MALARIA in 2014: An Unprecedented Opportunity at the Dawn of a New Era

Report for the All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases
We are much indebted to Professor David Schellenberg, London School of Hygiene and Tropical Medicine, who once again masterminded and authored this report.

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- Medicines for Malaria Venture
- Malaria Consortium
- Malaria No More UK
- Sabin Foundation Europe
- The UK Coalition against Neglected Tropical Diseases
- PATH Malaria Vaccine Initiative

As we come to the end of this Parliament, we would like to thank the Medicines for Malaria Venture for generously funding the printing of this and all previous reports since 2005.
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Abbreviations

ACT.............................. Artemisinin-based Combination Therapy
APPG............................ All Party Parliamentary Group
APPMG.......................... All Party Parliamentary Group on Malaria and Neglected Tropical Diseases
DFID............................. UK Department for International Development
FIND............................. Foundation for Innovative New Diagnostics
GFATM.......................... Global Fund for AIDS, Tuberculosis and Malaria
GMP............................. WHO’s Global Malaria Programme
IPT............................. Intermittent Preventive Treatment
IPTi............................. Intermittent Preventive Treatment in infants
IPTp............................. Intermittent Preventive Treatment in pregnancy
IRS............................. Indoor Residual Spraying
ITN............................. Insecticide Treated Mosquito Net
IVCC............................. Innovative Vector Control Consortium
LLIN............................. Long Lasting ITN
MDG............................. Millennium Development Goal
MiP............................. Malaria in Pregnancy
MMV............................. Medicines for Malaria Venture
MVI............................. PATH Malaria Vaccine Initiative
MPAC............................. Malaria Policy Advisory Committee
PDP............................. Product Development Partnership
R&D............................. Research and Development
RBM............................. Roll Back Malaria Partnership
RDT............................. Rapid Diagnostic Test
SMC............................. Seasonal Malaria Chemoprevention
SP............................. Sulfadoxine-pyrimethamine
WHO............................. World Health Organization
Key recommendations

For the Government:

• In recognition of the UK’s attainment this year of the United Nations’ target that 0.7% of Gross National Income be committed to Overseas Development Assistance, make every effort to **enshrine into law this commitment**.

For DFID:

• **Ensure DFID’s support for malaria reaches the £500M commitment by 2015.** There is just one year left to achieve DFID’s landmark Malaria: Framework for Results commitment to “help at least halve deaths in at least ten of the highest burden countries”. Important resource gaps remain - the UK’s support is more important now than ever.

• **Maintain the UK’s commitment to the fight against malaria beyond 2015.** The UK can play a critical role and secure the future success of malaria control programmes through investment in malaria control and the development - and deployment - of new insecticides, drugs, diagnostics and vaccines.

• **Use the UK’s leadership to support increased malaria investment from other donor countries, the European Union and the Private Sector.**

For all funders:

• **Support the development of capacity** for robust disease surveillance, monitoring of service delivery quality, and evidence based action at national and sub-national levels, and do this in coordination with domestic and international agencies.

• **Invest in operational research and information systems** to unlock the full potential of the malaria control tools that already exist.

• **Support the global plans** to counter insecticide and drug resistance.

• **Ensure that malaria prevention and control measures are integrated into - and strengthen - national health systems.**

“Enshrine in law that 0.7% of UK Gross National Income is committed to Overseas Development Assistance”
For the APPMG:

• Increase engagement with the diaspora from malaria endemic countries.

• Increase efforts to publicise the importance of the UK and international community’s work on malaria.

For all stakeholders:

• Encourage endemic country governments to fulfil their pledges to commit 15% of government expenditure to health and support efforts to strengthen health systems to deliver essential malaria interventions.
In June, I had the privilege of visiting Sierra Leone and seeing at first hand the results of the mass distribution of mosquito nets. In all the homes I visited, the nets were clearly being used and appreciated. This fairly straightforward public health measure has saved hundreds of thousands of lives, mainly of children and women, over the past decade.

Since the visit, Sierra Leone has experienced a devastating increase in Ebola cases and deaths. The thoughts of all members of our Group are with the people of Sierra Leone, Liberia, Guinea and their neighbours at this extraordinarily difficult time. We welcome the additional support which DFID is providing, including helping to provide and fund 700 additional treatment beds as an emergency measure.

Bed net distribution in many countries still depends very much on grant aid – whether from the Global Fund or donors such as the UK’s Department for International Development (DFID). Last year, I called on endemic countries in sub-Saharan Africa to fulfil their pledge made at Abuja in 2001 to commit 15% of their national budget to health. They would then be more able to support rolling programmes of bed net distribution and replacement without being dependent on grants.

This public health measure – carried out through the national health system, rather than relying on a parallel programme – would help both cut the burden of disease and increase trust in that system.

I have been reflecting on this as I have listened to evidence presented to the UK’s International Development Select Committee during its inquiry on strengthening health systems, which has just been published.

There was some criticism of the ‘silo’ or ‘vertical’ approach to health. This refers to programmes running outside – or without much contact with – national health systems, aimed at tackling specific diseases such as HIV/AIDS, TB and malaria. Instead, it was argued that there should be much more time and effort spent on supporting and strengthening those national health systems.

But both are essential. The programmes tackling specific diseases have had substantial success – not least in malaria where we have succeeded in almost halving child death rates since 2000, saving over 3 million lives in Sub-Saharan Africa alone. We must not lose the focus which such programmes have brought. That has happened before in some places – malaria in Zanzibar in the 1960s for instance - and the disease returned with a vengeance.

At the same time, it is only through strong health systems which reach every part of a country that the work can be sustained. Many more clinical and support staff need to be trained for treatment, prevention and education; logistics must be improved to ensure that every community has the supplies and support it needs; and, something which is often forgotten, local communities must be fully involved in their health services so that they can point out the gaps and challenge poor care.

The news that the Tanzanian National Voucher Scheme for distribution of insecticide treated bed nets to pregnant women and children (which we visited at the end of 2012 and was mentioned in last year’s report) has been closed by DFID due to possible irregularities is very disappointing. But the decision rightly sends a clear signal that poor control of programmes will not be tolerated.

Chairman: Jeremy Lefroy MP
Vice Chairmen: Pauline Latham MP OBE; Lord Rea; Kevin Barron MP; Baroness Hayman GBE, PC
Secretary: Fiona Bruce MP Treasurer: Andrew George MP
Coordinator: Susan Dykes e-mail susanmdykes@gmail.com

www.appmg-malaria.org.uk
We have seen remarkable progress, with UK funding to fight malaria tripled 2008 – 2014, making a life-saving, life-changing difference to millions around the world; something I have been fortunate enough to witness examples of first hand. I hope to see this effort at least sustained into the next 2015-2020 Parliament: with a child still dying every minute from this preventable, treatable disease, we cannot afford to lose focus.

There is more which our All Party Group can do – especially in making its work better known and involving UK citizens whose families come from countries where malaria is endemic. That will also be a task for the next Parliament.

In the meantime, I would like to thank and pay tribute to Mrs Pauline Latham OBE MP, Baroness Hayman, Lord Rea, Kevin Barron MP, Andrew George MP and Fiona Bruce MP for all they contribute.

Susan Dykes has coordinated the group since its formation. I and my colleagues owe a great debt of gratitude to her for all she has done over the years. She will be stepping down as coordinator in March, at the end of this Parliament. I wish to place on the record my heartfelt thanks to Susan.

Jeremy Lefroy MP
Chairman of the All-Party Parliamentary Group on Malaria and Neglected Tropical Diseases

This is the fourth and final malaria report from our APPG during the 2010-2015 Parliament. When I look back over the previous reports, I see common themes:

• Solid progress in reducing deaths and sickness from malaria;
• The value of UK support and global partnerships to tackle the disease such as Roll Back Malaria and the Global Fund to Fight AIDS, TB and Malaria; I was particularly heartened by the UK Government’s decision to commit twice as much (£1 billion) to the Global Fund (2014-16) replenishment as it had to the previous three years;
• A continuing and very substantial gap between the sums needed to control malaria effectively, and what is available; funding remains the single biggest threat to future success against malaria;
• The vital need for wealthy countries to fulfill their commitment to increase Overseas Development Assistance to 0.7% of Gross National Income (GNI) – only the United Kingdom in the G8 has done this;
• A parallel need for endemic countries who signed the Abuja declaration to fulfill that commitment;
• New challenges, in particular growing resistance to artemisinin-based drugs and to the insecticides used to treat bed nets.

I sincerely hope that this All Party Parliamentary Group will be formed again in the next Parliament. There is little doubt in my mind that it was the work of this group in the last Parliament, under the leadership of its founder, Rt Hon. Stephen O’Brien MP, which played a major part in ensuring that the UK Government pledged to increase funding for the fight against malaria up to £500 million every year, a goal which I hope will be achieved in 2014/15.

Our role in this Parliament has been to enable all those involved in the fight to keep colleagues up to date on progress; to provide a place in which experts can meet and discuss each other’s work; and to support, encourage and challenge the Government and DFID.
Summary

Malaria is a preventable and treatable disease which was allowed to cause 207 million cases and 627,000 deaths in 2012. The heaviest burden continues to fall on young, African children.

However, we have seen major progress since 2000, the result of dramatic increases in investment for malaria control and research. Deaths amongst children in Sub-Saharan Africa have fallen by 54% since 2000 - saving over 3 million lives - and malaria has been eliminated from 4 countries, with others nearing the point at which elimination is a real prospect.

The recent dramatic improvements in malaria control give no cause for complacency: history has repeatedly shown that when efforts and funds to control malaria are relaxed, it comes roaring back (Figure 1). Reducing malaria control efforts at this point risks failing to capitalise on the strategic advantage we are developing – jeopardising millions of lives and billions of dollars.

We are now at a tipping point in the fight against this disease: sustained investment will drive down the number of malaria cases and deaths still further. These health benefits will be complemented by economic development as the expenditure on treatment of cases decreases and benefits accrue for the health system and the wealth of malaria-affected communities. A recent estimate suggests a potential net economic return on malaria investment of over $200 billion by 2035. Healthier communities will be more economically productive, and educational outcomes will be enhanced.

Non-health sectors can play an important role in malaria control. Improvements in housing, regulation and infrastructural developments can all help to decrease the burden of malaria. The time is right to view all policies and developments through the malaria lens.

Malaria control requires tools to prevent and treat the infection. The corner stone of prevention is vector control: insecticide-treated nets (ITN) can kill mosquitoes and have been shown to reduce malaria cases by up to half and child deaths by over 20%. Artemisinin-based combination treatment (ACT) is the best malaria therapy and is increasingly accessible and affordable to infected communities. However, both insecticides and drugs are threatened by the scourge of resistance. This is a biological inevitability which, until we succeed in eradicating the disease entirely, will require ongoing investment in research to develop new classes of insecticides and treatments. Historically, it has proved difficult to ensure adequate investment in research and development of new malaria products: malaria is a disease of the poor and the poor are unable to afford the prices which would normally motivate industries to invest in the development of new products. Product Development Partnerships (PDPs) are a mechanism to overcome this challenge. Research and development is needed now to find new tools not just to stay ahead of resistance, but also to accelerate progress towards our ultimate goal, a malaria free world.

We are at the dawn of a new era in the fight against malaria. In 2015 we will celebrate the major milestone of the Millennium Development Goals (MDGs) which have done so much to strengthen global partnerships, investment and support for malaria. We are poised to build on the early successes of the new millennium. Health will feature in the Sustainable Development Goals. The World Health Organization’s Global Malaria Programme is developing a Global Technical Strategy to accelerate progress with malaria control and to move towards elimination and eventual eradication of malaria. The Roll Back Malaria partnership is updating its Global Malaria Action Plan (GMAP) to ensure that the technical strategy is adequately implemented and that maximum benefits are secured. And the world’s first malaria vaccine - RTS,S - may soon be added to the arsenal at our disposal to fight this deadly disease.

The All Party Parliamentary Group on Malaria and Neglected Tropical Disease (APPMG) recognises the major contribution that the UK has made in driving global progress against malaria since 2000, and the UK’s leadership role in research and development towards a world free of malaria.

Now is the time to renew our commitment to this fight. The next five years can be decisive in determining the future of malaria: never before has the global community been better placed to make malaria a disease of history.

As we approach the general election the APPMG strongly encourages a unified, cross-party and increased commitment to the fight to end malaria.

“Malaria is a preventable and treatable disease which was allowed to cause 207 million cases and 627,000 deaths in 2012.”

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Burkitt's Lymphoma is a terrible cancer which particularly affects children living in malaria endemic African countries. It is the most common paediatric cancer in Africa, accounting for almost 75% of all childhood malignancies in the equatorial belt, and is responsible for the majority of all recorded child cancer deaths. Burkitt’s Lymphoma most commonly affects boys aged between four and seven years and presents as a large, painful facial or abdominal tumour which can double in size every 24 hours. Almost all patients are infected with the Epstein-Barr virus - best known as the cause of glandular fever - a virus which is easily transmitted by saliva and which infects almost everyone in the world. Whilst almost everyone develops immunity to Epstein-Barr; chronic malaria infection reduces this immunity and the virus then causes genetic changes that turn certain white blood cells into cancer. If caught early, Burkitt’s Lymphoma can be completely cured in 90% of cases with drugs alone. The effects of chemotherapy are often miraculous – children undergoing successful treatment can be transformed from being tragically disfigured to appearing normal, sometimes within a matter of a few days.

The tumour was first described in 1957 in Uganda. Ensuing research revealed the virus-cancer linkage and has redirected cancer research and treatment throughout the world. While the people of the West have benefitted enormously from the legacy of these discoveries, in the development of research and treatments for cancer and other diseases, children in Africa have not been so fortunate.

The cure rates for those children lucky enough to be diagnosed is 10-30%, with the majority of children suffering and dying in their communities without any access to effective treatment or pain relief. Even today, access to chemotherapy and other drugs — particularly pain killers — is an ongoing struggle. Many children suffer an unnecessary and painful death.

Burkitt’s Lymphoma can be prevented by eliminating malaria. But until malaria disappears, the work of groups such as the Burkitt’s Lymphoma Fund for Africa, which strives to make life-saving treatments available to affected patients, will continue to be invaluable.

Figure 1: The risk of interrupted investment: malaria resurgences. Source: Cohen et al. Malaria Journal 2012 11:122

Health impacts beyond malaria: Repeated malaria infection increases children’s cancer risk.
Prevention of malaria

Effective malaria control depends on strategies to prevent and to treat malaria. The cornerstone to malaria prevention is control of the mosquito vector. Insecticide-treated mosquito nets (ITN). Figure 2) have been shown in well-designed and conducted research studies to reduce malaria episodes, severe disease and death. There have been major improvements in the deployment of insecticide-treated nets since 2000 (Figure 3) and improvements in the technology itself - in the form of Long Lasting Insecticide treated Nets (LLIN). In some settings, Indoor Residual Spraying (IRS) – where insecticide is sprayed onto the walls of buildings – is also useful. Figure 4 shows the increasing number of high malaria risk countries which have high coverage of vector control tools.

Another approach is to target the larval forms of malaria-transmitting mosquitoes. This requires the use of insecticides and sometimes larvicide-eating fish in mosquito breeding sites. However, malaria-carrying mosquitoes can breed in very small collections of water; such as the hoof prints of cattle, and treating all breeding sites is a challenge.

Drugs also play an important role in preventing malaria (Figure 5). For example, Intermittent Preventive Treatment in pregnancy (IPTp) is the administration of a malaria treatment at pre-scheduled times during pregnancy. IPTp reduces anaemia in mothers and increases the birth weight of babies. Currently, however, there is only one drug, sulfadoxine-pyrimethamine (SP), recommended for IPTp by the World Health Organization (WHO), and there are high levels of resistance to this drug in some populations: new drugs for IPTp are needed.

Seasonal Malaria Chemoprevention (SMC) is another drug-based approach to prevent malaria.
A specific combination of drugs is recommended by WHO for SMC in young children living in parts of the sub-Saharan region where malaria transmission is concentrated into 3-4 months per year (Figure 6). Well-conducted trials have shown that SMC can reduce malaria cases by over 80% and reduce deaths by 57%.

There is no magic bullet for malaria prevention; it is important to ensure an appropriate combination of effective tools is available for those at risk.

I have no protection from malaria: Angela’s story

Angela Kangulumais is a teacher at one of the primary schools in Ndola, in the Copper belt Province of Zambia. She is six months pregnant with her second child and is no stranger to the sickness of malaria.

The last time she suffered with it was in 2010, just before her first pregnancy with Kelvin who is pictured in the photograph. She nursed a headache for over a week and woke up one morning unable to see properly or to walk unaided. With the help of her husband, she went to the local clinic where she was diagnosed with malaria and prescribed ACT. She felt much better within a day of commencing treatment.

In the same year, she learnt she was expecting her first child. At her first antenatal visit, she was urged to take sulfadoxine-pyrimethamine (SP) as intermittent preventative treatment (IPTp) to protect her from malaria during pregnancy; SP is a safe anti-malarial drug to administer to pregnant women and currently the only drug available for IPTp. Being familiar with the terrible symptoms of malaria, she agreed to take the drug. But after taking SP, she soon became nauseous and started to vomit. The only option she was left with for protection was a mosquito net. “This method alone is inadequate as I can’t always be under the net,” she said.

Today, with her second child on the way, Angela is at a loss regarding how to protect herself and her unborn child, given the way she reacts to SP, currently the only available drug for IPTp.

Story courtesy of Prof. Christine Manyando, Tropical Diseases Research Centre, Zambia and MMV
Malaria diagnosis and treatment

A major change in recent years has been the introduction of Rapid Diagnostic Tests for malaria diagnosis (Figure 7). These are simple kits which identify the malaria parasite in blood from a finger-prick. They do not require electricity, laboratory facilities or a trained laboratory technician. For the first time this makes it possible to diagnose malaria even in remote rural settings. This helps to ensure that malaria treatments go to the patients who really need them, and at the same time makes it possible to count cases with confidence. As a result, RDTs enable progress with malaria control to be monitored and resources better targeted to places where they are most needed. RDTs are being rolled out widely in malaria endemic countries (Figure 8).

Artemisinin-based combination treatments (ACTs) have been increasingly deployed over the last 10 years (Figure 9). Combining two antimalarial drugs into a single tablet means that the parasite faces a tougher challenge to develop resistance to both components and therefore the threat of resistance is considerably less than when a single drug is used to cure malaria. ACTs depend on the agricultural production of Artemisia and there are major challenges in forecasting artemisinin needs and then translating these forecasts into the material needed to produce the medicines. Developments in synthesising artificial artemisinins are encouraging but have yet to reach the stage where they can satisfy demand.

Recent studies have demonstrated that getting the dose of treatment right is more complicated than previously appreciated. This is important to ensure patients are cured and to minimise the risk of drug resistance. Recommendations are being formulated, based on new research, to ensure that the majority of malaria patients get the right dose. There are also challenges in understanding how ACTs interact with other drugs which are...
widely used in Africa. Unfortunately, HIV and malaria frequently co-exist and the treatments most commonly used for each are now known to interact with each other. There is an ongoing need to ensure that new malaria treatments are developed, and that the optimal dosing regimens in different age groups and co-morbidities are achieved.

Beyond treating uncomplicated malaria there is also a need for new medicines to treat relapsing malaria and to help block the transmission of malaria from patient to patient. Relapsing *Plasmodium vivax* malaria causes about 70–80 million clinical episodes each year yet the only medicine approved to cure it, primaquine, has been in use for 60 years. It is an inconvenient treatment to take - requiring a two week course - and can have potentially fatal side effects. Investment in research and development of new drugs remains a high priority.

“RDTs enable progress with malaria control to be monitored and resources better targeted to places where they are most needed”


>212 million treatments
delivered and counting

Renewed investment in research and development (R&D), including by the UK, is starting to yield dividends. Strong development pipelines are producing safe and effective insecticides and drugs, and sensitive and reliable diagnostic tests, and a potential first malaria vaccine.

**Vaccines**

Scientists have been working for decades to develop a vaccine against malaria (Figure 10). Many vaccines are life-saving interventions and have so far targeted viruses and bacteria, which are relatively small, simple organisms. The development of a vaccine to tackle the complex *Plasmodium falciparum* parasite has proved far more challenging.

This year marks the completion of the Phase 3 trial of the RTS,s vaccine – which the British pharmaceutical company GSK has now submitted for regulatory review by the European Medicines Agency. The vaccine reduces by one third to a half the number of clinical episodes of malaria in small children living in endemic countries. Although such levels of protection are considerably lower than normally expected of a vaccine, the extraordinary burden of malaria disease and death mean that even modest reductions may have major public health impacts. RTS,s has been developed through an innovative partnership involving African research centres, scientists from three continents, GSK, and the PATH Malaria Vaccine Initiative.

The global malaria community awaits the results of the regulatory review and the policy deliberations of the World Health Organization to see to what extent RTS,s is likely to play a part in the ongoing fight against malaria. There will be a need for post-approval phase IV studies to consolidate safety information and to document the vaccine’s

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*Fig 10: Tanzanian scientists host British MPs in a malaria vaccine research laboratory in Korogwe, Tanzania.*
The development of new tools

**MMV Portfolio: October 2008**

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**New chemical entities since 2007**

2017+ 2015+ 2013 2011 Submission Probability

10% 20% 68% >90%

**New presentations of existing molecules**

2022+ 2020+ 2018 2016 Launch

*Fig 11: Medicines for Malanias Venture’s expanding drug development portfolio*
effectiveness when deployed as part of routine immunisation programmes in sub-Saharan Africa. And of course, research should continue to develop a next generation of vaccines that more effectively prevent infection or even block transmission of the parasite altogether.

Countering Resistance to Medicines and Insecticides

The development of resistance is an almost inevitable result of large scale use of insecticides and drugs. In 2009, resistance was described to artemisinin in south east Asia. This is the same part of the world which first reported resistance to other malaria drugs such as chloroquine, sulphadoxine-pyrimethamine and mefloquine. Resistance to these drugs spread through south east Asia, south America and Africa. It seems inevitable that resistance to artemisinin will also spread to Africa where, if no new drugs are available, a public health disaster will result. The Medicines for Malaria Venture (MMV) has developed the strongest anti-malaria drug development pipeline that has ever existed and has developed and brought to registration four new treatments between 2009-2013 (Figure 11). However there is no room for complacency as new classes of drugs are urgently needed if malaria treatment is to stay ahead of resistance.

Many factors that are thought to have contributed to the emergence and spread of artemisinin resistance in south east Asia. One important factor is likely be the use of oral artemisinins alone – as a monotherapy – instead of the WHO-recommended artemisinin combination therapy or ACTs. Other contributing factors are the use of substandard and counterfeit anti-malarial drugs and the difficulty of controlling malaria within migrant and hard to reach populations.

For health workers and patients alike, it is all too obvious when a malaria drug starts to fail. Recovery times are protracted at low levels of resistance, but this develops into a failure to prevent the development of severe disease and death. Insecticide resistance, on the other hand, is insidious. It is not so obvious that mosquitoes are failing to respond to insecticides. A high level of insecticide resistance is needed before the impact on the number of malaria cases and deaths becomes apparent. It will be too late if we wait until this happens to take insecticide resistance seriously.

The molecular and biological assays to detect insecticide resistance in the laboratory are very sensitive. They show that insecticide resistance is now present in 64 countries in Sub Saharan Africa (Figure 12) and that mosquitoes are much
The development of new tools

less sensitive to the previously lethal effects of insecticides. Resistance to all four classes of insecticide has been described in some countries. The Liverpool-based Innovative Vector Control Consortium is leading the development of new insecticides and has a strong development pipeline.

It takes time to develop new drugs and insecticides and to make sure they are safe and effective. In the mean time WHO’s Global Malaria Programme (GMP) has issued guidance to delay the spread of drug and insecticide resistance. The Global Plan for Insecticide Resistant Management (GPIRM) and the Global Plan for Artemisinin Resistance Containment (GPARC) describe strategies to help countries ameliorate resistance (Figure 13). Investment in the GPARC has been swift – with DFID, The Global Fund against Aids, TB and Malaria and other key funders responding to the need to improve surveillance and intensify activities to prevent the spread of artemisinin resistance outside South East Asia. Support for the GPIRM has been less marked - a situation which merits urgent and serious action.

Medicines for Malaria Eradication

The goal to eradicate malaria cannot be achieved with current medicines. An initiative called the Malaria Eradication Research Agenda (malERA) drew on the knowledge of malaria experts from around the world to consider what properties new drugs would need in order to achieve malaria eradication from the world. Two types of drug were defined - Single Exposure Radical Cure and Prophylaxis (SERCaP) and Single Exposure Chemoprotection (SEC). MMV and partners are actively pursuing the identification and development of these drugs.

Novel Approaches for Vector Control

Current approaches to vector control target the most important malaria transmitting mosquitoes, which tend to bite in the middle of the night when people can be protected by sleeping under insecticide treated mosquito nets. However, a small but significant amount of malaria is transmitted by less efficient vectors which bite outside, in the early evening. The relative importance of these mosquitoes is growing as malaria control improves. If control is to be maximised it will be essential to develop strategies and new tools to attack these early biting mosquitoes. Approaches being evaluated include insecticidal medicines - which reduce a mosquito’s survival if they feed on someone who has taken the drug; insecticidal lotions; repellents; insecticidal and / or repellent clothing; and odour baited traps.
The World Health Organization’s Global Malaria Programme (GMP) is responsible for making evidence-based decisions about which interventions and strategies should be used in which situations. GMP benefitted enormously from five years of exemplary leadership by Dr Rob Newman who, amongst other things, established a rigorous and transparent approach to setting global malaria policy. The APPMG warmly welcomes GMP’s new Director, Dr Pedro Alonso, and assures him of its support.

The Roll Back Malaria partnership is a global forum for the many different stakeholders in the malaria community to coordinate efforts in resource mobilisation, strategy deployment, data gathering and advocacy to ensure that the strategies recommended by WHO are implemented effectively.
Effective malaria control requires effective tools to prevent and treat malaria. However, they also need to be available, affordable, acceptable and usable by the target populations. A substantial increase in operational research is required to make the most of the tools which already exist.

Malaria Consortium’s Stop Malaria Project in Uganda is an example of such work, supporting the Ugandan Ministry of Health to understand what is needed to implement Intermittent Preventive Treatment in pregnancy (IPTp) in 34 districts. The study shows that barriers exist on the supply side (resources, policies, human capacity, etc.), on the demand side (accessibility, affordability, acceptability), and in the quality and completeness of the data needed to track IPTp coverage. The project is identifying measures which should increase IPTp coverage, including dissemination of clear policies, strengthening technical working groups on malaria in pregnancy (MiP) at national and district level, better training of health workers, development of job aids, tracking and provision of commodities and use behaviour change communication to increase IPTp uptake. IPTp uptake is increasing, but is still far from meeting the target of 85% of women receiving at least two doses.

Malaria in pregnancy is a serious public health problem but is preventable. However, many opportunities to provide IPTp are missed. There is a need to tailor interventions strategically to the needs of pregnant women in different contexts, to develop better data recording and reporting systems, and to overcome the demand and supply-side barriers.

“A substantial increase in operational research is required to make the most of the tools which already exist.”
The first 12 years of this millennium saw a 25% reduction in the incidence of malaria... a 42% reduction in deaths... 3.3 million deaths averted.

The first 12 years of this millennium saw a 25% reduction in the incidence of malaria (Figure 14). These gains have been associated with a 42% reduction in deaths overall, with higher reductions amongst young children and a total of about 3.3 million deaths averted in the same period (Figure 15). Furthermore, four countries have been certified malaria free - UAE, Morocco, Turkmenistan, Armenia - and 15 other countries are getting close to elimination.

These dramatic changes are a result of the increased availability and use of interventions to prevent and treat malaria. Access to insecticide-treated nets increased to 42% of at-risk populations in sub-Saharan Africa in 2013 (Figure 3). In addition, approximately 135 million people (4% of the global population at risk) were protected by indoor residual spraying (IRS) in 2012.

Access to treatment has also improved. Rapid diagnostic tests (RDTs) are increasingly used to distinguish malaria fevers from other causes, enabling the improved targeting of artemisinin-combination therapies (ACTs). Around 331 million courses of these highly effective drugs were delivered in 2012. There have also been improvements in the management of severe disease with intravenous artesunate now being recommended as first line treatment.

However, in 2012 (most recent data available), there were still 207 million cases of malaria globally and 627,000 deaths. In sub-Saharan Africa, 57% of the population continued to be exposed to this deadly, but preventable, disease (Figure 16).

Mathematical modelling suggests we can do a lot more with better use of the tools available today. By improving the use of insecticide-treated nets and ACTs it should be possible to reduce malaria cases and deaths by 40% by 2020. Anticipated improvements in the use of malaria control tools mean that a 90% reduction in cases and deaths is...
The burden of malaria

“In 2012 there were still 207 million cases of malaria globally and 627,000 deaths.”

“We can do a lot more with better use of the tools available today.”

possible by 2030. With appropriate investment, we can also expect malaria to be eliminated in ten countries by the end of 2020 and in 35 countries by 2030. The introduction of new tools, such as the malaria vaccine RTS,S, should lead to even greater gains. Such improvements will dramatically improve not only health and survival but also educational outcomes and economic productivity.
The Mundia family – Living with the frequent burden of malaria

"Malaria is a nightmare for us," was the immediate reaction from Christopher Mundia when asked about the malaria situation in his home area of Chipulukusu Township, Ndola, Zambia. Swampy vegetation surrounds the township, contributing to high malaria transmission all year round. Christopher's daughter, Phyllis, is just recovering from the disease. "Phyllis was treated last week. Look at her, she still looks pale," Christopher commented.

Unfortunately, a child suffering from malaria is not a rare occurrence in the Mundia household. "We have two children less than five years old who get malaria six to seven times a year," said Mr Mundia. "We also have a seven-year-old and a nine-year-old who both needed to be hospitalised with severe malaria. Our home is devastated by malaria."

"Malaria seriously affects our economic situation," said Agness Mundia, Phyllis's mother. "I cannot engage in any form of productive activity to supplement my husband’s salary, as I am often at home nursing one child after another. Sometimes I have to be in hospital with the children, nursing them because they are severely ill and require quinine in a drip for treatment." Mr Mundia added "my workplace has cautioned me several times because of the repeated need to assist my wife with our sick children."

Fortunately, the family live just three kilometres away from the nearest clinic, where they can access high-quality artemisinin-combination therapies at no cost. "If there were no drugs in the health facilities, we would never be able to afford to keep buying them to give to the children. These drugs are very important to us; they form part of our daily lives because of the situation we live in."

Story courtesy of Prof. Christine Manyando, Tropical Diseases Research Centre, Zambia and MMV
In last year’s report we presented a vision of what will be required to achieve a world without malaria. “The ambition has to be to eliminate malaria deaths by optimised malaria control and, eventually, to eradicate malaria across the world.” This will need full deployment of the tools and strategies to prevent and treat malaria. However, to realise their full potential a number of other factors must be considered.

**Reliable health information** systems are needed to produce and process complete, reliable information to monitor progress with malaria control and to forecast commodity needs. Rapid Diagnostic Tests and mobile phone technology can produce a step change in information use for malaria control decisions.

In order to target investments where they are most needed it is essential to measure malaria cases and deaths and to track the level of resistance to insecticides and drugs. There is an urgent need to strengthen the information systems required to capture key data to enable national and global policy makers and programme implementers to track progress with malaria control decisions.

Malaria transmission varies in time and space within countries, regions, districts and even villages. Improved information systems are required to map malaria cases so that efforts can be targeted where they are most needed. By so doing, not only will malaria control improve but malaria control programmes will provide better value for money.

**Development of local capacity** to enable appropriate responses to information and to research local solutions to local problems. Health staff at district and national levels need to respond appropriately to new information. For example, an upsurge of cases should prompt local health workers to check ITN coverage in households, the availability of treatment in health facilities and shops etc. Systems are needed

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**Improved data systems for malaria control in Odisha, India.**

The National Institute of Malaria Research and the National Vector Borne Disease Control Programme (NVBDCP), Odisha, India, with technical and financial support from MMV, are implementing a programme in four districts of Odisha state, across four different transmission settings. The goal is to ensure universal access to timely diagnosis, treatment and radical cure at the community level, and to assess its impact on malaria transmission.

In each district, there is an intervention and control “block”, an area comprising 100,000–150,000 people. In all the blocks, Accredited Social Health Activists (ASHAs) work at the community level to diagnose malaria, including *Plasmodium vivax*, with the recent introduction of rapid diagnostic tests (RDTs), and treat patients in line with national guidelines. In the intervention blocks, the uninterrupted supply of RDTs and antimalarials is assured along with supportive supervision of ASHAs. The programme has also introduced patient cards to identify repeat attendances as well as an electronic data-management system to enable the proactive use of data for timely action.

“The programme allows us to reattribute patient data from outpatient clinics in towns to the village where a patient lives. This means that we can identify high-burden areas and really focus our resources accordingly. For example, the microscopist in Hindol block realised that more cases were coming from a certain area, which led us to conduct a mass survey, and detect and treat a large reservoir of asymptomatic carriers. We believe this averted a malaria outbreak.”

*Dr Madan Mohan Pradhan, Deputy Director Health Services, NVBDCP, Ministry of Health & Family Welfare, Odisha.*
to mobilise resources outside the district, such as insecticide spray teams to respond to local needs. Dry data can be turned into powerful knowledge-based strategies where trained staff act on data and deliver effective malaria prevention and treatment. These systems will enable funders to focus on outcomes and impact, and not just inputs. Building capacity needs to be prominent in the development and malaria control agendas. We commend the investments of DFID and the Wellcome Trust to strengthen capacity for malaria research and control.

**Engagement with the private sector**, an important player in malaria control, will be essential in three broad areas. First, private sector investment is required to bring new products to market. Second, the private sector plays a key role in service and commodity provision in many settings: the vast majority of anti-malarials in Nigeria and DR Congo, the two countries most heavily burdened with malaria in the world, are sourced from the private retail sector. The private sector must be integrated into the broad picture of the health systems in such settings. The power of the private sector to make commodities available, even in remote rural settings, was clearly demonstrated by the Affordable Medicines Facility for malaria (AMFM): the public sector could take advantage of this capacity. It will be important to capture data from the private sector in routine health information systems. Finally, there is considerable potential for the local and international private sector to play a role in domestic investment for malaria control through the provision of services in the workplace and as part of corporate social responsibility programmes.

**A plan for elimination** – interrupting the transmission of malaria in a country – can be developed when malaria transmission is reduced to low levels through the supply of effective commodities and recognised by enhanced information systems. No commitment to elimination should be made before a thorough evaluation of what will be required, especially in terms of finance and time, to complete the job.

**The Millennium Development Goals and Beyond**

Malaria features as a specific indicator for MDG 6 and contributes to other MDGs, including poverty, education, child survival and maternal health. Great progress has been made with 50 countries on track to reduce malaria cases by 75% by 2015 in comparison with 2000. However, these account for only 3% of the total estimated cases worldwide. The malaria and global health communities must commit to completing the “unfinished business” of the MDGs. Malaria will be relevant to the post-2015 agenda, and should feature as a sub-target under the Sustainable Development Goal on Health. Malaria control efforts need to be better integrated into the overall development agenda and the work of non-health sectors – including water and sanitation, housing, infrastructure, environment, finance, mining, industry, tourism and education. All sectors should use a malaria lens to consider the potential broader economic, environmental and social impacts of their activities in endemic countries.

A better appreciation of the inter-dependencies between sectors is beginning to dawn, as evidenced by the July 2013 multi-sectoral Roll Back Malaria (RBM) meeting on the social determinants of malaria. Strengthened cross border collaboration can lead to harmonisation of approaches and methods, synchronisation of activities, exchanges of information and experience, as well as cross sector work on malaria. Strong government commitment is critical, though it takes time to bring colleagues from other sectors on board and to recognise the malaria considerations as an added benefit rather than a complication to their activities. The potential for impact is considerable: the elimination of malaria in England was less due to specific interventions than to progressive social, economic, educational, medical and public health improvements, which also had major non-malarial benefits.

“The ambition has to be to eliminate malaria deaths by optimised malaria control and, eventually, to eradicate malaria across the world..”
“Renewed financial commitment now will bring an era of unprecedented benefits for health, survival and development.”

Finance for Malaria Control

International funding for malaria control increased from less than US$ 100 million in 2000 to US$ 1.60 billion in 2011. This figure rose to US$ 1.94 billion in 2012 and US$ 1.97 billion in 2013 (Figure 17). Increased UK support has been a major contributor to this change, second only to the US for international funding. Domestic funding for malaria control has also increased, albeit modestly (Figure 18). The increase in funding has resulted in marked increases in the use of ACTs and ITNs, and this has translated to a 25% reduction in the incidence of malaria cases and a 42% reduction in deaths - equivalent to approximately 3.3 million lives (Figure 19). With the given resources, no other global initiative can boast such gains.

However, only a fraction of the needed finance has been made available to date and lack of funding remains the greatest barrier to progress against malaria. Global requirements for malaria control were estimated to exceed US$ 5.1 billion per year between 2011 and 2020 in the RBM 2008 GMAP. The enormity of the additional potential benefits is clear given the dramatic improvements already seen in survival with today’s modest levels of ITN and ACT use. Renewed financial commitment now will bring an era of unprecedented benefits for health, survival and development.

Finance for Research and Development

The last two decades have seen a five-fold increase in annual funding for malaria research and development (R&D)—from US$131 million in 1993 to $610 million in 2011. However, recent projections estimate that malaria R&D will require up to $8.3 billion over a decade (2013–2022) to develop the new tools needed to sustain efforts to combat the
disease, with a midrange projection for investment of about $700 million annually. R&D investments are critical, given the emergence of drug resistance in the malaria parasite and insecticide resistance in the mosquito and the potential benefits of improved diagnostics and vaccines.

It is crucial to sustain the momentum created by an R&D pipeline that has never been healthier, with nearly 90 products in development. With almost 40 drugs, ten of which are in late-stage clinical trials; the first vaccine candidate to reach late-stage testing, with dozens of others in development; more than a dozen new mosquito control tools; and a host of new diagnostic tools, we have never been better-placed to accelerate efforts to control and eliminate malaria.

*Fig 18 Domestic funding for malaria control, 2005-2012. Source: WHO. World Malaria Report, 2013.*

"It is crucial to sustain the momentum created by an R&D pipeline that has never been healthier."
The role of the UK

The APPMG recognises the leadership role that the UK government has played in malaria research, development and control. The fight against malaria remains a leading example of cost-effective, impactful investment of UK aid. The UK Government’s commitment to the 0.7% of Gross National Income (GNI) for international development has set a powerful example. The APPMG is particularly proud of the recent parliamentarian support for the International Development (Official Development Target) Private Member’s Bill during its second reading on 12 September 2014 - which saw 164 MPs support enshrining in law the UK’s 0.7% commitment. The Bill has strong support to move forward to committee stage and we urge parliamentarians to ensure that this is enshrined in law.

Thanks to the UK’s support, working in partnership with global efforts, we have shown that it is possible to turn the tide against the malaria parasite. Millions of people are accessing effective malaria prevention, diagnosis and treatment thanks to DFID’s direct bilateral and multilateral support. DFID and the Wellcome Trust have made major investments in developing the capacity of endemic country scientists to conduct high-quality research to test new interventions and strategies for malaria control. The joint DFID/Wellcome Trust/MRC Global Health Trials initiative has raised the bar for quality research into priority diseases in low and medium income countries. DFID is also in the process of supporting the improved use of data to inform decision making for malaria control. However, further investments in malaria control and research and development are needed to yield still greater results.

Britain has a long and distinguished history of investment and leadership in the fight against malaria, from the discovery over 100 years ago that mosquitoes transmit the disease to the development now of the first malaria vaccine. We are making progress against this disease faster now than at any other point in history. We can be proud to recognise the pivotal role played by UK aid investments, world leading British businesses, scientists and research institutions, working together with partners around the world towards a common goal – a world free from malaria.

“The UK Government’s commitment to the 0.7% of Gross National Income (GNI) for international development has set a powerful example.”

Case Study: UK Leadership in the fight against Malaria

The UK is considered a global leader in the fight against malaria, contributing significant resources each year to tackle the disease. There have been many notable successes of this bilateral investment which have shown tremendous impact.

With DFID support, the Malaria Consortium has managed the Support to National Malaria Programme (SuNMaP). This £89 million, seven year project is designed to strengthen malaria control efforts at the national level and across ten states through technical assistance, institutional strengthening and commodities support.

Ending in 2015, some highlights from this project include:

- The mass distribution of over 2.5 million long lasting insecticide treated nets directly and coordination for distribution of over 57.7 million nets nationwide. An additional 5.38 million have been distributed through continuous distribution channels, including the commercial sector.
- Building the capacity of over 15,000 service providers and managers
- Working with commercial sector partners to increase access by expanding retail market for nets and antimalarial drugs / commodities
- Harmonising partners’ activities in malaria control
The impact of the DFID-supported Medicines for Malaria Venture

DFID has been a long-term supporter of MMV from its founding in 1999. MMV and its partners have achieved considerable impact on the lives of malaria sufferers. We have brought forward four new antimalarial drugs three of which are already saving lives, the fourth having just recently been approved by regulators.

- Over 200 million treatments of Coartem® Dispersible (artemether-lumefantrine) have been distributed to 50 malaria-endemic countries since product launch in 2009. Using a conservative estimate of 60-75 million infected children under the age of five years treated for malaria with Coartem Dispersible, this implies 400,000-500,000 lives saved.
- Over 20 million vials of Guilin Pharmaceuticals’ injectable artesunate, Artesun® for severe malaria, have been delivered, saving an estimated 130,000 additional young lives compared to treatment with quinine.
- More than 400,000 treatments of Eurartesim® have been shipped to Cambodia. The drug has been submitted for registration in 13 other countries throughout Africa and Asia, and approved in four (the others are currently pending).

We are confident that the strength of the MMV portfolio gives us a proven platform for future impact. It comprises numerous exciting drug projects in various phases of development including:

- Progress into the final development of tafenoquine, a single-dose cure for P.vivax that has demonstrated potential to reduce malaria relapses by 90%.
- Compounds such as OZ439 and KAE609 that have completed early clinical trials. The activity of these two drugs have demonstrated their potential as components of a single-dose cure that could improve patient compliance.

Fatimah’s Story: A community care worker’s perspective

Fatimah Ibrahim, a community care giver in the rural area of Gada in Niger State took part in a SuNMaP-supported training of community care givers. Fatimah learned how to spot, and treat, malaria in under-fives, as well as malaria prevention information that she could share with members of her community.

“The parents keep bringing their children. Sometimes I see ten people a day. It is very important that their parents should bring the children as soon as they spot signs of fever, and after that make sure they take the medicine correctly. Then they recommend me to others. This saves a lot of money and many hours work for the health facility.”
### Useful websites

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APPMG’s Malaria Events & Speakers: October 2013 - June 2014

2013

October | Launch of the 9th Annual Malaria Report: Malaria at the Cross Roads
Launched by Stephen O’Brien MP, Former Minister of International Development, and presented by the report’s author, Professor David Schellenberg, LSHTM.

December | APPMG and APPG Global Health Host Launch of the Policy Cures G-FINDER Report
Speakers included: Professor Chris Whitty, Chief Scientific Adviser and Director of Research and Evidence Division (acting Director of Policy), DFID, Professor Alan Fenwick, Imperial College, Director of the Schistosomiasis Control Initiative in the Department of Infectious Disease Epidemiology and Dr Tim Wells, Medicines for Malaria Venture.

2014

February | The Challenge of Drug Resistance
Speakers included: Professor John Watson, Deputy Chief Medical Officer, Honorary Professor in the Department of Infectious and Tropical Diseases at the London School of Hygiene and Tropical Medicine and Visiting Professor in the Department of Primary Care and Population Sciences at University College London, and Professor Hilary Ranson, Head of the Department of Vector Biology at the Liverpool School of Tropical Medicine.

March | Financing Malaria and NTDs Research, Development and Control
Speakers included: Professor Jeremy Farrar, Director, Wellcome Trust, Dr. Sue Kinn, Team Leader and Research Manager, DFID and Chairman, PDP Funders Group, Dr Julia Fan Li, Lion Head Global and Dr David Reddy, Chief Executive, Medicines for Malaria Venture.

April | World Health Day - The Malaria Experience
This was a drop-in event which included a Malaria Awareness Travel Centre, an African Malaria Clinic and an interactive Mosquito Box.

May | Focus on the Democratic Republic of Congo & Nigeria – Innovation and Action
Speakers included: Prudence Hamade, Senior Technical Adviser, Malaria Consortium, Pierre Hugo, Director, Access and Delivery Africa, Medicines for Malaria Venture with the aid of Professor Christian Burri, Head Department of Medicines Research, Swiss Tropical and Public Health Institute and Asif Ali, Programme Manager, Clinton Health Access Initiative.

June | Financing the Fight: Reaching the Tipping Point Against HIV, TB and Malaria
Speakers included: Mark Dybul, Executive Director, The Global Fund to Fight AIDS, Tuberculosis and Malaria, Azra Ghani, Professor in Infectious Disease Epidemiology, Imperial College and Lucica Ditiu, Executive Secretary, Stop TB Partnership.