

## Mosquitoes use gut bacteria to fight the malaria they transmit—scientists are exploring how to use this

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Anopheles gambiae complex mosquito species can transmit malaria. Credit: CDC/James Gathany via Wikimedia Commons

The months of September to May are an unfortunate season in South



Africa: <u>malaria season</u>. The mosquito-borne disease is found in the northeastern districts of KwaZulu-Natal, Mpumalanga and Limpopo provinces.

There are fewer <u>malaria</u> cases in South Africa compared to other African countries. The World Health Organization estimated there were more than 10 million cases of malaria <u>in Mozambique in 2022</u>. South Africa, that country's neighbor, recorded <u>5,183 malaria cases</u> between September 2022 and August 2023.

Its relatively low case numbers may be a result of South African health authorities' excellent work in controlling the disease (control efforts began more than <u>120 years ago</u>). The last major malaria outbreak in South Africa was in <u>2000</u>, when more than 60,000 cases were recorded. Also notable was the <u>2017 outbreak</u>, with 28,264 cases.

This combination of control efforts and low numbers may mean that South Africans think malaria is not something they need to worry about unless they travel to provincial hotspots in the months of September to May. But it remains a disease of concern—not just within the country's borders, but in the broader southern African region. Many researchers like ourselves are working towards eliminating or even, one day, totally eradicating the disease.

"<u>Elimination</u>" doesn't mean there will be no malaria in the region at all. Instead, it would mean that local mosquitoes no longer spread the disease in South Africa.

The reason that South Africa has not fully eliminated malaria is precisely because its local mosquito populations are still transmitting the disease. In fact, in 2023, about 17% of people who got sick from malaria had caught it in South Africa and not from traveling to neighboring African countries.



Scientists are using and developing many different "weapons" in the fight against malaria. Our approach involves using mosquitoes' own gut bacteria to prevent them from spreading malaria. This is a form of biocontrol, which involves the use of living organisms or natural substances to control harmful pests.

The groundwork we're laying with this <u>ongoing research</u> will, we believe, allow us and other scientists to create a powerful malaria-beating tool.

## **Current control methods**

No single control method can eliminate malaria. South Africa is home to a range of mosquito species that can pass on malaria, and all behave differently.

For example, some of the mosquitoes that transmit malaria in the local malaria-endemic areas are active outdoors. They bite people outside and, rather than resting inside homes, they tend to rest outdoors. Outdoor mosquitoes are difficult to control because most control methods target indoor mosquitoes.

There is also a continuing problem of mosquitoes <u>developing resistance</u> to the insecticides that are used to spray the walls inside houses. <u>New</u> <u>insecticides</u> are not being produced fast enough to keep up with the demand.

One promising biocontrol method that's been developed in recent years is, essentially, a form of mosquito "birth control." Sterile Insect Technique involves the release of massive numbers of sterile male mosquitoes. Male mosquitoes do not bite, and therefore are not a disease or biting nuisance risk. However, they will mate with the local female mosquitoes. When female mosquitoes have mated with a sterile male, they will <u>lay unfertilized eggs which won't hatch</u>. Over time, this



decreases the number of mosquitoes that hatch. The technique is <u>being</u> <u>trialed</u> in northern KwaZulu-Natal.

While this is exciting, the trial program has not been rolled out for general malaria control yet. However, it's good to see South Africa testing biocontrol options—and that's where our work comes in.

## The power of bacteria

Bacteria are tiny single-celled organisms. As happens in humans, there are "good" bacteria in the gut of mosquitoes that affect their survival and overall well-being. These bacteria are also known as the microbiota. A mosquito's gut microbiota is needed for the insect to <u>become an adult</u> and <u>digest food</u>. These bacteria can also help the mosquito survive insecticide exposures by breaking them down into <u>smaller</u>, less toxic <u>compounds</u>.

Most importantly, the gut bacteria of mosquitoes are an integral part of their immune system, because they can help the insects fight off infections including malaria. The parasite that causes malaria infects the mosquito when an adult female mosquito takes an infected blood meal from a human. Malaria parasites are likely <u>bad for the insect</u> and so they try to fight the infection. Most mosquitoes are quite good at fighting off the infection.

However, there are a few mosquito species that cannot fight off the parasite infection. These mosquitoes become unhealthy as the infection circulates through their body, and then <u>pass on the parasite to humans</u> when they bite them.

In a sense, therefore, a malaria-transmitting mosquito is a sick mosquito. This is where bacteria can help. If the mosquito has the right set of gut bacteria, she will be able to fight off the malaria parasite. In turn, she



will not get infected by the malaria parasite and can no longer pass it on to humans. Scientists can help the mosquitoes to halt malaria infections by providing them with the correct bacteria. This is a type of biocontrol known as <u>paratransgenesis</u>.

In our lab, we are interested in finding the right bacteria that can be used to help stop the spread of malaria. We <u>have found</u> that different types of mosquitoes have different sets of bacteria. We have also found that there are several anti-parasitic bacteria in mosquitoes that do not spread malaria well. Since these bacteria can boost the immune system of the mosquito, they could help to prevent the mosquitoes from transmitting the malaria parasite.

If we understand exactly which bacteria are involved, they can be used as biocontrol. These candidates could be given to a malaria-transmitting mosquito through a blood-meal (that contains the bacteria) or through genetic modification.

Paratransgenesis was first successfully performed in the <u>kissing bug</u> more than 30 years ago in the U.S. to control <u>Chagas disease</u> (American trypanosomiasis). The work sparked many more paratransgenesis strategies for the control of other <u>blood-sucking insects</u>, not just mosquitoes.

However, there is still some time before we see paratransgenesis being rolled out for mosquitoes. Like with most insects, this research is still in the lab testing phase. This type of biocontrol might not be used in South Africa within the next decade or even 20 years. The reason for the relatively slow progress is to ensure safety and to follow the many strict regulations that come with these technologies. But, with our work, we are contributing to making paratransgenesis control programs for mosquitoes a reality in South Africa one day in the future.



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