacia studies have not found the skull to be an affected area (Le May
and Blunt, 1949; Chalmers et al., 1967; Brickley, Mays, and Ives, 2005; Rothschild and Martin, 2006; Brickley, Mays, and Ives, 2007; Ives and Brickley, 2014). Focusing on the postcrania also helped to maintain uniformity in methodology between the first and second samples used in this study.

No minimum number of osteomalacia indicators was required for scoring in both samples; any individual exhibiting visible indications of osteomalacia, namely deformities associated with pseudofractures in any of the examined postcranial elements were accordingly scored as showing evidence of osteomalacia. An additional criterion was applied to scoring the pelvis: besides visible evidence of pseudofractures, individuals with evidence of protrusio acetabuli were scored as having evidence of osteomalacia. This condition has been associated with osteomalacia status, therefore serves as an additional indicator in this study (Bible et al., 1983; Brickley, Mays, and Ives, 2007).

Hamann-Todd Osteological Collection

The Hamann-Todd Collection began modestly in the late 19th century with the efforts of Carl August Hamann, a talented surgeon, and prominent faculty member of Western Reserve University, now Case Western Reserve University (Iscan, 1992; Hunt and Albanese, 2005; Kern, 2006). Hamann expressed interest in creating an institution dedicated to the study and appreciation of anatomy and began the collection with various animal and human specimens he had personally collected; this effort would become the Hamann Museum of Comparative Anthropology and Anatomy (Kern, 2006). Hamann then appointed Thomas Wingate Todd in the early 1900s as director of this museum (Cobb, 1959; Iscan, 1992; Kern, 2006). Todd then worked for over twenty years to acquire the 3,000+ human individuals and impressive

Most of the human individuals within the collection were bodies that remained unaccounted for at the Cuyahoga County Morgue and major hospitals in the area in the years when Todd was expanding the collection (Kern, 2006). This was made possible by a change in local legislature that required “unclaimed bodies” at local institutions to be formally reported to Todd (Kern, 2006 p. 10). The bodies could then be taken to Western Reserve Medical School where formal documents were produced on each individual including photographs and “anthropometric and demographic data” (Kern, 2006 p. 11). After being used for student cadaver dissections, the remains became a permanent part of the growing osteological collection with their associated records (Kern, 2006). Due to the nature of how these specimens were incorporated into the collection, these individuals represent a population that was “more socio-economically disadvantaged” within their urban setting (Iscan, 1992; McNulty, 2009 p. 78).

Both the overall size and the inclusion of these extensive records with each set of remains makes this collection highly unique (Kern, 2006). The collection has been and still is avidly used to evaluate various research questions deriving from students, researchers, and medical personnel. A few of the research questions explored since the creation of the collection have focused on trends in the aging process of the human skeleton, diagnostic elements of different fracture types, and how this collection compares in terms of general demographics with other osteological collections throughout the United States (Lovejoy et al., 1985; Mensforth and Latimer, 1989; Iscan, 1992; Hunt and Albanese, 2005; McNulty, 2009).

The individuals comprising the Hamann-Todd collection serve as a valid study population for exploring the skeletal effects of vitamin D deficiency due to various features. This
large collection includes roughly 2,900 complete skeletons (Cooperman et al., 1992). The majority of individuals are male and of European-derived ancestry or white; however there are over 500 females and roughly 1,000 individuals, both male and female, of African-derived ancestry (Cooperman et al., 1992). Ages at death also widely range within this collection (Cooperman et al., 1992). Although the oldest individual in the collection died over the age of 90, there are individuals representative of every decade of life, including several children (Cooperman et al., 1992). This diversity ultimately allows for this study to explore vitamin D deficiency by sex, ancestry, and age among other factors.

The individuals of this collection lived in a significant location for evaluating skeletal manifestations of vitamin D deficiency. These individuals were born in the United States or areas of Europe before dying in the Cleveland metropolitan area (Cobb, 1935; Mensforth and Latimer, 1989; Iscan, 1992). Cleveland, Ohio resides at a latitude of approximately 41° N, far north of the equator (Harkness and Cromer, 2005). Yearly UVB rays are inherently decreased and fluctuate; higher levels are available beginning in May and only much lower levels are available beginning in November (Harkness and Cromer, 2005; Chaplin and Jablonski, 2009). This seasonality consequently increased the risk of vitamin D deficiency in this population (Harkness and Cromer, 2005; Chaplin and Jablonski, 2009).

In addition to demographic profiles and location, the period in which these individuals lived and aspects of their lifestyle also increase their risk of hypovitaminosis D. All individuals were born between the early 1800s and early 1900s; therefore they represent a “contemporary American” human population (Mensforth and Latimer, 1989; Kern, 2006 p. 10). In addition, Cleveland, Ohio during this time was already “highly industrialized” suggesting a diverse amalgamation of people living an urban lifestyle (Iscan, 1992 p. 39; McNulty, 2009). It is also
important to note that these individuals were born before the mass use of vitamin supplements, such as those for vitamin D, fortification of foods with vitamin D, and the availability and use of “antimicrobial drugs” (Mensforth and Latimer, 1989 p. 461; Welch, Bergstrom, and Tsang, 2000; McNulty, 2009).
CHAPTER III

Results

Statistics

For the statistical analysis of this study, we employed the use of Statistical Package for the Social Sciences (SPSS) by IBM, version 24. Due to the nature of this dataset, analysis focused on nonparametric statistical tests in addition to general frequencies and proportions. Pearson Chi-square tests of independence were utilized to test the distribution of nominal variables, such as presence or absence of indicators of osteomalacia, namely pseudofractures, in relation to sex, ancestry, and reported cause of death. A Mann-Whitney Rank Sum (Wilcoxon Rank Sum) test was used to assess differences among groups in terms of age, the primary continuous variable in this analysis. \( p < 0.05 \) was considered significant for all tests.

Sex, Ancestry, and Reported Cause of Death

A total of 1,295 individuals from the Hamann-Todd Human Osteological Collection were sampled for this study. Out of these individuals, 813 (62.7%) were male, and 482 (37.2%) were female. These individuals represent two major ancestry types, European-derived and African-derived. A total of 692 (53.4%) European-derived individuals and 603 (46.6%) African-derived individuals were included. Of the European-derived group 473 (68.4%) were males and 219 (31.6%) were females. The African-derived group consisted of 340 (56.4%) males and 263 (43.6%) females. These frequencies are consistent with the overall demographics of the available complete skeletons in the Hamann-Todd Collection, which are mostly male (82.7%) and mostly
individuals of European-derived ancestry (54.5%) (Cooperman et al., 1992).

A total of 217 (16.8%) individuals were found to have at least one identifiable indicator of osteomalacia in this study, most commonly the presence of pseudofractures. Of these individuals, 128 (59.0%) are male, and the remaining 89 (41.0%) female. These individuals represent 15.7% of males sampled and 18.5% of females sampled (Figure 1). Despite more women proportionally being affected, and the fact that many previous studies on vitamin D deficiency status (Jacques et al., 1997; Zamboni et al., 2002; Plotnikoff and Quigley, 2003; Bonilla et al., 2014), and demographics of osteomalacia (Nowell, Evans, and Kurrein, 1951; Chalmers et al., 1967), indicate that women are more likely to be affected than men, sex was not found to be a significant indicator of osteomalacia status among these Hamann-Todd individuals ($p = 0.205$) (Table 1).

Of the 217 individuals with indicators of osteomalacia, 166 (76.5%) were European-derived, with the remaining 51 (23.5%) being of African-derived ancestry. These data comprise 23.4% of all European-derived individuals sampled, but only 8.5% of all African-derived individuals sampled (Figure 2). Ancestry was found to be a significant correlate of osteomalacia status within this population ($p = 0.000$) (Table 2); however, this significant association was evaluated to be mild in strength ($\phi = 0.207$). These results do not support the findings of many previous studies on vitamin D status, which indicate that individuals with darker skin tones are more at risk for deficiency, the cause of osteomalacia (Albright et al., 1946; Albright and Reifenstein, 1948; Nesby-O’Dell et al., 2002; Harkness and Cromer, 2005; Bodnar et al., 2007; Lee et al., 2007; Freedman et al., 2013; Vierucci et al., 2013; Bonilla et al., 2014).

Reported cause of death for each Hamann-Todd individual sampled was also considered in this study. This classification was diverse within this sample; therefore it was pertinent to
Figure 1. Frequency of osteomalacia indicators by sex
Table 1. Crosstabulation Table (Sex* Osteomalacia Status)

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<td>393</td>
<td>89</td>
<td>482</td>
</tr>
<tr>
<td></td>
<td>401.2</td>
<td>80.8</td>
<td>482.0</td>
</tr>
<tr>
<td></td>
<td>685</td>
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<td>813</td>
</tr>
<tr>
<td></td>
<td>676.8</td>
<td>136.2</td>
<td>813.0</td>
</tr>
<tr>
<td></td>
<td>1078</td>
<td>217</td>
<td>1295</td>
</tr>
<tr>
<td></td>
<td>1078.0</td>
<td>217.0</td>
<td>1295.0</td>
</tr>
</tbody>
</table>
Figure 2. Frequency of osteomalacia indicators by ancestry type
Table 2. Crosstabulation Table (Ancestry* Osteomalacia Status)

<table>
<thead>
<tr>
<th>Ancestry</th>
<th>Status</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No Osteomalacia Indicators</td>
<td>Osteomalacia Indicators</td>
</tr>
<tr>
<td>European-derived</td>
<td>Count</td>
<td>526</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
<td>576.0</td>
</tr>
<tr>
<td>African-derived</td>
<td>Count</td>
<td>552</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
<td>502.0</td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>1078</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
<td>1078.0</td>
</tr>
</tbody>
</table>
truncate these causes into 6 relevant categories for analysis. These categories are: infectious diseases, such as tuberculosis; heart disease and cardiac complications; cancer; unnatural causes of death such as accidents, homicides, and suicides; records that included lethal pathologies from multiple categories; and those with an unknown cause of death. Of the 1,295 individuals sampled 564 (43.6%) died of infectious disease, 272 (21.0%) of heart disease or cardiac complications, 47 (3.6%) of various forms of cancer including reproductive cancers such as ovarian, breast, and prostate, 186 (14.4%) of unnatural deaths, 32 (2.5%) of combined lethal pathologies, and 194 (15.0%) of unknown cause (see Appendix A).

Of the 217 total individuals with indicators of osteomalacia in at least one area, 73 (33.6%) died of infectious disease, 71 (32.7%) of heart disease and cardiac complications, 29 (13.4%) of unknown cause, 25 (11.5%) of unnatural deaths, 10 (4.6%) of combined lethal pathologies, and 9 (4.1%) of cancer. Therefore, 12.9% of the infectious disease group, 26.1% of the heart disease group, 14.9% of those with unknown cause of death, 13.4% of the unnatural death group, 12.5% of the combined lethal pathologies group, and 19.1% of the cancer group showed indications of pseudofractures (Figure 3). This difference in osteomalacia status based on reported cause of death was found to be significant within this population ($p=0.000$) (Table 3), although this association was evaluated to be somewhat weak in strength ($Goodman and Kruskal’s Tau = 0.023$). These results provide support for the bulk of previous literature exploring potential nonskeletal impacts of poor vitamin D status (John et al., 1999; Ahonen et al., 2000; Wilkinson et al., 2000; Freedman, Dosemeci, and McGlynn, 2002; Li et al., 2002; Feskanich et al., 2004; Xiang et al., 2005; Garland et al., 2006; Garland et al., 2007; White et al., 2008; Gombart, 2009; Kestenbaum et al., 2011; Ritterhouse et al., 2014; Schmidt et al., 2014; Kim, 2015).
Figure 3. Frequency of osteomalacia indicators by reported cause of death
<table>
<thead>
<tr>
<th>Reported Cause of Death</th>
<th>Status</th>
<th>No Osteomalacia Indicators</th>
<th>Osteomalacia Indicators</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>Count</td>
<td>Expected Count</td>
<td></td>
</tr>
<tr>
<td>Infectious Disease</td>
<td>Count</td>
<td>491</td>
<td>469.5</td>
<td>564.0</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
<td>73</td>
<td>94.5</td>
<td></td>
</tr>
<tr>
<td>Heart Disease/Complications</td>
<td>Count</td>
<td>201</td>
<td>226.4</td>
<td>272.0</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
<td>71</td>
<td>45.6</td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td>Count</td>
<td>161</td>
<td>154.8</td>
<td>186.0</td>
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<tr>
<td></td>
<td>Expected Count</td>
<td>25</td>
<td>31.2</td>
<td></td>
</tr>
<tr>
<td>Cancer</td>
<td>Count</td>
<td>38</td>
<td>39.1</td>
<td>47.0</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
<td>9</td>
<td>7.9</td>
<td></td>
</tr>
<tr>
<td>Combined Lethal Pathologies</td>
<td>Count</td>
<td>22</td>
<td>26.6</td>
<td>32.0</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
<td>10</td>
<td>5.4</td>
<td></td>
</tr>
<tr>
<td>Unknown</td>
<td>Count</td>
<td>165</td>
<td>161.5</td>
<td>194.0</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
<td>29</td>
<td>32.5</td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>Count</td>
<td>1078</td>
<td>1078.0</td>
<td>1295.0</td>
</tr>
<tr>
<td></td>
<td>Expected Count</td>
<td>217</td>
<td>217.0</td>
<td></td>
</tr>
</tbody>
</table>
**Age**

The Hamann-Todd individuals sampled in this study ranged in age from 18 to 99 years old, with a mean age of 50.59 ± 17.38 years old (\(\bar{x} \pm \text{SE}\)). In terms of frequency, 186 (14.4%) individuals were between the ages of 18 and 29, 217 (16.8%) were between 30 and 39 years old, 197 (15.2%) between 40 and 49 years old, 271 (20.9%) between 50 and 59 years old, 204 (15.8%) between 60 and 69 years old, and 220 (16.9%) who were 70 years old or older. Previous literature indicates that risk of vitamin D deficiency (Omdahl et al., 1982; Ebeling et al., 1992; Gloth et al., 1995; Adams et al., 1999; Rucker et al., 2002) and osteomalacia (Nowell, Evans, and Kurrein, 1951; Ives and Brickley, 2014) increases with age. A Mann-Whitney Rank Sum (Wilcoxon Rank Sum) test supported this notion; frequency of osteomalacia indicators such as pseudofractures significantly increased with age in this sample \((p = 0.000)\) (Figure 4).

**Affected Anatomical Areas**

The majority of cases of scored osteomalacia were found in areas of the axial skeleton, with the addition of the pelvis, and some bones of the feet also being affected relatively frequently. The sternum was the most commonly affected site, with 142 cases found in this sample (65.4%) (Figures 5.1-5.2). Other affected sites, in order of frequency are the ribs (Figures 6.1-6.2), sacrum (Figures 7.1-7.2), pelvis (Figures 8.1-8.2), the thoracic vertebrae (Figure 9), and the bones of both feet (Figures 10.1-10.2a,b; also see Appendix B and C).

Much smaller frequencies of pseudofractures were found in the scapulae, the clavicles, the cervical and lumbar vertebrae, the hand bones (Figure 11), and the long bones on both sides of the body (see Appendix D).

Of the 217 individuals found to have indicators of osteomalacia, individuals ranged from
Figure 4. Frequency of osteomalacia indicators by age in years

Human-Food Human Collection:

Frequency of Osteomalacia Indicators by Age

Age in Years

Number of Individuals
Figure 5.1. Evidence of pseudofractures in the sternum; unaffected sternum, left vs. affected sternum, right. (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
Figure 5.2. Evidence of pseudofractures in the sternum; unaffected sternum, far left vs. 3 affected specimens. (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
Figure 6.1. Evidence of pseudofractures in the ribs; 3 rib specimens affected at the vertebral ends. (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
Figure 6.2. Evidence of pseudofractures in the ribs; 2 ribs affected at the sternal end by an infection, left and middle vs. rib specimen affected by pseudofractures, right. (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
Figure 7.1. Evidence of pseudofractures in the sacrum: unaffected sacrum, left vs. sacrum affected by pseudofractures, right. (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
Figure 7.2. Evidence of pseudofractures, middle, right (Photo courtesy of L. Jellema, Cleveland Museum of Natural History).
Figure 8.1. Evidence of pseudofractures in the pelvis; left innominate bone exhibiting a true fracture, left vs.
left innominate bone affected by pseudofractures, right. (Photo courtesy of L. Jellema, Cleveland Museum of
Natural History)
Figure 8.2. Evidence of pseudofractures in the pelvis: left innominate bone exhibiting a true fracture, left vs. left innominate bone affected by pseudofractures, right. (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
Figure 9. Evidence of pseudofractures in the vertebrae; 2 thoracic vertebrae affected by pseudofractures, top and middle vs. osteoporotic thoracic vertebra, bottom. (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
Figure 10.1. Evidence of pseudofractures in the metatarsals; metatarsal affected by pseudofractures, right vs. unaffected metatarsal, left. (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
Figure 10.2a. Evidence of pseudofractures in the metatarsals; 2 metatarsals affected by pseudofractures, top vs. 2 unaffected metatarsals, bottom (view a). (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
Figure 10.2b. Evidence of pseudofractures in the metatarsals; 2 metatarsals affected by pseudofractures, top vs. 2 unaffected metatarsals, bottom (view b). (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
Figure 11. Evidence of pseudofractures in the metacarpals; metacarpal affected by pseudofractures, left vs. unaffected metatarsal, right. (Photo courtesy of L. Jellema, Cleveland Museum of Natural History)
having only one area affected to up to eight; this range was used to create categories of the relative degree of involvement present within this sample. Individuals affected in one to three areas were considered to have “mild” involvement, those with four to six affected were considered to have “moderate” involvement, and those with seven or more affected areas were considered to have “severe” involvement.

A total of 201 individuals were classified as having mild involvement; these individuals make up 15.4% of all males sampled and 15.8% of all females sampled. These individuals also constitute a much higher percentage of the European-derived group (21.7%) than the African-derived group (8.5%) in the total sample.

Twelve individuals were categorized as having moderate involvement. These individuals make up less than 1% of all males sampled, but over 2% of all females sampled. All 12 individuals are European-derived; no African-derived individuals were classified as having moderate involvement.

Severe involvement was seen in four individuals. These individuals make up less than 1% of males and females sampled, however it is clear that moderate and severe cases are more likely to be female than male. In addition, all four of these individuals were of European-derived ancestry. Only European-derived individuals were found to have four or more areas affected by indicators of osteomalacia in this study (see Appendix E).
CHAPTER IV

Discussion and Conclusions

This study of osteomalacia within the Hamann-Todd Collection is to our knowledge the largest survey of osteomalacia within a historical osteological collection. This sample was not only large, but also highly inclusive of those available to study within this collection; we included males and females, European- and African-derived individuals, individuals with ages ranging from as young as 18 to as old as 99 years old, in addition to evaluating individuals with a variety of reported causes of death. Efforts toward inclusiveness were based on the recognition that this collection is its own unique population, based on how it was assembled from Cleveland inhabitants in the early 1900s (Cobb, 1959; Mensforth and Latimer, 1989; Iscan, 1992; Hunt and Albanese, 2005; Kern, 2006; McNulty, 2009). Analysis of this population for osteomalacia primarily enhances discussions of how to identify this condition in the skeleton. It also serves as another example of how this disease may distribute demographically based on sex, ancestry, and age, along with highlighting possible nonskeletal effects of prolonged affliction. We also hope this analysis will assist in reconstructing the potential living conditions, and ultimately the identities, of these specific past Clevelanders.

Sex

As these data indicate, there was no significant difference in the frequency of osteomalacia indicators observed between males and females. Previous studies on vitamin
D deficiency indicate females are at a much higher risk of deficiency, and in turn osteomalacia, than males (Nowell, Evans, and Kurrein, 1951; Chalmers et al., 1967; Whitehead et al., 1981; Jacques et al., 1997; Jablonski and Chaplin, 2000; Mensforth, 2002; Zamboni et al., 2002; Plotnikoff and Quigley, 2003; Herm, Killguss, and Stewart, 2005; Chaplin and Jablonski, 2009; Bonilla et al., 2014). However, other hypovitaminosis D studies did not find females to be any more likely than males to be deficient (Vierucci et al., 2013), while some have even found high incidence in males (Armas, Hollis, and Heaney, 2004; Tsur, Metzger, and Dresner-Pollack, 2011; Ritterhouse et al., 2014).

The dataset presented in this study does corroborate results of a similar osteomalacia study completed on human remains from the 1700s and 1800s in England (Brickley, Mays, and Ives, 2007). These authors found indications of osteomalacia in both males and females, with little difference in frequency by sex; approximately 4% of males and 5% of females were found to have osteomalacic indicators (Brickley, Mays, and Ives, 2007). The authors point out that those affected in their study were from “poorer sections of the community” and circumstances associated with poverty in that time period, such as malnutrition and persistent bombardment from industrialized pollution, are to blame for the observed frequencies (Brickley, Mays, and Ives, 2007 p. 78). Various other studies have also confirmed the existence of such a severely detrimental relationship between urbanization and prevalence of hypovitaminosis D (Harris et al., 2000; Nesby O’Dell et al., 2002; Gordon et al., 2004; Harkness and Cromer, 2005).

Although the Hamann-Todd Collection is composed of individuals in the United States from a later period (Kern, 2006), similar circumstances could have led to the lack of a significant difference in osteomalacia status by sex in this study. After all, these individuals were living in the setting of Cleveland, Ohio in the late 19th and early 20th centuries (Mensforth and Latimer,
1989; Kern, 2006). Cleveland in this time period was a verifiably urban setting, with booming industries associated with steel, automobile production, and electric power (Iscan, 1992; Lamoreaux, Levenstein, and Sokoloff, 2006; McNulty, 2009). In addition there were major jumps in population from circa 1870 to 1920, coinciding well with collection acquisition by Carl August Hamann and T. Wingate Todd (Cobb, 1959; Iscan, 1992; Hunt and Albanese, 2005; Kern, 2006; Lamoreaux, Levenstein, and Sokoloff, 2006). In addition, constituents of the collection were “more socio-economically disadvantaged” contributing to them being incorporated into the collection in the first place (Iscan, 1992; Kern, 2006; McNulty, 2009 p. 78). As in similar collections, health status of these individuals can be assumed to be poorer than those in greater society (Brickley and Ives, 2008; Komar and Grivas, 2008; Ives and Brickley, 2014).

**Ancestry**

These data also demonstrate a higher likelihood of osteomalacia indicators among individuals of European-derived ancestry, relative to those of African-derived ancestry. These results do not support several studies of hypovitaminosis D that indicate individuals with darker skin tones are of higher risk, especially at a northern latitude, due to the enhanced protective nature of their skin (Jablonski and Chaplin, 2000; Nesby-O’Dell et al., 2002; Jablonski, 2004; Harkness and Cromer, 2005; Bodnar et al., 2007; Carson, 2009; Chaplin and Jablonski, 2009; Shoben et al., 2011; Jablonski and Chaplin, 2012). However, other studies indicate an enhanced risk for those with lighter skin tones, such as a study that found a genetic proclivity for hypovitaminosis D in “individuals of European descent” (Wang et al., 2010 p. 182).
Additionally, a study completed in Scandinavia with a “mostly Caucasian” sample, found high levels of vitamin D deficiency (Larose et al., 2014 p. 165).

A potential reason for the lack of affected African-derived individuals in this study may be important osteological differences between this group and those of European ancestry (Wang et al., 1997; Taaffe et al., 2001; Mensforth, 2002; Kalkwalf et al., 2007). Levels of bone mineral density, and “bone mineral content” are found to be higher in “Blacks compared with non-Blacks” (Kalkwalf et al., 2007 p. 2093). Earlier studies have also found differences in bone mineral density among different ancestry types, with African-derived, or black, individuals having higher levels (Wang et al., 1997; Taaffe et al., 2001). This relationship was also demonstrated between African-derived and European-derived individuals within the Hamann-Todd Collection in a previous study in the late 1980s (Mensforth, 2002).

Gutiérrez et al. (2011), found that bone mineral density became poorer and poorer with worsening vitamin D status in “whites and Mexican-Americans but not in blacks;” despite scant concentrations of 25(OH)D and levels of calcium consumption, bone mineral density was “remarkably preserved” in those of African-derived ancestry (Gutiérrez et al., 2011 p. 1750). This study suggests part of this occurrence may be due to differences in how those in this ancestry category produce and respond to levels of parathyroid hormone (Gutiérrez et al., 2011). African-derived individuals may require lower levels of vitamin D to ward off high levels of parathyroid hormone, which can degrade bone health and bone mineral density over time (Holick, 1996; Mensforth, 2002; Vieth and Fraser, 2002; Bilezikian, 2003; Holick, 2003; Holick, 2004a; Holick, 2004b; Kamycheva, Sundsfjord, and Jorde, 2004; Holick, 2007; Gutiérrez et al., 2011; Lila et al., 2012; Gasser, 2013). Although there is evidence of higher levels of parathyroid hormone in African-derived individuals (Shoben et al., 2011), spectrums commonly used to
assess levels of this hormone and of vitamin D, may need to be adjusted for different groups of people; levels of parathyroid hormone that are high and accrue bone mineral density degradation may vary among ancestry groups (Gutiérrez et al., 2011). Other issues of vitamin D metabolism, such as the ability to more effectively save calcium from being excreted, have also been suggested for African-derived, or black individuals (Cosman et al., 1997; Bryant et al., 2003).

**Age**

As expected, these data do indicate a significant increase in the frequency of osteomalacia indicators with increasing age. These results support many studies associated with hypovitaminosis D risk and older age (Omdahl et al., 1982; Ebeling et al., 1992; Gloth et al., 1995; Jacques et al., 1997; Adams et al., 1999; Mensforth, 2002; Rucker et al., 2002; Shoben et al., 2011; Holmund-Suila et al., 2013), along with several studies that specifically focused on osteomalacia in both the clinical setting and in skeletal remains (Nowell, Evans, and Kurrein, 1951; Chapuy et al., 1997; Mensforth, 2002; Mosekilde, 2005; Ives and Brickley, 2014). This positive association is potentially due to changes that occur with natural aging such as: alterations in how the skin reacts to UVB rays and the beginning stages of vitamin D synthesis (MacLaughlin and Holick, 1985; Holick, 1989; Need et al., 1993; Mosekilde, 2005), lower levels of vitamin D receptors within the intestines (Ebeling et al., 1992), and increases in parathyroid hormone secretions (Harris et al., 2000; Rucker et al., 2002; Kamycheva, Sundsfjord, and Jorde, 2004; Tsur, Metzger, and Dresner-Pollack, 2011; Giusti et al., 2006 as cited by Gorter et al., 2017). Additionally, Gloth et al. (1995), found better vitamin D status in older individuals being cared for in a nursing home setting, than those who were “homebound” and “community-dwelling” (Gloth et al., 1995 p. 1683). Due to the time period, older individuals in the Hamann-
Todd Collection were most likely not receiving the kind of care observed in that study (Mensforth and Latimer, 1989; Gloth et al., 1995; Kern, 2006).

Despite a clear relationship between indicators of pseudofractures and age it was not possible to tease out any sense of progression of this disease from this sample. The sternum was found to be the most highly affected bone in this sample with 142 cases and therefore was tested to see if it was a possible starting point in osteomalacia. However, affected sternums were found in both an individual in their twenties, along with several individuals in their eighties. In addition, some of the oldest individuals in this grouping had only an affected sternum, while some of the younger individuals had an affected sternum and several other skeletal regions. Therefore, within this sample, this condition appears to affect the same general areas in different people at different times in their lives with no standardized starting location.

*Reported Cause of Death*

In this study, a significant relationship was found between frequency of osteomalacia indicators and reported cause of death. It would be pertinent to further test this association to evaluate which of these reported causes of death have strong relationships with osteomalacia status. As the risk of many diseases does naturally increase with age, it would also be appropriate to evaluate such potential interactions that may affect this evaluation of variation (Niccoli and Partridge, 2012).

These preliminary results do contribute to the bulk of previous literature that details the potential impacts of poor vitamin D status on nonskeletal body systems (Wilkinson et al., 2000; Li et al., 2002; Xiang et al., 2005; White et al., 2008; Gombart, 2009; Kestenbaum et al., 2011; Ritterhouse et al., 2014; Schmidt et al., 2014; Kim, 2015). Vitamin D deficiency has been
explored in relation to infectious diseases, such as tuberculosis, due to its impact on immune system function (Wilkinson et al., 2000; White et al., 2008; Gombart, 2009; Ritterhouse et al., 2014; Kim, 2015). It has also been implicated in studies of cardiovascular health (Li et al., 2002; Xiang et al., 2005; Kestenbaum et al., 2011; Schmidt et al., 2014), while an increased risk of many cancers is also linked with vitamin D status (John et al., 1999; Ahonen et al., 2000; Freedman, Dosemeci, and McGlynn, 2002; Mensforth, 2003; Feskanich et al., 2004; Garland et al., 2006; Garland et al., 2007).

Location of Pseudofractures

These data indicate that the sternum was the most commonly affected bone among these Hamann-Todd individuals with 142 cases found. Although this bone has not been cited in osteomalacia studies nearly as often as areas such as the scapulae, ribs, pelvis, and femur (Albright and Reifenstein, 1948; Le May and Blunt, 1949; Chalmers et al., 1967; Mensforth, 2002; Brickley, Mays, and Ives, 2005; Rothschild and Martin, 2006; Brickley, Mays, and Ives, 2007; Ives and Brickley, 2014), these results do support its inclusion as another potential site in further osteomalacia studies. We speculate developmental and biomechanical specificities of the sternum within the context of this unique population may explain the high prevalence observed.

The sternum is composed of the manubrium, the body or corpus sterni, and the xiphoid process (White and Folkens, 2005; White, Black, and Folkens, 2012; Bayaroğullari et al., 2014). The body of the sternum ultimately begins as multiple elements, or sternebrae, that fuse together in a “caudo-cranial direction” at different stages in life (White and Folkens, 2005; White, Black, and Folkens, 2012; Bayaroğullari et al., 2014 p. 87). The development of ossification centers and associated penetrating vasculature is inconsistent in the sternum; the manubrium usually has one
center of ossification, while the sternebrae have been shown to have one or two centers each
(White and Folkens, 2005 p. 184; White, Black, and Folkens, 2012 p. 151; Bayaroğullari et al.,
2014). In addition, this bone is located close to the internal thoracic artery, which has “sternal”
specific “branches” of vessels; many other “collateral vessels” that shunt blood to the sternum
have also been identified (de Jesus and Acland, 1995 p. 163, 167).

Degree of fusion of this bone is also complex and variable; the manubrium does not
always fuse with the body even in old age and the xiphoid process is a “highly variable element”
in terms of both shape and fusion (White and Folkens, 2005 p. 184; White, Black, and Folkens,
2012 p. 151; Bayaroğullari et al., 2014). Whether this relative variability in ossification centers,
fusion, and degree of vascular interactions contribute to the susceptibility of this bone to
deformations from prolonged osteomalacia is worthy of further research. This would further
support a previous hypothesis that claims indicators of osteomalacia, like pseudo fractures, do not
distribute simply in areas of “muscle strain;” a more complex explanation including close
proximity of major blood vessels that create consistent “vascular stress” is more plausible (Le

It is also important to note that a normal sternum has “very low density” (White and
Folkens, 2005 p. 184; White, Black, and Folkens, 2012 p. 151), which may suggest a relationship
between osteomalacia and areas of bone with lower “volume fractions of solids” or areas of bone
with a higher proportion of trabeculae and a smaller proportion of cortical bone (Gibson, 1985 p.
317; Keaveny et al., 2001; White and Folkens, 2005; White, Black, and Folkens, 2012). This
could be due in part to the fact that trabecular bone has a quicker “turnover” rate than cortical
bone (Brickley, Mays, and Ives, 2007 p. 75). The most commonly cited areas of osteomalacic
pseudo fractures, which include the scapulae, ribs, and proximal end of the femur, along with the
sternum, are each made up of more trabeculae (Gibson, 1985; Keaveny et al., 2001); this supports a potential relationship between the presence of osteomalacia indicators with trabecular bone. Interestingly, these areas are also all major sites of red bone marrow in adults (Piney, 1922; Ellis, 1961; White and Folkens, 2005; White, Black, and Folkens, 2012).

The position of the sternum within the body may also affect why it was a commonly affected bone in this sample. The sternum is located anteriorly in the chest and articulates on either side with the ribs. Biomechanically the sternum together with the ribs and vertebrae constitute the “functional” units of the “thoracic spine” (Berg, 1993 as cited by Horton et al., 2005 p. 2015). These elements and surrounding tissues work together “controlling and restricting” movement in the thorax (Horton et al., 2005 p. 2014). In exceptional cases, this bone can be variably influenced by deformations in the spine (Chen et al., 1990; Sapherson and Mitchell, 1990; Klaase, Zimmerman, and Veldhuis, 1998; Horton et al., 2005); one such condition, Scheuermann’s kyphosis, has previously been identified within the Hamann-Todd Collection (Digiovanni, Scoles, and Latimer, 1989). Therefore, further investigation should be undertaken to evaluate any indications of kyphosis in the spines of specimens with these sternal pseudofractures.

The positioning of the sternum places it under consistent pressure from respiration; the chest essentially functions as a “pressure vessel” (Casha et al., 2014 p. 617). Any fluctuations in normal respiration, such as coughing, can add additional strain; this extra pressure in the chest is much different than the “ambient pressure” (Casha et al., 2014 p. 617). This observation is significant for this sample considering Hamann-Todd individuals originate from a time before “antimicrobial drugs” (Mensforth and Latimer, 1989 p. 461; McNulty, 2009). Consequently, many individuals within this collection suffered from infectious respiratory diseases such as
tuberculosis, which is characterized by severe, prolonged coughing and difficulty breathing normally (Harries, Maher, and Graham, 2004). Further investigation into individuals in this collection, specifically those who died of respiratory infections, could confirm the sternum and even the ribs, to be the bones most affected.

In this study 96 of the 217 cases (44.2%) that displayed indications of osteomalacia had them in two or more areas. The appearance of multiple pseudofractures in an individual is consistent with an earlier study (Chalmers et al., 1967), which found that the majority of individuals sampled had multiple skeletal indicators of the condition (Chalmers et al., 1967). Although there was no significant difference in frequency of osteomalacia indicators based on sex, females were found to be more likely to show four or more affected areas in this sample. European-derived individuals also displayed more affected areas than African-derived individuals. We speculate these results may ultimately also have to do with differences in bone mineral density associated with sex and ancestry (Wang et al., 1997; Taaffe et al., 2001; Mensforth, 2002; Kalkwalf et al., 2007; Gutiérrez et al., 2011).

Culture

Indicators of osteomalacia were found in 217 individuals or rather 16.8% of the 1,295 individuals sampled. We speculate that the time period, location, and economic circumstances of the individuals within this collection may have contributed to this result. Nonetheless, there are several other aspects of culture that could also have impacted the relatively high frequency of osteomalacia observed among Hamann-Todd individuals in comparison with other studies (Brickley, Mays, and Ives, 2005; Brickley, Mays, and Ives, 2007; Ives and Brickley, 2014). This collection is reflective of a “contemporary American” human population (Mensforth and
Latimer, 1989; Kern, 2006 p. 10), however, this population is from a time when styles of dress were far more modest than they are today; fashion for both men and women often included covering most of the legs and arms (National Cloak & Suit Co., 1992; Cunningham, 2003; Jno J. Mitchell Co., 2012). The harmful effects of certain clothing styles on vitamin D status have been previously explored (Plotnikoff and Quigley, 2003; Baroncelli et al., 2008; El-Rassi, Baliki, and El-Hajj Fulheihan, 2009; Tsur, Metzger, and Dresner-Pollack, 2011). Tanned skin was also not avidly in fashion until the late 1920s (Martin et al., 2009); it is well established that avoiding the sun is detrimental for vitamin D status (Holick, 1996; Jablonski 2000; Jablonski 2004; Holick, 2007; Holick and Chen, 2008; Chaplin and Jablonski, 2009; Genius et al., 2009; Holick, 2012b; Jablonski and Chaplin, 2012; Vierucci et al., 2013).

The use of both alcohol and tobacco were in high flux during this period, especially in Ohio (Marino, 1999; Duvall, 2007). Tobacco farming was essential to Ohio’s economy, especially in the late 1800s and early 1900s when it was the “single most important cash crop” in the Ohio River Valley (Duvall, 2007 p. 2). Alcohol was also popular, even after Prohibition; approximately 100,000 people in Cleveland still consumed alcohol routinely, much of which was imported illegally from Canada (Marino, 1999). These two habits are significant for evaluating this past population due to the detriment smoking, and alcohol can have on vitamin D status and bone health (Krall and Dawson-Hughes, 1999; Harris et al., 2000; Cheng et al., 2014; Larose et al., 2014; Ogunsakin et al., 2016).

Conclusions

In summary, visible indicators of osteomalacia, most namely pseudofractures, were found within postcranial remains of sampled individuals within the Hamann-Todd Osteological
Collection. These indicators were found most commonly in the sternum and several individuals were found to have pseudofractures in several areas. Ancestry type, age, and reported cause of death all showed significant relationships with osteomalacia status within this study. While biological sex was also tested, it was not found to be a significant predictor of osteomalacia status; both males and females within this sample were affected by this pathology. Based on how and when this collection was assembled, lifestyle factors such as living in a city in relative poverty at a northern latitude (Iscan, 1992; Kern, 2006; McNulty, 2009), where rampant use of tobacco and alcohol were common (Marino, 1999; Duvall, 2007), and there was adherence to more modest clothing styles (National Cloak & Suit Co., 1992; Cunningham, 2003; Jno J. Mitchell Co., 2012), may have also impacted the relative frequency of osteomalacia indicators found within this population. Several of these circumstances are not dissimilar to those in other historical collections (Mensforth and Latimer, 1989; Iscan, 1992; Kern, 2006; Brickley and Ives, 2008; Komar and Grivas, 2008; McNulty, 2009; Ives ad Brickley, 2014; Nystrom, 2014).

It is clear from this analysis that both biological and cultural factors work together to create a more complete and complex image of the health status of this vitamin D deficient past group. This is not surprising considering how complex an issue health status is for present human populations, especially those also in relative poverty (Farmer, 2004; Ho, 2007; Mukherjee et al., 2011; Lee, 2017). Although this is not an evaluation of a modern-day living population, Hamann-Todd individuals were living in a city setting with limited or no access to beneficial foods and medical care (Mensforth and Latimer, 1989; Iscan, 1992; Kern, 2006; McNulty, 2009). This is similar to what many modern populations are facing and is ultimately a form of “structural violence” (Farmer, 2004 p. 307; Ho, 2007; Mukherjee et al., 2011; Nystrom, 2014; Lee, 2017). Considering the number of people globally suffering from avoidable conditions due
to unacceptably inaccessible health care and nutritious foods (Farmer, 2004; Ho, 2007; Mukherjee et al., 2011; Lee, 2017), it would be pertinent to recognize such suffering in this past population to make moves toward better protecting modern populations from similar fates.

Overall, we assert that these conclusions enhance discussions of what osteomalacia can do to the skeleton, which groups of people may be at risk, and how vitamin D deficiency may relate to overall health status and mortality. In addition, on a broad scale, we hope this study helps to illuminate how aspects of culture and society can have as strong, if not stronger, an impact on health than biological factors, both in the past, and into the present and future. On a smaller, but still significant scale, we also hope this study provides a means of preserving just one of the stories these Hamann-Todd individuals have to tell, even in death.
REFERENCES


Albright F, et al. 1946. Osteomalacia and late rickets: The various etiologies met in the United States with emphasis on that resulting from a specific form of renal acidosis, the therapeutic indications for each etiological sub-group, and the relationship between osteomalacia and Milkman's syndrome Medicine. 2:399–479.


Harris SS, et al. 2000. Vitamin D insufficiency and hyperparathyroidism in a low income, multiracial, elderly population.


Marino J. 1999. Did the Old Arcade once harbor a speakeasy? Cleveland Scene (October 7th).


APPENDICES
APPENDIX A

Demographics (Reported Cause of Death)

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total (Sex)</th>
<th>European-derived</th>
<th>African-derived</th>
<th>Total (Ancestry)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Infectious Disease</strong></td>
<td>388</td>
<td>176</td>
<td>564</td>
<td>280</td>
<td>284</td>
<td>564</td>
</tr>
<tr>
<td><strong>Heart Disease and Complications</strong></td>
<td>176</td>
<td>96</td>
<td>272</td>
<td>160</td>
<td>112</td>
<td>272</td>
</tr>
<tr>
<td><strong>Cancer</strong></td>
<td>27</td>
<td>20</td>
<td>47</td>
<td>34</td>
<td>13</td>
<td>47</td>
</tr>
<tr>
<td><strong>Unnatural Deaths</strong></td>
<td>114</td>
<td>72</td>
<td>186</td>
<td>107</td>
<td>79</td>
<td>186</td>
</tr>
<tr>
<td><strong>Multiple Lethal Pathologies</strong></td>
<td>26</td>
<td>6</td>
<td>32</td>
<td>22</td>
<td>10</td>
<td>32</td>
</tr>
<tr>
<td><strong>Unknown</strong></td>
<td>82</td>
<td>112</td>
<td>194</td>
<td>89</td>
<td>105</td>
<td>194</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>813</td>
<td>482</td>
<td>1295</td>
<td>692</td>
<td>603</td>
<td>1295</td>
</tr>
</tbody>
</table>
APPENDIX B

Demographics (Most Affected Postcrania)

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total (Sex)</th>
<th>European-derived</th>
<th>African-derived</th>
<th>Total (Ancestry)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sternum</td>
<td>71</td>
<td>71</td>
<td>142</td>
<td>116</td>
<td>26</td>
<td>142</td>
</tr>
<tr>
<td>Ribs</td>
<td>37</td>
<td>22</td>
<td>59</td>
<td>49</td>
<td>10</td>
<td>59</td>
</tr>
<tr>
<td>Sacrum</td>
<td>13</td>
<td>28</td>
<td>41</td>
<td>37</td>
<td>4</td>
<td>41</td>
</tr>
<tr>
<td>Pelvis*</td>
<td>12</td>
<td>26</td>
<td>38</td>
<td>25</td>
<td>13</td>
<td>38</td>
</tr>
<tr>
<td>Thoracic Vertebral</td>
<td>22</td>
<td>13</td>
<td>35</td>
<td>31</td>
<td>4</td>
<td>35</td>
</tr>
<tr>
<td>Left Foot**</td>
<td>13</td>
<td>22</td>
<td>35</td>
<td>29</td>
<td>6</td>
<td>35</td>
</tr>
<tr>
<td>Right Foot</td>
<td>13</td>
<td>16</td>
<td>29</td>
<td>23</td>
<td>6</td>
<td>29</td>
</tr>
<tr>
<td>Total</td>
<td>181</td>
<td>188</td>
<td>379</td>
<td>310</td>
<td>69</td>
<td>379</td>
</tr>
</tbody>
</table>

* Scoring indicators used were presence of pseudofractures and/or presence of protrusive acetabuli

** 2 individuals sampled missing bones of the left foot.
### APPENDIX C

**Demographics (Pelvis Indicators)**

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total (Sex)</th>
<th>European-derived</th>
<th>African-derived</th>
<th>Total (Ancestry)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Presence of Pseudofractures/Folding (Pelvis)</td>
<td>11</td>
<td>16</td>
<td>27</td>
<td>22</td>
<td>5</td>
<td>27</td>
</tr>
<tr>
<td>Presence of Protrusio Acetabuli (Pelvis)</td>
<td>1</td>
<td>10</td>
<td>11</td>
<td>3</td>
<td>8</td>
<td>11</td>
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<tr>
<td>Total</td>
<td>12</td>
<td>26</td>
<td>38</td>
<td>25</td>
<td>13</td>
<td>38</td>
</tr>
</tbody>
</table>
APPENDIX D

Demographics (Least Affected Postcrania)

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total (Sex)</th>
<th>European-derived</th>
<th>African-derived</th>
<th>Total (Ancestry)</th>
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<tbody>
<tr>
<td>Right Scapula</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Left Scapula</td>
<td>0</td>
<td>2</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Right Clavicle</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Left Clavicle</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Cervical Vertebrae</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Lumbar Vertebrae</td>
<td>3</td>
<td>2</td>
<td>5</td>
<td>5</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>Right Hand</td>
<td>1</td>
<td>1</td>
<td>2</td>
<td>1</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Left Hand*</td>
<td>2</td>
<td>1</td>
<td>3</td>
<td>2</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Right Long Bones</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Left Long Bones</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>6</td>
<td>8</td>
<td>14</td>
<td>11</td>
<td>3</td>
<td>14</td>
</tr>
</tbody>
</table>

* 2 individuals sampled missing bones of the left hand.
### APPENDIX E

**Demographics (Degree of Involvement)**

<table>
<thead>
<tr>
<th></th>
<th>Male</th>
<th>Female</th>
<th>Total (Sex)</th>
<th>European-derived</th>
<th>African-derived</th>
<th>Total (Ancestry)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Mid Involvement</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(1-3 areas affected)</td>
<td>125</td>
<td>76</td>
<td>201</td>
<td>150</td>
<td>51</td>
<td>201</td>
</tr>
<tr>
<td><strong>Moderate Involvement</strong></td>
<td>2</td>
<td>10</td>
<td>12</td>
<td>12</td>
<td>0</td>
<td>12</td>
</tr>
<tr>
<td>(4-6 areas affected)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Severe Involvement</strong></td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>0</td>
<td>4</td>
</tr>
<tr>
<td>(7+ areas affected)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>No Involvement</strong></td>
<td>685</td>
<td>393</td>
<td>1078</td>
<td>526</td>
<td>552</td>
<td>1078</td>
</tr>
<tr>
<td>(0 areas affected)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td>813</td>
<td>482</td>
<td>1295</td>
<td>692</td>
<td>603</td>
<td>1295</td>
</tr>
</tbody>
</table>