



# Regional heterogeneity of malaria healthcare seeking and diagnosis in China (2017–2022): Implications in preventing re-establishment of malaria transmission

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## ABSTRACT

**Background:** Enhancing regional collaboration in malaria prevention and control is a pivotal strategy for malaria control and elimination in China. The objective of this study is to examine the regional heterogeneity of malaria healthcare-seeking behaviors and diagnosis across various regions in China from 2017 to 2022.

**Methods:** Individual case data from national malaria surveillance databases were utilized. An analysis was conducted to discern the regional variations in the healthcare-seeking behaviors and diagnosis among regions.

**Results:** From 2017 to 2022, a total of 10,943 malaria cases were reported in China, predominantly imported cases (10,929), with significant variations in the distribution of different *Plasmodium* species among regions ( $P < 0.001$ ) and annually ( $P < 0.001$ ). There was a notable lack of timeliness in healthcare seeking (56.1 %) and case confirmation (67.3 %) with substantial regional disparities ( $P < 0.001$ ). These delays predominantly occurred in county and prefectural-level medical institutions ( $P < 0.001$ ), where misidentification of *Plasmodium* species was also prevalent ( $P < 0.001$ ). Furthermore, an initial diagnosis of malaria was observed in 76.6 % of cases ( $P < 0.001$ ), yet 87.8 % of malaria cases were ultimately confirmed correctly ( $P < 0.001$ ). Notably, *P. ovale* (21.0 %) and *P. malariae* (10.8 %) were easily misidentified as *P. vivax* ( $P < 0.001$ ).

**Conclusion:** The development of regional-specific interventions is essential to raise public awareness regarding malaria-related knowledge and to enhance the vigilance of health workers and their capacity of malaria testing. This will strengthen the nation's malaria surveillance and response system. Concurrently, fostering technological innovations for the rapid and precise identification of *Plasmodium* species, along with effective coordination of cross-regional mechanisms, is imperative to prevent re-establishment of malaria transmission in China.

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## Introduction

Malaria remains one of the "Big Three" infectious diseases, alongside HIV/AIDS and tuberculosis [1,2], presenting a serious threat to global health and life [3]. In 2022, despite substantial progress since the year 2000, it was estimated that approximately 249 million malaria cases persisted across 85 malaria-endemic countries, with 608,000 malaria-related deaths [3]. Notably, around

94 % of these cases and 95 % of malaria-related deaths occurred in Africa [3].

In China, malaria has a long history of epidemic and posed a significant threat to the health of the Chinese people and restricted economic and social development for decades [4,5]. However, through relentless efforts over several generations, China has made remarkable strides. Since 2017, no indigenous cases of mosquito-borne malaria have been reported [6], and on June 30, 2021, the World Health Organization (WHO) certified China as malaria-free [7]. The journey to this milestone has been bolstered by the establishment of multiple inter-regional cooperation mechanisms for malaria control and prevention, which have played an indispensable role. The cooperation mechanisms such as those in the five provinces of Jiangsu, Shandong, Henan, Anhui and Hubei in 1973 [8], Guizhou and Guangxi in 1976 [9], and Guangdong, Guangxi and Hainan in 1992 [10], respectively, have been instrumental in significantly reducing malaria morbidity and mortality.

However, as globalization and international travel intensify, China continues to confront a challenge that a substantial number of annual imported malaria cases returning from malaria-endemic areas abroad. This not only brings a continuous risk of re-establishment of malaria transmission after elimination but also continues to endanger public health [11–13]. Thus, China has implemented a new division of the areas for malaria control and prevention cooperation mechanisms among 24 historical malaria endemic provinces [14,15]. It aims to enhance the timely sharing of information and experience, improve case management among the migrant population, and bolster the capacity of foci disposal, thereby facilitating the prevention of re-establishment of transmission.

In the present study, we analyzed the epidemiological characteristics of reported malaria cases among different regions in China from 2017 to 2022. Concurrently, we assessed the performance of healthcare-seeking behaviors and case diagnosis under the new regional cooperation framework for malaria prevention and control. This analysis aims to inform strategies that can effectively address the potential challenges in the post-elimination phase, thereby aiding in the prevention of re-establishment of malaria transmission in China.

## Methods and materials

### Data source and collection

Data on malaria cases reported in Chinese mainland (not include Hong Kong, Macao, and Taiwan) from January 1, 2017, to December 31, 2022, were extracted from the China Information System for Disease Control and Prevention and Parasitic Diseases Information Reporting Management System. Epidemiological and demographic data were collated, including the onset of symptoms, the timeline for seeking healthcare and receiving a diagnosis, results of initial diagnosis, and the confirmation and verification. Additionally, the data encompassed the identification of *Plasmodium* species, health facilities for initial diagnosis and confirmation, types of malaria cases (imported, introduced, recurrent, or induced), and the geographical distribution in China.

All reported malaria cases were diagnosed and confirmed by laboratories within the malaria diagnostic laboratory network according to the criteria on Diagnosis of Malaria (WS259–2015) in China [16]. Moreover, each case underwent verification by provincial laboratories using polymerase chain reaction (PCR).

Additionally, healthcare seeking is deemed prompt if the individual seeks medical treatment within 3 days of symptom onset. Similarly, a diagnosis is considered timely if the case can be confirmed within 3 days following the initial diagnosis.

### Case definition

First, imported malaria case refers to the malaria case who traveled to malaria-endemic areas or had the previous malaria infection in history outside of China before the onset of illness, with evidence of case epidemiological investigation related to importation. Second, recrudescence case refers to a malaria case attributed to the recurrence of asexual parasitemia after antimalarial treatment, due to incomplete clearance of asexual parasitemia of the same genotype(s) that caused the original illness. In this study, it is specially referred to *Plasmodium malariae*, which can persist for extremely long periods, even for the life of the human host, but the mechanisms remain unclear as no dormant liver stages of hypnozoites have been reported. Third, induced case refers to a case whose origin of infection can be traced to a blood transfusion or other form of parenteral inoculation of the parasite but not to transmission by a natural mosquito-borne inoculation. Fourth, introduced case refers to a case contracted locally with strong epidemiological evidence linking it directly to a known imported case (first-generation local transmission).

### Regional division

The 24 historically malaria-endemic provinces have been divided into four distinct regions for malaria prevention and control as follows: five provinces of Shandong, Jiangsu, Anhui, Hubei and Henan are classified as the central region; six provinces of Jiangxi, Shanghai, Zhejiang, Fujian, Hunan and Chongqing are the southeastern region; seven provinces of Guangxi, Guangdong, Hainan, Sichuan, Guizhou, Yunnan, Xizang are the southern region; six provinces of Liaoning, Hebei, Shanxi, Shaanxi, Gansu and Xinjiang are the northern region [14,15]. Furthermore, Nei Mongol, Qinghai, Heilongjiang, Jilin, Ningxia, Beijing and Tianjin are the non-endemic areas in the history [17].

### Classification of health facilities

Health facilities were categorized into four distinct administrative levels: Below the county level and others (Individual clinics, Village clinics, Township health center and others), County level (County CDC and County medical institutions), Prefectural level (Prefectural CDC and Prefectural medical institutions), and Provincial level (Provincial CDC and Provincial medical institutions).

### Statistical analysis

The collation and cleaning of raw data extracted from the database was performed using WPS Office (Kingsoft Office, Beijing, China), and each step meticulously reviewed by two independent authors. Figures were done using WPS Office, RAWGraphs 2.0 (<https://app.rawgraphs.io/>), and CNSKnowall (<https://cnsknowall.com/#/HomePage>). Statistical differences were examined using either Pearson Chi-square tests or Fisher's Exact Test, conducted with IBM SPSS Statistics Version 26.0 (IBM Corp., Armonk, NY, USA). And SAS Version 9.3 (SAS Inst., Cary, USA) was used when SPSS was running out of memory. The level of significance was set at  $P < 0.05$  (two-sided).

## Results

From 2017 to 2022, a total of 10,943 malaria cases were reported in China, including 7031 *Plasmodium falciparum* cases, 1879 *P. vivax* cases, 1525 *P. ovale* cases, 332 *P. malariae* cases, 1 *P. knowlesi* case, 156 cases of mixed infections, and 19 clinically diagnosed cases (Table 1). Notably, there were statistically significant differences in the

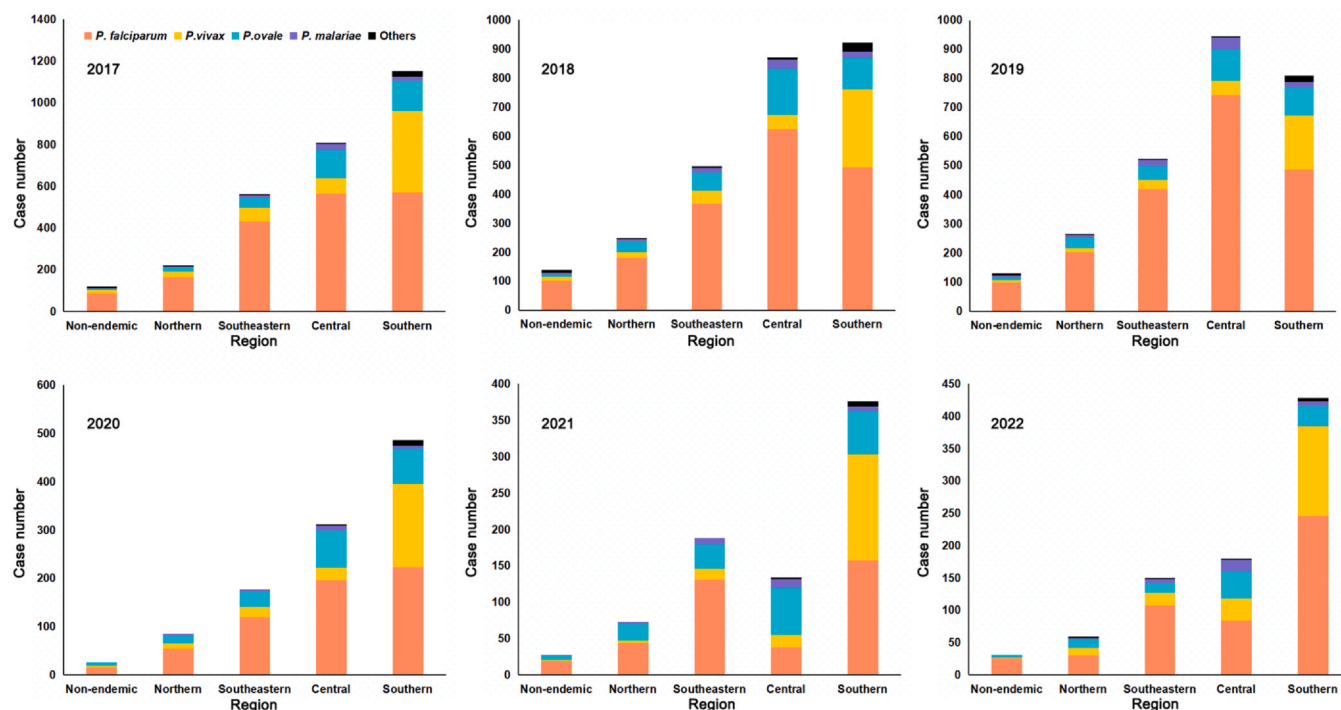
**Table 1**  
Malaria cases reported among different regions in China, 2017–2022.

Region	Infection					Total (%)
	<i>P. falciparum</i> (%)	<i>P. vivax</i> (%)	<i>P. ovale</i> (%)	<i>P. malariae</i> (%)	Others (%)	
<b>Non-endemic</b>	350 (73.4)	44 (9.2)	40 (8.4)	16 (3.4)	27 (5.7)*	477 (4.4)
<b>Northern</b>	678 (71.5)	84 (8.7)	148 (15.6)	29 (3.1)	9 (0.9)*	948 (8.7)
<b>Southeastern</b>	1575 (75.1)	201 (9.6)	239 (11.4)	67 (3.2)	14 (0.7)**	2096 (19.2)
<b>Central</b>	2250 (69.3)	250 (7.7)	583 (18.0)	143 (4.4)	21 (0.6)***	3247 (29.7)
<b>Southern</b>	2178 (52.2)	1300 (31.1)	515 (12.3)	77 (1.8)	105 (2.5)**	4175 (38.2)
<b>Total</b>	7031 (64.3)	1879 (17.2)	1525 (13.9)	332 (3.0)	176 (1.6)	10,943

\* Mixed infection and clinically diagnosed cases.

\*\* Mixed infection.

\*\*\* *P. knowlesi* infection and mixed infection.



**Fig. 1.** Malaria cases reported annually among different regions in China, 2017–2022.

**Table 2**  
Distribution of the proportion of timely healthcare seeking of reported malaria cases among different regions in China, 2017–2022.

Region	Year						Total (%)
	2017 (%)	2018 (%)	2019 (%)	2020 (%)	2021 (%)	2022 (%)	
<b>Non-endemic</b>	65 (53.7)	76 (54.3)	70 (53.8)	12 (46.2)	20 (71.4)	19 (61.3)	262 (54.9)
<b>Northern</b>	95 (43.4)	127 (51.4)	131 (49.2)	41 (48.2)	45 (61.6)	30 (51.7)	469 (49.5)
<b>Southeastern</b>	297 (52.9)	278 (55.9)	314 (59.9)	106 (59.9)	156 (83.0)	102 (68.5)	1253 (59.8)
<b>Central</b>	423 (52.5)	487 (55.9)	587 (62.1)	177 (56.7)	80 (59.7)	116 (64.8)	1870 (57.6)
<b>Southern</b>	540 (46.8)	517 (56.0)	435 (53.8)	287 (59.1)	240 (63.8)	270 (63.1)	2289 (54.8)
<b>Total</b>	1420 (49.6)	1485 (55.5)	1537 (57.5)	623 (57.4)	541 (67.7)	537 (63.6)	6143 (56.1)

distribution of cases infected with *Plasmodium* species among different regions ( $\chi^2 = 1140.3$ ,  $df = 16$ ,  $P < 0.001$ ) (Table 1), and the variations were also observed in each year (2017:  $\chi^2 = 332.7$ ,  $df = 16$ ,  $P < 0.001$ ; 2018:  $\chi^2 = 286.9$ ,  $df = 16$ ,  $P < 0.001$ ; 2019:  $\chi^2 = 228.8$ ,  $df = 16$ ,  $P < 0.001$ ; 2020:  $P < 0.001$ , Fisher's Exact Test; 2021:  $P < 0.001$ , Fisher's Exact Test; 2022:  $P < 0.001$ , Fisher's Exact Test) (Fig. 1).

In other words, there were 10,929 imported malaria cases reported, with 7026 of those cases being infected with *P. falciparum* (64.3%), followed by *P. vivax* (1875, 17.2%), *P. ovale* (1525, 14.0%), *P. malariae* (327, 3.0%), mixed-infection (156, 1.4%) and *P. knowlesi* (1 case), along with 19 clinically diagnosed cases (0.2%). The majority of these imported cases originated from Africa (9454, 86.5%),

followed by cases from Asia (1379, 12.6%), Oceania (65, 0.6%) and South America (31, 0.3%). Particularly, the majority of cases from Africa were infected with *P. falciparum* (73.6%, 6960/9454), whereas *P. vivax* cases predominantly made up the imported cases from Asia (93.5%, 1289/1379). In addition, there were 5 induced *P. falciparum* cases, 5 recrudescence *P. malariae* cases, and 4 introduced *P. vivax* cases.

#### Timeliness of healthcare seeking

In total, 56.1% (6143/10,943) of the reported cases sought healthcare within 3 days of symptom onset from 2017 to 2022. This

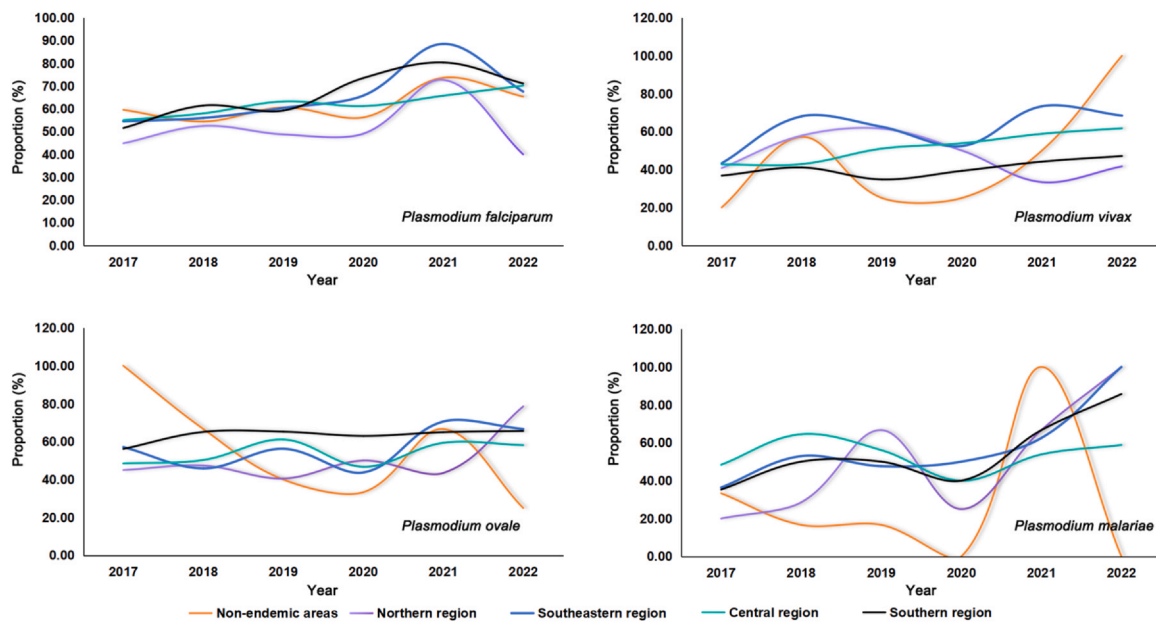


Fig. 2. Timeliness in healthcare seeking of reported cases infected with different *Plasmodium* species each year among different regions in China, 2017–2022.

varied by region, with significant differences among different regions ( $\chi^2 = 34.4$ ,  $df = 4$ ,  $P < 0.001$ ) (Table 2). In each year, statistically significant differences were found in the years of 2017 ( $\chi^2 = 12.8$ ,  $df = 4$ ,  $P = 0.013$ ), 2019 ( $\chi^2 = 22.2$ ,  $df = 4$ ,  $P < 0.001$ ) and 2021 ( $\chi^2 = 28.0$ ,  $df = 4$ ,  $P < 0.001$ ), while no such differences were noted in 2018 ( $\chi^2 = 1.9$ ,  $df = 4$ ,  $P = 0.746$ ), 2020 ( $\chi^2 = 5.3$ ,  $df = 4$ ,  $P = 0.257$ ) and 2022 ( $\chi^2 = 5.3$ ,  $df = 4$ ,  $P = 0.260$ ) (Table 2).

From the perspective of *Plasmodium* species, 59.8% of *P. falciparum* cases, 43.2% of *P. vivax* cases, 56.0% of *P. ovale* cases and 51.5% of *P. malariae* cases, sought healthcare promptly. There were significant statistical differences in the timeliness of healthcare seeking in *P. falciparum* cases ( $\chi^2 = 32.8$ ,  $df = 4$ ,  $P < 0.001$ ), *P. vivax* cases ( $\chi^2 = 29.6$ ,  $df = 4$ ,  $P < 0.001$ ), and *P. ovale* cases ( $\chi^2 = 14.5$ ,  $df = 4$ ,  $P = 0.006$ ), with the exception of *P. malariae* cases ( $\chi^2 = 6.0$ ,  $df = 4$ ,  $P = 0.201$ ), among different regions (Fig. 2).

Additionally, annual regional differences in the timeliness of healthcare seeking were also analyzed for cases infected with four *Plasmodium* species: *P. falciparum* (2017:  $\chi^2 = 7.7$ ,  $df = 4$ ,  $P = 0.101$ ; 2018:  $\chi^2 = 5.8$ ,  $df = 4$ ,  $P = 0.218$ ; 2019:  $\chi^2 = 14.1$ ,  $df = 4$ ,  $P = 0.007$ ; 2020:  $\chi^2 = 15.1$ ,  $df = 4$ ,  $P = 0.004$ ; 2021:  $\chi^2 = 12.9$ ,  $df = 4$ ,  $P = 0.012$ ; 2022:  $\chi^2 = 12.2$ ,  $df = 4$ ,  $P = 0.015$ ), *P. vivax* (2017:  $\chi^2 = 3.9$ ,  $df = 4$ ,  $P = 0.426$ ; 2018:  $\chi^2 = 13.9$ ,  $df = 4$ ,  $P = 0.007$ ; 2019:  $\chi^2 = 14.2$ ,  $df = 4$ ,  $P = 0.005$ ; 2020:  $\chi^2 = 3.7$ ,  $df = 4$ ,  $P = 0.470$ ; 2021:  $\chi^2 = 5.8$ ,  $df = 4$ ,  $P = 0.213$ ; 2022:  $\chi^2 = 6.1$ ,  $df = 4$ ,  $P = 0.167$ ), *P. ovale* (2017:  $\chi^2 = 6.9$ ,  $df = 4$ ,  $P = 0.138$ ; 2018:  $\chi^2 = 9.2$ ,  $df = 4$ ,  $P = 0.055$ ; 2019:  $\chi^2 = 8.5$ ,  $df = 4$ ,  $P = 0.073$ ; 2020:  $\chi^2 = 6.1$ ,  $df = 4$ ,  $P = 0.191$ ; 2021:  $\chi^2 = 4.8$ ,  $df = 4$ ,  $P = 0.308$ ; 2022:  $\chi^2 = 4.5$ ,  $df = 4$ ,  $P = 0.346$ ) and *P. malariae* (2017:  $\chi^2 = 2.0$ ,  $df = 4$ ,  $P = 0.764$ ; 2018:  $\chi^2 = 6.5$ ,  $df = 4$ ,  $P = 0.165$ ; 2019:  $\chi^2 = 4.2$ ,  $df = 4$ ,  $P = 0.382$ ; 2020:  $\chi^2 = 0.5$ ,  $df = 4$ ,  $P = 1.000$ ; 2021:  $\chi^2 = 1.1$ ,  $df = 4$ ,  $P = 0.969$ ; 2022:  $\chi^2 = 5.0$ ,  $df = 4$ ,  $P = 0.193$ ) (Fig. 2).

#### Timeliness of case diagnosis

Overall, 67.3% (7360/10,943) of reported malaria cases were confirmed within 3 days of initial diagnosis from 2017 to 2022, with statistical significance among different regions ( $\chi^2 = 135.8$ ,  $df = 4$ ,  $P < 0.001$ ) (Table 3). Similarly, a significant difference was found year over year (2017:  $\chi^2 = 122.5$ ,  $df = 4$ ,  $P < 0.001$ ; 2018:  $\chi^2 = 28.7$ ,  $df = 4$ ,  $P < 0.001$ ; 2019:  $\chi^2 = 19.2$ ,  $df = 4$ ,  $P = 0.001$ ; 2020:  $\chi^2 = 16.8$ ,  $df = 4$ ,  $P = 0.002$ ; 2021:  $\chi^2 = 16.7$ ,  $df = 4$ ,  $P = 0.002$ ; 2022:  $\chi^2 = 25.8$ ,  $df = 4$ ,  $P < 0.001$ ) (Table 3).

Meanwhile, 68.5% of *P. falciparum* cases ( $\chi^2 = 45.7$ ,  $df = 4$ ,  $P < 0.001$ ), 72.0% of *P. vivax* cases ( $\chi^2 = 155.8$ ,  $df = 4$ ,  $P < 0.001$ ), 60.1% of *P. ovale* cases ( $\chi^2 = 32.7$ ,  $df = 4$ ,  $P < 0.001$ ) and 52.1% of *P. malariae* cases ( $\chi^2 = 10.5$ ,  $df = 4$ ,  $P = 0.032$ ) were confirmed promptly (Fig. 3).

Additionally, yearly regional differences in the timeliness of case diagnosis were analyzed for cases infected with each *Plasmodium* species: *P. falciparum* (2017:  $\chi^2 = 66.8$ ,  $df = 4$ ,  $P < 0.001$ ; 2018:  $\chi^2 = 12.2$ ,  $df = 4$ ,  $P = 0.016$ ; 2019:  $\chi^2 = 7.5$ ,  $df = 4$ ,  $P = 0.112$ ; 2020:  $\chi^2 = 9.9$ ,  $df = 4$ ,  $P = 0.042$ ; 2021:  $\chi^2 = 12.2$ ,  $df = 4$ ,  $P = 0.016$ ; 2022:  $\chi^2 = 17.1$ ,  $df = 4$ ,  $P = 0.002$ ), *P. vivax* (2017:  $\chi^2 = 72.0$ ,  $df = 4$ ,  $P < 0.001$ ; 2018:  $\chi^2 = 51.1$ ,  $df = 4$ ,  $P < 0.001$ ; 2019:  $\chi^2 = 33.8$ ,  $df = 4$ ,  $P < 0.001$ ; 2020:  $\chi^2 = 3.7$ ,  $df = 4$ ,  $P = 0.442$ ; 2021:  $\chi^2 = 4.1$ ,  $df = 4$ ,  $P = 0.377$ ; 2022:  $\chi^2 = 12.5$ ,  $df = 4$ ,  $P = 0.013$ ), *P. ovale* (2017:  $\chi^2 = 37.7$ ,  $df = 4$ ,  $P < 0.001$ ; 2018:  $\chi^2 = 14.8$ ,  $df = 4$ ,  $P = 0.004$ ; 2019:  $\chi^2 = 3.1$ ,  $df = 4$ ,  $P = 0.545$ ; 2020:  $\chi^2 = 4.7$ ,  $df = 4$ ,  $P = 0.330$ ; 2021:  $\chi^2 = 8.7$ ,  $df = 4$ ,  $P = 0.066$ ; 2022:  $\chi^2 = 1.8$ ,  $df = 4$ ,  $P = 0.783$ ) and *P. malariae* (2017:  $\chi^2 = 4.1$ ,  $df = 4$ ,  $P = 0.434$ ; 2018:  $\chi^2 = 7.0$ ,  $df = 4$ ,  $P = 0.136$ ; 2019:  $\chi^2 = 10.4$ ,  $df = 4$ ,  $P = 0.030$ ; 2020:  $\chi^2 = 0.8$ ,  $df = 4$ ,  $P = 0.934$ ; 2021:  $\chi^2 = 3.4$ ,  $df = 4$ ,  $P = 0.575$ ; 2022:  $\chi^2 = 2.5$ ,  $df = 4$ ,  $P = 0.526$ ) (Fig. 3).

#### Health facilities of case diagnosis

Prefectural (33.3%) and county medical institutions (29.0%) were the primary destinations for initial medical treatment and diagnosis of malaria cases. There was a notable disparity in the utilization of health facilities at different administrative levels, with significant regional differences observed ( $\chi^2 = 2346.6$ ,  $df = 12$ ,  $P < 0.001$ ) (Fig. S1). Similarly, these institutions were also the main sites where cases were confirmed (prefectural: 41.8%; county: 25.6%) ( $\chi^2 = 3169.4$ ,  $df = 12$ ,  $P < 0.001$ ) (Fig. S1).

#### Case verification

From 2017 to 2022, only 76.6% (8377) of total malaria cases were initially diagnosed as malaria, with significant regional differences ( $\chi^2 = 151.8$ ,  $df = 4$ ,  $P < 0.001$ ) (Non-endemic areas: 73.4%; Northern region: 82.3%; Southeastern region: 72.7%; Central region: 71.2%; Southern region: 81.7%) (Fig. S2).

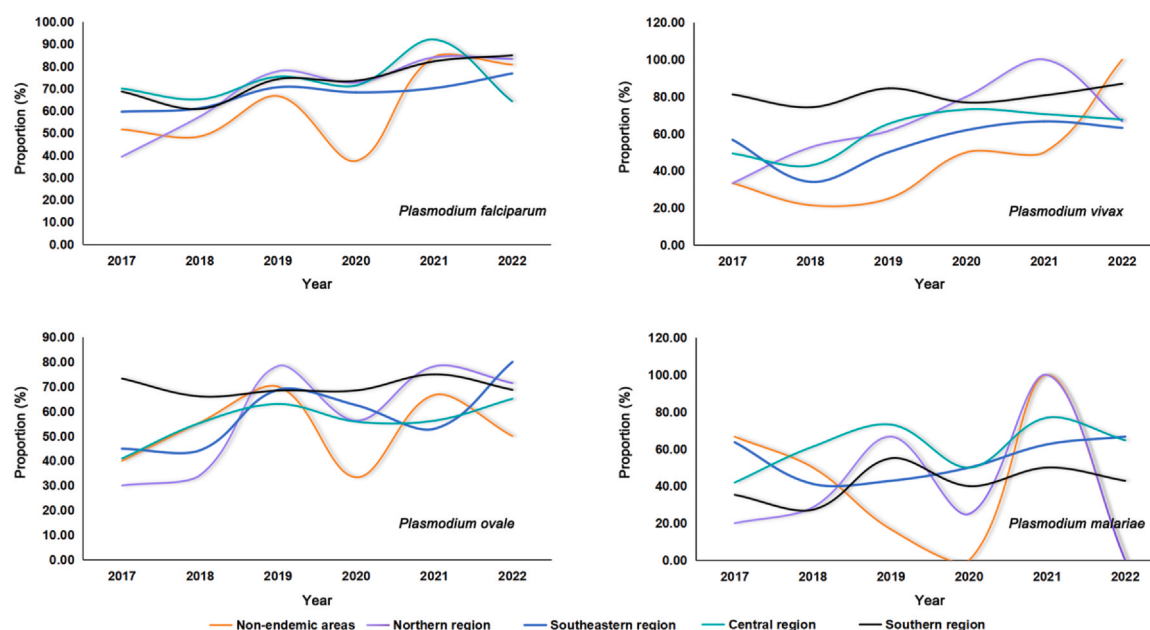
Furthermore, 9613 (87.8%) malaria cases (6616 *P. falciparum* cases, 1742 *P. vivax* cases, 1012 *P. ovale* cases, 243 *P. malariae* cases)



**Table 3**

The proportion of prompt confirmation of reported malaria cases among different regions in China, 2017–2022.

Region	Year						Total (%)
	2017 (%)	2018 (%)	2019 (%)	2020 (%)	2021 (%)	2022 (%)	
<b>Non-endemic</b>	59 (48.4)	64 (45.7)	82 (63.1)	10 (38.5)	22 (78.6)	24 (77.4)	261 (54.7)
<b>Northern</b>	82 (37.4)	131 (53.0)	207 (77.8)	58 (68.2)	61 (83.6)	44 (75.9)	583 (61.5)
<b>Southeastern</b>	326 (58.1)	277 (55.7)	355 (67.7)	117 (66.1)	125 (66.5)	112 (75.2)	1312 (62.6)
<b>Central</b>	501 (62.2)	538 (61.8)	692 (73.2)	209 (67.0)	94 (70.1)	117 (65.4)	2151 (66.2)
<b>Southern</b>	835 (72.4)	593 (64.2)	610 (75.4)	356 (73.3)	300 (79.8)	359 (83.9)	3053 (73.1)
<b>Total</b>	1803 (63.0)	1603 (59.9)	1946 (72.8)	750 (69.1)	602 (75.3)	656 (77.6)	7360 (67.3)

**Fig. 3.** Timeliness in case confirmation of reported malaria cases infected with different *Plasmodium* species each year among different regions in China, 2017–2022.

were verified with species identification that matched the initial diagnosis, revealing significant regional differences ( $\chi^2 = 209.3$ ,  $df = 4$ ,  $P < 0.001$ ) (Non-endemic areas: 73.8%; Northern region: 80.8%; Southeastern region: 90.5%; Central region: 91.4%; Southern region: 90.6%) (Fig. S2). In terms of the accurate identification of *Plasmodium* species, *P. ovale* (21.0%, 321/1525) and *P. malariae* (10.8%, 36/332) were most easily misidentified as *P. vivax* ( $\chi^2 = 1120.5$ ,  $df = 3$ ,  $P < 0.001$ ). There were also significant regional differences in the precise identification of *P. falciparum* ( $\chi^2 = 191.0$ ,  $df = 4$ ,  $P < 0.001$ ), *P. vivax* ( $\chi^2 = 40.2$ ,  $df = 4$ ,  $P < 0.001$ ), *P. ovale* ( $\chi^2 = 83.8$ ,  $df = 4$ ,  $P < 0.001$ ), and *P. malariae* ( $\chi^2 = 23.5$ ,  $df = 4$ ,  $P < 0.001$ ) (Fig. S2).

Regarding the misidentification of *Plasmodium* species, namely *P. falciparum*, *P. vivax*, *P. ovale*, and *P. malariae*, a total of 1154 malaria cases (415 *P. falciparum* cases, 137 *P. vivax* cases, 513 *P. ovale* cases, and 89 *P. malariae* cases) were misidentified during confirmation. This discrepancy was marked by significant differences ( $\chi^2 = 382.1$ ,  $df = 12$ ,  $P < 0.001$ ) in health facilities at different administrative levels among different regions (Fig. 4). Moreover, statistical differences ( $P < 0.001$ , Fisher's Exact Test) were also found in the cases caused by each single *Plasmodium* species (Fig. 4).

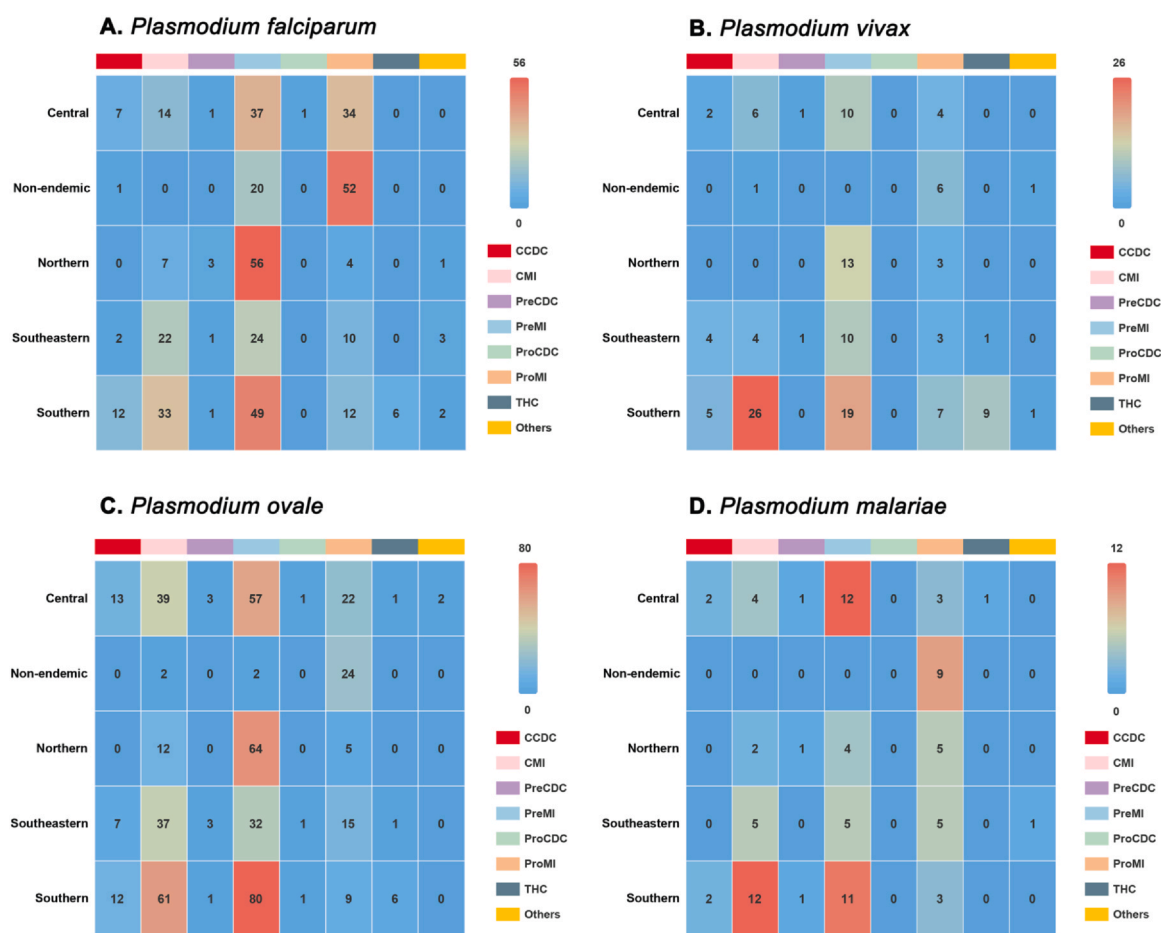
## Discussion

In the present study, we systematically examined the characteristics of healthcare-seeking behaviors, case diagnosis and verification of 10,943 malaria cases reported in different health facilities in five regions in China from 2017 to 2022. Our focus was particularly on identifying the challenges in the prompt and precise detection of

these cases, which are crucial for preventing re-establishment of malaria transmission within the country.

Since 2017, China has been free of indigenous cases of mosquito-borne malaria. However, the country continues to grapple with the persistent threat of imported cases, predominantly from Africa (mainly *P. falciparum* cases) and Asia (mainly *P. vivax* cases). Prompt diagnosis followed by effective treatment are pivotal for preventing fatalities and reducing transmission, forming the core of strategies for malaria control and elimination as well as the prevention of re-establishment of transmission [18,19]. Untreated cases could lead to severe illness or even death from *P. falciparum* malaria, and there is a potential for the introduction of new cases due to the extensive presence of *Anopheles* mosquitoes in China that are capable of transmitting malaria, particularly *P. vivax* [20–24]. Therefore, there is an urgent need for an enhanced surveillance and response system to prevent the re-establishment of malaria transmission.

Firstly, the perception of malaria and the adoption of timely healthcare-seeking behaviors are critical for promptly detecting and treating cases. This approach is crucial for reducing morbidity and mortality, and preventing onward malaria transmission [25]. Delays in treatment, often driven by patients' late initiation of healthcare, are linked to a higher risk of severe malaria. Factors contributing to delays in seeking healthcare include ethnic or religious features, low levels of education and socio-economic status, and the degree of available social support [26–28]. In the present study, there is an urgent need to enhance the timeliness of healthcare seeking, particularly in the northern region (less than 50% overall), where was the lowest almost every year. Moreover, regardless of the type of malaria parasite infected, less than 60% of cases sought healthcare in a



**Fig. 4.** Malaria cases infected with four *Plasmodium* species misidentified during confirmation in different health facilities among different regions in China, 2017–2022. CCDC: County CDC; CMI: County medical institutions; PreCDC: Prefectural CDC; PreMI: Prefectural medical institutions; ProCDC: Provincial CDC; ProMI: Provincial medical institutions; THC: Township health center.

timely manner, with *P. vivax* cases faring even worse at less than 45%. Notably, delays in seeking healthcare have been a primary factor of diagnostic delays among imported malaria cases [29–31]. Hence, it is imperative to develop targeted interventions aimed at increasing knowledge about malaria among international migrant populations, especially those traveling to and from malaria-endemic areas, as well as people living at the border areas, such as the China-Myanmar border [11,32]. It is equally important to emphasize the necessity for those individuals to seek healthcare immediately upon experiencing malaria-related symptoms and to inform the doctors about their travel and residence history in malaria-endemic areas.

Secondly, the vigilance and diagnostic competency of medical practitioners in identifying malaria is crucial for the timely detection of any malaria cases. Unfortunately, knowledge, awareness, and vigilance regarding malaria is always declined in this population after elimination [33,34]. The current study's findings indicate that the overall timeliness from initial diagnosis to confirmation is also not high, regardless of the type of malaria parasite infected. Moreover, timely confirmation of cases is particularly challenging, especially in the northern region and non-endemic areas. It is imperative to strengthen capacity building nationwide, moving beyond a focus on historically endemic areas during the elimination phase [17]. In addition, while the majority of cases were diagnosed and confirmed in county and prefectural-level medical institutions, only 76.6% (71.2–82.3%) of total malaria cases were initially diagnosed correctly. Furthermore, 89.3% (9613/10,767) of malaria cases infected with four *Plasmodium* species individually were confirmed correctly, highlighting the challenge of the identification of *P. ovale* and *P.*

*malariae*. Misidentifications were predominantly found in the same county and prefectural-level medical institutions. Therefore, it is essential to keep vigilance and implement ongoing training programs for health workers at all levels, especially those from medical institutions. In cases of febrile patients, it is advisable to inquire about additional epidemiological factors, such as travel and residence history in malaria-endemic countries or border areas like China-Myanmar border within the past 2 years, blood transfusion history within the last 2 weeks, previous episodes of malaria or fever of unknown origin, and to conduct immediate laboratory testing for malaria parasites. Besides, there is a need to strengthen technological innovation to facilitate rapid and precise identification of *Plasmodium* species, thereby supporting the appropriate treatment of malaria cases [35]. Thirdly, effective malaria prevention and control hinges the timely detection, precise diagnosis, and treatment of malaria cases. This requires the coordination between disease prevention and control institutions, medical institutions and other relevant departments in China. It is essential to strengthen joint efforts in capacity building, real-time information sharing, and case investigations and follow-ups. This should be complemented by bolstering the vigilance of front-line medical practitioners to ensure timely detection of malaria cases [36]. Furthermore, there is a need for cross-regional collaboration in the fight against the cross-border and cross-regional movement of imported cases after elimination. Upon identifying a suspected malaria case, medical practitioners must confirm it and report it immediately to the disease prevention and control institutions. This should activate a multi-sectoral or potentially cross-regional cooperation mechanism and ensure the

high quality of implementation of the "1-3-7" approach [37,38], so as to realizing the prevention of the re-establishment of malaria transmission in China.

## Limitations

Owing to the lack of data pertaining to the behavioral determinants of healthcare-seeking behaviors, as well as the initial diagnosis and confirmation, it is unable to dissect the factors that may impact the timeliness of seeking medical care and obtaining a diagnosis. In the future, it is recommended to carry out epidemiological investigations, such as case-control studies and cohort studies, to further understand the influencing factors and furnish the necessary evidence for crafting targeted interventions moving forward.

## Conclusions

China continues to grapple with numerous challenges in consolidating the achievements of malaria elimination in the post-elimination phase. These challenges include a large number of imported cases, coupled with delays in healthcare seeking and case confirmation with low diagnostic capacity. Consequently, malaria remains a non-negligible concern. It is imperative to develop regional-specific interventions aimed at raising public knowledge about malaria, elevating the vigilance of health workers, and bolstering their capacity for malaria detection. This will strengthen the nation's malaria surveillance and response system. Simultaneously, there is a pressing need to bolster technological innovations for rapid and accurate identification of *Plasmodium* species. Additionally, coordination of cross-regional cooperation mechanisms should be strengthened, so as to realize the prevention of the re-establishment of malaria transmission in China.

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## Declaration of Competing Interest

The authors declare that they have no competing interests.

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## Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at [doi:10.1016/j.jiph.2024.102601](https://doi.org/10.1016/j.jiph.2024.102601).

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