

Control and Eradication of Malaria: Past, Present and Future

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The problem of malaria

To the great surprise of many well-informed people in developed countries, malaria remains a major problem in the world today. Although figures may not be very reliable, it was estimated that in 2008 one fifth of the world's population was at risk of malaria, leading to 240 million episodes and some 850,000 deaths, the majority occurring in Africa.¹ The impact falls mainly on children under five and in 50 million pregnant women at risk annually, where effects on mother and baby can be disastrous.

Apart from the major problem of deaths and serious illness from the potentially lethal form, *Plasmodium falciparum*, very large numbers of individuals suffer from the less serious form of malaria, *Plasmodium vivax*, that is a particular problem in the Asia-Pacific region, where some 2 billion people are at risk of infection. Despite the horrific burden of malaria today, it is noteworthy that the situation is substantially improved compared with a century ago when many more countries were susceptible to malaria transmission. The number has now fallen to about 100, in many of which the number of cases is relatively small, as control efforts are effective, and some countries are moving towards elimination. Thus the major burden of death and illness that leads to complications of

serious anaemia or complications for mother and baby during pregnancy, is largely confined to Africa, and five countries, namely Nigeria, Democratic Republic of Congo, Uganda, Sudan, United Republic of Tanzania account for 50% of deaths. Just 15 countries now account for 80% of all deaths.

The vast direct and indirect costs of malaria

The excessive cost of malaria is not confined to illness and direct deaths from infection, but magnified by its contribution to all causes of illness and death and its huge economic impact on the countries in malaria-endemic regions. When malaria specific interventions are introduced, the effects on health are greater than may have been anticipated from the best estimates of malaria-specific illness and death. Estimates of economic cost have been the subject of a number of studies, championed by Jeffrey Sachs and others. In a landmark paper of 2002, Sachs and Malaney concluded that ‘countries in which a high proportion of the population lived in regions of *P. falciparum* malaria transmission in 1965 had annual economic growth rates that were 1.3% lower than other countries over the period 1965–1990, even after controlling for the other standard growth determinants used in macroeconomic analyses’.² The many possible reasons for this huge impediment to development include medical costs, absenteeism from work for self or child care, high infant mortality, failure to open new areas for agriculture, tourism, or other development, and effects on fertility, population growth, saving and investment, absenteeism and worker productivity.

What is malaria: the infection and the disease?

There are four species of malaria that predominantly infect humans, with a recent addition being a parasite of monkeys (*Plasmodium knowlesi*) that has been found in Malaysia and neighbouring countries, where forest-dwelling communities are close to monkeys and the mosquitoes responsible for transmitting the infection. The malaria parasites are transmitted by the bite of infected Anopheline mosquitoes as the females of

this species seek a blood meal on humans prior to egg-laying. Many anopheline species carry human malaria, each with characteristic habitat, feeding behaviour and feeding sources (human, and sometimes other animals).

Some understanding of the life cycle is required in order to appreciate the limited number of targets for prevention of transmission of disease. After a blood meal, the parasites circulate for a short time before lodging in the liver. Here they undergo maturation without provoking symptoms until after a variable period, normally about 10 days, but up to several weeks, they emerge and invade red blood cells, then circulate in the blood stream. At this stage, a non-immune person develops characteristic symptoms of fever and shaking chills as parasites are released from host blood cells. Maturation and multiplication of parasites inside blood cells followed by rupture enables the next brood to invade another group of cells to multiply again. As the cycle progresses with red cell destruction, the patient may become anaemic and without treatment can suffer dysfunction of organs including kidney, liver, placenta and lung. The most serious consequence is cerebral malaria, caused by only one of the species (*P. falciparum*), as a result of distorted malaria-infected red cells adhering to capillaries of the brain leading to potentially fatal consequences. Organ damage is of major consequence when malaria infects the placenta causing maternal anaemia, and placental dysfunction leading to poor outcomes for the baby. In addition to the asexual forms of the parasite responsible for disease, sexual forms are produced that are taken up at the time of mosquito feeding. Fertilisation occurs in the mosquito gut producing forms of the parasite that migrate to the salivary glands where they can invade humans at a subsequent episode of mosquito feeding.

Challenges of malaria diagnosis and management in underserved environments

The diagnosis and management of malaria at an individual level presents major challenges for health care providers. The

first challenge is that symptoms may be indistinguishable from many other simple or serious conditions from viral illness or dengue fever to life-threatening cerebral malaria or epidemic meningitis. A diagnosis of malaria infection is confirmed by taking a blood sample, adding a chemical stain, then examining under a microscope. This is made more difficult in a rural region where microscopes and skilled microscopists are not available, and a low concentration of parasites in the blood may be virtually undetectable yet still cause symptoms. Newer rapid diagnostic tests relying on a simple colour change when blood is added to filter paper may partly overcome this problem. Another complication is that a child or adult with a degree of immunity may have parasites present in the blood yet be quite well, or suffering from another cause of fever.

A second challenge is to provide the correct medication on the assumption of a correct diagnosis, at the correct dose, and ensure that all medication is consumed by a patient who may be crying, vomiting, or disinclined to continue treatment when symptoms start to subside. A third challenge is the emergence of resistance of malaria to cheap, easily available drugs and the need to use combinations of drugs that may have side-effects, or require longer terms of administration. A fourth challenge is that drugs effective for acute treatment of symptomatic disease may neither be effective against the sexual forms of the parasite that maintain transmission when a mosquito bites again, nor for eradication of long-lasting forms of two species (*P. vivax* and *P. ovale*) that have the troublesome characteristic of relapsing from dormant liver stages months or years following initial infection, to cause recurrent illness.

History of efforts to control malaria

The economic devastation and human impact of malaria has been known for a long time. In 1898 Fortunato and Franchaneti wrote a letter to their sponsor indicating the devastation caused by this disease in Italy. 'Malaria disease leaves uncultivated 200 million hectares of land ... It poisons every year about 2 million inhabitants and kills 15,000 of them

... Whoever could quantify the extent to which this disease reduces the welfare, the human resources in the wealth of the land? There is no other health problem so deeply linked to the prosperity of our country.³ The Italians were aware of the devastation caused by the febrile illness that they had referred to as malaria (bad air), recognised since time immemorial as being associated with the swamps around Rome. In 1880 Laveran identified the cause of malaria while undertaking autopsies on people who died of malaria in Algeria. However, the mechanism of transmission was not known until 1897, when Ronald Ross, working with the British Army in India, proved that malaria could be transmitted by mosquitoes. Immediately he recognised that with this discovery he had found a mechanism by which malaria could potentially be controlled.

On the day Ross refers to as 'Mosquito Day' in August 1897, he noted that 'this day relenting God has placed within my hand a wondrous thing', and he went on, 'I know this little thing a myriad men will save'.⁴ Soon after this, experimental proof of transmission of human malaria was obtained and research commenced to control malaria by the elimination of breeding sites, screening of houses, and prevention of mosquito bites. Ross became extremely interested in mechanisms to control malaria, recognising the value of removing mosquito breeding sites by adequate drainage of swamps and free-lying water, and the value of protecting individuals from bites of mosquitoes that were mainly active in the evenings. Such was the success of early efforts that many believed application of then available knowledge would be sufficient to eradicate malaria completely. In 1930, the mosquito with the most profound capacity to transmit malaria in Africa (*Anopheles gambiae*) was discovered in Brazil and through an amazing effort using a military approach, Soper and colleagues were able to eliminate this mosquito, by methods similar to those achieved through eradication of the mosquitoes that caused yellow fever.

While Ross was working in India and making discoveries about transmission of malaria, the great German microbiologist Koch was studying malaria throughout the German colonies. In landmark studies in what is now Papua New Guinea, he made astute observations on the development of immunity to malaria in individuals repetitively and frequently exposed in an endemic area. He noted high rates of malaria in Europeans working on plantations, and that migrants from China and Malaya had high rates initially, but over time had gradually reduced rates of malaria, but never as low as those seen in lifelong residents of the area. Thus he made the observations describing the development of immunity, and also noted that individuals could be carrying malaria parasites and yet be quite well, therefore requiring treatment of a whole population for malaria to be eradicated. He believed that malaria could be prevented by using the drug quinine that had been brought to Europe from Peru ('Jesuit's bark'), and was being produced in large scale to reduce its cost. He believed that the world had the tools to make every malarious region virtually free from malaria. Of course, at that time, Koch was not aware of the relapsing malaria that may lie dormant in the liver, or that sexual forms taken up by mosquitoes were not susceptible to quinine that would be given to prevent clinical disease. The optimism of discovery was soon replaced by understanding of the limitation of knowledge and practical reality of treating whole populations, let alone the emergence of drug resistance.

The Australian experience

The Australian population also suffered malaria, with first reports in 1843 at Port Essington. By the late 1840s, reports of clinical illness similar to malaria were described by explorers, and febrile illnesses reported as far south as Gosford, although they may have been caused by diseases of viral origin. In 1897–1899, it was said that 10% of admissions to Darwin Hospital were a result of malaria. Such was the concern of tropical infectious diseases that an Institute of Tropical

Medicine was opened in Townsville in 1910 and the School of Public Health and Tropical Medicine in Sydney in 1930. Studies in Papua New Guinea showed that atebrine was equally effective as quinine when treating malaria and authorities issued regulations to spray aeroplanes to prevent introduction to Australia. It was only in the middle of the 20th Century that Australia was finally declared malaria free.

Australian malariologists made enormous contributions to global knowledge of malaria through the work of Fairley and others during the World War II. His superb understanding of malaria in endemic countries was vital to establishing experimental proof of the potential value of drug treatment for prevention of malaria in non-immune troops as they entered endemic areas. Under his guidance a unit was established at Townsville as 'No adequate experimental centre for critical investigations on human volunteers existed in any Allied country, and it was felt imperative that the Australian Army should be in a position to assess rapidly the value of new synthetic antimalarial drugs'.⁵ His astute clinical observations and experimentation in human volunteers to demonstrate the role of malaria prophylaxis in preventing illness in battlefields to the north of Australia made an enormous difference to the wellbeing of troops. The powerful evidence provided, particularly at the unit in Townsville, was put into practice in military situations, making enormous contribution to the health, wellbeing and ultimate success of the military campaigns. Beyond the practical implications of his work, it was noted by Ford that 'It was rightly said that (Fairley's) great enterprise, in a few years, had brought greater advances to the knowledge of malarial prophylaxis than had occurred in the past fifty years, or was to occur in the subsequent twenty. Its value to the world was inestimable'.⁶

The impact of DDT on malaria and the malaria control strategy

From the time of the discovery of mosquito transmission of malaria, experts looked for opportunities to prevent the disease

by reducing the number of mosquitoes capable of carrying the disease. Removal of breeding sites with skilful sanitary engineering to prevent accumulation of water, application of larvicides where this was possible, and introduction of sprays to reduce the numbers of mosquitoes could all make a contribution, but what was required was a long-lasting insecticide requiring infrequent application. The solution came with the discovery of dichloro diphenyl trichloroethane, otherwise known as DDT. This insecticide from the GEIGY company was found to kill a variety of pests, but its particular asset was that it could be sprayed on walls of houses at relatively infrequent intervals, providing a toxic landing place for mosquitoes whose habit was to bite indoors and rest on the nearest vertical surface. This being the behaviour pattern for a wide variety of mosquitoes that carried malaria, an obvious means for control was to put this insecticide in a place where it would specifically kill mosquitoes that had fed on human beings, thus preventing transmission of the infection by attacking the mosquitoes liable to spread the disease.

Success and failures in the Global Malaria Eradication Campaign

Recognition of the profound effects that such an insecticide could produce fuelled the belief that available tools could eliminate malaria not only from a region, but also eradicate the disease from the whole world. The contention was disputed by those who believed over-optimistic promises would be followed by inevitable failure, and that a better strategy would be to devote available resources to control of illness and deaths where the burden of disease was at its greatest. The ambitious goal inspired donors to try to achieve a dream, and thus in 1955 the World Health Organization launched the Global Malaria Eradication Program, based on the assumption that the new insecticide could reduce transmission in the mosquito, and that infected individuals could be treated with the use of the widely available drug, chloroquine, that appeared to be effective against all forms of malaria infecting humans.

The DDT story ... loss of a powerful weapon

Coincident with attempted implementation of global eradication came the emerging threat of drug resistance, and more importantly and significantly, growing concern about the effects of residual chemicals on the environment highlighted by the writing of Rachel Carson.⁷ Although the use of insecticides for personal protection and residual spraying of houses was small in comparison with huge amounts used in agriculture, the potential benefits were forgotten in comparison to the emotive issues raised in respect of environmental pollution. The United Nations Environment Programme had the goal of restricting and potentially eliminating non-degradable organic pollutants (POPs), and was supported in its efforts by environmental activists in donor countries. The overall effect was that even though DDT was not universally banned for malaria control, it was in practice not readily available where it was needed in many countries.

Fortunately, a minority group maintained its efforts to restore DDT to the therapeutic armamentarium, arguing that when used appropriately, the benefits clearly outweighed the harmful effects of the pesticides. As stated by Tren and Bate, 'Malaria kills a few million every year. Each life lost is a potential Mandela, Shakespeare or Edison, and nothing is less reversible than death, nor more tragic than the death of a child. Hundreds of millions suffer chronic illness, which creates a painful economic burden and perpetuates poverty. This may not be the intention of those who propose a DDT ban, but it surely will be the outcome.'⁸ Fortunately, DDT is now being deployed for indoor residual spraying once again.

Why have past efforts at eradication failed?

There were several reasons why the Global Malaria Eradication Program succeeded in eliminating malaria in some countries, but overall did not achieve its full objective. Of the many reasons cited, perhaps the most important were the naivety about the size of the task in hand when confronting

mosquitoes in Africa that were so efficient in transmitting malaria, the political will required, and the duration of campaign required to eliminate the last parasites. The tools and programs were simply not able to achieve the task.

Aside from this, it was already known that mosquitoes could develop resistance to DDT or any other insecticides in two ways, first by developing chemical resistance to those insecticides and therefore requiring alternative and far more expensive drugs for their containment, and second, by behavioural resistance favouring transmission by mosquitoes that avoided insecticides by resting safely outdoors after feeding indoors. Mosquitoes of forest fringes that were likely to bite during daylight hours would never have been challenged by indoor residual insecticides.

Malaria became resistant to the antimalarial drug chloroquine, and second line drugs were more expensive, had side-effects, and were hard to obtain. Not only were parasites resistant to these drugs, but there was no effective agent against the forms of *P. vivax* malaria that persisted for a long time in the liver, giving rise to relapses months or years after the initial infection. An asymptomatic individual could transmit malaria many years after transmission had first occurred, thus requiring the continuation of the program for many, many years in order to achieve eradication.

The Global Malaria Eradication Program had amazing successes in many countries but because it was never effective in heartland Africa where highly efficient carriers of malaria produced insuperable obstacles, it was considered overall to have been a failure. This provided a moral victory for those malariologists who argued that it was more important to put effort into control of malaria in 'heartland' areas where the burden of disease was greatest, rather than trying to eliminate malaria from areas with low morbidity where by definition the public health impact was very small.

A failed eradication campaign caused disillusion and resurgent disease

The failure of eradication had some more disastrous effects because malaria came back into many areas where control had been achieved, but financial resources and political will declined so that the effort was not maintained. When malaria control removes the repeated infections that boost immunity, populations of all ages become susceptible and resurgent malaria into a non-immune population can have disastrous consequences and negate benefits achieved over many years. This was particularly noted with epidemics of malaria in Sri Lanka at the end of the 1960s and Madagascar in the 1980s. Thus the battle between those who favoured inputs to control disease and those who promoted efforts to attempt its elimination for all time, continued in the middle part of the last century and is still alive today.

Analysis of the failed global malaria eradication has continued for the past 40 years, even though it remains the goal in the background of every global plan to combat malaria. Major mistakes appear to have been a lack of insight into the complexity of the problems being addressed, and the fact that tools were simply not available to achieve the desired goals. Such a lesson had not been learnt from 'one weapon wars against malaria' that had attempted to control malaria with measures directed only at mosquitoes or only at patients, with tools that were inadequate for the task. A particular problem was the failure to interact with the health systems that would be absolutely critical for continuation of the attack when malaria elimination was reaching the final stages.

Donors became fatigued with the process that they had been led to believe would be achievable in a relatively short time, and with failure of the campaign, funds were directed towards other worthy goals for international development. Those engaged with the process at the time now say that inadequate attention was given to the ongoing research required and a quote from a senior malariologist in 1982 bears

tribute to such a view: ‘Throughout the world support for further research into malaria, even that concerned with insecticides and chemotherapeutic contracted swiftly. Worse still, the apparent imminent demise of the once important disease removed the necessity for training scientists in malariology. It took ten years and a war to halt this tragic trend.’⁹

Malaria control replaces malaria eradication as the predominant paradigm

The failure of the eradication campaign, donor fatigue and lack of political will led to a period of inactivity with respect to malaria control, breakdown in control programmes, and as stated above, resurgent malaria, now accompanied by increased and extensive resistance to antimalarial drugs and increased insecticide resistance. By the early 1990s a redesigned malaria strategy was presented, focusing on malaria control, with specific interventions tailored for different transmission conditions. It was recognised that control required early diagnosis and treatment, combined with preventive measures such as spraying and control of mosquitoes where appropriate, but most importantly, strengthened health systems to support focused programs for malaria. The approach needed to be holistic in providing resources known to be effective, safe drugs, nets, and services, coupled with research for new drugs and ideally an effective vaccine. Goals of preventing mortality, reducing direct and indirect morbidity, and reducing social and economic loss predominated over the longer-term goal of eradication.

Renewed efforts in malaria research and malaria control

As the World Health Organization was introducing its Global Malaria Control Program in the 1990s, there was a rebirth of research funded by those who saw the emerging resistance to antimalarial drugs and lack of alternatives, and the promise that biotechnology could yield a vaccine that could eventually be introduced to prevent the disease. Techniques developed in molecular biology, cell biology and immunology were applied to malaria, enabling an understanding of mechanisms of

genetic diversity and drug resistance (and in some cases tests for their presence); simpler methods for testing whether mosquitoes were infected; genetically engineered prototype vaccines, and potential of genetically modified parasites to be used as attenuated vaccines. Arguably, a new age of malaria research had been introduced, stimulated both from altruism and the desire to apply new tools to an old problem.

In addition, global funding for infectious disease increased in response to recognition that poor health was an impediment to global development. Infectious diseases contribute to poverty and under-development characteristic of unstable societies that are at risk of civil disturbances associated with 'failed states': in this sense AIDS, TB and malaria are threats to world peace, and should be addressed for a safer world.

Major initiatives included creation of the Global Fund to Fight AIDS, Tuberculosis and Malaria to increase dramatically the resources to fight three of the world's most devastating diseases, and to direct those resources to areas of greatest need. As a partnership between governments, civil society, the private sector and affected communities, the Global Fund represents a new approach to international health financing.

Increased support for malaria research also came from other sources, stimulated and spearheaded by the amazing generosity of Bill and Melinda Gates. In rapid succession the Foundation added support for the Global Fund for AIDS, tuberculosis and malaria, and the Malaria Vaccine Initiative; United States Government (Civilian and Military) increased funding, and the Multilateral Initiative against Malaria was created. Public/private partnerships included the Medicines for Malaria Venture and, among others, 'Rotary against Malaria' also made a contribution. In September 2008, the umbrella organisation for malaria control 'Roll Back Malaria' launched a Global Malaria Action Plan,¹⁰ part of which was to suggest that the end game should be eradication of malaria from the globe. It was noted at that time that there were several countries of the world or regions, up to 30 or so, that

were already approaching the last stages of elimination with intense application of available tools.

Challenges of the changing architecture of funding for global health

The surge in funding for single 'vertical' programs for infectious disease control has been welcomed, but has caused some distortions of funding and services in countries of need. Critics argue that country managers are forced to accept priorities of donors rather than their priorities based on local disease burden and accept onerous responsibilities to provide multiple reports to meet specifications for targets of individual donors. Abundant resources for a single disease may attract staff (and their time) with resultant weakening of other parts of the system. A big challenge is to determine how funds for a single program can be used wisely to strengthen health systems with donor aid facilitating transformation to sustainable development.

A renewed call for eradication

At a landmark meeting in October 2007, Melinda and Bill Gates challenged the malariologists of the world to develop a plan for the eradication of malaria. They recognised that this was a very big challenge, and that all efforts should continue for the control of malaria where it was causing illness and deaths, but that scientists should take a critical longer term view if ever such a goal was to be achieved. Just as 50 years earlier the debate of control versus elimination and eradication led to much disagreement amongst scientists in the field, there were legitimate questions as to whether malaria could actually be eliminated from all endemic countries with currently available tools, particularly in conditions of conflict, poor communications, and even in some cases civil war. Many were concerned that efforts towards eradication would replace efforts currently directed to control the immense burden of malaria.

Recognising the need for a long term view towards malaria eradication, and noting that a new medication, vaccine or insecticide may take 20 years from discovery to intervention, the

initial action was to establish a research agenda to identify road blocks or bottlenecks for eventual eradication. In this renewed paradigm of elimination, tools should be considered more for their long-term value in reducing transmission of malaria from human to mosquito to human, than on control of disease and reduction of deaths. In addition, treatments would need to be found for the relapsing parasite *Plasmodium vivax*. It was also recognized that new tools that would be of benefit for eradication were highly likely also to play a very important role in ongoing efforts to control the disease.

Where are we now?

The world malaria report estimates that there are 240 million cases of malaria per year and 860,000 deaths, with 90% of the deaths occurring in Africa, and 85% in children less than five years of age. Undoubtedly major progress is being made in applying the tools that are available to control malaria, even though much remains to be done. Estimates suggest that 30% of households in the 35 high-burden countries in the African region owned at least one insecticide-treated net in 2008 and about one quarter of children less than five slept under a treated net. However, averages hide realities when some of the worst-affected countries, such as Democratic Republic of Congo and Nigeria, had some of the lowest rates of net ownership and usage. The reintroduction of indoor residual spraying has allowed protection to be delivered to increased numbers of people, from approximately 10 million in 2004–2005 to something like 60 million in 2008. The aim for better treatment has seen increased numbers of countries adopt standardised combinations of antimalarial drugs as recommended treatment policy, and more than 50% of countries have now put these policies into action.

Substantial successes have now been seen in the last decade, with reduction in more than half of the cases in nine African countries, and more than 25 outside Africa. Spectacular reductions have been seen in Zambia, Rwanda, Sao Tome and Principe and Eritrea and, as anticipated from

earlier studies, reduction in deaths attributable to malaria has been paralleled by a decrease in all causes of mortality. It is estimated that since 2006, some 350,000 lives have been saved by the introduction of insecticide treated bednets and provision of therapy for prevention of malaria in children.

Hopes for a vaccine

Vaccination is one of the most cost-effective approaches in medicine and everyone believes an effective vaccine could produce enormous benefits. Almost 40 years ago it was shown that mice could be vaccinated against malaria, and soon afterwards, small numbers of humans were protected in a proof of principle that vaccination is possible, even though the duration of protection was limited, and the method was not amenable to being scaled up for mass production. With the revolution in molecular biology, a genetically engineered vaccine was produced based on results of some of the early animal studies, and is now being tested in a large-scale experimentation in Africa to determine whether early evidence of 50% protection is confirmed in large-scale field testing.¹¹ Trialists are optimistic of a partially effective vaccine, and additional supplementary candidates are in the research and development pipeline, producing a climate of cautious optimism that a major new first-stage weapon may soon be available.

Efforts for control or elimination and the challenge of drug resistance

The gratifying response to implementation of currently available interventions in some regions has inspired some to champion efforts towards eradication, and others to emphasise what is needed to maintain and extend improvements in malaria control. With chemotherapy being the dominant mechanism of treatment of illness, every effort needs to be made to prevent the emergence of resistance to antimalarial drugs by preventing the use of ineffective monotherapy and ensuring that combination therapy is used for all active treatment. To prevent rising drug resistance, it is important to track

the emergence of resistance against individual drugs. A strategy being considered is to develop an effective rapid test for identification of resistance that could lead to immediate introduction of expensive second-line drugs and a control strategy in the area to prevent that parasite being transmitted further into the community.

Coupled with this improved management of individual episodes of illness, is the need to find better diagnostic tests for malaria, and other causes of fever presenting in the same way, so that drugs will not be used unnecessarily, thus reducing the pressure for induction of drug resistance. As mentioned previously, identification of a drug that had efficacy against both asexual stages and those transmitted by mosquitoes would ensure that resistant parasites emerging following treatment would not be transmitted. Above all it is essential for the world to work through mechanisms such as Medicines for Malaria Venture (MMV) to develop new drugs that are also affordable when resistance inevitably arises to current agents.

Funding this initiative

The Global Malaria Action Plan presented by Roll Back Malaria in 2008 with the Global Fund, the World Bank and the United States President's Malaria Initiative suggests that between 6 and 5 billion dollars US per year is required between 2010 and 2015 to build control, then sustain control efforts. It is notable that total funding actually committed in the years 2009 and 2010 was only one third of this total. In addition to the required costs for implementing the strategy, there is additional need for approximately \$1 billion for research and development of the new agents that will be required to achieve control, and be effective in achieving elimination, and finally eradication of malaria as emphasized above. All nations of the world including Australia should be making their contributions, in particular, to support the World Health Organization for its normative function and guiding role for countries in greatest need of support for policy and practice guidelines.

Conclusion

The burden of disease is intolerable yet tools are available to make an enormous impact on death and suffering. Investment in control and elimination will have enormous returns for personal health and cumulative benefits for a safer and healthier future for the whole world. It is up to the leaders of this generation to ensure that future generations will benefit from a massive investment in the next decade.

Endnotes

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