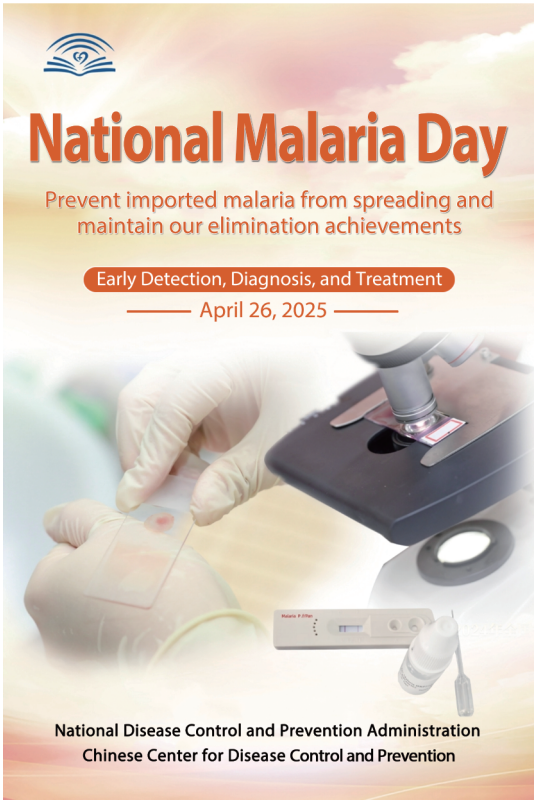
ISSN 2096-7071 (Print)
ISSN 2096-3101 (Online)
CN 10-1629/R1

CHINA CDC WEEKLY

Vol. 7 No. 18 May 2, 2025

中国疾病预防控制中心周报



NATIONAL MALARIA DAY ISSUE

ISSN 2096-7071

China CDC Weekly

Cover Image: adapted from National Disease Control and Prevention Administration, https://www.ndcpa.gov.cn/jbkzzx/c100008/common/content/content_1914247731118247936.html.

This week's issue was organized by Guest Editor Qiyong Liu.

Commentary

Malaria Ends with Us — Time to Reinvest, Reimagine, and Reignite

Simon I. Hay[1,#]

ABSTRACT

On World Malaria Day 2025 under the banner "Malaria Ends with Us", China's experience offers timely lessons for global malaria elimination. Certified malaria-free in 2021, China achieved this milestone through decades of reinvestment, local innovation, and strong political will. This commentary highlights key strategies: reinvestment after resurgence in the Huai River Basin, adaptive local leadership in Hainan, and cross-border collaboration in Yunnan. China's integrated approach — combining ecological vector control, community engagement, and sustained surveillance — shows that ending malaria requires more than technology. It demands long-term commitment, innovation, and collective action.

In 2021, China was certified malaria-free by the World Health Organization — a historic milestone and a testament to over 70 years of unrelenting public health commitment (*1*). Yet the global picture remains daunting: malaria remains endemic in more than 80 countries, with approximately 244 million cases and nearly 700,000 deaths in 2022, the vast majority from *Plasmodium falciparum* in Africa (*2*). On World Malaria Day 2025, the imperative is clear: we must reinvest in proven strategies, reimagine our response for a changing world, and reignite political and scientific will to finish the job. China's experience offers a roadmap — and a warning pertinent to these times (*3*).

Reinvest: The Cost of Complacency

China's malaria elimination was not linear. As the case of the Huai River Basin (HRB) demonstrates, early success can invite complacency. After achieving "basic elimination" by 1987, the HRB experienced a severe resurgence between 2003 and 2006. The causes were telling: dramatic reductions in funding, dismantled surveillance infrastructure, loss of trained personnel, and underestimation of the transmission potential of *Anopheles sinensis* — a mosquito species thought to be low-risk (*4*).

Reinvestment turned the tide. Mass drug administration campaigns, vector control using *Bacillus sphaericus*, and a revitalized public health network restored elimination by 2012. The lesson is clear: malaria resurgence was not a failure of tools, but of sustained commitment. It is a lesson that has been reinforced repeatedly in many other global settings (*5*). Endemic and recently certified countries alike must plan now for the decades ahead. That means financial reinvestment, but also political leadership, workforce development, and robust surveillance systems that remain vigilant even when cases dwindle.

Reimagine: Innovations in Vector Control

While insecticide-treated nets (ITNs) and indoor residual spraying (IRS) have been global mainstays, China's experience demonstrates the value of reimagining vector control. Environmental management — particularly larval source management — played a critical role in China's success (*6*).

In agricultural regions, innovative irrigation and cropping practices — including intermittent irrigation, paddy-upland crop rotation, and rice-fish co-culture — effectively reduced *Anopheles* breeding sites while simultaneously improving agricultural yields and water use efficiency. These strategies proved cost-effective, scalable, and particularly relevant for low- and middle-income countries where vector control budgets face increasing constraints.

Biolarvicides such as *B. thuringiensis israelensis* and *B. sphaericus* have further expanded the vector control toolkit, offering targeted, environmentally friendly interventions. When combined with improved residential hygiene and infrastructure development, these measures provide sustainable and community-led approaches to malaria prevention.

Vector control, in short, need not be limited to

insecticide-treated surfaces. It can be designed into landscapes, livelihoods, and local economies — by reimagining the environments in which mosquitoes thrive.

Reignite: The Power of Local Leadership and Cross-border Collaboration

Elimination requires passion as much as precision (*7*). China's national campaign to eliminate the "four pests" — mosquitoes, flies, rats, and cockroaches — mobilized communities, trained tens of thousands of health workers, and drove a health literacy movement that reached every province (*8*). These efforts extended beyond top-down mandates to encompass cross-sectoral action and local accountability.

Through strong local government leadership and interdepartmental cooperation, Hainan established flexible, adaptive strategies for malaria control. Leadership continuously refined intervention methods across different phases of the elimination campaign (*9*). Hainan's approach offers valuable insights for regions with high malaria transmission risk.

Yunnan Province, China's final frontier for indigenous transmission, exemplified the power of tailored responses in complex border settings. Facing multiple vector species, challenging terrain, and shared borders with Myanmar, Laos, and Vietnam, Yunnan confronted substantial risk of imported cases. The province implemented stratified risk management, the now-famous "1-3-7" strategy (case reporting within 1 day, investigation within 3 days, focused response within 7 days), and extensive cross-border sentinel surveillance (*10*). Today, it stands as a global model for malaria elimination in high-mobility, cross-border settings.

Sustained elimination also requires new regional partnerships. China's cooperation with neighboring countries to monitor vectors, share data, and harmonize interventions demonstrates that malaria cannot be eliminated one country at a time. Cross-border frameworks must be reinvigorated, particularly in sub-Saharan Africa and the Greater Mekong Subregion.

Lessons for a Changing World

Climate change, urbanization, land-use shifts, and growing drug and insecticide resistance present evolving threats to malaria control. China's journey demonstrates that resilience lies in adaptability. Its phased strategy — transitioning from integrated mosquito management to sustainable vector management — underscores the necessity for interventions that are locally tailored, environmentally attuned, and continuously evolving.

China's success against malaria resulted not from a single innovation but from the synergy of many factors: strong political will, stratified risk approaches, ecological insight, and relentless operational adaptation. As we approach 2030 — the target year for malaria elimination in multiple global strategies — we must integrate these lessons with next-generation tools: vaccines, genetic technologies, AI-driven surveillance, and climate-informed early warning systems.

Yet technology alone cannot end malaria. What remains essential is the human element: reinvestment in health systems, reimagined strategies for the most complex settings, and reignition of collective will.

A Call to Action

As we mark World Malaria Day under the banner "Malaria Ends with Us", let us recognize that "us" encompasses national governments, local communities, scientists, funders, and every individual at risk. Ending malaria is possible — but only if we sustain what works, embrace innovation, and remain vigilant for emerging challenges. China's 70-year journey is not merely a triumph to be admired from afar. It is a playbook to be adapted, invested in, and reimagined — until malaria ends with all of us.

Conflicts of interest: No conflicts of interest.

Acknowledgements: Thanks to Profs Qiyong Liu and Pete Gething for useful comments and catches.

doi: 10.46234/ccdcw2025.099

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Submitted: April 20, 2025
Accepted: April 26, 2025
Issued: May 02, 2025

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Vital Surveillances

Risk Factors for Imported Severe Malaria Cases — China, 2019–2023

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ABSTRACT

Objective: To analyze the epidemiological characteristics of imported malaria in China from 2019 to 2023 and to explore risk factors for severe malaria cases, thereby providing a theoretical basis for early clinical identification and intervention of severe malaria.

Methods: National malaria case data were retrospectively collected from 2019 to 2023 through the Chinese Center for Disease Control and Prevention Parasitic Disease Prevention and Control Information System. Study subjects were divided into severe and non-severe malaria cases, and the characteristics of both groups were analyzed. Multivariate logistic regression analysis was used to explore risk factors for developing severe malaria.

Results: From 2019 to 2023, a total of 7,892 imported malaria cases were reported nationwide, including 673 severe cases and 7,219 non-severe cases. There were 7,353 (93.2%) male and 539 (6.8%) female patients. Compared to non-severe malaria patients, severe malaria patients were older (43.9±10.4 years), predominantly originated from Africa (643,95.5%), had a higher frequency of recent overseas residence within the past month (609,90.5%), were typically infected with *P. falciparum* (527,78.3%), and had a higher mortality rate (47,7.0%). Severe cases had longer median time intervals from symptom onset to medical visit (4 days), from visit to diagnosis (2 days), and from diagnosis to treatment (2 days), and a longer median medication time (7 days), all $P<0.05$.

Conclusions: This study identified risk factors for severe malaria and recommends focusing on monitoring patients' age, infection source, *Plasmodium* species, time from onset to hospital visit, and recent history of foreign residence. These findings provide a valuable reference for effectively managing malaria cases and reducing the incidence of severe malaria in the future.

Malaria remains a major global public health challenge and one of the most significant infectious diseases worldwide. According to the latest data released by the World Health Organization (WHO), there were approximately 263 million malaria cases and 597,000 deaths caused by malaria globally in 2023. Notably, the majority of these cases were attributed to *Plasmodium falciparum* infections in Africa (*1*). Malaria has been endemic in China for over 3,000 years. Through generations of effort, both the number of malaria cases and the extent of malaria-endemic areas have significantly decreased (*2*). In response to the global malaria elimination initiative outlined in the United Nations Millennium Development Goals, the Chinese government launched a nationwide campaign in 2010. This initiative set ambitious targets: to eliminate malaria in most regions in China by 2015 and to achieve nationwide malaria elimination by 2020. No local cases have been reported since 2017. On June 30, 2021, China was officially certified as a "malaria-free country" by the World Health Organization after successfully achieving the goals of its malaria elimination program.

However, in recent years, with the continuous advancement of economic globalization and the "Belt and Road" infrastructure initiative, China's exchanges with countries around the world have become increasingly frequent. In particular, the number of workers traveling to malaria-endemic regions, such as Africa and Southeast Asia, has risen. As a result, imported malaria cases are now the primary source of malaria cases in China, presenting new challenges for malaria prevention and control in the country (*3*). Since 2017, China has reported zero indigenous mosquito-borne malaria cases. However, the risk of imported cases and their potential for secondary transmission persists. Therefore, malaria prevention and case management remain critical in China, with the goals of reducing severe malaria cases and deaths,

and of preventing local secondary transmission (*4*).

Severe malaria is a potentially life-threatening complication of malaria infection. The pathophysiological progression from non-severe malaria to severe malaria involves complex host–parasite interactions that are influenced by both intrinsic factors, such as age and genetic susceptibility, and extrinsic factors, such as delayed diagnosis and chemoprophylaxis compliance (*5*).

Large-scale epidemiological assessments to describe trends and identify risk factors for severe malaria may improve imported malaria case management and prevent severe cases. To better understand and address this challenge, we retrospectively collected data on malaria case information nationwide from 2019 to 2023, using the Chinese Center for Disease Control and Prevention Parasitic Disease Prevention and Control Information System (NIPD-PCIS). We conducted case-based epidemiological investigations on each imported malaria case and described its epidemiological characteristics, identified risk factors associated with severe malaria, and provided information for early detection and clinical management of severe malaria and to inform malaria treatment strategies early in the disease.

METHODS

Inclusion Criteria of Malaria Cases

Malaria is an infectious parasitic disease caused by *Plasmodium* parasites. Diagnosis of malaria cases in this study was based on a comprehensive assessment of epidemiological history, clinical manifestations, and laboratory examinations, in accordance with the Health Industry Standards of the People's Republic of China.

Criteria for Classification as Severe and Non-Severe Malaria

In confirmed malaria cases, the presence of one or more of the following clinical manifestations indicates severe malaria: coma, severe anemia (hemoglobin <5 g/dL or hematocrit <15%), acute renal failure (serum creatinine >265 μmol/L), pulmonary edema or acute respiratory distress syndrome, hypoglycemia (blood glucose <2.2 mmol/L or <40 mg/dL), circulatory collapse or shock (systolic blood pressure <70 mmHg in adults or <50 mmHg in children), and metabolic acidosis (plasma bicarbonate <15 mmol/L) (*6*). In clinical practice, physicians comprehensively evaluate patients' symptoms, physical signs, laboratory findings, and disease progression to determine the presence of severe malaria. Patients infected with malaria parasites who present with mild symptoms, absence of high parasitemia, and no vital organ dysfunction or additional concerning laboratory indicators are classified as non-severe malaria cases.

Data Collection

China has established a comprehensive nationwide malaria reporting system that requires healthcare institutions at all levels, including hospitals and public health departments, to immediately report any diagnosed malaria case through the Disease Surveillance Information Reporting and Management System. Mandatory reporting fields include: 1) demographic data (name, age, sex, occupation, and current residence); 2) disease-related information (date of symptom onset, date of medical consultation, and history of prior malaria infections); 3) clinical manifestations (fever, chills, headache, and generalized myalgia); and 4) diagnostic results (parasitological test outcomes and *Plasmodium* species identification). For this study, epidemiological data of malaria cases from 2019 to 2023, including both clinical and parasitological information, were extracted from the Chinese Center for Disease Control and Prevention Parasitic Disease Prevention and Control Information System (NIPD-PCIS).

Data Analysis

Summary statistics of normally distributed quantitative variables were expressed as means and standard deviations. For non-normally distributed variables, we used medians and interquartile ranges (IQRs), and categorical data were summarized by ratios and percentages. The Mann–Whitney U test was used to compare median differences in continuous variables between groups, while the χ^2 test and Fisher's exact test were used to examine proportional differences. Logistic regression was used to identify factors associated with severe malaria, and the association between exposure variables and severe cases was estimated by odds ratios (*OR*s) and 95% confidence intervals (*CI*s). A two-sided *P* value <0.05 was considered statistically significant. All statistical tests were performed using SPSS (version 22.0; IBM Corp., Armonk, NY).

RESULTS

Epidemiological Profile

From 2019 to 2023, a total of 7,892 imported malaria cases were reported. All cases were divided into two groups according to the inclusion criteria mentioned in the methodology: severe malaria (673 cases) and non-severe malaria (7,219 cases), with a significant surge in severe cases in 2023 (Figure 1A). National distribution of imported malaria from 2019 to 2023 shows that the top five regions with the highest number of malaria cases are Yunnan, Guangdong, Henan, Sichuan, and Shandong provinces, while the top five provinces with severe malaria cases are Henan, Shandong, Sichuan, Guangdong, and Hubei (Figure 1B). Case characteristics are presented in Table 1, which showed that 7,352 (93.2%) patients were male and 539 (6.8%) patients were female, with a mean age of 41.0±11.3 years. The severe malaria group had an older mean age (43.9±10.4 years) compared to the non-severe malaria

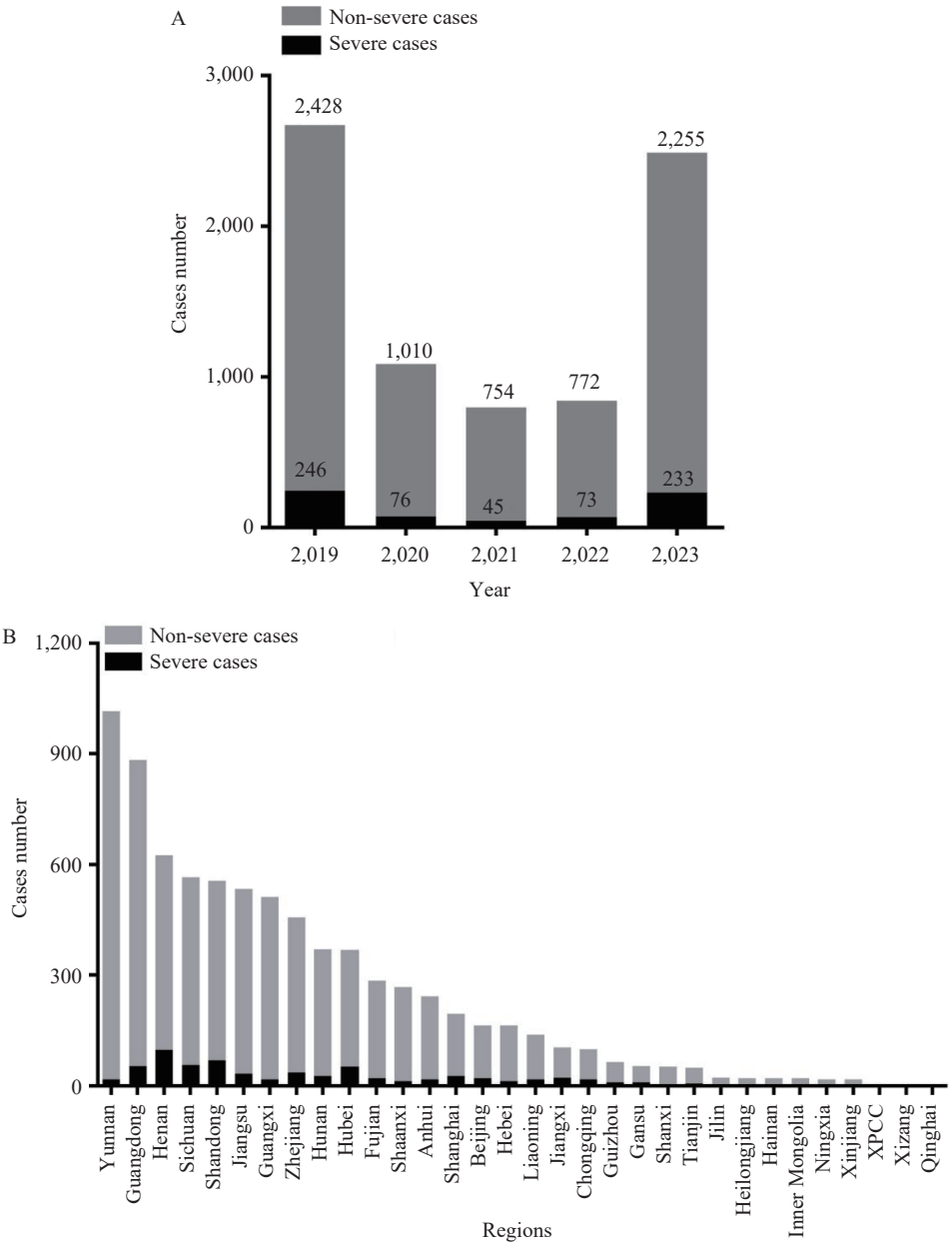

FIGURE 1. Distribution of severe and non-severe imported malaria in China. (A) Distribution of severe and non-severe imported malaria in China from 2019 to 2023; (B) National distribution of severe and non-severe malaria from 2019 to 2023. Abbreviation: XPCC=Xinjiang Production and Construction Corps.

TABLE 1. Epidemiological characteristics of malaria in China from 2019 to 2023.

Factors	Total (*N*=7,892)	Non-severe patient (*N*=7,219)	Severe patient (*N*=673)	Statistical value	*P*
Gender, *N* (%)				0.403	0.294
Male	7,353 (93.2)	6,721 (93.1)	631 (93.8)		
Female	539 (6.8)	497 (6.9)	42 (6.2)		
Age	41.0±11.3	40.7±11.4	43.9±10.4	−6.97	0.005
Purpose of travel, *N* (%)					
Labor	6,300 (79.8)	5,788 (80.2)	512 (76.1)	8.03	0.18
Tourism	92 (1.2)	86 (1.2)	6 (0.9)		
Others	1,500 (19.0)	1,345 (18.6)	155 (23.0)		
Source, *N* (%)					
Africa	6,690 (84.8)	6,047 (83.8)	643 (95.5)	93.92	0
Asia	1,137 (14.4)	1,113 (15.4)	24 (3.6)		
Oceania	49 (0.6)	45 (0.6)	4 (0.6)		
South America	16 (0.2)	14 (0.2)	2 (0.3)		
History of living abroad within one month, *N* (%)					
No	1,665 (21.1)	1,601 (22.2)	64 (9.5)	59.369	0
Yes	6,227 (78.9)	5,618 (77.8)	609 (90.5)		
History of living abroad in the past year, *N* (%)					
No	2,994 (37.9)	2,734 (37.9)	260 (38.6)	0.149	0.364
Yes	4,898 (62.1)	4,485 (62.1)	413 (61.4)		
Initial diagnosis, *N* (%)					
Malaria	6,071 (76.9)	5,555 (76.9)	516 (76.7)	0.026	0.871
Other diseases	1,821 (23.1)	1,664 (23.1)	157 (23.3)		
Species, *N* (%)					
Plasmodium falciparum	5,005 (63.4)	4,478 (62.0)	527 (78.3)	72.33	0
Plasmodium vivax	1,524 (19.3)	1,445 (20.0)	79 (11.7)		
Plasmodium ovale	1,031 (13.1)	984 (13.6)	47 (7.0)		
Plasmodium malariae	248 (3.1)	235 (3.3)	13 (1.9)		
Mixed	79 (1.0)	72 (1.0)	7 (1.0)		
others	5 (0)	5 (0)	0 (0)		
Previous malaria, *N* (%)					
No	1,431 (18.1)	1,325 (18.3)	106 (15.8)	2.789	0.51
Yes	6,461 (81.9)	5,894 (81.7)	567 (84.2)		
Outcome, *N* (%)					
Death	47 (0.6)	0 (0)	47 (7.0)	461.017	0
Survival	7,845 (99.4)	7,219 (100)	626 (93.0)		

group (40.7±11.4 years). The majority of patients were overseas workers (79.8%). Among all the cases, 84.8% of the patients originated from Africa, 14.4% from Asia, 0.6% from Oceania, and 0.2% from South America. Notably, 95.5% of the severe malaria cases were from Africa. A total of 6,227 (78.9%) patients had a history of overseas residence within the past month and 4,898 (62.1%) within the past year, including 609 (90.5%) in the severe malaria group. Among the 7,892 patients, 76.9% were initially diagnosed with malaria. The malaria species were identified as 5,005 cases of *P. falciparum*, 1,524 cases of *P. vivax*, 1,031 cases of *P. ovale*, 248 cases of *P. malariae*, and 79 cases of mixed infection. Of the

severe cases, 527 (78.3%) were caused by *P. falciparum*. Among all of the patients, 6,461 (81.9%) had a history of malaria infection. A total of 47 deaths occurred, all in the severe malaria group (7.0% of severe cases). Statistical analysis showed significant differences between the severe and non-severe malaria groups in terms of age, infection source, history of overseas residence within the past month, malaria species, and patient outcomes (P<0.05).

Diagnosis and Treatment Information

The median time was 2 days (IQR: 1–4 days) from symptom onset to medical visit, 1 day (IQR: 0–2 days) from visit to diagnosis, and 1 day (IQR: 0–2 days) from diagnosis to treatment. In the severe malaria group, the median time was 4 days (IQR: 2–6 days) from symptom onset to medical visit, 2 days (IQR: 1–4 days) from visit to diagnosis, and 2 days (IQR: 0–3 days) from diagnosis to treatment. The corresponding times of the non-severe malaria group were 2 days (IQR: 1–4 days), 1 day (IQR: 0–2 days), and 1 day (IQR: 0–2 days), respectively. The median duration of medication was 7 days (IQR: 3–8 days) overall, 7 days (IQR: 5–9 days) in the severe malaria group, and 7 days (IQR: 3–8 days) in the non-severe malaria group. The median length of hospital stay was 5 days (IQR: 0–7 days) overall, 7 days (IQR: 5–10 days) in the severe malaria group, and 5 days (IQR: 0–7 days) in the non-severe malaria group. Mosquito nets for malaria prevention were used when traveling abroad by 5,634 patients (71.4%) overall, 498 patients (74%) in the severe malaria group, and 5,136 patients (71.1%) in the non-severe malaria group (Table 2). Statistical analyses showed significant differences between severe and non-severe malaria groups in the time from symptom onset to medical visit, time from visit to diagnosis, and time from diagnosis to treatment, and in the duration of medication and length of hospital stay (P<0.05).

Abbreviation: Risk Factors for Severe Malaria

In a univariate analysis, factors were associated with an increased risk of severe malaria, including age, source of infection, malaria type, history of living abroad within the past month, time from onset to visit, time from visit to diagnosis, and time from diagnosis to treatment. A multivariable logistic regression analysis revealed that age (*OR*: 1.022, 95% *CI*: 1.014, 1.031), Africa as the infection source (*OR*: 2.902, 95% *CI*: 1.958, 4.299), *Plasmodium falciparum* as the causal pathogen (*OR*: 1.442, 95% *CI*: 1.159, 1.793), time from onset to visit (*OR*: 1.035, 95% *CI*: 1.021, 1.05), and a history of living abroad within the past month (*OR*: 2.207, 95% *CI*: 1.649, 2.955) were independent risk factors for developing severe malaria (Table 3).

DISCUSSION

In 2017, China achieved zero reporting of indigenous malaria cases, marking a significant milestone in the country's journey toward malaria elimination (*7*). However, with increasing international exchanges, the number of imported malaria cases has been rising in recent years, and the severe malaria rate among imported *P. falciparum* cases has reached 8.5% (673/7,892). Severe malaria is characterized by an acute onset, multiple severe complications, and high mortality (*6*). Therefore, rapid and effective diagnosis and treatment of imported malaria to prevent progression to severe malaria is critically important.

In this study, we retrospectively analyzed risk factors associated with severe imported malaria cases in China from 2019 to 2023. The results showed that increased age was associated with a higher risk of severe malaria. This finding aligns with WHO surveillance data showing that patients over 45 years had a 1.5 times higher mortality than younger adults (*1*). This may be attributed to weakened cellular immune functions and

TABLE 2. Diagnosis and treatment characteristics of malaria in China from 2019 to 2023.

Factors	Total (*N*=7,892)	Non-severe patient (*N*=7,219)	Severe patient (*N*=673)	Statistical value	*P*
From onset to visit/d, median (IQR)	2 (1–4)	2 (1–4)	4 (2–6)	−14.153	0
From visit to diagnosis/d, median (IQR)	1 (0–2)	1 (0–2)	2 (1–4)	−15.39	0
From diagnosis to treatment/d, median (IQR)	1 (0–2)	1 (0–2)	2 (0–3)	−3.48	0.003
Medication time/d (IQR)	7 (3–8)	7 (3–8)	7 (5–9)	−9.298	0
Use bed nets during stay abroad, *N* (%)					
No	2,258 (28.6)	2,083 (28.9)	175 (26.0)	2.457	0.063
Yes	5,634 (71.4)	5,136 (71.1)	498 (74.0)		

TABLE 3. Multivariate logistic analysis of factors associated with the risk of severe malaria.

Factors	β	SE	Wald	*P*	*OR* (95% *CI*)
Age	0.022	0.004	29.531	0	1.022 (1.014, 1.031)
Source					
Others					
Africa	1.033	0.201	26.509	0	2.902 (1.958, 4.299)
Species					
Others					
Plasmodium falciparum	0.37	0.111	11.042	0.001	1.442 (1.159, 1.793)
From onset to visit	0.05	0.008	43.024	0	1.035 (1.021, 1.05)
From visit to diagnosis	0	0	0.001	0.971	1 (1, 1)
From diagnosis to treatment	−0.026	0.015	3.125	0.077	0.974 (0.946, 1, 003)
History of living abroad within the past month					
No					
Yes	0.792	0.149	28.298	0	2.207 (1.649, 2.955)
Constant	−7.381	0.310	567.888	0	0.001

Abbreviation: SE=standard error; *OR*=odd ratio; *CI*=confidence interval.

reduced splenic filtration capacity in elderly patients, thus reducing parasite clearance (*8*). Additionally, older patients often have comorbidities such as diabetes and cardiovascular diseases with associated endothelial dysfunction, which may exacerbate malaria-related complications (*9*).

Since the Forum on China–Africa Cooperation (FOCAC) in 2000, China's labor exports to Africa have continuously increased. Africa has the highest malaria burden globally, and infection in Africa is predominantly caused by *P. falciparum* (*1*). Previous studies and our data indicate that *P. falciparum* infection is a risk factor for severe malaria (*10*). These factors contribute to a significantly higher risk of severe malaria in patients from Africa compared to other regions, consistent with previous reports (*11*). Therefore, malaria education for travelers to Africa is particularly important.

Our study found that the time from symptom onset to medical visit was positively associated with the risk of severe malaria, consistent with many other studies (*12*). These findings emphasize the need for implementing standardized "test and treat" protocols within 24 hours of symptom onset, as recommended in the latest guidelines (*6*). The high risk associated with recent overseas residence within 1 month suggested that strengthened malaria diagnosis and treatment measures are needed for recent returnees, and that education and adoption of malaria knowledge among inbound and outbound travelers needs to be improved.

This study has several limitations: 1) The data were retrospectively analyzed. 2) Potential inconsistencies in adherence to malaria control measures among healthcare facilities in different regions may have introduced confounding variables. 3) The inclusion criteria were limited; clinical characteristics, such as comorbidities and genetic factors, and laboratory indicators, such as complete blood count and blood biochemistry, were not collected.

CONCLUSIONS

In summary, from 2019 to 2023, severe cases accounted for 8.5% of all malaria cases in China. Independent risk factors for severe malaria included advanced age, African infection source, *P. falciparum* infection, prolonged time from symptom onset to seeking medical attention, and history of residing abroad within the past month. Therefore, identifying these epidemiological characteristics and implementing prompt interventions are crucial for reducing the incidence and preventing re-transmission of severe malaria, thereby alleviating socioeconomic burdens and strengthening malaria eradication efforts. This study enriches the knowledge base regarding severe malaria risk factors and provides a valuable reference for effective case management strategies in the future.

Conflicts of interest: No conflicts of interest.

Ethical statement: Routine data were used from the NIPD-PCIS. All data were anonymized during the analysis.

doi: 10.46234/ccdcw2025.100

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Submitted: March 04, 2025
Accepted: April 24, 2025
Issued: May 02, 2025

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Preplanned Studies

Application of Remote Sensing Methods in Predicting the Dynamics of *Anopheles sinensis* — Anhui Province, China, 2019–2023

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Summary

What is already known about this topic?

Remote sensing information provides indirect insights into infectious disease dynamics. Public health practice has significantly benefited from the increasing availability and accessibility of remote sensing data.

What is added by this report?

This study explores the relationship between meteorological and environmental factors and malaria vector abundance using remote sensing technology, establishing predictive models for *Anopheles sinensis* population dynamics.

What are the implications for public health practice?

Identifying reliable predictors of malaria vector abundance enables policymakers to allocate resources more efficiently to regions at high risk of malaria transmission. In areas where an abnormal increase in malaria vector populations is predicted, proactive measures can be implemented, including environmental management, enhancement of local malaria diagnostic capabilities, and strengthening of targeted public health education campaigns.

ABSTRACT

Introduction: Malaria is a mosquito-borne infectious disease that poses a serious threat to human health. Although Anhui Province achieved malaria elimination in 2019, the risk of retransmission from imported cases persists due to cross-border human mobility. Given the strong correlation between meteorological and environmental factors and malaria transmission, this study selected four distinct geographic regions in Anhui Province to investigate the relationship between these factors and malaria vector abundance using remote sensing technology.

Methods: We collected density data of *Anopheles sinensis* (*An. sinensis*), meteorological parameters (temperature, humidity, rainfall), and normalized difference vegetation index (NDVI) from 18 surveillance sites in Anhui Province from 2019 to 2023. The data underwent preprocessing through multi-band composition, image mosaicking, and surface reflectance calibration to construct a spatiotemporal database. A generalized additive model (GAM) was developed using data from 2019 to 2022 and subsequently validated by predicting mosquito vector density in 2023.

Results: Univariate GAM analysis revealed that nonlinear models provided a better fit than linear models based on Akaike Information Criterion (AIC) values. Temperature, lagged temperature (temperature_1), humidity, lagged humidity (humidity_1), rainfall, lagged rainfall (rainfall_1), NDVI, and lagged NDVI (NDVI_1) all demonstrated significant nonlinear relationships with *An. sinensis* density ($P<0.05$). Specifically, NDVI (0.34–0.81), temperature (10.55 ℃–30.68 ℃), humidity (46.82%–97.61%), and rainfall (9.67 mm–440.52 mm) showed significant positive correlations with *An. sinensis* density. The optimal multivariate GAM incorporated lagged variables: humidity_1, NDVI_1, rainfall_1, and temperature_1. This model achieved an R^2 value of 0.76 on the test set, with a mean squared error (MSE) of 0.19 and a mean absolute error (MAE) of 0.28.

Conclusions: NDVI, temperature, humidity, and rainfall constitute the key environmental drivers influencing temporal patterns of *An. sinensis* density in Anhui Province. The GAM-based prediction model provides quantitative decision support for dynamic mosquito vector monitoring and resource allocation for malaria control.

Malaria is a significant global health challenge, currently endemic in 83 countries that collectively represent 40% of the world's population (*1*). In recent years, the gradual resumption of cross-border human mobility has led to continued occurrences of imported malaria cases in Anhui Province. Despite the achievement of local elimination, environmental conditions conducive to malaria transmission remain unchanged, creating a persistent risk of re-establishment (*2–3*). Malaria is fundamentally an environment-related disease, with transmission dynamics directly influenced by environmental factors such as rainfall, temperature, and humidity. Advancements in remote sensing technology now enable these environmental parameters to be derived from satellite data, providing valuable support for malaria epidemiological studies and control efforts (*4–5*). This study aims to explore the relationship between meteorological and environmental factors and malaria vector abundance using remote sensing technology. By leveraging these capabilities, we seek to enhance spatial risk modeling and identify reliable predictors of malaria receptivity, ultimately assisting policymakers in more effective allocation of limited resources.

Anhui Province is located in the transitional zone between warm temperate and subtropical climates, characterized by a typical monsoon climate. The annual average temperature ranges from 14 °C to 17 °C, with average annual precipitation between 800 mm and 1,800 mm. The Yangtze and Huai Rivers flow from west to east across the province, dividing Anhui into four distinct natural geographic regions: the area north of the Huai River, the Jianghuai Hills, the southern Anhui mountainous area, and the Yangtze River Plain. Based on historical malaria prevalence, *Anopheles* mosquito distribution, imported case incidence, and re-transmission risk, 18 counties and districts from 16 cities were selected as surveillance sites. At each site, a representative natural village was chosen as the survey point, considering factors such as natural geographic environment, crop distribution, and livestock farming (Supplementary Table S1, available at https://weekly.chinacdc.cn/). Mosquito surveillance was conducted biweekly from May to October during 2019–2023, with each session lasting overnight (from 18:00 to 07:00 the following day). The outdoor human-baited double net trap was used for mosquito collection. An unsealed single-layer mosquito net was suspended in a residential area near an *Anopheles* mosquito breeding site, with its base touching the ground. One individual sat inside the inner net to attract mosquitoes. A larger open mosquito net was placed outside the inner net, and another individual entered the outer net for 15 minutes per hour to capture *Anopheles* mosquitoes resting on or around the inner and outer nets using a mosquito aspirator. Surveillance activities were conducted under standardized conditions, including fixed personnel, time, and locations. Data on the normalized difference vegetation index (NDVI) and humidity were obtained from the Sentinel-2A remote sensing dataset. The raw satellite data were processed through multi-band composition, image mosaicking, and surface reflectance calibration, and all bands were resampled to a uniform spatial resolution of 10 meters. A 2-km radius buffer zone was created around each surveillance site, within which environmental variables were extracted. Temperature and precipitation data were obtained from the National Meteorological Information Center of the China Meteorological Administration (http://data.cma.cn) and the Anhui Provincial Meteorological Bureau (http://ah.cma.gov.cn). To study the lag effect of environmental variables, data from the preceding surveillance cycle (approximately two weeks prior) were also collected.

A generalized additive model (GAM) was used to model the data, with a negative binomial regression link function selected to address the issue of overdispersion in the data. The model was trained using data from 2019 to 2022 and then used to predict data for 2023. First, univariate analyses were conducted for each explanatory variable to identify those with a significant impact on mosquito density. Explanatory variables that showed statistical significance in univariate analyses and had relatively lower Akaike Information Criterion (AIC) values were included in the multivariate model. Stratified analyses were performed based on different geographic types. The full multivariate regression model is expressed as follows:

$$Y = f_1(Rainfall_{-1}) + f_2(Temperature_{-1}) + f_3(Humidity_{-1}) + f_4(NDVI_{-1}) + \beta_0$$

Where the function Y is the negative binomial link function, β_0 is the constant intercept term, and f is the spline smoothing function that connects the explanatory variables. All analyses were conducted in R software (version 4.4.3; R Core Team, Vienna, Austria).

From May 2019 to October 2023, a total of 12,094 female *An. sinensis* mosquitoes were captured. The

highest number was recorded in early July, with 2,674 specimens accounting for 22.11% of the total catch. In the univariate GAM analysis, nonlinear models demonstrated a better fit than linear models based on the AIC. Results showed that temperature, lagged temperature (temperature_1), humidity, lagged humidity (humidity_1), rainfall, lagged rainfall (rainfall_1), NDVI, and lagged NDVI (NDVI_1) were all significant nonlinear explanatory variables for *An. sinensis* density (P<0.05). Among these, NDVI (0.34–0.81), temperature (10.55 ℃–30.68 ℃), humidity (46.82%–97.61%), and rainfall (9.67 mm–440.52 mm) showed significant positive correlations with *An. sinensis* density (Supplementary Figure S1 and Supplementary Table S2, available at https://weekly.chinacdc.cn/). The optimal parameters for the multivariate GAM model were lagged humidity (humidity_1), lagged NDVI (NDVI_1), lagged rainfall (rainfall_1), and lagged temperature (temperature_1). The model's AIC value was 7764.05, explaining 56% of the deviance. When tested, the model achieved an R^2 value of 0.76, with a mean squared error (MSE) of 0.19 and a mean absolute error (MAE) of 0.28 (Table 1 and Figure 1). The changes in *An. sinensis* density across different geographical regions of Anhui Province in relation to environmental factors are shown in Figure 2 and Supplementary Figure S2 (available at https://weekly.chinacdc.cn/).

TABLE 1. Outputs of multivariate regression from the GAM.

Variable	Estimate	edf	χ^2	*P*
Intercept	−4.43			<0.001
s (NDVI_1)	Smooth	3	5.43	<0.01
s (Rainfall_1)	Smooth	3	4.50	<0.001
s (Temperture_1)	Smooth	3	7.69	<0.001
s (Humidity_1)	Smooth	3	5.25	<0.5

Abbreviation: *s( )*=Smooth*( )*; edf=effective degrees of freedom; GAM=generalized additive model.

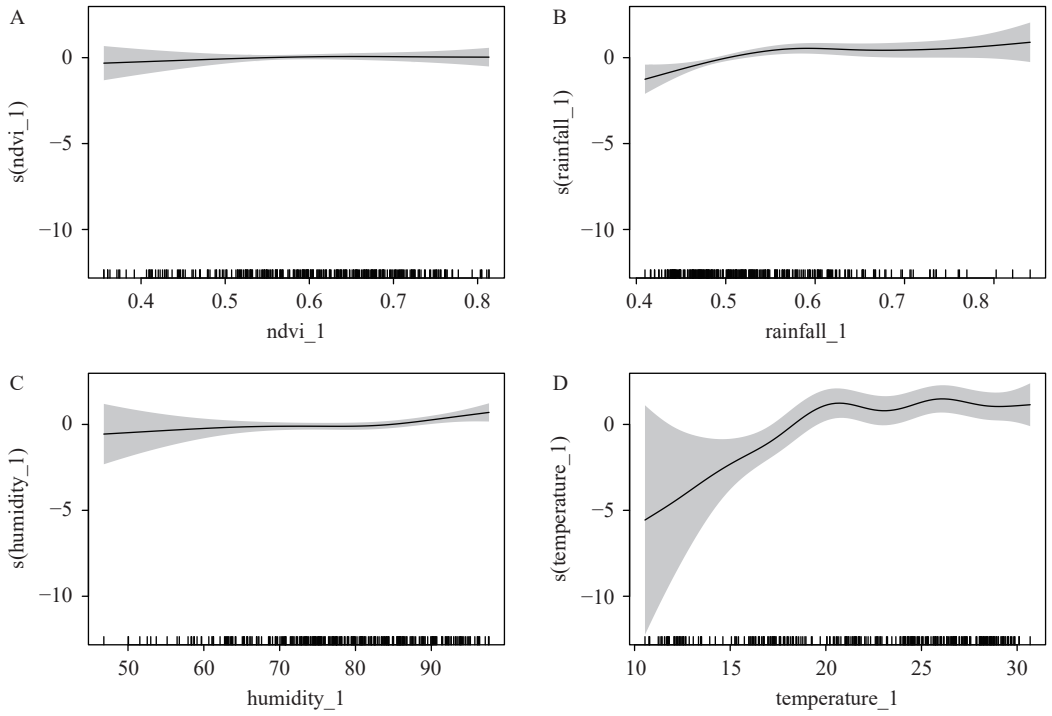

FIGURE 1. Multifactor analysis of environmental factors' impact on *Anopheles* density. (A) impact of lagged NDVI (ndvi_1); (B) impact of lagged rainfall (rainfall_1); (C) impact of lagged humidity (humidity_1); (D) impact of lagged temperature (temperature_1).
Note: The vertical axis represents the smoothed effect value, indicating the magnitude of impact on *Anopheles* density.

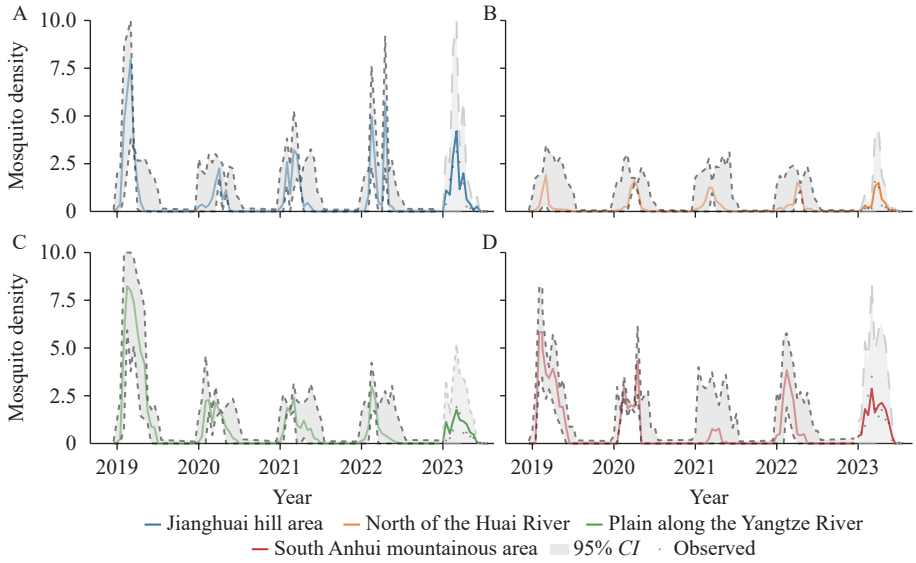

FIGURE 2. Comparison of observed *Anopheles* density values from 2019 to 2022 with fitted and predicted values for 2023. (A) Jianghuai hill area; (B) North of the Huai River; (C) Plain along the Yangtze River; (D) South Anhui mountainous area. Abbreviation: *CI*=confidence interval.

DISCUSSION

In this study, we identified NDVI, temperature, humidity, and rainfall as the key factors influencing the temporal patterns of *An. sinensis* density in Anhui Province. The seasonal pattern of mosquito infestation closely correlates with seasonal variations in these environmental parameters. Low temperatures adversely affect *An. sinensis* survival, significantly reducing adult mosquito infestation rates and egg hatching rates, which leads to substantial population decline (*6*). Nevertheless, mosquito populations rebound during summer months.

David Roiz et al. (*7*) suggested that environmental data from weeks preceding the emergence of high-risk populations should be prioritized to facilitate effective vector control strategies and malaria prevention planning. Accordingly, we incorporated the nonlinear effects of NDVI, temperature, humidity, and rainfall with a two-week lag into our multivariable GAM. The model demonstrated that *Anopheles* mosquito density exhibits an overall increasing trend with NDVI. Additionally, mosquito density increases with rainfall, but this effect gradually diminishes after rainfall exceeds 190 mm. Previous studies have indicated that NDVI can serve as an indicator of suitable mosquito habitat conditions. Increased rainfall and NDVI may create more favorable breeding sites and reduce human activity, thereby contributing to higher mosquito densities (*8*).

When temperature falls below 20 °C, even slight variations have a markedly pronounced effect on *Anopheles* density. As temperature increases, the number of *Anopheles* rises sharply. Above 20 °C, the relationship between temperature and mosquito density is approximately linear and positive. However, when maximum temperature reaches around 28 °C, the influence of temperature fluctuations on *Anopheles* density becomes less apparent. This phenomenon may be attributed to the mosquito population already achieving a relatively high density in the environment. Under optimal thermal conditions, *Anopheles* density tends to stabilize, thereby diminishing the impact of temperature variations on population dynamics. When humidity ranges between 70% and 80%, it exhibits a roughly linear negative effect on mosquito populations. Both temperature and humidity are known to influence mosquito biting rates (*9*) and survival rates (*10*). The observed negative impact of humidity in this range may result from complex interactions among multiple climatic factors (*11*). Our multivariable model explained 56% of the deviance, indicating that it captured over half of the variability in the target variable. The predictive performance, assessed using the coefficient of determination (R^2), yielded an R^2 value of 0.76, demonstrating a strong correlation between predicted and observed values. Furthermore, through regional faceted visualizations, the model effectively captured the spatial heterogeneity and temporal dynamics of *Anopheles* density. The banded

regions of the confidence intervals further validated that the model's uncertainty was within a reasonable range, providing reliable predictions of mosquito density dynamics. These results offer valuable insights for informing malaria control strategies. The strength of this study lies in our use of high-resolution remote sensing imagery to extract environmental factors, ensuring the reliability and accuracy of the independent variables. Additionally, we have accounted for lag effects. However, this study did not account for other factors that influence malaria transmission, such as agricultural irrigation, urbanization, and human mobility.

This study highlights the importance and usefulness of remote sensing technology in vector population monitoring, which will benefit efforts to prevent the re-establishment of malaria transmission. It investigates trends in vector population dynamics and the combined effects of environmental factors, emphasizing their significance in predicting and assessing the risk of local malaria re-introduction. The application of multivariate models and an understanding of climate impacts on the mosquito life cycle provide valuable insights for malaria control managers, aiding in the spatial and temporal allocation of resources to formulate cost-effective decisions and policies. In areas where an abnormal surge in malaria vector populations is forecasted, it is imperative to increase investment in managing mosquito breeding sites. This encompasses removing stagnant water and enhancing environmental sanitation. Furthermore, efforts should be intensified to improve the diagnostic capabilities of local primary healthcare institutions. Concurrently, targeted awareness-raising campaigns should be launched to heighten preventive awareness among residents.

Conflicts of interest: No conflicts of interest.

Funding: This study was supported by the Anhui Provincial Health Commission Research Project (AHWJ2024Aa20278).

doi: 10.46234/ccdcw2025.101

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Submitted: January 14, 2025
Accepted: April 21, 2025
Issued: May 02, 2025

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SUPPLEMENTARY MATERIALS

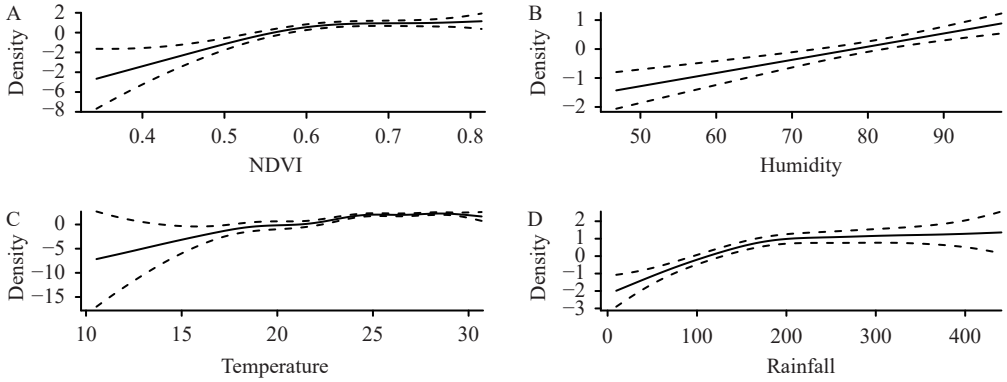
SUPPLEMENTARY TABLE S1. Details for 18 surveillance sites in the study areas.

Regions	Cities	Counties	Geographical coordinates
North of the Huai River	Bengbu	Huaiyuan	33.06°N, 117.24°E
North of the Huai River	Bengbu	Guzhen	33.18°N, 117.25°E
North of the Huai River	Bozhou	Guoyang	33.60°N, 116.15°E
North of the Huai River	Bozhou	Mengcheng	33.38°N, 116.67°E
North of the Huai River	Fuyang	Yingshang	32.43°N, 116.18°E
North of the Huai River	Huaibei	Suixi	33.94°N, 116.71°E
North of the Huai River	Huainan	Tianjiaan	32.50°N, 117.01°E
North of the Huai River	Suzhou	Yongqiao	33.89°N, 117.15°E
Jianghuai hill area	Chuzhou	Dingyuan	32.47°N, 117.64°E
Jianghuai hill area	Lu'an	Shucheng	31.14°N, 116.77°E
South Anhui mountainous area	Huangshan	Huangshan	30.26°N, 118.21°E
Plain along the Yangtze River	Anqing	Tongcheng	30.91°N, 116.99°E
Plain along the Yangtze River	Anqing	Wangjiang	30.19°N, 116.66°E
Plain along the Yangtze River	Chuzhou	Quanjiao	32.07°N, 118.27°E
Plain along the Yangtze River	Hefei	Feidong	32.21°N, 117.39°E
Plain along the Yangtze River	Maanshan	Hexian	31.73°N, 118.34°E
Plain along the Yangtze River	Tongling	Tongguan	30.91°N, 117.86°E
Plain along the Yangtze River	Xuancheng	Guangde	31.03°N, 119.26°E

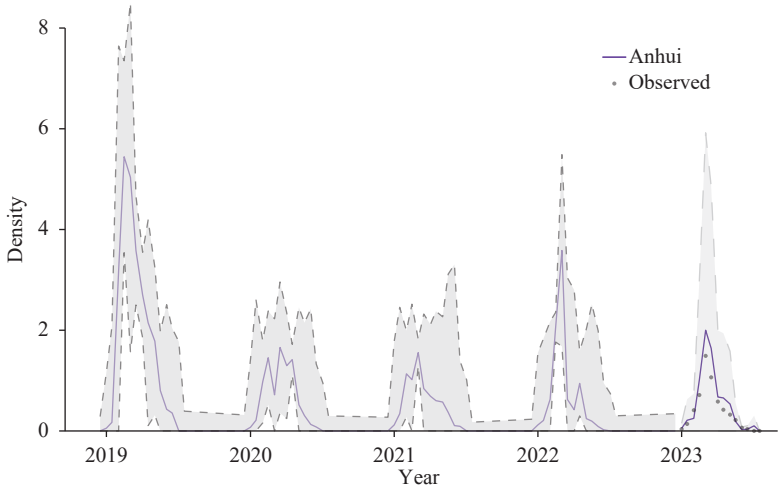
SUPPLEMENTARY TABLE S2. Comparison of AICs for univariate models with variables and time lags.

Model	Variable	Estimate	Standard error	edf	X^2/F	*P*	AIC
NDVI	*Intercept*	−4.19	6.40	1		<0.001	6873
	s (NDVI)	Smooth		3	6.19	<0.001	
$NDVI_{-1}$	*Intercept*	−2.42	3.79	1		<0.01	6704
	s ($NDVI_{-1}$)	Smooth		3	6.76	<0.001	
		Model with variable explanatory Humidity					
Humidity	*Intercept*	−3.77	0.04	1		<0.001	6729
	s (Humidity)	Smooth		3	1.02	<0.001	
$Humidity_{-1}$	*Intercept*	−3.00	0.04	1		<0.001	6650
	s ($Humidity_{-1}$)	Smooth		3	2.78	<0.05	
		Model with variable explanatory Temperature					
Temperature	*Intercept*	−6.06	0.24	1		<0.001	7342
	s (Temperature)	Smooth		3	11.36	<0.001	
$Temperature_{-1}$	*Intercept*	−3.27	0.13	1		<0.001	6930
	s ($Temperature_{-1}$)	Smooth		3	10.66	<0.001	
		Model with variable explanatory Rainfall					
Rainfall	*Intercept*	−1.38	0.01	1		<0.001	7150
	s (Rainfall)	Smooth		3	6.40	<0.001	
$Rainfall_{-1}$	*Intercept*	−1.26	0.01	1		<0.001	7047
	s ($Rainfall_{-1}$)	Smooth		3	6.61	<0.001	

Abbreviation: *s( )*=Smooth; edf=Effective Degrees of Freedom; AIC=Akaike Information Criterion; NDVI=normalized difference vegetation index.



SUPPLEMENTARY FIGURE S1. Univariate analysis of the impact of environmental factors on *Anopheles* density. (A) impact of NDVI; (B) impact of Humidity; (C) impact of Temperature; (D) impact of Rainfall.
Abbreviation: NDVI=normalized difference vegetation index.



SUPPLEMENTARY FIGURE S2. A comparison chart of the observed *Anopheles* density values in the whole province from 2019 to 2022, along with the fitted and predicted values in 2023.

Preplanned Studies

Echinococcus Infection and Metacestode Fertility in Yaks and Sheep — Four Provincial-Level Administrative Divisions, Northwestern China, 2023

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Summary

What is already known about this topic?

Echinococcosis is a parasitic zoonosis caused by the larval stage of cestode species belonging to the genus *Echinococcus*, which is highly prevalent in northwestern China. *Echinococcus* spp. includes numerous species/genotypes that have different infectivity and parasitism patterns in livestock hosts, potentially affecting the transmission dynamics of the parasite.

What is added by this report?

In four PLADs of China, the prevalence of *Echinococcus* was 16.5% in yaks and 9.41% in sheep. The predominant species/genotype was *E. granulosus* s.s. (G1/G3), which mainly infected sheep liver and yak lung. However, fertile cysts were more frequent in sheep than in yaks.

What are the implications for public health practice?

Understanding the livestock infection rate, prevalent species/genotypes, and cyst fertility is essential for elucidating the mechanisms of *Echinococcus* transmission and pathogenesis. This knowledge lays the foundation for developing accurate prevention and control strategies.

ABSTRACT

Introduction: Echinococcosis is a zoonotic parasitic disease caused by the larval stage of *Echinococcus*, prevalent in northwestern China. It poses a serious threat to human health and causes significant economic losses in the livestock industry. This study aims to investigate the infection and development of *Echinococcus* in livestock in northwestern China, providing scientific basis for precise prevention and control of echinococcosis.

Methods: This study utilized a combination of slaughterhouse and household investigations. Liver and lungs from slaughtered livestock in Sichuan Province, Qinghai Province, Xizang Autonomous Region, and Xinjiang Uygur Autonomous Region were examined through visual inspection and palpation, and *Echinococcus* cysts were collected. The cyst fertility was analyzed via microscopic examination. Metacestode DNA was extracted for PCR amplification of the mitochondrial *Cox1* gene. Sequence alignment with the GenBank database was conducted to identify the genotypes of *Echinococcus*. Phylogenetic tree was constructed using MEGA 7.0 software. Haplotypes were analyzed using DnaSP 6, and a haplotype network was constructed using PopART 1.7. Data analysis was performed using SAS 9.4, and $P<0.05$ indicates statistical significance.

Results: Between October and December 2023, 400 yaks and 808 sheep were surveyed in Qinghai, Xizang, and Xinjiang. The infection rate of *Echinococcus* in yaks was 16.5%, significantly higher than that in sheep (9.41%, $\chi^2=12.9802$, $P<0.001$). The fertility rate of *Echinococcus* cysts in sheep was 71.79%, significantly higher than that in yaks (15.57%, $\chi^2=64.1670$, $P<0.0001$). The cysts were mainly parasitizes in the liver of sheep (82.89%) and the lungs of yaks (63.89%). A total of 169 *Cox1* sequences were successfully amplified, of which 98.82% (167/169) corresponded to *E. granulosus* sensu stricto (s.s.) G1/G3, while one sequence was identified as *E. canadensis* G6, and one from *E. multilocularis*. A total of 48 haplotypes were detected, with H3 being the predominant haplotype.

Conclusions: In the four survey provincial-level administrative divisions (PLADs) of China, the infection rate in yaks (16.5%) was significantly higher than in sheep (9.41%). *Echinococcus* was found preferably infect sheep liver and yak lungs, with a higher cyst fertility rate in sheep compared to yaks. Livestock infections are mainly caused by *E. granulosus* G1/G3, and this study, for the first time, identified *E.*

multilocularis infection in yaks from Xizang. The findings provide a crucial foundation for further research into the molecular epidemiology, genetic evolution, and the development of precise prevention and control strategies for *Echinococcus* in the regions.

Echinococcosis is a serious and potentially fatal parasitic zoonosis with worldwide distribution, caused by the larval stage of cestodes in the genus *Echinococcus*. Cystic echinococcosis (CE) caused by *Echinococcus granulosus* sensu lato (s.l.) and alveolar echinococcosis (AE) caused by *E. multilocularis* are the two main forms of the disease and represent major public health problems in northwestern China. *E. granulosus* s.l. is a species complex comprising *E. granulosus* sensu stricto (s.s.) (G1/G3), *E. equinus* (G4), *E. ortleppi* (G5), *E. canadensis* (G6, G7, G8, and G10), and *E. felidis*. Among these, G1/G3 and G6/G7 are commonly found in human infections, while the other genotypes are either rare or absent in human cases (*1*). *E. granulosus* s.l. can infect wild mammals and domestic livestock, while humans may become infected through accidental ingestion of infective eggs (*2*). The infection leads to the development of *Echinococcus* cysts primarily in the host's liver or lungs (*3*–*4*). The larval metacestodes can develop into fertile cysts containing infectious protoscoleces, thereby promoting the cycle and transmission of *Echinococcus* between intermediate and definitive hosts. However, field investigations frequently reveal infertile and calcified cysts that cannot continue the parasite life cycle, thus reducing transmission risk in local areas. In China, developmental differences in cysts among intermediate hosts remain poorly understood, which impacts the risk assessment of *Echinococcus* transmission. Understanding the genotype distribution and cyst development patterns in different hosts is crucial for implementing effective prevention and control strategies against echinococcosis.

This study was conducted in four provincial-level administrative divisions (PLADs) in northwestern China: Xinjiang Uygur Autonomous Region, Sichuan Province, Qinghai Province, and Xizang Autonomous Region, with average altitudes ranging from 1,500 to 4,700 meters. From October to December 2023, livestock infection investigations were conducted at slaughterhouses in Shiquan County, Sichuan; Yushu County, Qinghai; and Hejing County, Xinjiang, as well as in herders' homes in Mozhugongka County and Dangxiong County, Xizang. Livestock cysts were examined and collected through autopsy. Cyst fertility was evaluated microscopically: the presence of protoscoleces indicated a fertile cyst, while their absence indicated an infertile cyst (Figure 1A). DNA was extracted from cysts using the DNeasy Blood and Tissue Kit (Qiagen, Hilden, Germany) following the manufacturer's instructions. The primers forward: TTGAATTTGCCACGTTTGAATGC and reverse: GAACCTAACGACATAACATAATGA were used to amplify an 874 bp fragment of the *cytochrome c oxidase subunit 1* (*Cox1*) gene. Polymerase chain reaction (PCR) reaction conditions followed the protocol described by Minoru Nakao et al (*5*). CE prevalence, cyst fertility, and organ preference were compared using χ^2 test or Fisher's exact test, with differences considered statistically significant at $P<0.05$. All statistical analyses were performed with SAS (version 9.4; SAS Institute; Cary, North Carolina, United States). All amplicons were sequenced and compared to sequences in GenBank (https://blast.ncbi.nlm.nih.gov/Blast.cgi). A phylogenetic tree based on *Cox1* sequences was constructed using MEGA (version 7.0; Center for Evolutionary Medicine at Temple University; Philadelphia, Pennsylvania, United States) and visualized with iTOL (https://itol.embl.de/). Haplotype diversity was analyzed with DnaSP (version 6) (*6*). The haplotype network and statistical calculations were performed using the Median-Joining network method in PopART software (version 1.7) (*7*).

The present study investigated the prevalence of echinococcosis in livestock across three PLADs. A total of 400 yaks (8–14 years old) and 808 sheep (2–5 years old) were examined. We identified 158 cysts across three PLADs, including 32 cysts in yaks from Qinghai, 48 cysts in yaks from Xizang, 20 cysts in sheep from Xizang, and 58 cysts in sheep from Xinjiang. The infection rate in yaks (16.5%, 66/400) was significantly higher than in sheep (9.41%, 76/808, $\chi^2=12.9802$, $P<0.001$). Notably, the prevalence of cysts in Xizang yaks (43.59%, 34/78) was significantly higher than in Qinghai yaks (9.94%, 32/322, $\chi^2=51.6105$, $P<0.0001$). Similarly, the prevalence in sheep from Xinjiang (17.06%, 58/340) was significantly higher than in Xizang (3.85%, 18/468, $\chi^2=40.3453$, $P<0.0001$). Additionally, 42 cysts from yaks in Sichuan and 5 cysts from cattle in Xinjiang were included in the genotype and fertility analyses.

Cox1 genes were successfully amplified in 169 samples, with an overall success rate of 82.44%

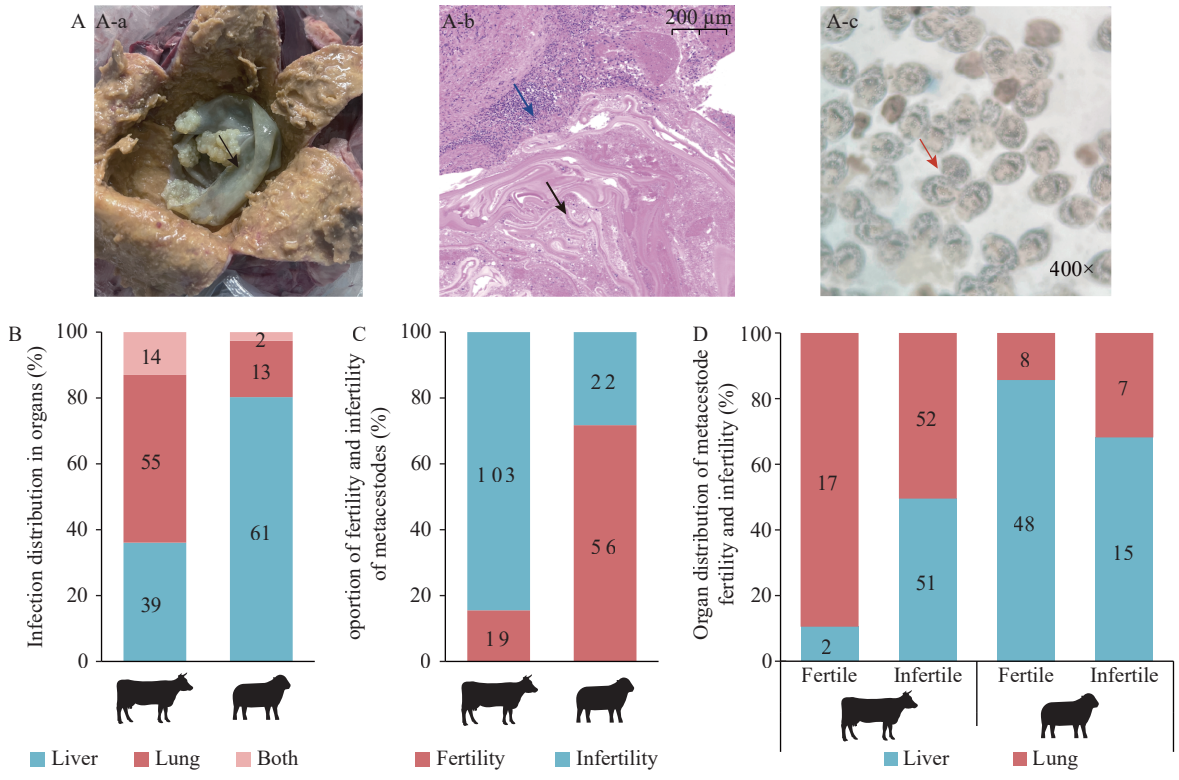

FIGURE 1. Metacestode fertility analysis. (A) Autopsy and microscopy examination. A-a: Cyst after fluid extraction; A-b: Histological analysis of cyst stained with haematoxylin-eosin (HE); A-c: Protoscoleces under the microscope. (B) Organ preference of *Echinococcus* in yaks and sheep; (C) Comparison of metacestode fertility rates between yaks and sheep. (D) Comparison of metacestode fertility rates in different organs of yaks and sheep.
Note: black arrow - endocyst; blue arrow - inflammatory reaction; red arrow - protoscoleces.

(169/205), comprising 78.69% (96/122) from yak cysts and 89.74% (70/78) from sheep cysts. Genotyping revealed that 167 isolates (98.82%) were identified as *E. granulosus s.s.* (G1/G3) from Qinghai (*n*=23), Xizang (*n*=52), Xinjiang (*n*=59), and Sichuan (*n*=33). One isolate was identified as *E. canadensis* (G6) from sheep, and one as *E. multilocularis* from yak. Three species/genotypes (G1/G3, G6, and *E. multilocularis*) were detected in Xizang, whereas only G1/G3 was found in the other three PLADs (Table 1). We identified 46 distinct haplotypes from G1/G3 samples. To explore relationships between different haplotypes, a Median-Joining Network was constructed (Figure 2). The network displayed a star-like structure with one predominant haplotype (Haplotype 3, H3), which accounted for 48.50% (81/167) of the total population and was distributed across all four PLADs. Among the haplotypes, 40 were exclusive to a single PLADs, while 5 haplotypes were prevalent in two geographically adjacent PLADs. *E. granulosus s.s.* shared haplotypes between yaks and sheep. Specifically, H3 was shared across all four PLADs, while haplotypes H9, H28, H31, H32, H34, and H37 were shared in Xizang.

In this study, the distribution of *Echinococcus* cysts in the parasitized organs of yaks and sheep showed statistically significant differences (χ^2=35.2831, P<0.0001). A total of 122 cysts were found in 108 yaks, including 69 cysts (63.89%) in the lung and 53 cysts (49.07%) in the liver. Multi-organ (both liver and lung) infections were found in 14 yaks. There was a significant difference in the distribution of *Echinococcus* cysts in yak organs (χ^2=4.8218, P<0.05). Meanwhile, a total of 78 cysts were identified from 76 sheep, including 15 cysts (19.74%) in the lung and 63 cysts (82.89%) in the liver. Multi-organ infections were found in 2 sheep. The distribution of *Echinococcus* cysts in sheep organs was significantly different (χ^2=60.6736, P<0.0001). These results indicate that *Echinococcus* shows a significant organ preference for the lungs in yaks and for the liver in sheep. Additionally, the fertility rates of cysts formed in the parasitized organs were compared. The fertility rate in sheep (71.79%, 56/78) was higher than that in yaks (15.57%, 19/122), with a statistically significant difference (χ^2=64.1670, P<0.0001). In sheep, the

TABLE 1. Prevalence, genotype diversity and cyst fertility of *Echinococcus* isolates from 4 PLADs in China.

PLAD	Host	No. of examination	Infection rate, %	No. of cysts	Fertile cyst rate, %	Genotype	No. Of isolate
Qinghai	Yak	322	9.94 (32/322)	32	3.13 (1/32)	G1/G3	23
Xizang	Yak	78	43.59 (34*/78)	48	29.17 (14/48)	G1/G3	39
						E. multilocularis	1
	Sheep	468	3.85 (18*/468)	20	35.00 (7/20)	G1/G3	13
						G6	1
Xinjiang	Sheep	340	17.06 (58/340)	58	84.48 (49/58)	G1/G3	56
	Cattle			5	0	G1/G3	3
Sichuan	Yak			42	9.52 (4/42)	G1/G3	33
Total	Yak	400	16.5 (66/400)	122	15.57 (19/122)	G1/G3	95
						E. multilocularis	1
	Sheep	808	9.41 (76/808)	78	71.79 (56/78)	G1/G3	69
						G6	1
	Cattle			5	0	G1/G3	3

Note: The four PLADs include Qinghai, Xizang, Xinjiang, and Sichuan. Infection rate (%) = Number of infected livestock ÷ Number of inspected livestock × 100% ; Fertile cyst rate (%) = Number of fertilecyst ÷ Number of cyst ×100%; No. of cysts was calculated based on the number of infected organs, with each infected organ being counted as one cyst.
Abbreviation: PLADs=provincial-level administrative divisions.
* indicates *Echinococcus* infection in multiple organs, including the liver and lung.

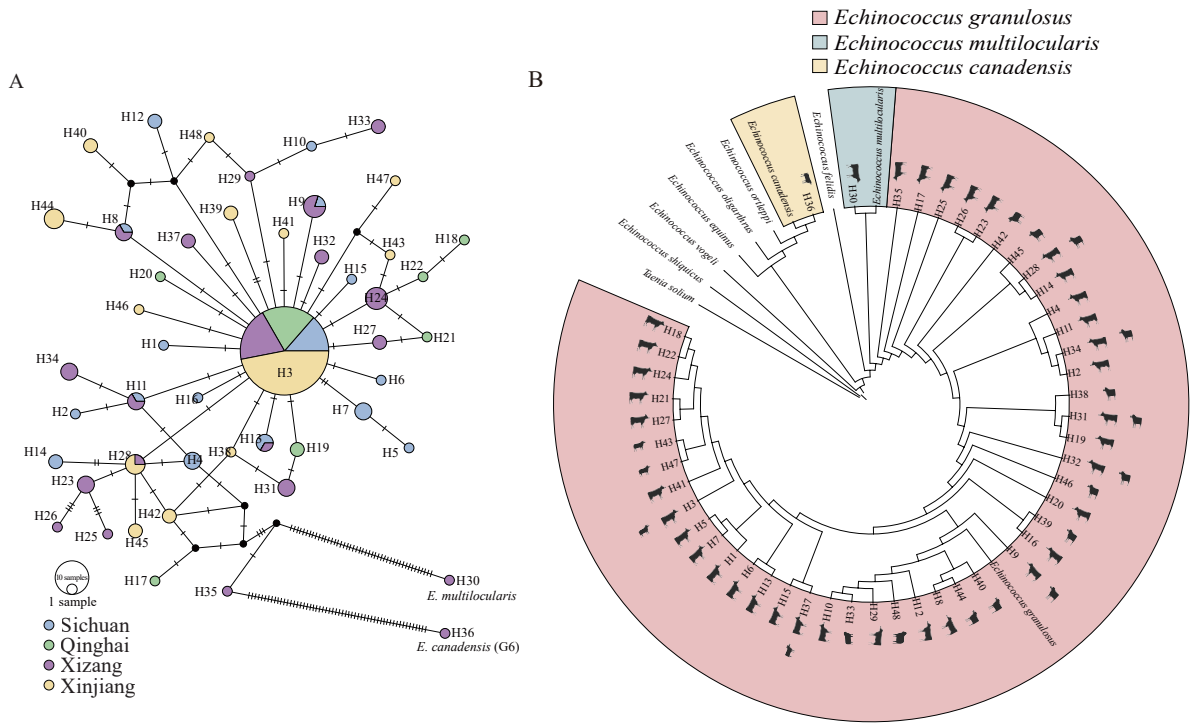

FIGURE 2. Haplotype network and phylogenetic analysis of the 735 bp *Cox1* gene of *Echinococcus*. (A) Haplotype network: Circle sizes represent the frequency of each haplotype. (B) Phylogenetic analysis: Different haplotypes belonging to the same species/genotype are colored accordingly.
Note: For (A), The number of mutations separating haplotypes is indicated by dash marks. Colors indicate the geographic origin. H: haplotype. Circle in blue corresponds to Sichuan (Number of haplotypes, *n*=16), circle in green corresponds to Qinghai (*n*=7), circle in purple corresponds to Xizang (*n*=18), and circle in yellow corresponds to Xinjiang (*n*=13). For (B), Intermediate hosts for a specific haplotype are indicated by black host silhouette.

fertility rate was 76.19% (48/63) in the liver and 53.33% (8/15) in the lungs, with no statistically significant difference. In yaks, the fertility rate was 3.77% (2/53) in the liver and 24.64% (17/69) in the lungs, indicating that the cyst fertility differed significantly (χ^2=9.9241, P<0.05) in the distribution of organs in yaks, with *Echinococcus* more likely to develop infertile cysts in the yak liver (Figure 1B–D).

DISCUSSION

Differences in susceptibility to *Echinococcus* infection among various hosts can significantly influence parasite growth and development. Understanding these host-parasite interactions is crucial for comprehending echinococcosis epidemiology and implementing effective control measures. Therefore, investigating *Echinococcus* infection and development in livestock across four PLADs provides essential information for designing accurate, targeted prevention and control strategies.

In this study, CE prevalence was 16.5% in yaks and 9.41% in sheep. The prevalence in Xizang yaks (43.59%) was significantly higher than the national average of 5.8% reported from 2016 to 2021 (*4*), highlighting the need for continued and enhanced control measures in this region. Conversely, the prevalence in sheep was lower than the post-2011 prevalence (13.86%) reported in a meta-analysis (*3*). This reduction in sheep prevalence can largely be attributed to the earlier implementation of intervention measures and increased efficacy of vaccines against echinococcosis in sheep (*8*). Furthermore, the yaks (8–14 years old) examined in this study were generally older than the sheep (2–5 years old), likely contributing to their extended exposure to contaminated environments and increased susceptibility to infection. Our survey identified three *Echinococcus* genotypes (G1/G3, G6, and *E. multilocularis*), with G1/G3 being the most prevalent across all four PLADs, consistent with previous findings in China (*9*–*10*). A case of *E. multilocularis* infection was found in a yak from Xizang. Although *E. multilocularis* infections in yaks and sheep in the Qinghai-Tibet Plateau have been previously reported (*11*–*12*), this is the first report of *E. multilocularis* infection in a Xizang yak, confirmed by PCR sequencing. Therefore, its impact on livestock should be considered in AE prevention and control efforts. Haplotype analysis identified H3 as the dominant haplotype, consistent with earlier studies (*10*). Additionally, our results show that sheep and yaks share the H3 haplotype, confirming transmission of this haplotype among livestock across the four PLADs.

Organ or tissue preferences are essential for the establishment, survival, and pathogenesis of many parasites (*13*). Previous studies (*14*) have demonstrated that *E. granulosus* G1/G3 preferentially parasitizes the liver of sheep. In our study, *E. granulosus* showed a clear predilection for sheep liver (84.06%) and yak lungs (67.06%). Additionally, the proportion of fertile cysts was significantly higher in sheep compared to yaks (Figure 1C). These findings suggest that the liver preference and higher cyst fertility of *E. granulosus* in sheep contribute more substantially to CE transmission than in yaks. However, the role of yaks should not be overlooked, particularly considering their high infection prevalence in Xizang. Despite these observations, the mechanisms underlying organ tropism and cyst fertility of *E. granulosus* remain incompletely understood. It is still unclear whether these patterns are driven by parasite factors, host factors, or a combination of both. Further investigation into the evolution, parasitism, and pathogenicity of *E. granulosus* may provide insights into this issue. Moreover, reliance on the mitochondrial *Cox1* gene alone is insufficient to fully understand *E. granulosus's* adaptation to endemic environments and its development in various hosts. More comprehensive analysis involving whole genome sequencing is needed. Currently, the control strategy for echinococcosis in the four PLADs of China primarily follows an integrated approach, emphasizing dog deworming, livestock vaccination, and centralized slaughtering. However, this survey revealed significant differences in infection rates, *Echinococcus* species distribution, and cyst fertility in yaks and sheep across the four PLADs. Therefore, we recommend developing region-specific control strategies based on local epidemiological data. In particular, molecular epidemiological monitoring should be implemented to investigate variations in *Echinococcus* populations across different regions, providing data support for the precise control of echinococcosis. This study has certain limitations: the sampling locations may not fully represent the overall situation in the four PLADs, and the sample size was constrained by the availability of livestock for autopsy.

In summary, this study investigated the prevalence of *Echinococcus* in livestock across four PLADs. The results showed that *E. granulosus* infection in Xizang yaks remains higher than the national average. Additionally, *E. multilocularis* infection was found in

Xizang yaks for the first time. *E. granulosus* G1/G3 is the most prevalent genotype across the four PLADs, with H3 as the dominant haplotype shared by sheep and yaks in these areas. Furthermore, *E. granulosus* exhibits a clear organ tropism for the liver in sheep and the lungs in yaks, with higher cyst fertility in sheep. This study provides crucial evidence and a foundation for developing more accurate echinococcosis prevention strategies.

Conflicts of interest: No conflicts of interest.

Acknowledgements: The staff from the Disease Control & Prevention Centers of Yushu Prefecture, Qinghai Province; Tibetan Autonomous Prefecture of Ganzi, Sichuan Province; and Hejing County, Bayingolin Mongolian Autonomous Prefecture, Xinjiang Uygur Autonomous Region.

Funding: This work was supported by the National Key Research and Development Program of China (No. 2021YFC2300800, 2021YFC2300803), State Key Laboratory for Reproductive Regulation and Breeding of Grassland Livestock (No. 2021KF0301), and NHC Key Laboratory of Echinococcosis Prevention and Control (No. 2022WZK1006); The National Parasitic Resources Center, the Ministry of Science and Technology fund (NPRC-2019-194-30).

doi: 10.46234/ccdcw2025.102

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Submitted: November 26, 2024
Accepted: April 18, 2025
Issued: May 02, 2025

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Methods and Applications

Global Assistance and the Cascade of Malaria Prevention and Control — Sub-Saharan Africa, 2011–2022

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ABSTRACT

Introduction: Approximately 70% of funding for malaria prevention and control (P&C) in Sub-Saharan Africa comes from global assistance, yet progress has stagnated over the past decade.

Methods: We constructed a cascade of malaria P&C services and analyzed its coverage and quality across 26 African countries from 2011–2022. Panel analysis was conducted to examine the effectiveness of four major donors [the United States of America (USA), the United Kingdom (UK), the Global Fund to Fight AIDS, Tuberculosis and Malaria (GF), and United Nations International Children's Emergency Fund (UNICEF)], which account for 90% of global funding, in implementing the cascade.

Results: Recommended practice coverage doubled during 2011–2016 but decreased by 10% by 2022. Unrecommended practices followed the same pattern. Total funding from 2011–2020 reached 7.15 billion USA Dollar (USD), with the USA and GF steadily contributing 94.65%, while the UK and UNICEF demonstrated notable funding reductions. Overall, the funding showed limited correlation with the cascade coverage and quality, promoting directly only the upstream measures.

Conclusion: Our findings highlight four key challenges: retrogression of cascade coverage since the late 2010s, persistent gaps between recommended and unrecommended practices, funding constraints, and limited direct effects of donor funding. Strengthening health system capacity at the farthest end of the cascade may provide a solution to this dilemma.

Sub-Saharan Africa accounted for over 90% of global malaria cases and deaths annually after 2010, with approximately 75% of the total malaria prevention and control (P&C) funding sourced from global donors (*1*). The United States of America (USA), the United Kingdom (UK), the Global Fund to Fight AIDS, Tuberculosis and Malaria (GF), and the United Nations agencies provided about 90% of total global assistance, covering most countries in this region over the past decade (*1*). Through combined local and global efforts, malaria prevalence and mortality nearly halved from 2000 to 2015; however, this momentum has not been maintained, with a notable rebound following the coronavirus disease 2019 (COVID-19) pandemic (*2*). Given the current challenges and limited funding, it is imperative to identify the obstacles to malaria P&C progress in Sub-Saharan Africa and maximize the effectiveness of available resources. Although service coverage and quality have been identified as major barriers to malaria P&C development in Africa, few studies in the past five years have comprehensively analyzed P&C service status across Sub-Saharan Africa, and even fewer have statistically examined donor effects on malaria-related service improvements. This study aims to construct a cascade of malaria P&C practices, analyze major donors' funding contributions to each level of the cascade and their effects, identify challenges, provide suggestions for improving global anti-malarial assistance effectiveness, and promote malaria P&C development in Africa.

METHODS

Data Sources

Data on malaria P&C practice coverage and febrile rates were obtained from the Demographic and Health Surveys (DHS) and the Malaria Indicator Surveys (MIS). These surveys provided data on: insecticide-treated mosquito net (ITNs) use and indoor residual spraying (IRS) implementation in households; intermittent preventive treatment during pregnancy (IPTp) among women aged 15–49; diagnostic blood

testing, and type and timing of treatment among febrile children under age 5 (U-5 children). Thus, the target population is limited to these groups. Data on country characteristics, including population, gross nation income (GNI), malaria incidence, and domestic malaria funding, were obtained from the World Bank dataset, the Global Burden of Disease Study 2021 (GBD 2021), and the World Health Organization (WHO)'s World Malaria Reports. Funding data for the major donors — USA, UK, GF, and United Nations International Children's Emergency Fund (UNICEF) — were obtained from official reports of the corresponding agencies and cross-checked with the World Malaria Reports and the Institute for Health Metrics and Evaluation (IHME) Development Assistance for Health (DAH) database. Links to all data sources are available in Supplementary Table S1(available at https://weekly.chinacdc.cn/).

Indicators

Based on WHO recommendations (*3*) and considering data availability, a comprehensive malaria P&C cascade was defined to include: 1) ITNs and IRS use, 2) IPTp service, 3) care-seeking when fever occurs, 4) blood testing, 5) timely medical treatment, and 6) full course of medicine use. Donor funding was categorized into 1) ITNs and IRS, 2) IPTp, 3) diagnosis, and 4) treatment, and estimated accordingly. Each level of the cascade was further classified as "recommended" or "unrecommended" based on the WHO Guidelines for Malaria (*3*). The definitions of recommended practices (RPs) and unrecommended practices (UPs) are listed in Supplementary Table S2 (available at https://weekly.chinacdc.cn/). As most countries lacked data on diagnostic results, it was impossible to determine whether children who received anti-malarial drugs were diagnosed with malaria; therefore, levels 5) and 6) in the cascade included all children treated with drugs. To describe trends in cascade coverage, considering the limited data points for each country, we developed a new indicator called balanced annual percentage change (BAPC). The formula is:

$$b_{ijk} = \frac{c_{ij(p+1)} - c_{ijp}}{L_{ijk}}$$

$$BAPC_{ij} = \frac{\sum_{k=1}^{k=n} L_{ijk} b_{ijk}}{\sum_{k=1}^{k=n} L_{ijk}}$$

where k is the sequence number of the periods between two available data points, and period k begins at year p and ends at year $p+1$; c_{ijp} is the coverage of measure j of country i in year p; L_{ijk} is the length of time of period k; n is the total number of the periods. This indicator describes and compares countries' overall trends in the coverage of each cascade measure.

Statistical Analysis

The frequency and timing of surveys varied greatly across countries. To include as many countries as possible, we divided the 2011–2022 time range into four periods: 2011–2013, 2014–2016, 2017–2019, and 2020–2022. One data point represented a country's condition in the corresponding period, and countries with two or more data points were included.

For analyzing donor funding effects, one-year lagged panel analysis (*4*) was selected, with control variables including 1) malaria incidence, 2) population, 3) GNI, and 4) domestic malaria funding. The dependent variables were interpolated and explanatory variables were min-max normalized. Data was processed with IBM SPSS Statistics 20 (IBM Corp., Armonk, NY, USA). Figures were created with Origin 2023 (OriginLab Corp., Northampton, MA, USA).

RESULTS

This study included 1,638,505 person-time observations across 26 countries. The average sample size per country in each period was 12,036 for children under age 5 (U-5) and 11,388 for women aged 15–49. Detailed demographic characteristics of the study countries and sample sizes are presented in Supplementary Tables S3–S5 (available at https://weekly.chinacdc.cn/).

The Cascade of Malaria P&C

The coverage of cascade components among U-5 children and women aged 15–49 by country and period are presented in Supplementary Table S4 and Table S5; and Figure 1 panels (A)–(D) illustrate the population-balanced coverage of the malaria P&C cascade, febrile rates, and malaria incidence among U-5 children across the four study periods. From 2011–2013 to 2014–2016, coverage of all P&C measures nearly doubled. However, since 2016, all rates have declined at different but nonetheless alarming rates. Notably, blood test rates were lower than treatment rates during 2011–2016, and by

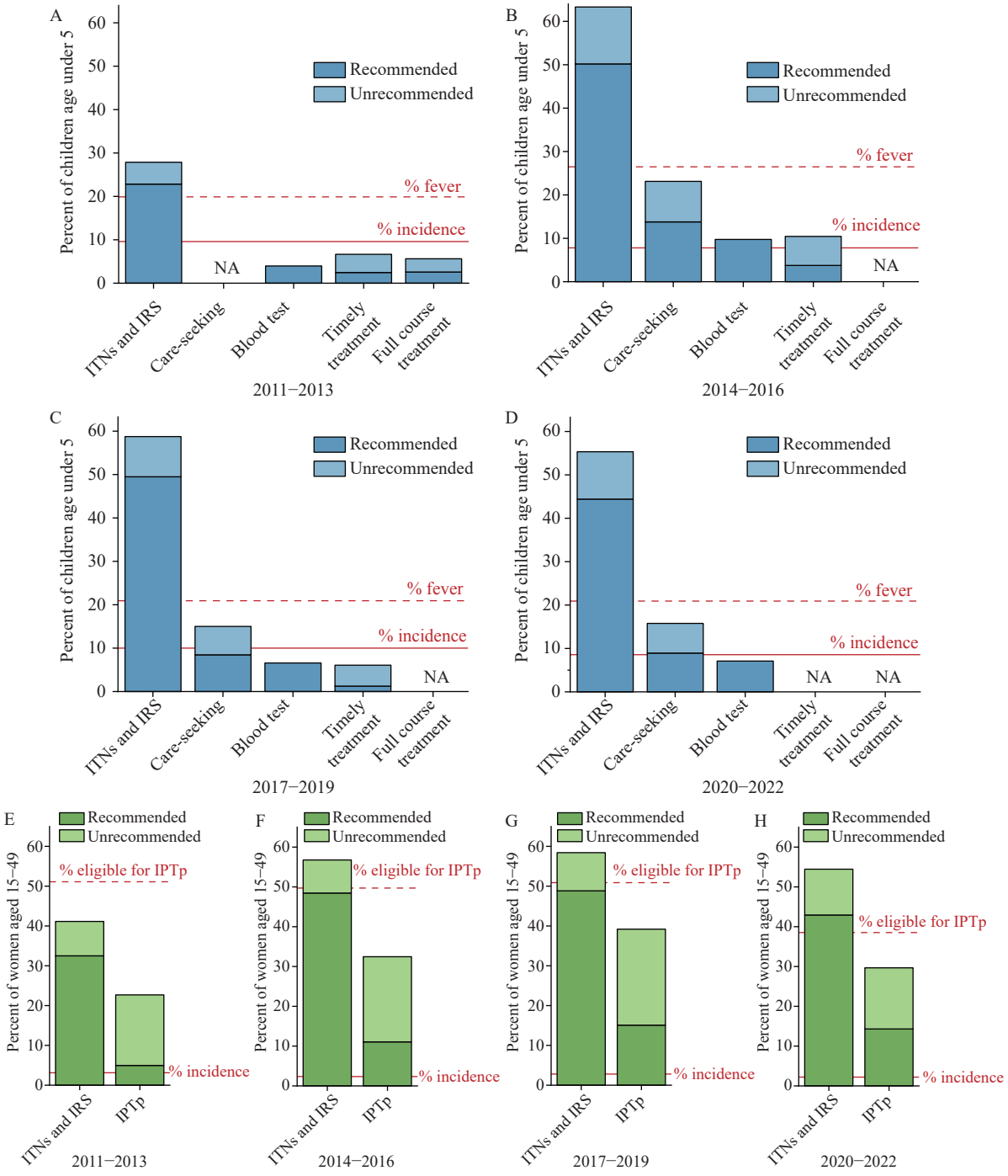

FIGURE 1. Coverage of the cascade of malaria prevention and control. (A) children under age 5 (U-5) in 2011−2013; (B) children under age 5 (U-5) in 2014−2016; (C) children under age 5 (U-5) in 2017−2019; (D) children under age 5 (U-5) in 2020−2022; (E) women aged 15−49 in 2011−2013; (F) women aged 15−49 in 2014−2016; (G) women aged 15−49 in 2017−2019; (H) women aged 15−49 in 2020−2022.

Note: The dotted red lines represent the average fever rates reported in the DHS: (A) 19.90%, (B) 26.49%, (C) 20.93%, and (D) 20.92%. The solid red lines indicate the average malaria incidence rates reported in the IHME GBD 2021: (A) 9.61%, (B) 7.79%, (C) 10.01%, and (D) 8.57%. The dotted red lines represent the pregnancy rates among surveyed women reported in the DHS: (E) 51.09%, (F) 49.71%, (G) 50.87%, and (H) 38.51%. The solid red lines indicate the average malaria incidence rates reported in the IHME GBD 2021: (E) 3.13%, (F) 2.35%, (G) 2.78%, and (H) 2.21%.

Abbreviation: NA=not available; ITNs=insecticide treated nets; IRS=indoor residual spraying; IPTp=intermittent preventive treatment during pregnancy; IHME=institute for health metrics and evaluation; GBD=global burden of disease.

2014–2016, treatment rates exceeded incidence rates. These findings suggest potential mistreatment of febrile children without confirmed diagnoses, although data quality limitations may have contributed to these discrepancies. By 2017–2019, blood test rates surpassed treatment rates, but without data on diagnostic results, it remained impossible to determine whether all treated children had confirmed malaria diagnoses. As shown in Figure 1 panels (E)–(H), among women aged 15–49, RP coverage of ITNs and IRS followed similar trends to those observed in U-5 children, while IPTp coverage increased throughout the 12-year period, albeit at a decreasing pace. Comparatively, RP coverage in women showed a faster and more sustainable growth.

Figure 2 presents the BAPC of cascade coverage. RP coverage of ITNs and IRS increased to varying degrees among both U-5 children and women in 16 countries. For IPTp, only Mali and Ghana exhibited declines in RP coverage, while most countries showed considerable progress; meanwhile, UP coverage decreased in approximately half of the countries. Changes in care-seeking rates varied substantially across countries; growth in blood test rates was most promising, while treatment rates trended downward in most countries. Countries exhibited three main types of practice changes: Type I (ideal) — overall increase with RP increasing while UP decreasing, or RP increasing faster than UP; Type II (less ideal) — widened RP-UP gap with UP increasing faster than RP, or RP decreasing while UP increased more rapidly; Type III (unideal) — overall decrease with RP increasing but UP decreasing faster, or RP decreasing while UP increasing more slowly, or both decreasing. For ITNs and IRS, IPTp, care-seeking, and treatment, 0.00%, 4.17%, 26.67%, and 19.05% of countries fell into Type II, while 38.46%, 18.18%, 60.00%, and 57.14% fell into Type III, respectively.

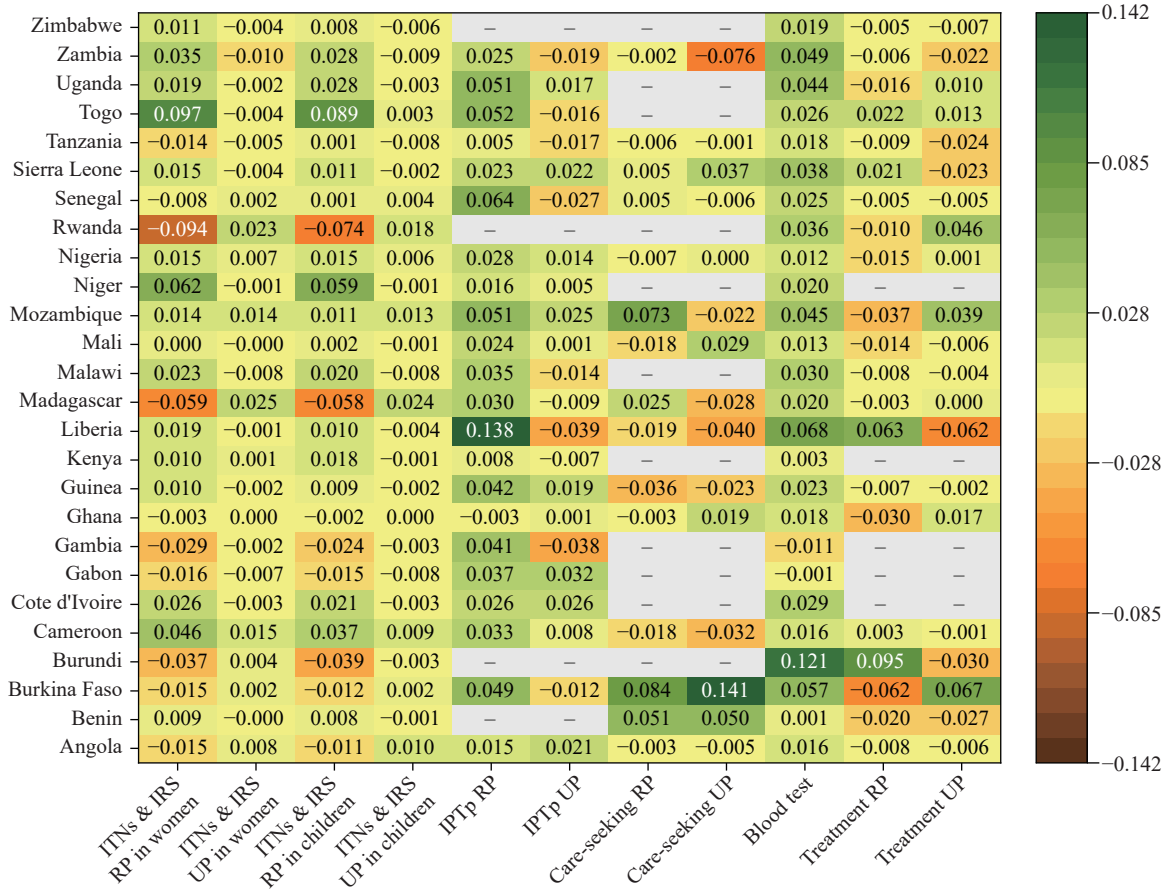

FIGURE 2. BAPC of the cascade coverage by country.
Note: − indicates missing values.
Abbreviation: BAPC=balanced annual percentage change; ITNs=insecticide treated nets; IRS=indoor residual spraying; IPTp=intermittent preventive treatment during pregnancy; RP=recommended practice; UP=unrecommended practice.

Funding to the Cascade and Effects

Figure 3 illustrates the funding contributions from the four major donors to the 26 study countries by component and year. During 2011–2020, total funding reached 7.15 billion USD, increasing from 627.24 million USD in 2011 to 721.89 million USD in 2020, with an annual average of 715.43 million USD. The USA and the GF contributed 94.65% of total funding with relatively stable patterns. In contrast, funding from the UK and UNICEF showed considerable volatility, with rapid austerity evident. The procurement and distribution of ITNs were the primary focus for the USA, UK, and UNICEF, accounting for 57.78%, 54.39%, and 56.33% of their annual funding, respectively. The GF emphasized medical supply and service optimization for IPTp (37.97%) and treatment (36.62%) simultaneously.

The results of the one-year lagged panel regression are presented in Table 1. Based on Breusch-Pagan and Hausman tests, random effect model was selected. For both U-5 children and women aged 15–49, aggregated funding was positively correlated with coverage of ITNs and IRS total coverage and RP. Among individual donors, only the USA demonstrated effectiveness in improving coverage of ITNs and IRS, care-seeking, and IPTp.

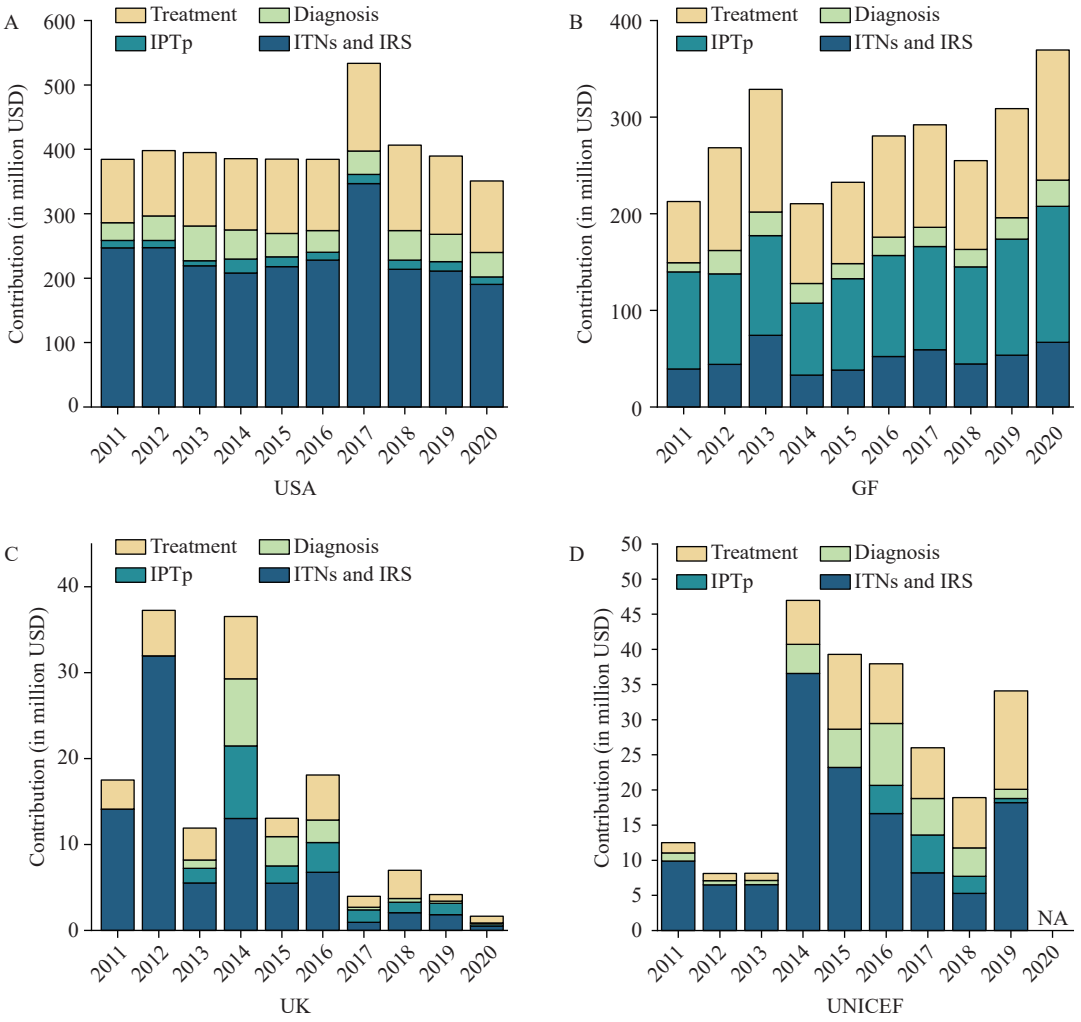

FIGURE 3. Funding from major donors by type of intervention. (A) United States of America (USA); (B) Global Fund to Fight AIDS, Tuberculosis and Malaria (GF); (C) United Kingdom (UK); (D) United Nations International Children's Emergency Fund (UNICEF).

Abbreviation: USA=United States of America; GF=Global Fund to fight AIDS, Tuberculosis and Malaria; UK=United Kingdom; UNICEF=United Nations International Children's Emergency Fund; ITNs=insecticide treated nets; IRS=indoor residual spraying; IPTp=intermittent preventive treatment during pregnancy.

TABLE 1. One-year lagged panel regression of cascade coverage and major donors' funding.

Population Donor	U-5 children					Women aged 15–49				
	USA	UK	GF	UNICEF	Total	USA	UK	GF	UNICEF	Total
ITNs and IRS										
As recommended	0.271* (0.062, 0.481)	−0.136 (−0.363, 0.090)	0.075 (−0.102, 0.253)	−0.045 (−0.301, 0.209)	0.251* (0.048, 0.454)	0.247* (0.052, 0.442)	−0.145 (−0.354, 0.063)	0.057 (−0.106, 0.222)	−0.032 (−0.267, 0.203)	0.226* (0.037, 0.415)
Unrecommended	0.002 (−0.106, 0.111)	−0.008 (−0.130, 0.113)	−0.039 (−0.133, 0.054)	−0.005 (−0.142, 0.130)	−0.016 (−0.121, 0.088)	−0.007 (−0.059, 0.045)	0.001 (−0.052, 0.054)	0.001 (−0.040, 0.043)	−0.012 (−0.072, 0.046)	−0.006 (−0.057, 0.044)
In total	0.279* (0.046, 0.513)	−0.137 (−0.393, 0.118)	0.036 (−0.164, 0.236)	−0.049 (−0.337, 0.238)	0.239* (0.012, 0.465)	0.248* (0.058, 0.439)	−0.144 (−0.349, 0.061)	0.205 (−0.074 0.484)	−0.038 (−0.419, 0.342)	0.227* (0.042, 0.412)
IPTp										
As recommended	–	–	–	–	–	0.189* (0.015, 0.363)	−0.182 (−0.446, 0.082)	−0.068 (−0.294, 0.157)	−0.026 (−0.289, 0.249)	−0.048 (−0.270, 0.174)
Unrecommended	–	–	–	–	–	0.092 (−0.035, 0.220)	−0.045 (−0.228, 0.137)	−0.007 (−0.194, 0.178)	−0.007 (−0.167, 0.152))	0.002 (−0.154, 0.159)
In total	–	–	–	–	–	0.285* (0.094, 0.475)	−0.204 (−0.480, 0.072)	−0.073 (−0.317, 0.171)	−0.016 (−0.302, 0.269)	−0.042 (−0.283, 0.197)
Care−seeking										
Within 24 h	0.201 (−0.039, 0.441)	−0.081 (−0.509, 0.346)	−0.285 (−0.532, 0.039)	0.194 (−0.159, 0.547)	−0.085 (−0.340, 0.169)	–	–	–	–	–
After 24 h	0.356* (−0.127, 0.584)	0.031 (−0.390, 0.454)	−0.139 (−0.388, 0.109)	0.039 (−0.304, 0.383)	0.102 (−0.149, 0.324)	–	–	–	–	–
In total	0.539 (−0.127, 0.951)	−0.049 (−0.800, 0.701)	−0.239 (−0.575, 0.150)	0.235 (−0.380, 0.851)	0.015 (−0.431, 0.465)	–	–	–	–	–
Blood test	0.061 (−0.130, 0.252)	−0.195 (−0.469, 0.078)	0.075 (−0.088, 0.239)	−0.053 (−0.259, 0.152)	−0.041 (−0.165, 0.082)	–	–	–	–	–
Treatment										
Within 24 h	−0.050 (−0.225, 0.124)	−0.005 (−0.204, 0.192)	0.002 (−0.218, 0.222)	−0.051 (−0.180, 0.283)	−0.024 (−0.219, 0.170)	–	–	–	–	–
After 24 h	0.116 (−0.062, 0.295)	0.010 (−0.192, 0.213)	0.137 (−0.088, 0.364)	0.043 (−0.199, 0.285)	0.160 (−0.033, 0.354)	–	–	–	–	–
In total	0.051 (−0.111, 0.215)	0.032 (−0.148, 0.212)	0.131 (−0.073, 0.335)	0.076 (−0.137, 0.289)	0.120 (−0.054, 0.296)	–	–	–	–	–

Note: – indicates missing values.
Abbreviation: USA=United States of America; UK=United Kingdom; GF=Global Fund to Fight AIDS, Tuberculosis and Malaria; UNICEF=United Nations International Children's Emergency Fund; ITNs=Insecticide Treated Nets; IRS=Indoor Residual Spraying; IPTp=Intermittent Preventive Treatment during Pregnancy.
* indicates $P<0.05$.

DISCUSSION

From 2011 to 2016, the coverage of each level of the prevention and control cascade nearly doubled. This finding aligns with a 2015 publication that reported care-seeking rates exceeding 50% and first-line medication compliance rates below one-third across 43 Sub-Saharan African countries (*5*). However, after 2016, most services experienced declining coverage at varying rates, with over half of the countries falling into the type III category for care-seeking and treatment. Such a decrease partially corresponds with World Malaria Reports 2017–2023, and warns of the difficulties in developing these health system components. Additionally, the type II countries of a considerable proportion require special attention due to the potential harm caused by the widening gap between UPs and RPs, as supported by substantial evidence (*6*–*8*).

The panel analysis results align with existing studies (*9*–*10*). Two potential concerns require attention: first, for services showing statistically significant relationships between assistance funding and service coverage, the effects may manifest in both RPs and UPs, suggesting limited control over implementation processes. Second, prevention and care-seeking represent upstream components of the malaria P&C cascade, which depend more directly on material supply and behavioral change advocacy. The downstream components — including parasitological diagnosis through blood testing and timely, full-course treatment — place higher demands on the individual capacities of doctors in public and private health facilities, community health workers, laboratory technicians, pharmacists, and even drug retailers, calling for greater attention from governments and external partners.

Meanwhile, most funding from the UK, the GF, and UNICEF showed no statistically significant impact on improving cascade coverage. Three possible explanations exist: 1) funding data exhibited little pattern, particularly for the UK amid Brexit and accompanying policy shifts (*11*); 2) considering the substantial investment needed to sustain various measures throughout the P&C system, donors' influence may lie in maintaining existing coverage; and 3) increased funding and materials alone had limited impact on service accessibility and availability, indicating the considerable mediating effect of overall health system capacity, as noted above.

Effective implementation of national malaria strategic plans requires a systematic approach involving enhanced political will and governance mechanisms, indigenous medical manufacturing capacity, well-maintained supply chains, and improved primary and secondary health services (*12*). Our results suggest that capacity building and quality assurance at the farthest end of the health system are urgently needed. For example, to correctly manage non-malarial febrile illnesses (*13*), strengthen supply chain management and stock-out reporting (*14*), and support public and private health facilities — including clinics, drug shops, and pharmacies — in their compliance with treatment guidelines based on adequate drug supply (*15*).

This study has several limitations: 1) seeing the retrospective nature of the DHS program, the data may be subject to recall bias; 2) due to the limited surveyed groups in the DHS, service coverage could only be measured in children under age 5 and women aged 15–49, rather than the entire population; and 3) the domestic malaria funding (as a controlled variable) could not be broken down into detailed programs. Overall, this study suggests that strengthening capacity at the farthest end of the health system, supported by increased global funding, may offer a pathway to avoid the gloomy outlook for malaria control and elimination.

Conflicts of interest: No conflicts of interest.

Funding: Supported by the Gates Foundation (Grant number: INV-018912).

doi: 10.46234/ccdcw2025.103

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Submitted: February 24, 2025
Accepted: April 25, 2025
Issued: May 02, 2025

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. Data sources.

Data	Source
Cascade coverage, from DHS and MIS	https://www.dhsprogram.com/topics/malaria/index.cfm
Malaria incidence, from IHME GBD 2021	https://ghdx.healthdata.org/ihme_data
Population and GNI, from World Development Indicators of the World Bank	https://databank.worldbank.org/source/world-development-indicators
Domestic funding for malaria, extracted from the WHO's World Malaria Reports (for example, Annex 4-C in the 2023 World Malaria Report)	https://www.who.int/teams/global-malaria-programme/reports
Funding of the USA, from annual funding tables of President's Malaria Initiative (PMI), the agency of the USA to deliver anti-malaria assistance abroad	https://www.pmi.gov/resources/malaria-operational-plans-mops/
Funding for international development of the UK	https://www.gov.uk/guidance/statistics-on-international-development
GF allocation for countries by disease	https://data-service.theglobalfund.org/downloads
Funding of UNICEF, from UNICEF Supply Annual Reports	https://www.unicef.org/research-and-reports

SUPPLEMENTARY TABLE S2. Definition of the recommended and the unrecommended practices.

Cascade level	Recommended practice (RP)	Unrecommended practice (UP)
ITNs and IRS	Only one measure was deployed in the household for the utmost cost-effectiveness; in the case of ITNs, the net was treated with insecticide within three years before the survey.	ITNs and IRS were co-deployed in the household, which would provide no additional benefit than a single measure; in the case of ITNs alone, the net was not treated with insecticide or was treated more than three years before the survey.
IPTp	At least three doses of Sulfadoxine-pyrimethamine (SP) for IPTp during antenatal care (ANC) visits.	Less than three doses of SP for IPTp during ANC visits.
Care-seeking when fever	The febrile child was taken to seek medical care within 24 hours of fever.	The febrile child was taken to seek medical care after 24 hours of fever.
Blood test	In all settings, suspected malaria should be confirmed with a parasitological test.	–
Timely medical treatment	Anti-malaria drug was given within 24 hours of fever.	Anti-malaria drug was given after 24 hours of fever.
Full course of medicine use	The drug was taken as any times as the guidance recommended.	The drug was taken less or more times than the guidance recommended.

SUPPLEMENTARY TABLE S3. Demographic characteristics of the included countries (2011–2022 average).

Country	Domestic funding for malaria (million USD)	Population (million)	GNI (million USD)	Incidence in children under 5 (%)	Incidence in women aged 15–49 (%)
Angola	35.84	28.75	59,250	7.14	2.55
Benin	3.53	11.13	11,575	15.76	3.55
Burkina Faso	27.90	19.03	12,250	15.25	3.58
Burundi	1.77	10.84	1,775	7.81	2.53
Cameroon	22.36	23.40	29,000	8.68	2.74
Cote d'Ivoire	16.60	24.05	43,500	11.58	3.00
Gabon	3.67	2.04	9,500	8.09	2.83
Gambia	0.86	2.29	1,128	4.97	2.89
Ghana	24.60	29.20	44,500	11.29	3.12
Guinea	3.64	11.80	7,925	15.52	3.55
Kenya	3.61	47.33	60,000	1.87	0.75
Liberia	10.01	4.65	1,600	13.25	2.98
Madagascar	0.03	25.23	10,350	2.63	1.26
Malawi	1.39	17.23	7,425	8.33	2.74
Mali	4.57	18.53	12,750	13.17	3.16
Mozambique	14.06	27.39	11,750	13.72	3.44
Niger	10.27	20.68	11,050	11.66	3.21
Nigeria	5.71	186.25	370,000	11.10	3.10
Rwanda	14.35	11.83	6,950	1.50	0.92
Senegal	15.59	14.63	18,000	1.12	1.35
Sierra Leone	0.35	7.42	3,325	16.15	3.60
Tanzania	27.43	53.80	42,000	4.43	1.85
Togo	3.27	7.58	4,850	11.04	3.03
Uganda	5.91	38.53	24,250	8.07	2.50
Zambia	16.00	16.55	18,000	6.32	2.09
Zimbabwe	1.51	14.33	14,000	1.73	1.79

Abbreviation: USD=United States Dollar; GNI=Gross National Income.

SUPPLEMENTARY TABLE S4. The malaria P&C cascade coverage in children under 5 by country, 2011–2022.

Country	Period	Sample size	Febrile number	ITNs and IRS RP	ITNs and IRS UP	Care-seeking RP	Care-seeking UP	Blood test	Treatment RP	Treatment UP
Angola	2011–2013	9,681	2,645	0.27	0.03	0.30	0.31	0.27	0.14	0.14
Benin	2011–2013	17,489	1,141	0.66	0.09	–	–	0.18	0.18	0.27
Burkina Faso	2011–2013	–	–	–	–	–	–	–	–	–
Burundi	2011–2013	4,985	1,690	0.48	0.07	–	–	0.28	0.07	0.18
Cameroon	2011–2013	147,276	2,680	0.01	0.01	–	–	–	0.12	0.14
Cote d'Ivoire	2011–2013	9,742	1,662	0.36	0.04	–	–	0.11	0.09	0.07
Gabon	2011–2013	7,446	1,315	0.30	0.25	–	–	0.13	0.14	0.11
Gambia	2011–2013	10,701	977	0.69	0.06	–	–	0.33	0.03	0.04
Ghana	2011–2013	–	–	–	–	–	–	–	–	–
Guinea	2011–2013	8,531	1,883	0.20	0.11	–	–	0.08	0.16	0.14
Kenya	2011–2013	–	–	–	–	–	–	–	–	–
Liberia	2011–2013	4,340	1,617	0.39	0.05	–	–	0.32	0.09	0.46
Madagascar	2011–2013	8,109	959	0.87	0.05	–	–	0.05	0.08	0.10
Malawi	2011–2013	2,813	676	0.47	0.13	–	–	0.22	0.23	0.09
Mali	2011–2013	12,882	809	0.63	0.09	–	–	0.12	0.14	0.13
Mozambique	2011–2013	12,683	1,313	0.44	0.06	–	–	0.31	0.22	0.08
Niger	2011–2013	15,291	1,563	0.16	0.10	–	–	0.14	0.04	0.19
Nigeria	2011–2013	35,361	3,691	0.16	0.05	–	–	0.11	0.20	0.15
Rwanda	2011–2013	3,779	876	0.70	0.06	–	–	0.30	0.02	0.09
Senegal	2011–2013	–	–	–	–	–	–	–	–	–
Sierra Leone	2011–2013	14,958	2,859	0.37	0.15	–	–	0.41	0.09	0.41
Tanzania	2011–2013	–	–	–	–	–	–	–	–	–
Togo	2011–2013	–	–	–	–	–	–	–	–	–
Uganda	2011–2013	9,839	2,860	0.41	0.15	–	–	0.27	0.14	0.53
Zambia	2011–2013	–	–	–	–	–	–	–	–	–
Zimbabwe	2011–2013	7,187	515	0.26	0.05	–	–	0.07	0.02	0.03
Angola	2014–2016	–	–	–	–	–	–	–	–	–
Benin	2014–2016	–	–	–	–	–	–	–	–	–
Burkina Faso	2014–2016	8,419	2,617	0.71	0.05			0.31	0.28	0.22
Burundi	2014–2016	15,544	4,640	0.37	0.08	0.54	0.19	0.64	0.35	0.09
Cameroon	2014–2016	–	–	–	–	–	–	–	–	–
Cote d'Ivoire	2014–2016	–	–	–	–	–	–	–	–	–
Gabon	2014–2016	–	–	–	–	–	–	–	–	–
Gambia	2014–2016	–	–	–	–	–	–	–	–	–
Ghana	2014–2016	4,159	894	0.18	0.00	0.46	0.27	0.34	0.14	0.35
Guinea	2014–2016	–	–	–	–	–	–	–	–	–
Kenya	2014–2016	4,724	1,290	0.45	0.13			0.39	0.15	0.09
Liberia	2014–2016	3,926	1,134	0.38	0.05	0.33	0.44	0.50	0.06	0.56
Madagascar	2014–2016	9,149	693	0.74	0.85	–	–	0.12	0.05	0.03
Malawi	2014–2016	2,621	594	0.63	0.07	–	–	0.35	0.30	0.09
Mali	2014–2016	9,539	2,104	0.65	0.09	–	–	0.14	0.09	0.18
Mozambique	2014–2016	–	–	–	–	–	–	–	–	–

Continued

Country	Period	Sample size	Febrile number	ITNs and IRS RP	ITNs and IRS UP	Care-seeking RP	Care-seeking UP	Blood test	Treatment RP	Treatment UP
Niger	2014–2016	–	–	–	–	–	–	–	–	–
Nigeria	2014–2016	8,292	2,622	0.35	0.09	0.36	0.31	0.13	0.16	0.25
Rwanda	2014–2016	9,505	1,388	0.55	0.10	–	–	0.35	0.04	0.08
Senegal	2014–2016	8,746	1,146	0.55	0.05	–	–	0.11	0.02	0.03
Sierra Leone	2014–2016	8,460	1,639	0.38	0.08	0.51	0.20	0.53	0.03	0.55
Tanzania	2014–2016	12,745	1,667	0.48	0.13	0.49	0.40	0.35	0.05	0.41
Togo	2014–2016	8,583	1,413	0.30	0.14	–	–	0.25	0.09	0.13
Uganda	2014–2016	6,108	1,413	0.67	0.11	–	–	0.36	0.07	0.70
Zambia	2014–2016	16,657	2,745	0.55	0.06	0.52	0.55	0.52	0.02	0.44
Zimbabwe	2014–2016	8,082	799	0.29	0.03	–	–	0.13	0.01	0.01
Angola	2017–2019	18,311	1,943	0.18	0.08	0.28	0.28	0.37	0.09	0.10
Benin	2017–2019	16,266	2,429	0.71	0.08	0.31	0.30	0.18	0.06	0.11
Burkina Faso	2017–2019	7,562	1,220	0.50	0.05	0.57	0.18	0.50	0.09	0.42
Burundi	2017–2019	–	–	–	–	–	–	–	–	–
Cameroon	2017–2019	12,595	1,388	0.59	0.02	0.37	0.35	0.21	0.14	0.14
Cote d'Ivoire	2017–2019	–	–	–	–	–	–	–	–	–
Gabon	2017–2019	–	–	–	–	–	–	–	–	–
Gambia	2017–2019	–	–	–	–	–	–	–	–	–
Ghana	2017–2019	4,159	929	0.17	0.00	0.40	0.30	0.38	0.05	0.40
Guinea	2017–2019	9,778	1,221	0.20	0.14	0.45	0.35	0.20	0.12	0.12
Kenya	2017–2019	–	–	–	–	–	–	–	–	–
Liberia	2017–2019	7,372	1,472	0.37	0.09	0.48	0.40	0.52	0.22	0.34
Madagascar	2017–2019	7,306	1,055	0.67	0.11	0.32	0.29	0.16	0.03	0.06
Malawi	2017–2019	2,950	794	0.61	0.08	0.32	0.25	0.40	0.18	0.07
Mali	2017–2019	11,760	1,503	0.62	0.14	0.31	0.30	0.16	0.05	0.09
Mozambique	2017–2019	5,691	1,275	0.69	0.13	0.41	0.31	0.50	0.00	0.31
Niger	2017–2019	–	–	–	–	–	–	–	–	–
Nigeria	2017–2019	38,097	7,536	0.39	0.11	0.39	0.39	0.14	0.00	0.23
Rwanda	2017–2019	3,548	870	0.68	0.08	0.36	0.20	0.37	0.00	0.18
Senegal	2017–2019	15,178	2,378	0.62	0.05	0.33	0.24	0.18	0.01	0.05
Sierra Leone	2017–2019	12,618	1,476	0.46	0.13	0.53	0.31	0.64	0.22	0.28
Tanzania	2017–2019	9,623	1,502	0.44	0.11	0.41	0.35	0.39	0.02	0.34
Togo	2017–2019	4,446	777	0.59	0.13	0.40	0.19	0.33	0.15	0.17
Uganda	2017–2019	9,748	1,973	0.52	0.13	0.60	0.27	0.54	0.04	0.59
Zambia	2017–2019	12,219	1,550	0.65	0.03	0.51	0.32	0.67	0.01	0.37
Zimbabwe	2017–2019	–	–	–	–	–	–	–	–	–
Angola	2020–2022	–	–	–	–	–	–	–	–	–
Benin	2020–2022	–	–	–	–	–	–	–	–	–
Burkina Faso	2020–2022	15,379	2,623	0.62	0.06	0.82	0.61	0.65	–	–
Burundi	2020–2022	–	–	–	–	–	–	–	–	–
Cameroon	2020–2022	5,548	1,344	0.43	0.14	0.32	0.25	0.26	–	–
Cote d'Ivoire	2020–2022	12,595	1,726	0.59	0.02	0.42	0.27	0.37	–	–

Continued

Country	Period	Sample size	Febrile number	ITNs and IRS RP	ITNs and IRS UP	Care-seeking RP	Care-seeking UP	Blood test	Treatment RP	Treatment UP
Gabon	2020–2022	8,291	1,311	0.16	0.19	0.43	0.30	0.12	−	−
Gambia	2020–2022	10,640	1,326	0.43	0.04	0.60	0.19	0.24	−	−
Ghana	2020–2022	−	1,451	−	−	0.44	0.38	0.45	−	−
Guinea	2020–2022	5,205	921	0.29	0.09	0.34	0.28	0.28	−	−
Kenya	2020–2022	5,200	745	0.51	0.14	0.31	0.30	0.41	−	−
Liberia	2020–2022	3,717	1,026	0.45	0.05	0.29	0.36	0.52	−	−
Madagascar	2020–2022	15,972	1,439	0.33	0.28	0.39	0.20	0.23	0.05	0.11
Malawi	2020–2022	−	−	−	−	−	−	−	−	−
Mali	2020–2022	11,567	2,424	0.63	0.09	0.26	0.39	0.24	−	−
Mozambique	2020–2022	12,163	1,039	0.31	0.12	0.64	0.24	0.53	−	−
Niger	2020–2022	6,212	1,569	0.71	0.09	0.38	0.28	0.32	−	−
Nigeria	2020–2022	13,721	3,732	0.29	0.11	0.32	0.31	0.22	0.00	0.06
Rwanda	2020–2022	9,709	−	0.41	0.13	−	−	−	−	−
Senegal	2020–2022	8,999	1,697	0.50	0.06	0.35	0.22	0.26	0.00	0.00
Sierra Leone	2020–2022	−	−	−	−	−	−	−	−	−
Tanzania	2020–2022	−	1,014	−	−	0.46	0.40	0.45	−	−
Togo	2020–2022	−	−	−	−	−	−	−	−	−
Uganda	2020–2022	−	−	−	−	−	−	−	−	−
Zambia	2020–2022	−	−	−	−	−	−	−	−	−
Zimbabwe	2020–2022	−	−	−	−	−	−	−	−	−

Note: missing values are marked by −. The tables present the cascade coverage in children under 5 (U-5 children) by country and period, along with the average coverage for each period. For ITNs and IRS coverage, the numerator represents the number of U-5 children with access to ITNs and IRS, while the denominator represents the total number of U-5 children (sample size). For care-seeking, blood test, and treatment coverage, the numerator represents the number of U-5 children with access to the corresponding services, while the denominator represents the number of febrile U-5 children. All averages are weighted by the corresponding denominator indicators.

SUPPLEMENTARY TABLE S5. The malaria P&C cascade coverage for women aged 15–49 by country, 2011–2022.

Country	Period	Sample size	Number of women aged 15-49 eligible for IPTp	ITNs and IRS RP	ITNs and IRS UP	IPTp RP	IPTp UP
Angola	2011–2013	8,849	5,331	0.26	0.03	0.09	0.25
Benin	2011–2013	17,957	–	0.65	0.10	–	–
Burkina Faso	2011–2013	–	–	–	–	–	–
Burundi	2011–2013	5,319	–	0.48	0.08	–	–
Cameroon	2011–2013	16,417	7,612	0.09	0.06	0.13	0.32
Cote d'Ivoire	2011–2013	11,381	5,412	0.37	0.04	0.07	0.25
Gabon	2011–2013	8,772	4,123	0.26	0.25	0.02	0.21
Gambia	2011–2013	11,928	5,375	0.62	0.06	0.06	0.88
Ghana	2011–2013	–	–	–	–	–	–
Guinea	2011–2013	9,561	4,983	0.20	0.11	0.12	0.22
Kenya	2011–2013	–	–	–	–	–	–
Liberia	2011–2013	4,188	2,311	0.40	0.06	0.28	0.37
Madagascar	2011–2013	8,550	4,334	0.83	0.07	0.04	0.28
Malawi	2011–2013	2,993	1,707	0.42	0.14	0.13	0.68
Mali	2011–2013	11,652	6,723	0.61	0.10	0.11	0.45
Mozambique	2011–2013	14,097	7,623	0.44	0.07	0.10	0.32
Niger	2011–2013	12,103	7,675	0.15	0.10	0.09	0.53
Nigeria	2011–2013	40,296	20,110	0.15	0.04	0.06	0.21
Rwanda	2011–2013	5,229	–	0.61	0.08	–	–
Senegal	2011–2013	–	–	–	–	–	–
Sierra Leone	2011–2013	17,368	8,488	0.37	0.16	0.21	0.46
Tanzania	2011–2013	–	–	–	–	–	–
Togo	2011–2013	–	–	–	–	–	–
Uganda	2011–2013	9,673	4,907	0.39	0.17	0.10	0.39
Zambia	2011–2013	–	–	–	–	–	–
Zimbabwe	2011–2013	10,105	4,395	0.24	0.06	0.05	0.10
Angola	2014–2016	–	–	–	–	–	–
Benin	2014–2016	–	–	–	–	–	–
Burkina Faso	2014–2016	8,442	4,875	0.71	0.05	0.27	0.44
Burundi	2014–2016	17,826	8,660	0.36	0.07	0.08	0.12
Cameroon	2014–2016	–	–	–	–	–	–
Cote d'Ivoire	2014–2016	–	–	–	–	–	–
Gabon	2014–2016	–	–	–	–	–	–
Gambia	2014–2016	–	–	–	–	–	–
Ghana	2014–2016	5,347	2,377	0.16	0.00	0.62	0.29
Guinea	2014–2016	–	–	–	–	–	–
Kenya	2014–2016	5,664	2,639	0.41	0.14	0.23	0.38
Liberia	2014–2016	4,629	2,259	0.38	0.05	0.25	0.60
Madagascar	2014–2016	11,094	3,873	0.70	0.08	0.04	0.30
Malawi	2014–2016	2,970	1,624	0.58	0.08	0.00	0.92
Mali	2014–2016	7,900	5,062	0.69	0.09	0.23	0.45

Continued

Country	Period	Sample size	Number of women aged 15-49 eligible for IPTp	ITNs and IRS RP	ITNs and IRS UP	IPTp RP	IPTp UP
Mozambique	2014–2016	–	–	–	–	–	–
Niger	2014–2016	–	–	–	–	–	–
Nigeria	2014–2016	8,218	4,340	0.33	0.08	0.23	0.35
Rwanda	2014–2016	13,765	–	0.57	0.10	–	–
Senegal	2014–2016	9,573	4,470	0.54	0.05	0.04	0.67
Sierra Leone	2014–2016	8,601	–	0.39	0.08	–	–
Tanzania	2014–2016	14,370	7,050	0.46	0.16	0.07	0.61
Togo	2014–2016	10,011	5,010	0.25	0.12	0.23	0.55
Uganda	2014–2016	5,747	3,017	0.66	0.11	0.27	0.38
Zambia	2014–2016	18,174	9,345	0.56	0.06	0.51	0.42
Zimbabwe	2014–2016	10,819	–	0.27	0.04	–	–
Angola	2017–2019	15,242	8,947	0.20	0.09	0.18	0.37
Benin	2017–2019	16,496	–	0.70	0.09	–	–
Burkina Faso	2017–2019	7,729	4,519	0.49	0.06	0.57	0.37
Burundi	2017–2019	–	–	–	–	–	–
Cameroon	2017–2019	15,378	6,463	0.56	0.02	0.31	0.44
Cote d'Ivoire	2017–2019	–	–	–	–	–	–
Gabon	2017–2019	–	–	–	–	–	–
Gambia	2017–2019	–	–	–	–	–	–
Ghana	2017–2019	5,347	2,308	0.15	0.00	0.61	0.31
Guinea	2017–2019	11,120	5,530	0.21	0.13	0.34	0.45
Kenya	2017–2019	–	–	–	–	–	–
Liberia	2017–2019	8,708	4,267	0.37	0.09	0.39	0.52
Madagascar	2017–2019	8,379	5,227	0.62	0.14	0.10	0.28
Malawi	2017–2019	3,923	1,941	0.54	0.09	0.34	0.59
Mali	2017–2019	10,945	6,368	0.60	0.15	0.25	0.46
Mozambique	2017–2019	6,404	3,377	0.68	0.13	0.42	0.45
Niger	2017–2019	–	–	–	–	–	–
Nigeria	2017–2019	42,407	21,792	0.37	0.11	0.17	0.47
Rwanda	2017–2019	5,096	–	0.70	0.09		
Senegal	2017–2019	18,094	8,486	0.61	0.05	0.20	0.73
Sierra Leone	2017–2019	16,487	7,377	0.43	0.15	0.35	0.59
Tanzania	2017–2019	10,443	5,364	0.46	0.13	0.20	0.61
Togo	2017–2019	4,867	2,488	0.52	0.13	0.39	0.50
Uganda	2017–2019	9,262	4,826	0.56	0.15	0.41	0.49
Zambia	2017–2019	14,922	7,372	0.65	0.04	0.59	0.36
Zimbabwe	2017–2019	–	–	–	–	–	–
Angola	2020–2022	–	–	–	–	–	–
Benin	2020–2022	–	–	–	–	–	–
Burkina Faso	2020–2022	18,284	6,446	0.63	0.06	0.56	0.37
Burundi	2020–2022	–	–	–	–	–	–
Cameroon	2020–2022	6,880	2,346	0.42	0.15	0.43	0.39

Continued

Country	Period	Sample size	Number of women aged 15-49 eligible for IPTp	ITNs and IRS RP	ITNs and IRS UP	IPTp RP	IPTp UP
Cote d'Ivoire	2020–2022	15,378	5,674	0.56	0.02	0.30	0.49
Gabon	2020–2022	10,051	4,457	0.12	0.18	0.35	0.50
Gambia	2020–2022	13,012	5,799	0.41	0.04	0.43	0.54
Ghana	2020–2022	−	5,189	−	−	0.60	0.30
Guinea	2020–2022	5,996	2,147	0.28	0.09	0.50	0.39
Kenya	2020–2022	7,210	2,064	0.52	0.14	0.32	0.30
Liberia	2020–2022	4,813	1,594	0.43	0.05	0.69	0.26
Madagascar	2020–2022	20,820	9,315	0.31	0.28	0.31	0.20
Malawi	2020–2022	−	−	−	−	−	−
Mali	2020–2022	11,156	4,934	0.63	0.10	0.34	0.42
Mozambique	2020–2022	14,570	5,153	0.30	0.13	0.24	0.43
Niger	2020–2022	6,236	2,734	0.68	0.09	0.24	0.57
Nigeria	2020–2022	14,837	5,497	0.29	0.10	0.31	0.33
Rwanda	2020–2022	14,776	−	0.39	0.14	−	−
Senegal	2020–2022	11,152	3,615	0.55	0.07	0.42	0.51
Sierra Leone	2020–2022	−	−	−	−	−	−
Tanzania	2020–2022	−	5,836	−	−	0.26	0.45
Togo	2020–2022	−	−	−	−	−	−
Uganda	2020–2022	−	−	−	−	−	−
Zambia	2020–2022	−	−	−	−	−	−
Zimbabwe	2020–2022	−	−	−	−	−	−

Note: missing values are marked by −. The tables present the cascade coverage in women aged 15–49 by country and period, along with the average coverage for each period. For ITNs and IRS coverage, the numerator represents the number of women aged 15–49 with access to ITNs and IRS, while the denominator represents the total number of women aged 15–49 (sample size). For IPTp coverage, the numerator represents the number of women aged 15–49 with access to IPTp service, while the denominator represents the number of women aged 15–49 who were pregnant and eligible for IPTp. All averages are weighted by the corresponding denominator indicators.

Methods and Applications

Impact of Implementation Interruptions of 1,7-Malaria Reactive Community-Based Testing and Response Approach on Malaria Control Efforts — Southern Tanzania

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ABSTRACT

Introduction: Surveys from the China-Tanzania Malaria Control Project demonstrated that the 1,7-malaria Reactive Community-Based Testing and Response (1,7-mRCTR) approach significantly reduced malaria incidence rates. However, implementation was disrupted by security concerns, infectious disease outbreaks, and supply shortages. This study evaluates how these interruptions affected intervention effectiveness to inform future malaria control strategies.

Methods: The study employed a two-phased design: Phase I (2016–2018) and Phase II (2019–2021). Weekly malaria incidence rates per 100 people were calculated from cases reported by local health facilities in the intervention areas during both phases. Seasonal and trend decomposition using loess (STL) and interrupted time series modeling with piecewise linear regression were used to evaluate the impact of disruptions on 1,7-mRCTR implementation effectiveness.

Results: In Tanzania's 1,7-mRCTR areas, malaria incidence peaked during November-December and June-July. Phase I's 8-month interruption reversed the weekly trend from a 0.17% decline to a 0.58% increase (P=0.001). After resumption, incidence dropped 8.96% (P=0.039) and maintained a 0.39% long-term decline (P=0.003). Even with seasonal adjustment, the interruption slowed the weekly decline from 0.08% to 0.07% (P=0.003). Phase II showed a similar pattern: a one-week interruption caused a 0.70% drop (P=0.007) but shifted the trend from a 0.02% decline to a 0.08% increase (P=0.001). After resumption, interventions stabilized the decline at 0.11% weekly (P=0.001).

Conclusions: This research demonstrates that Tanzania's malaria incidence is closely linked to seasonal patterns and consistent intervention efforts. Phase I's 8-month security-related interruption reduced 1,7-mRCTR effectiveness by 12.5%, while Phase II's 3-month pandemic-induced interruption caused only short-term fluctuations with minimal long-term impact. Rapid resumption of interventions after disruptions allowed for prompt recovery, highlighting the importance of adaptive strategies to maintain progress toward malaria control goals.

Malaria is a significant mosquito-borne parasitic disease that substantially impedes social and economic development in endemic countries (*1*). According to the World Health Organization's malaria report (*2*), global malaria incidence and mortality rates slightly increased in 2022. Compared to 2021, there were an additional 5 million malaria cases worldwide in 2022, totaling approximately 249 million cases. In 2022, 94% of all malaria cases (233 million cases) and 95% of all malaria deaths (580,000 cases) occurred in the African region of the WHO (*2*). Tanzania is among the 11 countries with the heaviest malaria burden globally, accounting for 3.1% of global cases and deaths in 2021, and 4.1% of global deaths (*3*). Since the early 2000s, Tanzania has expanded malaria prevention and control efforts by improving case management, distributing insecticide-treated nets (ITNs), implementing indoor residual spraying, and combining these measures with malaria treatment. These interventions successfully reduced the country's malaria parasite prevalence by 50%. However, malaria remains a leading cause of death and morbidity across all age groups in Tanzania, particularly among pregnant women and children under five (*4*).

China was once a region with high malaria incidence. After launching its malaria elimination

program in 2010, China implemented the "1-3-7" strategy, achieving zero local malaria cases in 2017. In 2021, China was certified as malaria-free by the World Health Organization. The National Institute of Parasitic Diseases (NIPD) at the China CDC and the Ifakara Health Institute in Tanzania jointly implemented the "China-Tanzania Pilot (Phase I) and Demonstration Projects (Phase II) on Malaria Control" from April 2015 to October 2021(*5*). The prevalence of malaria in the pilot areas was reduced from 25.7% to 4.9%, representing an 81% reduction (*6*).

Malaria morbidity control requires long-term and sustained interventions. Interruptions in 1,7-mRCTR implementation are consequences of undesirable incidents that may influence malaria control effectiveness. Due to security problems, the implementation of the Phase I project in the Rufiji intervention area was interrupted for 8 months (January 2017–August 2017). During the implementation stage of the Phase II project, an epidemic of infectious diseases caused the project to be temporarily interrupted again (March 2020–May 2020), and malaria prevention and control work in the intervention area stagnated. Although cross-sectional survey data confirmed the effectiveness of our implementation, the impact of these two interruptions on intervention effectiveness is currently unknown. Therefore, this study used data on malaria cases reported by local health facilities in the intervention area to analyze the impact of implementation interruptions using an interrupted time-series model, which provides a theoretical basis for further optimizing preventive and control measures and improving intervention effectiveness.

Methods

Study Area

The China-Tanzania Pilot and Demonstration Projects on Malaria Control were implemented in two phases: Phase I (January 2016 to April 2018) and Phase II (September 2019 to October 2021). The project proposed and tested an integrated package of intervention measures called 1,7-malaria Reactive Community-Based Testing and Response (1,7-mRCTR) at two intervention sites (Chumbi and Ikwiriri) in the Rufiji Region, South Tanzania, which has been described previously (*7*). Phase II expanded 1,7-mRCTR from two to six sites in Tanzania, funded by the Bill and Melinda Gates Foundation (BMGF). It covered Kilwa District (Lindi Region) and Rufiji and Kibiti Districts (Pwani Region) in southeastern Tanzania, with two wards per district representing four catchment populations. However, as Rufiji District received additional interventions beyond larvicidal treatment, only Kilwa and Kibiti Districts were included in assessing Phase II interruption impacts.

Data Sources

We obtained patient registration data from health institutions through an information reporting system developed by professional technicians at the Ifakara Health Institute. The data included demographic information of patients, their village addresses, and malaria status. Weekly malaria incidence per 100 people was calculated based on all confirmed malaria cases.

Statistical Analysis

All individuals registered in health facilities within the study period were included in the analysis. During Phase II, there were very few weeks with missing values for malaria case numbers in the intervention areas' health facilities, which were addressed using multiple imputation (MI). MI was selected over complete-case analysis due to its ability to preserve statistical power and reduce bias under the missing-at-random (MAR) assumption, implemented via the R mice package. We decomposed the weekly malaria incidence changes by applying seasonal and trend decomposition using loess (STL) (*7*–*8*).

Interrupted time series analysis (ITSA) (*9*–*10*) was used to evaluate the impact of the 1,7-mRCTR implementation interruption on intervention effectiveness. Considering the seasonal nature of malaria incidence, the decompose function in *R* was first used to remove the effect of seasonal factors, and one-period lagged Newey-west regression was used to assess the effect of intervention interruptions on malaria control in the intervention area. Statistical analyses were performed using Stata version 15 (StataCorp, College Station, USA) and R statistical software, version 4.3.2 (R Foundation for Statistical Computing, Vienna, Austria). All reported *P* values are two-tailed, with *P* value <0.05 considered statistically significant.

RESULTS

Description of Malaria Incidence Changes

As shown in Figure 1, during Phase I, the Rufiji intervention area experienced a 0.13% weekly decline in malaria incidence, while the control area showed a 0.10% weekly increase (Figure 1A). In Phase II, the Kilwa and Kibiti intervention areas maintained a declining trend of 0.08% weekly, outperforming the control area which decreased at a rate of 0.04% weekly (Figure 1B).

Time Series Feature Decomposition

Figure 2 demonstrates that despite the overall downward trend in malaria incidence in Phase I intervention areas, a substantial rebound occurred from January to May 2017. Similarly, malaria incidence in Phase II intervention areas showed a sharp increase during the pre-intervention period, approximately from January to May 2020. Additionally, clear seasonal patterns in malaria incidence were observed across the implementation areas. Further analyses revealed that the peak malaria transmission season in the Tanzanian intervention area occurred from November to December, with a secondary peak from June to July (Supplementary Figure S1, available at https://weekly.chinacdc.cn/).

Interruption Time Series Analysis

As shown in Figure 3 and Table 1, Phase I intervention areas initially demonstrated a 51.10% weekly malaria incidence with a 0.17% weekly decline. A one-week interruption caused an immediate 6.69% drop (P=0.116) but reversed the trend from a 0.17% decline to a 0.58% increase. Following resumption (Figure 3B), incidence dropped by 8.96% (P=0.039) with a sustained 0.39% long-term decline (P=0.003). Seasonally adjusted analysis revealed that the interruption reduced the downward trend from 0.08% to 0.02%, with post-resumption recovery maintaining a 0.07% weekly decline (P=0.003).

Phase II intervention areas began with 44.48% incidence and an early 0.87% weekly increase (Table 2). A one-week interruption caused a 0.35% rise but reversed the trend from increasing 0.87% to decreasing by 1.16% weekly (P<0.001). Following resumption (Figure 4A), incidence surged 10.3% (P=0.007) but stabilized to a 0.19% long-term decline (P<0.001). Seasonally adjusted data revealed an initial

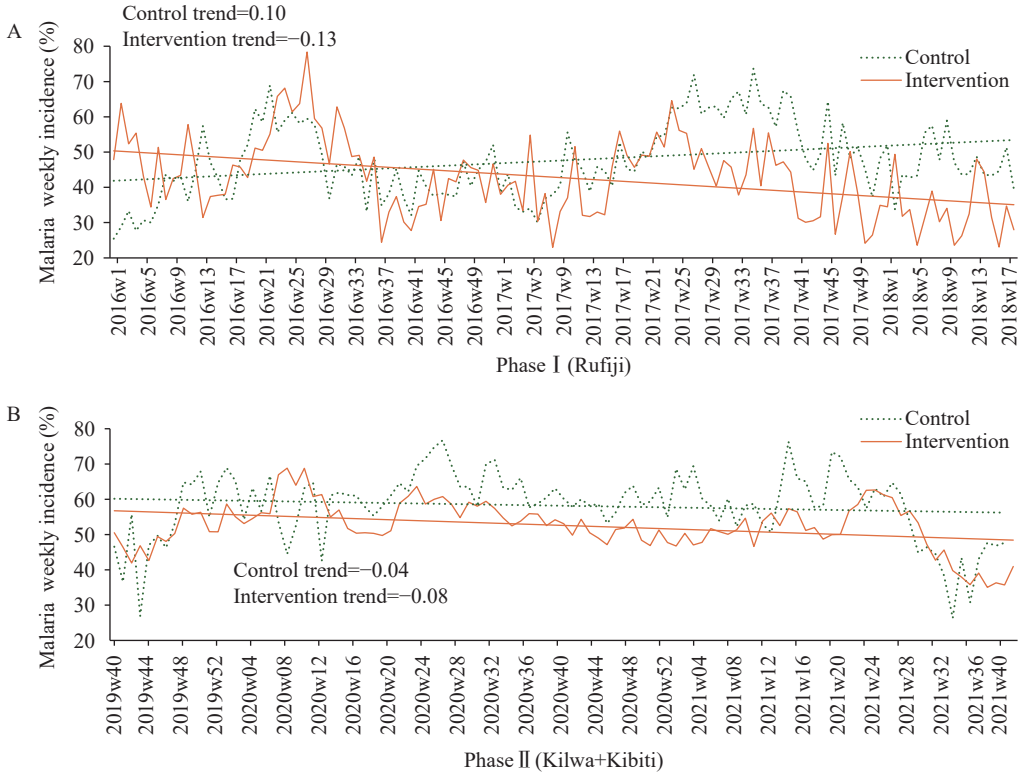

FIGURE 1. Weekly incidence changes of malaria in 1,7-malaria Reactive Community-Based Testing and Response intervention and control areas in Tanzania. (A) Phase I; (B) Phase II.

0.02% decline (Figure 4B), interrupted by a 0.70% drop and a trend shift from a decrease of 0.02% to an increase of 0.08%. Post-resumption, malaria weekly incidence decreased by 0.30% [95% confidence interval (*CI*): −0.62, 0.02; *P*=0.063] in the first week, though this effect was not statistically significant. After continuous implementation, the incidence trend changed by 0.18% and maintained a long-term decline of 0.11% (95% *CI*: 0.09, 0.12; *P*=0.001) per week.

DISCUSSION

Disease control requires sustained, long-term efforts which are vulnerable to disruptions from program continuity issues, climate shifts, and policy changes.

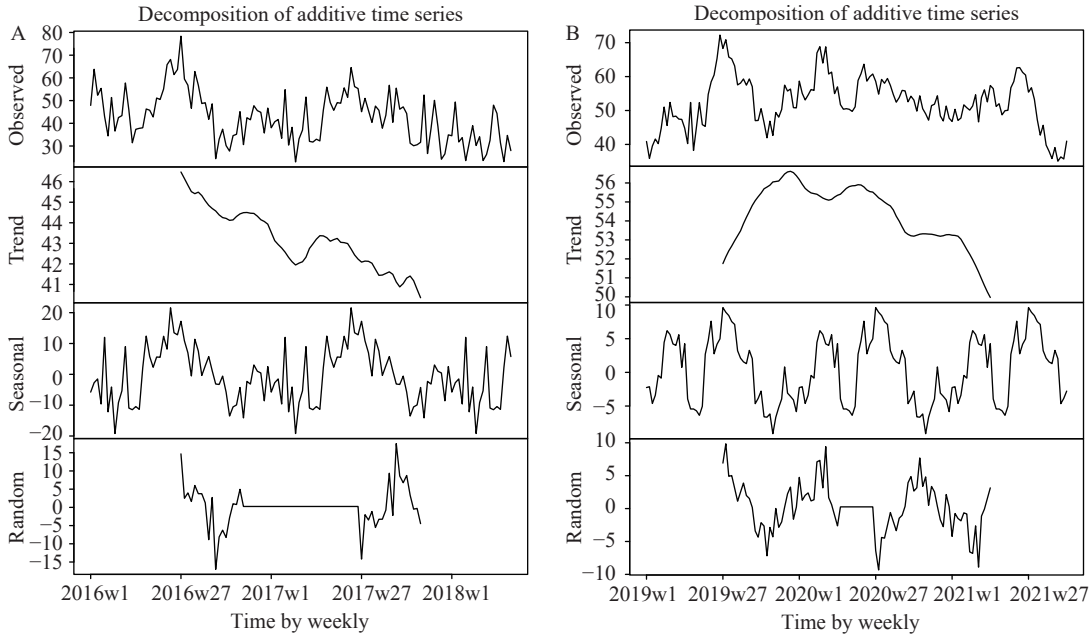

FIGURE 2. Time series decomposition plot of malaria incidence in 1,7-malaria Reactive Community-Based Testing and Response implementation areas. (A) Phase I; (B) Phase II.

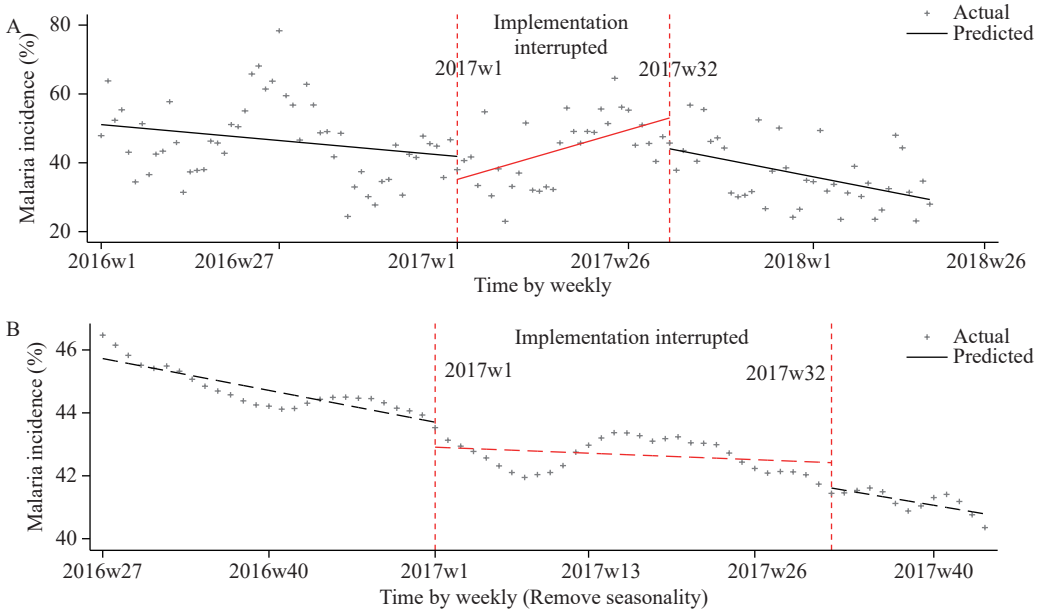

FIGURE 3. ITS scatter plot of the weekly malaria incidence in Phase I implementation areas, Tanzania. (A) Implementation interrupted; (B) Implementation interrupted after removing seasonality.

TABLE 1. Estimated level and trend changes of malaria weekly incidence before and after 1,7-malaria Reactive Community-Based Testing and Response interruption (Phase I).

Period	Variables	Phase I			Phase I (Adjust seasonality)		
		Coefficient	95% *CI*	*P*	Coefficient	95% *CI*	*P*
2016w1–2016w12	Initial level	51.1	45.01, 57.19	<0.001	45.73	45.33, 46.12	<0.001
	Trend	−0.17	0.01, −0.36	0.049	−0.08	0.05, 0.10	<0.001
2017w1–2017w32	Immediate level change after interrupted 1 week	−6.69	−15.06, 1.68	0.116	−0.79	0.22, 1.37	0.008
	Trend changes after interrupted	0.75	0.37, 1.14	<0.001	0.06	0.03, 0.10	0.001
	Trend	0.58	0.23, 0.92	0.001	−0.02	−0.04, 0.01	0.209
2017w33–2018w18	Immediate level change after implementation recovery 1 week	−8.96	0.45, 17.48	0.039	−0.81	0.33, 1.29	0.001
	Trend changes after implementation recovery	−0.96	0.55, 1.38	<0.001	−0.05	0.01, 0.11	0.047
	Trend	−0.39	0.15, 0.63	0.002	−0.07	0.02, 0.11	0.003

Abbreviation: *CI*=confidence interval.

TABLE 2. Estimated level and trend changes of malaria weekly incidence before and after 1,7-mRCTR interruption (Phase II).

Period	Variables	Phase II			Phase II (Adjust seasonality)		
		Coefficient	*P*	95% *CI*	Coefficient	*P*	95% *CI*
2019w40–2020w8	Initial level	44.48	<0.001	40.75, 48.21	56.15	<0.001	55.69, 56.62
	Trend	0.87	<0.001	0.48, 1.25	−0.02	0.293	−0.06, 0.02
2020w9–2020w22	Immediate level change after interrupted 1 week	0.35	0.918	−6.47, 7.18	−0.7	0.007	0.20, 1.21
	Trend changes after interrupted	−2.03	<0.001	1.12, 2.94	0.1	0.001	0.06, 0.14
	Trend	−1.16	0.006	0.34, 1.98	0.08	<0.001	0.06, 0.09
2020w23–2021w40	Immediate level change after implementation recovery 1 week	10.3	0.007	2.89, 17.71	−0.3	0.063	−0.62, 0.02
	Trend changes after implementation recovery	0.98	0.021	0.15, 1.81	−0.18	<0.001	0.16, 0.21
	Trend	−0.19	<0.001	0.09, 0.29	−0.11	0.001	0.09, 0.12

Despite these challenges, limited guidance exists for addressing implementation interruptions, which often compromise study outcomes (*11*). By examining implementation gaps in the China-Tanzania Malaria Control Project, we assessed the impacts of both short- and long-term disruptions to inform strategies for minimizing interruptions and optimizing interventions. In Rufiji, Tanzania — the first site to implement China's 1,7-mRCTR approach — malaria incidence in intervention villages decreased by over 15.7% by the end of Phase I (*12*). Longitudinal health facility data confirmed a consistent downward trend in intervention areas during Phase I, validating the effectiveness of the 1,7-mRCTR strategy.

Phase I data revealed that malaria incidence increased by 0.58% weekly during the 8-month interruption, returning to pre-implementation levels. Despite Tanzania's ongoing long-term insecticidal net campaigns, seasonally adjusted analysis showed that the interruption reduced the downward trend to 25% of pre-interruption rates, with post-resumption weekly declines decreasing from 0.08% to 0.07% (a 12.5% reduction). The infectious disease pandemic disrupted malaria control efforts globally (*13–14*), halting Tanzania's interventions for 3 months (March–May 2020) due to logistical challenges and RDT shortages, with an additional 13 weeks of intermittent interruptions following resumption. Phase II incorporated larval control and insecticide spraying in Rufiji (*15*), so this district was excluded from our analysis to avoid confounding effects.

In Phase II (beginning October 2019), malaria incidence initially increased before the infectious disease pandemic (likely due to seasonal peaks) but showed a downward trend when adjusted for seasonality. During the pandemic, reported cases decreased (possibly due to reduced mobility), though seasonally adjusted data revealed a transient upward trend, indicating that interrupted interventions allowed a slow resurgence of malaria. Phase II's post-

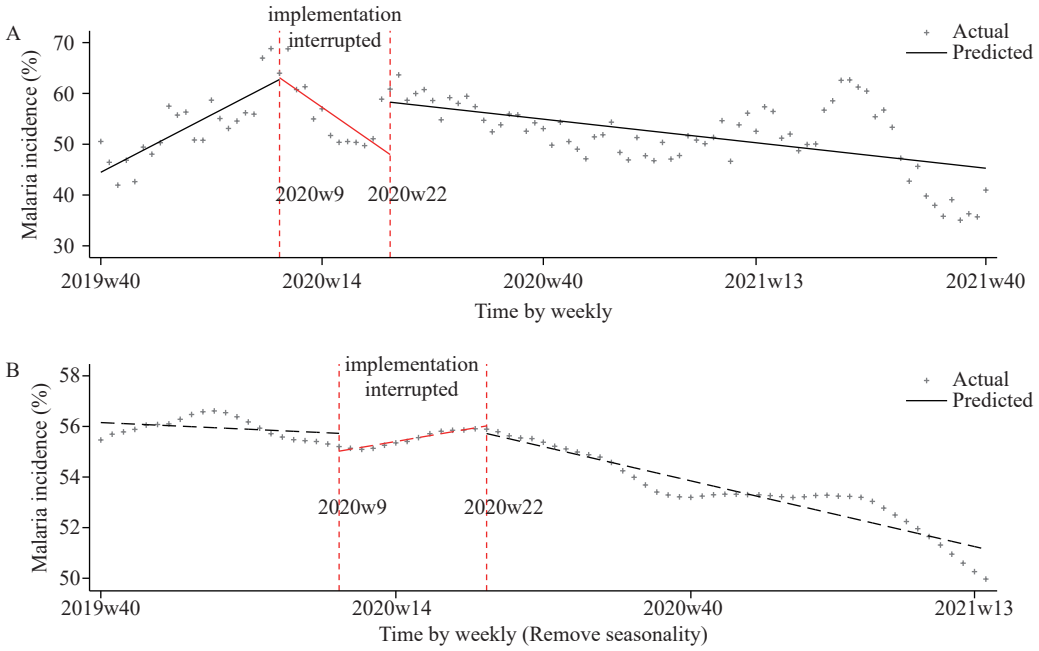

FIGURE 4. ITS scatter plot of the weekly malaria incidence in Phase II implementation areas, Tanzania. (A) Implementation interrupted; (B) Implementation interrupted after removing seasonality.

resumption RDT shortages caused sporadic interruptions over 13 weeks with irregular, brief disruptions, so their impact was not separately analyzed. Our analysis demonstrated that while weekly malaria incidence fluctuated during supply shortages, seasonally adjusted data showed minimal long-term effect. This highlights the importance of stockpiling malaria supplies, particularly in high-transmission areas. We recommend that healthcare facilities pre-stock RDTs and treatments based on local population needs to maintain screening capabilities during emergencies.

This study has several limitations: its retrospective design potentially introduced uncontrolled biases and confounders; reliance on RDTs may have missed low-density malaria infections; and the infectious disease pandemic could have delayed malaria case reporting.

CONCLUSION

The eight-month interruption during Phase I reduced the effectiveness of the 1,7-mRCTR implementation by 12.5%. In contrast, the three-month passive interruption during Phase II caused only minor transient fluctuations with minimal impact on the overall effectiveness of the 1,7-mRCTR approach. Additionally, temporary shortages of RDT reagents had negligible effects on implementation effectiveness.

Conflicts of interest: No conflicts of interest.

Acknowledgements: Ifakara Health Institute.

Ethical statement: The Medical Research Coordination Committee of the National Institute for Medical Research (NIMR) granted the permit to conduct this study (NIMR/HQ/R.8a/Vol.IX/2005 and 3634). Institutional ethical approval was also obtained from the Ifakara Health Institute Institutional Review Board (IHI/IRB/No: 18-2015 and 18-2020) and the Chinese Center for Disease Control (201,505).

Funding: Supported by the UK Department for International Development (DFID) through the China-UK Global Health Support Programme (GHSP-CS-OP4-D02) and the Bill & Melinda Gates Foundation (OPP1198779, OPP1213975).

doi: 10.46234/ccdcw2025.104

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Submitted: July 09, 2024
Accepted: April 11, 2025
Issued: May 02, 2025

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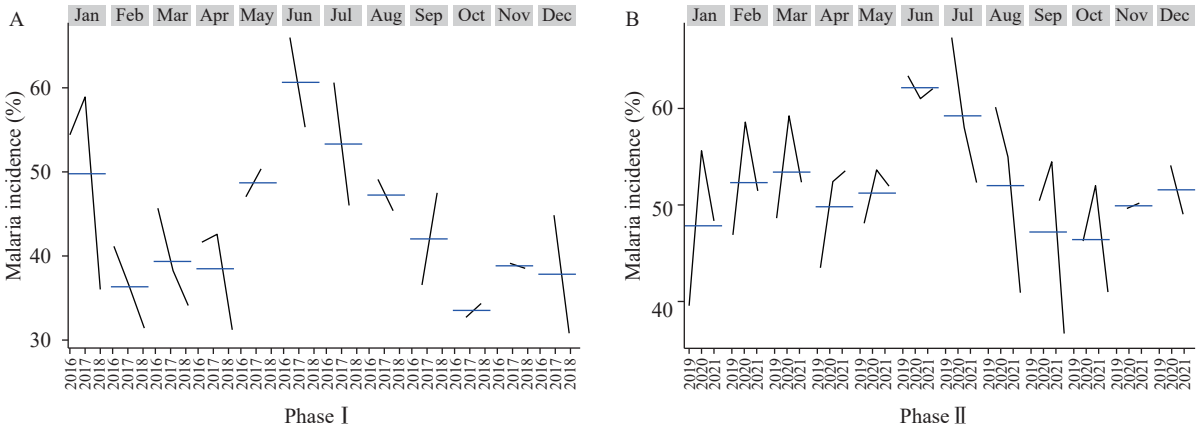
SUPPLEMENTARY MATERIAL



SUPPLEMENTARY FIGURE S1. Time series seasonal feature extraction of malaria incidence in intervention areas, Tanzania. (A) Phase I; (B) Phase II.

Review

China's Malaria R&D Innovations: A Scoping Review from 2013–2023

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ABSTRACT

Malaria remains a major global health challenge. Understanding the research progress of the potential innovative tools is important for malaria elimination. This scoping review aims to explore China's research and development (R&D) advances from 2013–2023 in addressing the current challenges and contributing to global malaria elimination. Using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR), this review searched the English and Simplified Chinese data sources from five databases. A total of 11,112 English articles and 2,944 Chinese articles were retrieved. After screening, 44 English and 13 Chinese articles were included. Key advancements were identified in three domains: vector control, pathogen screening and diagnosis, and prevention and treatment. Innovations in vector control include studies such as the use of *Serratia* strains and symbiont-mediated RNAi approaches to block malaria transmission. Advances in pathogen screening and diagnosis feature biosensor development, AI monitoring technologies, and novel amplification gene and nucleic acid detection technologies. In prevention and treatment, artemisinin-based combination therapies (ACTs) remain a cornerstone, with additional progress in industrial pharmaceuticals and technologies already in field and semi-field-testing stages. This review underscores the importance of leveraging China's R&D capacity to meet global challenges. To maximize impact, we call for global attention to strengthening international collaboration with China in malaria R&D to accelerate the commercialization, regulatory approval, and large-scale deployment of innovations.

Malaria, one of the 'Big Three' infectious diseases, contributed 249 million cases and 608,000 deaths to the global disease burden in 2022, with the WHO African Region bearing a disproportionately high share (*1*). Recent years have witnessed innovative advancements in malaria control that offer new hope for elimination. The RTS,S/AS01 malaria vaccine now provides additional protection for children living in endemic areas (*2*–*3*), while modern malaria rapid diagnostic tests (RDTs) have significantly improved in sensitivity and specificity, delivering fast and reliable results (*2*). Additionally, emerging engineering technologies that deploy transgenic methods against mosquitoes, such as gene drive, show potential to modify mosquito populations to reduce their reproductive capacity and transmission ability, though these remain in experimental stages (*4*). However, these advancements face significant challenges. The RTS,S/AS01 vaccine demonstrates compromised efficacy, highlighting the need for more robust vaccines (*5*). Widespread *pfhrp2* gene deletions compromise RDT reliability (*6*), while emerging drug resistance to artemisinin-based combination therapy (ACT) and mosquito resistance to insecticides driven by evolving vector behaviors (*7*) present ongoing threats. Ecological concerns regarding gene drive technologies further complicate implementation (*8*). These challenges, combined with longstanding impediments such as limited service delivery capacity, insufficient operational expertise, and inadequate laboratory infrastructure in endemic areas, underscore the critical need for continued innovation in malaria control to achieve global elimination.

Malaria has historically been one of China's most serious health challenges. In the 1940s, China reported over 30 million malaria cases annually (*9*). Nevertheless, China has achieved remarkable progress: zero local transmission cases since 2016 and World Health Organization (WHO) certification as malaria-

free in 2021. China's success in combating malaria can be attributed to a comprehensive range of prevention and control strategies, including strong government commitment to science, evidence-based interventions, and financial support; the establishment of a robust and adaptive surveillance and response system; and continuous capacity building alongside demand-oriented scientific research (*10*). The 1-3-7 strategy — developed by the National Malaria Elimination Program in 2010 and extensively implemented in early 2012 — has been recognized as critical to China's malaria elimination. This strategy refers to reporting malaria cases within one day, confirming and investigating cases within three days, and implementing appropriate responses to prevent further transmission within seven days (*11*).

In parallel, China has made significant strides in malaria-related research and product development (*12*). The discovery of artemisinin, originating from "Project 523" in 1967 and later earning Professor Tu Youyou the Nobel Prize in Physiology or Medicine in 2015, revolutionized malaria treatment globally (*13*). ACTs, endorsed by WHO as first-line and second-line treatments for malaria, have saved millions of lives (*14*). Beyond artemisinin, China's research progress in other innovative products is also noteworthy, including insecticide-treated nets (ITNs) for preventing mosquito bites (*15*), genetically modified mosquitoes for transmission control (*16*), the PfCP-2.9 blood-stage vaccine for malaria, which has entered clinical studies, and additional vaccine candidates in various R&D stages (*17*).

Despite growing international recognition of China's malaria elimination achievements, there remains a lack of systematic, evidence-based documentation, particularly regarding advances in diagnosis and vector control. This gap hinders further innovation and limits the global application of China's contributions. While the Malaria Eradication Research Agenda (malERA) emphasizes the importance of R&D to interrupt transmission (*18*), the increasing global malaria burden highlights the need for more effective tools and strategies. Given these challenges and the limited literature summarizing China's malaria innovation from a global health perspective, this scoping review aims to provide a comprehensive overview of malaria R&D in China from 2013 to 2023, identifying progress, gaps, and opportunities to contribute to global malaria elimination efforts.

METHODOLOGY

Study Design

This study was meticulously designed following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses extension for Scoping Reviews (PRISMA-ScR) checklist (*19*) to ensure methodological rigor and international generalizability. We implemented a pilot review phase where two reviewers jointly screened approximately 20 publications during in-person and online meetings under the guidance of an experienced reviewer. Following this initial screening, the team conducted collaborative discussions to critically evaluate outcomes and make necessary adjustments to the screening and data extraction protocol before proceeding to the full scoping review.

Search Strategies

Our review incorporated search strategies encompassing both English and Simplified Chinese data sources to comprehensively capture emerging innovation information. English data sources included PubMed (https://www.ncbi.nlm/nih.gov/pubmed/), Web of Science (https://www.webofscience.com/), and ScienceDirect (https://www.sciencedirect.com), while Chinese data sources comprised local databases including China National Knowledge Infrastructure (CNKI, https://www.cnki.net/) and Wanfang (https://www.wanfangdata.com.cn/). The specific search strategies employed for each database are presented in Table 1. To address potential meaning discrepancies arising from English-Chinese language translation, two independent researchers conducted reverse translation verification. Translation references for keywords used in the Chinese literature search strategy are provided in Supplementary Table S1 (available at https://weekly.chinacdc.cn/). The final literature search was completed in December 2023.

Inclusion and Exclusion Criteria

The inclusion and exclusion criteria were developed through two rounds of internal discussions among researchers. Initially, we defined innovation products in malaria based on the framework identified by Chibi et al. (*20*): technology and device developments in surveillance, microplanning, prevention, diagnosis, and treatment of malaria. Subsequently, we established our specific inclusion and exclusion criteria, which are detailed in Table 2.

TABLE 1. Search strategies applied in the databases.

Database	Search time	Key words	Article type	Publication time range
PubMed	2023.12.2	(Malaria [title] OR malaria [Mesh] OR plasmodium [title] OR anopheles [title] OR artemisinin [title] OR quinine [title]OR vector [title] OR parasite [title])AND (control [title] OR product* [title] OR technolog*[title] OR prevention[title] OR vaccin*[title] OR screening [title] OR diagnosis [title] OR treatment [title] OR rehabilitation [title] OR recovery [title] OR medicine [title] OR biology* [title] OR pathway [title] OR mechanism [title] OR novel [title] OR drug* [title] OR residual spraying [title] OR potential [title] OR efficacy [title])AND (China [all fields] OR Chinese [all fields])	All	2013–2023
Web of Science	2023.12.2	AB=((Malaria OR plasmodium OR anopheles OR artemisininOR quinine OR vector OR parasite)AND (control OR product* OR technolog* OR prevention OR vaccin* OR screening OR diagnosis OR treatment OR rehabilitation OR recovery OR medicine OR biology* OR pathway OR mechanism OR novel OR drug* OR residual spraying OR potential OR efficacy)AND (China OR Chinese))	All	2013–2023
ScienceDirect	2023.12.2	Term: "control" OR "product" OR "products" OR "technology" OR "technologies" OR "prevention" OR "vaccine" OR "vaccines" OR "vaccination" OR "screening" OR "diagnosis" OR "treatment" OR "rehabilitation" OR "recovery" OR "medicine" OR "biology" OR "pathway" OR "mechanism" OR "novel" OR "drug" OR "drugs" OR "residual spraying" OR "potential" OR "efficacy" AND TI:"Malaria" OR "plasmodium" OR "anopheles" OR "artemisinin" OR "quinine" OR "vector" OR "parasite" Find articles with these terms:"China" OR "Chinese"	Research Articles	2013–2023
CNKI	2023.12.2	((TI='疟疾') OR (TI='疟原虫') OR (TI='蚊') OR (TI='青蒿素') OR (TI='奎宁') OR (TI='寄生虫')) AND ((TI='控制') OR (TI='产品') OR (TI='技术') OR (TI='预防') OR (TI='疫苗') OR (TI='筛查') OR (TI='诊断') OR (TI='治疗') OR (TI='康复') OR (TI='药物') OR (TI='生物') OR (TI='通道') OR (TI='机制'))	Academic Study	2013–2023
Wanfang	2023.12.2	题名或关键词:((疟疾 OR 疟原虫 OR 蚊 OR 青蒿素 OR 奎宁) AND (控制 OR 产品 OR 技术 OR 预防 OR 疫苗 OR 筛查OR诊断 OR治疗OR康复 OR药物OR生物OR通道OR机制))	All	2013–2023

TABLE 2. Inclusion and exclusion criteria of the scoping review.

Category	Inclusion	Exclusion
Language	English and Chinese	Languages other than English and Chinese
Author affiliation information	At least one of the first or corresponding authors' primary (first listed) affiliation is an institute located in China	None of the first or corresponding authors' primary affiliation is an institute located in China
Accessibility	Open access	Limited access
Study design	Empirical studies: Observational studies (clinical trials, cohort, case–control, cross-sectional, case-crossover, ecologic, case series, case reports) assessing the effectiveness of certain interventions; Health technology Assessment (HTA) studies qualitative studies; reviews (systematic, scoping) and meta-analyses. Non – empirical studies: (e.g., commentary, some of the editorial pieces, erratum etc.)	Study of animals, cells, or other non-human subjects Basic research at genetic or molecular levels without field or semi-field experimental data; Development of analytical tools or strategies; clinical guidelines and interpretation of them; causal inference studies to identify risk factors; Non – empirical studies: (e.g., commentary, some of the editorial pieces, erratum etc.)
Objective	To introduce or examine an innovative malaria product satisfying the definition*	Other objectives than introducing or examining an innovative malaria product satisfying the definition*
Result	Result of the study should expose the application information of the product.	No focus on the product or no expose of the product application information.
Study time	2013 to 2023	Before 2013 or after 2023

* The definition: technology and device developments in surveillance, microplanning, prevention, diagnosis, and treatment of malaria (*20*).

Quality Assessment

Critical appraisal checklists developed by the Joanna Briggs Institute (JBI), an international research organization specializing in evidence-based healthcare, were utilized for quality assessment of the studies, including Diagnostic Test Accuracy Studies, Quasi-Experimental Studies, and Case Reports (*21*–*23*). For each study meeting the inclusion criteria, the corresponding critical appraisal aligned with its study design was applied to evaluate quality. Two independent researchers conducted the data inclusion-exclusion process using EndNote X9 (Clarivate, Philadelphia, USA) before submitting the individual checklist outcomes for each study to the entire research

team for final inclusion-exclusion determination.

Data Analysis

Evidence charting and synthesis were performed in accordance with the 2020 updated scoping review methodological guidelines by the JBI team (*24*). For included studies, evidence charting focused on a) the major research institution of the first author or corresponding author, b) the innovative products introduced in the study, c) the nationality of the participating institutes, d) the major challenges and opportunities, e) the study language, and f) research progress. During the evidence synthesis process, we categorized the data into clusters of prevention, diagnosis, and treatment based on the definition of malaria product innovation from Chibi, Wasswa, Ngongoni, Baba and Kalu (*20*). Two researchers conducted evidence extraction and data charting using Microsoft Excel 2016 (Microsoft Corp., Redmond, WA, USA).

RESULTS

Description of Included Studies

A total of 11,112 English articles were retrieved, including 1,311 from PubMed, 7,102 from Web of Science, and 2,699 from ScienceDirect. After removing 269 duplicates, 10,615 articles were excluded based on title and abstract review. Full-text review led to the exclusion of 151 articles that did not meet inclusion criteria, 27 articles with unavailable full texts, and 1 article duplicated in Chinese literature. Following JBI quality assessment, 5 papers were rejected due to inadequate experimental design. Ultimately, 44 English articles were included in the final analysis.

For Chinese literature, 2,944 relevant articles were retrieved, including 1,275 from Wanfang and 1,669 from CNKI. After removing 362 duplicates, 2,468 articles were excluded based on title and abstract review. Full-text review led to the exclusion of 91 articles that did not meet inclusion criteria and 8 articles with unavailable full texts. One article published in both Chinese and English was included only in its Chinese version. Following JBI quality assessment, 2 papers were rejected due to inadequate experimental design. Ultimately, 13 Chinese articles were included in the final analysis.

Annual Distribution of Chinese and English Publications

Figure 2 illustrates the annual distribution of Chinese and English publications from 2013 to 2023. The number of English publications consistently exceeded Chinese publications throughout the study period. From 2017 to 2023, English publications maintained relative stability at approximately six publications per year. In contrast, Chinese publications were fewer in number and showed greater fluctuations.

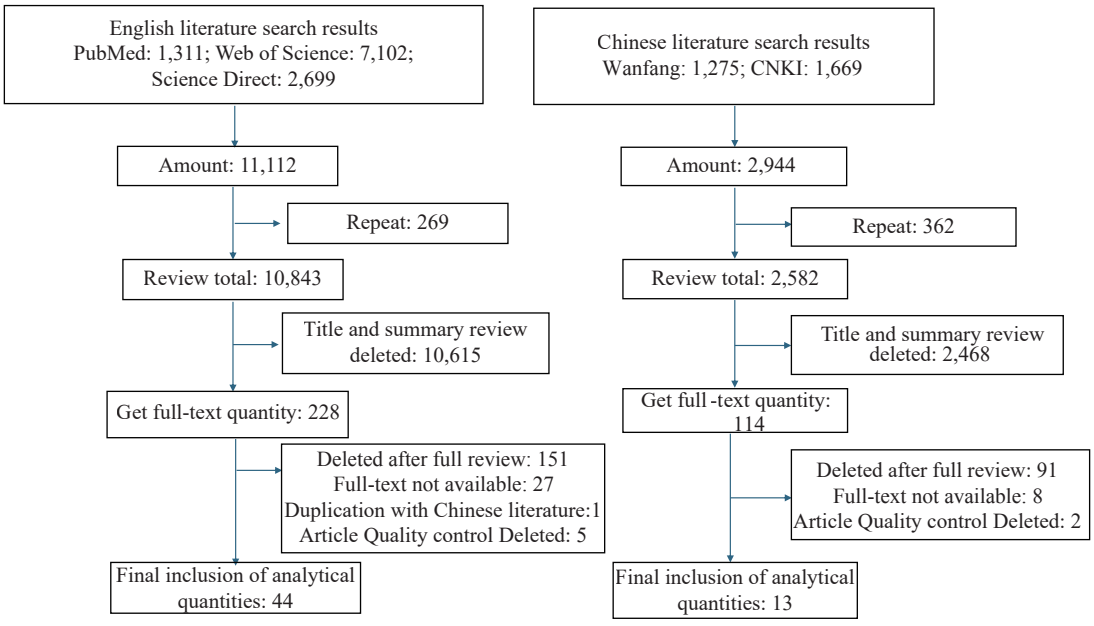

FIGURE 1. Screening process and results of literature review.

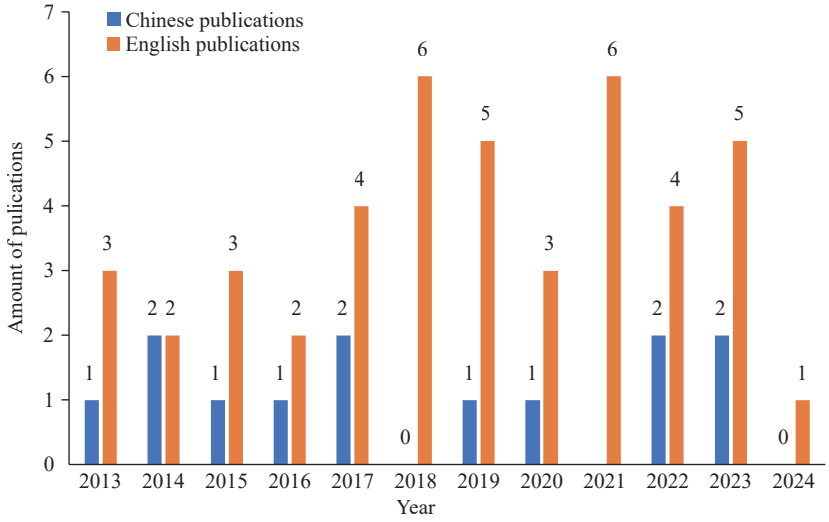

FIGURE 2. Distribution of publications by year.

English publications peaked in 2018 and 2021 with six entries each, followed by a slight decline while maintaining stability. Chinese publications remained scattered across other years with only one or two entries annually. The predominance of English publications in both quantity and yearly consistency suggests either greater international attention to the research topic or a more globally oriented approach to disseminating research outcomes.

Affiliated Institutions and Collaborators

The affiliated institutions in China conducting malaria research primarily include universities, research institutes, hospitals, disease control centers, and enterprises. Among the publications reviewed, 36 had first or corresponding authors from universities, 12 from research institutes, 9 from hospitals, 3 from disease control centers, and 2 from firms, with 3 from other enterprises or institutions.

In our literature review, 37 articles represented collaborations exclusively among Chinese institutions (11 in Chinese and 26 in English), while 10 involved collaborations with the United States and 2 with Pakistan. Additional collaborative research was conducted with institutions in Australia, Sweden, France, Germany, Italy, Colombia, India, Gabon, Niger, Sierra Leone, and Iraq.

Applicable Technologies in Malaria Prevention, Diagnosis, and Treatment

Based on our research review, malaria control technologies primarily focus on three key areas: vector control, pathogen screening and diagnosis, and prevention and treatment. For detailed information regarding specific Malaria R&D innovations, their development stages, and other related information mentioned in these results, please refer to the Supplementary Table S1. Significant advancements have been achieved in each area, as detailed below:

Vector control Research on vector control primarily focuses on larval control and adult mosquito interventions. In larval control, two published studies have examined Capture and Ligation Probe-PCR (CLIP-PCR) and recombinase-mediated constant temperature amplification (RAA). For adult mosquito control, Professor Sibao Wang's team has conducted two studies on *Serratia* strains (Y1 and J1) isolated from field-caught female *Anopheles sinensis* from China, assessing their effect on *Plasmodium* development in *An. stephensi*, as well as the symbiont-mediated RNAi (smRNAi) approach. Additionally, Professor He Qi's team has investigated the efficacy of *Zanthoxylum acanthopodium* essential oil as a vector control agent.

Pathogen screening and diagnosis In the area of pathogen screening and diagnosis, we categorize advancements into instrument innovation, technological innovation, and analytical method innovation.

Instrument innovation primarily focuses on biosensor Development, such as the Portable Microfluidic Aptamer-Tethered Enzyme Capture (APTEC) Biosensor for Malaria Diagnosis, which detects changes in red blood cell and platelet parameters in patients with malignant malaria.

Technological Innovation encompasses AI monitoring, software and big data integration, and

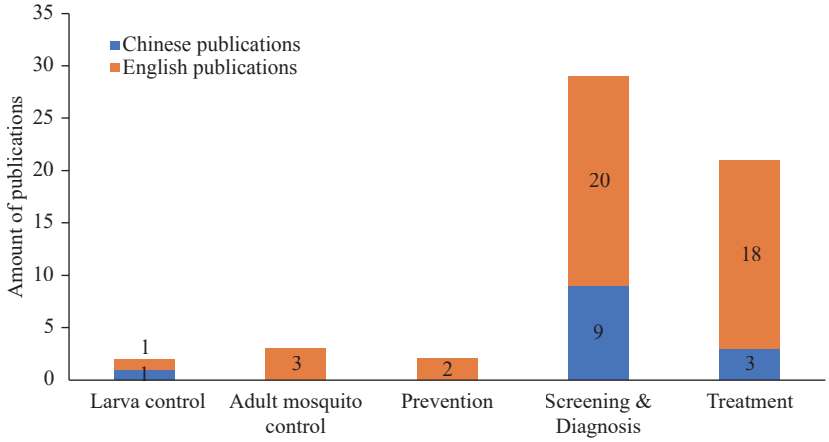

FIGURE 3. Prevention and treatment phases cited by literature.

platform construction. The University of Hong Kong has developed whole genome sequencing and big data analysis technology for *Plasmodium falciparum*, establishing a genome polymorphism database and variation and evolution analysis model.

Analytical method innovation represents significant progress beyond traditional pathogen screening methods that relied on blood films and malaria antigen detection. Currently, there are 8 advancements in staining malarial parasites and serological detection, alongside 20 new amplification gene, nucleic acid, and protein detection technologies.

Prevention and treatment Artemisinin-based combination therapy, currently the most important weapon in the global fight against malaria, is the first-line antimalarial treatment vigorously promoted by the World Health Organization. Among the treatment and prevention advancements identified, 8 (57.1%) are related to artemisinin. Currently, 15 technologies have progressed to field and semi-field testing stages. Additionally, 11 advancements have been made in industrial pharmaceuticals.

Through this literature review, we found that malaria research in China is primarily conducted by universities, with major international collaborations involving institutions in the United States, Europe, and Australia. Research efforts concentrate on pathogen screening and diagnosis, with several technologies having advanced to field and semi-field testing stages.

DISCUSSION

This scoping review identified key innovations in China's malaria-related R&D across three domains: vector control, diagnostic technologies, and prevention and treatment.

Significance and Potential of China's Innovations

Despite global progress in malaria R&D, significant gaps persist in addressing drug and insecticide resistance, RDT sensitivity, cost-effectiveness, and detection of asymptomatic cases (*25–30*). China's R&D trends offer promising solutions to these challenges and complement global efforts, with many innovations focused on improving the sensitivity, cost-effectiveness, and accessibility of malaria interventions. Non-chemical vector control methods, including the smRNAi approach and the use of *Zanthoxylum acanthopodium* essential oil, provide alternatives that reduce dependence on insecticides (*31*). These environmentally sustainable approaches can mitigate the rise of insecticide resistance, particularly in regions where traditional methods have become less effective (*32*). Additionally, China's advancements in vector control, such as CLIP-PCR technology, enhance the precision and efficiency of vector management, enabling more targeted interventions in areas with diverse *Anopheles* species. In diagnostics, aptamer-mediated diagnostic systems and AI-based platforms for analyzing thin-blood smears address critical shortcomings of existing tools. These technologies potentially offer higher sensitivity, rapid results, and simpler application in field conditions. By making malaria diagnostics more accessible and affordable, these advancements show promise for strengthening surveillance systems and ensuring timely treatment. China has also made significant contributions to next-generation malaria vaccines by enhancing the

immunogenicity of *Plasmodium* antigens and developing novel vaccine candidates. In drug delivery and chemoprevention, China's innovations include novel delivery systems such as lipid emulsions for intravenous administration of artemisinin and other antimalarial drugs (*33*). These systems improve drug absorption and address challenges in treating severe malaria and multidrug-resistant strains.

Promoting China's R&D to Accelerate Global Malaria Elimination

Globally, malaria R&D has been supported by robust funding mechanisms, partnerships, and the application of innovations in malaria-endemic regions. In contrast, China faces limited R&D partnerships, funding mechanisms, and global application of innovative tools. In terms of partnerships, global efforts often emphasize collaborations with private enterprises and international organizations through public-private partnerships (PPPs). These collaborations have driven the rapid translation of innovations into field applications. In China, however, partnerships with private enterprises remain underdeveloped, limiting the scalability and deployment of novel tools. Regarding funding mechanisms, most of China's malaria R&D relies on domestic funding, such as the National Natural Science Foundation of China (NSFC). International funding mechanisms such as the Bill & Melinda Gates Foundation (BMGF) and PATH are currently supporting China's malaria R&D and their application to malaria-endemic regions. Nevertheless, there remains a substantial funding gap for China's malaria R&D. In terms of application of China's innovative malaria products, the country's malaria-free status makes it difficult for researchers to find suitable fields for applying their products domestically. Applying these products in malaria-endemic regions outside China would be an alternative, but insufficient funding and lack of local partners and experience, including unfamiliarity with foreign regulations and additional coordination requirements, restricts their global impact. These factors inhibit China's R&D from contributing effectively to global malaria elimination efforts.

To maximize the global impact of China's malaria-related R&D, the following strategies should be considered. First, strengthening partnerships with international organizations, such as the WHO, Global Fund, and the Roll Back Malaria Partnership. These partnerships can not only ensure China's innovations are aligned with global health priorities, but also help to refine existing technologies and ensure their successful deployment in malaria-endemic regions, ultimately facilitating faster uptake of Chinese innovations on the global stage. Second, developing close collaboration with local research institutions and government agencies such as malaria programmes. China's innovations must be adapted to local contexts in malaria-endemic regions. Collaboration with local institutions, malaria programmes, and health authorities will ensure solutions developed in China are accessible and culturally appropriate (*34*). Third, increased investment and PPPs in translational research are needed to bridge the gap between laboratory research and field implementation. This includes support for clinical trials, regulatory approvals, and the commercialization of products. Promoting policies that foster collaboration between research institutions, government agencies, and private enterprises is essential to accelerate the development and deployment of malaria-related products (*35*). Fourth, streamlining the process for regulatory approvals of China's malaria innovations. Collaborations with WHO and other international, regional, and local health organizations such as the African Medicines Agency (AMA), can facilitate the approval of malaria-related products in various markets, ensuring their widespread use (*20*,*36*–*37*). Fifth, capacity building should be delivered within local health systems for healthcare workers, researchers, and policymakers during the implementation of these innovations. This will not only ensure that new technologies are used effectively, but also support local malaria programmes in strengthening their ability to achieve elimination goals (*38*). Lastly, the competencies of those engaging in China's global malaria efforts should also be strengthened to ensure a smooth translation and application of China's domestic products and expertise to foreign contexts (*39*–*40*). Improved global health competencies will promote trust with local counterparts and facilitate the adaptation of products and technologies.

This scoping review has several limitations. Firstly, we only searched the peer-reviewed literature and did not include grey literature from government, institutional, and enterprise websites. This omission could result in missed information, particularly from companies. Our previous investigations have shown that many Chinese companies do not publish their technologies unless collaborating with research entities. Secondly, although we used an appraisal checklist to

assess the quality of the publications, we were unable to evaluate the effectiveness of the identified advancements. Lastly, the final literature search was conducted at the end of 2023, which may limit the timeliness of the findings.

CONCLUSION

China's malaria R&D offers innovative solutions to global challenges. Advancements in non-chemical vector control, diagnostics, and vaccines demonstrate China's potential to complement global malaria elimination efforts. To maximize impact, we call for global attention to strengthening international collaboration with China in malaria R&D to accelerate the commercialization, regulatory approval, and large-scale deployment of innovations.

Conflicts of interest: No conflicts of interest.

Funding: Supported by the Bill and Melinda Gates Foundation (INV-061480) and the National Key R&D Program of China (grant number 2024YFC2309900).

doi: 10.46234/ccdcw2025.105

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Submitted: February 28, 2025
Accepted: April 28, 2025
Issued: May 02, 2025

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SUPPLEMENTARY MATERIAL

SUPPLEMENTARY TABLE S1. China's Malaria R&D Innovations Identified in This Scoping Review (2013–2023).

Stage of control	Year of publication	Language	Affiliation	Study type	Product or technology	Phase of the study
Adult mosquito control	2018	English	University	Experimental	Zanthoxylum acanthopodium essential oil	Laboratory
	2019	English	University	Observational	Two Serratia strains (Y1 and J1) isolated from field-caught female *Anopheles sinensis* from China and assessed their effect on *Plasmodium* development in *An. Stephensi*	Laboratory
	2023	English	University	Experimental	Symbiont-mediated RNAi (smRNAi) approach	Laboratory
Screening and diagnosis	2013	English	University	Observational	Sandwich RNA hybridization assay	Laboratory
	2013	English	University	Experimental	*Plasmodium vivax* aldolase-specific monoclonal antibodies	Laboratory
	2014	Chinese	Research institute	Observational	The small subunit ribosomal ribonucleic acid gene amplified by nested polymerase chain reaction for the diagnosis of three-day *Plasmodium* infection	Field
	2014	English	Research institute	Observational	The Wondfo Rapid diagnostic Kit (Pf-HRP2/PAN-pLDH)	Laboratory
	2014	Chinese	Hospital	Observational	A highly sensitive visual closed-tube detection method for *Plasmodium falciparum* based on Loop-mediated Isothermal Amplification (LAMP) technology	Laboratory
	2015	Chinese	Hospital	Observational	SYBR Green Real-time PCR	Laboratory
	2015	English	University	Experimental	The immunogenicity of HRP 2 exon II and the novel monoclonal antibodies (mAbs) against HRP 2 for Point-of-Care Test (POCT)	Laboratory
	2017	Chinese	CDC	Observational	Parallel diagnosis composed of thick blood smears and rapid *Plasmodium* detection (RDT)	Laboratory
	2017	English	University	Observational	The LAMP assay with the primer set PF3D7_1253300-5	Laboratory
	2017	English	University	Observational	A rapid antibody-free diagnostic method of malaria infection with *Plasmodium falciparum* and *Plasmodium vivax* in whole blood with Surface-enhanced Raman Spectroscopy using Nanostructured Gold Substrate	Semi-Field
	2018	English	University	Observational	A Portable Microfluidic Aptamer-Tethered Enzyme Capture (APTEC) Biosensor for Malaria Diagnosis.	Laboratory
	2018	English	University	Observational	A novel aptamer-based electrochemical biosensor (aptasensor) for malaria detection by impedance. Spectroscopy, through the specific recognition between a highly discriminatory DNA aptamer and its target *Plasmodium falciparum* lactate dehydrogenase (PfLDH).	Laboratory
	2018	English	University	Observational	Aptamer-mediated *Plasmodium*-specific diagnosis of malaria	Laboratory
	2019	English	Hospital	Observational	Mindray BC-6800 hematology analyzer	Laboratory
	2019	Chinese	University	Observational	nABPs obtained by recombinant expression and purification using genetic engineering technology, and a colloidal gold immunochromatography detection method	Laboratory
	2020	Chinese	Research institute	Observational	Loop-mediated isothermal amplification technology for capture and connection	Laboratory
	2020	English	University	Observational	A novel fluorescence probe of *Plasmodium vivax* lactate dehydrogenase based on adenosine monophosphate protected bimetallic nanoclusters	Laboratory
	2022	Chinese	Hospital	Observational	Changes of red blood cell and platelet parameters in patients with malignant malaria	Field
	2022	English	University	Observational	The novel LAMP assay based on the *P. falciparum* actin I gene	Semi-Field
	2022	English	University	Observational	Multi-section Capture and Ligation Probe PCR (mCLIP-PCR).	Semi-Field
	2022	Chinese	Other	Observational	A group of primer pairs with better amplification effects; The amplification of the entire RAA system could be completed in 20 minutes at 37 ℃ using the best primer pairs.	Laboratory
	2022	English	Other	Experimental	An assay using recombinase-aided amplification (RAA) and a lateral-flow dipstick (LFD) (RAA-LFD) to detect the 18S ribosomal RNA gene of *Plasmodium* species	Laboratory

Continued

Stage of control	Year of publication	Language	Affiliation	Study type	Product or technology	Phase of the study
Screening and Diagnosis	2022	English	Research institute	Observational	The mμLAMP detection system: a new detection system, i.e., multiplex microfluidic loop-mediated isothermal amplification (mμLAMP) array, was developed to provide a convenient, rapid and economical detection system for malaria diagnosis.	Laboratory
	2023	Chinese	Hospital	Observational	The blood cell histogram of the BC-5300 blood cell analyzer combined with blood smear microscopy to detect *Plasmodium*	Semi-Field
	2023	English	Research institute	Observational	AIDMAN: An AI-based object detection system for malaria diagnosis from smartphone thin-blood smear images	Semi-Field
	2023	English	Hospital	Observational	A rapid multiplex assay of human malaria parasites by digital PCR	Semi-Field
	2023	English	CDC	Experimental	An Innovative Point-of-Care Rapid Diagnostic Test for the identification of imported malaria parasites in China	Field
	2023	English	University	Observational	A simple alkaline lysis method for DNA extraction from blood samples on filter paper.	Laboratory
	2024	English	University	Observational	A field-applicable, ultrasensitive malaria diagnostic tool based on CRISPR-Cas13a for the detection of *P. falciparum* in whole blood samples	Laboratory
Larva control	2015	English	University	Observational	Capture and Ligation Probe-PCR (CLIP-PCR)	Laboratory
	2016	Chinese	Other	Observational	Recombinant enzyme-mediated isothermal amplification RAA technology	Laboratory
Prevention	2015	English	University	Observational	The discovery of a novel virulence factor of *P. falciparum*, a TatD-like DNase (PfTatD) that is expressed primarily in the asexual blood stage and is likely utilized by the parasite to counteract NETs.	Laboratory
	2016	English	University	Experimental	The cryptic epitopes of different antigens in the sporozoite and liver stages of *Plasmodium falciparum* to increase their immunogenicity without changing T cell antigen receptor (TCR)-peptide binding specificity	Laboratory
Treatment	2013	Chinese	Hospital	Experimental	Artesunate combined with CVVH treatment	Field
	2013	English	University	Observational	Novel Selective and Potent Inhibitors of Malaria Parasite Dihydroorotate Dehydrogenase: Dihydrothiophenone Derivatives	Laboratory
	2014	English	University	Observational	Endoperoxide polyketides from a Chinese Plakortis simplex	Laboratory
	2016	English	University	Experimental	Prototypes of lateral flow dipstick assays	Field
	2017	English	University	Observational	Inosine monophosphate dehydrogenase (IMPDH), an important target for antimalarial drug discovery	Laboratory
	2017	English	University	Observational	The component in A. annua extracts (MAE) leading to enhanced antiplasmodial potency of QHS via regulation of its metabolism	Laboratory
	2017	Chinese	Hospital	Experimental	The efficacy of acupuncture combined with artemisinin-based drugs in the treatment of malaria	Field
	2018	English	University	Observational	The supplementation of L-Arg may be a promising adjunctive therapy to reduce malaria-associated mortality in endemic areas. susceptibility to parasite synchronously by regulating host immune responses against P.y17XL, producing better outcomes for malaria infection	Laboratory
	2018	English	University	Experimental	Lipid emulsions for intravenous co-delivery of artemether and lumefantrine in severe malaria treatment	Laboratory
	2019	English	University	Observational	Identified a novel series of dual inhibitors through fragments assembly	Laboratory
	2019	English	Research institute	Observational	4-Aryl pyrrolidines as a novel class of orally efficacious antimalarial agents	Laboratory
	2019	English	University	Experimental	Overexpression of AaPIF3	Semi-Field
	2020	English	University	Observational	A series of artemisinin-sulfonamide hybrids (1–16)	Laboratory
	2020	English	University	Observational	Drug Repurposing of Quisinostat to Discover Novel *Plasmodium falciparum* HDAC1 Inhibitors with Enhanced Triple-Stage Antimalarial Activity and Improved Safety	Laboratory

Continued

Stage of control	Year of publication	Language	Affiliation	Study type	Product or technology	Phase of the study
Treatment	2021	English	Research institute	Experimental	Naphthoquine-Azithromycin Coformulation	Field
	2021	English	Hospital	Observational	Employed comparative genomics analysis and identified parasite-infected erythrocyte-specific protein 2 (PIESP2) to be a CM-related protein; further experimental investigations found that PIESP2 is an immunogenic protein	Laboratory
	2021	English	University	Observational	PfDXR inhibitors with improved pharmacology/safety	Laboratory
	2021	English	Research institute	Observational	The identification of a *Plasmodium*-blocking symbiotic bacterium, *Serratia ureilytica* Su_YN1	Laboratory
	2021	English	University	Observational	An HMFN-based delivery system with considerable antimalarial efficacy	Laboratory
	2021	English	University	Experimental	Heparin-decorated nanostructured lipid carriers of artemether-protoporphyrin IX-transferrin combination for therapy of malaria	Laboratory
	2023	Chinese	CDC	Experimental	The treatment of vivax malaria in children with Wumei Pills combined with Compound dihydroartemisinin Tablets and primaquine regimens	Field

Youth Editorial Board

Indexed by Science Citation Index Expanded (SCIE), Social Sciences Citation Index (SSCI), PubMed Central (PMC), Scopus, Chinese Scientific and Technical Papers and Citations, and Chinese Science Citation Database (CSCD)

The inauguration of *China CDC Weekly* is in part supported by Project for Enhancing International Impact of China STM Journals Category D (PIIJ2-D-04-(2018)) of China Association for Science and Technology (CAST).

CCDC weekly

Vol. 7 No. 18 May 2, 2025

Responsible Authority
National Disease Control and Prevention Administration

Sponsor
Chinese Center for Disease Control and Prevention

Editing and Publishing
China CDC Weekly Editorial Office
No.155 Changbai Road, Changping District, Beijing, China
Tel: 86-10-63150501, 63150701
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CSSN
ISSN 2096-7071 (Print)
ISSN 2096-3101 (Online)
CN 10-1629/R1