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Malaise and mosquitos: osteoarchaeological evidence for malaria in the medieval Netherlands

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Malaria was an important disease in the history of the Netherlands. For the period after 16th century AD, there is solid documentation indicating the presence of the disease, specifically in the marshy areas of Holland and Zeeland. For the medieval period (AD 1000-1600), however, no such data exist which has resulted in the absence of malaria in discussions on past health and disease. Therefore, this article explores the possibility of medieval malaria by analysing the relationship between skeletal pathology and habitation in marshy areas. Results indicate that malaria was a highly significant illness in these regions of the Netherlands. This demonstrates that ignoring malaria as an important disease may result in wrong conclusions about the health status of medieval populations.

1 Introduction

Ziet ge muggen, lang van poot
Aarzel niet, maar sla ze dood!
Klein is de mug, maar groot het leed
Veroorzaakt door een muggebeet.
Beter dan chinine slikken,
Is het muggen dood te tikken!

A mosquito is neither friend nor pet
So don't hesitate and kill him dead
Small the bug but big the blight
Caused by a mosquito bite
Better than swallowing lots of pills
Is to give a mighty whack that kills

(translation Kelly Fennema)

Malaria, a debilitating and often chronic disease, is a major health problem in the non-western world. Although currently absent in the Netherlands, historical evidence suggests that malaria was endemic here as well, specifically in the marshy areas (Swellengrebel and de Buck 1938, 9; Van Seventer 1969, 9; Van der Heide 1988, 2374). This is demonstrated by the quote displayed above. The short poem encouraging people to kill mosquitos was displayed in the offices of general practitioners in the 1930s (Van der Heide 1988, 2372). This is a clear example of the fact that also in the Netherlands, malaria presented a health problem up to the 20th century. Unfortunately, in historical sources references to malaria concerning the period before the 17th century are scarce (Bruce-Chwatt and de Zulueta 1980, 106). While it is expected that the disease was also present in the medieval Netherlands based on the abundance of marshy areas in this period, the lack of solid documentation impairs the assessment of the impact and spread of malaria during this time.

Given the lacunae in our knowledge of malaria in the medieval Netherlands from historical records, we have to turn to archaeological data, specifically to human skeletal remains. The study of osteoarchaeology has proven an excellent source for knowledge about disease in the past. However, the fact that malaria does not result in specific skeletal lesions makes it difficult to study the disease in the archaeological record. Recently however, Gowland and Western (2012) were able to demonstrate a clear relationship between a pathological lesion called cribra orbitalia and regions they considered to be malarial (Gowland and Western 2012). This led them to conclude that even though malaria is not the only disease causing the orbital lesions, it can be used as an indicator for malaria in the UK. Therefore, building on research of Gowland and Western (2012), this paper aims to research the prevalence of cribra orbitalia in Dutch skeletal collections dating to the medieval period to investigate if a similar relationship between the pathology and possible malaria endemic areas exist. If so, this study will provide the first indirect evidence for malaria in the medieval period and will emphasise the importance of considering this aetiology in future skeletal research in the Netherlands.

2 Malaria: an overview

Malaria is an infectious mosquito-borne disease caused by parasitic protozoans of the *Plasmodium* genus. Only mosquitos of the *Anopheles* genus can transmit the malaria parasites: from the saliva, they are transferred to the circulatory system of the host where the parasites reproduce and mature (Sinden and Gilles 2002, 8). Of the approximately 200 species of the *Plasmodium* genus, there are currently four which directly infect humans: *P. vivax, P. falciparum, P. malariae,* and *P. ovale*. The *P. vivax* parasite is still the most globally distributed one. Since the *P. vivax* species is able to develop at lower temperatures than the other species and has a long incubation period, it was this species that was present in the Netherlands in the past, (Martens *et al*. 1999, S92). In contrast to the species prevalent in Africa (*P. falciparum*), the *P. vivax* malaria is considered to be less fatal (Warrell 2002, 200). The other two species have a limited distribution and are rarely associated with fatalities (Warrell 2002, 202).

One of the most important symptoms of malaria are the intermittent fevers, a feature of the disease also recognised throughout history, as will be discussed below. The fevers are the result of the typical life cycle of the parasites. Once they enter the human body, they invade the liver and red blood cells where parasite reproduction takes place. Once enough parasites are produced, which takes approximately 48 to 72 hours, the red blood cells burst releasing malaria organisms in the blood stream. This sudden increase of parasites in the blood results in an immune response of the body which is responsible for the fevers, but also for chills and muscle pain associated with malaria (Pinello 2008, 28). The symptoms are relieved when the parasites invade new blood cells, but will return once the cells burst again, explaining the intermittent fevers so well known for malaria. This destruction of red blood cells also results in another important symptom: anaemia. The cells are destroyed faster than the body can produce them, leading to a low red blood cell count. Although this does not have to be fatal, weaker individuals such as the sick, elderly or children can easily die as a result of anaemia (Douglas *et al*. 2012), which suggests that this could have been the case in the past as well.

3 Malaria in the past

Although it is difficult to identify malaria on the basis of past descriptions of symptoms, malaria appears to be a disease of great antiquity. Even though the name of the disease only dates to the 18th century, referring to the then assumed cause (corrupted air = *mala aria*) (van Seventer 1969, 9), references to seasonal and intermittent fevers are found much earlier in ancient Assyrian, Chinese, and Indian medical texts. Additionally, early scholars from Europe also seem to note the presence of the disease. Hippocrates, for example, described symptoms which can be associated with malaria (Gilles 2002, 1; Packard 2007, 37). In the third century BC, malaria appeared to have been omnipresent in Rome and its surroundings taking substantial numbers of lives (Packard 2007, 37). Plinius prescribed bread with woodlice as remedy for the fever that was plaguing the citizens (van der Heide 1988, 2372). From this period onwards, it is assumed that malaria spread to Northern and Central Europe. Historical documents indicate its presence in England in the 16th century AD. English marshlands were considered to be extremely unhealthy since inhabitants and visitors were plagued by *ague*, a term which refers to the high, intermittent fevers (Dobson 1989, 3). In the centuries that followed, references to what appears to have been malaria are regularly found throughout Europe, suggesting that it was a common disease. From the 19th century onwards, improved agricultural methods, medication, and other eradication techniques resulted in a decrease of malaria in Europe (Packard 2007, 37).

Malaria is also known to have had a long history in the Netherlands. From the 17th century onwards, references to symptoms which could be related to the disease are found in several historical documents. Sylvius de le Boë, a Dutch doctor and anatomist, describes an epidemic of fevers in Leiden in 1669 and the famous Dutch physician Herman Boerhaave also has written extensively about the fevers causing many deaths in the Netherlands (Bruce-Chwatt and de Zulueta 1980, 106). In 1826, a severe outbreak of fevers, apparently related to flooding of the North Sea, caused many deaths. In Amsterdam, for example, 2400 of the 200,000 inhabitants are reported to have died as a result of ‘malarial disease’. Several more outbreaks would plague the Netherlands in this century (Bruce-Chwatt and de Zulueta 1980, 107), although the infection rates became somewhat lower in this time. This was most likely as a result of the increased availability and reduced price of the medicine quinine (van Seventer and De Buck 1938, 24-26).

What is clear throughout time is the relationship between marshy areas, especially regions that were reclaimed from the sea, and the prevalence of malaria. The current provinces of Zeeland, Friesland, North-Holland, and Groningen appear to have been most heavily affected by ‘malarial disease’ (Bruce-Chwatt and de Zulueta 1980, 108). In the 20th century, it became clear that this is a result of the preference of *Anopheles atroparvus,* the mosquito species which was transmitting malaria in the Netherlands, for breeding in brackish water. In the peat and clay areas reclaimed on the sea, water salinity would have been high, creating the perfect breeding ground for malaria mosquitos. In these areas, mosquito density would be very high (fig. 1) resulting in a high prevalence of malaria. This is also why the damming of the Zuiderzee with the Afsluitdijk in 1932 reduced the disease rates in the Netherlands: the once large body of brackish water now became fresh water. Additionally, a combination of measures in the form of supplementary medication and treatment of houses (and stables) with insecticide (Dichloordifenyltrichloorethaan or D.D.T.) resulted in the disappearance of the disease in the 20th century (van der Heide 1988, 2374). After 1958, no patient with autochthonous malaria has been reported in the Netherlands (van Seventer 1969, 2055).

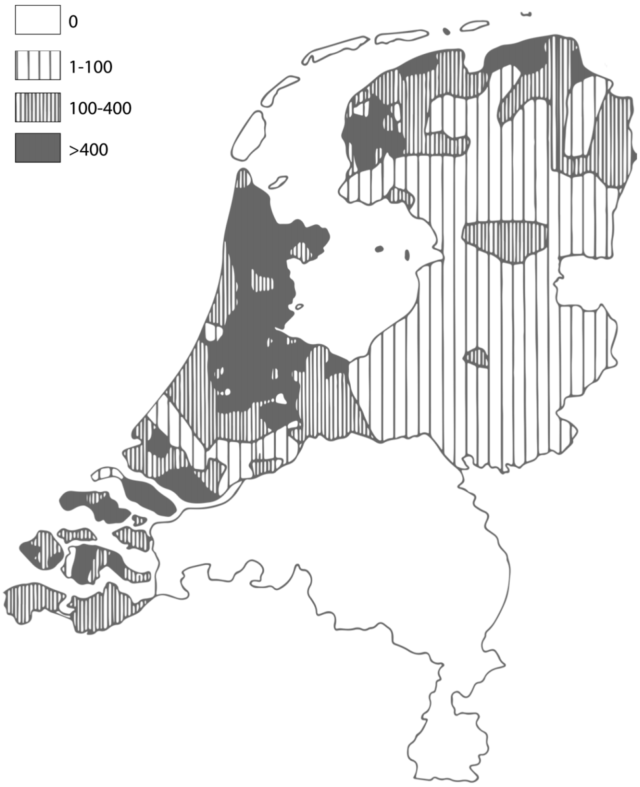

Figure 1 Map of the Netherlands indicating mosquito density as estimated by the number of mosquitos found in stables in 1938: black=more than 400 mosquitos, narrow lines=100-400 mosquitos, wide lines=1-100 mosquitos, white=0 mosquitos (adapted from Swellengrebel and de Buck 1938, 71)

Information on geology and climate from the medieval period suggests that malaria could have been prevalent during this time. Land reclamation was one of the most important activities in the medieval period in the coastal regions, starting around AD 1000, resulting in large areas of drained peat and clay surrounded by brackish water (Hoppenbrouwers 2002, 116). This would have created the perfect circumstances for endemic malaria in the medieval period. Since no historic documentation on malaria in this period exists, osteoarchaeological data from skeletal assemblages provide the only means by which evidence for this hypothesis can be gained.

4 Malaria in the skeleton

4.1 Direct evidence: biomolecular

Palaeopathology aims at diagnosing disease in human remains. Unfortunately, it is not always possible to identify the specific disease that is the cause of lesions observable in the skeleton through macroscopic examination alone. This is due to the fact that bone has a limited response to disease. As a result, skeletal lesions caused by a number of diseases are indistinguishable from each other. Recent advances in ancient pathogen research, however, have made it possible to identify ancient disease directly in bone, resulting in a definitive diagnosis. This approach worked particularly well for tuberculosis (*e.g.* Mays *et al.* 2001; Mays and Taylor 2003), leprosy (Donoghue *et al.* 2005) and the Black Death (Bos *et al.* 2012; Harbeck *et al.* 2013). However, identifying malaria parasites in ancient human remains proved to be more difficult. Parasite DNA has been successfully found in soft tissues of Egyptian mummies (Nerlich *et al.* 2008), however, the detection appears to be more challenging in skeletal remains. Although ancient malaria pathogen DNA was found in the skeleton of a child from Italy (Sallares *et al.* 2004), several other researchers failed to retrieve the parasite DNA from bone. For example, Pinello (2008) analysed over a hundred skeletons from malaria endemic areas in England but was unable to identify malaria DNA. The author hypothesises that this is most likely due to poor pathogen DNA survival or to inadequate detection techniques at the time (Pinello 2008, 12).

Other methods for identifying ancient disease in skeletal remains include lipid biomarkers analysis and antibody detection. Lipid biomarker research has shown to be valuable for diagnosis of tuberculosis and leprosy (*e.g.* Gernaey *et al.* 2001), however, this has not been attempted for malaria. The detection of antibodies has had some success in archaeology. Kolman *et al.* (1999) were able to detect syphilis antibodies, although other researchers were unable to confirm their results (*e.g.* Cattaneo *et al.* 1992). For the detection of malaria, this approach has proved to be successful in soft tissue samples from Egyptian mummy remains (Bianucci *et al.* 2008). Fornaciari and colleagues (2010) were able to detect malaria antibodies in members of the Medici family in Italy who were known to have died from malaria. Currently, Kendall and colleagues are working on improving the immunological assays to be able to apply this method on a more regular (cost efficient) basis in archaeology (Kendall *et al.* 2014).

4.2 Indirect evidence: skeletal

As direct detection methods for malaria in ancient skeletal remains are currently not providing clear and consistent results, indirect skeletal evidence for the disease has to be considered to be able to gain insights in the distribution in the past. Although malaria does not result in clear pathognomonic lesions in the skeleton, the fact that anaemia is one of the most common symptoms allows it to be studied osteoarchaeologically. Anaemia results in a deficiency of red blood cells which the body will try to replace by generating more. Most of the red blood cell production in the human body takes place in the bones, specifically in the marrow.

In response to the low red blood cell count, the bone marrow becomes enlarged in an effort to produce more cells. Occasionally, this expansion of the marrow can be seen macroscopically in the skeleton since it results in the disappearance of the outer layer of bone. Especially in places where the cortex is thin, such as the cranium, the effects of anaemia can be seen. The eye orbits are prone to show the lesions associated with marrow enlargement since the bone cortex is very thin. This marrow hyperplasia in the eye orbits is termed cribra orbitalia and gives the surface a porous, sieve-like appearance (fig. 2) (Aufderheide and Rodríguez-Martín 1998; Walker *et al*. 2009; Gowland and Western 2012).

It is, however, important to note that anaemia is not a specific disease, but a pathological symptom and can be related to many causal factors, not just malaria (Walker 1985; Walker *et al*. 2009, 110). The causes of anaemia in archaeology have been extensively debated over the last few years. Although controversy on the actual aetiology still exists (see Waldron 2009; Walker *et al*. 2009), cribra orbitalia is generally described to be the result of general nutritional stress (Waldron 2009). High prevalence of orbital lesions in a population will commonly lead to the conclusion that the individuals were deprived of certain nutrients. Although vitamin deficiencies are a good explanation for cribra orbitalia in areas without malaria, in regions where this disease was prevalent it has to be considered as possible cause for the orbital lesions as well. While the fact that anaemia is an important symptom in malaria would suggest that the disease is a likely cause of orbital lesions, due to its clinical insignificance and difficulty of observing this lesion radiologically, medical literature does not currently support this hypothesis (Gowland and Western 2012, 303). Recently, however, Gowland and Western (2012) were able to demonstrate a clear relationship between cribra orbitalia and marshy areas in Anglo-Saxon England. No such correlation was found with enamel hypoplasia, another skeletal stress marker, suggesting that the orbital lesions can be a good indicator for malaria in the archaeological record (Gowland and Western 2012, 309).

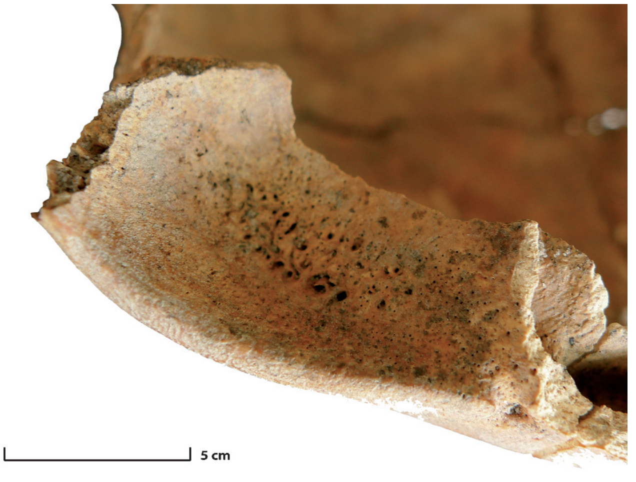

Figure 2 Healed cribra orbitalia in the left eye orbit of an adult female from the Paardenmarkt collection, Alkmaar

In Dutch skeletal collections, cribra orbitalia is a relatively common pathology. However, malaria is rarely mentioned as a possible cause for the orbital lesions in skeletal reports, even though it is possible that this disease is responsible for the observed cribra orbitalia, especially when individuals came from a region with malaria endemicity. Currently, however, there is no strong indication for malaria being present in the medieval period. Therefore, the relationship between marshy areas and the prevalence of cribra orbitalia is studied in an effort to provide indirect evidence for the presence of malaria.

4 Cribra orbitalia in Dutch skeletal collections

4.1 *Materials and methods*

For this study, the prevalence of cribra orbitalia in 13 urban and rural skeletal collections, a total of 1838 individuals, are compared. An overview of the collections and cribra orbitalia prevalence are shown in table 1. Unfortunately, the percentages of cribra orbitalia displayed in the table are crude prevalences which mean that all individuals in the collection are taken into account, not just the individuals with eye orbits. Ideally, a true prevalence, including only individuals with eye orbits, should be used for this kind of analysis. However, this was not available for all collections. If only assemblages for which a true cribra orbitalia prevalence was recorded were used, the sample size and geographic spread would become too limited for valuable analysis. Therefore, it was decided to use the crude prevalence, but it is important to keep in mind that this may have been influenced by post-mortem factors such as taphonomic alteration or destruction of bones.

The seventh column in the table indicates whether the collection came from an area considered to be high in malaria mosquitos. Since no direct evidence is available for the medieval period, the categorisation is based on counts from the 1930s. When the skeletal collection originated from an area with more than a hundred mosquitos in 1938, it is considered malarial. Although it is possible that mosquito density changed during time, information on past geological circumstances would suggest that areas classified as malarial in 1938 would have been preferred by malaria mosquitos in the medieval period as well. The skeletal assemblages classified as malarial according to the

Site number	Site	Dating	Number of individuals	Cribra orbitalia	Crude prevalence (%)	Malarial?	Reference
1	Beguinage cemetery, Breda	1267-1530	120	0	0,0%	No	Rijpma and Maat 2005
2	Blokhuizen, Niedorp	1000-1200	119	13	10,9%	Yes	Schats, in prep.
3	Catharinakerk, Eindhoven	1200-1500	186	3	1,6%	No	Baetsen and Weterings-Korthorst 2013
4	Cruyskerke	1200-1421	316	6	1,9%	No	Sannen 2010
5	Julianaplein, Wijk aan Zee	1420-1573	17	3	17,6%	Yes	Baetsen 2008
6	Klaaskinderkerke	1268-1573	54	7	13,0%	Yes	Schats, in prep.
7	Koningsveld, Delft	1450-1572	220	4	1,8%	No	Groen, in prep.
8	Minderbroeder-sklooster, Dordrecht	1275-1572	316	5	1,6%	No	Maat et al. 1998
9	Nieuwlichtklooster, Utrecht	1392-1580	57	8	14,0%	Yes	d'Hollosy 2012
10	Oude en Nieuwe Gasthuis, Delft	1265-1652	101	1	1,0%	No	Onisto et al. 1998
11	Paardenmarkt, Alkmaar	1448-1572	189	17	9,0%	Yes	Schats, in prep.
12	Stiftskapel, Maastricht	1070-1521	27	0	0,0%	No	Jansen and Maat 2002
13	Vroner Kerkhof, St. Pancras	1000-1297	116	8	6,9%	Yes	Alders and van der Linde 2011

Table 1 Prevalence of cribra orbitalia in the collections under study and corresponding 'malarial' or 'non-malarial' categorisations

20th century data are mostly from North-Holland and Zeeland where regions of peat and clay reclaimed on the sea were very common. Figure 3 shows the same map as above but now includes the skeletal assemblages used for comparison in this study.

4.2 Results

The comparison of the prevalence of cribra orbitalia between the areas considered malarial and those which are deemed non-malarial shows a marked difference. In total, 56 individuals (10.1%) showed orbital lesions in the malarial regions and in the non-malarial areas only 19 of 1286 (1.5%) individuals were affected by this pathology (table 2). This difference in prevalence between the malarial and non-malarial regions can be analysed using a chi-square test of independence to assess whether the difference also meets statistical significance. The results indicate that the difference is highly statistically significant (X^2= 74.131, df=1, $p<0.001$, N=1838), pointing to a clear relationship between cribra orbitalia presence and regions considered to be malarial.

5 Malaria in medieval Netherlands

The results indicate a strong link between areas deemed malarial and the prevalence of cribra orbitalia. Much higher frequencies of the orbital pathology are reported for the skeletal assemblages that originated from areas where malaria mosquitos are assumed to have been prevalent in the medieval period. This would suggest that cribra orbitalia, as was shown by Gowland and Western (2012) for the UK, is also a good indicator for malaria in the Netherlands. Consequently, while this was previously only assumed, the results of this study potentially provide evidence for the occurrence of malaria in the medieval period.

Even though sample size in this study is modest and the geographic spread does not cover the entire Netherlands, the results have important implications for the understanding of health and disease in the medieval period. This research has demonstrated that malaria is most likely a significant cause of cribra orbitalia in the regions where the disease was endemic, such as large parts of North-Holland and Zeeland. Ignoring malaria as a factor in the discussion of disease in a

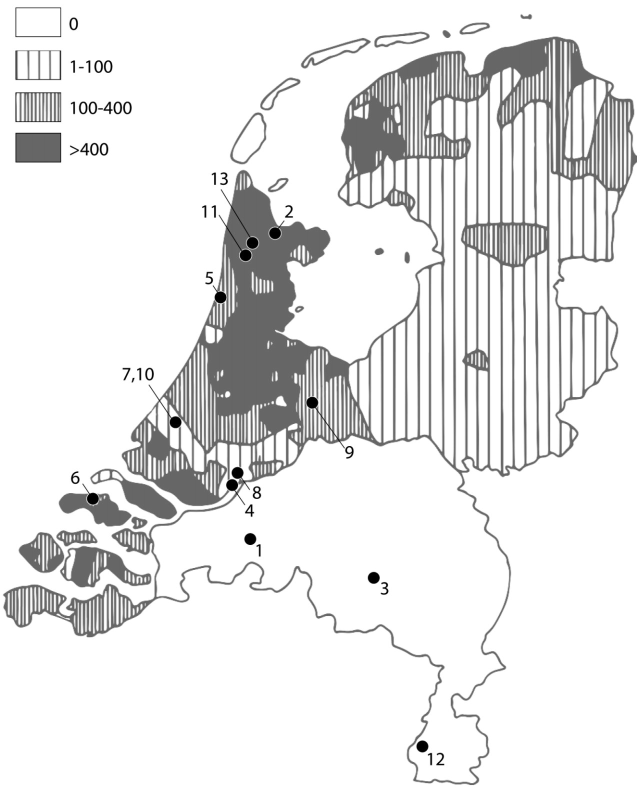

Figure 3 Map of the Netherlands indicating mosquito density in 1938 (adapted from Swellengrebel and de Buck 1938, 71) with the sites used in this study indicated as dots (numbers correspond with those in table 1)

population from these regions could potentially result in wrong conclusions. For example, the high prevalence of cribra orbitalia in the skeletal collection from Wijk aan Zee is explained in the skeletal report by high levels of nutritional stress (Baetsen 2008, 74). Considering that Wijk aan Zee was located in a region with high malaria endemicity, this disease should have been taken into account as a possible cause of the orbital lesions.

To conclude, this paper has demonstrated that malaria could have been an important disease in the medieval period in the marshy areas of the Netherlands. By showing a relationship between malarial areas and cribra orbitalia prevalence, this study has demonstrated the potential of using the lesions as malaria indicators in Dutch archaeology. Consequently, the results have significant implications for the interpretation of cribra orbitalia. Rarely malaria has been discussed as a possible cause, more often cribra orbitalia is associated with nutritional stress. Even though many factors can be responsible, not taking into account malaria-related anaemia can result in incomplete discussion on health and disease, specifically when dealing with skeletons from marshy areas. The incorporation of malaria in the differential diagnosis of cribra orbitalia could potentially completely change the interpretation of the health status of some archaeological populations.

In the future, more conclusive evidence could be provided through the incorporation of new biomolecular techniques. As discussed above, some studies focusing on malaria detection in skeletal remains using DNA techniques have been performed, unfortunately with limited success (*e.g.* Sallares *et al.* 2004; Pinello 2008). However, recently, new DNA techniques have been developed which may improve the detectability of the ancient pathogen in human bones (Kobolt *et al.* 2013). Additionally, the analysis of human dental calculus has shown to have great potential for the analysis of disease in past populations (Warinner *et al.* 2015) which may also be of use in the search for the malaria parasites. With these new methods, it will be possible in the future to gain a full and definitive understanding of the spread of malaria in the medieval period. The present study has created a starting point from which further research can be undertaken.

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	Number of individuals with cribra orbitalia	Number of individuals without cribra orbitalia	Total number of individuals	Crude prevalence
Malarial	56	496	552	10,1%
Non-malarial	19	1267	1286	1,5%

Table 2 Prevalence of cribra orbitalia in malarial and non-malarial areas

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