

ZERO Malaria

THE ZERO MALARIA EXPERIENCE

SHOWCASING THE POWER OF SCIENCE IN THE FIGHT AGAINST MALARIA

THE "STATE OF MALARIA" IN 2024 - WHY THE ZERO MALARIA EXPERIENCE HAS BEEN CREATED.

The fight against malaria is one of humankind's oldest battles, and in 2022 nearly a quarter of a billion cases were estimated¹. Through political commitment and the power of scientific innovation, huge strides have been made against the disease over the last 70 years, and particularly since the turn of the millennium. Since 2000, malaria mortality rates have halved, and 16 countries have been certified for eliminating the disease entirely.² As we reach the end of the first quarter of the 21st century, it is possible to imagine a "Zero Malaria" world.

Building from the powerful African-led 'Zero Malaria Starts With Me' campaign, the Zero Malaria movement seeks to unite citizens everywhere and acknowledge that a world free of malaria makes all nations safer, stronger and more prosperous.³

At this pivotal moment, Malaria No More UK, working closely with partners ranging from the scientific powerhouse of Imperial College London to the visual creatives at The Mill, have used cutting edge creative technology to demonstrate what the future of the malaria fight can achieve through the new immersive Zero Malaria Experience.

The Zero Malaria Experience (The Experience), launched in November 2024 by Zero Malaria ambassador David Beckham, alongside other leaders and champions, focuses on the role of innovation and scientific research to bring about the end of malaria. It uses modelling from Imperial College London **to show that more than 13 million lives, the majority of which are children under-five**, can be saved if key tools and treatments are rolled out in the next 15 years.

Scientific innovations have always been at the forefront of the collective, global effort to control and eliminate malaria. From the discovery of the disease's cause by British scientist Dr Ronald Ross in the late 19th century, to the deployment of the first insecticide treated nets (ITNs) almost a century later, it has always been science, research and development that has provided the upper hand against malaria.



As we enter the second quarter of the 21st century, success in research and development means the toolbox against malaria has grown significantly. In 2024, vaccines approved by the World Health Organization (WHO) began rollout in routine immunisation programmes (outside of the pilot programme) for the first time in several African countries. When delivered equitably to the populations who need them, these vaccines will help further control and drive towards elimination of the disease. Used alongside existing tools like second generation ITNs and augmented by future generations of the vaccines and potential new treatments like monoclonal anti-bodies, it will be possible to save millions more lives.

Controlling and eliminating malaria saves lives in endemic countries. The infrastructure used to do this also helps strengthen health systems. Countries with stronger health systems are better able to diagnose and prevent diseases with pandemic potential, so these investments are to the benefit of all nations.

The funding required to control and progressively eliminate malaria has been unlocked by tireless leadership by endemic country leaders supported by the solidarity of international donors, particularly the nations of the G7. Initiatives including The Global Fund to Fight AIDS, Tuberculosis and Malaria (Global Fund), and Gavi, the Vaccine Alliance (Gavi) are made possible by international financing from countries across the world. This international financing is bolstered by bilateral investments, particularly those made by the Government of the USA through the President's Malaria Initiative (PMI). Thanks to this leadership, funding to defeat malaria now totals over an estimated \$4.1 billion each year.⁴ Yet there remains a sizeable gap between this funding, and what is needed to end malaria. As the next section of this briefing shows, investments are now more necessary than ever in the face of a perfect storm of challenges.

FACING A "PERFECT STORM" – WHY FUNDING FOR THE MALARIA TOOLS AND TREATMENTS HIGHLIGHTED IN THE ZERO MALARIA EXPERIENCE ARE NEEDED NOW MORE THAN EVER.

Despite huge progress in the early 21st century, malaria remains a leading cause of illness and deaths globally, with the burden overwhelmingly in low-income countries in Africa. The World Malaria Report 2023 published by the WHO's Global Malaria Program (GMP) showed there were an estimated 249 million cases and 608,000 deaths from the disease in 2022 - 76% of which were children under five.⁵

A disease of poverty, malaria weakens health systems, disrupts economies, and threatens global health, and economic security. Although there has been great progress over the last two decades, mortality and case rates are now above pre-COVID-19 pandemic levels. Despite increases in domestic spending and private sector contributions, low-income malaria-endemic countries still have a significant dependence on donor funding with 66% of malaria resources coming from external funders⁶. The global malaria campaign is now facing a 'perfect storm' of converging challenges including funding shortfalls, drug and insecticide resistance, climate change and humanitarian crises. Components of the perfect storm include:

• Humanitarian and health emergencies: Between 2019 and 2022, 41 malaria-endemic countries suffered such crises. Many of these countries saw substantial increases in malaria cases and deaths.

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- **Biological threats:** Insecticide, drug and parasite resistance are impacting the effectiveness of existing malaria interventions, whilst the recently discovered species of mosquito An. stephensi, which thrives in both rural and urban areas, has been detected in ten countries in Africa and threatens greater malaria transmission in urbanised areas.
- **Climate change** is making malaria more unpredictable and harder to control. Short-term extreme weather events are now causing large spikes in malaria, as seen in 2022 in Pakistan and 2023 in Mozambique.
- **Insufficient funding levels to maintain coverage:** The last Global Fund replenishment, whilst achieving a record level of funding, fell short of its target, which combined with the impact of the ongoing global financial crises and pressures on domestic resourcing, has resulted in significant resource gaps for malaria. Recently released modelling from the Malaria Atlas Project for the RBM Partnership to End Malaria (RBM) and the African Leaders Malaria Alliance (ALMA) shows that if resources for malaria received through the Global Fund continue to flatline from 2027 to 2029 there will be an estimated additional 112 million cases and up to 280,700 additional malaria deaths, leading to upsurges and outbreaks of malaria right across the continent of Africa⁷.

To weather the perfect storm, investment must be prioritised to ensure malaria tools and treatments can reach those who need them most. The Zero Malaria Experience shows the huge potential that investment in, and deployment of, these tools have for saving lives.

THE STORY OF THE ZERO MALARIA EXPERIENCE.

The Zero Malaria Experience is an immersive and interactive installation which uses new research to tell the story of how a 'toolbox' of scientific innovations has helped to reduce malaria over the past 60 years. It illustrates the potential of existing interventions, like ITNs and vaccines, alongside future ones, such as gene-drive technologies and next-generation vaccine products, to save millions more lives in years to come.

The Zero Malaria Experience allows visitors to select different combinations from this 'toolbox' of cutting-edge malaria innovations to demonstrate how many millions of lives they can save when used together. It uses new research from Imperial College London which estimates that more than 13.2 million lives could be saved in Africa over the next 15 years (from 2025 until 2040) from existing and viable future tools. This is an average of nearly 900,000 lives a year and equates to just under the population of Rio de Janeiro (13.8 million), where this year's G20 Summit will gather world leaders to discuss building a more 'just world and sustainable planet'.

As malaria disproportionately impacts children, 10 million of the lives saved would be those under five years of age. The top five countries where the most lives are projected to be saved in the time period are Nigeria (2,767,000 or 20.8%), The Democratic Republic of Congo (1,191,000 or 9.0%), Ethiopia (929,000 or 7.0%), Tanzania (833,000 or 6.3%) and Kenya (652,000 or 4.9%).

To develop the model behind this research, scientists at Imperial College London compiled existing data sources on the historical malaria burden and spread. They then used mathematical modelling to project the impact of malaria interventions on clinical malaria cases and deaths over time. The model incorporates real-world data, expert insights, and predictive analysis to estimate how many lives can be saved from the expansion of key malaria control measures.





The model focuses on two key outcomes:

- **Clinical incidence:** the model predicts a reduction in malaria clinical incidence by 2040 (as compared to present time) as a result of introducing new tools and increasing coverage of existing tools.
- **Lives saved:** The model estimates that 13.2 million lives could be saved in Africa from 2025 until 2040 by introducing new tools, with 10 million lives saved among children under 5 years.

The modelling focused on the rollout and deployment of several key interventions. Some of these interventions are already available, others are due to come 'on stream' during the 15-year period analysed.

INNOVATION IN ACTION – THE NEW TOOLS AND TREATMENTS THAT CAN SAVE MILLIONS OF LIVES.

The Zero Malaria Experience allows users to see how millions of lives can be saved through the successful delivery of a range of tools and treatments. Over the next 15 years, the malaria toolbox is expected to grow substantially. When delivered with mainstay tools and treatments like preventative chemotherapy, indoor residual spraying and rapid diagnostic tests, these new entrants promise to deliver huge changes for millions around the world.

Malaria vaccines

The RTS,S vaccine was the world's first WHO-approved vaccine for malaria and marked a significant milestone in malaria prevention. It was soon joined by the R21 vaccine, approved for usage by the WHO in 2023⁸. The vaccines have been shown to reduce severe malaria cases and deaths in young children when used in combination with other tools. Supported by Gavi, the WHO and UNICEF, the rollout of RTS,S and R21 reached a significant new phase in 2024 as they entered routine immunisation programmes outside of the pilot phase. Beginning in Cameroon in January 2024, 23 countries in total have been approved for the vaccines, with 15 expected to introduce them in 2024 alone.⁹

Not only are malaria vaccines strengthening the malaria fight today, they also offer a bright future. There are now several 'next generation' vaccines in the research and development pipeline. For example, blood-stage vaccine candidates are being developed which target the malaria parasite at its most devastating stage—the rapid replication of the organism in human red blood cells. The blood stage is where clinical disease and all malaria-associated illness and death occurs. Scientists are currently investigating the possibility of combining a vaccine like R21 or RTS,S (anti-infection vaccines) with a blood stage vaccine called RH5 (anti-disease vaccines). In doing so, a multi-stage vaccine is created which targets multiple stages of the parasite's lifecycle, increasing the overall efficacy of the vaccine. Other vaccines in the pipeline include mRNA and transmission blocking vaccines.

New forms of protection - Long lasting injectables and monoclonal antibodies

Monoclonal antibodies (mAbs) are the fastest-growing class of drug and currently used for some cancers, inflammatory diseases and infections including COVID-19 and Ebola virus. They are given directly to an individual to protect rapidly against, or fight an illness, rather than being produced by the body and can work even in people with compromised immune systems. Unlike vaccines,





which require multiple doses, mAbs offer the benefit of long-lasting protection from a single healthcare visit, simplifying prevention efforts in high-burden areas. With Phase 2 trials showing 80% efficacy in children, the excitement for these potentially game-changing drugs is growing.

In addition to mAbs, one dose, long lasting injectable treatments are a cause for significant optimism. These game changing additions to the malaria arsenal will offer longer and more accessible protection of seasonal malaria chemoprevention (SMC).

Controlling the mosquito - Insecticide-Treated Nets and Gene Drive technology

Insecticide-treated nets

ITNs have long been a cornerstone of malaria prevention, reducing bites from mosquitoes at night when they are most active. Traditionally, ITNs were treated with insecticides that kill mosquitoes on contact. However, rising insecticide resistance has begun to undermine their effectiveness, prompting the development of next-generation nets. The New Nets Project (NNP) piloted dual-action ITNs across sub-Saharan Africa, combining two insecticides to combat resistant mosquito strains¹⁰. Between 2018 and 2022, the project demonstrated these nets' effectiveness in high-transmission areas. These ITNs have been deployed in over 17 countries, averting an estimated 13 million malaria cases and saving 24,600 lives, thanks to initial project funding from The Global Fund and Unitaid¹¹.

Gene Drive Technology

Gene Drive technology offers a revolutionary approach to reducing malaria transmission by genetically modifying mosquito populations to either reduce their numbers or render them incapable of carrying the malaria parasite. A recent experiment, which introduced modified mosquitoes to make up 12.5 and 25% of the study population, led to complete population collapse in just one year: the first time a gene drive has been shown to be effective when tested in conditions that mimic the natural environment¹².

This has exciting implications for use in the real world where, in appropriate settings, it could considerably reduce the number of malaria-carrying mosquitoes and therefore the number of malaria cases and deaths. Gene drives do not require regular distribution and can be effective by releasing just a few thousand mosquitoes in several locations, making them low cost to implement. They are also less affected by resistance and could be used in hard to-reach areas that are not adequately tackled by existing methods, or alongside the scale up of existing tools such as ITNs and insecticides.

COLLABORATING TO END MALARIA.

The power of the tools and treatments required to achieve the projections used in the Zero Malaria Experience will only be realised through collaboration between a significant number of actors. This section draws out just some of those crucial actors in the process (and as such is intended as an illustrative and non-exhaustive list).

At the core of this collaboration are the local, regional, and national government officials of endemic countries, with resources stewarded by National Malaria Control Programmes and Ministries of Health, and funding drawn down from national treasuries. They are in turn supported by a multitude of non-governmental organisations and civil society groups based within affected communities.





Working to support countries are the global health initiatives and technical support agencies funded through multilateral channels. Historically the largest of these for malaria has been the Global Fund which is responsible for around two thirds of international financing for malaria control and elimination efforts. With the advent of vaccines for malaria, Gavi, the Vaccine Alliance has now become an important part of the malaria fight. In its next replenishment event due to complete in 2025, malaria vaccinations will become a significant part of Gavi's portfolio. Both the Global Fund and Gavi receive support from, and work in collaboration with, specialised agencies and funds of the UN, including WHO, UNICEF and the World Bank group.

Research and development of new tools and treatments to fight malaria takes in a significant network of connected institutions working collaboratively. This includes academic institutions in endemic countries like the Ifakara Health Institute in Tanzania, as well as those based out of traditional donor countries such as Imperial College London and the London School of Hygiene and Tropical Medicine in the UK, and the John Hopkins Malaria Research Institute in the US. Through the painstaking scientific research into, and testing and field assessment of, new tools and treatments, these networks of organisations are at the frontline of the malaria campaign's effort to stay one step ahead of the disease.

Product development partnerships (PDPs) play a vital role in connecting research institutions, academic organisations, manufacturers, donors and local and national governments in the delivery of new tools and treatments. For malaria, Medicines for Malaria Ventures (MMV) and the Innovative Vector Control Consortium (IVCC) are two particularly significant actors, playing a key role in catalysing research and development of tools and treatments including the achievement of Next Generation Nets, as well as the promising opportunity of mAbs and long-lasting injectables. Working closely with the PDPs, as well as other actors in the wider community is Unitaid, which plays a key role in supporting and catalysing the development of new tools and treatments.

Private sector actors, including biotech and pharmaceutical companies, as well as manufacturing organisations, are also hugely important in the process. GSK, Novartis, Vestergaard and the Serum Institute of India are just a few examples of the businesses playing a vital role in the research, development and manufacture of tools and treatments. The private sector also plays an important role in funding malaria control and elimination through donations bilaterally and multilaterally, and through direct action to ensure that their workforces and communities served are protected. Sitting alongside these include philanthropic organisations and foundations such as the Gates Foundation, Open Philanthropy and the JC Flowers Foundation.

Finally, national governments of non-endemic countries standing in solidarity with malariaendemic nations play a vital role in providing funding and support to the actors noted above. G7 nations in particular provide the majority of the funding to Gavi and the Global Fund; and their continued contributions will be vital to achieving the vision set out in the Zero Malaria Experience. In addition to multilateral support through the Global Fund and Gavi, the Government of the USA makes a significant bilateral contribution through the efforts of the President's Malaria Initiative.



A CALL TO ACTION - HOW TO MAKE THE ZERO MALARIA EXPERIENCE A REALITY.

The Zero Malaria Experience shows that investment in research and development, paired with funding for the vital global health initiatives that allow tools and treatments to reach those most in need, can save millions of lives in the next 15 years. Through collaboration across research institutions, private sector companies, product development partnerships, philanthropic organisations, and national and local governments, the next generation of tools and treatments will set malaria on the path to eradication.

For this to be achieved, it is imperative for leaders to prioritise the following:

- Ensure full funding for the Global Fund and Gavi at their next replenishments 2025 will see both global health initiatives hold their replenishment events. It is vital that full funding is received for both initiatives, especially given the mutual interdependence between the tools and treatments which their funding supports countries to access.
- Increase funding for research and development The Zero Malaria Experience demonstrates the huge number of lives that can be saved from malaria with the investment in research and development. Despite huge achievements in recent years with the successful roll out of next generation ITNs and the introduction of vaccines for malaria, the most recent World Malaria Report shows funding for research and development against the disease has hit a 10-year low. It is imperative that full investment to maintain the pipeline of new tools and treatments is achieved.
- **Support Product Development Partners and market shaping initiatives –** As new science develops ever more effective tools, it is vital that the PDPs and market shaping initiatives required for their successful roll out are in place. Donor nations are critical to the funding of these partners and initiatives and should sustain their leading role in making scientific research become reality for those most in need.

¹ World Malaria Report 2023: Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. Pp 18.

² World Health Organization, <u>https://www.who.int/teams/global-malaria-programme/elimination/countries-and-territories-certified-malaria-free-by-who</u>

³ More information on the Zero Malaria movement can be found at <u>https://zeromalaria.org/</u>

⁴ World Malaria Report 2023: Geneva: World Health Organization; 2020. Licence: CC BY-NC-SA 3.0 IGO. Pp 45.

⁵ lbid, pp 8.

⁶ Ibid, pp 47.

⁷ The RBM Partnership To End Malaria, <u>https://endmalaria.org/news/malaria-kill-300000-more-people-if-critical-funding-not-received</u> ⁸ World Health Organization, <u>https://www.afro.who.int/countries/cameroon/news/cameroon-kicks-malaria-vaccine-rollout</u>

⁹ Countries introduced in 2024 to date: Cameroon (22/01); Burkina Faso (05/02); Benin (25/04); Sierra Leone (25/04); Liberia (25/04); Cote d'Ivoire (15/07); South Sudan (16/07); Mozambique (05/08); Central African Republic (22/08); and Niger (19/09).

¹⁰ Innovative Vector Control Consortium, <u>https://www.ivcc.com/market-access/new-nets-project/</u>

¹¹ The Global Fund to Fights Aids, Tuberculosis and Malaria, <u>https://www.theglobalfund.org/en/news/2024/2024-04-17-new-nets-prevent-13-million-malaria-cases-sub-saharan-africa/</u>

¹² Hammond, A., Pollegioni, P., Persampieri, T. et al. (2021) Gene-drive suppression of mosquito populations in large cages as a bridge between lab and field. Nat Commun, 12, 4589. <u>https://doi.org/10.1038/s41467-021-24790-6</u>

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