Malaria: the last mile
Can we sustain the political will to eliminate malaria in south-east Asia and beyond?

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Elimination is the answer

Despite huge progress in fighting malaria over the past decade, the parasite that causes the disease has evolved to become more difficult to treat in some parts of Asia. Growing resistance to artemisinin, the key ingredient of the most effective treatment available, poses a great challenge to malaria control. Should this resistance spread to Africa it could reverse the present downward trend and lead to large-scale epidemics.

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The last mile

Maintaining investment and political engagement will be vital to tackling drug-resistant malaria
The fight continues

By Charles Nelson

The only way to stop the antimalarial drug resistance found in south-east Asia from spreading to other parts of the world is to accelerate towards elimination.

Malaria, a completely preventable and treatable disease, still kills more than 580,000 people a year. Some 90 per cent of these deaths occur in Africa, where an estimated 437,000 children die before their fifth birthday. These numbers are unacceptable.

This is despite significant progress having been made. A rapid expansion of malaria interventions since 2000 has helped to reduce the number of malaria deaths by an estimated 47 per cent worldwide and by 54 per cent across Africa. This is due predominantly to activity in support of the malaria-specific Millennium Development Goal, which not only created a cause that people working for international development could rally behind, but also helped to mobilise political advocates on the issue. The gains, though impressive, are fragile and malaria has resurged significantly on many occasions.

The parasite that causes the disease, *P. falciparum*, as with many other organisms, is mutating, and in some parts of south-east Asia it has become more difficult to treat. Mutations are resulting in growing resistance of the parasite to artemisinin. This is the vital ingredient of the most effective treatment currently available for malaria. Any resistance to it poses a great challenge to our ability to control the disease.

The Greater Mekong subregion, which comprises the countries bound by the Mekong River in south-east Asia, has been the cradle of resistance to previous antimalarial drugs and is once again the origin on this occasion. Responding to antimalarial drug resistance in this region – and preventing the potential spread of resistance through Asia to Africa and beyond – is a global public health priority. If allowed to reach malaria-endemic parts of Africa and south Asia, it could have a devastating impact on the achievements of focused malaria control. Given the lack of any alternative drug to treat malaria, there is a very real risk that the arrival of an artemisinin-resistant parasite would trigger a huge rise in deaths from malaria.

In south-east Asia there is relatively low transmission of malaria. Containment programmes are now aimed at accelerating the elimination of *P. falciparum* since, in practice, the only way to eliminate the resistant parasites, and the risk of them migrating, is to eliminate malaria.

Malaria Consortium is contributing to these efforts by helping countries establish stronger surveillance systems for drug-resistant malaria, which can have added value for other disease surveillance. The people most at risk of suffering from and spreading drug-resistant malaria, which can have biotic and tuberculosis drug resistance, a problem with causes and effects similar to those of antimalarial drug resistance.

The UK, led by the Department for International Development (DFID), remains a global leader in investment in the fight against malaria. In 2011 it pledged to halve malaria deaths in at least ten of the worst-affected countries by the end of 2015, and has renewed that pledge to work to extend these reductions in the future. With DFID expected to sustain an investment of £500m a year on malaria by the end of this year, tackling drug-resistant malaria will have to be high on the priority list.

The fight continues. Round tables such as the one convened by the New Statesman, in partnership with Malaria Consortium, at the Houses of Parliament in December last year demonstrate the cross-party support for tackling malaria, and outline the need for the UK and other countries to address antimalarial drug resistance. Political advocates have done an excellent job ensuring malaria is kept high on the development agenda in the UK, internationally and in endemic countries. However, the international and domestic funding available combined is still only just over half of what is required to achieve the global targets for malaria control and elimination forecast by the World Health Organisation.

If we want to stay ahead of the game in malaria control and continue making steady progress towards elimination, current and new political advocates need to help close this funding gap and boost prioritisation of efforts to control the spread of drug-resistant malaria, as well as accelerate towards elimination.
In a year marred by the continuing ebola outbreak in West Africa, one of the worst global health crises in recent memory, the story of malaria offered something different to hold on to: hope.

The World Health Organisation (WHO) released its annual malaria report on 9 December 2014 and its findings gave cause for celebration. Between 2000 and 2013, malaria mortality rates decreased by 47 per cent, and by 54 per cent in the WHO African region (which comprises all nations in Africa except for Egypt, Liberia, Morocco, Somalia, Sudan and Tunisia).

It is believed that 4.3 million deaths have been averted. Some 64 countries are on track to meet the Millennium Development Goal to reverse the number of malaria cases, and of these, 55 will reduce malaria rates by 75 per cent, if the present trend continues.

“We meet at a tremendously significant time,” remarked Stephen O’Brien, a Conservative MP and the Prime Minister’s envoy and special representative for the Sahel. “Technical and political willpower has been galvanised to make the differences that saved lives.”

His comments came the very day after the WHO’s report was released, and were made at a round-table forum hosted by the New Statesman, in partnership with Malaria Consortium.

Delegates at the round table agreed that the past decade had been a period of remarkable scientific and political progress in the battle against the disease. Funding for the cause has grown threefold since 2005 and now stands at $2.7bn. This has meant more access to medicines and preventive tools, such as insecticide-treated mosquito nets (now available to almost half of the at-risk population in sub-Saharan Africa, compared to just 2 per cent in 2004). Vocal philanthropic champions – most notably Bill and Melinda Gates – have also lent weight to the cause.

Yet the round-table delegates felt there were still challenges ahead. Some of these challenges are biological, others political. Chief among biological concerns is the growing resistance of malaria parasites to artemisinin, the primary ingredient used in the most effective antimalarial drugs.

The emergence and spread of artemisinin resistance is an acute concern in the Greater Mekong subregion of south-east Asia, where lifestyle factors and poor surveillance systems make local situations...
exceedingly complex. The round table considered the political challenges, and discussed whether the current momentum could be maintained into the next stages of the global malaria strategy.

For O’Brien, who opened the debate, the WHO’s report proved that continued political investment had been “money well spent”. He said the UK had shown “tremendous leadership” on the issue and commended the 166 MPs who in September 2014 voted in favour of committing 0.7 per cent of gross national income to international development.

“This is a real opportunity,” he said. “It is a prospect, within our lifetimes, to be the generation that eventually got ahead of the mosquito.”

Sir Malcolm Bruce, the deputy Liberal Democrat leader and chair of the House of Commons select committee on international development, agreed that the UK had both the “capacity and commitment” to increase overseas aid. “If we can sustain economic growth, then that budget will continue to rise in line with the economy,” he said.

Yet for him the job was not yet done and risks could lie in complacent congratulation. “The ebola outbreak shows what happens when you take your eye off the ball,” he warned.

“That could happen with malaria. It’s about reminding people that even though the stats are moving in the right direction, if you don’t keep investment going it can come back and bite you.”

Even the most positive figures still show great gaps: if 50 per cent of the targeted populations are using mosquito nets, that still leaves half of the total number of households vulnerable.

Pedro Alonso, director of the WHO Global Malaria Programme, noted that simply getting more mosquito nets into homes in Africa was still “the number-one challenge”.

He reminded the group of other figures, noting: “Around 60 million cases still go undiagnosed and untreated with effective antimalarials. Fifteen million pregnant women who should be receiving preventive treatment are not actually getting it. All of this speaks to a massively unfinished agenda.”

Resolving this unfinished agenda means urgently addressing threats, Alonso explained. For example, resistance to insecticides (such as those used to treat nets) is “an issue that could hit us very...”
significantly over the coming years.” More than 42 countries in sub-Saharan Africa have reported insecticide resistance, according to WHO. “We may be standing at the edge of a precipice,” Alonso said. “WHO has put in place a programme that gives clear guidelines as to what countries should be doing to manage this, but we still probably need to step up our game.”

Of all the challenges, it was that of artesinin resistance that remained the focus of much of the conversation.

For Alonso, and many others around the table, the only way to tackle resistant parasites was to focus on programmes that had an ambitious goal: elimination. “The only reasonable way forward for artesinin resistance in south-east Asia is elimination of malaria and interruption of transmission,” Alonso said.

Could such an ambitious goal really be achieved? It is important here to note the terminology. Disease “eradication” is defined as the extinction of a disease worldwide—something that has been achieved only once (for a human infectious disease), and that was with smallpox, in the late 1970s. “Elimination” is the extinction of a disease within a defined geographical area, such as polio in the United States. While nominally more feasible than eradication, elimination could hardly be called straightforward.

Pascal Ringwald, co-ordinator of drug resistance and containment for WHO’s Global Malaria Programme, believed it could be possible. “Elimination in the region is technically an operation that is feasible at a reasonable cost,” he said, going on to make a second point: “This project needs to be owned by the countries. It is extremely important the countries involved understand the strategy and are convinced it’s the way to go.”

Such local engagement presents particular challenges, said Malcolm Bruce, raising the reticence of governments in countries such as Myanmar (Burma) to engage with the issue. “These places are not only difficult to access, but their policies are a long way from being stable,” he explained. “The Burmese government isn’t keen on letting people in. I perceive, in principle, but our agenda is about making sure that gets translated from principle to practice—and the pace at which we do this is critical.”

David Reddy, chief executive of Medicines for Malaria Venture, joined in to advise how medical research and development could combat resistance. He also explained how vital it is that continued investment remains. “We know that resistance is by its nature a moving target, so the UK has been investing in clinical studies and surveillance as well as developing the next generation of drugs,” he said. “Two important things are happening as a result: one is that we have two classes of antimalarial drugs now in clinical studies. The second is that some countries like South Africa and Thailand are beginning to step up and match British government funding. The leadership that’s been shown by DFID (the Department for International Development) is bearing fruit and we hope that continues.”

The prospect of new drugs on the horizon is encouraging, but what can be done with the ones we already have? Colin Sutherland, head of the department of immunology and infection at the London School of Hygiene and Tropical Medicine, explored some of the experiments in progress. “We are waiting to reap the benefits of new drugs in the pipeline, and they’re not going to be saving lives in the next five years,” he said. “So we’re thinking about trialling the impact of two ACT [artesinin combination therapy] regimens in a row, because we know they push the parasite in opposite directions.”

“These are some of the interesting ways in which we can deploy the tools we currently have, and maybe buy ourselves more time.”

“If a country reports a single case of malaria, including imported malaria, a report is made to the local health authority,” she said. “A successful system must be designed to enable teams to react promptly to an emerging outbreak. Currently, countries have limited capacity into the surveillance systems. To do that, malaria has to become a reportable disease where every case is an emergency.”

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In a political environment, that getting co-operation is high-on impossible.” Alonso agreed, saying, “Elimination will only be achieved by the countries themselves with their own workers, not outside groups or experts,” but conceded that the capability to achieve this was limited. “Capacity-building is the often-forgotten part of the equation here, and in south-east Asia we have a significant problem.”

For Celine Zegers de Beyl, monitoring and evaluation specialist at Malaria Consortium, we must urgently build more capacity into the surveillance systems. “It is so important that we detect every case,” she said. “A successful system enables teams to react promptly to an emerging outbreak. Currently, countries are quite diverse in their surveillance systems. In Cambodia we have a successful system where every month they produce a malaria bulletin, and everyone can access trends at country and district level. Myanmar is much further behind; there is no reliable information on the malaria burden available at a national level and that’s a big problem.”

“Consensus is very strong that dealing with artesinin resistance through elimination has to be the solution,” added Charles Nelson, chief executive of Malaria Consortium. “To do that, malaria has to become a reportable disease where every case is an emergency. The ability is there in principle, but our agenda is about making sure that gets translated from principle to practice—and the pace at which we do this is critical.”

MALARIA CONTROL AND ELIMINATION
Education and awareness-raising are also part of the picture, as François Bompart, vice-president of Access to Medicines, a division of the health-care company Sanofi, reminded the panel. “We talk about access to medicine but the first thing is access to diagnosis,” he said, reiterating just how important it is to match the right patient with the right drug. “Sometimes the marketing of drugs is seen as a ‘dirty word’, but it can be a very good tool when it comes to educating and helping local actors become more effective.”

Cautious optimism regarding the prospect of elimination in south-east Asia was underscored by an awareness of just how difficult it will be. Many felt the final mile might prove the most difficult. Umberto d’Alessandro, director of the Medical Research Council’s unit in Gambia, put it this way: “It’s easier to go from a presence of 40 per cent to 10 per cent than it is to go from 10 per cent to 1 per cent, or even zero. The parasite is a biological system and it can adapt to different conditions.”

Not only does biology make it difficult to cross the finish line, but human nature poses its own limitations, too. Christopher Whitty, chief scientific adviser to DfID, described the “political paradox” that often arises under similar conditions. “Elimination is most popular when it is least possible,” he said. “By the time you get down to these extraordinarily low levels, there are many other priorities for public health. The enthusiasm dries up as the disease dries up. People often underestimate this political difficulty.”

A further sticking point was identified by Tom Feilden, science correspondent for BBC Radio 4’s Today programme, who said that although enthusiasm was no doubt permeating the mood in the room, it was difficult to get a clear picture of what the next steps had to be. “Is it solving the political problems in south-east Asia, or do we need to do more technically?” he asked. “How do we move away from the rich west bestowing something on other parts of the world? I’m really interested in this narrative – I’m just not sure how we get on that road.”

The need for a clearer narrative resonated with the group. Colin Sutherland agreed that public engagement required an ongoing story – not a simple task in a field as volatile as malaria. “We need to be doing everything at once. It’s a complicated pattern of activity to weave into a story. Data collection is dull, but it is so important. It needs to be part of the fabric.”

Lord Collins of Highbury, the Labour peer and shadow spokesperson for international development, saw a compelling story in the transformative power that disease elimination can have on developing countries. “The economic impact of these diseases is huge and it’s holding countries back, countries with a huge amount of resource and talent that could grow,” he said. “It is absolutely in our interest to ensure these places thrive. Ebola taught us that we do not know what’s around the corner, so we’ve got to keep investing in these health-care systems.”

For O’Brien, this final point was perhaps the most critical. “We’re leaving the pioneering phase and entering the mature phase. We’re going to have to find a complementary narrative that is equally inspiring, otherwise the danger is that politicians move on. “The next stage has got to be not just about saving lives, but helping people live fuller lives. That means full realisation of economic opportunities, and full participation in society and democracy.”

The next era in the fight against malaria is under way. If local and international partners are to go boldly into it, the conversation must consider more than the number of lives saved, or the quantity of new drugs developed, and instead move towards discussing a fuller picture of what a disease-free world could achieve – economically, politically and socially.
A child is tested for malaria using a rapid diagnostic test kit. By ensuring an accurate diagnosis prior to treatment, the risk of drug resistant malaria can be reduced through avoiding the overuse of drugs.