Diagnosing Tuberculosis

A critical review of palaeopathological literature on tuberculosis in human skeletal and mummified remains

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Abstract

To analyse tuberculosis both in present and historic times becomes very important in order to understand the magnitude of this disease. The presented information in this thesis was based on a quantitative analysis of skeletal traits and aDNA used to diagnose tuberculosis in skeletal material and mummified remains. The material was collected from 51 articles, books and theses from the year 2000 until present. Two exceptions were made with one article from 1994 and one doctoral thesis from 1999. The geographical selection included materials from Africa, Asia, Europe, North America and South America. The oldest materials were from the European Neolithic and the youngest were from 1990-2000. The aim of this thesis was to investigate what diagnostic traits have been used to diagnose tuberculosis, at what quantity they are present and how they appear in relation to the use of aDNA analysis. 46% of the total amount of diagnosed individuals were males and 34% females. The adults diagnosed with tuberculosis represent 61% of the material. Previous research has shown Pott´s disease as the diagnostic trait for tuberculosis. In the materials studied here, calcification and structural changes on ribs were the most often used diagnostic trait. Pott´s disease has been used as a diagnostic trait 57 times, ribs 157 times. Of the materials included in this study, the most common method to study human remains was to analyse skeletal remains without aDNA with 413 cases.

Keywords: *tuberculosis, critical review, methods, palaeopathology, Pott´s disease, ribs*

Preface

Thank you…

… Anna Tornberg, for your counselling during this process

… Amanda Casselstål, for your aid in the final steps

… Gustaf Olsson, for your never-ending support

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1. Introduction

As one of our oldest known diseases, tuberculosis has left a mark on our society. The still visible traces of the sanatoriums and institutions, to which the sick were confided to, tells us a story about the reality of tuberculosis and what it meant for people. Some of these places are still used today for other purposes, some are ruins and other have been lost to time. Art and texts from our past shows us how people viewed and handled the disease they were exposed to. An old ceramic sculpture from Egypt shows us a man doubled over with a deformed back (Dubos, Dubos, 1952. p. 5), which is one of the earliest artistic evidence of the disease. Various texts tells us about the suffering they faced, with symptoms like coughing up blood, pain, stiffness in joints and the disability it left them with. Still, they lived their lives and worked to the best of their abilities. Tuberculosis affected both their everyday life and their skeletons. With a good immune system, the body can survive with the disease for years. When the disease has been active for long enough, it can affect the bones. The skeletal changes caused by tuberculosis, will be the main focus of this thesis. The focus will be on the palaeopathological approach to skeletal and mummified remains. This will be done by investigating the methods applied to the materials and the palaeopathological changes used to diagnose individuals. The journey tuberculosis has made with the human species is not short nor easy. From the earliest evidence of the disease in cattle and humans it has travelled alongside us for thousands of years. From

sparsely populated groups with great access to fresh air and nutritious food it was a disease like many others, it mostly affected the weak. With the founding of cities and with more densely populated areas, tuberculosis began to spread like never before. Not including the waves of plague that tormented establishments around the populated areas, tuberculosis was the deadliest disease for a very long time. With the development of sciences and an understanding of how disease and the human body works, legislation began to change in an attempt to limit the spread of the disease. Later with the development of treatments, tuberculosis was finally being challenged and began retreating. At one point it was even declared as no longer a threat in Europe. The impact tuberculosis had as a disease changed again with the overuse of antibiotics and mutations of diseases. Today, there are multidrug-resistant and extreme multidrug-resistant strings of tuberculosis that are increasing the difficulties to fight and eliminate the disease (Gagneux, 2012. p. 850, World Health Organization, 2018. 230421). With the increase of tuberculosis over time, it also becomes more and more relevant to study the disease, as it is still very prominent today. However, fewer individuals develop severe skeletal changes today than before scientists began to understand the disease and develop a cure. It is therefore important to study the disease as it was before a cure, a debilitating one. With the use of skeletal changes such as Pott´s disease, calcified pleura and calcification of the ribs I will carry out a quantitative analysis of the available published materials on tuberculosis in the past 20 years.

1.1. Aims and research questions

The aim of this thesis is to investigate the methods applied to materials diagnosed with tuberculosis to see what palaeopathological changes they use to diagnose. This will be done by reviewing previously analysed and published materials where they have diagnosed tuberculosis with the use of skeletal changes, aDNA or visual changes in lung tissue in mummified remains. With the aid of modern data, the discussion will address if the traditional osteological changes used for diagnosis are the ones providing the most accurate results both on a population level and for case studies. With the use of previous research, the aim is to establish a foundation regarding the development of tuberculosis research that can be applied globally.

- Does aDNA provide a reliable alternative when diagnosing both individuals and populations, and when it is confirmed, are palaeopathological changes present?
- Are traditional osteological traits such as Pott´s disease adequate to indicate tuberculosis for cases as well as in a population?

- To what extent is Pott´s disease used as a diagnostic trait and is it the most common one?
- Has the frequency of tuberculosis changed over time?
- Is there a correlation between certain skeletal changes, age and sex?

2. Background

In this chapter, background information regarding tuberculosis will be presented. The chapters are divided into three larger sub-chapters; tuberculosis, mummified remains and previous research. The subjects presented in Tuberculosis are as follows.

A section regarding the disease today and who it affects the most will be brought forth with the aid of statistics from the World Health Organization and The World Bank. The first signs of tuberculosis in history and its origin will be discussed based on various sources. A presentation of the various names and cures used for the disease is placed in the end of the first sub-chapter. The next sub-chapter includes an account of the various genetic strings within the tuberculosis complex. The last sub-chapter in tuberculosis presents the various ways tuberculosis affects and manifests itself in the body as well as how tuberculosis spread from human to human .

In the section of mummified remains some different aspects to mummification is presented. How it occurs, natural versus artificial mummification and what part it can play in palaeopathological research.

In the section of previous research, a history of the studying of tuberculosis is presented. This section consists of some examples from Scandinavia with the purpose of discussing the development in tuberculosis research. For the researched materials, the selection is global to get varied materials and to see if there exists a differentiation over time.

2.1. Tuberculosis

Tuberculosis has a long-standing position as a very efficient killer of mankind. Before modern diseases such as Acquired Immunodeficiency Syndrome (AIDS) / Human Immunodeficiency virus (HIV), it was the disease that killed most people in non-plague years (Waldron, 2009. p. 90f). According to World Health Organization, the highest group at risk today are those with a positive HIV diagnosis. Out of the 1.4 million people that died in 2019 of tuberculosis, 208 000 of those was diagnosed with HIV (World Health Organization, b240221). One problem with

diagnosing tuberculosis both palaeopathologically and medically, is the latent and asymptomatic manifestations of the disease, individuals carrying the disease without them knowing. The latent version can be identified with the use of DNA (BlueCross BlueShield of North Carolina, 2021). There are at least four different ways that tuberculosis can manifest itself: Pulmonary tuberculosis (affects the lungs), tuberculous adenitis (lymph nodes), scrofula (skin) and gastrointestinal tuberculosis (intestines) (Lewis, 2007. p. 146). Any of these can cause skeletal changes if left untreated.

Today, one third of the world's population is infected with the tuberculosis bacteria and annually, around 10 million people become ill because of it. Of those carrying the tuberculosis bacteria, about 5-15% have active tuberculosis, the remaining 95-85% has got the latent and asymptomatic version that could become active if the immune system is compromised (World Health Organization, 080321). The latent version of the disease is non-transmittable (Gagneux, 2012. p. 852). Of those with both latent tuberculosis and positive HIV, a minimum of 10% develop active tuberculosis every year (Lawn, Bekker, 2009. p. 96). The changes caused in the host body by either tuberculosis or HIV are ideal for the other to thrive. The tuberculosis bacteria cause a dysfunction in cells that are part of the hosts response to viruses. This leads to a microenvironment ideal for HIV (Lawn, Bekker, 2009. p. 104). The presence of both diseases can cause problems when diagnosing. In some cases, the sputum test, used to diagnose tuberculosis in resource-poor settings, can show a false negative when the patient is infected with both diseases (Nachega, Maartens, 2009. p. 524).

Tuberculosis affects all parts of the world, but in 2019 South-East Asia was the most affected with 44% of new registered cases, followed by Africa with 25% and Western Pacific 18% (World Health Organization, 080321). Given a longer time perspective, Africa is the most affected continent (figure 1). The 17 worst affected areas of Europe are eastern or south-eastern located countries, with Portugal in place 18 being the worst affected western European country (World Health Organization, c220321). In the Americas, it is almost exclusively south and central America that are affected (World Health Organization, 220321).

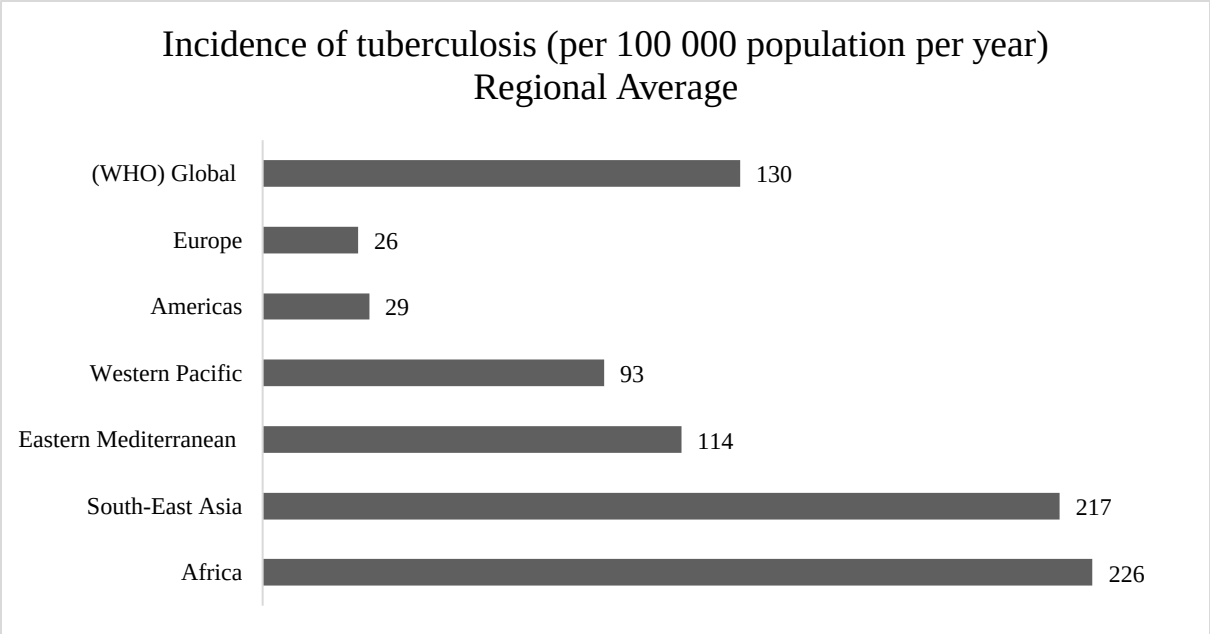

Figure 1. Statistics on "Incidence of tuberculosis (per 100 000 population per year)". The image shows regional averages: Global, Europe, Americas, Western Pacific, Eastern Mediterranean, South-East Asia and Africa. Information from World Health Organisations webpage (World Health Organization, 080321).

The exact number of individuals that develop skeletal changes in the past due to tuberculosis is difficult to assess. They are required to have had an active form of the disease and for the skeletal changes to be severe enough to be detected. The skeletal changes also need to correspond to what is traditionally thought of as a diagnostic traits. The general percentage presented by archaeological scholars vary between 2 and 7% (Arcini, 2003. p. 110, Waldron, 2009. p. 91f, Roberts, Manchester, 2010. p. 188, Brown, Brown, 2011. p. 250, Buikstra, DeWitte, 2019. p. 15). The specific number varies between "no more than 2%" to "5-7%". Regardless of the exact percentage, it is a very small amount of people that exhibit the skeletal changes. This can become rather problematic when trying to investigate tuberculosis on a population level (Arcini, 1999. p. 115, Arcini, 2003. p. 110, Waldron, 2009. p. 91f, Roberts, Manchester, 2010. p. 188).

Just like in the past, the poor and unprivileged are the ones who suffer the most (Roberts, Buikstra, 2003. p. 55ff, Gandy, 2009. p. 925, Squire, Thomson, 2009. p. 908, Gagneux, 2012. p. 850). Small spaces with poor ventilation and a lack of hygiene continues to be the main cause behind the rapid spread of the disease (Roberts, Buikstra, 2003. p. 3ff, Roberts, Buikstra, 2019. p. 321). As seen in figure 2, the highest frequencies originate from countries and areas with low income and lower-middle income, examples found in table 1. Due to the high frequency deaths

of those with HIV, they have been excluded from this table by World Health Organization therefore mitigating bias towards areas highly affected by HIV and AIDS.

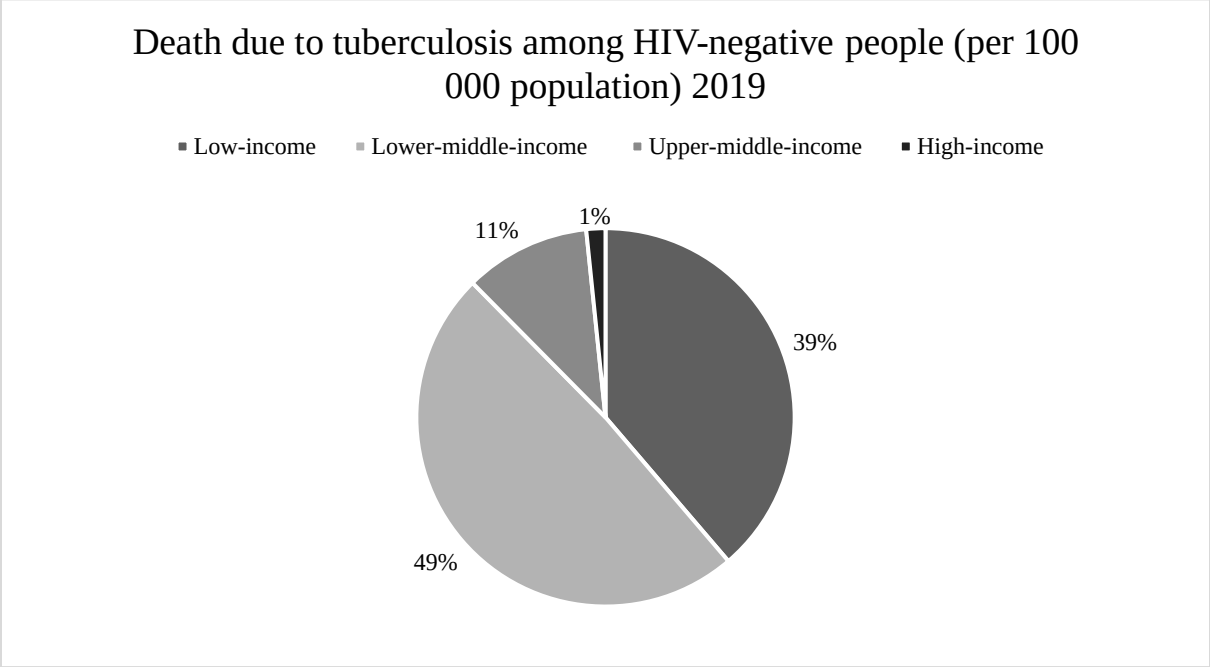

Figure 2. Statistics on "Deaths due to tuberculosis among HIV-negative people (per 100 000 population) 2019". The image shows low-, lower-middle-, upper-middle, high-income World Bank income group. Information from World Health Organisations webpage (World Health Organization, 080321).

The grading done by The World Bank, is based on a countries GNI (Gross National Income) per capita score (The World Bank, 220321). The calculated amount and example of countries can be seen in table 1.

Table 1. Income groups as divided by The World Bank, GNI and example countries (The World Bank, 220321).

Income group	GNI	Example countries
Low-income economies	$1,035 or less	Afghanistan, Liberia, Rwanda, Somalia, Sudan, Uganda
Lower-middle income economies	$1,036 to $4,045	Algeria, Bangladesh, Cambodia, Egypt, India, Ukraine
Upper-middle income economies	$4,046 to $12,535	Argentina, Botswana, Brazil, China, Iran, Serbia
High income economies	$12,536 or more	Australia, Canada, Chile, Japan, Sweden, Trinidad and Tobago

The first diagnosed cases of tuberculosis in humans originate from the Neolithic, a case of Pott´s disease from Liguria, Italy dated to around 3500 years BCE (Nuorala et al., 2004. p. 2, Zink et

al., 2007. p. 386). Another early case originates from Zealand, Denmark, dated to 2500-1500 BCE and was published by Møller-Christensen in 1982 (Møller-Christensen, 1982. Ch. 5, Nuorala et al., 2004. p. 2). The earliest known case of tuberculosis in England originates from the Iron Age (400-230 BCE) in Dorset. Lumbar vertebra 2 and 3 have been affected by Pott´s disease and a biomolecular study of the remains provides a positive result on the *Mycobacterium tuberculosis* complex. The results did not specify whether it was *Mycobacterium tuberculosis* or *Mycobacterium bovis* that caused the infection (Mays, Taylor, 2003. p. 189ff). The second oldest evidence in England comes from the Roman period (300 CE) (Roberts, 2002. p. 106).

The origin of tuberculosis is well debated, Nuorala et al. (2004. p. 2) refers to studies of modern tuberculosis strains from around the world that concludes that it is approximately 15 000-20 400 years old (Kapur, Whittam & Musser, 1994, Sreevatsan et al., 1997). The debate has been a long-standing one weather tuberculosis is a zoonosis or anthroponosis. A date prior to the domestication of cattle would hopefully settle the debate, did humans infect cattle or did cattle infect humans (Waldron, 2009. p. 92f)? This has been even more problematised with traces of tuberculosis in wild animals (Roberts, 2002. p. 110). Lewis (2007. p. 148) states that it is believed to be a zoonosis, developed from the bovine form to the human form during the Neolithic. In the book Palaeopathology, Waldron (2009. P. 92) makes the case that it is an antroponosis and the human form developed into a version that could affect cattle as well. Waldron bases this on aDNA studies referenced in the text (Brosch et al., 2002). The same conclusion is discussed by Charlotte Roberts and Keith Manchester (2010. P. 184f) and Larsen (2015, p. 102f) with reference to a study done by Brosch et al. (2002) regarding the *Mycobacterium complex.* Zink et al. (2007) also discusses this in their paper on the molecular history of tuberculosis. The case presented is that the *Mycobacterium tuberculosis* strand is the ancestral strand of tuberculosis and therefor represents the beginning of the *Mycobacterium complex* (Zink et al., 2007. p. 386). Both Nuorala et al. (2004. p. 2) and Roberts (2002. p.110f) discusses evidence from a bison dated to 17 000 BCE. The conclusion is that the tuberculosis strands that affects humans did not originate from *Mycobacterium bovis*. According to this case, the split between *Mycobacterium tuberculosis* and *bovis* occurred 15 000-20 000 years ago. The bison came from the Natural Trap Cave in Wyoming, United States of America (Donoghue et al., 2004. p. 588). In the same accumulation of bones (more than 40 000 bone samples accumulated for 100 000 years), traces of skeletal changes due to tuberculosis has been found in sheep, bison and musk oxen. In Brosch et al. (2002. p. 3688) they present evidence that

suggests that *Mycobacterium tuberculosis* is the original part of the complex and that *Mycobacterium bovis* and the other parts of the complex broke off at various points in history, with *M. bovis* and *M. africanum* being the last to part (Brosch et al., 2002. p. 3687).

An article presented by Sabin et al. (2020. p. 2) discusses different possibilities for the origin of the *Mycobacterium* bacteria. One estimation is that it originates 70 000 years ago and spread with the major migration of humans from Africa (Sabin et al., 2020. p. 2). The data for this originates from a large global dataset of modern *Mycobacterium tuberculosis* genomes. Another estimation is that it is 6000 years old, based on radiocarbon dates as a direct calibration point to get mutation rates. These have also been supported by other mutation rates using *Mycobacterium tuberculosis* genomes from late eighteenth and early nineteenth centuries (Sabin et al., 2020. p. 2). Based on the mummified remains of Bishop Peder Winstrup and the aDNA samples collected, Sabin et al. (2020. p. 9f) states that the *tuberculosis* genome cannot be older than the Neolithic. Sebastien Gagneux (2012. p. 852) discusses a study (Kappelman et al., 2008) that found skeletal changes possibly due to tuberculosis in a 500 000-year-old fossil of a *Homo erectus*. This finding has been questioned, but it does raise some questions regarding the actual age of tuberculosis. In a response to this article, Roberts, Pfister & Mays (2009) concludes that the case presented by Kappelman et al. (2008) is most likely not caused by tuberculosis.

During the middle ages, tuberculosis was known as the ´King's evil´, especially in England and France. It was widely believed that the illness could be cured by a royal's touch (Barberis et al., 2017. p. 10). In historic times and in records such as church books, the term for tuberculosis as the cause of death was by consumption. This covers primary lung infection and pulmonary tuberculosis (Roberts, Manchester, 2010. p. 183). One can however not assume that all cases of consumption were caused by tuberculosis. Since the visible symptoms of breathlessness and coughing up blood could be caused by other lung affecting diseases (Roberts, Manchester, 2010. p. 183). The terminology of phthisis and consumptions was used until mid-nineteenth century when the term tuberculosis was coined by Johann Lukas Schönlein. During the nineteenth century, there was a large debate regarding the origin and what caused the disease. In southern Europe it was believed to be an infectious disease. In Norther Europe, a hereditary one or a form of cancer (Barberis et al., 2017. p. 10). The discussion also included if the diseases scrofula, tubercles and phthisis was in fact the same one.

The first cures based on scientific research against tuberculosis were developed in the 1880s. After the discovery of the *mycobacterium tuberculosis* bacillus, there was a rapid development in treatments for the disease. After establishing that the disease was infectious and curable, new laws and guidelines were established in order to control the disease (Bates, 1992. p. 1). The first successful attempt at a remedy for tuberculosis was the introduction of sanatoriums. A sanctuary of sort where the sick could rest and breath fresh air (Barberis et al., 2017. p. 11). The idea was first published by botanic student Hermann Brehmer in 1854 who himself suffered from tuberculosis. He claims to have been healed after a trip to the Himalayan Mountains. With sanatoriums, the sick were isolated and given a chance to recover in a calm and relaxing environment. By limiting the contact with family and the rest of the society, the hopes were to stop the spread.

2.1.1. Infections and spread of disease

The effect a disease can have on a community or society is very dependent on the population size. In the case of measles, if a population is fewer than 250 000 individuals the disease will cause major periodic outbreaks (Roberts, Manchester, 2010. p. 26). In a population larger than 250 000 individuals it is more likely that the infected individual dies or becomes immune due to a minor infection. Therefore, it is more efficient for the bacteria or virus to develop a latent version of the disease to make sure that the bacteria or virus does not die out after the outbreak. Any reoccurring outbreaks of the disease in smaller populations is only achieved with reintroduction from an outside source (Roberts, Manchester, 2010. p. 26). The size of the population has been proven to be very relevant in regard to mutations and active versus latent versions of tuberculosis (Gagneux, 2012. p. 855). According to Gagneux, when a society becomes larger it favours a higher virulence in the bacteria and a shorter latency period. If a society is too small, this would most likely eliminate a large portion of the people and with them, the disease (Gagneux, 2012. p. 855). With the urbanisation and development of cities during most part of the last 2000 years, tuberculosis has developed with this expansion. In tests made with both ancient and modern strings of tuberculosis, the modern version shows signs of being much more aggressive and viral (Gagneux, 2012. p. 855). This fits with the Ecological theory presented by Gagneux (2012. p .855) that larger groups of people triggers the bacteria or virus to change its potency and tendency to lay latent in its host.

When analysing an excavated material, one must keep in mind that it is most likely not representative of the living community. It is very unlikely that the entire cemetery is excavated

at the same time (Roberts, Manchester, 2010. p. 28). This could lead to large parts of the material not being prioritised, destroyed or missing after a long time in storage. Without extensive documentation, we cannot assume that the entire population is buried in the same cemetery either. It is also unlikely that no one from another population is buried there (Roberts, Manchester, 2010. p. 28). Origin can be analysed with the use of strontium analysis, this does however, not guarantee a specific location, but it can tell if someone is not a local (Roberts, Manchester, 2010. p. 28).

During the middle ages, laws regarding who was allowed to be buried in a cemetery was very strict. The examples that follow are from Swedish medieval law. However, similar laws or tradition are very likely to exist elsewhere. Only those who died a "good" death, according to the church, would be allowed to be buried in a cemetery. Those that were executed or committed suicide were not allowed to be buried in consecrated grounds (Fendin et al., 2009. p. 42). This resulted in a part of the population being excluded from the communal burial ground. Another displacement in Christian burial grounds were with unbaptised children. They are often found outside the cemetery, in the walls surrounding the cemetery or hidden under floors. Then there are those that choose to be buried elsewhere (Roberts, Manchester, 2010. p. 28). This creates an inconsistency in the burial context, it makes investigating disease on a population level somewhat troubling when part of the population is missing from the start. Based on stereotypical beliefs, most that were executed belonged to a lower socioeconomical status. This can in some cases be investigated by the means of the execution. Those beheaded with a sword was considered to be of a higher status than those that got beheaded with an axe. The different weapons used leave distinct markings on the bones (Fendin et al., 2009. p. 89). Giving us somewhat of an indication of the socioeconomical status of the individual. There is another problem here as well, that we cannot draw any conclusions regarding the populations health by only looking at a small number of individuals without their context (Roberts, Manchester, 2010. p. 28). Where in the cemetery the sample is taken from is also a factor. Specific sections for male, females, children and poor versus wealthy affects the analysed sample significantly (Roberts, Manchester, 2010. p. 30). In locations such as a monastery, battleground or a ship wreak (containing soldiers) are more likely to compose of a large quantity of males. Therefor creating a sex bias in the result.

The way a disease can spread varies greatly. The tuberculosis bacteria can spread in a few different ways. From human to human, the disease spreads via droplets in coughs, sneezes and saliva (Waldron, 2009. p. 90f, Roberts, Manchester, 2010. p. 187, Roberts, 2011. p. 435, Larsen,

2015. p. 103). This could also be the case for *M. bovis* in cases where farmers and caretakers came in close contact with the cattle. The spread of the disease from animal to human can also come from unpasteurized milk or infected meat (Lewis, 2007. p. 103, Waldron, 2009. p. 92f, Roberts, Manchester, 2010. p. 185f, Müller, Roberts & Brown, 2014. p. 178f, Larsen, 2015. p. 103). In a study done between the years 1958 and 1962, a researcher tested the hypothesis that tuberculosis was an airborne disease. At a tuberculosis ward in Baltimore, United States, a group of guinea pigs were placed in connection to the ventilation system (Dharmadhikari, Nardell, 2009. p. 9). The idea was that the air breathed by the tuberculosis infected patients would travel through the ventilation shafts into a space filled with guinea pigs. There were no other contact between the patients and guinea pigs. The results were clear, the guinea pigs were infected by the air (Dharmadhikari, Nardell, 2009. p. 9).

The ideal environment for the tuberculosis bacilli to spread is in small, crowded spaces with poor ventilation containing individuals with compromised immune system (Waldron, 2009. p. 91). The environments people lived in during early cities and the urbanisation caused by the industrial revolution was ideal for this. The initial infection of tuberculosis can be upon first contact. However, the symptoms might never appear, or they start to develop years after initial contact. Other diseases such as lepra and syphilis spread very differently. To become infected with lepra, one must be in direct contact with someone infected frequently. Like tuberculosis, lepra also takes a very long time for the symptoms to develop. All three of these diseases can only be seen in the bones after a very long time but they have been very common throughout history, with syphilis being the last one to spread in Europe.

2.1.2. The tuberculosis complex and how it affects the body

Today we know of 5 forms of the tuberculosis complex that can affect humans (table 2). There are other mycobacterium complexes that affect humans but are regarded as their own disease (Roberts, Buikstra, 2003. p. 6). It was not until the last 150 years that researchers began to fully understand the disease. In 1882, the first isolation of the tubercle bacillus was presented by Robert Koch. He managed to identify, isolate and cultivate the bacillus and later tested it on laboratory animals. This became the first major step in the fight against tuberculosis. He later won a Nobel prize in medicine in 1905 for his contributions (Barberis et al., 2017. p. 11).

Table 2. The Mycobacterium tuberculosis complex and what species they affect (Stone et al., 2009. p. 66f, Roberts, Buikstra, 2019. p. 322).

Part of the tuberculosis complex	Affects	Human as secondary host
Mycobacterium tuberculosis	Humans	no
Mycobacterium bovis	Domesticated and wild mammals	yes
Mycobacterium africanum	Humans in specific parts of Africa	no
Mycobacterium canetti	Humans	no
Mycobacterium caprae	Goats	yes
Mycobacterium pinnipedii	Seals and sea lions	very rare
Mycobacterium microti	Voles, hyrax and llamas	very rare
Mycobacterium mungi	Banded mongoose in Botswana	very rare

Primary tuberculosis appears when an individual is infected for the first time, often in childhood. The initial trace of tuberculosis activates the bodies response. If the host is strong and the immune system is well developed, it contains the bacteria and heals the lesions this caused the lungs or intestines. As a result, it inactivates the bacteria, which is the expected response in 90% of infected cases (Waldron, 2009. p. 90f, Roberts, 2011. p. 435). If the body is in other ways compromised or if the immune system is not functioning properly, the person dies without much trace on the bones (Roberts, 2011. p. 435). The bacteria can later be activated if the host becomes weak, if the immune system is compromised or if the host is infected again (Waldron, 2009. p. 91, Roberts, Manchester, 2010. p. 187). Also called secondary tuberculosis, and this causes the skeletal changes used for diagnosing the disease.

If the immune system is weak, the bacteria can spread rather rapidly through the body. After a successful infection, the bacteria spreads through the circulatory and lymphatic systems, and can grow in both organs and bones, affecting a large part of the body. If the disease is spread through droplets and enters the body through the lung, it is the most severely affected organ and the surrounding bones, ribs and spine, could show traces of this. If the disease is not treated or the host is too weak, the disease spreads through the bloodstream and settles in bones and other organs, causing permanent and semi-permanent changes to the structure and integrity of the bones and joints.

Today, one third of the world's population carries the tuberculosis bacteria. Of these, 5-15% carry an active and destructive version of tuberculosis. Of those with active tuberculosis, up to 7% develop the skeletal changes that can be used to diagnose an individual based on their skeleton. Depending on the path the tuberculosis spreads through the body it can manifest itself in the skeleton in three different ways: the most common type which occurs in more than 50 % of the skeletally diagnosed cases are spinal tuberculosis or tuberculosis spondylitis also known

as Pott´s disease (Spekker et al., 2018. p. 344). The other two are: tuberculosis osteomyelitis that affects the non-spinal bones and tuberculosis arthritis affecting the non-spinal joints (Spekker et al., 2018. p. 344). In the book *Palaeopathology* (2009. p. 95), Waldron has created a small box for each pathology where he lists the diagnostic traits. A modified version of this can be found on page 21. When addressing the extra-spinal bones in regard to an active tuberculosis, there needs to be destructive changes on the bone with no signs of the body creating new bone to heal itself and for the changes not to be evenly affecting elements and sides (Waldron, 2009. p. 95).

Tuberculosis can manifest itself on any organ in the human body, the pulmonary form becomes the most infectious one due to its formation in lung cavities (Gagneux, 2012. p. 852). By infecting the lung tissue, it becomes a location for bacteria to multiply and to have an easy path to other hosts. On the other hand, we have the extra-pulmonary versions of tuberculosis that seem to be less infectious in comparison. This makes the extra-pulmonary tuberculosis less of a public health priority. Children are believed to be particularly susceptible to the bovine form due to their consumption of cow's milk for infant feeding (Lewis, 2007. p. 149). This becomes particularly fatal in the first 2-3 years of life. Tuberculosis can be passed on from child to mother through breastmilk, it can also spread from mother to foetus, this does often result in miscarriages, stillbirths or causing the child to die shortly after birth (Lewis, 2007. p. 146).

The different elements are listed below with more specific pathological changes. Most of the terminology is based on White, Black & Folkens book *Human Osteology* (2012).

2.1.2.1. Ankle and tarsal bones

The tibiotalar joint is more commonly affected than the talocalcaneal joint. Similar to the hip and knee joints, this kind of lesion most commonly affects children. The talus bone is more commonly affected, the distal tibia is less common, and the distal fibula is rarely affected (Roberts, Buikstra, 2019. p. 337f). If the area begins to heal, there is a very high risk of ankylosis to occur (Roberts, Buikstra, 2019. p. 338). The epiphysial part of the bone could begin to swell and the spongious bone becomes unstable. Due to the weight bearing nature of the ankle, this can result in structural changes of the bones involved.

2.1.2.2. Bones of the hands and feet

One of the characteristics of childhood tuberculosis is the expansion of the tubular bones in the hands and feet. Tuberculous dactylitis also known as spina ventosa creates a blown-up appearance of the tubular bones. Magilton et al. (2008. p. 221) describes it as to have an eggshell like effect. In one study, 15% of those with skeletal tuberculosis showed evidence of these changes (Roberts, Buikstra, 2019. p. 339). Another estimation suggest that it occurs in 0,6%-6% of cases with skeletal tuberculosis in children (Magilton et al., 2008. p. 222). They also found that these changes rarely occur after the age of 10. If the individual survives the tuberculosis, these changes could disappear with age (Roberts, Buikstra, 2019. p. 339).

2.1.2.3. Calcified Pleura

A trait that might be hard to distinguish is what is the remnants after calcification of pleura, a membrane that surrounds the lungs (Arcini, 2003. p. 108, Roberts, Manchester, 2010. p. 191). A trained archaeologist or osteologist is required to anticipate the possible presence of calcified tissues and other rarities during excavation in order to locate them. The most time efficient technique is to save the soil surrounding and underneath the ribs, spine, abdomen and pelvis to ensure that minor calcified items are saved and can be processed later during cleaning. The shape, form and size of the pleura can vary, it is often irregular and has got a combination of smooth and sharp parts, depending on the location in relation to the lung. Other reasons calcified pleura might be present are caused by neoplasia and congestive heart failure (Valdés et al., 1996. p. 158). Example image of calcified pleura can be seen in figure 3 & 4.

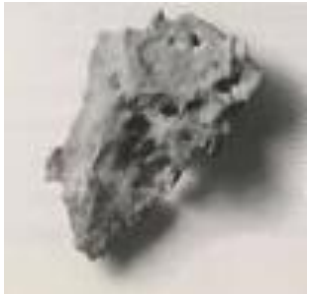

Figure 3. Example of calcified pleura. Image from (Arcini, 2003. p. 109) . Picture taken by Staffan Hyll. Published with permission from author.

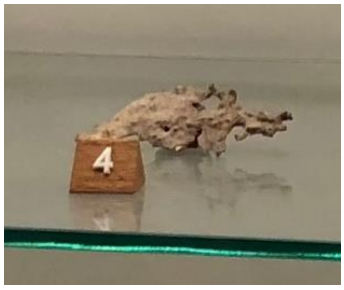

Figure 4. Example of calcified pleura. On display at Æbelholt museum in Denmark. Published with permission from museum.

To be aware of the presence of other materials possibly present during excavation is not only important for calcified pleura but also for kidney stones, urinary stones, shells or other traces of worms or parasites in the intestines. As well as calcified arteries of the brain and heart (Arcini, 2003. p. 92). Even though the excavation process is done correctly and by professionals, it is not guaranteed that these things will be found even though they were present during burial.

2.1.2.4. Cranium

Some skeletal changes due to tuberculosis can manifest itself on the cranium. In some individuals this occurs on the mandibula and some on the calvarium. One example made by Haagen and Lynnerup (2019. p. 76ff), shows what they call "moth-eaten" irregular margins on a hole located over the lambdoid suture. This change causes an acute situation where the brain becomes exposed. Another kind of skeletal change are calcified plaques on the inside of the cranium (Lewis, 2007. p. 143). The direct cause of these changes is believed to be meningitis. Some theories suggest that the tuberculosis bacteria targets the meninges and the infection it causes is likely to kill the individual. This most often occurs during primary infection and therefor most often affects children. If the child survives the infection, it can cause blindness, deafness and mental retardation (Lewis, 2007. p. 147f). The skeletal manifestations of meningitis are however not a definitive sign of tuberculosis.

2.1.2.5. Elbow

Of the upper extremities, the elbow is the most affected joint, it mostly occurs in children and young adults. The distal end of humerus is the mostly affected, followed by proximal ulna and lastly proximal radius (Roberts, Buikstra, 2019. p. 340). With severe and long-standing tuberculosis, all three joints could be affected. Active tuberculosis manifests in a very deteriorating way. If the joint is given a chance to heal, all three elements are likely to fuse as the body tries to heal itself, a fusion would leave the joint unmovable.

2.1.2.6. Hip

The hip joint is the second most affected part of the body after the spine (Lewis, 2007. p. 147, Roberts, Buikstra, 2019. p. 332). The changes are however almost always develop during childhood and rarely appears for the first time in those over 25 years old. Due to the anatomy of the hip joint, it is easy access for the bacteria to develop and settle there (Roberts, Buikstra,

2019. p. 333). The breakdown of the joint affects the acetabulum, femoral head and both the left- and right-hand side. The result can end in the complete dissolving of acetabulum forcing the femoral head to find a new point on the iliac wing (Roberts, Buikstra, 2019. p. 333f). In some cases, the destruction of the acetabulum is so severe that it disintegrates completely, leaving only a gaping hole in the medial aspect of the pelvis (Roberts, Buikstra, 2019. p. 335). Erosive changes to the femoral head to the point of complete destruction is rarely seen and then only in infants with septic arthritis as well. Other areas of the pelvis that can be affected by tuberculosis is the sacroiliac joint, it is often observed in young adults rather than children (Roberts, Buikstra, 2019. p. 334ff).

2.1.2.7. Knee

The knee is affected almost as often as the hip. Like the hip, the palaeopathological changes in the knee mostly appears in childhood and adolescence (Lewis, 2007. p. 147). The tuberculosis can manifest itself in all three parts of the knee: distal femur, proximal tibia and posterior side of the patella. If left untreated the knee can, like the vertebral bodies, disintegrate to the point of a collapse (figure 5). The result could become an unmovable joint where the once smooth surfaces have been replaced with osteophytes (Arcini, 2003. p. 109).

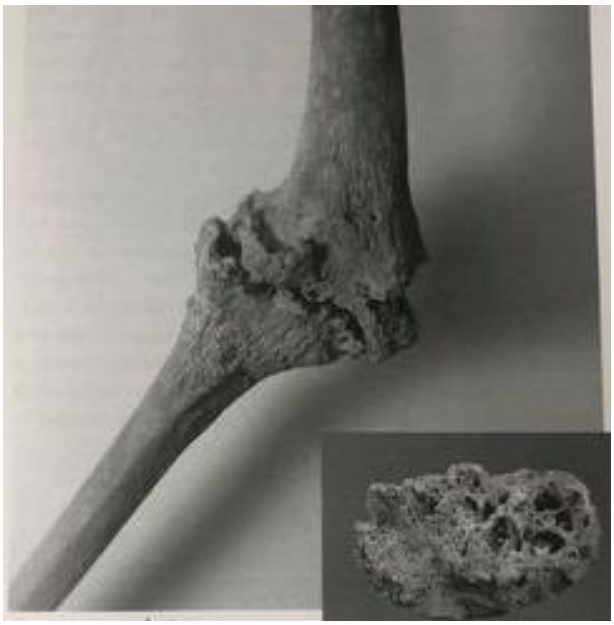

Figure 5. Example of skeletal changes to the knee due to tuberculosis. Smaller image is a detailed view of the joint surface. Image from (Arcini, 2003. p. 109). Picture taken by Staffan Hyll. Published with permission from author.

2.1.2.8. Ribs

One manifestation of tuberculosis in the skeleton is calcification on the medial part of the ribs (Waldron, 2009. p. 94f, Roberts, Manchester, 2010. p. 190f, Larsen, 2015. p. 103ff). One estimation suggests that the ribs are involved in approximately 5% of cases with skeletal tuberculosis (Davidson M.D., Horowitz M.D., 1970. p. 78, Roberts, Buikstra, 2003. p. 101). Mays, Fysh & Taylor (2002. p. 27) estimates skeletal change in ribs to be involved in 1-8% of cases with skeletal tuberculosis. Roberts et al. (1998. p. 57) refers to various studies that contain skeletal changes on ribs and they vary from 1.4% to 22.9%. The ribs in direct contact with the lungs are the most likely to become affected. The ribs in the middle (5-8) are more likely to become calcified than 1-4 and 9-12 (Roberts, Buikstra, 2003. p. 88, Roberts, Buikstra, 2019. p. 344). As stated by Roberts and Buikstra (2019. p. 344), research on modern documented individuals known to have died from tuberculosis, results in the conclusion that rib involvement is more likely to occur in people with tuberculosis than for any other pulmonary disease. However, other diseases that could cause similar changes are pleurisy, pneumonia and bronchiectasis (Magilton et al., 2008. p. 222). The result of the calcification is a chalky residue that builds on the bones as well as erosive changes to the structure of the bone, which primarily affects the part of the rib facing the lungs. Many believe that the pathological changes to the medial part of the ribs is non-specific and can therefore not be used as a guarantee for tuberculosis (Lewis, 2007. p. 149).

2.1.2.9. Shoulder

Tuberculosis in the shoulder is much more uncommon than hips and knees. In one study, only 4.7% of those affected with skeletal tuberculosis developed changes in the shoulder (Roberts, Buikstra, 2019. p. 339). The palaeopathological change to the shoulder can appear in any age, however, it is more common in adults than children. The skeletal change is biased towards males and three times more likely to affect the right side than left. The proximal end of humerus is mostly affected, very rarely does the tuberculosis affect the scapula. Shoulder tuberculosis is more likely to heal in children than adult, it is common in affected adults that the humeral head and the glenoid fossa are destroyed (Roberts, Buikstra, 2019. p. 339). An untreated tuberculosis can cause a hollow like effect on the humeral head.

2.1.2.10. Spine

The most common skeletal change caused by tuberculosis affects the spine and is called vertebral tuberculosis, tuberculosis spondylitis or Pott´s disease. In the spine, the tuberculosis bacteria attacks the vertebral body and causes it to weaken to the point of collapse. This results in a kyphosis, which is named Pott´s disease or Pott´s gibbus (Roberts, Buikstra, 2003. p. 92, Stone et al., 2009. p. 69, Roberts, Buikstra, 2019. p. 330). An example of this can be seen in figure 6, 7 and 8. The kyphosis is named after Sir Percival Pott, a surgeon in London who described the condition in 1779 (Roberts, Manchester, 2010. p. 189f). The development of Pott´s disease is common during childhood (Lewis, 2007. p. 147). All three parts of the spine, cervical, thoracic and lumbar, can be affected. Depending on the placement of the collapse, it can lead to some serious consequences. The most frequently affected part of the spine is the lower thoracic and lumbar, the first lumbar being the most affected and one to four vertebrae are usually involved (Roberts, Buikstra, 2003. p. 92, Roberts, Manchester, 2010. p. 188f, Roberts, Buikstra, 2019. p. 327). A kyphosis in the lower part of the spine could affect the bladder, intestine and digestive system and result in weakness of limbs and paralysis (Roberts, Manchester, 2010. p. 189f). A kyphosis in thoracic could affect most of the organs in the abdomen depending on the placement, a kyphosis in the first few cervical and thoracic vertebrae could affect the lungs, heart or breathing, possibly leading to death. If the individual survived the collapse, the body would start to repair itself by covering the damaged bones with new bones. An example of this can be seen in figure 6. The vertebrae are left with a wedge-shaped body and the vertebral foramen and lamina are left mostly unaffected (figure 7 & 8).

Figure 6. Picture of Pott´s disease. Kyphosis of L3-4. Specimen from Æbelholt museum, Denmark. Published with permission from museum. Picture taken by author.

Figure 8. Example of new bone surrounding a vertebrae collapse. The affected vertebrae in this case were thoracal 11 and 12. This individual comes from S:t Jakob's monastery in Lund. Image from (Andersson, 2019. p. 19)

Figure 7. Example of wedge-shaped vertebral body. This individual comes from S:t Jakob´s monastery in Lund. Image from (Andersson, 2019. p. 19)

2.1.2.11. Wrist and carpal bones

Out of all of the joints in the wrist, the radiocarpal, intercarpal and carpometacarpal are the ones that becomes affected by tuberculosis most often. The actual manifestation of the disease varies between age groups. The carpometacarpal joint is mostly affected in childhood and the radiocarpal joint is spared. In adults, the process originates from the radiocarpal joint and can spread rapidly to the others (Roberts, Buikstra, 2019. p. 340).

2.1.3. Skeletal changes required to diagnose

In *Tuberculosis in England* (2002), Charlotte Roberts states that without the skeletal changes of Pott´s disease, possible joint and non-specific bone changes are not enough to diagnose a skeletal material (Roberts, 2002. p. 102). However, the presence of rib periostitis could be seen as a possible indicator, although it is not certain enough to base the diagnosis solely on this (Roberts, 2002. p. 103). Further, Roberts discusses the possibility that hypertrophic pulmonary osteoarthropathy (a combination of periostitis, thickening of the distal part of the diaphysis and arthropathy, in the larger joints (Kumari et al., 2018. p. 2)) and endocranial new bone formation could be caused by tuberculosis. In the book *Palaeopathology*, Waldon (2009. p. 95) lists some requirements for diagnosing skeletal tuberculosis. Below is a modified version of that.

Operational definition for tuberculosis

Spinal: Erosive changes predominantly affecting the vertebral bodies with the vertebral foramen intact in combination with no new bone formation.

There may be stiffness in joints with possible fusion, vertebral collapse and kyphosis of the vertebrae.

Extra-spinal: Single location erosive changes with no new bone formation.

Dactylitis: Cystic expansion in the joints of the fingers with swelling, loss of bone but no new replacing bone.

Figure 9. Modified version of Operational definition for tuberculosis from Palaeopathology by Waldron. A list of requirements to diagnose tuberculosis both spinal and extra-spinal.

2.2. Mummified remains

The definition of mummies are the complete or partial preservation of soft tissue, including skin, organs, muscles and ligaments (Lynnerup, 2019. p. 799). There are two kinds of mummification processes: natural and artificial. The natural process occurs when the remains, both human and animal, are exposed to extreme cold or heat, dry climate, a climate low in oxygen or a large quantity of a material that absorbs/draws fluids like salt (Lynnerup, 2012. p. 1, Lynnerup, 2019. p. 799). The artificial process is mimicking or copying these processes, which can be done by removing the organs and drying them separately. The body is then treated with chemicals (Lynnerup, 2012. p. 1f). These processes can affect both the soft tissue and bones in various ways. The skin changes colour due during this process, the organs can shrink or change form completely and some organs are removed during the mummification process. A well-preserved mummy can hold a lot of information such as tattoos, scars, traces of pathologies, trauma or pathogen DNA (Lynnerup, 2012. p. 2f). When studying tuberculosis, the lungs are some of the most informative parts. Tuberculosis can be diagnosed from the lung tissue and any surviving organic materials could be suitable for aDNA testing (Lynnerup, 2012. p. 4f). The negative aspect of studying mummies as an osteologist is the very limited access to the bones. Mummies excavated today are being taken care of in a very different ways than those excavated 100 years ago. If the mummies are intact, the only way to see the bones are with radiographic scans.

2.3. Previous research

The first documents describing tuberculosis originates from India and were written 1300 BCE. Followed by a document from China, written in 300 BCE (Barberis et al., 2017. p. 9). In Ancient Greece, Hippocrates described Phthisis, the then known name for tuberculosis, accurately when compared with today's standard (Roberts, Buikstra, 2003. p. 8, Barberis et al., 2017. p .9). He highlighted the fatality regarding young adults and the effect it had on the body (Barberis et al., 2017. p. 9). Tuberculosis was discovered and discussed in Greece by Isocrates and Aristotle and in the Roman empire by Celso, Aretaeus of Cappadocia and Caelius Aurelianus around the same time (Barberis et al., 2017. p. 10).

Prior to the development of techniques and methods such as DNA, tuberculosis was studied solely based on skeletal changes. When a skeletal sample with changes consistent with the traditional approach was found, it was analysed and published as a case find. Only the presence of Pott´s disease was considered to be sufficient for a diagnosis.

One of the first Swedish researchers who identified tuberculosis in human skeletal remains was Carl Magnus Fürst (Fürst, 1920. p. 19, Fürst, 1922. p. 29, Henschen, 1962. p. 99, Ahlström, Arcini, 2012. p. 3f). In 1920 he published a report from an excavation of Vreta monastery in the province of Östergötland. In this material, he found an eight-year-old child with spinal tuberculosis in the lumbar vertebral (Fürst, 1920. p. 19, Fürst, 1922. p. 29, Henschen, 1962. p. 100). This child is believed to have belonged to the oldest Swedish royal line, the *Stenkilska* family. Due to its placement in the church, perhaps this was the last male heir (Henschen, 1962. p. 99).

In the book *Sjukdomarnas historia och geografi*, Henschen (1962. p. 97ff) discusses how tuberculosis has been viewed in the past. One important belief regarding tuberculosis in the past was that it was hereditary (Henschen, 1962. p. 98). This fact was established by Greek and Roman physicians and was common knowledge amongst scholars for a very long time. The fact that it was hereditary was often used as an argument to impose hierarchies and social classes on society (Henschen, 1962. p. 98). Henschen further discusses the impact tuberculosis has had on the Scandinavian royal households. In the oldest Norwegian history, there are tails of an old king named *Inge Krokrygg* (Inge Bent Stine) who died in 1161. His name could indicate a healed tuberculosis which gave him his characteristic appearance (Henschen, 1962. p. 99). Another story includes one of the noble men under *Knud den Store* (Canute The Great) who

died after a long-time struggle with a damaged lung in 1086. A third story regards king Oscar I who lost two of his sons after he hired a teacher for them who later died of the disease. A surviving son and the succeeding king, Oscar II struggled for the rest of his life with chronic pulmonary tuberculosis.

Møller-Christensen (1982. Ch. 5) refers to five findings of tuberculosis: three cases of Pott´s disease and two cases of calcified pleura, in the material from Æbelholt monastery in Denmark. A large amount of the graves found at Æbelholt show signs of trauma or illness, some of them are in display in the local museum. Two of the findings of tuberculosis are of men around 40 years of age. Examples can be found in figure 6 & 10. One man displayed the traditionally characteristic trait of Pott´s disease from vertebrae thoracic 9 to lumbar 3. During excavation, they found remnants of buckles that the excavators believed to have belonged to a girdle like structure that supported the weakened muscles of the back (Møller-Christensen, 1982. Ch. 5). He was buried in a coffin in the frat yard and is therefore believed to have been a member of the monastic family and perhaps one of the caregivers (Møller-Christensen, 1982. Ch 5). The spine of this individual can be seen in figure 10. Figure 6 is an example of what a healed and not so severe Pott´s disease can look like from the Æbelholt material.

Figure 10. Extreme kyphosis (Pott´s disease) of thoracic and lumbar vertebrae. On display in Æbelholt museum, Denmark. Published with permission from museum. Picture taken by author.

An extensive work on tuberculosis was done by Roberts & Buikstra in *Bioarchaeology of tuberculosis* (2003). The book covers the physical aspects of the disease as well as the social, political and psychological aspects. Roberts & Buikstra also discusses the impact tuberculosis has got on us as individuals and who is most likely to become affected (Roberts, Buikstra, 2003. p. 44ff). In chapters discussing age, sex and ethnicity the authors address the biases the disease shows with males and those in age groups 15-30 and 60+ with children being the most affected group (Roberts, Buikstra, 2003. p. 45ff). The book applies to both modern and historic cases.

One of the sources that indicates that tuberculosis was common infection was the church books (Arcini, 2008. p. 88). Some provide a lot of information regarding not only cause of death but also symptoms, family relations and living conditions. All of this varied in degree of information depending on the knowledge and interest of the priest who wrote it down. In an article written by Arcini (2008. p. 88f) she discusses this problematic situation when she studies

a material with the church records still intact. However, this also provides a great opportunity if the individuals are identifiable. In this material, Arcini was able to diagnose one individual with Pott´s disease. Based on the church records Arcini also attempted to identify the remains of a 9-year-old child named Eva Maria whom, based on the priests' notes, died of tuberculosis (Arcini, 2008. p. 89). Arcini´s study was based on parts of a population, and she brings focus to the various diseases and pathological changes she identifies in the material.

One study of tuberculosis was done by Anna Kjellström (2012) on a material from Sigtuna, Sweden. The material originated from a cemetery belonging to an early medieval church, 227 skeletons were excavated and analysed during the process. Of these, one individual was diagnosed with tuberculosis. The individual was affected by Pott´s disease, which Kjellström used as a diagnostic feature. Extra-spinal changes occurred on both tibiae with longitudinal strides (Kjellström, 2012. p. 268). The diaphysis of fibulae was also affected with a thickening of the shaft.

One of the most well preserved Scandinavian mummified human remains belonged to Bishop Peder Winstrup. He passed away in 1679 and was buried in the Cathedral of Lund (Karsten, Manhag, 2017. p. 75ff). His remains were kept in a family crypt below the floor in the cathedral until 1833 when the cathedral was being renovated (Karsten, Manhag, 2017. p. 77). His remains were then placed in the main crypt under the cathedral and kept there until it was re-opened for scientific analyses of his grave. Countless times during his rest in the crypt, the coffin was opened and viewed by student, priests and an invited public. This cost him part of his beard (Karsten, Manhag, 2017. p. 89). When the coffin was opened in 2013, it was the last chance to analyse his remains. The coffin was to be buried in a nearby cemetery. His placement in the crypt had been ideal for the preservation of his remains. Skin, hair, clothes and most of his organs were still intact. During the extensive investigation of his remains, some calcifications of lung tissue was found still located in his lungs during a CT scan (Karsten, Manhag, 2017. p .120). These calcifications was believed to have been caused by tuberculosis or a similar disease (Karsten, Manhag, 2017. p. 115). The calcifications were removed and later tested for tuberculosis (Sabin et al., 2020). There were no other indications of tuberculosis in the rest of his remains.

Only recently with the development of DNA methods is it possible for larger samples to be tested and individuals who do not demonstrate skeletal changes have a chance at being diagnosed. This kind of research has increased in the past twenty years, with the result of it

taking up a much larger part of the discussion than before. Research with the use of aDNA has many applications, the application of aDNA in combination with mummies can provide some very interesting results (Zink et al., 2001, Konomi et al., 2002, Fletcher et al., 2003, Zink et al., 2003, Donoghue et al., 2004, Zink et al., 2004, Zink et al., 2007, Sabin et al., 2020). With a more non-destructive approach to mummified remains, aDNA become an important tool to find answers without tearing the remains apart.

3. Material and method

In this chapter, the materials used in this analysis and how they have been selected are presented. Factors that affect the analysis such as case versus population, alternative diagnoses, age and sex estimations and geographical origin are discussed.

A literary review was carried out to see how many articles found skeletal changes characteristic with tuberculosis in the bones and with the use of aDNA. Due to tuberculosis being a very well researched topic, it was impossible to cover all of the published material within this thesis. To make the available material more comprehensible and updated, materials published from the year 2000 and forward were included in the analysis. Two exceptions were made, one article from 1994 and one doctoral thesis from 1999. Further narrowing of literature was done by doing a wide searches in the following journals: International Journal of Osteoarchaeology, Journal of Osteoarchaeology and American Journal of Physical Anthropology. Keywords used: Tuberculosis, TB and Pott´s disease. The approach was a quantitative analysis of the characters used to diagnose tuberculosis in published materials. This was limited by access to libraries and published materials, not all journals and issues were open access online. Some literature available through these searches was deemed irrelevant or were using the same material as an already processed article. When possible, the original publication was used. For the literature used in previous research, bibliographies were the primary source of information. The quantitative analysis was divided into categories in both sex and age estimations to see if patterns emerged regarding specific palaeopathological changes.

Some of the articles discussed alternative diagnoses for the remains they analysed, it is a very important factor in understanding the process of diagnosing the individuals. Some diseases display very similar skeletal changes, it might not be possible to distinguish between them, an important point to make when presenting the results. That with the information provided, a diagnosis could not always be made with certainty. Some of the most common alternative

diagnoses was brucellosis, Scheuermann´s disease, echinococcosis, treponematosis, spondylitis, fungal infections and trauma.

Table 3. Number of articles using the methods/materials. Based on Appendix 9.5.

Method/material	Number of articles
Skeletal	48
aDNA	22
Mummies	10

Of the processed articles, 48 used skeletal material, 10 used mummified remains and 22 diagnosed the remains with aDNA. There is some overlap in what materials the research is based on and aDNA studies were performed on both skeletal and mummified remains. More specific information can be found in appendix 9.6. The skeletal material originates from all over the world and are from the Neolithic to the year 2000 CE.

When dividing the sample into case or population, a few things were taken into consideration. The main one was the type of sample. The kind of articles that were suggested to be case articles often addressed one or a few individuals with no large discussion regarding what kind of spread the disease would have had in the population the individual originated from. In most cases, the individual presented originated from a large sample where the authors diagnosed one or several individuals with tuberculosis. This was later written as an article discussing that specific case. Those categorized as population often had a larger discussion regarding the health status of the larger community. The population group also often included a large sample that were presented with more data than in the case category. The dividing of case versus population was to see if there were different attributes, methods and socioeconomic groups addressed in the sample.

Age and sex estimations were not conducted as part of this analysis, any information regarding this is based on the original analysis. No additional age or sex estimations were conducted by the author of this thesis. To make the tables clearer, the sex estimations are presented as male, indeterminate and female. Male? And female? have been placed under male and female respectively. The original dividing of sex remains in appendix 9.6.

Table 4. All of the articles with their method, material and if the studied case or population. Based on Appendix 9.5.

Author	aDNA	Skeletal	Mummified remains	Case or population
(Andersson, 2019)	0	1	0	Population
(Anderson, 2001)	0	1	0	Case
(Arcini, 2003)	0	1	0	Population
(Arcini, 1999)	0	1	0	Population

(Arcini, 1994)	0	1	0	Case
(Arcini, 2008)	0	1	0	Case
(Arrieta, Bordach & Mendonça, 2014)	0	1	0	Case
(Bertoldi et al., 2005)	0	1	0	Case
(Bianucci et al., 2012)	1	0	0	Case
(Canci et al., 2005)	0	1	0	Case
(Dabernat, Crubézy, 2010)	0	1	0	Case
(de la Cova, 2011)	0	1	0	Case
(Donoghue et al., 2004)	1	0	1	Case
(Fletcher et al., 2003)	1	1	1	Population
(Haagen, Lynnerup, 2019)	0	1	0	Case
(Haas et al., 2000)	1	1	0	Case
(Hartzell, 2008)	0	1	0	Case
(Kjellström, 2012)	0	1	0	Case
(Konomi et al., 2002)	1	0	1	Case
(Köhler et al., 2014)	0	1	0	Case
(Lambert, 2002)	0	0	0	Case
(Larentis et al., 2020)	0	1	0	Case
(Larsen, 2015)	0	1	0	Case
(Magilton et al., 2008)	0	1	0	Population
(Mariotti et al., 2015)	0	1	0	Population
(Matos, Marques & Lopes, 2011)	0	1	0	Case
(Matos, Santos, 2006)	0	1	0	Case
(Mays, Taylor, 2003)	1	1	0	Case
(Mays, Fysh & Taylor, 2002)	1	1	0	Case
(Mays et al., 2001)	1	1	0	Case
(Molnár, Marcsik, 2002)	1	1	0	Population
(Müller, Roberts & Brown, 2014)	1	1	0	Population
(Nicklisch et al., 2012)	1	1	0	Case
(Nuorala et al., 2004)	1	1	0	Case
(Paja et al., 2012)	0	1	0	Case
(Pálfi et al., 2015)	1	1	0	Population
(Sabin et al., 2020)	1	1	1	Case
(Santos, Roberts, 2006)	0	1	0	Population
(Santos, Roberts, 2001)	0	1	0	Case
(Sparacello et al., 2017)	1	1	0	Case
(Spekker et al., 2018)	0	1	0	Case
(Spigelman, Pap & Donoghue, 2006)	1	1	0	Case
(Spigelman et al., 2002)	1	0	0	Case
(Suzuki, Fujita & Choi, 2008)	0	1	0	Case
(Suzuki, Inoue, 2007)	0	1	0	Case
(Tayles, Buckley, 2004)	0	1	0	Case
(Zink et al., 2001)	1	1	1	Population
(Zink, Grabner & Nerlich, 2005)	1	1	0	Population
(Zink et al., 2007)	1	1	0	Population
(Zink et al., 2004)	1	1	1	Population
(Zink et al., 2004)	1	1	1	Population

The materials used in this study originates from most continents, figure 11. One of the studies including specimens from the Andean mountain chain without specifying which countries (Konomi et al., 2002). Therefor South America is slightly underrepresented.

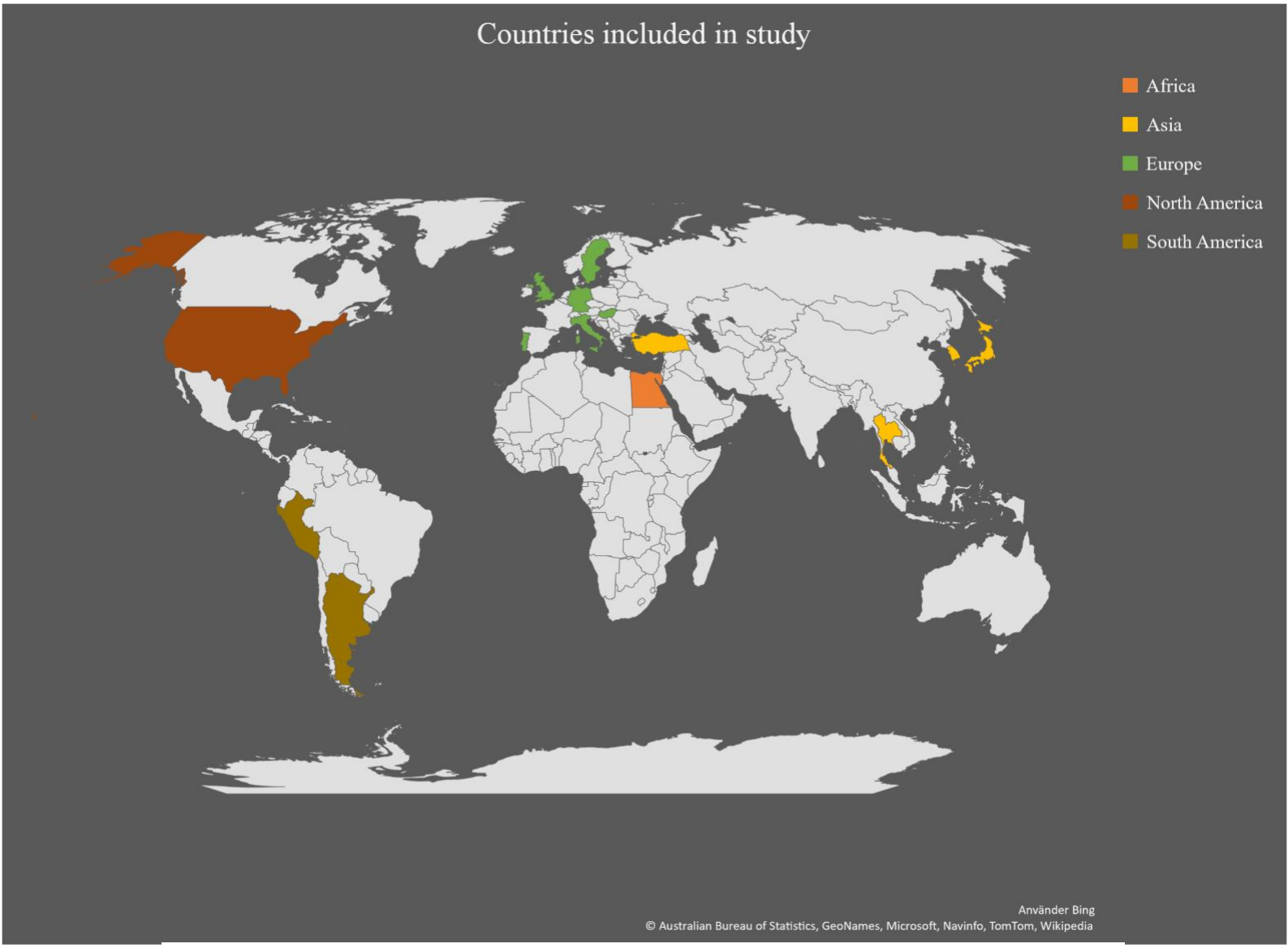

Figure 11. Map of the included countries in study. Map constructed with the use of excel. Based on appendix 9.2.

4. Theory

In this chapter, various factors that affect the remains and how we view them are presented. The Osteological Paradox is an important part of this and is presented from the perspective of what researchers needs to be aware of and how to relate to a material. As well as pros and cons with the use of aDNA to study diseases.

4.1. Osteological paradox

In 1992, a number of osteologists and anthropologists wrote a critical article to the problems they face while studying human remains (Wood et al., 1992. p. 343ff). What can we actually see in the bones? They wanted to address the issues with skeletal remains and that what is seen in the bones might not be representative of the living society (Wood et al., 1992. p. 344f). If they died of a disease, was it something that killed them in matter of days and therefor did not leave any trace on the bones. Or were they not strong enough to survive something they should have been able to if they had a better immune system. This becomes especially problematic when looking at diseases that have got the highest risks at a certain age.

One of the main parts of the osteological paradox is selective mortality (Wood et al., 1992. p. 344). This refers to the issue that those studying remains face, we only see the individual at the stage of their life when they died. We do not see those that struggled with the disease but survived miraculously or those that were at risk but somehow did not get sick. When studying younger individuals this can affect the results (Wood et al., 1992. p. 344). The majority of individuals with the disease might have survived and they no longer show skeletal changes consistent with the disease. This makes it incredibly hard to estimate the real impact the disease had on society and the community.

An individual's frailty, health and chances of survival is affected by many factors. This can also be defined as hidden heterogeneity in risks. Some are genetic composition, socioeconomical background, environmental variations, diet and cultural influences (Wood et al., 1992. p. 345). Hereditary diseases and a genetical weakness can shorten the lifespan significantly (Wood et al., 1992. p. 345). Smoke from fires, soot from chimneys, chemicals and exhausts from cars and factories, these all have a very negative impact on your health. Diet is a very well discussed subject and the impacts it has on our lives. A deficiency can leave us susceptible to some diseases and an overconsumption to others. Diet causes issues on either end of the socioeconomical spectrum. The poor and unprivileged do not have enough access to food and the rich and wealthy can overindulge. This can result in obesity, gout, calcification of arteries and veins, lung and heart disease.

If a third of those that got a certain disease died immediately without traces on the bones, one third recovered without traces of the disease and died at a much later age and one third struggled with the disease for a long time and developed skeletal changes. We would only be able to see

one third of the total spread of the disease when looking at the bones of that specific age group, it becomes very un-representative of the actual spread and impact it had on the society (Wood et al., 1992. p. 344f). To look at a skeletal material and determine the individuals and the general health of the society only by looking at their bones is troublesome and to estimate the health based on the modern qualifications is almost impossible. On an individual level it becomes hard due to the fact that we can only see the pathological changes that have affected the body for quite some time and the traumatic changes that occurred within the last years. On a population level it is even harder due to the fact we only see the individuals at their weakest point, at death. There is also the factor of demographic nonstationarity (Wood et al., 1992. p. 344), that no population remains the same throughout history. There will always be an uneven amount of births in relation to deaths in a community. This in combination with emigrations and immigrations, results in an ever-changing demography.

"*Health is a state of complete physical, mental and social well-being and not merely the absence of disease or infirmity"* (World Health Organization, a030321). As seen in this quote from World Health Organization, it is not just the physical health that matters when discussing health, the psychological and social aspects are equally important, however it is not something we can see or analyse in a skeletal material. Does this mean that we should not discuss health at all when we can only measure some parts of the requirements, and in those we can measure, we have a limited amount of knowledge about? In conclusion: the absence of evidence is not evidence of absence; it becomes very difficult to make statements and diagnosis when we cannot see the full picture. For more detail into the subject, graphs and calculations, see Wood et al. (1992).

4.2. aDNA

Not all of those who are infected with tuberculosis have symptoms. Of those carrying the disease today, approximately 85-95% have a latent and asymptomatic version (World Health Organization, 080321). The latent version of the disease does not cause bone changes until it becomes active. This could become a factor of error when interpreting results of aDNA. If the modern data (that one third of the world population is carrying tuberculosis) is appliable to societies in the past then we could discuss the existence of a disease with the aid of aDNA. If the remains of a whole town was tested with aDNA, approximately one third would provide a positive result. However, out of one third of the population, only 5-15% would have been

affected by the disease. The use of aDNA in this case would prove the existence of the disease, not the actual level of sickness in the community.

The use of aDNA as a tool to diagnose tuberculosis when the skeletal changes are not present has been discussed and tested by many. It has limitations such as cost, risk of contamination and the need for organic material to be present. It is not as easily accessible as the visual appearance of Pott´s disease. However, one of the major advantages with using aDNA, when studying pathologies, is the chance to diagnose more individuals than what is possible with skeletal changes since it takes some time for skeletal changes to occur (Donoghue et al., 2004. p. 585). With aDNA, the pathologies can be detected much sooner. It can also be used as a confirmation on a diagnosis when the skeletal material is not sufficient (Donoghue et al., 2004. p. 585). As discussed in some examples in the background section, aDNA can also be used to study the evolution of a disease (Nuorala et al., 2004. p. 3ff, Sabin et al., 2020. p. 4ff). When aDNA is applied to a larger sample, it provides us with the chance of diagnosing individuals that otherwise would have been completely overlooked.

One issue with aDNA is the risk of contamination. The aDNA molecules are unstable and gets easily affected by the environment it is surrounded by. They can get contaminated by the surrounding materials, excavators, sampling tools, investigators or other specimens. To prevent this, several steps have been taken to prevent contamination. As stated by Donoghue et al. (2004. p. 584), physical separation of activities before and after sampling, strict protocols to prevent and monitor modern DNA contamination, using negative controls and sampling in more than one laboratory. This has been a problem for a very long time, but with the development of new and better methods, most of these risks have been eliminated. The use of aDNA is today a standardised method and it is possible to differentiate between modern and aDNA. aDNA breaks at the ends of the segment while deteriorating and is therefore easily separated. By analysing the DNA, the broken segments can be used to confirm the presence of aDNA (Malmström et al., 2019. p. 2). By studying the deterioration of the aDNA, scientists can differentiate between old and new DNA.

According to Donoghue at el. (2004. p. 585) the mycobacteria is the ideal microorganism for studying aDNA and was for that reason one of the first to be discovered. The chemical composition of the mycobacteria gene increases its stability and therefor its chance at survival. The cell walls are thick and rich with lipids which protects it from enzymes that focuses on the breakdown of cells even during the necrosis of the hosts own cells (Donoghue et al., 2004.

p.585). In some cases, it is even transmittable from the diseased remains to a new host after one year of decomposition.

An aDNA sample could cost around 10000-15000 SEK per sample (personal communications with supervisor). The initial test cost a minimum of 6000 SEK per sample to analyse, this only shows if there is aDNA present and possibly the sex of the individual. The pathological analysis of aDNA could cost an additional 5000-10000 SEK. This varies between laboratories.

5. Result

Firstly, overall results are presented with focus on diagnostic traits in relation to age estimations and total amount of individuals. Lastly, the results are divided into four subcategories: frequency over time, sex estimations, age estimations and element representation.

In the process of this analysis, the author analysed 51 articles from the year 2000 until present with the exception of one from 1994 and one from 1999. Of these, 36 articles presented case studies. The remaining 15 presented either a population or are discussing their individual(s) within the population they were found. The data has been divided into diagnostic traits (figure 12 & table 5), differentiation between case and population (table 6), timelines (figure 13 & 14, focus on total number of individuals versus diagnosed individuals), sex estimations (table 6 & 7, figure 15 & 16, male, female, indeterminate and not specified), age estimations (table 6, figure 17 & 18, juvenile, adolescent, adult, mature adult, indeterminate and not specified) and element representation (table 8). The total number of individuals included in the analysed materials were 17389 and of these 868 were diagnosed with tuberculosis. This represent 5% (0.0499) of the material. There were 712 cases of skeletal changes due to tuberculosis, 717 if lymph nodes are included. Some of these belong to the same individuals. The data in figure 12 is based on the information in table 5 (below). This was made to create a visualisation of the information.

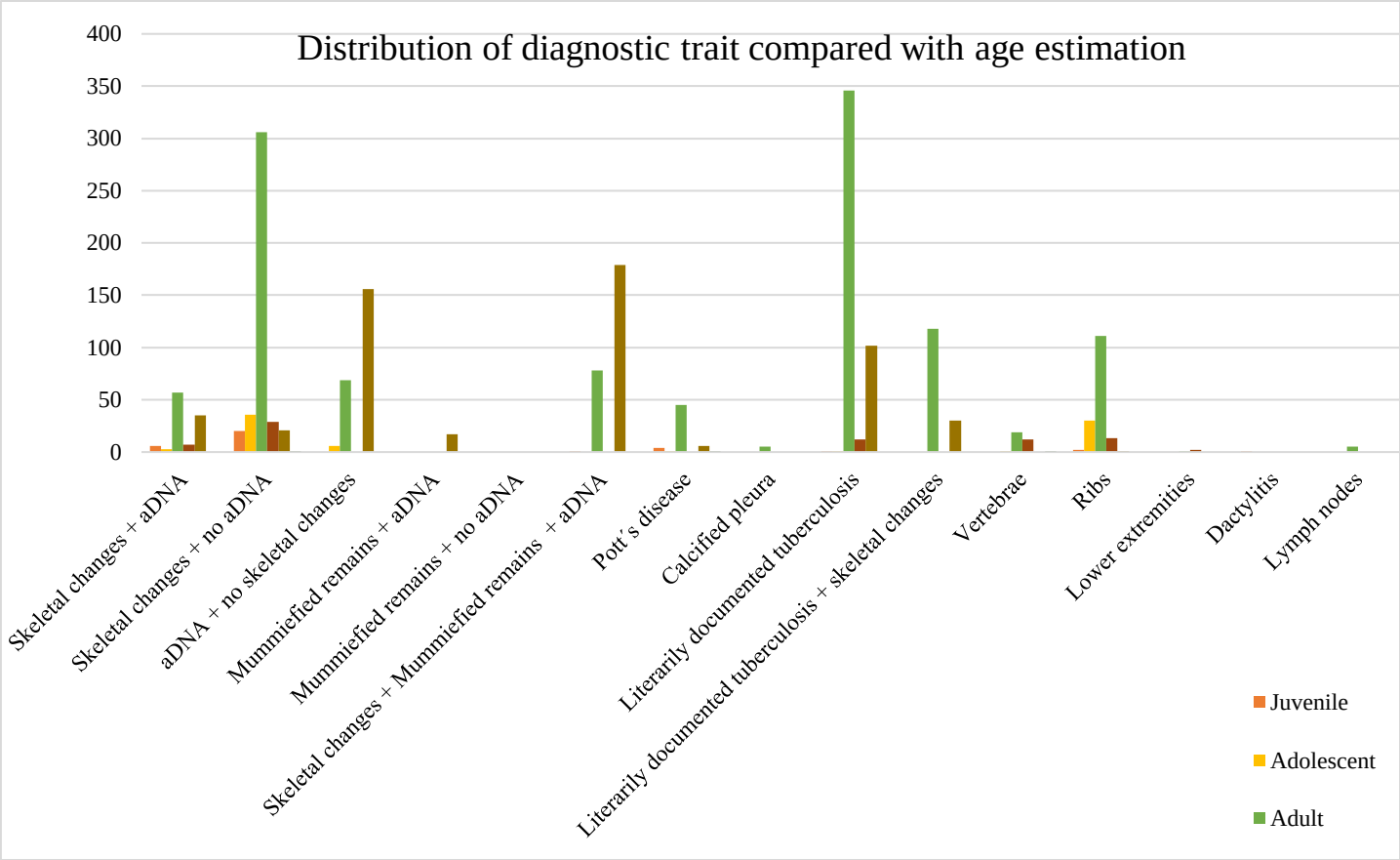

Figure 12. Distribution of diagnostic traits in relation to age estimations. A diagram of table 5.

In figure 12, the adults are the largest specified age group in every category except for dactylitis (juveniles) and lower extremities (mature adults). The group containing the largest number of individuals was the group that analysed literarily documented tuberculosis with 462 individuals. The second largest was the material composed of skeletal changes with no use of aDNA, 413 individuals. In three cases the "not specified" age group was the most prominent, in "aDNA and no recorded skeletal changes", "mummified remains and aDNA" and "skeletal changes, mummified remains and aDNA".

The category with a visible quantity of the most age groups are "skeletal changes + no aDNA", with all age groups except "indeterminate" being visible in the figure. The category with the second highest is "skeletal changes + aDNA" with "adolescent" and "indeterminate" being the only two missing. "Mummified remains + no aDNA" is the only category with no cases. It is included to demonstrate the differences between methods. Perhaps if older articles discussing mummified remains and tuberculosis had been included then there would have been some that would have fallen under this category. "calcified pleura", "lower extremities", "dactylitis" and "lymph nodes" are the skeletal changes that were the least frequent in this study. Dactylitis and

lymph nodes are used as a diagnostic trait each time they are present. Based on the results in this thesis, they do not seem to be relevant in diagnosing a large quantity of individuals and should perhaps be viewed as a rarity.

There is a large inconsistency between the groups "Literarily documented tuberculosis " and "Literarily documented tuberculosis + skeletal changes". The cases where there are both a documented tuberculosis diagnosis and skeletal changes provides the investigator with a great opportunity to see a correlation between the two. Investigating those with a documented tuberculosis diagnosis with no prominent skeletal changes provides an opportunity to investigate early signs of tuberculosis. These might be not visible or be too damaged when the more severe skeletal changes have developed. Skeletal changes on ribs used as a diagnostic trait are used slightly more often than documented tuberculosis with skeletal changes (157 compared to 148, table 5). Making the case that ribs are the most reoccurring skeletal change.

The category "aDNA + no skeletal changes" illustrated more than twice the number of individuals than the group "skeletal changes + aDNA". This provides a change for a diagnosis to be made before the skeletal changes has become too severe to be visible. aDNA is used to diagnose tuberculosis with 614 individuals.

Table 5. Distribution on type of material in relation to age estimation. Skeletal changes used as a diagnostic trait. Based on Appendix 9.6.

Age/Type of material/ Diagnostic trait	Juvenile	Adolescent	Adult	Mature adult	Not specified	Indeterminate	Total
Skeletal changes + aDNA	6	3	57	7	35	0	108
Skeletal changes + no aDNA	20	36	306	29	21	1	413
aDNA + no skeletal changes	0	6	69	0	156	0	231
Mummified remains + aDNA	0	0	0	0	17	0	17
Mummified remains + no aDNA	0	0	0	0	0	0	0
Skeletal changes+ Mummified remains + aDNA	1	0	78	0	179	0	258
Pott´s disease	4	1	45	0	6	1	57
Calcified pleura	0	0	5	0	0	0	5
Literarily documented tuberculosis	1	1	346	12	102	0	462
Literarily documented tuberculosis + skeletal changes	0	0	118	0	30	0	148
Vertebrae	0	1	19	12	0	1	33
Ribs	2	30	111	13	1	0	157

Lower extremities	0	0	1	2	0	0	3
Dactylitis	1	0	0	0	0	0	1
Lymph nodes	0	0	5	0	0	0	5

The information in table 6 is divided into case and population to demonstrate differences between the two. In most cases the population column contains the most individuals, except for the juveniles where the cases are of a much higher number. The total number of individuals included in the study is larger in the case category. However, the population category has got a higher number of tuberculosis diagnosed individuals. The cases have 246 diagnosed individuals and a total number of individuals of 10298, this represent 2.3% (0.0238) of the analysed individuals. The population category has got 622 cases of diagnosed tuberculosis and a total of 7091 individuals. This represents 8.8% (0.0877) of the total amount of cases.

Table 6. Result of age estimation, sex estimation, number of individuals diagnosed with tuberculosis and total number of individuals in study. Divided between case or population. Last row is the total amount of individuals in the study. Blank space is intentional to make a differentiation between age and sex. Based on Appendix 9.3. and 9.4.

Age / Sex/ Tuberculosis diagnosis	Case	Population
Juvenile	73	18
Adolescent	60	20
Adult	206	545
Mature Adult	32	14
Indeterminate	1	0
Not specified	24	227
Female	181	339
Indeterminate	7	45
Male	234	479
Not specified	32	234
Tuberculosis diagnosis	246	622
Number of individuals in study	10298	7091
Total number of individuals	17389	

In the case of Eleonora of Toledo (Bianucci et al., 2012) the investigation was on her remains alone and an existing record of her illness was used. In two cases, the material studied was three selected individuals from different parts of the world (Spigelman et al., 2002, Haagen, Lynnerup, 2019). One case with individuals with no contextual background is presented by Spekker et al. (2018), this differentiates from the rest of the anatomical collections. The anatomical collections over all provide a great sample for studying pathologies due to its well-preserved recorded remains. It does however often not convey facts regarding the community.

5.1. Frequency over time

To make it easier to differentiate between the different time periods they have been divided into two different figures, one prior to year 500 in figure 13 and one after year zero in figure 14. The overlap here is due to wide dating done by the authors of the analysed articles. With the use of a logarithmic scale is it possible to see a difference between the low and high quantity of both the total amount of individuals and those identified with tuberculosis.

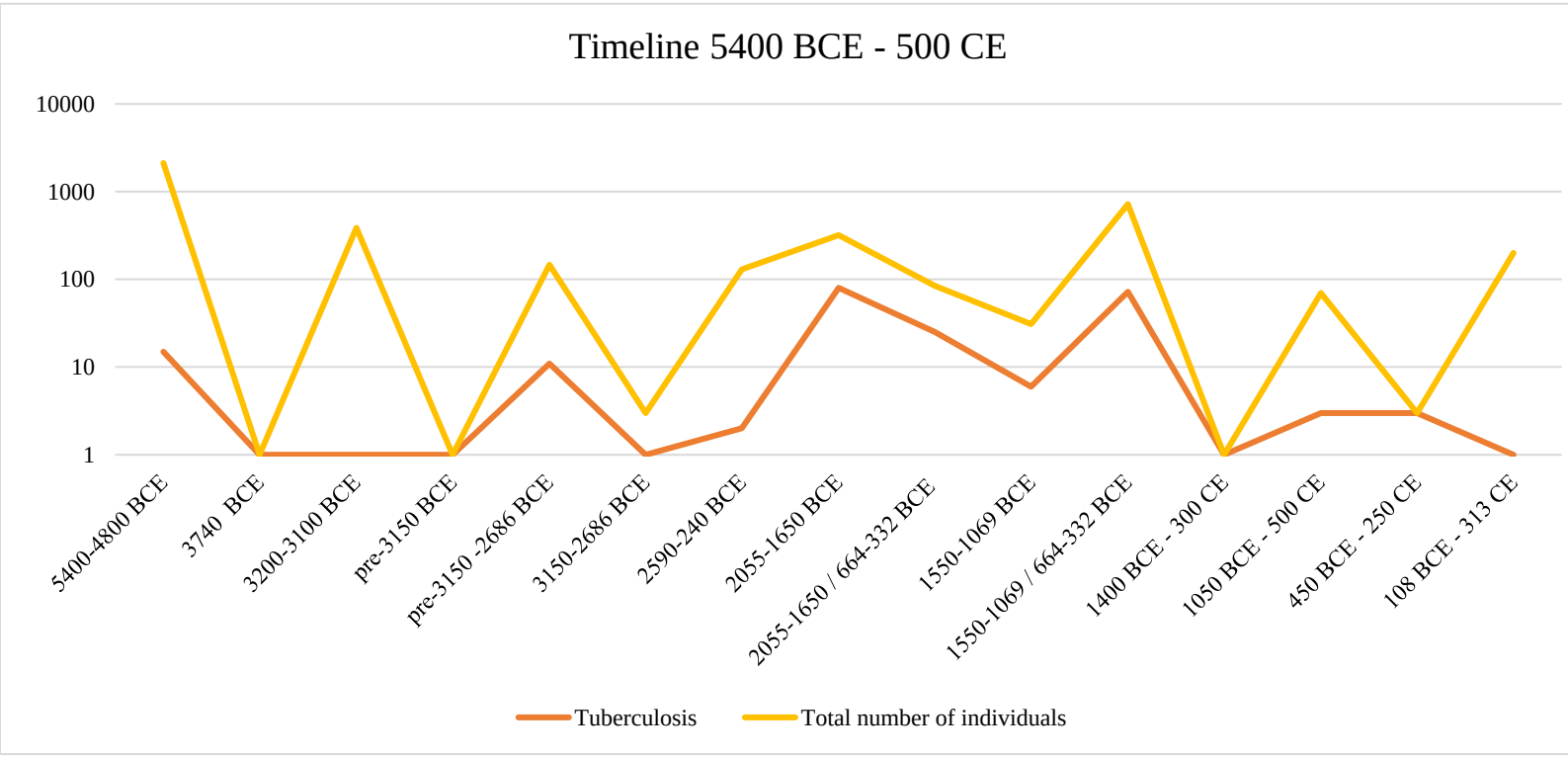

Figure 13. Logarithmic scale. 1 -10, 10-100, 100-1000, 1000- 10 000. Timeline 5400 BCE – 500 CE. Focus on relation between total number of individuals versus individuals diagnosed with tuberculosis. Based on Appendix 9.1.

In figure 13, some materials appear to have a rather large amount of positive tuberculosis. For example, "5400-4800 BCE", "pre-3150-2686 BCE", "2055-1650 BCE", "2055-1650 / 664-332 BCE" and "1550-1069 / 664-332 BCE". With "2055-1650 BCE" including 80 positive tuberculosis diagnosis of 317 total individuals being the one with the largest amount. The highest total number of individuals originate from "5400-4800 BCE" with 2118 individuals, 15 of these being diagnosed with tuberculosis.

In other materials, their number can appear to be rather insignificant. In the cases of "3200-3100 BCE", "2590-240 BCE" and "108 BCE-313 CE" there is a significant difference between the total number of individuals and those diagnosed with tuberculosis. "3200-3100 BCE" has got a total of 388 individuals but only one with tuberculosis. "2590-240 BCE" consists of 130

individuals in total with two cases of tuberculosis. “108 BCE-313 CE” consists of 200 individuals with one case of tuberculosis.

There does not appear to be any increase in frequency over time prior to year zero according to figure 13. A number of the articles used did not specify the total amount of individuals in the population or burial context. In some cases, this was because it was not possible to calculate due to extensive breakage.

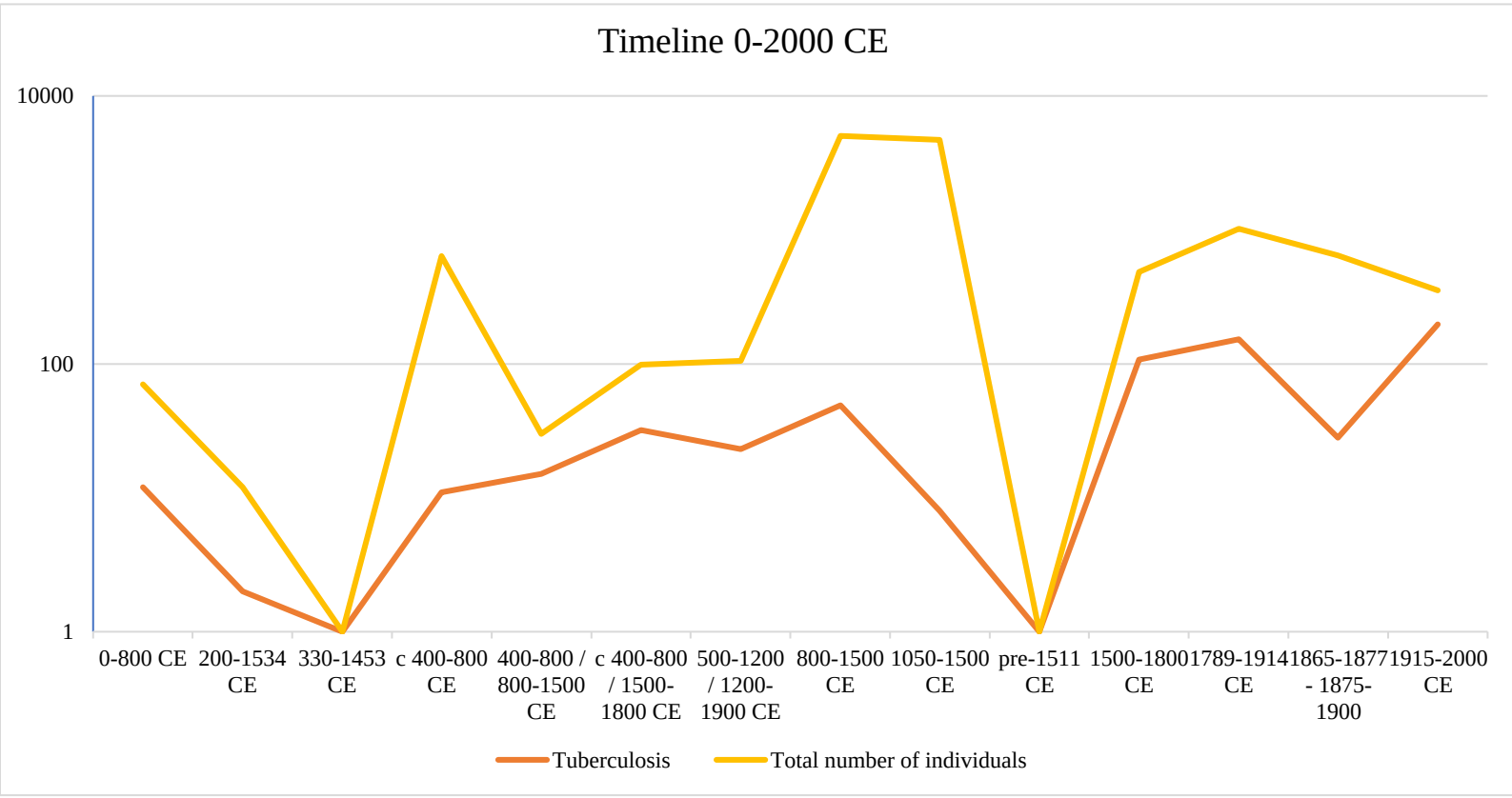

Figure 14. Timeline 0-2000 CE. Logarithmic scale. 1-100, 100-10 000. Focus on relation between total number of individuals versus individuals diagnosed with tuberculosis. The timeline is highly affected by the variation in sample size. Individuals from “800-1500” and “1050-1500” demonstrates a large sample size but very few tuberculosis cases in comparison. Based on Appendix 9.1.

The highest quantities of individuals included in the study are dated to “c 400-800 CE”, “800-1500 CE”, “1050-1500 CE”, “1500-1800 CE” and “1789-1914 CE”. The highest number of individuals diagnosed with tuberculosis can be found in “1915-2000 CE” with 197 out of 353 in total amount of individuals. If the periods that only include one individual (“330-1453 CE” and “pre-1511 CE”) is excluded, there is an increase, with some ups and downs from year zero until “1915-2000 CE”. “800-1500 CE” and “1050-1500 CE” are the two time periods that have the highest number of individuals included in the study. “800-1500 CE” containing 5028 individuals with 49 of them being diagnosed with tuberculosis, this equals 0.9% (0.009). “1050-

1500 CE" contains 4687 individuals and 8 of them being diagnosed with tuberculosis, equals 0.1% (0.001).

5.2. Sex distribution

In the sex distribution, there is an overrepresentation of males, which is consistent with Roberts & Buikstra (2003. p. 45). Even though some larger materials consist only of males (de la Cova, 2011), their amount is not sufficient enough to explain this overrepresentation of males. To see a differentiation between case and population, view table 6 above. In materials with a larger sample, there are more males than females (table 7).

In cases where it is possible, the sex distribution is based on the individuals with a positive tuberculosis diagnosis. In some cases, this was not possible since the authors did not include that information in the text (Haas et al., 2000, Santos, Roberts, 2001, Lambert, 2002, Fletcher et al., 2003, Zink, Grabner & Nerlich, 2005, Matos, Santos, 2006, Santos, Roberts, 2006, Nicklisch et al., 2012, Müller, Roberts & Brown, 2014, Mariotti et al., 2015). Some texts did not specify the sex of the involved individuals and they are placed under "not specified". Which takes up 17% of the total material (figure 15). On the other hand, there are some examples of a material with more females than males. In Santos & Roberts (2001) there is 36 females and 30 males in the material consisting of 66 individuals. In Nicklisch et al. (2012) there were 31 females and 24 males out of 118 individuals.

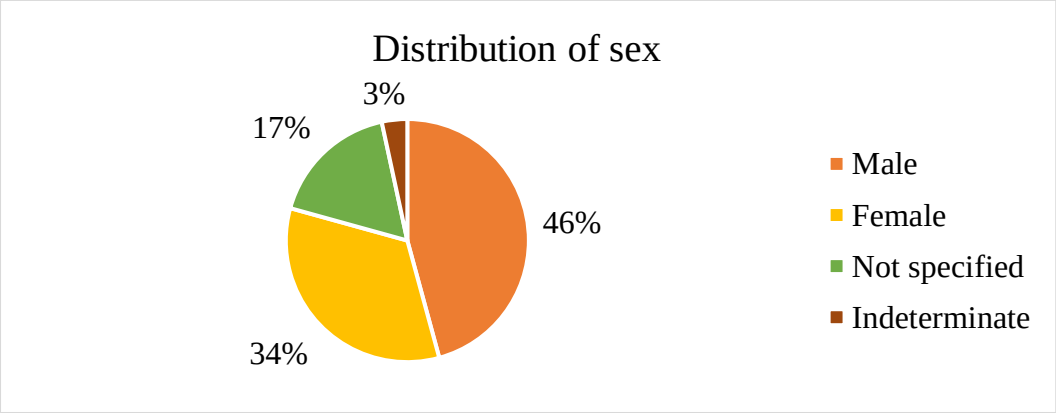

Figure 15. Total distribution of sex estimation.46% male, 34% female, 17% not specified, 3% indeterminate. Based on Appendix 9.3

There is a clear over representation of males in the results. Males represent 46% of the materials analysed while females represent 34%. As mentioned in 3. Material and Method, male? and female? have been placed under male and female respectively to visualise the figure better. 17% of the individuals are not specified to sex, this does not mean that they were impossible to

estimate, merely that the authors did not include the information in the article. 3% of the individuals in this study have been placed under "indeterminate". These individuals were not possible to provide a sex estimation for various reasons. The most common is breakage of the traits used to estimate sex or the traits being neither characteristic of male nor female. Juveniles have not been included in this section even though some juveniles have had an estimation of sex in the article based on aDNA analysis or documentation.

Table 7 shows the specific publications that contain more male individuals than female. It has been divided into male, female and total number of individuals to show the clear differences in sex distribution. This differentiation between male and female is regardless of the size of the materials. Articles of only a few individuals have not been included in this table because they are more dependent on the specific individuals than these that demonstrate a more significant pattern. Some of these do and some do not equal the total number of individuals. This can be due to some of the remaining individuals not being mentioned, consisting of juvenile or deemed as "indeterminate".

Table 7. Articles with a overrepresentation of males. Reference to article, male, female and total number of individuals included in study. Based on Appendix 9.6.

Publication	Male	Female	Total number of individuals
(Santos, Roberts, 2006)	157	106	263
(Mariotti et al., 2015)	138	106	244
(Matos, Santos, 2006)	109	88	197
(Fletcher et al., 2003)	95	70	168
(Müller, Roberts & Brown, 2014)	28	23	70
(Zink, Grabner & Nerlich, 2005)	17	6	36
(Zink, Grabner & Nerlich, 2005)	15	9	24
(Zink et al., 2001)	14	6	41

5.3. Age distribution

The age groups have been divided into larger categories to make the analysis more efficient and consistent. Juvenile represent 0-12 years, adolescent 13-18, adult 19-60, mature adult 60+ (figure 17 & 18). The largest age group was the adults. In the total analysis (figure 16), they represent 61% of the material. The second largest group were the "not specified" with 22 %. Juveniles occupy 7% of the material, adolescent take up 6% and mature adult 4%. One reason for the adult groups being the largest is that it includes the most age groups. The age group of juveniles span over 13 years, adolescent 6 years, adult 51 years and mature adult includes all those over the age of sixty. This actually tells us that there is a large quantity of juveniles and

adolescent and quite few mature adults. The indeterminate group only contains one individual, and the percentage is therefore less than 1 %, this is shown in the figure as 0%.

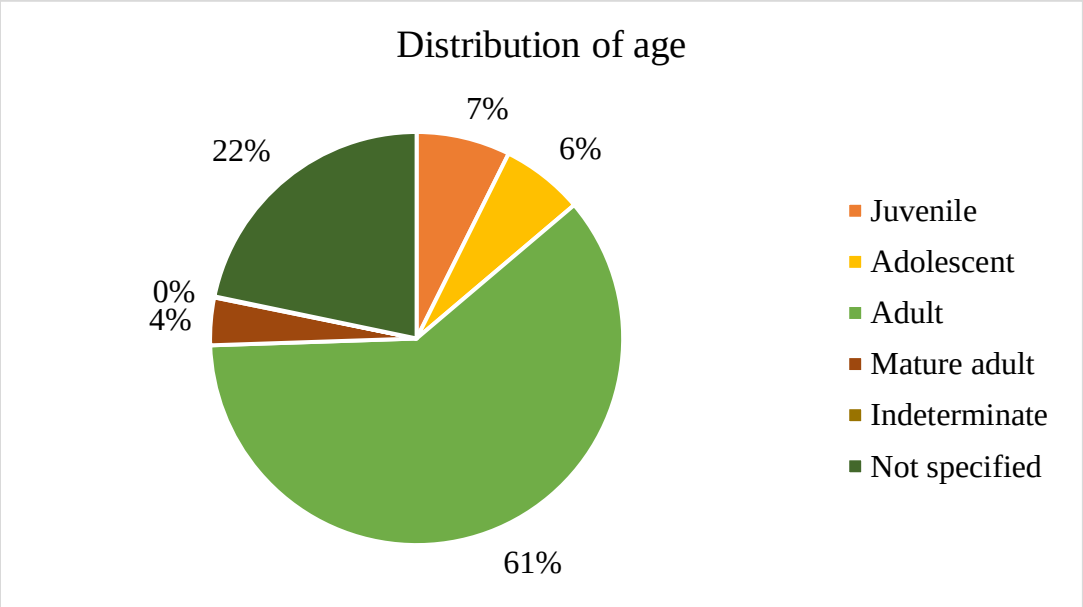

Figure 16. Total distribution of age. 7% juveniles, 6% adolescent, 61% adult, 4% mature adult, 0% indeterminate, 22% not specified. Based on appendix 9.4.

5.4. Element representation

The most affected element in the studied articles were the ribs. 301 individuals had some sort of pathological change to the surface of the ribs (table 8). Not all of these were diagnosed with tuberculosis. Only Pott´s disease, lymph nodes and dactylitis was used as a diagnostic trait in all of the cases which it appeared. Erosive changes in vertebrae were in 33 cases used as an indicator of tuberculosis even though there was no kyphosis. Only 261 skeletal changes were used as a diagnostic trait and 717 skeletal changes due to tuberculosis was recorded.

Table 8. Element representation in the studied materials. Based on Appendix 9.6.

Affected element	Number of individuals	Used as diagnostic trait	Percentage
Ribs	301	157	52%
Lower extremities	145	3	2%
Vertebrae	132	33	25%
Pott´s disease	57	57	100%
Upper extremities	28	0	0%
Cranium	22	0	0%
Pelvis	14	0	0%
Calcified pleura	12	5	42%
Lymph nodes	5	5	100%
Tuberculosis dactylitis	1	1	100%
Total	717	261	36%

Out of all the included articles, six used pathological changes to the surface of the ribs as an indicator of tuberculosis (Santos, Roberts, 2001, Lambert, 2002, Bertoldi et al., 2005, Matos, Santos, 2006, Santos, Roberts, 2006, Suzuki, Inoue, 2007). Out of the 301 registered cases of surface changes to the ribs, 157 individuals were diagnosed based on these changes and no aDNA analysis was conducted to confirm. The largest number of individuals was from Matos & Santos (2006) and Santos & Roberts (2006) with 76 and 54 individuals respectively. In addition to these, there were 74 cases with changes to the ribs that were not deemed as a diagnostic trait and where they did not use aDNA as part of the analysis. The article with the most individuals in this category was published by Mariotti et al. (2015) with 48 individuals. Most of the individuals in this category was diagnosed based on either Pott´s disease, erosive changes to the vertebral body or had documented tuberculosis. There were 70 cases of skeletal changes to the ribs that the tuberculosis was diagnosed with aDNA, the articles with the most skeletal changes to the ribs were by Müller, Roberts & Brown (2014) and Nicklisch et al. (2012) with 27 and 22 individuals respectively. There were 12 cases of registered calcified pleura. A few of the cases consisted only of the calcified pleura (Haas et al., 2000, Molnár, Marcsik, 2002, Hartzell, 2008, Hartzell, 2010, Müller, Roberts & Brown, 2014, Sabin et al., 2020). Only one had other skeletal changes involved in the diagnosis (Arcini, 2003). Calcified pleura was used as a diagnostic trait in 5 out of 12 cases. There were 32 articles with 57 identified cases of Pott´s disease (Arcini, 1994, Arcini, 1999, Haas et al., 2000, Anderson, 2001, Santos, Roberts, 2001, Zink et al., 2001, Spigelman et al., 2002, Mays, Taylor, 2003, Nuorala et al., 2004, Tayles, Buckley, 2004, Zink et al., 2004, Canci et al., 2005, Zink, Grabner & Nerlich, 2005, Suzuki, Inoue, 2007, Zink et al., 2007, Arcini, 2008, Magilton et al., 2008, Suzuki, Fujita & Choi, 2008, Dabernat, Crubézy, 2010, Matos, Marques & Lopes, 2011, Kjellström, 2012, Nicklisch et al., 2012, Arrieta, Bordach & Mendonça, 2014, Köhler et al., 2014, Müller, Roberts & Brown, 2014, Larsen, 2015, Mariotti et al., 2015, Pálfi et al., 2015, Spekker et al., 2018, Andersson, 2019, Haagen, Lynnerup, 2019, Larentis et al., 2020). In all cases Pott´s disease was found, it was used as a diagnostic trait of tuberculosis. Pott´s disease was used as a diagnostic trait in case articles 28 times and 29 times in population articles. In the population articles, there was one article with 11 cases of Pott´s disease and one with 5 cases. Out of the 51 articles used in this analysis, 27 articles used aDNA as a method of diagnosing tuberculosis in both skeletal and mummified remains (Haas et al., 2000, Mays et al., 2001, Zink et al., 2001, Konomi et al., 2002, Mays, Fysh & Taylor, 2002, Molnár, Marcsik, 2002, Spigelman et al., 2002, Fletcher et al., 2003, Mays, Taylor, 2003, Zink et al., 2003, Donoghue et al., 2004, Nuorala et al., 2004, Zink et al., 2004, Zink, Grabner & Nerlich, 2005, Spigelman, Pap & Donoghue, 2006, Zink et

al., 2007, Bianucci et al., 2012, Nicklisch et al., 2012, Müller, Roberts & Brown, 2014, Pálfi et al., 2015, Sparacello et al., 2017, Sabin et al., 2020). This involved 3343 individuals and 418 of these were diagnosed with tuberculosis (appendix 9.6.).

6. Discussion

Based on this study, I believe that aDNA does provide a reliable alternative to visual diagnosing of palaeopathological changes. Both as a confirmation in cases where there are palaeopathological changes as well as when a larger sample is tested to see if tuberculosis is present in the material. In most of the cases included in this study, aDNA was used when there were no skeletal changes present or when they were difficult to see due to soft tissue still being present. According to most of the literature used in this thesis, Pott´s disease is *the* palaeopathological trait used to diagnose tuberculosis. It is present in both case and population articles equally (28 and 29) which is quite low compared with other traits. A kyphosis of the back with no involvement of the vertebral foramen is used as a diagnostic trait each time it is present in the articles studied within this thesis. Based on the results presented in this thesis I believe that it is possible to diagnose individuals using skeletal changes. However, I believe that there needs to be even more research done regarding the specific skeletal changes and their appearance to make it available and as accurate as possible. As demonstrated here, a diagnosis can be made on additional traits than Pott´s disease and calcified pleura, but there needs to be more method developing research in order to fully use this knowledge. What this process can conclude is that there are more traits than Pott´s disease that provide us with, according to the respective authors, a positive tuberculosis diagnosis. Ribs are the most commonly used skeletal trait for a positive tuberculosis diagnosis. Pott´s disease is used as a diagnostic trait 57 times and ribs 157 times in the materials analysed in this thesis. There is no clear increase in frequency over time prior to year zero. There is however an increase in figure 14 that shows the dates between year zero and 2000. Some skeletal changes are indicators of childhood tuberculosis, such as dactylitis, hip joint, knee joint, ankle and tarsal bones, elbow joint, carpometacarpal joint and the cranium. If these are found in adult individuals it is most likely an indicator of childhood tuberculosis. Pathological changes to the knee and elbow joint could manifest itself as late as during adolescence and in the hip to as late as 25 years of age. Only two joints are more commonly developed in adulthood, the shoulder and radiocarpal joint. When estimating at what age the infection of the hand began, it requires that only one of the joints are affected. With time the erosive changes tend to spread to the surrounding joints, making it more difficult

to estimate the original one. Based on the results here and in accordance with earlier studies, for example Roberts & Buikstra (2003. p. 45), there is a male bias in the number of individuals diagnosed with tuberculosis. There are several factors in the osteological paradox that can be applied here. They will be discussed further below.

With even more materials to study and from a larger selection timewise, the outcome might have appeared different. It is possible that before the use of aDNA that fewer individuals were diagnosed due to Pott´s disease being underrepresented in the material. However, out of these 17389 studied individuals, only 5% (868) were diagnosed with tuberculosis, within the expected limits based on previous studies. Does this mean that we are doing an accurate job overall? I believe that looking at a larger perspective, yes. When over 17000 individuals are taken into consideration we are within the expected ranges. However, when we are studying materials with over 3000 individuals and only find one or two (Arcini, 1999. 1/3305=0.0003 = 0.03%) (Paja et al., 2012. 2/3872=0.0005 = 0.05%) or cases with 24 individuals and find eight (Zink, Grabner & Nerlich, 2005. 0.33 = 33%) it does not fit the expected statistics. It requires a large number of individuals to see enough data to draw any conclusions. In three cases it required more than 2000 individuals to find more than two individuals with tuberculosis based on traditional skeletal changes. In other cases, only a few individuals were needed. One error to this is all of those materials that no tuberculosis was found in. If every material excavated was included in this study, the ratio between those included and the number of diagnosed individuals would differentiate even more. There is also a problem with lack of evidence from a large part of the world. This could be due to the type of journals that were accessible.

aDNA was used as a method for diagnosing tuberculosis on 614 out of 868 individuals that were diagnosed with tuberculosis. In 71% of the cases included in this study, aDNA was used either on its own or as a compliment to palaeopathological changes to diagnose tuberculosis. Even though it is an analysis that takes longer time and cost more than a visual interpretation, it is used in 71% of the cases included here. Skeletal changes without the use of aDNA is used in 413 individuals, which equals 48%. There is a rather significant difference between the two. aDNA as a method is used much more frequently to confirm a diagnosis than only the visual changes. There were 108 cases with both a positive aDNA test and skeletal changes. There were also 258 cases where skeletal changes, mummified remains and aDNA was used for a diagnosis. aDNA in combination with skeletal changes occur in 42% of the cases included in this study. The factor of latent and asymptomatic tuberculosis must be considered here. As latent tuberculosis can be seen in aDNA, how can we be sure if they died from the disease or carried

it latently and died of something else? If we can draw some conclusions regarding the latent versions of the disease, it can also provide some information regarding the spread of disease in a community or geographical area. When an aDNA analysis is applied to remains, it provides a definitive proof that the literary sources or skeletal changes are accurate. It is also a good method when investigating materials that are delicate and the bones become inaccessible, such as mummies.

As the results demonstrates, Pott´s disease is not the most commonly used diagnostic trait. Many articles however discuss it as if it was the most reliable trait. In Roberts (2002)With the use of anatomical collections and aDNA, skeletal changes on other elements such as ribs are being investigated with the hope that it might become a reliable and scientifically proven trait for diagnosing tuberculosis. When processing the results, it was surprising how low the quantity of which Pott´s disease and calcified pleura was present and used compared with skeletal changes on the ribs. Pott´s disease was used as a diagnostic trait 57 times and skeletal changes on ribs 157 times. Ribs was the most commonly used trait, both in presence and as a diagnostic trait. The only skeletal changes that was used as a diagnostic trait when they were present were Pott´s disease (57), calcification of lymph nodes (5) and dactylitis (1). According to the materials used here, neither appear to be a common trait. According to Spekker et al (2018. p. 343) in cases with skeletal tuberculosis, Pott´s disease occurs in approximately 50% of the cases. According to this study, that is not accurate. Out of 712 cases of skeletal changes due to tuberculosis (717 if lymph nodes are included) only 57 cases of Pott´s disease were presented. That accounts for 8%, not 50%. If we only count the cases where the skeletal changes are used for a diagnosis it is 57 out of 261 (261 being the number of skeletal changes used for a diagnosis), approximately 22% (0.218). It is possible that the kind of statistic used by Spekker et al. (2018) are more consistent with Pott´s disease and calcified pleura being the most secure or the only trait used. One estimation made by Davisson & Horowitz (1970. p. 78) regarding the statistic of ribs states that it occurs in approximately 5% of cases of skeletal tuberculosis, also referenced by Roberts & Buikstra (2003. p. 101). Mays, Fysh & Taylor (2002) estimates that ribs are present in 1-8% of skeletal changes. The referenced studies that resembles the results here the closest are presented by Roberts et al. (1998) with results ranging from 1.4%-22.9%. In this study, 60% of the skeletal changes used as a diagnostic trait for tuberculosis were caused by ribs used as a diagnostic traits (157/261=0.60). Out of all the skeletal changes recorded in this study, 42% were caused by ribs as they were recorded (301/717=0.419). That

is substantially larger than 5% or 1-8%. This inconsistency in statistics are further proof that a larger scale research project with focus in method development needs to be conducted.

In the total material diagnosed with tuberculosis, only 7% were juveniles. This does not provide a large enough sample to identify skeletal changes. There were 7 cases of palaeopathological changes consistent with tuberculosis that were specified to an element in juveniles. Four of these were Pott´s disease, two were changes on ribs and one were the dactylitis case. The dactylitis case represents 0.1% (0.0014) of the total of skeletal changes due to tuberculosis. It could be that the study conducted by Roberts & Buikstra (2019. p. 339) that indicated 15% presence of dactylitis included more juveniles than the materials included in this study and therefore included a higher number of dactylitis cases. In the book by Magilton et al. (2008. p. 221f) they presented the statistics that 0.6-6% of juveniles that has skeletal tuberculosis showed signs of dactylitis. 0.6-6% closer to the result presented here, however, it is still much larger. Dactylitis disappears with remodelling and is therefore most often found when it is active or in a young individual where the remodelling is not complete yet. Given that skeletal changes on hips, knees, elbow, feet and hands and ankle and tarsal bones most often affects children, these changes can be used to estimate when the individual got infected. Erosive changes to the weight bearing joins do not disappear with remodelling, they often collapse under the weight of the individual, with time, leaving the joint stiff and unusable. Given the number of skeletal changes that originate from childhood, we should see more changes in the juvenile categories. The lower extremities (hip, knee, feet, ankle and tarsal bones) were present in 145 cases, but only used as a diagnostic trait in 3. For the palaeopathological study of tuberculosis, I believe that there needs to be even more research with focus on developing methods and techniques to enable this knowledge to be used to its fullest potential. Only one case in the previous research chapter discusses a juvenile individual (Fürst, 1920, 1922). In this case, it was a child affected with Pott´s disease. Unfortunately, there is not a lot of information regarding the rest of the elements and what other skeletal changes the individual might have had.

The research done by Santos and Roberts (2001) discussed three juveniles that were documented to have died from *tuberculosis meningitis*. However, none of them demonstrated the skeletal changes that this could have caused. The most likely scenario is that the passed away before the disease left a mark on the bones. The presence or lack of skeletal changes is a reoccurring problem when studying juveniles, they often die before the skeletal changes manifests itself or they survive the disease and most of the changes disappear with natural remodelling. There has been some theories that there is a correlation between juvenile

tuberculosis and *Mycobacterium bovis.* Lewis (2007. p. 149) bring up the possibility of this being due to children's high consumption of cow's milk as a substitute for breastfeeding. This becomes especially relevant for new-borns who cannot breastfeed and those weaning. This could be the cause to many cases of childhood tuberculosis. It is also possible for the child to contract the human form of tuberculosis through breastmilk (Lewis, 2007. p. 146).

The main question that I hoped to answer in this thesis was if Pott´s disease is the only real skeletal trait that we can use to diagnose tuberculosis. Based on a large quantity of research, this has been the skeletal trait to look for when it comes to tuberculosis. Waldron's (2009. p. 95) statement that any extra-spinal change is not enough to make a diagnosis would mean that those that based the diagnosis on the ribs alone wrongfully diagnosed their individuals. It is a difficult point to consider, if we only base a diagnosis on Pott´s disease do we then miss a large number of individuals? Or if we base a diagnosis on other skeletal changes such as ribs, how many of them are wrongfully diagnosed with tuberculosis? Applying a pathological aDNA analysis could answer the question on individuals. But to truly answer the question, there needs to be conducted further investigations into the origin of surface changes on ribs and other elements. All of the articles included in this study have been approved by peer review, which means that the methods and results they presented have been accepted by the academic community. They might not have been agreed with, but they have been accepted enough to be published. This is a very interesting phenomenon, that a diagnosis is being made with traits that are not considered strong enough on their own. None of those that based the diagnosis on ribs used aDNA. Meaning that the case itself is strong enough for the authors to publish their diagnosis on the subject.

In the materials discussed in previous history, most of them used Pott´s disease as the only diagnostic trait. For example, Fürst (1920, 1922) and Møller-Christensen (1982) shows clear example of the kyphosis and discusses tuberculosis as the only diagnosis. In the materials presented in the last 20 years, more various traits are taken into consideration. This provides researchers with a greater change to diagnose those that died in the past based solely on skeletal changes. When or if skeletal changes such as ribs are established as a diagnostic skeletal traits of tuberculosis, some of the older published materials should be studied again, perhaps with a change of diagnosing more individuals. Since Pott´s disease is not as frequent as one would like, at least according to this study, more established skeletal changes could change the fundamentals of tuberculosis diagnosing.

In regard to frequency over time, it becomes very dependent to the materials included in the study. If the process were to start over, I would try to find more diverse materials from a larger geographical area and from a larger time selection. This could hopefully provide a more accurate result in regard to frequency over time. In accordance with the Ecological theory presented by Gagneux (2012. p. 855) the increase in frequency from year zero until 2000 CE seen in figure 14 follows the drastic increase in people and capacity of cities. If points in figure 14 that only includes one individual had been excluded, then this increase would be even clearer. The increase in cases of diagnosed tuberculosis is also in accordance with the fact that the bacteria becomes more aggressive as times passes. One factor that disturbs the lineage in figure 13 is the material that originate from Egypt. They had a civilisation long before the rest and show higher figures than the rest of the world. The Egyptian cases occupy most of figure 13 and present a significant inconsistency. This could also be due to the long timespan some of the cases are presenting. Some articles did not or were not able to specify the exact date an individual originated from and therefore some of the time periods covers a large time span.

To draw any conclusions regarding the frequency of which tuberculosis presents itself and its increase with time becomes however problematic when considering those that were not included in this study. To include all the published materials both on tuberculosis and on human remains in the past would have been a huge task, but that might be the only way to truly get the proper statistic. One way to make it more manageable is to choose a geographical location, such as a town or county and a time period. By taking all the published material from this specific region, from a specific time and to study the quantity of individuals diagnosable with tuberculosis. This could be a way to see the real statistics for that time and place. This approach is for too large for a master thesis, but it could provide the answers to how common tuberculosis actually is. For the time limitations of this thesis, I believe that this approach it the one providing the best results. This thesis also provides a lot of material that can be used for future tuberculosis research projects. The bibliography contains quite a few books and articles that can make a tuberculosis study more manageable.

The overrepresentation of males in the materials could be causes by various factors. In the cases where morphology has been used to estimate sex, the male traits were perhaps better preserved. Therefor making the males more easily identifiable. In the cases originating from cemeteries, perhaps a section consisting mostly of males were exhumed. One possibility is that males had a better immune system or a better health and therefore could fight the disease for much longer, leaving the body with palaeopathological changes. This problematic situation is in accordance

with the osteological paradox. We do not see as many women as men and therefore we might assume that fewer women had the disease. It is a possibility, however it is just likely that more males survived the disease due to their physique and them perhaps being more outdoors than women. Later with the establishment of sanatoriums, perhaps it was the men that they could afford to send there and rest while the women had to remain home. The two discussed cases of Pott´s disease from Møller-Christensen (1982. Ch. 5) are classic examples of a kyphosis. They were also both males in their forties. The child discussed by Fürst (1920, 1922) is believed to have been a young male due to his positioning in the church. Kjellström´s (2012) article includes one individual with skeletal tuberculosis, this individuals was indeterminate and therefore we do not have any sex estimation in this case. In the case of Bishop Peder Winstrup (Karsten, Manhag, 2017, Sabin et al., 2020), we have a powerful and prominent man who did not have a documented tuberculosis diagnosis but who had calcified nodes in his lungs. One case by Arcini (2008) includes a female with Pott´s disease. Arcini presents the only known female individual out of the articles included in the previous history chapter.

When the study is focused on a smaller material, I do not think that we can or should discuss tuberculosis in a population perspective. Analysing a larger material and processing the individuals showing skeletal changes is a way of bringing awareness to the existence of the disease. But I do not believe that we can estimate the rest of the population's health in relation to tuberculosis in a small material. It is also a very diffuse line to draw, what counts as a large or small material? It becomes very dependent on funding, experience and time limitations. For example, the bachelor thesis presented by Andersson (2019) provides too small of a sample to draw any conclusions regarding the entire medieval population of Lund. Arcini (1999) processes a material consisting of 3305 individuals as part of her doctoral thesis. The aim of the thesis was to investigate the pathological condition of these remains and to diagnose those that were possible. Of these 3305 individuals, only one was diagnosed with tuberculosis. This individual was an adult female with Pott´s disease. Perhaps if aDNA had been applied to this material, even more individuals could have been diagnosed. Sense Arcini based the diagnosis on traditional skeletal characteristics, this would have been the only true case of tuberculosis. However, if the ribs on these individuals were intact and existing, perhaps more individuals could have been diagnosed today if ribs proved to be a diagnosable trait of tuberculosis.

There are many factors involved in the preservation of remains. One of the biggest factors in the sample composition is the degree of preservation and completeness of the original community. If only one third of a cemetery is exhumed, it is hard to make a statement regarding

the entire community. There is also the factor of who did the estimation. With aDNA, the result should be rather certain. With morphology, the estimation is based on the analyst's experience, knowledge and access to the physical remains. Also, the method applied and the reference materials available could affect the certainty of the estimation.

The numbers presented in table 8 regarding element representation in the studied materials, are not entirely precise. Some articles did not specify the specific number of individuals affected with certain skeletal change. Those articles were represented with a 1 for present. This actively demonstrates that the skeletal changes should be of a larger amount on each of the categories. One problem encountered during this process was the inconsistency with how the skeletal changes, age estimation and sex estimation was presented. In a number of cases, neither of these facts were stated in the text. Thus, making it more difficult to compare results and methods used to diagnose the remains. When the aim of a scientific paper is to present and describe the process to enable others to repeat, such facts are essential. The inconsistency in the processed articles becomes a factor of error. A minor misunderstanding or a fact not chosen to include could have serious effects on the results. If all those "not specified" regarding sex were females, then the total statistics would have looked very different. If, regarding age, they had all been juveniles, then there could have been a discussion regarding the high mortality rates of juveniles in the materials. If aDNA was used by all researchers to confirm the sex of an individual, perhaps the distribution of sex would have looked very different. And it would have provided an opportunity to divide the individuals into more precise groups, with 10- or 20-year intervals to investigate how various skeletal changes occur at different ages. With the large age span that is used here, such dividing will be hard to do in the adult category.

One palaeopathological changes that I thought I would find more of during this process was visual changes in lung tissue in mummified remains. The only finding in this category was the calcifications in the lungs of Peder Winstrup (Karsten, Manhag, 2017, Sabin et al., 2020). Perhaps it was more common prior to the use of aDNA to base a diagnosis on this and therefore it is not as present in recent articles.

Certain materials that were excavated some time ago is not as complete today as they appeared during excavation. For example, the material from S:t Jakob's cemetery in Lund (Andersson, 2019) where only a few ribs were still present. This could be caused by many factors, such as taphonomy and excavation techniques. However, due to the completion of the remainder of the bones, it is more likely that they were discarded or severely fragmented during excavation. The

material in Andersson (2019) was excavated in the 1980s. Materials from earlier then that are even more likely to be missing certain elements, for a long time only the cranium was considered useful.

7. Conclusion

The research needs to be conducted on a rather large material in order to get an accurate estimation on the presence of tuberculosis when analysing populations based on palaeopathological changes recommended for a diagnosis. The result of this thesis is that Pott´s disease is not the only trait that can be used to diagnose tuberculosis. Based on the results from table 8, ribs are the palaeopathological changes that provides the highest quantities of tuberculosis diagnoses. Whether it is the most accurate requires much more research to provide a sufficient answer to. It does however provide promising results regarding a possible method development. Ribs have not always been saved during excavation and have therefor not been studied as often as many other elements. Their fragility is also a factor in this. Another traits that has been discussed in this thesis is calcified pleura, which can be hard to find, and it is also not guaranteed to be caused by tuberculosis. As shown by several authors before, the is a male bias in those diagnosed with tuberculosis. One factor can be explained by the osteological paradox, that more males could survive the disease for longer than females and therefor have more males diagnosed. This can be problematised to an extent but that there are more males diagnosed with tuberculosis than females is a fact. In accordance with the Ecological theory, there is an increase in the number of individuals who are diagnosed with tuberculosis that follows the increase in cities and urbanisation. With more people living in close proximity to each other there are more hosts to infect. With more people the disease no longer require latens versions to keep the disease from dying out to the same extent. Most of the palaeopathological changes that is caused by tuberculosis originates from childhood. This can be used to estimate when an individuals was infected and became ill by the disease. Changes to the hips, knees, elbows, hand and feet are some that originates from childhood. To sum up everything that has been stated so far, there are more ways to diagnose tuberculosis than just Pott´s disease. aDNA is proving to become more and more reliable with new developments and techniques. Ribs as well are showing increasingly promising results as a reliable diagnostic tool. However, I believe that more method developing research needs to be conducted and published in order to truly establish ribs and other elements as diagnostic traits.

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9.1. Appendix - Time periods

The table is organized after the earliest number in the date estimations.

Region	Time period	Year	Tuberculosis	Total number of individuals
Europe	Neolithic	5400-4800 BCE	15	2118
Europe	Bronze Age	3740 BCE	1	1
Egypt	Predynastic - Early dynastic	3200-3100 BCE	1	388
Egypt	Predynastic	pre-3150 BCE	1	1
Egypt	Predynastic - Early dynastic	pre-3150 -2686 BCE	11	146
Egypt	Early Dynastic Period	3150-2686 BCE	1	3
Scandinavia	Bronze Age - Iron Age	2590-240 BCE	2	130
Egypt	Middle Kingdom	2055-1650 BCE	80	317
Egypt	Middle Kingdom - Late Period of Ancient Egypt	2055-1650 / 664-332 BCE	25	85
Egypt	New Kingdom	1550-1069 BCE	6	31
Egypt	New Kingdom - Late Period of Ancient Egypt	1550-1069 / 664-332 BCE	72	720
Thailand	Iron Age	1400 BCE - 300 CE	1	1
Europe	Iron Age	1050 BCE - 500 CE	3	70
Japan	Yayoi	450 BCE - 250 CE	3	3
East Asia	Han dynasty	108 BCE - 313 CE	1	200
Europe	Iron Age - Medieval	0-800 CE	12	70
South America	Early Intermediate, Middle Horizon, Late Intermediate, Late Horizon	200-1534 CE	2	12
West Asia	Byzantine Empire	330-1453 CE	1	1
Europe	Early medieval	c 400-800 CE	11	639
Europe	Early medieval/ Medieval	400-800 / 800-1500 CE	15	30
Europe	Early medieval - early modern	c 400-800 / 1500-1800 CE	32	99
North and South America	Classical / post-classical	500-1200 / 1200-1900 CE	23	105
Europe	Medieval	800-1500 CE	49	5028
Scandinavia	Medieval	1050-1500 CE	8	4687
Southeast Asia	Pre-European contact	pre-1511 CE	1	1
Europe	Early modern	1500-1800 CE	108	224
Europe	Long nineteenth century	1789-1914 CE	152	1014
North America	Reconstructed era - Gilded Age	1865-1877 - 1875-1900 CE	28	644
Europe	Modern	1915-2000 CE	197	353

9.2. Appendix - Geographic distribution

Town	Country	Continent	Number of materials in articles in said town/country/continent
	Egypt	Africa	6
	Borneo	Asia	2
	Japan	Asia	1
	Korea	Asia	1
	Thailand	Asia	1
	Turkey	Asia	2
		Europe	2
Chichester	England	Europe	1
Towcester	England	Europe	1
Wharram Percy	England	Europe	1
	Germany	Europe	2
Munich	Germany	Europe	1
	Hungary	Europe	8
Bologna	Italy	Europe	1
Liguria	Italy	Europe	1
Lombardy	Italy	Europe	1
Modena	Italy	Europe	1
Rome	Italy	Europe	1
	Portugal	Europe	2
Castelo Branco	Portugal	Europe	1
Lisbon	Portugal	Europe	1
	Scandinavia	Europe	1
	Scotland	Europe	1
Linköping	Sweden	Europe	1
Lund	Sweden	Europe	3
Helsingborg	Sweden	Europe	1
Sigtuna	Sweden	Europe	1
Tierp	Sweden	Europe	1
Åhus	Sweden	Europe	1
	United Kingdom	Europe	2
	United States of America	North America	3
Colorado	United States of America	North America	1
Mississippi	United States of America	North America	1
	Argentina	South America	1
	Peru	South America	1
Andean mountains	Argentina, Bolivia, Chile, Colombia, Ecuador, Peru, Venezuela	South America	1

9.3. Appendix - Distribution of sex

Total	
Sex	Amount
Female	515
Female?	5
Indeterminate	52
Male?	10
Male	703
Not specified	266
Total	1551

Case	
Sex	Amount
Female	181
Female?	0
Indeterminate	7
Male?	3
Male	231
Not specified	32
Total	454

Population	
Sex	Amount
Female	334
Female?	5
Indeterminate	45
Male?	7
Male	472
Not specified	234
Total	1097

9.4. Appendix - Distribution of age

Total	
Age	Amount
Juvenile	91
Adolescent	80
Adult	751
Mature adult	46
Indeterminate	1
Not specified	269
Total	1238

Case	
Age	Amount
Juvenile	73
Adolescent	60
Adult	206
Mature adult	32
Indeterminate	1
Not specified	24
Total	396

Population	
Age	Amount
Juvenile	18
Adolescent	20
Adult	545
Mature adult	14
Not specified	245
Total	842

9.5. Appendix – Method and case versus population

Author	Title	aDNA	Skeletal	Mummified remains	Case or population
Andersson, L.	Tuberkulos i medeltida Lund	0	1	0	p
Anderson, T.	A case of skeletal tuberculosis from Roman Towcester	0	1	0	c
Arcini, C.	Åderförkalkning och portvinstår	0	1	0	p
Arcini, C.	Health and disease in early Lund	0	1	0	p
Arcini, C.	Ett fall av tuberkulos i det medeltida Helsingborg	0	1	0	c
Arcini, C.	Lacunae to fill: combining palaeopathological and documentary research in investigations of individuals from a post-medieval Swedish cemetery	0	1	0	c
Arrieta, M.A. Bordach, M.A. Mendonça, O.J.	Pre-Columbian Tuberculosis in Northwest Argentina: Skeletal Evidence from Rincón Chico 21 Cemetery	0	1	0	c
Bertoldi, F. Lora, S. Bullegato, C. Ghezzo, M. Librenti, M. Gelichi, S.	The cemetery of nonantola (Modena, Italy): A preliminary study of the health status of the medieval population	0	1	0	c
Bianucci, R. Giuffra, V. Bachmeier, B.E. Ball, M. Pusch, C.M. Fornaciari, G. Nerlich, A.G.	Eleonora of Toledo (1522-1562): Evidence for tuberculosis and leishmaniasis co-infection in Renaissance Italy	1	0	0	c
Canci, A. Nencioni, L. Minozzi, S. Catalano, P. Caramella, D. Fornaciari, G.	A case of healing spinal infection from Classical Rome	0	1	0	c
Dabernat, H. Crubézy, É.	Multiple bone tuberculosis in a child from predynastic upper Egypt (3200 BC)	0	1	0	c
de la Cova, C.	Race, Health and disease in 19th-century-born males	0	1	0	c
Donoghue, H. D. Spigelman, M. Greenblatt, C. L. Lev-Maor, G. Bar-Gal, G. K. Matheson, C. Vernon, K. Nerlich, A. Zink, A. R.	Tuberculosis: from prehistory to Robert Koch, as revealed by ancient DNA	1	0	1	c
Fletcher, H. Donoghue, H. Holton, J. Pap, I. Spigelman, M.	Widespread occurrence of Mycobacterium tuberculosis, DNA from 18th-19th century Hungarians	1	1	1	p
Haagen, K. Lynnerup, N.	Abnormal Bone: Considerations for Documentation, Disease Process Identification, and Differential Diagnosis	0	1	0	c
Haas, C. Zink, A. Molnár, E. Szeimies, U. Reischl, U. Marcsik, A. Ardagna, Y. Dutour, O. Pálfi, G. Nerlich, A.	Molecular evidence for different stages of tuberculosis in ancient bone samples from Hungary	1	1	0	c
Hartzell, L.	En tidigmedeltida begravningsplats i Tierp	0	1	0	c

Kjellström, A.	Possible cases of leprosy and tuberculosis in medieval Sigtuna, Sweden	0	1	0	c
Konomi, N. Lebwohl, E. Mowbray, K. Tattersall, I. Zhang, D.	Detection of Mycobacterial DNA in Andean Mummies	1	0	1	c
Köhler, K. Pálfi, GY. Molnár, E. Zalai-Gaál, I. Osztás, A. Bánffy, E. Kirino, K. Kiss, K. K. Mende, B. G.	A late Neolithic case of Pott´s disease from Hungary	0	1	0	c
Lambert, P. M.	Rib lesions in a prehistoric Puebloan sample from Southwestern Colorado	0	0	0	c
Larentis, O. Tonina, E. Tesi, C. Rossetti, C. Gorini, I. Ciliberti, R. Licata, M.	A probable case of subligamentous tuberculosis spondylitis: The concealed body of the late modern period (early 16th century to early 20th century), Franciscan crypt of St. Anthony and St. Eusebius church, Lombardy, Italy	0	1	0	c
Larsen Spencer, C.	Bioarchaeology - interpreting behaviour from the human skeleton	0	1	0	c
Magilton, J. Lee, F. Boylston, A. Judd, M. Kenny, J. Lewis, M. Manchester, K. Ogden, A. Ortner, D. Storm, R. Sture, J.	Lepers outside the gate	0	1	0	p
Mariotti, V. Zupello, M. Pedrosi, M. Bettuzzi, M. Brancaccio, R. Peccenini, E. Morigi, M. Balcastro, M.	Skeletal evidence of tuberculosis in a modern identified human skeletal collection (certosa cemetery, Bologna, Italy)	0	1	0	p
Matos, V. Marques, C. Lopes, C.	Severe vertebral collapse in a juvenile from the graveyard (13th/14th-19th centuries) of the São Miguel Church (Castelo Branco, Portugal): Differential palaeopathological diagnosis	0	1	0	c
Matos, V. Santos, A. L.	On the trail of pulmonary tuberculosis based on rib lesions: results from the human identified skeletal collection from the meseu Bocage (Lisbon, Portugal)	0	1	0	c
Mays, G. S. Taylor, M.	A first prehistoric case of tuberculosis from Britain	1	1	0	c
Mays, S. Fysh, E. Taylor, G.M.	Investigation of the link between visceral surface rib lesions and tuberculosis in a medieval skeletal series from England using ancient DNA	1	1	0	c

Mays, S. Taylor, G.M. Legge, A.J. Young, D.B. Turner-Walker, G.	Paleopathological and biomolecular study of tuberculosis in a medieval skeletal collection from England	1	1	0	c
Molnár, E. Marcsik, A.	Paleopathological evaluation of Hungarian skeletal remains from the 7th-9th centuries AD	1	1	0	p
Müller, R. Roberts, C. Brown, T.	Biomolecular identification of ancient mycobacterium tuberculosis complex DNA in human remains from Britain and continental Europe	1	1	0	p
Nicklisch, N. Maixner, F. Ganslmeier, R. Friederich, S. Dresely, V. Meller, H. Zink, A. Alt, K. W.	Rib lesions in skeletons from early Neolithic sites in central Germany: on the trail of Tuberculosis at the onset of agriculture	1	1	0	c
Nuorala, E. Götherström, A. Ahlström, T. Donoghue, H.D. Spigelman, M. Lidén, K.	MTB complex DNA in a Scandinavian Neolithic passage grave	1	1	0	c
Paja, L. Coqueugniot, H. Dutour, O. Willmon, R. Farkas, G.L. Palkó, A. Pálfi, G.	Knee ankyloses associated with tuberculosis from the Medieval Hungary - Differential Diagnosis Based on Medical Imaging Techniques	0	1	0	c
Pálfi, G. Maixner, F. Maczel, M. Molnár, E. Pósa, A. Kristóf, L. A. Marcsik, A. Balázs, J. Masson, M. Paja, L. Palkó, A. Szentgyörgyi, R. Nerlich, A. Zink, A. Dutour, O.	Unusual spinal tuberculosis in an Avar Age skeleton (Csongrád-Felgyő, Ürmös-tanya, Hungary): A morphological and biomolecular study	1	1	0	p
Sabin, S. Herbig, A. Vågene, Å. Ahlström, T. Bozovic, G. Arcini, C. Kühnert, D. Bos, K.	A seventeenth-century Mycobacterium tuberculosis genome supports a Neolithic emergence of the Mycobacterium tuberculosis complex	1	1	1	c
Santos, A. L. Roberts, C. A.	Anatomy of a serial killer: Differential diagnosis of tuberculosis based on rib lesions of adult individuals from the Coimbra identified skeletal collection, Portugal	0	1	0	p
Santos, A. L. Roberts, C. A.	A picture of tuberculosis in young Portuguese people in the Early 2oth century: a multidisciplinary study of the skeletal an historical evidence	0	1	0	c
Sparacello, V. Roberts, C. Kerudin, A. Müller, R.	A 6500-year-old Middle Neolithic child from Pollera Cave (Liguria, Italy) with probable multifocal osteoarticular tuberculosis	1	1	0	c
Spekker, O. Hunt, D.R. Váradi,O.A. Berthon, W. Molnár, E. Pálfi, G.	Rare manifestations of spinal tuberculosis in the e Robert J. Terry Anatomical Skeletal Collections (National Museum of Natural History, Smithsonian Institution, Washington, DC, USA)	0	1	0	c

Spigelman, M. Pap, I. Donoghue, H.D.	A death from Langerhans cell histiocytosis and tuberculosis in 18th century Hungary - what palaeopathology can tell us today	1	1	0	c
Spigelman, M. Matheson, C. Lev, G. Greenblatt, C. Donoghue, D. H.	Confirmation of the presence of Mycobacterium tuberculosis complex-specific DNA in three archaeological specimens	1	0	0	c
Suzuki, T. Fujita, H. Gyu Choi, J.	Brief communication: New evidence of tuberculosis from prehistoric Korea - population movement and early evidence of tuberculosis in Far East Asia	0	1	0	c
Suzuki, T. Inoue, T.	Earliest evidence of spinal tuberculosis from the Aneolithic Yayoi period in Japan	0	1	0	c
Tayles, N. Buckley, H.R.	Leprosy and tuberculosis in Iron age southeast Asia	0	1	0	c
Zink, A. Haas, C. Reischl, U. Szeimies, U. Nerlich, A.	Molecular analysis of skeletal tuberculosis in an ancient Egyptian population	1	1	1	p
Zink, A.R. Grabner, W. Nerlich, A.G.	Molecular identification of human tuberculosis in recent and historic bone tissue samples: the role of molecular techniques for the study of historic tuberculosis	1	1	0	p
Zink, A.R. Molnár, E. Motamedi, N. Pálfy, G. Marcsik, A. Nerlich, A.G.	Molecular history of tuberculosis from ancient mummies and skeletons	1	1	0	p
Zink, A.R. Sola, C. Reischl, U. Grabner, W. Rastogi, N. Wolf, H. Nerlich, A.G.	Molecular identification and characterization of Mycobacterium tuberculosis complex in ancient Egyptian mummies	1	1	1	p
Zink, A.R. Sola, C. Reischl, U. Grabner, W. Rastogi, N. Wolf, H. Nerlich, A.G.	Characterization of Mycobacterial tuberculosis complex DNAs from Egyptian Mummies by Spoligotyping	1	1	1	p

9.6. Appendix - Database

MTB = Mycobacterium tuberculosis

MTC = Mycobacterium tuberculosis complex

MA = Mycobacterium africanum

MB = Mycobacterium bovis

MM = Mycobacterium microti

N = negative or no result

When possible, the number of individuals affected with the pathological change is specified. If not, a 1 is used as an indicator of presence.

A **fat** number indicates the skeletal change used for diagnosing.

To ensure that all columns were to fit, an empty one is placed in the right side.

0 indicates no changes reported

9.6. Appendix Database

Author	Titel	Published	Radiographic	aDNA	Tuberculosis complex	Skeletal	Post x disease	Placement of Kyphosis	Vertebrae	Costae	Upper extremities	Lower extremities	Pelvis	Cranium	Calcified pleura	Tuberculosis dactylitis	Mummie	Lymph node	Documented tuberculosis	Juvenile	Adolescent	Adult	Mature adult	Indeterminate	Not Specified	Male	Male?	Female	Female?	Indeterminate	Not specified	Date	Case or Population	Tuberculosis diagnosis	Total amount	Country/region	Alternative diagnosis	
Andersson, L.	Tuberkulos i medeltida Lund	2019	0	0	0	1	1	T11-12	2	0	0	1	0	0	0	0	0	0	0	0	1	1	0	0	0	0	1	1	0	0	0	1 medieval 1 1200-1560	p	2	326	Lund, Sweden	Yes	
Andersson, T.	A case of skeletal tuberculosis from Roman Towcester	2001	0	0	0	1	1	T2-9	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	2nd-4th C AD	c	1	27	Towcester, England	Yes	
Arcini, C.	åderförkalkning och portvinstår	2003	0	0	0	1	0	0	0	0	0	0	1	0	0	1	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	early medieval - 1200	p	1	249	Åhus, Sweden	No	
Arcini, C.	Health and disease in early Lund	1999	0	0	0	1	1	T3-7	1	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	early medieval - 1050-1100	p	1	3305	Lund, Sweden	No	
Arcini, C.	Ett fall av tuberkulos i det medeltida Helsingborg	1994	0	0	0	1	1	T9-12	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	1000-1200	c	1	567	Helsingborg, Sweden	No	
Arcini, C.	Lucosis to tbc: combining palaeopathological and documentary research in investigations of individuals from a post-medieval Swedish cemetary	2008	0	0	0	1	1	T12-L2	1	1	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	1780-1810	c	1	570	Linköping, Sweden	No	
Arrieta, M.A. Bordach, M.A. Mendonça, O.J.	Pre-Columbian Tuberculosis in Northwest Argentina: Skeletal Evidence from Rincón Chico 21 Cemetery	2011	1	0	0	1	2	C7-T1	4	2	2	2	2	0	0	0	0	0	0	0	0	4	4	0	1	0	3	0	5	0	1	0	850-1400 AD	c	9	70	Argentina	Yes	
Bertoldi, F. Lora, S. Bellegato, C. Ghezzo, M. Liberati, M. Gelichi, S.	The cemetery of nonantola (Modena, Italy): A preliminary study of the health status of the medeival population	2005	0	0	0	1	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	1100-1300 CE	c	1	185	Modena, Italy	No	

9.6. Appendix Database

Bianucci, R. Giuffra, V. Bachmeier, B.E. Ball, M. Pusch, C.M. Fornaciari, G. Nerlich, A.G.	Eleonora of Toledo (1522-1562): Evidence for tuberculosis and leishmaniasis co-infection in Renaissance Italy	2012	0	**1**	MTC	1	0	0	0	0	0	0	0	0	0	0	0	0	0	**1**	0	0	1	0	0	0	0	0	1	0	0	0	1522-1562	c	1	1	Italy	No	
Canci, A. Nencioni, L. Minozzi, S. Catalano, P. Caramella, D. Fornaciari, G.	A case of healing spinal infection from Classical Rome	2005	1	0	0	1	**1**	T5-9	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	0-100 CE	c	1	28	Rome, Italy	Yes	
Dabernat, H. Crubézy, É.	Multiple bone tubeculosis in a child from predynastic upper Egypt (3200 BC)	2009	1	0	0	1	**1**	T12-L1	0	1	1	1	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	3200-3100 BC	c	1	388	Egypt	Yes	
de la Cova, C.	Race, Health and disease in 19th-century-born males	2011	0	0	0	1	0	0	**1**	1	0	0	0	0	0	0	0	0	**28**	0	0	16	12	0	0	28	0	0	0	0	0	0	1800	c	28	644	United states of America	No	
Donoghue, H. D. Spigelman, M. Greenblatt, C. L. Lev-Maor, G. Bar-Gal, G. K. Matheson, C. Vernon, K. Nerlich, A. Zink, A. R.	Tuberculosis: from prehistory to Robert Koch, as revealed by ancient DNA	2004	0	**1**	MTB	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	15	0	0	0	0	0	15	300-1400	c	15	30	Mixed (Europe, Turkey and Borneo)	No	
Fletcher, H. Donoghue, H. Holton, J. Pap, I. Spigelman, M.	Widespread occurence of Mycobacterium tuberculosis, DNA from 18th-19th century Hungarians	2003	27 individuals	**1**	MTB	1	0	0	0	0	0	0	0	0	0	0	0	1	0	**93**	0	6	69	0	0	18	95	0	70	0	3	0	1731-1838	p	93	168	Hungary	No	

9.6. Appendix Database

Haagen, K. Lynnerup, N.	Abnormal Bone: Considerations for Documentation, Disease Process Identification, and Differential Diagnosis	2019	0	0	0	1	**1**	T6-8	2	0	0	0	0	1	0	0	0	0	0	0	1	2	0	0	0	1	0	0	0	2	0	1 modern collection 1 pre-hispanic Peru 1 middle/late colonia period Peru	c	3	3	1 United states 2 Peru	Yes	
Haas, C. Zink, A. Molnár, E. Szeimies, U. Reischl, U. Marcsik, A. Ardagna, Y. Dutour, O. Pálfi, G. Nerlich, A.	Molecular evidence for different stages of tuberculosis in ancient bone samples from Hungary	2000	14	**1**	MTB	1	**3**	T3-6 T12-L1 L5-S1	10	3	0	2	1	0	2	0	0	0	0	1	1	12	0	0	0	10	0	4	0	0	0	7-8th and 17th C AD	c	8	14	Hungary	No	
Hartzell, L.	En tidigmedeltida begravningsplats i Tierp	2008	0	0	0	1	0	0	0	1	0	0	0	0	1	0	0	0	0	0	0	2	0	0	0	1	1	0	0	0	0	1050-1210	c	2	13	Tierp, Husbyborg, Sweden	No	
Kjellström, A.	Possible cases of leprosy and tuberculosis in medieval Sigtuna, Sweden	2010	0	0	0	1	**1**	L1-3	1	0	0	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	1	0	medieval	c	1	227	Sigtuna, Sweden	Yes	
Konomi, N. Lebwohl, E. Mowbray, K. Tattersall, I. Zhang, D.	Detection of Mycobacterial DNA in Andean Mummies	2002	0	**1**	2 MTB, 10 MTC	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	2	0	0	0	0	0	2	140-1200 AD	c	2	12	Andes mountain, South America	No	
Köhler, K. Pálfi, GY. Molnár, E. Zalai-Gaál, I. Osztás, A. Bánffy, E. Kirino, K. Kiss, K. K. Mende, B. G.	A late neolithic case of Pott´s disease from Hungary	2014	1	0	0	1	**1**	T8-9, T10-L4	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	4000-3000 BCE	c	1	2000	Hungary	No	

9.6. Appendix Database

Lambert, P. M.	Rib lesions in a prehistoric Puebloan sample from Southwestern Colorado	2002	0	0	0	1	0	0	12	**11**	1	4	0	0	0	0	0	0	0	13	0	19	0	0	0	7	0	7	0	3	0	1075-1125: 11 1225-1280: 1 1075-1280: 16 1125-1175: 4	c	11	32	Colorado, United States of America	Yes	
Larentis, O. Tonina, E. Tesi, C. Rossetti, C. Gorini, I. Ciliberti, R. Licata, M.	of subligamentous tuberculosis spondylitis: The concealed body of the late modern period (early 16th century to early 20th century), Franciscan crypt of St. Anthony and St. Eusebius church, Lombardy, Italy	2019	1	0	0	1	**1**	T2-5	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	1600-1800	c	1	1	Lombardy, Italy	No	
Larsen Spencer, C.	Bioarchaeology - interpreting behavior from the human skeleton	2015	0	0	0	1	0	0	**1**	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	1	AD 1050-1400 Mississippian	c	not specified	not specified	Mississippi, United States	No	
Larsen Spencer, C.	Bioarchaeology - interpreting behavior from the human skeleton	2015	0	0	0	1	**1**	0	1	3	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	0	0	0	3	not specified	c	3	3	not specified	No	
Larsen Spencer, C.	Bioarchaeology - interpreting behavior from the human skeleton	2015	0	0	0	1	0	0	1	0	2	1	0	0	0	0	0	0	0	0	0	0	0	0	3	0	0	0	0	0	3	not specified	c	3	3	not specified	No	
Magilton, J. Lee, F. Boylston, A. Judd, M. Kenny, J. Lewis, M. Manchester, K. Ogden, A. Ortner, D. Storm, R. Sture, J.	Lepers outside the gate	2008	0	0	0	1	**3**	L1-5	10	14	1	1	2	4	0	**1**	0	0	0	3	5	3	4	0	15	4	0	4	0	0	22	medieval	p	30	374	England, Chichester	Yes	

9.6. Appendix Database

Mariotti, V. Zupello, M. Pedrosi, M. Bettuzzi, M. Brancaccio, R. Peccenini, E. Morigi, M. Balcastro, M.	Skeletal evidence of tuberculosis in a modern identified human skeletal collection (certosa cemetery, Bologna, Italy)	2015	1	0	0	1	3	1: T5-12 2: T10-L3	3	48	0	102	0	0	0	0	0	0	**64**	0	8	46	10	0	0	138	0	106	0	0	0	1891-1944	p	64	244	Bologna, Italy	No	
Matos, V. Marques, C. Lopes, C.	Severe vertebral collapse in a juvenile from the graveyard (13th/14th-19th centuries) of the São Miguel Church (Castelo Branco, Portugal): Differential palaeopathological diagnosis	2011	1	0	0	1	**1**	T3-7	1	1	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1200/1300-1800 CE	c	1	10	Castelo Branco, Portugal	No	
Matos, V. Santos, A. L.	On the trail of pulmonary tuberculosis based on riblesions: results from the human identified skeletal collection from the museu Bocage (Lisbon, Portugal)	2006	1	0	0	1	0	0	0	**76**	0	0	0	0	0	0	0	0	**84**	0	24	49	11	0	0	109	0	88	0	0	0	1800-1900	c	84	197	Lisbon, Portugal	No	
Mays, G. S. Taylor, M.	A first prehistoric case of tuberculosis from Britain	2003	0	**1**	MTC	1	1	L2-3	1	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	0	0	0	(iron age) 400-230 BC	c	1	15	Britain	Yes	

9.6. Appendix Database

Mays, S. Fysh, E. Taylor, G.M.	Investigation of the link between visceral surface rib lesions and tuberculosis in a medieval skeletal series from England using ancient DNA	2002	0	**1**	MTB	1	0	0	1	7	2	2	2	1	0	0	0	0	0	2	2	1	2	0	0	2	1	2	0	0	0	medieval	c	7	687	England	No	
Mays, S. Taylor, G.M. Legge, A.J. Young, D.B. Turner-Walker, G.	Paleopathological and biomolecular study of tuberculosis in a medieval skeletal collection from England	2001	1	**1**	MTB	1	0	0	7	4	2	5	1	0	0	0	0	0	0	0	0	0	4	5	0	0	5	1	3	0	0	0	medieval (generally 890-1400 AD) see p. 302	c	9	"	northern England, Wharram Percy	Yes	
Molnár, E. Marcsik, A.	Paleopathological evaluation of hungarian skeletal remains from the 7th-9th centuries AD	2002	1	**1**	MTB	1	0	0	1	1	0	0	0	0	2	0	0	0	0	0	0	0	3	0	0	0	2	0	1	0	0	0	600-800 AD	p	10	423	Hungary	No	
Müller, R. Roberts, C. Brown, T.	Biomolecular identification of ancient mycobacterium tuberculosis complex DNA in human remains from Britain and continental Europe	2014	0	**1**	MTB	1	**11**	not specified	24	27	6	6	2	4	1	0	0	0	0	10	0	60	0	0	0	28	6	23	5	8	0	1-9th c AD	p	12	70	europe	No	
Nicklisch, N. Maixner, F. Ganslmeier, R. Friederich, S. Dresely, V. Meller, H. Zink, A. Alt, K. W.	Rib lesions in skeletons from early neolithic sites in central Germany: on the trail of Tuberculosis at the onset of agriculture	2012	1	**1**	MTB	1	2	lower C, Lower T	2	22	3	6	1	8	0	0	0	0	0	31	0	57	0	0	0	24	0	31	0	0	0	5400-4800 BC	c	14	118	Germany	No	

9.6. Appendix Database

Nuorala, E. Götherström, A. Ahlström, T. Donoghue, H.D. Spigelman, M. Lidén, K.	MTB complex DNA in a Scandinavian Neolithic passage grave	2004	0	**1**	MTB, MB, MM or MA	1	1	T + L	0	0	1	1	0	0	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	0	2	4590-2440 BP	c	2	130	Scandinavia	Yes	
Paja, L. Coqueugniot, H. Dutour, O. Willmon, R. Farkas, G.L. Palkó, A. Pálfi, G.	Knee ankylses associated with tuberculosis from the Medieval Hungary - Differental Diagnosis Based on Medical Imaging Techniques	2012	1	0	0	1	0	0	0	0	0	0	**2**	0	0	0	0	0	0	0	0	0	0	2	0	0	2	0	0	0	0	0	12th-16th AD	c	2	3782	Hungary	No	
Pálfi, G. Maixner, F. Maczel, M. Molnár, E. Pósa, A. Kristóf, L. A. Marcsik, A. Balázs, J. Masson, M. Paja, L. Palkó, A. Szentgyörgyi, R. Nerlich, A. Zink, A. Dutour, O.	Unusual spinal tuberculosis in an Avar Age skeleton (Csongrád-Felgyő, Ürmös-tanya, Hungary): A morphological and biomolecular study	2015	1	**1**	MTB	1	**1**	T10-L3	1	1	0	0	1	0	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	7-8th century AD	p	1	216	Hungary	Yes	
Sabin, S. Herbig, A. Vågene, Å. Ahlström, T. Bozovic, G. Arcini, C. Kühnert, D. Bos, K.	A seventeenth-century Mycobacterium tuberculosis genome supports a Neolithic emergence of the Mycobacterium tuberculosis complex	2020	1	**1**	MTB	1	0	0	0	0	0	0	0	0	0	1	0	1	0	1	0	0	1	0	0	0	1	0	0	0	0	0	1600	c	1	1	Lund, Sweden	Yes	

Santos, A. L. Roberts, C. A.	Anatomy of a serial killer: Differential diagnosis of tuberculosis based on rib lesions of adult individuals from the coimbra identified skeletal collection, Portugal	2006	1	0	0	1	0	0	0	**54**	0	0	0	0	0	0	0	0	**171**	0	0	263	0	0	0	157	0	106	0	0	0	1904-1936	p	171	263	Portugal	No	
Santos, A. L. Roberts, C. A.	A picture of tuberculosis in young Portuguese people in the Early 20th century: a multidisciplinar y study of the skeletal an historical evidence	2001	1	0	0	1	**1**	C7-T8	**1**	**13**	2	4	0	1	0	0	0	0	**18**	19	27	20	0	0	0	30	0	36	0	0	0	1904-1936	c	18	66	Portugal	No	
Sparacello, V. Roberts, C. Kerudin, A. Müller, R.	A 6500-year-old Middle Neolithic child from Pollera Cave (Liguaria, Italy) with probable multifocal oateoarticular tuberculosis	2017	1	**1**	N	1	0	0	1	1	1	0	1	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	5740 +- 30 BP	c	1	1	Liguria, Italy	Yes	
Spekker, O. Hunt, D.R. Váradi,O.A. Berthon, W. Molnár, E. Pálfi, G.	Rare manifestations of spinal tuberculosis in th e Robert J. Terry Anatomical Skeletal Collections (National Museum of Natural History, Smithsonian Institution, Washington, DC, USA)	2018	1	0	0	1	0	0	**1**	1	0	1	0	0	0	0	0	0	**1**	0	0	1	0	0	0	1	0	0	0	0	0	1902-1926	c	1	1	United states of America	No	

9.6. Appendix Database

Spekker, O. Hunt, D.R. Váradi,O.A. Berthon, W. Molnár, E. Pálfi, G.	Rare manifestations of spinal tuberculosis in th e Robert J. Terry Anatomical Skeletal Collections (National Museum of Natural History, Smithsonian Institution, Washington, DC, USA)	2018	1	0	0	1	0	0	**1**	1	1	1	0	0	0	0	0	0	**1**	0	0	1	0	0	0	1	0	0	0	0	0	1895-1931	c	1	1	United states of America	No	
Spekker, O. Hunt, D.R. Váradi,O.A. Berthon, W. Molnár, E. Pálfi, G.	Rare manifestations of spinal tuberculosis in th e Robert J. Terry Anatomical Skeletal Collections (National Museum of Natural History, Smithsonian Institution, Washington, DC, USA)	2018	1	0	0	1	**1**	C6-7 L1-2	1	0	0	0	0	0	0	0	0	0	**1**	0	0	1	0	0	0	0	0	1	0	0	0	1899-1949	c	1	1	United states of America	No	
Spigelman, M. Pap, I. Donoghue, H.D.	A death from langerhans cell histiocytosis and tuberculosis in 18th century Hungary - what palaeopatholog y can tell us today	2006	1	**1**	MTB	1	0	0	0	1	0	0	1	1	0	0	0	0	0	1	0	0	0	0	0	0	0	0	0	0	0	1750-1770	c	1	263	Hungary	Yes	
Spigelman, M. Matheson, C. Lev, G. Greenblatt, C. Donoghue, D. H.	Confirmation of the presence of Mycobacterium tuberculosis complex-specific DNA in three archaeological specimens	2002	0	**1**	0	1	**2**	L-S	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	2	0	0	0	0	0	3	1 pre-european-contact Borneo, 1 Byzantine Turkey, 1 17th c Scotland	c	3	3	1 Borneo, 1 Turkey, 1 Scotland	No	

9.6. Appendix Database

Suzuki, T. Fujita, H. Gyu Choi, J.	Brief communication: New evidence of tuberculosis from prehistoric Korea - population movement and early evidence of tuberculosis in Far East Asia	2008	1	0	0	1	**1**	T11-L1	1	1	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	1	0	0	0	100-0 BCE	c	1	200	Korea	Yes	
Suzuki, T. Inoue, T.	Earliest evidence of spinal tuberculosis from the Aneolithic Yayoi period in Japan	2007	0	0	0	1	**2**	1: T3-7 2: T7-11	0	**1**	0	0	0	0	0	0	0	0	0	0	0	2	0	0	1	1	0	0	0	0	2	300 BC - 300 AD	c	3	3	Japan	No	
Tayles, N. Buckley, H.R.	Leprosy and tuberculosis in Iron age southeast asia	2004		0	0	1	**1**	T11-L1 T2-6	1	0	0	0	0	1	0	0	0	0	0	0	0	1	0	0	0	0	0	1	0	0	0	iron age	c	1	1	Thailand	Yes	
Zink, A. Haas, C. Reischl, U. Szeimies, U. Nerlich, A.	Molecular analysis of skeletal tuberculosis in an ancient Egyptian population	2001	1	**1**	9 MTB	1	1	T12-L1	13	3	0	0	0	0	1	0	1	0	0	2	0	39	0	0	0	14	0	6	0	21	0	New kingdom (1550-1069 BCE): 6/31 Middle kingdom (2050-1650 BCE): 1/6 predynastic (pre-3150 BCE): 1/1 Early-dynastic (3150-2686 BCE): 1/3	p	9	41	Egypt	No	

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Zink, A.R. Grabner, W. Nerlich, A.G.	Molecular identification of human tuberculosis in recent and historic bone tissue samples: the role of molecular techniques for the study of historic tuberculosis	2005	1	**1**	0	1	0	0	1	0	0	0	0	0	0	0	0	**5**	0	0	0	24	0	0	0	15	0	9	0	0	0	1990-2000	p	8	24	Munich	No	
Zink, A.R. Grabner, W. Nerlich, A.G.	Molecular identification of human tuberculosis in recent and historic bone tissue samples: the role of molecular techniques for the study of historic tuberculosis	2005	1	**1**	0	1	5	L4-5 L4-S1 T12-L1 L1-4 T10-11	17	0	0	0	0	0	1	0	0	0	0	2	0	34	0	0	0	17	0	6	0	13	0	1550-1070 BC used until 500BC	p	7	36	Egypt	No	
Zink, A.R. Molnár, E. Motamedi, N. Pálfy, G. Marcsik, A. Nerlich, A.G.	Molecular history of tuberculosis from ancient mummies and skeletons	2007	0	**1**	MTC	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	10	0	0	0	0	0	10	1400-1800 AD	p	10	51	Southern Germany	No	
Zink, A.R. Molnár, E. Motamedi, N. Pálfy, G. Marcsik, A. Nerlich, A.G.	Molecular history of tuberculosis from ancient mummies and skeletons	2007	0	**1**	MTC	1	1	T	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	23	0	0	0	0	0	23	600-1700 AD	p	23	75	Hungary	No	
Zink, A.R. Molnár, E. Motamedi, N. Pálfy, G. Marcsik, A. Nerlich, A.G.	Molecular history of tuberculosis from ancient mummies and skeletons	2007	0	**1**	2 MA	1	1	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	0	37	0	0	0	0	0	37	13: 3500-2650 BCE 68: 2050-1650 BCE 79: 1500-500 BCE	p	37	160	Egypt	No	

9.6. Appendix Database

Zink, A.R. Sola, C. Reischl, U. Grabner, W. Rastogi, N. Wolf, H. Nerlich, A.G.	Molecular identification and characterization of Mycobacterium tuberculosis complex in ancient Egyptian mummies	2004	0	**1**	MTB	1	1	T + L	1	0	0	0	0	0	1	0	1	0	0	0	0	0	0	0	7	0	0	0	0	0	7	3500-2800 BC	p	7	133	Egypt	No	
Zink, A.R. Sola, C. Reischl, U. Grabner, W. Rastogi, N. Wolf, H. Nerlich, A.G.	Molecular identification and characterization of Mycobacterium tuberculosis complex in ancient Egyptian mummies	2004	0	**1**	MTB + MA	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	64	0	0	0	0	0	64	2100-1650 BC	p	64	243	Egypt	No	
Zink, A.R. Sola, C. Reischl, U. Grabner, W. Rastogi, N. Wolf, H. Nerlich, A.G.	Molecular identification and characterization of Mycobacterium tuberculosis complex in ancient Egyptian mummies	2004	0	**1**	MTB + MA	1	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	0	0	0	47	0	0	0	0	0	47	1450-500 BC	p	47	605	Egypt	No	
Zink, A.R. Sola, C. Reischl, U. Grabner, W. Rastogi, N. Wolf, H. Nerlich, A.G.	Characterization of Mycobacterial tuberculosis complex DNAs from Egyptian Mummies by spoligotyping	2003	0	**1**	12 MTB or MA	1	0	0	0	0	1	0	0	0	1	0	1	0	0	1	0	0	0	0	24	1	0	0	0	0	24	2050-500 BC	p	25	85	Egypt	No	