

Review

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Posted Date: 21 October 2025

doi: 10.20944/preprints202510.1682.v1

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Review

Decoding Malaria: An African Perspective of the Journey from Microscopy to Genomics

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Abstract

Malaria remains one of the most pressing public health challenges in Africa, a continent that bears a significant percentage of the global malaria morbidity and mortality. From the earliest microscopic discoveries of *Plasmodium* to the era of genomics and vaccine innovations, Africa has stood both as the epicentre of the disease, and the focal point of global research and control efforts. The continent's unique ecological, genetic, and socio-political contexts have also shaped the evolution of the parasite, the host, and the mosquito vector. African scientists, institutions, and communities have progressively transitioned from being subjects of investigations to active contributors in malaria research; advancing studies in epidemiology, molecular biology, pharmacogenomics, and vaccine development. This review traces the journey of malaria science from its microscopic origins to genomic breakthroughs; emphasising how Africa's contributions, challenges, and innovations have redefined global understanding. It also highlights the importance of locally-driven research, surveillance, and policy frameworks to translate genomic data into practical solutions, aiming towards equitable and sustainable malaria elimination on the continent.

Keywords: Africa; genomics; malaria; plasmodium; research; vaccine

1. Introduction

Malaria is a life-threatening yet preventable and curable mosquito-borne disease. Malaria infection arises from the transmission of a protozoan parasite to humans following the bite of an infected female Anopheles mosquitoes (Siao et al., 2020; Sato, 2021; Gozalo et al., 2024; Long et al., 2024). The typical symptoms of malaria include headaches, fever, chills, and muscle aches, progressing to severe complications including anaemia, cerebral malaria, multiorgan failures and coma if not treated rapidly (Sypniewska et al., 2017; Mamudu et al., 2025). Despite being curable and preventable, it remains a major global health problem particularly in Africa and other tropical regions (Doumbia et al., 2022; Ounjaijean and Somsak, 2025). In sub-Saharan Africa, malaria remains a major health challenge accounting for a vast majority of infections and mortality, disproportionately affecting children aged zero to five, and pregnant women (Anjorin et al., 2023). While the sub-Saharan African region continues to face persistent challenges including poverty, weak healthcare systems, climate change, drug resistance and the emergence of new vectors; significant progress has been achieved in malaria prevention and cure through interventions like the provision of insecticide-treated bed nets, insecticides, artemisinin-based combination therapies, and intermittent prophylactic treatment in high-risk groups, which resulted in a significant reduction in malaria incidence and mortality rates within the region (World Health Organization, 2023; Li et al., 2024).

The African subregion is intricately linked to the history of malaria; indeed, no other infectious disease has shaped Africa's health, history, and development as profoundly as malaria (Bashir et al., 2025). Endemic across much of sub-Saharan Africa, malaria has not only imposed a staggering public

health burden but has also influenced patterns of settlement, agricultural productivity, trade, and colonial enterprise. Over centuries, recurrent malaria epidemics have curtailed population growth, impeded economic progress, and strained fragile health systems (Badmos et al., 2021; Merga et al., 2025). The persistence of *Plasmodium falciparum* transmission, coupled with ecological and socio-economic vulnerabilities, continue to define the continent's epidemiological landscape. Thus, malaria in Africa is not merely a biomedical problem; it is a developmental, historical, and psychosocial challenge intertwined with the region's evolution and well-being (Msellemu et al., 2016; Nkumama et al., 2017; Li et al., 2024).

The history of malaria research is also inextricably linked with the African subregion, and the high burden of malarial infection in the region led to several foundational discoveries, advancing our understanding of the parasite's co-evolution with human populations (Cox, 2010; Drouin et al., 2024). This history began with the first microscopic observation of *Plasmodium* parasite by Alphonse Laveran in Algeria in 1880, to the 1890s research by Ronald Ross that associated the *Anopheles* mosquito with transmission of the parasite, and the completion in 2002 of the first draft sequence of the *plasmodium falciparum* genome (Laveran, 1978; Rajakumar and Weisse, 1999; Gardner et al., 2002; Hoffman et al., 2002; Institute of Medicine, 2004; Sinden, 2007; Tan and Ahana, 2009; Su et al., 2019; Talapko et al., 2019; Pande et al., 2024). For more than a century, the African continent has served simultaneously as the laboratory of malaria science and the frontline of global control efforts, shaping and being shaped by every major advance in parasitology, vector biology, and therapeutic discovery (Institute of Medicine, 2004; Li et al., 2024). In recent decades, however, this narrative has evolved, with sustained capacity building and experience resulting in African institutions, scientists, and regional networks shifting from being peripheral contributors to central architects in the areas of malaria genomics, epidemiology, and translational research (Ghansah et al., 2014, 2019; Ishengoma et al., 2019; Tessema et al., 2019). In this narrative review, malaria's scientific evolution (Table 1) is examined through an African lens, exploring the historical milestones, genomic breakthroughs, local innovations, and enduring challenges that continue to define the continent's path from microscope to genome.

Table 1. Timeline of Malaria Research Milestones in Africa (1880–2025).

Year / Period	Milestone / Event	Significance (with African Focus)
1880	Charles Louis Alphonse Laveran observes <i>Plasmodium</i> parasites in Algeria.	Marks the first identification of a protozoan parasite in humans; discovery occurred on African soil.
1897	Sir Ronald Ross demonstrates mosquito transmission of malaria.	Foundation for vector control strategies later applied extensively in Africa.
1898–1900	Giovanni Battista Grassi confirms mosquito transmission of <i>P. falciparum</i> in humans.	Clarifies parasite life cycle, directly relevant to African <i>Anopheles</i> species.
1900–1950	Expansion of malaria research and control under colonial health systems.	Establishment of early laboratories in Nigeria, Ghana, Sudan, and Kenya; focus on vector ecology and habitat management.
1940s	Introduction of chloroquine and DDT.	Synthetic antimalarials and insecticides revolutionise malaria treatment and control across tropical Africa.
1955	WHO launches the Global Malaria Eradication Programme (GMEP).	Africa largely excluded due to logistical, ecological, and infrastructural challenges.
1950s–1960s	Creation of regional research institutes.	Establishment of tropical medicine centres (e.g., East African Institute of Malaria, Nigeria's Trypanosomiasis Institute).
1969–1976	The Garki Project (Nigeria).	WHO–Nigeria collaboration providing realistic mathematical models of malaria transmission; exposed limits of vector spraying and mass drug administration in African settings.
1970s–1980s	Widespread chloroquine resistance.	Resistance of <i>P. falciparum</i> spreads across Africa; drives the search for new drug therapies.

1980s	Strengthening of African research institutions.	Growth of KEMRI (Kenya), Noguchi Memorial Institute (Ghana), and Ifakara Health Institute (Tanzania).
2002	<i>Plasmodium falciparum</i> genome sequenced.	Major genomic breakthrough; African samples and scientists contributed to understanding drug resistance genes.
2005	Roll Back Malaria & President's Malaria Initiative (PMI) expanded.	Renewed global and African focus on malaria funding, control, and elimination strategies.
2010	Scale-up of insecticide-treated nets (ITNs).	Significant reduction in malaria morbidity and mortality across sub-Saharan Africa, especially among children.
2015	African Union's "Catalytic Framework to End AIDS, TB, and Eliminate Malaria by 2030."	Integration of malaria control within Africa's broader health and development agenda.
2018	RTS,S/AS01 (Mosquirix) pilot vaccine rollout in Ghana, Kenya, and Malawi.	First large-scale real-world vaccine trials conducted in Africa; pivotal step toward immunological control.
2020	WHO recognises Africa as the global epicentre of malaria research and challenge.	Over 90% of global malaria cases and deaths occur in Africa, making it central to global policy and innovation.
2021	WHO recommends RTS,S for widespread use.	Historic milestone in malaria vaccination; evidence driven by African trial data.
2022	Reports of <i>pfkelch13</i> mutations in East Africa.	Confirms partial artemisinin resistance in <i>P. falciparum</i> strains from Rwanda and Uganda.
2023	R21/Matrix-M vaccine approved and endorsed by WHO.	Developed with major African participation (notably Burkina Faso); efficacy surpasses 75%.
2024–2025	Expansion of genomic surveillance networks (PDNA, MalariaGEN Africa Hub).	African-led genomic initiatives enable cross-border tracking of parasite evolution, drug resistance, and vector genomics.

From Laveran's 1880 discovery in Algeria to Africa's leadership in malaria genomics and vaccine development by 2025, this timeline illustrates the continent's transformation from a site of colonial experimentation to a global driver of innovation, policy, and molecular research in the fight against malaria.

2. From Microscopic Discovery to Molecular Technologies

The microscopic era of malaria research began in 1880, when French military physician, Charles Louis Alphonse Laveran who was stationed in Algeria, first identified motile pigmented parasites in the blood of soldiers; this marked the discovery of *Plasmodium* as the causative agent of the disease (Cox, 2010; Pande et al., 2024). This breakthrough, achieved through meticulous light microscopy, was significant in transforming previously-held beliefs that malaria was a mysterious "miasmatic" illness, and entrenching its place as a parasitic infection (Awoyemi, 2005; Hempelmann and Krafts, 2013; Lalchandama, 2014). In the decades that followed, improvements in microscopic and histological techniques, most notably the introduction of the Romanowsky–Giemsa staining methods aided the characterisation of the biology and life cycle of different members of the plasmodium species, and also increased diagnostic accuracy of the infection. (Barcia, 2007; Wongsrichanalai et al., 2007; Krafts et al., 2011). Since the early 1900s when the German chemist, Gustav Giemsa introduced the stain that bore his name (which is a mixture of methylene blue and eosin stains), the microscopic examination of Giemsa-stained blood smears has remained a standard diagnostic technique for malaria infection.

These early discoveries not only enabled the diagnosis of malaria but also established the taxonomic foundation of malaria science, allowing the identification of four species of the Plasmodium parasite including *Plasmodium falciparum* (*P. falciparum*), *Plasmodium vivax*, *Plasmodium malariae*, and *Plasmodium ovale*. These species have now been confirmed to predominate across different geographical regions, with *P. falciparum* prevailing in Africa (Zekar and Sharman, 2023). Across Africa, microscopy also became the cornerstone of malaria diagnosis, surveillance, and research, remaining a primary method for diagnosis in most parts for more than a century (Nkrumah

et al., 201; Ugah et al., 2017; Comfort et al., 2024); and till today, it continues to remain indispensable in clinical and field settings across Africa (Dhorda et al., 2020; Prah et al., 2021; Aninagyei et al., 2024; Tegegn et al., 2024).

In recent times, while microscopy remains the gold standard for malaria diagnosis, it is increasingly being complemented and, in some settings, surpassed by molecular and imaging technologies. These advanced methods offer greater speed, specificity, and sensitivity; enabling the detection of low-density parasitaemia and the identification of parasite genotypes associated with drug resistance (Calderaro et al., 2024). Techniques such as polymerase chain reaction (PCR), quantitative PCR (qPCR), loop-mediated isothermal amplification (LAMP), and next-generation sequencing (NGS) have expanded diagnostic capacity and deepened understanding of parasite diversity and evolution. In parallel, innovations in digital microscopy and artificial intelligence–assisted image analysis are transforming diagnostic accuracy and workflow efficiency (Maturana et al., 2023; Dantas de Oliveira et al., 2024; Fong Amaris et al., 2024; Rubio Maturana et al., 2024), particularly in resource-limited African laboratories. Collectively, these advances underscore the fact that while the microscope era established the cornerstone of malaria diagnosis, the field is fast transitioning toward a new phase of molecular precision and genomic insight, with Africa increasingly positioned to benefit from and contribute to this transformation.

3. The Transmission Revolution: Vector Discovery and Control in the African Context

At the turn of the 20th century, the discovery of the mosquito vector involved in the transmission of malaria marked a significant milestone in malaria research (Table 1). Sir Ronald Ross, working in Secunderabad, India, demonstrated that *Anopheles* mosquitoes transmit *Plasmodium* parasites, confirming the disease's vector-borne nature (Capana, 2006; Cox, 2010; Ruele et al., 2024). Almost simultaneously, Giovanni Battista Grassi, an Italian medical doctor/zoologist and his colleagues identified the specific *Anopheles* species responsible for human transmission, providing conclusive evidence of the parasite's complex life cycle between mosquito and human hosts (Institute of Medicine, 1991; Capana, 2006; Gachelin, et al., 2018; Chaudhury, 2021; Ruele et al., 2024). Though the mosquito transmission cycle was established through research in India and Italy, the field observation centres established across West and Central Africa were important in confirming the ecological link between mosquitoes, swamps, and seasonal fevers (Ferroni et al., 2012). Colonial medical services during the early 20th century documented extensive microscopic surveys in regions that are now Nigeria, Sierra Leone, the Gambia, and the Congo; laying the foundation for modern malariology in Africa (Bump and Aniebo, 2022). Though these early efforts were led largely by colonial scientists, they produced enduring data on the distribution, vector behaviour, and parasite species diversity of the *Anopheles* mosquito. The earliest foundational public health institutions in Africa including the Yaba Malaria Research Station in Nigeria (Now placed within Nigerian Institute for Medical Research) and Kampala's East African Malaria Institute were centres for training and surveillance, nurturing the first generation of African parasitologists and entomologists (Talisuna et al 2015; Nankabirwa et al., 2022; Namuganga et al., 2022). Today, these institutions were the foundation of the various centres of excellence for malaria research across sub-Saharan Africa.

The paradigm shift from considering malaria as a disease resulting from "bad air" to discovering the mosquito vector charted the path for malaria control and eradication. For the first time, prevention strategies could target the mosquito vector rather than only treating human infection. The implications for Africa, a region disproportionately affected by malaria were profound (Wilson et al., 2020; Kaura et al., 2023). The continent's ecology, characterised by diverse *Anopheles* species, favourable climatic conditions, and extensive breeding habitats, provided ideal environments for sustained transmission (Ayala et al., 2009; Mattah et al., 2017; Getachew et al., 2020; Msugupakulya et al., 2023; Ebhodaghe et al., 2024). The recognition of *Anopheles gambiae* as the primary African vector later became a cornerstone for malaria entomology and control initiatives. Detailed understanding of the life cycle and ecological characteristics of the *Anopheles gambiae* provided a cornerstone for the

scientific field of malaria vector entomology and the practical application of malaria control programs across sub-Saharan Africa (Killen et al., 2002; Alves et al., 2024; Takken et al., 2024).

Early vector control efforts, which included environmental management, larva source reduction, and the use of insecticides such as DDT (dichloro-diphenyl-trichloroethane) were implemented during the colonial and early postcolonial periods. These interventions which achieved variable levels of success were also constrained by socioeconomic inequities, limited infrastructure, and resistance to insecticides. Nonetheless, they laid the groundwork for modern integrated vector management programs (van den Berg, 2009; Raghavendra et al., 2011; Maheu-Giroux et al., 2021).

In post-independence Africa, the transmission era also brought scientific and institutional evolution. Field stations such as the Garki Project in Nigeria provided critical epidemiological data and modeling tools that informed global malaria strategies. The Garki Project which was conducted in northern Nigeria immediately after independence, was a landmark field study aimed at understanding malaria transmission and control in real-world African settings. From 1969 to 1976, researchers gathered extensive epidemiological data that culminated in the development of a mathematical model of malaria transmission that was far more reflective of African realities than earlier theoretical models (Nedelman, 1988). This project jointly implemented by the World Health Organisation (WHO) and the Nigerian government, tested interventions such as indoor residual spraying and mass drug administration strategies, offering critical evidence that these strategies alone were insufficient to achieve long-term malaria elimination under local ecological and social conditions (Molineaux and Gramiccia, 1980). The findings demonstrated that, despite aggressive vector control and chemotherapy, malaria elimination in high-transmission African settings required sustained, multifaceted interventions, a lesson that continues to shape policy today (Abeku et al., 2019).

The understanding of malaria transmission also stimulated behavioural and socio-environmental research, linking human activity, housing quality, and agricultural practices to transmission risk. This intersection between entomology, ecology, and social science paved the way for community-based interventions such as insecticide-treated nets (ITNs) and indoor residual spraying (IRS), that would later dominate control efforts in the late 20th and early 21st centuries (Hershey et al. 2017; Thwing et al., 2019; Kayentao et al., 2018; van den Berg et al., 2018; Win Han et al., 2019; Karemere et al., 2021). Thus, the transmission revolution not only clarified malaria's biological ecology but also redefined its public health identity, establishing Africa as both the epicentre of the disease and the testing ground for innovation in vector control, community engagement, and policy formulation.

4. The Vector and the Environment: Africa's Ecological Uniqueness

Malaria transmission in Africa is shaped by an intricate interplay of vector biology, environmental factors, and human behaviour; creating conditions that are both unique and challenging for control efforts. The African landscape, with its diverse climate zones from humid rainforests to dry savannahs and highlands provides optimal breeding habitats for *Anopheles* mosquitoes, the most efficient malaria vectors in the world. Understanding this ecological uniqueness is key to designing context-specific interventions.

Africa hosts more than 140 species of *Anopheles*, but only a few dominate malaria transmission. The predominant ones are *Anopheles gambiae sensu stricto*, *Anopheles arabiensis*, and *Anopheles funestus*, whose exceptional anthropophily and endophilic behaviour make them highly effective vectors (Msugupakulya et al., 2023). *Anopheles gambiae*, in particular, is often described as "the most efficient malaria vector known to man," capable of transmitting *Plasmodium* with remarkable precision and adaptability (Shaw et al., 2021). This efficiency, coupled with genetic plasticity, contributes to persistent malaria transmission even in areas of high intervention coverage.

The ecological settings of Africa foster continual malaria transmission. Rainfall patterns, temperature, and humidity directly influence mosquito breeding and parasite development rates. In tropical regions, the perennial availability of stagnant water ranging from puddles and rice paddies

to urban drainages ensures sustained vector populations (Chaptoterera et al., 2025). In contrast, semi-arid zones experience seasonal transmission, with peaks corresponding to the rainy season. Climate change, through rising temperatures and altered precipitation patterns, is increasingly expanding the geographic range of vectors into previously non-endemic highland regions of East Africa and southern Africa (Chaptoterera et al., 2025).

Rapid and often unplanned urban growth in African cities introduces new ecological dynamics. Poor drainage, overcrowding, and intermittent water supply create artificial breeding habitats, while shifts in housing structures and human activity patterns affect exposure risk. Meanwhile, agricultural practices such as irrigation and deforestation alter local ecologies, expanding vector habitats and changing species composition (Aliyu and Amadu, 2017). The overlap of rural and peri-urban transmission patterns complicates vector control, requiring integrated approaches that consider local livelihood systems.

Addressing Africa's ecological complexity requires interventions tailored to local environmental and social contexts. Current strategies include the deployment of dual-insecticide nets, larva source management, biological control agents (e.g., larvivorous fish, *Bacillus thuringiensis israelensis*), and environmental engineering. Additionally, innovative tools such as gene-drive mosquitoes, developed with contributions from African research institutions, aim to suppress or modify vector populations in the long term. Africa's ecological uniqueness defined by its biodiversity, climatic diversity, and socio-environmental interactions makes malaria control both a biological and ecological challenge. Recognising and leveraging these unique conditions are essential for sustainable malaria elimination. As vector ecology continues to evolve under the pressures of climate change and human development, Africa's environmental research will play a pivotal role in shaping adaptive, eco-smart malaria control strategies.

5. Chemotherapeutic Advances and Roadblocks: From Quinine to Artemisinin Resistance in Africa

The history of malaria therapy is deeply intertwined with the global evolution of the science of pharmacology and Africa's colonial and postcolonial experience (Table 2). For centuries, the use of traditional herbal remedies, including using the bark of the cinchona tree (which contains the antimalarial drug quinine) and the neem tree were used to treat malaria. The successful extraction of quinine from the bark of the cinchona tree in the 17th century provided the first antimalarial agent (Baird et al., 1996; Garforth, 2007; Nosten and White, 2007; Dkarani et al., 2008; Butler et al., 2010; Permin et al., 2016; Kokori et al., 2024). The discovery of quinine would go on to shape both military and colonial expansion into tropical Africa by providing a means to survive in endemic regions once deemed the "white man's grave" (Brockway, 1979; (Fredj, 2016; Ratschiller Nasim, 2023). However, while quinine saved countless lives, it also symbolised the uneven power dynamics of colonial medicine, as its availability and use were often restricted to colonial officials and elites, leaving local populations with limited access. Quinine remained the only known antimalarial agent until the 19th century. The global shortage of quinine prompted an urgent scientific drive to develop synthetic alternatives (Goss, 2014; Cassauwers, 2015). This effort accelerated the discovery of novel compounds such as chloroquine in 1934, and its official adoption in 1946 as the drug of choice for malaria treatment worldwide, capable of replacing quinine as the principal antimalarial therapy (US Institute of Medicine, 2004; MMV, 2025). Nonetheless, quinine has retained its therapeutic relevance as a secondary or backup medicine, particularly in severe malaria cases.

Table 2. Timeline of Malaria Chemotherapy in Africa (1880–2025).

Period / Year	Therapeutic Milestone	Significance in the African Context
Pre-1880s	Traditional African Antimalarial Remedies	Indigenous use of plants such as <i>Cryptolepis sanguinolenta</i> , <i>Azadirachta indica</i> (neem), <i>Morinda lucida</i> , and <i>Vernonia amygdalina</i> for

		treating fever and malaria-like symptoms; foundation for later pharmacognostic studies.
17th–19th Century	Introduction of Quinine from Cinchona bark	Used by colonial powers and missionaries in Africa; first effective therapy against malaria; limited access for native populations during colonial expansion.
1880–1930s	Refinement of Quinine Therapy	Quinine becomes standard treatment across Africa; issues of cost, supply, and resistance begin to emerge.
1940s	Synthesis of Chloroquine (CQ)	Affordable, potent antimalarial; rapidly adopted across Africa as a first-line therapy; marked a new era in mass treatment.
1950s–1970s	Golden Age of Antimalarial Chemotherapy	Introduction of amodiaquine, pyrimethamine and sulfadoxine-pyrimethamine (SP); widespread prophylaxis and treatment programmes implemented during and after colonial rule.
1960s–1970s	Mass Drug Administration Trials (e.g., Garki Project, Nigeria)	Evaluated large-scale CQ and SP distribution; revealed challenges of sustainability and resistance in high-transmission African settings.
1980s	Emergence of Chloroquine Resistance in Africa	Chloroquine resistance spreads from Southeast Asia to Africa; genetic basis later linked to <i>pfcr1</i> and <i>pfmdr1</i> mutations; marks beginning of drug- resistance era.
1990s	Transition to Sulfadoxine-Pyrimethamine (SP) and Other Alternatives	SP temporarily replaces CQ; resistance soon follows; combination therapies explored to delay resistance.
2000s	Adoption of Artemisinin-Based Combination Therapies (ACTs)	ACTs became WHO-recommended first-line treatment; Africa leads global implementation through national malaria control programmes; major decline in mortality observed.
2010s	Widespread Distribution and Policy Integration of ACTs	Rollout supported by Roll Back Malaria, Global Fund, and PMI; local studies validate safety and efficacy; artemisinin resistance monitoring begins in East Africa.
2012–2020	Integration of Pharmacovigilance and Molecular Surveillance	African researchers identify key resistance markers (<i>pfkelch13</i> mutations); routine genotyping incorporated into surveillance systems.
2021–2023	Emergence of Artemisinin Partial Resistance in East Africa	Reports from Rwanda, Uganda, and Eritrea confirm reduced susceptibility; renewed emphasis on surveillance and combination therapy refinement.
2023–2025	Renewed Focus on Traditional and Nutraceutical Antimalarials	Growing research on African botanicals (e.g., <i>Spondias mombin</i> , <i>Cryptolepis sanguinolenta</i>) and their molecular targets; integration of ethnomedicine with modern pharmacology.
2025 and beyond	Toward Personalised and Genomic-Guided Malaria Therapy	Africa's genomic networks (e.g., PDNA, MalariaGEN Africa Hub) enable tracking of resistance alleles and design of tailored treatment policies; exploration of host-genetic factors guiding therapy and vaccine response.

From quinine's introduction to the continent-wide deployment of ACTs and genomic surveillance, Africa's therapeutic landscape reflects both the burden and brilliance of adaptation. Each stage of antimalarial therapy has been shaped by Africa's unique ecology, parasite evolution, and growing research independence. Today, with African scientists leading genomic, pharmacological, and ethnomedicinal investigations, the continent stands poised to redefine the next generation of precision antimalarial therapies.

The mid-twentieth century witnessed the rise of other synthetic antimalarials, including amodiaquine, and sulfadoxine-pyrimethamine (SP), which were affordable and widely distributed across Africa during the 1950s–1970s (Vestergaard and Ringwald, 2007; Onalapo et al., 2018). Chloroquine in particular, became a mainstay of malaria control and was considered at the time a "miracle drug." Yet, by the 1980s, resistance of *Plasmodium falciparum* to chloroquine had spread rapidly across Africa, undermining decades of progress (von Seidlein et al., 1997, Baird, 2004; Wurtz et al., 2012; Tse et al., 2019; Pandey et al., 2023). This wave of resistance was later traced to mutations in two transmembrane transporter including *P. falciparum* multidrug resistance protein 1 (*PfMDR1*)

and *P. falciparum* chloroquine resistance transporter (*PfCRT*) genes, which have provided some of the earliest molecular insights into the adaptive capacity of the parasite (EANMAT, 2003; Viegas et al., 2006; Zhou et al., 2020; Silva et al., 2022). Moreover, the persistent burden of malaria, coupled with the emergence of chloroquine resistance has led to sustained global efforts to develop more effective chemotherapeutic agents and consider multidrug therapy for malaria infections.

In response to the failure of monotherapies, the late twentieth and early twenty-first centuries saw the global adoption of artemisinin-based combination therapies (ACTs), derived from *Artemisia annua*, a plant long used in traditional Chinese medicine (Eastman and Fidock, 2009; Su and Miller, 2015; Morua et al., 2025). Artemisinin-based combination therapies quickly became the first-line treatment for *P. falciparum* malaria, and their deployment in Africa dramatically reduced malaria morbidity and mortality, particularly among children under five (Bhattarai et al., 2007; Nosten and White, 2007; Maiga et al., 2021). Africa became both the largest consumer and the primary testing ground for ACT efficacy. The emergence of partial artemisinin resistance, a phenomenon first observed in Southeast Asia and now appearing in countries like Rwanda, Uganda, and Eritrea (Mihreteab et al., 2023, 2025; Agaba et al., 2024) underscores another urgent threat to the continent's malaria control achievements. This resistance, caused by mutations in the parasite's *k13* gene, means that artemisinin-based drugs take longer to clear parasites from the blood, increasing the risk of treatment failure and further spread of resistance (Agaba et al., 2024; Milong et al., 2024; Zheng et al., 2024; Oyegbade et al., 2025)

Molecular surveillance has become a cornerstone of contemporary malaria pharmacology. African researchers are at the forefront of monitoring resistance-associated mutations in *pfkelch13*, *pfprt*, and *pfmdr1* genes using genomic and molecular diagnostic tools (Zhou et al., 2019; Cheng et al., 2021; Zhao et al., 2021; Martín Ramírez et al., 2025). The monitoring of resistance patterns assists in the understanding of the prevalence and spread of drug resistance; enabling informed public health policies and the development of more effective treatment strategies, especially as new mutations emerge and spread (Zhao et al., 2021; Wang et al., 2022; Alruwaili et al., 2025; Dakorah et al., 2025; Martín Ramírez et al., 2025). These efforts are supported by regional initiatives such as the Malaria Genomic Epidemiology Network, West African Network for Clinical Trials of Antimalarial Drugs, the Pathogenic Diversity Network Africa, and the Plasmodium Diversity Network Africa, which are strengthening genomic surveillance capacity and promoting data sharing across national borders. The rise of multidrug-resistant *Plasmodium* strains and emerging partial resistance to newer drugs have further intensified the urgency for continuous research and innovation in antimalarial therapy.

Beyond conventional chemotherapy, renewed attention is being directed toward traditional medicinal plants, reflecting a shift towards *Afrocentric pharmacognosy* which is driven by the need to combat drug-resistant malaria, the high cost, and accessibility problems of modern drugs, and the rich biodiversity of the continent (Onukansi et al., 2025). Several African botanicals including *Azadirachta indica* (neem), *Cryptolepis sanguinolenta*, *Morinda lucida*, *Vernonia Amygdalina*, *Markhamia tomentosa*, *Polyalthia longifolia*, and *Trichilia heudelotii* are being systematically evaluated for their antiplasmodial and immunomodulatory properties, integrating indigenous knowledge into contemporary drug discovery pipelines (Osunderu, 2009; Alebie et al., 2017; Onukansi et al., 2025). Thus, the history of malaria therapeutics in Africa represents more than a pharmacological evolution; it is a chronicle of adaptation, resistance, and rediscovery. From quinine to artemisinin, Africa has not only endured the shifting tides of drug efficacy but has also increasingly become a critical contributor to global malaria pharmacogenomics, policy, and innovation.

6. The African Genomic Awakening

The decoding of the *P. falciparum* genome in 2002 opened new possibilities for understanding malaria biology; however, it also revealed a crucial reality that most genomic data were derived from African isolates (Mobegi et al 2014; Ajibaye et al., 2020; Kassegne et al., 2020; Metoh et al., 2020), where the infrastructure to analyse this data was lacking. This created a bottleneck, limiting the ability of local researchers to participate in and benefit from advancements, although significant efforts have

since been made to improve sequencing and data analyses capabilities in Africa. Also, Africa, being the heart of *P. falciparum* diversity, became central to understanding parasite evolution and resistance mechanisms. Subsequent initiatives such as the MalariaGEN Consortium, Human, Heredity and Health (H3) Africa, and Plasmodium Diversity Network Africa (PDNA) to mention a few have continued to empower African researchers to generate and analyse high-quality genomic data locally (MalariaGEN et al., 2023, 2025). These platforms have uncovered patterns of drug resistance gene spread (e.g., *pfprt*, *pfmdr1*, *kelch13*) and mapped regional population structures of *Plasmodium* and *Anopheles* species (MalariaGEN, 2008).

African scientists now leverage next-generation sequencing to lead malaria research, monitor parasite adaptation, vector evolution, and host–parasite genetic interactions. Studies in Ghana, Mali, Uganda, and Nigeria are decoding how local immunity and genetic traits (e.g., sickle cell haemoglobin, G6PD deficiency, Duffy negativity) influence malaria susceptibility and treatment outcomes. This genomic renaissance marks Africa’s transition from data scarcity to data leadership in malaria research.

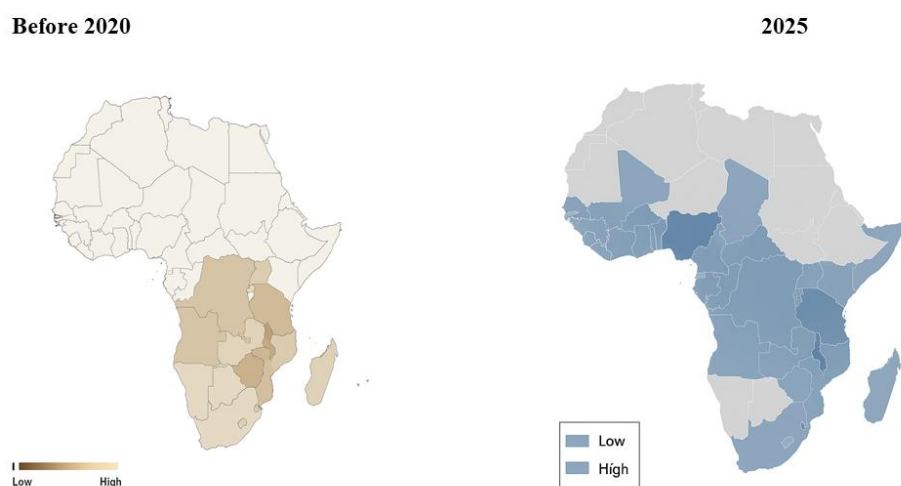


Figure 1. Genomic Surveillance Networks for Malaria across Africa, then and now. Image generated using ChatGPT. The image was generated in response to this prompt: 'Create an image that shows genomic surveillance networks for Malaria across Africa before the year 2020 and now in the year 2025.'

7. Vaccines and Immunity: African Contributions to the Next Frontier in Malaria Control

The quest for an effective malaria vaccine represents one of the most ambitious endeavours in global health, and Africa has been central to every phase of this journey (Effiong et al., 2022; Alum et al., 2025). Given that the continent bears over 90% of the global malaria burden, African populations, scientists, and institutions have been both the recipients and the drivers of vaccine innovation, immune profiling, and clinical evaluation (Table 3). African scientists and institutions are actively driving innovation, with initiatives like the African Malaria Network Trust (AMANET) focusing on vaccine research and capacity building (Sibomana et al., 2025). Unlike many other infectious diseases, malaria presents a formidable immunological challenge owing to the complex life cycle of *Plasmodium* species, their capacity for antigenic variation, and the parasite’s co-evolution with the human immune system in endemic regions (Crutcher and Hoffman, 1996; Crompton et al., 2014;

Pikor et al., 2016; Gross et al., 2021). For centuries, efforts to understand natural immunity in African populations have informed global vaccine design, reflecting Africa's centrality to malaria immunology and translational research (Crutcher and Hoffman, 1996; Crompton et al., 2014; Pikor et al., 2016; Gross et al., 2021; Kalkal et al., 2022).

Table 3. Key African Malaria Vaccine Trials and Their Outcomes.

Vaccine Candidate	Target Antigen / Platform	Trial Locations (Africa)	Trial Phase / Period	Efficacy / Key Findings	Lead Institutions / Partners
RTS, S/AS01 (Mosquirix™)	Circumsporozoite protein (<i>Plasmodium falciparum</i>) + Hepatitis B surface antigen; AS01 adjuvant	Ghana, Kenya, Malawi, Mozambique, Tanzania, Gabon	Phase III (2009–2014); Pilot Implementation (2019–2023)	~30–50% efficacy against clinical malaria in children (5–17 months); protection wanes over time; reduced severe malaria	GSK, PATH, WHO, African research consortia
R21/Matrix-M	Circumsporozoite protein (modified RTS,S antigen) with Matrix-M adjuvant	Burkina Faso, Mali, Ghana	Phase IIb (2019–2021); Phase III (2021–2024 ongoing)	Up to 75% efficacy over 12 months; high antibody titers; favourable safety profile	University of Oxford, Serum Institute of India, African clinical trial partners
SPf66	Synthetic multi-epitope peptide	The Gambia, Tanzania	Phase II (1990s)	Low and inconsistent efficacy (<30%); abandoned	Colombian and African collaborators
DELVAC/AMA1-C1	Apical Membrane Antigen-1 (AMA1) recombinant protein	Mali	Phase I–II (2005–2010)	Safe; induced strong antibody response but limited protective efficacy	NIH, Malaria Vaccine Initiative (MVI), African trial sites
PfSPZ Vaccine	Attenuated whole sporozoite vaccine (IV route)	Mali, Tanzania, Burkina Faso, Kenya	Phase I–II (2015–2023 ongoing)	40–55% efficacy in field trials; durable immune memory in controlled settings	Sanaria Inc., NIH, African collaborators
Transmission-Blocking Vaccines (TBVs)	Pfs25 / Pfs230 antigens (gametocyte stages)	Tanzania	Phase I (ongoing)	Safe and immunogenic; target parasite transmission rather than infection	PATH, NIH, African research institutions

Africa's involvement in malaria vaccine trials has progressed from passive participation to active scientific leadership. The continent has hosted pivotal efficacy trials, developed clinical and immunological infrastructure, and contributed critical data that informed global malaria vaccine policy. Current research continues to expand into multi-stage, transmission-blocking, and next-generation vaccines, with African scientists increasingly steering design and implementation.

The early recognition that individuals in endemic regions develop partial immunity to malaria after repeated exposure provided the conceptual foundation for vaccine development (Dolan et al., 2009; Barry and Hansen, 2016; Chan et al., 2020; Opi et al., 2021). African epidemiological studies including those conducted in The Gambia, Nigeria, and Tanzania assisted in defining the dynamics of naturally-acquired immunity, distinguishing between protection against severe disease, and sterile immunity (Pinkevych et al., 2012; Deroost et al., 2016). Observations of asymptomatic parasitaemia, age-dependent immunity, and protection conferred by genetic traits such as the sickle-cell mutation and the glucose-6-phosphate dehydrogenase deficiency offered profound insights into host-parasite interactions (Moormann et al., 2003; Awah et al., 2012; Gong et al., 2012). These findings not only explained regional variations in malaria burden but also guided vaccine development strategies targeting pre-erythrocytic and blood-stage antigens. These insights guided the identification of

immunogenic parasite antigens, including circumsporozoite protein, merozoite surface (MSP), and apical membrane antigens (AMA), which remain key targets for subunit vaccine development (Woehlbier et al., 2010; El-Moamly and El-Sweify, 2023).

Malaria vaccines are broadly classified based on the developmental stage of the parasite they are designed to target. These include pre-erythrocytic vaccines, which aim to prevent infection at the liver stage; erythrocytic or blood-stage vaccines, which seek to limit parasite multiplication and disease severity; and transmission-blocking vaccines, which interrupt the parasite's transmission from humans to mosquitoes (El-Moamly and El-Sweify, 2023). While most candidates focus on a single stage, a few are being developed to act across two or more phases of the parasite's life cycle (El-Moamly and El-Sweify, 2023). A landmark breakthrough in the field was the RTS, S/AS01 (Mosquirix™) vaccine, the first vaccine candidate to achieve regulatory approval for use in humans (Laurens, 2022; Egbewande, 2022; Praet et al., 2022). Developed through collaboration between GlaxoSmithKline (GSK) and PATH, RTS, S was extensively evaluated in phase II and III clinical trials conducted in several African countries, including Ghana, Kenya, Malawi, and Tanzania (Laurens, 2022; Egbewande, 2022; Praet et al., 2022). The vaccine, which targets the circumsporozoite protein (CSP) of *Plasmodium falciparum*, offered modest yet meaningful protection, particularly among African children. With an efficacy of approximately 30–50% against clinical malaria, these pivotal trials provided the scientific basis for its pilot introduction in 2019 under the coordination of the World Health Organisation (WHO), a milestone in global and African malaria control efforts (Laurens, 2022; Egbewande, 2022; Praet et al., 2022). The R21/Matrix-M vaccine, developed by Oxford University and the Centre National de Recherche et de Formation sur le Paludisme (CNRFP), is a malaria vaccine that has shown similar or better efficacy than RTS, S, with a lower cost and acceptable safety profile; it also achieved over 75% efficacy in Phase II trials (Oduoye et al., 2024; Schmit et al., 2024; Venkatraman et al., 2025; WHO, 2025). African institutions and scientists played a pivotal role at every stage from its clinical evaluation to implementation. The large-scale pilot trials in these countries provided the decisive data on vaccine safety, efficacy, and feasibility that underpinned the WHO's 2021 recommendation for widespread use (WHO, 2021). This represents a profound paradigm shift with Africa as the epicentre of both discovery and validation in global vaccine science. In 2023, the WHO endorsed R21 for broad use, marking not only a scientific breakthrough but also a symbolic achievement for African-led research capacity. This success reflects a shift from dependency to partnership, where African laboratories, data systems, and ethics frameworks now underpin the next generation of vaccine innovation and deployment strategies.

African immunologists and epidemiologists have also provided invaluable insights into host-parasite interactions and immune correlates of protection (Kibwana et al., 2024; Ogwang et al., 2025). Studies conducted in endemic areas revealed that antibody-mediated and T-cell-dependent mechanisms vary with transmission intensity, age, and genetic background. Moreover, research from institutes such as KEMRI-Wellcome Trust (Kenya), MRC Unit in The Gambia, and Noguchi Memorial Institute (Ghana) has refined understanding of how immunity develops over time, and how vaccine responses differ among African populations (Mannan et al., 2003; Shelton et al., 2015; Odhiambo et al., 2025).

As parasite diversity and antigenic variation continue to challenge vaccine durability, African laboratories are increasingly participating in genomic and immune epidemiological research to design next-generation vaccines (Gunawardena and Karunaweera, 2015; Shelton et al., 2015; Hafalla et al., 2025). Multi-stage formulations combining pre-erythrocytic, blood-stage, and transmission-blocking components are now under evaluation in African sites, reflecting a shift toward integrated, locally-relevant vaccine strategies (Tachibana et al., 2025). Africa's role in malaria vaccine research has evolved from that of a passive testing ground to that of a scientific collaborator and innovator. The continent's immunological diversity, clinical research infrastructure, and growing cadre of trained vaccine scientists position it at the forefront of the next phase in malaria control and elimination. As the world moves toward more durable, multi-stage vaccines, Africa's sustained

leadership will remain indispensable in ensuring that immunological discoveries translate into equitable, context-sensitive public health gains.

8. From Policy to Practice: Translating Science into Sustainable Malaria Control in Africa

Scientific advances in malaria research, spanning diagnostics, therapeutics, and vector control—have significantly shaped global and regional malaria policies. However, translating these scientific insights into sustainable, community-level impact across Africa has remained a persistent challenge. The success of malaria control depends not only on innovation but on the effective integration of research outcomes into national health systems, policies, and behavioural practices (Table 4).

Table 4. Major Policy Milestones and Implementation Outcomes in African Malaria Control (1955–2025).

Period / Year	Policy or Initiative	Key Objectives / Focus	African Context & Implementation Outcomes
1955	WHO Global Malaria Eradication Programme (GMEP)	Eradicate malaria globally through vector control and drug treatment.	Limited success in Africa due to weak infrastructure, resistance to DDT, and poor healthcare systems; many regions excluded.
1969–1976	The Garki Project (Nigeria)	Develop realistic models of malaria transmission and evaluate IRS and MDA interventions.	Revealed challenges of eradication in high-transmission settings; established basis for integrated malaria control models.
1988	African Malaria Control Strategy (OAU/WHO)	Strengthen national malaria control programmes (NMCPs).	Marked Africa's renewed regional ownership of malaria response post-GMEP failure.
1998	Roll Back Malaria (RBM) Initiative	Global partnership to reduce malaria burden through ITNs, IRS, and access to treatment.	Expanded ITN use, improved treatment access, but uneven national implementation.
2000	Abuja Declaration (AU Summit)	Commit African leaders to halve malaria deaths by 2010.	Catalysed political commitment, increased donor funding, and national strategic plans.
2005–2010	Scaling Up for Impact (SUFi)	Universal coverage of prevention and treatment interventions.	Notable reductions in malaria mortality; emphasis on ITN distribution and IPT in pregnancy.
2015	WHO Global Technical Strategy (GTS) 2016–2030	Reduce malaria incidence and mortality by $\geq 90\%$.	Guided by data from African surveillance networks; adaptation to local epidemiology.
2018–2021	RTS,S Pilot Implementation (Ghana, Kenya, Malawi)	Evaluate first malaria vaccine in real-world settings.	Demonstrated feasibility, modest efficacy, and community acceptance of vaccination.
2022–2025	R21/Matrix-M Vaccine Roll-out & Genomic Surveillance Expansion	Strengthen immunity and integrate molecular tools into control strategies.	Improved vaccine coverage; genomic data guiding resistance monitoring and localised interventions.
Ongoing (2020s)	One Health & Climate-Resilient Malaria Policies	Integrate environmental, vector, and human health frameworks.	Focus on sustainability, adaptation to ecological change, and Africa-led research networks (e.g., MARA, PAMAfrica).

Following the Roll Back Malaria (RBM) Initiative launched in 1998, African governments, through partnerships with the World Health Organisation (WHO), African Union (AU), and local research networks, began implementing evidence-based strategies such as insecticide-treated nets (ITNs), indoor residual spraying (IRS), and intermittent preventive treatment (IPT). These

interventions were guided by data from entomological and epidemiological studies that demonstrated their cost-effectiveness and population-level benefits (Pyrce et al., 2022; Obembe et al., 2024). Yet, varying ecological conditions, resource limitations, and health system disparities across the continent often determined the degree of implementation success.

Recent years have seen a shift towards data-driven and adaptive malaria control policies, integrating insights from genomic surveillance, real-time mapping of vector resistance, and community-based participatory approaches (Obeagu and Obeagu, 2024). Countries such as Ghana, Rwanda, and Zambia have incorporated national malaria control programmes (NMCPs) with continuous feedback mechanisms linking researchers, policymakers, and frontline health workers. This approach has strengthened accountability, resource allocation, and response to local transmission dynamics.

Nevertheless, sustainable malaria control in Africa must extend beyond biomedical interventions to address socioeconomic, behavioural, and environmental determinants. Poverty, inadequate housing, and weak infrastructures perpetuate malaria transmission cycles, while climate change and population displacement introduce new ecological pressures. As a result, future policy frameworks must embrace a One Health perspective, integrating human, environmental, and animal health for comprehensive resilience. Ultimately, bridging the gap between scientific discovery and practical implementation requires capacity building, local innovation, and sustained investment. Empowering African scientists, expanding regional manufacturing of diagnostics/ vaccines, and ensuring equitable access to preventive tools are critical steps toward self-reliant and sustainable malaria control across the continent.

9. The Future of Malaria Research in Africa

Africa's scientific landscape is rapidly changing. The integration of artificial intelligence, metabolomics, and spatial genomics is transforming malaria surveillance and control. Regional networks are developing AI-driven early warning systems and portable sequencing platforms capable of field-level resistance monitoring. Innovations such as gene drive mosquitoes, microbiome engineering, and precision medicine approaches hold promise, but must be guided by ethical frameworks rooted in African contexts. Ultimately, malaria elimination in Africa will require more than biomedical tools, it demands an integrated approach combining molecular science, socio-economic reform, community engagement, and environmental management.

10. Conclusions

Africa's malaria story has been one of pain, persistence, and progress. From the first microscopic discovery of *Plasmodium* in Algeria to the sequencing of African parasite genomes, the continent has transitioned from a passive subject of research to a leading voice in global malaria science. The journey from microscope to genome mirrors Africa's broader scientific awakening characterised by resilience, innovation, and self-determination. As genomic and molecular tools become increasingly accessible, Africa's greatest opportunity lies in translating knowledge into context-specific solutions that save lives, strengthen systems, and ultimately end malaria's centuries-long reign. The next chapter of malaria control will not be written in foreign laboratories alone; it will also be authored in African research centres, field stations, and communities, where science and survival continue to meet.

Funding: None declared.

Conflicts of Interest: The authors declare no conflict of interest.

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