



## RESEARCH ARTICLE

# Estimating malaria disease burden in the Asia-Pacific [version 1; peer review: 2 approved with reservations]

Richard James Maude <sup>1-3</sup>, Chris Erwin Gran Mercado <sup>1,4</sup>, Jennifer Rowley<sup>1</sup>, Nattwut Ekapirat<sup>1</sup>, Arjen Dondorp<sup>1,2</sup>

<sup>1</sup>Mahidol-Oxford Tropical Medicine Research Unit, Faculty of Tropical Medicine, Mahidol University, Bangkok, Bangkok, 10400, Thailand

<sup>2</sup>Centre for Tropical Medicine and Global Health, Nuffield Department of Medicine, University of Oxford, Oxford, Oxfordshire, UK

<sup>3</sup>Harvard TH Chan School of Public Health, Harvard University, Boston, MA, USA

<sup>4</sup>Department of Tropical Hygiene, Faculty of Tropical Medicine, Mahidol University, Bangkok, Bangkok, 10400, Thailand

**v1** First published: 01 Apr 2019, 4:59 (<https://doi.org/10.12688/wellcomeopenres.15164.1>)

Latest published: 01 Apr 2019, 4:59 (<https://doi.org/10.12688/wellcomeopenres.15164.1>)

## Abstract

**Background:** The Asia-Pacific aims to eliminate malaria by 2030. Many of the 22 endemic countries have earlier targets. To track progress towards elimination and predict timelines and funding required it is essential to have an accurate picture of the true burden of malaria over time. Estimating this is a major challenge with most countries having incomplete data on numbers of cases and wide variation between health system access and performance. Regular estimates are published by the World Health Organization (WHO), but these are not split by species, can have a wide range of uncertainty, change over time and are not available for every year.

**Methods:** For the Asia Pacific Leaders Malaria Alliance, the burden of malaria for the 22 malaria-endemic countries in the Asia-Pacific from 2000 to 2015 was estimated by combining data submitted by countries to WHO with a systematic review to estimate the proportion of cases recorded. Due to a lack of suitable data, it was only possible to apply this method to 2013-2015. A simplified method was then derived to estimate the annual burden of *falciparum* and *vivax* malaria as inputs to a mathematical model to predict the cost of elimination, which is described elsewhere.

**Results:** The total number of estimated cases was around double the number of confirmed cases reported in the Asia Pacific with a broad range of uncertainty around these estimates due primarily to sparsity of data with which to estimate proportions of cases reported. The ranges of estimated burdens were mostly like those published for countries by WHO, with some exceptions.

**Conclusions:** The accuracy and precision of malaria burden estimates could be greatly improved by having more regular large surveys on access to healthcare in malaria-endemic areas and making subnational data on malaria incidence and reporting completeness publicly available.

## Keywords

malaria, Asia-Pacific elimination, burden, *falciparum*, *vivax*

## Open Peer Review

Reviewer Status ? ?

	Invited Reviewers	
	1	2
<b>version 1</b>		
published	report	report
01 Apr 2019		

- Fe-Esperanza-Caridad J. Espino** ,  
Research Institute for Tropical Medicine,  
Department of Health, Muntinlupa City,  
Philippines  
**Alvin Tan**, Research Institute for Tropical  
Medicine, Department of Health, Muntinlupa  
City, Philippines
- Patrick Walker**, Imperial College London,  
London, UK

Any reports and responses or comments on the article can be found at the end of the article.

This article is included in the [Mahidol Oxford](#)



[Tropical Medicine Research Unit \(MORU\)](#)  
gateway.



This article is included in the [Predicting the cost of malaria elimination in the Asia-Pacific](#) collection.

**Corresponding author:** Richard James Maude ([richard@tropmedres.ac](mailto:richard@tropmedres.ac))

**Author roles:** **Maude RJ:** Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Investigation, Methodology, Project Administration, Resources, Supervision, Visualization, Writing – Original Draft Preparation; **Mercado CEG:** Data Curation, Investigation, Writing – Review & Editing; **Rowley J:** Data Curation, Investigation, Methodology, Writing – Review & Editing; **Ekapirat N:** Data Curation, Investigation, Writing – Review & Editing; **Dondorp A:** Supervision, Writing – Review & Editing

**Competing interests:** No competing interests were disclosed.

**Grant information:** RJM was funded by the BMGF (OPP1110500), Asian Development Bank (TA-8763), Australian Department of Foreign Affairs and Trade (71215) and the Wellcome-Trust Major Overseas Programme in SE Asia (106698/Z/14/Z). CEGM was funded by Asian Development Bank (TA-8763) and the Australian Department of Foreign Affairs and Trade (71215). JR was funded by the Australian Department of Foreign Affairs and Trade (71215). NE was funded by the Australian Department of Foreign Affairs and Trade (71215). AMD was funded by the Wellcome-Trust Major Overseas Programme in SE Asia (106698).

*The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.*

**Copyright:** © 2019 Maude RJ *et al.* This is an open access article distributed under the terms of the [Creative Commons Attribution Licence](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

**How to cite this article:** Maude RJ, Mercado CEG, Rowley J *et al.* **Estimating malaria disease burden in the Asia-Pacific [version 1; peer review: 2 approved with reservations]** Wellcome Open Research 2019, 4:59 (<https://doi.org/10.12688/wellcomeopenres.15164.1>)

**First published:** 01 Apr 2019, 4:59 (<https://doi.org/10.12688/wellcomeopenres.15164.1>)

## Introduction

The Asia-Pacific aims to eliminate malaria by 2030, with individual countries having much earlier national targets for each of *P. falciparum* and *P. vivax*. For malaria elimination to succeed, it is essential to have an accurate picture of malaria incidence over time and space. However, in many countries the burden of malaria is grossly under-reported. Under-reporting of malaria incidence greatly impedes allocation of appropriate resources within governments and impairs efficient targeting of appropriate malaria control interventions. It also constrains allocation of external funding from donors (e.g. The Global Fund), which is determined predominantly by the disease burden and economic capacity of the country<sup>1,2</sup>. A complete and accurate picture of malaria incidence is essential for a country to show reliable evidence they are moving towards elimination. Additionally, harmonization of reliable and complete data between countries facilitates direct comparability of datasets across international borders. Ongoing efforts to increase this harmonisation will help underpin regional conversations about malaria elimination and greatly improve coordination between National Malaria Control Programmes (NMCPs).

There are several contributors to under-reporting of malaria. Most NMCPs routinely collect malaria incidence data from government health centres, but the extent to which data from hospitals and community health workers are included in the national dataset varies greatly<sup>3</sup>. Information on patients presenting to other health services, including non-governmental organizations (NGOs) and the private sector, as well as the military and mobile and migrant populations (both often higher risk for malaria), are also frequently omitted from the national totals and from the data reported to the World Health Organization (WHO) as many NMCPs do not have access to this information. For those facilities that do report data to the NMCP, the data itself may be incomplete due to missing reports. This may not always be apparent to the NMCP in countries where facility-level data is aggregated at the district or province level prior to collation in the national database. Finally, not all malaria cases may receive a diagnostic test, thus excluding them from the number of confirmed cases.

Several methods have been developed to estimate the true burden of malaria. Two of these are used by the World Health Organization for the annual World Malaria Report (WMR) published towards the end of each year which provides a point estimate together with a range from lower and upper estimates for total cases in each country<sup>4,5</sup>. In high-transmission countries in Africa, a geostatistical model including environmental and sociodemographic covariates is used to estimate annual cases from malaria prevalence surveys. In countries outside of Africa and low-transmission countries in Africa, the number of reported malaria cases is adjusted for completeness of reporting, the likelihood that cases were parasite-positive, and the extent of health-service use to estimate numbers of cases. This method uses data submitted annually by NMCPs and nationally representative household surveys of healthcare use, which are not done in many countries. Although widely quoted, the burden estimates by WHO are not broken down by species, can have a wide range of uncertainty, are not published for every year (e.g. 2014) and the

numbers are revised periodically. Country-level estimates have been published for 2006<sup>4</sup>, 2010<sup>6</sup>, 2012<sup>7</sup> and 2013<sup>8</sup> with revised estimates for 2000, 2005, 2010 and 2015 in 2016<sup>5</sup>. In 2017<sup>9</sup>, annual country-level estimates were published for 2010–2016. These were different to those published previously and were substantially revised with new estimates for 2010–2017 in WMR 2018<sup>10</sup>. These gaps and changes over time make it impossible to reconstruct an annual trend in estimated incidence by country since 2000 from these reports. However, annual detailed data on numbers of cases reported by each country including a breakdown by species and diagnostic method and a wealth of other information are provided in the annexes of these reports.

In 2014, the Asia Pacific Leaders Malaria Alliance (APLMA) secured agreement from the East Asia Summit Heads of Government for the Asia Pacific region to become free of malaria by 2030. Supported by the Australian government and Asian Development Bank, APLMA worked with a range of partners, including Mahidol Oxford Tropical Medicine Research Unit (MORU) in 2016 and 2017, to build an evidence base to inform decisions on malaria elimination. As part of this, MORU developed a report on the status of malaria elimination in the Asia Pacific including a survey on current sources of malaria surveillance data collected by NMCPs and the role of the private sector in malaria treatment in the Asia Pacific region<sup>3</sup>, together with estimates of the range of possible annual disease burdens in each country in 2014 and 2015. This required development of a new and transparent methodology using publicly available data. In a follow-on project for APLMA supported by Asian Development Bank, these annual estimates were then extended to cover the period 2000 to 2015. This was done in order to parameterise a mathematical and economic model to predict the cost of regional elimination and the return on investment under a range of scenarios. Details of the model and results of the economic analysis are published in other manuscripts in this collection<sup>11,12</sup>.

The methodology and results of the disease burden estimates are presented in this paper including a systematic review on treatment-seeking behaviour and comparison with WHO estimates for selected years.

## Methods

### Data analysis

Data were analysed in Excel 2016 (Microsoft, WA, USA) and GraphPad Prism 8.0.1 (GraphPad Software Inc., CA, USA) in 2016 and 2017. Three methods were used to estimate the burden of malaria, the choice of method depending on the available data in each year.

### Method 1

The true burden of clinical malaria ( $B_{\text{TRUE}}$ ) in 2013, 2014 and 2015 was estimated at country level for each of total burden, *P. falciparum* and *P. vivax* using the method described here. This combined information on malaria incidence and completeness of reporting from the WHO World Malaria Reports (WMR) 2014<sup>13</sup>, 2015<sup>8</sup> and 2016<sup>5</sup> with the sensitivity of diagnostic tests used and estimates of the proportions of patients recorded by the malaria surveillance systems in each country. The latter were

obtained from a systematic review of published reports on treatment-seeking behaviour. The burden estimates for 2015 were compared with estimates derived by WHO for the WMR 2016<sup>5</sup>. Details of the methods used by the WHO can be found in the 2008 WMR<sup>4</sup>. Briefly, for the Asia-Pacific, these use data reported by NMCPs on numbers of cases, completeness of reporting and the likelihood that cases were parasite positive and data from nationally representative surveys on the extent of health service use. It was not possible to compare estimates for 2014 with WHO estimates as no estimates were published for that year, the 2015 WMR<sup>8</sup> containing estimates from 2013.

The true burden of malaria ( $B_{TRUE}$ ) in 2013, 2014 and 2015 was estimated to derive national median, minimum and maximum estimates for each of total malaria burden, *P. falciparum* and *P. vivax* per country using the following equation:

$$B_{TRUE} = \frac{1}{P_{rec}} * \left( \frac{B_{confTOT} * P_{mic}}{S_{mic}} + \frac{B_{confTOT} * P_{RDT}}{S_{RDT}} \right) * \frac{1}{P_{comp}}$$

Where:

$P_{rec}$  = the proportion of those with malaria who are recorded in each country. As it is not possible to measure this parameter directly, as a proxy, the proportion of individuals with malaria or undiagnosed fever presenting to health facilities or community based treatment programmes in each country was used. This assumed these cases would be recorded in the national surveillance database and that cases who presented to the private sector would not. To estimate  $P_{rec}$ , a range of values for each country were derived from a systematic review of published literature on treatment seeking behaviour in each country, described below with search terms in extended information, Table S1.

$B_{confTOT}$  = the total number of confirmed malaria cases in each country in 2013, 2014 and 2015. This was the sum of the number of confirmed malaria cases in Public Health Facilities and Community Treatment Programs in each country in the WMR 2014<sup>13</sup>, WMR 2015<sup>8</sup> and WMR 2016<sup>5</sup>. Mixed infections (*P. falciparum* plus *P. vivax*) were included in the numbers for each species. Numbers of unconfirmed cases were not included due to the large uncertainty in the proportions of these cases likely to have malaria and the introduction of mandatory malaria testing in all the Asia-Pacific countries prior to 2012. These data are provided in the appendices of the respective WMRs.

$P_{mic}$  = the proportion of confirmed cases diagnosed in each country by microscopy in 2013<sup>13</sup>, 2014<sup>8</sup> and 2015<sup>5</sup>. These data are provided in the extended data, Table S2<sup>14</sup>.

$P_{RDT} = (1 - P_{mic})$  = the proportion of confirmed cases diagnosed in each country by rapid diagnostic test (RDT) in 2013<sup>13</sup>, 2014<sup>8</sup> and 2015<sup>5</sup>. These data are provided as extended data, Table S2<sup>14</sup>.

$S_{mic}$  = sensitivity of microscopy = 95% (range 90–100%). The lower end of this range was set at the WHO minimum level of competency for malaria microscopists<sup>15</sup>.

$S_{RDT}$  = sensitivity of RDT = 95% (75–100%) for *P. falciparum* and 90% (50–100%) for *P. vivax* and other *Plasmodium* species. The true sensitivity of RDTs in field conditions varies widely between manufacturers and in different field conditions, as well as being greatly affected by parasitaemia, as reported in detail following extensive testing by WHO. The values used were derived from the ranges of sensitivities found in these tests<sup>16</sup>.

$P_{comp}$  = the completeness of reporting i.e. the proportion of expected reports which were received by the NMCP. Values for this were taken directly from the data provided by countries to WHO for the WMRs on completeness of reporting by public health facilities.  $P_{comp}$  was calculated by the countries from the total number of health facility reports received by a ministry of health during a year, divided by the total number of facility reports that were expected in that year. The expected number of facility reports was the number of health facilities multiplied by the frequency of reporting; that is, if 100 facilities were expected to report each month, 1200 reports would be expected during a year. Where no values were available, this was assumed to be 100% to give the most conservatively high disease burden estimate. These data are provided in the extended data, Table S2<sup>14</sup>. No data on completeness of reporting were available for cases at community level so this was assumed to be the same as public health facility cases.

**Systematic review.** The methodology for the systematic review is described in detail on PROSPERO, under registration [CRD42016032564](https://doi.org/10.1111/CRD4.2016032564). The following inclusion criteria were used: English language, human studies, quantitative or mixed methods, enumeration of public and/or private sector health-care seeking behaviour for malaria/fever/febrile illness and/or published from 2000 onwards. Sources included Pubmed (fixed search terms are given as extended data, Table S1<sup>14</sup>), hand search of reference lists from identified articles, publicly available grey literature, [Demographic and Health Surveys](#) (DHS) and [UNICEF Multiple Indicator Cluster Surveys](#) (MICS). The search was done in 2015. Studies were screened for duplications and assessed for quality using published criteria<sup>17</sup>. In total, 2637 relevant sources were identified. Of these, 20 could not be obtained in full-text. Of the remainder, 70 studies met the inclusion and quality criteria and were thus used for this analysis. A value for  $P_{rec}$  was derived from the results of each included study and the median, minimum and maximum values for each country used in the analysis. The surveys were all treated equally with no weighting for recency, geographic or demographic coverage of the data in order to output the widest range of possible values.

Results were correlated with estimates for 2013 and 2015 in the WMRs.

## Method 2

For 2000 to 2008, data on completeness of reporting were not available. From 2000 to 2012, numbers of confirmed cases at community level, and numbers of cases by diagnostic method for community cases were not available. Therefore as an alternative approach, the burden estimates calculated for 2014

were used to calculate the ratio of estimated cases to reported cases in public health facilities for each species and this ratio was used to derive estimates of *P. falciparum* and *P. vivax* for 2000 to 2013 for the modelling. This was done by multiplying this ratio by the annual number of reported confirmed public health facility-reported cases of each species in 2000 to 2013, provided in the appendices of the WMR 2015<sup>8</sup>. These data are provided as extended data, Table S3<sup>14</sup>. This carried the assumptions that the proportion of confirmed cases identified in the community and completeness of reporting did not change during this period. The ratios are provided as extended data (Table S3)<sup>14</sup>. To validate this method, the median, minimum and maximum burdens for each species were correlated with those derived for 2013 using Method 1 and the trends over time compared with the burden estimates for total cases in the 2016 WMR.

### Method 3

In the data in the WMRs, there were found to be some discrepancies in the total numbers of cases by diagnostic method and by species. To address this, a third alternative method was applied to data from 2000 to 2014 to estimate the numbers of confirmed *falciparum* and *vivax* cases at public health facilities

by multiplying the numbers of confirmed cases diagnosed by microscopy and RDT by the proportion reported with each *Plasmodium* species. This was then adjusted for the sensitivity of microscopy and RDT, access to healthcare and completeness of reporting, as outlined for Method 1. For years in which completeness of reporting was not available for a particular country, it was assumed to be 100%. Validation was then done by comparing the estimated median, minimum and maximum with calculated values using Method 2 for 2013. Trends over time by country for 2000 to 2015 using Methods 2 and 3 were then compared to the available data from the World Malaria Report to select the preferred method to derive estimates for the modelling.

## Results

### Proportion of cases recorded

The results of the systematic review on proportion of cases recorded are in Table 1. Out of the included 70 surveys, 22 covered the whole country, of which 20 were DHS or MICS, and the others were mostly limited to a single subnational unit (subdistrict, district, province). Most of the data were from before 2013. In three countries, the most recent data were from

**Table 1. Results of systematic review to estimate the proportion of those with malaria who are recorded in each country.**

Country	Number of sources	References	Most recent data	Cover whole country	Estimated proportion recorded		
					Median	Minimum	Maximum
Afghanistan	2	18,19	2011	1	67.6%	63%	72.1%
Bangladesh	6	20–25	2013	4	70%	9.4%	79%
Bhutan	1	26	2010	1	74.2%		
Cambodia	9	27–35	2014	3	61%	16%	90.7%
DPR Korea	1	36	2009	1	74.6%		
India	10	37–46	2011	1	60%	7.1%	93%
Indonesia	5	47–51	2012	1	42%	28%	74%
Lao PDR	4	52–55	2012	1	46%	9%	61%
Malaysia	1	56	2009	0	81.6%		
Myanmar	7	57–63	2013	1	48%	6.8%	91.4%
Nepal	4	64–67	2014	2	44%	26.4%	51%
Pakistan	5	68–72	2014	1	65%	11%	77%
Papua New Guinea	0			0	N/A		
Philippines	3	73–75	2013	1	50%	45.40%	93.1%
PR China	0			0	N/A		
Republic of Korea	0			0	N/A		
Solomon Islands	1	76	1999	0	97%		
Sri Lanka	2	77,78	2001	0	75.9%	71.7%	80.1%
Thailand	4	29,79–81*	2013	1	58.1%	35%	83%
Timor-Leste	0			0	N/A		
Vanuatu	1	82	2007	1	73.2%		
Viet Nam	6	53,83–87*	2014	2	56%	10.7%	94.7%
<b>Total</b>	<b>70*</b>			<b>22</b>			

\*Actual total was 72 but two sources had data for two countries.



2014 (whole country: Cambodia and Viet Nam, one province: Pakistan) and in four from 2013 (whole country: Bangladesh and Philippines; one township: Myanmar; five provinces: Thailand). The DHS and MICS surveys were the largest with mostly whole country coverage but were specific only to children whereas much of the burden of malaria in the Asia-Pacific is in adults. Nationally representative surveys were found for 15 countries, only subnational for three (Malaysia, Solomon Islands and Sri Lanka) and no surveys were found for four countries. Regarding national surveys, 12 countries had data from MICS, seven from DHS and four from both DHS and MICS.

### Burden Estimates for 2013 to 2015

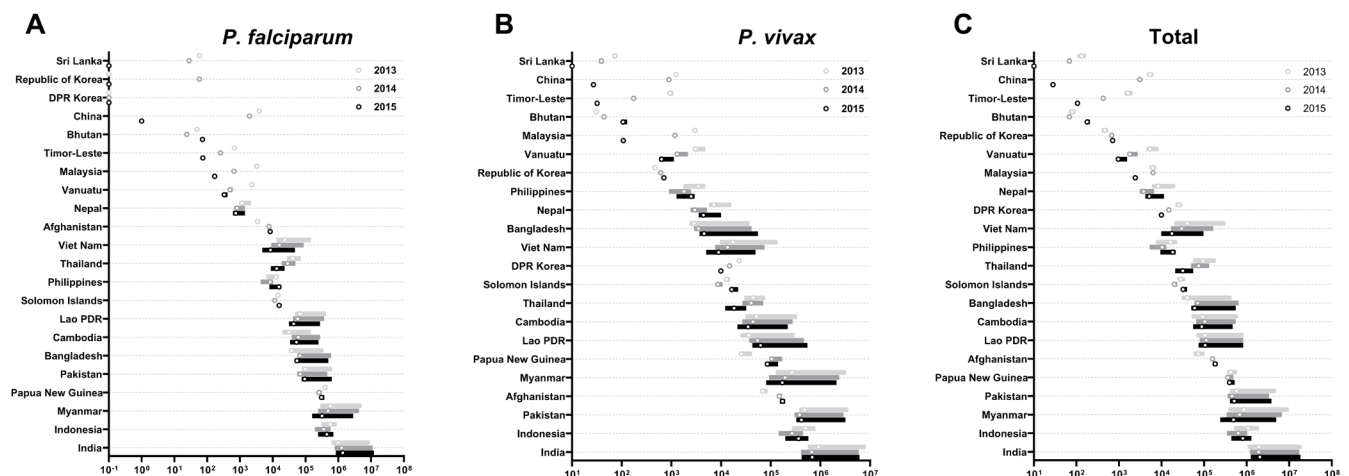
The malaria burden estimates for each country in 2013, 2014 and 2015 derived using Method 1 are presented in [Figure 1](#) and extended data, Table S5A-C<sup>14</sup>. The total estimated burden for the 22 countries in 2015 was median (range) 2,784,441 (1,764,116–17,864,485) *P. falciparum*, 2,056,221 (1,372,338–13,281,356) *P. vivax*, 5,222 (4,684–7,782) other species and 4,809,884 (3,141,137–31,153,623) total cases. This total was around two times greater than the total number of confirmed cases reported to WHO in each of these years.

The precision of these estimates was greatly influenced by the lack of suitable recent studies on access to healthcare to estimate the proportion of cases reported for the 22 countries and by a lack of data on completeness of reporting for confirmed community cases. For comparison, the estimates for total malaria burden in 2015 published in the WMR 2016 are also shown as extended data, Table 5C<sup>14</sup> and graphically in [Figure 2](#). The median, minimum and maximum estimates by country correlated strongly with the WHO estimates ( $r=0.9661$ ,  $0.9570$  and  $0.8778$ , respectively). Although estimates for many countries were quite similar between the two methods, the overall WHO point estimate was 3.6 times higher. This discrepancy was mainly due to an almost eight times higher point estimate by WHO for India due to inclusion of the number of unconfirmed malaria cases in the WHO calculation. Of note, both methods found a similar upper

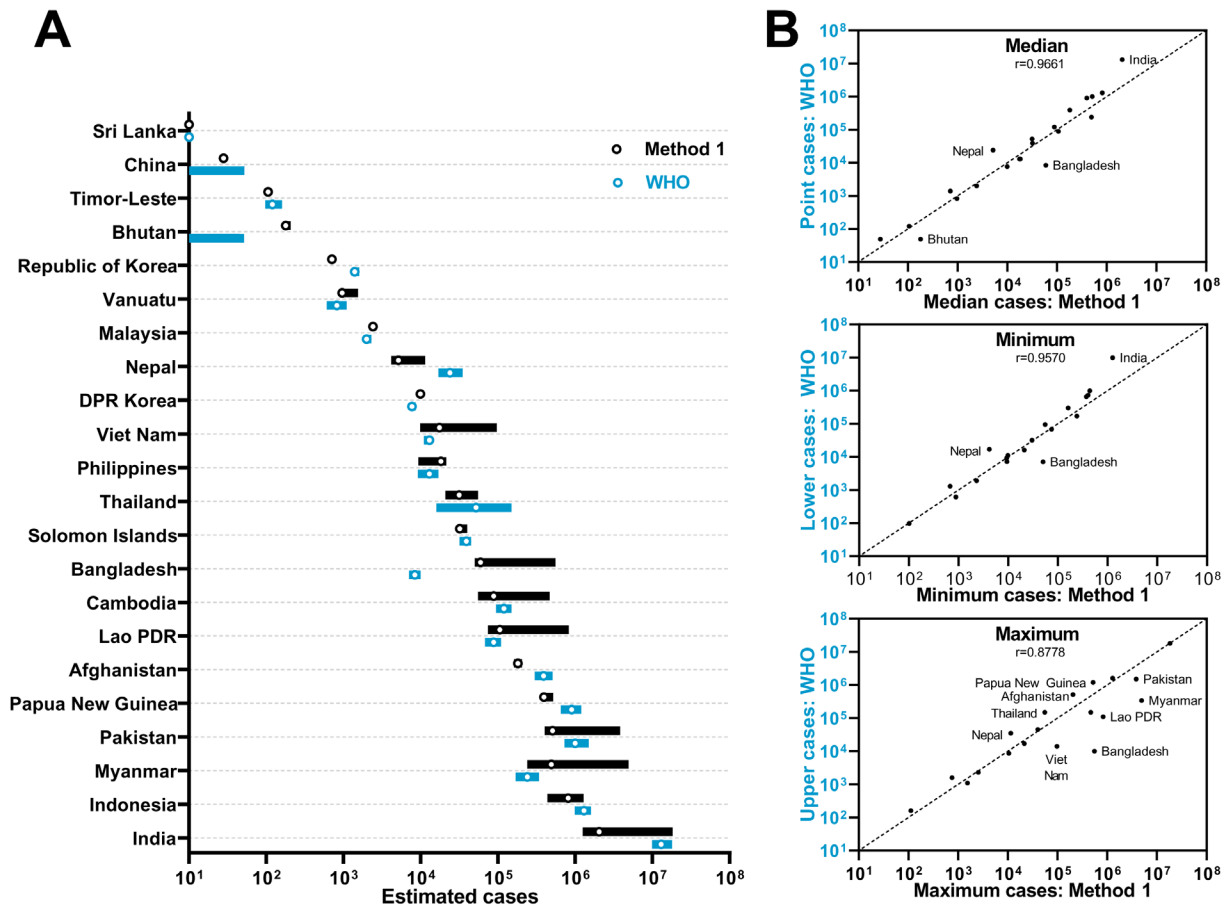
bound for total cases in India of around 18,000,000. Other countries with substantial differences between the two were Bangladesh, where the WHO estimate was lower, and Nepal, where it was higher. In Bangladesh this was due to most confirmed cases being reported at community level (6,608 public health facility vs 32,992 community in 2015)<sup>5</sup> as most malaria testing and treatment in the country is done by the Bangladesh Rural Advancement Committee (BRAC) consortium and not at public health facilities run by the government. The reason for the WHO estimate for Nepal being much higher is not clear, although at 1,112 reported cases and 24,000 (17,000–35,000) estimated cases, this represents a 21.6-fold increase for the Point estimate, which is by far the highest of any country in the Asia-Pacific. For comparison, Method 1 found a median of a 3.4-fold increase.

The burden estimates for 2014 could not be compared with WHO estimates for that year as no estimates were published for 2014. In the 2015 WMR, country-level estimates were provided for 2013 and regional level estimates were provided for 2015. These 2015 estimates were then revised downwards in the 2016 WMR.

Comparing median, minimum and maximum estimates for 2013 using Method 1 with those for 2013 from WHO ([Figure 3](#)), again found them to be highly correlated ( $r=0.8970$ ,  $0.9109$  and  $0.8409$ , respectively), although less strongly than for 2015. There were some notable differences between Method 1 and WHO. Median estimates for Timor Leste, Bangladesh, India and Indonesia were markedly lower than those from WHO. These countries all had very high ratios of estimated cases to reported cases in 2013 in the WMR (59, 26, 15 and 10, respectively). Both Timor Leste and Bangladesh had very large decreases in cases estimated by WHO from 2013 to 2015 (750-fold and 83-fold). With reported confirmed cases decreasing only 12-fold in Timor and increasing 1.8-fold in Bangladesh in the same period, and no other clear explanation for such a large change, the estimates in 2013 seem to be too high. India had a 1.3-fold decrease



**Figure 1.** Numbers of estimated *P. falciparum*, *P. vivax* and total malaria cases in 2013, 2014 and 2015 by country using Method 1. Median and range are shown.



**Figure 2.** Number of estimated total malaria cases in 2015 by country using Method 1 and from WHO WMR 2016. Median and range are shown. Dashed lines in B are the identify lines.

in cases estimated by WHO from 2013 to 2015 and Indonesia 3.2-fold. Similar to 2015, the higher number of cases in the WHO estimates appear to be due to inclusion of the large numbers of unconfirmed cases in the calculations. Maximum estimates for Cambodia, Lao PDR, Viet Nam and Myanmar were much higher than those from WHO due primarily to the wider range of sources used to quantify the proportion of cases which are reported.

A comparison of results for 2013 using Methods 1 (calculation method) and 2 (ratio method) is shown in Figure 4. The results were very similar for all countries for both *P. falciparum* and *P. vivax* ( $r=0.9873$ ,  $0.9782$  and  $0.9873$  for median, minimum and maximum *P. falciparum* and  $0.9870$ ,  $0.9896$  and  $0.9922$  for *P. vivax*) with no marked differences for any country.

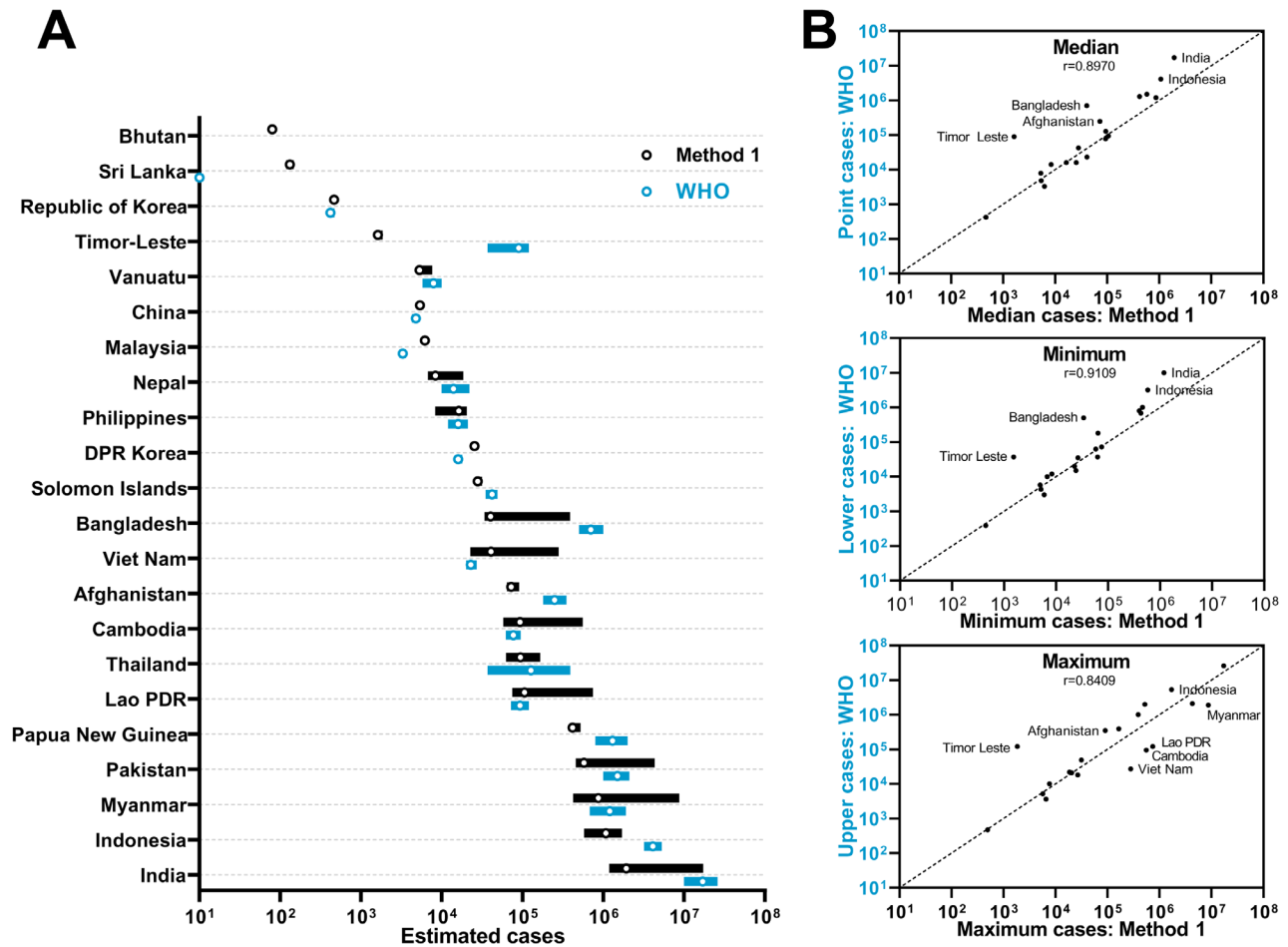
#### Burden estimates for 2000 to 2014

Numbers of reported confirmed cases, and disease burden estimates for each species by country from 2000 to 2015 using Methods 2 and 3 are shown in Figure 5 with reported numbers of confirmed cases in Figure 6A-C. Methods 2 and 3 differed in that Method 3 generally gave lower overall estimated totals for the Asia-Pacific before 2009 with a relatively flat trend over time.

The two methods gave very similar overall results from 2012 onwards. In contrast, Method 2 produced a clear downward trend in both *falciparum* from 2000 to 2015 and *vivax* from 2005 to 2015. WHO estimates for 2000, 2005, 2010 and 2015 also showed a marked downward trend, especially from 2005 to 2015 (Figure 6D-F)<sup>5</sup>. Using Method 2, the estimated cases were lower in Myanmar in 2007 to 2011 and in Papua New Guinea in 2012 and 2013 due to the numbers of confirmed cases by microscopy and RDT being far higher than the total numbers reported for each species. Compared to Method 2, Method 3 produced lower numbers of *P. falciparum* in Bangladesh prior to 2012. This was due to the majority of cases being diagnosed in the community in Bangladesh and numbers of cases by species in the community only being included in the totals before 2012. In the Philippines in 2000 to 2006, Method 3 was found to give fewer estimated cases as there were no data on numbers of confirmed cases by microscopy and RDT but there were data on numbers of each species.

#### Burden estimates for modelling

Method 2 was chosen to derive estimates for the modeling as it better captured the trend in estimated cases over time seen in the estimates from WHO. Results of the disease burden estimates



**Figure 3.** Number of estimated total malaria cases in 2013 by country using Method 1 and from WHO WMR 2015. Median and range are shown. Dashed lines in B are the identify lines.

for 2000 to 2014 derived using Method 2 that were used in the modelling are provided in the extended data (Tables S6A-F)<sup>14</sup>.

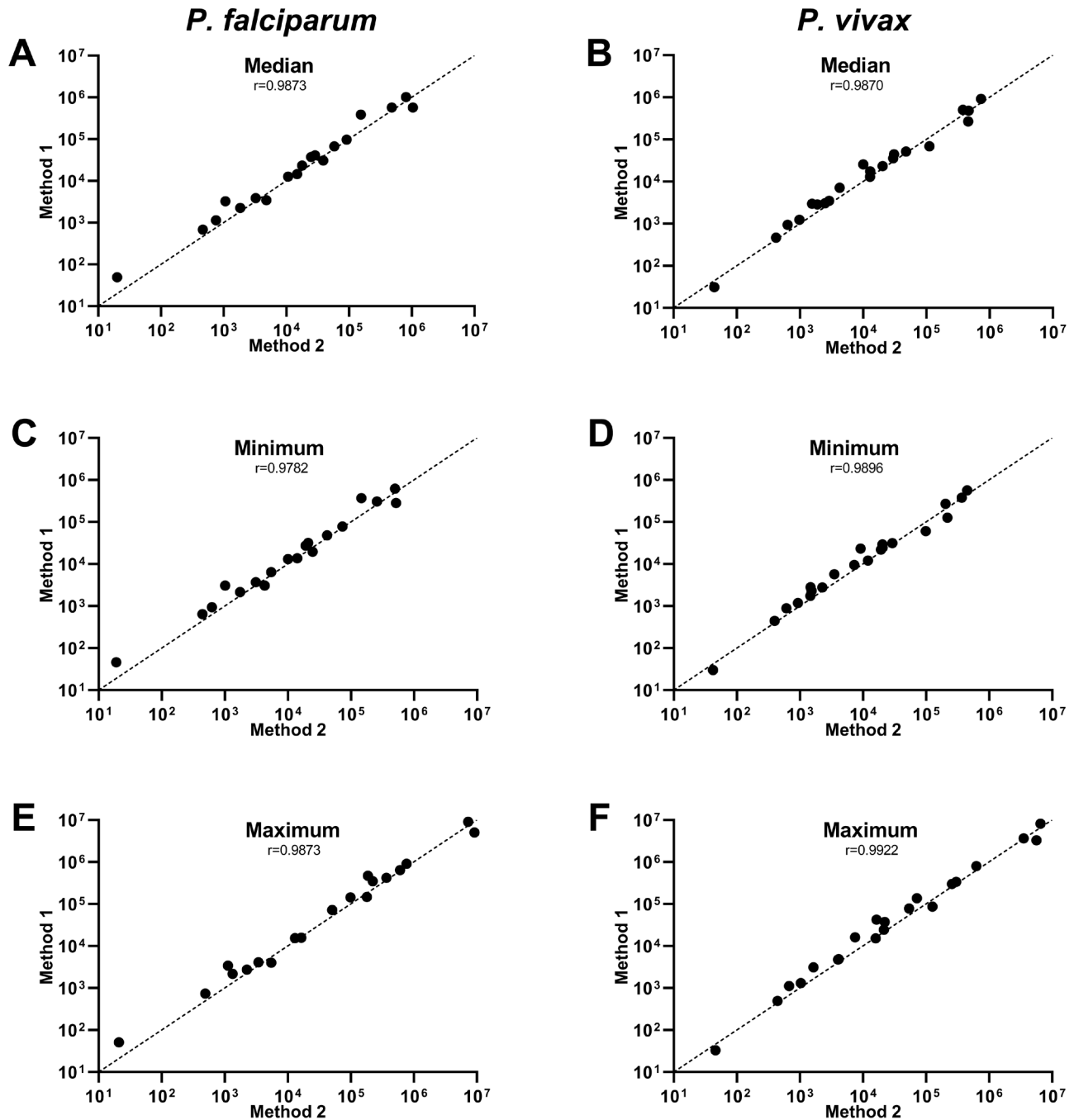
## Discussion

The study attempted to develop a simple method to calculate annual estimates by parasite species of malaria disease burden for the 22 endemic countries in the Asia-Pacific from 2000 to 2015 using publicly available data. It was found that the overall resulting estimated numbers of cases were roughly double the numbers that were reported. However, there was an approximate 10-fold range of uncertainty around these estimates. This uncertainty was similar in scale to the estimated total numbers of cases in the same countries published by WHO in the annual WMRs. Although the methods were broadly similar, estimates for particular countries varied between the two due to differences in the data used. One major difference is that the WHO estimates include numbers of unconfirmed cases, whereas this study did not. In India, this may have caused the point estimates from WHO to be more than 10 times higher due to the more than 100 million suspected cases reported each year, although this was compensated for by the broader range of values for the

proportion recorded in the present study which resulted in similar maximum estimates. It was decided not to include unconfirmed cases in the present analysis as mandatory diagnostic testing for malaria has been widely adopted in health facilities in the Asia-Pacific, as recommended by WHO since 2010, and those who do not attend a health facility would be included in the proportion of unrecorded cases.

The primary contributor to the uncertainty of the derived estimates in the present study was the wide range of values for the proportion of cases which are recorded. In an attempt to include data from a broad range of sources, these were collected from a systematic review of the published literature. Despite widely searching both the academic and grey literature, there were relatively few suitable studies and none at all in some countries. Thus many of the studies that were included were not recent and there was insufficient data to assess how much this value might change over time in each country. An analysis of estimates from DHS and MICS by WHO in 2008 found that the proportion of people with fever using health facilities covered by the reporting system did not change substantially over time<sup>4</sup>.

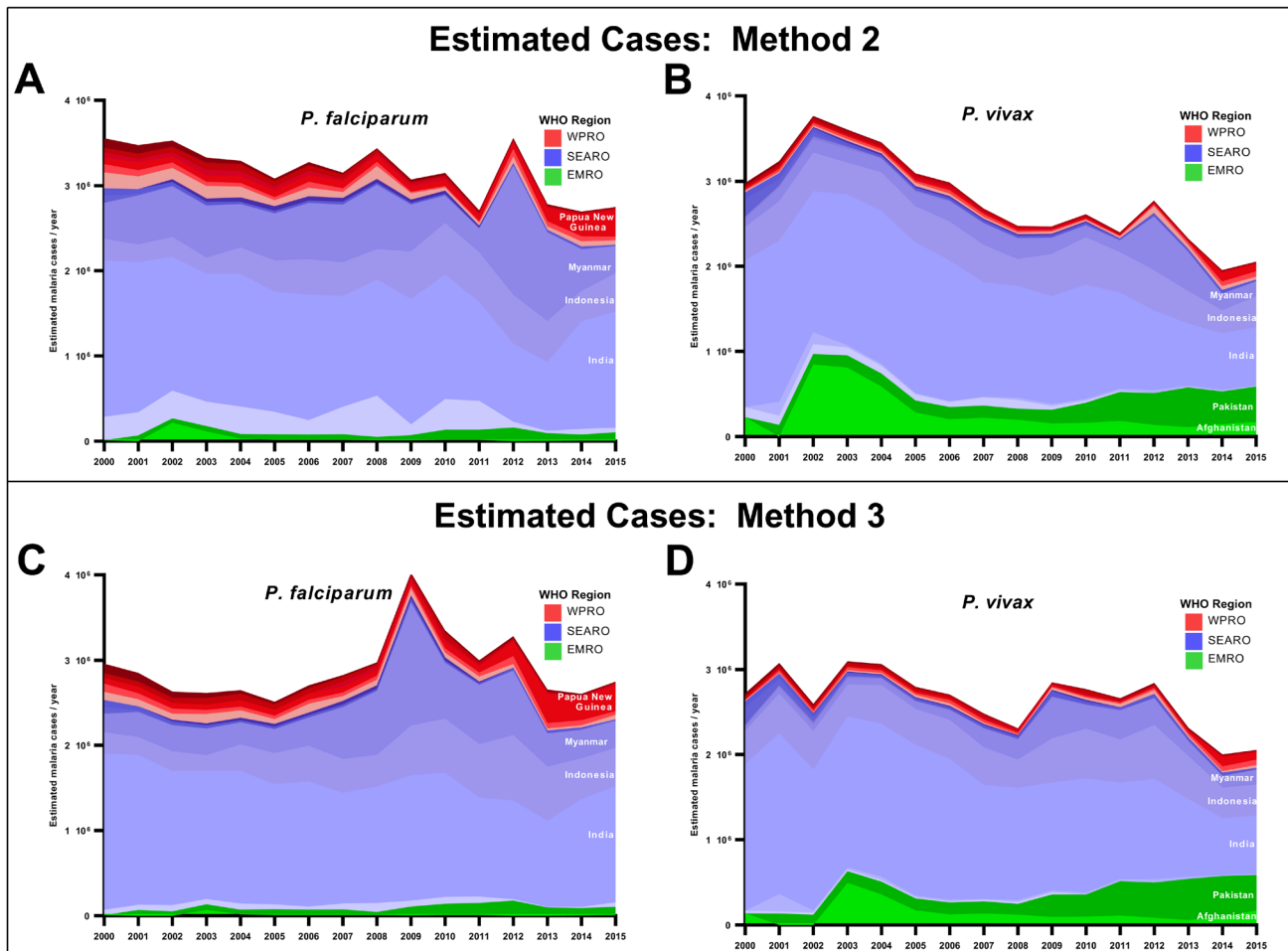




**Figure 4.** Comparison of malaria burden estimates for each species in 2013 using calculation method (Method 1) vs ratio method (Method 2). Dashed lines are the identity lines.

However, data for any particular country was sparse with only 58 year-to-year comparisons across all malaria endemic countries. With substantial investments in malaria in recent years across the Asia-Pacific, and expansion of village malaria worker networks particularly in the Greater Mekong Subregion<sup>88</sup>, it seems likely that access to healthcare should have improved since 2000, but this is difficult to measure with current available evidence.

DHS and MICS are large nationally representative surveys that were included among the sources for quantifying the proportion of cases recorded in the present study. They are also the primary source of this data for this parameter used in the WHO WMR estimates for the Asia-Pacific. The DHS and MICS are surveys of children under 5 years of age. A limitation of this for the Asia-Pacific is that a high proportion of those with malaria are older children and adults<sup>89,90</sup> and it is not clear if their



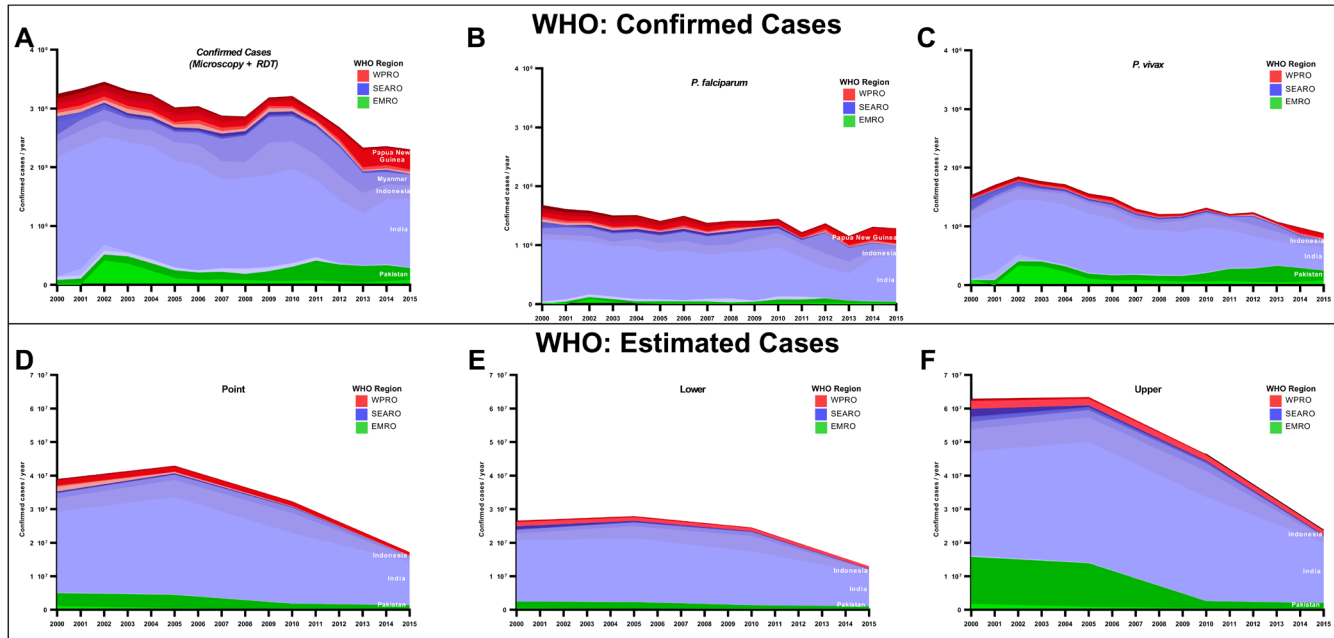
**Figure 5.** Median annual estimated numbers of cases using Methods 2 and 3 of *P. falciparum* and *P. vivax* in the Asia-Pacific 2000–2015.

health-seeking behaviour is different to young children as suggested in some studies<sup>37</sup>. Another limitation is that these surveys are not always representative of malaria endemic areas whose populations may have lower income and poorer access to healthcare<sup>90,91</sup>.

It is worth focusing a little more on India, as the country with by far the highest reported and estimated burden. The difficulty estimating, and high degree of uncertainty of, the true burden of malaria in India have been highlighted by previous studies<sup>89,92</sup>. One used a geostatistical method to estimate the number of cases and deaths in 2006 to be far higher than that estimated by WHO<sup>92</sup>. Inadequacies in reporting and the health management information system were highlighted as contributing to the uncertainty. In the present study, 10 citations from India were included for estimating the proportion of cases reported, the most from any country; however, only one of these was nationally representative and the most recent was from 2011 and estimates ranged from 7% to 93%. Since then, a further DHS was done in India in 2015–16, which had no specific questions about malaria but found that 73% of children with fever are taken to a health facility

or provider<sup>93</sup>. There is clearly a need for more robust measures of access to healthcare to improve estimates for India.

In this study, detailed calculations could be made only for 2013–2015 due to a lack of data on the required parameters. Although the initial intention was to apply a single method to annual data from 2000 to 2014 to use in modelling the cost of elimination, it was found that some of the parameters used in the estimates were not available for earlier years. Therefore two simplified versions of the equation using fewer parameters were also developed and the method that most closely reproduced the trends in reported cases and the WHO estimates was adopted for the modelling. The final approach adopted for these estimates was calculation of a ratio of estimated cases to reported confirmed health facility cases. This is similar to a method that has been proposed for estimating the burden of dengue where the number of reported cases is multiplied by an expansion factor (EF)<sup>94</sup>. Available data for dengue is much less comprehensive than for malaria and therefore EF has been calculated from published studies and from extrapolation based on available metrics of the quality of healthcare. The limitations of the former are that there are few



**Figure 6.** Annual numbers of confirmed cases reported in the 2015 and 2016 WMRs (**A.** all confirmed by microscopy or RDT, **B.** *P. falciparum* and **C.** *P. vivax*) and estimated numbers of cases reported in the 2016 WMR (**D.** Point, **E.** Lower and **F.** Upper) in the Asia-Pacific from 2000 to 2015.

relevant studies and that the studies mostly only covered small parts of each country and a limitation of the latter is that it uses broad metrics of healthcare quality, e.g. physician density and child mortality that are not proven to be related to dengue reporting rates. Unlike malaria, most cases of dengue do not have a confirmatory diagnostic test so the number of reported cases includes people who do not have dengue. These all contribute to wide uncertainty in estimates of dengue but may be worth considering for malaria, for which the data, despite the problems, is generally better.

For the present study, in addition to the limitations due to lack of available data for particular years, there are a number of other limitations to the analysis which should be highlighted. Over the period 2000 to 2015, there have been changes to the health systems in each country, which are difficult to account for in the analysis. Examples include the initiation of a mandatory requirement to confirm all reported cases with a diagnostic test and the introduction and subsequent roll-out of falciparum RDTs followed by RDTs for multiple species, particularly in the community in different years in different countries. There have also been changes in coverage of health services (mostly improvements) during this time. All of these have occurred gradually and have the potential to increase numbers of confirmed malaria cases in the data, but their impact on the totals is difficult to quantify and adjust for. The simple approach adopted here, to use ratios based on 2014 estimates, would at least partially account for these as all countries had adopted mandatory testing and most had adopted RDTs by this time.

It was also not possible to fully account for some differences between health systems which impact on the way data are

reported. For example, the numbers of cases reported to WHO are divided into those reported by public health facilities and cases at community level. The estimates by WHO use numbers of public health facility cases as these are usually the majority and are thought to be more reliable. Much less information is therefore provided in the WMR for the cases at community level, with data not broken down by species and completeness of reporting not being included. For example, in Bangladesh the majority of malaria testing is done by Bangladesh Rural Advancement Committee (BRAC), and reported as community cases with only a minority being public health facility cases. This resulted in much lower estimates of cases in Bangladesh by WHO compared to this study in 2013 and 2015.

The direct consequence of uncertainty in the burden estimates for this particular study was uncertainty in the modelling results that are driven by this data. In this case, the predicted cost and return on investment for elimination are the main results of the modelling and had a range of possible values for any possible scenario. Whilst it may be helpful as a general indication of the scale of investment required, to inform detailed budget planning, particularly for individual countries, and to guide allocation of finite resources between countries would require much more precise estimates.

Other methods which have been used to estimate malaria burden estimates include the Global Burden of Disease Study<sup>95</sup>, which used three different techniques depending on the availability and quality of malaria incidence data: 1) using regression on mortality data, age group and modelled parasite positivity ratio (PfPR); 2) by regression on national level PfPR estimates; and 3) using case data from the WMR. For Asia-Pacific countries, all three

methods were used. There were substantial differences from the WHO estimates and the authors discuss the various contributors to these differences in detail including challenges of inadequate available data. An alternative approach for areas with very poor data has been to use incidence and prevalence data from published studies in Africa to develop a transmission dynamic mathematical model including immunity, which predicts the age distribution and annual incidence of clinical disease<sup>96</sup>. Such an approach is limited by available research data from heterogeneous study designs, is affected by measures of health-seeking and requires a number of assumptions to be made including about malaria biology and transmission in the country being modelled. The geostatistical model used to derive estimates for WHO for high burden countries in Africa has also been applied to estimate global malaria burden<sup>97</sup>. This uses a Bayesian framework with multiple spatially highly resolved covariates to generate detailed predicted prevalence surfaces from which an estimated range of incidence is derived. This method continues to be refined and updated maps and predicted estimates are published on the project website (<https://map.ox.ac.uk/>). One recent development has been the use of serology data to quantify recent malaria infections<sup>98</sup>. Studies are ongoing to assess how well seropositivity rates might predict malaria incidence.

The precision and accuracy of malaria burden estimates could be improved by changes in the collection and availability of data. Examples highlighted by the present analysis include having more regular household surveys on access to healthcare for people with fever in malaria-endemic areas to estimate the proportion of cases reported in all countries, e.g. DHS and MICS. This would be most informative if done in malaria-endemic areas in the populations at risk of malaria. Completeness of reporting of cases at community level is not currently collected but could be included in the annual WMR. A lack of publicly available subnational data is a major constraint to deriving more accurate estimates with current estimates only possible at national level. As well as malaria incidence rates, it is likely that completeness of reporting, access to healthcare, and the proportion of community to public health facility cases all vary across space and these should be included in the estimates. This will also have the advantage of allowing subnational burden estimates, which will be much more informative for NMCPs when deciding on allocation of resources.

## Conclusions

Estimating the true burden of malaria is essential to help guide allocation of resources for malaria elimination. Limitations in the available data make estimating true burden and predicting cost of elimination very imprecise. Having more publicly available data from NMCPs, more regular surveys on access to healthcare and access to subnational data could greatly improve these estimates.

## Data availability

### Underlying data

The data used in this manuscript are taken from the WHO World Malaria Reports, which are available online at: [https://www.who.int/malaria/publications/world\\_malaria\\_report/en/](https://www.who.int/malaria/publications/world_malaria_report/en/).

## Extended data

Zenodo: Estimating malaria disease burden in the Asia-Pacific. <https://doi.org/10.5281/zenodo.2592931><sup>14</sup>.

The following extended data are available:

- Supplementary Material Tables S1 to S3.doc.
  - Table S1. Search terms for literature review on healthcare seeking behaviour.
  - Table S2. Completeness of reporting by health facilities ( $P_{comp}$ ), proportion of cases diagnosed by microscopy ( $P_{mic}$ ) and proportion of cases diagnosed by RDT ( $P_{RDT}$ ).
  - Table S3. Composite ratio of burden estimates to public health facility cases in 2014 for *P. falciparum* and *P. vivax* for Method 2.
- Supplementary Material Table S4 Pf\_Pv\_reportedcases.xlsx (Table S4. Numbers of confirmed *P. falciparum* (A) and *P. vivax* (B) cases reported by public health facilities in the WHO World Malaria Reports).
- Supplementary Material Table S5 Pf\_Pv\_Total\_WHO burden 13-15.xlsx (Table S5. Estimated malaria disease burden for 22 countries in the Asia-Pacific in 2013 compared to 2015 (A), 2014 (B) and 2015 compared with 2016 (C) using Method 1).
- Supplementary Material Table S6 Pf\_Pv\_burdenestimates\_00-14.xlsx (Tables S6A-F. Estimated burden of *P. falciparum* and *P. vivax* malaria by country from 2000 to 2014 used in the modelling).

Extended data are available under the terms of the [Creative Commons Zero “No rights reserved” data waiver](#) (CC0 1.0 Public domain dedication).

## Reporting guidelines

Zenodo: PRISMA checklist for study “Estimating malaria disease burden in the Asia-Pacific”. <https://doi.org/10.5281/zenodo.2592931><sup>14</sup>.

## Grant information

RJM was funded by the BMGF (OPP1110500), Asian Development Bank (TA-8763), Australian Department of Foreign Affairs and Trade (71215) and the Wellcome-Trust Major Overseas Programme in SE Asia (106698). CEGM was funded by Asian Development Bank (TA-8763) and the Australian Department of Foreign Affairs and Trade (71215). JR was funded by the Australian Department of Foreign Affairs and Trade (71215). NE was funded by the Australian Department of Foreign Affairs and Trade (71215). AMD was funded by the Wellcome-Trust Major Overseas Programme in SE Asia (106698).

*The funders had no role in the design or writing of this paper, or the decision to submit the paper for publication. The authors were not paid to write this manuscript.*

## References

1. The Global Fund: **35th Board Meeting Allocation Methodology 2017-2019**. The Global Fund; 2016.  
[Reference Source](#)
2. The Global Fund: **Funding Model**. The Global Fund; 2019.  
[Reference Source](#)
3. Mercado CE, Ekpirat N, Dondorp AM, *et al.*: **An assessment of national surveillance systems for malaria elimination in the Asia Pacific**. *Malar J*. 2017; 16(1): 127.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
4. World Health Organization: **World malaria report 2008**. Geneva: World Health Organization; 2008.  
[Reference Source](#)
5. World Health Organization: **World malaria report 2016**. Geneva: World Health Organization; 2016.  
[Reference Source](#)
6. World Health Organization: **World malaria report 2012**. Geneva: World Health Organization; 2012.  
[Reference Source](#)
7. World Health Organization: **World malaria report 2013**. Geneva: World Health Organization; 2013.  
[Reference Source](#)
8. World Health Organization: **World malaria report 2015**. Geneva: World Health Organization; 2015.  
[Reference Source](#)
9. World Health Organization: **World malaria report 2017**. Geneva: World Health Organization; 2017.  
[Reference Source](#)
10. World Health Organization: **World malaria report 2018**. Geneva: World Health Organization; 2018.  
[Reference Source](#)
11. Shretta R, Silal SP, Celhay OJ, *et al.*: **Malaria elimination transmission and costing in the Asia-Pacific: Developing an investment case [version 1; peer review: awaiting peer review]**. *Wellcome Open Res*. 2019; 4: 60.  
[Publisher Full Text](#)
12. Silal SP, Shretta R, Celhay OJ, *et al.*: **Malaria elimination transmission and costing in the Asia-Pacific: a multi-species dynamic transmission model [version 1; peer review: awaiting peer review]**. *Wellcome Open Res*. 2019; 4: 62.  
[Publisher Full Text](#)
13. World Health Organization: **World malaria report 2014**. Geneva: World Health Organization; 2014.  
[Reference Source](#)
14. Maude RJ: **Estimating malaria disease burden in the Asia-Pacific (Version 1.0) [Data set]**. *Zenodo*. 2019.  
<http://www.doi.org/10.5281/zenodo.2592932>
15. World Health Organization, Regional Office for the Western Pacific: **Malaria microscopy quality assurance manual: version 1**. Manila: WHO Regional Office for the Western Pacific; 2009; 125.  
[Reference Source](#)
16. UNICEF/UNDP/World Bank/WHO Special Programme for Research and Training in Tropical Diseases, Centers for Disease Control (U.S.), Foundation for Innovative New Diagnostics: **Malaria rapid diagnostic test performance results of WHO product testing of malaria RDTs: round 3 [2010-2011]**. Geneva: World Health Organization. (in press).  
[Reference Source](#)
17. Hawker S, Payne S, Kerr C, *et al.*: **Appraising the evidence: reviewing disparate data systematically**. *Qual Health Res*. 2002; 12(9): 1284–99.  
[PubMed Abstract](#) | [Publisher Full Text](#)
18. Howard N, Shafi A, Jones C, *et al.*: **Malaria control under the Taliban regime: insecticide-treated net purchasing, coverage, and usage among men and women in eastern Afghanistan**. *Malar J*. 2010; 9: 7.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
19. Central Statistics Organisation (CSO) and UNICEF: **Afghanistan Multiple Indicator Cluster Survey 2010-2011**. Kabul: Central Statistics Organisation (CSO) and UNICEF; 2013.  
[Reference Source](#)
20. Haque U, Hashizume M, Sunahara T, *et al.*: **Progress and challenges to control malaria in a remote area of Chittagong hill tracts, Bangladesh**. *Malar J*. 2010; 9: 156.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
21. Haque U, Sunahara T, Hashizume M, *et al.*: **Malaria prevalence, risk factors and spatial distribution in a hilly forest area of Bangladesh**. *PLoS One*. 2011; 6(4): e18908.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
22. Ahmed SM, Hossain MS, Kabir M: **Conventional or interpersonal communication: which works best in disseminating malaria information in an endemic rural Bangladeshi community?** *PLoS One*. 2014; 9(6): e90711.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
23. Bashir K, Al-Amin HM, Reza MS, *et al.*: **Socio-demographic factors influencing knowledge, attitude and practice (KAP) regarding malaria in Bangladesh**. *BMC Public Health*. 2012; 12: 1084.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
24. National Institute of Population Research and Training (NIPORT) MaA, and ICF International: **Bangladesh Demographic and Health Survey 2011**. 2013.  
[Reference Source](#)
25. Pathy P: **Bangladesh Multiple Indicator Cluster Survey 2012-2013**. Dhaka: Bangladesh Bureau of Statistics (BBS) and UNICEF Bangladesh; 2014.  
[Reference Source](#)
26. National Statistics Bureau: **Bhutan Multiple Indicator Survey**. May 2011, Thimphu, Bhutan: National Statistics Bureau; 2011.  
[Reference Source](#)
27. Hasegawa A, Yasuoka J, Ly P, *et al.*: **Integrating child health services into malaria control services of village malaria workers in remote Cambodia: service utilization and knowledge of malaria management of caregivers**. *Malar J*. 2013; 12: 292.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
28. Lim S, Yasuoka J, Poudel KC, *et al.*: **Promoting community knowledge and action for malaria control in rural Cambodia: potential contributions of Village Malaria Workers**. *BMC Res Notes*. 2012; 5: 405.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
29. Wangroongsarb P, Satimai W, Khamsiriwatchara A, *et al.*: **Respondent-driven sampling on the Thailand-Cambodia border. II. Knowledge, perception, practice and treatment-seeking behaviour of migrants in malaria endemic zones**. *Malar J*. 2011; 10: 117.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
30. Gryseels C, Uk S, Erhart A, *et al.*: **Injections, cocktails and diviners: therapeutic flexibility in the context of malaria elimination and drug resistance in Northeast Cambodia**. *PLoS One*. 2013; 8(11): e80343.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
31. Meessen B, Bigdeli M, Chheng K, *et al.*: **Composition of pluralistic health systems: how much can we learn from household surveys? An exploration in Cambodia**. *Health Policy Plan*. 2011; 26 Suppl 1: i30–44.  
[PubMed Abstract](#) | [Publisher Full Text](#)
32. Littrell M, Gatakaa H, Phok S, *et al.*: **Case management of malaria fever in Cambodia: results from national anti-malarial outlet and household surveys**. *Malar J*. 2011; 10: 328.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
33. ACTwatch Group and PSI/Cambodia: **Kingdom of Cambodia Household Survey Report, 2011**. Population Services International: DC; 2011.  
[Reference Source](#)
34. Yeung S, Van Damme W, Socheat D, *et al.*: **Access to artemisinin combination therapy for malaria in remote areas of Cambodia**. *Malar J*. 2008; 7: 96.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
35. National Institute of Statistics DGfH, and ICF International: **Cambodia Demographic and Health Survey 2014**. Phnom Penh, Cambodia, and Rockville, Maryland, USA: National Institute of Statistics, Directorate General for Health, and ICF International; 2015.  
[Reference Source](#)
36. CBS: **DPR Korea Multiple Indicator Cluster Survey 2009, Final Report**. Pyongyang, DPR Korea: CBS; 2010.  
[Reference Source](#)
37. Yadav SP: **A study of treatment seeking behaviour for malaria and its management in febrile children in rural part of desert, Rajasthan, India**. *J Vector Borne Dis*. 2010; 47(4): 235–42.  
[PubMed Abstract](#)
38. Deshmukh PR, Dongre AR, Sinha N, *et al.*: **Acute childhood morbidities in rural Wardha: some epidemiological correlates and health care seeking**. *Indian J Med Sci*. 2009; 63(8): 345–54.  
[PubMed Abstract](#) | [Publisher Full Text](#)
39. Chaturvedi HK, Mahanta J, Pandey A: **Treatment-seeking for febrile illness in north-east India: an epidemiological study in the malaria endemic zone**. *Malar J*. 2009; 8: 301.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
40. Mazumdar S: **Prevalence, risk factors and treatment-seeking behaviour for malaria: the results of a case study from the Terai region of West Bengal, India**. *Ann Trop Med Parasitol*. 2011; 105(3): 197–208.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
41. Das A, Ravindran TS: **Factors affecting treatment-seeking for febrile illness in a malaria endemic block in Boudh district, Orissa, India: policy implications for malaria control**. *Malar J*. 2010; 9: 377.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
42. Borah PK, Dutta P, Phukan AC, *et al.*: **Health Seeking Behavior Among the Fever Cases During an Outbreak of Malaria in Assam**. *J Human Ecol*. 2004; 15(3): 195–7.  
[Publisher Full Text](#)
43. Sarkar J, Murhekar MV, Shah NK, *et al.*: **Risk factors for malaria deaths in Jalpaiguri district, West Bengal, India: evidence for further action**. *Malar J*. 2009; 8: 133.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
44. Srivastava NM, Awasthi S, Agarwal GG: **Care-seeking behavior and out-of-pocket expenditure for sick newborns among urban poor in Lucknow, northern India: a prospective follow-up study**. *BMC Health Serv Res*. 2009; 9: 61.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)



45. Lalchhuanawma R, Murhekar MV: **Health-seeking behaviour for febrile illness in malaria-endemic Kolasib district, Mizoram, India.** *Int Health.* 2012; 4(4): 314–9. [PubMed Abstract](#) | [Publisher Full Text](#)
46. International Institute for Population Sciences (IIPS) and Macro International: **National Family Health Survey (NFHS-3), 2005-06.** India: Key Findings. Mumbai: IIPS; 2007. [Reference Source](#)
47. Sanjana P, Barcus MJ, Bangs MJ, *et al.*: **Survey of community knowledge, attitudes, and practices during a malaria epidemic in central Java, Indonesia.** *Am J Trop Med Hyg.* 2006; 75(5): 783–9. [PubMed Abstract](#) | [Publisher Full Text](#)
48. Karyana M, Burdarm L, Yeung S, *et al.*: **Malaria morbidity in Papua Indonesia, an area with multidrug resistant *Plasmodium vivax* and *Plasmodium falciparum*.** *Malar J.* 2008; 7: 148. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
49. Statistics Indonesia (Badan Pusat Statistik—BPS) NPafPBB, and, Kementerian Kesehatan (Kemenkes—MOH) all: **Indonesia Demographic and Health Survey 2012.** Jakarta, Indonesia: BPS, BKKBN, Kemenkes, and ICF International; 2013. [Reference Source](#)
50. BPS: **The Selected Districts of Papua Province Multiple Indicator Cluster Survey 2011, Final Report.** Jakarta, Indonesia: BPS; 2013. [Reference Source](#)
51. BPS: **The Selected Districts of West Papua Province Multiple Indicator Cluster Survey 2011, Final Report.** Jakarta, Indonesia: BPS; 2013. [Reference Source](#)
52. Nonaka D, Vongseththa K, Kobayashi J, *et al.*: **Public and private sector treatment of malaria in Lao PDR.** *Acta Trop.* 2009; 112(3): 283–7. [PubMed Abstract](#) | [Publisher Full Text](#)
53. Pongvongsa T, Ha H, Thanh L, *et al.*: **Joint malaria surveys lead towards improved cross-border cooperation between Savannakhet province, Laos and Quang Tri province, Vietnam.** *Malar J.* 2012; 11: 262. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
54. Shirayama Y, Phompida S, Kuroiwa C: **Monitoring malaria control in Khammouane province, Laos: an active case detection survey of *Plasmodium falciparum* malaria using the Paracheck rapid diagnostic test.** *Trans R Soc Trop Med Hyg.* 2008; 102(8): 743–50. [PubMed Abstract](#) | [Publisher Full Text](#)
55. Ministry of Health and Lao Statistics Bureau: **Lao Social Indicator Survey 2011-12.** Vientiane, Lao PDR; 2012. [Reference Source](#)
56. Al-Adhroey AH, Nor ZM, Al-Mekhlafi HM, *et al.*: **Opportunities and obstacles to the elimination of malaria from Peninsular Malaysia: knowledge, attitudes and practices on malaria among aboriginal and rural communities.** *Malar J.* 2010; 9: 137. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
57. Thandar MM, Kyaw MP, Jimba M, *et al.*: **Caregivers' treatment-seeking behaviour for children under age five in malaria-endemic areas of rural Myanmar: a cross-sectional study.** *Malar J.* 2015; 14: 1. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
58. Xu JW, Xu QZ, Liu H, *et al.*: **Malaria treatment-seeking behaviour and related factors of Wa ethnic minority in Myanmar: a cross-sectional study.** *Malar J.* 2012; 11: 417. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
59. Lwin MM, Sudhinaraset M, San AK, *et al.*: **Improving malaria knowledge and practices in rural Myanmar through a village health worker intervention: a cross-sectional study.** *Malar J.* 2014; 13: 5. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
60. Richards AK, Banek K, Mullany LC, *et al.*: **Cross-border malaria control for internally displaced persons: observational results from a pilot programme in eastern Burma/Myanmar.** *Trop Med Int Health.* 2009; 14(5): 512–21. [PubMed Abstract](#) | [Publisher Full Text](#)
61. PSI/Myanmar AG: **Household Survey: Baseline The Republic of the Union of Myanmar 2012 AMTR Survey Report.** PSI; 2012. [Reference Source](#)
62. Kyawt-Kyawt-Swe, Pearson A: **Knowledge, attitudes and practices with regard to malaria control in an endemic rural area of Myanmar.** *Southeast Asian J Trop Med Public Health.* 2004; 35(1): 53–62. [PubMed Abstract](#)
63. Ministry of National Planning and Economic Development and Ministry of Health M: **Myanmar Multiple Indicator Cluster Survey 2009 - 2010 Final Report.** Nay Pyi Taw, Myanmar: Ministry of National Planning and Economic Development and Ministry of Health, Myanmar; 2011. [Reference Source](#)
64. Sreeramareddy CT, Shankar RP, Sreekumaran BV, *et al.*: **Care seeking behaviour for childhood illness—a questionnaire survey in western Nepal.** *BMC Int Health Hum Rights.* 2006; 6: 7. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
65. Ministry of Health and Population (MOHP) [Nepal] NE, and ICF International Inc: **Nepal Demographic and Health Survey 2011.** Kathmandu, Nepal: Ministry of Health and Population, New ERA, and ICF International, Calverton, Maryland; 2012. [Reference Source](#)
66. Central Bureau of Statistics: **Nepal Multiple Indicator Cluster Survey 2010, Mid- and Far Western Regions, Final Report.** Kathmandu: Central Bureau of Statistics and UNICEF Nepal; 2012. [Reference Source](#)
67. Central Bureau of Statistics: **Nepal Multiple Indicator Cluster Survey 2014, Final Report.** Kathmandu, Nepal: Central Bureau of Statistics and UNICEF Nepal; 2015. [Reference Source](#)
68. Rehman A, Shaikh BT, Ronis KA: **Health care seeking patterns and out of pocket payments for children under five years of age living in Katchi Abadis (slums), in Islamabad, Pakistan.** *Int J Equity Health.* 2014; 13: 30. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
69. Zaidi SS, Seidlein LV, Nizami SQ, *et al.*: **Health care utilization for diarrhea and fever in 4 urban slums in Karachi.** *J Coll Physicians Surg Pak.* 2006; 16(4): 245–8. [PubMed Abstract](#)
70. National Institute of Population Studies (NIPS) [Pakistan] and ICF International: **Pakistan Demographic and Health Survey 2012-13.** Islamabad, Pakistan, and Calverton, Maryland, USA: NIPS and ICF International; 2013. [Reference Source](#)
71. Sindh Bureau of Statistics and UNICEF: **Sindh Multiple Indicator Cluster Survey 2014, Final Report.** Karachi, Pakistan: Sindh Bureau of Statistics and UNICEF; 2015. [Reference Source](#)
72. Bureau of Statistics PaDD, Government of the Punjab: **Multiple Indicator Cluster Survey, Punjab 2011.** Bureau of Statistics, Planning and Development Department, Government of the Punjab; 2012. [Reference Source](#)
73. Matsumoto-Takahashi EL, Tongol-Rivera P, Villacorte EA, *et al.*: **Patient Knowledge on Malaria Symptoms Is a Key to Promoting Universal Access of Patients to Effective Malaria Treatment in Palawan, the Philippines.** *PLoS One.* 2015; 10(6): e0127858. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
74. Espino F, Manderson L: **Treatment seeking for malaria in Morong, Bataan, the Philippines.** *Soc Sci Med.* 2000; 50(9): 1309–16. [PubMed Abstract](#) | [Publisher Full Text](#)
75. Philippine Statistics Authority (PSA) [Philippines] all: **Philippines National Demographic and Health Survey 2013.** Manila, Philippines, and Rockville, Maryland, USA: PSA and ICF International; 2014. [Reference Source](#)
76. Dulhunty JM, Yohannes K, Kourleoutov C, *et al.*: **Malaria control in central Malaita, Solomon Islands 2. Local perceptions of the disease and practices for its treatment and prevention.** *Acta Trop.* 2000; 75(2): 185–96. [PubMed Abstract](#) | [Publisher Full Text](#)
77. Attanayake N, Fox-Rushby J, Mills A: **Household costs of 'malaria' morbidity: a study in Matale district, Sri Lanka.** *Trop Med Int Health.* 2000; 5(9): 595–606. [PubMed Abstract](#) | [Publisher Full Text](#)
78. Reilley B, Abeyasinghe R, Pakianathar MV: **Barriers to prompt and effective treatment of malaria in northern Sri Lanka.** *Trop Med Int Health.* 2002; 7(9): 744–9. [PubMed Abstract](#) | [Publisher Full Text](#)
79. Sonkong K, Chaikien S, Neave P, *et al.*: **Factors affecting delay in seeking treatment among malaria patients along Thailand-Myanmar border in Tak Province, Thailand.** *Malar J.* 2015; 14: 3. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
80. Chaiwan J, Sudathip P, Khantiku N, *et al.*: **Understanding malaria prevention and treatment strategies among migrants in Thailand's Cambodia and Myanmar border areas.** *Joint International Tropical Medicine Meeting 2014; 3/11/14;* Bangkok, Thailand. 2014. [Reference Source](#)
81. NSO U, MOPH, NHSO, THPF, IHPP: **Thailand Multiple Indicator Survey 2012.** Bangkok, Thailand: NSO, UNICEF, MOPH, NHSO, THPF, IHPP; 2013. [Reference Source](#)
82. Ministry of Health GoV: **Vanuatu Multiple Indicator Cluster Survey 2007, Final Report.** Port Vila, Vanuatu: Ministry of Health, Government of Vanuatu; 2008. [Reference Source](#)
83. Okumura J, Wakai S, Umenai T: **Drug utilisation and self-medication in rural communities in Vietnam.** *Soc Sci Med.* 2002; 54(12): 1875–86. [PubMed Abstract](#) | [Publisher Full Text](#)
84. Erhart A, Thang ND, Bien TH, *et al.*: **Malaria epidemiology in a rural area of the Mekong Delta: a prospective community-based study.** *Trop Med Int Health.* 2004; 9(10): 1081–90. [PubMed Abstract](#) | [Publisher Full Text](#)
85. Morrow M, Nguyen QA, Caruana S, *et al.*: **Pathways to malaria persistence in remote central Vietnam: a mixed-method study of health care and the community.** *BMC Public Health.* 2009; 9: 85. [PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
86. General Statistics Office (GSO): **Viet Nam Multiple Indicator Cluster Survey 2011, Final Report.** Ha Noi, Viet Nam: General Statistics Office (GSO); 2011. [Reference Source](#)
87. General Statistics Office and UNICEF: **Viet Nam Multiple Indicator Cluster Survey 2014, Final Report.** Ha Noi, Viet Nam: General Statistics Office and UNICEF; 2015. [Reference Source](#)

88. Dondorp AM, Smithuis FM, Woodrow C, *et al.*: **How to Contain Artemisinin- and Multidrug-Resistant *Falciparum* Malaria.** *Trends Parasitol.* 2017; **33**(5): 353–63.  
[PubMed Abstract](#) | [Publisher Full Text](#)
89. Kumar A, Valecha N, Jain T, *et al.*: **Burden of malaria in India: retrospective and prospective view.** *Am J Trop Med Hyg.* 2007; **77**(6 Suppl): 69–78.  
[PubMed Abstract](#) | [Publisher Full Text](#)
90. Hanandita W, Tampubolon G: **Geography and social distribution of malaria in Indonesian Papua: a cross-sectional study.** *Int J Health Geogr.* 2016; **15**: 13.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
91. Yiengprugsawan V, Lim LL, Carmichael GA, *et al.*: **Tracking and decomposing health and disease inequality in Thailand.** *Ann Epidemiol.* 2009; **19**(11): 800–7.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
92. Hay SI, Gething PW, Snow RW: **India's invisible malaria burden.** *Lancet.* 2010; **376**(9754): 1716–7.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
93. International Institute for Population Sciences (IIPS) and ICF: **National Family Health Survey (NFHS-4), 2015-16: India.** Mumbai, India: IIPS; 2017.  
[Reference Source](#)
94. Undurraga EA, Halasa YA, Shepard DS: **Use of expansion factors to estimate the burden of dengue in Southeast Asia: a systematic analysis.** *PLoS Negl Trop Dis.* 2013; **7**(2): e2056.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
95. Murray CJ, Ortblad KF, Guinovart C, *et al.*: **Global, regional, and national incidence and mortality for HIV, tuberculosis, and malaria during 1990-2013: a systematic analysis for the Global Burden of Disease Study 2013.** *Lancet.* 2014; **384**(9947): 1005–70.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
96. Griffin JT, Ferguson NM, Ghani AC: **Estimates of the changing age-burden of *Plasmodium falciparum* malaria disease in sub-Saharan Africa.** *Nat Commun.* 2014; **5**: 3136.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
97. Hay SI, Okiro EA, Gething PW, *et al.*: **Estimating the global clinical burden of *Plasmodium falciparum* malaria in 2007.** *PLoS Med.* 2010; **7**(6): e1000290.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)
98. Helb DA, Tetteh KK, Felgner PL, *et al.*: **Novel serologic biomarkers provide accurate estimates of recent *Plasmodium falciparum* exposure for individuals and communities.** *Proc Natl Acad Sci U S A.* 2015; **112**(32): E4438–47.  
[PubMed Abstract](#) | [Publisher Full Text](#) | [Free Full Text](#)

# Open Peer Review

Current Peer Review Status: ? ?

---

## Version 1

Reviewer Report 31 May 2019

<https://doi.org/10.21956/wellcomeopenres.16544.r35408>

© 2019 Walker P. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution Licence](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



**Patrick Walker**

Department of Infectious Disease Epidemiology, Imperial College London, London, UK

This article concerns a fundamental topic relevant to malaria control in the Asia-Pacific: what is the actual burden and how has it changed in the face of interventions? It is clearly a substantial piece of work and analysis and I agree wholeheartedly with their conclusions around the difficulties of this process and the benefits of more regular reporting and surveys of treatment seeking behaviour. However, I have some quite major concerns about the methodology as it currently stands and, as a result, the extent to which the estimates are a reasonable reflection of burden, particularly in places with imperfect diagnosis and where a substantial proportion of individuals access care within the private sector.

Inevitably newly derived estimates of malaria burden will be compared with those that exist already, particularly those released by WHO in their annual malaria report. Alternative estimates should be welcomed – there's more than one good way to cook an egg - particularly if the methods used reflect an alternative, but justifiable, way to handle the uncertainty which, for estimation on this scale, is likely to be substantial. However, I'm confused as to why in this analysis, when comparing their estimates to WHO, the authors use those from the 2016 World Malaria Report, rather than the more recently released estimates in the 2018 version[ref-1]. I'm going to advocate that the authors amend their analysis to reflect these more up-to-date estimates for two reasons:

1) I disagree with the authors when they make the following statement: "In 2017, annual country-level estimates were published for 2010–2016. These were different to those published previously and were substantially revised with new estimates for 2010–2017 in WMR 2018. These gaps and changes over time make it impossible to reconstruct an annual trend in estimated incidence by country since 2000 from these reports". I think that revising historical estimates as new data and methods become available is a hugely important process and should be welcomed (not least because it's precisely what the authors themselves are attempting to do), as long as discrepancies are understood and carefully investigated this process should make reconstructing annual trends more reliable rather than impossible and subsequent revisions, or attempts to improve upon estimates, should use the most up-to-date methodology and data as the gold standard. The current estimates by WHO also have estimates for each year.

2) The latest version of the WMR has a comprehensive section which detailed the methods used to obtain

estimates, making understanding differences between the WHO estimates and those in this paper far more straightforward (especially as they are often using the same data inputs). It reveals two key differences from the methods used by the authors – firstly WHO attempts to account for individuals with suspected malaria who do not receive a diagnostic test by extrapolating the test positivity for malaria in those tested, secondly they provide a clear accounting of how private sector is incorporated. In contrast the authors in this analysis do not include individuals suspected for malaria who are not tested on the basis that:

“It was decided not to include unconfirmed cases in the present analysis as mandatory diagnostic testing for malaria has been widely adopted in health facilities in the Asia-Pacific, as recommended by WHO since 2010, and those who do not attend a health facility would be included in the proportion of unrecorded cases.”

This seems a very hard argument to sustain without data – inevitably there is going to be a gap between policy (mandatory testing) and its implementation. It doesn't take long to find examples where this isn't the case (for example in PNG in 2014 about 40% of children with fever accessed care, of these about 25% - 10% of all fevers - received a test for malaria<sup>2</sup>). Clearly WHO's method where they extrapolate test positivity in the 25% receiving a test to the remaining 75% accessing care contains assumptions but personally I would pick that approach over the implicit assumption the authors make that there is no burden to be accounted for within that 75%...

In contrast to the WHO who now give a clear accounting for how private sector care seeking (and uncertainty) is incorporated, in particular for India where this is done at a sub-national level, here the authors incorporate all of this uncertainty (private/public/seek care/don't seek care etc.) within a single term  $P_{rec}$  and provide no formula for how either the median or range of these values are calculated (at least that I can find – many apologies if I missed it buried in the S.I! – if so I would suggest moving to main text).

A more careful accounting for this calculation by the authors would allow the reader to assess the reasons and merits of the major discrepancies between some estimates: for example, in my opinion, the 10 fold, >10 million case discrepancy between the estimates of WHO and the authors can, and should, be explained and investigated in more detail than simply because “[WHO] include numbers of unconfirmed cases”. I agree that some other discrepancies seem harder to explain (e.g. Nepal) from WMR 2016 but it is noticeable in the Nepal example that the estimates for WMR 2018 are broadly in-line with the authors' which I think is another argument for amending the analysis to contrast with the most up-to-date version.

Other suggestions/questions:

When the authors can find no estimate for reporting completeness they “assume 100% to give the most conservatively high burden of disease” – apart from questions as to why it is necessarily advantageous to be conservatively high, and that other assumptions do not err towards high burden – is this not contrarily the least conservative assumption in that respect? From the formula and intuition I would guess assuming less complete reporting would revise estimates upwards? Apologies again if I've misconstrued.

The authors do what appears to be a highly comprehensive review of the literature but my guess is that, as it was done in 2015 and given publication timelines, there will be a lot of additional data out there now, particular for 2015 estimates. Even more recent estimates might have added value, particularly for settings like PNG where no previous data was found (e.g. the 2016-17 survey referenced<sup>2</sup>). I'd recommend repeating the search and updating.

It's really not clear how uncertainty is accounted for, as well as having more information as to how the % of cases reported is obtained from the literature I'd like to know how the range was defined and how uncertainty is propagated throughout the analysis. In particular for their region-wide total upper and lower bounds of burden they simply sum the upper and lower bounds of each individual country. I don't think this is the optimal way to represent uncertainty (akin to representing the uncertainty range of 1000 coin tosses as [0-1000], in some ways it's true but it isn't very useful...). Even doing something simple like drawing values from triangle distributions between ranges of uncertainty and representing 95% interval would probably give more informative overall indication of the likely range.

## References

1. World Health Organisation: World malaria report 2018. *WHO*. 2019.
2. Hetzel MW, Saweri OPM, Kuadima JJ, Smith I Ura, Tandrapah A, Jamea-Maiasa S, Siba PM, Pulford J: National malaria control programme evaluation Papua New Guinea malaria indicator survey 2016-2017: Malaria prevention, infection, and treatment. 2018. [Accessed 31st May 2019]. [Reference Source](#)

**Is the work clearly and accurately presented and does it cite the current literature?**

Partly

**Is the study design appropriate and is the work technically sound?**

Partly

**Are sufficient details of methods and analysis provided to allow replication by others?**

No

**If applicable, is the statistical analysis and its interpretation appropriate?**

No

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Partly

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Mathematical modelling and data analysis applied to malaria epidemiology.

**I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.**

Reviewer Report 23 April 2019

<https://doi.org/10.21956/wellcomeopenres.16544.r35191>



© 2019 Espino F et al. This is an open access peer review report distributed under the terms of the [Creative Commons Attribution Licence](#), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.



**Fe-Esperanza-Caridad J. Espino**

Department of Parasitology, Research Institute for Tropical Medicine, Department of Health, Muntinlupa City, Philippines

**Alvin Tan**

Department of Epidemiology and Biostatistics, Research Institute for Tropical Medicine, Department of Health, Muntinlupa City, Philippines

The manuscript is a comprehensive evaluation of the disease estimates of the only global official source of country malaria data, the WHO World Malaria Report. The authors have also raised in their discussion a number of factors that affect quality data not only for malaria but for other health indicators. They estimated malaria disease burden using the information obtained from the WHO World Malaria Report during the period after the introduction of two interventions that have positively affected disease burden in the Asia Pacific region – deployment of malaria RDTs and ACTs.

1. The heterogeneity of malaria among, and within countries of the Asia Pacific is becoming more pronounced, and it is likely that countries might give less attention to the quality of sub-national malaria data as disease reporting approaches zero cases. What other routinely collected data at sub-national facilities, including community health facilities, could possibly serve as an indicator of coverage? Could the authors provide what are there to be learned from other disease programs?
2. Details of WHO estimation described in 2008 WMR discloses that the Organization uses SPR in its equation. Because countries test for malaria in all individuals who are suspected to have the disease (i.e., have fever), the SPR is dependent upon disease prevalence. The trend of the confirmed number of malaria cases is towards overall decrease in numbers. How could this have affected the differences between WHO overall estimates and the authors' (illustrated in Figure 2)? Further, the sensitivity of the test procedures as proposed in the manuscript is better than positivity rates in Cibulskis' article (Cibulskis et al., 2007<sup>1</sup>; and see WMR 2008) since positivity rates are greatly affected by disease prevalence whereas sensitivity is inherent to the test.
3. WHO WMR 2008 (page 153/215) adjusts the for the number of positive-parasite cases. The authors define  $B_{\text{confTOT}}$  as the number of confirmed malaria case in the WMR. Thus, when estimating for true burden of malaria, could the authors clarify whether  $B_{\text{TRUE}}$  is a value that has been adjusted two times?
4. What was the purpose of using the incidence estimates from the WMR? Was it to demonstrate the mechanics of the proposed formulae? Or to estimate malaria burden? If it was to estimate malaria burden, there might have been an accidental overestimate as the WMR estimates were already adjusted for reporting completeness and health seeking patterns. This could also be one of the reasons why the estimates for the manuscript are almost always higher than the WMR figures even if some of the assumptions used (particularly 100% reporting rate) was supposed to underestimate the burden.

## References

1. Cibulskis RE, Bell D, Christophel EM, Hii J, Delacollette C, Bakayita N, Aregawi MW: Defining and

Defeating the Intolerable Burden of Malaria III: Progress and Perspectives: Supplement to Volume 77(6). 2007; **77** (6).

**Is the work clearly and accurately presented and does it cite the current literature?**

Yes

**Is the study design appropriate and is the work technically sound?**

Yes

**Are sufficient details of methods and analysis provided to allow replication by others?**

No

**If applicable, is the statistical analysis and its interpretation appropriate?**

I cannot comment. A qualified statistician is required.

**Are all the source data underlying the results available to ensure full reproducibility?**

Yes

**Are the conclusions drawn adequately supported by the results?**

Partly

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** I am a pediatric infectious diseases specialist with a PhD in tropical health. I have been involved in projects regarding malaria surveillance and reporting of the Philippines' Department of Health. My co-referee has an MSc in epidemiology.

**We confirm that we have read this submission and believe that we have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however we have significant reservations, as outlined above.**

---