

ACTs: Efficacy, Resistance and Urgent Global Action

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Introduction

Artemisinin-based Combination Therapies (ACTs) are crucial for uncomplicated malaria, especially in children. Reviews affirm their vital role, highlighting maintained efficacy and a generally favorable safety profile. Yet, continuous surveillance is essential to monitor potential resistance, ensuring these drugs remain effective for pediatric populations [1].

Here's the thing: artemisinin resistance in African *Plasmodium falciparum* parasites is a significant concern. Genetic markers, like kelch13 mutations, are linked to this resistance, with dire implications for current ACT efficacy. This demands accelerated drug development and resistance containment to prevent a major public health setback [2].

Developing new ACTs faces substantial hurdles. Progress continues, but persistent challenges remain in bringing novel therapies to market. An urgent necessity exists for innovative compounds to outpace drug resistance, maintaining effective treatment options against malaria [3].

Implementing ACTs in sub-Saharan Africa involves complex practicalities. Systematic reviews identify both facilitating factors that aid successful deployment and persistent barriers hindering widespread, effective use. These insights are crucial for strengthening malaria control programs [4].

What this really means is understanding resistance is foundational. The genetic basis of artemisinin resistance in *Plasmodium falciparum* focuses on the critical role of kelch13 gene mutations. This elucidates how these genetic changes impact drug efficacy, providing knowledge for designing new drugs and surveillance strategies [5].

Let's break it down: a thorough assessment of ACT safety and tolerability for uncomplicated *Plasmodium falciparum* malaria in Africa confirms these therapies are generally well-tolerated and safe. This finding is crucial for public health acceptance and broad application [6].

Understanding varied drug pharmacokinetics in special populations is important. Factors like age, pregnancy, and co-infections can alter drug absorption, distribution, metabolism, and excretion. This stresses the importance of tailored dosing strategies to optimize treatment efficacy and safety in vulnerable groups [7].

ACTs have significantly reduced malaria incidence across sub-Saharan Africa. Quantitative analyses underscore their profound success as a cornerstone of malaria control efforts. This demonstrates their indispensable role in public health interventions aimed at disease reduction [8].

This review uncovers the alarming prevalence and underlying causes of substandard and falsified ACTs in sub-Saharan Africa. These illicit drugs undermine

malaria treatment efficacy, contribute to resistance, and hinder global eradication efforts, demanding robust regulatory action [9].

A critical assessment of artemisinin and partner drug efficacy across Africa reinforces the need for consistent, high-quality surveillance programs. These programs are necessary to promptly detect and respond to any emerging drug resistance, safeguarding the future of malaria treatment [10].

Description

Artemisinin-based Combination Therapies (ACTs) are the frontline treatment for uncomplicated malaria, particularly for children, where their efficacy and safety profiles are consistently affirmed [1, 6]. These therapies have significantly reduced malaria incidence across sub-Saharan Africa, establishing ACTs as an indispensable tool in malaria control programs [8]. However, this success is continually challenged by various factors, most notably the insidious threat of drug resistance.

A paramount concern is the emergence and spread of artemisinin resistance in *Plasmodium falciparum* parasites, particularly in Africa [2]. What this really means is understanding the genetic basis of this resistance is crucial. Mutations in the kelch13 gene are strongly implicated, acting as key genetic markers for resistance [2, 5]. These genetic changes directly impair how effectively ACTs clear parasites, posing a severe threat to current treatment protocols and potentially leading to widespread treatment failures. This situation urgently calls for accelerated drug development and robust strategies to contain resistance, preventing a major public health crisis [2].

Here's the thing: developing new ACTs to combat evolving resistance is a complex and challenging endeavor. There's a persistent need for innovative compounds to outpace drug resistance, ensuring treatment options remain effective against malaria [3]. Beyond drug development, implementing ACTs in regions like sub-Saharan Africa presents operational hurdles. Systematic reviews identify both facilitating factors that aid successful deployment and significant barriers hindering widespread, effective use. These insights are vital for tailoring and strengthening malaria control programs [4].

Adding to these challenges is the issue of substandard and falsified ACTs, an alarming problem particularly prevalent in sub-Saharan Africa [9]. These illicit drugs, often containing insufficient or incorrect active ingredients, not only fail to treat patients effectively but also contribute directly to the development and spread of drug resistance. Their presence undermines legitimate malaria treatment efforts and severely impedes global eradication goals, necessitating urgent and robust regulatory action [9]. Furthermore, the pharmacokinetics of ACTs can vary significantly in special populations, such as young children, pregnant women, or

individuals with co-infections. Factors like age, pregnancy, and co-infections can alter drug absorption, distribution, metabolism, and excretion [7]. This variability underscores the importance of developing tailored dosing strategies to optimize both efficacy and safety in these vulnerable groups [7].

To maintain the gains made against malaria and effectively counter drug resistance, consistent and high-quality surveillance of artemisinin and its partner drug efficacy across Africa is indispensable [10]. This proactive monitoring allows for prompt detection and informed response to any emerging drug resistance, safeguarding the future of malaria treatment. Without such vigilance, the advances achieved through ACTs could be jeopardized, highlighting the continuous commitment required in research, development, implementation, and surveillance to sustain the fight against malaria [10].

Conclusion

Artemisinin-based Combination Therapies (ACTs) are unequivocally vital for treating uncomplicated malaria, especially in pediatric populations, consistently demonstrating sustained efficacy and a favorable safety profile. These therapies have profoundly impacted global health, significantly reducing malaria incidence across sub-Saharan Africa and establishing themselves as a cornerstone of public health interventions. Yet, despite their proven success and indispensable role, the ongoing challenge of artemisinin resistance presents a critical threat. This resistance, driven by specific genetic mutations such as kelch13 in *Plasmodium falciparum*, gravely undermines treatment efficacy and poses a significant risk to global malaria control efforts. This situation urgently calls for accelerated action in developing new antimalarial drugs and implementing robust resistance containment strategies.

Beyond the biological challenge of resistance, the practical implementation of ACTs faces considerable hurdles in regions like sub-Saharan Africa. Both facilitating factors and persistent barriers impact their widespread and effective use. Further complicating matters is the alarming prevalence of substandard and falsified ACTs, which not only compromise treatment outcomes but also actively fuel the development and spread of drug resistance. Additionally, the varied pharmacokinetics of ACTs in special populations, including young children and pregnant women, necessitate tailored dosing strategies to ensure optimal efficacy and safety. To safeguard the long-term effectiveness of ACTs, continuous, high-quality surveillance of drug efficacy across Africa is indispensable, allowing for prompt detection and effective response to any emerging resistance, thus ensuring these critical treatments remain viable for future malaria eradication goals.

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Conflict of Interest

None.

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