



Malaria vaccine rollout begins in Africa: the need to strengthen regulatory and safety surveillance systems in Africa

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INTRODUCTION

Malaria kills over 600 000 people annually, with most deaths occurring on the African continent.¹ The increase in a number of cases is further precipitated by the impact of climate change and the emergence of anti-malarial drug resistance.² These two factors significantly threaten effective malaria treatment and control. An effective vaccine has the potential to reduce resistant infections.² The WHO's recommendation of two malaria vaccines, RTS, S/AS01 in 2021 and R21/Matrix-M in 2023 is a significant breakthrough in vaccine development.³ As efforts are made to introduce these vaccines, it is important to ensure the presence of a resilient and robust pharmacovigilance (PV) system to monitor vaccine safety effectively, building on the experiences gained from the introduction of the COVID-19 vaccine. PV is key for providing timely and accurate data on vaccine safety, influencing data-driven decision-making and addressing public concerns to improve vaccine acceptance. However, PV frequently continues to be overlooked in the context of global health. In this article, we explore the importance of leveraging COVID-19 vaccine safety surveillance lessons through the Africa Centres for Disease Control and Prevention (Africa CDC) Saving Lives and Livelihoods (SLL) interventions, experiences and strategies that could be adopted to support the current malaria vaccines rollout in malaria-endemic countries.

18 million doses of RTS, S/AS01 have been allocated to 12 African countries to be rolled out from 2023 to 2025, with support from Gavi, The Vaccine Alliance, WHO, UNICEF and other partners.⁴ The introduction of the malaria vaccine will revolutionise the fight

SUMMARY BOX

- ⇒ Despite the critical role of pharmacovigilance in providing timely and accurate data on vaccine safety and influencing data-driven decision-making, it frequently continues to be overlooked in the context of global health.
- ⇒ Given the current heterogeneous situation of pharmacovigilance in different African countries, improving capacity in countries introducing malaria vaccines should be given the highest priority.
- ⇒ Leveraging the experiences of existing systems and the successes of COVID-19 vaccine safety surveillance can help ensure a more confident and efficient rollout of malaria vaccines.
- ⇒ This article underscores the significance of using the lessons and strategies derived from COVID-19 vaccine safety surveillance to bolster the ongoing malaria vaccine rollout in countries affected by malaria.

against this deadly disease that affects millions of children and pregnant women worldwide, especially in Africa. However, in this bright panorama, one additional element must be considered and appropriately funded: robust PV systems that help monitor the safety of vaccines and immunisation campaigns. Successful vaccination campaigns will hinge on robust PV systems that are well-prepared for monitoring and research on adverse events following immunisations (AEFIs) in the countries.

CONSEQUENCES OF POOR PHARMACOVIGILANCE SYSTEM

Given the current heterogeneous situation of PV in different African countries, primarily due to limited or intermittent funding and a lack of qualified personnel, improving PV capacity in countries introducing malaria vaccines should be given the highest priority.



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With only a few countries having a well-established PV system, it is imperative to focus on improving PV capabilities during the vaccine deployment to prevent or reduce any potential repercussions on vaccination campaigns.⁵ A valuable lesson gained from introducing new vaccines highlights the significance of addressing safety concerns. This became apparent in the Philippines, where the rollout of a dengue vaccine led to increased dengue morbidity and mortality from dengue. As a result, the entire national immunisation programme was disrupted due to a generalised lack of confidence in all vaccines. As a consequence, there was a resurgence of measles and polio.⁶ In the case of COVID-19 vaccines, a scoping review on COVID-19 vaccine hesitancy in Africa highlights that public perception and acceptance were negatively impacted by a range of factors including fear of AEFIs, distrust of the pharmaceutical industry, as well as myths surrounding immunisation.⁷ Misinterpretation of raw data can easily lead to misinformation. For example, during the rollout of the COVID-19 vaccine under the SLL, we noted that a single incidence of unrelated deaths in Cameroon to the vaccine derailed our entire intervention. Even though an investigation revealed the cause of death was unrelated, intensive Risk Communication and Community Engagement activities were necessary to regain confidence in the COVID-19 vaccination efforts.

CHALLENGES

In most African countries, the absence of legal provisions that compel Marketing Authorisation Holders (MAHs) to address local safety concerns generated from spontaneous reporting and to conduct post-marketing studies hinders the effectiveness of PV systems. These systems are already constrained by limited budgets and skilled personnel to track, monitor and rapidly investigate suspected AEFIs efficiently.⁵ It is also important to note that only five of the African countries' National Regulatory Authorities (NRAs), namely Egypt, Ghana, Nigeria, South Africa and Tanzania, have achieved the WHO Global Benchmarking maturity level 3.⁸ To address these challenges, countries must establish internal procedures for PV operations of MAHs that are in line with international guidelines and cater to local requirements. Additionally, given the administration of these new vaccines to children, there is an urgent need for thorough surveillance to detect any emerging safety issues in this population and to explore potential genetic and age group variations that could impact a significant cohort of vaccine recipients before they can harm additional vaccine beneficiaries.⁹

It is necessary, therefore, to leverage the global support and momentum surrounding the malaria vaccine rollout as a catalyst for countries to establish and strengthen their PV systems.¹⁰ This presents an opportunity to create solid frameworks for monitoring and managing AEFIs and enhance public health surveillance and response mechanisms. The effective PV systems will play a crucial role in providing timely and accurate data on vaccine safety,

especially on the risks associated with the vaccines vis-a-vis the benefits of preventing malaria disease.¹¹ This will bolster public confidence in immunisation programmes and further support the introduction of new vaccines that are becoming increasingly urgently needed to combat emerging and re-emerging infectious diseases.

THREE KEY PILLARS IMPORTANT TO STRENGTHEN PHARMACOVIGILANCE SYSTEM

Safety surveillance programmes are necessary for all countries in order to respond to specific adverse events to vaccines that are influenced by intrinsic and environmental factors. Countries should institute continuous monitoring of vaccines by strengthening three pillars: legislation, promoting well-trained PV personnel and encouraging high-quality reporting as part of the public health commitment of health professionals. In relation to this, Africa CDC is deeply involved in addressing these gaps and in the introduction of malaria vaccines across the continent. This consists of allocating funds and playing a key role in distributing vaccines in partnership with other organisations to support National Public Health Institutes. This aims to ensure effective immunisation coverage and seamless integration of the malaria vaccine into existing immunisation programmes, committing funds and serving as a key player in the allocation of vaccines in collaboration with partners to support National Public Health Institutes for effective immunisation coverage.¹² With Cameroon and Burkina Faso taking the lead to start the World's First Malaria Vaccine Programme for Children,¹³ it is paramount to use the WHO global benchmarking assessment tool and the following checklist for a quick evaluation of the readiness of PV programmes for a successful introduction of the malaria vaccine: the existence of an effective PV system in place; the mechanisms of how AEFIs will be collected, monitored, reported, analysed and communicated; how will signals be routinely searched, detected, investigated and communicated; the existence of plans to collaborate with regional, continental or global PV networks to enhance surveillance capabilities; strategies in place to address vaccine hesitancy; intends to collaborate with key PV stakeholder, communities and healthcare providers to ensure vaccine safety; and, plans in place to contribute to the global efforts in monitoring the safety of the malaria vaccine and informing future recommendations through data sharing.

COLLABORATION

The collaborative and transparent approach adopted during the COVID-19 pandemic, involving PV key stakeholders such as Public Health Organisations, Vaccine Safety Networks, NRAs, vaccine manufacturers, healthcare workers and the public, was crucial in monitoring the safety of the COVID-19 vaccines. This highlights the importance of a unified effort in ensuring vaccine safety and building public trust. Harmonisation and

collaborations provide a proactive solution to promote and protect public health through timely information sharing, strengthening weak management structures, resource mobilisation and processes, and reconstructing fragile and fragmented legal frameworks.¹⁴

LESSON FROM COVID-19 VACCINE SAFETY SURVEILLANCE

The post-licensure safety monitoring systems used for COVID-19 vaccines and during the introduction of new therapeutic medicines such as tuberculosis and HIV medicines could serve as a model that can be ameliorated for monitoring the safety of malaria vaccines. This means leveraging the experiences of existing systems and successes of COVID-19 vaccine safety surveillance, particularly in regulatory involvement, collaboration among PV actors and effective surveillance systems, can pave the way for a more confident and efficient rollout of malaria vaccines. While bridging some gaps, such as improving the reporting and investigation efficiency, sharing information between countries and ensuring good practical training the PV personnel are key to improve the PV system.

INNOVATION

Once the challenges, such as resource constraints and lack of skilled human resources, have been identified, it is essential to develop innovative solutions like digital safety applications to help identify and report suspected cases and contribute to more efficient risk communication. The role of artificial intelligence in PV will undoubtedly increase in the forthcoming years, specially if it is possible to link specific aid tools to electronic medical records.¹⁵ The implementation of real-time surveillance through digital solutions for reporting AEs and integration of dynamic data management systems and analytical methods presents a practical and highly customisable strategy for the early identification of AEs following the release of new vaccines.¹⁶ International collaboration is key to overcome these hurdles and to ensure safe and equitable access to these life-saving vaccines. While the Health Information System Programme-supported District Health Information System 2 is one notable example of a safety monitoring system in use at Africa CDC and many African and Asian countries, it is essential to harmonise various data collection tools and databases such as VigiBase and the Med Safety application from African Union Smart Safety Surveillance across the continent to support the joint effort to ensure the safety of vaccines.¹⁷

CONCLUSION

Addressing these challenges in nations requires a concerted effort to mobilise resources, strengthen regulatory frameworks and engage communities. The active involvement and training of healthcare providers and the establishment of vaccine safety

advisory committees implemented during COVID-19 vaccine introduction are essential steps toward achieving robust PV systems.

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REFERENCES

- World Health Organization. Malaria. 2023. Available: <https://www.who.int/news-room/fact-sheets/detail/malaria>
- Hamilton A, Haghpanah F, Hasso-Agopsowicz M, *et al*. Modeling of malaria vaccine effectiveness on disease burden and drug resistance in 42 african countries. 2023. Available: <https://www.nature.com/articles/s43856-023-00373-y>
- World Health Organization. WHO recommends R21/Matrix-M vaccine for malaria prevention in updated advice on immunization. WHO; 2023. Available: <https://www.who.int/news/item/02-10-2023-who-recommends-r21-matrix-m-vaccine-for-malaria-prevention-in-updated-advice-on-immunization>
- 18 million doses of first-ever malaria vaccine allocated to 12 african countries for 2023–2025: GAVI, WHO and UNICEF. WHO; 2023. Available: <https://www.who.int/news/item/05-07-2023-18-million-doses-of-first-ever-malaria-vaccine-allocated-to-12-african-countries-for-2023-2025--gavi--who-and-unicef>
- Ndagije HB, Walusimbi D, Atuhare J, *et al*. Drug safety in Africa: a review of systems and resources for pharmacovigilance. *Expert Opin Drug Saf* 2023;22:891–5.
- Dayrit MM, Mendoza RU, Valenzuela SA. The importance of effective risk communication and transparency: lessons from the dengue vaccine controversy in the Philippines. *J Public Health Policy* 2020;41:252–67.
- Ackah BBB, Woo M, Stallwood L, *et al*. COVID-19 vaccine hesitancy in Africa: a scoping review. *Glob Health Res Policy* 2022;7:21.
- World Health Organization (WHO). List of national regulatory authorities (NRAs) operating at maturity level 3 (ML3) 1 and maturity level 4 (ML4) 2 (as benchmarked against who global benchmarking tool (GBT)). 2023. Available: <https://www.who.int/publications/m/item/list-of-nras-operating-at-ml3-and-ml4>
- Yue QY. The International Society of Pharmacovigilance (ISoP) Pharmacogenomic Special Interest Group: Pharmacogenomics in Pharmacovigilance. *Drug Saf* 2021;44:615–7.
- World Health Organization. *COVID-19 Vaccines: Safety Surveillance Manual*. 2nd edn. 2021.
- European medicines agency. COVID-19 vaccines: development, evaluation, approval and monitoring | European medicines agency. EMA website; 2021. Available: <https://www.ema.europa.eu/en/human-regulatory-overview/public-health-threats/coronavirus-disease-covid-19/covid-19-public-health-emergency-international>

- concern-2020-23/covid-19-vaccines-development-evaluation-approval-and-monitoring
- 12 Africa CDC. Africa CDC renews its commitment to reduce vaccine-preventable diseases and outbreaks in Africa – Africa CDC. 2024. Available: <https://africacdc.org/news-item/africa-cdc-renews-its-commitment-to-reduce-vaccine-preventable-diseases-and-outbreaks-in-africa/>
 - 13 Time. Cameroon starts world-first malaria vaccine program for kids. 2024. Available: <https://time.com/6565005/cameroon-malaria-vaccines/>
 - 14 Ndomondo-Sigonda M, Miot J, Naidoo S, *et al*. Harmonization of medical products regulation: a key factor for improving regulatory capacity in the East African Community. *BMC Public Health* 2021;21:187.
 - 15 Pons-Mesquida MÀ, Oms-Arias M, Diogène-Fadini E, *et al*. Safer prescription of drugs: impact of the PREFASEG system to aid clinical decision-making in primary care in Catalonia. *BMC Med Inform Decis Mak* 2021;21:349.
 - 16 Lieu TA, Kulldorff M, Davis RL, *et al*. Real-Time Vaccine Safety Surveillance for the Early Detection of Adverse Events. *Med Care* 2007;45:S89–95.
 - 17 Kiguba R, Olsson S, Waite C. Pharmacovigilance in low- and middle-income countries: A review with particular focus on Africa. *Brit J Clin Pharma* 2023;89:491–509.