Case Study

Increasing uptake of the most effective treatment to reduce severe malaria mortality

TREATING SEVERE MALARIA WITH INJECTABLE ARTESUNATE INSTEAD OF QUININE CAN SUBSTANTIALLY REDUCE MORTALITY. TO INCREASE UPTAKE AND IMPROVE HEALTH OUTCOMES, CHAI SUPPORTED MINISTRIES OF HEALTH IN SIX HIGH-BURDEN COUNTRIES TO OVERCOME BARRIERS TO ADOPTION.

OVERVIEW

Severe malaria is a medical emergency in which the disease has progressed to a life-threatening state, most commonly the result of delayed or improper treatment of uncomplicated malaria. If left untreated, severe malaria is thought to lead to almost 100 percent mortality.[1] To date, injectable quinine is the most widely used treatment for severe malaria. However, this treatment has significant drawbacks with side effects such as hypoglycemia and administration by rate-controlled infusion over four hours. Studies show that over 10 percent of patients treated with quinine still die, accounting for many of the estimated 600,000 malaria deaths annually, of which approximately 80% are children under the age of five in sub-Saharan Africa.

As an alternative, injectable artesunate (Inj AS) reduces mortality from severe malaria by 22.5 percent compared with quinine. In other words, for every 42 children suffering from severe malaria who are treated with Inj AS instead of quinine, one additional life will be saved.[2] Recognizing this, in 2011, the World Health Organization (WHO) recommended Inj AS as the preferred treatment for severe malaria. Despite the clear benefits, and the WHO recommendation, the uptake of Inj AS has been slow due to several demand- and supply-related barriers.

In collaboration with partners, CHAI has been working with the governments of **Nigeria, Uganda, Cameroon, Malawi, Kenya,** and **Zambia** to address these barriers and increase the use of Inj AS for the treatment of severe malaria.

THEORY OF CHANGE

Inj AS has been shown to be a clinically superior alternative to quinine for the treatment of severe malaria, substantially reducing mortality. CHAI is facilitating rapid uptake in select focal countries, thus reducing mortality caused by severe malaria and providing a model for more widespread adoption.

IMPACT

This project has resulted in the increased adoption and uptake of Inj AS in six high malaria burden African countries: Nigeria, Uganda, Cameroon, Malawi, Kenya, and Zambia. Orders have been placed since 2011 that will allow close to 1.3 million patients to be treated with this superior medicine, with the potential to save up to 30,000 additional lives.

KEY PARTNERS

- **DFID**
- **UNITAID**
- **MMV**

Partners critical to the success of this project include the Department for International Development (DFID), UNITAID, and the Medicines for Malaria Venture (MMV). This work began in 2011 in Uganda and Nigeria and through demonstration of an impactful and replicable approach, rapidly expanded to the other countries in 2012-2013

APPROACH

CHAI identified demand-side hurdles as the greatest drivers of slow uptake of Inj AS. These barriers to uptake were as follows:

- Resistance to policy change at the country level;
- Lack of training on the use of the new treatment;
- Difficulty with forecasting requirements during a transition period; and
- High cost of Inj AS, at three to five times more expensive than quinine on a per vial basis.

Because most countries have traditionally procured severe malaria commodities using national financing, many have indicated that new international donor funding will be required to support a switch to Inj AS.

Through the initial work in Nigeria and Uganda, CHAI defined a clear approach to overcoming these demand-side hurdles involving three steps that could be replicated in other countries:

1. **Raising awareness of the clinical benefits and supporting the Ministry of Health (MOH) with the update of national treatment guidelines.**
2. **Working with partners, such as MMV, to support the National Malaria Control Program with the planning and implementation of a national rollout of Inj AS.**
3. **Supporting countries to obtain funding from international donors, such as the Global Fund to Fight Aids, Tuberculosis, and Malaria (GFATM), for the sustained procurement of Inj AS.**

CHAI's goal is to work itself out of a job; completion of this work will sustainably put Inj AS into the standard national malaria case management practices and funding streams.

IMPACT

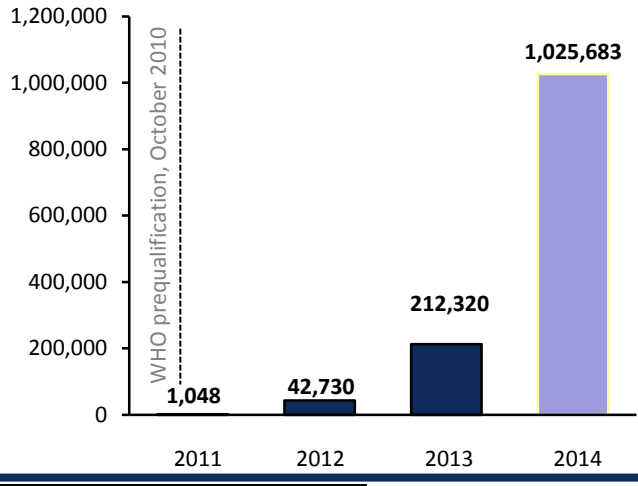
By mid-2013, CHAI had championed the update of the malaria case management guidelines to align with the WHO policy for Inj AS in all six focus countries. Relevant trainings have been conducted or scheduled for each country to help healthcare workers understand and adhere to the new guidelines. The progress made in these countries has helped to lay the groundwork for more widespread adoption in additional countries, thus contributing to a greater number of lives saved through improved treatment.

From 2011–2014, with support from CHAI, the MOHs in the six focus countries placed orders for a total of over eight million vials of Inj AS; prior to intervention, these countries were not procuring Inj AS for the treatment of severe malaria. This increased uptake (with the greatest volumes in Nigeria and Uganda) will allow for the treatment of up to 1.3 million patients, saving approximately 30,000 lives. In 2015, it is expected that CHAI's effort will help save up to another 28,000 additional lives[i,3] (see Figure I, below).[4,5]

Furthermore, the impact achieved across these countries, specifically through the early work in Nigeria, resulted in additional funding commited by UNITAID in early 2013 for procurement of Inj AS. This funding will provide treatment with Inj AS for an additional 2.3 million patients.[ii,iii]

Lastly, all countries have made significant progress securing funding from the national government, GFATM, or the United States President's Malaria Initiative for sustainable ongoing implementation and use of Inj AS for severe malaria in 2014. The results achieved in each of these focus countries were made possible in large part due to funding provided by DFID and UNITAID.

FIGURE I. ANNUAL ORDERS OF INJ AS REPRESENTED AS NUMBER OF PATIENTS TO BE TREATED ACROSS CHAI FOCUS COUNTRIES SINCE WHO PREQUALIFICATION



[i] Accounts for projected orders in 2015 based on 2014 forecasts.
[ii] Figure is based on current price of Inj AS, which is projected to decrease in 2015.
[iii] Figures relating to the number of patients treated and lives saved are estimated based on total orders placed and not directly linked to a defined time period. Given the lack of available data, CHAI is unable to confirm with certainty the number of patients that receive treatment as a result of increased uptake.

LIMITATIONS AND LESSONS LEARNED

Obtaining funding to catalyze the procurement of Inj AS proved to be an early and formidable hurdle. To overcome this barrier, CHAI partnered with MMV to submit a proposal to UNITAID to fund the procurement of Inj AS for five of the six focus countries: Nigeria, Uganda, Cameroon, Kenya, and Malawi.

This proposal was successful largely due to the demonstration of a clear approach through the work in Nigeria. It is therefore important to demonstrate scalable impact in the early stages of a project, thus building a compelling case for the involvement of additional partners and donors.

FUTURE OUTLOOK

Despite the substantial loss of life caused by severe malaria, national governments and international donors have often deprioritized its treatment in favor of interventions for treating and preventing uncomplicated malaria. This project has encouraged governments and other stakeholders to reconsider how they approach the treatment of severe malaria.

As a result of more widespread adoption, the vast majority of malaria-endemic countries have incorporated Inj AS into their applications to the GFATM's New Funding Mechanism. This shift is paving the way towards the ultimate goal of ensuring that all severe malaria cases are treated with Inj AS instead of quinine, potentially saving up to an additional 190,000 lives per year.[6]

Contact Information
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[2] Dondorp A, Fanello C, Hendriksen I, et al. Artesunate versus quinine in the treatment of severe falciparum malaria in African children (AQUAMAT): an open-label, randomised trial. *Lancet*. 2010. 376(9753): 1647–1657 http://www.thelancet.com/journals/lancet/article/PIIS0140-6736%2810%2961924-1/abstract. Accessed August 2014.

[3] Calculation for number of lives saved and treatment with Inj AS is based on the mortality rate and average doses per treatment (adult and children) identified in the AQUAMAT clinical trial.

[4] Vials/Treatment: WHO Body Mass Index Statistics.

[5] World Health Organization. Guidelines for the treatment of malaria. Second edition. *World Health Organization Website*. http://whqlibdoc.who.int/publications/2010/9789241547925_eng.pdf?ua=1. March 2010. Accessed August 2014.

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