Provider and household costs of Plasmodium vivax malaria episodes: a multicountry comparative analysis of primary trial data


Objective To determine household and health-care provider costs associated with Plasmodium vivax infection across a range of endemic settings.

Methods We collected cost data alongside three multicentre clinical trials of P. vivax treatment in Afghanistan, Brazil, Colombia, Ethiopia, Indonesia, Philippines, Peru, Thailand and Viet Nam conducted between April 2014 to December 2017. We derived household costs from trial participant surveys administered at enrolment and again 2 weeks later to determine the costs of treatment and transportation, and the number of days that patients and their household caregivers were unable to undertake their usual activities. We determined costs of routine care by health-care providers by micro-costing the resources used to diagnose and treat P. vivax at the study sites.

Findings The mean total household costs ranged from 8.7 United States dollars (US$; standard deviation, SD: 4.3) in Afghanistan to US$ 254.7 (SD: 148.4) in Colombia. Across all countries, productivity losses were the largest household cost component, resulting in mean indirect costs ranging from US$ 5.3 (SD: 3.0) to US$ 220.8 (SD: 158.40). The range of health-care provider costs for routine care was US$ 3.6–6.6. The cost of administering a glucose-6-phosphate-dehydrogenase rapid diagnostic test, ranged from US$ 0.9 to 13.5, consistently lower than the costs of the widely-used fluorescent spot test (US$ 6.3 to 17.4).

Conclusion An episode of P. vivax malaria results in high costs to households. The costs of diagnosing and treating P. vivax are important inputs for future cost-effectiveness analyses to ensure optimal allocation of resources for malaria elimination.

Introduction

Outside Sub-Saharan Africa, Plasmodium vivax is now the predominant cause of malaria, affecting 14.0 million patients in 2016. While cost-effectiveness analyses can inform the efficient provision of health-care interventions, information on the costs for providers, patients and their households should be available. The costs of P. vivax malaria infection are potentially different from those infection caused by P. falciparum, since P. vivax forms liver stages (hypnozoites), which lie dormant for weeks or months after the primary infection before reactivating to cause symptomatic infections (relapses). Hence, one infectious mosquito bite can result in multiple episodes, with the risk and frequency of relapses varying significantly between geographical regions.

Accordingly, the clinical management of patients with P. vivax requires a radical cure with a drug regimen that kills both the blood and liver stages of the parasite. The only widely available compound with activity against the dormant liver stages is primaquine, which is usually prescribed as a 14-day regimen. The efficacy of primaquine is dependent upon the total weight-adjusted dose administered. Patents’ adherence to 14-day primaquine courses varies considerably and failure to complete a full course is common. Therefore, adherence and effectiveness can potentially be improved by administering the same total dose while reducing the duration of treatment. In a recent multicentre clinical trial, the safety and efficacy of a 7-day primaquine regimen was compared with a 14-day primaquine and placebo regimen (short-course primaquine trial). Clinical trials have also been conducted of tafenoquine compared to a 14-day primaquine and placebo regimen (tafenoquine trials).

Tafenoquine is a single-dose drug for radical cure of malaria that has recently received regulatory approvals in Australia and the United States of America, with further submissions underway in malaria-endemic countries. Both drugs can cause haemolysis in individuals with glucose-6-phosphate-dehydrogenase (G6PD) deficiency, an inherited enzymopathy. For this reason, the World Health Organization (WHO) treatment guidelines recommend that, where possible, G6PD status should be ascertained in all patients before administration. Due to operational and financial constraints, screening...
for G6PD deficiency is rarely offered. This may change as new rapid diagnostic tests become more widely available to facilitate point-of-care testing. For G6PD-deficient individuals, an 8-week course of weekly primaquine doses is recommended with monitoring for anaemia.

Little research has been conducted on the costs of diagnosing and treating P. vivax malaria. In a recent review, only nine relevant studies were identified with varying percentages of cases due to P. vivax. Given the increasing options available for testing and radical cure treatment, cost surveys were included in the study design of the short-course primaquine trial and adapted to the tafenoquine trials. We aimed to describe the costs of treating uncomplicated P. vivax malaria in a range of endemic settings using data from both households and health-care providers, collected alongside these trials. The results can inform economic evaluation and policy-making for P. vivax malaria testing and treatment strategies.

### Methods

#### Household costs

We collected household cost data at study sites in nine countries: Afghanistan, Brazil, Colombia, Ethiopia, Indonesia, Philippines, Peru, Thailand and Viet Nam (Box 1). Using questionnaires translated into local languages, patients, or informants on the patients’ behalf, were interviewed by study staff at enrolment (day 0) and again 2 weeks later. We analysed data on the direct and indirect costs to the patient's household for individuals with P. vivax malaria. Here, we report only the costs from the first episode of malaria, to minimize bias arising due to changes in treatment-seeking behaviour that might result from being enrolled in the study.

Direct costs included all out-of-pocket expenditure for the entire episode for the patient’s household: (i) treatment seeking: the cost of treatment-seeking before enrolment in the study (medications, tests and fees); (ii) transport for treatment seeking: the cost of transportation for treatment seeking before enrolment in the study; (iii) visit cost: payments for treatment at the study health-care facility (medications, tests and fees); and (iv) transport cost: the cost of transportation to the health-care facility (medications, tests and transport for treatment seeking before, during or after treatment: the cost of treatments, tests and fees).

#### Provider costs

We collected data on health-care provider costs only at four study sites in the short-course primaquine trial: Jalalabad in Afghanistan, Arba Minch in Ethiopia, North Sumatra in Indonesia and Dak-O in Viet Nam. Using data from clinic records and interviews with providers, we collected all costs of routine care and of potential additions to care for patients with P. vivax malaria, but not the costs of care related to the trial. Cost items included blood draws (finger prick or venous), malaria diagnosis (rapid diagnostic test and microscopy) and treatment (blood-stage and liver-stage), G6PD tests (rapid diagnostic test and fluorescent spot test) and the HemoCue test (HemoCue AB, Angelholm, Sweden) for anaemia. G6PD testing was not routine at any of the sites, so we calculated the cost of rapid diagnostic test and fluorescent spot test as additional costs. The site in Ethiopia was a research facility, so we adjusted inputs to reflect a routine clinical care setting.

We made the following assumptions about provider costs. One blood draw per patient would be sufficient for all tests undertaken. Since the throughput of malaria patients was generally low at all facilities, the fluorescent spot test would be used as a point-of-care test (i.e. only one test run in a batch). The fluorescent spot test consumables would be stored in a freezer (or a refrigerator with a −20 °C freezer compartment) as this offered a more conservative estimate of long-term costs. The annual number of malaria patients per facility was used for equipment throughputs. We combined the country-specific costs of diagnosis and treatment for P. vivax malaria with

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**Box 1. Clinical trial details in the multicentre study of the economic costs of P. vivax malaria episodes**

The design of the Improving the Radical Cure of Vivax trial has been previously described. The trial was conducted from 20 July, 2014 to 31 December, 2017. Outpatients in Afghanistan, Ethiopia, Indonesia and Viet Nam were treated with locally recommended schizontocidal treatment (chloroquine or dihydroartemisinin–piperaquine) and randomized to receive either 14 days of primaquine (total dose 7 mg/kg), 7 days of primaquine (total dose 7 mg/kg) followed by 7 days of placebo or 14 days of placebo. Patients were screened for glucose-6-phosphate-dehydrogenase (G6PD) deficiency before enrolment, and individuals with G6PD deficiency were excluded from the randomized study and given standard schizontocidal treatment plus eight doses of weekly primaquine. All patients gave informed consent before enrolment. Follow-up was 12 months.

In the Global Assessment of Tafenoquine Haemolytic Risk Trial and Dose and Efficacy Trial Evaluating of Chloroquine and Tafenoquine In Vivax Elimination trial, adult patients (≥17 years) with P. vivax malaria from Brazil, Cambodia, Colombia, Ethiopia, Peru, Philippines, Thailand and Viet Nam were treated with either 14-day primaquine (3.5 mg/kg) or single-dose tafenoquine (300 mg) and followed for 6 months. These trials were conducted from April 2014 to November 2016. No patients in Cambodia completed the cost survey. Patients were excluded if G6PD enzyme activity was less than 70%. In both these trials, patients were hospitalized for days 1–3 to evaluate drug safety; the costs related to this stay are not included here.

The surveys used to collect household cost data were similar for all trials, with some minor differences. The short-course primaquine trial asked about travel and payments for the current clinic while the tafenoquine trials asked about facilities where patients were diagnosed. For patient and caregiver time off due to illness, short-course primaquine surveys asked about usual activity whereas the tafenoquine trials asked about usual work. Patients specified the number of days off for themselves and caregivers in the short-course primaquine trial, whereas the tafenoquine trials had one category for more than 7 days. The tafenoquine trials did not ask what activity caregivers would normally be doing. The follow-up visit was on day 15 for the tafenoquine trials. For the short-course primaquine trial, this was day 13 for G6PD normal patients and day 14 for those with G6PD deficiency.

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*Economic costs of P. vivax malaria episodes*
the cost of patient visits using the WHO global cost database for an outpatient centre with beds.15,16

Analysis

We report all costs in United States dollars (US$) for the year 2016. We collected costs using local currencies, then adjusted them for inflation if from a different year,15,16 before conversion to US$.17 We also converted key unit entries were made: we assumed these were zero since treatment fees were paid by the study. For patients in the tafenoquine studies who reported more than 7 days of lost productivity, we assumed they had lost 8 days. All data are presented by country, pooling data from Ethiopia and Viet Nam, which were included in all the trials. We report the mean, standard deviation (SD), median and interquartile ranges for household-level costs and days lost per episode of malaria. For provider costs, point estimates are presented. The incremental costs of switching from fluorescent spot test to G6PD rapid diagnostic test are reported.

Ethical approval

Ethical approval for the original Improving the Radical Cure of Vivax Malaria protocol and included amendments (Version 7) was obtained from the following review boards: Oxford Tropical Research Ethics Committee OxTREC (Ref number 101413) and the Human Research Ethics Committee of the Northern Territory Department of Health, Australia HREC (Ref Number 131991). In addition local approvals were obtained from the Institutional Review Board, Ministry of Public Health, Afghanistan, the Health Research Ethics Committee, Faculty of Medicine University of Indonesia, Cipto Mangunkusumo Hospital, Jakarta, Indonesia, the Ministry of Health Evaluation Committee on Ethics in Biomedical Research Vietnam, the Institutional Scientific & Ethical Review Committee of the Ethiopian Public Health Institute, the National Research Ethics Review Committee, Ethiopia and the Institutional Review Board of the Columbia University Medical Centre, US. The Global Assessment of Tafenoquine Haemolytic Risk trial (NCT 02216123) and Dose and Efficacy Trial Evaluating Chloroquine and Tafenoquine In Vivax Elimination (NCT 01376167) studies are registered.

Results

Patient characteristics

Of 3159 patients enrolled in the studies, 2951 (93%) completed cost surveys at both the initial and follow-up visit: 2236 patients from the short-course primaquine trial and 715 from the tafenoquine trials (Fig. 1). Most patients were male (1897; 64%) and ≥ 15 years old (1980; 67%). The percentage of enrolled females in the tafenoquine trials (211 out of 715; 30%) was lower than in the short-course primaquine trial (843/2236, 38%). In the short-course primaquine trial, 43% (971/2236) were children aged < 15 years, with the proportion of children varying by country from 14% (46/334) in Viet Nam to 60% (211/354) in Afghanistan (Fig. 1). Since children younger than 17 years were excluded from the tafenoquine trials, only 33% (971/2951) of patients overall were children. Patients ranged in age from 10 months to 94 years.
**Household costs**

**Productivity losses**

Patients reported a mean loss of 3.5 days (SD: 3.1) from their usual activities over the entire episode of malaria (Table 1). More details of the data are available from the data repository.21 Of the 2883 patients who reported their usual activities, 1007 (35%) would have been at school, 436 (15%) were subsistence farmers, 391 (14%) missed paid employment, 378 (13%) would have been doing housework and 671 (23%) reported another activity. Most patients (78%, 2243/2883) reported needing someone to cut back on usual activities to care for them, with a mean loss of 1.8 days (SD: 2.8). In Viet Nam, 59% (221/377) of patients reported needing a caregiver, compared with 98% in both Brazil (204/208) and Peru (247/251). The highest mean number of lost days was in Colombia and the Philippines for both patients and caregivers (Table 1). Half (823/1633) of caregivers from the short-course primaquine trial reported that they would normally be doing housework, 216 (13%) were unable to farm, 101 (6%) missed school, 179 (11%) missed paid employment and 314 (19%) reported that they would be doing another activity (the tafenoquine trials did not ask about usual activities for caregivers). Further information on activities by country is available from the data repository.20 When multiplied by the GDP per capita for each country, these productivity losses resulted in mean indirect costs that ranged from US$ 5.3 (SD: 3.0) per episode in Afghanistan to US$220.8 (SD: 158.4) in Colombia (available from the data repository).21

**Treatment-seeking costs**

Overall, 1671 (57%) of the 2951 patients were seeking treatment for the first time. This proportion ranged widely by country from 0% (0/251) in Peru to 91% (322/354) in Afghanistan (available from the data repository).22 For this episode of malaria, 659 patients (22%) had sought treatment once before, 598 (20%) had sought treatment twice before and 23 (1%) had sought treatment three times before the enrolment visit. While many patients reported spending a mean of US$ 2 or less, patients in Colombia and Thailand spent a mean of US$ 19.2 (SD: 27.1) and US$22.0 (SD: 39.2), respectively (available from the data repository).21

While transportation to the study clinic cost over US$ 10 for a return journey in Brazil, Colombia and Thailand, these costs were low in most countries. Overall, 93% (2745/2951) of patients reported a journey of under 1 hour. The majority of those with long travel times were in Afghanistan, where 28% (99/354) reported journeys of over 1 hour to get to the clinic, with correspondingly higher mean transportation costs of US$ 3.1 (SD: 1.5).

Considering all transport and treatment costs, the mean direct household expenditure was US$ 6.6 (SD: 12.2), varying from US$ 1.6 (SD: 2.2) in the Philippines to US$ 35.3 (SD: 46.6) in Thailand (available from the data repository).21

**Total household costs**

The mean total costs to households due to illness (indirect costs from lost productivity plus direct costs of transportation and treatment) varied by country, ranging from US$ 8.7 (SD: 4.3) in Afghanistan to US$ 254.7 (SD: 148.4) in Colombia (available from the data repository).21 Costs were higher for women in Afghanistan, Ethiopia, Indonesia and Viet Nam and for men in Brazil and Peru. Viet Nam was the only country where no age-related differences were apparent, a likely reflection of nearly all patients being older than 15 years (available from the data repository).21

**Provider costs**

The total cost of routine care by healthcare providers per patient visit in the four settings ranged from US$ 3.6 in Afghanistan to US$ 6.6 in Indonesia (Table 2). The cost per test and associated laboratory processing time are available from the data repository.24 In these settings with relatively low patient throughputs, implementing fluorescent spot testing resulted in a cost range of US$ 6.3–17.4 compared with US$ 0.9–13.5 for G6PD rapid diagnostic tests. Some settings reported that fluorescent spot tests and G6PD rapid diagnostic tests had to be repeated for some patients, thereby increasing the costs. G6PD rapid diagnostic testing was consistently cheaper per patient than fluorescent spot testing, even in Indonesia where the unit cost of a G6PD rapid diagnostic test was US$ 13.0. Potential cost savings per test using a G6PD rapid diagnostic test instead of the fluorescent spot test ranged from US$ 3.5 in Indonesia to US$ 16.1 in Viet Nam. The cost of monitoring for anaemia with the HemoCue test ranged from US$ 1.2 in Viet Nam to US$ 3.0 in Ethiopia.

**Total costs**

Fig. 2 summarizes the total costs per *P. vivax* malaria episode in the nine countries, including all provider (direct) costs and the household direct and indirect costs. As shown, the indirect household costs due to productivity losses were

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**Table 1.** Productivity losses to patients and their caregivers due to an episode of *P. vivax* malaria illness in malaria-endemic settings in nine countries, 2014–2017

<table>
<thead>
<tr>
<th>Country</th>
<th>No. of clinical episodes</th>
<th>No. of days patient unable to do usual activities</th>
<th>No. of days caregiver was required</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean (SD)</td>
<td>Median (IQR)</td>
<td>Mean (SD)</td>
</tr>
<tr>
<td>Afghanistan</td>
<td>354</td>
<td>2.2 (1.3)</td>
<td>2.0 (1.5–3.0)</td>
</tr>
<tr>
<td>Brazil</td>
<td>276</td>
<td>1.3 (1.9)</td>
<td>1.0 (0.0–1.3)</td>
</tr>
<tr>
<td>Colombia</td>
<td>18</td>
<td>7.0 (5.4)</td>
<td>7.0 (3.0–11.0)</td>
</tr>
<tr>
<td>Ethiopia</td>
<td>618</td>
<td>3.3 (2.5)</td>
<td>2.5 (2.0–4.0)</td>
</tr>
<tr>
<td>Indonesia</td>
<td>982</td>
<td>3.8 (3.7)</td>
<td>3.0 (0.5–5.0)</td>
</tr>
<tr>
<td>Peru</td>
<td>251</td>
<td>6.3 (2.5)</td>
<td>6.0 (5.0–8.0)</td>
</tr>
<tr>
<td>Philippines</td>
<td>6</td>
<td>9.8 (5.2)</td>
<td>10.0 (4.0–15.0)</td>
</tr>
<tr>
<td>Thailand</td>
<td>69</td>
<td>4.1 (2.7)</td>
<td>5.0 (2.0–6.0)</td>
</tr>
<tr>
<td>Viet Nam</td>
<td>377</td>
<td>3.2 (2.5)</td>
<td>2.5 (1.5–4.0)</td>
</tr>
<tr>
<td>Overall</td>
<td>2951</td>
<td>3.5 (3.1)</td>
<td>3.0 (1.0–5.0)</td>
</tr>
</tbody>
</table>

IQR: interquartile range; SD: standard deviation.

Notes: We collected data alongside three multicentre clinical trials of *P. vivax* malaria treatment from April 2014 to December 2017.24 Patients reported the length of time they could not perform usual activities due to illness and the length of time caregivers stopped doing usual activities to care for them. We pooled data from different trials in Ethiopia and Viet Nam. More details are available from the data repository.21

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**Table 2.** Productive losses to patients and their caregivers due to an episode of *P. vivax* malaria illness in nine countries, 2014–2017

<table>
<thead>
<tr>
<th>Country</th>
<th>No. of clinical episodes</th>
<th>No. of days patient unable to do usual activities</th>
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IQR: interquartile range; SD: standard deviation.

Notes: We collected data alongside three multicentre clinical trials of *P. vivax* malaria treatment from April 2014 to December 2017.24 Patients reported the length of time they could not perform usual activities due to illness and the length of time caregivers stopped doing usual activities to care for them. We pooled data from different trials in Ethiopia and Viet Nam. More details are available from the data repository.21
Transportation
Productivity losses

Table 2. Costs to health-care providers of routine care for a patient with *P. vivax* malaria illness in four malaria-endemic settings

<table>
<thead>
<tr>
<th>Care item</th>
<th>Afghanistan</th>
<th>Ethiopia</th>
<th>Indonesia</th>
<th>Viet Nam</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patient visit</td>
<td>1.68</td>
<td>0.98</td>
<td>0.08</td>
<td>1.74</td>
</tr>
<tr>
<td>Malaria diagnosis</td>
<td>1.14</td>
<td>3.51</td>
<td>2.86</td>
<td>3.47</td>
</tr>
<tr>
<td>Blood-stage drugs</td>
<td>0.28</td>
<td>0.36</td>
<td>2.65</td>
<td>0.27</td>
</tr>
<tr>
<td>Liver-stage drugs</td>
<td>0.19</td>
<td>NA*</td>
<td>0.43</td>
<td>0.43</td>
</tr>
<tr>
<td>Other medications</td>
<td>0.33</td>
<td>0.43</td>
<td>0.59</td>
<td>0.09</td>
</tr>
<tr>
<td>Total cost</td>
<td>3.62</td>
<td>5.28</td>
<td>6.61</td>
<td>6.01</td>
</tr>
</tbody>
</table>

* Liver-stage drugs are not included as routine care in Ethiopia.

Notes: We collected data on health care provider costs on the typical costs per *P. vivax* malaria patient alongside a multicentre clinical trial in the study countries. Basic visit costs were taken from the World Health Organization CHOICE unit cost estimates for service delivery at an outpatient centre with beds. Diagnosis costs included microscopy in Afghanistan, Ethiopia and Viet Nam, plus rapid diagnostic test for malaria in Indonesia and Viet Nam. Costs of blood-stage drugs included dihydroartemisinin–piperaquine in Indonesia and chloroquine in Viet Nam. In Afghanistan, 90% received chloroquine tablets and 10% received chloroquine syrup. In Ethiopia, 78% of patients received chloroquine tablets, 20% received chloroquine syrup and 2% of patients received artether–lumefantrine. Liver-stage drugs included low-dose primaquine for all patients in Indonesia and Viet Nam, while 50% of patients received low-dose primaquine in Afghanistan. Costs of other medications included drugs frequently prescribed for malaria (but not antimalarials) were multiplied by the percentage of patients receiving those medications. All drug costs are for adult prescriptions. More details of the test costs are available from the data repository.

Fig. 2. Total mean costs per episode of *P. vivax* malaria in malaria-endemic settings in nine countries


Notes: We collected household and provider costs using local currency and adjusted to 2016 US$. Cost components include household visit costs (including treatment seeking) and transportation (for the visit and treatment seeking), indirect costs to households (productivity losses) and direct costs of health-care providers (visit including diagnosis and treatment of *P. vivax* malaria). Household cost data were collected alongside three multicentre clinical trials of *P. vivax* malaria. Unlike previous studies, the costs reported here are due solely to individuals infected with *P. vivax*. The mean total household cost per episode varied considerably (from around US$ 9 to US$ 255), reflecting differences in both the duration of time off normal activities and GDP per capita in the country. When productivity losses are excluded, these costs fall to around US$ 2 to US$ 35. While time is a scarce resource with economic value, productivity losses are rarely included in economic evaluations as costs to society as whole (i.e. including costs to patients and their households) are not often presented. While the costs from the health-care provider perspective is appropriate for priority-setting within the health sector, indirect productivity losses can be the larger cost component for households.

Even when days lost to illness and caregiving are captured by surveys, the cost of these days can be difficult to value. The impact of ill health on members of the household (spillover effects) is a rapidly evolving area in health economics and a consensus has not been reached on whether to include spillover effects in economic evaluations, even when taking the societal perspective. A recent review on measuring and valuing time losses due to informal caring demonstrates that much of the thinking in this area has been focused on chronic conditions in developed nations. Changing the scope of economic evaluations could exacerbate inequalities in health and access to health-care technologies. Our results rely on revealed preference methods that focus on the monetary value of time losses to the caregivers without consideration of (dis)utility due to the patients’ illness; accordingly, there is no risk of double counting.

The most common approach for valuing the time of those not in paid employment is to collect information on daily wages for those in paid employment and use the average cost as a shadow wage. Most patients in this...
study were not in paid employment, so this approach would provide limited data. Reassur-
ingly, a study in Timika, Indonesia found a shadow wage of US$11 (2014), demonstrating that our use of one GDP per capita per day of US$10 (2016) may be conservative. Similar methods of valuation are being implemented in other global health studies, and it is important to note that this figure is equivalent to 1/365th of a disability-adjusted life-year when using a willingness-to-pay threshold of one GDP per capita.

Malaria exerts a greater burden on poorly resourced communities and families who are likely to have lower shadow wages; hence, the use of GDP per capita per day for lost wages may have overestimated the indirect costs of P. vivax malaria. Days lost to illness can be catastrophic for a family reliant on subsistence farming and may contribute to a cycle of poverty. We assumed no one else within a household made up the lost income, although this could be a mitigating strategy. The valuation of productivity losses may be overestimated for children; however, this would be offset by decreased performance at school, which were excluded. A study in Ethiopia also found significant differences in indirect and total costs of care by malaria species. Since P. vivax malaria is a disease epitomized by recurrent episodes and long-term morbidity with limited direct mortality, quantifying and valuating these productivity losses are essential for a comprehensive analysis of the economic burden of the disease. Indeed, previous research indicated that countries with a high percentage of the population at risk of P. falciparum infection were likely to experience reductions in growth as great as 2% GDP per capita. Testing for G6PD deficiency, as recommended by WHO, resulted in additional costs ranging from US$1 for the rapid diagnostic test in Ethiopia and Viet Nam to US$17 for the fluorescent spot test in Indonesia and Viet Nam. At US$6–17 per test, the fluorescent spot test is an expensive option. Due to the limited shelf life of the reagents, the cost per patient will increase as the number of cases at a facility decrease. While this would be less expensive in the short-term, the overall cost per test would increase as the reagents last twice as long in the freezer unless the refrigerator has a –20 °C compartment as the facilities in Ethiopia and Viet Nam did. While the G6PD rapid diagnostic test was consistently less expensive than the fluorescent spot test, the cost savings per test given were dependent on the in-country costs of consumables, ranging from US$4 per person in Indonesia to US$16 in Viet Nam. In Indonesia, where primaquine is prescribed without G6PD testing, the incremental cost per person treated is likely to be a major obstacle to convincing policy-makers to implement routine testing. Furthermore, if primaquine treatment is to be routinely administered, the use of a HemoCue test (or equivalent) might be viewed as necessary to monitor patients for anaemia. While it is a relatively inexpensive test (US$3 or less), it may be required more than once per P. vivax episode.

This study has several limitations. Household visit costs may have been lower in a research context than in routine care. Cost data were missing for 7% of the patients in the short-course primaquine trial and 8% of patients in the tafenoquine trials, potentially creating a bias. For example, fewer patients in Afghanistan returned at day 13, which could reflect higher travel costs for those individuals. Furthermore, the tafenoquine trials required hospitalization, which may have created a bias in those who enrolled. While we have data from a large and diverse set of sites in nine countries, these sites may not fully reflect the considerable heterogeneity within countries. Productivity losses were a key driver of the total costs, but there is no consensus on how best to valuate these, particularly for children in whom the incidence of P. vivax malaria is highest in many settings.

In conclusion, the economic burden of P. vivax malaria is substantial at the household level, with the largest component arising from lost productivity. Ensuring safe radical cure through G6PD rapid diagnostic testing would reduce this burden, but uptake of tests may be impeded if associated with high test costs. We propose that this large collection of P. vivax malaria costs is an important resource with which to embark upon more robust cost-effectiveness analyses in the future.

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Competing interests: JAG and GK are employed by and hold stock in GlaxoSmithKline. KG was employed by GlaxoSmithKline and holds stock in GlaxoSmithKline, Bristol Myers Squibb and AstraZeneca.
Objective Determining the costs, for the menages and the prestataires of soins, associated to the infection by Plasmodium vivax vivax in different zones endémiques.

Methods We have collected the data on the costs in the use of 3 medical centers in the treatment of Plasmodium vivax menés in Afghanistan, in Brazil, in Colombia, in Ethiopia, in Indonesia, in the Philippines, in Peru in Thailand and in the Viet Nam from April 2014 and December 2017. We have calculated the costs for the ménages to partir d’enquêtes réalisées auprès des participants aux essais, lors de leur admission puis 2 semaines plus tard, afin de déterminer les coûts de traitement and of transport as well as the number of jours où les patients and their aids who were concerned by the activities. We have determined the cost of the soins courants by the prestataires of soins in calculant le coût individuel des ressources utilisées for diagnostiquer and treat Plasmodium vivax in the site of the studies.

Results The costs total moyen in 8.7 dollars des États-Unis ($ 8.7 US, 4.3 US$) in Ethiopia to 154.8 dollars in Zimbabwe. Tout pays confondus, les pertes de productivité étaient la principale composante des coûts for the ménages, puisqu’elles entraînaient des coûts indirects moyens allant de 5.3 US dollars (ET: 3.0) à 220.8 dollars (ET: 154.80) in Colombia. En ce qui concerne les prestataires de soins, le coût des soins courants allait de 3.6 à 6.6 US dollars. Le coût de réalisation d’un test de diagnostic rapide basé sur le glucose-6-phosphate-déshydrogénase variait de 0.9 $ US à 13.5 $ US, un coût toujours inférieur à celui du expériences test par fluorescence (6.3 $ US à 17.4 $ US).


Resume

Les coûts totaux moyens pour les ménages allaient de 8,7 dollars des États-Unis ($8.7 US) à 154.8 dollars (ET: 154.80) in Colombie. Tout pays confondus, les pertes de productivité étaient la principale composante des coûts pour les ménages, puisqu’elles entraînaient des coûts indirects moyens allant de 5.3 US dollars (ET: 3.0) à 220.8 dollars (ET: 154.80) in Colombie. En ce qui concerne les prestataires de soins, le coût des soins courants allait de 3.6 à 6.6 US dollars. Le coût de réalisation d’un test de diagnostic rapide basé sur le glucose-6-phosphate-déshydrogénase variait de 0.9 $ US à 13.5 $ US, un coût toujours inférieur à celui du test par fluorescence (6.3 $ US à 17.4 $ US).

Conclusion Un épisode de paludisme à P. vivax entraîne des coûts élevés pour les ménages. Connaître les coûts du diagnostic et du traitement de P. vivax sera fort utile aux futures analyses coût-éfficacité. Cela permettra d’affecter les ressources de manière optimale en vue d’éradiquer le paludisme.
period с апреля 2014 года по декабрь 2017 года. Затраты семьи определялись по данным анкетирования участников клинического исследования, проведившегося в момент включения в исследование и в 2 недели спустя для определения затрат на лечение и проезд, а также для определения количества дней, в течение которых пациенты и ухаживавшие за ними члены семьи были не в состоянии вести обычный образ жизни. Затраты медицинских учреждений на обеспечение стандартного набора медицинских услуг оценивались посредством микрокалькуляции расходов на ресурсы, необходимые для диагностики и лечения инфекции P. vivax в центрах проведения исследований.

Результаты Средняя общая величина затрат семьи находилась в диапазоне от 0,7 до 8,7 долл. США (среднеквадратичное отклонение, СО 4,3) в Афганистане до 254,7 долл. США (СО 148,4) в Камбодже. Во всех странах потери трудоспособности составляли наибольший компонент затрат семьи, при этом средние косвенные затраты составляли от 5,3 до 220,8 долл. США (СО 158,4). Затраты медицинских учреждений на обеспечение стандартного набора медицинских услуг составляли от 3,6 до 6,6 долл. США. Затраты на проведение экспресс-теста для диагностики заболевания по глюко-6-фосфат-дегидрогеназе составляли от 0,9 до 13,5 долл. США, что было во всех случаях ниже затрат на широко используемый тест флуоресцентного питания (от 6,3 до 17,4 долл. США).

Вывод Вспышка заболеваемости малярией, вызванной P. vivax, дорого обходится семьям пациентов. Затраты на диагностику и лечение P. vivax должны обязательно учитываться в последующих анализах эффективности затрат с целью обеспечения оптимальных ресурсов для искоренения малярии.

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