



Racing Against Time: Protecting the Gains Achieved in Malaria Control Against Drug Resistance

This report is dedicated to the memory of Dr Sylvia Meek, its co-author, who dedicated her life to the fight against malaria and neglected tropical diseases.





Migrant workers are tested for asymptomatic malaria to help track and reduce transmission at the Thai-Cambodia border

Resistance to Artemisinin Combination Therapies (ACTs), the most effective drugs we have to tackle malaria, is growing. It is already a significant threat to health in Southeast Asia and will be a global threat if it spreads further.

Given the urgency of the situation, the All-Party Parliamentary Group has decided to publish a special report on the situation with the action needed. We are grateful to Dr Sylvia Meek and the team at Malaria Consortium for their assistance with this.

We know that governments in the region recognise the threat and have already taken action. We also know that the UK has provided money for doing so, and we welcome that. However, an even greater focus is needed. Only by effectively eliminating malaria from the region can we be sure resistance will not spread.

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Declaration of past interest: Jeremy Lefroy was previously involved in a business growing and processing artemisia annua for the production of artemisinin.

Foreword

Introduction



Malaria case data are collected from private providers

In the early 1900s, malaria was endemic to most countries in the world. Following failed malaria elimination efforts in the 1950s and 1960s, there was a reduction of malaria control efforts which resulted in a significant resurgence in cases in many countries. Even 20 years ago, the idea that malaria could be eradicated was unthinkable. The disease was killing more than one million people a year worldwide, most of them children.

The story of the fight against malaria is one of great progress. Through the work of governments, donors, the private sector, NGOs,

scientists and affected communities, and thanks to the development of new preventive, diagnostic and treatment tools, the picture of malaria today is quite different. Since 2000, there has been a 60% decline in malaria deaths globally: 6.2 million fewer deaths across the world. Taking population growth into account, the incidence rate of new malaria cases is down by 37% since 2000. Indeed, global malaria control is one of the success stories of the Millennium Development Goals (MDGs).¹ The change has come through a newfound determination and political will, increased funding, concerted action and the

deployment of effective new prevention and treatment tools. Malaria control globally is at an all-time peak.

As we enter the era of the Sustainable Development Goals (SDGs), there is still much to be done; the fight against malaria is far from finished. Malaria remains one of the world's deadliest diseases, with 214 million new cases and 438,000 deaths in 2015. Approximately 80% of these deaths were concentrated in 15 countries, mainly in Africa. Pregnant women and children are particularly vulnerable.² Malaria also places heavy burdens on families and communities

through disruptions to education and work, as well as diverting household incomes to pay for treatment. Malaria can account for up to 40% of public health expenditure in countries where it is endemic. The disease also disproportionately affects the poor, exacerbating poverty by reducing the life chances of vulnerable populations.

The gains already made in tackling malaria are fragile and could be easily lost if efforts are not sustained and redoubled. If efforts do not continue, we risk worse than a job half done: malaria resurgence will undo the progress of decades of

investment and lead to a dramatic increase in malaria cases and deaths. The global community must work towards the total elimination of malaria. To achieve this, we require effective tools to prevent, diagnose and treat the disease. As has been demonstrated by the past loss of effective treatments, one of the greatest challenges ahead is the rise and spread of drug resistant malaria.



Testing for malaria in Thailand using a malaria rapid diagnostic test. Photo: Mimi Mollica

¹ World Health Organisation and UNICEF: 'Achieving the Malaria MDG Target', 2015

² WHO: 'World Malaria Report', 2015

Artemisinin is the key ingredient in the most effective treatment currently available for malaria. However, the parasite that causes the most deadly form of the disease, *Plasmodium falciparum*, is becoming increasingly resistant to this compound. In order to counter the development of artemisinin resistance (AR), a fast-acting, artemisinin-based compound is combined with one of several drugs from a different class. Companion drugs include lumefantrine, mefloquine, amodiaquine, sulfadoxine/pyrimethamine and piperazine; these combinations are known as Artemisinin-based Combination Therapies (ACTs). Where possible, the two drugs are brought together to create a co-formulated drug in a single tablet.

Resistance was first detected along the Thai-Cambodia border in 2008 and has subsequently been detected in five countries of the Greater Mekong Subregion (GMS): Cambodia, Myanmar, Thailand, Vietnam and Lao People's Democratic Republic.

Currently, in the large majority of areas where AR is found, patients with resistant parasites still recover after treatment, provided that they are treated with an effective ACT. However, the clearance time is prolonged,

increasing the risk of transmission of the resistant parasite. In Cambodia, resistance has emerged to both components of ACTs currently in use, and therefore *P. falciparum* is now resistant to almost all available antimalarials along the Thai-Cambodia border. There is also evidence that AR not only spreads from one country to another but can emerge independently in several locations.

If drug resistant malaria spreads to other parts of South Asia and on to Africa, a global public health crisis will occur. Drug resistant malaria parasites have not yet been detected in Africa, but following the pattern of the spread of previous resistant strains, drug resistant malaria is a distinct possibility. Despite the ongoing work to develop replacement drugs, no new treatment for malaria is in the pipeline if ACTs become ineffective. If resistance were to reach Africa where the malaria burden is greatest, the impact could be devastating, leading to a massive increase in deaths. Much of the progress achieved with the substantial resources invested in malaria control since 2000 would be undone. In short, AR could have severe, global consequences for the future of malaria control and elimination.

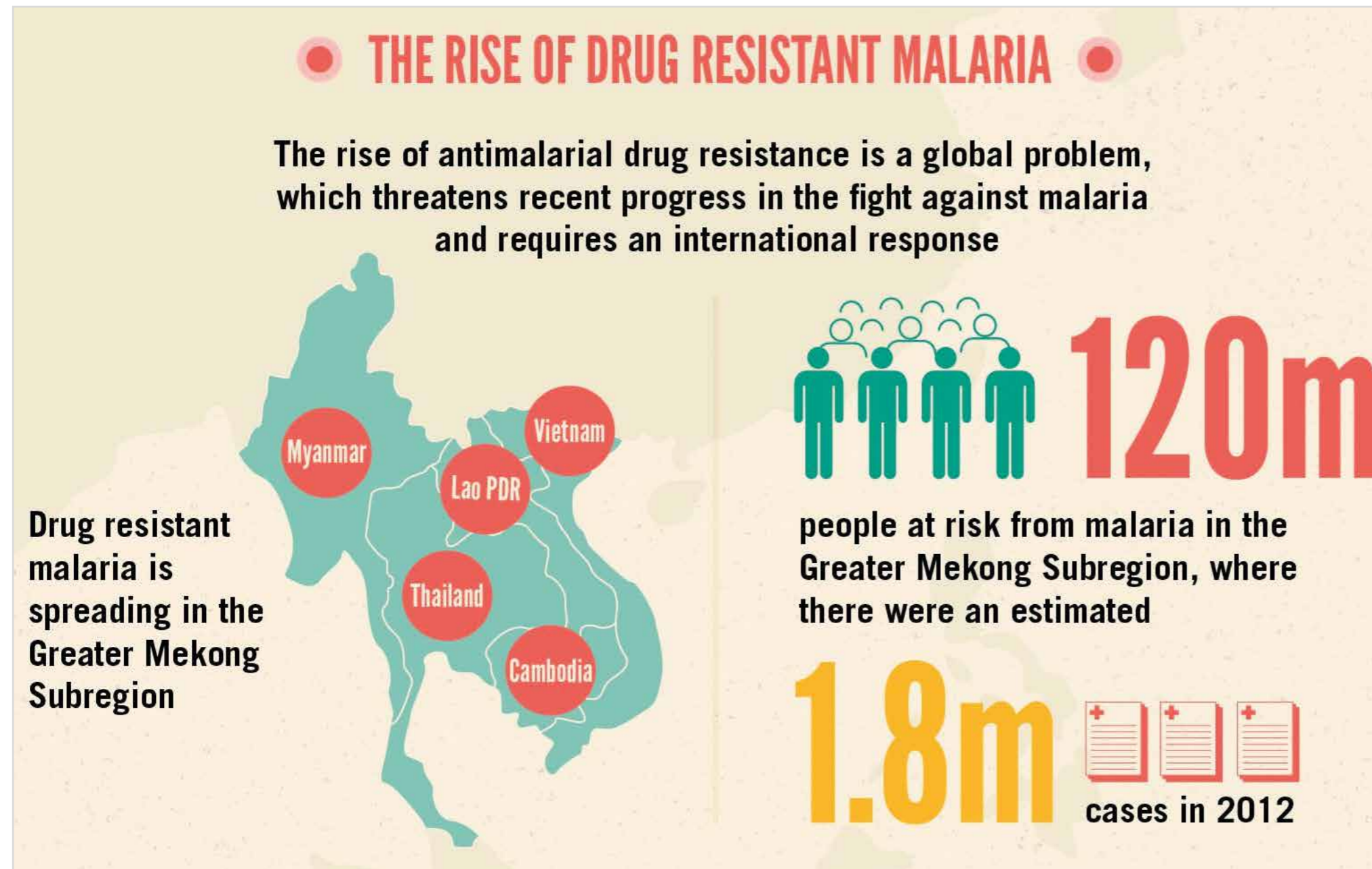
Artemisinin Resistance

Cambodian migrant workers in Thailand taking part in an antimalarial drug resistance study



The global importance of AR is increasingly being realised

If resistance to partner drugs develops further in the GMS, or if AR breaks beyond the borders of Southeast Asia and spreads to Africa, the result would be a global health crisis. The scale of the impact would demand an international response. Besides the increase in malaria-related illnesses and deaths, the economic impact of drug resistant malaria could become significant. One study estimated that an ACT failure rate of just 30% - a conservative estimate - would lead to medical costs of US \$32 million and productivity losses of US \$385 million every year.³



The Ebola crisis in Western Africa was a stark reminder of the impact of an untreatable disease outbreak and reinforced the importance of building strong health systems that offer effective services to everyone. Widespread AR would place an overwhelming burden on already overstretched health systems throughout Asia and Africa. Further, the Ebola crisis highlighted the role that migration plays in spreading diseases rapidly between countries, which contributes to the spread of drug resistant malaria in the GMS.

Ebola also demonstrated the importance of dealing with disease outbreaks early before they become larger epidemics. In the 1960s and 1970s, *P. falciparum* parasites resistant to the antimalarial drugs chloroquine and sulfadoxine-pyrimethamine emerged in Southeast Asia and spread to Africa over the next 30 years, doubling malaria deaths among children. The spread of drug resistance was not recognised for decades, after which time it was too late to launch an effective public health response. Widespread resistance therefore required the replacement of chloroquine and sulfadoxine-pyrimethamine with new and costly alternatives that took time to develop, resulting in a situation that accelerated unnecessarily.⁴

³ Joel Lubell et al, 'Artemisinin resistance – modelling the potential human and economic costs' Malaria Journal 2014: 13: 452

⁴ Worldwide Antimalarial Resistance Network



Mon San works in a rubber farm in Southern Myanmar and is helping her community through demonstrating positive behaviours to prevent malaria

The key to tackling drug resistance is to eliminate malaria in affected areas

Much work has already been done in the GMS to eliminate *P. falciparum*. There has been a move towards more targeted programmes in areas where AR is prevalent. After intensified efforts from 2009, the World Health Organisation (WHO) called for an emergency response in 2013 to AR, setting up a regional hub in Phnom Penh in Cambodia. The focus has been on ensuring a comprehensive and rapid scale-up of interventions in the region.

The key aspects to eliminating malaria and therefore tackling the spread of AR are:

- 1) Strengthened surveillance systems to identify, track and treat every case of malaria (see case study);
- 2) Universal coverage and use of insecticide-treated mosquito nets for people at risk;
- 3) Increased access to effective treatment and universal availability of sensitive diagnostics to ensure every case is confirmed prior to treatment;
- 4) Development of innovative tools to improve the timeliness and quality of data, including the use of real-time systems to report and respond immediately to every case and better access to data to support malaria research, monitoring, evaluation and surveillance;
- 5) Improved access to treatment and education for hard-to-reach mobile and migrant communities who travel within countries and across borders and play an important role in transmitting malaria. Such communities are particularly significant because they may lack knowledge about malaria prevention;
- 6) Development of tailored tools and approaches to provide protection from mosquito bites to all individuals at risk, through the use of new technologies and novel methods. This is particularly important in areas where conventional preventive tools are less effective due to the biting habits of the local mosquitoes;
- 7) Tackling poor quality, fake and counterfeit drugs and discontinuing the use of artemisinin monotherapies, which are considered a major contributing factor in the development of resistance.



Malaria Consortium staff at a border check point between Cambodia and Thailand encourage people crossing the border to be tested for malaria

Case Study:



Border-crossers are screened at a checkpoint on the Cambodia-Laos border as part of efforts targeting malaria infection and artemisinin resistance

Targeting malaria infection and AR on the Cambodia-Laos border

To tackle AR, it is imperative to eliminate malaria in the Greater Mekong Subregion, where AR is already entrenched and which has historically been the epicentre of resistance to antimalarial drugs. A key challenge to malaria elimination in this region lies in understanding better how the disease is spread in and between countries. Cross-border population movement is one of the biggest challenges to eliminating malaria. Because communities are mobile and often live in remote areas, however, the full extent of their role in spreading AR and reintroducing the disease into neighbouring areas is not entirely known.

“These people are really hard for us to reach,” said Sophal Uth, Programme Coordinator for Malaria Consortium in Cambodia.

“Sometimes they just get one or two doses of malaria treatment and then they go away – they move to another place. This is our big concern. Right now we want to find and treat every case of malaria so that drug resistance cannot spread further.”

In order to gain a better understanding of the impact of cross-border migration, Malaria Consortium completed screenings at the

official border crossing between Cambodia and neighbouring countries as part of a project diagnosing and treating migrant populations. The second phase of this survey is targeting the highly porous Cambodia-Laos border that also has 12 unofficial crossing points. Population movements across these points are frequent and may be a root cause of malaria transmission. However, the extent of the problem is currently unknown.

People crossing at the chosen sites are screened for malaria and, if the diagnosis is positive, are treated on the spot. A short interview is then conducted to gain a better understanding of the knowledge that existing migratory populations have about the disease. The interviews serve to identify what behaviours are most associated with malaria infection so that control initiatives can be targeted better in the future.

This project is strengthening the evidence base around the effect that cross-border population movements have on the spread of malaria, including AR, and will help to refine approaches to target malaria prevention and control activities for hard-to-reach populations. In addition, the project is providing diagnosis, treatment and preventive education directly to these migrant communities.

The strategies at the heart of elimination in this region have many added benefits contributing to greater health security. In particular, investing in malaria elimination will result in better surveillance systems, stronger health services and a greater engagement of affected communities. Strategies developed and lessons learnt in Asia can also be applied to countries in Africa as they move towards malaria elimination over the next fifteen years.

Realising this accelerated elimination strategy will not be easy. It will require investment in areas that do not currently have a high malaria burden, where the need to continue to allocate resources to malaria control will not be obvious to policy makers. The benefits, however, are significant, not only in reducing the malaria burden in the GMS and tackling drug resistance but also in showing the world that with enough will and determination elimination can be achieved. Success in the GMS could ultimately become a model for other regions to eliminate malaria.

The need for political advocates is more pressing than ever

As we move forward from the MDGs and begin work towards achieving the SDGs, sustained political will for combating malaria is crucial. MDG 6(c), which called on the international community to halt and then reverse malaria rates by 2015, provided the impetus for a large mobilisation of resources and political will. However, with 17 goals covering a broader range of areas of development, the SDGs do not include such a strong focus on malaria. There is a risk, therefore, of losing the momentum of the past 15 years and the substantial progress made in tackling the disease. This is despite the significant impact that reducing malaria will have on a wide number of the SDGs; from reducing poverty, tackling hunger and increasing school attendance, to boosting economic growth, supporting gender equality and tackling climate change.⁵ It is therefore important that political advocates continue to press for investment in malaria elimination.



Migrant and mobile populations, such as this family working in a plantation in Pailin, Cambodia, are most at risk of malaria

⁵ WHO 'Action and Investment to Defeat Malaria 2016-2030'

Conclusion

The growth of resistance to antimalarial drugs, as well as antimicrobials, with which the issue shares many similarities, threatens to return the world to a time when parasitic diseases or simple bacterial infections often resulted in death. If we are to sustain progress in the fight against malaria and achieve the ambitious SDG for health, it is vital that we limit and prevent resistance. Continued investment in all areas of the elimination strategy outlined above will be required. In particular, it is crucial that funding is maintained in countries that are close to elimination, which is often a challenge for resource allocation when the disease burden decreases and other health concerns become more pressing. As a world leader in tackling malaria, the UK has an important role to play in keeping malaria high on the international agenda. The UK can continue to encourage other donors and endemic countries' governments to keep investing in elimination efforts until every case has been treated and the threat from drug resistance has been defeated.



Community members in Kyun Su township, Myanmar gather to learn about health-seeking behaviours for malaria

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