

# Malaria burden and control in Bangladesh and prospects for elimination: an epidemiological and economic assessment



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## Summary

**Background** Malaria is endemic in 13 of 64 districts in Bangladesh. About 14 million people are at risk. Some evidence suggests that the prevalence of malaria in Bangladesh has decreased since the the Global Fund to Fight AIDS, Tuberculosis and Malaria started to support the National Malaria Control Program (NMCP) in 2007. We did an epidemiological and economic assessment of malaria control in Bangladesh.

**Methods** We obtained annually reported, district-level aggregated malaria case data and information about disbursed funds from the NMCP. We used a Poisson regression model to examine the associations between total malaria, severe malaria, malaria-attributable mortality, and insecticide-treated net coverage. We identified and mapped malaria hotspots using the Getis-Ord  $G_i^*$  statistic. We estimated the cost-effectiveness of the NMCP by estimating the cost per confirmed case, cost per treated case, and cost per person of insecticide-treated net coverage.

**Findings** During the study period (from Jan 1, 2008, to Dec 31, 2012) there were 285 731 confirmed malaria cases. Malaria decreased from 6·2 cases per 1000 population in 2008, to 2·1 cases per 1000 population in 2012. Prevalence of all malaria decreased by 65% (95% CI 65–66), severe malaria decreased by 79% (78–80), and malaria-associated mortality decreased by 91% (83–95). By 2012, there was one insecticide-treated net for every 2·6 individuals (SD 0·20). Districts with more than 0·5 insecticide-treated nets per person had a decrease in prevalence of 21% (95% CI 19–23) for all malaria, 25% (17–32) for severe malaria, and 76% (35–91) for malaria-associated mortality among all age groups. Malaria hotspots remained in the highly endemic districts in the Chittagong Hill Tracts. The cost per diagnosed case was US\$0·39 (SD 0·02) and per treated case was \$0·51 (0·27); \$0·05 (0·04) was invested per person per year for health education and \$0·68 (0·30) was spent per person per year for insecticide-treated net coverage.

**Interpretation** Malaria elimination is an achievable prospect in Bangladesh and failure to push for elimination nearly ensures a resurgence of disease. Consistent financing is needed to avoid resurgence and maintain elimination goals.

**Funding** None.

## Introduction

Bangladesh has a history of endemic malaria transmission in 13 of 64 districts. Up to 70 000 laboratory-confirmed and 900 000 clinical cases (appendix p 1), with more than 500 deaths per year, were reported in the late 1990s.<sup>1–3</sup> Unreported cases might have been as high as 250 000 each year.<sup>4</sup> A cross-sectional survey in 2007 reported a crude prevalence of 4% in the 13 malaria-endemic districts.<sup>5</sup> More than 90% of cases were *Plasmodium falciparum*.<sup>5</sup> The highest prevalence (>10%) was identified in three districts of the Chittagong Hill Tracts in southeastern Bangladesh.<sup>5</sup>

The Global Fund to fight AIDS, Tuberculosis and Malaria (Global Fund) approved funds in 2006<sup>4</sup> (Round 6) and 2009<sup>6</sup> (Round 9) to support the Bangladesh National Malaria Control Program (NMCP). The NMCP was implemented by the Bangladesh Ministry of Health with BRAC (a national non-governmental development organisation). The goals were to: (1) reduce malaria morbidity and mortality; (2) provide community-based services that increased access to diagnosis and treatment with artemisinin-based combination therapies in hard-to-reach regions; (3) provide longlasting insecticidal nets

(LLINs) to 100% of households in the three malaria-endemic districts with the highest malaria burden and 80% coverage in the other ten malaria-endemic districts; (4) strengthen the malaria epidemiological surveillance system; (5) strengthen partnerships in malaria control; and (6) provide periodic (every 3 years) treatment of non-LLIN with suitable insecticides.<sup>4,6</sup>

These interventions started in late 2007, and were fully implemented in the 13 malaria-endemic districts in 2008. There has been a general reduction in malaria cases, presumably through high coverage of and increased use of insecticide-treated nets, increased use of rapid diagnostic tests and antimalarial treatments, and a high number of community health workers and health facilities.<sup>7–9</sup> The interventions have also reached marginalised populations.<sup>8</sup> Bangladesh is moving from control to elimination in parts of the country, but evidence in favour of these actions has been more descriptive than quantitative so a robust cost-benefit analysis is crucial. Cost-effectiveness analysis is needed to maintain sustainable control programmes and assess the future needs for malaria elimination.

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See Online for appendix

Malaria elimination also has substantial indirect benefits and economic attractiveness.<sup>10,11</sup> A systematic assessment of the effect of the programme has not been done in Bangladesh. Both donors and policy makers should have information about the costs and benefits of interventions. To address this gap, we did an epidemiological and economic analysis using the country's number of malaria episodes, total costs of the programme, and disbursed funds from 2008 to 2012 in the 13 malaria-endemic districts. We compared international donor assistance to control malaria in Bangladesh with other malaria-endemic countries.

## Methods

### Study area

The population of Bangladesh is about 150 million; 14 million people live in the 13 malaria-endemic districts.<sup>12</sup> Eight of these districts are in the north of Bangladesh, sharing a border with India, and five districts are in southeast Bangladesh, sharing borders with India and Myanmar (Burma).

### Data sources

The main methods of malaria surveillance in Bangladesh are passive case detection at hospitals and rapid diagnosis and treatment at the community level by community health workers. We obtained annually reported, district-level aggregated malaria case data from the NMCP. Uncomplicated malaria, severe malaria (defined by clinical and laboratory variables associated with an increased risk of death and the presence of *P falciparum* parasitaemia)<sup>13,14</sup> involving admission to hospital, and malaria-associated mortality, were confirmed by microscopy or rapid diagnostic tests done in hospitals or by community health workers. Appendix p 2 shows the malaria reporting system in Bangladesh in more detail. We obtained data for the number of LLINs distributed and nets treated (new available non-LLIN) with K-O-tab 123<sup>15</sup> (together designated

as insecticide-treated nets) annually from the NMCP. LLINs were costed at \$6.00 per net, and insecticide treatment of nets at \$0.50 per net. We took demographic data from the Bangladesh Bureau of Statistics.<sup>16</sup> Populations were projected for 2008, 2009, 2010, and 2012 using an exponential population growth model based on Bangladesh Bureau of Statistics 2001 and 2011 data.<sup>16</sup>

We obtained detailed data from the Bangladesh NMCP for funds disbursed to the NMCP from the donors (Global Fund, Bangladesh Government). Once the investments from the Global Fund arrived in Bangladesh, they were deposited in the Ministry of Health according to the US dollar rate. Inflation rates were calculated on the basis of differences between the rate at the time the funds were received and the reporting time at the end of the fiscal year. We obtained cost data in US dollars from the Bangladesh NMCP manager. All costs were cross-checked with budgets outlined in the original proposals submitted to the Global Fund and through reviews of available reports.

### Data analysis

We analysed yearly aggregated district-level age (0.0–4.0 years, 4.1–14.0 years, and >14.0 years) and sex-specific malaria data for all 13 malaria-endemic districts. We used detailed demographic data from the Bangladesh Bureau of Statistics as the denominator. We calculated the prevalence<sup>17</sup> of any malaria, severe malaria, and malaria-associated mortality per 1000 population. For all 13 districts, we calculated coverage of insecticide-treated nets per 1000 population, assuming an average net life of 3 years.<sup>18</sup> We used Poisson regression to explore the association between malaria prevalence and insecticide-treated net coverage at the district level. We used STATA (version 11) for all statistical analyses.

Yearly malaria data (total number of malaria episodes, *P falciparum*, *Plasmodium vivax*, and mixed infections) were linked with district shape files (geographic data). District-level malaria prevalence in each year and the percentage of *P falciparum*, *P vivax*, and mixed infections were mapped separately and analysed for spatial clustering using the Getis-Ord  $G_i^*$  statistic<sup>19</sup> in ArcGIS software (version 10). This statistic established whether differences between the local mean (ie, the prevalence for a district and its nearest neighbouring districts) was significantly different from the global mean (ie, the prevalence for all districts).<sup>20</sup> A significant positive Z score identified a hotspot for high prevalence and a significant negative Z score for a district identified local clustering of low prevalence.<sup>21–23</sup>

For the economic analyses, all costs were treated as capital costs (eg, transportation, human resources, training, infrastructures, institutional overhead, operational research), except costs for drugs, diagnoses, health education (information education communication or behaviour change communication), LLINs, and impregnation of nets to prevent malaria, which were treated as operating costs. The population (14 million

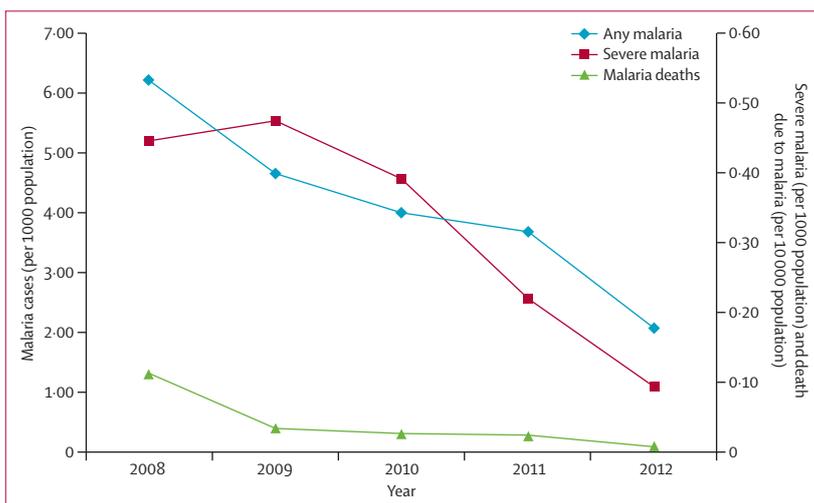


Figure 1: Prevalence of total malaria, severe malaria, and malaria mortality in Bangladesh (2008–12)

	Any malaria	Severe malaria	Malaria-associated mortality	0-0-4-0 years	4-1-14-0 years	>14-0 years	Male	Female
<b>Year</b>								
2008	1	1	1	1	1	1	1	1
2009	0.74 (0.74-0.75)	1.13 (1.08-1.17)	0.34 (0.23-0.48)	0.54 (0.52-0.55)	0.69 (0.68-0.71)	0.83 (0.82-0.84)	0.77 (0.76-0.78)	0.72 (0.71-0.73)
2010	0.65 (0.65-0.66)	0.89 (0.85-0.94)	0.34 (0.22-0.54)	0.50 (0.49-0.52)	0.63 (0.62-0.65)	0.72 (0.71-0.73)	0.70 (0.69-0.71)	0.61 (0.60-0.62)
2011	0.62 (0.62-0.63)	0.53 (0.51-0.56)	0.34 (0.21-0.54)	0.47 (0.46-0.49)	0.64 (0.63-0.66)	0.66 (0.65-0.67)	0.69 (0.68-0.70)	0.56 (0.55-0.57)
2012	0.35 (0.34-0.35)	0.21 (0.20-0.22)	0.09 (0.05-0.17)	0.23 (0.22-0.24)	0.32 (0.31-0.33)	0.40 (0.40-0.41)	0.39 (0.38-0.40)	0.30 (0.30-0.31)
<b>ITN coverage (number of nets per person)*</b>								
0.00-0.10	1	1	1	1	1	1	1	1
0.11-0.30	0.97 (0.95-0.99)	1.17 (1.09-1.26)	0.39 (0.18-0.85)	0.84 (0.77-0.91)	0.84 (0.80-0.88)	0.99 (0.96-1.02)	0.94 (0.91-0.96)	0.99 (0.96-1.03)
0.31-0.50	0.78 (0.76-0.79)	0.92 (0.84-0.99)	0.31 (0.14-0.68)	0.49 (0.45-0.53)	0.53 (0.50-0.56)	0.86 (0.83-0.88)	0.82 (0.80-0.84)	0.68 (0.65-0.70)
>0.50	0.79 (0.77-0.81)	0.75 (0.68-0.83)	0.24 (0.09-0.65)	0.48 (0.43-0.53)	0.49 (0.46-0.52)	0.93 (0.91-0.96)	0.83 (0.81-0.86)	0.68 (0.66-0.71)

ITN=insecticide-treated net. \*Average coverage for 2008-12.

**Table: Malaria prevalence rate ratio (95% CI) in Bangladesh according to year and coverage of ITN**

people) living in malaria-endemic districts of the country was used as the denominator.

For the analysis of international donor assistance to control malaria, we calculated each malaria-endemic country's total expenditures from international donors to control malaria from 2008 to 2012, and their populations living in malaria-endemic regions. We compared the total population living at risk and disbursed funds for malaria control in Bangladesh with other malaria-endemic countries.

### Role of the funding source

There was no funding source for this study. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

### Results

During the study period (from Jan 1, 2008, to Dec 31, 2012) there were 285731 confirmed malaria cases in the 13 malaria-endemic districts. There was a steep decrease in malaria from 6.2 cases per 1000 population in 2008, to 2.1 cases per 1000 population in 2012 (figure 1). Between 2008 and 2012, prevalence of all malaria decreased by 65% (95% CI 65-66), severe malaria decreased by 79% (78-80), and malaria-associated mortality decreased by 91% (83-95) (table). Malaria prevalence among male individuals was 1.3 times higher than in female individuals over the course of the study (table). Malaria prevalence decreased between 2008 and 2012 in all age groups (table), but the highest decrease was in children aged 0-4 years: 77% (95% CI 76-78; appendix p 3).

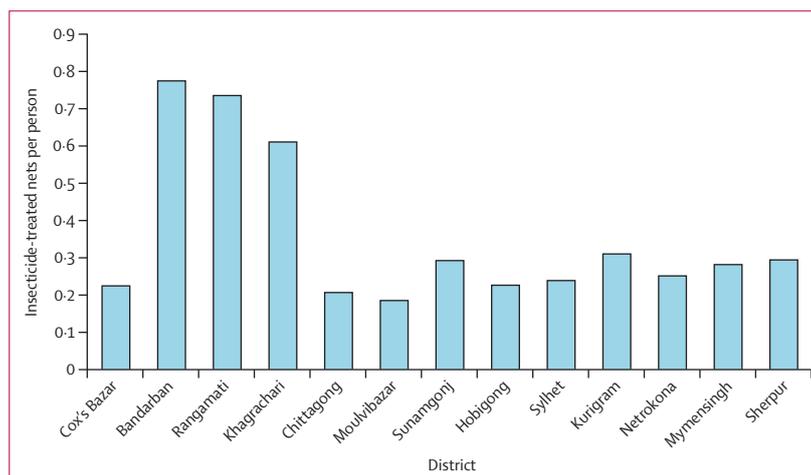
From 2008 to 2012, the Bangladesh NMCP did 2.2 million diagnostic tests for malaria (71% microscopy, 29% rapid diagnostic tests). Of 285731 tests that were positive for malaria, 56% (160715) were confirmed by rapid diagnostic test (Paracheck-Pf, Orchid, Biomedical System, Verna, Goa, India)<sup>24</sup> and 44% (125863) were confirmed by microscopy (appendix p 4). Treatments

provided by the Bangladesh NMCP for patients with malaria were artemether-lumefantrine, chloroquine, primaquine, and quinine (appendix pp 9-11).

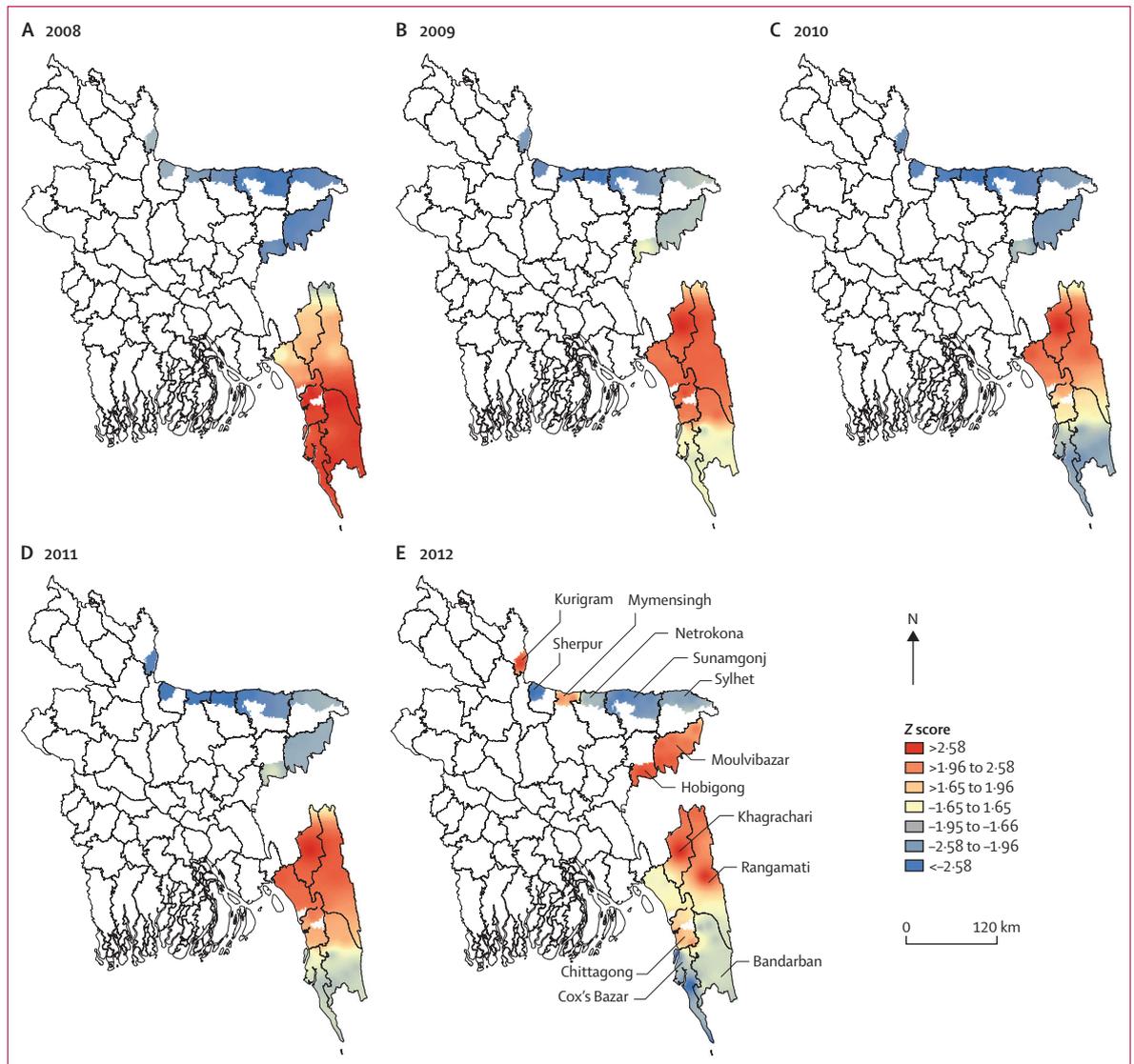
Most malaria cases were *P falciparum* (89.3%, 255 266), 10.3% (29 367) were *P vivax*, and 0.4% (1089) were mixed infections (*P falciparum* plus *P vivax*; appendix pp 5-7).

During the study period, 3.11 million new LLINs were supplied and an additional 3.77 million nets were treated with insecticide.<sup>15</sup> By 2012, there was one insecticide-treated net for every 2.6 individuals (SD 0.20) in the 13 malaria-endemic districts (figure 2).

The decrease in malaria prevalence in all age groups was associated with increased insecticide-treated net coverage (table). Districts with more than 0.5 insecticide-treated nets per person had an annual decrease in prevalence of 21% for all malaria, 25% for severe malaria, and 76% for malaria-associated mortality among all age groups (table). Coverage of more than 0.5 insecticide-treated nets per person was associated with a greater



**Figure 2: Mean number of insecticide-treated nets per person in the 13 malaria-endemic districts of Bangladesh, 2008-12**



**Figure 3:** Malaria prevalence in Bangladesh in 2008, and progress in malaria control from 2009 to 2012. For 2009–2012, red areas show the regions with the largest decreases in malaria prevalence.

annual decrease in malaria prevalence in female individuals (prevalence rate ratio 0.68; 95% CI 0.66–0.71) than in male individuals (0.83; 0.81–0.86; table).

Three districts in the Chittagong Hill Tracts and four districts in northeastern Bangladesh (Sylhet, Moulvibazar, Hobigong, and Netrokona) reported continuous malaria hotspots for *P falciparum* from 2008 to 2012; the number of cases of *P vivax* and mixed infections fluctuated in all endemic districts (appendix pp 5–7). There was a continuous reduction of malaria cases in all endemic districts in the northeast and in the Chittagong and Rangamati districts in southeast Bangladesh until 2011 (figure 3). In 2012, the number of malaria cases was reduced compared with 2008 in all five districts in the south; Kurigram and

Mymensingh in the north; and Hobigong and Moulvibazar in the northeast of Bangladesh (figure 3).

Bangladesh spent US\$39.81 million (89% from the Global Fund and 11% from the Bangladesh Government) to control malaria from 2008 to 2012. The yearly average investment per person to control malaria was \$0.41 from 2008 to 2012.

Assuming one insecticide-treated net provides cover for two individuals, the amount spent for distribution of 6.88 million insecticide-treated nets (LLINs and non-LLINs) was \$0.68 (SD 0.30) per person per year during 2008–12. During the study period, the mean cost per diagnosed malaria case was \$0.39 (SD 0.02) and the average cost per malaria case treated was \$0.51 (0.27). Bangladesh also spent an average of \$0.05 (0.04) per person yearly for health education.

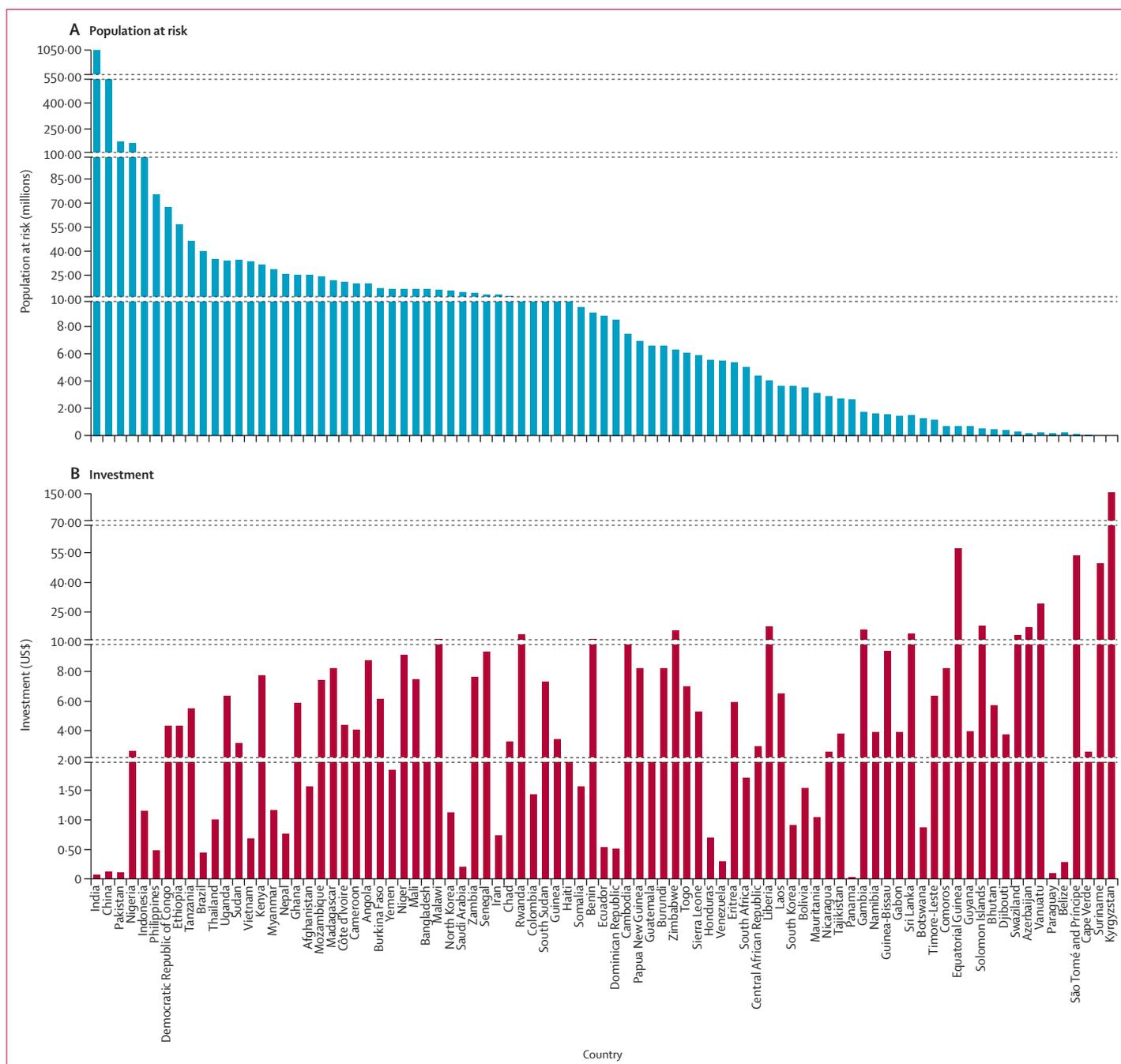


Figure 4: Mean population living at risk of malaria (2008–12) and spend per person on malaria control from international donor funds (2008–12)

From 2008 to 2012, 87 malaria-endemic countries received financial support from international donors to control malaria.<sup>25,26</sup> In terms of size of population living at risk of malaria, of 91 endemic countries, Bangladesh (14 million people living in endemic districts) ranked 29th.<sup>25,26</sup> However, Bangladesh ranked 57th in terms of amount of international funding invested (\$2.04 per person; figure 4).<sup>25,26</sup>

## Discussion

The prevalence of all malaria, severe malaria, and malaria-associated mortality decreased in Bangladesh after 5 years of interventions. The annual number of cases declined, especially in children aged 0–4 years. Bangladesh achieved high insecticide-treated net coverage and the extent of coverage was associated with the reduction in cases. Cost per diagnosis,<sup>27,28</sup> cost per

treated case,<sup>27</sup> and cost of insecticide-treated net coverage<sup>27,29–32</sup> were lower than for malaria control programmes in other countries, suggesting that the Bangladesh NMCP is cost-effective.

Despite limited funds, the Bangladesh NMCP has achieved success in reducing malaria.<sup>27,33,34</sup> Increased prevention and control measures have reduced the malaria burden in Bangladesh, although some of the decreases might have been a result of external factors.

Bangladesh provided one insecticide-treated net for every 2.6 individuals in the 13 malaria-endemic districts, higher than many other malaria-endemic countries.<sup>35–37</sup> Results of another study in the Bandarban district showed that more than 90% of individuals slept under nets during the night before the interview.<sup>38</sup> Of the nets used, about 80% were reported to be insecticide-treated and more than 95% of children younger than 5 years used an insecticide-treated net.<sup>38</sup> Since increased insecticide-treated net coverage was associated with a reduction in malaria cases in the present study, maintenance of high coverage of insecticide-treated nets will probably be crucial in future.

For diagnosis of malaria, the proportional use of rapid diagnostic tests (29%) was much lower than that of microscopy (71%; appendix p 8). However, the proportion of confirmed cases diagnosed by rapid diagnostic tests was higher (56%) than for microscopy (44%). This finding might have arisen because microscopy is mainly used in government hospitals to which most people refer for treatment but which are mainly located in urban areas where malaria-infection rates are low. Rapid diagnostic tests are mainly used by community health workers working in hard-to-reach regions in which prevalence is thought to be higher.

The lower prevalence of malaria in female individuals than male individuals might relate to the high risk of exposure in typically male occupations, such as agricultural and forestry.<sup>4,39</sup> Behavioural differences might also play a part; for example, women are generally well covered with clothing, prefer to sleep earlier (therefore spending more time under nets), and tend to sleep with their children under nets.<sup>4,38,39</sup>

After 5 years of malaria control interventions, hotspots persist in the Chittagong Hill Tracts. More intensive and targeted surveillance systems, including mapping of asymptomatic carriers, is needed.<sup>7</sup> Identification and targeting of transmission in the Chittagong Hill Tracts and Cox's Bazar district on a regular basis will be crucial to reduce the malaria burden.<sup>5,8,12,40,41</sup>

Currently, Bangladesh has elimination programmes (begun in 2012) in four districts in northeast Bangladesh. The programmes monitor annual malaria cases at the district level. Monthly malaria maps at the lowest administrative level (mauza) could further help control programmes to be more cost-effective by more accurately targeting resources.

The costs per person for diagnosis (\$0.39) and treatment (\$0.51) of malaria in Bangladesh were low compared with other countries (range \$0.88–9.54).<sup>27,28,42</sup> Bangladesh also spent a small amount of funds on health education with a radio, leaflet, and advertisement campaign. So far, artemisinin-based combination therapies (lumefantrine-artemether, artesunate; appendix pp 9–11) are highly effective for treatment of malaria in Bangladesh.<sup>43,44</sup> However, close monitoring of drug resistance is essential in Bangladesh because resistance to artemisinin-based combination therapies has been reported at the Thai–Cambodia border<sup>45</sup> and more recently at the Thai–Myanmar border.<sup>46</sup> Monitoring of the potential spread of resistance of artemisinin-based combination therapies should be a high priority in Bangladesh.

In addition to providing relatively expensive LLINs, the NMCP also supported cheaper insecticide treatment of nets,<sup>15</sup> thus Bangladesh maintained highly cost-effective insecticide-treated net coverage compared with other malaria-endemic countries.<sup>29–32</sup>

The average international donor support for malaria control worldwide to malaria-endemic countries was US\$1.86 per person per year.<sup>47</sup> The corresponding figure for Bangladesh was \$0.41 per person per year for the population living at risk of malaria, which is less than the \$0.70 per person per year given to the countries in the southeast Asian and western Pacific regions.<sup>47</sup>

The greatest threat to a successful elimination plan for Bangladesh is the border areas with Myanmar and Indian states of Assam, Tripura, Meghalaya, and Mizoram.<sup>48–54</sup> Areas adjacent the porous border are malaria endemic, largely mountainous, and composed of forest reserves. A cross-border malaria strategy with India and Myanmar is crucial to maintain the gains that have been achieved. One way could be to implement border screening and develop cross-border and regional malaria collaborations that will move Bangladesh forward in malaria elimination.

This study has a number of limitations. For example, it is known that economic development and urbanisation can be associated with reduced malaria.<sup>55</sup> It is, therefore, possible that not all improvements in the malaria situation were attributable to the control activities of the NMCP. Bangladesh has undergone substantial progress in terms of general societal development. This progress and improved access to health care in general could have contributed to a decrease in malaria prevalence irrespective of the activities of the NMCP. The number of malaria cases identified for the present study might be underestimated if substantial numbers of people acquire antimalarial drugs from vendors that do not report to the country's malaria record. The rapid diagnostic test used by the Bangladesh NMCP (Paracheck-Pf) only detects *P falciparum*, leaving *P vivax* infections (which can be detected by microscopy) undetected. False positives or

**Panel: Research in context****Systematic review**

We searched PubMed from inception to Nov 12, 2013, with the keywords "malaria" and "Bangladesh". We also searched PubMed, with the keywords "malaria India", or "malaria Assam", or "malaria Meghalaya", or "malaria Tripura", or "malaria Mizoram", or "malaria Myanmar", or "border malaria" or "malaria cost-effectiveness", or "malaria cost", or "malaria bednet", or "malaria LLIN" or "malaria ITN", or "malaria treatment". 109 articles have been reported regarding malaria research and control in Bangladesh, including about antimalarial drug resistance, epidemiology, entomology, and diagnosis. We also searched in the Global Fund website, Google, and the World Malaria Reports for 2012 and 2013. We searched all unpublished reports available from the Bangladesh National Malaria Control Program. From these searches we identified progress of malaria control, diagnosis, and treatment in Bangladesh since 2008. Although there were no precise estimates in the scientific literature, reported studies<sup>7,9</sup> suggested that the prevalence of malaria in Bangladesh had decreased since 2008.

**Interpretation**

Bangladesh is moving closer to elimination of malaria. On the basis of the reductions in malaria prevalence that we have identified, malaria elimination is an achievable prospect in Bangladesh; however, resurgence of malaria is nearly assured if control and surveillance measures are scaled back. Consistent financing will be needed to avoid resurgence and maintain elimination goals.

negatives with either microscopy or rapid diagnostic tests were not considered. Importation risk from India or Myanmar has not been considered and the cost calculations also did not take into account expired antimalarial drugs and rapid diagnostic tests or loss in the government stocks.

Malaria control in Bangladesh is mostly donor-dependent. The country has been successful in securing \$39.81 million from the Global Fund for its malaria programme from 2008 to 2012 and obtained a further \$25 million until June, 2015, from the Global Fund. However, the Bangladesh NMCP is currently underfunded relative to the size of the population living at risk of malaria, and improved funding will be crucial for elimination efforts. The present assessment will support future malaria control strategies by the Ministry of Health in Bangladesh and donors. A resurgence of malaria in Bangladesh is nearly assured if control and surveillance measures are scaled back before elimination has been achieved (panel).<sup>56,57</sup> Consistent financing, which will require a substantial change in the approach to malaria funding, is necessary to avoid resurgence. The case for elimination is already sufficiently compelling for Bangladesh. The benefits are not only local, but also international if Bangladesh can act as a buffer against the

spread of artemisinin resistance from the Mekong region to the Indian subcontinent. Furthermore, experiences from the field in countries involved in malaria control, such as Bangladesh, will also be of importance for programme design in other malaria-endemic countries.

**Contributors**

UH was responsible for the design of the study; gathering, collation, preparation, analysis, and interpretation of the data; and drafted the report. HJO, ACAC, and DEN assisted in the interpretation of results and writing the report. NI, JK, SR, MK, and WH facilitated the data and contributed to writing. GEG and DLS were responsible for study design, interpretation of results, and drafting the report.

**Conflicts of interest**

We declare that we have no conflicts of interest.

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