Malaria Elimination 1

Shrinking the malaria map: progress and prospects

Richard G A Feachem, Allison A Phillips, Jimee Hwang, Chris Cotter, Benjamin Wielgosz, Brian M Greenwood, Oliver Sabot, Mario Henry Rodriguez, Rabindra R Abeyasinghe, Tedros Adhanom Ghebreyesus, Robert W Snow

In the past 150 years, roughly half of the countries in the world eliminated malaria. Nowadays, there are 99 endemic countries—67 are controlling malaria and 32 are pursuing an elimination strategy. This four-part Series presents evidence about the technical, operational, and financial dimensions of malaria elimination. The first paper in this Series reviews definitions of elimination and the state that precedes it: controlled low-endemic malaria. Feasibility assessments are described as a crucial step for a country transitioning from controlled low-endemic malaria to elimination. Characteristics of the 32 malaria-eliminating countries are presented, and contrasted with countries that pursued elimination in the past. Challenges and risks of elimination are presented, including Plasmodium vivax, resistance in the parasite and mosquito populations, and potential resurgence if investment and vigilance decrease. The benefits of elimination are outlined, specifically elimination as a regional and global public good. Priorities for the next decade are described.

Introduction

A three-part strategy to eradicate malaria has been developed1–4 and is now widely endorsed,5–10 (1) aggressive control in highly endemic countries, to achieve low transmission and mortality in countries that have the highest burden of disease and death; (2) progressive elimination of malaria from the endemic margins, to shrink the malaria map; and (3) research into vaccines and improved drugs, diagnostics, insecticides, and other interventions, and into delivery methods that reach all at-risk populations.

Much effort and investment has rightly been devoted to part one of this strategy, aggressive control in highly endemic countries, and has resulted in a massive scale-up of effective interventions11–13 and substantial reductions in mortality and morbidity from malaria in some endemic countries.14–18 Investment and activity in part three of the strategy, research into new interventions and delivery methods, have increased in the past decade, and a research agenda for malaria eradication has been developed.19 By contrast, part two of the strategy, shrinking the malaria map, has received less attention, which has resulted in a deficit of evidence-based knowledge and guidance. This four-part Series about malaria elimination begins to fill this gap.20–22

Historical summary

Efforts to control and eliminate malaria on a large scale date back to the late 19th century, with the discovery of the plasmodium parasite and its transmission by anopheline mosquitoes. During the first half of the 20th century, when 178 countries had endemic malaria, little progress was made, partly because efforts were disrupted by World Wars 1 and 2. However, from 1945 to 2010, 79 countries eliminated malaria.23–25 Despite exponential population growth in malaria-endemic areas during the past 60 years, an estimated 50% of the world’s population live in malaria-free areas, compared with only 30% in 1950.26

With few exceptions, elimination in the northern hemisphere proceeded systematically from north to south, and in the southern hemisphere, from south to north. Thus, the concept of shrinking the malaria map was born. Most of this progress was achieved in temperate regions where climatic conditions are not as conducive to endemic malaria as they are in the tropics. Notable exceptions to this pattern include elimination on tropical islands, such as Maldives, Mauritius, Reunion, Taiwan, and much of the Caribbean, and in rapidly developing small tropical countries, such as Brunei, Hong Kong, and Singapore.14,27–29

This remarkable success was propelled by the Global Malaria Eradication Program, launched by WHO.30

Key messages

• A three-part strategy is now agreed to move the world to eventual malaria eradication: aggressive control in the high-burden regions; elimination from the endemic margins inwards; and research and development into new interventions and technologies.
• 99 countries have endemic malaria; of these, 67 are controlling malaria and 32 are pursuing an elimination strategy.
• The 32 malaria-eliminating countries span all geographic locations, sizes, and incomes. Many of them have the prospect of eliminating malaria within the next decade.
• Countries contemplating elimination should comprehensively assess the feasibility of malaria elimination.
• 25 of the 32 malaria-eliminating countries are solely or mainly fighting a battle against Plasmodium vivax malaria. New interventions and techniques are urgently needed to detect and treat this infection.
• Although malaria elimination has risks, the alternative of maintaining controlled low-endemic malaria for a long period also has risks, many of them similar in nature and magnitude.
• The benefits of malaria elimination are not sufficiently understood, but include substantial positive externalities in the form of benefits to neighbouring countries (regional public goods) and worldwide (global public goods).
• Various overarching challenges exist, including improved methods for diagnosis and surveillance, multicountry collaboration, and ensuring long-term commitment and resources to achieve elimination and maintain it for decades thereafter.
in all parts of the world apart from Africa in 1955. The programme relied on vector control, mainly indoor residual spraying, and systematic detection and treatment of cases. However, because of administrative, financial, and technical issues, it was abandoned in 1969.4 Lessons learned from the Global Malaria Eradication Program have been well documented, are discussed in this Series, and are important as the international community once again focuses on progressive elimination and eventual eradication of malaria.19–21

After the abandonment of the Global Malaria Eradication Program, most countries that had eliminated malaria continued to maintain their malaria-free status. Many of the countries remaining malarious were left with demotivated programmes, chloroquine and DDT resistance,46 and insufficient local and international commitment, finance, or guidance.47 Such circumstances led to substantial increases in malaria worldwide during the 1970s and 1980s. Other causes of malaria resurgence included changes in political and economic conditions, as seen in former Soviet republics like Tajikistan, where malaria endemicity was re-established after the post-Soviet economic collapse and the deterioration of the public health system.48 These experiences provide important lessons about the need to maintain investment and vigilance during the latter stages of elimination efforts.5,14,21

Despite the setbacks, we have many reasons to be optimistic. Scale-up of malaria control has resulted in progress towards elimination in several countries since the early part of the 21st century, driven by large increases in available finance for malaria39–42 and by the widespread use of longlasting insecticide-treated bednets, artemisinin-based combination therapy, and rapid diagnostic tests.

Definition of elimination
The terms elimination, eradication, and control are often used loosely, which results in misunderstanding.48 The word eradication has previously been used to describe what we now call elimination,49 but is used only to mean the “permanent reduction to zero of the worldwide incidence of infection caused by a specific agent as a result of deliberate efforts. Interventions are no longer needed.”50 Generally, cessation of malaria transmission in a defined geographic area, such as an island or an entire country, is now called elimination. WHO defines malaria elimination as: “interrupting local mosquito-borne malaria transmission in a defined geographical area—ie, zero incidence of locally contracted cases, although imported cases will continue to occur. Continued intervention measures are required.”51

The WHO definition of elimination, taken literally, is achieved almost nowhere. Most countries that have achieved elimination and are maintaining their WHO-certified malaria-free status, such as Italy or the USA, have occasional, small outbreaks of secondary cases that are contracted from primary imported cases. For example, despite 12 outbreaks of malaria in the USA between 1993 and 2009, and 26 secondary cases,46 no one is suggesting that the USA has not eliminated malaria. WHO addressed this issue in 2006 by proposing an operational criterion of elimination as “nationwide per year fewer than three ‘epidemiologically linked’ cases of a malaria infection without an identifiable risk factor other than local mosquito transmission, for 3 consecutive years.”57

Cohen and colleagues58 reviewed the use of the terms control, elimination, and eradication and proposed a new definition of elimination as “a state where interventions have interrupted endemic transmission and limited onward transmission from imported infections below a threshold at which risk of re-establishment is minimised. Both capacity and commitment to sustain this state indefinitely are required.”59 This new definition recognises that maintaining “zero incidence of locally contracted cases”60 is not always an achievable target. Furthermore, as addressed in the third paper61 in this Series, this definition emphasises the maintenance of a highly functional surveillance and outbreak response system that is capable of preventing re-establishment of local transmission.

Although many stages occur between the control and the elimination of malaria, this Series regards the alternative to malaria elimination as a state of malaria epidemiology that is typically achieved before launching an elimination effort, often referred to as sustained control. Definition of this state is important because a country that decides not to eliminate is not deciding to do nothing, but is deciding to continue investments and programmatic activities to maintain a state of malaria control indefinitely.

WHO defines malaria control as “reducing the disease burden to a level at which it is no longer a public health problem”,62 which allows for a contextual and disease-oriented endpoint. Cohen and colleagues60 introduced a new term, controlled low-endemic malaria, which they define as “a state where interventions have reduced endemic malaria transmission to such low levels that it

Panel 1: Definitions used in this Series

Elimination
“A state where interventions have interrupted endemic transmission and limited onward transmission from imported infections below a threshold at which risk of re-establishment is minimised. Both capacity and commitment to sustain this status indefinitely are required.”59

Malaria-eliminating country
• A country that has formally declared a national, evidence-based elimination goal, has assessed its feasibility, and has embarked on a malaria elimination strategy.
• A country that is strongly considering an evidence-based national elimination goal, and that has already made substantial progress in spatially progressive elimination (eg, by eliminating malaria from specific islands, provinces, or geographic areas) and in greatly reducing malaria nationwide.

Controlled low-endemic malaria
“A state where interventions have reduced endemic malaria transmission to such low levels that it does not constitute a major public health burden, but at which transmission would continue to occur even in the absence of importation.”63
does not constitute a major public health burden, but at which transmission would continue to occur even in the absence of importation.4 Generally, this term applies to areas where malaria-specific mortality and severe disease outcomes are rare and malaria’s contribution to all-cause childhood mortality is small.48 These definitions of elimination and controlled low-endemic malaria from Cohen and colleagues10 are adopted in this paper and throughout this Series (panel 1). WHO categorises countries in four programme phases by use of malaria slide positivity and incidence rates: control, pre-elimination, elimination, and prevention of re-introduction. For example, a country in the elimination phase has an annual parasite incidence of less than one case per 1000 people at risk.9

This Series builds on WHO’s categorisations and other work.2,3 We propose a new term, a malaria-eliminating country, which refers to a country in the process of moving from controlled low-endemic malaria towards elimination. There are two proposed categories for malaria-eliminating countries: the first includes countries that have formally declared a national, evidence-based elimination goal, have assessed the feasibility of such a goal, and have embarked on a malaria elimination strategy; the second includes countries that are strongly considering an evidence-based national elimination goal, and that have already made substantial progress in spatially progressive elimination (eg, by eliminating malaria from specific islands, provinces, or geographical areas) and in greatly reducing malaria nationwide.

Ten countries in the WHO elimination phase, eight in the pre-elimination phase,10 and 14 that may or may not have met WHO’s epidemiological criteria for pre-elimination or elimination (because data are insufficient or ambiguous, or, in some cases, controversy exists with respect to data interpretation)—such as Cape Verde, Namibia, and Swaziland (webappendix pp 3–11)—qualify as malaria-eliminating under the first definition category. Several countries that have not declared a national elimination goal, but are on a plausible pathway to elimination, and that are participating in active scientific, technical, and financial discussions about how to achieve and sustain elimination (eg, Bhutan, Costa Rica, Dominican Republic, São Tomé and Príncipe, and South Africa; webappendix pp 3–11)7,8 qualify as malaria-eliminating countries under the second definition category. Webappendix pp 3–11 provides data for each of the 32 malaria-eliminating countries and clarifies present categorisations.

This categorisation of malaria-eliminating countries is closely aligned with the geographical distribution of elimination feasibility that is described in the second paper of this Series.20 We have identified a third of all malarious countries as malaria-eliminating countries, and thus draw attention to the need for greater support, research, and investment into elimination and the difficult task of preventing re-introduction. The definitions and categorisations used in this Series address all Plasmodium species that infect human beings. However, some countries might choose to set interim elimination targets by parasite species in recognition of the added challenge of eliminating Plasmodium vivax malaria. The second paper in this Series, which presents worldwide rankings of malaria elimination feasibility, underscores this challenge and does not rank the technical feasibility of P vivax elimination because of the poor understanding of its epidemiology and the likely species-specific strategies and interventions that will be needed.

Elimination

Figure 1 shows a world map with countries categorised by their epidemiological status: 109 countries are malaria free, 67 are controlling endemic malaria, and 32 are malaria-eliminating countries. There are, necessarily, discretionary judgments to be made with respect to marginal countries that could be categorised as either controlling or eliminating malaria. We have been conservative when making these judgments. For example, Madagascar and Haiti have both adopted elimination goals,9,10 but in view of their present malaria burden and other factors affecting the feasibility of elimination,10 we do not categorise either country as a malaria-eliminating country. Country conditions and progress towards elimination will change with time, and we will continue to reassess the epidemiological status and revise the categorisation of each country.

The epidemiological status of the countries shown in figure 1 is not intended to be prescriptive. We believe, on the basis of country-specific evidence and policies, assessments, and judgments made by WHO, national leaders, and malaria experts, that the countries defined as malaria-eliminating countries all have a reasonable prospect of eliminating malaria within the next decade or so.1 Some countries, such as the Solomon Islands, will find elimination more difficult than will others, such as Argentina. Some countries defined as controlling malaria, especially those in Latin America, might think that figure 1 is overly conservative and believe that they too can achieve elimination in the next decade or so.

For a country to decide to move from controlled low-endemic malaria to elimination will always be a matter of judgment for national decision makers, and should be based on a comprehensive understanding of the technical, operational, financial, and socioeconomic viability of the task.1,10 Countries should be discouraged from embarking on elimination programmes on the basis of national ambitions that are not founded on detailed evidence. All countries contemplating elimination should comprehensively assess the feasibility of malaria elimination, as recently done in Zanzibar,10 and make their decision on the basis of the results. Further work and experience will clarify the feasibility of elimination in diverse settings. In
the second paper in this Series, Tatem and colleagues present global rankings of the overall feasibility (a combination of technical and operational feasibility) of \textit{Plasmodium falciparum} elimination, and the operational feasibility of \textit{P. vivax} elimination. Figure 2 shows the key factors that determine the technical feasibility of elimination. There is a close, but not perfect, association between the designation of malaria-eliminating countries in this paper and the model-based estimations of elimination feasibility presented by Tatem and colleagues. For example, the data that they present lend support to a higher level of ambition for some Latin American countries than we have recognised.

Characteristics of malaria-eliminating countries

Malaria-eliminating countries share three important characteristics. First, most of them lie at the margins of malaria-endemic regions (figure 1). For example, Algeria, China, and Mexico are situated at the most northern margins of endemic malaria transmission, and Argentina, South Africa, and Vanuatu are situated at the most southern margins of endemic malaria transmission. Second, malaria-eliminating countries already have substantial malaria-free areas. Third, transmission in malaria-eliminating countries has typically been greatly reduced in recent years and incidence is generally low. These characteristics, for obvious reasons, make the task of malaria elimination much easier.

\textit{P. vivax} malaria is the dominant challenge across the malaria-eliminating countries. Figure 3 maps the proportion of human malaria caused by \textit{P. falciparum} and \textit{P. vivax} by country. Comparison of figures 1 and 3 shows that in only seven of the malaria-eliminating countries (Botswana, Cape Verde, Dominican Republic, Namibia, São Tomé and Príncipe, South Africa, and Swaziland) the malaria burden is due solely or mainly to \textit{P. falciparum}. The other 25 malaria-eliminating countries either have a mix of \textit{P. vivax} and \textit{P. falciparum}, or have predominantly or solely \textit{P. vivax} malaria. The prevalence of \textit{P. falciparum} malaria in these countries is falling at a faster rate than is the prevalence of \textit{P. vivax} malaria, and, therefore, the proportion of malaria due to \textit{P. vivax} is increasing. Thus, for countries outside Africa, the final stages of elimination will be the elimination of \textit{P. vivax} malaria, as was the case for most countries that have already achieved elimination.

---

**Figure 1:** Categorisation of countries as malaria free, eliminating malaria, or controlling malaria, 2010

Source: adapted from reference 2 with permission from authors and publisher.

**Figure 2:** Factors that determine technical feasibility of elimination

Source: adapted from reference 3 with permission from authors and publisher.

**Figure 2:** Factors that determine technical feasibility of elimination

Source: adapted from reference 3 with permission from authors and publisher.
This reality and other challenges have sparked a renewed interest in *P. vivax*.56,57

The table lists the 32 malaria-eliminating countries, with their socioeconomic and other defining characteristics. Generally, small countries with few people will find elimination easier than will large countries with large populations, although this association will not necessarily be the case if the small countries are also poor.28 of the malaria-eliminating countries are middle-income or high-income countries, in which the gross national income is greater than US$975 per head per year.58 The remaining four countries (Kyrgyzstan, North Korea, Tajikistan, and Uzbekistan) will find the task of elimination much more challenging.

Life expectancy at birth is a good indicator of a country’s overall health. Life expectancy in malaria-eliminating countries ranges from 48 years in Swaziland to 79 years in Costa Rica and South Korea (table).59 The countries with the lowest life expectancies are those with high child mortality, a weak health infrastructure, and a high prevalence of HIV/AIDS. Such countries have tough decisions to make about resource allocation amidst competing disease priorities.

An important issue for many countries embarking on elimination is whether they are eligible for grants from the Global Fund to Fight AIDS, Tuberculosis and Malaria; the US President’s Malaria Initiative; or the World Bank’s International Development Association.22 of the malaria-eliminating countries are Global Fund eligible and ten are not (table). The countries that are not eligible are upper-middle-income countries or high-income countries and should therefore be able to finance malaria elimination with their domestic resources. The President’s Malaria Initiative concentrates on malaria control in 15 high-burden African countries60 and also provides support to São Tomé and Príncipe. Eligibility for funding from the International Development Association is, with some exceptions for very small countries, based on gross national income per head. 11 of 32 malaria-eliminating countries are eligible for funding from the International Development Association (table) and are therefore receiving, or can receive, highly concessional loans for malaria elimination.

Another key variable is the present total health expenditure per head per year. If this amount is small, malaria elimination can constitute a substantial (and possibly unjustifiable) proportion of all funds available for health. If the total health expenditure is large, malaria elimination can be financed without interfering with other health priorities or the health sector as a whole. Total health expenditures per head per year of malaria-eliminating countries varies from $14 to $1168 (table).61 The economics and financing of elimination is discussed in greater detail in the fourth paper of this Series.21

The proportion of all private health-care expenditure (typically paid for out-of-pocket) in malaria-eliminating countries ranges from 8% to 78%. For countries in which this proportion is high, it will be especially necessary to enlist non-governmental health-care providers in the task of malaria elimination.7 Additionally, the development of social health insurance and other risk-pooling mechanisms will greatly improve the financial feasibility of malaria elimination.62–64

---

Figure 3: Categorisation of countries according to whether human malaria is predominantly caused by *Plasmodium falciparum*, *Plasmodium vivax*, or both *P. falciparum* and *P. vivax*, 2010

Source: adapted from reference 3 with permission from authors and publisher.
Comparison of past and present malaria-eliminating countries

Countries that have successfully eliminated malaria tend to be wealthier than those that are seeking to eliminate. This finding raises two important questions. When they were in the process of eliminating malaria, were the countries that have achieved elimination wealthier than the countries that are currently trying to eliminate? And, at the time, did they have stronger health-care systems than malaria-eliminating countries do at present?

We reviewed the economic situation in the 32 present malaria-eliminating countries and in 99 countries that attempted elimination since 1948. Webappendix p 12 shows methods, data sources, and analysis.

<table>
<thead>
<tr>
<th>Population (millions)</th>
<th>Life expectancy at birth (years)</th>
<th>GNI per head (US$)*</th>
<th>Health expenditure per head (US$)*</th>
<th>Private health expenditure (% of total health expenditure)</th>
<th>GFATM R10† malaria eligibility (Y/N)</th>
<th>PMI selected (Y/N)</th>
<th>World Bank IDA eligible (Y/N)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low-income economies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kyrgyzstan</td>
<td>5.2</td>
<td>66</td>
<td>740</td>
<td>35</td>
<td>57</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>North Korea</td>
<td>23.8</td>
<td>66</td>
<td>14</td>
<td>14</td>
<td>14</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Tajikistan</td>
<td>6.8</td>
<td>67</td>
<td>600</td>
<td>21</td>
<td>77</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Uzbekistan</td>
<td>27.3</td>
<td>68</td>
<td>910</td>
<td>30</td>
<td>49</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td><strong>Lower-middle-income economies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Azerbaijan</td>
<td>8.6</td>
<td>68</td>
<td>3830</td>
<td>102</td>
<td>73</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Bhutan</td>
<td>0.7</td>
<td>63</td>
<td>1900</td>
<td>49</td>
<td>27</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Cape Verde</td>
<td>0.5</td>
<td>70</td>
<td>3130</td>
<td>112</td>
<td>21</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>China</td>
<td>124.6</td>
<td>74</td>
<td>2940</td>
<td>94</td>
<td>59</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>El Salvador</td>
<td>6.1</td>
<td>72</td>
<td>3480</td>
<td>181</td>
<td>38</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Georgia</td>
<td>4.3</td>
<td>72</td>
<td>2470</td>
<td>147</td>
<td>78</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Iran</td>
<td>17.9</td>
<td>72</td>
<td>3540</td>
<td>215</td>
<td>49</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Iraq</td>
<td>5.0</td>
<td>66</td>
<td>1810</td>
<td>117</td>
<td>61</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Paraguay</td>
<td>6.2</td>
<td>74</td>
<td>2180</td>
<td>117</td>
<td>61</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Philippines</td>
<td>90.3</td>
<td>71</td>
<td>1890</td>
<td>52</td>
<td>67</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>São Tomé and Príncipe</td>
<td>0.1</td>
<td>61</td>
<td>1020</td>
<td>49</td>
<td>25</td>
<td>Y</td>
<td>Y††</td>
</tr>
<tr>
<td>Solomon Islands</td>
<td>0.5</td>
<td>67</td>
<td>1180</td>
<td>44</td>
<td>8</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Sri Lanka</td>
<td>20.1</td>
<td>71</td>
<td>1780</td>
<td>62</td>
<td>52</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Swaziland</td>
<td>1.1</td>
<td>48</td>
<td>2520</td>
<td>155</td>
<td>34</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Vanuatu</td>
<td>0.2</td>
<td>69</td>
<td>2330</td>
<td>67</td>
<td>35</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td><strong>Upper-middle-income economies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Algeria</td>
<td>34.3</td>
<td>71</td>
<td>4260</td>
<td>148</td>
<td>18</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Argentina</td>
<td>39.8</td>
<td>75</td>
<td>7200</td>
<td>551</td>
<td>54</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Botswana</td>
<td>1.9</td>
<td>56</td>
<td>6470</td>
<td>379</td>
<td>23</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Costa Rica</td>
<td>4.5</td>
<td>79</td>
<td>6060</td>
<td>402</td>
<td>31</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>9.9</td>
<td>72</td>
<td>4390</td>
<td>206</td>
<td>63</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Malaysia</td>
<td>27.0</td>
<td>72</td>
<td>6970</td>
<td>259</td>
<td>55</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Mexico</td>
<td>106.3</td>
<td>76</td>
<td>9980</td>
<td>527</td>
<td>55</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Namibia</td>
<td>2.1</td>
<td>59</td>
<td>4200</td>
<td>281</td>
<td>33</td>
<td>Y</td>
<td>N</td>
</tr>
<tr>
<td>Panama</td>
<td>3.4</td>
<td>76</td>
<td>6180</td>
<td>380</td>
<td>31</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>South Africa</td>
<td>48.6</td>
<td>54</td>
<td>5820</td>
<td>425</td>
<td>62</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>Turkey</td>
<td>73.9</td>
<td>73</td>
<td>9340</td>
<td>352</td>
<td>27</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td><strong>High-income economies</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Saudi Arabia</td>
<td>24.6</td>
<td>71</td>
<td>15590</td>
<td>492</td>
<td>23</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td>South Korea</td>
<td>48.6</td>
<td>79</td>
<td>21590</td>
<td>1168</td>
<td>44</td>
<td>N</td>
<td>N</td>
</tr>
<tr>
<td><strong>Total population</strong></td>
<td>2053.9</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Atlas method (US dollars): the Atlas conversion factor is used by the World Bank to facilitate cross-country comparisons of national income and health expenditure. The method uses the 3-year average of the local currency exchange rate to US dollars, adjusting for inflation. †R10 refers to applicant eligibility for Round 10 in 2010. ‡São Tomé and Príncipe is not among the PMI 15 focus countries but is receiving support from the governments of Brazil and the USA for its elimination programme. Adapted from reference 2 and reproduced with permission of the authors.

Table: Demographic, economic, health, and aid characteristics of the 32 malaria-eliminating countries
Achieving elimination

A conducive environment, including political, social, financial, operational, and technical factors, is imperative for successful elimination. As history has taught us, a universal approach is ineffective, and each country or region pursuing elimination should thoroughly assess their situation and develop a strategy for elimination and prevention of reintroduction. The second paper in this Series outlines the details of technical considerations, the third paper presents operational considerations, and the fourth paper discusses financial considerations.

Most of the activity that a malaria programme must take on to achieve elimination is similar to the activities needed to maintain controlled low-endemic malaria, and should already be well established before the launch of an elimination effort. High coverage with appropriate vector control interventions, and with diagnostic and case management services should be established and maintained. Data collection should be well designed and rigorously undertaken, and a high standard of programme management is essential. As elimination approaches, these activities should continue, but will become more focal as the heterogeneity of malaria transmission increases.

Elimination needs a relentless focus on surveillance and response, and especially on the identification and rapid elimination of foci of all infections, both symptomatic and asymptomatic. In the third paper in this Series, Moonen and colleagues review the specific operational requirements for elimination programmes. In addition to the need for sophisticated surveillance and response systems, they detail the onerous requirements for active case detection at borders, screening of high-risk migrants, and implementation of cross-border and regional initiatives. To support these activities at the necessary level of sensitivity, improved laboratory facilities, including capacity to undertake PCR testing, genotyping, and serology, are needed.

A further elimination-specific intervention is mass drug administration or some form of mass or focused screening and treatment. Although experience of these techniques in some parts of the world has been discouraging, several countries, including China and Vanuatu, have successfully used mass drug administration. A comprehensive review of country experience with mass drug administration, screening, and treatment is urgently needed, with a particular focus on Asia. An improved understanding of past and present practice and results from such reviews will help in the development of appropriate recommendations to malaria-eliminating countries for the suitability and timing of these interventions, and for which techniques and combinations of drugs are most effective.

Challenges of elimination

The specific challenges in elimination of malaria vary substantially between countries and regions and, although common agendas exist, some countries and regions need unique solutions. The long-term research agenda, as defined by MalERA, will enable the development of new generations of diagnostics, drugs, vaccines, and insecticides during the next decades. For the 32 malaria-eliminating countries, most of these new interventions will come too late to assist their elimination efforts, although they will be helpful in the long term for prevention of reintroduction. The research agenda that is especially relevant to countries trying to eliminate malaria consists of short-term operational research to improve the effectiveness of present antimalarial interventions. The Malaria Elimination Group, the Asia Pacific Malaria Elimination Network, and the Southern African Malaria Elimination Research Group, along with other...
organisations, are stimulating and supporting applied research of this type.7,10,73

For countries in Latin America, the Middle East, and the Asia Pacific region that are trying to eliminate malaria, elimination of \textit{P vivax} poses particular challenges that require constant emphasis and attention. The pressing challenges in the fight against \textit{P vivax} malaria include the dormant hypnozoite stage; the unavailability of a quick, point-of-care glucose-6-phosphate dehydrogenase test for those at risk of haemolysis if treated with primaquine (the only available drug); and the limitations of primaquine.10,74,75

**Risks of elimination**

Risks of malaria elimination exist both globally and nationally. Globally, concern focuses mainly on issues of finance and resistance. Some are concerned that too much emphasis on or investment into elimination will take funds away from the important and life-saving goal to reduce malaria morbidity and mortality in high-burden countries.10,76 We agree fully that shifting investments from part one of the three-part strategy, aggressive control in highly endemic countries, to part two, shrinking the malaria map, would not be justified, especially in view of the high returns on investment achieved by the prevention of severe illness and deaths from malaria, particularly in children and pregnant women. At present, only 8% of all commitments to malaria made by the Global Fund are directed towards the 32 malaria-eliminating countries.77

For the other major international funder of malaria, the President’s Malaria Initiative, this figure is close to zero. Clearly, only a small amount of international finance is allocated to elimination. Any increased focus on or investment into elimination will take funds away from the important and life-saving goal of adults living in previously or currently malaria-endemic regions. However, outbreaks with high adult mortality are rare, perhaps because in low-transmission areas specific immune responses can be maintained for many years after a malaria infection.78 More information is needed about whether there are levels of controlled low-endemic malaria below which effective antimalarial immunity is not preserved, and about the length of time after exposure to malaria infection before immunity is lost completely.

**Benefits of elimination**

Although the benefits of controlling malaria are well documented and understood,74 the benefits of eliminating malaria are understood to a lesser extent, are difficult to quantify, and need further research. Many differences between the benefits of elimination and controlled low-endemic malaria will be negligible. Development of a standardised set of indicators to help a country measure and monitor the benefits of elimination will help to gain and sustain political commitment and community engagement, and guide countries and donors in their decision making and long-term strategic planning processes. The fourth paper of this Series discusses the economic and social benefits that a country might expect to gain from elimination.

From an operational perspective, a benefit that will differ noticeably between maintenance of controlled low-endemic malaria and elimination is the system for detecting, reporting, and responding to any imported cases and potential outbreaks. For elimination to succeed, this system will need to be robust, private and public sector providers will need to work together, and the health system will need to be well managed.20

Concerns about artemisinin resistance in the Greater Mekong subregion—the traditional epicentre of antimalarial resistance—are growing.74,76 Modelling suggests that the elimination of \textit{P falciparum} from this subregion is needed to prevent the spread of artemisinin-resistant parasites.81 Such efforts are a global public good and essential to the entire fight against malaria.

3330 years ago, King Tutankhamun died, possibly from malaria.83 Egypt only recently eliminated malaria.84 One cannot overlook the benefits of national pride after a country’s health sector successfully eliminates a disease that has killed its people and blighted its economy for thousands of years.

With the appropriate levels of documentation and assessment, every country’s elimination experience benefits all countries remaining endemic. Countries attempting to eliminate malaria use a wide range of techniques in areas such as surveillance, mass drug administration, and cross-border collaboration. The documentation, assessment, and dissemination of these experiences will inform other countries that will face similar challenges.85

The regional benefits and positive externalities85 of malaria elimination are substantial. If a country
eliminates malaria, its neighbours are assisted in very definite ways. Importation of malaria cases from the country that eliminated malaria to its neighbouring countries will end. Cross-border collaboration will have already been established to allow the country to achieve elimination, and this collaboration might bring many benefits to the health sector and other sectors. Thus, the elimination of malaria from Botswana, Namibia, South Africa, and Swaziland, is of tangible benefit to their four northern neighbours, Angola, Mozambique, Zambia, and Zimbabwe. This regional public good needs to be factored into calculations about the benefits of investment in malaria elimination. Such benefits suggest that regional bodies, such as the Southern African Development Community, should continue supporting malaria elimination. Panel 2 details several multicountry elimination efforts.

Spatially progressive elimination during the past century has brought tangible benefits to millions of people, and has allowed many countries to take up the elimination challenge as their neighbouring countries have completed the task. Shrinking the malaria map steadily increases the focus of international investments and attention on a decreasing number of countries that are fighting malaria, and brings us closer to the last battles against residual malaria in lowland, high rainfall, and tropical parts of Africa. Malaria elimination is unquestionably a high-value global public good that deserves international investment.

Future strategies
When planning the elimination agenda for the next decade, the first point to emphasise is that efforts directed at shrinking the malaria map should in no way detract from control in highly endemic countries or the development of new interventions and delivery methods. However, greater attention to shrinking the malaria map is crucial for global malaria eradication.

Gaining international consensus on the circumstances under which a country can regard itself as a malaria-eliminating country, and be regarded as such by the international community, would assist the clarity and focus of international efforts. We hope that this paper will contribute to clarification of a reasonable set of criteria for determination of the categorisation of a country as malaria eliminating, and that the evidence presented in this Series will lend support to countries that are striving to eliminate the disease. Enabling the development of an international consensus on elimination is clearly the role of WHO, and the process should be supported by other partners and stakeholders.

The first comprehensive elimination feasibility assessment that included a qualitative and quantitative approach was recently done in Zanzibar. Continued development of such feasibility assessment so that it can be applied in a user-friendly way by national malaria programme leaders would be of great assistance to countries that are contemplating elimination, but do not yet have the evidence base to build a fully informed strategy. This work is being taken forward jointly by, among other organisations, WHO; the Global Health

Panel 2: Multicountry elimination efforts
Multicountry approaches to elimination can be incredibly useful to countries considering or embarking on elimination. Collaborative efforts have many benefits, including increased joint political support, advocacy and global awareness, alignment of strategies, collaboration on control and prevention activities, and learning from each other’s successes and challenges. Collaboration between malaria-endemic neighbours will be especially important for countries that share borders, but it also applies to island countries. Several examples of collaborative efforts are described below.

Asia Pacific Malaria Elimination Network (APMEN)
Countries: Bhutan, China, Indonesia, Malaysia, North Korea, Philippines, Solomon Islands, South Korea, Sri Lanka, Vanuatu.
APMEN comprises ten countries from the Asia Pacific region that are aiming for elimination on a national or substantial subnational scale, together with the southeast Asian and western Pacific regional offices of WHO and regional partners. APMEN supports elimination within the region through research, collaboration, and knowledge exchange, with a particular focus on Plasmodium vivax malaria. APMEN is supported by the Australian Government and has its secretariat in Brisbane and San Francisco. It has held two meetings, one in Brisbane, Australia (in 2009) and one in Kandy, Sri Lanka (in 2010), and has launched fellowship and research grant programmes.

Elimination Eight (E8) Regional Initiative
Front-line countries: Botswana, Namibia, South Africa, Swaziland.
The E8 is a regional initiative in southern Africa comprised of four front-line malaria-eliminating countries, which have collectively set a goal of elimination by 2015, together with their northern neighbours, the four second-line countries. The E8 have pledged to work together to eliminate malaria through a spatially progressive approach by achieving elimination in the front-line four and, subsequently, in the second-line four. For elimination in southern Africa to succeed, close collaboration between all of the eight countries is crucial. An inaugural meeting of the E8 was held in Windhoek, Namibia in 2009.

The Tashkent Declaration
Countries: Armenia, Azerbaijan, Georgia, Kazakhstan, Kyrgyzstan, Tajikistan, Turkey, Turkmenistan, Uzbekistan.
The Tashkent Declaration is a commitment to action signed by the ministers of health from nine countries, which reaffirms previous commitments to scale up the response with the goal of elimination by 2015. These nine countries, with the support of the WHO Regional Office, have been successful in developing strategies for elimination. Armenia, Kazakhstan, and Turkmenistan have achieved elimination and are making efforts to prevent reintroduction. The remaining endemic countries in this region have very low levels of transmission and, with continued collaborative efforts, are also on the path to elimination.

Saudi-Yemeni Partnership in Combating Malaria
Countries: Saudi Arabia, Yemen.
In 2001, a partnership to combat malaria between Saudi Arabia and Yemen began with the goal to free the Arabian Peninsula from malaria by 2020. With most of the endemic transmission occurring along the border between the two countries, the partnership provides an opportunity for Saudi Arabia to prevent imported malaria cases and for Yemen to reduce its burden of disease due to malaria, and, ultimately, to eliminate malaria on the peninsula.
Group at the University of California, San Francisco; and the Clinton Health Access Initiative.

Comprehensive documentation of experiences with past and present elimination efforts has shown great value in providing lessons for malaria-eliminating countries. Country-specific case studies are completed or are being prepared for Bhutan, Mauritius, Morocco, and Sri Lanka, while more focused studies of specific aspects of elimination programmes are underway in Botswana, China, Namibia, Philippines, Solomon Islands, Swaziland, Vanuatu, and Zanzibar.

The fourth paper in this Series presents what is known about the financial and economic aspects of elimination; however, not much is known. The first priority is to gain a better understanding of the costs of elimination and of preventing reintroduction, by comparison with the costs of the maintenance of controlled low-endemic malaria. A detailed assessment and quantification of the benefits of elimination to a country, a region, and the world, would also be very helpful.

Previous interventions have allowed 79 countries to eliminate malaria since 1945. Present interventions are allowing for steady, and in some cases rapid, progress towards elimination in the 32 malaria-eliminating countries. Improved evidence and guidance about the most effective use of interventions in an elimination setting would be very valuable. For example, when and how should indoor residual spraying be partially withdrawn or made more focal when infection rates are low and when transmission is highly localised? What is the appropriate role of mass drug administration in both the early and late stages of an elimination programme?

Current interventions are good, but they are not good enough. Although MalERA sets out a long-term agenda for research to assist the next generation of malaria-eliminating countries, we urgently need new and improved interventions that can be applied soon, to assist malaria-eliminating countries. Specifically, we now need three technologies for the diagnosis and treatment of P. vivax: an improved rapid diagnostic test with greater specificity and sensitivity for P. vivax; an improved test for glucose-6-phosphate dehydrogenase deficiency that can be used accurately in non-laboratory settings; and a treatment for P. vivax that is better and safer than primaquine.

A pervasive assumption exists that, when it comes to malaria control and elimination, governments have to do everything; they have to employ all staff, procure all products, and deliver all services. This is an unnecessary shouldering of a heavy burden. Every country has willing and competent non-governmental partners whose help should be harnessed through effective collaborations. For example, the mining industries, faith-based organisations, and other groups have been active in many malaria programmes and could do much more.

With immunisation, the maintenance of an expensive public health intervention in the absence of disease is commonplace and thought to be a cost-effective investment. However, experience in malaria shows that when the disease falls to low rates and is no longer an obvious threat, political leadership, support, and investment diminish and interventions are often discontinued. New approaches are needed to maintain the necessary political commitment, community engagement, and investment to eliminate malaria and prevent its reintroduction. Some countries, such as Singapore, have achieved this aim by responding to malaria through a broader capacity for other vector-borne diseases, especially dengue fever. In 2009, Sri Lanka had 428 cases of malaria and no malaria deaths. In the same year, it had 35 000 cases of dengue fever and 360 deaths. Joining forces with efforts to control dengue fever, which kills wealthy and influential people in urban areas, can help to maintain political commitment and investment for both diseases. Integrated vector-borne disease control efforts need to be documented and widely disseminated.

The average yearly growth rate of GDP per head in the 32 malaria-eliminating countries from 1998 to 2008 was 3.3%; during this period, the GDP per head fell in only three of these countries. This per head growth is causing landscapes, work patterns, and housing styles to change. These changes tend to reduce a country’s receptivity to malaria. For example, a study in northeastern South Africa showed that higher incomes and modern house construction were strongly associated with a lower risk of malaria. Better data are needed for the effect of economic growth on malaria.

Conclusion
Deliberate shrinking of the malaria map started over 150 years ago and countries have continued to make remarkable progress since. As history has taught us, a decision to pursue elimination needs thoughtful consideration of the many challenges, risks, and benefits, and planning for the prevention of reintroduction. With 32 countries working towards elimination, appropriate recognition and support for their efforts is crucial. This Series seeks to initiate a process of developing evidence that will support and inform their efforts, and draws attention to the gaps in knowledge that need to be filled to realise the vision of a malaria-free world.

Contributors
All authors participated in the development of the ideas for this paper. The text was drafted by RGAF, AAP, JH, and CC, with contributions from all other authors. RWS helped shape the key messages. Data analysis was done mainly by CC and BW. All authors took part in the review, preparation, and final approval of the paper.

Conflicts of interest
RGAF, CC, and AAP, work at the Global Health Group of the University of California, San Francisco, CA, USA. The Global Health Group exists in part to support countries that are embarked on an evidence-based pathway towards elimination. BRA, TAG, and MHR play leading roles in the malaria elimination programmes of Sri Lanka, Ethiopia, and Mexico, respectively. OS leads the malaria programme at the Clinton Health Access Initiative which actively supports malaria elimination in southern Africa.

Published online October 29, 2010 DOI:10.1016/S0140-6736(10)61270-6
Africa. RGA, AAP, BMG, OS, MHR, RRA, and RWS serve as members of the Malaria Elimination Group. RWS has received funding from Novartis for chairing meetings of national control programmes in Africa and has received a research grant from Pfizer. The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of their employing organisations nor of the sources of funding.

Acknowledgments
The work of the Global Health Group on malaria elimination is supported by grants from the Bill & Melinda Gates Foundation and ExxonMobil. RWS is a Wellcome Trust Principal Research Fellow (#078925) and has received a research grant from Pfizer. The findings and conclusions in this paper are those of the authors and do not necessarily represent the views of their employing organisations nor of the sources of funding.

For more on the Malaria Elimination Group see http://www.malariaelimination.org/


44 Andrews JM. Malaria Eradication in the US. In: Sixth International Congress on Tropical Medicine and Malaria. Lisbon, Portugal: Instituto de Medicina Tropical, 1959: 652–64.


