

Tools for Malaria Disease Reduction and Elimination in Endemic Sub-Saharan Africa Countries: A Rapid Evidence Review



Background

Malaria remains a major public health concern despite the massive global control and elimination efforts [1]–[3]. Malaria-endemic countries accounted for the highest incidence (95%) and mortality (96%) due to the disease in 2022 [3]. Over half (54.8%) of these malaria cases were from six sub-Saharan countries namely: Nigeria, the Democratic Republic of Congo, Uganda, Mozambique, Angola and Burkina Faso [3] (Figure 1). Malaria disease burden is exacerbated by the deterioration of the health care systems in some countries [4], increasing urbanization, climate change [5], changes in mosquito biting behaviour [9], and insecticide and drug resistance [6]–[8].

The World Health Organization (WHO) developed the Global Technical Strategy for Malaria (GTSM) to guide malaria control and elimination efforts from 2016 to 2030. The key targets included the reduction of malaria case incidence and mortality by at least 90% by 2030, eliminating Malaria in at least 35 countries by 2030, and preventing the re-establishment of Malaria in all malaria-free countries by 2030 [10]. To attain the GTSM targets, more innovative tools and superior approaches to malaria prevention and case management are required.

Key Messages

- Massive scale up of targeted malaria interventions can lead to a substantial decrease in malaria cases.
- Leveraging on participatory planning and decision-making for malaria tools development and deployment is key for public awareness, trust and acceptance.
- Malaria advocacy and multisectoral approaches provide opportunities for malaria prevention efforts.
- The gene drive mosquitoes for malaria disease control and elimination could be a game changer if successfully developed and proven safe.

This evidence brief provides information on the existing tools for malaria incidence reduction and elimination, including the tools' strengths, limitations, and the implementation/adaptation barriers within the sub-Saharan Africa region.

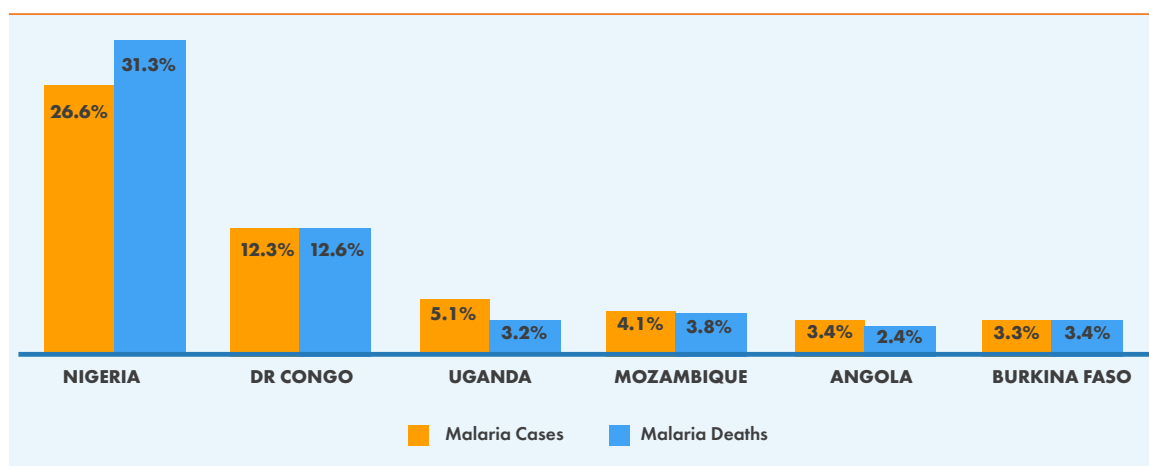


Figure 1: Malaria cases and deaths in endemic sub-Saharan Africa; World Malaria Report, 2022

Objectives

To provide a rapid evidence summary of sub-Saharan Africa's existing malaria control and elimination tools.

Methods

This rapid evidence review searched for literature from the database's inception to January 2023 in electronic publication databases and grey resources. This evidence summary included malaria interventions in the Malaria endemic sub-Saharan African countries.

Results

The tools used for malaria control and reduction in sub-Saharan Africa include anti-malarial drugs, including artemisinin combination therapies; malaria vaccines; vector control, including indoor residual spraying (IRS) and insecticide-treated nets (ITNs). Other potential

tools still under development include novel genetic approaches such as gene drives and sterile insect techniques. For effective treatment of malaria disease, prompt diagnosis plays a critical role in early detection and control. Table one below summarizes Malaria control intervention across sub-Saharan Africa.

Challenges associated with malaria control tools

The challenges identified with the use of anti-malaria drugs include parasite resistance attributed to the increasing circulation and usage of counterfeit drugs [11] and side effects from some drugs, compromising their widespread use in mass administration for elimination [12]. Additionally, there are high drug or vaccine development costs requiring logistical and research investments [13]–[15].

Table 1 Summary of malaria elimination interventions

| Malaria elimination approach | Examples of tools for malaria reduction and eradication |
|--------------------------------|--|
| Vector prevention & control | Larvicides, attractive sugar baits, long-lasting insecticidal treated nets (LLINs), indoor residual spraying, novel genetic approaches such as gene drive mosquitoes, sterile insect technique, and heritable bacterial endosymbionts (Wolbachia). |
| Malaria therapeutic treatments | Amodiaquine, Artemisinin-based combination therapies, Artemisinin monotherapies and novel malaria medicines. |
| Vaccines | These include pre-erythrocytic, blood stage and transmission-blocking vaccines. Currently, only RTS, S Vaccine has been approved by WHO for widespread use in the prevention of Malaria among children in Africa. |

Vector prevention and control presents a couple of challenges highlighted, such as vector resistance to pyrethroids [16] and vector mutations that present a particular threat to the small gains in malaria reduction and control in sub-Saharan Africa [17]. Furthermore, the changing biology and epidemiology of malaria vectors, including the feeding and resting patterns with the increased ITN use, significantly deter the efforts and gains made in malaria control. These behavioural patterns thereby allow the mosquitoes to avoid contact with the toxic product or limit the duration of contact.

Additionally, using the sterile insect technique, where mass-reared insects are sterilized and released to the wild to compete with wild males, may lead to reproductive fitness loss and leave the environment where the mosquito thrives unchanged. Consequently, the mosquito populations revert to their original density as soon as treatments end or when mosquitoes become resistant to the insecticide [18]. Furthermore, the slow acceptance of new technologies affects mosquitoes' gene drive due to mutation controversy [13].

The challenges posed by malaria diagnostics include misdiagnosis due to high asymptomatic prevalence in tropical communities [19], weak health and information systems and uncertain funding streams [14], and limited high-level diagnostic laboratory capacity [20]. Important to note is the fragile health systems in the sub-Saharan region which were further weakened by the COVID-19 pandemic that disrupted health services [2].

Strategies to eliminate malaria

Identifying new and long-lasting insecticide formulations is a key ingredient of vector control strategies. Additionally, designing interventions that address the altered feeding and resting behavioural patterns of malaria vectors may serve to reduce vector populations further [15].

Vaccines play an important role in malaria elimination and clinical disease reduction [21]. For example, the WHO-approved RTS, S vaccine for use among children who are a high-risk group [2], [22] confers 30% protection against clinical infection for 4 years [21]. Further, it is worth noting that several malaria vaccines are under development [15].

Malaria elimination strategies should include advocacy and multisectoral approaches. For example, integrating poverty alleviation programmes that improve housing as part of malaria control interventions [1] and strengthening the community's socio-behavioural change in the malaria prevention efforts [23].

Discussion

Malaria persists in sub-Saharan Africa despite the massive global efforts towards its elimination and control. To accelerate malaria elimination efforts, malaria drug and vector resistance require urgent innovative solutions [16], [24]–[28]. Further, to address drug resistance, investments and research are needed to develop new drugs and formulations [29].

Vector resistance to pyrethroids has hampered the effectiveness of LLIN and IRS in malaria control efforts [16]. Additionally, tool development for vector control is faced with significant barriers, including financial and infrastructural deficiencies [30]. One strategy by WHO and The Global Fund is engaging with industries to increase market production for non-pyrethroid IRS formulations and low-cost models [30]. Moreover, countries need to invest in national insecticide resistance monitoring and management plans [30].

The vaccine for malaria prevention among children in Africa is a major stride to malaria prevention and control [31]. Some recent achievements in the malaria vaccine development are the R21 /Matrix-M vaccine which has shown over 74% efficacy in a randomized control trial from Burkina Faso [32], [33]. Importantly, Ghana has taken the lead in authorising and including the R21 malaria vaccine for children (5 to 36 months) with the highest risks of death from the disease [34].

These, therefore, illustrate country-level efforts in the uptake and rollout of an effective and safe vaccine that is yet to be recommended by WHO to acquire international funding.

Using integrated approaches and the gene drive mosquitoes for malaria disease control and elimination could be a game changer if successfully developed and proven safe. It is therefore important to prioritize the resources for the development, testing and deployment of these innovative tools in malaria endemic regions [2], [10], [14]. Over and above, it is important to invest in country-specific needs and strengthen regional collaborations and resource mobilization to develop and adopt effective malaria elimination strategies.

Conclusion

The application and use of malaria control tools need to consider safety concerns, cost-effectiveness, efficacy and regulatory landscapes in sub-Saharan African countries to gain the social license they need to be successfully deployed.

REFERENCES



- 1 T. A. Tizifa, A. N. Kabaghe, R. S. Mccann, H. Van Den Berg, M. Van Vugt, and K. S. Phiri, "Prevention Efforts for Malaria," 2018.
- 2 World malaria report 2021.
- 3 World malaria report 2022.
- 4 R. G. A. Feachem et al., "Malaria eradication within a generation: ambitious, achievable, and necessary," *The Lancet*, 2019.
- 5 The malERA Consultative Group on Vector Control, "A research agenda for malaria eradication: vector control," *PLoS Med*, 2011.
- 6 Global technical strategy for malaria 2016-2030, 2021 update.
- 7 R. W. Steketee, J. M. Miller, and C. Kawesha, "Implications of the MDA Trial in Southern Province, Zambia, for Malaria Control and Elimination," *Am J Trop Med Hyg*, 2020.
- 8 T. P. Eisele et al., "Impact of Four Rounds of Mass Drug Administration with Dihydroartemisinin-Piperaquine Implemented in Southern Province, Zambia," *Am J Trop Med Hyg*, 2020.
- 9 K. Marwa et al., "Therapeutic efficacy of artemether-lumefantrine, artesunate-amodiaquine and dihydroartemisinin-piperaquine in the treatment of uncomplicated Plasmodium falciparum malaria in Sub-Saharan Africa: A systematic review and meta-analysis," *PLoS One*, 2022.
- 10 World malaria report 2020: 20 years of global progress and challenges.
- 11 A. M. Dondorp, F. M. Smithuis, C. Woodrow, and L. von Seidlein, "How to Contain Artemisinin- and Multidrug-Resistant Falciparum Malaria," *Trends Parasitol*, 2017.
- 12 P. L. Alonso et al., "A research agenda to underpin malaria eradication," *PLoS Med*, 2011.
- 13 R. G. A. Feachem et al., "Malaria eradication within a generation: ambitious, achievable, and necessary," *Lancet*, 2019.
- 14 J. Hemingway et al., "Tools and Strategies for Malaria Control and Elimination: What Do We Need to Achieve a Grand Convergence in Malaria?" *PLoS Biol*, vol. 14, no. 3, Mar. 2016, doi: 10.1371/JOURNAL.PBIO.1002380.
- 15 "malERA: An updated research agenda for diagnostics, drugs, vaccines, and vector control in malaria elimination and eradication," *PLoS Med*, 2017.
- 13 R. G. A. Feachem et al., "Malaria eradication within a generation: ambitious, achievable, and necessary," *Lancet*, 2019.
- 16 C. Sokhna, M. O. Ndiath, and C. Rogier, "The changes in mosquito vector behaviour and the emerging resistance to insecticides will challenge the decline of malaria," *Clin Microbiol Infect*, 2013.
- 17 K. Karunamoorthi, "Malaria Vaccine: A Future Hope to Curtail the Global Malaria Burden," *Int J Prev Med*, 2014.
- 18 S. Wang and M. Jacobs-Lorena, "Genetic approaches to interfere with malaria transmission by vector mosquitoes," *Trends Biotechnol*, 2013.
- 19 N. A. V. Beare, S. Lewallen, T. E. Taylor, and M. E. Molyneux, "Redefining cerebral malaria by including malaria retinopathy," *Future Microbiol*, vol. 6, no. 3, pp. 349–355, Mar. 2011, doi: 10.2217/FMB.11.3.
- 20 N. A. V. Beare, S. Lewallen, T. E. Taylor, and M. E. Molyneux, "Redefining cerebral malaria by including malaria retinopathy," *Future Microbiol*, vol. 6, no. 3, pp. 349–355, Mar. 2011, doi: 10.2217/FMB.11.3.
- 21 I. A. Cockburn and R. A. Seder, "Malaria prevention: from immunological concepts to effective vaccines and protective antibodies," *Nature Immunology*, 2018.
- 22 WHO recommends groundbreaking malaria vaccine for children at risk." <https://www.who.int/news/item/06-10-2021-who-recommends-groundbreaking-malaria-vaccine-for-children-at-risk> (accessed Mar. 10, 2023).
- 23 I. R. Moshi et al., "Community perceptions on outdoor malaria transmission in Kilombero Valley, Southern Tanzania," *Malar J*, 2017.

- 24 T. Gari and B. Lindtjørn, "Reshaping the vector control strategy for malaria elimination in Ethiopia in the context of current evidence and new tools: Opportunities and challenges 11 Medical and Health Sciences 1108 Medical Microbiology," *Malar J*, 2018.
- 25 N. Noreen, A. Ullah, S. M. Salman, Y. Mabkhot, A. Alsayari, and S. L. Badshah, "New insights into the spread of resistance to artemisinin and its analogues," *J Glob Antimicrob Resist*, 2021.
- 26 G. Benelli and J. C. Beier, "Current vector control challenges in the fight against malaria," *Acta Trop*, 2017.
- 27 C. F. Oliva et al., "Current status and future challenges for controlling malaria with the sterile insect technique: technical and social perspectives," *Acta Trop*, 2014.
- 28 E. B. Esu, C. Oringanje, and M. M. Meremikwu, "Intermittent preventive treatment for malaria in infants," *Cochrane Database Syst Rev*, 2019.
- 29 J. Achan, J. Mwesigwa, C. P. Edwin, and U. D'alessandro, "Malaria medicines to address drug resistance and support malaria elimination efforts," 2017.
- 30 A. P. Mnzava et al., "Implementation of the global plan for insecticide resistance management in malaria vectors: Progress, challenges and the way forward," *Malar J*, 2015.
- 31 A. Brooks, O. J. T. Briët, D. Hardy, R. Steketee, and T. A. Smith, "Simulated impact of RTS,S/AS01 vaccination programs in the context of changing malaria transmission," *PLoS One*, 2012.
- 32 M. S. Dattoo et al., "Efficacy of a low-dose candidate malaria vaccine, R21 in adjuvant Matrix-M, with seasonal administration to children in Burkina Faso: a randomised controlled trial," *The Lancet*, 2021.
- 33 M. S. Dattoo et al., "Efficacy and immunogenicity of R21/Matrix-M vaccine against clinical malaria after 2 years' follow-up in children in Burkina Faso: a phase 1/2b randomised controlled trial," *Lancet Infect Dis*, 2022.
- 34 "Ghana sets milestone as first country to authorize new malaria vaccine."

Authors

Sandra Y. Oketch¹, Pauline Soy¹, Adauo Anyiam-Osigwe¹, Edel Sakwa¹, Patricia Wamukota¹, Wolfgang Richard Mukabana¹, Rose Oronje¹

Institutional affiliation

1 African Institute for Development Policy (AFIDEP)

AFIDEP

African Institute for
Development Policy

Kenya Office

6th Floor (Block A), Westcom Point Building,
Mahiga Mairu Avenue, Off Waiyaki Way, Westlands
P.O. Box 14688-00800, Nairobi, Kenya
Phone: +254 20 203 9510 | +254 716 002 059



African Institute for Development Policy

@Afidep

Malawi Office

3rd floor, Public Service Pension Fund Building, Presidential Way, City Centre,
P.O. Box 31024, Lilongwe 3, Malawi
Phone: +265 995 495 143
Email: info@afidep.org



@htp_Africa



African Institute for Development Policy



AFIDEP



afidep_org