Articles



Malaria burden and costs of intensified control in Bhutan, 2006-14: an observational study and situation analysis



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Summary

Introduction The number of malaria cases has fallen in Bhutan in the past two decades, and the country has a goal of complete elimination of malaria by 2016. The aims of this study are to ascertain the trends and burden of malaria, the costs of intensified control activities, the main donors of funding for the control activities, and the costs of different preventive measures in the pre-elimination phase (2006–14) in Bhutan.

Methods We undertook a descriptive analysis of malaria surveillance data from 2006 to 2014, using data from the Vector-borne Disease Control Programme (VDCP) run by the Department of Public Health of Bhutan's Ministry of Health. Malaria morbidity and mortality in local Bhutanese people and foreign nationals were analysed. The cost of different control and preventive measures were calculated, and the average numbers of long-lasting insecticidal nests per person were estimated.

Findings A total of 5491 confirmed malaria cases occurred in Bhutan between 2006 and 2014. By 2013, there was an average of one long-lasting insecticidal net for every 1.51 individuals. The cost of procuring long-lasting insecticidal nets accounted for more than 90% of the total cost of prevention measures. The Global Fund to Fight AIDS, Tuberculosis and Malaria was the main international donor, accounting for more than 80% of the total funds.

Interpretation The malaria burden in Bhutan decreased significantly during the study period with high coverage of long-lasting insecticidal nets. The foreseeable challenges that require national attention to maintain a malaria-free status after elimination are importation of malaria, especially from India; continued protection of the population in endemic districts through complete coverage with long-lasting insecticidal nets and indoor residual spraying; and exploration of local funding modalities post-elimination in the event of a reduction in international funding.

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Introduction

Bhutan is one of more than 30 countries with a stated goal of malaria elimination.1 Bhutan has endorsed the goal of an Asia-Pacific region free of malaria by 2030 and is one of 18 countries pursuing this goal through membership of the Asia-Pacific Malaria Elimination Network.2 The Vectorborne Disease Control Programme (VDCP), run by the Department of Public Health of Bhutan's Ministry of Health, aims to eliminate malaria by 2016 and obtain WHO certification of elimination by 2020.3

Malaria transmission in Bhutan occurs in seven of 20 districts (figure 1). Malaria-endemic districts have a subtropical climate with hot and humid conditions and abundant rainfall during the monsoon period, which lasts up to 3 months. 4 Plasmodium falciparum and P vivax are the main malaria parasite species in Bhutan and the main vector species are Anopheles pseudowillmori and A culicifacies.3,5

A malaria eradication programme was first established in Bhutan in 1964. However, following a rapid increase in cases, Bhutan transitioned to a malaria control programme from 1971 to 1995. This increase might have been caused by a reduction in the frequency of indoor residual spraying from three times a year during 1965-74 to twice a year from 1974, the coverage of which also fell from 80% in 1973 to below 50% in 1974.6 Moreover, active case detection was initiated in 1969 and continued until 1989, meaning that a higher proportion of cases was identified, thereby increasing the number of cases recorded.7 From 1996 to 2003, Bhutan began to reinvest in malaria control activities with goals of improved access to remote and rural areas and difficult-to-reach populations, initiating cross-border prevention and increasing awareness of malaria.8 In 2004-14, control and preventive measures focused on the scale-up of control and preventive measures in high-risk areas.

The main control and preventive measure during the eradication era (1964-71) was indoor residual spraying with dichlorodiphenyltrichloroethane (DDT); however, because of reports of resistance to DDT in some areas of the world, global concern over its environmental effects and safety, and reduced public acceptance, DDT was replaced by deltamethrin (a synthetic pyrethroid) from 1995 to 1997. In 1998, insecticide-treated bednets were introduced, as a result of the Roll Back Malaria initiative, which aimed to rely on personal protection sustained by community involvement and participation.7 In 2003, focal indoor residual spraying was introduced for use

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Research in context

Evidence before this study

We searched PubMed for relevant articles using "malaria" AND "Bhutan" as search terms with no specified start date up to Feb 25, 2016, and with no language restrictions. Our search identified 22 studies, of which 14 specifically related to malaria. Two studies described malaria control in Bhutan. Both reports draw attention to importation of malaria across Indian states as a critical issue. One paper outlined Bhutan's plan to screen at border points and major construction sites with expatriate workers, to prevent importation of malaria.

Added value of this study

The study presents a detailed analysis of the trends of malaria in the pre-elimination period in Bhutan with regard to types of infection, age-specific and sex-specific burden, occupation, deaths, and the nationality of patients with malaria. It further analyses the costs associated with malaria elimination, incorporating sources of funding for scale-up of activities

leading to pre-elimination. Cost analysis studied individual control and preventive measures including long-lasting insecticidal nets, indoor residual spraying, drugs, and other commodities. Additionally, the ratio of long-lasting insecticidal net coverage per person over three mass distribution periods was presented.

Implications of all the available evidence

The risk of importation of malaria from India necessitates coordinated malaria control activities between India and Bhutan. Additionally, populations in the malaria-endemic districts will need complete coverage with long-lasting insecticidal nets and indoor residual spraying. Local funding modalities post-elimination of malaria need to be explored if a reduction in international funding occurs. Initiation of public-private partnerships in cost sharing and social marketing of long-lasting insecticidal nets is one possible way forward.

during outbreaks and emergencies and in areas of high *P falciparum* transmission with an annual parasite incidence higher than 10 per 1000 population.¹¹ In 2006, the existing preventive approach was initiated, using long-lasting insecticidal nets and two rounds of indoor residual spraying every year (figure 2).

Malaria control activities are decentralised and integrated into the general health-care system in Bhutan. Microscopic diagnostic facilities for examination of blood for malaria parasites are available to all health facilities in endemic areas. Rapid diagnostic tests are used when microscopists are not available (out of hours) or during outbreaks or emergencies when the demand for microscopy is high. Treatment for *P vivax* malaria has not changed since 1965, and remains chloroquine for 3 days and primaquine over 14 days (figure 2), whereas treatment options for *P falciparum* malaria have changed over the years, and are presently artemether—lumefantrine and quinine (figure 2).

Malaria surveillance in Bhutan is done through passive case detection and fever surveillance, which involves submitting numbers of fever cases at the end of each week to the VDCP from the field through district offices. The latter is an important ongoing surveillance method—an increase of fever cases over the weekly mean of the preceding 5 years triggers an investigation of a possible outbreak of malaria. A spatial decision support system based on geographic information systems (GIS) has been set up to help surveillance in malaria-reporting districts.⁷

This study is a situation observational analysis, defined as an assessment of the present health situation, which is fundamental to designing and updating national policies, strategies, and plans. We aimed to determine the trends and burden of malaria, the costs of intensified control

activities, the main donors of the control activities, and the costs of different preventive measures in the preelimination phase (2006–14).

Methods

Study design and data collection

We obtained nationwide data about malaria cases in Bhutan from 2006 to 2014 from the national malaria surveillance system, hosted by the VDCP. These data contained laboratory-confirmed malaria cases, which were defined as clinically diagnosed cases with either malaria parasites confirmed by microscopy or a positive rapid diagnostic test result. Since all health services in Bhutan are free of charge with good coverage and no private practices, we can assume that this dataset is complete for clinical malaria cases. Additionally, every health centre in malaria-endemic areas has dedicated malaria technicians who are able to monitor fever cases in their small catchments, thus increasing the likelihood of fever cases being tested for malaria. The infections were categorised by species: P falciparum and P vivax or mixed infections. The following patient information was extracted for each case: whether the patient was a Bhutanese citizen or a foreign national (foreign nationals were classified as non-Bhutanese citizens visiting or residing in Bhutan), age, occupation, and sex.

Historical information was obtained through searches of databases such as PubMed, MEDLINE, and Google Scholar, using the search terms "Bhutan", "malaria elimination", "long-lasting insecticidal nets", and "indoor residual spraying" between Feb 1, 2015, and March 30, 2016. Search was not restricted to published studies, but included conference presentations, abstracts, and government reports. No language restrictions were imposed.

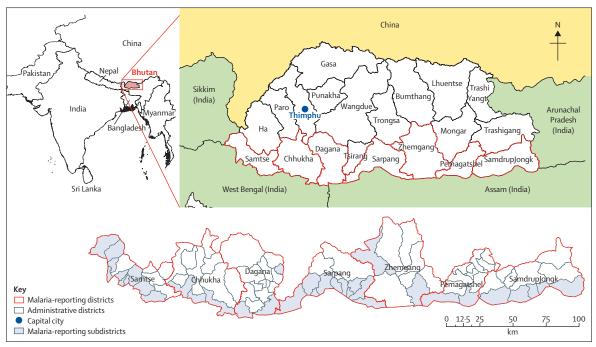


Figure 1: Map of Bhutan showing malaria-reporting districts and subdistricts

Malaria indicators

The total number of long-lasting insecticidal nets distributed from 2006 to 2014 was obtained from the VDCP. Long-lasting insecticidal nets were distributed to all the population residing in 36 subdistricts of seven districts. These subdistricts were selected based on the presence of malaria vectors. The average number of people per net was calculated for the years 2006, 2010, and 2013 (the mass distribution years) using the corresponding population of the 36 subdistricts. Population estimates used in this study were from publications from the National Statistical Bureau and the Office of the Census Commissioner of Bhutan (estimates of uncertainty regarding the population are not available). 13,14

Test positivity rate was calculated by dividing the total number of malaria cases by the number of blood slide examinations and rapid diagnostic tests used, multiplied by 100 (and expressed as a percentage). Annual malaria incidence was calculated as the annual cumulative incidence of malaria cases reported by each district divided by the total population of the districts of the same year, multiplied by 1000.

Cost analysis

Data about the funds disbursed to the VDCP from international donors (The Global Fund to Fight AIDS, Tuberculosis, and Malaria; WHO; and the Government of India), and from the Royal Government of Bhutan, were obtained from the VDCP for the 2008–14 financial years. The costs of different commodities such as drugs,

long-lasting insecticidal nets, chemicals and equipment (eg, pumps) for indoor residual spraying, microscopes, and rapid diagnostic tests, were obtained from the VDCP. All the funds were converted into US dollars (US\$) for analysis. Costs were analysed based on different preventive measures, running of programme offices, and fuel for vehicles.

Statistical analysis and ethics clearance

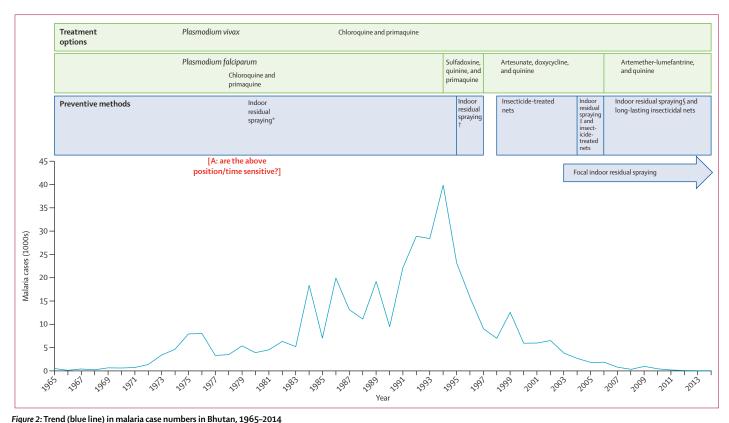
Data were extracted into Microsoft Excel and Stata 12.1 was used for statistical analysis. Permission to use the data was approved by the Ministry of Health of the Royal Government of Bhutan. Since the datasets did not contain information about individual patients, ethical clearance was not required.

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 9 years from 2006 to 2014, a total of 5491 cases of malaria were reported in Bhutan. Malaria in Bhutanese citizens accounted for 4377 cases: 80% of the total. In the Bhutanese population, the highest number of malaria cases was reported in 2006 with 1751 cases, followed by 883 cases in 2009. The lowest number of cases was 21 cases in 2014. In 2006, monoinfections with *P vivax* accounted for 895 (52%) of



*With dichlorodiphenyltrichloroethane (DDT). †With deltamethrin. ‡One round per year. §Two rounds per year.

1751 cases, followed by *P falciparum* (733 [42%]) and mixed infections (124 [7%]). In 2014, *P falciparum* infected 11 (52%) of the 21 cases, and there were no mixed infections (table 1, figure 3).

Two types of foreign national status were recorded in the malaria patient records in Bhutan. The first group of foreigners includes those staying in Bhutan on a longerterm basis, mostly Indians working in developmental projects; the second category includes Indian nationals visiting Bhutan on day visits for business and employment. Malaria in the foreign nationals residing in Bhutan accounted for 384 (7%) of the total cases (table 1). In 2006, 116 cases were reported in this group, with numbers decreasing to 21 (6%) of 384 cases in 2014. Malaria in foreign national daily visitors accounted for 730 cases (13% of the total) during the study period. The highest number of cases reported in foreign national daily visitors was in 2006 (408 cases). After this timepoint, a decreasing trend occurred, with just three cases in 2014. Most of the infections were caused by P falciparum throughout the study period, with the exception of 2013, when *P vivax* was more frequent than P falciparum. No mixed infections were reported in foreign national daily visitors since 2011. Overall, foreign nationals (both those residing in Bhutan and daily visitors) contributed more than half of all malaria cases since 2013 (table 1).

A total of 15 deaths were recorded during the study period. The highest numbers of deaths were reported in 2006 and 2009, with four (27%) deaths each. No deaths have been reported since 2013. All deaths were caused by *P falciparum* or mixed infections (table 1). Women accounted for the most deaths (ten) and there were four deaths in children. Samdrup Jongkhar district reported the highest number of deaths (five), followed by Sarpang district (three).

Malaria indicators showed that numbers of blood samples collected for testing malaria parasites decreased during the study period, as did the test positivity rate (table 1). Annual malaria incidence fell during the study period from 12·9 cases per 1000 population in 2006 to less than one case per 1000 population from 2012 to 2014 (table 1).

During the study period, 357091 new long-lasting insecticide-treated nets were distributed to residents in 36 subdistricts in endemic districts. In 2006, 93 269 were distributed, achieving an average of one long-lasting insecticidal net per 1·44 people. In 2010 and 2013, 99 697 and 99 617 long-lasting insecticidal nets were distributed, with averages of one net per 1·45 people in 2010 and one per 1·51 people in 2013. Follow-up distributions of long-lasting insecticidal nets were continued in the years between mass distributions as a mechanism to achieve universal population coverage (table 1).

	2006	2007	2008	2009	2010	2011	2012	2013	2014
Cases in the Bhutanese p	population								
Overall	1751	744	314	883	410	172	64	18	21
P falciparum	733 (42%)	274 (37%)	129 (41%)	433 (49%)	137 (33%)	83 (48%)	31 (48%)	8 (44%)	11 (52%
Pvivax	895 (52%)	384 (52%)	142 (45%)	374 (42%)	239 (58%)	78 (45%)	31 (48%)	10 (56%)	10 (48%
Mixed	124 (7%)	86 (12%)	43 (14%)	76 (9%)	34 (8%)	11 (6%)	2 (3%)	0	0
Cases in foreign nationa	als residing in Bh	utan							
Overall	116	49	16	89	26	22	18	27	21
P falciparum	39 (34%)	14 (29%)	7 (44%)	41 (46%)	3 (12%)	4 (18%)	2 (11%)	5 (19%)	3 (149
P vivax	68 (59%)	30 (61%)	7 (44%)	39 (44%)	22 (85%)	14 (64%)	16 (89%)	21 (78%)	18 (699
Mixed	9 (8%)	5 (10%)	2 (13%)	9 (10%)	1 (4%)	15 (8%)	0	1 (4%)	0
Cases in foreign nationa	als who are daily	visitors to Bhutan	1						
Overall	408	60	32	126	29	45	24	3	3
P falciparum	255 (63%)	28 (47%)	18 (56%)	99 (79%)	14 (48%)	35 (78%)	14 (58%)	1 (33%)	2 (67
P vivax	139 (42%)	26 (43%)	13 (41%)	24 (19%)	10 (35%)	10 (22%)	10 (42%)	2 (67%)	1 (33
Mixed	14 (3%)	6 (10%)	1 (3%)	3 (2%)	5 (17%)	0	0	0	0
Total deaths									
Overall	4	1	2	4	2	1	1	0	0
P falciparum	3 (75%)	0	1 (50%)	3 (75%)	0	1 (100%)	1 (100%)	0	0
Mixed	1 (25%)	1 (100%)	1 (50%)	1 (25%)	2 (100%)	0	0	0	0
Malaria indicators									
Population at risk	135 281	137 445	139 645	141879	144149	146 455	148799	151179	153 598
Long-lasting insecticidal nets	93 269	7413	9063	20 963	99 697	8942	11041	99617	7086
Long-lasting insecticidal nets per person	1-44				1.45			1.51	
Blood sample collection	66 079	51 446	47566	62 496	54617	44481	42 512	31632	30691
Malaria test positivity rate, %	2.8%	1.5%	0.7%	1.6%	0.8%	0.4%	0.2%	0.1%	0.1%
Annual malaria incidence per 1000 population	12.9	5∙4	2.2	6-2	2.8	1.2	0-4	0.1	0.1

Farmers were infected more than any other occupation group, accounting for more than half of the 961 cases in 2006 (table 2). A similar trend continued until 2012. However, since 2013, labourers have been infected more than other occupations, accounting for 29 (60%) of 48 cases in 2013 and 20 (44%) of 45 cases in 2014 (table 2). More than half of all cases in all years were in the 20–39 years age group and in men, for both types of infection (appendix pp 2–3).

The Global Fund to Fight AIDS, Tuberculosis and Malaria was the main donor supporting the Bhutan malaria programme. The highest amount was provided in the 2009–10 financial year by the Global Fund, amounting to US\$1·23 million (73%) of the total \$1·7 million. The Royal Government of Bhutan contribution was \$0·17 million (12% of the total \$1·4 million) in the 2008–09 financial year but increased to \$0·22 million (32% of the total \$0·7 million) in the 2012–13 financial year. Overall, the total funds provided to the VDCP decreased from the 2009–10 to 2012–13

financial years, but increased again in the 2013-14 financial year (table 3).

International funding was used solely for preventive and control measures, and ranged between \$0.5 million in 2006 and \$0.02 million in 2014 (appendix p 4). Most of the money was spent on the purchase of long-lasting insecticidal nets, with more than \$0.45 million (89%) of the total spent on procuring these nets in 2006. The proportion of money spent on buying drugs fell from 1.4% (\$0.07 million) in 2006 to just 0.08% (\$15.34 million) in 2014. The proportionate cost of rapid diagnostic tests increased from 7.8% (\$0.04 million of \$0.5 million) of total costs in 2006 to 29.4% (\$0.02 million of \$0.05 million) in 2007 and fell again to 16.4% (\$0.01 million) in 2008. There was a further reduction in 2009 (to 6.1%; \$0.009 million of \$0.2 million) but it increased gradually to reach 11% (\$0.002 million of \$0.02 million) in 2014. Other commodities, such as pumps for spraying chemicals for indoor residual spraying, and microscopes, were also purchased in different years (appendix p 4).

See Online for appendix

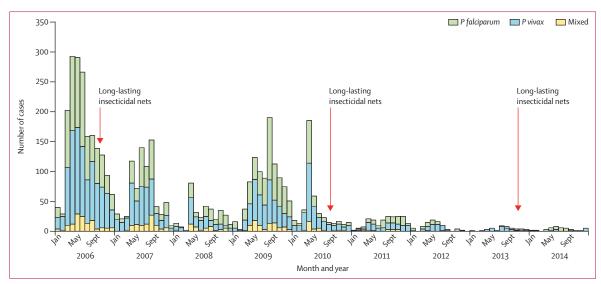


Figure 3: Changes in types of malaria infection, treatment, and preventive measures in Bhutan, 2006-14 P falciparum=Plasmodium falciparum. P vivax=Plasmodium vivax.

	2006	2007	2008	2009	2010	2011	2012	2013	2014
	(n=1973)	(n=798)	(n=322)	(n=968)	(n=424)	(n=217)	(n=99)	(n=48)	(n=45)
Business person	68 (4%)	23 (3%)	14 (4%)	27 (3%)	6 (1%)	7 (3%)	2 (2%)	3 (6%)	2 (4%)
Farmer	1143	452	158	410	201	83	28	7	12
	(58%)	(57%)	(49%)	(42%)	(47%)	(38%)	(28%)	(15%)	(27%)
Government	76	30	24	34	20	19	6	2	3
employee	(4%)	(4%)	(7%)	(4%)	(5%)	(9%)	(6%)	(4%)	(7%)
Housewife	0	0	0	119 (12%)	35 (8%)	16 (7%)	13 (13%)	1 (2%)	0
Labourer	160	77	25	69	41	22	29	29	20
	(8%)	(10%)	(8%)	(7%)	(10%)	(10%)	(29%)	(60%)	(44%)
Monk	9 (1%)	17 (2%)	4 (1%)	6 (1%)	4 (1%)	1 (1%)	0	0	0
Armed forces	177	53	30	31	17	12	2	1	1
	(7%)	(7%)	(9%)	(3%)	(4%)	(6%)	(2%)	(2%)	(2%)
Student	340	146	67	272	100	57	19	5	7
	(17%)	(18%)	(21%)	(28%)	(24%)	(26%)	(19%)	(10%)	(16%)
ata are n (%).									

Discussion

During the study period (2006–14) the number of *P falciparum* and *P vivax* malaria cases has decreased in Bhutan. This reduction corresponded with the mass distribution of long-lasting insecticidal nets and scaling up of indoor residual spraying, whereas other services such as diagnosis and treatment did not change during the study period. Cases dropped substantially following mass distribution of long-lasting insecticidal nets in 2006. However, cases resurged in 2009 and 2010, possibly because of the waning effect of the impregnated insecticide in the fibres of the nets. Reductions in malaria cases

occurred and were maintained once new long-lasting insecticidal nets were distributed in 2010 and 2013. This success could be attributed, at least in part, to robust GIS-based surveillance systems that are in place, aligning with the global and regional strategies to eliminate malaria. 15,16

This analysis suggests that the greatest threat to successful elimination efforts for Bhutan is importation of malaria, especially from India and other nearby countries. The two Indian states of Assam and West Bengal, which both border Bhutan, report the highest malaria burden in India. ^{17–21} The areas adjoining the international border in India are forested and are inhabited by indigenous people with poor access to

	2008-09	2009-10	2010-11	2011-12	2012-13	2013-14		
Royal Government of Bhutan	\$0.17 (12%)	\$0.21 (12%)	\$0.20 (26%)	\$0.26 (29%)	\$0.22 (32%)	\$0.20 (21%)		
Global Fund to Fight AIDS, Tuberculosis and Malaria	\$1.0 (73%)	\$1.23 (73%)	\$0.38 (49%)	\$0.42 (47%)	\$0.28 (40%)	\$0.60 (63%)		
Government of India	\$0.17 (12%)	\$0.19 (11%)	\$0.17 (22%)	\$0.16 (18%)	\$0.18 (26%)	\$0.14 (14%)		
WHO	\$0.04 (3%)	\$0.05 (3%)	\$0.02 (3%)	\$0.05 (6%)	\$0.02 (3%)	\$0.01 (2%)		
Total	\$1.4	\$1.7	\$0.78	\$0.9	\$0.7	\$0.95		
Data are millions of US\$ (%).								
Table 3: Funding source for various malaria control activities in Bhutan								

Indian health facilities and services. These areas are subject to ethnic violence, which can impede health services efforts.²² A strategy to address cross-border malaria with India is crucial to maintain the gains that have been achieved by Bhutan so far. Emigrants entering and staying overnight in Bhutan usually undergo blood examination for malaria parasites. However, day visitors do not undergo such a screening process, and therefore pose a substantial risk of onward transmission to the local population.²³ A potential risk of transmission of malaria across the borders by infected mosquitoes also exists, in view of the very close proximity of villages on both sides of the international border.

International donors were the major contributors to control and preventive measures, with funds spent on procuring antimalarial drugs, long-lasting insecticidal nets, indoor residual spraying, rapid diagnostic test kits, microscopes, and chemicals and pumps for indoor residual spraying. Funds from the Royal Government of Bhutan have mainly been used to pay the salaries of the officials working in the national programme, to run the offices, and for purchasing fuel for vehicles. International funding has allowed the ratio of one long-lasting insecticidal net per person to better the WHOrecommended ratio of one long-lasting insecticidal net per two people for malaria-endemic areas with low transmission.²⁴ This effort aims to interrupt local malaria transmission by mosquitoes despite a continued presence of malaria vectors and importation of parasites.²⁵ Recent prospective research has confirmed high coverage of long-lasting insecticidal nets in Bhutan with regular use.26

Bhutan received major funding from the Global Fund in grant round 4 (US\$1·3 million) and grant round 7 (US\$1·6 million) and from the Global Fund Transitional Funding Mechanism (\$0·8 million).⁷ The average international donor support worldwide to malaria-endemic countries for malaria control was less than \$1 per person per year in 2007.²⁷ The corresponding figure for Bhutan was \$2·2 per person per year, which is more than the \$0-1 per person per year for 2009.²⁸ With the decreasing burden of malaria, international support will probably wane, exerting pressure on the Royal Government of Bhutan exchequer to fund malaria elimination activities. However, to maintain universal coverage of long-lasting insecticidal nets post-elimination,

the Royal Government of Bhutan might need to consider two modalities through public–private partnership with cost sharing and social marketing of long-lasting insecticidal nets.

This study had some limitations. The cost calculations did not include the cost of expired drugs and rapid diagnostic tests, nor the cost of training malaria technicians or of quality assurance programmes. Furthermore, the cost analysis was restricted to long-lasting insecticidal nets and indoor residual spraying because no information could be obtained about other costs, such as the costs of buildings and equipment. The treatment of malaria was provided by physicians and other relevant health workers so these costs could not be included in the study because of difficulties in calculating the proportion of their time involved in providing treatments. The underlying cause of deaths from malaria could not be analysed because data were not recorded in the surveillance system.

In conclusion, the results of this study show that the malaria burden in Bhutan fell substantially during the study period, with high coverage of long-lasting insecticidal nets in the country. This study identified four foreseeable challenges that need national attention to maintain a malaria-free status in Bhutan after elimination. First, importation of malaria, especially from India, necessitates coordinated malaria control activities between Bhutan and India. Second, protection of the population in the endemic districts will necessitate complete coverage with long-lasting insecticidal nets and indoor residual spraying. Third, exploration of local funding modalities post-elimination will be needed in the event of a reduction in international funding. Last, initiation of public-private partnerships through cost sharing and social marketing of long-lasting insecticidal nets to maintain universal coverage of at-risk populations should be explored.

Contributors

KW and ACAC conceived the study. KW did data extraction, statistical analysis, interpreted the results, and drafted the report. ACAC assisted in statistical analysis and interpretation of results and was involved in the critical revision of the report. CB, MLG, GCK, and RN assisted in interpretation and revision of the report.

Declaration of interests

We declare no competing interests.

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