

THE IMPACT OF SELF-MEDICATION AND INCOMPLETE TREATMENT OF MALARIA ON DEVELOPMENT OF DRUG RESISTANCE: A NARRATIVE REVIEW

*¹Mahmood MOHAMMED, ²Sani Dahiru, ³Bidazum Ishaka Dahiru, ³Faisal Adamu

¹Department of Biological Sciences, Federal University Gusau, Zamfara, Nigeria

²Department of Pharmacology, Ahmadu Bello University, Zaria, Kaduna State, Nigeria

³Department of Biotechnology, Nigerian Defence Academy, Kaduna, Nigeria

*Corresponding Author Email Address: mmohammed@fugusau.edu.ng

ABSTRACT

Malaria remains a major infectious disease, particularly in sub-Saharan Africa, where it continues to pose a significant public health challenge. Although substantial progress has been made in malaria control, the emergence and spread of antimalarial drug resistance threaten efforts toward elimination. This review adopted a narrative literature review approach, examining available literature on the contribution of incomplete antimalarial treatment and self-medication to the development and transmission of drug-resistant *Plasmodium* parasites. It focused on factors contributing to poor treatment adherence, patterns of self-medication, and resistance mechanisms associated with commonly used antimalarial drugs. Poor adherence to prescribed treatment, premature discontinuation of therapy, economic difficulties, limited health literacy, adverse drug reactions, and restricted access to healthcare may result in inadequate drug exposure and selective pressure favouring resistant parasites. Self-medication further contributes through incorrect diagnosis, inappropriate drug selection, under-dosing, medication sharing, and the use of counterfeit or substandard medicines. The review discusses resistance mechanisms involving genetic mutations associated with chloroquine, sulfadoxine-pyrimethamine, and artemisinin. The consequences include treatment failure, increased morbidity and mortality, higher healthcare costs, and setbacks to malaria elimination. Effective control requires improved public health education, access to diagnostic and healthcare services, stronger pharmaceutical regulation, surveillance, adherence support, and continued research. Preserving the effectiveness of existing antimalarial medicines is essential for reducing malaria burden and achieving sustainable malaria control and elimination.

Keywords: Malaria; antimalarial drug resistance; incomplete treatment; self-medication; *Plasmodium* parasites.

INTRODUCTION

Malaria is a life-threatening, vector-borne infectious disease caused by protozoan parasites of the genus *Plasmodium*, which are transmitted to humans through the bites of infected female *Anopheles* mosquitoes (Agwu, 2026). While there are 156 known species of *Plasmodium*, five are primary causes of natural infection in humans: *P. falciparum*, *P. vivax*, *P. ovale*, *P. malariae*, and *P. knowlesi*. Among these, *P. falciparum* is the most virulent and is responsible for more than 99% of global cases, including the majority of severe outcomes and fatalities (Alharbi & Ahmed, 2026; Sant et al., 2026). Once injected into the human host, the parasites complete a developmental stage in the liver before entering the

bloodstream to begin the intra-erythrocytic development cycle, which triggers characteristic symptoms such as fever, aches, and chills (Scovino et al., 2026). If untreated, the infection can progress to severe health issues, including severe anemia, respiratory distress, blood clumping, and neurological complications (Idro & Newton, 2026).

The global burden of the disease remains a critical public health priority. In 2024, the World Health Organization (WHO) estimated that malaria caused approximately 282 million cases and 610,000 deaths worldwide. Sub-Saharan Africa carries a disproportionate share of this burden, accounting for over 90% of all malaria-related infections and deaths (WHO, 2026). Within this region, countries like Nigeria and the Democratic Republic of Congo consistently report the highest numbers, with Nigeria alone contributing roughly 25.9% of global cases and 30.9% of global mortality (Akinwale et al., 2026). Pregnant women and children under five years of age are the most vulnerable populations; in pregnancy, malaria can lead to adverse birth outcomes such as preterm birth, low birth weight, and increased infant mortality (Xie et al., 2026).

A primary challenge to malaria elimination is the continuous evolution of antimalarial drug resistance. Historically, first-line treatments like chloroquine (CQ) and sulfadoxine-pyrimethamine (SP) were abandoned after widespread resistance led to massive treatment failures across Asia and Africa (Patrick et al., 2026). Currently, artemisinin-based combination therapies (ACTs) are the cornerstone of malaria management, but their efficacy is increasingly threatened. Artemisinin partial resistance (ART-R), characterized by delayed parasite clearance, emerged initially in the Greater Mekong Subregion of Southeast Asia but has recently been reported indigenously in several African countries, including Rwanda, Uganda, Eritrea, Ethiopia, and Tanzania. Molecular studies have identified mutations in the parasite's *pfk13* gene as reliable genetic markers for this resistance (Mediavilla et al., 2026; Nima et al., 2026; Obeagu et al., 2026).

The development and spread of antimalarial drug resistance are driven by a complex interplay of biological, environmental, and behavioral factors. Human behavioral factors, including poor adherence to treatment regimens—where patients discontinue medication once symptoms subside but before complete parasite clearance—and widespread self-medication, significantly accelerate the selection and spread of resistant parasite strains. In many endemic communities, malaria is frequently self-treated without laboratory confirmation of diagnosis (Diallo et al., 2026; Mahmood et al., 2026). In High Burden to High Impact (HBHI) countries, healthcare facilities are often concentrated in urban centers, resulting in “medical deserts” in rural areas where

populations commonly rely on indiscriminate drug use or herbal remedies, thereby increasing the risk of treatment failure and mortality (Kojom Foko & Sharma, 2026). In addition, biological and environmental factors further complicate malaria control efforts, including the emergence of insecticide resistance in mosquito vectors and the invasion of new species such as *Anopheles stephensi*. Furthermore, genetic deletions of the *pfhrp2* gene in malaria parasites can lead to diagnostic failure, as rapid diagnostic tests (RDTs) may produce false-negative results, thereby delaying appropriate treatment (Mazigo et al., 2023; Gleiser et al., 2026).

MATERIALS AND METHODS

This study adopted a narrative literature review approach to provide a descriptive and interpretative synthesis of published evidence relevant to the review topic. Literature was identified through searches of PubMed, Scopus, Web of Science, Google Scholar, and African Journals Online (AJOL), alongside reference lists and relevant reports from recognised organisations such as WHO and FAO.

The review considered English-language publications published between 2000 and 2026. Relevant peer-reviewed articles, scholarly publications, and credible technical reports addressing epidemiological, diagnostic, clinical and public health. Duplicate, irrelevant, insufficiently informative, non-English, and unverified sources were excluded.

Selected publications were assessed for relevance, and information was organised thematically and synthesised narratively, highlighting key findings, similarities, differences, emerging patterns, and knowledge gaps. No statistical pooling or meta-analysis was conducted, and the review did not follow a formally registered protocol or systematic screening process.

Limitations of the Narrative Review

This review has limitations inherent in the narrative review approach, including possible selection and interpretation bias due to the authors' judgement. The search may not have captured all relevant publications, and restricting the review to English-language literature may have excluded useful evidence published in other languages. The review did not use a formally registered protocol, comprehensive reproducible screening, or a structured risk-of-bias assessment. Therefore, the findings should be interpreted as a descriptive synthesis rather than an exhaustive or quantitatively pooled assessment. Nevertheless, the review provides an overview of the subject, identifies knowledge gaps, and highlights areas for further research.

Definition and Overview

Incomplete antimalarial treatment is defined as the failure of a patient to adhere to the prescribed dosage, frequency, and duration of a medication regimen. This practice, often referred to as non-adherence, allows malaria parasites to survive and proliferate even after the host has received some medication, providing the selective pressure necessary for the evolution of drug-resistant strains (Bhuyan and Goud, 2026; Obeagu et al., 2026). Factors driving this behavior include clinical mismanagement, poor medication quality, and various socioeconomic barriers that prevent patients from completing their therapy.

Early Symptom Relief

A primary cause of non-adherence is the cessation of treatment once a patient experiences symptomatic relief. (Dalvi and Mekoth,

2026) In many endemic regions, individuals stop taking their medication after only two or three tablets because their fever, aches, or pains have subsided (Gerstenlauer, 2019). Patients often mistakenly believe they have fully recovered, even though asymptomatic parasites may still persist in the bloodstream and continue the transmission cycle.

Adverse Drug Reactions

The experience of adverse drug reactions is a significant deterrent to completing therapy. Side effects such as nausea, vomiting, dizziness, and gastrointestinal discomfort can discourage patients from finishing the full course of a drug (Leporini et al., 2014). While many modern treatments like Artemisinin-based Combination Therapies (ACTs) are generally well-tolerated, the fear or presence of these untoward medical occurrences often leads to treatment abandonment (Mekasha et al., 2026).

Economic Constraints and the Poverty-Disease Cycle

In low-income settings, the poverty-disease cycle forces many households to make difficult choices regarding healthcare. High out-of-pocket expenditures mean that a single malaria episode can be a major financial shock, leading some patients to purchase only a portion of a prescribed dose from unregulated street vendors or "chemists". (Obeagu and Obeagu, 2026) Because visiting a formal clinic is more expensive than buying a few tablets from a vendor, economic barriers directly drive irrational drug use and the selection of resistant parasites.

Poor Health Literacy and Misconceptions

A lack of public awareness regarding infection risks and the necessity of targeted treatments contributes heavily to resistance (Mbane et al., 2026). Studies indicate a strong correlation between education levels and medication adherence; for instance, university graduates are significantly less likely to engage in the risky practice of self-medicating with leftover or incomplete drug courses (Diallo, 2026;).

Drug Supply Interruptions and "Medical Deserts"

The existence of "medical deserts" remote or rural areas where healthcare facilities are absent or inaccessible prevents many from obtaining complete treatment. Rural health centers are frequently understaffed, under-equipped, and suffer from chronic shortages of essential medicines. When facilities run out of first-line ACTs, clinicians may be forced to rely on older, less effective drugs, or patients may be unable to find enough medication to finish a full course of treatment (Ntissi et al., 2026).

Cultural Beliefs and Social Networks

Deep-seated traditional beliefs and misinformation significantly impact medication-taking behavior. In some communities, there is a heavy reliance on the opinions of family members or local social networks over professional medical guidance. This often leads to the informal sharing or borrowing of medications within families, which frequently results in inappropriate dosing and the use of leftover, potentially expired drugs. Addressing these gaps requires engaging with trusted community structures, such as religious institutions and traditional leaders, to foster collective action for appropriate care-seeking (Alfian et al., 2026).

Biological Mechanisms of Antimalarial Drug Resistance Development

The development of antimalarial drug resistance is an evolutionary process driven by natural selection and genetic variation within parasite populations. This phenomenon occurs when malaria parasites evolve mechanisms to evade the effects of drugs that were previously effective, rendering standard treatment protocols ineffective (Patrick et al., 2026).

1. The Selective Pressure Mechanism

Resistance typically arises from spontaneous mutations in the parasite's genome that occur independently of drug exposure (Tenorio, 2025). Drug resistance can occur through several mechanisms, including reducing drug binding by altering the target site so that the medication can no longer attach to its intended enzyme or protein. Resistance may also develop through increased drug efflux, where transport mechanisms actively remove the drug from the parasite's digestive vacuole. Additionally, parasites can increase the production of specific proteins or enzymes—often through increased gene copy numbers—so that standard drug doses are no longer sufficient to inhibit their activity (Vivekanandan et al., 2025; Agwu, 2026).

When a patient follows a complete treatment regimen, drug concentrations remain high enough to eliminate both highly susceptible and partially resistant parasites. However, premature interruption of treatment or under-dosing (often due to self-medication or poor-quality drugs) creates "drug pressure". Under these conditions, drug levels decline before all parasites are cleared. Highly susceptible parasites are eliminated first, while partially resistant strains survive and reproduce. Over multiple transmission cycles, these resistant traits become increasingly prevalent, and mosquito vectors spread the dominant resistant strains throughout communities (Zhang et al., 2026).

Historical Examples of Resistance

Chloroquine (CQ) Resistance

Chloroquine was the primary first-line treatment throughout the mid-20th century due to its safety and low cost (Chikwaro et al., 2026). Chloroquine resistance first emerged in the late 1950s along the Thai–Cambodian border and simultaneously in South America. It subsequently spread to East Africa, including Kenya and Tanzania, by 1978 and reached West Africa by 1980 (Patrick et al., 2026). The primary molecular marker of chloroquine resistance is a single nucleotide polymorphism (SNP) in the *pfcr* gene, specifically the K76T mutation at codon 76, while mutations in the *pfmdr-1* gene also contribute to the resistant phenotype (Dinzouna-Boutamba et al., 2026; Getie and Birhane, 2026). In chloroquine-sensitive parasites, the drug accumulates within the digestive vacuole and disrupts the heme detoxification pathway, causing the buildup of toxic byproducts that kill the parasite (Sanaullah et al., 2025). In resistant parasites, however, the mutant PfCRT protein actively transports chloroquine out of the digestive vacuole, preventing the drug from reaching effective concentrations at its target site (Agwu, 2026).

Sulfadoxine–Pyrimethamine (SP) Resistance

As CQ failed, many countries switched to SP, an antifolate combination drug. Sulfadoxine–pyrimethamine (SP) acts synergistically by inhibiting the folate biosynthetic pathway, which is essential for parasite DNA synthesis. Sulfadoxine targets and inhibits the dihydropteroate synthase (DHPS) enzyme, while

pyrimethamine inhibits dihydrofolate reductase (DHFR) (Mishra et al., 2026). Resistance to SP develops through the stepwise accumulation of point mutations, particularly in the *pfdhfr* gene at codons 108, 59, 51, and 164, and in the *pfdhps* gene at codons 436, 437, 540, 581, and 613 (Yan et al., 2026). These mutations reduce the binding affinity of the drugs to their target enzymes, thereby diminishing their effectiveness. The widespread occurrence of "triple" and "quadruple" mutant parasite strains has rendered SP largely ineffective for the treatment of clinical malaria across most of Africa; however, the drug remains in use for Intermittent Preventive Treatment in Pregnancy (IPTp) (Roux et al., 2021).

Artemisinin (ART) Resistance

Artemisinin-based combination therapies (ACTs) are currently the cornerstone of global malaria treatment (Mekasha et al., 2026). Resistance to artemisinin, characterized by delayed parasite clearance following treatment, was first identified in the Greater Mekong Subregion between 2007 and 2008 (Nima et al., 2026). Although resistance was initially confined to Southeast Asia, indigenous artemisinin-resistant parasite populations have since been confirmed in Rwanda, Uganda, Eritrea, Ethiopia, and Tanzania. At the molecular level, resistance is primarily associated with mutations in the propeller domain of the *pfk13* gene (Kojom Foko et al., 2025; Mohammadi et al., 2026).

Recent genomic studies have also identified mutations in the *PfRAD5* and *PfWD11* genes as important genetic factors associated with delayed parasite clearance (Vishwanatha et al., 2025). Biologically, the K13 protein plays a role in hemoglobin uptake and degradation within the parasite. Mutations in K13 reduce hemoglobin endocytosis, resulting in lower heme availability for artemisinin activation and thereby enhancing parasite survival during drug exposure. Furthermore, resistant parasites may undergo prolonged ring-stage arrest, allowing additional time to recover from drug-induced damage and increasing their likelihood of survival (Dutta et al., 2025).

Self-Medication and Antimalarial Drug Resistance

Definition and Prevalence

Self-medication is the practice of using drugs to treat self-diagnosed symptoms without the consultation, diagnosis, prescription, or supervision of qualified healthcare professionals (Afzal et al., 2025). In many malaria-endemic countries, antimalarial medications are highly accessible through community pharmacies, patent medicine vendors (PMVs), street markets, and informal sellers (Obiobasi et al., 2026).

The prevalence of self-medication remains alarmingly high due to a combination of systemic and socioeconomic factors. In many rural areas, long distances to healthcare facilities create "medical deserts," making formal healthcare services difficult to access (Aljinović-Vučić, 2025). The problem is further compounded by chronic shortages of healthcare workers and essential medicines, which often force patients to seek quicker alternatives outside the formal health system. Economic barriers, including consultation fees and laboratory testing costs, also make self-medication a more affordable option than visiting a healthcare facility. Additionally, individuals who have previously experienced malaria may develop a false sense of confidence in their ability to recognize and treat recurrent symptoms without professional guidance. The convenience and immediate symptomatic relief provided by readily available medications, such as analgesics, often encourage individuals to prioritize self-treatment over seeking a definitive

diagnosis and appropriate medical care (Bouwe et al., 2026).

The Risk of Incorrect Diagnosis

A major danger of self-medication is the high likelihood of misdiagnosis. Because fever is a non-specific symptom that occurs in many infectious and non-infectious diseases, individuals often assume that any febrile illness is malaria and initiate treatment without proper diagnostic testing (Kumar et al., 2025). As a result, antimalarial drugs are frequently used to treat conditions such as typhoid fever, dengue fever, COVID-19, respiratory infections, pneumonia, bacterial sepsis, and other systemic infections. The inappropriate use of antimalarial medications for non-malarial illnesses not only delays accurate diagnosis and appropriate treatment but also increases unnecessary drug exposure (Belay et al., 2025). This unnecessary exposure can exert selective pressure on malaria parasites that may be present at subclinical levels, thereby contributing to the emergence and spread of antimalarial drug resistance.

Incorrect Drug Selection

Individuals who self-medicate often choose treatments based on personal preference, outdated prescriptions, or recommendations from family members and friends rather than current clinical guidelines (Aljinović-Vučić, 2025). This practice frequently results in the use of ineffective, including antimalarial monotherapies, which involve the use of artemisinin derivatives or partner drugs alone despite their prohibition by the World Health Organization (WHO) due to the risk of resistance development. Self-medication may also involve the continued use of outdated drugs such as chloroquine (CQ) or sulfadoxine-pyrimethamine (SP) in regions where widespread resistance has rendered these medications ineffective for clinical treatment (Amaka et al., 2025). In addition, misconceptions that antibiotics can cure malaria or nonspecific symptoms such as body pains contribute to the inappropriate use of antimicrobial agents and the growing problem of antimicrobial resistance (AMR). The selection of unsuitable treatments often results in incomplete parasite clearance, prolonged infections, and increased opportunities for the transmission and spread of drug-resistant malaria parasites (Kabli, 2025).

Inappropriate Dosage and Treatment Duration

Self-medication is strongly associated with irrational drug-use practices that often fail to achieve therapeutic drug concentrations necessary for effective treatment (Wang, 2026). One common practice is under-dosing, in which individuals take fewer tablets than prescribed in an attempt to reduce costs or reserve medication for future use. Another frequent behavior is the premature discontinuation of treatment once symptoms such as fever or headache improve, leaving behind surviving parasites that may possess partial resistance to the drug. Medication sharing is also widespread, with a single prescribed treatment course being divided among multiple family members, resulting in each individual receiving an inadequate dose (Sharma et al., 2025). These practices reduce treatment effectiveness, promote treatment failure, and create favorable conditions for the selection and spread of drug-resistant malaria parasites.

These behaviors create "drug pressure," where drug concentrations are high enough to kill susceptible parasites but low enough to allow mutant, resistant strains to survive and multiply.

Use of Counterfeit and Substandard Medicines

The global market for counterfeit and substandard antimalarial drugs represents a major driver of antimalarial resistance, particularly in low- and middle-income countries (Mekasha et al., 2026). These poor-quality medicines often contain inadequate amounts of the active pharmaceutical ingredient, with analyses of some chloroquine (CQ) and sulfadoxine-pyrimethamine (SP) products obtained from informal markets revealing only a fraction of the required therapeutic dose. In other cases, counterfeit drugs may contain incorrect, substituted, or degraded chemical components that provide little or no therapeutic benefit. Some falsified antimalarial products contain no active medicinal ingredients whatsoever, resulting in complete treatment failure. The use of such substandard and counterfeit medications exposes parasites to subtherapeutic drug concentrations, promotes the survival of resistant strains, and contributes significantly to the emergence and spread of antimalarial drug resistance (Onwujekwe et al., 2009).

Exposure to these substandard products essentially "vaccinates" the parasite population against the drug, as the low concentrations allow the parasites to adapt and evolve mechanisms—such as increased drug efflux or target site mutations—to survive future treatments. Strengthening regulatory oversight and supply chain management is essential to removing these dangerous products from the market.

Contribution to Community-Level Resistance

The development of resistance within a single individual does not remain an isolated clinical event; rather, it fuels a cycle of community-wide transmission (Heseltine, 2000). When a patient receives sub-therapeutic doses due to non-adherence or self-medication, a "drug pressure" is created that eliminates susceptible parasites while allowing resistant strains to survive and reproduce. These surviving parasites are then ingested by female *Anopheles* mosquitoes during a blood meal and subsequently transmitted to healthy members of the population (Chikwendu et al., 2019).

This spread is further exacerbated by human movement, such as migration for economic, religious, or conflict-related reasons, which allows resistant parasites to bypass geographic barriers and establish themselves in new regions. Furthermore, in "medical deserts" remote areas lacking formal healthcare neglected populations often act as significant reservoirs for resistant parasite transmission, as they may indiscriminately use ineffective herbal medicines or poor-quality drugs (Chikwendu et al., 2019; Janjoter et al., 2026).

Combined Public Health Impact

1. Increased Treatment Failure

As resistance to primary therapies like Artemisinin-based Combination Therapies (ACTs) increases, the ability of clinicians to cure infections is fundamentally compromised. Patients experience recrudescence, where the initial infection is not cleared, and symptoms return shortly after therapy (Wu et al., 2025). In some African sites, the PCR-corrected efficacy of Artemether-Lumefantrine (AL) has already dropped below the critical WHO threshold of 90%, necessitating urgent changes to national treatment protocols (Van Wyk et al., 2026).

2. Increased Morbidity and Mortality

The rise of drug-resistant malaria fundamentally changes the treatability of the disease by transforming otherwise manageable

infections into potentially life-threatening conditions. Drug-resistant malaria infections are associated with prolonged disease duration due to slower parasite clearance, resulting in patients remaining ill for extended periods (White et al., 2026). These infections also increase the risk of severe complications, including severe anemia, respiratory distress, and neurological impairment associated with severe malaria. In addition, drug resistance contributes to higher fatality rates, with antimicrobial resistance (AMR) in Nigeria alone being linked to an estimated 60,000 deaths annually, a burden that continues as first-line antimalarial drugs progressively lose their effectiveness (Alabi et al., 2025).

Vulnerable populations carry the heaviest burden. Children under five and pregnant women are at the highest risk; for example, malaria in pregnancy is estimated to cause hundreds of thousands of infant deaths annually through low birth weight and preterm delivery (Minwuyelet et al., 2026).

Economic Consequences

Drug resistance imposes a significant financial burden on both national economies and individual households, contributing to a self-reinforcing cycle of poverty and disease (Mbanefo et al., 2026). At the macroeconomic level, malaria-endemic countries experience an average annual reduction of approximately 1.3% in GDP due to lost productivity, while antimicrobial resistance (AMR)-related costs in Nigeria alone are estimated to reach billions of naira. At the household level, out-of-pocket health expenditure in Nigeria accounts for more than 75% of total healthcare spending, and a single episode of malaria can cost nearly ₦10,000 in direct treatment expenses, often leading to catastrophic health expenditure in which families are forced to divert funds from essential needs such as food and children's education (Elendu, 2026). In addition, productivity losses are significant, as repeated illness episodes and caregiving responsibilities reduce workforce participation, particularly among low-income households whose livelihoods depend heavily on physical labor.

Threat to Malaria Elimination Goals

The emergence of resistance represents the single greatest threat to the WHO Global Technical Strategy goal of a 90% reduction in malaria burden by 2030. While global incidence declined significantly between 2000 and 2015, progress has since stalled, with case numbers rising in high-burden countries like Nigeria and the DRC (Alharbi & Ahmed, 2026).

Resistance undermines the entire "test and treat" framework by rendering current diagnostic antigens invisible to tests and current medicines ineffective. If resistance continues to spread unchecked, it threatens to reverse decades of public health gains, potentially plunging communities back into an era where common malaria infections are untreatable. Sustaining progress requires multisectoral solutions, strengthened surveillance, and a massive investment in next-generation therapies (Olebo et al., 2025).

Strategies for Reducing Antimalarial Resistance Development

To preserve the efficacy of current antimalarial therapies and combat the rise of resistant strains, a multifaceted approach combining clinical, regulatory, and community-based interventions is required.

1. Strengthening Public Health Education

Low public awareness regarding infection risks and appropriate treatment practices contributes significantly to the spread of drug resistance. Community-based interventions are therefore

necessary to address the misconception that medicines such as antibiotics are "cure-alls" and to reinforce the fact that they are not effective against malaria. Effective communication strategies should include the use of radio messages delivered in local languages, market-day outreach programs, and social media platforms to ensure wide population coverage. Targeted education initiatives, particularly school-based health education, are also important, as children can serve as agents of behavioural change within their households. The participation of trusted community figures, including religious leaders, traditional rulers, and celebrities, can strengthen public confidence in health messages and encourage appropriate medication use and timely healthcare-seeking behavior.

2. Expanding Access to Diagnostic Testing

The "test and treat" guideline is often not followed in malaria-endemic regions, resulting in presumptive treatment and unnecessary drug pressure that contributes to drug resistance. Strengthening diagnostic capacity requires significant investment in laboratory infrastructure, equipment, and trained healthcare personnel, particularly in rural health facilities that currently lack adequate microbiology services. The adoption of innovative diagnostic tools, including automated rapid diagnostic tests (RDTs) and molecular techniques such as polymerase chain reaction (PCR), is necessary to detect low-density malaria infections that are often missed by traditional microscopy and standard RDTs. In addition, effective monitoring and regulation of private sector drug vendors is essential.

3. Improving Access to Healthcare Services

The existence of "medical deserts," which are rural regions without accessible healthcare facilities, forces many populations to rely on informal and often inappropriate self-medication practices. Addressing this challenge requires the strengthening of grassroots healthcare delivery through the training and deployment of Community Health Workers (CHWs) to provide essential services to hard-to-reach populations. In addition, innovative service delivery models such as telemedicine support and improved sample transport systems are necessary to bridge the gap between rural patients and secondary or tertiary diagnostic facilities. Economic interventions, including the reduction of high consultation fees and the provision of subsidized health commodities such as artemisinin-based combination therapies (ACTs) and insecticide-treated nets, are also essential in breaking the poverty–disease cycle that contributes to irrational drug use.

4. Regulation of Drug Distribution

Strict enforcement of existing pharmaceutical policies is necessary to close the gap between "prescription-only" classifications and real-world dispensing practices. The implementation of digital verification systems for real-time prescription authentication can empower consumers while discouraging illegal and unauthorized drug sales. Furthermore, addressing the widespread circulation of substandard and counterfeit medicines is critical, as it is estimated that up to 30% of antimalarial drugs in sub-Saharan Africa are of poor quality or falsified. Strengthening regulatory oversight across the pharmaceutical supply chain is therefore essential to eliminate these low-quality products, which expose malaria parasites to sub-therapeutic drug concentrations and inadvertently contribute to the development of drug resistance (Al-Jedai et al., 2022; Fadlallah et al., 2016).

5. Enhancing Adherence Support

Improving adherence requires moving beyond simple instructions to a deeper understanding of the behavioral beliefs that influence

patient decisions and treatment practices. Behavioral interventions, such as video-based health messages, have shown promise in improving the uptake of preventive therapies among vulnerable populations. In addition, antimicrobial stewardship training for frontline health workers is essential, as it equips them with the knowledge and communication skills needed to clearly explain why patients must complete a full course of treatment even after symptoms begin to subside.

6. Strengthening Surveillance Systems

Continuous monitoring is considered the “gold standard” for identifying when malaria treatment protocols need to be revised. Therapeutic Efficacy Studies (TES) must be routinely conducted at sentinel sites, with patients followed for 28 to 42 days to accurately distinguish between reinfection and true treatment failure (recrudescence). The integration of molecular surveillance, including genetic analysis of markers such as *pfk13* (associated with artemisinin resistance) and *pfhrp2* (associated with diagnostic failure), into routine monitoring systems enables the early detection of emerging indigenous resistance. In addition, the use of centralized, near-real-time digital reporting systems allows policymakers to proactively adjust treatment and control strategies based on up-to-date epidemiological data.

7. Research and Development

Staying ahead of evolving malaria parasites requires sustained investment in new technologies and therapeutic strategies. Research into next-generation medicines should prioritize hybrid drug development, resistance-reversal agents, and new combination therapies that incorporate drugs with independent or opposing resistance pressures. The rollout of malaria vaccines represents a major advancement in malaria prevention, while future research and development efforts should focus on transmission-blocking vaccines and the application of mRNA technology to further reduce disease transmission and burden. In addition, organizations such as the Medicines for Malaria Venture (MMV) play a crucial role in the development of affordable, child-friendly antimalarial formulations aimed at protecting the most vulnerable populations.

Conclusion

Malaria remains a major global health challenge, especially in sub-Saharan Africa, where *Plasmodium falciparum* causes most cases and deaths among vulnerable groups like children and pregnant women. Its persistence is worsened by biological, environmental, and human factors, with growing antimalarial drug resistance threatening the effectiveness of treatments such as ACTs. Drug resistance results from multiple interconnected causes, including poor treatment adherence, self-medication, limited healthcare access, weak diagnostic systems, substandard medicines, and parasite and vector evolution. These factors drive treatment failure, increased illness and death, economic burden, and strain on health systems, putting malaria control gains at risk. Effective control requires a coordinated global response focused on strengthening health systems, improving diagnosis and treatment access, enforcing drug quality regulations, increasing public awareness, and investing in surveillance and research. Sustained political commitment and innovation are essential to prevent reversal of progress and support malaria elimination.

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