Targeting the End of Malaria by 2050

Malaria continues to have a significant impact on half of the world's population who live in tropical regions. It claims 600,000 lives each year, the majority of whom are children under 5-years of age. Over the last century, scientific advances have managed to bring the death toll down from its historic annual peak of around five million fatalities, but even with today's vaccines, mosquito nets, and indoor residual pesticide spraying programmes, we have not yet eradicated the disease's threat.

Some would go further and express concerns that we are losing momentum. As Peter Sands, Executive Director of the Global Fund puts it: "More than ever, we are at risk of losing our fight against this disease. Progress has ground to a halt, and in some places is reversing. Unless we act now, malaria could resurge dramatically."[1]

Malaria is caused by a parasite, transmitted to the human bloodstream through the bites of infected mosquitoes. Once the parasite is inside the body, it multiplies, attacking red blood cells. This causes symptoms like chills, flu-like symptoms, extreme exhaustion, and more. Without treatment, the effects of malaria can become severe and even fatal, especially for children and pregnant women. Severe malaria can even cause permanent brain damage to unborn children.

The Relationship Between Malaria and Economic Development

It is undeniable that the prevalence of malaria in modern day is linked to inequities in access to health innovation. There is a direct correlation between health access and economic development. While the efforts to prevent and manage malaria have significantly lowered the disease's impact in numerous nations in recent years, such as India, Sri Lanka, and Vietnam, more detailed evaluations of health outcomes reveal that poor and vulnerable populations miss out on the benefits of these malaria control initiatives.

An estimated 58% of malaria deaths occur among the poorest 20% of the world's population.[2] This staggering figure results from numerous contributing factors: inadequate housing and overcrowding without use of mosquito preventatives, poorly paid farming occupations, nearby mosquito-filled forests, malnutrition that limits the body's ability to fight malaria, and lack of access to preventative agents. Note that in many of these contexts, infrastructure related to economic development impacts the lifestyle of communities which increases the risk of contracting malaria and vector borne diseases in general.

Malaria control relies heavily on prevention, with prompt treatment being the most crucial method to avoiding malaria-related deaths. However, when the poorest, most vulnerable in society lack access to preventative measures or quality treatment, the disease is free to spread.

As reported by WHO in 2022, four African countries accounted for almost 50% of all malaria deaths worldwide: Nigeria (26.8%), the Democratic Republic of the Congo (12.3%), Uganda (5.1%) and Mozambique (4.2%).[3]

This data showcases the inequity in treatment of the disease in countries where large populations are living in poverty, extreme poverty, or beginning to recover from poverty. In these nations, poverty is heavily linked to lack of healthcare access, and therefore, lack of access to preventative measures and treatments of malaria.

Several high-GDP countries with subtropical and tropical regions once struggled with the prevalence of malaria but saw the incidence of malaria cases decline rapidly in line with the development of their economies. The United States of America is a clear example of this often-untold history.

Malaria was brought to the Americas during the transatlantic slave trade, primarily through infected African slaves and European colonisers. In particular, the strain of malaria (*P. falciparum*) carried by enslaved Africans was deadly. It led to the establishment of malaria as a major health problem in the southern region of the USA.

In hot climates such as South Carolina, the disease was rampant in sugar, cotton, and rice plantations. The US was plagued by malaria until the mid-20th century, infecting presidents from Washington to Lincoln, weakening Civil War soldiers by the hundreds of thousands, and draining the country's physical and economic health in the process.

The nation saw a burst of hope in the 1930s when the Tennessee Valley Authority modernised the rural south with hydroelectric power. But just as the United States was eradicating its last pockets of infection, malaria wormed back into the USA's spotlight during World War II. During the early days of the Pacific campaign, more soldiers were killed by malaria than by enemy forces.

The leading public health agency in the United States, the Centers for Disease Control and Prevention (CDC) was founded in 1946 to combat malaria. Through heavily funded mosquito control programmes, surveillance, and publicity campaigns denouncing the insects, in combination with a robust private market, malaria was officially eradicated from the USA in 1951. Today, the CDC remains very involved with malaria research around the globe.

This history of malaria in the USA is a prime example of the power of economic development when combatting the mosquito-transmitted disease. As the USA transformed into a developed country, the nation had the national resources and the private sector market to eradicate malaria, even back in 1951. Economic development also brought changes to how people lived. Better sewage and waste management systems, transition away from unclean

tight living quarters, and changes to animal rearing and agricultural practices all changed proximity to breeding grounds for mosquitoes.

In contrast, nations with high levels of poverty remain disproportionally plagued by the disease today.

Vaccines – The Latest Breakthrough in Malaria Prevention

The high-profile research breakthroughs we have seen in the last decade include the development and rollout of the RTS,S vaccine, commonly known as Mosquirix.[4] In Phase 3 clinical trials conducted between 2009 and 2014, the RTS,S vaccine that was given in 4 doses over 18 months reduced severe malaria cases by 22% and deaths by 13%4 in children aged 5–17 months. With repeated booster vaccines over a 4-year period, efficacy can reach up to 36%.[5]

Since then, we have seen pilot programmes start in 2019 in Ghana, Kenya, and Malawi which vaccinated over 1.7 million children. The World Health Organization's (WHO) modelling study estimates the vaccine could prevent 5.4 million cases of malaria and 23,000 deaths annually in the vaccinated population. Global estimates of malaria cases are 249 million.[6]

Based on the success of pilot programmes, in October 2021 WHO recommended the widespread use of the RTS,S vaccine for children in areas of moderate to high malaria transmission. The decision represented a landmark in global malaria control efforts, but we do not yet have the panacea the world is waiting for.

RTS,S is seen as a complementary tool, rather than a standalone solution. Mosquirix offers approximately 30% protection against malaria in children during the first year after vaccination,[7] with its efficacy dropping over time which requires the need for booster doses. These efficacy numbers are only attainable in areas where insecticide-treated nets are widely used and there is good access to diagnosis and treatment.

Plus, malaria vaccines on the market do not provide complete immunity, meaning that vaccinated individuals can still contract the disease, though they are likely to experience less severe symptoms. Protection provided by vaccines is also strain-specific, primarily targeting Plasmodium Falciparum, the deadliest species of malaria parasite, and offering limited defence against other species such as *P. vivax*.

Vaccines are part of the solution, but beyond the scientific challenge of discovery, safety, and efficacy, there are also logistical challenges such as cold storage of the vaccine and the practicalities of multi-dose programmes, and high costs of widespread administering of vaccinations, especially in resource-limited areas.

Other Interventions

When used properly, mosquito nets are one of the most effective tools for preventing mosquito-borne diseases. However, as a preventative measure it does suffer from several drawbacks. It is common for untreated nets to have holes in them, trapping mosquitos inside and attracting more bites as a result. In hot, humid conditions, such as the subtropical regions where malaria is rife, the netting can also be too thick and uncomfortable to sleep underneath, limiting air circulation and discouraging people from using them altogether.

Other options include residual sprays that can help reduce the mosquito population in specific areas by coating surfaces where mosquitoes are likely to land with insecticides. While effective to deter mosquitos, these sprays can also affect other species, including beneficial insects like bees and butterflies, and can even pose health risks to humans when stringent safety guidelines aren't followed.

Symptoms of exposure can include respiratory issues, skin irritation, or more severe health effects with long-term exposure – again, deterring individuals from using the sprays. This preventative method is also less effective in very high humidity or when washed away by rain, limiting its convenience in high malaria-risk areas.

The reality is there is no silver bullet. We need an integrated vector control system that gives people and public health agencies more options to design the best system to suit their context.

Battling a Mutating Species

Fighting malaria is like fighting several diseases at once. There are 156 different species of Plasmodium, the parasite that carries malaria. Five of these species infect humans. This doesn't count other vector borne disease such as dengue, zika, and others.

Each species goes through six different lifecycles and each lifecycle is like dealing with a completely different creature, similar to the difference between a pupa and a butterfly. This is why creating a vaccine is extremely difficult. This is further complicated by the speed the parasite mutates. Mosquito mutation also compounds this challenge. This is why insecticides become increasingly less effective over time for insecticide treated bed nets and indoor residual sprays, the primary tools currently used to eliminate the spread of malaria.[8]

Recently, it's been reported that the species of mosquitos which carry malaria, typically night biters, are biting earlier in the day. This limits the effectiveness of pesticides and indoor residual sprays which focus on protection in the home.

This complex context is why there is a need to expand the pool of integrative tools. This is already common practice in many parts of the United States where a combination of local government control measures combined with private sector activities play an important role in mosquito population control. These government programmes, such as on-going seasonal surveillance, larvicide, and aerial fumigation work best in combination with private sector practices like mosquito repellent use and home pest control services. Therefore, developing countries must find the right integrative solutions that fit their circumstances.

Mosquito repellents have significant potential as part of an integrative set of tools to combat mosquito borne diseases. Unlike pesticides, because repellents do not kill, insects do not become resistant over time.

The Case for a New Generation of Mosquito Repellents

Historically, mosquito repellents have proven inconclusive as an effective prevention tool in community-wide studies for vector control. Discussions with vector control experts indicate this has primarily been due to problems with adoption and adherence during studies. In short, people don't like using the current mosquito repellent options on a daily basis.

A new type of repellent is needed, one that solves the adoption and adherence challenges in current repellents. A generation of mosquito repellents that are safe for daily use, do not require reapplication, and can fit into the daily skincare routine of communities most at risk of vector borne diseases.

The UK has many public health challenges, but malaria is not one of them. Nevertheless, the country has some of the world's leading scientists and institutions focused on infectious disease. These include the major research-led universities and other specialist research centres such as Liverpool School of Tropical Medicine.

Based around a famous deep-water port with a long history of global trade, Liverpool City Region is also the UK location of LivFul. Our organisation joined the conversation in 2015 from a strategic base on the Sci-Tech Daresbury campus, a national science and innovation campus. The organisation set out to develop an improved repellent designed to prevent mosquito-borne infections.

As a Co-CEO and Co-Founder of LivFul, I grew up in Nigeria and suffered several malaria infections by the age of 10. I saw first-hand its impacts in my community and family. But motivated to change my situation, I created my own repellent in my bathroom from simple household products. Only later did I learn that repellents already existed – I just didn't have access to them. The experiences I had as a child all helped me to realise that lack of access is a systemic issue, so I co-founded LivFul to find a holistic way to solve health access.

After moving to the United States as a teenager, I devoted my career to forming a company to work on a more effective insect repellent. Our small team at LivFul began research into tangibility by speaking with individuals in developing countries who attend to the malaria epidemic every day – including health professionals and locals in malaria-afflicted communities.

We sought to create a product that avoided some of the common complaints about existing mosquito repellents – that they were often sticky, uncomfortable, not long lasting, and carried an unpleasant odour.

LivFul went on to produce an enhanced insect repellent (EIR) featuring IR3535®, a well-known active ingredient recognised in the scientific community for effectively repelling mosquitoes without posing health or environmental risks. To enhance its effectiveness, LivFul also developed a patented technology, STAYTEC™, which works alongside IR3535® to ensure the repellent lasts on human skin for over 14 hours.

LivFul has set out to make long-lasting, affordable repellents desirable to fit into daily skincare routines, comparable to the use of moisturiser.

In partnership with the pharmaceutical and chemical manufacturers Merck KGaA, LivFul tested the repellent (consisting of the active ingredient IR3535® and LivFul's patented STAYTEC™ technology).

The 16-hour study involved placing the arms of volunteers into boxes filled with 200 female mosquitos to test the effectiveness of the repellent over long time periods. Prior to the study, mosquitos were starved for 24 hours to ensure they would be most aggressive and hungry during this time. Upon fully passing this study, the same test was carried out in Ghana in partnership with the University of Ghana's Noguchi Memorial Institute for Medical Research.

The next study involved testing against the Anopheles Gambie species of mosquito, the deadliest in the world. LivFul partnered with Noguchi in Ghana to test their repellent's success against this species, as many repellents fail to achieve consistent success against the Anopheles Gambia species due to their erratic, aggressive nature. However, LivFul's repellent passed with flying colours, where no volunteers were bitten or therefore infected during the study.

During their continued success throughout Africa, LivFul began gathering data in Congo and Uganda, showcasing their repellent's

more than 90% adoption and adherence rate. Everyone was surprised to see that when using LivFul's repellent, people weren't getting bitten at all – despite concerns over human error and the possibility of 'missing a spot'. LivFul measured the levels of malaria in the blood of users, and after 60 days, users were clearer of the disease than ever.

Earlier this year, LivFul received the final report of a study conducted with the Noguchi Medical Institute in Ghana. The significant results of the study were shared by Merck KGaA at the American Mosquito Control Association annual meeting, the National Malaria Eradication Program meeting in Ghana, and by LivFul to the NMEP in Nigeria.

Not only did its EIR demonstrate maintained repellency (reaching 100%–96.2% over 9 hours), the test had a significant impact on the Entomological Inoculation Rate, while also showing high efficacy against mutating mosquitoes; more than 98% fewer landings over a 16-day period.

To assess the repellent's economic viability in impoverished regions, LivFul conducted a trial with Ghanian security guards who earn $3 a day. At the end of the trial, security guards talked about the quality-of-life improvement as a result of using the repellent, which not only protects them from a deadly disease but acts as a luxury item in everyday life. While security guards couldn't justify the purchase of items like lotion or deodorant, LivFul's repellent sachets offer an array of benefits such as a pleasant odour, moisturising properties, as well as 14 hours of mosquito protection, rationalising the purchase.

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Hogan Bassey

LivFul Founder, Hogan Bassey, was a typical child growing up in the suburbs of Lagos, Nigeria. He went to school, played sports with the neighbourhood kids, and contracted malaria multiple times. As he grew up, he realised a lack of access to basic health solutions an endemic and structural problem in global healthcare. His "success" in disease prevention motivated him first to pursue a solution to the problem of insect-borne diseases. Hogan's determination resulted in the creation of a new generation of repellent. LivFul Inc. is a company that supports better health with ground-breaking science and one-of-a-kind products, beyond vector-borne disease control.