Economic and Resource Use Associated With Management of Malaria in Children Aged <5 Years in Sub-Saharan Africa: A Systematic Literature Review

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Background. Malaria is a major health, economic, and social burden in sub-Saharan Africa. Purpose. The objective is to help understanding the economic impact of malaria and informing estimates of the potential economic impact of malaria prevention. To achieve this, we conducted a systematic review of published information on health system costs, health care resource use, and household costs for the management of malaria episodes in children aged <5 years in sub-Saharan Africa. Data Sources and Study Selection. We conducted searches in Medline, EMBASE, and Cochrane Library for studies reporting data on economic cost or resource use associated with management of malaria in children aged <5 years in sub-Saharan Africa. Searches were limited to articles published in English or French between January 1, 2006, and September 1, 2016. Conference abstracts from 2014 to 2016 were hand-searched. Data Extraction and Data Synthesis. We identified 1846 publications, of which 17 met the selection criteria. The studies covered nine countries: The Democratic Republic of Congo, Ghana, Kenya, Malawi, Mozambique, Nigeria, Tanzania, Uganda, and Zambia. All costs were standardized to 2016 US dollars (US$). Seven studies estimated the costs of a malaria episode to health systems, and 10 publications plus one abstract reported household costs. The cost to the health system was US$1.94 to US$31.53 for outpatient malaria cases to US$20 to US$136 for inpatient cases. Families bear a large share of the burden through out-of-pocket payments of medical care and lost income due to time off work. Limitations. Data were missing for many countries and few comparisons could be made. Conclusions. Severe malaria is associated with much higher costs than uncomplicated malaria, and families bear a large share of the cost burden.

Keywords
economic impact, malaria, sub-Saharan Africa, systematic review

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Introduction

Malaria is a potentially life-threatening infectious disease caused by protozoan parasites of the genus Plasmodium. Plasmodium falciparum causes the most severe disease. The parasites are vectored by Anopheles mosquitoes and trigger symptoms when they multiply in human red blood cells (erythrocytes).
Malaria is characteristically an acute febrile illness. The symptoms of uncomplicated malaria are nonspecific and include fever, chills, headache, and vomiting. If not treated within 24 hours, malaria can progress to severe illness and can be fatal. In children, severe malaria can include symptoms such as severe anemia, respiratory distress in response to metabolic acidosis, or convulsions and coma in cases of cerebral malaria. Long-term neurological abnormalities such as ataxia, palsy, speech impairment, deafness, and blindness may persist after cerebral malaria, especially in children.

Interventions to prevent malaria include vector control methods (mainly the use of insecticide-treated nets and indoor residual spraying), chemoprevention, and potentially vaccination. Artemisinin-based combination therapies (ACT) are recommended by the World Health Organization (WHO) for the treatment of uncomplicated malaria caused by *P. falciparum*, and have been shown to reduce malaria mortality by 97% to 99% in children aged <5 years.

Despite the increase of prevention and control methods, malaria is still a major public health burden in sub-Saharan Africa, being in the top three causes of childhood death. In 2015, there were an estimated 191 million cases of malaria and 394,000 malaria deaths in the WHO Africa region. The malaria burden is concentrated in young children. In 2015, there were an estimated 292,000 malaria deaths in children aged <5 years in the WHO Africa region, accounting for 74% of malaria deaths.

Malaria is therefore associated with a high economic and social burden. Malaria costs may be substantial in relation to household income in sub-Saharan Africa, especially in poorer socioeconomic groups. After taking into account factors such as initial poverty, economic policy, and tropical location, the rate of economic growth per capita in countries with malaria was estimated to be 1.3% per year slower between 1965 and 1990, compared with countries without malaria. The long-term effect of this lower growth rate is an income per capita, in a country with intensive malaria, that is only around one third of that in a country without intensive malaria.

The objective of this study is to conduct a systematic review of information available from the peer-reviewed literature on health system costs, health care resource use, and household costs for the management of malaria episodes in children aged <5 years in sub-Saharan Africa. It should help identify information that can be applied to improve understanding of the economic burden of malaria to health systems and households, and to help assess the potential economic impact of malaria prevention.

### Methods

#### Search Strategy

Three electronic databases, Medline, EMBASE, and the Cochrane Library, were searched to identify studies reporting information on economic impact and resource use associated with malaria management in children aged <5 years in sub-Saharan Africa. For example, search terms in Medline for disease included ‘Malaria (MeSH),’ ‘plasmodium (MeSH),’ or ‘plasmodium falciparum’ (MeSH),’ search terms for economics included ‘budgets (MeSH)’ or ‘economic (MeSH),’ and search terms for the geographical area included ‘sub-Saharan Africa (MeSH)’ or ‘West Africa (MeSH)’ together with individual country names. Detailed search terms are presented in Supplementary Material: Search terms. The searches were limited to studies published in English or French, and added to the database between January 1, 2006, and September 1, 2016. In addition, hand searches were conducted to identify relevant conference abstracts from key conferences between 2014 and 2016.

#### Study Selection

Studies before 2006 were excluded. Studies were selected according to the predefined PICOS (Population, Intervention, Comparison, Outcome, Study type) framework. As this was a review of information on cost of illness, “Intervention” and “Comparison” were not applicable, and the “Outcome” of interest was cost data. Full details of the PICOS criteria used are presented in Supplementary Material: PICOS criteria. Studies were included if they met the following criteria:

- **Population:** children aged <5 years with malaria (including uncomplicated, severe, or other manifestations of malaria, with or without laboratory/rapid diagnostic test [RDT] confirmation), living in sub-Saharan Africa.

- **Costs reported:** costs per disease episode; costs of antimalarial treatments; diagnosis and treatment of uncomplicated or severe malaria, including late manifestations of severe malaria; treatment of symptoms attributable to malaria (e.g., fever). Studies on the cost of management of febrile illnesses without malaria confirmation were included only if indirect costs associated with productivity loss and opportunity costs (travel time and waiting time) were reported. The selected studies reported costs from either the health care sector or household perspective. Health care sector costs were defined as the direct...
cost of malaria per episode or total cost of malaria over a known number of episodes. Household costs included direct and indirect costs associated with episodes of malaria including out-of-pocket payments, transportation, self-medication, and traditional therapy.

- **Study type:** observational studies, pragmatic trials, and clinical trials of therapeutic interventions were included. Model-based studies were included only if they estimated costs of treatment provision for diagnosed malaria cases.

Studies were excluded as follows:

- Studies in North Africa or South Africa, or studies in populations not receiving treatment in the context of routine health care delivery (e.g., displaced populations) were excluded.
- Studies on disease recurrence, reinfection, incorrect treatment administration, screening and mass administration of interventions, or studies reporting information that could not be attributed to a uniquely identifiable disease episode were not included.
- Case reports, letters, comments, and historical articles were excluded.

Publications identified by the electronic searches were first screened for relevance by reviewing the title and abstract. Studies that were eligible after primary screening underwent full-text review against the selection criteria above. Two reviewers conducted the screening and full-text review. Any discrepancies were resolved by discussion or the involvement of a third reviewer.

Data including country, study period, population, study type, and reported costs were extracted from studies meeting the selection criteria. All costs were inflated and converted to 2016 US dollars using the CCEMG-EPPI Centre online cost converter tool using the International Monetary Fund dataset for purchasing power parity values and the year of data collection if available, otherwise the year of study publication.15

**Risk of Bias Assessment**

A risk assessment was performed by one reviewer on the studies reporting resource use and cost data. The included studies in this review were analyzed separately, and potential limitations in the methods (i.e., study design, data collection, and data entry) were flagged as well as potential self-reported biases.

The PRISMA checklist completed for this literature review can be found in the supplementary material.

**Results**

**Search Results**

A total of 1846 publications were identified from the searches and screened using title and abstract. Of these, 101 underwent full-text review, and 16 met the selection criteria.16–31 One additional study was identified from the hand searches of conference abstracts,32 resulting in a total of 17 studies included (Figure 1). The most recent publication date was 2016.29

The studies covered nine countries, the Democratic Republic of Congo (DRC), Ghana, Kenya, Malawi, Mozambique, Nigeria, Tanzania, Uganda, and Zambia.

**Studies on Malaria Costs to Health Systems**

**Characteristics of Included Studies.** Seven studies16–22 estimated health care costs for episodes of malaria in a range of settings. Five studies were costing studies,16,17,19–21 one analyzed the pattern of medicine prescribing in the community,18 and one was an expenditure study.22 In addition, a model-based study estimated health care system costs and private expenditure in three countries (Ghana, Kenya, and Tanzania).30 Table 1 summarizes the study characteristics.

**Cost of Health Care Associated With an Episode of Malaria.** Five studies16,19,20,22,30 reported data on inpatient costs for an episode of malaria, and three17,18,20 reported data on outpatient costs (Table 2). Health care costs included the costs of diagnostics and treatment, drug costs, administration costs, and hospitalization costs.

Most studies reported cost for severe malaria or malaria hospitalization with a total cost ranging from US$18.35 to US$136.35 per patient depending on the type of facility (health center or hospital) and complication to be treated (cerebral malaria, anemia) (Figure 2). If a patient was treated in a national hospital, the costs were higher (US$115.18) than if that same patient was treated in a mission hospital (US$106.26).22 Treatment per inpatient episode of malaria was more expensive in hospitals compared with health centers.16 The type of malaria was an important cost driver. Treatment for cerebral malaria with anemia or neurological sequelae was more expensive than uncomplicated and severe malaria in Kenya, Ghana, Tanzania, and Zambia.19,30

Two studies reported data covering Kenya. Costs reported by Ayieko et al.22 (National: US$115.18, District: US$75.22) were slightly higher than those reported by Sicuri et al.30 (range US$3.07–63.19). This could reflect limitations in the cost-analysis methodology used by
Ayieko et al.,\textsuperscript{22} which reported a bed-day cost of hospitaliza-
tion based on results of two studies each representing a
single hospital. Bed-day costs vary significantly between
hospitals especially due to differences in occupancy rates.
The study authors mentioned that overcoming this limita-
tion was difficult given the expense of conducting multiple
formal hospital costing studies. In addition, a high level of
presumptive malaria treatments (due to lack of accurate
diagnosis) may have encouraged the use of the wrong drug,
so total treatment costs could have been overestimated.

Fewer studies reported cost for outpatient or uncomplic-
ated malaria with a total cost per episode from US$1.94 to
US$7.47 mainly based on drug cost (Figure 3). One study
in Nigeria reported higher costs of US$ 31.53 per outpatient
case due mainly to personnel costs.\textsuperscript{20}

In Uganda, antimalarial drugs delivered at health
facilities were free for children aged <5 years with a
diagnosis of uncomplicated malaria, thus placing the
economic burden on the health care system rather on
households.\textsuperscript{27}

\textit{(text continues on p. 9)
Figure 2  Cost per inpatient malaria case with cost components when available. QNN, quinine; ART, artesunate.

Figure 3  Cost per outpatient malaria case with cost components when available.
| Study | Country | Study Period | Type of Malaria | Age Group | Study Type | Primary Outcomes | Data Sources | Patient Recruitment | Costs Included |
|-------|---------|--------------|-----------------|-----------|------------|------------------|--------------|---------------------|-----------------|
| Ferrari16 | Democratic Republic of Congo | October 2012 to June 2013 | Severe | ≤ 6 years, excluding infants < 6 months | Prospective comparative observational study | Cost per episode | Prospective collection; time and motion data collection | Consecutive cases | Inpatient, outpatient, and medication costs |
| Ezenduka17 | Nigeria | January to June 2013 | Uncomplicated | ≤ 5 years (10% of total) | Retrospective cohort | Cost of diagnostics and medication per case | Hospital medical records | Patient lists | Medication, diagnostics, co-medication |
| Ezenduka18 | Nigeria | May to August 2013 | Not reported | < 5 years | Prospective cross-sectional sample | Cost per prescription | Medicine retail outlets survey | People who obtained medications from pharmacy outlets | Testing and medication costs |
| Comfort19 | Zambia | 2005–2008 | Severe, malaria with anemia, cerebral or cerebral with moderate anemia | < 5 years | Longitudinal retrospective based on non-random sample of available record | Cost per hospitalization | Electronic medical records | Patient lists of all cases admitted during study period | Admission costs |
| Onwujekwe20 | Nigeria | Not reported | Not reported | < 5 years | Cross-sectional survey design with proportionate sampling | Cost per episode | Medical records, patient exit interviews | Patient lists and consecutive patients presenting for treatment | Cost of outpatient treatment to HC provider; out-of-pocket and other costs supported by patients |
| Osei-Kwakye21 | Ghana | January 2009 to February 2010 | Uncomplicated | 1–59 months | Cross-sectional observational study | Cost per prescription/cost per encounter per diagnosed case | Hospital OPD data (medical record) | Consecutive patients presenting for malaria treatment | Testing and medication costs |
| Ayicko22 | Kenya | November 2004 to October 2005 | Not reported | < 5 years | Prospective and retrospective cross-sectional study | Caretakers | Medical records, patient interviews | All consecutive admissions to the health center | Inpatient costs |
| Sicuri30 | Ghana, Kenya, Tanzania | Not reported | Uncomplicated malaria, cerebral malaria, cerebral malaria + neurological sequelae | < 5 years | Model-based estimation of total cost of malaria episodes | Mean cost of care per episode and per child | Secondary sources derived from other literature; for comorbidity and complications: interviews with clinicians, health workers, managers of the malaria control program | Not applicable | Cost of treatment of uncomplicated malaria; cost of treatment of hospitalized cases; costs of comorbidity and cost of complications; household costs (health care services, transport, and other costs) |

HC, health care; OPD, outpatient department.
Table 2  Inpatient and Outpatient Costs per Episode of Malaria to the Health Systems

| Study                                      | Cost Base Year; Unit | Malaria Type                        | Type of Health Facility | Drug Costs | Diagnostics | Other Costs | Hospital Stay Costs | Total Cost per Episode   |
|-------------------------------------------|----------------------|-------------------------------------|-------------------------|------------|-------------|-------------|---------------------|--------------------------|
| Health care delivery type: Inpatient      |                      |                                     |                         |            |             |             |                     |                          |
| Onwujekwe (Nigeria)³⁹                      | Base year NR, US$    | NR                                  | 6 facilities (public, health care centers, mission) | 2.48       | 0.34        | NR          | National: 90.43     | 49.78                    |
| Ayieko et al. (Kenya)⁷²                    | 2005, US$            | NR                                  | 7 hospitals, mixed facilities | National: 4.90  | National: 19.38 | NR          | National: 51.91     | Per admission National: 115.18 |
| Comfort (Zambia)¹⁰                        | 2008, US$            | Severe, malaria with anemia, cerebral malaria | Government, second-level (Livingstone General Hospital) | NR         | NR          | Total costs for all malaria admissions in 2008: US$2557.88 | NR                       |
| Ferrari (DRC)¹⁶                            | 2014, US$            | Severe malaria                      | Mixed facilities        | Injectable drug cost QNN group Hospitals: 0.63 Health centers: 1.22 ART group Hospitals: 5.0 Health centers: 7.45 Oral drug cost QNN group Hospitals: 0.80 Health centers: 1.34 ART group Hospitals: 0.52 Health centers: 0.54 | Injectable QNN Hospitals: 4.08 Health centers: 1.09 | Injectable ART Hospitals: 4.32 Health centers: 4.48 ART group Hospitals: 1.16 Health centers: 1.76 | Injectable QNN Hospitals: 44.96 Health centers: 15.45 ART group Hospitals: 43.86 Health centers: 14.96 | Per patient Injectable QNN Hospitals: 53.99 Health centers: 22.24 Injectable ART Hospitals: 54.1 Health centers: 25.26 Oral QNN Hospitals: 54.16 Health centers: 25.19 Oral ART Hospitals: 49.62 Health centers: 18.35 |
| Sicuri (Kenya, Ghana, Tanzania)³⁰         | 2009, US$            | Uncomplicated malaria, malaria hospitalization, severe anemia, cerebral malaria, cerebral malaria + neurological sequelae | NR                      | NR         | NR          | NR          | NR                  | Health system cost per episode Kenya: 3.07–63.19 Ghana: 3.20–136.35 Tanzania: 1.94–53.21 |

(continued)
Table 2 (continued)

| Study            | Cost Base Year; Unit | Malaria Type | Type of Health Facility | Drug Costs | Diagnostics        | Other Costs | Hospital Stay Costs | Total Cost per Episode |
|------------------|----------------------|--------------|-------------------------|------------|--------------------|-------------|--------------------|------------------------|
| Onwujekwe (Nigeria)\(^{10}\) | Base year NR, US$    | NR           | 6 facilities (public, health care centers, mission) | 1.93       | Diagnostics: 1.45  | NR          | NA                 | 31.54                  |
| Ezenduka (Nigeria)\(^{17}\)  | Base year NR, US$    | Uncomplicated | Public (medical center and teaching hospital)\(^{c}\) | 7.47       | NR                 | NR          | NA                 | NR                     |
| Ezenduka (Nigeria)\(^{18}\)  | Base year NR, US$    | Uncomplicated | Public                  | 3.71\(^{d,e}\) | NR                 | NR          | NA                 | Per prescription: 3.71 |

ACT, artemisinin-based combination; ART, artesunate; CI, confidence interval; DRC, Democratic Republic of Congo; NA, not applicable; NR, Not reported; QNN, quinine; US, United States.

\(^{a}\)Public health hospital (Institut Médi­cal Evangélique, Kimpese, Bas Congo); one medium-sized, nonprofit, missionary hospital (St Luc Kisan­tu); and a medium-sized, government hospital (Centre Hospitalier Roi Baudouin). In addition, five rural health centers were selected within the same Health Zones (HZs; Health Centre Bita, Health Centre Menkao, Health Centre Ngeba, Health Centre CECO, and Health center La Famille).

\(^{b}\)Mean cost for oral quinine and Artesunate-Amodiaquine (AS-AQ).

\(^{c}\)Medical center is a health care facility which provides outpatient services. Teaching hospital is a tertiary health care facility providing a variety of specialized clinical and teaching services. It is the main referral public health facility in the state run by the federal government. Patients pay for services and their drugs at the point of delivery.

\(^{d}\)Artemether-pyrimethamine was the most used antimalarial drug (50.6%), followed by monotherapy sulphadoxine-pyrimethamine (18.8%). For all study age groups, total cost of medication (including co-medications) with artemisinin-based combination (ACT) averaged US$4.10 per prescription about twice the mean cost of treatment with monotherapy US$2.06 but the average medication cost varied noticeably across age categories. While it was highest for children under 5 years at US$3.74 (95% CI; US$3.11 to US$4.35), the lowest was observed for children aged between 5 and 12 at US$2.75 (95% CI; US$2.43 to US$3.06) per case.

\(^{e}\)The mean cost of medication (including co-medication such as antibiotics) per patient at the two public health facilities for children under <5 years was 1062 Naira. Costs data were standardized with US dollars, as calculated for the 2014 price year (Nigeria) [US$1 = 158.553 Naira (2014)]. Exchange rates were obtained from the World Bank Data.
Inpatient care of an uncomplicated episode (US$5.15) was more expensive than outpatient care (US$2.65), with health personnel and medications being the major cost drivers. Limited data on outpatient delivery were reported.

Length of Stay in Hospital. Only two studies reported data on hospital length of stay. Ferrari et al. reported that the average length of stay for patients with severe malaria ranged from 1.7 to 7.1 days, depending on treatment and type of health facility. Ayieko et al. evaluated patients with an unspecified malaria diagnosis, and reported an average length of stay ranging from 3.1 days in a mission hospital to 4.8 days in a district hospital.

Studies of Malaria Costs to Households

Characteristics of Included Studies. Ten studies reported malaria costs to households (Table 3). Two of these also reported costs to health systems. In addition, one abstract reported some information on hospitalization costs associated with severe malaria to households in Malawi. Two publications reported results from the same study, a cross-sectional survey of household expenditure for children with malaria in Nigeria. Similarly, two publications reported data from the same sample in Uganda. Only one study provided data on the distance to the closest health facility, and only one reported data on the average household income.

Out-of-Pocket Costs Borne by Households. Studies reporting data on health care out-of-pocket costs to households for an episode of malaria are summarized in Table 4. Out-of-pocket costs include direct costs attributed to drugs, consultation, diagnostics and hospitalization, and indirect costs attributed to caregiver transportation.

The studies reported out-of-pocket payment as cost per episode or as cost per month. Values reported ranged from US$0.23 to US$36.56 per episode and US$0.29 to US$23.43 per month. Although the studies were heterogeneous in malaria severity and cost items reported, some trends were observed. The elements that made the largest contribution to total out-of-pocket costs per episode were transportation and complications in relation to malaria severity.

Transportation costs made the largest contribution to direct costs to households in Malawi, Mozambique, and Uganda. In Mozambique, subjects spent US$7.6 per episode, of which 39% was attributable to medicines and more than half to transport for the sick person and the caregiver. In Malawi, even though consultation is free for children aged <5 years, households incurred costs for transportation to public health facilities. It was also estimated that overall 27% of formal services users with children aged <5 years paid out-of-pocket costs for services received as a result of fever, related either to travel (16%) or medication (11%) costs. Malawian households living in villages far from hospital incurred greater out-of-pocket costs. Travel costs made the largest contribution to direct cost and increased significantly for those living in hard-to-reach villages between the dry and wet seasons (Dry: US$0.36; Wet: US$1.04, P = 0.04). Direct costs for malaria episodes were greater for those living in hard-to-reach locations compared with villages near the hospital in both dry (US$0.44 v. US$0.23, P = 0.04) and wet (US$1.11 v. US$0.47, P = 0.08) seasons.

In Uganda, caregivers living in urban areas spent significantly more on transport to reach health centers than those in rural areas. This is because people in urban areas tended to hire motor cycles or public transport vehicles to reach health centers, while those from rural areas walked or used their own (or borrowed) bicycles. On average, caregivers in the urban areas spent four times more than those in rural areas.

Although malaria severity type was not reported by some studies, it was possible to see a trend in out-of-pocket costs associated with hospitalization and treatment. The treatment costs for severe malaria cases were higher and potentially catastrophic to the majority of households particularly in Nigeria, Uganda, Ghana, Kenya, and Tanzania. In a study by Sicuri et al., Ghanaian households needed to support higher direct costs (US$36.56/episode) compared with Tanzania (US$5.46/episode) and Kenya (US$11.83/episode), due to more expensive treatment and higher medical service costs, which include high health personnel salary. For cerebral malaria with neurological sequelae, households in Ghana had the highest direct medical costs (US$40.74) followed by Kenya (US$22.17) and Tanzania (US$8.71). In Nigeria, inpatient costs were greater than outpatient costs averaging to US$12.69 and US$23.43 per episode, respectively. This was due to the cost of hospitalization, special services, comorbidities, and other systemic complications of severe malaria. These complications increase the time spent in hospital, thereby increasing costs. Nigerian households also bear the costs of microscopy tests in inpatient departments. Although the national health insurance scheme was launched in Nigeria years ago to reduce the economic burden of illness borne by individuals, none of the respondents had any form of health insurance. In Uganda, caregivers inured
Table 3  Characteristics of Included Studies on the Cost of Malaria Episodes to Households

| Study          | Country       | Study Period                  | Definition of Malaria          | Age Group | Study Type   | Outcomes                                                                 | Data Sources                                                                 | Patient Recruitment/ Sampling Technique                                                                 | Costs Included                                                                 |
|----------------|---------------|-------------------------------|--------------------------------|-----------|--------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|--------------------------------------------------------------------------------|
| Etiaba23       | Nigeria       | Not reported                  | Not reported                  | <5 years  | Survey       | Household expenditure per case                                           | Medical records/lists of admissions in study period                           | Two-stage sample; Purpose sample of 6 health facilities; systematic random sampling (households with children ≤5 years old) | Costs of all HC services privately paid for before and after the index date; Health care costs during episode |
| Onwujekwe20    |               |                               |                                |           |              |                                                                          |                                                                                | Adamo selected villages; cluster random sampling (target sample: 483 children ≤5 years) | Health care expenditure for services privately paid for; Travel and assistance direct costs; foregone income |
| Ewing24        | Malawi        | June 2009 to February 2010    | Uncomplicated (mild to severe) | <5 years  | Cross-sectional survey | Household cost of seeking health care (self-initiation) given the number of children with febrile episodes (cost per case) | Direct interviews of caregivers                                                | Two-stage cluster sampling based on enumeration areas and random household (as per expanded immunization program evaluation sampling) | For febrile episodes reported: Health care expenditure for formal services, self-prescribed drugs, traditional medicine; time used to obtain care |
| Mujica-Mota26  | Malawi        | November 2003 to March 2004   | Not reported                  | <5 years  | Survey       | Mean reported household out-of-pocket cost                               | Direct interviews to household heads, complemented by participation of other household members | Two-stage cluster sampling based on enumeration areas and random household (as per expanded immunization program evaluation sampling) | Direct expenditure for health care, out-of-pocket expenditure and accessory expenditure (food, travel); Days taken off work |
| Castillo-Riquelme25 | Mozambique    | June to August 2002           | Not reported                  | <5 years  | Survey       | Health care expenditure, out-of-pocket expenditure, catastrophic expenditure | Family caretaker interviews                                                  | Purpose sample of six clusters in two countries and all households in cluster (high risk areas) or all patients' lists in low low-risk areas | Direct expenditure for health care, out-of-pocket expenditure and accessory expenditure (food, travel); Days taken off work |
| Matovu27       | Uganda        | March to June 2012            | Uncomplicated                 | <5 years  | Randomized controlled trial | Difference in direct and indirect cost of seeking care from centers compared with care obtained from community medicine distributors | Exit interviews of consecutive caregivers presenting for RCT follow-up         | Convenience sample from participants into a clinical trial; versus two-stage cluster random sample of children visited by community medicine distributors | Direct expenditure for health care, out-of-pocket expenditure and accessory expenditure (food, travel); cost of time spent for travel and waiting time |

(continued)
Table 3 (continued)

| Study                     | Country          | Study Period          | Definition of Malaria | Age Group | Study Type | Outcomes                                                                 | Data Sources                                                                 | Patient Recruitment/ Sampling Technique                                                                 | Costs Included                                                                                           |
|--------------------------|------------------|-----------------------|-----------------------|-----------|------------|---------------------------------------------------------------------------|--------------------------------------------------------------------------------|---------------------------------------------------------------------------------------------------------|----------------------------------------------------------------------------------------------------------|
| Menon²⁹ Orem²⁸            | Uganda           | November to December 2009 | Not reported          | < 5 years | Survey     | Total expenditure incurred for episodes of febrile children in 2 weeks prior to survey | Individual questionnaire administered to women aged 16-49 years from households in each cluster | Two-stage cluster sample—enumeration areas and systematic sampling with equal probability in the enumeration area | Expenses related to the medical consultations, hospitalization, medicines, and transportation, time off work |
| Sicuri²⁰                  | Ghana, Kenya, Tanzania | Not reported          | Uncomplicated malaria, cerebral malaria, cerebral malaria + neurological sequelae | < 5 years | Model-based estimation of total cost of malaria episodes | Mean cost of care per episode and per child | Secondary sources derived from other literature; for comorbidity and complications: interviews with clinicians, health workers, managers of the malaria control program | Not applicable                                                                                           | Cost of treatment of uncomplicated malaria; cost of treatment of hospitalized cases; costs of comorbidity and cost of complications; household costs (health care services, transport, and other costs) |
| National Population Commission³¹ | Nigeria          | 2006–2010            | Not reported          | < 5 years | Cross-sectional survey | Mean expenditure for treatment of episode of fever | Interviews to all women aged 15-49 years from sampled households using Roll-Back Malaria questionnaires | Stratified two-stage cluster design based on administrative areas of the Population and Housing Census | Cost of medications, hospitalizations, visits, testing                                                                 |
| Njau³²                    | Malawi           | Not reported          | Severe                | < 5 years (51%) | Not reported | Not reported | Not reported | Not reported | Hospitalization costs                                                                                                           |

HC, health center; RCT, randomized controlled trial.
Table 4 Out-of-Pocket Costs of Malaria Episodes to Households

| Study                                      | Cost Base Year | Mean Direct Medical Costs (US$) | Caregiver Transportation (US$) | Other (US$) | Total Out-of-Pocket Costs per Episode (US$) |
|--------------------------------------------|----------------|---------------------------------|--------------------------------|-------------|------------------------------------------|
| **Nigeria**                                |                |                                 |                                |             |                                          |
| Etiaba\textsuperscript{23}                 | Not reported   | Inpatient: 23.43/month          | —                              | —           | Inpatient: 23.43/month                   |
|                                            |                | Outpatient: 12.69/month         |                                |             | Outpatient: 12.69/month                  |
|                                            |                | Inpatient (drugs): 5.15         |                               |             | Inpatient: 23.43/month                   |
|                                            |                | Inpatient (diagnostics): 1.25   |                                |             | Inpatient: 13.03/month                   |
|                                            |                | Inpatient (administration fees): 0.28 |                            |             |                                        |
|                                            |                | Total direct medical (inpatient): 6.98 |                            |             |                                        |
|                                            |                | Outpatient (drugs): 2.65         |                                |             |                                        |
|                                            |                | Outpatient (diagnostics): 0.13   |                                |             |                                        |
|                                            |                | Outpatient (administration fees): 0.31 |                            |             |                                        |
|                                            |                | Total direct medical (outpatient): 3.16 |                          |             |                                        |
|                                            |                |                                 |                                |             |                                        |
| Onwujekwe\textsuperscript{20}              | Not reported   | Inpatient: 6.98                 | Inpatient: 0.62                | Inpatient: 0.43 | Inpatient: 3.11                          |
|                                            |                |                                  |                                  | Costs before IPD: 3.11 | Outpatient: 0.21                        |
|                                            |                |                                  |                                  | Others: 0.21 | Others: 0.1                             |
|                                            |                |                                  |                                  |              |                                        |
| National population survey in Nigeria\textsuperscript{31,a} | 2010           | Mean expenditure for treatment of episode of fever\textsuperscript{1}: 6.35 | Not reported | Not reported | Not reported                           |
| Mozambique                                 |                |                                 |                                |             |                                          |
| Castillo-Riquelme\textsuperscript{25}      | 2006           | Consultation: Free for <5 years of age | 2.09                          | While waiting: 0.21 | 7.6/month                             |
|                                            |                | Medication: 2.96                |                                |             |                                        |
|                                            |                | Malaria test: 0.06              |                                |             |                                        |
| Malawi                                    |                |                                 |                                |             |                                          |
| Mujica-Mota\textsuperscript{26}            | 2006           | Formal health facility          | Formal: 0.30                   | Not reported | Formal: 0.44/month                      |
|                                            |                | Consultation: Free for <5 years of age | Informal: 0.12                |             | Informal: 0.29/month                    |
|                                            |                | Medication: 0.14                |                                |             |                                        |
|                                            |                | Informal health facility        |                                |             |                                        |
|                                            |                | Consultation: 0.01              |                                |             |                                        |
|                                            |                | Medication: 0.16                |                                |             |                                        |
|                                            |                |                                 |                                |             |                                        |
| Ewing\textsuperscript{24}                  | Not reported   | Childhood febrile episode by distance to formal health facility | Dry season: &lt;5 km from hospital: 0.2 | Not reported | Dry season: &lt;5 km from hospital: 0.23 |
|                                            |                |                                 | Hard to reach: 0.36            |             | Hard to reach: 0.44                      |
|                                            |                |                                 | Wet season: &lt;5 km from hospital: 0.33 |             | Wet season: &lt;5 km from hospital: 0.47 |
|                                            |                |                                 | Hard to reach: 1.04            |             | Hard to reach: 1.11                      |

(continued)
| Study            | Cost Base Year | Mean Direct Medical Costs (US$) | Caregiver Transportation (US$) | Other (US$) | Total Out-of-Pocket Costs per Episode (US$) |
|------------------|----------------|---------------------------------|--------------------------------|-------------|--------------------------------------------|
| Njau (abstract)³² |                | Admission costs                 |                                | Non-hospital costs: 4.74 | Not reported                               |
|                  |                | Hospitals managed by CHAM: 14.75 |                                |              |                                            |
|                  |                | Government hospitals: 5.42      |                                |              |                                            |
| Kenya            |                |                                 |                                |              |                                            |
| Sicuri³⁰         | 2009           | UM: 0.81                        | Not reported                    | Not reported | 11.83/episode                              |
|                  |                | MO: 12.06                       |                                |              |                                            |
|                  |                | MO + SA: 12.06                  |                                |              |                                            |
|                  |                | CerM: 12.06                     |                                |              |                                            |
|                  |                | CerM + NS: 22.17                |                                |              |                                            |
| Tanzania         |                |                                 |                                |              |                                            |
| Sicuri³⁰         | 2009           | UM: 0.47                        | Not reported                    | Not reported | 5.46/episode                               |
|                  |                | MO: 6.05                        |                                |              |                                            |
|                  |                | MO + SA: 6.05                   |                                |              |                                            |
|                  |                | CerM: 6.05                      |                                |              |                                            |
|                  |                | CerM + NS: 8.71                 |                                |              |                                            |
| Ghana            |                |                                 |                                |              |                                            |
| Sicuri³⁰         | 2009           | UM: 4.92                        | Not reported                    | Not reported | 36.56/episode                              |
|                  |                | MO: 27.17                       |                                |              |                                            |
|                  |                | MO + SA: 82.77                  |                                |              |                                            |
|                  |                | CerM: 27.17                     |                                |              |                                            |
|                  |                | CerM + NS: 40.74                |                                |              |                                            |
| Uganda           |                |                                 |                                |              |                                            |
| Matovu³⁷         | 2009           | Medication: Free for < 5 years of age | Urban³: 0.78 | Not reported | Urban: 0.47                               |
|                  |                |                                  | Rural³: 0.111                   |              | Rural: 0.18                               |
| Menon²⁹          | 2009           | Private health facility: 7.14   | Not reported                    | Not reported | 7.58/month                                 |
|                  |                | Public health facility: 8.64    |                                |              |                                            |

CerM, cerebral malaria; CHAM, Christian Health Association of Malawi; IPD, inpatient department; MO, malaria hospitalization; NS, neurological sequelae; SA, severe anemia; UGX, Ugandan shilling; UM, uncomplicated malaria.

³Cost data were standardized with US dollars, as calculated for the 2010 price year (Nigeria) and the 2009 price year (Uganda). Nigeria survey data originally reported average cost of treatment to be 871.7 Naira [US$1 = 150.298 Naira (2010)]. Study by Matuvo et al. (2009)³³ originally reported mean travel costs to be 1,417 UGX and 257.9 UGX for urban and rural settings, respectively [US$1 = 2030.488 UGX (2009)]. Exchange rates were obtained from the World Bank data.
US$7.58 total costs per episode, and costs were similar at either a private or public health facility. The authors also estimated that among those families with a febrile child who sought care, expenses were 4.3% of an average total monthly income per febrile episode. However, it is not clear whether these costs were largely attributed to medication, diagnostics, or other medical elements.

Non–Health Care Costs Associated With Productivity Loss Due to Malaria and Value of Time Lost to Households Due to Seeking Health Care. Table 5 summarizes information from studies reporting data on productivity loss in monetary value or days and time lost to households due to seeking health care for malaria. Three studies reported monetary value of productivity losses ranging from US$0.43 to US$235.34 per episode. The number of days lost were reported from three studies and ranged from 4.8 to 6 days per episode. Regarding the time spent to seek for health care, two studies reported ranges from 16 to 158 minutes.

Two studies reported information on productivity loss covering Tanzania, Ghana, Kenya, and Malawi. In the study by Sicuri et al., households experiencing cerebral malaria with neurological sequelae in Kenya had the highest economic burden with large productivity losses. Average indirect costs were higher in Kenya, at close to US$8 per uncomplicated episode. This figure fell to US$1.4 in Ghana, where productivity losses were lower due to the lower minimum wage. Indirect costs increased sharply for hospitalized cases, and cases with neurological sequelae had the highest costs: US$77.82, US$99.46, and US$235.23 in Ghana, Tanzania, and Kenya respectively. In Malawi, people living in hard-to-reach villages were less likely to attend a formal health facility compared with those living near the hospital. Hard-to-reach villages were as likely to attend in both dry and wet seasons. Indirect costs represented the main economic burden for households. Most indirect costs were due to time caring at home (Table 5). The cost of time spent caring was greater in hard-to-reach villages (US$4.69) compared with villages near the hospital (US$2.81) in the dry season (P = 0.02), but did not differ significantly in the wet season (P = 0.12). In addition, Malawian carers of feverish young children were as likely to lose earnings in a formal health care facility as in informal care (P = 0.60). It was not possible to make a comparison between Malawi and the other three countries, due to lack of information on malaria-confirmed diagnosis.

Four studies reported information on the time lost to households due to seeking health care, covering Mozambique, Malawi, and Uganda. The number of days lost was higher in Uganda (close to 5 days) than in Mozambique and Malawi (close to 3 days; Table 5). Information on episode duration from Uganda was not reported, so it is not possible to say whether the higher average number of days lost in Uganda could be associated with a longer duration of malaria episodes in Uganda compared with the duration of 6 days in Malawi (Table 5). Travel and waiting times at the facility were longer in Uganda (up to 90 minutes) than in Malawi (up to 30 minutes) regardless of malaria diagnosis and urban/rural setting (Table 5). Households in rural areas in Uganda travelled for significantly longer (P < 0.001), but their waiting time was shorter than for urban households (P < 0.001). The combined effect of travel and waiting time was not significantly different between rural and urban households (P = 0.289). Caregivers travelled an average of 1.5 km to reach a health facility.

Risk of Bias Assessment. Table 6 reports the limitations associated to the studies included in the review. Potential inaccuracy of the data due to the retrospective design was the most common limitation raised across studies. Data collected might have been overestimated/underestimated as patients and/or caregivers had to recall the cost incurred to treat an episode of malaria. Additionally, most of the studies failed to describe the diagnosis procedure (often due to inadequate documentation) and thus reliability of diagnosis remained questionable.

Discussion

To our knowledge, this is the first systematic review of published cost data on the management of malaria episodes in children aged <5 years in sub-Saharan Africa. Seventeen studies covering nine countries allowed us to understand how malaria is managed in sub-Saharan countries and served to answer the research question of this systematic literature review.

Several studies estimated the cost of a malaria episode in the health system perspective, in inpatient or outpatient settings. These costs varied between the type of facility in which malaria was treated and the severity of malaria. The mean cost per severe malaria case treated as inpatient was US$60.44 (Min: 18.35; Max: 136.35), with the lowest costs reported from health centers in the Democratic Republic of Congo and highest cost in Ghana hospitals. Regarding outpatient care, the costs reported showed broader disparity with an
| Study             | Cost Base Year, Currency | Caregivers’ Reported Productivity Loss for Entire Episode of Malaria | Mean Duration of Episode | Mean Days Lost | Travel Time to Facility | Waiting Time at Facility |
|-------------------|--------------------------|-------------------------------------------------------------------|--------------------------|---------------|------------------------|-------------------------|
| **Tanzania**      | Sicuri30 2009, US$       | Uncomplicated malaria: US$3.48                                   | Not reported             | Not reported   | Not reported           | Not reported            |
|                   |                          | Malaria hospitalization: US$15.92                                 |                          |               |                       |                         |
|                   |                          | Malaria hospitalization + severe anemia: US$22.17                 |                          |               |                       |                         |
|                   |                          | Cerebral malaria: US$15.92                                        |                          |               |                       |                         |
|                   |                          | Cerebral malaria with neurological sequelae: US$99.46             |                          |               |                       |                         |
| **Ghana**         | Sicuri30 2009, US$       | Uncomplicated malaria: US$1.4                                    | Not reported             | Not reported   | Not reported           | Not reported            |
|                   |                          | Malaria hospitalization: US$26.83                                 |                          |               |                       |                         |
|                   |                          | Malaria hospitalization + severe anemia: US$59.31                 |                          |               |                       |                         |
|                   |                          | Cerebral malaria: US$27.34                                        |                          |               |                       |                         |
|                   |                          | Cerebral malaria with neurological sequelae: US$77.82             |                          |               |                       |                         |
| **Kenya**         | Sicuri30 2009, US$       | Uncomplicated: US$8.81                                            | Not reported             | Not reported   | Not reported           | Not reported            |
|                   |                          | Malaria hospitalization: US$23.72                                 |                          |               |                       |                         |
|                   |                          | Malaria hospitalization + severe anemia: US$38.8                  |                          |               |                       |                         |
|                   |                          | Cerebral malaria: US$23.72                                        |                          |               |                       |                         |
|                   |                          | Cerebral malaria with neurological sequelae: US$235.23            |                          |               |                       |                         |
| **Malawi**        | Ewing24 Base year not reported, US$ | Childhood febrile episode by distance to formal health facility\(a\)   | Not reported             | Not reported   | Not reported           | Not reported            |
|                   |                          | Dry season < 5 km from hospital: US$2.81                         |                          |               |                       |                         |
|                   |                          | Hard to reach: US$4.69                                           |                          |               |                       |                         |
|                   |                          | Wet season < 5 km from hospital: US$3.66                         |                          |               |                       |                         |
|                   |                          | Hard to reach: US$4.47                                           |                          |               |                       |                         |
| **Mujica-Mota**   | 2006, US$                | Overall earnings losses (median) for childhood febrile illness by health facility\(b\) | Formal: 6 days           | Overall work/study days missed (median) | Formal: 30 min          | Formal: 30 min          |
|                   |                          | Formal: US$0.43                                                 | Informal: 4.8 days       | Formal: 2.8 days  | Informal: 15 min       | Informal: 1 min         |
|                   |                          | Informal: US$0.64                                                |                           |               |                       |                         |
average cost of US$8.49 and median cost of US$3.46 (Min: 1.94; Max: 31.53).

The current data provide a good level of information on the cost of malaria in some sub-Saharan countries; however, several data gaps were noted. Studies reporting out-of-pocket costs of malaria episodes to households were heterogeneous, covering Nigeria, Mozambique, Malawi, Kenya, Tanzania, Ghana, and Uganda. No studies reported data from other sub-Saharan African countries (i.e., data were missing for more than 20 countries). Furthermore, cost components varied between studies. Only two studies\(^20\) stated clearly how malaria cost was reported (“cost per case of malaria” and “cost per episode per child,” respectively). The lack of a clear case definition was a major limitation when analyzing the data, leading to heterogeneous cost results in different studies. Few studies specified the type of antimalarial treatment assigned to patients. Only Ezenduka et al.\(^18\) and Ferrari et al.\(^16\) clearly reported that participants were either on monotherapy (quinine) or ACTs, with ACTs being more expensive.

It was not possible to make meaningful comparisons between countries and studies. Only one publication, a model-based study, reported cost estimates from several countries obtained using consistent methods and thus allowed direct between-country comparisons. Total costs per episode in this study were lower in Tanzania than in Ghana or Kenya. Most other studies lacked information on malaria severity and the method of diagnosis for malaria treatment within health care facilities, indicating a potentially high incidence of overdiagnosis and overuse of antimalarial drugs.

Ten full publications\(^20,23–31\) and one abstract\(^32\) estimated the costs of an episode of malaria to households, covering aspects such as out-of-pocket costs, time lost in travelling to and/or waiting at health care facilities, and productivity costs associated with caring for a child with malaria. Transportation costs made the largest contribution to direct costs to households. Findings illustrate the large economic burden to households for treating one episode of malaria.

It is important to note that household cost studies were mainly relying on the participants’ ability to recall costs accurately, while the provider cost studies relied on formal records. Another important difference relates to the case definition employed. Cost studies conducted at health facilities allow identifying patients who have been medically diagnosed with malaria, although this is not always well stated as mentioned above. In contrast, household surveys may use a less specific diagnosis for recruitment, such as families with a child who has

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**Table 5 (continued)**

| Study | Cost Base Year, Currency | Mean Duration of Episode | Mean Days Lost | Travel Time to Facility | Waiting Time at Facility |
|-------|--------------------------|--------------------------|---------------|-------------------------|-------------------------|
| Mozambique Castillo-Riquelme\(^25\) | 2006 Not reported | 6 days | Not reported | Not reported | Not reported |
| Uganda Matovu\(^27\) | Not reported | Not reported | Not reported | Uncomplicated malaria by setting | Rural: 90 min; Urban: 58 min |
| Menon\(^29\) | 2009 Not reported | Time away from regular duties: 4.9 days | Not reported | Not reported | Not reported |

\(^a\)This cost represents cost of time caring.

\(^b\)Formal health care facility (hospital inpatient, health center, dispensary, and private clinic), informal drug use (drug self-medication, pharmacy/chemist, shop).

\(^c\)Labor substitution is defined as another person doing the job of the sick person.

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| Study                        | Risk Flagged (Yes/No) | Limitations Associated to the Study                                                                                                                                                                                                 |
|-----------------------------|-----------------------|----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Ferrari 16      | Yes       | - Limitations in the study design (e.g., a new vial of quinine was used for every dose, which is not reflective in the real world)  
- Underestimation of total treatment costs (e.g., costs related to supportive measures and the presence of comorbidities were not analyzed) |
| Onwujekwe 20 | Yes       | - Potential inaccuracy of the data due to the retrospective design                                                                                                           |
| Ayieko 22      | Yes       | - Limitations in the approach used to determine bed-day costs  
- Underestimation of pre-admission costs, as outpatient facilities were not included in this study                         |
| Menon 29       | Yes       | - Overestimation of costs as the survey was conducted during peak malaria transmission season  
- Potential bias in the selected sample size                                                                                   |
| Orem 28        | Yes       | - Survey used does not serve the purpose of assessing the patterns of treatment seeking behavior for children under five with malaria  
- Potential data collection errors  
- As household real income were not included in the survey, wealth had to be used as a proxy  
- Regression diagnostic tests were not performed to ensure that the binomial logit and Log-lin models were the most appropriate |
| Comfort 19     | Yes       | - Limitation in the quality of the hospital data gathered  
- Small sample size that is unrepresentative of the entire population  
- Lack of comprehensive data across subgroups, which creates large variations in costs (i.e., overestimating the real cost difference)  
- Overestimation of number of malaria visits due (authors not able to distinguish between confirmed malaria and clinical malaria) |
| Matovu 27      | Yes       | - Potential inaccuracy of the data due to the retrospective design and limitations associated to the collection of data                                                                                                    |
| Mujica-Mota 26 | Yes       | - Limitations associated to the method of household selection (non-representative sample size)                                                                           |
| Ezenduka 18    | Yes       | - Potential bias in the selected sample size  
- Lack of comprehensive diagnostic information gathered (due to inadequate documentation)                                                                                 |
| Castillo-Riquelme 25 | Yes | - Collected results might represent the “worst case” scenario, as the survey was conducted just after the high malaria season                                                                                           |
| Ezenduka 17    | Yes       | - Potential bias in the selected sample size                                                                                                                             |
| Sicuri 30      | Yes       | - Underestimation of true costs (e.g., underestimation of incurred costs in households)                                                                               |
| Ewing 24       | Yes       | - Potential inaccuracy of the data as findings are based on the caregiver’s responses to recall an episode of malaria that had happened in the past                                                                         |
| Osei-Kwakye 21 | Yes       | - No follow-up of patients due to the cross-sectional design  
- Potential bias in the data collection method (e.g., uncertainty if a child was treated for malaria or not)                                                                 |
| Etiaba 23      | Yes       | - The data collected for health seeking and comorbidity were collected on different study groups and so statistical conclusions could not be drawn                                                                 |
| Njau 32        | Yes       | - Potential bias in the selected sample size  
- Potential inaccuracy of the data as patients had to recall cost incurred after being discharged from the hospital                                                        |
| National Population Commission 21 | Yes | - Nonsampling errors (i.e., mistakes made in implementing data collection and data processing, such as failure to locate and interview the correct household and misunderstanding of the questions)  
- Data entry errors                                                                                                                                 |

Table 6: Identification of Risks of Bias (i.e., Limitations) to the Identified Studies Reporting Resources Use and Cost Data
experienced an episode of fever and may therefore include conditions other than malaria.

Despite a policy of free treatment for children aged < 5 years at public health facilities in some sub-Saharan African countries such as Malawi, Uganda, Mozambique, and Nigeria, many households still pay for malaria treatment as a result of frequent scarcity of antimalarial drugs in government health facilities, and bear a proportion of diagnosis costs particularly at inpatient departments.\textsuperscript{20,25} Our review showed that out-of-pocket payments for malaria episodes ranged from US$5.46 in Tanzania to US$36.56/episode in Ghana. Out-of-pocket costs increased sharply in relation to malaria severity and complications. Studies from Nigeria and Kenya implied that most households were uninsured, paying for their health care directly from earnings and savings. In Kenya, all public health facilities charge user fees at the point of care which can be at similar levels to the user fees charged by mission hospitals, and these payments were a major challenge to households.

Our review indicated that the burden on households of transportation to health care facilities varied depending on location and seasonality. Transportation costs were identified for Nigeria, Mozambique, Malawi, and Uganda with the highest burden observed in Mozambique.

Considering the out-of-pocket payments, our findings highlight the potentially catastrophic payments incurred by care for a febrile child in sub-Saharan African countries, which could push households into extreme poverty because of health expenses.

Our review reported that indirect costs related to productivity loss also increased sharply for severe hospitalized cases and cases with neurological sequelae. The number of days lost by caregivers ranged from 3 to 5 days.

Our findings are comparable with other reviews conducted on the economic burden of malaria treatment to households, one of which concluded,

For many people in sub-Saharan Africa the costs for the treatment of one case of malaria are such a high percentage of monthly income/expenditure that they lead to (household) catastrophe; on top of this, few countries in sub-Saharan Africa have healthcare insurance or subsidies for malaria treatment available, leading to extra catastrophe; and lastly, not every healthcare facility has appropriate treatment for malaria available, resulting in many ill people receiving incorrect or less effective treatment.\textsuperscript{35}

Several limitations were noted in the studies included in this systematic literature review. First, some papers did not state the cost base year, an important consideration since prices change over time. When costs were converted, the year of publication was used to inflate and convert cost. This approach might be subject to underestimation or overestimation of costs. Second, there was a lack of information regarding the number of episodes and the definition of an episode of malaria was not always well specified in the publications. Some provided specific information, for example, that an episode was equivalent to having fever 2 weeks prior to data collection,\textsuperscript{26,29} but the majority did not describe it. As a result, it was not possible to link costs to the treatment of particular symptoms. Some of the studies had a retrospective design, which is a limitation for household studies as people are unlikely to have detailed records of the costs incurred, and their recollections may be incomplete or inaccurate. Information on the duration of malaria episodes was also missing from some studies, so it was not possible to assess whether differences in the number of days lost between countries could be associated with differences in duration of malaria episodes. The systematic review process was also limited as not all languages were included. However, we included studies written in English and French, which decreases the potential for language bias.

**Conclusion**

The cost to the health system varied from US$1.94 to US$31.53 for outpatient cases to a range of US$18.35 to US$136.35 for inpatient cases. The highest cost was related to severe cases, particularly cerebral malaria cases with neurological sequelae. Families bear a large share of the burden through out-of-pocket payments of medical care and loss in income due to time off work. Overall, the publications identified in this systematic review provided information focused on a small number of sub-Saharan countries with some methodological gaps.

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**Author Contributions**

All authors comply with the ICMJE criteria for authorship. AE-H, EC, and CS were involved in the conception or the design of the study/project. AE-H, JC, and EC participated in the collection or generation of the data. AE-H, JC, EC, and CS
performed the study/project. AE-H and CS contributed to the material/analysis tools. AE-H, JC, EC, and CS were involved in the analyses or interpretation of the data. All authors read and approved the final manuscript.

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