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Tracing Leprosy: The paleopathological study of the individuals excavated from the Sant Llàtzer leprosarium in Barcelona, Spain (12th-18th c.)

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ABSTRACT

Objective: Our objectives are twofold: to analyse the frequency of leprosy-related pathological lesions in the cemetery of Sant Llàtzer Hospital (12th-18th c.); and to examine how individuals affected by the disease were perceived and integrated into society during that period in Barcelona.
Materials: The skeletal remains of 87 individuals recovered from the cemetery.
Methods: All remains were analysed macroscopically and, when required, radiographed.
Results: Of the total number of individuals (n=87), 21 (24.1 %) showed evidence indicative of leprosy. Notably, the frequency of leprosy cases was lower in the 13th-15th c. (10 %; n = 50), the only period for which multi-person graves were documented.
Conclusions: The frequency of leprosy-related lesions in Sant Llàtzer is similar to that observed in other European Christian leprosaria, although it varies across the centuries. There is no funerary evidence that leprosy sufferers were treated differently than other citizens.
Significance: The cemetery of Sant Llàtzer, the first in Spain directly linked to a leprosarium, uniquely spans a significant period of activity. Its exceptionally preserved remains and rich records have offered unparalleled insight into the disease and its profound social implications.
Limitations: Leprosy affects the bone in only a small percentage of untreated cases. Moreover, poor preservation of skeletal remains may prevent diagnosis.
Suggestions for Further Research: Biochemistry, genomics, and proteomics might provide new insights into the disease, the origin and migrations of the individuals buried in Sant Llàtzer, as well as other aspects of their daily lives.

1. Introduction

Leprosy, or Hansen's disease, is an infectious disease caused by *Mycobacterium leprae* or *Mycobacterium lepromatosis*, primarily affecting the skin, peripheral nerves, and nasal and mouth tissues (WHO, 2023). Despite being curable, leprosy remains a significant health concern in some regions due to the stigma that hinders patients from seeking proper medical treatment, leading to an increased risk of developing disabilities (Cooreman, 2021).

Due to its chronic nature, leprosy can affect the facial skeletal structures, the hand and feet bones, and the tibiae and fibulae, making it identifiable in skeletal remains. However, not all changes occur in all individuals (Ortner, 2008; Roberts, 2020). Leprosy's clinical form is highly conditioned by the immunological response of the host, which

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implies that the course of the disease can differ between individuals (Ridley and Jopling, 1966). Patients with low resistance to the pathogen may develop severe lesions, including the characteristic changes in the rhinomaxillary area. This form is known as lepromatous leprosy (LL) or multibacillary form (Ridley and Jopling, 1966; Lockwood, 2010). On the other end of the spectrum, tuberculoid leprosy (TL) patients exhibit higher immunological response and no rhinomaxillary changes (paucibacillary form) (Ridley and Jopling, 1966; Lockwood, 2010).

Atrophy of the anterior nasal spine, widening and rounding of the nasal aperture, and recession of the prosthion in the maxilla (which may result in loss of the anterior teeth) are the three main facial skeletal changes that LL sufferers may experience (Ortner, 2008; Roberts, 2020). The internal structures of the nasal cavity and the oral surface of the palatine may also be affected (Andersen and Manchester, 1992).

In contrast, lesions in the limbs are generally linked to neglected trauma secondary to sensory loss rather than the direct action of the pathogen (Ortner, 2008; Lockwood, 2010). This sensory loss can lead to repetitive injuries, ulceration, and infection, which are not properly addressed due to the lack of pain perception. One of the characteristic effects of leprosy on hand bones is the destructive remodelling and resorption of the distal phalanges, resulting in significant bone loss and deformation (Ortner, 2008; Roberts, 2020). Additionally, diaphyseal remodelling in leprosy is marked by a reduction in the diameter of the long bones of the hands and feet, without the cortical bone appearing thinner (Andersen et al., 1992). The enlargement of the nutrient foramen of the hands may also occur in leprosy, due to the dilation of the arterioles (Roberts, 2020). This process leads to functional impairments and deformities, exacerbating the challenges faced by individuals suffering from the disease.

An infection in the soft tissues may result in an inflamed periosteum and the deposition of new bone layers onto the extracortical surface of the bone (Lewis et al., 1995). Specifically, tibial and fibular periosteal reaction with striated new bone deposits is characteristic of leprosy, although this reaction is again usually associated with sensory loss and neglected trauma rather than the direct action of *M. leprae* (Lewis et al., 1995; Roberts, 2020). Periosteal reaction may also occur on the upper limbs (Lewis et al., 1995; Taylor et al., 2024). However, periosteal new bone formation may be due to multiple causes (Roberts, 2020).

Some authors have argued that there is no pathognomonic lesion for leprosy (Matos, 2009; Antunes-Ferreira et al., 2013) and hence, the combination of lesions in a skeleton must be taken into consideration to perform a differential diagnosis (Ortner, 2008; Antunes-Ferreira et al., 2013). Lupus vulgaris (tuberculosis of the facial skin) and treponematosis share similar rhinomaxillary lesions to leprosy, whereas acro-osteolysis can be caused by seronegative spondyloarthropathies, traumatic injuries (including frostbite), and neuropathies derived from diabetes or treponematoses (Ortner, 2008).

Despite the variability in leprosy expression making its diagnosis from skeletal remains difficult, bioarchaeological studies have provided valuable insights into the disease's past epidemiology (Boldsen and Mollerup, 2006; Boldsen, 2008), evolution (Donoghue et al., 2015a; Donoghue et al., 2015b; Schuenemann et al., 2018; Pfrengle et al., 2021), and social perception (Baker and Bolhofner, 2014; Roffey et al., 2017). Almost every modern European country has provided bioarchaeological evidence for leprosy (see Roberts, 2020), the oldest one dating from the Late Copper Age (Köhler et al., 2017). Documentary sources indicate a rise in the establishment of hospitals across Europe in the 12th century, including those specifically for people with leprosy (leprosaria) (Rawcliffe, 2006; Demaitre, 2007; Brenner and Touati, 2021). However, the cemeteries directly associated with these institutions that have been located and excavated are few. Currently, the most extensive skeletal collections linked to medieval leprosaria are those of Chichester (Magilton et al., 2008) and Winchester (Roffey and Tucker, 2012) from England, and Naestved from Denmark (Møller-Christensen, 1978). The pioneer work by Møller-Christensen on Naestved served as the precedent for all bioarchaeological research on leprosy, establishing the basis for diagnosing leprosy from skeletal remains. Hungary has also provided substantial bioarchaeological evidence for leprosy (e.g. Pálfi et al., 2002; Köhler et al., 2017; Donoghue et al., 2005; see also Roberts, 2020 compendium), including the oldest ones (Köhler et al., 2017), but only one site with a cemetery directly linked to a leprosarium (Pálfi et al., 2002).

In Spain, only a few isolated cases of leprosy have been described from human skeletal remains (Etxebarria et al., 1997; Guijo Mauri et al., 1999; Calvo, 2000; López Flores and Barrionuevo Contreras, 2009; De Miguel Ibáñez et al., 2011; Rascón Pérez et al., 2013; González-Garrido et al., 2017; Herrerín et al., 2019), while in Portugal, two leprosaria cemeteries have been excavated (Antunes-Ferreira et al., 2013; Ferreira et al., 2013). Written sources show that at least nineteen leprosaria existed in Catalonia (northeastern Spain) between the 12th and 15th centuries (Jáuregui 2018a), although a definitive number is difficult to provide. However, many of these leprosaria were eventually absorbed by other institutions, and their original location remains unknown (Jáuregui 2018a). The cemetery of Sant Llàtzer Hospital is the only one directly associated with a leprosarium excavated in Spain, and the skeletons of its cemetery are the subject of study in this paper.

1.1. The leprosarium of Barcelona

The Sant Llàtzer (Saint Lazarus) Hospital in Barcelona was intended to provide shelter for leprosy patients in the city. The institution's earliest reference dates back to 1172 (Jáuregui, 2018b; Archive of the Cathedral of Barcelona (ACB), 2024). Its church, initially Santa Maria and Santa Margarida (Saint Marie and Saint Margaret, later Sant Llàtzer in the 14th century) was first mentioned in 1218, suggesting a proto-house for the sick before the construction of the Romanesque chapel, which is still preserved today at Plaça del Padró (Ciutat Vella).

The leprosarium was situated at the intersection of two main paths leading to the city gates (Portal de la Boqueria and Porta Ferrissa) in an area of orchards and vineyards outside the walls (Castellano, 1994; Busquets et al., 2009). Then, during the 14th century, as the city expanded, the leprosarium became enclosed within new walls and linked to a new gate, Portal de Sant Antoni (1377) (Fig. 1), and the vicinity rapidly developed into an urbanised section (Hinojo, 2015).

In 1320, numerous leprosaria were attacked in the south of France, alongside Jewish communities, in a crusade known as the Shepherds' Crusade, which led to the dismantling of several leprosaria in Catalonia and the absorption of some by other hospitals (Nirenberg, 1996; Jáuregui, 2018a). Despite this, the leprosarium of Barcelona remained active and received numerous donations during the 13th-14th centuries (Jáuregui, 2018a). By the late 14th century, it accommodated an average of 4–5 patients, playing a crucial role in the city's assistance network, and continued operating at the same location until the 20th century (Castellano, 1994).

Vital information about daily life in the leprosarium was recorded in seven account books from 1379 to 1395, including patient arrivals, departures, diagnostic processes, and perceptions of the sickness, which provide detailed information about the treatment given to the patients (Jáuregui, 2018b; Jáuregui et al., 2023). During that time, leprosy, though incurable, received palliative care primarily from surgeons who performed periodic bloodletting, or from hospital workers (Demaitre, 2007; Rawcliffe, 2006; Jáuregui et al., 2023; Roberts, 2020). Doctors were involved in providing additional care and prescribing medicines, as documented in their purchases. However, there was no on-site doctor at the leprosarium. Furthermore, the account books indicate that the patients suffered from other diseases, some of which were related to their tenuous health condition.

1.2. Excavations in the necropolis of Sant Llàtzer Hospital

Two archaeological interventions were conducted in the chapel of Sant Llàtzer and Santa Margarida (Plaça del Padró, Ciutat Vella)

Fig. 1. Map of Barcelona from 1492, showing the outline of the walls and the location of the leprosarium. S. Sanpere i Miquel (19th c.) - Arxiu Històric Ciutat de Barcelona, adapted by Vanesa Triay.

between 1989 and 1991. The excavations revealed several structures related to the hospital and church's construction and evolution. Eleven burials from the 15th-16th centuries and twelve from the 18th century were found inside the main nave (Beltrán de Heredia Bercero, 1991; Campillo, 1991; López Mullor and Beltrán de Heredia Bercero, 1994). Additionally, eleven east-west-orientated pits from the early phase (12th-13th centuries) of the hospital were discovered under the chapel of Sant Sepulcre, with no accompanying funerary objects. From this, one individual had their head resting on stones, and two were prone burials (López Mullor and Beltrán de Heredia Bercero, 1994).

As the hospital expanded, the burial site had to be relocated north of the church (Castellano, 1994). A third archaeological intervention (2007–2009) was carried out in this sector, which revealed new structures, water wells, silos, and 46 burials from which 79 skeletons were recovered, dating from the 12th to the 18th century (Triay, 2010).

In the first phase of the hospital (12th - 13th centuries), most burials were simple oval-shaped southwest-oriented structures, which were systematically aligned. Some of them were located around the church apse. Only one burial (UF 104 UE 56) showed strictly canonical orientation (heading west), which stands out for being the only tomb with a trapezoidal shape and built with flat stones (Triay, 2010).

The largest number of burials belonged to the 13th-15th centuries, with eight simple individual pits and nine oval-shaped collective graves. The individuals were wrapped in shrouds and deposited following the canonical orientation when possible (Triay, 2010). Few had associated funerary objects (Triay, 2010).

During the 15th century, the burial area was relocated to the present-day Plaça del Pedró (Castellano,1994; López Mullor and Beltrán de Heredia Bercero, 1994; Triay, 2010). Burials from the 15th-16th and 17th-18th centuries followed a similar typology as in former periods, but now some funerary objects like medals, rosaries, and rings, were present (Triay, 2010). Iron nails and buckles were also associated with the most recent burials, suggesting that the individuals were dressed in their clothes and buried in wooden coffins (Triay, 2010).

1.3. Previous studies

The skeletal remains recovered during the 1990s excavations inside Sant Llàtzer's main nave were previously studied by Campillo (1991), who found no signs indicative of leprosy, and these remains were subsequently reburied. In contrast, the skeletons recovered from beneath the chapel of Sant Sepulcre and those excavated during the 2007–2009 archaeological works had not been previously studied. These skeletons were housed in the History Museum of Barcelona and are the focus of this paper.

A previous study by Pfrengle et al. (2021) selected 35 samples from 18 skeletons recovered from the necropolis of Sant Llàtzer for DNA extraction (see Supplementary Information Table S1). Genetic research has enabled the identification of *M. leprae* in archaeological human remains, representing a breakthrough in the study of leprosy history. Pfrengle and colleagues were able to reconstruct nine genomes of *M. leprae* from nine of these individuals. Additionally, five individuals for whom the recovery of the pathogen's genome had been attempted (with both positive and negative results) were sampled for a proteomics study (Wilkin et al., 2024). In two cases, this allowed the recovery of host immune proteins related to modern leprosy (see Supplementary

Information Table S2).

The study of the Sant Llàtzer necropolis offers a unique opportunity to gain valuable insights into the history of leprosy in southern Europe. By combining historical, archaeological, genetic, and palaeopathological evidence, we aim to provide a comprehensive understanding of the disease and its social dimension during the Medieval to Early Modern periods in Barcelona. Our objectives are twofold: firstly, to analyse the frequency of leprosy-related pathological lesions among the individuals recovered from the cemetery of Sant Llàtzer Hospital; secondly, to examine how leprosy sufferers were perceived and integrated into society.

2. Materials and methods

The skeletal remains of 87 human individuals were recovered from the necropolis of Sant Llàtzer Hospital (Table 1). Of these, 45 were recovered from single graves and 42 were recovered from nine collective burials. The remains were macroscopically examined at the osteology laboratory of the Universitat Autònoma de Barcelona, Bellaterra, Spain.

According to old historiography, only those affected by leprosy were buried in the cemetery of Sant Llàtzer Hospital, as the stigma associated with the sickness led to isolation during life and in the afterlife (Roca, 1899). Therefore, the majority of individuals buried in its cemetery were expected to be patients of the hospital.

Sex estimation of the individuals under study was based on the morphology of the cranium and os coxae (Ferembach et al., 1980). Age at death was estimated using the changes in the auricular surface of the ilium (Lovejoy et al., 1985) and the pubic symphysis (Todd, 1921a; Todd, 1921b). Late fusing epiphyses were also considered in order to distinguish young adults from older adults (Ubelaker, 1989; Scheuer and Black, 2004; Falis and Prangle, 2015). Regarding non-adult individuals, age estimations were made based on long bone length (Fazekas and Kósa, 1978), epiphyseal fusion (Ubelaker, 1989), and dental development (Crétot, 1978a; 1978b). The individuals have been classified into seven age categories, following Buikstra and Ubelaker (1994): foetus (before birth), infant (0–2 years), child (3–11 years), adolescent (12–19 years), young adult (20–34 years), middle adult (35–49 years), and old adult (>50 years).

Palaeopathological investigation was carried out with reference to Aufderheide and Rodríguez-Martín (1998), Buikstra and Ubelaker (1994), and Roberts and Manchester (2010). The criteria for the diagnosis of leprosy were based on Møller-Christensen (1978), Andersen and Manchester (1992), Andersen et al. (1992), Ortner (2008), and Matos (2009). Following these authors, rhinomaxillary bone changes and hand and foot lesions were evaluated to conduct an osteological diagnosis (see Supplementary Information Table S3). Odontodysplasia was also assessed, an anomaly in the development of the root of the upper permanent incisors that has been observed in some leprosy cases among children (Kjellström, 2012; Matos and Santos, 2013; Taylor et al., 2024). However, leprosy has no pathognomonic lesion, as many diseases share similar bony changes (Ortner, 2008). Supplementary Information Table S4 summarises the other conditions that have been considered and ruled out in the differential diagnosis. When necessary, radiological analyses were performed on the skeletal remains at the Hospital General de Catalunya, Barcelona, Spain. The radiographs were performed using anteroposterior and lateral projections with a Philips DigitalDiagnost C50 system.

Finally, one individual (UF 104 UE 56) was newly radiocarbon dated for this study, revealing that it belongs to the High Medieval Period (1038–1179 cal AD, 2σ, 90.8 %). The ^{14}C analysis was conducted at the Scottish Universities Environmental Research Centre (SUERC), Glasgow, UK. The radiocarbon age was calibrated using the Oxford Radiocarbon Accelerator Unit calibration program OxCal 4 (Bronk Ramsey, 2009) and the IntCal20 atmospheric calibration curve (Reimer et al., 2020). Pfrengle et al. (2021) provided ^{14}C dates for five other individuals, three belonging to the High Medieval Period (from around AD 1000–1300 s), and two to the Early Modern Period (from AD 1500–1815) (see Supplementary Information Table S5). The rest of the burials have been dated based on pottery and other archaeological evidence (Triay, 2010). Overall, the radiocarbon dating aligns with those date estimations.

Table 1
Number of individuals studied from each chronological period.

	Skeletons recovered from individual graves	Skeletons recovered from collective graves	Total number of skeletons studied
12th c. – 13th c.	22	0	22
End of the 13th c. – 15th c.	8	42	50
15th–16th c.	5	0	5
17th c.	3	0	3
18th c.	7	0	7

3. Results

3.1. Demographic profile

The 87 individuals recovered from the cemetery of Sant Llàtzer Hospital represented three broad age categories: 66 (75.8 %) adults, of which 13 individuals (14.9 %) were identified as young adults, and 10 (11.4 %) were categorised as middle adults; 11 (12.6 %) adolescents; and 10 (11.5 %) children between 3 and 12 years old (Table 2). Many tombs were disrupted due to modern construction or overlapping graves, resulting in incomplete skeletal remains (see Supplemental Information Table S6). Consequently, estimating the sex and age at death for all individuals was not possible. Nevertheless, seventeen individuals were identified as male (22.1 %) and 27 as female (35.0 %). Sex was not estimated for children.

Most burials, comprising 50 individuals, were dated to the late 13th to 14th centuries. Among these, nine collective graves contained up to 10 skeletons each on different levels. Notably, eight out of ten individuals under 12 years of age were recovered from these collective graves, and none were buried in individual tombs between the late 13th century and 15th century.

3.2. Palaeopathology

The palaeopathology study has been structured into sections below, based on the affected anatomical regions. These sections include rhinomaxillary changes, upper limb lesions, and lower limb lesions. A summary can be found in Supplementary Information Table S3.

3.2.1. Rhinomaxillary changes

Out of the 87 recovered individuals, only 26 preserved the rhinomaxillary region. Among them, 11 exhibited rhinomaxillary bone changes (see Supplementary Information Table S7). The most frequently recorded lesion is the remodelling of the margins of the nasal aperture, observed in 10 individuals. Three individuals had lost their central incisors, and one had lost both lateral incisors (Fig. 2).

Destruction of the nasal septum was observed in two individuals, and the other two showed resorption of the anterior nasal spine (Fig. 3). However, the frequency of these lesions can be easily underestimated due to erosion and postmortem destruction of the area. Additionally, five skeletons showed pitting on the palatal surface of the maxilla, and four displayed porosity on the nasal floor. New bone formation on the nasal floor was observed in two cases.

Among the non-adult skeletons, three exhibited rhinomaxillary changes. The youngest individual affected was UF 32 UE 1225, who died at the age of 7–8 years. The other two individuals (UF 10 UE 1124 and UF 21 UE 1137) were 13–15 years old and 14–15 years old, respectively. None of them showed odontodysplasia (UF 10 UE 1124 and UF 21 UE

Table 2
Age and sex distribution of individuals recovered from the Sant Llàtzer Hospital.

Chronology	Attributed sex	Infants	Children	Adolescents	Young adults	Middle adults	Old adults	Adults (indeterminate)	Total
12th –13th c.	**Male individuals**	-	-	3	2	2	-	1	8
	Female individuals	-	-	2	2	3	-	1	8
	Indeterminate sex	-	1	2	-	-	-	3	6
	Total	0	1	7	4	5	0	5	22
13th- 14th c.	**Male individuals**	-	-	1	2	2	-	3	8
	Female individuals	-	-	-	4	1	-	8	13
	Indeterminate sex	-	8	1	1	1	-	19	30
	Total	0	8	2	7	4	0	30	51
15th–16th c.	**Male individuals**	-	-	1	-	-	-	-	1
	Female individuals	-	-	-	-	-	-	2	2
	Indeterminate sex	-	-	1	-	-	-	1	2
	Total	0	0	2	0	0	0	3	5
17th- 18th c.	**Male individuals**	-	-	-	-	-	-	-	0
	Female individuals	-	-	-	1	1	-	2	4
	Indeterminate sex	-	1	-	1	-	-	3	5
	Total	0	1	0	2	1	0	5	9
Total		0	10	11	13	10	0	43	87

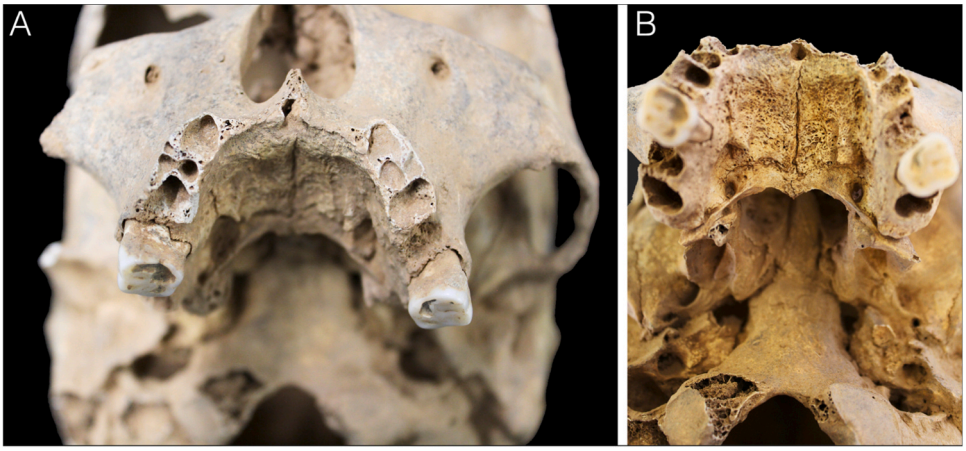

Fig. 2. Detail of the skull of the individual UF 803 UE 8020 (female, 25–30 y.). A) Resorption of the alveoli of the upper incisors. B) Pitting on the palate.

Fig. 3. Detail of the nasal aperture of individual UF 703 UE 7027 (female, 25–35 y.). The margins of the nasal aperture and the anterior nasal spine are smooth and rounded. The nasal septum is partially resorbed.

113 preserved all the permanent upper incisors; UF 32 UE 1225 preserved two). However, individual UF 21 UE 1137 displayed severe pitting on the palate and extensive bone formation within the nasal cavity (Figs. 4A and 4B), as well as a periapical lesion on the right lateral upper incisor (Fig. 4C).

3.2.2. *Upper limb lesions*

Sixteen individuals showed lesions in the hand bones. However, most of the individuals did not preserve all hand bones, particularly distal phalanges, making it challenging to assess potential early cases.

Acro-osteolysis was observable in the right first proximal phalanx of the individual UF 702 UE 7019 (Fig. 5), with destruction on its distal end. It can also be seen on individual UF 104 UE 56 (Fig. 6), with almost complete destruction of the distal end of the second intermediate phalanx of the left hand, which was ankylosed to the distal end of the proximal phalanx. Radiologically, concentric destructive remodelling is evident on the proximal phalanx, as well as on the left first proximal phalanx of the same individual, which shows complete destruction of its distal joint surface.

Furthermore, three individuals exhibit enlarged foramina on their hand bones. In one case, the enlarged foramen is surrounded by new bone formation (Fig. 7).

Periosteal reaction was observed on the diaphysis of the upper limbs in two cases: on the distal end of the left humerus, left ulna, and radius of individual UF 14 UE 1109 and on the distal ends of both radii and the left ulna of individual UE 479. Additionally, both individuals showed hand lesions (Figure S1).

3.2.3. *Lower limbs*

Thirteen skeletons exhibited periosteal reaction on the tibiae and fibulae, along with other lesions related to leprosy (see Supplementary Information Table S3). In most cases, the periosteal reaction was bilateral and symmetrical.

Foot lesions were found in nine individuals, with seven showing new bone deposits. Destructive remodelling was noted in the metatarsals of

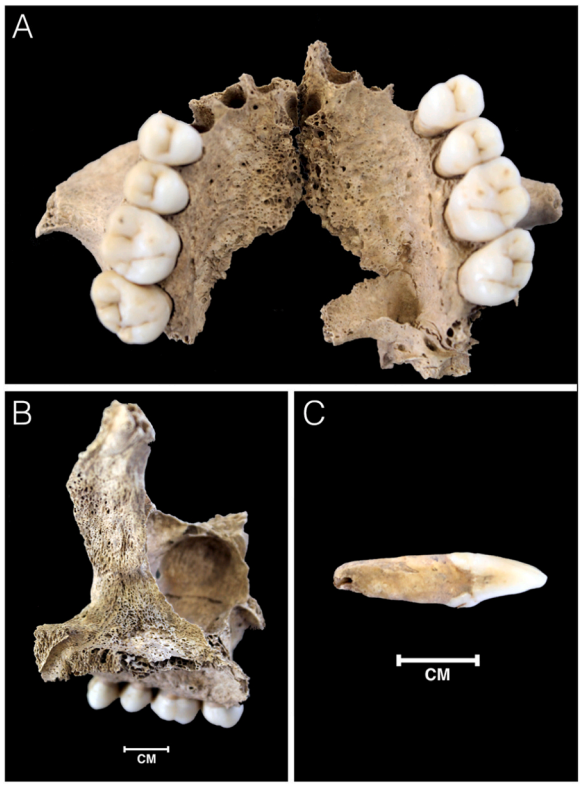

Fig. 4. Detail of the rhinomaxillary area of individual UF 21 UE 1137 (male, 14–15 y.). A) Pitting on the palate. B) New bone formation on the nasal surface of the right portion of the maxilla. C) Periapical lesion on the right lateral upper incisor.

two individuals. The most notable lesions were observed in individual UF 3 UE 1097 on the left first, second, and third metatarsals. The proximal spicules' resorption due to acro-osteolysis had already begun on the first and third metatarsals of individual UF 3 UE 1097 (Figs. 8A and 8B). The medullary cavity of the first metatarsal was almost completely obliterated (Fig. 8C).

4. Discussion

4.1. Frequency of leprosy-related lesions in Sant Llàtzer

The cemetery of Sant Llàtzer Hospital is the largest one related to a leprosarium excavated in the Iberian Peninsula and the first one excavated in Spain. In Portugal, only two have been located and excavated: one near the leprosarium of Beja, which was used between the 14th and 16th centuries (Antunes-Ferreira et al., 2013), and one associated with the Lagos leprosarium, in use between the 15th and 17th centuries (Ferreira et al., 2013). In contrast, the years of activity of Sant Llàtzer Hospital extended from the Early Medieval Period to the 20th century.

The cases of leprosy that have been previously described in Spain were diagnosed on skeletons from necropoli unrelated to leprosaria and did not show evidence of differential mortuary treatment than their communities (Etxebarria et al., 1997; Guijo Mauri et al., 1999; López Flores and Barrionuevo Contreras, 2009; González-Garrido et al., 2017). Of these, six cases were recorded in Islamic cemeteries corresponding to the 11th - first half of the 13th century (Guijo Mauri et al., 1999; López Flores and Barrionuevo Contreras, 2009), and one was associated with the Visigothic period (7th-9th century) (Etxebarria et al., 1997). Only one case corresponded to an individual buried in a Medieval Christian cemetery (12th - early 13th century) (González-Garrido et al., 2017).

The first objective of this study was to analyse the frequency of leprosy-related pathological lesions in the cemetery of Sant Llàtzer Hospital. The osteological analysis allowed the identification of five individuals probably suffering from leprosy based on the distribution of their lesions; eleven were considered possible cases of leprosy, and fifteen showed lesions that could be related to leprosy but were too incomplete to diagnose (see Supplementary Information Table S3). The conditions considered in the differential diagnosis are listed in Supplementary Information Table S4. The incomplete preservation of some of the skeletons can lead to underestimating the frequency of the illness since the paleopathological diagnosis of leprosy depends on the distribution of lesions in the skeleton and hence, on the skeletal elements available (Ortner, 2008). Combining aDNA, proteomics, and paleopathology results, we may conclude that 21 individuals of the total studied from the site (24.1 %) exhibit strong evidence of having suffered from leprosy (Tables 3 and 4). Nevertheless, it is important to recall that the absence of skeletal leprosy-related lesions or even negative results in aDNA or proteomics analyses do not rule out that the individual may have suffered from leprosy, as they may have not developed lesions or some elements required for the diagnosis may have not been preserved (including the DNA or the proteome) Wood et al., 1992).

One individual (UF 102 UE 46) did not show any lesion that could be

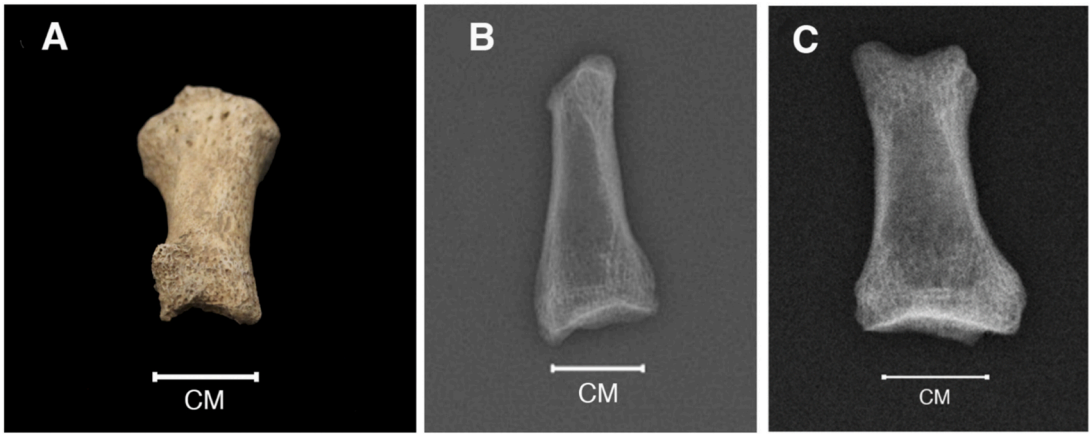

Fig. 5. A) Detail of bone destruction on the distal end of the first proximal phalanx of the UF 702 UE 7019 right hand (male, indeterminate age at death). Palmar view. B) Sagittal view radiograph of the right first proximal phalanx. Bone destruction can be noticed on its distal end, which affects the joint surface. C) Frontal view radiograph.

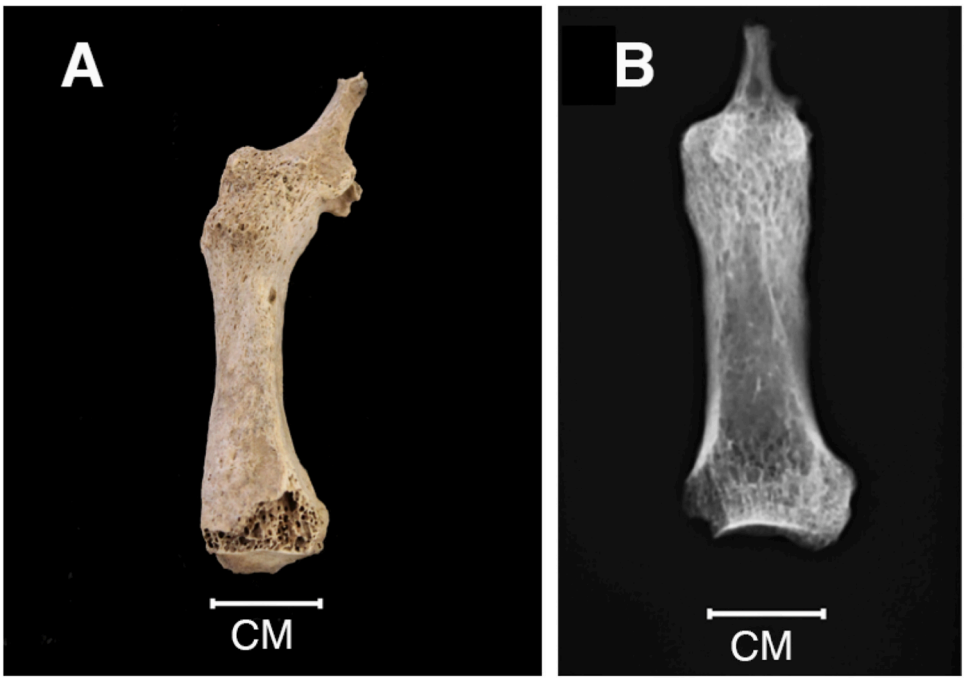

Fig. 6. A) Acro-osteolysis of the second intermediate phalanx and fusion with the second proximal phalanx of the left hand of individual UF 104 UE 56 (female, indeterminate age at death). Medial view. B) Coronal view radiograph of the left second intermediate and proximal phalanx.

Fig. 7. Enlarged foramen surrounded by pitted new bone on the diaphysis of the third left metacarpal of individual UF 703 UE 7027 (female, 25–35 y.).

related to leprosy but yielded positive results regarding the recovery of immune proteins associated with the disease (Wilkin et al., 2024). The presence of immune proteins associated with leprosy is indicative of an active leprosy infection. Immunoglobulins, haptoglobin, complement component proteins (C-reactive protein and Apolipoprotein A-1), and alpha, beta, and gamma fibrinogen chains were recovered from two individuals (UF 700 UE 7006 and UF 102 UE 46) in a previous study, which indicates that they were combating leprosy infection at the time of death (Wilkin et al., 2024). Individual UF 102 UE 56 did not preserve the lower limbs, but they did not show any skeletal lesions that could be related to leprosy on the cranium, upper body, or hand bones. As mentioned previously, not all leprosy patients develop skeletal changes (Ortner, 2008), or in the case of individual UF 102 UE 56, maybe only the lower limbs and foot bones were affected.

The percentage of individuals with evidence of having suffered from leprosy in Sant Llàtzer hospital is similar to that observed in other medieval cemeteries associated with Christian leprosaria, such as the cemetery of St James and St Mary Magdalene Hospital in Chichester (19.5 %) (Ortner, 2008; Magilton et al., 2008) or the cemetery of St John Timberhill in Norwich (19.4 %) (Shepherd Popescu, 2009). In contrast, 77 individuals (61.6 %) of the 125 excavated in the cemetery of St Mary Magdalen Hospital in Winchester showed evidence of leprosy (Taylor et al., 2024). In Portugal, seven skeletons were recovered from the leprosarium of Beja, of which one was considered a probable case of leprosy and four were possible cases (Antunes-Ferreira et al., 2013). The archaeological work in the Valle da Gafaria ("Leprosarium Valley") at Lagos, recovered 11 adult skeletons, of which two were highly suggestive of having suffered from leprosy and three showed other pathological conditions; namely, treponematosis, brucellosis, and Legg-Calvé-Perthes disease (Ferreira et al., 2013).

Nevertheless, the frequency of lesions observed in Sant Llàtzer is higher amongst the individuals dated from the 12th - early 13th centuries (50 % of the skeletons showed evidence of having suffered from leprosy) and amongst the skeletons from the 15th-16th centuries (60 %). In contrast, it is especially low in the group of skeletons from the 13th-14th centuries (10 %). The small number of skeletons recovered from the 15th-16th centuries (only five individuals) may explain the lack of results for this period. Roffey and Tucker (2012) point out that these high frequencies of lesions might be explained by a higher accuracy of the medieval procedure for diagnosing leprosy than previously assumed, and suggested that some of these institutions may have sheltered leprosy sufferers and individuals with other diseases. This seems to be the case for Lagos leprosarium (Portugal), where different pathologies were reported (Ferreira et al., 2013). Taylor et al. (2024) note a drop in the proportion of individuals with evidence of leprosy observed in St Mary Magdalen leprosarium (Winchester) once later burials are taken into consideration, which is similar that documented in Sant Llàtzer.

Regarding the drop in the frequency of lesions observed in the burials from the 13th-14th centuries, it might be associated with the general decline of leprosy in Europe and/or with a change in the use of the

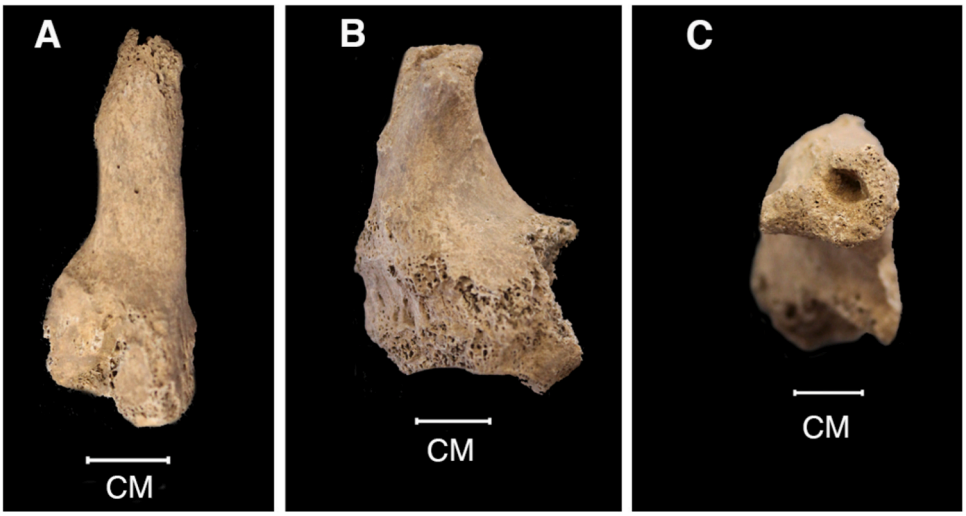

Fig. 8. A) Acro-osteolysis of the third left metatarsal of individual UF 3 UE 1097 (indeterminate age and sex). B) Detail of the remodelling of the first left metatarsal. C) Axial view of the first left metatarsal. The medullary cavity is almost obliterated.

Table 3
Summary of skeletons showing signs of leprosy from the Sant Llàtzer Hospital.

Code	Chronology	Sex	Age at death	Osteological diagnosis	aDNA evidence for leprosy	Leprosy-associated immune proteins
UF 101 UE 43	12th–13th c.	Male	25–30 years	Not diagnosable	Positive	Negative
UF 102 UE 46	12th–13th c.	Male	17–20 years	Not diagnosable	Negative	Positive
UF 103 UE 49	12th–13th c.	Male	27–35 years	Probable case of leprosy	Negative	n. a.
UF 104 UE 56	12th–13th c.	Female	n. a.	Probable case of leprosy	Negative	n. a.
UF 700 UE 7006	12th–13th c.	Female	17–20 years	Not diagnosable	Positive	Positive
UF 701 UE 7016	12th–13th c.	Female	n. a.	Probable case of leprosy	Negative	n. a.
UF 702 UE 7019	12th–13th c.	Male	n. a.	Possible case of leprosy	Negative	n. a.
UF 703 UE 7027	12th–13th c.	Female	25–35 years	Probable case of leprosy	Positive	n. a.
UF 800 UE 8008	12th–13th c.	Female	12–14 years	Not diagnosable	Positive	Negative
UF 803 UE 8020	12th–13th c.	Female	25–30 years	Probable case of leprosy	Positive	n. a.
UE 479	12th–14th c.	Male?	Middle adult	Possible case of leprosy	n. a.	n. a.
UF 3 UE 1097	13th–14th c.	n. a.	n. a.	Possible case of leprosy	n. a.	n. a.
UF 10 UE 1104	13th–14th c.	Male	30–39 years	Possible case of leprosy	n. a.	n. a.
UF 10 UE 1124	13th–14th c.	Male?	13–15 years	Possible case of leprosy	n. a.	n. a.
UF 15 UE 1111	13th–14th c.	Male	n. a.	Possible case of leprosy	n. a.	n. a.
UF 32 UE 1225	13th–14th c.	n. a.	7–8 years	Possible case of leprosy	n. a.	n. a.
UF 25 UE 1174	15th c.	n. a.	17–20 years	Possible case of leprosy	Positive	n. a.
UF 8 UE 1054	16th c.	Female	n. a.	Not diagnosable	Positive	n. a.
UF 21 UE 1137	16th c.	Male	14–15 years	Possible case of leprosy	Positive	n. a.
UF 14 UE 1109	17th c.	Female?	n. a.	Possible case of leprosy	n. a.	n. a.
UF 11 UE 1069	18th c.	Female	Young adult	Possible case of leprosy	Positive	n. a.

"Not diagnosable", skeleton too incomplete. "n. a.", not available. "Male?", possible male; "Female?", possible female. Ancient DNA data from Pfrengle et al. (2021). Proteomics data from Wilkin et al. (2024).

Table 4
Summary of leprosy cases observed in individuals from the Sant Llàtzer Hospital.

	Total number of skeletons studied	**Confirmed cases (aDNA or proteomics evidences)**	**Probable cases**	**Possible cases**	**Total**	**Percentage of cases**
11th – 13th centuries	22	6	3	2	11	50.0 %
13th – 14th centuries	50	0	0	5	5	10.0 %
15th – 16th centuries	5	3	0	0	3	60.0 %
17th – 18th centuries	10	1	0	1	2	20.0 %
Total	**87**	**9**	**3**	**8**	**21**	**24.1 %**

Ancient DNA data from Pfrengle et al. (2021). Proteomics data from Wilkin et al. (2024).

necropolis. Leprosy prevalence started to decline in Europe in the late medieval period, coinciding with the increase of the frequency of leprosy (Donoghue et al., 2005; Hohmann and Voss-Böhme, 2013; Rawson et al., 2014). The theories for explaining this phenomenon are several: some authors argued that tuberculosis infection may have provided some immunity to leprosy (Rawson et al., 2014), while others consider that LL patients were more susceptible to tuberculosis and this led to an increase of their mortality (Donoghue et al., 2005; Hohmann

and Voss-Böhme, 2013). Taylor et al. (2024) document a similar decline in the lesion frequency in the last phases of activity of St Mary Magdalen leprosarium in Winchester. The authors argue that this tendency may be related to the fact that the decline of leprosy led to a change in the use of the leprosarium, which might have started admitting patients with other conditions. Further research, including aDNA and proteomics studies, on the impact of tuberculosis in the Sant Llàtzer leprosarium may provide new insights into the coexistence between leprosy and tuberculosis in Barcelona and its epidemiological consequences.

4.2. Sant Llàtzer funerary practices and their social implications

While most individuals at Sant Llàtzer were buried following the Christian tradition, with their heads facing west or southwest, a few burials deviated from this norm. One burial from the 12th-13th centuries had a north-south orientation (UF 103 UE 49), and two others were oriented east-west (UE 481 and UE 502), which stood in stark contrast to the surrounding tombs. Additionally, two individuals from the same period were buried facing down (individuals UE 494 and UE 502) (Beltrán de Heredia Bercero, 1991), an unconventional burial position that could not result from any movement of the soil or post-deposition handling.

Prone burials, although infrequent, have been observed in various historical contexts. While they have been associated with punishment or fear in Late Medieval and Modern burials (Arcini, 2009), they might have held different meanings during the Early Medieval Period (Alterauge et al., 2020). For instance, the voluntary prone burial of *King Pepin the Short*, King of the Franks, in the 8th century was seen as an act of devotion and redemption of his father's sins (Toplak, 2015; Alterauge et al., 2020), and it occupied a privileged location in front of the entrance of the Basilica of Saint Denis in Paris.

In medieval Western Europe, individuals afflicted with leprosy were often viewed as sinners chosen for redemption during their lifetime, deserving of compassion (Brenner, 2010). This perception sheds light on why leprosy hospitals played a crucial role as centres of piety and charity in medieval society. Written sources dating from the 12th century onwards reveal that donations and bequests to Sant Llàtzer Hospital were common, indicating it was a regular recipient of charity (Jáuregui, 2018b). Interestingly, some donors specifically selected the hospital cemetery as their burial place, without any explicit reference to illness or connection to the institution (ACB, Perg. 3–35–130). Moreover, the practice of burying individuals facing down, as observed in some cases at the hospital cemetery, could also be interpreted within a religious context. It likely served as another expression of religious piety, especially during the early phase of the hospital, reflecting societal beliefs surrounding sin and redemption.

Notably, some of the burials at Sant Llàtzer dating from the 12th-13th centuries and belonging to leprosy sufferers were situated in privileged locations around the apse of the church. This suggests that leprosy sufferers were respected even after their death, indicating a level of social acceptance or sympathy towards their condition. Similar practices have been documented at St. Mary Magdalen leprosarium in Winchester, where individuals with leprosy were buried at the apse of the church (Taylor et al., 2024). In fact, most leprosy cases reported from archaeological contexts are not associated with leprosaria (see Roberts, 2020), as can be observed throughout Spain (Etxeberria et al., 1997; Guijo Mauri et al., 1999; López Flores and Barrionuevo Contreras, 2009; González-Garrido et al., 2017). This shows that leprosy sufferers were generally not treated differently, at least upon death, than other individuals in their communities.

The funerary practices at the Sant Llàtzer Hospital evolved over the centuries. Initially, burials were simple, with no grave goods, and the individuals were modestly wrapped. However, in the post-medieval period, the funeral practices changed. The graves potentially included goods and wooden boxes, and the individuals were dressed for burial. During the 13th to 15th centuries, mass graves were documented. Collective graves stand out in such a small hospital, where, according to the account books preserved from 1379 to 1395, the density of patients did not surpass five. An explanation might be found in the account book of 1385, where there is a reference that someone left money on behalf of their aunt who had been buried at the cemetery because of the "great mortality of years ago", suggesting that the cemetery might have been used during an epidemic episode (Jáuregui et al., 2023). Further research, including the use of ancient DNA analysis to confirm the presence of *Yersinia pestis,* is needed to assess whether these burials might be related to the plague outbreaks of 1348 in Barcelona or some other catastrophic event. An epidemic or catastrophic event may also explain the presence of immature skeletons in these collective graves, although written sources do not provide evidence of non-adults staying at the hospital, particularly between 1379 and 1395 (Jáuregui, 2018b; Jáuregui et al., 2023). However, it cannot be ruled out that some of them could have been patients of the hospital and that they might not appear in the account books due to the short period that the surviving books cover. In fact, three individuals under 15 years of age (UF 10 UE 1124, UF 21 UE 1137, and UF 32 UE 1225) exhibited rhinomaxillary changes, although rhinomaxillary changes are rare among juvenile skeletons (Matos and Santos, 2013; Taylor et al., 2024), likely because lesions develop a few years after the initial infection (Roberts, 2020).

There is no archaeological evidence to support the notion that leprosy sufferers faced marginalisation in Barcelona before the 19th century. However, only one individual (UF 21 UE 1137, 16th c., with positive results for *M. leprae* aDNA) exhibited irregular arm and leg positions, suggesting a lack of care during the burial process. This individual's burial stands out as an anomaly. However, the account books from the end of the 14th century show that hospital administrators saw some individuals as problematic (the enslaved individual at the hospital, for example, and some patients), and they might have been treated with less reverence upon death.

Recent research has been critical in rethinking the social perception of leprosy, making obvious the complexity and differences across territories and centuries (Rawcliffe, 2006; Demaitre, 2007; Brenner and Touati, 2021). The study of burials from Sant Llàtzer Hospital offers valuable insights into the complexities of the perception of leprosy and the social dynamics surrounding the disease in the Medieval and Early Modern periods in Barcelona and the Iberian Peninsula. The account books from the 14th century reveal a diverse group of patients in the facility coming from varied origins and social backgrounds, including former enslaved individuals to wealthy donors, and from Christian and non-Christian origins. The necropolis reflected this heterogeneity (Jáuregui, 2018b).

Our findings also suggest that the hospital held significant societal importance in the region for several centuries, attracting benefactors who made charitable donations driven by piety and the desire for redemption. Leprosy sufferers were buried with respect, even with reverence in some cases, and following Christian customs.

5. Conclusions

The objectives of this study were twofold: firstly, to analyse the frequency of leprosy-related pathological lesions in the cemetery of Sant Llàtzer Hospital (12th-18th c.); secondly, to examine how individuals affected by the disease were perceived and integrated into society during that period in Barcelona. Although it was expected that most all burials located around Sant Llàtzer chapel were associated with patients of the leprosarium, evidence of leprosy has been observed in 24.1 % (21 individuals) of the recovered individuals (n=87), with a reduced frequency (10 %) among individuals from the 13th-14th centuries (n=50); the only chronological period for which collective burials were documented. A previous genomic study confirmed the presence of *M. leprae* in 9 individuals.

Over the centuries, funerary practices at the hospital changed, possibly reflecting shifts in the institution's purposes. However, these

changes do not indicate any mistreatment or marginalisation of leprosy sufferers. On the contrary, the privileged burial locations they occupied during the 12th-13th centuries might imply that these individuals were respected, at least during the first period of activity of the hospital. In the 14th-15th centuries, the necropolis might have also served as a burial site during epidemics or catastrophic events, which may explain the mass graves documented only during this period and the lower frequency of leprosy-related lesions observed. Sant Llàtzer Hospital was undoubtedly ingrained in the social fabric of Barcelona, functioning as a key healthcare provider and serving important religious and charitable roles.

This study, spanning from the Medieval to Early Modern periods, provides invaluable insights into the history and pathology of leprosy in Barcelona and in a wider European context. It sheds light on the evolving perceptions of the disease and the social dynamics surrounding it, allowing for a deeper understanding of the complexities involved. Furthermore, this research highlights the significance of interdisciplinary research, integrating historical and archaeological methods with paleopathological and bioarchaeological techniques, including genomic data analysis. This comprehensive approach is essential for revealing the intricate relationships between disease, society, and culture in historical contexts.

CRediT authorship contribution statement

Andrea Fernández-Vilela: Writing – review & editing, Investigation, Formal analysis. **Vanesa Triay:** Writing – review & editing, Writing – original draft, Visualization, Investigation, Formal analysis, Conceptualization. **M. Eulàlia Subirà:** Writing – review & editing, Conceptualization. **Jordi Ruiz:** Writing – review & editing, Methodology, Investigation, Formal analysis. **Maria Fontanals-Coll:** Writing – review & editing, Writing – original draft, Visualization, Supervision, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Nuria Montes:** Writing – review & editing, Writing – original draft, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Rosa Dinarès:** Writing – review & editing, Writing – original draft, Visualization, Software, Methodology, Investigation, Formal analysis, Data curation. **Clara Jáuregui:** Writing – review & editing, Writing – original draft, Investigation, Conceptualization.

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Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.ijpp.2024.11.005.

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