

A child receiving the second of four malaria vaccine doses at Lumumba Hospital in Kisumu, Kenya.

## At Long Last, Can Malaria Be Eradicated?

Two new vaccines may finally turn back an ancient plague. But in unexpected ways, their arrival also complicates the path to ending the disease.

By Apoorva Mandavilli Photographs by Kang-Chun Cheng Oct. 4, 2022 NYT All through childhood, Miriam Abdullah was shuttled in and out of hospitals, her thin body wracked with fever and ravaged by malaria. She was so sick so often that her constant treatments drained her parents, who also cared for her many siblings, both financially and emotionally.

"At some point, even my mum gave up," recalled Ms. Abdullah, now 35. In Nyalenda, the poor community in Kisumu, Kenya, where Ms. Abdullah lives, malaria is endemic and ubiquitous. Some of her friends developed meningitis after becoming infected; one died. "Malaria has really tormented us as a country," she said.

There are tens of millions of horror stories like Ms. Abdullah's, handed down from generation to generation. But now change is in the air: Malaria is the rare global

health scourge about which experts are sanguine — so much so that some have begun to talk about <u>eradicating the disease</u>.

"I think there's so much room for optimism," said Philip Welkhoff, director for malaria programs at the Bill and Melinda Gates Foundation. "Later this decade, we could actually launch a push that gets us all the way to zero."

<u>China</u> and El Salvador were <u>certified malaria-free</u> last year, and the six countries in the Greater Mekong region, including Vietnam and Thailand, have driven down cases by about 90 percent. About 25 countries are expected to have eliminated malaria by 2025.

The bulk of infections now <u>occur in Africa</u>. Even there, despite the limitations <u>imposed by</u> the coronavirus pandemic, nearly 12 million more African children received preventive malaria drugs in 2020 than in 2019.

But it is the arrival of two new vaccines that portend a sea change. The <u>first</u>, called Mosquirix, was 35 years in the making. It was approved by the World Health Organization just last year and may be distributed as soon as late next year. A more powerful malaria vaccine, developed by the Oxford team that created the AstraZeneca Covid vaccine, may be just a year or two away. Many experts believe it is this formulation, which has shown an efficacy of up to <u>80 percent in clinical trials</u>, that may transform the fight against malaria.



Miriam Abdullah at home in Nyalenda, a poor community in Kisumu. Some of her friends developed meningitis after becoming infected with malaria; one died. "Malaria has really tormented us as a country," she said.



Malaria medication in Ms. Abdullah's purse.



A woman, shrouded by a blue mosquito net, smiling at her son while sitting on a bed.

Still <u>more options</u> are on the <u>horizon</u>, including <u>an mRNA</u> vaccine being developed by the German company BioNTech; <u>monoclonal antibodies</u> that can <u>prevent</u>

<u>malaria</u> for <u>six months or longer</u>; bed nets coated with long-lasting insecticides or with chemicals that <u>paralyze mosquitoes</u>; as well as new ways to trap and kill mosquitoes.

"It's an exciting time," said Dr. Rose Jalang'o, who led a pilot test of the Mosquirix vaccine in Kenya, where it was given to children alongside other immunizations.

But getting to a malaria-free world will require more than promising tools. In many African countries, distribution of vaccines, drugs and bed nets requires overcoming myriad challenges, including rough terrain, other urgent medical priorities and misinformation.

While the funding for malaria programs is more generous than for many other diseases that plague the poorest nations, resources are still limited. Money devoted to one approach often leads funders to neglect others, fueling competition and sometimes rancor.

Mosquirix cost more than \$200 million to develop over more than 30 years, but its efficacy is roughly half that of the Oxford vaccine, called R21. The first doses of Mosquirix will not be delivered to African children until late 2023 or early 2024. The supply will be <u>severely constrained</u> for a number of reasons, and is expected to remain so for years.

In December, Gavi, a nongovernmental organization that supports vaccinations worldwide, <u>committed \$156 million</u> to distribute Mosquirix. And in August, Unicef granted the vaccine's manufacturer, GlaxoSmithKline, a \$170 million contract, enough to produce 18 million doses over the next three years.

But that is a far cry from the estimated 100 million doses that will be needed each year.

R21, the second vaccine, appears to be more powerful, cheaper and easier to manufacture. And the Serum Institute of India is prepared to produce more than 200 million doses of R21 per year.

Some malaria experts note that given the urgent need, the world needs every option it can get. But <u>others worry</u> that every dollar directed to Mosquirix now is a dollar less for developing other tools.

"Existing malaria control measures are already underfunded," said Dr. Javier Guzman, director for global health policy at the Center for Global Development in Washington. "I don't want to be negative, but a new tool without additional for director has included as a series are and measure as a restriction and "

funding basically means sacrifices and means an opportunity cost."



A sunset on the banks of the Wigwa River, which flows through Nyalenda and is a breeding site for mosquitoes.

Malaria is among the oldest infectious diseases and one of the deadliest. Years of rapid progress stalled about a decade ago, leaving the toll in 2019 at a staggering 229 million new infections and 558,000 deaths.

While the Covid pandemic did not send malaria infections skyrocketing, as happened with tuberculosis, the pandemic reversed a slow downward trend in malaria deaths, which ratcheted up to 627,000 in 2020.

Nearly all of the lives lost to malaria are <u>in sub-Saharan Africa</u>, where about 80 percent of the deaths are in children younger than 5.

Many strategies to fight malaria are dated, yet still inaccessible to millions. Only about <u>half of African children</u> sleep under insecticide-treated bed nets, for instance, and even fewer receive seasonal drugs that prevent the infection.

Malaria <u>compounds</u> social inequities. It robs children of the ability to fight other pathogens, overwhelms health care systems and devastates entire communities. One untreated person with malaria can remain ill for six months, giving mosquitoes the opportunity to spread the parasite to as many as 100 other people.

Designing a vaccine against a parasite has proved much more <u>challenging</u> than creating one against a virus or bacterium. Plasmodium falciparum, the organism that causes malaria in Africa, rapidly cycles through several life stages, morphing into a new form each time.

The body struggles to recognize and defend itself against this shape-shifter, leaving people vulnerable to repeated bouts of disease.

A mosquito bite delivers only about 10 "sporozoites," the form of the parasite that can be transmitted. But within 30 minutes of infection, the sporozoites invade the liver and begin to multiply into an unbeatable army of thousands. Mosquirix and R21 target sporozoites in the few minutes before they enter the liver.

The parasite wrecks the body so quickly that by the time children are taken to the hospital, many are in dire need of a blood transfusion. But blood is often in short supply in sub-Saharan Africa, and using a bag for a small child can mean that half or more will be discarded, said Dr. Mary Hamel, who leads the W.H.O.'s malaria vaccine implementation program.

"You see a child who is so pale and floppy and breathing so rapidly, and they're just splayed on the cot — and there's nothing you can do," she said.
"You've got to *prevent* malaria — it just progresses too fast," she added.



A girl about to receive a dose of malaria vaccine at the Ring Road Clinic in Nyalenda.



A laboratory at the Ring Road Clinic.



A boy getting tested for malaria at Dunga Nursing and Maternity Ward in Kisumu. Roughly a third to half of the patients they see have malaria concerns or infections.

Mosquirix, the first vaccine against any parasite, is a technical triumph. But its efficacy, at about 40 percent, is much lower than scientists had hoped. Ideally, the vaccine would be deployed alongside existing controls, like insecticide-treated bed nets and preventive drugs, based on data indicating where the tools are most needed and delivered by a robust health care work force. "If you combine with the right tool, you can get a much, much bigger impact," said Dr. Thomas Breuer, chief global health officer at GlaxoSmithKline, which manufactures Mosquirix.

The vaccine, which can be refrigerated, was tested in Kenya, Ghana and Malawi in children younger than 2 years — and more easily than some experts had feared. "It is more deliverable in rural, remote settings than many other vaccines have been," said Prashant Yadav, an expert in health care supply chains at the Center for Global Development.

Community health workers went door-to-door to publicize Mosquirix, and governments spread the word via local television and radio shows. Despite

misinformation that circulated on WhatsApp and social media, uptake of the vaccine was comparable to that of routine immunizations.

But in many African countries, mistrust of vaccines is high. In one survey, about half of people in Niger and the Democratic Republic of Congo said they would not trust a malaria vaccine.

Moreover, Mosquirix must be given in four doses, the first at 5 months of age and the fourth after 18 months of age. But few other vaccines are given to children older than 18 months, and many parents in Africa face enormous logistical hurdles in taking children to a clinic.

Parents may also wrongly assume that the first three doses of Mosquirix are protective enough, researchers said. (By contrast, R21 has an efficacy of 70 percent after three doses given before 17 months of age. A booster given a year later maintains and even enhances its potency.)

"It would be easier if the last shot was at 18 months," Dr. Kwame Amponsa-Achiano, a physician and epidemiologist who leads the vaccine program at Ghana's ministry of health, said of Mosquirix.



A physician at the Ring Road Clinic.

Compared to the billions of dollars poured into Covid vaccines, the funds for malaria are a pittance. The Gates Foundation spends about \$270 million a year fighting the disease, not counting its contributions to the Global Fund to Fight AIDS, Tuberculosis and Malaria.

The scarcity of resources means that people — and organizations — end up picking favorite strategies. Some maintain that controlling mosquitoes is the logical path, while others push vaccines. Still others say monoclonal antibodies are the way forward.

In such a highly competitive arena, Mosquirix does not emerge as the obvious winner.

"Deploying a tool which is expensive, and not that effective, with a short duration of action, may not be the thing that you want to lead to first," said Dr. Scott Filler, head of malaria programs for the Global Fund, which supports more than half of malaria programs worldwide.

The money might be better spent increasing use of bed nets, or ensuring that people have access to basic primary health services, including testing, treating and tracking for malaria, Dr. Filler said.

Even the Gates Foundation, which has poured more than \$200 million into the development of Mosquirix, is now lukewarm on the vaccine and is focusing instead on speeding newer tools to Africa.

"Some of this other stuff in the portfolio is going to be better, cheaper, easier to deploy and easier to scale up," Dr. Welkhoff said.

But other experts believe that given malaria's devastation, a vaccine with low efficacy is better than none.



A woman changing a baby's diaper at the Dunga Nursing and Maternity Ward.



Mosquito nets in a garden in Kisumu.

**Image** 



Ms. Abdullah in her daughter's room. Next to the baby photos on the wall are letters the child wrote thanking her mother for protecting her from mosquitoes with nets and vigilance.

"We have this vaccine that has been tested very, very extensively — more than any vaccine prior to approval," said Michael Anderson, a former director general of Britain's Department for International Development who now heads MedAccess, a nonprofit group financed by the British government.

R21 has cost less than \$100 million to develop. If regulators are as fast and nimble as they were with Covid vaccines, it could be authorized a few months after the researchers submit final data at the end of this year.

The two vaccines are not necessarily in competition, said Dr. Adrian Hill, R21's architect and director of the Jenner Institute at the University of Oxford. The biggest problem with Mosquirix "is there isn't enough of it," Dr. Hill said. Still, R21 would be simpler to deliver because it's "a more modern product," he added. "It was designed in 2012, not in the 1980s and 1990s."

For many parents in Africa, a vaccine cannot come soon enough. In Kisumu, Ms. Abdullah is anxious to immunize her 2-year-old daughter, who has already had malaria once, against the illness that marred her own childhood.

"I would go for it immediately," she said. "In fact, I would go for it before I even go for the Covid-19 vaccine."

Odera Wickliffe contributed reporting from Kisumu, Kenya.