Despite progress, existing treatments and pesticides are losing their effectiveness, says Andrew Jack.

This will be a decisive year for malaria. From the jungles of the Greater Mekong or the urban shanties of Haiti, new tools and tactics are being used to combat the spread of the disease and to alleviate its huge economic and human costs.

It still infects 200m people each year and kills nearly 600,000, yet enormous progress has been made since the start of the millennium – the death rate has halved and an estimated 4.3m lives have been saved but there are concerns over funding and biological resistance.

Pedro Alonso, director of the World Health Organisation’s global malaria programme, says: “Malaria has been a success story. The progress made is really unprecedented. But we are at a tipping point. We are worried about losing the gains achieved over the past decade.”

In total, 30 countries are moving towards elimination. Argentina is set to be declared malaria-free this year, while other nations including Sri Lanka and Saudi Arabia have done so.

Leaders of countries where malaria is endemic have stepped up their cross-border commitments spearheaded by organisations such as the African Leaders’ Malaria Alliance and the Elimination Eight of southern African countries as well as the Asia Pacific Leaders’ Malaria Alliance. Some prominent business people have also increased support, such as Mike Ilitch in Nigeria.

Increased funding to disseminate existing tools – including indoor residual spraying and insecticide treated bed nets, rapid diagnostic tests for accurate confirmation of malaria and artemisinin combination drug therapy for treatment – has helped strengthen the fight against the disease. New experimental approaches are also advancing. The Medicines for Malaria Venture and its academic and pharmaceutical industry partners report progress towards a single-dose malaria treatment.

GlaxoSmithKline’s RTS,S, a vaccine it is developing against the parasite, is being scrutinised regulators. Meanwhile, Oxitec is developing genetically modified sterile mosquitoes to eradicate the insects that transmit the infection.

There is fresh momentum on yet more ambitious goals. The Bill & Melinda Gates Foundation is reviving a decades-old discussion about eradication. “The great debate now is a malaria-free world,” says Alan Magill, in charge of work on the disease at the Seattle-based organisation. “Do we just accept the status quo or start to chart paths towards a new vision?”

Already the World Health Organisation is set to seek approval next month from ministers of health at the World Health Assembly in Geneva of a bolder plan for 2016-2030 that envisages elimination of malaria in at least 35 more countries, with a 90per cent reduction in death and infection.

In the Greater Mekong, a growing number of studies have shown that the parasite has become resistant to artemisinin and the other drugs with which it is combined on the Thai-Cambodia border. There are plans for a rapid shift towards elimination of the disease using techniques including mass drug administration to the entire population.
**War on Anopheles mosquitoes heats up**

**Research** Scientists are learning more about how the insects target humans, writes Clive Cookson

Malaria depends on a complex triad of biological relationships between the Plasmodium parasite, the mosquito vector, and its two hosts: humans and mosquitoes. Although most scientists, including those in recent years who have focused on tackling the parasite itself through drugs and vaccines, the one on the Anopheles mosquitoes, which spread Plasmodium, people, and the environment. But progress in understanding these relationships is mounting, driven by recent research. 

In January, researchers from the University of California, Merced reported evidence that Anopheles mosquitoes may be able to sense the emergence of “super” mosquitoes. In fact, they can detect the chemical cue that prompts mosquitoes to switch to breeding in pools that are less than 100 mm deep, even when the water is not as clear and the mosquitoes are not as numerous. This finding has implications for understanding how malaria may spread in urban areas, where pools of water are more common and mosquitoes may be more numerous.

In February, researchers from Oxford University and the University of California, Los Angeles, published a study showing that Anopheles mosquitoes can detect the presence of human odours even when they are not near people, suggesting that mosquitoes may be able to find humans from a distance, even from many kilometers away. This finding has implications for understanding how malaria may spread in urban areas, where pools of water are more common and mosquitoes may be more numerous.

Anopheles mosquitoes are a major contributor to the spread of malaria, which affects millions of people each year. In recent years, researchers have been focusing on understanding how mosquitoes target humans, in order to develop new strategies for controlling malaria. The findings from these recent studies suggest that Anopheles mosquitoes may be able to sense the emergence of “super” mosquitoes, even when the water is not as clear and the mosquitoes are not as numerous. This finding has implications for understanding how malaria may spread in urban areas, where pools of water are more common and mosquitoes may be more numerous.

**Lethal gene relies on law of attraction**

**Genetics** Impressive results as biological warfare to combat deployed into insects, reports Clive Cookson

Chemical insecticides are the mainstay of malaria control today, but future campaigns could focus on targeting the mosquitoes themselves, with genetically modified insects. In this issue, a company based out of Oxford University in 2015, to skip the advancement phase, using the gene drive to insert a “dominant lethal” gene into mosquitoes, which would make the male offspring sterile and males that survived would philander with all females in the population.

The strategy, tested over the past five years in Hualien in southern Taiwan and the Loneliness Parry, chief executive of Oxitec, says the company’s technology is a “promising new tool in the fight against malaria,” and has the potential to be a “key component of a broader malaria strategy.”

But, as in any new technology, there are challenges to be overcome. One of the biggest challenges is the issue of resistance, as mosquitoes can develop resistance to the modified mosquitoes over time. This raises questions about the sustainability of the strategy, and whether it will be effective in the long term.”

Another important issue is the ethical and social implications of releasing genetically modified mosquitoes into the wild. There are concerns about the potential for these mosquitoes to spread their modified genes to other mosquito populations, and the potential for these genes to affect other species or the environment. These issues must be carefully considered before any large-scale releases of modified mosquitoes are approved.

Despite these challenges, there is growing interest in the use of genetically modified mosquitoes as a potential tool for controlling malaria. In the United States, for example, a company based out of Pennsylvania, Oxitec, is currently testing its technology in the field, and has received approval from the US government to begin releasing genetically modified mosquitoes in Florida.

But the technology is not without controversy. Some people are concerned about the potential for the modified mosquitoes to affect other species or the environment, and the ethical implications of releasing genetically modified mosquitoes into the wild. These issues must be carefully considered before any large-scale releases of modified mosquitoes are approved.

Overall, the strategy of using genetically modified mosquitoes to control malaria is promising, but there are still many challenges to be overcome. As more research is conducted and the technology improves, it is likely that this approach will become a more important tool in the fight against malaria in the future.”

**Prevention** As bed nets begin to lose their effectiveness, researchers are coming up with new approaches, writes Sarah Murray

The World Health Organization (WHO) has recently launched a campaign to combat malaria, with a focus on increasing the use of insecticide-treated bed nets. These nets are effective at preventing mosquito bites, and thus reducing the risk of malaria transmission. However, studies have shown that the effectiveness of these nets is decreasing, due to the development of resistance to the insecticides used in their production.

One of the key challenges in controlling malaria is the emergence of resistance to insecticides. In recent years, there have been several cases of resistance to insecticides, such as pyrethroid and organophosphate insecticides, in different parts of the world. This has led to a decrease in the effectiveness of these nets, as mosquitoes are able to survive and reproduce in areas where these insecticides are being used.

In addition to the development of resistance to insecticides, there are other factors that contribute to the decrease in the effectiveness of bed nets. These include the use of sub-optimal insecticides, the lack of proper maintenance and replacement of the nets, and the use of nets that are not effective at preventing mosquito bites.

One of the key strategies for improving the effectiveness of bed nets is to use insecticides that are less likely to develop resistance, such as the neonicotinoids and the carbamates. In recent years, there has been a shift towards using these classes of insecticides, as they are less likely to develop resistance.

Another key strategy is to use nets that are more effective at preventing mosquito bites. This can be achieved by using nets that are impregnated with a variety of insecticides, or by using nets that are treated with a single, strong insecticide.

Overall, the key to improving the effectiveness of bed nets is to use insecticides that are less likely to develop resistance, and to use nets that are more effective at preventing mosquito bites. With these strategies in place, it is possible to increase the effectiveness of bed nets, and thus reduce the risk of malaria transmission.
I imagine volunteering to be infected with malaria costs bills near 600,000 people a year. That is what Colleen Cooper, a psychologist at the University of Queensland, had in mind when she decided to do it in order to help researchers develop drugs to treat malaria. “It’s healthy, but there are plenty of peers who would disagree,” she says. “It is important for people to donate their bodies to help others.”

Ms Farmer is one of 230 volunteers who have taken part in trials using the “challenge model”, in which healthy people out there who are not, she says. The trials are helping to develop new drug treatments.

“While many new drugs and vaccines are being developed, it is difficult to determine which areas to hit for infections where malaria is in the throbbing stage,” says Prof James McCarthy, a professor at QIMR. “A malaria in a more advanced stage may be using treatments, which may make the develop activity of new drug trials. This trials are helping to achieve this,” he says.

The World Health Organization reports that there were about 100,000 cases in 2013 in Asia and South America which had led to an estimated 360,000 deaths.

Under QIMR’s challenge model, particularly those trials are infected with a sample of malaria that is much higher than the infection rate in the developing world. This makes the disease a more serious illness.

“We use these trials, clearly monitored using tests that measure the DNA of the bacteria normal children who are treated to the volunteers perfectly. This will involve trials to monitor their effectiveness at tackling the disease and capture valuable information that can help develop treatments.”

The critical component of any clinical trials in which people are infected with malaria is the development of a 90-100 per cent cure rate. This is one of the reasons that the model was developed. This would increase the speed of drug testing and provides a valid path to develop new malaria drugs. “With this method, we have ruled out three different approaches to developing a full clinical development – and MMV has been able to apply for two of the drugs based on the data provided by the challenge model,” she says.

“It saved us a year at least, which is important knowing that we are very unlikely to see anything new treatments,” says Prof Andrew Jack, chief scientific officer at Malaria Venture (MMV), a Switzerland-based not-for-profit organisation.

“We have a history of one of a new challenge,” he says. “It’s not going to be an easy task, but that may just have been the hospital environment.”

“I had a headache at one stage, but that may just have been the hospital environment,” he says. “I had a complete test and medical people.”

The challenge-model research has attracted support from Medicines for Malaria Venture, a Switzerland-based not-for-profit organisation. “A big international team would identify and develop a new drug,” he says.

“The sponsor often is somebody else that has been interested in the work before.”

**Fight intensifies against a killer disease**

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Haiti revives eradication aim

Case study

Recent experience and limited funding point to the need for a more targeted approach, writes Andrew Jack

A century ago, the Dominican Republic and Haiti combated malaria but ultimately were unable to eliminate it. Now, after decades of inaction, the island nation is working to make it a malaria-free region.

This week we mark World Malaria Day. The day has been set aside for health workers to bring attention to the disease, which is responsible for killing an estimated 400,000 people a year, and is among the major causes of illness and death for children and pregnant women.

Today, the island of Hispaniola is the last place in the region where the disease is endemic, and its elimination has been a priority for governments and international organizations. Haiti is the world’s poorest country, and one of the regions most severely affected by malaria.

In 2010, Haiti had a national malaria control programme, but it was not effective in controlling the disease. Since then, the country has been working to improve its malaria control efforts, and has made progress in reducing the number of cases.

In 2015, Haiti announced its goal of eliminating malaria by 2020. The country has made significant strides in reducing the number of cases, and has implemented a range of interventions, including malaria case management, indoor residual spraying, and expansion of the national malaria control programme.

However, the country still faces many challenges, including insufficient funding, inadequate infrastructure, and a lack of political commitment. The government has been working to improve its malaria control efforts, and has received support from international organizations, including the World Health Organization (WHO) and the United Nations Development Programme (UNDP).

Haiti’s success in reducing the number of malaria cases has been impressive, and the country is making progress towards eliminating the disease. However, the country still faces many challenges, and additional support and resources are needed to fully eliminate malaria from the island.

Malaria is a preventable and treatable disease, and with the right interventions, Haiti can achieve its goal of eliminating malaria by 2020. The country is making progress towards this goal, and is working to improve its malaria control efforts. With continued support from international organizations and the international community, Haiti can achieve its goal of eliminating malaria and improve the health of its population.
Researchers hope vaccines can work on several fronts

The first malaria vaccine will be a milestone but not a magic bullet, explains Andrew Wang

For years, researchers have been hunting for a vaccine to protect people against malaria, but what about a vaccine that can prevent the disease from transmitting the disease? That is one of the approaches being worked on by the Malawi Vaccine Initiative, an offshoot of the Seattle-based Bill and Melinda Gates Foundation. Andrew Birkett, director of the initiative, says such “transmission-blocking” vaccines could become a powerful weapon against malaria if they are developed.

“I hope in them reflects the limitations of the parasite that cause the disease,” he says. “Researchers are really trying to get to the point where they have a vaccine that will be effective.”

This approach would prevent a vaccinated person from contracting malaria, but it would trigger antibodies in the parasite that would stop it being passed on to other people by mosquitos.

“Going forward, it would be especially useful in reducing the many instances of asymptomatic malaria carriers, who spread the disease without knowing they have it. Many people do not feel sick and, therefore, are not seeking medical treatment,” he adds.

Some in the global health community have expressed apprehension that these prevention vaccines will not be ready after 25 years of work on the vaccine.

Mr Birkett says such sentiments are unfounded.

“We don’t want 10 per cent efficacy, but we are talking about 60 per cent efficacy. The fact that people who are vaccinated will not be infected is a big step forward,” he says.

Approved by European regulators, it met our expectations for recommendations from the World Health Organizations for its use. It would then be followed in countries in Africa and other malaria-endemic regions around the world to decide whether to adopt the vaccine.

Mr Birkett, whose organization helped Glaxo develop the product, says RTS,S is an “important first milestone”, but it “will never go to be a magic bullet”.

In clinical trials, the vaccine cut infections by almost half in children aged between five months and 17 months and by about 30 per cent in younger babies.

Some in the global health community have expressed apprehension that these prevention vaccines will not be ready after 25 years of work on the vaccine.

Mr Birkett says RTS,S is “the beginning of the end of the story. It’s not going to be a portfolio approach where we are trying to hit all the right targets.”

There are many ways to approach vaccine development, from the traditional to the novel. Other organizations are also entering the race. One of the most promising and advanced alternatives to RTS,S is being developed by a local Thai-based biotech company called Sanaria. The vaccine, known as KAE609, successfully completed early-stage clinical trials last year.

Only three of 15 participants who received a high dose of the vaccine developed malaria after being exposed to infected mosquitoes.

Mr Birkett says RTS,S cannot be used as a definitive solution to combat malaria, but it “will go on to be a useful step in combating”.

Other organisations include the Medicines for Malaria Venture (MMV), which in May last year launched an ACT using semi-synthetic artemisinin to reduce dependence on volatile supplies of the sweet wormwood plant. The French company needed to produce 200 kg of artemisinin per year of the ingredient using genetically modified yeasts, enough to meet a third of the global demand.

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Race against time to kill resistant mosquitoes

Insecticides

Scientists and manufacturers must innovate to avoid a catastrophic failure in decades to come, says Andrew Bounds.

At the turn of the millennium, health experts hit on a way to curb the scourge of malaria in the developing world: impregnating bed nets with a pyrethroid insecticide that would kill mosquitoes when they bit. But it worked well. Human deaths rates have almost halved while mosquito populations were killed in untold numbers for the tiny numbers immune to pyrethroids.

The World Health Organization estimates that without new approaches, an extra 120,000 people will die each year. The Innovative Vector Control Consortium (IVCC), a disease research centre, says “resistance can occur at a low frequency for many years until a tipping point is reached, when resistance then spreads rapidly, which can result in catastrophic failure of an intervention.” We are almost at that point in many countries in sub-Saharan Africa.

The IVCC, based at the Liverpool School of Tropical Medicine in the UK, is not a for-profit organisation that works with companies such as Syngenta, Bayer, BASF, Sumitomo, DuPont and the IVCC last year won a £6m grant from Wellcome Trust for developing new insecticides, hoping they will work on resistant mosquitoes. Another priority is to reduce the use of pyrethroids, says Prof Andrew Hemingway, director of the School and an expert on malaria. “There is nothing as cheap as pyrethroids,” says Prof Hemingway. “It is going to be more expensive.”

The WHO is trialling nets with a combination of insecticides, hoping they will work on resistant mosquitoes. Another new design has insecticide impregnated into yarn before the net is woven rather than sprayed after it is made, increasing efficacy. But costs could mount.

“For many, the problem is we do not have the baseline of which insecticides to use on resistant mosquitoes,” says Luke Lucas, business development manager for its Sumitomo product, the Olyset Duo, in South-east Asia.

“Resistance can occur at a low frequency for many years until a tipping point is reached, when resistance then spreads rapidly, which can result in catastrophic failure of an intervention,” says the IVCC. We are almost at that point in many countries in sub-Saharan Africa.

Prof Hemingway says donors are “wary of putting all their eggs in one basket with all the research and development (R&D) in pyrethroids . . . it is going to be more expensive.” There is nothing as cheap as pyrethroids . . . it is going to be more expensive.”

“We need the ministry of health and the ministry of agriculture working together for the Ministry of Agriculture to be investing in resistance-free alternatives. The message is getting through.”

Andrew Bounds

A Tribute To Dr. Joel Jones

A Malaria Hero To Inspire Us All

Dr. Joel J. Jones, former manager of Liberia’s National Malaria Control Program (NMCP), died suddenly on March 19, 2015. Dr. Jones was a physician and surgeon with a Masters in Public Health from the Institute of Tropical Medicine in Belgium. His education, coupled with his deep experience managing his network of private laboratories, FFW Diagnostics, which he founded and named in honor of his mother, Frances Eminda Wood, set him well as the NMCP program manager.

Dr. Jones had led national malaria control efforts in Liberia for more than ten years as a doctor, educator, and medical manager. He was a strong leader with a keen intellect and an amazing sense of humor. He focused on addressing the many personal, social and economic obstacles that left people in endemic areas at risk of malaria. He was known widely for his wit, energy, creativity and leadership support, all preserved with fear and loss. He worked hard to achieve the goals of malaria control, not just politically but personally.

Dr. Jones’ family believes the media will miss a good friend and an important advocate for what a passionate and dedicated public health professional he was. We remember him with pride, passion and respect.

FT Health: Combating Malaria

Pradeep Srivastava

Friday 24 April 2015


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