THE IMPACT OF *Mycobacterium leprae*: A COMPREHENSIVE META-ANALYSIS

OF THE PALEOPATHOLOGICAL LITERATURE

by

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DEDICATION

To my mom and dad. Thank you for everything.

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ABSTRACT

Leprosy, caused by the bacteria *Mycobacterium leprae and Mycobacterium lepromatosis*, is a chronic, infectious disease that eventually causes disfiguring skin lesions, nerve damage, and muscle weakness. Even though leprosy has been nearly eliminated in many parts of the world today, it remains endemic in India, Myanmar, Nepal, Brazil, and a few African countries. Unfortunately, this infectious disease is not limited to just modern populations. In the past, leprosy spread globally and was a pervasive, degenerating disease. The literature traces leprosy back to 1550 BCE although there is possible skeletal evidence of leprosy in Rajasthan, India from 2000 BCE, suggesting it originated there and spread on a larger scale, but leprosy's dissemination remains uncertain.

Presently, numerous scientific articles exist on the paleopathology of leprosy, but no meta-analysis of leprosy has ever been done. In this paper, a meta-analysis was conducted on 1,645 paleopathological cases of leprosy found in 102 sites ranging from 3125 BCE to 1905 CE. This meta-analysis statistically tested the prevalence of leprosy based on the paleopathological literature to chart the pathogen's occurrence. First, a comprehensive search was conducted on previously published peer-reviewed literature to identify archaeological sites where leprosy was reported. These were geographically and temporally grouped together to trace the disease's effect in the varying populations over time. Second, the null hypotheses that the frequency and distribution of bone lesions due to leprosy did not change through time were tested. Results suggest that the frequency

and distribution of bone lesions did change over time, increasing in frequency in the Iron Ages and the Middle Ages, contrary to the null hypotheses.

Additionally, the average age at death of a leprosy sufferer rose almost 12 years from the Bronze Age to the Iron Age (26.6 years versus 38.3 years). Age at death remained relatively constant through the Middle Ages. There were more male skeletons than female skeletons (N = 312 versus N = 221) although females died at a younger age than males in all time periods analyzed except the Bronze Age.

This project suggests that *Mycobacterium leprae* originated in South Asia, slowly reaching Europe where it spread quickly and prospered for over 400 years, dramatically declined worldwide, and was eventually introduced to the New World likely through colonialism and the slave trade. Due to a rise in co-infection with other pathogens and improved social conditions, Europeans likely developed a natural resistance to leprosy. Leprosy's current global situation is also discussed, with 1.15 million infected individuals as of 2013 (World Health Organization, 2016). This is the first meta-analysis examining leprosy's global imprint in the archaeological record and provides evidence for how bone lesion frequency and distribution changed across time and space.

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LIST OF ABBREVIATIONS

APM	Alveolar Process of the Maxilla
ANS	Anterior Nasal Spine
BA	Bronze Ages
EME	Early Modern Era
ENIC	Endonasal Inflammatory Changes
F	Female
HD	Hansen's Disease
IA	Iron Ages
M	Male
MA	Middle Ages
MNI	Minimum-Number of Individuals
MDT	Multidrug Therapy
M. leprae	*Mycobacterium leprae*
SE	Standard Error
TB	Tuberculosis
U	Unknown

CHAPTER ONE: INTRODUCTION

Brief Introduction

Paleopathology is defined as the study of pathological conditions found in human remains or contexts. Pathological studies of skeletal data have demonstrated that health and diet were at an all-time low in the medieval period (Porter, 1999:25). Today, meanwhile, medicines and antibiotics serve to cure some of the worst infectious diseases. Modern medicine and medical research work toward furthering disease and injury prevention, cure, and individual wellbeing.

<u>Leprosy</u>

Leprosy, also known as Hansen's disease, is a chronic, curable infectious disease mainly causing disfiguring skin lesions, nerve damage, and muscle weakness. It is transmitted by nasal or oral droplets although only about 10% exposed to the disease actually get it (Covey, 2001:315). Although it is curable, blindness, paralysis, and severe disfigurement can manifest if unchecked and untreated.

More than 1.15 million people suffer from leprosy worldwide, with 215,557 new cases reported in 2013, mainly in South Asia, Africa, and South America (World Health Organization, 2016). However, except for pockets in Angola, Brazil, the Central African Republic, India, Madagascar, Nepal, Myanmar, and Tanzania, the disease is classified as eliminated, defined as below one case per 10,000 population (ibid).

There are two species of bacteria that cause leprosy: *Mycobacterium leprae* and *Mycobacterium lepramatosis*. *Mycobacterium lepramatosis* was discovered in 2008 in

Mexican populations and is a lesser agent of leprosy than *Mycobacterium leprae* (Han et al., 2008). *M. leprae* is an aerobic bacillus bacteria, enclosed in a characteristic waxy coating, resembling *Mycobacterium tuberculosis* in its size and shape.

Leprosy can be diagnosed as paucibacillary, a more moderate form of leprosy containing just a few lesions, or multibacillary, which is more severe and indicates more than five lesions present. Based on the severity of the symptoms, WHO classifies the disease into six classes through a Ridley-Jopling system, beginning with early indeterminant (I) leprosy and continuing with polar tuberculoid (TT) leprosy, borderline tuberculoid (BT) leprosy, mid-borderline (BB) leprosy, borderline lepromatous (BL) leprosy, and polar lepromatous (LL) leprosy (Pardillo et al., 2007:1096). Lepromatous leprosy (BL and LL) is the more contagious form of leprosy since the body is unable to form a resistance. Usually, BL or LL sufferers develop nodules all over body and face. Tuberculoid leprosy (TT and BT) is a less contagious form of leprosy. The skin grows dry, discolored, and loses feeling and most often affects the fingers and toes and is a common cause of blindness.

Furthermore, this chronic infectious disease is difficult to acquire, but a weakened immune system increases risk of disease, and signs of it may not show for 6 months up to a few decades after initial contact. *M. leprae* is extremely slow growing after contact and needs to be in an intracellular environment within its host (Donoghue et al., 2015:5141). Even after a diagnosis of leprosy, it can be years until lesions appear on the body. In the first stages of the disease, lesions are barely noticeable and do not itch and therefore, are often ignored by the individual. As the disease progresses, nerve damage and other

complications arise, including the characteristic deformities on the face and extremities (World Health Organization, 2016).

Historical Background

Today, the diagnosis and treatment of leprosy is unproblematic and most countries have achieved elimination at a national level (Bennett et al., 2008:198-9). In the past, before a cure was available, there was widespread fear of contracting leprosy which lead to the social exclusion of individuals who displayed symptoms of the disease. It is believed that it was first recorded on an ancient Egyptian papyrus document written around 1550 BCE, and around 600 BCE, Indian writings describe a skin disease that appears to have been leprosy (Hulse, 1972; Dharmendra, 1947). Numerous hymns of the four thousand year old Sanskrit text, *Atharva Veda,* discuss health problems that some scholars believe to be leprosy. The *Sushruta Samhita* (600 BCE), an ancient Sanskrit text describing primeval surgery and Indian medicine, is considered the oldest Indian writing describing the physical malformations of leprosy (Bloomfield, 2004).

The word *tsara'ath* in the Leviticus 13:9-46 (the Torah or the Old Testament), translated as 'leprosy,' used to be considered the oldest reference to the disease in history. *Tsara'ath* in Hebrew was later translated into Greek as *lepra*, or "scaly." However, it is now thought that 'leprosy' was used to categorize a broad variety of skin diseases (Møller-Christensen, 1967; Aufderheide and Rodriguez-Martin, 1998; Lechat, 2002), designating a state of moral uncleanness and ritual impurity for all sufferers (Grmek, 1991; Roberts and Manchester, 1995; Zias, 2002; Mariotti et al., 2005:311). The New Testament also contains references to lepers, but describes malformations that are unlikely characteristic of clinical leprosy.

For many years, leprosy was feared and misunderstood since many people thought of it as a hereditary disease, a curse, or even a punishment from God or some higher deity (Bennett et al., 2008:199). European sufferers were outcasts from society and had to ring bells to warn others of their approach. Victims were also pressured to not procreate, believing that the disease was hereditary. The public perception that people with the disease were unclean was derived from biblical scriptures, fearing that leprosy was a "moral disease" (Covey, 2001:316). Leviticus 13:44-46 states, "Now whosoever shall be defiled with the leprosy [*tsara'ath*], and is separated by the judgement of the priest, shall have his clothes hang lose, his head bare, his mouth covered with a cloth, and he shall cry out that he is defiled and unclean. All the time that he is infected and unclean, he shall dwell alone without the camp" (ibid).

This social stigma continued for most of its history, contributing to the barrier in self-reporting and medical treatment. It is nearly impossible to quantify the patients of centuries past based on the historical literature, so scholars have turned to other sources to help portray leprosy's history, especially demographic information such as church records and bioarchaeology. Leprosariums, usually sustained by the church, maintained some of the best medical records during the medieval ages.

Leprosy became a serious health problem in the medieval era and leprosy asylums, or "leprosariums," also called "lazar houses," typically run by monastic orders, were established in mass quantities in the United Kingdom, Denmark, Portugal, France, Germany, Sweden, Czech Republic, Italy, and Hungary (Robbins et al., 2009:5669; Antunes-Ferreira et al, 2013; Boldsen, 2001; Magilton et al., 2008). While episcopal support and private endowments financed most medieval European leprosariums,

leprosariums in Western Europe "had other unique sources of income" (Miller and Nesbit, 2014:130). In most cases, these leprosariums charged an admission fee by its patrons and their families or ran a business on the side to earn revenue. The business set-up of these leprosariums excluded some needy candidates who could not afford its services. Outside of Europe, leprosariums also became widespread in India during the medieval period (Granoff 1998:220). After the medieval era, leprosariums grew popular outside of Europe and were built in countries such as Japan, Syria, Israel, South America, and a few in the United States (Miller and Nesbitt 2014:73).

There is debate in the paleopathological literature on the oldest known skeleton with leprosy. Recently, a skeleton dating to 2000 BCE in Rajasthan, India was excavated bearing signs of leprosy (Robbins et al., 2009). Also in 2009, Köhler and colleagues, published a site report from Abony-Turjányos dűlő, Hungary on 2 probable leprous skeletons from 3215 BCE, but as of 2015, this article has not been translated into English (Köhler et al., 2009). This case from Hungary has not been cited in any subsequent paleopathological publications on leprosy.

In the 2007, Roberts provided an account of two burial cists dating to 2300 c. – 2000 c. BCE in Dryburn Bridge, East Lothian, Scotland. One of these cists (burial 11) contained a leprous 6-8 year old child pathological by identified with rhinomaxillary changes (2007:18-25). In contrast to Köhler et al., this report has been cited in the subsequent paleopathological literature yet articles published in 2015 still refer to the burial in Balathal, Rajasthan, India as the "oldest" documented case of leprosy (Kjellström, 2012; Taylor et al., 2013:17). In light of this confusion, one of the main

goals of this systematic review of the literature is to provide evidence to resolve this debate.

Since leprosy does not act as an immediate killer, it has remained more stable than most other infectious diseases (Boldsen, 2009:409; Monot et al., 2005). Modern leprosy is a disease that the sufferers die with, not from (Boldsen, 2005:165). Leprosy is frequently seen in co-infection with other diseases, observed in burials dating to the *Yersinia pestis* and *Mycobacterium tuberculosis* epidemics a few hundred years ago (Pálfi and Molnár, 2011; Donoghue et al., 2005).

Additionally, according to Monot et al. (2005), leprosy was much more of an epidemic in the past than it is today. The skeletal pathology and epidemiology of another well-known *Mycobacterium*, *Mycobacterium tuberculosis*, also an epidemic in the past, remains a big threat to global health. Both *M. tuberculosis* and *M. leprae* grow remarkably slow for bacteria, taking tuberculosis and leprosy, respectively, months or sometimes years to develop. Around one-third of the world's population are infected with tuberculosis and about 2 million people die each year from the disease while mortalities from leprosy number around 4,000 annually (Stone et al., 2009).

Both leprosy and tuberculosis were prevalent, or a common threat, in Europe throughout the first thousand years after the fall of the Roman Empire, but thereafter leprosy suddenly declined. It is not known why this occurred, but Donoghue et al. (2005:389), Roberts & Manchester (1995), and Lietman et al. (1993; 1997) suggest that cross-immunity protected tuberculosis patients from leprosy. They coexisted in antiquity, but tuberculosis sufferers had increased mortality and therefore, there was a historical decline in leprosy to where it is almost non-existent today.

Leprosy, unlike TB, is an Old World disease. Most historians agree that the disease originated in Asia as early as 2000 BCE. By 400 CE, the first leprosariums were built in Cappadocia and in Europe (Aufderheide and Rodriguez-Martin, 1998). Skeletal evidence of the disease is scarce until 400 CE, when the disease emerges in the UK (although not for the first time), likely spreading by the Roman army (Donoghue et al., 2015; Monot et al., 2005). The Crusades resulted in high leprosy infection rates throughout most of medieval Europe, with hundreds of leprosariums emerging in Denmark and the UK. All pre-16th century leprous skeletal remains are from Old World contexts (Table 1; Stone et al., 2009:71). Leprosy only reached the New World (North and South America) in the 16th and 17th centuries, likely by European explorers and migration. During the 19th century CE, Europeans spread the disease into Oceania (Aufderheide and Rodriguez-Martin, 1998; Smith, 2010:12). However, the earliest bioarchaeological cases of leprosy in Western Micronesia date from the 7th to the 15th centuries, making them the oldest known leprous individuals in Oceania (Trembly, 1995).

In the past millennium or two, however, leprosy spread like the common cold and was a chronic, widespread disease. After possibly originating in Asia, the disease was ubiquitous in Europe in the medieval period, but many people were likely misdiagnosed. Before standard terminology for different pathologies were invented, leprosy served as the "de facto" term for anyone suffering from a skin infection that left lesions on the bone. Therefore, early reports of leprosy could have been discussing another disease entirely, affecting the accuracy of the numbers. This problem persisted until Gerhard Armauer Hansen described the bacteria causing the disease in 1873 (Monot et al., 2005; Taylor et al., 2006). Despite this supposed "misdiagnosis" with syphilis, yaws, bejel,

pinta, tuberculosis, and numerous other skin conditions, leprosy was at full force for two thousand years. To keep up with the "demand," the United Kingdom instituted hundreds leprosariums within 12th to 16th centuries alone (Roberts, 2002a).

Leprosy has since nearly died out in Europe and most of the Western World; with rare cases appearing in the skeletal record within the past 450 years after a sudden decline in cases in the 16th century. This is remarkable considering the infection did not arrive in the New World until the 18th century likely through colonization and the slave trade (Stone et al., 2009).

Multiple hypotheses to explain leprosy's drastic decline beginning in 1400 CE have been proposed. One explanation that has been suggested is that late medieval people eventually developed increased resistance to the disease after the widespread death of those most vulnerable to the disease (Mendum et al., 2014; Monot et al., 2009). Additionally, it is possible that the power of leprosy faltered due to the heavy competition with other diseases such as *Mycobacterium tuberculosis* and *Yersinia pestis*, or the "Black Death" (Monot et al., 2009:1287). The Black Death spread throughout Europe in 1346-1353 CE, killing 30%-60% of Europe's population and 25% of the world population. Lastly, the improved living conditions, better sanitation, and strict quarantine efforts/superior medicine practices, especially after the Black Death, have been offered as reasons for leprosy's unexpected decline (Bennett et al., 2008:199).

Currently, leprosy is a curable disease with the use of multi-drug treatment (MDT) which may last from 6 to 24 months. Treatment should be provided in the early stages of the disease in order to prevent permanent disability. Before the World Health Organization introduced MDT in 1981, the possibility of curing leprosy through medical

treatment was not possible as the disease itself was little understood, particularly its transmission and how to care for someone who had it (World Health Organization, 2016). Not much is known about medical treatments for leprosy before the medieval ages but for the most part, early attempts at medicine were basic, naturalistic, and medicated by herbal remedies.

Medieval physicians, especially during the Renaissance era, used a wide variety of treatments to try to care and cure the disease. Some of these methods included rubbing hydnocarpus oil on the body, eating white lilies or the soil of ant-hills, spilling blood, drinking mercury, and amateur dissection and amputation (Covey, 2001:319; Rasmussen et al., 2008). Spiritual health was also closely linked to physical health as prayer and religion served as the most prescribed medicine. To answer the spiritual aspects of leprosy, many churches and monasteries ran and maintained leprosariums and promoted pilgrimages (Covey, 2001:319).

Although tremendous advances have occurred in the past three decades in the understanding and treatment of the disease, much remains unknown about the disease's transmission and pathogenesis (Bennett et al., 2008:198). It is a considerable debate as to whether the bacteria *Mycobacterium leprae* originated in ancient Europe, Eastern Africa, India, or the Near East centuries ago. One study, using comparative genomics from 21 countries, traced the strain of *M. leprae* by sequencing rare single-nucleotide polymorphisms of leprosy back to Eastern Africa or the Near East (SNP-type 1) and showed that leprosy was likely then spread through human migration and colonialism (Monot et al., 2005). The disease then grew rampant in Western Africa and Europe until about 450 years ago. This 2005 study is further explored in Chapter 5.

The most accepted hypothesis, similar to that in Monot (2005) is that leprosy originated in Southern Asia, spread through the Old World, and was introduced to the New World by Spaniards, through the African slave trade, and colonialism. The possibility of an African origin has been thoughtfully considered as well but that is likely no longer an option after the discovery of skeletal evidence for leprosy in Rajasthan, India, the oldest known case of leprosy at 2000 BCE (Grmek, 1991; Robbins et al., 2009)

Leprosy Today

With the introduction of multidrug therapy (MDT) by the World Health Organization in 1981, leprosy is curable and treatment in the early stages prevents permanent disability. Since 1995, the World Health Organization has supplied the triple antibiotic course free of charge to all leprosy patients. MDT regimens combine rifampin, clofazamine, and dapsone in the treatment of leprosy (Bennett et al., 2008:201; Setia et al., 2006:162). Despite WHO providing MDT free of charge, a 2015 study found that leprosy affects poor and marginalized communities in developing countries, pushing affected households deeper into poverty (Chandler et al., 2015). Further out of pocket expenses and lost productivity (ability to earn an income) keeps disabled individuals at a constant disadvantage.

Even though leprosy is nearly eliminated, it remains endemic in parts of the world, with India accounting for about 60% of all registered cases (as of 2012; WER 2012 Index). In regions considered European or 'New World,' it remains endemic only in Brazil (1-2 cases per 10,000 people). Although more rare, there have been cases reported issue in Venezuela, Paraguay, and the Dominican Republic (based on rate detected per 10,000 in 2011; Figure 1) (ibid).

Leprosy prevalence rates, data reported to WHO as of beginning January 2011

Prevalence rates (per 10 000 population)

>2
1.0 - 2.0
<1
0 cases reported
No data available
Not applicable

The boundaries and names shown and the designations used on this map do not imply the expression of any opinion whatsoever on the part of the World Health Organization concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted lines on maps represent approximate border lines for which there may not yet be full agreement. © WHO 2011, All rights reserved

Data Source: World Health Organization
Map Production: Control of Neglected
Tropical Diseases (NTD)
World Health Organization

World Health Organization

Figure 1.   **Frequency of leprosy in 2011 worldwide per 10,000 population (WHO, 2012)**

Purpose

<u>The Value of a Meta-Analysis</u>

A meta-analysis fills the gaps in knowledge using a large set of archaeological findings. Thus, a meta-analysis of the prevalence and impact of leprosy throughout history is useful to trace the pathways of the disease in addition to providing insight into why *M. leprae* died out in most of the Western hemisphere over 450 years ago, yet still remains a problem in other countries. A meta-analysis takes effect sizes from individual studies that investigate the same question, quantify the observed effect in a standard way, and then combines these effects to get a more precise idea of the true effect in the population (Field, 2013:879).

The purpose of this research project is to expand our understanding of the impact of leprosy on past populations through a meta-analysis on the paleopathological literature by compiling and categorizing published and unpublished independent archaeological data on leprosy. A meta-analysis serves to provide a more comprehensive overview of this ancient chronic disease and its effect through time. This project uses statistical techniques to identify patterns among the study results.

While Roberts (*forthcoming*) is publishing a compendium of leprosy through history and numerous scientific articles exist on the archaeology of leprosy, no meta-analysis of leprosy has ever been done. This research is the first meta-analysis examining leprosy in the archaeological record, although there are meta-analyses on other pathologies (tuberculosis, Holloway et al., 2011; malaria, Setzer, 2014; Smith-Guzmàn, 2015, os acromiale, Yammine, 2014; syphilis, Boekhout, 2009). Bratschi et al. (2015) recently published a systematic literature review in *Leprosy Review* on the current knowledge of the transmission of *Mycobacterium leprae*, concluding that there are no studies that indisputably demonstrate the mechanisms behind the transmission of leprosy.

A paleopathological-based meta-analysis has the potential for enormous broader impacts in bioarchaeology and paleopathology. Despite considerable excellent work done studying leprosy, much about the infectious disease remains unknown, including its origin, initial transmission routes, and the timing of the spread of the disease (Robbins et al., 2009). This study is organized two-fold: First, I grouped archaeological findings on leprosy geographically and traced the disease's effect, or frequency, in the varying populations. Second, I tested two null hypotheses; (1) the frequency of bone lesions due to leprosy did not change through time and (2) the distribution of lesions throughout the

skeleton did not change over time. These null hypotheses are based on two research questions asking how the frequency of leprosy changes through time and how the distribution of lesions throughout the skeleton changes through time. It is assumed that the distribution of lesions throughout the skeleton correspond to the type of leprosy the individual had: lepromatous leprosy or tuberculoid. If the null hypotheses are confirmed, then leprosy has remained constant throughout time and the type of leprosy has not changed. If the null hypotheses are falsified, however, then the frequency and type of leprosy have changed over time. With higher frequencies of leprosy, it is assumed that there was increased migration, increased population density, and overall decreased sanitation.

CHAPTER TWO: LITERATURE REVIEW

Review of Past Studies: Geographical Division

Leprosy in Northern Europe

Due to the pioneering work of Møller-Christensen and Boldsen, bioarchaeological information on leprosy in Denmark is exhaustive (Møller-Christensen, 1978, 1967, 1965, 1952; Boldsen, 2013, 2009, 2008, 2006, 2005a, 2005b, 2001). Sixty-nine percent of this project's skeletal sample derives from Denmark. Regardless of large numbers of *Mycobacterium leprae* in its Scandinavian neighbors, there is no physical evidence of leprosy in Finland's skeletal record, although Vuorinen reported a leprosy hospital in Finland in 1355 CE (Vuorinen, 2002). Explanations for the absence range from environmental factors to TB co-infections leading to a nonsurvival of identifying leprosy lesions.

Leprosy is rare in the UK until the Roman period (4th century CE) and then increases in the early and late Medieval periods; only one case is seen in the post-Medieval period (Roberts et al., 2007, Roberts, 2002a; Walker, 2009). Eleven percent of the entire sample used in this data came from the UK. The data also includes Northern European skeletons from Sweden (Arcini, 1999; Nuorala et al., 2004; Linderholm and Kjellström, 2011) and Ireland (Murphy and Manchester, 2002). Even though leprosy disappeared from Middle Europe almost completely by the 18th century, the disease remained in the Baltic and Scandinavian countries (Nerlich and Zink, 2008:109).

Norway, Iceland, and the UK still had issues with leprosy after the medieval ages ended

but by the 1920s, new cases rarely occurred.

Leprosy in Central and Western Europe

Much like Denmark and the UK, Hungary has also received a significant amount

of attention in the paleopathological literature due to leprosy's large presence before and

during the medieval period (Csóri et al., 2009; Pálfi, 1991; Pálfi et al., 2002; Pálfi and

Molnár, 2009; Marcsik and Molnár, 2007, 2002; Molnár et al., 2015; Mészáros et al.,

2005; Donoghue et al., 2005; Donoghue et al., 2015; Köhler et al., 2009). After the

medieval era, leprosy became rare in Hungary. In the Czech Republic, the discovery of

two Czech individuals by Likovský et al. (2006) suggest that leprosy existed there prior

to the Crusades (2006:1276). Historical evidence cites confirmation of leprosy hospitals

in Czech Republic back to the later medieval period (Strouhal et al., 2002).

Much like the rest of Central and Western Europe, Portugal had a surge in leprosy

cases in the 14th to 16th centuries (Antunes-Ferreira et al., 2013; Ferreiera et al., 2013).

This rise in leprosy is typically associated with increased population density, migration,

and decreased sanitation, leading to a virulent environment for the disease to spread in.

This project includes the data from two leprosariums in Portugal, the Lagos leprosarium

and the Beja leprosarium. Other Central and Western European countries, such as Austria

and Germany, had cases of leprosy in the Iron Age and the medieval era (Gausterer et al.,

2015; Boldsen, 2008; Boldsen et al., 2013; Szilvássy, 1980).

Leprosy in the Mediterranean

Leprosy in Italy has a long history, thanks to human migration and trading. The

earliest case of leprosy in Italy, in Casalecchio di Reno, Bologna, dates to the 4th and 3rd

centuries BCE (Mariotti et al., 2005). Paleopathological literature references multiple cases of leprosy in the Iron Age, but most cases date to the early/middle medieval period (Rubini and Zias, 2009; Rubini et al., 2012; Rubini et al., 2014; Belcastro et al., 2005).

While only a few skeletons used in this data originate from France (Blondiaux et al., 2015; Blondiaux et al., 2002), social stigma against leprosy in France has a long place in the historical literature. In 1321, King Philip V was informed of a plot to poison the wells and springs of Aquitaine and subsequently, issued a decree that led to riots across France against lepers. French towns like Pamiers, Toulouse and Rouen, Normandy erected leprosariums to contain these "vagrants" and soon saw large crowds of people burn leprosy sufferers alive without trail (Miller and Nesbitt, 2014:96-7). King Charles V of France followed suit and complained that they "were overtaking Paris" (Covey, 2001:319).

Besides the historical literature and religious texts, Israel and Egypt have documented bioarchaeological evidence proving that leprosy existed in those two countries for a long time, providing some of the oldest samples in this project (Matheson et al., 2009; Molto, 2002; Dzierzykray-Rogalski, 1980). Rafi et al. (1994), Spigelman et al. (2002), and Møller-Christensen et al. (1966) have also recorded skeletal evidence for leprosy in Israel and Egypt. Turkey (Rubini et al., 2012), Cyprus (Baker and Bolhofner, 2014), Croatia (Watson and Lockwood, 2009), and Spain (Montiel et al., 2003) also have skeletal evidence for leprosy.

Leprosy in Asia, Oceania, and the New World

Most of the oldest leprosy cases are found in Asia and the Middle East. The oldest accepted osteological evidence for leprosy is found in India. Robbins et al. (2009)

published findings of the earliest skeletal evidence for leprosy, traced to a Late Indus Age burial in India from 2000 BCE. Additionally, two individuals with leprous lesions from Noen U-Loke, Thailand have been dated to 300-200 BCE and 1st to 2nd centuries CE and six from Armenia date to the 2nd to 1st centuries BCE (Tayles and Buckley, 2004; Khudaverdyan, 2010). Burial context tells us that leprosy was present, if not prevalent, in Asia centuries before it was ubiquitous in Europe.

Leprosy traveled throughout Asia during the Iron Age. A single leprous individual from the Ustyurt Plateau in Uzbekistan dates to the 1st to 4th centuries CE and two have been found in Georgia dating to the 6th to 10th centuries CE (Blau and Yagodin, 2005; Neil, 2003). Two dating to the Han Dynasty (206 BCE to 200 CE) were excavated in Shanxi Province, China (Zhang, 1994). A few centuries later, leprosy was recorded in Syria (Miller and Nesbit, 2014) and Japan. Historical literature documents leprosy in Japan as early as the medieval period; however, the earliest skeletal evidence dates to the 18th century CE (Suzuki et al., 2010, 2014).

Leprosy travels to the Pacific through China and Japan during the late Iron Age/ early medieval era and grows virulent after the medieval era ends. In Guam and Saipan, western Micronesia, six cases of leprosy were found across three Oceanic sites ranging in date from 7th to 11th centuries CE (Trembly, 1995). People born in Oceania had one of the highest prevalence of leprosy during the 18th to early 20th centuries outside of India and it remains an issue in Federated States of Micronesia, the Marshall Islands, Kiribati, Papua New Guinea, and the Philippines today (WPRO, 2016).

Meanwhile, skeletal evidence for leprosy in Chile and the Netherlands Antilles date to the Early Modern Era (post-1536 CE) (Gilmore, 2008; Polet, 2011). Since leprosy

did not exist in the Americas until post-Columbus exploration and conquest, there are no leprous skeletal remains dating to the Bronze Age, the Iron Age, or the medieval era.

Leprosy was never endemic in the United States (none of the skeletal samples originate from there and leprosy was not documented in Hawaii until 1823 CE), but cases of leprosy in Louisiana were first reported in the 18th century, likely resulting from migration and the slave trade (Nerlich and Zink, 2008:109). It was endemic in Louisiana between 1835 and 1970 and relatively high rates were found in Texas, although nowhere near the rate found in medieval Europe. The first leprosarium in the US existed in Carville, Louisiana from 1894-1999 and Baton Rouge's National Hansen's Disease Clinical Center remains a leader in research into multidrug therapy (Boeckl, 2011:22).

Bioarchaeological Considerations

All these things considered, there are other factors that affect the placement of leprous remains in the archaeological record. A frequent problem in correctly assessing health status in past populations is the conflicting interpretations pathological lesions in archaeological skeletal populations leave. The "Osteological Paradox," as Woods et al. (1994) deems this phenomena, is the problem that arises in bioarchaeological interpretations since the frequency of lesions in a skeletal sample(s) will always be higher than in the living population due to heterogeneity of risk and selective mortality (635). Specifically, those individuals that are most likely to enter the sample (or at the most risk of dying at any given age from any given factor) with osteological lesions were those old enough to have lesions form on their skeleton. Those suffering from a pathogen that died too young or before they endured the disease for too long, lack visible osteological lesions, appearing as if they never suffered from the disease at all. Donoghue et al. (2005)

lamented that, since only about 5% of pre-antibiotic lepromatous leprosy cases involve

bone changes, the number of paleopathology-reported leprosy cases will always be

under-estimate (251). Thus, using skeletal remains to determine leprosy rates may

underestimate the actual numbers of people who experienced the disease. In spite of this

setback, the number of leprosy cases reported from paleopathological literature compared

against the number of the total population examined for lesions provides valuable clues

into the rates of leprosy over space and time. Nevertheless, the Osteological Paradox is

crucial to remember in any bioarchaeological assessment of a past population.

Useful biocultural information is further restricted by present political,

socioeconomic, cultural, and preservation issues. Osteological attempts measuring

leprosy's distribution are hindered by these factors, which ultimately compromises

accurate estimations of the disease's proportion and impact throughout time. While

bioarchaeological interpretations suggesting an increase in leprosy in medieval Europe is

supported by the historical literature, the distribution of leprosy in the archaeological

record in many under-represented countries are affected by the aforementioned factors.

Political and socioeconomic instability affect the progression of archaeological

work in a country. The impact leprosy's had in many Middle Eastern, Asian, and African

countries is likely incorrectly assessed since it is difficult for archaeologists to acquire

permits to work in those places. Archaeology has also been impacted by government

propaganda, protests, wars, disinterest, and lack of funding. Bioarchaeology in Denmark

and the UK are very well-funded and supported by academics and locals, leading to a rise

in publications in those countries (Gamble, 2014).

Lastly, issues in preservation and diagnosis also impact leprosy's representation. There are a few problems found in many osteological investigations (i.e., poor bone preservation, inter-observer error, variations in recording lesions, and difficulties in aging) (Judd and Roberts, 1998:44). Leprosy lesions look similar to those caused by syphilis and tuberculosis, which have caused misidentifications and overestimations in the past (Suzuki et al., 2010; Holst, 2012). Additionally, diagnosing leprosy by scoring lesions using a technique that is over 60 years old is not as secure of a diagnosis method as DNA analysis (Møller-Christensen, 1952). Studies that exclude DNA analysis might suffer from inaccuracy in their estimations of leprosy's prevalence.

CHAPTER THREE: METHODS AND MATERIALS

Data Collection

Literature Search

A literature search was conducted using a number of online databases including Academic Search Premier, Google Books, Google Scholar, JSTOR, ProQuest, PubMed, ScienceDirect, SpingerLink, Web of Science, and Wiley Online Library. Peer-reviewed articles were also searched for within *Leprosy Review*, the *International Journal of Leprosy and Other Mycobacterial Diseases*, *AJPA*, the *International Journal of Osteoarchaeology*, the *International Journal of Paleopathology*, and The Past and Present of Leprosy, edited by Roberts et al. (2002).

Additionally, online publication sharing websites ResearchGate and Academia were utilized to aid in the search. They were primarily used to find full-text documents. Through these websites and through email, numerous authors were generous enough to send copies of their work and answer any further questions. A bioarchaeologist specializing in tuberculous and leprosy was contacted to inquire about the existence of any unpublished meta-analyses and thirteen articles were received by the author themselves.

Criteria for Consideration and Exclusion

The search terms included: "paleopathology," "leprosy," "history," "Hansen's [disease]," "skeletal," "remains," "lesions," "*Mycobacterium leprae*," "infectious disease," "meta-analysis," and "archaeological remains." Articles were searched using

four different combinations of terms in order to maximize the scope of references used (Table 3). The four search combinations were: (1) "leprosy" and "paleopathology"; (2) "leprosy" and "history" or "leprosy" and "skeletal" and "remains"; (3) "leprosy" and "lesions" or "leprosy" and "paleopathology" and "lesions"; (4) "leprosy" and "meta analysis" or "leprosy" and "archaeology." The results of the search terms are explained and discussed further in Chapter 5.

This review removed duplicate references, book reviews on sources already considered, publications not related to leprosy, and non-peer reviewed publications (e.g. letters). All publication dates were considered although some earlier dates were re-evaluated for accuracy and relevancy. If articles had overlapping skeletal samples, the more recently published article was used. The earliest article with data used in this project (supplementary text Appendix B) was published in 1958 and the most recent article was published in June 2015. The literature search is up to date as of December 2015. All documents returned from searches that were deemed relevant to this study are included in Appendix A. See Appendix B for articles/book chapters that were not included. Sources in all languages were considered and publications were found in English, French, Spanish, Danish, Hungarian, Russian, Ukrainian, German, Swedish, Czech, Croatian, Hebrew, Italian, Polish, Arabic, Portuguese, Japanese, Afrikaans, and Turkish.

In a Microsoft excel document (Table 3), the details of the literature search was carefully organized under each database and sorted by search terms. More details about the results from the literature search are provided in the Results section (Chapter 4). From August-September 2015, each of the aforementioned databases were searched for

relevant articles using four search term combinations and their results counted. Additionally, the following topics were not included in the meta-analysis despite being related to the impact and exposure of *M. leprae*:

- Articles describing signs and symptoms in living people, not skeletal signs,

- Cases of leprosy that were non-human,

- If cases of leprosy were mentioned but no description was given,

- Only drug treatment for leprosy was described but without bone signs,

- Articles reviewing cases already included from other sources,

- Other diseases than leprosy were the primary focus of the article (leprosy only mentioned as an example).

- The total number of skeletons at the site, with and without leprosy, was not provided.

"Not accessible" means that they could not be accessed by public domain or by the Boise State University library (see supplementary text Appendix B, column C). Useful articles that were not accessible were acquired either through inter-library loan or by contacting the author directly.

The meta-analytic approach was developed in 1976 by Gene V. Glass to increase diagnostic accuracy and address methodological validity in statistical studies (Glass, 1976). It is most often used to assess clinical effectiveness of healthcare or medical interventions by combining data from two or more randomized control trials (ex: BCG vaccine in regards to leprosy, Zodpey, 2007; Setia et al., 2006). Its use is not limited to clinical studies; systematic reviews and meta-analyses are possible and have been done

on paleopathological literature (Zweifel et al., 2009; Holloway et al., 2011; Setzer, 2014; Bratschi et al., 2015).

As Rothstein and Hopewell (2009) noted in the <u>Handbook of Research Synthesis and Meta-Analysis</u>, "the aim of a high quality research synthesis is to generate as comprehensive a list as possible of both published and unpublished studies" (105). Similarly, Johnson and Eagly. (2014) recommend that "every effort should be made to obtain unpublished studies. Meta-analyses properly have the goal of describing the universe of studies on a topic or at least an unbiased sample of that universe" (682). This proved to be difficult for this study, although four relevant unpublished studies were acquired and used in this project.

<u>Geographic and Chronological Groupings:</u>

Cases were grouped into six regions: Northern Europe, Central and Western Europe, Mediterranean, Asia, Oceania, and New World. Within each geographical regions, cases were also organized by cultural time periods. These were termed "Bronze Age", "Iron Age", "Middle Age", and "Early Modern Era." The corresponding dates of these groups are listed in Table 1. Note, that the chronological term MA represents the Middle Ages, which refers to the same period of time as the medieval era.

The European Middle (or medieval) Ages, listed in Table 1 as 1050 CE-1539 CE, is a major scheme for analyzing the crux of European history. However, the Post-classical Era (e.g., any period that immediately follows ancient history), in China began with the start of the Sui dynasty (600 CE) and ended 100 years before Europe's medieval ages (Marks, 2015:24). This seems to be the case for most of the rest of the Asian countries. Thus, the way these four periods were defined was somewhat restricted, yet out

of statistical necessity, some simplifications had to be made (Stone et al., 2009; Roberts, 2002a; Boldsen, 2009).

Table 1. **Descriptions of temporal groups and the corresponding dates for each geographical region. Groupings based on information gathered from: Stone et al. (2009); Roberts (2002a), and Boldsen (2009)**

Geographical Region and Description (Total = 1,645)	Bronze Age (pre-600 BCE): Total Cases	Iron Age (500 BCE – 1050 CE): Total Cases	Middle Ages (1050 CE-1536 CE): Total Cases	Early Modern Era (1536 CE – 1905 CE): Total Cases
Northern Europe	1	80	1,290	2
Central and Western Europe	2	39	137	0
Asia	1	12	0	3
Mediterranean	0	23	45	0
New World	0	0	0	4
Oceania	0	0	6	0
	Total = 4 (0.24%)	Total = 154 (9.36%)	Total = 1,478 (89.9%)	Total = 9 (0.55%)

Distribution of Lesions

Osteological lesions were recorded on the skeleton that were characteristic of leprosy. In this study, lesion distribution was based on *facies leprosa*-only (or rhinomaxillary syndrome), post-cranial only, or on both (*facies leprosa* and other) which acted as epithets to summarize the lesions reported in publications. These publications attributed their paleopathological system of lesions to Møller-Christensen (1978). More recent methodology is illustrated in Boldsen (2005, 2008, 2013), but the sequence remains practically the same as Møller-Christensen's (Table 2). The term *facies leprosa*,

introduced by Møller-Christensen in 1952, serves to represent the following skeletal

pathological changes of the skull:

1. "Atrophy of the *a*nterior *n*asal *s*pine (ANS);

2. Atrophy and recession of the *a*lveolar *p*rocess of the *m*axilla (APM)
   confined to the incisor region, beginning centrally at the prosthion and
   resulting in loosening and eventually loss of relevant teeth;

3. Endonasal inflammatory changes. These *e*ndonasal *i*nflammatory
   *c*hanges (ENIC) constitute the pathological basis of the complex,
   which should always be present for the diagnosis of "*facies leprosa*",
   together with one or both of the other symptoms mentioned" (Møller-
   Christensen, 1952, 1978).

Table 2.   Descriptions of leprosy lesions (Boldsen, 2008; Møller-Christensen, 1952, 1978).

Number	Lesion Description
1	The remodeling of the edge of the nasal aperture
2	Atrophy of the anterior nasal spine
3	Atrophy of the alveolar process on the premaxilla
4	Porosity or perforation of the palate
5	Subperiostal exostoses on fibula
6	General hypertrophy of the fibula
7	Changes to the plantar surface on the fifth metatarsal

The distributions of lesions were compared using chi-square tests. Four

contingency tables were created, each representing a different region, to test whether the

proportion of lesion type differed by time period. A Fisher's exact test was calculated for each contingency table to deal with the small samples.

<u>Frequency of Lesions</u>

The frequency of lesions where sample size was known, was evaluated by dividing the total number of skeletons with leprosy lesions by the total number of skeletons at the site. This was not possible in all cases due to insufficient information (supplementary text Appendix B). For comparative purposes, a regression analysis was performed using linear, power, logarithmic, and exponential models (to determine which model fit the data best) to examine the frequency of leprosy at each site. The results were charted in histograms.

Measurement of Variables

<u>Data Analysis</u>

The meta-analysis started with an exhaustive systematic review of the literature. The next research stage was setting boundaries for the sample of studies and selecting the determination criteria. After that, the third step was locating relevant studies, published and unpublished. Next, I created the meta-analytic database and decided on how the variables should be coded. A meta-analysis is the synthesis of compatible effects, giving greater weight to studies with less variance and more precision (Kovalchik, 2013). This project analyzed data using the R software (cran.r-project.org).

I used the R package metaprop to examine how proportions of leprosy varied across different time periods. By examining the forest plots, I inspected whether there was a trend in proportion of leprosy skeletons by time period. Chi-squared tests were also examined to determine if a) the proportion of leprosy between the different geographical

regions varied; b) the proportion of leprosy varied between the BA, IA, MA, and EME individuals; and c) if the distribution of lesions between four of the six geographical regions varied. Since the expected value of cells fell below 5 in at least one cell of each contingency table, Fisher's exact test was used to determine if there were differences in the proportions between the groups.

CHAPTER FOUR: RESULTS

Sample Size

A literature search conducted from August to September 2015 from 10 academic

databases using a combination of four search terms (see Table 3) returned a combined

total of 21,641 references. After additional searches (by searching through particular

journals, for instance), the total number of references totaled 21,880. Of these references,

77 met the inclusion criteria, 73 published and 4 unpublished (see Chapter 3).

Every continent, except Antarctica, had data, although the data varied drastically

in quantity. The exact number of leprosy cases reported across 77 papers was 1,645 from

a total number of 102 gravesites. Additionally, 533 of these individuals were sexed and

1,112 were unable to be sexed or the sex was not provided. From these 102 gravesites,

there was a total number of 18,787 skeletons excavated. Thus, the percentage of

individuals showing osteological signs of leprosy expressed in relation to total number of

individuals is 8.76%.

A few search term options were explored to determine the best choice to narrow

down the search and ultimately, the combination "leprosy AND paleopathology" was

deemed most responsive for acquiring relevant references. The other search

combinations, listed in Table 3 and discussed in the next paragraph, were searched as

well, but most relevant articles overlapped with any found in the "leprosy AND

paleopathology" combination, and therefore these search terms were not used. In all,

2,104 articles were returned from the search term combination "leprosy AND paleopathology." These articles were read and organized by database and relevance.

An additional 107 articles were found via references from papers included in the study, even though these articles were not found through a database. An additional 58 references were found not through a database, but they were categorized as "not accessible" (supplementary text Appendix B, column C). In an excel document, all 1,661 articles found through databases were read to determine if they were "useful" or "somewhat useful" to the project. 208 references were deemed "useful," 232 references were deemed "somewhat useful," and 1,221 references were deemed "not useful." "Useful" references contained data that was used in this project, whereas the "somewhat useful" references were primarily used for supporting information.

In every database listed after the first one (for example, ProQuest; see supplementary text Appendix B, row 980), there is a column added on whether the article is a duplicate or "new to the search". It is a "NO" if it is a duplicate and is a "YES" if it is not a duplicate. In column D, those that were repeats contained "Repeat" in the row. The results from Google Books, in all four search combinations, revealed similar results to those found in Google Scholar. Thus, the references from Google Books are not included in the Microsoft Excel document (supplementary text Appendix B).

After the literature search was completed, 432 references were removed as duplicates, 1,221 yielded no relevant information, and 555 were not accessible. "Not accessible" means that they could not be accessed by public domain or by the Boise State University library. Most of these "not accessible" articles were either repeats or not relevant to the study according to its abstract. Useful articles that were not accessible

were acquired either through inter-library loan or by contacting the author directly. Refer to Table 3 for details on the literature search. Additionally, 107 publications were acquired by following up references from papers included in the study and 13 were received from Dr. Charlotte Roberts, Dr. Helen D. Donoghue, Dr. Joel Blondiaux, Dr. Francisco J. Silva, and Dr. Kristin Snopkowski.

Table 3.   Details on the literature search from mentioned databases. Completed December 2015

Table 3.
Details of the literature search from numerous databases completed during August-September 2015

Database	Search 1	Results	Additional Searches	Results
Academic Search Premier	"leprosy" and "paleopathology"	12	Followed up references	107
Google Books	"leprosy" and "paleopathology"	435	Received from other authors (includes ResearchGate and Academia)	13
Google Scholar	"leprosy" and "paleopathology"	978		Total=120
JSTOR	"leprosy" and "paleopathology"	137		
ProQuest	"leprosy" and "paleopathology"	71	Also searched articles within these journals:	Results
PubMed	"leprosy" and "paleopathology"	47	Leprosy Review	12
Science Direct	"leprosy" and "paleopathology"	66	International Journal of Leprosy and Other Mycobacterial Diseases	8
SpringerLink (Not Available Through BSU)	"leprosy" and "paleopathology"	57	AJPA	17
Web of Science	"leprosy" and "paleopathology"	32	The Past and Present of Leprosy: Archaeological, Historical, Palaeopathological and Clinical Approaches Edited by Roberts et al. (2002).	24
Wiley Online Library (Not Available Through BSU)	"leprosy" and "paleopathology"	269		Total=61
		Database Total = 2,104		
Combined Total = 2,285	Not relevant = 1,221	Duplicates = 432	Not Accessible = 555	Final = 77

Figures 2 and 3 show histograms charting the number of leprous skeletons at each site (referred to as 'Events' for here on) and the total number of skeletons at each site (referred to as 'Total' for the remainder of the thesis). Both figures do not have a normal distribution and produced very positively skewed data. This indicates that the majority of sites have small samples (both in the number of leprous skeletons and the total number of skeletons), while a few sites have large sample sizes. A Shapiro-Wilk test shows that these distributions are non-normal; Events ($W = 0.2248$, $p < 0.001$) and Total ($W = 0.7324$, $p < 0.001$). A histogram of proportion of Events at each site (Figure 4) also shows that the proportion data is not normally distributed, although most sites have less than 10% leprous skeletons.
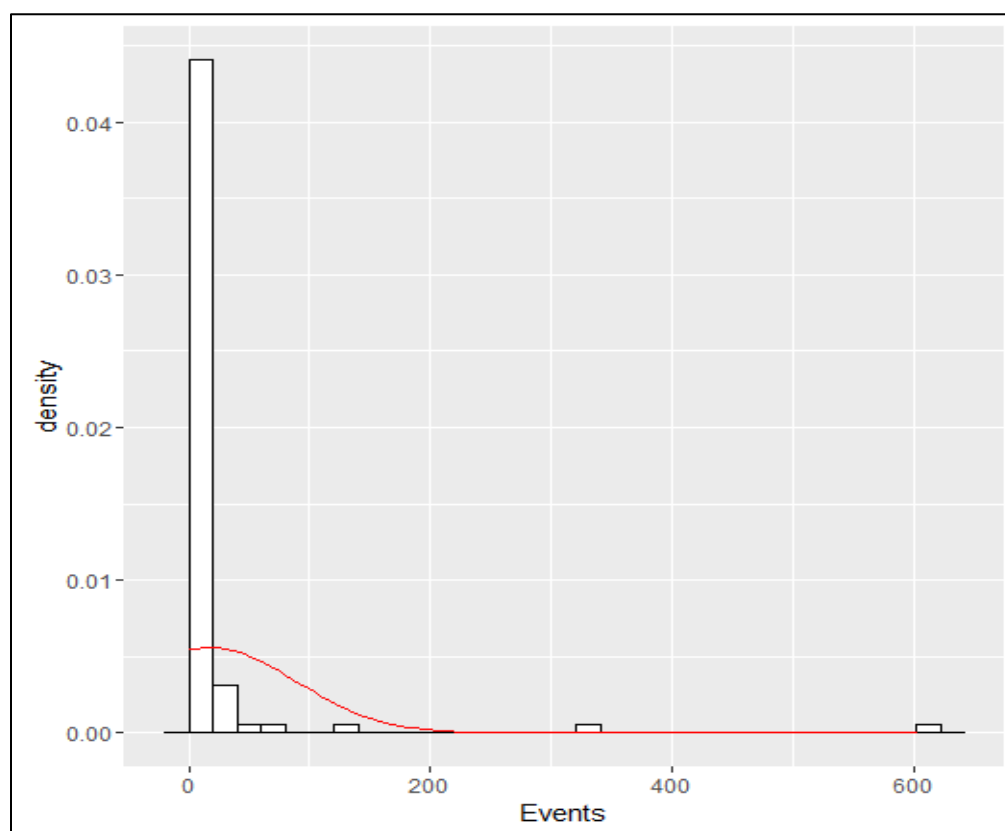
Figure 2. **Histogram overlaid with a normal curve of density (y) to number of Events (x) where Events represents number of leprous individuals at a site**
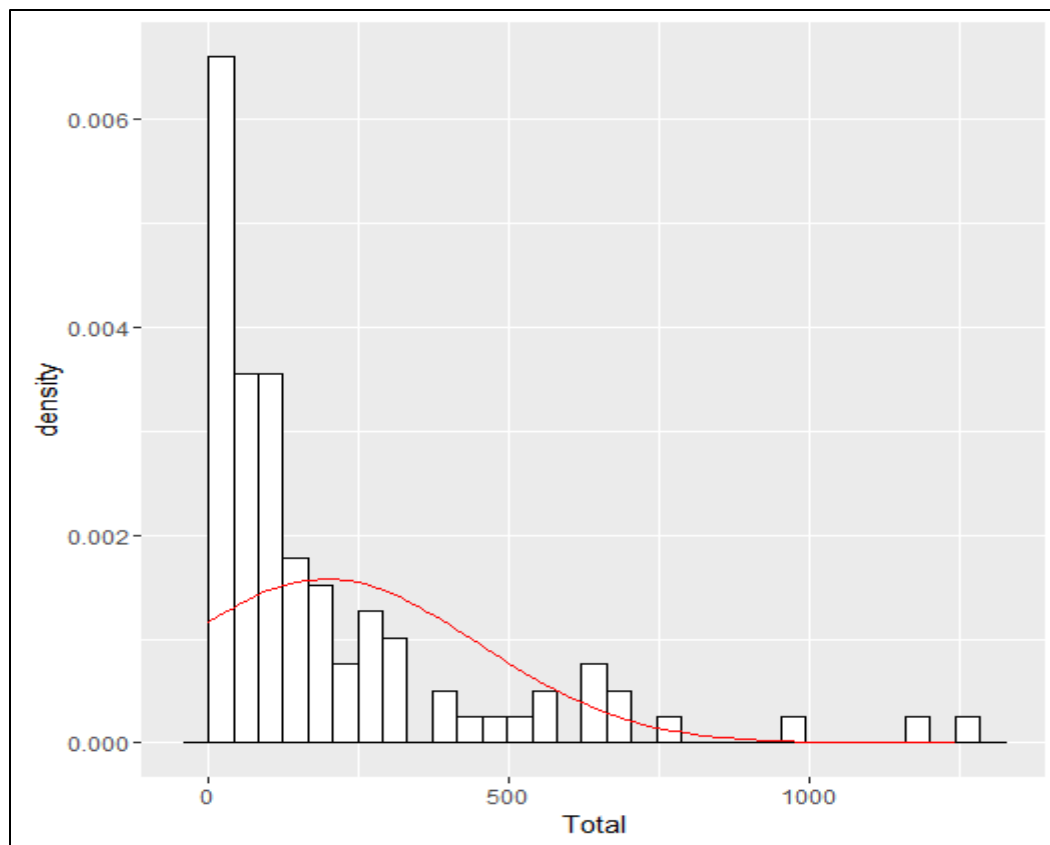
Figure 3. **Histogram overlaid with a normal curve measuring density (y) the distribution of the Total (x) number of skeletons at each site**
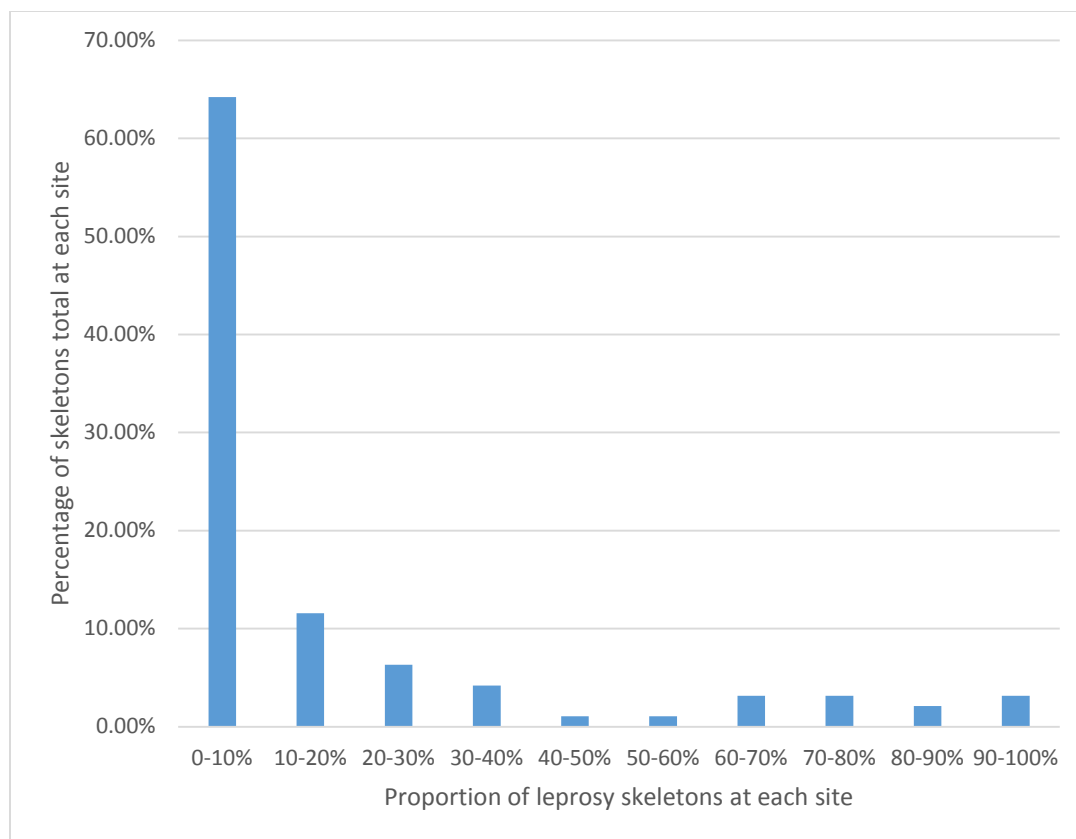
Figure 4.   **Histogram of the proportion of leprosy skeletons at each site**

<u>Sex</u>

The sample is composed of 312 males (59%) and 221 females (41%) (Figure 5). In this study, *M* represents males, *F* represents females, *U* represents those with unknown sex, and NA represents individuals where sex was not reported. Combined, sexed skeletons only amounted to 32.4% of the total sample. Those that were unknown or not reported cumulated 67.6% of the total (combined distribution depicted in Figure 6). Sexing was not possible for most individuals less than 18 years old ("infants" and "juveniles") and are placed in the unknown category.

LEPROUS SKELETONS: MALE AND FEMALE

■ Males ■ Females

Females, 221, 41%

Males, 312, 59%
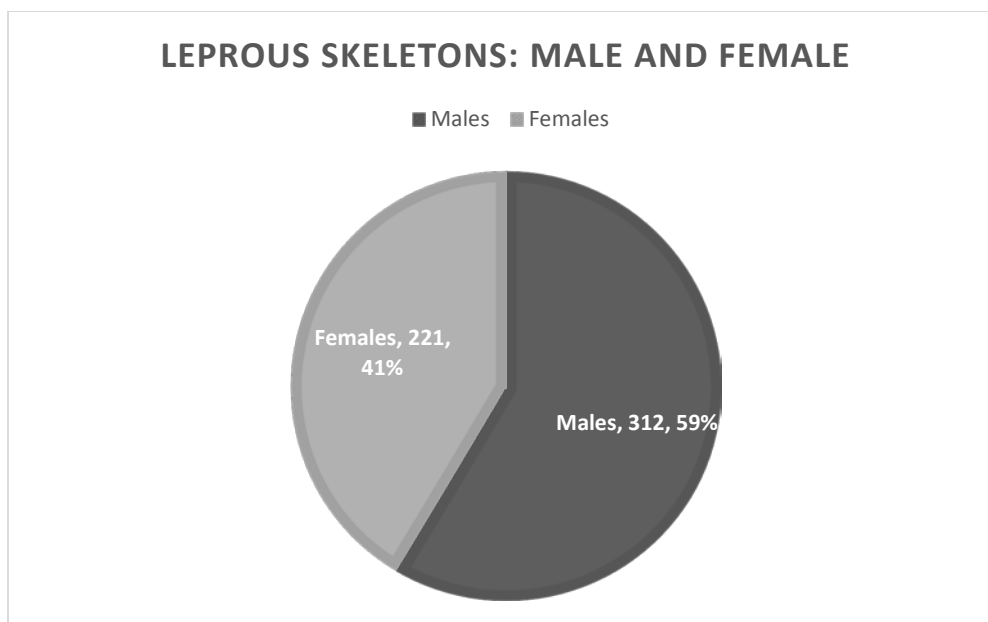
Figure 5.   **Number of males and females (only for those reporting sex, N = 533)**

DIVISION OF TOTAL SKELETON BY SEX

■ Males   ■ Females   ■ Unknown   ■ Not Reporting

19%

13%

65%

3%
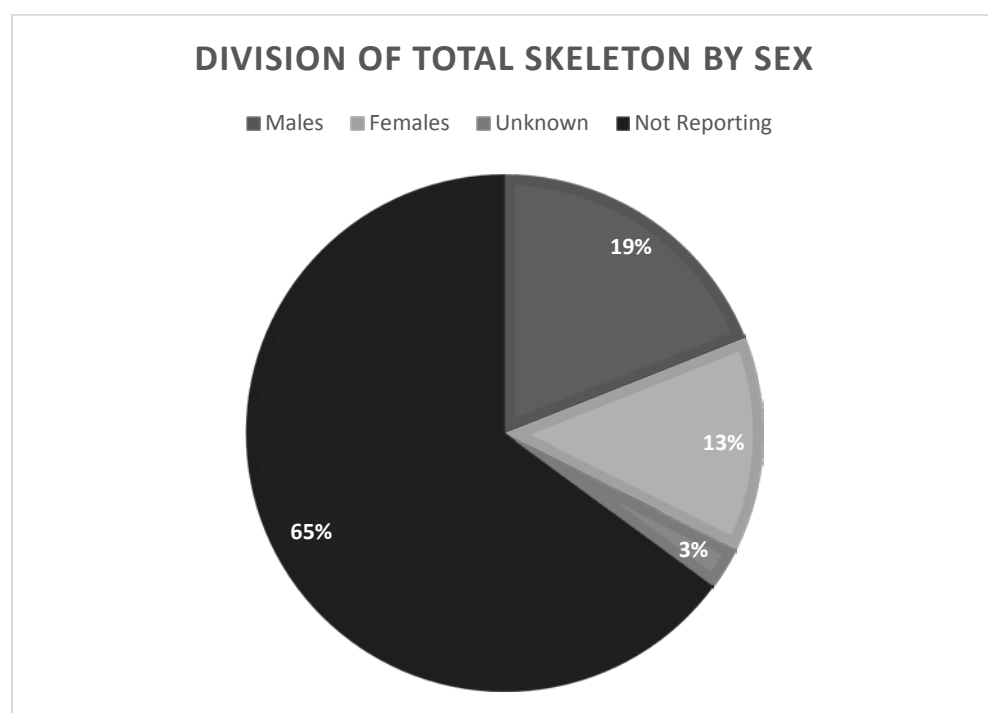
Figure 6.   **Number of males, females, unknown, and not reported (N = 1,645)**

<u>Age</u>

Age at death categories follow the organization used by Møller-Christensen

(1978). The age composition of the study sample were sorted into these eight categories:

0-6 years old, 7-13 years old, 14-19 years old, 20-29 years old, 30-39 years old, 40-49

years old, 50-59 years old, and 60+ years old. Some references did not report the exact

estimated age of death, using monikers such as *adult*, *young adult*, *elderly*, *adolescent*,

and *middle-aged*. In those cases, an age was estimated: *adult* (40 years old), *young adult*

(25 years old), *elderly* (65 years old), *adolescent* (14 years old), and *middle-aged* or

mature (50 years old). The age composition *with* (N = 611) and *without* (N = 428) the

estimated ages included are combined in Table 5.

The average ages of death of the total sample, male only, female only, and

unknown only were also calculated. In some instances, the average age of death fell

below the other estimates, so averages excluding 0-6 years and 7-14 years values were

also incorporated in Tables 4, calculating an average that did not account for instances of

child mortality.

Table 4. **Average ages of study sample – with estimation of terminology on the left and without estimation on the right. 'Adults' are assumed to be 40 years old, 'young adults' are 25 years old, 'middle-aged adults' and 'mature' are 50 years old, 'elderly' adults are 65 years old, and 'adolescents' are 14 years old. M stands for male, F stands for female, and U stands for unknown**

Average ages of all eight groups	With estimated-aged skeletons included	Without estimated-aged skeletons included
Total	29.91	30.76
M Only	34.02	34.27
F Only	38.03	38.4
U Only	27.33	22.9
Excluding individuals less than 14 years old		
Total	37.65	38.77
M Only	37.73	38.02
F Only	38.03	38.4
U Only)	41.12	39.15

Table 5. **Age composition within the study sample – includes the distribution with and without estimated ages, where 'adults' are assumed to be 40 years old, 'young adults' are 25 years old, 'middle-aged adults' and 'mature' are 50 years old, 'elderly' adults are 65 years old, and 'adolescents' are 14 years old**

	With estimated-aged skeletons included		Excluding estimated-aged skeletons	
Age category	Number of skeletons	Percent of total	Number of skeletons	Percent of total
0-6	4	0.65%	4	0.93%
7-13	21	3.44%	21	4.90%
14-19	51	8.35%	50	11.68%
20-29	35	5.73%	34	7.94%
30-39	137	22.42%	137	32.00%
40-49	187	30.60%	15	3.50%
50-59	156	25.53%	149	34.81%
60+	20	3.27%	18	4.20%
Total	611	100%	428	100%

Does Frequency of Leprosy Lesions Change through Time?

The frequency of leprosy lesions at each burial site (Table 6) was plotted by time (measured in years BP). Figure 7 includes all time periods in years BP (N = 95) whereas Figure 8 excludes Bronze Age (BA) lesions (N = 92). Figure 8 excluded BA skeletons because those values were outliers. In both figures, the best-fit line and the r^2 fit statistic are presented. Both figures show an upward trend in the frequency of leprosy lesions at each burial site through time. Figure 7, which includes all skeletal data, demonstrates that leprosy frequency is slowly increasing throughout the BA and IA, but drastically increases around 1000 BP. Figure 8, by excluding the BA skeletons, shows the upward trend clearly, with a large cluster of skeletons dating from 1000 BP to 500 BP.
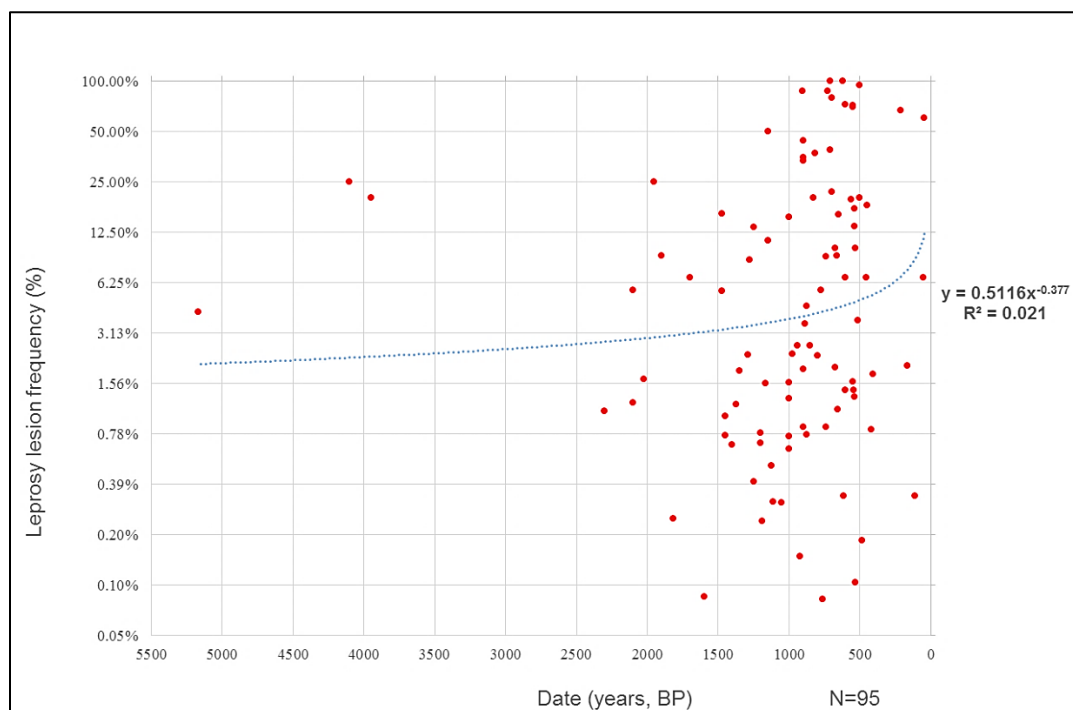
Figure 7. **Frequency of leprosy lesions at each burial site to time period in BP (N = 95). Includes Bronze Age skeletons. The x-axis is years BP in 500 year intervals and the y-axis is the frequency of leprosy at a site in intervals multiplied by two and includes the power function trend line**
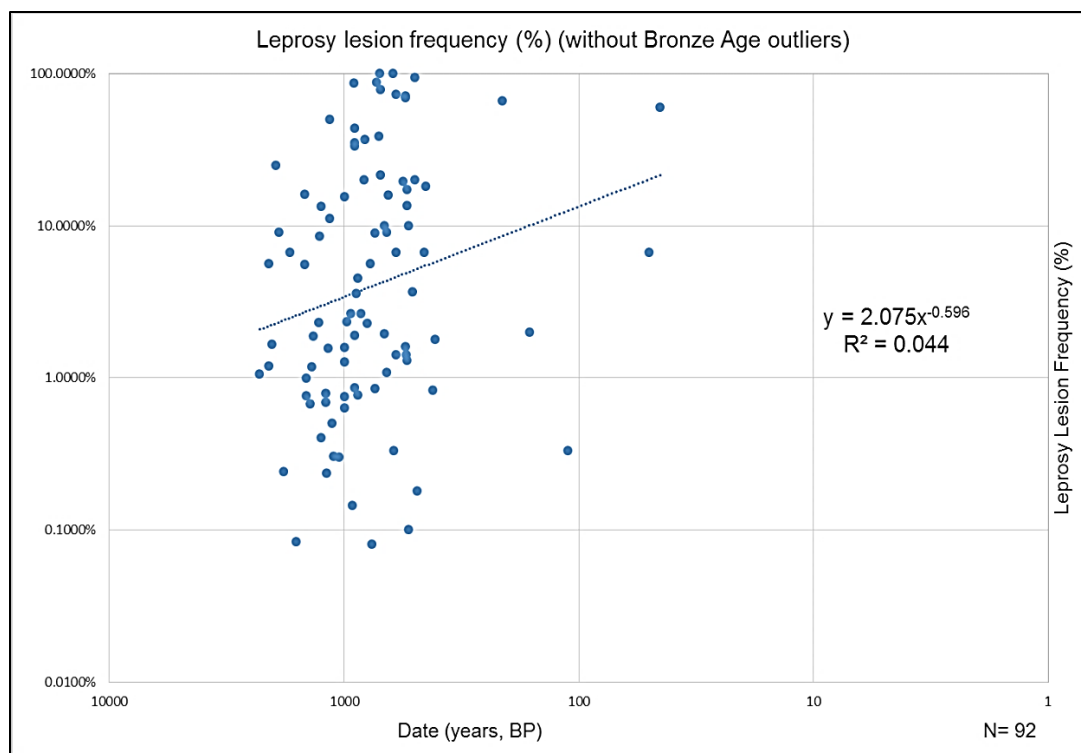
Figure 8. **Frequency of leprosy lesions at each burial site to time period in BP (N = 92). Does not include Bronze Age skeletons. Both axes are plotted as natural logarithms and includes the power function trend line**

Lesion Distribution

Lesions

Ninety-five out of 102 sites (93%) of the references that met the inclusion criteria of the survey reported leprosy lesion type. Osteological changes indicative of leprosy were recorded in seven locations on the skeleton (Table 2) (Boldsen, 2008; Møller-Christensen, 1952, 1978). Most references utilized the osteological method of reporting leprosy lesions developed by Møller-Christensen in 1978. Since not all the articles utilized a seven-step system, three monikers were used that broadly segregate the different types: *facies leprosa* (also known as skull-only), post-cranial-only, and both. Lesion count of each site based on these three types are recorded in Table 6.

Does Distribution of Lesions Change over Time?

To examine the relationship between the proportions of lesions across different time periods, a Fisher's exact test was conducted. A Fisher's exact test is a non-parametric version of the chi-square test and was conducted because the assumption of expected value greater than five was not met. The Fisher's exact test produced a p-value <0.001 indicating that there is a significant difference in leprosy distribution across time.

Table 6. **Lesion distribution total (N = 301), based on *facies leprosa*-only (or face-only), post-cranial only, or on both (*facies leprosa* and other). BA is Bronze Age, IA is Iron Age, MA is Middle Age, and EME is Early Modern Era**

Lesion-Type	BA	IA	MA	EME
Face-Only	0	34	45	1
Post-Cranial Only	0	4	56	1
Both	1	13	140	6

How does the Proportion of Lesion Type Change across Time Period?

Next, a Fisher's exact test was conducted to examine the relationship between the proportion of lesion types and time. There was a significant relationship between the number of lesions in each category across region and time, with a p-value<0.001 indicating a significant difference in these lesion distributions across time. Therefore, the distribution of lesions is changing over time from both types to *facies-leprosa* back again to both types.

Does Lesion Type Change through Time by Region?

Four contingency tables consisting of the number in each lesion type in each time period were made to conduct tests by geographical region: Northern Europe, Central and Western Europe, Mediterranean, and Asia (Tables 7A, 7B, 7C, and 7D). There were no

specific place of lesions indicated in any Oceania samples and the New World skeletons

were only found in the Early Modern Era (EME) so only four contingency tables were

made. Northern Europe had the largest amount of leprosy lesions (N = 203) in all, with

66.1% falling under MA Northern European skeletons with both lesion-types. There were

only 22 Central and Western European skeletons with lesions, 45% of whom dated to the

IA and only had *facies leprosa*. There were 59 Mediterranean skeletons with lesion-types,

primarily *facies leprosa* only in the IA and the MA. In Asia, 69% of the 13 total skeletons

with lesions were from the IA with *facies leprosa* and 2 EME Asian skeletons had both

lesion-type. Fisher's exact tests determined that, out of the four geographic areas tested,

only Asia was significant. See Chapter 5 for further discussion on the results from Tables

7A-D.

**Table 7A.   Contingency table of Chi-square test measuring lesion types –
Northern Europe**

Lesion-Type	IA	MA	EME
Face-Only	1	5	0
Post-Cranial Only	3	55	1
Both	3	134	1

Fisher's Exact Test: p-value = 0.1596

Table 7B.   Contingency table of Chi-square test measuring lesion types – Central and Western Europe

Lesion-Type	IA	MA
Face-Only	10	4
Post-Cranial Only	1	1
Both	5	1

Fisher's Exact Test: p-value = 0.7988

Table 7C.   Contingency table of Chi-square test measuring lesion types – Mediterranean

Lesion-Type	IA	MA
Face-Only	14	36
Both	4	5

Fisher's Exact Test: p-value= 0.434

Table 7D.   Contingency table of Chi-square test measuring lesion types – Asia

Lesion-Type	BA	IA	EME
Face-Only	0	9	0
Both	1	1	2

Fisher's Exact Test: p-value = 0.014

Tables 8 and 9 chart mean age at death by male, female, unknown and total across the four time periods. Table 8 provides calculated average age with estimated terminology of age included whereas Table 9 provides averages without the terminology included.

Figures 9 and 10 consist of the same information as Tables 8 and 9 but categorize average ages by geographical region as well. All 8 age categories are not represented in

some geographical regions and thus, have N/A next to it. Figure 9 includes results with

the estimated terminology of age and Figure 10 excludes those results.

Table 8. **Frequency distribution of median age at death for each time period in the combined sex sample – with estimated terminology (N = 611). Numbers in parenthesis represent the number of each calculated for each average**

Calculated Average Age at Death for Each Time Period: With Estimated Terminology:				
	Average Culmulated Age (and number of each)	Average Male Age (and number of each)	Average Female Age (and number of each)	Average Unknown Age (and number of each)
Bronze Age: pre-600 BCE	26.625 (4)	28.5 (2)	42.5 (1)	7 (1)
Iron Age: 500 BCE - 1049 CE	38.29 (67)	39.5 (30)	38.66 (18)	36.04 (19)
Middle Ages: 1050 CE - 1535 CE	37.25 (530)	40.75 (193)	33.87 (170)	36.47 (167)
Early Modern Era: 1536 CE - 1905 CE	36.44 (8)	35.8 (5)	22.5 (1)	45 (2)

Table 9. **Frequency distribution of median age at death for each time period in the combined sex sample – without estimated terminology (N = 424). Numbers in parenthesis represent the number of each calculated for each average**

Calculated Average Age at Death for Each Time Period: Without Estimated Terminology:				
	Average Culmulated Age	Average Male Age (and number of	Average Female Age (and number	Average Unknown Age (and number
Bronze Age: pre-600 BCE	26.625 (4)	28.5 (2)	42.5 (1)	7 (1)
Iron Age: 500 BCE - 1049 CE	35.9 (35)	37.07 (22)	38.03 (11)	2.43 (2)
Middle Ages: 1050 CE - 1535 CE	36.87 (378)	40.65 (185)	33.76 (167)	16.98 (26)
Early Modern Era: 1536 CE - 1905 CE	34.5 (7)	32.25 (4)	22.5 (1)	45 (2)

Two multi-way ANOVA's were conducted to see whether age is significant by

groups: sex (M, F, and U) and time period (BA, IA, MA, and EME). Levene's test was

used to test for homogeneity of variance. The Levene's test for Figure 9, which includes

data with estimated terminology, was significant (D.F. =11, F-value=5.37, p-

value=<0.001), suggesting the assumption of homogeneity of variance is not met. The

ANOVA in Figure 9 states that, with the estimated terminology included, sex by itself is

significant (p<0.001) but time period by itself as well as the combination of sex and time

period together are not significant (p=0.26; p=0.13).

Additionally, the Levene's test for Figure 10, which does not include data with

estimated terminology, is also significant (DF=11, F-value=1.85, p-value=<0.05). The

ANOVA in Figure 10 states that, without the estimated terminology included, sex by

itself is significant (p<0.001) but time period by itself is not significant (p=0.55).

However, sex and time period together are significant (p<0.01).

These results suggests that the sex (M, F, and U) of the leprous skeletons is a

significant factor to the age at death whether estimated terminology was used in the

ANOVA or not. Time period was a significant factor to the age at death only when

combined with sex and only when estimated terminology is not included (Figure 10).

Since the culminated average ages at death between the four time periods only varied

slightly, it is apparent that sex would need to be significant for the ANOVA's to be

significant.

```
> Anova(AnovaModel.1)
Anova Table (Type II tests)

Response: Age
                 Sum Sq  Df F value     Pr(>F)
Sex                4050   2 12.9173 3.219e-06 ***
Time.Period         636   3  1.3517    0.2567
Sex:Time.Period    1571   6  1.6705    0.1258
Residuals         93895 599
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure 9. **Multi-Way ANOVA of median age at death for each time period and geographical region in the combined sex sample – includes estimated terminology of age (N = 611)**

```
> Anova(AnovaModel.2)
Anova Table (Type II tests)

Response: Age
                 Sum Sq  Df F value    Pr(>F)
Sex                16657   2 53.4419 < 2.2e-16 ***
Time.Period          326   3  0.6964  0.554677
Sex:Time.Period     3001   6  3.2096  0.004332 **
Residuals          62338 400
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
```

Figure 10.   **Multi-Way ANOVA of median age at death for each time period and geographical region in the combined sex sample – does not include estimated terminology of age (N = 412)**

Does the Proportion of Leprosy Skeletons per Site Change?

Leprosariums likely affect the proportion of leprous individuals in the study.

Table 10 lists the 13 leprosariums used in this study and Table 11 lists the 4 leprosariums

that were not included in the data since they did not include the total number of skeletons.

While leprosariums are crucial in bioarchaeology, the overall representation of leprosy's

effect was skewed towards those sites with leprosariums. In particular, the data found at

three leprosariums in Denmark made up 69% of this data's total number of leprous

individuals. Figures 12 and 13 show two forest plots arranged chronologically by date

and time period, respectively, that excludes all leprosariums and samples less than 10

individuals (total) Leprosariums are further discussed in Chapter 5.

Table 10.   Leprosariums used in the study organized by date (N = 13)

References	Leprosarium	Year (Mid-point)
Mendum et al (2014); Magilton et al (2008)	St. Mary Magdalen, Winchester, UK	1043 CE
Wells (1967)	Castle Acre, Norfolk, UK	1225 CE
Blondiaux et al (2015)	Saint-Thomas d'Aizier, Haute-Normandy, France	1250 CE
Chundun et al (1995)	St. Giles, North Yorkshire, UK	1290 CE
Manchester et al (1986)	St. Mary and St. Thomas hospital, Ilford, Essex, UK	1300 CE
Farley et al (1989)	St. Margaret's Hospital, Buckinghamshire, UK	1350 CE
Primeau et al (2014)	Maribo, Lolland, Denmark	1350 CE
Lee et al (1989); Magilton et al (2008)	St James and St Mary Magdalene, Chichester, UK	1388 CE
Antunes-Ferreira et al (2013)	Beja, Portugal	1400 CE
Møller-Christensen (1978)	St. Jorgen Hospital, Næstved, Denmark	1400 CE
Boldsen (2001)	Kvarteret S:t Jörgen leprosy hospital, Malmö, Skåne, Sweden	1420 CE
Jensen et al (1983)	St. Jørgen, Odense, Denmark	1450 CE
Ferreira et al (2013)	Lagos, Algarve, Portugal	1500 CE

Table 11.   Leprosariums that were not used in the study organized by date (N = 4)

References	Leprosarium	Year (Mid-point)
Schultz et al (2002)	Lihou Island, Guernsey, UK	1250 CE
Bishop (1983)	St. Leonard's, Nottinghamshire, UK	1350 CE
Matos et al (2013)	St. Jørgen leprosarium cemetery, Odense, Denmark	1350 CE
Schmitz-Cliever (1972)	Aachen, Germany	1390 CE

Three forest plots (Figures 11, 12, and 13), which serves as a graphical representation of a meta-analysis, describe the meta-analysis of overall proportion from studies reporting a single proportion using the package 'metaprop.' The prevalence is measured based on the proportion of leprous skeletons at the site (N = 3,978). One forest plot (Figure 11) excludes any "Totals" under 10 so small sample sizes did not affect the data but includes data from leprosariums (listed in Table 10). The second forest plot (Figure 12) also excludes data taken from leprosariums, given that these may overestimate the prevalence of leprosy, in order to see how the proportions of leprosy skeletons changed through time.

The last forest plot (Figure 13) takes the data used in Figure 12 and organizes it by region instead of by date. Therefore, two forest plots are ordered chronologically by date whereas the last forest plot is organized chronologically by geographic region. This will demonstrate what factor influenced heterogeneity the most or if at all. Heterogeneity, which examines the amount of variation that exists between studies, was tested in order to determine the likelihood that the rates of leprosy prevalence were either changing over time or by geographic region. Greater levels of heterogeneity suggest that the samples are not consistent across time or place (Chen and Peace, 2013). If neither time period nor geographic region affect heterogeneity, then there is an unknown factor influencing the rate of leprosy.

The first forest plot had fixed and random effect proportions of 0.35 (I^2=98.6%; T^2=2.4; p<0.0001), indicating a significant difference in proportion across the 16 studies in the meta-proportion. The second and last forest plots have fixed effect and random effect proportions of 0.20 and 0.21 (I^2=94.4%; T^2=0.7043; p<0.0001), suggesting a

slighter smaller difference in heterogeneity between the 10 studies in this meta-proportion than the first plot. Therefore, running a meta-proportion that included leprosariums had more heterogeneity than a meta-proportion that was conducted without them, as expected. The heterogeneity tells us whether there are significant differences between those proportions.

The sites with the largest proportion of leprosy were found at leprosariums (Studies 3, 10, 12, and 16 in Figure 11). By removing those sites, the highest proportion is in St. Nicholai Kirche in Schleswig Germany at 44% versus the highest proportion of 95% at St. Jørgen, Denmark when leprosariums are included. Additionally, Figures 11 and 12 do not show a clear trend of proportion in those sites dating to the Iron Ages versus the medieval aged sites, suggesting that proportion is independent of time period.

Study	Events	Total		Proportion	95%-CI	W(fixed)	W(random)
1	17	110		0.15	[0.09; 0.24]	2.9%	6.2%
2	28	181		0.15	[0.11; 0.22]	4.8%	6.3%
3	33	38		0.87	[0.72; 0.96]	0.9%	5.9%
4	15	34		0.44	[0.27; 0.62]	1.7%	6.1%
5	38	108		0.35	[0.26; 0.45]	5.0%	6.3%
6	27	756		0.04	[0.02; 0.05]	5.3%	6.3%
7	44	120		0.37	[0.28; 0.46]	5.7%	6.3%
8	22	57		0.39	[0.26; 0.52]	2.8%	6.2%
9	135	622		0.22	[0.19; 0.25]	21.5%	6.4%
10	34	43		0.79	[0.64; 0.90]	1.5%	6.1%
11	75	384		0.20	[0.16; 0.24]	12.3%	6.4%
12	329	472		0.70	[0.65; 0.74]	20.3%	6.4%
13	20	200		0.10	[0.06; 0.15]	3.7%	6.3%
14	11	66		0.17	[0.09; 0.28]	1.9%	6.1%
15	20	152		0.13	[0.08; 0.20]	3.5%	6.3%
16	603	635		0.95	[0.93; 0.97]	6.2%	6.3%
Fixed effect model		3978		0.35	[0.33; 0.37]	100%	--
Random effects model				0.35	[0.20; 0.53]	--	100%

Heterogeneity: I-squared=98.6%, tau-squared=2.4, p<0.0001

0.2 0.4 0.6 0.8

Figure 11. **Forest plot of a meta-analysis of single proportions. Excludes Events under 10 but includes leprosariums. Organized chronologically by date where Study 1 occurred furthest back in time and Study 16 most recently. Studies: 1 (478 CE; Lauchheim, Germany), 2 (950 CE; St. John, Norfolk), 3 (1043 CE; St. Mary Magdalen, Winchester), 4 (1050 CE; St. Nicolai Kirche, Schleswig, Germany), 5 (1050 CE; St. Clemens Kirche, Schleswig, Germany), Study 6 (1065 CE; Lund,**

Sweden), Study 7 (1133 CE; Rathaus Markt, Schleswig, Germany), 8 (1239 CE; Dominikaner Kloster, Schleswig, Germany), 9 (1250 CE; Tirup, Denmark), 10 (1250 CE; Saint-Thomas d'Aizier, France), 11 (1388 CE; St. James and St. Mary Magdalene, Chichester), 12 (1400 CE; St. Jorgen, Denmark), 13 (1420 CE; Malmö, Denmark), 14 (1410 CE; St. Knud, Odense, Denmark), 15 (1410 CE; St. Albani, Odense, Denmark), 16 (1450 CE; St. Jørgen, Denmark)
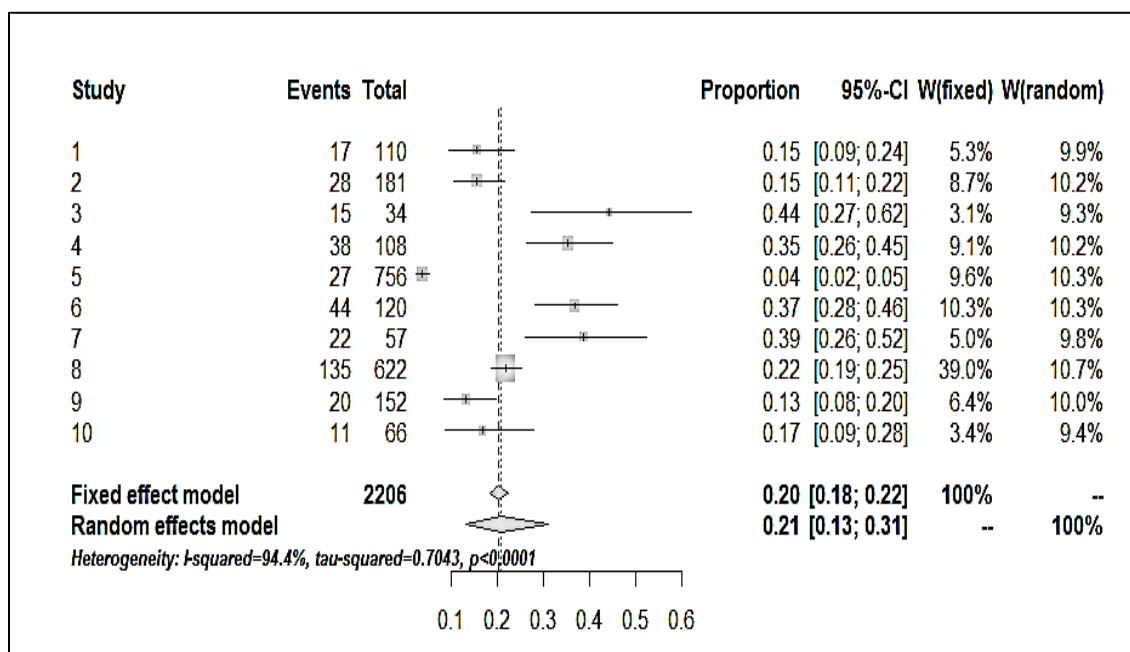
Figure 12. Forest plot of a meta-analysis of single proportions. Excludes Events under 10 and leprosariums. Organized chronologically by date where Study 1 occurred furthest back in time and Study 10 most recently. Studies: 1 (478 CE; Lauchheim, Germany), 2 (950 CE; St. John, Norfolk), 3 (1050 CE; St. Nicolai Kirche, Schleswig, Germany), 4 (1050 CE; St. Clemens Kirche, Schleswig, Germany), 5 (1065 CE; Lund, Sweden), 6 (1133 CE; Rathaus Markt, Schleswig, Germany), 7 (1239 CE; Dominikaner Kloster, Schleswig, Germany), 8 (1250 CE; Tirup, Denmark), 9 (1410 CE; St. Knud, Odense, Denmark), 10 (1410 CE; St. Friars, Odense, Denmark)
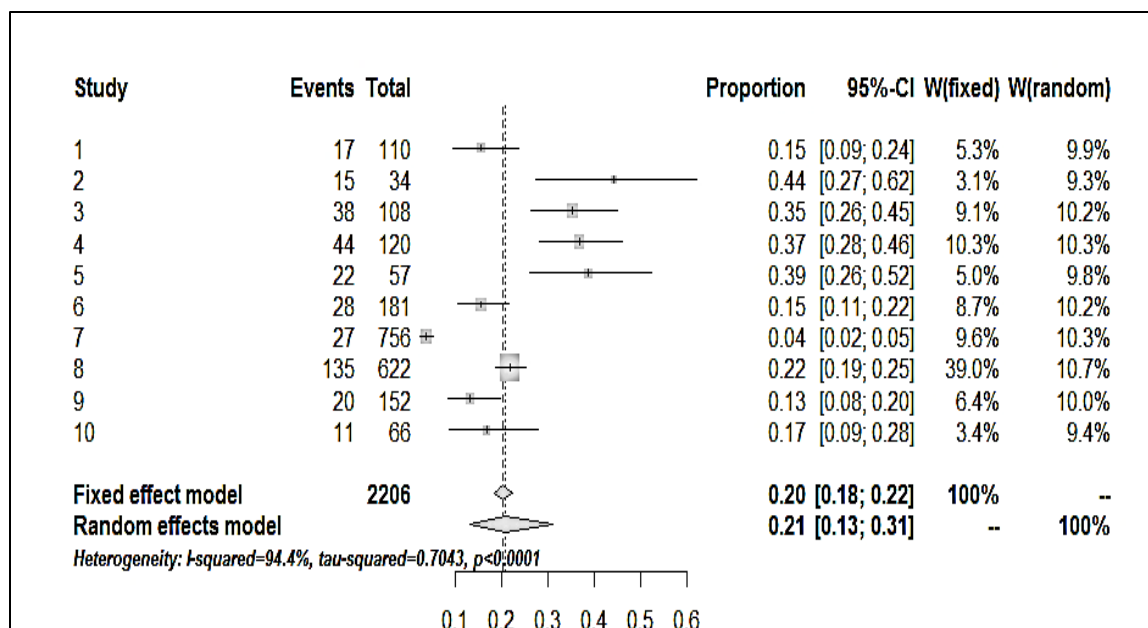
Figure 13. Forest plot of a meta-analysis of single proportions organized temporally by region. Excludes Events under 10 and leprosariums. Organized by geographic region where Studies 1 through 5 represent Central and Western Europe and Studies 6 through 10 represent Northern Europe. Studies: 1 (478 CE; Lauchheim, Germany), 2 (1050 CE; St. Nicolai Kirche, Schleswig, Germany), 3 (1050 CE; St. Clemens Kirche, Schleswig, Germany), 4 (1133 CE; Rathaus Markt, Schleswig, Germany), 5 (1239 CE; Dominikaner Kloster, Schleswig, Germany), 6 (950 CE; St. John, Norfolk), 7 (1065 CE; Lund, Sweden), 8 (1250 CE; Tirup, Denmark), 9 (1410 CE; St. Knud, Odense, Denmark), 10 (1410 CE; St. Friars, Odense, Denmark)

CHAPTER FIVE: DISCUSSION

Does Bone Lesion Type Vary by Time Period?

The frequency and distribution of bone lesions was found to vary depending on the geographical region and time period. All regions except for the New World, saw a rise in bone lesions after the Bronze Age but significantly decreasing after the Middle Ages (Tables 7A-D). This finding suggests that leprosy's large prevalence in most medieval, non-New World countries correlates with the poor health and high frequency of disease before the Early Modern Era. The New World only had bone lesions found post-1536 CE, which corresponds to other research made by comparative genomic studies that leprosy entered the Western hemisphere after the medieval period. The only significant result came from Asia, proposing that Asian bone lesions proportions varied by time period from both to *facies-leprosa* to both. No significant differences were found between the proportions of bone lesions across time for the other three geographical regions.

Additionally, the values of the chi-square test measuring lesion distribution suggests that there are significant differences in proportion of lesion types by time periods (BA, IA, MA, and EME) and geographic regions (NE, CWE, M, A, NW, and O). Skeletons from Northern Europe in the medieval ages are more likely to display both lesion types than *facies-leprosa* or post-crania only. Skeletons from Central and Western Europe in the Iron Age has a greater proportion of *facies-leprosa*. Skeletons from medieval Mediterranean countries have a greater proportion of *facies leprosa*, and Iron Age Asia has a greater proportion of *facies leprosa* (Tables 7A-D). This suggests that

different parts of the world suffered from either tuberculoid or lepromatous leprosy, which affects different parts of the body. Additionally, some results are biased towards one type since there were skeletons that were missing parts of their body, either due to poor preservation or to burial preference (i.e., ossuary jars in the Czech Republic).

<center>**How Does the Rate of Leprosy Change over Time?**</center>

Two of the forest plots (Figure 11 and 12) were organized by time to see if there was a trend of proportions through time while one (Figure 13) was organized chronologically by region. The studies with the highest proportions of leprosy came from were from leprosariums (Figure 11), such as the St. Mary Magdalen leprosarium in Winchester, UK and the Saint-Thomas d'Aizier in France. When the leprosariums were removed from the data and put in new forest plots, the sites with the highest proportions were all from Schleswig, Germany.

Organizing by region did not change the proportion values in the forest plot, predictably, but displayed the pattern the proportions made by region instead of time period. Notably, Figure 12, which is organized by date, shows a larger frequency of sites from the 11th and 12th centuries to any other time period. Even without leprosarium data included, this suggests that leprosy was prevalent in the early to middle medieval ages. Geographically, Figure 13 has a large proportion of non-leprosarium sites from Schleswig, Germany and Tirup, Denmark (Studies 2, 3, 4, 5, 8; Figure 13) (Boldsen et al., 2013; Boldsen, 2005b). Denmark has always been well-represented in leprosy during the medieval period, but this finding from Germany is unique. Possibly, Schleswig, Germany did not act as a leprosarium but as a town for leprosy sufferers and non-leprosy

sufferers alike could live together and be buried together. More data on this topic is required, however.

As for the rest of the data, the forest plots show that Denmark had large cases (10+) of leprosy throughout the 13th and 14th centuries whereas other countries that were represented early on in the forest plot with large leprosy cases – UK, Germany, and Sweden – had decreased in frequency. Based on the chronological and temporal distribution of these sites with 10+ leprosy cases (excluding leprosariums), leprosy was prevalent throughout Europe but did not impact Denmark until the 13th century, after it had decreased everywhere else.

Demographics

Leprosy more commonly occurs in males, who are more susceptible to the disease, than females in most regions of the world, although leprosy can affect all age groups (Walker, 2009:364). The data set confirms this, as 312 male skeletons had leprosy whereas only 221 females had it. Individuals under 18 years old and over 60 years old were poorly represented in the sample, likely because it takes years to develop bone lesions but most will not survive over the age 60 (Lynnerup and Boldsen, 2012). Although all age groups were represented, this infectious disease is not spread equally among the age groups. Based on the information from Table 8, or with the estimated terminology, the average cumulated ages ranged from 26.6 years to 38.3 years whereas the average cumulated ranged from 26.6 years to 36.9 years without estimated terminology factored in (Table 9). Subsequently, providing an estimate of age for those reported as *adult, middle-aged*, *young adult*, *adolescent*, and *elderly* did not change the numbers drastically. Tables 8 and 9 also show that males lived longer in the medieval era

than any other time period (40.75 years or 40.65 years) whereas females lived their longest in the Bronze Age (42.5 years) although this might be due to the small sample from the BA. While this demographic information is significant and suggests variation in health and sex-roles through time, the values are not significantly different from one another so a conclusion about age at death and sex can be made.

When the estimated terminology is included, 40-49 year old adults comprise the largest portion of the eight age groups (N = 187). This is likely because 173 of those numbers were "adults" of unknown age, subsequently estimated to be 40 years old. The appellative "adults" is a common term to call an older skeleton when age is generally unknown but the range could be anywhere between 20 to 60 years. With an estimation of 40 years for these 173 "adults," the distribution is predictably skewed towards a large number of 40 year olds in the sample. Most likely, based on historical information of the time period, the average age at death for those suffering from leprosy would have ranged anywhere from 30 to 39 years old (Blondiaux et al., 2015; Boldsen, 2005; Weiss and Møller-Christensen, 1971), a result that is confirmed by the paleopathological skeletons used in this study (see Table 5, which includes and excludes data where age was estimated by this project's author).

Health

Out of all the 1,645 leprosy cases used in this study, 0.24% were from the BA, 9.4% were from the IA, 89.9% were from the MA, and 0.55% were from the EME. There was an decrease in prevalence rates from BA (7.02% of cases from that time period) to IA (1.95% of cases from that time period) then a drastic increase in the MA (14.2% of cases from that time period) then a drop in cases in the EME (2.1% of cases from that

time period). Roberts (2002a) attributes MA's large increase in leprosy cases to denser living conditions and decreased sanitation, stimulating the rate of transmission.

There is a steep decline in prevalence rates once the medieval period came to an end in the 16th century likely due to the aftermath of the Black Death and increased competition with TB. Skeletal evidence of chronic infectious disease, according to Larsen (2009), "are primarily associated with agricultural-based populations living in close, densely crowded communities" (2009:7). It is assumed that, due to a rise in population, skeletons dating to the Iron Age, Middle Age, and Early Modern Era were from densely populated, agricultural communities. Agriculture was a relatively new phenomenon to the Bronze Age skeletons so it is possible that small number of skeletons in the dataset (N = 4) is related to agriculture's recent introduction. An agriculture-based diet is less healthy and more labor intensive than a hunter-gatherer diet. It also creates densely-populated areas, promoting the spread of disease.

A trend observed in the data was that females died at a younger age than males in all time periods except the Bronze Age (Tables 8 and 9). This finding is significant because assessing age at death and sex portrays the health conditions and trends of the population in a given time and place. In contrast to the pattern seen today where females live longer than males, a significant proportion of women in the Iron Ages and medieval ages died in association with childbirth. Life expectancy varied by location, but the trend remained the same. In the mid-late medieval UK, for example, the average life expectancy at birth for an aristocratic male was around 35 years whereas a female at birth was expected to live to age 30 (Lancaster, 1990:8). Surprisingly, the average ages for leprous individuals of both sexes in the data fall within 30 to 40 years, matching

estimates of the life expectancy at birth for the time period. This could be because leprosy, while a disfiguring disease, does not cause death unless it co-infects the individual with other diseases. In this dataset, the average age at death is higher than life expectancy at birth in the mid-late medieval UK because not many infants/children are dying with leprosy, whereas there were likely higher rates of infant/child mortality in the general population. Those children that did die from leprosy would skew that data towards a lower average age of death, a trend that is observed for the "unknown" individuals in Table 4. Assessing the average age of death is affected by the "Osteological Paradox," since many children do not have time to develop telling bone lesions before they die.

In reality, these estimates of life expectancy are at birth but once a person survives the first few years of life, life expectancy goes up by many years. A 21-year old individual's life expectancy in 13th century UK is 64 years. Therefore, it is also reasonable to conclude that the individuals in the dataset did not outlive non-infected individuals who, if they lived past the first few years of life, could expect to live well into their 50s and 60s. The leprosy sufferers usually died at an average age of 35 to 40 years of age.

However, life expectancy for the general population and those suffering from leprosy dropped drastically in the 1300-1400s, reflecting the high mortality rates caused by the Black Plague (see Chapter 1). A 21-year old aristocratic male in the UK was only expected to survive an additional 25 years in the 14th to 15th centuries (Lancaster, 1990). Therefore, the average age of death of a non-leprous individual and a leprous individual during the 1300-1400s were almost the same.

Leprosariums

Since successful medical treatment for leprosy did not exist until recently, past efforts focused on segregating and caring for those individuals afflicted with the disease. Leprosariums became common during the medieval era, often existing outside the city limits (Covey, 2001:320). Historical reports relaying accurate numbers of leprosariums at a given time vary drastically. Roffey (2012) reports "over 300 documented leper hospitals in the medieval period" (2012:203). Meanwhile, Matthew of Paris, a medieval-era Benedictine monk, roughly estimated there to be more than 19,000 "lazar houses" in Europe in the eleventh century (Simpson, 1872:3).

Estimates for the leprosarium count also differ depending on the country. Covey (2001) reports that by the mid-12th century CE, France had around 2,000 leprosariums, although there are none from that time period used in the dataset for this thesis, while England and Scotland had about 220 leprosariums (2001:317). Denmark had 31 leprosariums between 1250 CE to 1550 CE (Bennike et al., 2005). In Portugal, there were around 70 small leprosariums during the medieval period (Antunes-Ferreira et al., 2013:149; Carvalho, 1932). Likely, Covey states, there was a misuse of the word "leprosarium" for hospitals that treated people with leprosy occasionally, exclusively, sometimes, or never at all (2001:317; Roffey, 2010:217; Rogers et al., 1946).

Due to this misrepresentation of terminology, opinions vary in the literature on the prevalence of leprosy in medieval Europe. For the most part, authorities of the period agree that leprosy was a familiar disease during the 11th to 15th centuries among Europeans, as the disease is consistently reported and referred to in medieval-aged texts. It is intriguing to see the contrast between the reported number of leprosy hospitals and

the cases seen in the bioarchaeological record. This could indicate that leprosy was over-reported in the historical literature, possibly confusing the disease for another pathogen.

It is interesting, although not surprising given the historical literature, that every leprosarium, save one, whether its data was used in the study or not, dates to the medieval era (1050 CE – 1536 CE). The only exception is St. Mary Magdalen in Winchester, UK, although at 1043 CE only makes this site seven years away from the MA cut-off. While the bioarchaeological record may not show it, Antunes-Ferreira et al. (2013) states that leprosy hospitals were around in Europe as far back as 5th century CE (149).

These results also show leprosariums in the paleopathological literature were *only* in Europe, primarily in the UK and Denmark. This is unsurprising as the only non-European paleopathological skeletal sites from the medieval period used in this study were in Polis Chrysochous, Cyprus, Dakhleh Oasis, Egypt, and western Micronesia for a combined total of 11 non-European medieval-aged individuals (Baker et al., 2014; Molto, 2002; Trembly, 1995). Out of a total 1,108 burials from these three sites, these 11 leprous individuals indicate a rate of leprosy in non-European MA to a paltry 0.992% according to this paleopathological data. In this regard, these results support studies suggesting *Mycobacterium leprae* and leprosariums primarily raged through Europe during the medieval era although this conclusion could be biased based on where bioarchaeological research occurs (Donoghue et al., 2005, 2015; Matheson et al., 2009; Robbins et al., 2009).

Transmission and aDNA

Comparative genomic studies have mapped genetic variability between populations through mapping SNP-types and variable number tandem repeat, or "VNTR"

types. "SNP" or single nucleotide polymorphisms, each represent a difference in a single nucleotide, and have been consistently proposed as participants in susceptibility towards diseases such as leprosy (Alvarado-Arnez et al., 2015:1; Economou et al., 2013; Donoghue et al., 2005; Monot et al., 2005). Monot et al. (2005) discovered four different SNP-types (1, 2, 3, and 4) and in 2009, divided these four types into sixteen SNP-subtypes.

The four main strains, or types, of *Mycobacterium leprae* are divided geographically. Monot et al. (2005) created a map (Figure 2 from Monot et al. 2005; Figure 14) showing the dissemination of the strains and their geographical pathways. According to their research, strain 1 occurs in East Africa, Asia, and the Pacific; strain 2 in New Caledonia, Nepal/north India, Ethiopia, and Malawi; strain 3 in North Africa, Europe, and the Americas; and strain 4 in West Africa, Brazil, and the Caribbean islands (from Monot et al. Table 3, 2005:1041).

Economou et al. (2013) found evidence of SNP-subtype 2G, a type that is found mainly in Asia/North Africa, in medieval Swedish remains (465). This finding is unique and remains one of the few tested samples from Europe that does not belong to SNP-type 3, providing genetic evidence that a transmission of a particular type of the pathogen from Asia to Scandinavia had occurred during the medieval ages. Mendum et al. (2014) found evidence for SNP-type 2 strains in two skeletons from the medieval leprosarium of St Mary Magdalen near Winchester, England (2014). Monot et al. (2005) and Taylor and Donoghue (2011) have found evidence that SNP-type 3, a predominantly European and North American type, was present in some parts of Asia/Middle East in the Iron Age and medieval era. A 1st- 4th century CE adult skeleton from Uzbekistan was of subtype 3L

and four young adults from 4th century CE Dakhleh Oasis in Egypt had genotype 3. A large study by Donoghue et al. (2015), mostly on Hungarian samples, found SNP-subtypes 3M and 3K, which was also found in a Turkish sample (253). Based on their results, the authors concluded that Avar (or Caucasus) migration from Central Asia into Byzantium and Central Europe exposed the disease to local populations.

The exact route of transmission remains unclear, but there are two possible schemes for the spread of leprosy based on SNP types. The first, which Cole and Singh (2012) deem more probable, is that *M. leprae* evolved in East Africa and spread to Central Asia (SNP-type 2 preceding SNP-type 1, which migrated eastward, and SNP-types 3 and 4 subsequently follow). The other scheme argues that *M. leprae* evolved in Central Asia and spread to East Africa following human migrations (SNP-type 1 preceding SNP-type 2 and SNP-types 3 and 4 subsequently follow). The earliest accepted evidence (excluding the Bronze Age Scottish and Hungarian samples) of leprosy was found in a north Indian individual in 2009 and makes a strong argument for scheme two (Robbins et al., 2009). Thus, this study deems the second scheme the most likely scenario.

Genotypes 1 and 4 remain mostly unique to their geographic regions – type 1 in Asia, the Pacific region, and East Africa and type 4 in West Africa and the Caribbean region, and South America (Monot et al., 2005; Cole and Singh, 2012). SNP-type 1 originated in Asia, spread into East Africa, and then spread into the Pacific region through possible contact with, or immigration from, China or Japan (Trembly, 1995).

SNP-type 4 was brought over into the Caribbean and South America through the 18th century CE West African slave trade by infected European or North African

colonialists, explorers, traders, or West African slaves (Monot et al., 2005:1042). Much

like how SNP-type 3 arrived in North America, infected Europeans with type-4 leprosy

likely brought over the disease into the Caribbean and South America through early

exploration, migration, and the slave trade.
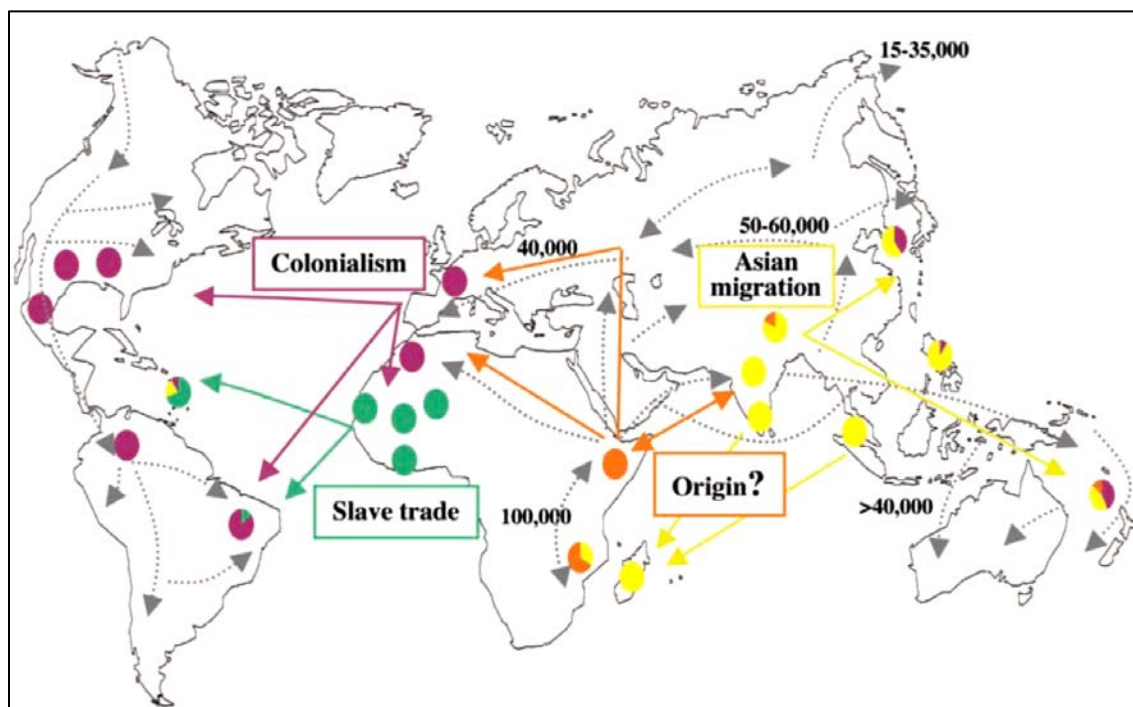
Figure 14.   Dissemination of leprosy in the world [from Monot et al. (2005)]. The colored circles indicate the country of origin sampled and their division into the four SNP types. SNP-type 1 is yellow, SNP-type 2 is orange, SNP-type 3 is purple, and SNP-type 4 is green. The colored arrows represent migrations (Monot et al., 2005:1042)

Limitations in a Meta-Analysis

Relying on data of human skeletons from bioarchaeological reports means relying

on the authors' quality of excavation and interpretation of skeletal pathologies.

Additional limiting factors include burial preservation and excavation and post-

excavation treatment which makes the quality of the data highly variable (see Chapter 2;

Roberts et al., 2003:13). Additionally, all articles that were not in English (the author's

native language), Spanish or Hebrew, were translated through an online website. This could have resulted in possible translation issues or incorrect information.

An apparent issue this project deals with is that several geographic areas and time periods have small samples sizes, or sometimes, none at all. One of the most obvious limitations in this study is its reliance on secondary sources. A possible bias lies in sample studies themselves as they are based on published studies available through the internet, the Boise State University library or its inter-library loan, or received from the authors themselves

There is a known bias since 44 sites from 29 different references did not include total number of individuals excavated and were subsequently thrown out since the frequency of lesions (or percent of skeletons with leprosy) could not be calculated. In these excluded sites, 5 were from Sweden, 3 from Denmark, 25 from UK, 1 from Egypt, 2 from Germany, 1 from Indonesia, 3 from Hungary, 2 from Israel, 1 from Poland, and 1 from Ukraine. This data was entered into an excel sheet similarly to the data that was used in this study (supplementary text Appendix C).

Bioarchaeological literature on leprosariums lead to a densely populated skeletal samples of people with leprosy in certain geographical areas, which may skew the results as skeletal samples without any leprosy lesions were not included. This suggests that the rate of leprosy may be lower than was calculated in this meta-analysis (given that skeletal samples with 0% leprosy prevalence were not included). Thus, the results of this meta-analysis are supported by the author with the full understanding that its reliability depends on the validity of the studies (Walker et al., 2008:438).

Biocultural Applications

This thesis' conclusions are strained by the biocultural considerations discussed in Chapter 2. The problem of accurate estimation of leprosy's impact continues to be an ongoing challenge for bioarchaeology and paleopathology. While this meta-analysis was successful in portraying leprosy's frequency and lesion distribution in past populations based on the available paleopathological literature, the Osteological Paradox, political instability, and socioeconomic issues creates misrepresentation in accurate bioarchaeological assessments. Some countries are over-represented and others are grossly under-represented. It should also be remembered that, due to leprosy's long incubation period which affects when bone changes develop, skeletons of children and those with a low resistant form of the disease are unlikely to show leprous lesions. The many intrinsic and extrinsic factors that affect whether or not someone shows signs of the infectious disease further complicates the picture. Clearly, it is unlikely that the frequency of leprosy was truly 8.76% of the total population. The skeletal material examined here only represents the individuals reported in the paleopathological literature and any assumptions on the demographic profile of the leprous individuals will be flawed. The data presented here tells us something about the impact of leprosy throughout time and space but the data is biased due to a number of different factors (Roberts, 2002b:216). More work is needed in order to obtain the real frequency of leprosy. Future careful excavation, recording, and analysis in additional geographic areas are needed to further interpretations on the impact and frequency of leprosy.

Conclusion and Further Directions

Review

Out of 18,787 total skeletal samples used in this data, the percentage of individuals that showed osteological signs of leprosy expressed in relation to total number of individuals was 8.756% (1,645 leprous skeletons). It is unlikely that leprosy was this prevalent in communities at any time, however. Leprosy was at its peak in Northern Europe in the high medieval period (1200-1400 CE), slowly declining in the mid-13th century CE, and then dropping off dramatically by the end of the period (Covey, 2001:320). This peak is correlated to the influx of leprosariums in that geographical region, especially in the UK and Denmark. Leprosy did not truly take effect in Europe until the late Iron Age, existing mostly in Asia and the Mediterranean until the sixth century.

Further Directions

The future of leprosy research is constantly marred by technological and methodological limitations. To keep up with curing leprosy today, research into leprosy's impact in the past will need to continue, especially in non-European and post-medieval populations. Additionally, continued methodological developments in lesion identification and prevalence is critical. As new paleopathological research continues to be published on leprosy, future meta-analyses will need to integrate this information with the new developing technique of aDNA analyses.

Although there is no vaccine available for the prevention of leprosy, there are numerous prevention programs ran by the World Health Organization, the Centers for Disease Control and Prevention, the National Institute of Allergy and Infectious Diseases,

the United Nations Children's Emergency Fund, LEPRA, the International Federation of

Anti-Leprosy Associations, and the Movement of Reintegration of Persons Afflicted by

Hansen's disease. Ever since the World Health Organization provided MDT for free

worldwide in 1995, leprosy rates keep decreasing every year (World Health

Organization, 2016). However, leprosy is still a problem in dozens of countries with India

accounting for over 60% of the total cases (as of 2012; WER 2012 Index). Despite these

setbacks and continued prevalence of the disease, substantial progress has been made by

providing free treatment to millions of affected individuals and in overcoming social

stigma and exclusion. Hopefully, this progress will be further advanced through

continued ongoing research into the basic understanding of the disease, the history and

cause of its transmission, and improved treatments and vaccines. If it does, leprosy will

one day no longer be one of the leading causes of physical disability and social stigma in

the world as it was in the past (Bennet et al., 2008).

REFERENCES

Alvarado-Arnez LE, Amaral EP, Sales-Marques C, Durães SMB, Sarno EN, Pacheco AG, Lana FCF, Moraes MO. 2015. Association of IL10 polymorphisms and leprosy: A meta-analysis. PLoS ONE 10:1-13.

Anderson S. 1998. Leprosy in a medieval churchyard in Norwich. In: Anderson S, editor. Current and recent research in osteoarchaeology. Proceedings of the 3rd meeting of the Osteoarchaeology research group. Oxford: Oxbow Books. p 31-37.

Antunes-Ferreira N, Matos VMJ, Santos AL. 2013. Leprosy in individuals unearthed near the Ermida de Santo Andre and leprosarium of Beja, Portugal. Anthropol Sci 121:149-159.

Arcini C. 1999. Health and disease in early Lund - osteopathologic studies of 3305 individuals buried in the first cemetery area of Lund 990-1536. Archaeologica Lundensia VIII. Lund: Department of Community Health Sciences.

Aufderheide AC, Rodríguez-Martín C. 1998. The Cambridge encyclopedia to human paleopathology. Cambridge: Cambridge University Press.

Baker B, Bolhofner KL. 2014. Biological and social implications of a medieval burial from Cyprus for understanding leprosy in the past. Int J Paleopathol 4:17-24.

Barber L, Sibun L. 1998. The medieval hospital of St Nicholas, Lewes, East Sussex: excavations 1994. Sussex archaeological collections ADS 148:1-42.

Bax L, Yu L-M, Ikeda N, Moons KGM. 2007. A systematic comparison of software dedicated to meta-analysis of casual studies. BMC Med Res Methodol 7:40.

Belcastro MG, Mariotti V, Facchini F, Dutour O. 2005. Leprosy in a skeleton from the 7th century necropolis of Vicenne-Campochiaro (Molise, Italy). Int J Osteoarchaeol 15:431-448.

Bennett BH, Parker DL, Robson M. 2008. Leprosy: steps along the journey of eradication. Pub Health Rep 123:198-205.

Bennike P, Lewis ME, Schutkowski H, Valentin F. 2005. Comparison of child morbidity in two contrasting medieval cemeteries from Denmark. Am J Phys Anthropol 128:734-746.

Blau S, Yagodin V. 2005. Osteoarchaeological evidence for leprosy from western Central Asia. Am J Phys Anthropol 126:150-158.

Blondiaux J, Naji S, Bocquet-Appel J-P, Colard T, de Broucker A, de Seréville-Niel C. 2015. The Leprosarium of Saint Thomas d'Aizier, the cementochronological proof of the medieval decline of Hansen disease in Europe? Int J Paleopathol. In press.

Blondiaux J, Durr J, Khouchaf L, Eisenberg LE. 2002. Microscopic study and X-ray analysis of two 5th century cases of leprosy: palaeoepidemiological inferences. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. BAR International series 1054. Oxford: Archaeopress. p 105-110.

Bloomfield M. 2004. Hymns of the Atharva Veda. Whitefish, MT: Kessinger Publishing.

Boekhout TA. 2009. The puzzle of syphilis: a literature review on putting the pieces together. [thesis].

Boeckl CM. 2011. Images of leprosy: disease, religion, and politics in European art. Kirksville, MO: Truman State University Press.

Boldsen JL, Rasmussen KL, Riis T, Dittmar M, Weise S. 2013. Schleswig: medieval leprosy on the boundary between Germany and Denmark. Anthropol Anz 70:273-287.

Boldsen JL. 2009. Leprosy in medieval Denmark - osteological and epidemiological analyses. Anthropol Anz 67:407-425.

Boldsen JL. 2008. Leprosy in the early medieval Lauchheim community. Am J Phys Anthropol 135:301-310.

Boldsen JL, Mollerup L. 2006. Outside St. Jørgen: leprosy in the medieval Danish city of Odense. Am J Phys Anthropol 130:344-351.

Boldsen JL, Freund UH. 2006. Osteological leprosy - epidemiology and diagnosis. Scan J Foren Sci 12:54-59.

Boldsen JL. 2005a. Testing conditional independence in diagnostic palaeoepidemiology. Am J Phys Anthropol 128:586-592.

Boldsen JL. 2005b. Leprosy and mortality in the medieval Danish village of Tirup. Am J Phys Anthropol 126:159-168.

Boldsen JL. 2001. An epidemiological approach to the paleopathological diagnosis of leprosy. Am J Phys Anthropol 115:380-387.

Boulter S. 1992. Death and disease in medieval Grantham. Unpublished Undergraduate Dissertation, University of Sheffield.

Brander T, Lynnerup N. 2002. A possible leprosy hospital in Stubbekøbing, Denmark. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. BAR International series 1054. Oxford: Archaeopress. p 145-148.

Bratschi MW, Steinmann P, Wickenden A, Gillis TP. 2015. Current knowledge on *Mycobacterium leprae* transmission: a systematic literature review. Lepr Rev 86:142-155.

Brothwell DR. 1958. Evidence of leprosy in British archaeological material. Med Hist 2:287-291.

Carvalho AS. 1932. História da lepra em Portugal. Oficinas Gráficas da Sociedade de Papelaria, Porto.

Chen D-G, Peace KE. 2013. Applied meta-analysis with R. Boca Raton: CRC Press.

Chundun Z, Roberts CA. 1995. Human skeletal remains, In: Cardwell P, editor. Excavation of the hospital of St Giles by Brompton Bridge, North Yorkshire. Archaeol J 152:214-220.

Cole ST, Singh P. 2012. History and phylogeography of leprosy. In: Nunzi E, Massone C, editors. Leprosy: a practical guide. London: Springer.

Covey HC. 2001. People with leprosy (Hansen's disease) during the Middle Ages. Soc Sci J 38:315-321.

Csóri ZS, Donoghue HD, Marcsik A. 2009. Leprosy in the 10th-13th century AD in Eastern Hungary. Ann Roum Anthropol 46:3-11.

Daniel TM. 2006. The history of tuberculosis. Resp Med 100:1862-1870.

Deeks JJ, Altman DG, Bradburn MJ. 2001. Statistical methods for examining heterogeneity and combining results from several studies in meta-analysis. In: Egger M, Smith GD, Altman DG, editors. Systematic reviews in health care: Meta-analysis in context, 2nd Edition. London: BMJ.

Dewey M. 2015. CRAN task view: meta-analysis. CRAN R-Project. CRAN. <https://cran.r-project.org/web/views/MetaAnalysis.html>.

Dharmendra R. 1947. Leprosy in ancient Indian medicine. Int J Lepr 15:424–430.

Donoghue HD, Taylor GM, Marcsik A, Molnár E, Pálfi G, Pap I, Teschler-Nicola M, Pinhasi R, Erdal YS, Veleminsky P, Likovsky J, Belcastro MG, Mariotti V, Riga A, Rubini M, Zaio P, Besra GS, Lee OY-C, Wu HHT, Minnikin DE, Bull ID, O'Grady J, Spigelman M. 2015. A migration-driven model for the historical spread of leprosy in medieval Eastern and Central Europe. Infect Genet Evol 31:250-256.

Donoghue HD, Marcsik A, Matheson C, Vernon K, Nuorala E, Molto JE, Greenblatt CL, Spigelman M. 2005. Co-infection of *Mycobacterium tuberculosis* and *Mycobacterium leprae* in human archaeological samples: a possible explanation for the historical decline of leprosy. Proc Biol Sci 272:389-394.

Duhig C. 1998. The human skeletal material In: The Anglo-Saxon cemetery at Edix Hill (Barrington A), Cambridgeshire. Council for British Archaeology Research Report.

Dzierzykray-Rogalski T. 1980. Paleopathology of the Ptolemaic inhabitants of Dakhleh Oasis (Egypt). J Hum Evol 9:71-74.

Farley M, Manchester K. 1989. The cemetery of the leper hospital of St Margaret, High Wycombe, Buckinghamshire. Med Arch 33:82-89.

Ferreira MT, Neves MJ, Wasterlain SN. 2013. Lagos leprosarium (Portugal): evidences of disease. J Archaeol Sci 40:2298-2307.

Field A. 2013. Discovering statistics using IBM SPSS statistics. London: Sage Publications. p 1-952.

Field A. 2012. Discovering statistics using R. 12th ed. London: Sage Publications. p 1-957.

Fornaciari G, Mallegni F, de Leo P. 1999. The leprosy of Henry VII: Incarceration or isolation? Lancet 353:758.

Gamble JA. 2014. A bioarchaeological approach to stress and health in medieval Denmark: dental enamel defects and adult health in two medieval Danish populations. [dissertation].

Gausterer C, Stein C, Teschler-Nicola M. 2015. First genetic evidence of leprosy in early medieval Austria. Wien Med Wochenschr 165:126-132.

Gilmore JK. 2008. Leprosy at the Lazaretto on St Eustatius, Netherlands Antilles. Int J Osteoarchaeol 18:72-84.

Gladykowska-Rzeczycka JJ. 1976. A case of leprosy from a medieval burial ground. Folia Morphol Warsz 35:253–264.

Glass GV. 1976. Primary, secondary, and meta-analysis of research. Educ Res 5:3-8.

Granoff P. 1998. Cures and karma: healing and being healed in Jain religious literature. In: Baumgarten AI, Assmann J, Stroumsa G, editors. Self, soul, and body in religious experience. Leiden, Netherlands: Koninklijke Brill.

Grmek MD. 1991. Diseases in the ancient Greek world. Baltimore: John Hopkins University Press.

Han XY, Seo Y-H, Sizer KC, Schoberle Y, May GS, Spencer JS, Li W, Nair RG. 2008.
A new *Mycobacterium* species causing diffuse lepromatous leprosy. Am J Clin
Path 130:856-864.

Holloway KL, Henneberg RJ, de Barros Lopes M, Henneberg M. 2011. Evolution of
human tuberculosis: a systematic review and meta-analysis of paleopathological
evidence. HOMO J Comp Hum Biol 62:402-458.

Holst M. 2012. Osteological analysis. Dixon Lane and George Street York. York
Osteoarchaeol Rep No 1612.

Hulse EV. 1972. Leprosy and ancient Egypt. Lancet 300:1024-1025.

Jensen KR, Tkocz I. 1983. Skeletmaterialet fra udgravningen af St. Jørgensgården i
Odense. Dansk Med Historisk Arbog 1983.

Johnson BT, Eagly AH. 2014. Meta-analysis of social-personality psychological
research. In: Reis HT, Judd CM, editors. Handbook of research methods in social
and personality psychology (2nd Ed.). Cambridge: Cambridge University Press. p
675-707.

Judd M, Roberts CA. 1998. Fracture patterns at the medieval leper hospital in Chichester.
Am J Phys Anthropol 105:43-55.

Khudaverdyan A. 2010. Pattern of disease in 2nd-1st millennium BC necropolis from
Lchashen, Armenia. Anthropologie 158:239-254.

Kjellström A. 2012. Possible cases of leprosy and tuberculosis in medieval Sigtuna,
Sweden. Int J Osteoarchaeol 22:261-283.

Köhler K, Marcsik A, Donoghue H, Márk L, Hajdu T. 2009. Előzetes eredmények az
Abony 36. lelőhely késő rézkori áldozati gödreiből feltárt embertani leletek
vizsgálata alapján.

Kovalchik S. 2013. Tutorial on meta-analysis in R. R useR! Conference 2013.

Kozak AD, Schultz M. 2006. Prokaza v drevnerusskom Kieve po dannym paleopatologii.
Vestnik Antropologii 14:34–40.

Lancaster HO. 1990. Expectations of life: a study in the demography, statistics, and history of world mortality. New York: Springer-Verlag. p 1-611.

Larsen CS. 2009. Emergence and evolution of agriculture: the impact on human health and lifestyle. In: Pond WG, Nichols BL, Brown DL, editors. Adequate food for all: culture, science and technology of food in the 21st century. Boca Raton, FL: CRC Press Taylor & Francis Group.

Lechat MF. 2002. The palaeoepidemiology of leprosy: an overview. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. BAR International series 1054. Oxford: Archaeopress. p 157-162.

Lee F, Magilton J. 1989. The cemetery of the hospital of St. James and St. Mary Magdalene, Chichester - A case study. World Archaeol 21:273-282.

Lietman T, Porco T, Blower S. 1997. Leprosy and tuberculosis: the epidemiological consequences of cross- immunity. Am J Publ Health 87:1923-1927.

Likovský J, Urbanová M, Hájek M, Cerny V, Cech P. 2006. Two cases of leprosy from Žatec (Bohemia), dated to the turn of the 12th century and confirmed by DNA analysis for *Mycobacterium leprae*. J Archaeol Sci 33:1276-1283.

Linderholm A, Kjellström A. 2011. Stable isotope analysis of a medieval skeletal sample indicative of systemic disease from Sigtuna, Sweden. J Archaeol Sci 38:925-933.

Lockwood DJ. 2002. Leprosy elimination – a virtual phenomenon or a reality? BMJ 324:1516-1518.

Lunt DA. 2013. The first evidence for leprosy in early mediaeval Scotland: two individuals from cemeteries in St. Andrews, Fife, Scotland, with evidence for normal burial treatment. Int J Osteoarchaeol 23:310-318.

Lynnerup N, Boldsen J. 2012. Leprosy (Hansen's disease). In: Grauer A, editor. A companion to paleopathology. Oxford: Wiley-Blackwell. p 458-471.

Magilton J, Lee F, Boylston A. 2008. 'Lepers outside the gate'. Excavations at the cemetery of the hospital of St James and St Mary Magdalene, Chichester, 1986-87

and 1993: Council for British archaeology research report 158 and Chichester excavations Volume 10, York.

Manchester K, Roberts CA. 1986. Palaeopathological evidence of leprosy and tuberculosis in Britain. Unpublished SERC Report (Grant 337.367), University of Bradford. Unpublished.

Marcsik A, Molnár, Osz B. 2007. Specifikus fertőző megbetegedések csontelváltozásai történeti népesség körében. JETE Press.

Mariotti V, Dutour O, Belcastro MG, Facchini F, Brasili P. 2005. Probable early presence of leprosy in Europe in a Celtic skeleton of the 4th-3rd century BC (Casalecchio di Reno, Bologna, Italy). Int J Osteoarchaeol 15:311-325.

Marks RB. 2015. The origins of the modern world: A global and environmental narrative from the fifteenth to the twenty-first century. 3rd edition, Lanham: Rowman & Littlefield.

Matheson CD, Vernon KK, Lahti A, Fratpietro R, Spigelman M, Gibson S, Greenblatt CL, Donoghue HD. 2009. Molecular exploration of the first-century Tomb of the Shroud in Akeldama, Jerusalem. PLoS ONE 4:e8319.

Mays S. 1991. The medieval burials from the Blackfriars Friary, School Street, Ipswich, Suffolk (Excavated 1983-1985). Ancient Monuments Laboratory Report 16/91. English Heritage: Portsmouth.

Mays S. 1989. The Anglo-Saxon human bone from School Street, Ipswich, Suffolk. Ancient Monuments Laboratory Report 115/89, English Heritage. Unpublished.

Mendum TA, Schuenemann VJ, Roffey S, Taylor GM, Wu H, Singh P, Tucker K, Hinds J, Cole ST, Kierzek AM, Nieselt K, Krause J, Stewart GR. 2014. *Mycobacterium leprae* genomes from a British medieval leprosy hospital towards understanding an ancient epidemic. BMC Genomics 15:270.

Mészáros P, Paluch T, Sóskuti K, Sz Wilhelm G. 2006 Felgyő, Kettőshalmi-dűlő. In: Régészeti Kutatások Magyarországon, 2005- Archaeological investigations in Hungary, 2005, Budapest, 199-200.

Meyer C, Jung C, Kohl T, Poenicke A, Poppe A, Alt KW. 2002. Syphilis 2001: a palaeopathological reappraisal. HOMO J Comp Hum Biol 53:39-58.

Miller TS, Nesbitt JW. 2014. Walking corpses: leprosy in Byzantium and the medieval west. Ithaca: Cornell University Press.

Møller-Christensen V. 1978. Leprosy changes of the skull. Odense: Odense University Press.

Møller-Christensen V. 1967. Evidence of leprosy in earlier peoples. In: Brothwell DR, Sandison AT, editors. Diseases in antiquity. Springfield, IL: Charles Thomas. p 295– 306.

Møller-Christensen, V. 1965. New knowledge of leprosy through paleopathology. Int J Lepr Other Mycobact Dis 33:603-610.

Møller-Christensen V, Faber B. 1952. Leprous changes in a material of medieval skeletons from the St. Georges Court, Næstved. Acta Radiol [Old Series] 37:308– 317.

Molnár E, Donoghue HD, Lee OY-C, Wu HHT, Besra GS, Minnikin DE, Bull ID, Llewellyn G, Williams CM, Spekker O, Pálfi G. 2015. Morphological and biomolecular evidence for tuberculosis in 8th century AD skeletons from Belmegyer-Csomoki Domb, Hungary. Tuberculosis 95:S35-S41.

Molnár E, Marscik A. 2002. Paleopathological evaluation of Hungarian skeletal remains from the 7th-9th centuries AD. Antropol Portuguesa 19:85-99.

Molto JE. 2002. Leprosy in Roman period skeletons from Kellis 2, Dakhleh, Egypt. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. BAR International series 1054. Oxford: Archaeopress. p 179-192.

Monot M, Honoré N, Garnier T, Zidane N, Sheradi S, Paniz-Mondolfi A, Matsuoka M, Taylor GM, Donoghue HD, Bouwman A, Mays S, Watson C, Lockwood D, Khamispour A, Dowlati Y, Jianping S, Rea TH, Vera-Cabrera L, Stefani MM, Banu S, Macdonald M, Sapkota BR, Spencer JS, Thomas J, Harshman K, Singh P, Busso P, Gattiker A, Rougemont J, Brennan PJ, Cole ST. 2009. Comparative

genomic and phylogeographic analysis of *Mycobacterium leprae*. Nat Gen 41:1282-1289.

Monot M, Honoré N, Garnier T, Araoz R, Coppée J-Y, Lacroix C, Sow S, Spencer JS, Truman RW, Williams DL, Gelber R, Virmond M, Flageul B, Cho S-N, Ji B, Paniz-Mondolfi A, Convit J, Young S, Fine PE, Rasolofo V, Brennan PJ, Cole ST. 2005. On the origin of leprosy. Science 308:1040-1042.

Montiel R, García C, Cañadas MP, Isidro A, Guijo JM, Malgosa A. 2003. DNA sequences of *Mycobacterium leprae* recovered from ancient bones. FEMS Microbiol Lett 226:413-414.

Murphy E, Manchester K. 2002. Evidence for leprosy in medieval Ireland. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. BAR International series 1054. Oxford: Archaeopress. p 193-199.

Neil B. 2003. 2003 Anglo-Georgian Nokalakevi expedition: Osteological assessment for trench A and B. p 1-21.

Nerlich AG, Zink AR. 2008. Past *leprae*. In: Raoult D, Drancourt M, editors. Paleomicrobiology: past human infections.

Nuorala E, Donoghue HD, Spigelman M, Götherström A, Hårding B, Grundberg L, Alexandersen V, Leden I, Lidén K. 2004. Diet and disease in Björned, a Viking-early medieval site in northern Sweden. Theses and Papers in Scientific Archaeology. Stockholm: Archaeological Research Laboratory.

Pálfi G, Molnár E. 2009. The paleopathology of specific infectious diseases from Southeastern Hungary: A brief overview. Acta Biol Szeged 53:111-116.

Pálfi G, Zink A, Haas CJ, Marcsik A, Dutour O, Nerlich AG. 2002. Historical and palaeopathological evidence of leprosy in Hungary. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. BAR International series 1054. Oxford: Archaeopress. p 205-212.

Pálfi G. 1997. Maladies dans l'antiquité et au Moyen-Âge. Paléopathologie comparée des anciens Gallo-Romains et Hongrois. Bulletins et Mémoires de la Société d'Anthropologie de Paris. Nouvelle série 9:1–206.

Pálfi G. 1991. The first osteoarchaeological evidence of leprosy in Hungary. Int J Osteoarchaeol 1:99-192.

Pardillo FEF, Fajardo TT, Abalos RM, Scollard D, Gelber RH. 2007. Methods for the classification of leprosy for treatment purposes. Clin Infect Dis 44:1096-1099.

Pearson K. 1904. Mathematical contributions to the theory of evolution. Philosophical transactions of the royal society of London. Series A, containing papers of a mathematical or physical character 195:1-47,405.

Pearson K. 1900. On the criterion that a given system of deviations from the probable in the case of a correlated system of variables is such that it can be reasonably supposed to have arisen from random sampling. Philosophical Magazine Series 50:157-175.

Polet C. 2011. Health and diet of ancient Easter Islanders: Contribution of paleopathology, dental microwear, and stable isotopes. Royal Belgian Institute of Natural Sciences. p 1-19.

Porter D. 1999. Health, civilization, and the state: a history of public health from ancient to modern times. London and New York: Routledge.

Powell F. 1996. The human remains. In: Raunds Furnells. The Anglo-Saxon church and churchyard. English Heritage Archaeological Report.

Primeau C, Linnerup N. 2014. Non-bony lesions and functional losses in leprosy [abstract]. Am J Phys Anthropol Suppl. p 16.

Rasmussen KL, Boldsen JL, Kristensen HK, Skytte L, Hansen KL, Mølholm L, Grootes PM, Nadeau M-J, Eriksen KMF. 2008. Mercury levels in Danish Medieval human bones. J Archaeol Sci 35:2295-2306.

Reader R. 1974. New evidence for the antiquity of leprosy in early Britain. J Archaeol Sci 1:205-207.

Robbins G, Tripthy VM, Misra VN, Mohanty RK, Shinde VS. 2009. Ancient skeletal evidence for leprosy in India (2000 B.C.). PLoS ONE 4:e5669.

Roberts CA. 2011. Chapter 9: The bioarchaeology of leprosy and tuberculosis. In: Agarwal SC, Glencross BA, editors. Social bioarchaeology. Oxford: Wiley-Blackwell. p 252-282.

Roberts CA, Cox M. 2007. The impact of economic intensification and social complexity on human health in Britain from 4000 BC (Neolithic) and the introduction of farming to the mid-19th century AD and industrialization (post-Medieval period). In: Cohen MN, Crane-Kramer GMM, editors. Ancient health: skeletal indicators of agricultural and economic intensification. Gainesville: University Press of Florida. p. 149-63.

Roberts CA, Cox M. 2003. Health and disease in Britain. From prehistory to the present day. Gloucester: Sutton.

Roberts CA, Lewis ME, Manchester K. 2002. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. BAR International series 1054. Oxford: Archaeopress.

Roberts CA. 2002a. Palaeopathology and archaeology: the current state of play. In: The archaeology of medicine. BAR International series 1046. Oxford: Archaeopress. p 1-20.

Roberts CA. 2002b. The antiquity of leprosy in Britain: the skeletal evidence. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. BAR International series 1054. Oxford: Archaeopress. p 213-222.

Roberts CA, Manchester K. 1995. The archaeology of disease. Ithaca, NY: Cornell University Press.

Roberts J. 2007. Human remains from the cists. In: Dunwell A, editors. Cist burials and an Iron Age settlement at Dryburn Bridge, Innerwick, East Lothian. Scottish Archaeological Internet Report 24:18-25.

Roffey S. 2012. Medieval leper hospitals in England: An archaeological perspective. Mediev Archaeol 56:203-233.

Rothstein HR, Hopewell S. 2009. Chapter 6: Grey literature. In: Cooper H, Hedges LV, Valentine JC, editors. The handbook of research synthesis and meta-analysis. New York: Russell Sage Foundation. p 103-128.

Rubini M, Zaio P, Roberts CA. 2014. Tuberculosis and leprosy in Italy-new skeletal evidence. HOMO J Comp Hum Biol 65:13-32.

Rubini M, Dell'Anno V, Giuliani R, Favia P, Zaio P. 2012. The first probable case of leprosy in Southeast Italy (13th-14th centuries AD, Montecorvino, Puglia). J Anthropol. p 1-7.

Rubini M, Erdal YS, Spigelman M, Zaio P, Donoghue HD. 2012. Paleopatholoical and molecular study on two cases of ancient childhood leprosy from the Roman and Byzantine empires. Int J Osteoarchaeol 24:570-582.

Rubini M, Zaio P. 2009. Lepromatous leprosy in an early mediaeval cemetery in central Italy (Morrione, Campochiaro, Molise, 6th-8th century AD). J Archaeol Sci 36:2771-2779.

Schmitz-Cliever E. 1972. Das mittelalterliche leprosarium Mela- tan bei Aachen. Clio Medica 7:13–34.

Schuenemann VJ, Singh P, Mendum TA, Krause-Kyora B, Jäger G, Bos KI, Herbig A, Economou C, Benjak A, Busso P, Nebel A, Boldsen JL, Kjellström A, Wu H, Stewart GR, Taylor GM, Bauer P, Lee OY-C, Wu HHT, Minnikin DE, Bersa GS, Tucker K, Roffey S, Sow SO, Cole ST, Nieselt K, Krause J. 2013. Genome-wide comparison of medieval and modern *Mycobacterium leprae*. Science 341:179-184.

Setia MS, Steinmaus C, Ho CS, Rutherford GW. 2006. The role of BCG in prevention of leprosy: a meta-analysis. Lancet Infect Dis 6:162-170.

Setzer TJ. 2014. Malaria detection in the field of paleopathology: A meta-analysis of the state of the art. Acta Trop 140:97-104.

Simpson SJY. 1872. On leprosy and leper hospitals in Scotland and England. In: Stuart J, editor. Archaeological Essays 2:1-184.

Smith SE. 2010. Human and mycobacterial coevolution: The role of genetic recombination in reconstructing the evolutionary history of these important human pathogens. [dissertation].

Smith-Guzmán NE. 2015. Cribra orbitalia in the ancient Nile Valley and its connection to malaria. Int J Paleopathol 10:1-12.

Stone AC, Wilbur AK, Buikstra JE, Roberts CA. 2009. Tuberculosis and leprosy in perspective. Yearb Phys Anthropol 52:66-94.

Stones JA, editor. 1989. Three Scottish carmelite friaries: excavations at Aberdeen, Linlithgow and Perth 1980-1986. Society of Antiquaries of Scotland.

Strouhal E, Ladislava H, Likovsky J, Vargova L, Danes J. 2002. Traces of leprosy from the Czech Kingdom. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. BAR International series 1054. Oxford: Archaeopress. p 223-232.

Suzuki K, Saso S, Hoshino K, Sakurai J, Tanigawa K, Luo Y, Ishido Y, Mori S, Hirata K, Ishii N. 2014. Paleopathological evidence and detection of *Mycobacterium leprae* DNA from archaeological skeletal remains of Nabe-kaburi (head-covered with iron pots) burials in Japan. PLoS ONE 9:1-9.

Suzuki K, Takigawa W, Tanigawa K, Nakamura K, Ishido Y, Kawashima A, Wu H, Akama T, Sue M, Yoshihara A, Mori S, Ishii N. 2010. Detection of *Mycobacterium leprae* DNA from archaeological remains in Japan using whole genome amplification and polymerase chain reaction. PLoS ONE 5:1-8.

Szilvássy J. 1980 Die Skelette aus dem awarischen Gräberfeld von Zwölfaxing in Niederösterreich. Anthropologische Forschungen 3, Wein, Austria.

Tayles N, Buckley HR. 2004. Leprosy and tuberculosis in Iron Age Southeast Asia? Am J Phys Anthropol 125:239-256.

Taylor GM, Donoghue HD. 2011. Multiple loci variable Number tandem repeat (VNTR) analysis (MLVA) of *Mycobacterium leprae* isolates amplified from European archaeological human remains with Lepromatous leprosy. Microbes Infect 13:923-929.

Taylor GM, Watson CL, Bouwman AS, Lockwood DNJ, Mays SA. 2006. Variable nucleotide tandem repeat (VNTR) typing of two palaeopathological cases of lepromatous leprosy from mediaeval England. J Archaeol Sci 33:1569-1579.

Trembly DL. 1995. On the antiquity of leprosy in Western Micronesia. Int J Osteoarchaeol 7:621-624.

Truman R. 2005. Leprosy in wild armadillos. Lepr Rev 76:198-208.

Vuorinen HS. 2002. History of leprosy in Finland. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. Oxford: Archaeo Press. p 239–246.

Walker D. 2009. The treatment of leprosy in 19th century London: a case study from St Marylebone cemetery. Int J Osteoarchaeol 19:364-374.

Walker E, Hernandez AV, Kattan MW. 2008. Meta-analysis: Its strengths and limitations. Cleve Clin J Med 75:431-439.

Watson CL, Lockwood DNJ. 2009. Single nucleotide polymorphism analysis of European archaeological *M. leprae* DNA. PLoS ONE 4:e7547.

Weiss D, Møller-Christensen V. 1971. Leprosy, echinococcosis and amulets: a study of a medieval Danish inhumation. Med Hist 15:260-267.

Wells C. 1967. A leper cemetery at South Acre, Norfolk. Mediev Archaeol 11:242-248.

Wiggins R, Boylston A, Roberts CA. 1993. Report on human skeletal remains from Blackfriars, Gloucester (19/91). Unpublished.

Wood JW, Milner GR, Harpending HC, Weis KM. 1992. The osteological paradox. Curr Anthropol 33:343-370.

World Health Organization (WHO). 2016. Leprosy elimination: WHO multidrug therapy (MDT). Geneva: The World Health Organization. <http://www.who.int/lep/mdt/en/>.

World Health Organization in the Western Pacific Region (WPRO). 2016. Eliminating leprosy in the Western Pacific. WHO Western Pacific regional office. <http://www.wpro.who.int/leprosy/elimination/en/>.

World Health Organization (WHO). 2012. Global leprosy situation. Weekly epidemiological record (WER) 87:317-328.

Yammine K. 2014. The prevalence of os acromiale: A systematic review and meta-analysis. Clin Anat 27:610-621.

Zhang Z. 1994. The skeletal evidence of human leprosy and syphilis in ancient China. Acta Anthropol Sin 13:294–299.

Zias J. 2002. New evidence for the history of leprosy in the Ancient Near East: an overview. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological and clinical approaches. BAR International series 1054. Oxford: Archaeopress. p 259-268.

Zodpey SP. 2007. Protective effect of bacillus Calmette Guerin (BCG) vaccine in the prevention of leprosy: A meta-analysis. Indian J Dermatol Venereol Leprol 73:86-93.

Zweifel L, Böni T, Rühli FJ. 2009. Evidence-based palaeopathology: Meta-analysis of PubMed-listed scientific studies of ancient Egyptian mummies. HOMO J Comp Hum Biol 60:405-427.

APPENDIX A

References Included in Data

Article	Year of Publication	Journal	Location	Year(s) of Excavation	Estimated Date of Remains	Midpoint Date of Remains/Date for Analysis	Number of Cases with Leprosy	Total Number of Burials	% of Skeletons with leprosy	Sex(# of each)	Age of Skeleton(s)	Location of Lesions	Skeletal Pathology Pattern	Notes
Antunes-Ferreira N, Matos VMJ, Santos AL. 2013. Leprosy in individuals unearthed near the Ermida de Santo Andre and leprosarium of Beja, Portugal. Anthropol Sci 121:149-159.	2013	Anthropol Sci	From survey number 6 cemetery near	2003	14th c. - 16th c. CE	1400 CE	5: 4 possible; 1 probable.	7 excavated in survey number 6 and observed (10	71.43% 1 M probable; 1 M and 3 M? possible.	Probable: adult M; Possible: 15-20 yo M?, 20-25 yo M,	Table 1	N/A	**Leprosarium:** skeletal remains from cemetery in the
Baker B, Bolhofner KL. 2014. Biological and social implications of a medieval burial from Cyprus for understanding leprosy in the past. Int J Paleopathol 4:17-24.	2014	Int J Paleopathol	Polis Chrysochous, Cyprus	Burial 11 in 2000	Lusignan period (1191-1489 CE)	1336 CE		1 300+	0.33% 1 F	20-34 yo F	N/A	Rhinomaxillary resorption; loss of maxillary incisors;	First archaeological evidence of leprosy in Cyprus; Baker
Møller-Christensen V. 1978. Leprosy changes of the skull. Odense: Odense University Press.	1978	Odense University Press	St. Jorgen Hospital, Næstved, South Zealand,	1948-1968	1250-1550 CE	1400 CE		329 472 analyzed (650 total excavated.)	69.70% 160 M; 151 F; 18 children aged 14 yo and under.	[See Table 5b for breakdown by leprosy lesions in	Observations on: face, hands, feet, tibia, fibia.	Table 5a. and 5b outline % with facies leprosa,	**Leprosarium:** Overlaps with multiple different
Jensen KR, Tkocz I. 1983. Skeletmaterialet fra udgravningen af St. Jørgensgården i Odense. Dansk Med Historisk Arbog 1983.	1983	Dansk Med Historisk Arbog 1983	St. Jørgen, Odense, Funen, Denmark	1979-1981	mid-13th c. - mid-17th c. CE	1450 CE	603 (estimated.)	635 estimated (1507 total excavated.)	95% N/A	N/A	N/A	Rhinomaxillary changes (facies leprosa, termed by	**Leprosarium:** ["Has yielded data on 635 individuals aged 15
Boldsen JL. 2001. An epidemiological approach to the paleopathological diagnosis of leprosy. Am J Phys Anthropol 115:380-387.	2001	Am J Phys Anthropol	Kvarteret S:t Jörgen, Malmö, Skåne, Denmark	1990-1991	1320-1520 CE	1420 CE	20 (estimated.)	200 analyzed (1600 total excavated.)	10.00% N/A	N/A	N/A	N/A	**Leprosarium:** From Boldsen 2001 - "a total of 200 [out of
Blau S, Yagodin V. 2005. Osteoarchaeological evidence for leprosy from western Central Asia. Am J Phys Anthropol 126:150-158.	2005	Am J Phys Anthropol	Devkesken 6, Ustyurt Plateau, Uzbekistan	1972,1975,1980,1 984, and 1985	1st c. - 4th c. CE	250 CE	1 (Devkesken 6, Kurgan 5b.)	15 (just in Devkesken 6 burial mound.)	6.67% 1 F	Middle-aged yo F	N/A	Rhinomaxillary changes: resorption of the	First skeletal evidence of leprosy from Central Asia (at Pg 243-248.
Wells C. 1967. A leper cemetery at South Acre, Norfolk. Mediev Archaeol 11:242-248.	1967	Mediev Archaeol	Castle Acre, South Acre, Norfolk, UK		1967	1100-1350 CE	1225 CE	7 (3 definite, 4 possible.)	8	87.50% 1 M; 6 F	26-45 yo M; 3 16-25 yo F; 2 26-45 yo F; adult F.	N/A	**"Leper cemetery":** Damaged by mechanical
Gausterer C, Stein C, Teschler-Nicola M. 2015. First genetic evidence of leprosy in early medieval Austria. Wien Med Wochenschr 165:126-132.	2015	Wien Med Wochenschr	Pottenbrunn, Austria	1965-1974	first half of the 9th c. CE	825 CE	1	199	0.50% 1 F	25 yo F	N/A	Terminal phalangeal absorption.	This is the first genetic evidence of an Austrian leprosy
Mariotti V, Dutour O, Belcastro MG, Facchini F, Brasili P. 2005. Probable early presence of leprosy in Europe in a Celtic skeleton of the 4th-3rd century BC (Casalecchio di Reno, Bologna, Italy). Int J	2005	Int J Osteoarchaeol	Casalecchio di Reno, Bologna, Italy	1991-1992	4th c. - 3rd c. BCE	350 BCE	1	94	1.06% 1 M	30-40 yo M	N/A	Rhinomaxillary syndrome and changes in tarsal	According to Mariotti et al, "t.74 could be the oldest skeleton
Likovský J, Urbanová M, Hájek M, Cerny V, Cech P. 2006. Two cases of leprosy from Žatec (Bohemia), dated to the turn of the 12th century and confirmed by DNA analysis of *Mycobacterium leprae* . J	2006	J Archaeol Sci	Chelčického nám chuch cemetery, Žatec in North-	1997-1998	second half of 11th c. CE	1075 CE	2	258	0.78% 1 M?; 1 F?	14-18 yo M?; adult F?	N/A	AO 9731-rhinomaxillary syndrome.	This discovery of the two leprous individuals is the first
Csóri ZS, Donoghue HD, Marcsik A. 2009. Leprosy in the 10th-13th century AD in Eastern Hungary. Ann Roum Anthropol 46:3-11.	2009	Ann Roum Anthropol	Hajdúdorog-Szállásföldek, Hungary		2004	1141-1235 CE	1188 CE	1	1245	0.08% 1 M	64-70 yo M	N/A	Rhinomaxillary syndrome (facies leprosa).	N/A
Pálfi G. 1991. The first osteoarchaeological evidence of leprosy in Hungary. Int J Osteoarchaeol 1:99-192.; Pálfi G. 1997. Maladies dans l'antiquité et au Moyen-Âge. Paléopathologie comparée des	1991; 1997	Int J Osteoarchaeol; Bull et Mém de la Soc d'Anthrop de Paris.	Sárrétudvari-Hízóföld, Eastern Hungary	N/A	10th c. CE	950 CE	2 (1 F, likely S-202; 1 M, possible S-237.)	264	0.76% 1 F; 1 M	50-60 yo F; middle-aged adult M.	N/A	1 F: rhinomaxillary syndrome (facies leprosa).	"[F]irst palaeopathological description of leprosy
Ferreira MT, Neves MJ, Wasterlain SN. 2013. Lagos leprosarium (Portugal): evidences of disease. J Archaeol Sci 40:2298-2307.	2013	J Archaeol Sci	Lagos leprosarium, Valle da Gafaria, Lagos,		2009	15th c. - 17th c. CE	1500 CE	2	11	18.18% 1 F; 1 M	25-30 yo F; 30-40 yo M.	N/A	N/A	**Leprosarium:** In addition to the results by Antunes-Ferreira
Gilmore JK. 2008. Leprosy at the Lazaretto on St Eustatius, Netherlands Antilles. Int J Osteoarchaeol 18:72-84.	2008	Int J Osteoarchaeol	The Lazaretto on St Eustatius, Netherlands	N/A	1886-1923 CE	1905 CE	3	5	60% 1 F; 2 U	20-25 yo F; 2 40-50 yo U.	N/A	Rhinomaxillary syndrome; bilaterally	N/A
Fornaciari G, Mallegni F, de Leo P. 1999. The leprosy of Henry VII: Incarceration or isolation? Lancet 353:758.	1999	Lancet	Cosenza Cathedral, Calabria, southern	November 1st, 1998	1242 CE	1242 CE	1	1	100% 1 M	30-35 yo M	N/A	Rhinomaxillary syndrome and severe femoral	Henry VII had lepromatous leprosy; "the first to be
Mendum TA, Schuenemann VJ, Roffey S, Taylor GM, Wu H, Singh P, Tucker K, Hinds J, Cole ST, Kierzek AM, Nieselt K, Krause J, Stewart GR. 2014. *Mycobacterium leprae* genomes from a British	2014; 2012	BMC Genomics; Mediev Archaeol	St. Mary Magdalen, Winchester,	2008-2011	955-1033 CE; 1020-1162 CE	1043 CE (taken from the midpoint of the midpoint of	33 show signs of leprosy; 2 (Sk14 and Sk27)	38	86.84% 1 M?; 1 U	1 adolescent M?; 1 middle-aged adult U.	N/A	N/A	**Leprosarium:** Same as Lee and Magilton 1989; once served as
Montiel R, Garcia C, Cañadas MP, Isidro A, Guijo JM, Malgosa A. 2003. DNA sequences of *Mycobacterium leprae* recovered from ancient bones. FEMS Microbiol Lett 226:413-414.	2003	FEMS Microbiol Lett	Capilla y Castillo de San Jorge, Seville, Spain		1998	12th c. CE	1150 CE	4 (A-43; A-326; A-120; A-343.)	175	2.29% 2 M; 1 F; 1 F?	24-30 yo M; 28-32 yo M; 20-24 yo F?; 45-55 yo F.	N/A	Diagnosis from lesions description is in Spanish.	DNA sequencing study; "Oldest Spanish cases of
Holst M. 2012. Osteological analysis. Dixon Lane and George Street York. York Osteoarchaeol Rep No 1612.	2012	York Osteoarchaeol	St Stephens Church, Dixon Lane and George	2005-2006	late 11th c. - mid 14th c. CE	1213 CE	1 probable.	117	0.85% 1 F	46+ yo F	N/A	Periosteal reactions on tibiae, fibulae,	Report commissioned to York
Lee F, Magilton J. 1989. The cemetery of the hospital of St. James and St. Mary Magdalene, Chichester - A case study. World Archaeol 21:273-282.; Magilton J, Lee F, Boylston A. 2008. 'Lepers outside the	1989; 2008	World Archaeol; Council for British Archaeology	St James and St Mary Magdalene, Chichester, UK (2	1986-87; (later 1993 again)	early 12th c. - mid-17th c. CE	1388 CE	75 (definite.)	384	19.53% 63 M; 10 F; 2 U	N/A (suggested ages of 1 child, 4 sub-adults, 78	N/A	In Magilton et al 2008: 72 have rhinomaxillary	**Leprosarium:** Additional information such as updated
Primeau C, Linnerup N. 2014. Non-bony lesions and functional losses in leprosy [abstract]. Am J Phys Anthropol Suppl. p 16.	2014	Am J Phys Anthropol Suppl	Leprosarium, Maribo, Lolland, Denmark	N/A	14th c. CE	1350 CE	4 with lesions (60 assumed.)	60	7% N/A	N/A	N/A	4 phalangeal lesions; none of the skeletons had	**Leprosarium:** Information based on a 250-word summary
Suzuki K, Takigawa W, Tanigawa K, Nakamura K, Ishido Y, Kawashima A, Wu H, Akama T, Sue M, Yoshihara A, Mori S, Ishii N. 2010. Detection of *Mycobacterium leprae* DNA from archaeological	2010	PLoS ONE	Hatanai, Aomori prefectue, Honshu Island, Japan	N/A	middle 18th c. - early 19th c. CE	1788 CE	1	50	2% 1 M	30-50 yo M	N/A	Rhinomaxillary syndrome; fibula; genome	Lepromatous leprosy; "[D]etected *M. leprae* DNA in
Suzuki K, Saso S, Hoshino K, Sakurai J, Tanigawa K, Luo Y, Ishido Y, Mori S, Hirata K, Ishii N. 2014. Paleopathological evidence and detection of *Mycobacterium leprae* DNA from archaeological skeletal	2014	PLoS ONE	Tawara-ga-yatsu, Kanto, Japan; Usukubo, Kanto,	N/A	early-mid 18th c. CE	1738 CE	2	3	66.67% 2 M	Late 20s yo M; middle-aged adult M.	N/A	"[R]ounding deformation seen in the lateral and	This study analyzed 3 Nabe burials out of 105 found. Out of
Tayles N; Buckey HR. 2004. Leprosy and tuberculosis in Iron Age Southeast Asia? Am J Phys Anthropol 125:239-256.	2004	Am J Phys Anthropol	Noen U-Loke, Mun River Valley, Khorat Plateau,	1996-1998	300-200 BCE (B107); first two c. CE (B42)	75 BCE (taken from the midpoint of the midpoint of	2	120	1.67% 2 M	16-20 yo M; older adult M.	Cranium, fibula, metacarpals, metatarsals.	N/A	"Noen U-Loke has provided the largest and best documented
Khudaverdyan A. 2010. Pattern of disease in 2nd-1st millennium BC necropolis from Lchashen, Armenia. Anthropologie 158:239-254.	2010	Anthropologie	Lchashen, Sevan pool, Armenia	1957-1967; Present?	2nd c. - 1st c. BCE	150 BCE	6	500	1.20% 4 M; 2 F	N/A	N/A	Rhinomaxillary syndrome.	N/A
Linderholm A, Kjellström A. 2011. Stable isotope analysis of a medieval skeletal sample indicative of systemic disease from Sigtuna, Sweden. J Archaeol Sci 38:925-933.	2011	J Archaeol Sci	Sigtuna, Sweden	2005-2006	10th c. - 14th c. CE	1100 CE	6	227 (according to Kjellström 2012.)	3% 1 F; 3 M; 2 U	N/A	N/A	Pg 927.	Overlaps with Kjellström 2012/2010; Study of

Boldsen JL, Mollerup L. 2006. Outside St. Jørgen: leprosy in the medieval Danish city of Odense. Am J Phys Anthropol 130:344-351.	2006 Am J Phys Anthropol	Gray Friars monastery, St. Albani parish	N/A	1000-1820 CE	1410 CE	St. Albani: 20; Gray Friars: 3; St. Knud: 11	461 total: St. Albani: 152; Gray Friars: 243; St.	St. Albani: π = 0.135; Gray Friars: π = 0.013; St … 15	N/A	N/A	N/A	Table 4: Observed and expected prevalence of	Overlaps with Matos 2013; focuses on four (three used here)
Neil B. 2003. 2003 Anglo-Georgian Nokalakevi expedition: Osteological assessment for trench A and B. p 1-21.	2003 Anglo-Georgian Nokalakevi expedition site Report	Nokalakevi, Georgia	1930; 2004	6th c. - 10th c. CE	700 CE	2 (307; 309.)	15	13.33%	1 M; 1 F	50-55 yo M; 48.8 yo +/- 10.5 y F.	N/A	"[S]keleton (307) did suffer with the early stages of	Other years of site reporting do not report leprosy.
Polet C. 2011. Health and diet of ancient Easter Islanders: Contribution of paleopathology, dental microwear, and stable isotopes. Royal Belgian Institute of Natural Sciences. p 1-19.	2011 Royal Belgian Institute of Natural Sciences	Easter Island, Chile	2004; 1934-2009	late 19th c. - early 20th c. CE	1900 CE	1	15	6.67%	1 M	40 yo M	N/A	Early stage of lepromatous leprosy.	"The individual from Ahu Motu Toremo Hiva could be one of
Rubini M, Zaio P. 2009. Lepromatous leprosy in an early mediaeval cemetery in central Italy (Morrione, Campochiaro, Molise, 6th-8th century AD). J Archaeol Sci 36:2771-2779.	2009 J Archaeol Sci	Morrione, Campochiaro, Molise, Central Italy	N/A	6th c. - 8th c. CE	600 CE	2 (Burial 68 and 108.)	107	1.87%	1 M; 1 F	50-55 yo M; 40-46 yo F.	N/A	Rhinomaxillary syndrome in both.	Molecular analysis in Donoghue et al 2015. T68 samples
Rubini M, Dell'Anno V, Giuliani R, Favia P, Zaio P. 2012. The first probable case of leprosy in southeast Italy (13th-14th centuries AD, Montecorvino, Puglia). J Anthropol. p 1-7.	2012 J Anthropol	Montecorvino, Foggia, Puglia, Italy		2008 end of 13th c. CE	1275 CE	1 (MCV2.)	10	10%	1 F? (Rubini 2014 says M).	35-40 yo M	N/A	Rhinomaxillary syndrome; postcrania: light	"This is the first case of leprosy in southeastern Italy
Rubini M, Zaio P, Roberts CA. 2014. Tuberculosis and leprosy in Italy-new skeletal evidence. HOMO J Comp Hum Biol 65:13-32.	2014 HOMO J Comp Hum Biol	Palombara, Rome, Central Italy	N/A	C14 475 +/- 25 y CE (5th c. CE)	475 CE (C_{14})	3	54	5.56% N/A	N/A	N/A	N/A	Rhinomaxillary syndrome.	See Table 2 and Figure 18 for a breakdown of leprosy
Taylor GM, Watson CL, Bouwman AS, Lockwood DNJ, Mays SA. 2006. Variable nucleotide tandem repeat (VNTR) typing of two palaeopathological cases of lepromatous leprosy from mediaeval England	2006 J Archaeol Sci	Wharram Percy, North Yorkshire, England (G708)	N/A	960-1100 CE	1030 CE	1	687	0.15%	1 M?	10 yo M?	N/A	The child: rhinomaxillary syndrome	Tested PCR for M. leprae aDNA in two mediaeval cases of
Boldsen JL. 2005b. Leprosy and mortality in the medieval Danish village of Tirup. Am J Phys Anthropol 126:159-168.	2005 Am J Phys Anthropol	Tirup, Jutland, Denmark	1984	1150-1350 CE	1250 CE	135 (25.6%)	622	21.704% (Boldsen calculates 25.6%.)	N/A	Adults; over 14 years.	N/A	Table 2: Epidemiological properties of	This was a rural parish cemetery. "The analyses
Boldsen JL. 2008. Leprosy in the early medieval Lauchheim community. Am J Phys Anthropol 135:301-310.	2008 Am J Phys Anthropol	Lauchheim, Ostalpkreis, Baden-	1986	second half of 5th c. - 680 CE	478 CE	17 (estimated.)	110 analyzed (1308 total excavated.)	16.2% (taken from Boldsen sample.)	"Nearly 1/5 of all men died with signs of leprosy	Adults; over 15 years.	N/A	Table 1: Frequency table of the observations	"16% of adult people showed osteological
Dzierzykray-Rogalski T. 1980. Paleopathology of the Ptolemaic inhabitants of Dakhleh Oasis (Egypt). J Hum Evol 9:71-74.	1980 J Hum Evol	Balat, Dakhleh Oasis, Egypt	1977	2nd c. BCE (Ptolemaic period)	150 BCE	4	71	5.63%	4 M	30 yo M; 55-60 yo M; 70-75 yo M; 75-80 yo M.	N/A	N/A	"It is well known that leprosy was common in ancient Egypt
Blondiaux J, Durr J, Khouchaf L, Eisenberg LE. 2002. Microscopic study and X-ray analysis of two 5th century cases of leprosy: palaeoepidemiological inferences. In: Roberts CA, Lewis ME,	2002 BAR International Series 1054	Vaison-la-Romaine, Southern France; (Neuville-sur-	N/A	500 CE (Vaison-la-Romaine); 500 CE (Neuville-sur-	500 CE; 500 CE	2 (1 at each place.)	131 Vaison-la-Romaine; 100 Neuville-sur-	0.763%; 1.0%	1 M (Vaison-la-Romaine); 1 F (Neuville-sur-	Adult M; adult F	N/A	N/A	Microscopy and x-ray explored; "They are believed to represent
Brander T, Lynnerup N. 2002. A possible leprosy hospital in Stubbekøbing, Denmark. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical,	2002 BAR International Series 1054	Stubbekøbing, Falster, Denmark	1994	1481-1505 CE	1493 CE	4	60	6.67%	1 M; 3 F	40-50 yo M; two 20-30 yo F; 30-40 yo F.	N/A	N/A	**Undeterminable leprosarium:** This article is trying to
Molto JE. 2002. Leprosy in Roman period skeletons from Kellis 2, Dakhleh, Egypt. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical,	2002 BAR International Series 1054	Kellis 2 cemetery, Balat, Dakhleh Oasis, Egypt	N/A	early-mid 4th c. CE (Roman times)	1438 CE	4 (2 likely, K2-B6 and K2-B116; 2 possible, K2-B9	108 analyzed (378 total excavated at K2 to date.)	3.70%	4 M	26-32 yo M; 24-38 yo M; 26-32 yo M [all rib	N/A	B6 and B116 show osseous lesions	"[A] crude prevalence rate of 3.7% indicates that leprosy was
Rubini M, Erdal YS, Spigelman M, Zaio P, Donoghue HD. 2012. Paleopatholoical and molecular study on two cases of ancient childhood leprosy from the Roman and Byzantine empires. Int J	2012 Int J Osteoarchaeol	Martellona, Rome, Central Italy	N/A	2nd c. - 3rd c. CE (1817 +/- 25 years BP)	133 CE (C14)	1 (GM162.)	412	0.24%	1 U	4-5 yo U	N/A	Rhinomaxillary syndrome.	"Shows strong palaeopathological evidence of
Rubini M, Erdal YS, Spigelman M, Zaio P, Donoghue HD. 2012. Paleopatholoical and molecular study on two cases of ancient childhood leprosy from the Roman and Byzantine empires. Int J	2012 Int J Osteoarchaeol	Kovuklukaya, Sinop, Northern Turkey	N/A	8th c. - 10th c. CE	800 CE	4 [3 adults (11/2; 20/1; 24;1); one infant SK9/1.]	36	11.11%	2 M; 1 F; 1 U	30-35 yo M; 40-50 yo M; 35-45 yo F; 4-5 month-old	N/A	Infant: lesions on the occipital and frontal bones;	"[SK9/1] the youngest individual known in the world to have had
Murphy E, Manchester K. 2002. Evidence for leprosy in medieval Ireland. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy. Archaeological, historical, palaeopathological	2002 BAR International Series 1054	St. Patrick's Church, Armoy, County Antrim,	Spring 1997	1444-1636 CE	1540 CE	1	56	1.79%	1 U	N/A	Only right and left foot present.	"[C]hanges indicative of lepromatous	"[W]hile there are three known Medieval leprosy
Pálfi G, Zink A, Haas CJ, Marcsik A, Dutour O, Nerlich AG. 2002. Historical and palaeopathological evidence of leprosy in Hungary. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present	2002 BAR International Series 1054	Püspökladány-Eperjesvölgy, Hajdú-Bihar,	N/A	10th c. - 11th c. CE	950 CE	4	629	0.64%	2 F; 2 M	22-40 yo M; 50-55 yo M; 30-35 yo F; 55-60 yo F.	Four skulls; all hands and feet are missing.	Early stage pathological alterations of the Facies leprosa;	The results are spread out among at least four different
Marcsik A, Molnár E, Ösz B. 2007. Specifikus fertőző megbetegedések csontelváltozásai történeti népesség körében. JETE Press.	2007 JETEPress	Hajdúdorog-Gyúlás, Hungary	N/A	10th c. CE	950 CE	1 (HG-56.)	63	1.59%	1 M	Mature aged M	N/A	"resorbed anterior nasal spine and	Information taken from Csóri et al 2009; "molecular analysis
Strouhal E, Ladislava H, Likovsky J, Vargova L, Danes J. 2002. Traces of leprosy from the Czech Kingdom. In: Roberts CA, Lewis ME, Manchester K, editors. The past and present of leprosy.	2002 BAR International Series 1054	Křtiny ossuary, near Brno, Moravia, Czech	N/A	13th c. - early 18th c. CE	1463 CE	1 (K12.)	554	0.18%	1 M	20-25 yo M	Skull.	Osseous changes suggestive of rhinomaxillary	"[W]e can consider the skull of K12 the first
Trembly DL. 1995. On the antiquity of leprosy in Western Micronesia. Int J Osteoarchaeol 7:621-624.	1995 Int J Osteoarchaeol	Guam and Saipan, Western Micronesia (3	N/A	7th c. - 11th c. CE; 11th c. - 13th c. CE; 13th c. - 15th	1050 CE (taken from the midpoint of the midpoint of	6	700	0.86% N/A	N/A	N/A	N/A	N/A	"The introduction of leprosy pre-dates western contact and
Brothwell DR. 1958. Evidence of leprosy in British archaeological material. Med Hist 2:287-291.	1958 Med Hist	Dunfermline Abbey, Fife, Scotland	1818 discovered (this is a plaster mold author is	1329 CE (when Robert the Bruce died)	1329 CE	1 ("Robert the Bruce, King of Scotland.")	1	100%	1 M	Robert the Bruce died at the age of 55.	N/A	Upper facial anomalies; extensive	Robert the Bruce; Møller-Christensen looked at his
Roberts J. 2007. Human remains from the cists. In: Dunwell A, editors. Cist burials and an Iron Age settlement at Dryburn Bridge, Innerwick, East Lothian. Scottish Archaeological Internet Report	2007 Scottish Archaeological Internet Report	Dryburn Bridge, East Lothian, Scotland	1978-1979	2300 c. - 2000 c. BCE (C14)	2150 BCE	1 (Burial 11.)	4	25%	1 U (child.)	6-8 yo U	"It was not possible to examine other	Rhinomaxillary syndrome; "These changes	Very detailed report in the cists (4,5,10,
Lunt DA. 2013. The first evidence for leprosy in early mediaeval Scotland: two individuals from cemeteries in St. Andrews, Fife, Scotland, with evidence for normal burial treatment. Int J	2013 Int J Osteoarchaeol	Hallow Hill cemetery; Kirkhill cemetery; both in	1975-1977 (Hallow Hill); 1980 (Kirkhill)	mid-8th c. CE (Hallow Hill); mid-7th c. - early 11th	750 CE; 838 CE	2 (1 at each place) [Hallow Hill cist 26; Kirkhill Skull	472 total [145 at Hallow Hill; 327 intact burials at	0.6897%; 0.3058%	1 F (HH); 1 F? (Kirkhill)	34-38 yo F (HH); 25-35 yo F? (Kirkhill).	N/A	Facies leprosa (Hallow Hill); HH post-cranial	"[T]he skeletons were not segregated but buried in the middle
Manchester K, Roberts CA. 1986. Palaeopathological evidence of leprosy and tuberculosis in Britain. Unpublished SERC Report (Grant 337.367), University of Bradford. Unpublished.	1986 Unpublished SERC Report	Guildford Dominican Friary, Surrey, UK	N/A	1275-1538 CE; Later and Post-Medieval	1407 CE	1	70	1.43%	1 M	16-25 yo M	N/A	N/A	Information taken from Roberts 2002; Age, specific dates,
Manchester K, Roberts CA. 1986. Palaeopathological evidence of leprosy and tuberculosis in Britain. Unpublished SERC Report (Grant 337.367), University of Bradford. Unpublished.	1986 Unpublished SERC Report	St. Mary and St. Thomas Hospital cemetery, Ilford,	N/A	11th c. - 17th c. CE; Later and Post-Medieval	1300 CE	4	25	16%	2 M; 2 F	N/A	N/A	N/A	**Leprosarium:** Basic information taken from Roberts 2002
Powell F. 1996. The human remains. In: Raunds Furnells. The Anglo-Saxon church and churchyard. English Heritage Archaeological Report.	1996 English Heritage Archaeological Report	Raunds, Northamptonshire, UK	1977-1984	500-1066 CE (Anglo-Saxon Britain)	783 CE	3 (Burials 5046, 5218, and 5256.)	191	1.57%	3 M	2 17-25 yo M; 25-35 yo M.	N/A	5046 facies leprosa and lower limb lesions. 5256	Field report online. 3 leprous individual not detailed in report but

Reference	Year	Source	Location	Excavation dates	Date range	Date (CE)	N	Analyzed	Frequency	Age/Sex	Completeness	Pathology notes	Information source
Duhig C. 1998. The human skeletal material In: The Anglo-Saxon cemetery at Edix Hill (Barrington A), Cambridgeshire. Council for British Archaeology Research Report.	1998 Council for British Archaeology Research Report	Edix Hill, Barrington, Cambridgeshire,	N/A	6th c. - 7th c. CE	550 CE	1	149	0.67% 1 F	N/A	N/A	N/A	Basic information taken from Roberts 2002.
Mays S. 1989. The Anglo-Saxon human bone from School Street, Ipswich, Suffolk. Ancient Monuments Laboratory Report 115/89, English Heritage. Unpublished.	1989 Unpublished Ancient Monuments Laboratory Report	School Street, Ipswich, Suffolk, UK	1983-1985	10th c. - 11th c. CE	950 CE	1 (Burial 1392.)	79	1.27% 1 F	21-25 yo F	N/A	Far too descriptive to summarize. See pg. 31-32.	Laboratory report. One case of leprosy.
Stones JA, editor. 1989. Three Scottish carmelite friaries: excavations at Aberdeen, Linlithgow and Perth 1980-1986. Society of Antiquaries of Scotland.	1989 Society of Antiquaries of Scotland	Carmelite Friary, Aberdeen, Grampian,	1980-1986	1500-1560 CE; Later and Post-Medieval	1530 CE	1 (Burial 2019.)	121	0.83% 1 M	46+ yo M	N/A	N/A	Basic information from Roberts 2002; Age, dates, and MNI.
Wiggins R, Boylston A, Roberts CA. 1993. Report on human skeletal remains from Blackfriars, Gloucester (19/91). Unpublished.	1993 Unpublished Report	Blackfriars, Gloucester, Gloucestershire,	N/A	13th c. - 16th c. CE; Later and Post-Medieval	1350 CE	2	140	1.43% 2 F	N/A	N/A	N/A	Basic information from Roberts 2002; Specific date and
Mays S. 1991. The medieval burials from the Blackfriars Friary, School Street, Ipswich, Suffolk (Excavated 1983-1985). Ancient Monuments Laboratory Report 16/91. English Heritage: Portsmouth.	1991 Ancient Monuments Laboratory Report 16/91	Blackfriars Friary, School Street, Ipswich, Suffolk,	1983-1985	1263-1538 CE; Later and Post-Medieval	1401 CE	4	249	1.61% 3 M; 1 F	2 26-45 yo M; 16-25 yo M; 46+ yo F.	N/A	On burial 1914 -> rhinomaxillary syndrome and	Basic information taken from Roberts 2002; Age, specific
Boulter S. 1992. Death and disease in Medieval Grantham. Unpublished Undergraduate Dissertation, University of Sheffield.	1992 Unpublished Undergraduate Dissertation,	Grantham, Lincolnshire, UK	1991	late-12th c. CE	1175 CE	3	53	5.66% 2 M; 1 F	N/A	N/A	N/A	Basic information taken from Roberts 2002.
Chundun Z, Roberts CA. 1995. Human skeletal remains, In: Cardwell P, editor. Excavation of the hospital of St Giles by Brompton Bridge, North Yorkshire. Archaeol J 152:214-220.	1995 Archaeol J	St. Giles, North Yorkshire, UK	1988-1990	1180-1400 CE; Later and Post-Medieval	1290 CE	3	33	9.09% 2 M; 1 F	2 adult M; 1 16-25 yo F.	N/A	N/A	**Served as a leprosarium for 300 years:** Basic
Anderson S. 1998. Leprosy in a medieval churchyard in Norwich. In: Anderson S; editor. Current and recent research in osteoarchaeology. Proceedings of the 3rd meeting of the	1998 Current and recent research in osteoarchaeology.	St. John, Timberhill, Norwich, Norfolk,	N/A	900-1000 CE	950 CE	28	181	15.47% 7 M; 11 F; 1 U adult; 9 juvenile.	N/A	N/A	N/A	Basic information taken from Roberts 2002. Date taken
Farley M, Manchester K. 1989. The cemetery of the leper hospital of St Margaret, High Wycombe, Buckinghamshire. Med Arch 33:82-89.	1989 Med Arch	St. Margaret's Hospital, High Wycombe,	N/A	13th c. - 16th c. CE; Later and Post-Medieval	1350 CE	8	11	72.73% 3 M; 1 F; 4 U	2 16-25 yo M; adult M; adult F; 4 adult U.	N/A	N/A	**Leprosarium:** skeletal remains uncovered from a
Belcastro MG, Mariotti V, Facchini F, Dutour O. 2005. Leprosy in a skeleton from the 7th century necropolis of Vicenne-Campochiaro (Molise, Italy). Int J Osteoarchaeol 15:431-448.	2005 Int J Osteoarchaeol	Vicenne-Campochiaro, Molise, Central	N/A	mid-late 7th c. CE	663 CE	3 (T18, T31, and T144.)	130 analyzed (167 total excavated.)	2.31% 2 F; 1 M	20-25 yo M; young adult F; mature adult F.	N/A	Near-lepromatous form of leprosy. Arco-osteolysis	Also cribra orbitalia; very good article for descriptive things to
Watson CL, Lockwood DNJ. 2009. Single nucleotide polymorphism analysis of European archaeological *M. leprae* DNA. PLoS ONE 4:e7547.	2009 PLoS ONE	Radasinovci, Croatia	N/A	8th c. - 9th c. CE	800 CE	2 (2A and 3A.)	4	50% 1 M; 1 F	50-60 yo M; 20-25 yo F.	N/A	Rhinomaxillary syndrome.	Information taken from Watson et al 2009 and Donoghue
Walker D. 2009. The treatment of leprosy in 19th century London: a case study from St Marylebone cemetery. Int J Osteoarchaeol 19:364-374.	2008 Int J Osteoarchaeol	St Marylebone cemetery, Westminster,	2004-2005	1839 CE	1839 CE	1 (Individual 825.)	301	0.33% 1 M	18-25 yo M (based on unfused clavicles.)	Complete skeleton.	Suffered from lepromatous leprosy;	A case when leprosy had become rare in Britain; this paper
Taylor GM, Donoghue HD. 2011. Multiple loci variable Number tandem repeat (VNTR) analysis (MLVA) of *Mycobacterium leprae* isolates amplified from European archaeological human remains with	2011 Microbes Infect	Prušánky, South Moravia, Czech Republic	N/A	9th c. - 10th c. CE	900 CE	1 (Burial 188.)	330 (176 adult individuals.)	0.30% 1 M	12-15 yo M	N/A	Atrophy of the anterior nasal spine and	Refer to Table 2 for VNTR typing results. 3M SNP type. Dates
Pálfi G, Molnár E. 2009. The paleopathology of specific infectious diseases from Southeastern Hungary: A brief overview. Acta Biol Szeged 53:111-116.	2009 Acta Biol Szeged	Szeged Castle, Kiskundorozsma-Daruhalom dűlő II,	N/A	late-7th c. CE	675 CE	8 (Donoghue 2015 references 3 as these are	94	8.51% 3 M	35-40 yo M; 40-45 yo M; 50-60 yo M.	N/A	Rhinomaxillary syndrome (517)/facies	Ages and dates taken from Donoghue et al 2015 and its
Pálfi G, Molnár E. 2009. The paleopathology of specific infectious diseases from Southeastern Hungary: A brief overview. Acta Biol Szeged 53:111-116.	2009 Acta Biol Szeged	Szentes-Kistőke, Hungary	first half of the 20th c.	7th c. - 8th c. CE (according to Donoghue et al	575 CE (taken from the midpoint of 650 CE or 500	1 (SK11.)	85	1.18% 1 F	Adult F	N/A	"[T]he morphological aspects of the	The ages and dates from Donoghue et al 2015. Individual
Molnár E, Donoghue HD, Lee OY-C, Wu HHT, Besra GS, Minnikin DE, Bull ID, Llewellyn G, Williams CM, Spekker O, Pálfi G. 2015. Morphological and biomolecular evidence for tuberculosis in 8th	2015 Tuberculosis	Bélmegyer-Csömöki domb, Southeast	1985-1989	7th c. - 9th c. CE	700 CE	1 (BC-51.)	248	0.40% 1 M	23-25 yo M	N/A	The skull shows rhinomaxillary remodelling, with	Most information taken from Donoghue et al 2015 and its S1.
Molnár E, Marcsik A. 2002. Paleopathological evaluation of Hungarian skeletal remains from the 7th-9th centuries AD. Antropol Portuguesa 19:85-99.	2002 Antropologia Portuguesa	Szarvas-Grexa Téglagyár, Hungary	N/A	late-7th c. - 9th c. CE	763 CE	1 (SG38.)	423	0.24% 1 F	30-35 yo F	N/A	Very fragmented, hands and feet bones missing	Most information taken from Donoghue et al 2015 and its S1.
Szilvássy J. 1980 Die Skelette aus dem awarischen Gräberfeld von Zwölfaxing in Niederösterreich. Anthropologische Forschungen 3, Wein, Austria.	1980 Anthropologische Forschungen	Zwölfaxing, Austria	1954-1959; 1977	8th c. - 9th c. CE	750 CE	2 (Grave 70 and 88.)	252	0.79% 1 F; 1 M	65-70 yo F; 25-30 yo M.	N/A	See Donoghue et al 2015 S1. Rib and palate tested	Information taken from Donoghue et al 2015 and S1. Both
Mészáros P, Paluch T, Sóskuti K, Sz Wilhelm G. 2006 Felgyő, Kettőshalmi-dűlő. In: Régészeti Kutatások Magyarországon, 2005-Archaeological investigations in Hungary, 2005, Budapest, 199-200.	2006 Archaeological investigations in Hungary, 2005,	Felgyő, Kettőshalmi dűlő, Hungary	2005	11th c. CE	1050 CE	2 (F-2467; F-3658.)	105	1.91% 1 F; 1 M	35-39 yo F; elderly M.	N/A	See Donoghue et al 2015 S1.	Information taken from Donoghue et al 2015 S1. F-3658
Donoghue HD, Marcsik A, Matheson C, Vernon K, Nuorala E, Molto JE, Greenblatt CL, Spigelman M. 2005. Co-infection of *Mycobacterium tuberculosis* and *Mycobacterium leprae* in human	2005 Proc Biol Sci B	Szombathely, Hungary.	N/A	15th c. CE	1450 CE	1 (Burial 10.)	5 analyzed (unknown total.)	20% N/A	N/A	N/A	"[T]here were no morphological changes on the	(DNA info taken from Donoghue et al 2005.)
Donoghue HD, Marcsik A, Matheson C, Vernon K, Nuorala E, Molto JE, Greenblatt CL, Spigelman M. 2005. Co-infection of *Mycobacterium tuberculosis* and *Mycobacterium leprae* in human	2005 Proc Biol Sci B	Basilica at Székesfehérvár, Hungary	N/A	Leprous individual from 11th c. CE; 11th c. - 16th c.	1050 CE; 1300 CE	1 (Burial 89.)	3 analyzed (unknown total.)	33.33% N/A	N/A	N/A	Typical leprotic morphological alterations around	(DNA info taken from Donoghue et al 2005.)
Nuorala E, Donoghue HD, Spigelman M, Götherström A, Hårding B, Grundberg L, Alexandersen V, Leden I, Lidén K. 2004. Diet and disease in Björned, a Viking-early medieval site in northern Sweden.	2004 Theses and Papers in Scientific Archaeology. Stockholm:	Björned, Ångermanland, Northern Sweden	N/A	late-10th c. - late 13th c. CE	1125 CE	1 (A4.)	5 analyzed (50 excavated.)	20% 1 M	Adult M	N/A	"[C]hanges indicating osteoarthritis can	(DNA info taken from Donoghue et al 2005 as well as Nuorala et
Boldsen JL, Rasmussen KL, Riis T, Dittmar M, Weise S. 2013. Schleswig: Medieval leprosy on the boundary between Germany and Denmark. Antropol Anz 70:273-287.	2013 Anthropol Anz	Rathaus Markt cemetery, Schleswig,	1970-present	1060-1205 CE	1133 CE	44 (estimated.)	120 analyzed (223 total excavated.)	$\pi = 0.37$; 95% c.i. = 0.28-0.48.	N/A	N/A	Table 1: Frequency table of the observations	The number of those with leprosy estimated. Age and
Boldsen JL, Rasmussen KL, Riis T, Dittmar M, Weise S. 2013. Schleswig: Medieval leprosy on the boundary between Germany and Denmark. Antropol Anz 70:273-287.	2013 Anthropol Anz	St. Nicolai Kirche cemetery, Schleswig,	1970-present	11th c. CE	1050 CE	15 (estimated.)	34 analyzed (127 total excavated.)	$\pi = 0.44$; 95% c.i. = 0.26-0.68.	N/A	N/A	Table 1: Frequency table of the observations	The number of those with leprosy estimated. Age and
Boldsen JL, Rasmussen KL, Riis T, Dittmar M, Weise S. 2013. Schleswig: Medieval leprosy on the boundary between Germany and Denmark. Antropol Anz 70:273-287.	2013 Anthropol Anz	St. Clemens Kirche cemetery, Schleswig,	1970-present	11th c. CE	1050 CE	38 (estimated.)	108 analyzed (206 total excavated.)	$\pi = 0.35$; 95% c.i. = 0.26-0.45.	N/A	N/A	Table 1: Frequency table of the observations	The number of those with leprosy estimated. Age and
Boldsen JL, Rasmussen KL, Riis T, Dittmar M, Weise S. 2013. Schleswig: Medieval leprosy on the boundary between Germany and Denmark. Antropol Anz 70:273-287.	2013 Anthropol Anz	Dominikaner Kloster cemetery, Schleswig,	1970-present	1239 CE	1239 CE	22 (estimated.)	57 analyzed (81 total excavated.)	$\pi = 0.39$; 95% c.i. = 0.19-0.66.	N/A	N/A	Table 1: Frequency table of the observations	The number of those with leprosy estimated. Age and

Reference	Year	Source	Site	Excavation dates	Date range	Date (CE)	Estimated	Analyzed	π / %	Additional	Sex/notes	Age	Other	Table 1 notes	Notes
Boldsen JL, Rasmussen KL, Riis T, Dittmar M, Weise S. 2013. Schleswig: Medieval leprosy on the boundary between Germany and Denmark. Anthropol Anz 70:273-287.	2013	Anthropol Anz	St. Johannis Kloster, Schleswig,	1970-present	1200-1225 CE	1213 CE	3 (estimated.)	31 analyzed (65 total excavated.)	π = 0.09; 95% c.i. = 0.02-0.17.	N/A	N/A	N/A		Table 1: Frequency table of the observations	The number of those with leprosy estimated. Age and Data taken from
Arcini C. 1999. Health and disease in early Lund - osteopathologic studies of 3305 individuals buried in the first cemetery area of Lund 990-1536. Archaeologica Lundensia VIII. Lund: Department of	1999	Lund University: Department of Community Health	Wooden church (T1-3) and Stone (T5) church in	N/A	T1: 990 CE - 1030 CE; T2-3: 1030 CE - 1100 CE; T5:	T1: 990 CE; T2-3: 1030 CE; T5:	1010 CE; 1065 CE; 1418 CE	T1: 7; T2-3: 27; T5: 1.	T1: 265; T2-3: 756; T5: 994	T1: 2.642%; T2: 3.571%; T5: 0.101%.	N/A (suggested ages of 21 M; 15 F; 7 U tossed out	Sex was not correlated with ages in Arcini	N/A	31 out of 34 of the older sample exhibited	Arcini 1999; pg. 118; mni and ages taken
Barber L, Sibun L. 1998. The medieval hospital of St Nicholas, Lewes, East Sussex: excavations 1994. Sussex archaeological collections ADS 148:1-42.	1998	Sussex archaeological collections	St. Nicholas Hospital, Lewes, East Sussex, UK		1994 late-12th c. - late-14th c. CE	1275 CE	2 (probable.)	103	1.94% 1 M; 1 U	16-25 yo M; adult U.	N/A			Only the feet survived for burial 6616 but showed	All information taken from Gilchrist and Sloane's 2005
Köhler K, Marcsik A, Donoghue H, Márk L, Hajdu T. 2009. Előzetes eredmények az Abony 36. lelőhely késő rézkori áldozati gödreiből feltárt embertani leletek vizsgálata alapján. Site Report.	2009	Site Report	Abony-Turjányos dűlő (Abony, site Nr. 36), Pest		2006 late Copper Age (5460-4870 cal. yr BP)	3215 BCE	2 (2 more less likely.)	48	4.17% 1 M; 1 F	18-22 yo M; 40-45 yo F.	N/A			Leprous pathological information in	Article is in Hungarian; only a preliminary site
Blondiaux J, Naji S, Bocquet-Appel J-P, Colard T, de Broucker A, de Sereville-Niel C. 2015. The Leprosarium of Saint Thomas d'Aizier, the cementochronological proof of the medieval decline of Hansen	2015	Int J Paleopathol	Saint-Thomas d'Aizier, Haute-Normandy, France		1998 Late Medieval Ages 12th c. - 15th c. CE	1250 CE	34	43 with facial bones (206 total excavated at Saint-	79% N/A	N/A	N/A			The 34 present at least two criteria of rhinomaxillary	Leprosarium: Refer to Niel et al. 2007 (in French). Leprosarium
Robbins G, Tripthy VM, Misra VN, Mohanty RK, Shinde VS. 2009. Ancient skeletal evidence for leprosy in India (2000 B.C.). PLoS ONE 4:e5669.	2009	PLoS ONE	Balathal, Rajasthan, India	1994-1997; 1999-2002	2000 BCE	2000 BCE	1 (1997-1.)	5	20% 1 M	37+/-5 yo M (pubic symphysis); 35+/-10 yo M (tooth	N/A			Rhinomaxillary syndrome and periostitis.	Lepromatous leprosy was present in India by 2000 BCE. This
Matheson CD, Vernon KK, Lahti A, Fratpietro R, Spigelman M, Gibson S, Greenblatt CL, Donoghue HD. 2009. Molecular exploration of the first-century Tomb of the Shroud in Akeldama, Jerusalem.	2009	PLoS ONE	Tomb of the Shroud, Hinnom Valley, Akeldama,		2000 1st c. CE	50 CE	1 (SC1.)	11	9.09% 1 M	N/A	N/A			N/A	Individual had both leprosy and tuberculosis. "This is
Reader R. 1974. New evidence for the antiquity of leprosy in early Britain. J Archaeol Sci 1:205-207.	1974	J Archaeol Sci	Poundbury Camp, Dorchester, Great Britain	1966-1982	mid-4th c. CE	350 CE		1 1200 (from Lewis 2010: 796 adults and 404	0.08% 1 M	Mature adult M	N/A			Inflammatory periostitis tibia and fibula; periostitis	"More severe level of deformity to the right foot than to the left"
Zhang Z. 1994. The skeletal evidence of human leprosy and syphilis in ancient China. Acta Anthropol Sin 13:294–299.	1994	Acta Anthropol Sin	Pinglu county, Shanxi Province, China	N/A	200 BCE - 200 CE (Han Dynasty)	0 CE	1	4	25% 1 F	30-35 yo F	Skull.			Lesion located mainly on the hard palate and the	Unable to acquire this article. Thus the information gathered
Arcini C. 1999. Health and disease in early Lund - osteopathologic studies of 3305 individuals buried in the first cemetery area of Lund 990-1536. Archaeologica Lundensia VIII. Lund: Department of	1999	Lund University: Department of Community Health	Wooden church in Kattesund, Lund, Skåne, Sweden	N/A	1050 CE - 1100 CE	1075 CE	8	176	4.55% N/A	2 7-14 yo U; 1 15-19 yo U; 2 20-39 U; 1 40-59 U; 2	N/A			N/A	Data taken from Arcini 1999; pg. 118; mni and ages taken
Arcini C. 1999. Health and disease in early Lund - osteopathologic studies of 3305 individuals buried in the first cemetery area of Lund 990-1536. Archaeologica Lundensia VIII. Lund: Department of	1999	Lund University: Department of Community Health	Fjälkinge, Skåne, Sweden	N/A	900 CE - 1050 CE	975 CE	3	128	2.34% N/A	N/A	N/A			N/A	Info taken from A6:tab 7:6 Arcini 1999:184 and pg. 49;
Arcini C. 1999. Health and disease in early Lund - osteopathologic studies of 3305 individuals buried in the first cemetery area of Lund 990-1536. Archaeologica Lundensia VIII. Lund: Department of	1999	Lund University: Department of Community Health	St. Clemens wooden and stone churches,	N/A	1050 CE - 1536 CE	1293 CE	6	551	1.09% N/A	N/A	N/A			N/A	Info taken from A6:tab 7:6 Arcini 1999:184 and pg. 49;

APPENDIX B

All References Searched

[See supplementary content in ScholarWorks.]

APPENDIX C

References Excluded from Data

[See supplementary content in ScholarWorks]