Review

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*Review*

# Ancient Pathogen Genomics in Africa - Current Evidence and Future Directions

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**Abstract**

Ancient pathogen genomics has redefined how infectious disease histories are reconstructed, revealing unexpected origins, transmission routes and lineage turnovers that are invisible from modern genomes alone. Yet this perspective remains heavily biased toward Eurasia and the Americas, leaving Africa, central to human evolution, biodiversity and zoonotic emergence, largely unexplored. In this review, we assess the current state of ancient pathogen research in Africa and synthesize insights from bacterial, parasitic and viral perspectives. We identify Africa as a pivotal frontier for the field and outline strategic priorities to move from isolated detections toward continent-scale reconstructions of past disease landscapes, with direct relevance for understanding present-day and future epidemic risk.

**Keywords:** paleogenomics; Africa; aDNA; pathogens; evolution

## Africa as a Frontier for Ancient Pathogen Genomics

As the continent where *Homo sapiens* evolved, Africa encompasses a wide range of environments and lifeways, including hunter-gatherers, herders, farmers and urban populations, offering an exceptional setting to examine how disease pressures have shaped mobility, health and adaptation over time [1]. Africa's ecological, climatic and socioeconomic conditions - including high biodiversity, humid environments, frequent human–animal contact and dense populations — make it a critical hotspot for emerging infectious diseases. In the first decades of this century, outbreaks of influenza A, Dengue, Ebola, Mpox and SARS-CoV-2 have caused major epidemics and pandemics, affecting millions of people and disrupting social and economic systems worldwide. Against the longer continuum of epidemic history, Africa is especially important, since rapid ecological change and shifting climate are expanding vector ranges and increasing opportunities for zoonotic spillover. Pathogens are dynamic evolutionary entities shaped by the same environmental and social transformations as their hosts. Holocene lifestyle transitions triggered an epidemiological shift, with closer contact to domesticated animals, as intensified human–animal contact, rising population

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densities and increased sedentism promoted both zoonotic and sustained human-to-human infection [2,3]. Over 60 % of emerging infectious diseases have zoonotic origins, and many pathogens still persist primarily as zoonoses [4,5]. Yet direct genomic evidence for how these processes unfolded in Africa remains limited.

Ancient pathogen genomics offers a direct means to investigate past disease dynamics by detecting pathogen DNA in metagenomes recovered from bone, teeth, and associated microbiota [2,6–10]. Advances in laboratory protocols and bioinformatic pipelines now allow robust identification and authentication of bacterial, viral and eukaryotic pathogens, including diseases that leave no skeletal lesions and predate written records [11,12] (Figure 1).

Despite Africa's central role in human evolution, biodiversity and pathogen emergence, ancient pathogen genomics on the continent remains in its infancy. Systematic ancient DNA (aDNA) studies in Africa are therefore crucial to reconstruct past disease burdens, clarify how infections shaped population history and provide an evolutionary framework for anticipating future threats. In this review, we draw on well-sampled studies from Eurasia and the Americas to provide a comparative basis and synthesize how ancient genomics has reshaped our knowledge of infectious microbes, with a particular focus on African ancient pathogens and future research priorities for the continent.

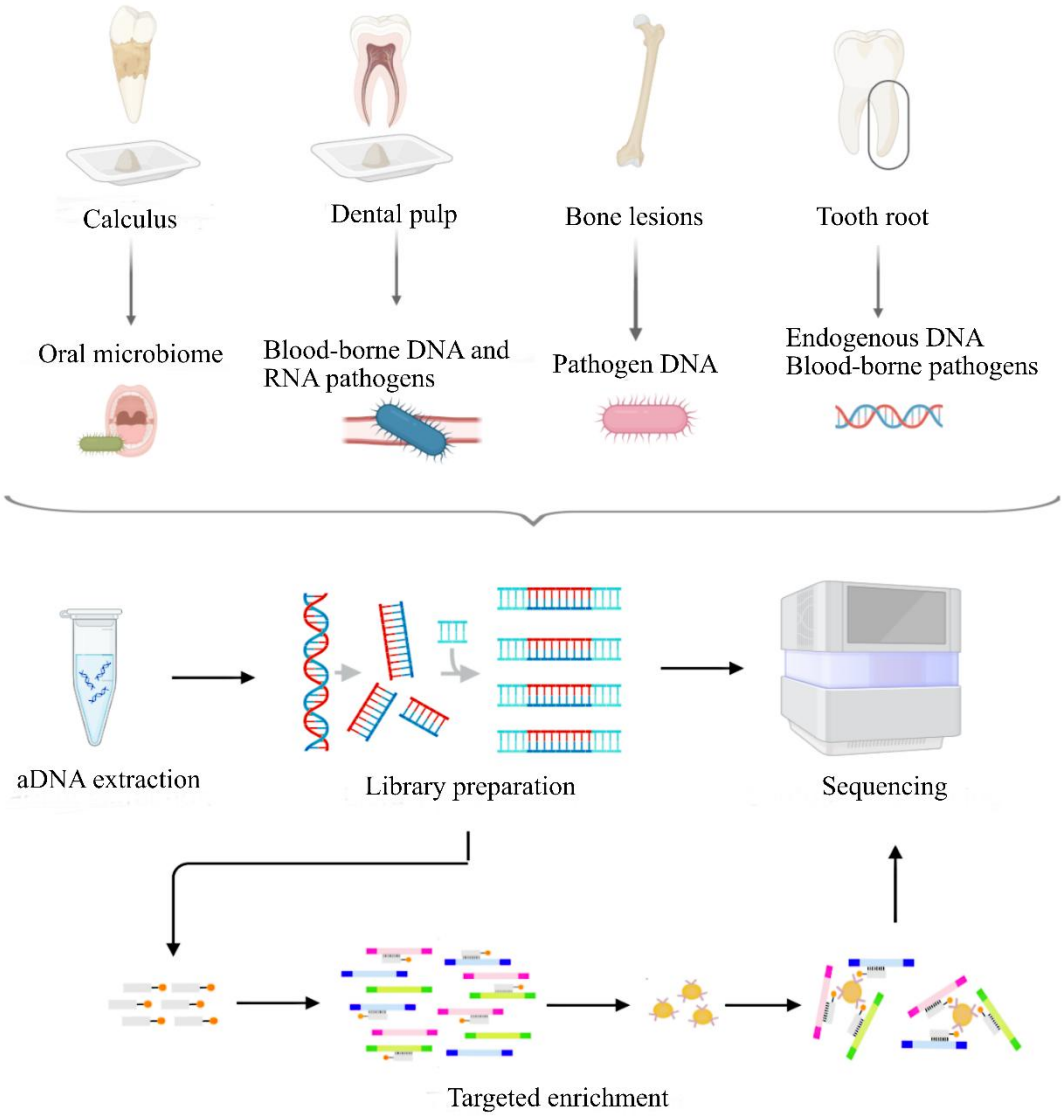


**Figure 1.** Sources and workflows for ancient pathogen genomics. Ancient pathogens can be detected from multiple biological substrates, including dental calculus, dental pulp, skeletal lesions and tooth roots. Following ancient DNA extraction, libraries are prepared for shotgun sequencing or targeted enrichment to increase

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pathogen recovery. Downstream bioinformatic analyses enable identification, authentication and genomic reconstruction of bacterial, viral and eukaryotic pathogens from archaeological remains.

## Ancient Pathogens - Revising Origins, Hosts and Spread

In Europe, ancient DNA studies have recovered genomes of *Mycobacterium tuberculosis* [13], *Yersinia pestis* [14], and viruses such as hepatitis B [15,16] and Herpes simplex virus 1 (HSV-1) [17], as well as protozoans including *Plasmodium falciparum* and *P. vivax* [18,19]. Similar research on human remains from the Americas [20–22] and Asia [23,24] has further expanded the ancient pathogen record. Together, these studies provide the clearest evidence that directly dated pathogen genomes can revise models of origin, transmission and dispersal that were previously inferred from modern genomes alone.

For *Y. pestis*, aDNA has shown that the same species caused the First plague pandemic, the Black Death and the third pandemic [25], and that the bacterium was already infecting humans over 5,000 years ago in Neolithic and Bronze Age Eurasia [26–28]. These early strains occupy basal positions in the *Y. pestis* phylogeny and lack key flea-associated virulence factors, indicating that efficient flea-borne transmission and high virulence evolved gradually over time [26,27]. In line with this early biology, the Late Neolithic Bronze Age (LNBA) *Y. pestis* has been identified at multiple sites across northern Europe, pointing to a broad geographic distribution [26,29]. This widespread presence occurred despite the absence of genomic features typically associated with classical flea-borne transmission. In Sweden, for example, *Y. pestis* was detected in 17% of individuals from Neolithic collective burials, a prevalence that is compatible with frequent human exposure during this period given the stringent detection limits of ancient pathogen analyses [27]. Genomic analyses have shown that *Y. pestis* strains responsible for the First plague pandemic formed a distinct, now-extinct or unsampled lineage, phylogenetically separate from later pandemic strains [30]. In contrast, dense sampling showed that the Black Death strains are highly clonal and derive from a lineage dated to 1338–1339 CE in the Tian Shan region [31,32], supporting a single introduction into Europe followed by centuries of local circulation and recurrent outbreaks. aDNA studies also contributed to shifts in understanding for the Mycobacterium tuberculosis complex (MTBC). Modern genomes-only analyses proposed that the MTBC emerged ~70,000 years ago, linked to human migrations out of Africa and inferred from parallels with human mitochondrial phylogenies [41]. In contrast, studies using ancient genomes as direct calibration points consistently produce much younger most recent common ancestor (MRCA) dates, generally under 6,000 years, supporting a Holocene origin and dispersal [22,35] (Box 1). Phylogenetic analyses of MTBC genomes from pre-colonial South American mummies did not fall within the main human-adapted lineages that dominate post-contact epidemics. Instead, they clustered with *Mycobacterium pinnipedii*, which today primarily infects seals and sea lions [22,33]. Bayesian dating placed the time to the most recent common ancestor (tMRCA) of the MTBC complex at ~2.8–5.8 kya and estimated that the South American *M. pinnipedii* cluster diverged from its closest relatives about 1,000 years ago, consistent with the radiocarbon ages [22]. These findings support seal-to-human transmission along the South American coast and show that an animal-derived tuberculosis lineage infected humans in the Americas before 1492 CE [22], contradicting the idea that tuberculosis in the New World derives solely from post-contact European introductions.

For malaria, *P. falciparum* and *P. vivax* account for most global disease burden today [36], with the WHO African Region carrying the vast majority of cases and deaths (https://www.afro.who.int/health-topics/malaria). *P. falciparum* appears to have arisen via a zoonotic spillover from gorillas in sub-Saharan Africa [37], with tMRCA estimates for extant strains ranging from <10,000 to ~450,000 years ago [38,39]. *P. vivax* is generally considered older [38]. While early mitochondrial and nuclear analyses supported a Southeast Asian origin based on clustering with macaque parasites [40,41], more recent studies identify African great-ape parasites (*P. carteri* and *P. vivax*-like) as its closest relatives [39,42]. This challenges a simple Asian-origin model. The high frequency of Duffy negativity in sub-Saharan Africa further suggests long-standing selective pressure

 doi:10.20944/preprints202603.0108.v1



from *P. vivax* and divergence estimates indicate separation from macaque parasites earlier than expected under a recent Asian origin [39]. Ancient data further indicate close relatedness of European and American *P. vivax* strains around the contact period, supporting introduction by European colonizers [38], whereas present-day American *P. falciparum* clusters with modern African lineages, consistent with dispersal via the trans-Atlantic slave trade.

Recovering viral genomes from ancient materials is more challenging because viral DNA and RNA are typically low in abundance and highly degraded [7]. Nevertheless, recent successes have transformed the field.

The sequencing of hepatitis B virus (HBV) from human remains spanning 400 to 10,500 years ago revealed lineages persisting in humans for over 11,000 years [16]. HBV circulated widely across western Eurasian hunter-gatherers (around ~10 kya), before the onset of agriculture and animal husbandry. Early Holocene genomes (~11–7.5 kya BP) fall into two Mesolithic clades [16]. Following the Neolithic transition, these HBV lineages were replaced by the Western Eurasian Neolithic–to–Bronze Age (WENBA) lineage, which spread with early European farmers from Anatolia and persisted for >4,000 years [16]. A second major turnover occurred at the end of the Bronze Age, when WENBA diversity collapsed and was superseded by the modern genotypes, indicating at least two major HBV lineage turnovers in known viral evolution [16]. A Bronze Age HBV genome from eastern Europe ancestral to modern African sequences suggests genotype A originated in western Eurasia and entered Africa, where it diversified by the end of the second millennium BCE [16,43]. Today, genotype A is highly diverse in Africa, and modern phylogenetic analyses link subgenotype A1 and A4 to introductions into the Americas during the transatlantic slave trade, with documented presence in Venezuela, Mexico, Haiti, Martinique and Colombia [44–47].

Ancient Herpes simplex virus type 1 (HSV-1) genomes recovered from four individuals across Northern Europe, dated to the past 2,000 years, provide the first direct time-stamped sequences of this virus [17]. These genomes place the tMRCA of circulating HSV-1 strains at ~4,000 years ago, implying a major lineage replacement, broadly coincident with the late Neolithic and Bronze Age migrations [17]. These findings conflict with earlier out-of-Africa scenarios inferred solely from modern sequences [48] and highlights the need for broader ancient sampling, particularly in Africa [17].

Across bacteria, protozoa and DNA viruses, these studies show how ancient genomic data can overturn long-standing models based on modern sequences alone, by refining MRCA estimates, revealing unexpected animal reservoirs, documenting repeated lineage turnovers and constraining the timing and routes of global dispersal. This basis is directly relevant for Africa, where equivalent ancient datasets are still scarce but have the potential to similarly reshape narratives of pathogen origins and spread on the continent and out of it.

Box 1. Timescale dependent rates and the interpretation of pathogen evolution

Estimating evolutionary rates and divergence times from genetic data requires temporal calibration. For most microbial pathogens, datasets are dominated by contemporary isolates, so molecular-clock analyses typically rely on tip dating using sequences sampled at known times. For rapidly evolving RNA viruses, sequences collected over only a few decades can provide sufficient temporal signal[49]. By contrast, for more slowly evolving pathogens, especially bacteria and DNA viruses, modern genomes often exhibit too little accumulated genetic change over the available sampling interval to support reliable inference [50,51].

Ancient genomes extend molecular-clock calibration beyond contemporary sampling by capturing pathogen genetic diversity from centuries to millennia in the past. For viruses, endogenous viral elements (EVEs) provide additional, independent calibration points on geological timescales [52,53]. Extending calibration across these longer timescales reveals a consistent pattern, the time-dependent rate phenomenon (TDRP), in which evolutionary rates estimated over short intervals are systematically higher than those inferred over longer timescales [54].

Time dependence of evolutionary rates has long been recognized in evolutionary biology, but its consequences are particularly pronounced for rapidly evolving pathogens [51,55,56]. When

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timescales are inferred primarily from short-term sampling, pathogen diversity accumulated over deep evolutionary time may be misinterpreted as having arisen much more recently, distorting inferences about the processes driving diversification. For example, ancient lineage divergence may be incorrectly attributed to recent ecological change, host population dynamics, or historical events, rather than to long-term evolutionary processes.

Long-term genomic records, such as ancient pathogen genomes and EVEs, expand the temporal window over which evolutionary rates can be evaluated, revealing the scale dependence of pathogen evolution and placing bounds on the extent to which short-term rate estimates can be extrapolated across deeper timescales. This perspective supports the development and empirical calibration of models that accommodate time-dependent rates, and clarifies both the possibilities and the limits of molecular-clock inference across pathogens [57,58] (Figure 2).

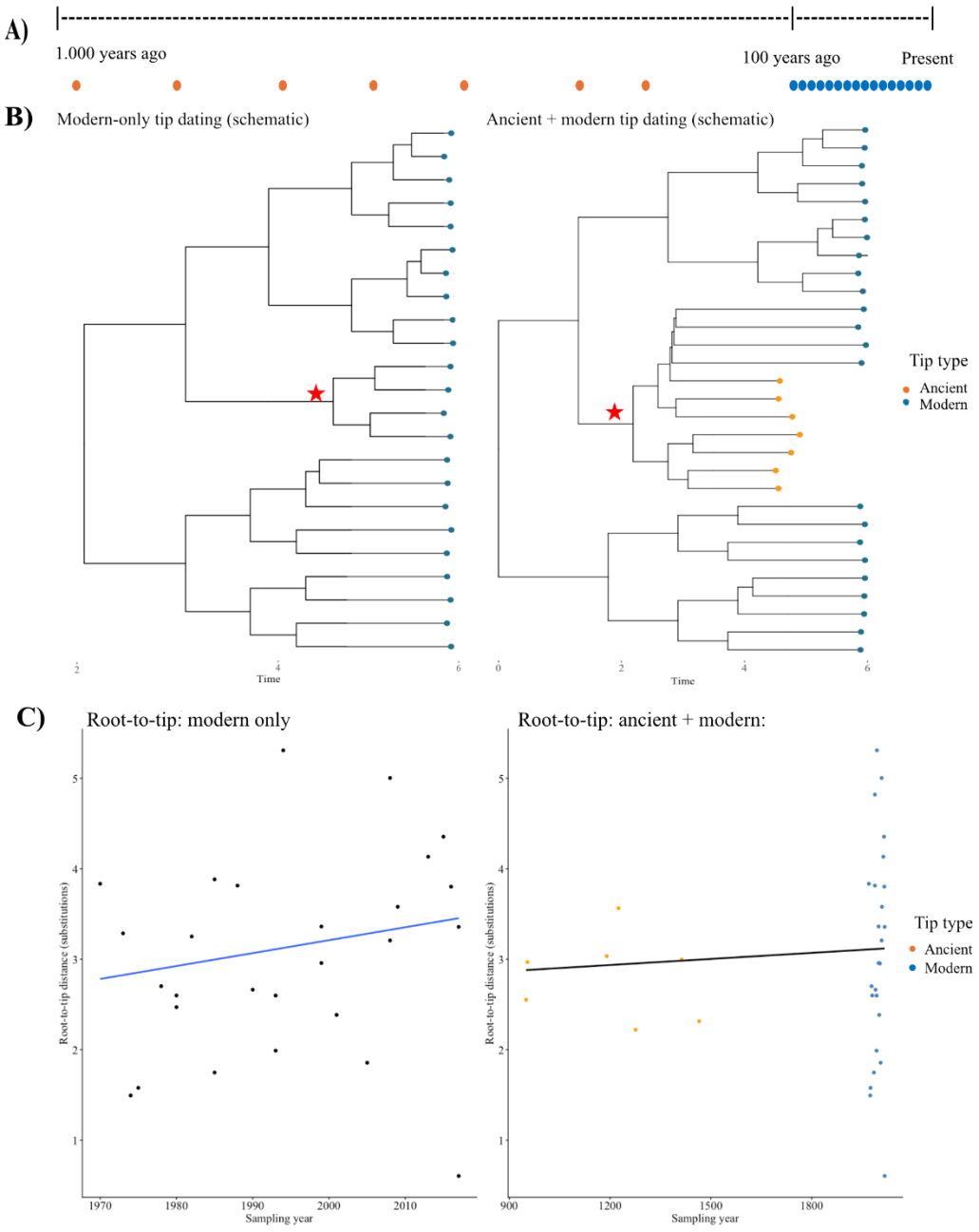


**Figure 2.** Ancient genomes provide temporal leverage for molecular clock calibration. (A) Conceptual schematic of sampling times. (B) Time-scaled phylogenies inferred using modern samples only (left) or combined ancient and modern samples (right). When only modern genomes are included, tips are clustered within a narrow

 doi:10.20944/preprints202603.0108.v1



temporal window, resulting in shallow trees and clock estimates dominated by short-term substitution dynamics. Incorporation of ancient genomes extends the phylogeny deeper in time and anchors internal nodes to absolute dates (red star), improving estimation of long-term evolutionary rates and divergence times. (C) Root-to-tip genetic distance plotted against sampling time. Modern-only data show limited temporal structure, whereas inclusion of ancient genomes broadens the timescale, strengthens temporal signal, and enables more reliable rate estimation.

## Recovering Ancient RNA Viruses - Challenges and Promise

Despite the success of ancient DNA virus retrieval, no authenticated RNA virus has yet been recovered from archaeological human remains. RNA viruses nevertheless include some of the most important human pathogens, responsible for diseases such as Ebola, Dengue, influenza and Lassa fever, with case-fatality rates that can be high in some outbreaks. If preserved in ancient specimens, viral RNA could illuminate long-term viral evolution, zoonotic emergence and host–pathogen interactions. RNA was long assumed too unstable for deep-time recovery because of its short cellular half-life and susceptibility to hydrolysis, which limited efforts to study ancient RNA. However, recent work has overturned this view, demonstrating that RNA can persist over extended periods. RNA has been recovered from ancient and non-human contexts, including a ~750-year-old ssRNA virus from barley and a ~1,000-year-old dsRNA virus from maize, alongside preserved host mRNA and miRNA from museum specimens and Late Pleistocene canids and historical wolf skins (14 kya) [59–63]. In the Tasmanian tiger sample, picorna-like RNA virus fragments of uncertain origin were detected [59]. A recent preprint reported near-complete viral RNA genomes from a 1908 *Drosophila melanogaster* specimen and suggested that ribonucleoprotein complexes may help stabilize RNA over time [64]. Most remarkably, Mármol-Sánchez et al. recovered transcriptional profiles from Pleistocene woolly mammoths, including a specimen dated to ~39,000 years ago, extending this proof of principle into deep prehistory [65]. Collectively, these results demonstrate RNA's potential longevity and establish ancient specimens as valuable archives for studying ancient RNA and, potentially, RNA viruses. Human historical specimens further demonstrate the value of RNA recovery for reconstructing origins and timescales. Analysis of influenza virus genomes from the 1918–1920 pandemic, amplified from formalin-fixed paraffin-embedded (FFPE) tissue, revealed an avian origin with specific mammalian host adaptations [66]. Similarly, a 1912 measles morbillivirus (MeV) genome from FFPE tissue is the oldest RNA genome of a human virus to date [67]. It showed that MeV and rinderpest diverged roughly 2,500 years ago after a cattle-to-human spillover, and it anchored the MeV MRCA estimate to around 528 BCE [67].

Together, these advances indicate that if archaeological human RNA virus recovery becomes feasible, it could substantially refine models of zoonotic origin, lineage replacement and epidemic emergence. In Africa, however, this goal faces additional hurdles: high ambient temperatures, fluctuating humidity and acidic or microbially active soils often reduce biomolecular preservation, making RNA survival even less likely. Success will likely depend on carefully targeted contexts with exceptional preservation potential and protocols optimized for ultra-short, highly degraded RNA fragments.

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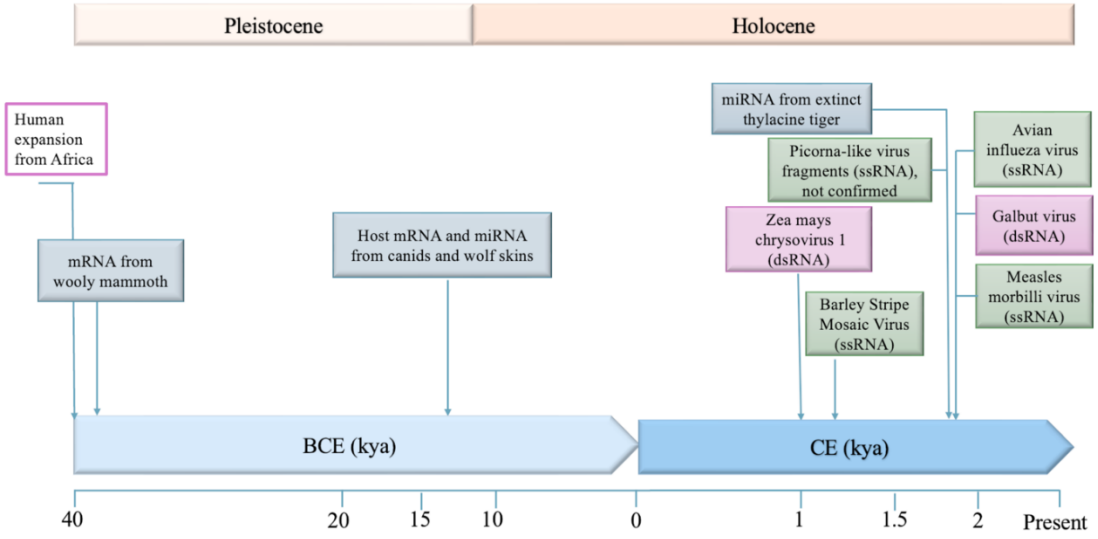


**Figure 3.** Timeline of ancient RNA and RNA virus recoveries. Schematic overview of reported ancient RNA virus detections from the late Pleistocene to the present.

## Ancient Pathogen Genomics in Africa - Current Limitations and Insights into Disease Landscape

In Africa, ancient pathogen research remains scarce, and no systematic survey of sub-Saharan contexts exists, with most research efforts concentrated on Egyptian mummies [68]. Many large African aDNA studies to date have relied on sequence capture techniques targeting only human DNA, which does not yield metagenomes for pathogen screening [69,70].

Ancient Egyptian remains nonetheless reveal a diverse infectious disease burden (Table 1). Molecular studies have repeatedly detected human-adapted MTBC DNA in Egyptian mummies, but to date no high-quality complete MTBC genome has been reported from this context [71–73]. The 2,200-year-old *Mycobacterium leprae* genome from Egypt is currently the earliest recovered and phylogenetically placed leprosy genome, clustering with present-day West African and Brazilian strains [43]. Including this genome in dated phylogenies shifts the inferred tMRCA to roughly 2.6–4.5 kya and the global *M. leprae* tMRCA to about 5.8 kya. This extends previous estimates by ~1.3 kyr and indicates that leprosy was established in North Africa by the late Iron Age. The ~2,000-year-old HBV genome recovered from Egyptian mummies falls within genotype A, between subclades A1 (Asia) and A3 (Africa), with a short branch length compatible with its ancient status [43]. Parasitic infections are likewise well represented among findings from Egypt. *Plasmodium falciparum* has been detected by PCR and NGS [73–75], while *Toxoplasma gondii* was detected in embalmed heads, plausibly linked to close human–cat contact [75]. This finding should be interpreted with caution, since an earlier study showed that the *T. gondii* reference genome is contaminated with human DNA [76], underscoring the importance of careful database selection prior to classification. *Schistosoma mansoni* and *S. haematobium were identified* in a canopic-jar liver from the Middle Kingdom and pointed to intestinal and urinary schistosomiasis [77]. *Leishmania donovani* appeared in Egyptian and Nubian material, with higher prevalence in Nubia [78]. Collectively, these data indicate a complex landscape of chronic bacterial, viral and parasitic infections.

Beyond Egypt, only one study has directly investigated metagenomes in sub-Saharan Africa: a 2,000-year-old hunter-gatherer child from Ballito Bay in South Africa [10]. The analysis recovered *Rickettsia felis*, a flea-borne pathogen that causes a typhus-like disease. A high-quality ancient *R. felis* genome was reconstructed with 11× mean coverage from petrous bone, suggesting that in severe infection in children, the petrous bone can potentially harbor sufficient pathogen DNA for genome reconstruction. Consistent with this, pathogen DNA has also been recovered from the petrous bone

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in other contexts, including *Treponema pallidum* in a human infant and *Brucella melitensis* in an adult sheep [79,80]. Skeletal evidence suggested that *R. felis* infection may have contributed to the child's poor health and early death, estimated at about seven years old [10]. These findings demonstrate that *R. felis* was already present at least 2,000 years ago among Later Stone Age hunter-gatherers who did not practice farming or herding [10]. This observation contradicts earlier assumptions that *R. felis* is a modern "emerging" pathogen associated with sedentism and animal domestication [81], instead suggesting persistence among mobile foragers.

**Table 1.** Overview of ancient pathogen detections in Africa.

| Pathogen (genome type) | Disease | Method | Sampling material | Location | Reference |
|---|---|---|---|---|---|
| Mycobacterium tuberculosis complex (dsDNA) | Tuberculosis | PCR | Mummified tissue/bones | Egypt | [71–73] |
| *Mycobacterium leprae* (dsDNA) | Leprae | NGS | Mummified tissue/bones | Egypt | [43] |
| HBV (partially dsDNA) | Hepatitis B | NGS | Mummified tissue/bones | Egypt | [43] |
| *Plasmodium falciparum* (dsDNA) | Malaria | PCR and NGS | Mummified tissue/bones | Egypt | [73–75] |
| *Toxoplasma gondii* (dsDNA) | Toxoplasmosis | PCR | Embalmed heads | Egypt | [75] |
| *Schistosoma mansoni* / *S. haematobium* (dsDNA) | Schistosomiasis | PCR | Canopic liver | Egypt | [77] |
| *Leishmania donovani* (dsDNA) | Leishmaniasis | PCR | Mummified tissue/bones | Egypt | [78] |
| *Rickettsia felis (dsDNA)* | Rickettsiosis | NGS | Petrous bone | South Africa | [10] |

## Future aDNA Research Perspectives on Africa's Disease History

Africa is poised to be a major frontier for ancient pathogen genomics, but progress will depend on framing testable questions that match the realities of preservation and sampling. A useful organizing principle is to treat Africa as both a point of comparison that helps test models built from Eurasian and American data and as a continent with its own endemic and zoonotic histories that require African ancient genomes to be understood. The priorities below emphasize pathogens with plausible preservation routes in teeth, bone, calculus and contextual sediments, and they highlight cases where ancient genomes could directly test competing models of origin, transmission mode and long-term persistence.

Written sources claimed that the plague of Justinian began in Ethiopia, and intensified military, diplomatic and economic ties between this region and the Byzantine Empire in the early sixth century likely provided an effective pathway for its spread into Europe [82]. Although the issue cannot be definitively resolved, an African origin for the plague of Justinian remains a plausible and arguably the most probable scenario [82]. This long view aligns with the present: Africa continues to carry a major share of the global plague burden, with Madagascar as a persistent hotspot. Understanding why plague persists there offers a testable model for long-term reservoir–vector–human dynamics. The key components (black rats and competent fleas) are widespread across Africa, but Madagascar appears to sustain particularly efficient transmission cycles shaped by highlands ecology, synanthropic mammal communities, household-level exposure and vector performance, together enabling self-sustaining persistence after introduction during the third pandemic [83,84].

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Beyond plague, Africa bears a high burden of bacterial and parasitic diseases including tuberculosis, cholera, malaria and schistosomiasis. Climate-driven shifts in vector ranges and habitats are likely to increase the broader relevance of several Africa-linked infections, reinforcing the need for deep-time baselines. These baselines are valuable not only for reconstructing past burdens but also for clarifying when key transmission systems became established, how often spillover events occurred and whether current endemic patterns reflect recent introductions or long-standing local persistence.

Future work should prioritize pathogens with realistic aDNA recovery potential. The Mycobacterium tuberculosis complex is a central target, given Africa's high modern burden and the distinctive presence of lineages 5 and 6 (*M. africanum*) in West Africa. Ancient genomes could test lineage emergence and replacement, refine divergence histories of African clades and clarify how local transmission systems evolved. Despite younger MRCA estimates from ancient calibration, the MTBC ancestor is still often inferred to have originated in Africa, followed by expansion and global dispersal via human movements [3,35]. An African MTBC genome substantially older than the currently available ancient calibrations would be particularly informative, helping to test the proposed African origin and to evaluate how tightly Holocene MRCA estimates bound deeper lineage history. *Salmonella enterica* is another high-value target: long historical records of enteric fever and a bloodstream phase increase the plausibility of recovery from teeth, enabling tests of introduction timing, lineage turnover and the deep history of antimicrobial resistance. For cholera and related gastrointestinal pathogens, direct detection in skeletal tissues is less reliable, thus targeted screening of burial-adjacent sediments and latrine-associated contexts may provide a more productive route.

Flea-borne bacteria also warrant systematic inclusion. *Rickettsia felis* has already been recovered from a ~2,000-year-old child in South Africa, and modern studies report widespread detection in humans, fleas and animal reservoirs across the continent, including asymptomatic infections [85,86]. This ecology makes *R. felis* a strong candidate for routine screening in African aDNA datasets, using curated reference panels and stringent authentication. A broader time series could determine whether *R. felis* persistence predates major Holocene shifts in settlement, livestock ecology and urbanization.

Parasitic pathogens should be integrated into the same approach, with *Plasmodium falciparum* as the key priority given its major contribution to Africa's disease burden. *Leishmania donovani* is feasible based on prior positives in North/Northeast Africa and remains a major cause of visceral leishmaniasis in East Africa today. *Trypanosoma brucei represents a historically important disease system whose ancient genomic record could contextualize modern low-level persistence and illuminate how vector ecology, human mobility and cattle farming have shaped regional transmission intensity over time.* Yet there is still little direct genomic evidence for how past African populations were affected by infectious diseases, how outbreaks unfolded before written records, or how hosts adapted over time. This gap is partly methodological: well-preserved human skeletons remain unevenly distributed across the continent due to heat, humidity and mortuary practices. Nonetheless, the growing body of African aDNA studies, including sub-Saharan genomes dating back ~10,200 years [87], demonstrates that suitable material is available, and systematic metagenomic screening of these sequences now offers a realistic avenue to address this gap.

Taken together, these priorities outline a practical, hypothesis-driven roadmap for African ancient pathogen research. Although no authenticated RNA virus has yet been recovered from archaeological human remains, even partial success in Africa would open a new temporal window on fast-evolving pathogens and clarify when major zoonotic lineages emerged or shifted. Broad, standardized screening across teeth, calculus, bone and contextual sediments (Table 2), should move the field from isolated detections toward continent-scale reconstructions of endemicity, emergence and long-term host–pathogen coevolution.

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**Table 2.** Expected recoverability of ancient pathogen DNA by substrate and transmission route. Dots indicate relative likelihood of detecting pathogen DNA/RNA consistent with transmission route and tissue tropism. Ratings reflect biological plausibility and preservation constraints rather than methodological sensitivity. ●●● high likelihood; ●● moderate; ● low; ○ speculative.

| | Parasites | | | Bacteria | | | DNA viruses | | | RNA viruses | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Blood borne | Oral-fecal | Mucosal | Blood borne | Oral-fecal | Mucosal | Blood borne | Oral-fecal | Mucosal | Blood borne | Oral-fecal | Mucosal |
| **Teeth** | ●● | ○ | ● | ●●● | ● | ●● | ●● | ○ | ● | ○ | ○ | ○ |
| **Bone lesions** | ● | ○ | ○ | ●●● | ○ | ● | ● | ○ | ○ | ○ | ○ | ○ |
| **Dental calculus** | ● | ●●● | ●● | ●●● | ●●● | ●●● | ● | ● | ● | ○ | ○ | ○ |
| **Sediment (skeletal remains associated)** | ● | ● | ○ | ●● | ● | ● | ● | ● | ○ | ○ | ○ | ○ |

## Conclusion

Understanding Africa's deep pathogen history is essential for anticipating future outbreaks. Ancient DNA studies in Europe, Asia and the Americas have shown how DNA viruses, bacteria and parasites shaped health, mobility and demography, but Africa remains profoundly understudied. Systematic ancient pathogen research on African human and animal remains could uncover infections that affected past populations but are undocumented today, and clarify how disease influenced migration, community stability, and the rise or decline of complex societies. Epidemics have been proposed as contributors to demographic downturns and societal collapse in parts of Africa [88,89], yet direct genomic evidence is still scarce.

Ancient African pathogen genomes could refine divergence rates and timescales, reconstruct long-term changes in virulence and transmission, and clarify the timing and ecological contexts of emergence, spread and persistence (Figure 4) (see Outstanding questions box). Combined with information on host identity and sampling location, phylogenetic analyses can also reveal past routes of disease dispersal and shifts in transmission dynamics. These insights will sharpen regional risk assessments, inform vaccine, antibiotic and antiviral development, and clarify historic spillover pathways at the wildlife–human interface, strengthening One Health strategies aimed at preventing future zoonotic pandemics.

With expanding archaeological access, rapidly improving biomolecular methods and growing interest in Africa's disease history, the coming years are likely to transform our understanding of ancient pathogens on the continent and their long-term impacts on African populations.

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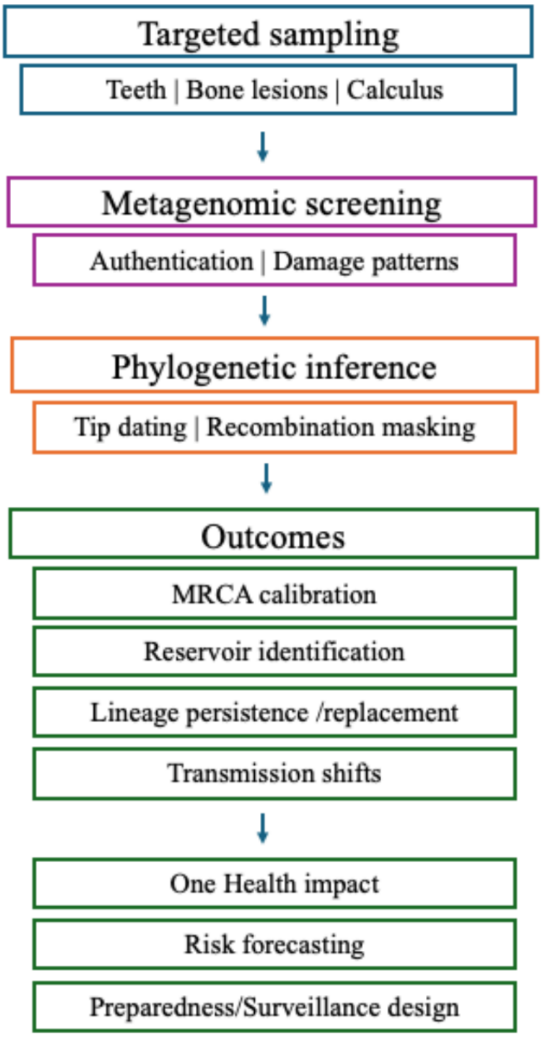


**Figure 4.** From ancient pathogen discovery to public health insight. Conceptual framework outlining how targeted sampling, metagenomic screening and phylogenetic inference in ancient pathogen genomics can inform evolutionary timescales, reservoir dynamics and transmission shifts, with downstream relevance for One Health risk forecasting and surveillance design.

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**Declaration of interests:** The authors declare no competing interests.

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