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High prevalence of adult and nonadult scurvy in an early agricultural transition site from Mainland Southeast Asia was associated with decreased survivorship

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Abstract

Objectives: The osteological paradox recognizes that the presence of lesions is not always directly related with increased mortality. When combined with the clinical, historical, and epidemiological literature on scurvy, survivorship analysis, a form of statistical analysis to assess the relationship between the presence of diseases in the archeological record and survival, helps determine the overall burden of the disease both in terms of morbidity and mortality. This article explores the relationship between scurvy and survivorship in 26 adults from Man Bac, a Neolithic site from northern Vietnam together with prepublished evidence of scurvy in the nonadult population ($n = 44$).

Methods: Diagnosis of scurvy included differential diagnosis combined with the Snoddy, A. M. E., Buckley, H. R., Elliott, G. E., Standen, V. G., Arriaza, B. T., & Halcrow, S. E. (2018). Macroscopic features of scurvy in human skeletal remains: A literature synthesis and diagnostic guide. *American Journal of Physical Anthropology*, *167*(4), 876–895. https://doi.org/10.1002/ajpa.23699 threshold criteria and the Brickley, M. B., & Morgan, B. (2023). Assessing diagnostic certainty for scurvy and rickets in human skeletal remains. *American Journal of Biological Anthropology*, *181*, 637–645 diagnostic certainty approaches. Kaplan–Meier survival curves were produced to assess the relationship between the presence of probable scurvy and age-at-death.

Results: The prevalence of probable scurvy in adults (35%) was considerably lower than reported for the nonadults (80%). Almost all lesions observed in the adults were in a mixed stage of healing. Kaplan–Meier analysis demonstrated no difference in survivorship between infants and children (<15 years) with or without probable scurvy, whereas a meaningful difference was observed for the adults and adolescents (15+ years).

Conclusions: The findings demonstrate that scurvy considerably decreased survivorship to older age categories. The degree of lesion remodeling, however, indicates that scurvy was not necessarily the direct cause of death but contributed to an overall disease burden that was ultimately fatal.

KEYWORDS
agricultural transition, demography, osteological paradox, survivorship, Vietnam

1 | INTRODUCTION

The question whether the Neolithic transition to domesticated rice, pigs, and dogs in Mainland Southeast Asia led to a decline in health has had significant attention in the last 20 years. However, a recent shift with the advancement of diagnostic methods accompanying a shift of paleopathological focus from nonspecific to specific disease has enabled considerably greater knowledge of the intricacies of the health profiles of prehistoric people in the region. Earlier work on nonspecific stress markers and dental disease suggested that there was little decline in health before and after the introduction of agriculture (Halcrow et al., 2013; Oxenham, 2006; Oxenham et al., 2018; Tayles et al., 2000). The recent work in combination with the previous literature however has demonstrated an epidemiological shift that is not strictly related to overall disease burden, but rather the types of diseases present changed significantly (Vlok, 2020; Vlok et al., 2020, 2021, 2022; Vlok, Oxenham, et al., 2024). In addition, clear intraregional variation in impact on health are beginning to emerge, that suggests any one trend for this region does not reflect the great variation of social and environmental factors that each human group experienced. Part of this new research by Vlok, Oxenham, et al. (2023) identified that an exceedingly high burden of scurvy (80%) was present in the nonadult cohort under 20 years of age-at-death in northern Vietnam at the beginning of the agricultural transition just over 4000 years ago. A combination of a diet of Vitamin C poor foods including domesticated rice and pigs, high fertility, high infectious disease and parasitic load, migration, subsistence transitions and climate change driving lower wild resource returns appear to be the main drivers for high scurvy burden.

In contrast to the high burden of scurvy at Man Bac, scurvy was not identified in the nonadults or adults from the Pre-Neolithic in the same region of northern Vietnam (6–7 kya), although it was recognized that poorer preservation may have contributed to lack of identification of scurvy in the earlier time period (Vlok, Oxenham, et al., 2023; Vlok, Snoddy, et al., 2023). Forthcoming research of nonadult and adult scurvy in the post-Neolithic Metal Periods of Vietnam however, where skeletal remains are excellently preserved, also appear to be very low (forthcoming research), suggesting good preservation is not the main driver for the identification of a high burden of scurvy at Man Bac. These findings indicate that the Man Bac individuals exhibited unusually high nutritional disease for the region, likely related to the unique characteristics of the initial agricultural transition described above.

Given that nonadults represent the cohort that did not survive to adulthood, it is difficult to determine from these findings alone, whether scurvy was pervasive throughout the Man Bac population, or whether nutritional deficiency was a side effect of the nonadults having experienced the greatest endogenous (e.g., inefficient metabolism of Vitamin C) and exogenous (e.g., Vitamin C poor diet) frailty. In addition, as is recognized by the osteological paradox, the presence of a disease does not directly relate to increased frailty in the population (Wood et al., 1992). As such, an assessment of scurvy in the Man Bac adults, an overall assessment of survivorship related to scurvy, as well as the role of nutrition throughout the Man Bac life course is necessary to capture a comprehensive understanding of overall health in the early agricultural period of Vietnam.

Regarding "frailty," we specifically refer here to the demographic (rather than the clinical) definition, which describes an individual's relative risk of death (see DeWitte, 2010; DeWitte & Hughes-Morey, 2012; Vaupel, 1988 for demographic and palaeodemographic examples where this definition is in operation). Risk of death is impacted by both endogenous (biological and genetic) and exogenous factors (social and environmental). If stress can be characterized as some form of disruption to homeostasis (Larsen, 2015), with scurvy as a specific example, then frailty and resilience can be seen as each end of a cline of the host's response (see discussion in McFadden & Oxenham, 2020). Lesions, or their lack, constitute aspects of the life history of any individual and only through exploring the interaction between the evidence for pathology in the context of demographic characteristics of an individual or population can we hope to understand interactions between disease and mortality in past populations. In this context, it is particularly important to assess frailty/resilience

questions in separate nonadult and adult analyses as proxies for survivors and nonsurvivors (see DeWitte & Stojanowski, 2015; McFadden & Oxenham, 2020; Wood et al., 1992; Wright & Yoder, 2003).

The developmental origins of health and disease (DoHAD) hypothesis postulates that stress in-utero have trade-off effects for health later on in life, a concept known as "adaptive plasticity" (Gowland, 2015; Temple, 2019). This hypothesis considers the fetal stage as one of programming for the postnatal environment, and if stressful, adapts to expect a stressful environment after birth as well. Maladaptation to the postnatal environment (e.g., the post-natal stage is associated with lower stress) has been linked to the development of chronic diseases later on in life, as adaptive plasticity has impacted form and function of various organs to the postnatal environment. Exposure beyond in-utero, such as during childhood and adolescence may also have significant implications for health later on in life, and health from a life history perspective can be thought of as an accumulation of biological and social events that do or do not contribute to physiological stress (Agarwal, 2016). Research suggests that early life stress accelerates maturity, decreases reproduction, and increases susceptibility to morbidity and mortality in later life (Ham et al., 2021; Temple, 2019). For example, early maturation leading to premature menarche in females increases the risk of osteoporosis in later adulthood due to lower bone modeling time in childhood (Lewis, 2022). Additionally, as a female fetus already carries all their ova, these adaptations can have multigenerational impact on health impacting not only their lifetime, but those of their children as well, and in this instance maternal health has implications for mother, daughter, and future grandchildren (Agarwal, 2016). These trade-offs impacting health both later on in a person's lifetime and potentially across generations makes sense from an evolutionary perspective, as organisms do not evolve to become healthier, but to pass off their genes to offspring, and survival to age of reproduction is an evolutionary priority over living to old age. Assessing scurvy in both the adults and nonadults at Man Bac provide an opportunity to investigate the role of nutritional stress from in-utero until old age, and important factors in health, such as the maternal-fetal interface and impacts of early life stress on later adulthood can be elucidated. Already evidence of congenital scurvy has been uncovered at Man Bac indicating scurvy of expecting mothers (Vlok, Oxenham, et al., 2023; Vlok, Snoddy, et al., 2023), but the adults need to be assessed in order to fully comprehend the disease context that placed these mothers and subsequently their babies at risk of scurvy.

This research attempts to address three key questions: (1) Is there evidence for scurvy in the adult cohort from Man Bac, (2) what is the relationship of scurvy with survivorship at the site in both adults and nonadults? and (3) what is the role of risk factors to scurvy from a life course perspective for the early agricultural transition of Vietnam?

1.1 | Clinical presentation of adult scurvy and relevance to diagnosis in archeology

Scurvy is a clinically diagnosable nutritional disease caused by prolonged Vitamin C deficiency. Prior research has demonstrated that for adults an estimate of 10 mg per day is sufficient to prevent the occurrence of clinical scurvy (Brickley et al., 2020; Hodges et al., 1969). However, this research has been limited to few studies that were conducted in unethical circumstances (e.g., experiments on prisoners in the 1960's), and the lack of controls, combined with our recognition of individual heterogeneity of thresholds for clinical expression in other micronutrient deficiencies (such as the relationship of Vitamin D and calcium levels to clinical rickets) means that it is likely that the minimal requirements of dietary Vitamin C to prevent scurvy vary from person to person (Hodges et al., 1969; Munns et al., 2016; Vlok, Snoddy, et al., 2023).

The classical symptoms of scurvy are reported as a hyperkeratotic papular rash, corkscrew hair growth, bleeding of the gums sometimes associated with tooth loss, lethargy, hemorrhage of superficial and deep muscles, edema due to blood pooling in the joint cavities, retro-orbital hemorrhage, and pseudo-paralysis due to the excruciating pain (Al-Tubaikh, 2010; Cook, 1945; Hirschmann & Raugi, 1999; Olmedo et al., 2006; Pimentel, 2003). These symptoms are caused by a single pathophysiological process. Vitamin C is essential to the synthesis of collagen, which is a group of fundamental proteins essential for the plasticity of soft tissues including blood vessels, and bone (Gould, 1961; Murad et al., 1981). Long-term Vitamin C deficiency results in defective collagen in the growth of new blood vessel tissue. As a consequence, the vessel walls rupture leading to internal hemorrhage. Regions of high friction between tissues such as around muscles are particularly susceptible to hemorrhage. The hyperkeratotic rash observed on the skin is a product of superficial vessel rupture around follicles and defective collagen in skin production (Fossitt & Kowalski, 2014).

The disease is associated with a high disability burden due to the debilitating pain and lethargy. If left untreated the disease is fatal often due to cardiac and/or respiratory failure (Hirschmann & Raugi, 1999). A return of Vitamin C to the diet is curative, with clinical manifestations disappearing within a few weeks (Hirschmann & Raugi, 1999), and spontaneous bleeding can stop within a few days of a return of adequate Vitamin C levels to the diet (Halligan et al., 2005). However, recovery from the multisystem damage caused by the condition is slow, and a person is susceptible to death and disease for months after. Therefore, a direct relationship of scurvy to frailty in the archeological record is not inferable. Theoretically, an individual can be recovering from scurvy and still die due to the disease as an ultimate cause, as the Vitamin C deficiency left them immunocompromised and susceptible to infectious disease, which is eventually fatal.

Scurvy affects three components of bone physiology. The first is modeling of new bone, which is exclusive to growing nonadults. As collagen is an essential component of osteoid, the deposit of new bone for longitudinal and appositional growth is disrupted. Children with scurvy have defective metaphyses, thin cortices, and generalized osteopenia of cortical and trabecular bone (Brickley et al., 2020). These features are not observed in adults. In both adults and children, osteoid deposit in bone remodeling causes generalized osteopenia (Brickley et al., 2020). Long-term Vitamin C deficiency is more likely

to have significant impacts on remodeling as osteoid deposition is disrupted for a longer period, and more severe osteopenia is expected in chronic cases. Lastly, subperiosteal hemorrhage results in irritation of the periosteum resulting in new bone formation at the hematoma site (Ortner & Ericksen, 1997). Increased vessel development (capillaries) occurs at the hematoma sites to drain the blood (Klaus, 2017). However, the Vitamin C deficiency means these vessels are also defective and as a consequence, result in even more bleeding. The subperiosteal new bone (SPNB) forms around these newly formed capillaries, and in dry bone these lesions are observable as discrete deposits of SPNB localized to the site of the hematomas in association with cortical porosity (Snoddy et al., 2018). These are not typically visible in adult radiographs in clinical contexts but are macroscopically observable in archeological dry bone. In contrast, the hematomas particularly of the long bones are more commonly radiographically visible in nonadults, especially infants (Brailsford, 1953).

Subclinical scurvy needs to be seriously considered in the archeological record, as physical evidence of the disease may be visible in bone at a higher prevalence than is reported in clinical literature where individuals have reached a particular severity of symptom presentation before they present for medical treatment. A 1930 study of seemingly healthy school children demonstrated that 18% of them had fragile vessels, which are at risk for hemorrhage. These fragile vessels disappeared when fed an orange a day (Göthlin, 1930). Vessel fragility has been observed within 48 h in guinea pigs who were fed a Vitamin C deficient diet (Dalldorf, 1933). Lowered capillary strength was also observed in 19 out of 27 adults with subclinical scurvy (observed by low plasma Vitamin C levels) (Rinehart & Greenberg, 1942). It is important to note that the term subclinical scurvy does not necessarily indicate asymptomatic expression, and individuals presented with nonspecific symptoms including mild gingivitis, small pharyngeal ulcers, slight swelling and stiffness in the joints, pins and needles, lethargy, and lack of appetite. Capillary strength was recovered within 2 weeks of an adequate diet (Rinehart & Greenberg, 1942). The potential of subclinical scurvy being overlooked in the clinical literature is significant since experimental evidence shows that classical signs in adults may only occur after a few months of deficiency (Fox, 1941). Even the historical clinical literature, which paleopathological diagnosis of scurvy remains heavily reliant on as the disease is rare in present day, is confounded by the individuals whose cases are reported. Cases were typically described in individuals with complex biosocial contexts (i.e., marginalized, disenfranchised, and lower socioeconomic individuals) that rendered them susceptible to a number of diseases or maladies from laborious activities, which would mask the symptoms of scurvy until they became severe (e.g., cases observed by Lind (1757) and Barlow (1883)). The above suggests that the prevalence of scurvy in bone may be more common in the archeological record than previously recognized. As more assemblages are studied, new diagnostic protocols are being produced, and more paleopathologists are trained to specifically diagnose the disease, it is expected that disease will become one that is common in a variety of archeological contexts around the world.

2 | METHODS AND MATERIALS

2.1 | The Man Bac site

Man Bac is a habitation and cemetery site in Ninh Binh province of northern Vietnam. The site is of great archeological significance for Mainland Southeast Asia as it is the only site that directly documents initial contact between local forager populations who first moved out of Africa to inhabit Southeast Asia, and a later southern migration of farmers from a northern route of Africa across Eurasia. This migration induced the early agricultural transition in Mainland Southeast Asia from around 4500 BP. The Man Bac site itself dates to between 4 and 3500 BP, during the 4.2 ka drying event (Oxenham et al., 2011; Vlok et al., 2020). This climate event is characterized by a period of drying and cooling experienced in many parts of the world with significant consequences for the collapse of major organized populations including in India, Egypt, Japan, and the Middle East (Ran & Chen, 2019). This event led to social transitions of human groups that had significant impact on their health (Robbins Schug et al., 2023). Man Bac appears to be associated with an adoption of agriculture, at least in part, as a response to ecological change during this period restricting wild flora and fauna resource returns (Oxenham et al., 2018).

Prior archeological and bioarcheological research has described a rich cosmopolitan community who were sedentary, had high fertility and population growth, low maternal mortality, were organized into kin-based hierarchical groups, suffered from a high burden of infectious, nutritional, and parasitic diseases, and had advanced forms of health care (McFadden et al., 2018, 2020; Oxenham et al., 2011, 2021; Tilley & Oxenham, 2011). It is extremely rare for sites in Southeast Asian prehistory to be as deeply contextualized as is the case at Man Bac, therefore assessing survivorship of specific disease at the site has great significance to the scope of future investigations within the region.

2.2 | Human osteological analysis

This analysis includes the differential diagnosis of 26 adults and survivorship analysis of a total of 70 adults and nonadults from Man Bac. Individuals needed to have at least two bones present with the potential to present with diagnostic scorbutic lesions in order to be included in the analysis. Analysis was also conducted on 84 adults from Con Co Ngua, a Pre-Neolithic site in northern Vietnam. No skeletal lesions consistent with scurvy were identified in the adults, as was the case with the nonadults (Vlok, Oxenham, et al., 2023). This publication focuses specifically on Man Bac where signs consistent with scurvy were found. The preservation of the Man Bac nonadults was previously reported by Vlok, Oxenham, et al. (2023) and Vlok, Oxenham, et al. (2024). To summarize, more than half of the nonadults were complete (>75% representation) with minimal to no cortical surface damage. Almost 75% of the adults were complete and again minimal to no cortical surface damage was observed.

Age-at-death estimation of the adults was assessed following standards for dental wear, auricular surface, and pubic symphysis (Brooks & Suchey, 1990; Buikstra & Ubelaker, 1994; Lovejoy et al., 1985; Oxenham, 2016). Sex was estimated using cranial and pelvic morphology (Buikstra & Ubelaker, 1994; Phenice, 1969; Walrath et al., 2004).

2.3 | Diagnosis of scurvy

Skeletal presentation of scurvy in adults is different to that of nonadults as the periosteum in an adult is more tightly attached and thinner (Dwek, 2010), and hematoma formation is more localized (see examples of adult lesions in Brickley et al. (2016), Buckley et al. (2014), Crist and Sorg (2014), Geber and Murphy (2012), and Maat (2004)). In theory, this means lesions should be more tightly restricted to regions of muscle attachments overlaying deep vessel systems which, when subject to micro or macro trauma hemorrhage blood, that in turn irritates the periosteum causing SPNB production (Ortner & Ericksen, 1997). What remains a challenge in adults is that lower abnormal bone response to irritation of the periosteal layer means that lesions are more subtle, a challenge that is compounded when considering the factor of remodeling of healing lesions (see Vlok (2023) and Brickley and Morgan (2023) for further discussion on the impact of lesion ambiguity to the application of diagnostic criteria). In addition, general porosity of the skull in regions of importance when assessing skeletons for scurvy (such as the pterygoid fossa) can occur in normal circumstances due to vascularization and the differentiation between subtle lesions and normal findings can be difficult.

To counter these issues, we conducted three different approaches to diagnosis of scurvy. The first is a traditional differential diagnosis followed by two inclusion criteria approaches: a threshold criteria approach by Snoddy et al. (2018), and a diagnostic certainty approach by Brickley and Morgan (2023). All approaches rely on individual experiences of scorbutic lesions, which differ amongst researchers depending on their exposure to various archeological human skeletal assemblages. As more cases of adult scurvy are published the application of these approaches will improve with more comparators available, as is the case already with the literature for nonadult scurvy. For this reason, the findings presented here are largely exploratory in recognition of the current lack of robust investigation into adult scurvy in the prehistoric past. The Snoddy et al. (2018) method and the Brickley and Morgan (2023) approaches apply different terms to the diagnostic process. The differences are based on the original sources for the terminology which were modified from the "United Nations Istanbul Protocol Manual on the Effective Investigation and Documentation of Torture and other Cruel, Inhuman or Degrading Treatment or Punishment" (Appleby et al., 2015; UN HCHR, 2004) and the "World Health Organization COVID-19 case definition" (World Health Organization, 2020), respectively. In addition, Brickley and Morgan (2023) classify lesions into three categories (diagnostic, highly consistent, and consistent), whereas Snoddy et al. (2018) only defines two categories (probable and possible). Vlok (2023) clarified and updated definitions from Snoddy et al. (2018) to operationalize them across multiple diseases where threshold diagnostic criteria are available, and these definitions are used here (Table 1). It is important to recognize that even in the clinical literature these terms are used inconsistently, and the most appropriate definition to use will be the one that is better aligned with the original research question. There are, however, some similarities between the definitions used by both approaches as can be seen in Table 1.

TABLE 1 Comparison of definitions in two inclusion criteria for scurvy diagnosis.

Brickley and Morgan (2023, pp. 641)	Snoddy et al. (2018) updated by Vlok (2023, pp. 327)
Definition: Diagnostic of: The pattern of lesions identified and discussed could not have been caused in any other way than described	Definition: No comparison. Vlok (2023) argues against definitive diagnosis based on lesions alone
Application: Unambiguous "Ortner" porosity of the greater wing of the sphenoid + other unambiguous lesions	
Definition: Highly consistent/typical: The lesion/s could have been caused by the condition described, but there are a few other possible causes that need consideration	Definition: Probable: A person who meets the clinical criteria for a disease
Application: A number of highly consistent lesions observed macroscopically	Application: Two or more clinically "diagnostic" lesions
Definition: Consistent with: The lesion/s could have been caused by the condition described, but it is nonspecific and there are many other possible causes	Definition: Possible/suspected: A suite of clinical signs that are suggestive of a particular disease category (respiratory, metabolic, infectious, and so forth) AND ecological, epidemiological, and archeological contexts supports the plausibility of this diagnosis
Application: Porotic lesions and/or SPNB that is consistent with scurvy but has various other possible causes. Less bone than might be anticipated (often referred to as osteopenia) assessed via microscopic evaluation	Application: At least one clinically "diagnostic" and/or at least two or more clinically "suggestive" lesions

2.3.1 | Traditional differential diagnosis

As Vlok (2023) argues, a differential diagnosis is an inherent step in any application of inclusion criteria, such as proposed by Snoddy et al.

(2018) and Brickley and Morgan (2023). The inclusion of this approach in diagnosis benefits both the reader and the researcher in identifying whether diseases with similar skeletal expression from a pathophysiological standpoint was sufficiently considered.

2.3.2 | Snoddy et al. (2018) threshold criteria approach

The Snoddy et al. (2018) criteria standardizes the diagnosis of probable, or possible cases of scurvy. In this method, lesions are considered to be "diagnostic" if they have a biological basis for the skeletal expression and have strong clinical or paleopathological backing by the literature (Table 2). Those that have been suggested to be associated with the disease both on the basis of biological sense and relationship to diagnosed cases of scurvy but are yet to be demonstrated to have high association, or are features that are generally observed in a number of overlapping diseases, are considered to be "suggestive." In order for a probable case to be recognized, at minimum two diagnostic lesions outlined by Snoddy et al. (2018) are required. If one diagnostic lesion and/or multiple suggestive lesions are present, the individual can be considered to have a possible case of scurvy.

The strengths of this approach are that lesions are cautiously considered in light of their anatomical intuitiveness, the specific relationship of the lesions in comparison to other diseases, and their real-world observation of the relationship of the lesion to clinical and paleopathological cases. That is, lesions that are well known to be associated to scurvy such as alveolar porosity from bleeding gums, do not make the standard for consideration of scurvy, as alveolar porosity is commonly associated and undiscernible from nonspecific periodontal disease. See critique by Snoddy et al. (2020) of a case where this lesion was misused in the diagnosis of a case of "scurvy." Condensing diagnosis into two categories (possible and probable) is statistically valid, due to the general low power of bioarcheological research, and recognition that there needs to be space for heterogeneity of lesion expression within these two categories (i.e., the definitions are not overprescribed as to render them statistically useless given limitations of bone expression). The use of these definitions is also beneficial for scientific communication purposes, particularly when considering engagement through multidisciplinary collaboration with neighboring fields, such as clinical medicine and epidemiology.

The limitations of this approach are that the threshold is focused on the number of different lesions present and that the diagnosis does not consider the severity and distinct pathological basis for a lesion. An individual with one clear "diagnostic" lesion would be considered a possible case, whereas an individual with multiple subtle "diagnostic" lesions would be considered a probable case. Preservation, particularly of the cranium and face considerably impacts whether a case is determined as a possible versus probable one (see Vlok, 2023 for detailed discussion on the limitations of this approach). Lastly, Snoddy et al. (2018) recommend regular review of "diagnostic" and "suggestive" lesions as research continues, and there have been more cases of scurvy published since (Morrone et al., 2021; Perry & Edwards, 2021; Srienc-Ściesiek et al., 2024; Vilumets et al., 2024). For example Simonit et al. (2023) identify new bone lesions extending from the hypoglossal canal on pars laterali from cases diagnosed with scurvy from

TABLE 2 Comparison of skeletal lesions secondary to hemorrhage contributing to diagnosis of adult scurvy by the Snoddy et al. (2018) compared with the Brickley and Morgan (2023) approach.

	Snoddy et al. (2018: 879–880)	Brickley and Morgan (2023: 639)
Lesions that are present in both diagnostic approaches		
Ectocranial parietal and/or squamous temporal bone	Diagnostic	Core
External surface of the greater wing of sphenoid bone	Diagnostic	Core
Foramen rotundum of sphenoid bone	Diagnostic	Core
Orbital wall	Diagnostic (orbital roof only)	Core
Anterior surface/ infraorbital foramen of maxilla	Diagnostic	Core
Posterior surface of maxilla	Diagnostic	Core
Palatal surface of maxilla	Diagnostic	Core
Medial surface/coronoid process of mandible	Diagnostic	Core
Supraspinous fossa of scapula	Diagnostic	Core
Infraspinous fossa of scapula	Diagnostic	Core
Long bones	Diagnostic (nonadults) Suggestive (in adults)	Core
Endocranial calvarium	Suggestive	Core
Visceral surface of the ilium	Suggestive	Core
Posterior/poster-medial aspect of zygomatic bone	Suggestive	Core
Lesions that are present in only one of the diagnostic approaches		
Pterygoid fossa/plate	Diagnostic	-
Antero-lateral shaft of rib	Suggestive	-
Antero-lateral aspect of zygomatic bone	Suggestive	-
Lesser wing of sphenoid bone	Suggestive	-
Mylohyoid line of mandible	Suggestive	-
Linea aspera of the femur	Suggestive	-
Inferior surface of pars basilaris	Suggestive	-
Maxillary and or/mandibular alveolar bone	-	Core

the 1st millennium Campana, Italy, which is anatomically intuitive, and worth future consideration.

2.3.3 | Brickley and Morgan (2023) diagnostic certainty approach

The Brickley and Morgan (2023) approach emphasizes the certainty that a lesion is pathological and is associated with the biological basis of scurvy. This approach differs to the Snoddy et al. (2018) approach by considering the ambiguity or lack thereof concerning lesions, which is the greatest limitation to the Snoddy et al. (2018) threshold criteria method (see Vlok (2023) for discussion). The limitations to the approach by Brickley and Morgan (2023) is that they do not provide photographic reference for the kinds of lesions that fit within each of their diagnostic definitions. A pictorial companion to this research that presents a variety of lesions, and their associated definitions will be very beneficial to the application of this approach, particularly in addressing uncertainty around what should be considered "normal" versus "abnormal." In addition, the requirement of the presence of the Ortner criteria of sphenoidal porosity and SPNB to implicate certain diagnosis of scurvy is one of legacy, rather than a reflection of the biological basis of a systemic disease, particularly as a great variety of lesions have been described since the original publication almost 30 years ago (Buckley et al., 2014; Geber & Murphy, 2012; Klaus, 2017; Ortner et al., 2001; Ortner & Ericksen, 1997; Snoddy et al., 2017; Stark, 2014). Lack of complete preservation of the greater wing of the sphenoid bone is particularly challenging when applying this approach to prehistoric assemblages. The Brickley and Morgan (2023) approach also differs from the Snoddy et al. (2018) approach in that with the exception of porosity and SPNB of the external greater wing of the sphenoid bone, all lesions are treated with equal weighting in the diagnostic process, such as alveolar porosity, which, as mentioned above we believe should be treated as nonspecific (Table 2). We applied the Brickley and Morgan (2023) approach with the exception of lesions of mandibular and maxillary alveolar bone. Photos of these lesions have nonetheless been included in Data S2. Fishers exact tests were applied to assess if there were any meaningful differences between the diagnostic outcome of two methods.

2.3.4 | Analysis of survivorship

Kaplan–Meier models were applied to assess survivorship in both (1) nonadult (<15 years) and (2) adult and nonadult adolescent cohorts (15+ years) as representative of survivors and nonsurvivors to skeletal maturity. The Snoddy et al. (2018) criteria were used for consistency across the adult and nonadult cohorts, as the nonadult cases were published prior to the publication of Brickley and Morgan (2023). Only probable cases were included in the analysis as lower diagnostic confidence is likely to introduce statistical noise.

Kaplan–Meier analysis is a nonparametric test that studies the difference in survival time of two cohorts. This survivorship test does not assume a uniform hazard, but its limitation is that effect size cannot be easily assessed. It is better suited to analysis for smaller sample sizes than the alternative Cox model, which is a semi-parametric model also applied in survivorship analysis. Statistical significance of the Kaplan–Meier was assessed using a log-rank test. SPSS v19 was used to analyze the models. Statistical significance was interpreted intuitively where no specific p-value cutoff was determined, but the p-value was used as an indicator alongside the mean 95% confidence interval (95% CI) to assess statistical validity. That is dichotic determination of statistical significance (e.g., commonly applied significance levels at $p < 0.05$ or $p < 0.1$) was not performed in this analysis. This approach (the use of the p-value as an indicator rather than in the relation to an arbitrary cutoff point) has gained significant ground in biological sciences, as it is well recognized that p-values simply are not replicable (Baker, 2016; Cohen, 2011; Halsey, 2019; Smith, 2020), a significant challenge for archeological data specifically, which can never be reproduced. Rather the p-value and the confidence interval are interpreted in comparison to the nature of the original sample, and contextual discussion about the relationship between the statistical model's output and its representation of a meaningful output is instead produced here. We recognize that while this approach has made significant ground in other fields it has yet to become commonplace in paleopathological literature but application of the p-value in combination with the CIs is already being applied in some studies (Kelmelis & DeWitte, 2021; Magalhães et al., 2023; Wang et al., 2023; Yaussy et al., 2023). We hope the analysis presented here provides groundwork for necessary change in our field as has been the case in other scientific fields.

3 | RESULTS

3.1 | Lesion patterning

At an assemblage level, the lesions of interest in scurvy diagnosis were predominantly symmetrical discrete and localized SPNB deposits, cortical porosity and/or vascular impressions associated with muscle attachments sites in 46% ($n = 12/26$) of the Man Bac adults. These symmetrical lesions were observed throughout the axial and appendicular skeleton and appear to be indicative of systemic disease rather than trauma. Lesions consistent with treponemal disease (diffuse new bone associated with cortical enlargement of the appendicular skeleton associated with regions of lymphatic drainage) were identified in 27% ($n = 7/26$) of adults. These lesions were discussed in Vlok et al. (2020) and excluded from analysis in this research. Lesions of interest to the differential diagnosis were predominantly observed on the cranial vault, face, and mandible (Figure 1). The region of the external greater wing of the sphenoid bones (21.7%, $n = 5/23$), temporal and parietal bones (20%, $n = 5/25$), and posterior and palatal maxillae were the most frequently affected with lesions clearly extending from the foramina (21.7%, $n = 5/23$). Lesions of the long bones were less likely to be symmetrical than in the skull and scapulae with only three

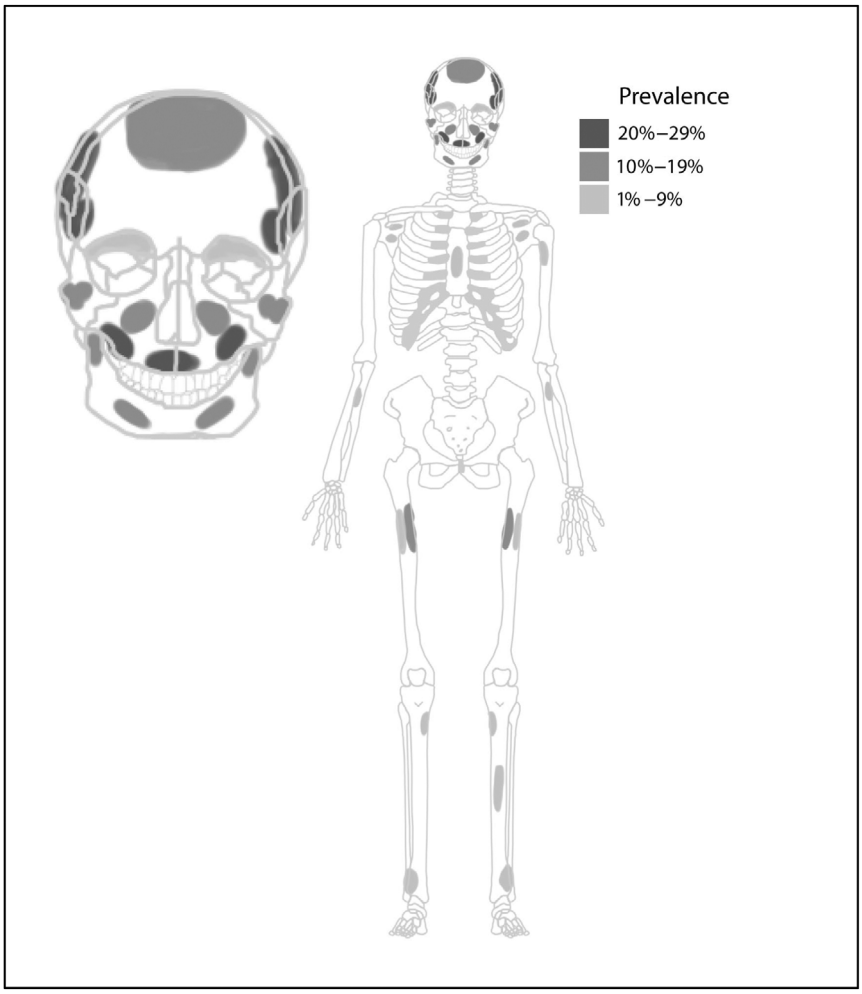

FIGURE 1 Distribution of discrete subperiosteal new bone, abnormal cortical porosity, and/or vascular impressions in the Man Bac adults.

cases of symmetrical discrete SPNB of the long bones recorded (12%, $n = 3/25$). Symmetrical discrete porosity and SPNB of the supraspinous and infraspinous fossae of the scapulae were only observed in one adult (MB05M29, middle-aged adult male, 4.5%, $n = 1/22$). However, the presence of diffuse lesions attributed to treponemal disease is likely obscuring the true pattern of discrete lesions in the long bones, so interpretation of symmetricity of appendicular discrete lesions is limited. All lesions considered for the diagnosis of each individual is available in Data S2.

3.2 | Differential diagnosis

3.2.1 | Treponemal disease

Given the evidence of treponemal disease in the Man Bac assemblage, it must be considered that the disease is the cause for the lesions. Treponemal disease can cause SPNB of the skull especially around the nasal region due to infection of the nasolabial lymph nodes causing inflammation known as goundou (Buckley & Dias, 2002; Mahachoklertwattana et al., 2003; Trenouth, 1975). However, the overall skeletal expression of treponemal disease is rarely symmetrical and is diffuse rather than discrete (Buckley & Dias, 2002). In addition, the lesions are focused around the frontal and parietal bones and lymph nodes due to the hematogenous and lymphatic spread of the disease and is dissimilar to the skeletal expression observed in the Man Bac adults that are strictly associated with muscle attachment sites (Figure 1). Therefore, while a proportion of the adults from Man Bac suffered from treponemal disease, the disease does not entirely describe all SPNB and porotic lesions observed in the adults. Similarly, nonspecific infection has been ruled out, as the skeletal expression of infection is more diffuse and not symmetrical due to the hematogenous spread of most bacteria and viruses (Buikstra, 2019).

3.2.2 | Pellagra

Pellagra is a disease caused by a combination of niacin (Vitamin B3) and tryptophan deficiency. The disease can cause nonspecific bone changes including the SPNB deposits of the limbs (Paine & Brenton, 2006). Preliminary studies of pellagra by Paine and Brenton (2006) and Miller et al. (2020), suggest that these lesions may be, but are not necessarily restricted to discrete regions of SPNB.

It also remains unknown whether pellagra causes any of these lesions directly or whether they are secondary to infection due to immunocompromization, or a result of comorbid micronutrient deficiency, such as scurvy. The dietary basis of Man Bac inclusive of pig and rice is rich in niacin and tryptophan, further indicating pellagra is an unlikely cause for the lesions, except in cases of extreme starvation.

3.2.3 | Osteomalacia

Osteomalacia, a condition caused by hypomineralization of osteoid (found alongside rickets in nonadults and on its own in adults) causes hypomineralized deposits of new bone at muscle attachments sites particularly of long bones (Brickley et al., 2020; Francis & Selby, 1997). However, these lesions are entirely dissimilar, appearing instead with clear disorganization of the lamellar bone rather than a result of hematoma formation (for a clear example see Brickley et al., 2007, p. 74). While rickets was present in the Man Bac nonadults (Vlok et al., 2020; Vlok, Oxenham, et al., 2024), there were no signs of bending deformities of the appendicular or axial skeleton, pseudofractures, or compression deformities and trauma to the spine consistent with osteomalacia (Brickley et al., 2020). Osteomalacia was ruled out as a possible cause for the lesion expression observed.

3.2.4 | Normal variation at muscle attachment sites

Given the ambiguity around lesions in adult scurvy, normal variation needs to be considered in the etiology of the new bone and cortical porosity. General vasculature of muscles, which also leave cortical pores, and robusticity of muscle attachments on the skull can be confused with abnormal cortical porosity and SPNB. As a comparator for normal versus abnormal porosity and subperiosteal new bone versus musculature, photographs of the same regions of the face and skull have been provided for the site of Con Co Ngua, a Pre-Neolithic site in the same region of northern Vietnam in Data S3 and cases from Man Bac who were not identified with scurvy in Data S4. Con Co Ngua individuals had a greater level of population activity and mobility than those at Man Bac, and overall have more robust cranio-morphology than most individuals from Man Bac (Huffer & Oxenham, 2015; Matsumura & Oxenham, 2013). Yet the adults from Con Co Ngua lack any of the porosity and new bone observed in the Man Bac adults with scurvy. Similarly, the Man Bac adults without scurvy also presented with no porosity. In addition, scorbutic lesion in the Man Bac adults were comparatively more distinct than presented in published adult scurvy cases in the literature (see Brickley et al. (2016, p. 96), Crist and Sorg (2014, pp. 99–101), Snoddy et al. (2017, p. 113) and similar to those reported by Vlok, McFadden, et al. (2024, p. 716) for the prehistoric Jomon of Japan). As such, the lesions identified were determined to be abnormal.

3.2.5 | Scurvy

Scurvy remains the most consistent explanation for the lesions. All lesions in Figure 1 are consistent with hematoma from vessel rupture due to microtrauma. The high prevalence of nonadults with scurvy at Man Bac also support evidence that scurvy is the underlying cause for the lesions in the adults (Vlok, Oxenham, et al., 2023).

3.3 | Snoddy et al. (2018) criteria outcome

Over 46% ($n = 12/26$) of the adults presented with at least one lesion diagnostic for scurvy at the site, with almost 35% ($n = 9/26$) having at least two diagnostic lesions consistent with a probable case (Figure 3; Table 3; Datas S1 and S2). These findings are considerably lower than those of the Man Bac nonadults where almost 80% were diagnosed with probable scurvy (Vlok, Oxenham, et al., 2023). Only one individual presented with a lesion that was entirely active, with the remainder of the adults presenting lesions with mixed/healing or remodeled new bone. Lesions along the zygomatic process of the temporal bone and pterygoid fossa were particularly clearly identifiable and reminiscent of hematomas pooling on the inferior margins of the temporalis muscle (Figure 2e). A clear decline in prevalence with increasing adult age-at-death cohort can be observed for possible and probable cases at Man Bac. No such trend is visible for the nonadults who all presented with high ratios of disease (Figure 3). Potential sex related differences were also observed with almost 50% ($n = 7/15$) of males and less than 20% of females ($n = 2/11$) presenting with probable scurvy, but a Fisher's exact test suggests there is no clear statistical difference ($p = 0.22$).

3.4 | Brickley and Morgan (2023) criteria outcome

Almost 35% ($n = 9/26$) of adults had unambiguous core scurvy lesions diagnostic of or highly consistent with scurvy (Table 4). Only one individual, a young adult male, had unambiguous lesions of the external greater wing of the sphenoid bone, which was diagnostic of scurvy. Males aged 20–29 had the most unambiguous lesions and represented five of the individuals diagnostic of and highly consistent with scurvy.

Very little difference in diagnosis was observed across the applications of both approaches for identifying scurvy in dry bone (Table 5). Only two individuals were differently classified across the two approaches. MB07H1M4, a female aged between 40 and 49, was diagnosed with probable scurvy with the Snoddy et al. (2018) approach, but due to well remodeled lesions and poor surface preservation, was only considered consistent with scurvy with the Brickley and Morgan (2023) approach. This individual had SPNB on the external greater wing of the sphenoid bone and temporal bone around the temporalis region, as well as endocranial SPNB. MB07H2M10, a male aged between 30 and 39, diagnosed with possible scurvy as they only

TABLE 3 Paleoepidemiology of adult scurvy at Man Bac (after Snoddy et al., 2018).

	Possible		Probable	
	Affected/observed	(%)	Affected/observed	(%)
Age (years)				
15–19[a]	0/4	0	3/4	75
20–29	0/9	0	5/9	55.6
30–39	2/6	33.3	1/6	16.7
40–49	1/8	12.5	2/8	25
50+	0/3	0	1/3	33.3
Males	2/15	13.3	7/15	46.7
Females	2/11	18.2	2/11	18.2
Total (20+)	3/26	11.5	9/26	34.6
Total (15+)	3/30	10	12/30	40

[a]A 15–19-year-olds were assessed in Vlok, Oxenham, et al. (2023).

had one diagnostic lesion according to the Snoddy et al. (2018) criteria but was highly consistent with scurvy with the Brickley and Morgan (2023) approach as he had multiple unambiguous core lesions for scurvy. Statistically, there was no difference in the use of the different criteria for classification of scurvy overall as well as when considering age-specific diagnoses, important when considering selective mortality (Table 5).

3.4.1 | Survivorship analysis of nonadults

A *p*-value of 0.399 and significant overlap between the 95% CI of the samples indicate no clear meaningful differences were observed in the survivorship of nonadults with and without probable scurvy (Figure 4; Table 6). These findings are not unexpected, as cases that were diagnosed as being only "possible" cases were those with poor preservation, and when these are also considered almost no child died before adulthood without having experienced malnutrition.

3.4.2 | Survivorship analysis of adults and adolescents

In contrast to the output of the nonadults under 15 years of age-at-death, Kaplan–Meier analysis of the adults and adolescents yielded potentially meaningful results. The Kaplan–Meier analysis demonstrated near separate mean 95% CI for the two samples tested in the analysis and a *p*-value of 0.052 (Figure 5; Table 7). The median findings were comparable to those of the mean.

4 | DISCUSSION

This research presents application of survivorship analysis on specific nutritional disease in an ancient cohort. We demonstrated that scurvy was consistently high in childhood, whereas from 15 years-at-death onwards, the prevalence of scurvy declined with increasing age. These findings suggest that scurvy is meaningful in regard to survivorship to adulthood, and in adulthood, survival to old age. The mean survival time for adults and adolescents with probable scurvy was 26.8 years whereas those who did not have probable scurvy had a mean survival time of 37.9 years. Our findings support the view that a high burden of scurvy reported at Man Bac was also associated with decreased survivorship. The outcome indicates that not only was scurvy pervasive throughout the population affecting all from birth to old age, but it also appears to be associated with an earlier age at death. The activity of the lesions (except for active lesions in one individual) was always partially or completely remodeled suggesting that the individuals were recovering from scurvy or suffering chronic episodes of the disease at the time of their deaths. Therefore, while there is decreased survivorship in adulthood with the presence of scurvy, as mentioned previously the disease cannot be concluded as the proximate cause of these individual's deaths. As discussed in Vlok, Oxenham, et al. (2023) scurvy is a proxy for a greater disease burden that may be invisible in bone including but not limited to multimicronutrient (and potentially in the case of starvation, macronutrient) deficiency, infection, and parasitosis. That is, while scurvy contributed significantly to their deaths, the proximate cause of death for each individual could have included an array of interacting factors. It is possible that sheaths of active new bone were lost postmortem and therefore very recent cases of scurvy may have been removed through postburial processes. An adult from 19th Century Ireland demonstrates how thin, active SPNB lesions can be in adults, which would be easily destroyed in the burial, excavation, and cleaning process of prehistoric assemblages (Geber & Murphy, 2012, p. 517). The one individual with active lesions (Figure 2c) also clearly has thin sheaths of active bone, that were preserved in the infraspinous fossae of the scapulae, protected from the burial environment by the scapular spine. Therefore, the relationship of lesion remodeling to survivorship is interpreted here with caution. Nevertheless, the findings suggest that each diagnosed individual was recovering from at least one episode of scurvy around time of death. A trend in increased mortality was not observed in nonadults as it appears this entire age cohort represents susceptibility to early death from all of the causes, comorbidities, and sequelae of scurvy (Vlok, Oxenham, et al., 2023). That is, the presence of scurvy was likely associated with failure to reach adult age at any point in childhood.

Females seemingly appeared to have lower prevalence of scurvy even though a high prevalence of fetal and neonate scurvy was identified at the site supported by both macroscopic and radiographic evidence of the disease. The interpretation of this finding should be considered with caution as the sample size was small and overall increased survivorship of females in relation to males may underlie this outcome. Almost 50% of the females ($n = 5/11$) as opposed to

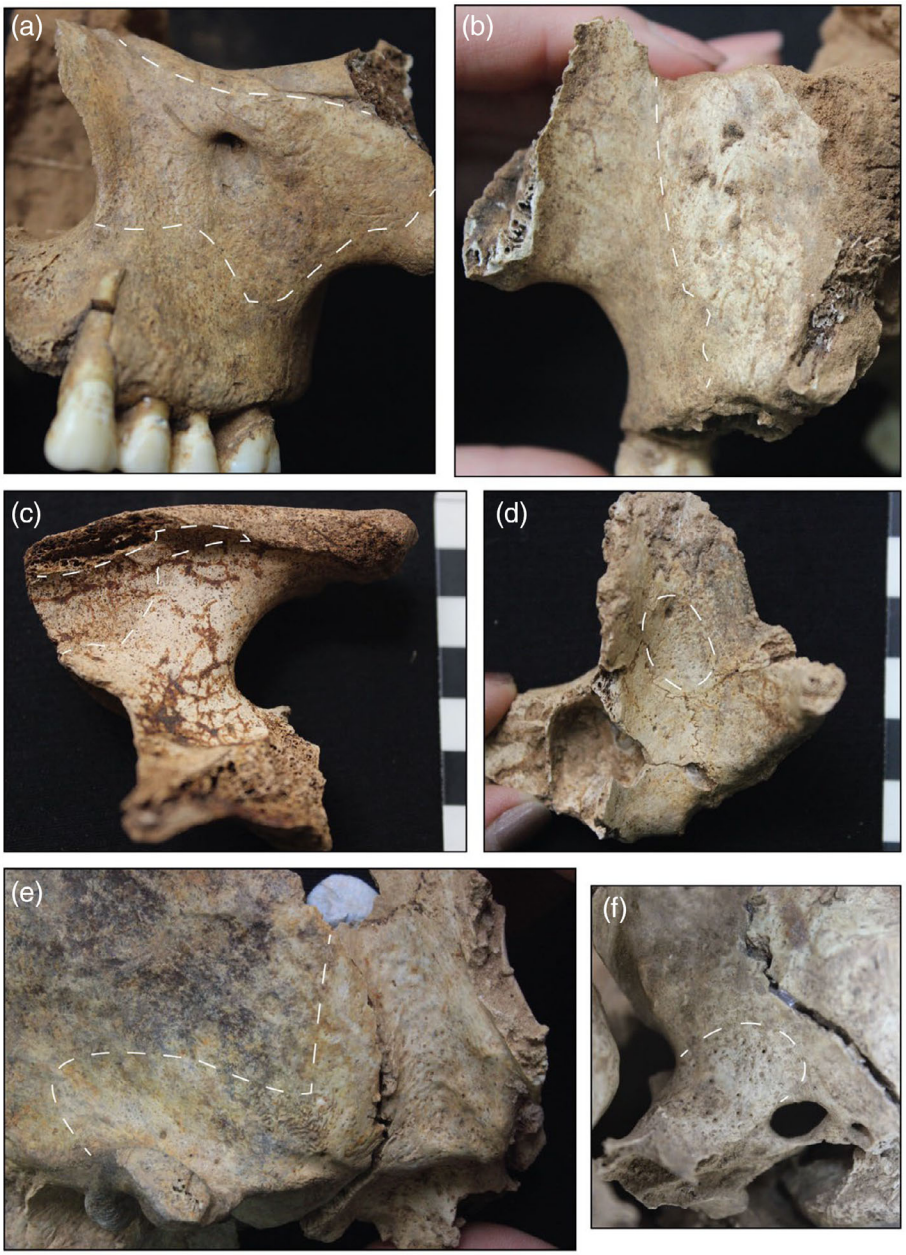

FIGURE 2 Macroscopic lesions in Man Bac adults and adolescents that are consistent with scurvy. Dashed lines represent margins of new bone. (a) Remodeled deposit of subperiosteal new bone (SPNB) with vascular impressions, and (b) mixed active/remodeled deposit of SPNB with abnormal cortical porosity and vascular impressions (MB05M11, young adult male). (c) Active SPNB inferior to scapular spine on infraspinous fossa of right scapula (MB05M29, middle-aged adult male). (d) Remodeled SPNB and abnormal cortical porosity on the posterior right zygoma, (e) right external greater wing of sphenoid and temporal squama (MB07H2M19, young adult male). (f) Mixed active/remodeled SPNB and abnormal cortical porosity on external left sphenoid around pterygoid region (MB07H2M18, male, 14–18 years).

20% of males ($n = 3/15$) were aged 40+ regardless of whether or not they were diagnosed with scurvy.

4.1 | Mortality and clinical presentation of scurvy in the literature

As scurvy is a highly fatal disease, this likely accounts for the strong statistical signature of decreased survivorship even in such a small sample size. In clinical and historical accounts, the presentation of scorbutic hemorrhaging and edema when not treated, eventually led to death. Jean, Sire de Joinville who wrote of the 13th Century Seventh Crusade describes the disease as one where "no man recovered of that sickness, but all had to die" (in Major, 1965, p. 586). Hakluyt who described the explorations of Jacques Cartier in the 16th Century notes that out of over 100 men who appear to have been stricken with scurvy, approximately a quarter died before the crew learnt that the local First Nations group used a bark of a tree that was curative (in Major, 1965, pp. 587–589). However, determining the total fatality rate of scurvy is difficult given the fact that (1) since the discovery of the role of ascorbic acid in preventing scurvy, epidemiological recording of the disease has been scant, and (2) death due to the immunological impact of Vitamin C deficiency and its sequelae (including anemia and diarrhea) means that in many cases the cause of death would not be directly attributed to scurvy. What is known is that death is an inevitable end if Vitamin C is not replenished in the diet. Amogne et al. (2021) report a prison population from Ethiopia who suffered scurvy in 2016. While those who were clinically diagnosed and treated did not die, retrospective analysis showed that when suspected cases were included

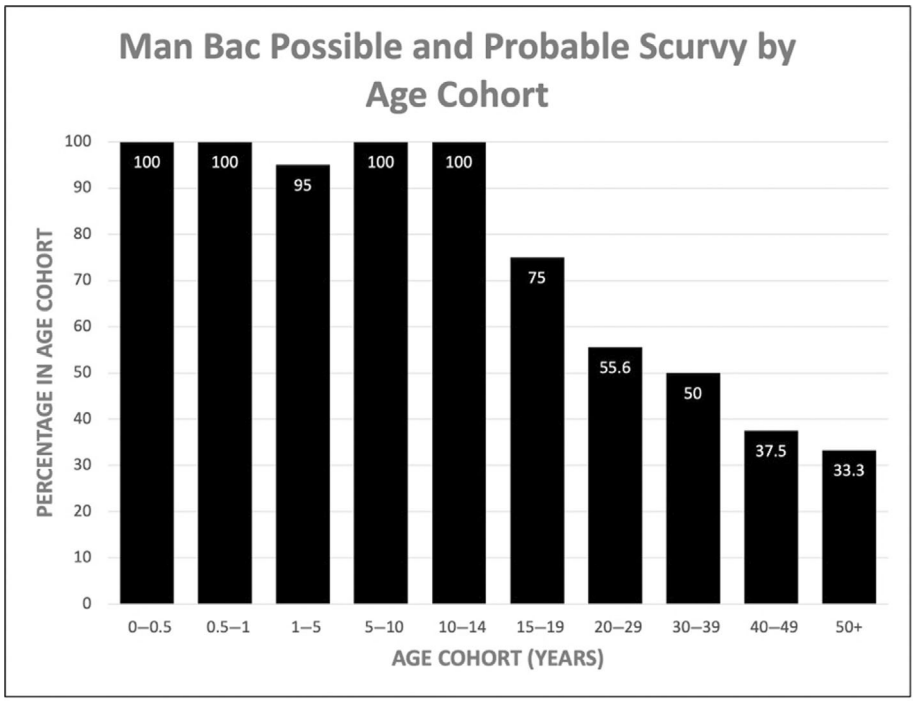

FIGURE 3 Prevalence of possible and probable cases of scurvy at Man Bac across different age cohorts.

TABLE 4 Paleoepidemiology of adult scurvy at Man Bac (after Brickley & Morgan, 2023).

	Consistent		Highly consistent		Diagnostic	
	Affected/observed	(%)	Affected/observed	(%)	Affected/observed	(%)
Age (years)						
20–29	0/9	0	4/9	44.4	1/9	11.1
30–39	1/6	16.7	2/6	33.3	0/6	0
40–49	1/8	12.5	1/8	12.5	0/8	0
50+	0/3	0	1/3	33.3	0/3	0
Males (20+)	0/15	0	7/15	46.7	1/15	6.7
Females (20+)[a]	3/9	33.3	0/9	0	0/9	0
Total (20+)	3/26	11.5	8/26	30.8	1/26	3.8

[a]Two females aged 15–19 were diagnosed with probable scurvy in Vlok, Oxenham, et al. (2023) with the Snoddy et al. (2018) approach.

TABLE 5 Age-specific diagnostic approach comparison.

Age	Snoddy et al. (2018)	Brickley and Morgan (2023)	Fishers exact (*p*-value)
Probable versus diagnostic/highly consistent			
20–29	5/9	5/9	1.0
30–39	1/6	2/6	1.0
40–49	2/8	1/8	1.0
50+	1/3	1/3	1.0
Total (adults)	9/26	9/26 (1 diagnostic)	1.0
Possible versus consistent			
20–29	0/9	0/9	1.0
30–39	2/6	1/6	1.0
40–49	1/8	2/8	1.0
50+	0/3	0/3	1.0
Total (adults)	3/26	3/26	1.0

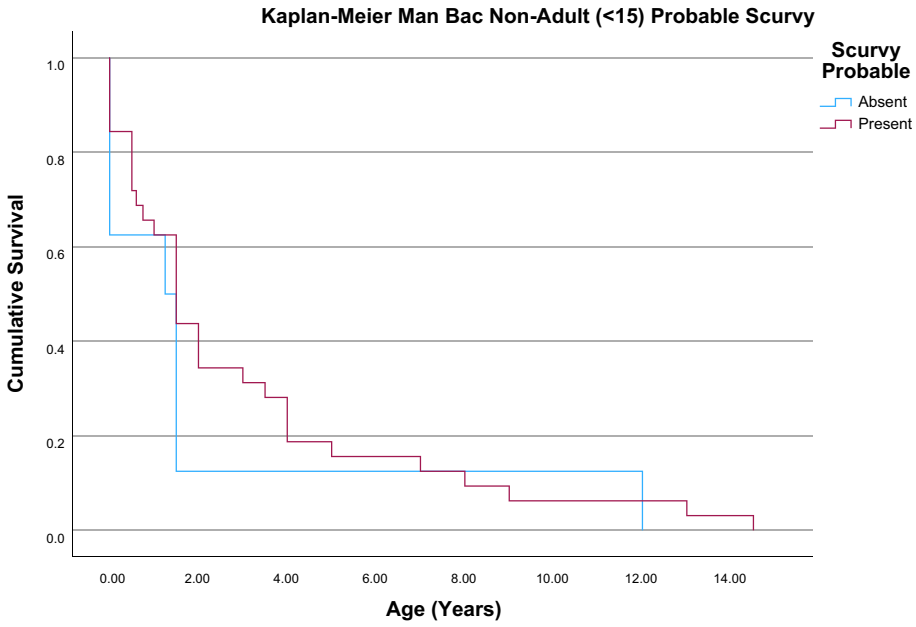

FIGURE 4 Cumulative survivorship curve for Kaplan–Meier analysis of Man Bac nonadults (<15 years).

TABLE 6 Statistical summary for Kaplan–Meier function of probable scurvy survivorship of nonadults (<15 years) at Man Bac.

Probable scurvy (<15 years)	Estimate	Std. error	95% CI
Mean			
Absent	2.219	1.420	0.000–5.002
Present	2.948	0.649	1.677–4.220
Overall	2.803	0.585	1.656–3.949
Median			
Absent	1.250	0.530	0.211–2.289
Present	1.500	0.234	1.042–1.958
Overall	1.500	0.085	1.333–1.667

Log rank (Mantel–Cox)		
Chi square	**DF**	***p*-value**
0.711	1	0.399

in the epidemiology the case fatality rate neared 10%. This population had been deprived of Vitamin C for 6 months due to food shortages. Cheung et al. (2003) reported as little as 6–31 days between symptom onset and death and a 7% case fatality rate in Afghans in 2002. A similar case fatality rate of 9% has been documented for troops in the Crimean War in the mid-19th Century (Huang et al., 2022; Pickavance et al., 2021). However, the fatality rate is highly variable dependent on knowledge of the curative properties and access to Vitamin C, whether partially or completely missing from the diet. For example, higher rates of death (over 60%) was recorded for Vasco da Gama's crew (15th Century) where at sea the crew lacked access to curative Vitamin C, and across two mid-19th Century hospitals in Southern New Zealand only one death from scurvy out of 42 cases (<3%) were recorded when treatment was available (Buckley et al., 2024; Mellinkoff, 1995).

Due to the osteological paradox, it is not possible to determine the fatality rate in archeological populations, but the application of the survivorship analysis in combination with the clinical literature indicates that instances of scurvy dramatically reduced survivorship, and the disease was pervasive throughout the population. The pervasiveness of the disease across age and sex suggests the Man Bac people did not recognize the relationship between fruits and vegetables and the amelioration of the disease's symptoms. Against a backdrop of diseases in the community including endemicity of yaws and malaria, it is even possible that the symptoms of scurvy were not recognized as disparate issues. Even as recent as the late 19th Century clinicians wrote of "malarial scurvy" in tropical India which occurred during the rainy season, an indicator of the difficulty to separate the conditions by their signs and symptoms alone. Even then, clinicians and surgeons inferred that the scurvy may be an extension of a malarial load in combination with insufficient diet that increased the clinical visibility of the disease (Buchanan, 1898; Murray, 1886). Again, the issue of the lack of specificity of symptoms in subclinical and early stages of scurvy would have made correlation to a dietary cause very difficult.

4.2 | Scurvy at Man Bac from a life history perspective

In regard to the osteological paradox, selective mortality is clearly identified in the Man Bac assemblage. That is, these individuals diagnosed with scurvy appear to represent the most susceptible to death of their age cohort and do not reflect the nutritional status of the living population. However, more can be elucidated from the epidemiological pattern of survivorship observed at Man Bac when considering a life history approach. Bioarcheologists have recorded evidence of reduced survivorship with early life stress. Temple (2014)

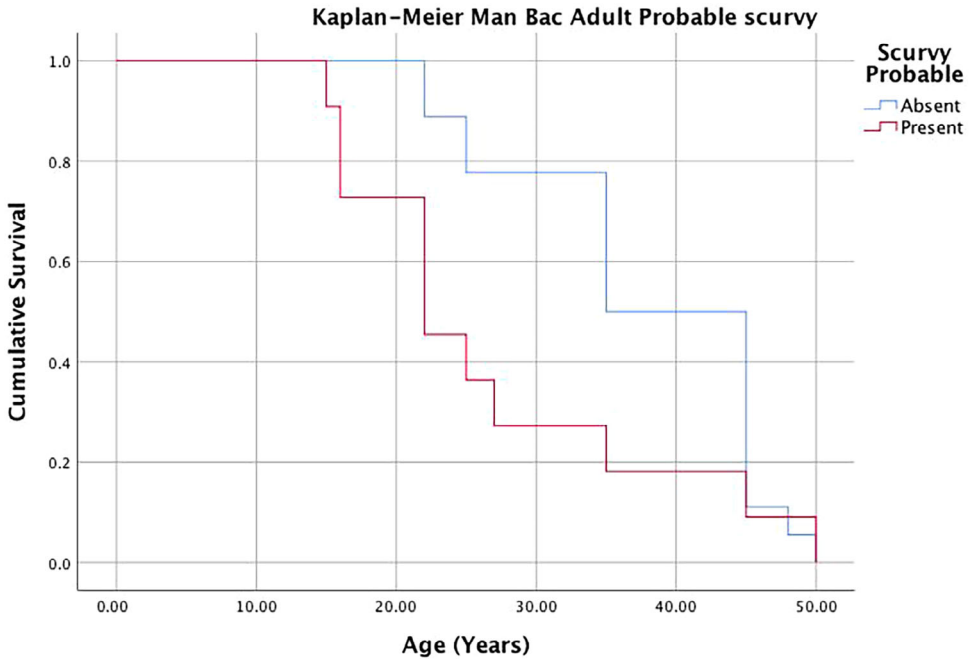

FIGURE 5 Cumulative survivorship curves for Kaplan–Meier of Man Bac adults/adolescents.

TABLE 7 Statistical summary for Kaplan–Meier function of probable scurvy survivorship of adults/adolescents (15+ years) at Man Bac.

Probable scurvy (15+ years)	Estimate	Std. error	95% CI
Mean			
Absent	37.889	2.201	33.576–42.202
Present	26.818	3.544	19.872–33.765
Overall	33.690	2.135	29.506–37.874
Median			
Absent	35.000	3.536	28.070–41.930
Present	22.000	3.716	14.717–29.283
Overall	35.000	3.484	28.171–41.829

Log rank (Mantel–Cox)		
Chi square	**DF**	***p*-value**
3.764	1	0.052

demonstrated that in the Jomon, Pre-Neolithic hunter-gatherers of Japan, linear enamel hypoplasia was linked to dying at a younger age. A similar study by Ham et al. (2021) for the Pueblo of the Southwest of North America found that a lower-status site demonstrated decreased survivorship for those with LEH, while a higher-status site demonstrated no difference in survivorship between those with or without LEH. The authors suggest that cultural buffering may be impacting the lack of different survivorship between those with and without LEH in the high-status site. At Man Bac, the high prevalence of scurvy from perinates to old adults demonstrates that some level of Vitamin C deficiency or insufficiency was pervasive throughout the entire population presenting a considerable burden of stress, which would have been a significant factor impacting adaptive plasticity. These findings suggest that those who survived to older age without signs of scurvy were likely exposed to some level of nutritional stress throughout their lifetime particularly in early life, rather than have skirted the nutritional stress entirely. The overall disease burden observed at Man Bac inclusive of malaria, treponemal disease, general dietary stress, genetic anemia, and parasitosis further supports most individuals in this community faced a stressful environment in early life (Oxenham & Domett, 2011; Vlok et al., 2021; Vlok & Buckley, 2022). Adaptive plasticity to stressful environments may then have been a key factor in survival to older age. When considering the relationship between general stress response and bone formation, the role of cortisol as an anti-inflammatory hormone is important as it inhibits SPNB response related to inflammation of the periosteum (Klaus, 2014). The hypothalamic–pituitary–adrenal axis (HPA), responsible for the production of cortisol in the short-term boosts immune system function and increases metabolic rate, important in times of nutritional stress and infection (Temple, 2019). A HPA axis adapted to a stressful environment may contribute to better survival, and a reduction of bone response to scurvy. However, as Klaus (2014) notes, the relationship between stressors, HPA response, and bone formation is not akin to an "on/off" switch, with a great variation in degree of biological impact. This factor is also particularly important when considering the development of lesions in subclinical scurvy where both stress and Vitamin C restriction may not be acute and only partially impact the deposit of osteoid at hematoma sites, increasing the likelihood that pathology is visible on the surface of the bone. From a physiological standpoint, this counters assumptions that have been made in the past (including by us) that lesions from scurvy only develop in the process of recovery as Vitamin C levels increase (Snoddy et al., 2017; Vlok, Oxenham, et al., 2023).

4.3 | Comparing the Brickley and Morgan (2023) and Snoddy et al. (2018) approaches

The similar outcomes regardless of using the Snoddy et al. (2018) compared with the Brickley and Morgan (2023) approach, should provide some level of ease to researchers, that either approach has value. It is perhaps necessary to apply both approaches at this current stage with diagnosis of adult scurvy as this area of research is still in its early stages of development. As previously mentioned, both approaches have their merits and their limitations, seemingly covering the limitations of the other. Nevertheless, as mentioned by Vlok (2023) and Brickley and Morgan (2023) any diagnostic approach should consider the biological and anatomical basis for lesion development. An accompanying differential diagnosis allows for this. In addition, ongoing discussion regarding which diagnostic terms to use is required. While the Brickley and Morgan (2023) approach applies terminology first adapted by Appleby et al. (2015) and already widely used within the paleopathological community, the probable/possible terminology by Vlok (2023) is one that is more recognizable beyond our discipline, and aligned with the terms used by public health bodies, such as the World Health Organization, which in turn apply terms that are readily understood by the public. Consideration of which terms are the most valuable should reflect aspects of diagnostic accuracy and the larger goals of our discipline going forward.

5 | CONCLUSION

Our research identified that a high prevalence of scurvy in the Neolithic assemblage of Man Bac (35% in adults and 80% in nonadults) was associated with decreased survivorship to adulthood, and when adulthood was achieved, decreased survivorship to old age. These findings together indicate that for the individuals who suffered from malnutrition during the early agricultural period of Vietnam, the impacts on individuals and the community as a whole were severe. The inhabitants of Man Bac, while they lived in a tropical environment with the capabilities to provide adequate Vitamin C were the victims of change. The combination of the 4.2 kya drying event, interaction between two groups with different subsistence patterns, the abundance of infectious diseases, the increasing proportion of their diet focused on rice, and a high fertility rate adding population pressure provided a unique set of challenging conditions within which the Man Bac community lived and died.

AUTHOR CONTRIBUTIONS

Melandri Vlok: Conceptualization (lead); data curation (lead); formal analysis (lead); funding acquisition (lead); investigation (lead); methodology (lead); project administration (equal); writing – original draft (lead); writing – review and editing (lead). **Marc Oxenham:** Data curation (supporting); funding acquisition (equal); investigation (supporting); project administration (equal); resources (equal); supervision (equal); writing – original draft (supporting); writing – review and editing (supporting). **Kate Domett:** Data curation (supporting); methodology (supporting); project administration (supporting); resources (supporting); writing – original draft (supporting); writing – review and editing (supporting). **Hiep Hoang Trinh:** Project administration (supporting); resources (supporting); writing – original draft (supporting); writing – review and editing (supporting). **Tran Thi Minh:** Data curation (supporting); formal analysis (supporting); investigation (supporting); writing – original draft (supporting); writing – review and editing (supporting). **Mai Huong Nguyen:** Project administration (supporting); resources (supporting); writing – original draft (supporting); writing – review and editing (supporting). **Hirofumi Matsumura:** Funding acquisition (supporting); project administration (supporting); resources (supporting); writing – original draft (supporting); writing – review and editing (supporting). **Hallie Buckley:** Conceptualization (supporting); data curation (supporting); formal analysis (supporting); investigation (supporting); methodology (supporting); project administration (supporting); resources (supporting); supervision (lead); writing – original draft (supporting); writing – review and editing (supporting).

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DATA AVAILABILITY STATEMENT

Data is provided as a supplementary file.

PERMISSIONS STATEMENT

Permission for analysis and publication of images of human skeletal remains were provided by the Institute of Archaeology, Hanoi, Vietnam in 2018.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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