

New studies show nobel prize-winning drug that knocks out parasitic worms could have second act fighting malaria

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A workhorse of a drug that a few weeks ago earned its developers a Nobel prize for its success in treating multiple tropical diseases is showing early promise as a novel and desperately needed tool for interrupting malaria transmission, according to new findings presented today at the American Society of Tropical Medicine and Hygiene (ASTMH) Annual Meeting.

Researchers from Colorado State University and the Institut de Recherche en Sciences de la Santé presented preliminary results from a trial in the West African country of Burkina Faso that show approximately 16 percent reduction in childhood malaria episodes caused predominantly by the deadly malaria parasite *Plasmodium falciparum* in four villages where, for the last few months, the majority of the population has been receiving a single dose of the anti-parasite [drug](#) ivermectin every three weeks. The villages are located in an area that experiences a high burden of both malaria and worm diseases, raising the possibility of addressing several health problems at once.

"These are preliminary results but we expect to see further reductions in malaria fevers as we continue with the trial, which is occurring during the rainy season when [malaria transmission](#) typically peaks," said Brian D. Foy, the lead investigator on the project. "The drop in malaria fevers we're seeing with the ivermectin treatment is in addition to whatever is being achieved with insecticide treated bednets, which are in widespread

use in all of the villages participating in the study."

There have been previous studies showing ivermectin, even at very low levels, is toxic to the *Anopheles* mosquitoes that carry malaria. But the trial in Burkina Faso is the only thus far to evaluate ivermectin solely as a strategy to fight malaria disease in sub-Saharan Africa, which is home to the majority of the 584,000 people—most them young children—who die from malaria each year.

Meanwhile, Kevin Kobylinski of the US Walter Reed Army Institute of Research (WRAIR) and its US component at the Armed Forces Research Institute of Medical Sciences in Thailand presented new data showing ivermectin can block development of *Plasmodium vivax* parasites in mosquitoes that are common in Southeast Asia. He said the results are further evidence of the potential of ivermectin to become a "powerful new tool to aid [malaria elimination](#) efforts" in a region where the spread of drug resistance threatens malaria control efforts worldwide.

Why Ivermectin for Malaria?

Over the last three decades more than 1 billion doses of ivermectin have been distributed in Africa and Latin America in mass drug administration (MDA) campaigns that have dramatically reduced the burden of lymphatic filariasis, which causes elephantiasis, and onchocerciasis, the disease that causes river blindness. Ivermectin also can kill several types of debilitating intestinal worms known as soil-transmitted helminths.

Earlier this month, the Nobel Prize in Physiology or Medicine was awarded to developers of ivermectin, William C. Campbell of Drew University and Satoshi Ōmura of Japan's Kitasato University, who [isolated the precursor of ivermectin](#) from an organism discovered in a

single soil sample collected in Japan in the 1970s. The drug was originally used to treat parasites in livestock and pets before becoming the mainstay of the global campaigns to combat lymphatic filariasis and onchocerciasis.

Lead investigator Foy noted that ivermectin's potential efficacy as a [malaria control](#) strategy differs from the drug's use against worm diseases because ivermectin is not intended to actually cure a [malaria infection](#). Rather, he said it is intended to reduce infections that lead to fevers in children by interrupting local transmission of *Plasmodium* parasites. Foy said laboratory studies indicate that when mosquitoes feed on the blood of people who have taken ivermectin, it interferes with the mosquito's ability to transmit malaria parasites to humans—sometimes by killing them outright, but more often by weakening them and interfering with their digestive system so they eventually die in the harsh conditions of nature.

"Even if the mosquitoes don't get enough ivermectin to directly kill them, we think a sub-lethal dose should be sufficiently toxic to reduce malaria transmission," Foy said.

But he noted that because the goal is to interrupt malaria transmission, the drug must be taken by a majority of the people in a town or village, who then pass it along to mosquitoes that bite them. In the trials in Burkina Faso, the drug distributions exclude children less than 90 centimeters (three feet tall), pregnant and newly breast-feeding women. The measure of success is a reduction in malaria incidence among children under age 5, most of whom will not actually take the drug. But this is the age group most at risk of serious illness and death from the disease.

Potential Role Fighting Spread of Drug Resistant

Malaria in Southeast Asia

WRAIR's Kobylinski said his most recent malaria study with ivermectin involved testing its potential to block malaria transmission by feeding blood meals containing ivermectin and *P. vivax* parasites to *Anopheles dirus* mosquitoes, the predominant malaria vector in Southeast Asia. While not as deadly as the *P. falciparum* [malaria parasite](#), *P. vivax* parasites can remain dormant in the liver and cause multiple, debilitating relapses.

Kobylinski and his colleagues found ivermectin effectively killed *Anopheles dirus* mosquitoes, and it also inhibited the ability of any surviving mosquitoes to develop *P. vivax* parasites in their bodies.

Kobylinski noted that malaria experts are considering combining ivermectin [with other medications](#) in MDA campaigns that would seek to stop the spread of drug resistant parasites in Southeast Asia by eliminating malaria from the entire region. He said ivermectin could help increase compliance with an MDA strategy in places like Thailand, where drug resistant malaria is spreading, but overall malaria infection rates are relatively low.

"There is a lot of interest in launching MDA campaigns to fight drug resistant malaria in Southeast Asia, but it can be hard to convince someone to take malaria medications if they don't have an active malaria infection," he said. "But if you put ivermectin into the mix, that could improve participation because many people recognize the benefits of taking ivermectin for more common problems, like scabies."

"We're at a critical moment in the fight against malaria where drug and insecticide resistance is threatening hard-won progress," said Christopher V. Plowe, president of the American Society of Tropical Medicine and Hygiene. "It's important to actively develop new tools and

strategies—including re-purposing old tools—to keep pushing down malaria."

Last year, growing interest in adding ivermectin to the malaria toolkit prompted the creation of the global [Ivermectin Research for Malaria Elimination Network](#) to set up a common research agenda for ivermectin-based [malaria](#) strategies.

Provided by Burness Communications

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