ONE PALEOPATHOLOGY: A DEEP-TIME FRAMEWORK FOR PREDICTING MALARIA RESURGENCE IN THE CLIMATE CRISIS

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Introduction

Malaria, the deadliest vector-borne disease in human history,[1,2] is resurging under climate change—but its past holds the key to our future resilience. This Viewpoint argues that *One Paleopathology*, a novel interdisciplinary framework bridging deep-time bioarchaeology, paleoclimatology, and disease ecology,[3,4] promises unparalleled insights into malaria's climate-driven expansions and contractions. By reconstructing 10,000 years of human-malaria-environment interactions, this approach can identify patterns critical for predicting and mitigating enhanced transmission and epidemics in a warming world.

Malaria remains endemic to sub-Saharan Africa, South and Southeast Asia,[5] and parts of Arabia, Oceania, South America, and the Korean peninsula (Fig. 1),[6,7] despite its mid-20th century eradication in most temperate zones. Its enduring prevalence reflects biological, political, and social forces. Historically, malaria's distribution shifted with climate, demographic, and ecological changes, emerging in regions currently at low risk. Today, as global warming extends *Anopheles* habitats in temperate areas, policymakers urgently need evidence-based projections to prioritize interventions—a need One Paleopathology can address. Because climate does not act alone and human activities have shaped malaria's burden for millennia—consider anthropogenic landscape modification, from early agriculture and urbanization to modern deforestation and dam building—One Paleopathology is well-suited to making the past actionable, as it situates the human disease experience in environmental and human contexts. Critically, it as well addresses socioeconomic and political inequities that have compounded malaria's toll, causing it to disproportionately impact marginalized communities.

By analyzing long-term trends and integrating bioarchaeological evidence of malaria during periods of climate change, we can uncover critical insights into the interactions between climate, environment, and biosocial factors in human health across deep time—knowledge essential for designing effective interventions. One Paleopathology transcends traditional disciplinary silos by synthesizing skeletal and historical (written) evidence, paleogenomics, and paleoclimate and paleoenvironmental proxies into predictive models. For example, malaria's wide prevalence in regions of Roman-era Britain and Italy seem to concentrate around former wetlands and expanded arable and to correlate with warmer summer temperatures,[8–10] a pattern now repeating in Europe's recent autochthonous cases.[11] One Paleopathology uniquely deciphers such correlations while quantifying long-term feedback loops between land use, immunity, and vector ecology, making malaria's past relevant today. It can demonstrate how malaria pathogens have often played a role in shaping human-environment interactions, population dynamics, social structures, and conflict.[12] It can, to give another example, also reveal long historical precedent for the malaria burden that children under the age of five now suffer.[8,13] The World Health Organization estimates there were 263 million malaria cases in 83 endemic countries in 2023 (an

increase of 11 million cases from the previous year), and 597,000 deaths.[7] Most of the victims were in their earliest years of life. [7]

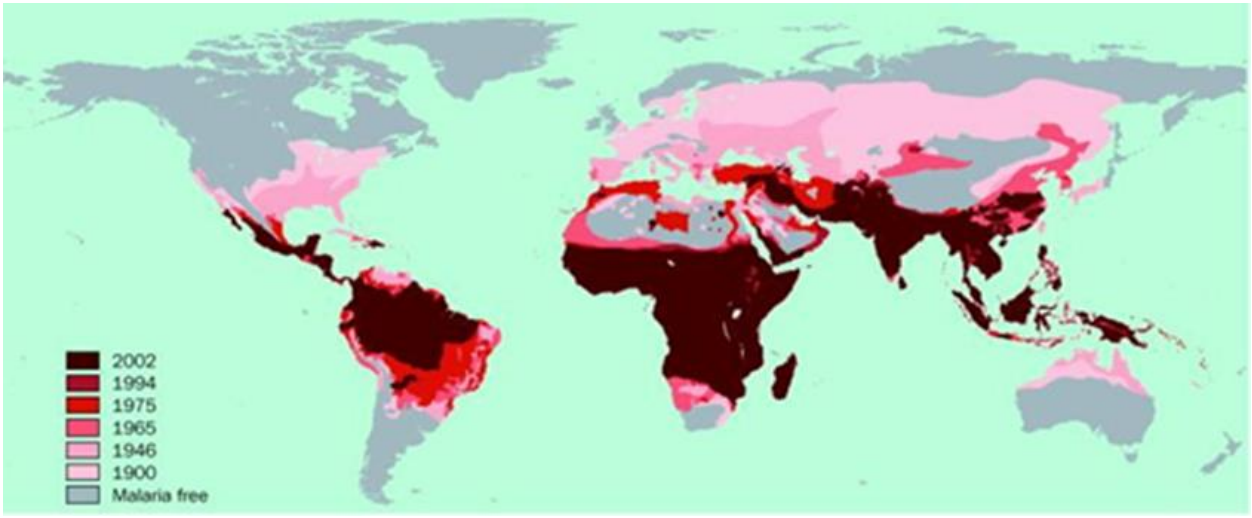

Fig. 1 *Malaria's global distribution prior to intervention.*[14]

Like other vector-borne diseases, malaria is predicted to resurge in the coming decades, with climate change altering vector habitats and its geographical range.[15–18] Intersecting anthropogenic factors further compound transmission risk: rapid urbanization and land use changes,[19] shifting public health priorities (exacerbated by COVID-19), human migration patterns,[20,21] and the destructive aspects of globalization.[22] Declines in global malaria funding intensify this threat—most notably with recent withdrawals of USAID support for mitigation programs. The consequences will be multi-systemic—overwhelming local health infrastructure, elevating morbidity and mortality rates, and triggering socio-economic ripple effects through disrupted migration, travel, and trade networks.[23]

Malaria demonstrates a long coevolution with humans and, crucially, can be reliably detected in past communities using combined bioarchaeological, paleogenomic, and historical evidence. There are numerous examples of human cultural adaptation to malaria under diverse and changing environmental, climatic, and social conditions. Historically, malaria has often declined when climate change intervenes (via cooling and aridity) and when humans employ integrated strategies for biocultural adaptation through wetlands management, housing design, and net provision, to name a few examples. For communities living under heightened or changing malaria risk, environmental variables are tightly linked with social and behavioral factors, such

as the effects of inequity, colonization, conflict, and displacement and their impact on population health over the long term.

We advance two key arguments for the One Paleopathology framework's value. First, the deep-time analysis of malaria can demonstrate how anthropogenic environmental modifications have shaped transmission dynamics across millennia. For example, historical irrigation systems (e.g., canals, aqueducts, drains), deforestation, and urban expansion created *Anopheles* breeding habitats in ancient Egypt, Mesopotamia, Anatolia, and the Greco-Roman world.[9,10,24] These patterns persist. Modern agricultural irrigation expands mosquito habitats, while wetland degradation creates ephemeral pools and reduces natural vector predators.[25] Poorly-planned urbanization maintains malaria risk through artificial water storage,[26] mirroring ancient Rome's urban malaria patterns shaped by seasonal and economic factors.[27]

Second, One Paleopathology informs modern risk modeling by establishing deep-time baselines. Using past disease outcomes—including ancient infant and child mortality rates and skeletal indicators of malaria or compromised health—as historical validation data, we can test predictive models against real epidemiological evidence.[28] This approach reveals how premodern environmental conditions interacted with human behavior, identity, lifeways, and social status to produce health outcomes in ways similar to modern experiences. By leveraging paleopathological insights about historical malaria transmission and environmental change and integrating them with modern climate science, researchers can predict evolving dynamics of malaria globally, including in areas where it has been eradicated.

Addressing the looming malaria crisis demands interdisciplinary collaboration. Disease ecologists, epidemiologists, climatologists, and social scientists are already uniting to address malaria's resurgence. One Paleopathology extends One Health and Planetary Health paradigms by integrating biocultural, evolutionary, and historical perspectives on humans-animals-pathogen-environment-climate relationships (Fig. 2).[3,4] Put differently, malaria's deep history can be viewed as a set of "completed experiments,"[29] from which we would do well to learn.

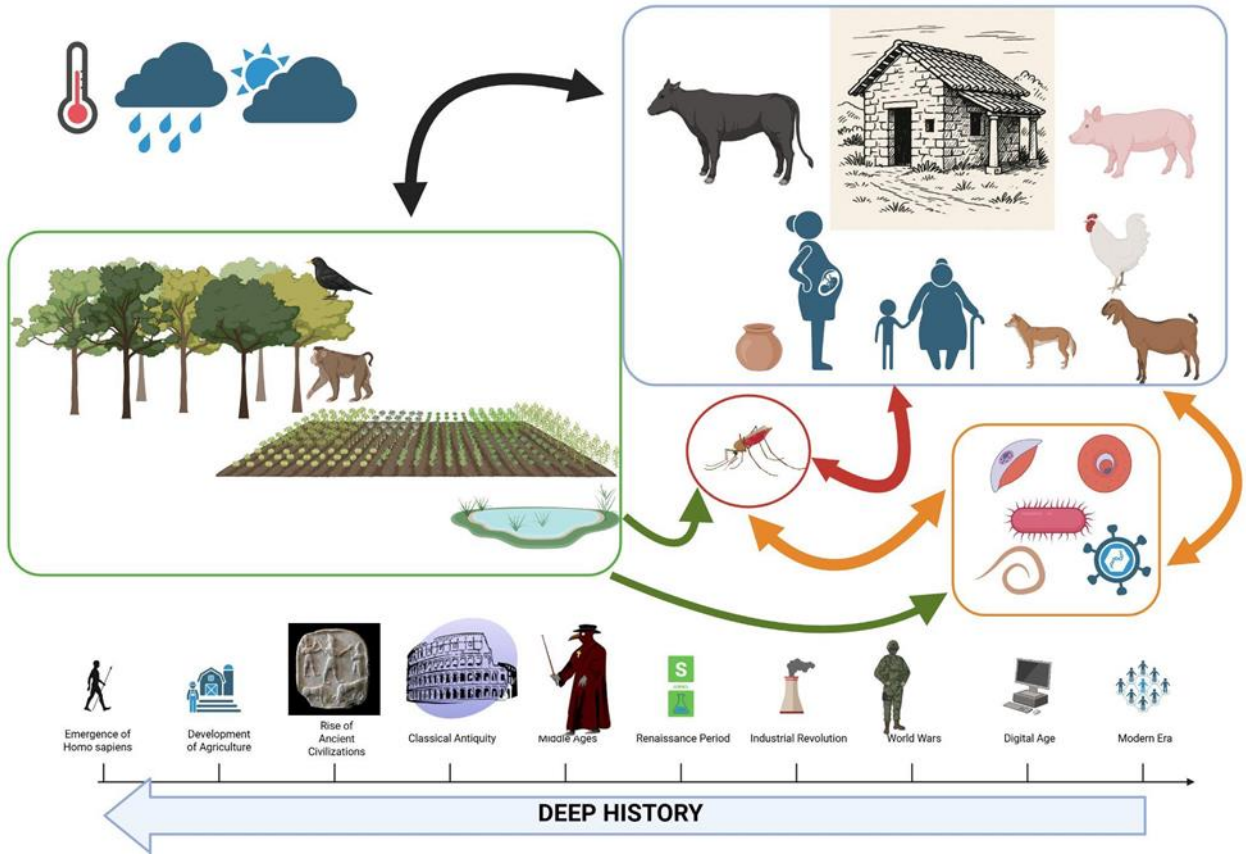

Fig. 2 One Paleopathology visualized: Human-Animal-Environment Relationships through Deep History

A deep-time perspective on malaria

The malaria parasite *P. falciparum* has influenced human health for over 10,000 years and *P. vivax* for perhaps 400,000.[30,31] Recent bioarchaeological studies from South Asia to the Americas,[32–34] including studies of past malaria,[35] demonstrate how paleoclimate changes affected agricultural viability and livestock health with cascading impacts on disease transmission and public health.

The evolution of the pathogen, and its host preference and vectors, is critical to understand to grasp zoonotic spillover potential, not to mention evolving transmission dynamics in already endemic areas and the emergence and occurrence of epidemics in areas once endemic and now at risk.[5] Paleogenomics tracks how malaria shaped selection pressures on human populations, leading to persistent sickle cell trait, thalassemia, and G6PD deficiency in endemic regions.[36] North Africa, Asia, and the Mediterranean are ideal breeding habitats for efficient *Anopheles* vectors. While agricultural expansion likely intensified malaria transmission historically,[37,38]

some protective mutations predate farming.[39] Shape-shifting internally and externally throughout history, malaria has adapted to environmental and societal changes.

Before mosquito transmission was identified in the late-19th century, multiple cultures recognized correlations between malaria's cyclical fevers and specific environmental and seasonal contexts. Early medieval European texts, for example, describe *lencten adl* (or spring fever), likely *P. vivax*.[40] Malaria's diagnostic symptoms appear in numerous ancient and medieval European and West Asian texts,[41] Chinese epigraphs from 2700 BCE,[42] Sumerian cuneiform tablets and early Egyptian papyri.[43] Such observations underpin scholarship linking malaria to societal changes, including the declines of ancient Greek and Roman civilizations.[10, 44–46]

Written evidence alone makes for tentative diagnoses,[47,48] but it becomes more reliable when combined with bioarchaeological[8,49] and paleogenomic evidence.[31,50] Regarding the former, malaria's systemic effects appear in skeletal tissue, as bone loss, delayed maturation, and increased susceptibility to infections (e.g., tuberculosis, geohelminths) that also manifest skeletally.[51] The most common indirect indicators are non-specific skeletal lesions formed during childhood in response to physiological disruption, particularly those affecting the orbital roofs (*cribra orbitalia*) and the cranial vault (*cribra cranii*, commonly referred to as porotic hyperostosis), though similar lesions affecting the femur (*cribra femoralis*) have also been specifically linked to malaria.[52] While these lesions indicate early childhood anemia, the underlying causes remain debated.[53] They occur more frequently in malaria-endemic regions, strongly associating them with malaria-induced hemolytic anemia.[8,49,52,54–56]

Separately, paleogenomic identifications of malaria parasites are beginning to help us fill out malaria's past, now placing it concretely in multiple premodern contexts.[31,46] Without paleogenomes or skeletal lesions, skewed demographic profiles in premodern funerary contexts, such as elevated infant mortality,[57] may signal past disease outbreaks.[58,59] At the same time, archaeological contexts reveal how past populations endured high risk for malaria for centuries while transforming landscapes through agriculture, settlement, migration, and trade. The One Paleopathology framework integrates these multi-disciplinary methods and datasets, providing critical tools to anticipate and combat malaria's possible resurgence.

One Paleopathology: Drawing on Biological, Ecological, and Social Entanglement

An understanding of modern transmission variables and risk factors is critical for reconstructing malaria's past. Monitoring vector population shifts and integrating climate-ecological data into models, in particular, is essential for identifying both emerging hotspots and revealing dynamic historical transmission patterns.[60] While robust disease modelling has proved particularly valuable in transitional zones, at malaria's endemic margins, where environmental changes can

pronouncedly alter vector ecology and disease risk, it also bridges present and past, ultimately enhancing our ability to predict future risk across unprecedented temporal scales.[61]

Climate-informed mechanistic models have predicted probable transmission patterns to guide efforts to control and eliminate malaria,[62,63] helping policymakers mitigate risks in an increasingly malaria-suited climate. These models also illuminate historical malaria patterns through risk factor analysis. Reconstructing past malaria transmission risk thus requires a interdisciplinary approach, integrating diverse paleoclimate and paleoenvironmental proxies with socio-political contexts,[64,65] and offering sophisticated approaches to understand malaria's evolving threat.

Modern modeling faces persistent scale-resolution challenges,[66] particularly when integrating paleoclimate data. Geographic variability in climate proxies further complicates regional extrapolation, necessitating interdisciplinary approaches that merge climate science, historical records, and ecological data.[67] Despite these challenges, advancing technologies, including computing capacities and collaborative frameworks, now enable effective translation of paleoclimate and paleoenvironmental reconstructions into disease ecology models.[68]

The One Paleopathology approach applies these novel methods to premodern contexts, combining 1) reconstructed environmental and physical landscape characteristics (e.g., elevation, basins, coastlines); 2) built environments (e.g., hydraulic infrastructure), subsistence strategies, proximity to domestic animals, and socio-economic factors; and 3) morbidity and mortality data. This integration will enable computer simulations of malaria's deep-time impacts across diverse ecological and cultural contexts.

Historical data significantly enhance predictive modeling. While current models effectively incorporate environmental factors (temperature and climatic events, landscape use, and mosquito ecology),[15,69] their predictive power remains limited without the inclusion of human variables, including demographic and socioeconomic dynamics and mitigating public health efforts.[16,22,69,70] These elements are crucial for addressing past and present emerging syndemics,[71] particularly "eco-syndemics" that link ecological change with health crises.[72–74] The expanded syndemic framework provides a more integrated perspective of population health in premodernity. This point is significant as social variables can be especially difficult to incorporate across varying spatial and temporal modern epidemiological models. Written history, archaeology, and bioarchaeology provide these human dimensions, completing models that already include environmental parameters.

Final Comments

The One Paleopathology framework integrates data from archaeological, bioarchaeological, and paleoclimatological contexts with epidemiological and ecological modeling to reconstruct

premodern disease landscapes. This approach, we argue, will offer crucial insights for addressing malaria resurgence amid environmental and climatic threats.

Deep-time One Paleopathology perspectives reveal malaria's evolutionary history, its complex relationship with humans, and inform current health policies related to risk mitigation and climate resilience. In doing so, they enhance predictive modeling of future risk zones and health outcomes, particularly in conditions of climate stress, social conflict, resource scarcity, and population displacement. As Michel and colleagues highlight,[31] human mobility has previously facilitated malaria's spread to new regions, a pattern now recurring through autochthonous (locally-acquired) outbreaks,[11,75] growing climate-induced population displacement, and expanding malaria geographies, all of which will expose susceptible populations with no preexisting immunity.[17] Effective response requires inter-disciplinary collaboration that includes scientific disciplines and local community knowledge,[16] bridging past patterns with present prevention strategies.

We urge planetary health researchers and policymakers to treat the past as a laboratory: One Paleopathology's evidence of malaria's resilience to environmental change must inform surveillance in climate-vulnerable regions, from the Mediterranean to the American South. Without this deep-time perspective, mitigation efforts risk repeating history's mistakes—misallocating resources to transient hotspots while overlooking systemic drivers.

Author contributions

Jordan A. Wilson led the initial drafting of the manuscript and coordinated the writing process. All authors contributed to the conceptual development of the paper and to the drafting, review, and editing of the manuscript. Jane Buikstra conceived the overarching idea for the paper and provided intellectual leadership throughout its development. All authors approved the final version for submission.

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