International Journal of
Life Sciences
International Peer Reviewed Open Access Refereed Journal

Int. J. of Life Sciences, 2023; 12 (1): 21-27
ISSN:2320-7817(p) | 2320-964X(o)

Research Article Open Access

Strategic reduction of *Plasmodium falciparum* infant mortality in Nigeria: Enhancing healthcare equity through medical drone delivery of the RTS,S/AS01 vaccine

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Manuscript details:
Received: 27.01.2024
Accepted: 24.02.2024
Published: 31.03.2024

Cite this article as:
Saumik Das, Brian Wolfe, Varchas Kukreja, Yubo Gao (2024) Strategic reduction of *Plasmodium falciparum* infant mortality in Nigeria: Enhancing healthcare equity through medical drone delivery of the RTS,S/AS01 vaccine, *Int. J. of Life Sciences*, 12 (1): 21-27.

Available online on http://www.ijlsci.in
ISSN: 2320-964X (Online)
ISSN: 2320-7817 (Print)

ABSTRACT

Malaria has been known to be a fatal disease that can be transmitted through the exchange of blood and is carried by the *plasmodium* parasite. Nigeria is one of the countries in Africa that has suffered the most from malaria, with the region accounting for 95% of malaria cases and 96% of malaria deaths. Malaria is the leading cause of child and infant mortality in Nigeria, due to the many healthcare disparities and inadequate access to current treatments. We researched the distribution and transportation issues around inefficient road systems, and vaccine storage surrounding malaria treatment, using a case study of a Rwandan drug transportation startup known as *Zipline*. When investigating through an ethical lens, we focused on the concepts of priority setting for malaria cases in Nigeria, specifically infant health groups, and the ethical mass distribution of vaccines. By integrating self-assembled, automated, GPS-routed, electronic drones and optimizing the storage system, our research aimed to propose a cutting-edge, sustainable ethical solution for the distribution of the RTS, S/AS01 vaccine. This research shines light on how to effectively combat similar health crises via the usage of medical delivery drones for mass administration.

Keywords: Malaria, vaccine, global health, bioethics, health inequity, United Nations Sustainable Development Goals (UN SDGs), global sustainability

INTRODUCTION

1.1 Disease Profile of Malaria

Malaria or *Plasmodium falciparum* is a single-celled parasite (shown in *Figure 1)* that is transmitted through either the bite of a female *Anopheles* mosquito or the transfusion of blood via contaminated needles (WHO, 2023).

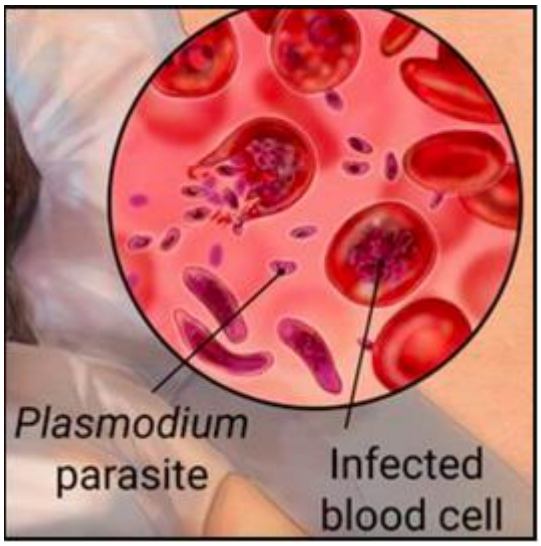

Figure 1. Plasmodium parasite in human bloodstream

As of 2021, malaria affected nearly half of the world's population, with cases being concentrated in warmer regions (CDC, 2019). After the parasite infects a mosquito during blood feeding, the parasites enter the gut of the mosquito and begin to multiply to form a new parasite. When a human is bitten, parasites from the mosquito's saliva enter the bloodstream, where they travel to the liver to mature and reproduce (WHO, 2023). It later grows inside red blood cells and destroys them, releasing daughter parasites. Symptoms typically occur within a week or two of infection. While most symptoms are mild such as headaches and sore throat, infants and pregnant women typically suffer worse symptoms such as vomiting or seizures (CDC, 2019). Regarding the infant mortality rate, 30% of infant deaths result from the transmission of malaria (Effiong et al., 2022). Malaria self-prevention methods include using mosquito nets, mosquito repellents after dusk, coils and vaporizers, protective clothing, and a window screen (WHO, 2023). Scientists are working on developing an effective vaccine to counteract this parasite and exploring options around transmission blocking vaccines (Arora et al., 2022).

1.2 Malaria in Nigeria

Malaria cases are concentrated in Sub-Saharan Africa, with the region accounting for 95% of malaria cases and 96% of malaria deaths (WHO, 2023). 80% of the deaths were children under five (WHO, 2023). Approximately, a child in Africa dies of malaria every five minutes, raising the urge to develop an effective vaccine for infants (UNICEF, 2023). Nigeria has the highest concentration of malaria in the world, with over 31% worldwide cases originating within the region (WHO, 2023).

1.3 Nigeria's Healthcare System

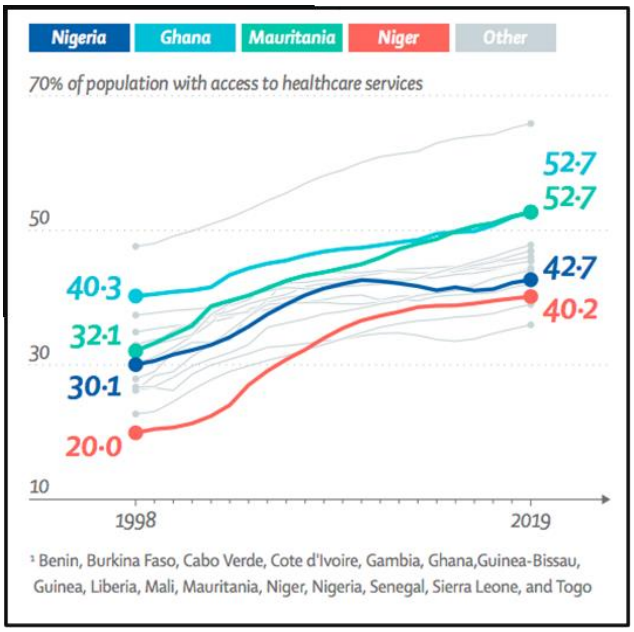

Figure 2. Access to healthcare facilities in Nigeria (Lancet, 2023)

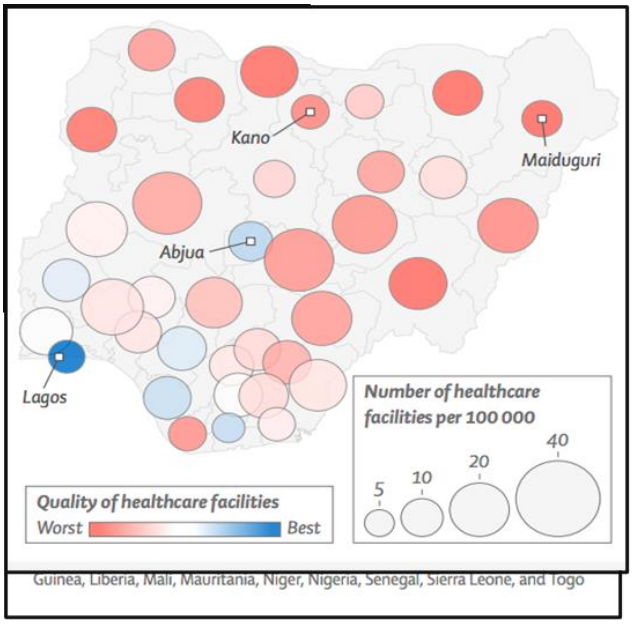

Figure 3. Availability and quality of healthcare facilities across Nigeria (Lancet, 2023)

Figure 2 depicts that among the West African countries, Nigeria has one of the lowest rates for access to healthcare services with just under 43% of the population having access to healthcare services.

Figure 3 portrays that healthcare facilities across Nigeria are of poor quality and are inadequate in serving the large population of approximately 214 million people. There are three areas for improvement in the Nigerian healthcare infrastructure resulting in healthcare disparities across Nigeria. There is a weak relation between the Nigerian government and academic institutions, a lack of funding for public health reform, and inadequate access to healthcare facilities across Nigeria (Lancet, 2023). Due to these healthcare inequalities and issues, the fight against malaria has been difficult for the Nigerian government's implementation of malaria control policies. To combat malaria, the National Malaria Strategic Plan (NMSP) by the Nigerian government aims to bring malaria-related mortality in Nigeria to zero and reduce the disease burden of malaria in Nigeria using various strategies (Maduka, 2018). These methods include testing patients with microscopy, as well as ensuring timely availability of necessary vaccines (Maduka, 2018). Moreover, the Nigerian government and other sub-Saharan nations have joined the *End Malaria Council*, to bring the malaria mortality rate close to zero by 2030.

1.4 Current Research on Vaccines

Two vaccines are currently under review. RTS,S/AS01 (*Mosquirix*) has passed Phase III trials, becoming the first WHO (World Health Organization) approved vaccine to combat malaria. Results from Phase III (refer to *Table 1*) show RTS, S/AS01 having a modest efficacy of 25.9% (circled in blue), in comparison to the other trials.

RTS, S/AS01is currently being piloted in Ghana, Kenya, and Malawi (WHO, 2023). Additional plans have been made to allocate the RTS, S/AS01 vaccine to nine more countries, including Benin, Burkina Faso, Burundi, Cameroon, the Democratic Republic of the Congo, Liberia, Niger, Sierra Leone, and Uganda. Nigeria is not one of the countries that has been selected to receive the RTS, S/AS01 vaccine. R21 is currently undergoing Phase III trials in Burkina Faso, Kenya, Mali, and Tanzania. Phase III results have not been reported yet but results from the previous Phase II.b show a high efficacy of 77%.1 (Datoo et al., 2021). While R21 has not yet been approved by the WHO, it has been approved for use by the Nigerian Government. The main difference between these two vaccines is that R21 contains additional circumsporozoite antigens. Although the R21 and RTS,S/AS01 vaccines are both transmission blocking vaccines (TBV) that interrupt malaria's life cycle (Laurens, 2019).

1.5 Transportation Crisis for Vaccines

To prevent spoilage and maintain their properties, vaccines are stored at a cold temperature range, which in the instance of the malaria vaccine is 2-8°C (Effiong et al., 2022). Due to frequent power outages in Nigeria, most hospitals have not invested in long-term facilities to store vaccines (Effiong et al., 2022). Nigeria has very few malaria vaccine distribution centers, making it difficult to access vaccines on-demand (Effiong et al., 2022). When vaccines are transported to hospitals, transportation vehicles must navigate poorly maintained and unpaved roads. Nigeria tops the list of African countries with most traffic accident-related fatalities, leading to unreliable delivery, which in turn makes rural communities susceptible (WHO, 2023). With all the road accidents, individuals may see benefits by the vaccines traveling by air, eliminating transportation issues. To eliminate transport issues from road accidents, we suggest delivering vaccines via air transport to improve efficacy.

Table 1. RTS, S/AS01 Phase III Efficacy Results (Laurens, 2020)

Age Group	6-12 weeks of age (n=6537
Vaccine Efficacy against clinical malaria, 3-dose group 95% CI)	18.3% (11.7 to 24.4)
Vaccine Efficacy against clinical malaria, 4-dose group 95% CI)	25.9% (19.9 to 31.5)
Vaccine Efficacy against severe malaria, 3-dose group 95% CI)	10.3% (-17.9 to 31.8)
Vaccine Efficacy against severe malaria, 4-dose group 95% CI)	17.3% (-9.4 to 37.5)

1.6 Overview of Ethical Issues

Infant or at-risk age groups such as pregnant women are prioritized for delivery of vaccines in the Nigerian healthcare system. Malaria disproportionately affects impoverished populations making it difficult for mass drug administration to reach all areas (Jamrozik et al., 2015). The current situation leaves other people in need of antimalarial drugs or vaccines excluded due to an unreliable transportation system. Through the healthcare disparities present in Nigeria and unpaved roads, rural areas are more susceptible. When we look at malaria control under an ethical lens, it is important to recognize that impoverished communities are disproportionately prioritized with vaccine delivery.

1.7 Novelty & Purpose

The study investigates medical delivery drones as a potential transportation system to improve mass vaccine administration for malaria in Nigeria. Out of the three areas of improvement our study investigates addressing the inadequate access to healthcare facilities by providing an ethical and sustainable way for long term mass drug administration across Nigeria. The novelty of this research is that the improved storage system, chute addition, and recently built delivery drones have not been used in Nigeria for mass drug administration. The significance of the research is to address the United Nations (UN) Sustainable Development Goals (SDGs) for "Good Health and Well Being" and "Reduced Inequalities" by reducing the mortality rate of malaria and addressing the healthcare disparities of malaria in Nigeria. This research can shine light on how to effectively combat similar health crises via the usage of medical delivery drones for mass administration.

2. MATERIAL AND METHODS

2.1 Case Study: Rwandan Drug Transportation

In Rwanda, a transportation startup called *Zipline* started delivering medical products via self-flying drones launched from a centralized *Zipline* facility. After an item is ordered, the medicine is packaged and placed in the body of a drone (Griffith et al., 2023). Wings and an electric battery are attached, and the item is launched from an electric catapult, accelerating from 0 to 70 miles per hour in 0.33 seconds (Griffith et al., 2023). Following a pre-programmed GPS route, the drone drops off the item in a protected box with a parachute and navigates back to its origin. Refer to *Figure 3* for schematics around the assembly and delivery process for *Zipline* medical drones. Since its introduction, *Zipline* has decreased in-hospital postpartum hemorrhage (PPH) deaths by 88% through efficient blood delivery (Zipline Fact Sheet, 2023). Drone delivery has reduced drug transportation time from six hours to nearly one hour, a time-efficient solution that could save thousands of Nigerian lives (Griffith et al., 2023). Naturally, there are some challenges, such as no-fly zones (military bases, natural parks), flight limits (*Zipline* drones cannot fly above 400 feet), and the inability to deliver to unmapped locations, resulting in delivery issues.

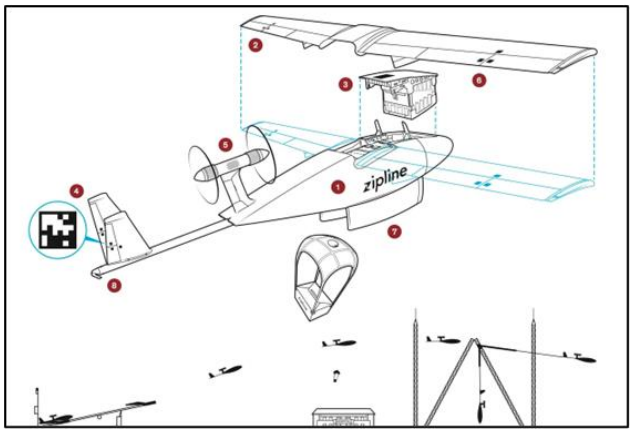

Figure 4. Zipline's medical delivery drone schematics (Ackerman & Koziol, 2022)

2.2 Selection Criteria for RTS,S/AS01 (*Mosquirix*) *Vaccine*

Efficacy, availability, and affordability were the three main selection criteria that we considered when selecting a vaccine. RTS,S/AS01 is one of the most efficacious malaria-combatting vaccines to date. The only vaccine that appears to be more efficacious is the R21 vaccine, but that leads to the next selection criteria. RTS,S/AS01 has been approved by the WHO and is available in select parts of Africa. In the coming years, RTS,S will be implemented across Africa, being more available than any other vaccine. R21 has not finished testing yet, so it is ruled out based on its availability concerns. RTS,S/AS01 is a relatively low-cost vaccine. The manufacturer, *GSK* (pharmaceutical company), has stated that pricing of RTS,S/AS01 will be set at manufacturing cost plus 5% that will be reinvested in vaccines against neglected tropical diseases. Having a relatively high efficacy, availability, and low cost are the reasons we chose the RTS,S/AS01

(*Mosquirix*) vaccine. R21 is a very recent innovation, so little is known about it compared to RTS,S/AS01. As more information becomes available about R21, it could prove to be a better option than RTS,S/AS01.

2.3 Connection to Nigeria's Applications

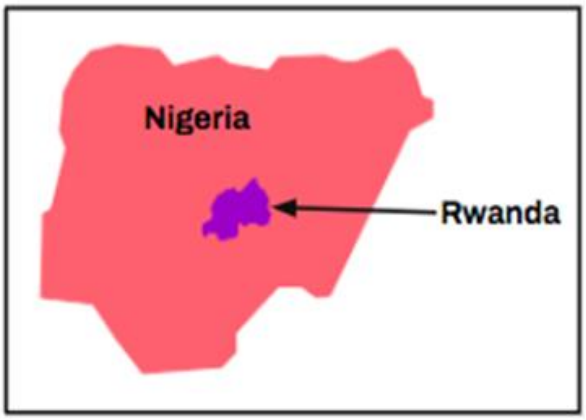

Figure 5. Comparison of size of Rwanda versus Nigeria

We believe we can use similar GPS-routed drones to *Zipline's* system to deliver malaria vaccines to areas in Nigeria that suffer from infrastructural issues such as flooding due to inadequate drainage systems and poor road maintenance. While *Zipline's* system is ideal for Rwanda, several features must be adapted for use in Nigeria. Nigeria is thirty-five times larger than Rwanda (shown in *Figure 5*), and therefore two centralized drone launching locations will not be sufficient to cover Nigeria's radius (Griffith et al., 2023). We would need closer to seventy launching sites, which will require significant expenditure. *Zipline* drones currently drop off medicine at a requested location outside the hospital. Our research group advises that facilities receiving medicine have a designated location within hospital boundaries where drones can safely drop off the medications, such as a delivery chute. Through implementing a chute, deliveries would directly enter the hospital, where they can be picked up and promptly administered by the healthcare workers.

2.4 A Sustainable Ethical Solution

Self-assembled automated drone delivery to chutes accounts for priority setting and does not rely on roads, overcoming the transportation crisis. This in turn allows for unbiased distribution of malaria vaccination, eliminating potential ethical concerns. Enhancing transportation time enables the distribution of a larger quantity of vaccines to the public, eliminating the need to concentrate solely on the infant population, instead making it possible to administer them to the entire public.

3. RESULTS

3.1 Participants & Study Design Plan

Infants, who account for 80% of all malaria deaths, are the utmost priority of the Nigerian healthcare system. Inspired by the *Zipline* medical delivery drone, we intend to implement GPS routed, self-assembly, electric automated drones to transport vaccines to unvaccinated families with infants and other age groups as well. Self-assembled automated drones deliver to chutes which can make the delivery more efficient by not relying on roads. This avoids traffic congestion and using unreliable roads in Nigeria. We will collaborate with local government groups and NGOs, to bridge the gap between academia and the Nigerian government. Furthermore, we plan on working with governmental organizations like the *End Malaria Council*, to reduce the mortality rate of malaria in Nigeria to zero by 2030.

4. DISCUSSION

4.1 Expected Outcomes

With an improved transportation system and vaccine, some potential public health implications include a lower disease burden and a lowered infant (and other groups) mortality rate. More people will gain exposure to medical drone delivery, and transportation problems with road traffic will be eliminated.

4.2 Review of Strengths & Limitations

Utilizing *Zipline* drones and the RTS, S/AS01 or the R21 vaccine will make mass drug administration possible for all groups of people. It will eliminate potential ethical concerns regarding priority settings and ensure fair distribution of vaccines to rural communities. Some limitations include the efficacy of the current RTS, S/AS01 vaccine, but future research into the R21 vaccine should minimize the consequences of this issue. Vaccine storage centers require expenses to build; however, the one-time investment will be useful for other public health and distribution crises. Based on the COM-B behavior change framework (Mitchie et al., 2014), we mapped out certain psychological and cultural barriers that may arise in our operation. Some of those include the resistance to drone operation as the Nigerian people are not as exposed to such technologies as seen in

Rwanda. There may be some political drawbacks as this would be the first time for medical drone operation to occur, causing concerns about regulation. While our study is limited to addressing the lack of healthcare facilities, we hope to expand our research in the context of public health reform to further improve their healthcare infrastructure.

4.3 Future Work

Further research into the new R21 vaccine is needed to evaluate its effectiveness on infants with mild and severe malaria. In the future we should aim to increase drone affordability by working to bridge the gap between academia and Nigerian governmental organization. Several sources indicated that civilians and healthcare workers may be unaware of *Zipline's* transportation efforts, so further advertising may be beneficial (Griffith et al., 2023). With a combination of the R21 vaccine and medical delivery drones, we believe this can be implemented in the efforts of the *End Malaria Council,* put forth by the Nigerian government to remove malaria by 2030.

5. CONCLUSION

Implementing the new RTS,S/AS01 vaccine along with improved cold storage systems and electric drones for transportation helps mitigate the infant mortality rate of malaria in response to the lack of medical facilities and a dysfunctioning healthcare system in Nigeria and addresses the ethical concerns surrounding priority setting of age groups on malaria control in Nigeria. We hope to expand our research to similar regions across sub-Saharan Africa, when dealing with diseases like malaria. Our research paves the way for decreasing the disease burden of malaria across Nigeria and works towards the UN SDGs "Good Health and Well Being" and "Reduced Inequalities" regarding the healthcare disparities present in Nigeria.

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Acknowledgements
We would like to thank our research mentors, Edwin Ruiz Fuentes, MPH (Yale University) and Durel Crosby, BA (Yale University), for their crucial guidance, insightful feedback, and consistent support throughout our project. We appreciate Yale University for allowing us to use their facilities and necessary resources to conduct our public health research

Conflict of interest: The authors declare that they have no conflict of interest.

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Peer review information
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