Tropical Biomedicine 41(2): 134-141 (2024)
https://doi.org/10.47665/tb.41.2.001

RESEARCH ARTICLE

Epidemiological characteristics and strategies for prevention and elimination of malaria in Qingdao, Shandong Province, China from 1949 to 2021

Shi, L.M.[1], Liu, S.Z.[1], Dou, X.J.[1], Liu, X.Y.[1], Feng, E.Q.[1], Liang, J.W.[1], Kong, X.L.[2], Ji, F.Y.[1*]

[1]Qingdao Municipal Center for Disease Control and Prevention/Qingdao Institute of Preventive Medicine, Qingdao, Shandong 266000, China
[2]Shandong Institute of Parasitic Diseases/Shandong Control Center for Digestive Diseases, Jining, Shandong 272000, China
*Corresponding author: jfy-5@126.com

ARTICLE HISTORY

Received: 24 September 2023
Revised: 19 January 2024
Accepted: 19 January 2024
Published: 30 June 2024

ABSTRACT

Malaria is an insect-borne disease transmitted by *Anopheles mosquitoes* or the importation of *Plasmodium*-infected blood, posing a serious threat to human health and life safety. This study aims to analyze the incidence of malaria in Qingdao at various stages from 1949 to 2021, to collate the control measures taken at different epidemic stages to assess the effectiveness of malaria control, and to identify a set of malaria control strategies suitable for Qingdao, while providing Chinese experience for other countries or cities in their malaria elimination efforts. A retrospective survey was used to collect information on malaria cases, control measures and prevention and control effects in Qingdao from 1949 to 2021, and to evaluate malaria control strategies and measures in Qingdao. 704 155 cases have been reported from 1949 to 2021, with three epidemic peaks: the incidence rate was 1715.9/100 000 in 1961, 1409.7/100 000 in 1965, and the most severe case occurred in 1972, with an incidence rate of 1635.6/100 000 and a case count exceeding 90 000. Throughout the various stages of malaria epidemics, Qingdao has effectively eliminated indigenous malaria by implementing diverse preventive and control measures. Since the last indigenous case of *Plasmodium vivax* was reported in 2002, all locally reported cases have been imported, mainly by returning migrant workers from Africa. This study examines a range of malaria prevention and control strategies and interventions that are appropriate for Qingdao. These measures have enabled Qingdao to successfully eliminate malaria and maintain malaria-free status for more than 20 years. These measures can also serve as a reference for similarly situated cities in Africa and Southeast Asia.

Keywords: Malaria epidemic; retrospective survey; eliminate malaria; control strategy; Qingdao.

INTRODUCTION

Malaria is a parasitic disease caused by *Plasmodium* species which are transmitted by *Anopheles* mosquito bites or the transfusion of blood containing malaria parasite gametophytes (Walter & John, 2022). According to the World Malaria Report 2022, there were 247 million cases in 2021 in 84 malaria endemic countries, an increase from 245million in 2020, and 619 000 deaths globally attributed to malaria in 2021 (WHO, 2022). There are four species of human malaria parasites that parasitize human red blood cells, namely: *Plasmodium vivax* (*P.v*), *Plasmodium falciparum* (*P.f*), *Plasmodium malariae* (*P.m*), and *Plasmodium ovale* (*P.o*) (Cox, 2002). Of these, *P. falciparum* and *P. vivax* are most common and deadly, respectively (Cox, 2002; Garcia, 2010).

Malaria is an old disease (Manson-Bahr, 1961; Garcia, 2010; Neghina *et al*., 2010), with an epidemic recorded more than 3,000 years in the Yin and Shang dynasties (Garcia, 2010; Neghina *et al*., 2010; Zhou, 2021), seriously affecting the health of the people and the development of the economy (Willey, 2014). A study of historical data revealed that in the 1940s, at least 30 million people were infected with malaria each year in China, with a death rate of about 1% (Feng *et al*., 2021; Zhou, 2021). After the founding of the People's Republic of China, the Chinese government developed a series of policies and programs (Qian & Tand 2000; Wang *et al*., 2022a), and following a 70-year effort, on June 30, 2021, China is certified malaria-free by WHO, which is a remarkable achievement (Wang *et al*., 2022a; Zhu & Cao, 2023). With the further development of global economic and cultural exchanges, imported malaria is now the biggest challenge facing China (Feng *et al*., 2015; Liu *et al*., 2021; Zhu & Cao, 2023).

Qingdao is located in the southern part of Shandong Peninsula, which is a single malaria endemic area (Su-Zhen *et al*., 2019), and the presence of the malaria vector *Anopheles mosquito* has led to a large-scale epidemic of *P. vivax*. Qingdao has adopted different control measures in different periods of malaria epidemics, and great achievements have been made in malaria control, with the annual incidence rate decreasing year by year. In 1985, Qingdao became the first city in Shandong Province to meet the basic malaria elimination criteria set by the Ministry of Health of the People's Republic of China (Su-Zhen *et al*., 2019). Since 2002, Qingdao has reported no indigenous malaria infections. Qingdao achieved the goal of malaria elimination ahead of schedule in 2016.

Indigenous malaria has been eliminated in Qingdao, but there are still a certain number of imported cases each year (Su-Zhen *et*

al., 2019; Yu *et al*., 2020). The vectors for malaria transmission in Qingdao still exist, and residents are generally susceptible to malaria (Liu & Liu, 2010). So the risk of local transmission caused by malaria imported from abroad persists (Feng *et al*., 2014). As a famous tourist city in China, Qingdao has an incomparably developed and convenient transportation, and a large number of people from all over the world come to Qingdao every year for tourism, family visits and trade activities (Su-Zhen *et al*., 2019). The gathering of mobile population in the city, especially during the malaria epidemic season is the peak of the gathering of mobile population, which greatly increases the risk of malaria re-transmission caused by imported cases (Tatarsky *et al*., 2011; Dharmawardena *et al*., 2015). Therefore, it is crucial to be able to develop a series of scientific measures that can prevent the re-transmission and outbreak of indigenous malaria caused by imported malaria.

Most of the studies on malaria epidemiology have been related to a single population such as children (Gondwe *et al*., 2021) and pregnant women (Osarfo *et al*., 2022), and few studies on the whole population for up to 70 years have been found. In this study, a retrospective survey was used to collect and summarize historical information on malaria control and elimination, and by describing the epidemiological characteristics of malaria incidence in Qingdao for more than 70 years, a comprehensive analysis was conducted to study malaria control strategies and prevention and control achievements in Qingdao since 1949, and an evaluation of the malaria control and elimination strategies in Qingdao was made. This study provides a practical basis for the prevention and control of indigenous retransmission caused by imported malaria and the maintenance of malaria-free status in Qingdao in the future. It also provides Chinese experience in malaria control and elimination to the current malaria endemic areas of the country such as Africa and Southeast Asia.

MATERIALS AND METHODS

Epidemiological data collection and source

We collected epidemiological data were from two main sources:

a) Data from passive surveillance:

In 1949, Qingdao established a health epidemic prevention station, which collected information on malaria cases from hospitals, health centers and other departments at all levels. Cases data from 1949-2005 were obtained from the Qingdao Epidemic Prevention Station (now called Qingdao Municipal Center for Disease Control and Prevention), including all years of malaria epidemic data, personnel statistical forms, case reporting records, and other original materials. In China, malaria was one of the infectious diseases under statutory surveillance, and the government required all malaria epidemiological information to be uploaded in the CDC surveillance system from 2004. Malaria cases in Qingdao were also reported online. 2005-2021 case-related data were obtained from the use of the China CDC parasitic disease control information management system.

b) Data from laboratory analysis:

From 1984 to 2021, blood smear examination data for "three fever" patients mainly came from laboratory examinations in primary care institutions, and surveillance data for mosquitoes transmitting malaria mainly came from on-site monitoring.

Population information was obtained from *Qingdao City statistical yearbook*.

Definitions

Based on the comprehensive analysis of the time of onset, the time of going out and returning, the place of going out and the length of stay, and the incubation period after infection with *Plasmodium*, the cases were divided into two categories: indigenous and imported cases. Imported cases include two types of infected persons who returned to the local area after being infected outside the city by residents of the city and those who returned to the local area after being infected outside the city by outsiders, and the rest are indigenous cases.

In China, confirmed cases were diagnosed based on the malaria diagnostic criteria issued by the country at different stages. The clinical diagnosed case was defined as patients with malaria-like symptoms but no parasite detected upon blood testing, while laboratory-confirmed case was defined as case confirmed by using any of the following methods including microscopy, rapid diagnostic tests (RDTs) or polymerase chain reaction (PCR) (Kong *et al*., 2017). In the outbreak epidemic stage, diagnosis was made based on clinical symptoms only because of the large number of malaria cases.

Blood testing of patients with the "four fevers" refers to the microscopic examination of blood samples from patients with four types of fevers: primary malaria, suspected malaria, colds and fevers of unknown origin. After the eradication of indigenous malaria, patients with fever caused by colds are no longer undergo microscopic examination of blood smears, and the remaining three types of patients are called "three fever" patients.

Statistical analysis

Annual incidence rates were calculated as the number of new cases per 100 000 population per year (January 1 to December 31 defined as the year). A retrospective analysis of historical information on malaria prevention and control in Qingdao from 1949-2021 was conducted by reviewing archives and collecting information on cases. The database was created using Microsoft office Excel 2021 (Microsoft Corporation, Redmond, WA, USA), and the chi-square test of malaria incidence changes was performed using GraphPad Prism 8.0 (GraphPad Software Inc., San Diego, CA, USA, https://www.graphpad.com/), with $P < 0.05$ set as a statistical difference. The spatial trend map of malaria incidence in Qingdao city was drawn with Arcgis 10.8 (Environmental Systems Research Institute Inc., RedLands, CA, USA, https://www.esri.com/en-us/home).

RESULTS

Epidemiological dynamics of malaria

During the malaria epidemic period, from 1949 to 2021, a total of 704 155 malaria cases were reported in Qingdao, including 703 893 indigenous and 262 imported cases. Within the period of 1950 to 1984, malaria was in a high-level epidemic stage in Qingdao, with three peak incidence rates: 1 715.9 per 100 000 (1961), 1 409.7 per 100 000 (1965), and the highest incidence rate in 1972 of 1 635.6 per 100 000, resulting in more than 90 000 cases (Figure 1). After 1972, the incidence of malaria in Qingdao decreased year by year, with it dropping to less than one thousandth in 1976 and one of

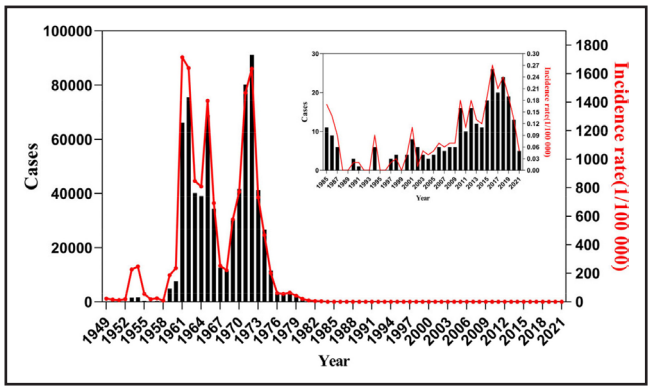

Figure 1. 1949-2021 malaria incidence and cases distribution in Qingdao.

ten thousand in 1981. The incidence dropped to 0.18 per 100 000 in 1985, meeting the basic elimination standard set by the Ministry of Health of the People's Republic of China (now called the National Health Commission of the People's Republic of China). The last indigenous case was reported in 2002. Since then, all malaria cases in Qingdao have been imported cases. There are no indigenous reports have been made to date.

Preventive measures and effects

After the founding of the People's Republic of China in 1949, the government has gradually eliminated indigenous malaria through the formulation of malaria prevention and control policies in different periods, such as the application of anti-malarial drugs and the modification of living environment. The process of malaria elimination in Qingdao followed the same path as the rest of the country. Qingdao has undergone five stages of eliminating indigenous malaria based on the malaria epidemiology, prevention, and control characteristics in different periods (Lai *et al*., 2019; Feng *et al*., 2022b). However, Qingdao has developed a set of malaria prevention and control strategies tailored to its own characteristics. These strategies are based on the national malaria prevention and control policy and take into account Qingdao's local living environment, economic development, and population. Innovative prevention and control strategies such as "delineating the stove to eliminate the source" and "focusing on prevention and control in accordance with local conditions" have been implemented.

The initial stage involves developing control structures for malaria, disseminating information on its prevention, and verifying the occurrence of malaria epidemics (1949-1959)

During the early years of founding of China, health organizations were incomplete, and their development was unbalanced. Moreover, due to the inadequate knowledge of malaria prevention and treatment among the populace, many people did not opt for medical treatment or adhere to science-based interventions when they fell sick, consequently leading to malaria outbreaks and epidemics. Due to the high prevalence of national control of infectious diseases, in the early 1950s, health institutions were established, patriotic health campaigns were publicized, and various efforts such as malaria prevention and control were carried out. In 1958-1959, the Qingdao Municipal Government vigorously publicized malaria prevention knowledge throughout the city and began comprehensive investigation and treatment of malaria patients. At the same time, the government has implemented various anti-mosquito measures including elimination of mosquito and fly breeding grounds, improvement of open toilets, dredging or upgrading sewage drains, and disinfecting the living environment. The annual incidence of malaria was reduced from 247.6 per 100 000 in 1954 to 8.2 per 100 000 in 1958 by a series of measures.

In the second phase, joint prevention and control measures are implemented to control outbreaks and epidemics (1960-1979)

The three malaria pandemics in Qingdao all took place during this period. Around 1960, a lack of funds for malaria control and natural disasters caused a significant shortage of antimalarial drugs. In Qingdao, the number of malaria cases increased sharply from 4 887 in 1959 to 66 087 in 1961 with the incidence rate increasing from 186.6 per 100 000 to 1 715.9 per 100 000. Currently, the primary objectives of the government are to enhance the epidemic reporting system and conduct outreach and educational activities. In areas with a high incidence of malaria, the government has established organizations that focus on controlling malaria. These organizations provide yearly training to grassroots health teams at every level, strengthen verifiable reporting of malaria outbreaks, and spread awareness of malaria prevention and treatment widely to the public. At the municipal level, medical and health teams were organized every year to verify malaria epidemics by going door-to-door. Those who were identified to have a history of malaria were registered and given medication. As a result of this initiative, the incidence of malaria decreased to 808.8 per 100 000 individuals during the 1963-1964 period.

In 1965, the incidence of malaria surged again due to poor control over the source of malaria infection, and inadequate implementation of anti-mosquito measures in addition to poor living conditions of the majority of the population. The incidence of malaria dropped significantly in 1966 due to the strengthening of the anti-relapse treatment for new and old patients. However, the discontinuation of prophylactic medication and anti-relapse treatment initiated the escalation of malaria cases in 1969. The increment persisted until 1972, and in that year, the incidence of malaria reached its highest level, with more than 90 000 cases reported.

The State Council approved the establishment of a five-province malaria joint prevention mechanism for Jiangsu, Shandong, Henan, Anhui, and Hubei Provinces in 1973. The five provinces jointly developed and synchronized malaria prevention and control measures which effectively solved the problem of inadequate implementation of malaria prevention and control measures in inter-provincial border areas. Malaria control measures have transitioned from eliminating breeding grounds of mosquito vectors and public education, to comprehensive measures that concentrate on controlling infectious agents. These include improving the management of current and past disease, implementing rest treatment in key districts with high morbidity, and district wide drug prevention during the epidemic season, implementing prophylactic drug administration at key infected sites in districts with general morbidity, organizing community health workers to provide and monitor drug administration to malaria cases, and achieving two "No" (No medication taken by third party to patients, No medication left at the treatment places), and keeping five "Arrival" (Patients arrival, medication arrival, water arrival, persuasion and mobilization arrival, observation of medication taken arrival).

The public's knowledge of malaria prevention and treatment has increased over the years, as has the rate of regular drug use, thanks to extensive publicity and education. In the six years from 1974 to 1979, a total of 51 432 current and suspected patients were treated, 135 819 patients with a history of malaria were treated during the malaria-free period, and 8 172 991 people took preventive medication, effectively reducing the number of recurrent cases and under reporting of epidemics. The incidence of malaria also continued to fall, from 1 635.6 per 100 000 in 1972 to 42.9 per 100 000 in 1979. In 1975, Qingdao began to set up microscopy stations in Jiaonan County (now Huangdao District) and Laixi County (now Laixi City), where the incidence of malaria was relatively high, for microscopy of blood smears from patients with fever, and from 1975 to 1980, the cumulative number of patients positive for *Plasmodium* parasites was 101 124, with a positivity rate of 12 620. From 1975 to 1980, the cumulative number of blood tests was 101 124 and 12 620 were positive for *P. vivax*, a positivity rate of 12.48%.

The third phase involves designating high malaria-endemic areas as foci, eliminating sources of infection, decontaminating malaria-endemic areas and reducing malaria incidence (1980-1999)

To further control the prevalence of malaria, Qingdao City selected Jiaonan County, where malaria was highly prevalent, as a pilot project in 1980-1982. A retrospective survey of malaria cases in Jiaonan County from 1977 to 1979 showed that of the 565 malaria patients, 492 cases were focal, accounting for 87.08 per cent, and 60 cases were dispersed, accounting for 10.62 per cent, with a further 13 cases distributed among key occupational groups vulnerable to *Anopheles* mosquitoes, such as night field workers. Therefore, in line with the characteristics of the late stage of malaria control, when the remaining foci are few and scattered, universal prophylactic administration during the rest period and the epidemic season has

been stopped and the focus of malaria control has been placed on households living on the outskirts of villages, key populations and populations around the foci. Villages where malaria is common and recurrence is frequent are used as "malaria foci", and the sources of malaria transmission are eliminated through repeated removal of the "foci". In 1982, a total of 564 people were randomly tested inside and outside the "foci", and the blood tests for *Plasmodium* were all negative, proving the success of "zoning the stoves and eliminating the sources of malaria", and in 1982 it began to be promoted in Qingdao, and the incidence of malaria declined rapidly, and in 1986 there were only 9 people suffering from malaria. At this stage, preventive medicine and anti-mosquito measures were also taken simultaneously, and blood tests for *Plasmodium* were actively carried out on patients with "four fevers". In 1980, Qingdao carried out blood tests for *Plasmodium* in patients with "four fevers", and all districts, counties and towns in the city set up microscopy stations or microscopy clinics. From 1980 to 1985, a total of 523 966 people were blood tested, of which 1 639 were positive, with a positivity rate of 0.31%. From 1988 to 1996, there were occasional new cases in Qingdao, and most malaria cases were imported from other provinces. There were imported cases from outside the country that started to appear in 1997, with a trend of increasing year by year.

Reinforcement of the management of mobile populations and consolidation of the results phase (2000-2009)

All malaria prevention management systems were further improved during this phase. Qingdao has established malaria case management methods, requirements for microscopic examination of febrile patients, and requirements for the treatment of lesions. Qingdao has further consolidated the results of malaria prevention and treatment by strengthening technical training and establishing a system of mobile community managers, so that the quality of malaria prevention and treatment work has been continuously improved and enhanced. The last indigenous case was reported in Qingdao in 2002, and since 2005, Qingdao has implemented a direct reporting network for malaria cases, which enables timely and accurate detection of malaria and other infectious diseases, and prevents the resurgence of indigenous epidemics by closely monitoring malaria outbreaks.

The final phase is malaria elimination and sustained compliance (2010-2021)

In this time, Qingdao followed the principles of adapting to local conditions, classifying and guiding, and scientifically preventing and controlling; taking control of the source of infection as the core and surveillance work as the leading role; strengthening capacity building; increasing the training of professional and technical personnel; and intensifying the work of blood testing for malaria. From 2010 to 2021, a total of 172 668 patients with "three fevers" were tested for *Plasmodium* in Qingdao, and 190 positive cases were found, all of which were imported cases, with a positive rate of 0.11% (Table 1). Since 2012, we have been managing each case found in accordance with the "1-3-7" surveillance and response strategy (Lu *et al*., 2016). Case reporting is required within 1 day of case discovery, case investigation and case review within 3 days, and targeted outbreak site investigation and disposal within 7 days to ensure that malaria cases are detected, reported, diagnosed and treated early.

From 2010 to 2021, the laboratory testing rate of imported malaria cases, the proportion of confirmed diagnoses and the standardised treatment rate in Qingdao City will all reach 100%. At this stage, large-scale training is conducted annually for malaria control specialists and technicians, with repeated and intensive training in all aspects of malaria blood film production and in identifying the morphology of various microscopic forms of *Plasmodium* to improve their malaria blood testing capacity, and skills competitions are held to further improve the detection and control capacity of specialists and technicians in the form of competitions as a substitute for training. In terms of malaria blood testing, Qingdao has set up municipal, district, county and township microscopy stations as sentinel sites for malaria case surveillance, so that malaria patients can be detected at the earliest opportunity through blood testing for *Plasmodium* parasites in patients with the "three fevers", and then designated fixed-point hospitals for those patients detected to receive a full course of standardised treatment with a full dose of free anti-malarial drugs.

During this period, Qingdao established a comprehensive malaria surveillance system and treatment network throughout the city, including three levels of sentinel microscopy stations to monitor patients with "three fevers" and designated hospitals for malaria treatment at the city, district and county levels. After 2017, Qingdao City continued to consolidate the results of malaria elimination, taking "timely detection and standardised and effective treatment of imported cases" as the core, consolidating joint prevention and control, improving monitoring and early warning, and strictly implementing the requirements of "1-3-7" imported malaria prevention and control work, timely blocking transmission and effectively controlling re-transmission of imported malaria.

Effectiveness of malaria control

We conducted a comparative analysis of malaria incidence in five phases from 1949 to 2021. 1949-1959 was the initial period of the country's establishment, when malaria was in the epidemic phase, with a cumulative total of 9 814 cases reported, accounting for 1.30%

Table 1. Blood testing for malaria in febrile patients in Qingdao, 2010-2021

Year	Number of blood testing	Blood testing rate	Number of positive cases	Positive rate	*Plasmodium* species		
					P. v	*P. f*	others
2010	24 548	0.28%	16	6.52%	3	2	11
2011	28 242	0.32%	10	3.54%	2	4	4
2012	24 548	0.27%	17	6.52%	4	13	0
2013	16 716	0.18%	11	7.18%	1	10	0
2014	14 056	0.15%	11	7.83%	2	9	0
2015	13 014	0.14%	18	13.83%	2	16	0
2016	11 867	0.12%	26	21.91%	1	23	2
2017	7 190	0.07%	21	27.82%	1	17	3
2018	7 766	0.08%	23	30.90%	1	20	2
2019	8 229	0.08%	19	23.09%	2	16	1
2020	8 084	0.08%	13	16.08%	4	7	2
2021	8 408	0.08%	5	5.95%	2	2	1
Total	172 688	0.15%	190	0.11%	25	139	26

Table 2. Incidence of malaria at different stages of the epidemic

Stage	Total population	Cases	Morbidity (1/100 000)	χ^2	*P* value
1949-1959	12 566 693	9 814	78.10	21 817 634	<0.0001
1960-1979	103 314 697	691 600	669.41		
1980-1999	130 183 271	2 499	1.92		
2000-2009	77 573 110	52	0.07		
2010-2021	114 038 500	190	0.17		

of the total number of reported cases. 1960-1979 was in the malaria outbreak epidemic phase, with a cumulative total of 691 600 cases reported, accounting for 98.33%. From 1980 to 1999, the incidence of malaria decreased significantly, new indigenous cases occasionally appeared, and imported cases from other provinces accounted for most of the cases. A total of 2 499 cases were reported in this period, accounting for 0.33% of the total number of reported cases. During 2000-2009, named the period of consolidating the results of malaria control, 52 malaria cases were reported in this period, accounting for 0.007% of the total number of reported cases. From 2010 to 2021, the period of complete elimination of indigenous malaria, the number of reported cases is 190, all of which are imported cases, accounting for 0.25% of the total number of reported cases. The incidence rates of the five phases showed a trend of increasing and then decreasing sharply (χ^2=21 817 634, *P*<0.0 001) (Table 2), which proved that the preventive and control measures we took were precise and effective.

Epidemiological characteristics of cases

Before 1985, most of the malaria patients in Qingdao were located in the rural areas, and all of them were clinically diagnosed cases of *P. vivax*, and the vector of malaria transmission was *Anopheles sinensis*. Cases occurred throughout the year, but there were obvious seasonal peaks, and the seasonal peaks are consistent at different stages, all rising in June, peaking in July-September, and starting to decline in October. With the continuous expansion of opening to the outside world and the increase of mobile people year by year, the proportion of imported malaria has increased. After 1985, indigenous malaria was basically eliminated, and imported malaria cases gradually increased, and the malaria epidemic no longer has obvious seasonality (Figure 2). Imported cases began to appear in 1986, and the last indigenous case was reported in 2002, after which imported cases have been reported every year (Figure 3). The type of infection with *Plasmodium* changed from a single *P. vivax* infection to a multi-species *Plasmodium* infection. The results of the analysis of *Plasmodium* species infected in 230 malaria cases in the last 20 years showed that *P. falciparum* infection was the majority, accounting for 63%, *P. vivax* infection accounted for 14%, and other types of *Plasmodium* infection accounted for 23% (Table 3).

Between 2010 and 2021, a total of 190 cases of imported malaria were reported (Table 2), out of which 176 were male and 14 were female. The maximum age reported was 64 years, including one year, with an average age of 39 years. Out of the 190 cases of malaria, 3 were imported from other provinces and 187 were imported from other countries. Out of these, 178 (95.19%) were from Africa and 9 (4.81%) from Asia. Among the 190 reported cases, 161 individuals resided in Qingdao. According to the spatial distribution analysis, patients were mainly concentrated in the coastal region of Qingdao. Additionally, the distribution of patients was closely associated with the level of local openness to the outside world (Figure 4).

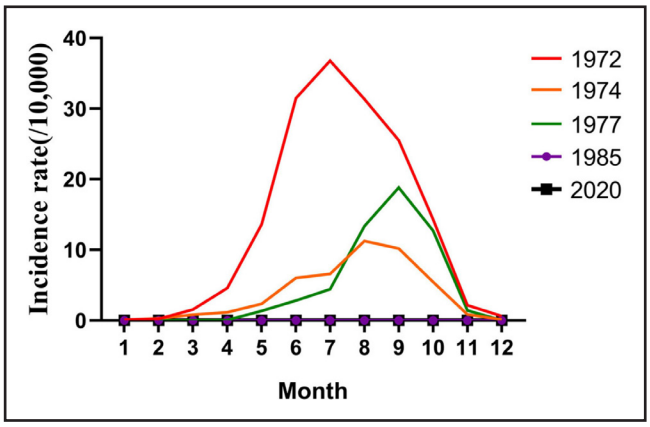

Figure 2. Seasonal distribution of malaria incidence in different epidemic stages.

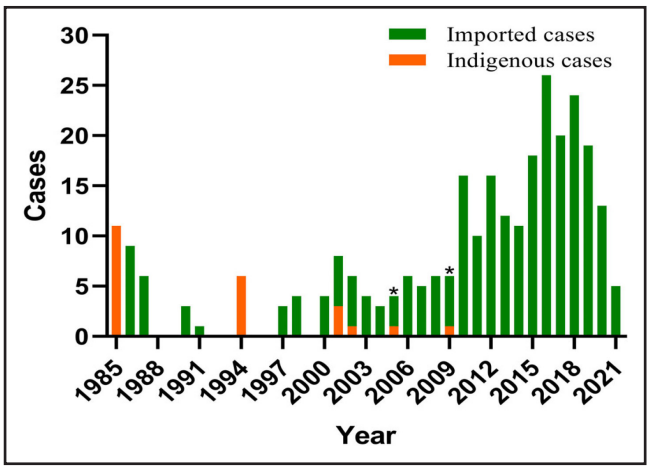

Figure 3. Composition of indigenous and imported cases in Qingdao from 1985-2021.
(*Indigenous cases of malaria in 2005, 2009 were recurrent cases.)

Table 3. Malaria case typings in Qingdao from 2002-2021

Plasmodium species	Cases	Proportion (%)
P. f	145	63
P. v	32	14
Others	53	23
Total	230	100

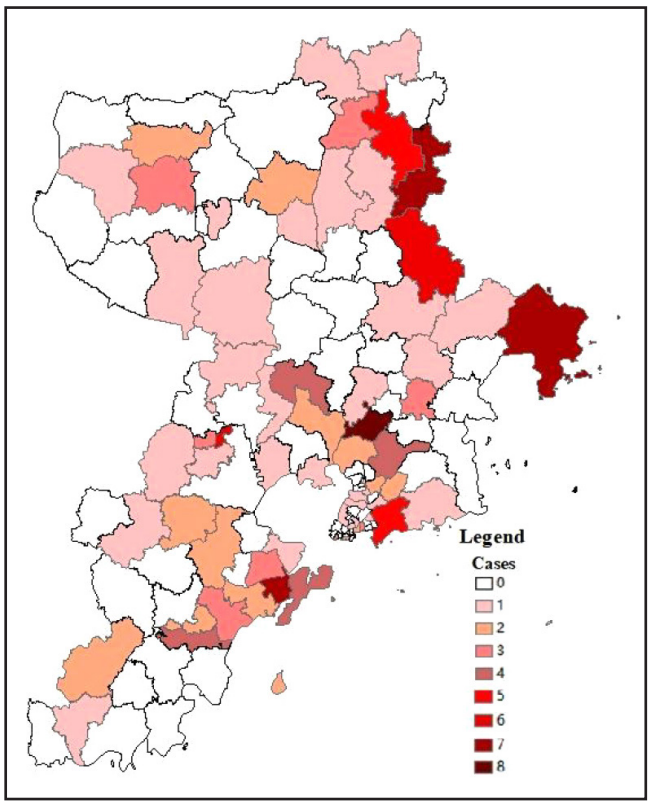

Figure 4. Spatial distribution of malaria cases in Qingdao from 2010 to 2021.

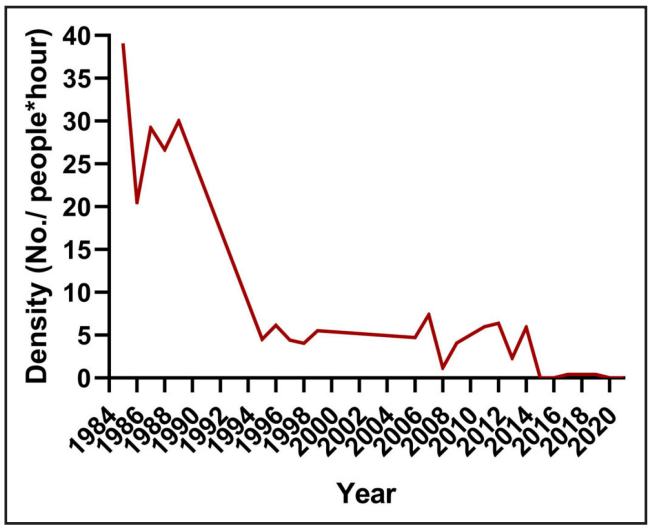

Figure 5. Media monitoring in Qingdao.

Characteristics of the medium

Mosquito species surveys and monitoring conducted in Qingdao over the past decades have revealed the presence of one type of *Anopheles* mosquitoes: *Anopheles sinensis*. Based on the observation of the number, lifespan, blood-sucking habits, seasonal growth, and seasonal distribution of malaria, and the sensitivity to *Plasmodium*. *Anopheles sinensis* has been identified as the sole vector of *Plasmodium* in Qingdao (Feng *et al*., 2017, 2022a; Wang *et al*., 2022b). Since 1981, Qingdao City has been monitoring *Anopheles mosquitoes*. Huangdao District was chosen as the malaria monitoring site in accordance with the requirements of the *Technical Programme for the Elimination of Malaria in Shandong Province*, based on the spatial distribution characteristics of malaria patients. The monitoring sites included the inlet wetlands and the areas of Poli and Dongjiakou. Twice a month vector monitoring was conducted between June and October every year. Mosquitoes were trapped using mosquito trapping lamps and artificial trapping methods. Monitoring results from the manual trapping method indicated a significant decline in the density of *Anopheles sinensis* after 1995, and by 2021, no more *Anopheles sinensis* were caught at the monitoring site (Figure 5).

DISCUSSION

The purpose of this study was to analyze the incidence and epidemiological characteristics of malaria in Qingdao over the past 70 years, evaluate a series of malaria control strategies adopted in different malaria epidemic stages in Qingdao, and identify a set of malaria control strategies and measures that are currently suitable for Qingdao to maintain the state of indigenous malaria elimination.

According to the WHO report, the European Region achieved the goal of eliminating endemic malaria in the 1970s (Danis *et al*., 2013). After the elimination of indigenous malaria, some European countries have only a few cases of imported malaria each year. Local government health budgets have been cut, and malaria surveillance and laboratory diagnostic capacity has declined over the years (Danis *et al*., 2013; Boccolini *et al*., 2020; Mironova *et al*., 2020). The presence of local malaria vectors and susceptible populations, together with increased economic and trade exchanges and an increase in mobile populations, led to the emergence of secondary cases of imported malaria and even outbreaks of malaria epidemics in areas such as Greece, Russia and Italy after the 1990s (Danis *et al*., 2013; Boccolini *et al*., 2020; Mironova *et al*., 2020). Similar to the situation in Greece and other countries, Qingdao has had imported malaria cases every year since the elimination of malaria in the area, and malaria vectors and susceptible populations have persisted, but Qingdao has succeeded in eliminating endemic malaria and has had no reports of endemic malaria for more than 20 consecutive years. What lessons can be learnt from the success of Qingdao in the elimination of endemic malaria and the sustainability of malaria elimination?

The statistical analysis of the epidemic data from 1949-2021 showed that the changing characteristics of the malaria epidemic in Qingdao over the past 72 years were basically similar to the historical process of malaria control in most cities in China (Qian & Tand, 2000; Yong-Liang *et al*., 2015; Hua-Yun *et al*., 2018). The findings of our research are specific technical approaches that have been used at different times and its contexts. We need to better understand the ways in which policies and approaches are developed on the ground, and the systems and capacities that make this possible.

There are some key factors here, the first of which is the importance the government attaches to malaria control. From the founding of the country in 1949 to the present day, the importance attached by the government has provided a strong organizational guarantee for the smooth running of the work. Malaria is an important parasitic disease that poses a serious threat to human health and life and affects socio-economic development, and the participation of the whole society is necessary to achieve the goal of eliminating indigenous malaria. The Qingdao Municipal Government attaches great importance to the elimination of malaria and has formulated appropriate policies at each historical stage of the elimination process. For example, every year the government organises the city's Spring Patriotic Hygiene Month, during which active measures are taken to eliminate a large number of dead-end sewers, improve environmental hygiene and household sanitation, reduce the number of mosquito breeding sites, cut off transmission routes and prevent the occurrence of malaria cases. Following the elimination of indigenous malaria, the government quickly adapted its strategies, shifting the focus of its malaria control efforts from controlling local malaria outbreaks to preventing local transmission caused by imported malaria, and ensuring the smooth implementation of its efforts by strengthening the public

health system and improving the malaria prevention and control network. Currently, the "1-3-7" surveillance and response strategy is being followed, and secondary cases of imported malaria have been effectively prevented by strengthening case finding and source management, and by timely treatment of potential transmission outbreaks.

In the 1950s, due to the lack of knowledge about malaria prevention and control among the public, who did not seek medical treatment or accept scientific treatment after falling ill, the phenomenon of under-reporting of cases occurred from time to time, and Qingdao experienced a number of malaria outbreaks and epidemics. Therefore, the second key factor is to strengthen public health education and raise awareness of malaria prevention and control among the entire population. Based on the World Malaria Day, China has established a National Malaria Day according to the actual situation in China. Qingdao takes advantage of the National Malaria Day each year by carrying out a variety of publicity activities in different forms and through different channels, so that the general public can have a better understanding of malaria prevention and treatment, raise their awareness of self-protection, and actively take preventive measures to stop the spread of malaria.

With the rise of tourism and the development of the foreign economy in Qingdao, a large number of transient people gather in the city every year. According to the *Qingdao Statistical Yearbook 2020*, the annual air passenger throughput reached 25 556 300 in 2019, and the city received a total of 11 303 000 tourists in 2019, of which 111 325 800 were domestic tourists and 1 702 600 were entrance tourists (Qingdao Municipal Bureau of Statistics Team, 2020). It is worth noting that among the entrance tourists, those from malaria-endemic areas such as South Korea and Southeast Asia accounted for 48.67% (Qingdao Municipal Bureau of Statistics Team, 2020). The WHO annual world malaria report indicates that *P. vivax* is mainly found in Southeast Asia (Feng *et al*., 2015; WHO, 2022). Of the 190 imported cases in Qingdao from 2010 to 2021, 25 were *P. vivax.* This greatly increases the risk of malaria importation and the potential threat of outbreak epidemics.

The third key factor is therefore the strengthening of the management of the floating population by the government and health care institutions. The CDC collaborated with customs, economic, tourism and other departments to target the migrant population from malaria-endemic areas, particularly those returning from overseas work. To keep these departments informed about malaria infection, morbidity and treatment, timely blood tests for *Plasmodium* parasites are carried out on febrile patients. If a person is found to be positive for *Plasmodium*, in addition to standard treatment, he or she is promptly followed up to investigate secondary infections.

The fourth key factor is continuous training of doctors to improve the diagnosis and treatment of malaria and to ensure that malaria cases are detected in time. Clinicians, public health workers, malaria microscopists and community health workers upgrading their skills through annual training, examinations and competitions to ensure that the three links of prevention, detection and treatment are closely integrated to further eliminate the incidence and prevalence of malaria.

The fifth key factor is that the establishment of a powerful malaria defence system has played an important role in the elimination phase. Between 2010 and 2017, the establishment of a three-tier surveillance network and a secondary treatment system in Qingdao enabled timely monitoring of patients with triple fever, timely identification of malaria patients, and timely and standardised treatment. It was also able to quickly close points and eliminate sources, preventing the re-transmission of imported malaria.

During the period of the indigenous malaria pandemic, seasonal peaks in malaria incidence were characteristic of the transmission of the vector insect *Anopheles sinensis*. After the elimination of indigenous malaria, the vectors of malaria still exist because the ecological environment of the Qingdao area has not fundamentally changed. Therefore, the sixth key point is to continue to monitor vector mosquitoes, treat possible infection sites in a timely manner, eliminate mosquito breeding sites, reduce the chances of mosquito bites and cut off transmission channels. In 1981, Qingdao began to establish a vector monitoring system, and the results of more than 40 years of monitoring show that the number and population of *Anopheles sinensis* in Qingdao have changed, and the catch of *Anopheles sinensis* has decreased year by year, with the density of *Anopheles sinensis* in 1985 was 39.07 per person*hour, and the density of *Anopheles sinensis* will decrease to 2.08 per person*hour by 2020. However, the recent monitoring results of vector population show that there is still a small amount of *Anopheles sinensis* in Qingdao. *Anopheles sinensis* is a semi-domestic mosquito species, which can feed on human and cattle blood. The significant decrease in the number of *Anopheles sinensis* may be related to the ecological habit of *Anopheles sinensis*. On the one hand, with economic development and accelerated urbanization, the number of farmers' cultivated land has been reduced and the mode of farming has been changed from cattle farming to mechanized farming, and the number of cattle kept in residents' homes has been greatly reduced. On the other hand, the increase in the use of insecticides and the scope of use also made the population of *Anopheles sinensis* change. Conducting mosquito vector surveillance is helpful to understand the geographical distribution of *Anopheles sinensis* and predict the risk of malaria retransmission, and at the same time, targeted epidemic site treatment can be carried out according to the incidence of imported malaria in different seasons and regions.

This study examined a group of strategies and measures for preventing and controlling malaria that are appropriate for Qingdao. These measures enabled the city to eliminate malaria and maintain that status for over 20 years without any indigenous cases. These measures include: 1. Government attention and support; 2. Census to verify malaria epidemics, cut off transmission routes and rapidly control epidemics; 3. Joint prevention and control to prevent outbreaks and epidemics; 4. Consolidation of malaria prevention and control achievements through elimination of foci and sources of the disease; 5. Elimination of malaria by adapting to local conditions and using prevention as the mainstay of prevention; 6. Establishment of a strong network system for malaria control, following the strategy of "1-3-7", strengthening monitoring and community health education and prevent the importation and re-transmission of malaria.

FUNDING

This work was supported by Projects of the Qingdao 2021 Medical and Health Research Program (2021-WJZD153).

Competing Interests

The author declares that they have no conflict of interests.

Author Contributions

Shi, L.M.: Investigation, Formal analysis, Data curation, Writing – original draft, Visualization. Liu, S.Z.: Methodology, Investigation, Formal analysis, Data curation. Dou, X.J.: Methodology, Investigation. Liu, X.Y.: Formal analysis. Feng, E.Q.: Investigation. Liang, J.W. & Kong, X.L.: Methodology, Project administration. Ji, F.Y.: Conceptualization, Resources, Writing – review & editing, Supervision, Project administration, Funding acquisition.

ACKNOWLEDGEMENTS

The authors extend their gratitude to Professor Ning Xiao of the Institute of Parasitic Disease Prevention and Control of the Chinese Center for Disease Control and Prevention for his invaluable guidance in this study. They also acknowledge the support of the Qingdao Districts (Municipal) CDCs in malaria prevention and control efforts in Qingdao.

REFERENCE

Boccolini, D., Menegon, M., Di Luca, M., Toma, L., Severini, F., Marucci, G., D'Amato, S., Caraglia, A., Maraglino, F.P., Rezza, G. *et al*. (2020). Non-imported malaria in Italy: paradigmatic approaches and public health implications following an unusual cluster of cases in 2017. *BMC Public Health* **20**: 857. https://doi.org/10.1186/s12889-020-08748-9

Cox, F.E. (2002). History of human parasitology. *Clinical Microbiology Reviews* **15**: 595-612. https://doi.org/10.1128/CMR.15.4.595-612.2002

Danis, K., Lenglet, A., Tseroni, M., Baka, A., Tsiodras, S. & Bonovas, S. (2013). Malaria in Greece: historical and current reflections on a re-emerging vector borne disease. *Travel Medicine and Infectious Disease* **11**: 8-14. https://doi.org/10.1016/j.tmaid.2013.01.001

Dharmawardena, P., Premaratne, R.G., Gunasekera, W.M., Hewawitarane, M., Mendis, K. & Fernando, D. (2015). Characterization of imported malaria, the largest threat to sustained malaria elimination from Sri Lanka. *Malaria Journal* **14**: 177. https://doi.org/10.1186/s12936-015-0697-0

Feng, J., Xia, Z.G., Vong, S., Yang, W.Z., Zhou, S.S. & Xiao, N. (2014). Preparedness for malaria resurgence in China: case study on imported cases in 2000-2012. *Advances in Parasitology* **86**: 231-265. https://doi.org/10.1016/b978-0-12-800869-0.00009-3

Feng, J., Xiao, H., Zhang, L., Yan, H., Feng, X., Fang, W. & Xia, Z. (2015). The *Plasmodium vivax* in China: decreased in local cases but increased imported cases from Southeast Asia and Africa. *Scientific Reports* **5**: 8847. https://doi.org/10.1038/srep08847

Feng, J., Zhang, L., Xia, Z.G., Zhou, S.S. & Xiao, N. (2021). Malaria-free certification in China: achievements and lessons learned from the National Malaria Elimination Programme. *Zoonoses* **1**. https://doi.org/10.15212/ZOONOSES-2021-1002

Feng, X., Feng, J., Zhang, L., Tu, H. & Xia, Z. (2022a). Vector control in China, from malaria endemic to elimination and challenges ahead. *Infectious Diseases of Poverty* **11**: 54. https://doi.org/10.1186/s40249-022-00971-3

Feng, X., Zhang, L., Tu, H. & Xia, Z. (2022b). Malaria elimination in China and sustainability concerns in the post-elimination stage. *China CDC Weekly* **4**: 990-994. https://doi.org/10.46234/ccdcw2022.201

Feng, X., Zhang, S., Huang, F., Zhang, L., Feng, J., Xia, Z., Zhou, H., Hu, W. & Zhou, S. (2017). Biology, bionomics and molecular biology of *Anopheles sinensis* Wiedemann 1828 (Diptera: Culicidae), main malaria vector in China. *Frontiers in Microbiology* **8**: 1473. https://doi.org/10.3389/fmicb.2017.01473

Garcia, L.S. (2010). Malaria. *Clinics in Laboratory Medicine* **30**: 93-129. https://doi.org/10.1016/j.cll.2009.10.001

Gondwe, T., Yang, Y., Yosefe, S., Kasanga, M., Mulula, G., Luwemba, M.P., Jere, A., Daka, V. & Mudenda, T. (2021). Epidemiological trends of malaria in five years and under children of Nsanje district in Malawi, 2015-2019. *International Journal of Environmental Research and Public Health* **18**: 12784. https://doi.org/10.3390/ijerph182312784

Hua-Yun, Z., Jun, C., Guo-Ding, Z., Wei-Ming, W., Yuan-Yuan, C., Ya-Ping, G., Ju-Lin, L., Jian-Xia, T., Yao-Bao, L., Sui, X. *et al*. (2018). Progress of malaria elimination of Jiangsu Province, China. *Chinese Journal of Schistosomiasis Control* **30**: 364-368. https://doi.org/10.16250/j.32.1374.2018165

Lai, S., Sun, J., Ruktanonchai, N.W., Zhou, S., Yu, J., Routledge, I., Wang, L., Zheng, Y., Tatem, A.J. & Li, Z. (2019). Changing epidemiology and challenges of malaria in China towards elimination. *Malaria Journal* **18**: 107. https://doi.org/10.1186/s12936-019-2736-8

Kong, X., Liu, X., Tu, H., Xu, Y., Niu, J., Wang, Y., Zhao, C., Kou, J. & Feng, J. (2017). Malaria control and prevention towards elimination: data from an eleven-year surveillance in Shandong Province, China. *Malaria Journal* **16**: 55. https://doi.org/10.1186/s12936-017-1708-0

Liu, Q.Y. & Liu, X.B. (2010). Prevention and control of vector *Anopheles*: a key approach for malaria elimination in China. *Chinese Journal of Vector Biology and Control* **21**: 409-413.

Liu, W., Hu, W., Dong, Z. & You, X. (2021). Travel-related infection in Guangzhou, China, 2009-2019. *Travel Medicine and Infectious Disease* **43**: 102106. https://doi.org/10.1016/j.tmaid.2021.102106

Lu, G.Y., Liu, Y.B., Beiersmann, C., Feng, Y. & M ller, O. (2016). Operational challenges to the 1-3-7 surveillance strategy for malaria elimination in China: a qualitative study. *Lancet* **388**: S15. https://doi.org/10.1016/S0140-6736(16)31942-0

Manson-Bahr, P. (1961). The malaria story. *Proceedings of the Royal Society of Medicine* **54**: 91-100.

Mironova, V.A., Shartova, N.V., Beljaev, A.E., Varentsov, M.I., Korennoy, F.I. & Grishchenko, M.Y. (2020). Re-introduction of vivax malaria in a temperate area (Moscow region, Russia): a geographic investigation. *Malaria Journal* **19**: 116. https://doi.org/10.1186/s12936-020-03187-8

Neghina, R., Iacobiciu, I., Neghina, A.M. & Marincu, I. (2010). Malaria, a journey in time: in search of the lost myths and forgotten stories. *The American Journal of the Medical Sciences* **340**: 492-498. https://doi.org/10.1097/MAJ.0b013e3181e7fe6c

Osarfo, J., Ampofo, G.D. & Tagbor, H. (2022). Trends of malaria infection in pregnancy in Ghana over the past two decades: a review. *Malaria Journal* **21**: 3. https://doi.org/10.1186/s12936-021-04031-3

Qian, H. & Tand, L. (2000). Prevention and control of malaria in China, in last 50 years. *Zhonghua Liu Xing Bing Xue Za Zhi* **21**: 225-227.

Qingdao Municipal Bureau of Statistics Team (2020). Qingdao City statistical yearbook 2020. http://qdtj.qingdao.gov.cn/tongjisj/tjsj_tjnj/tjnj_2020/202204/t20220414_5486359.shtml Accessed 19 January 2024.

Su-Zhen, L., Feng-Ying, J. & Xue-Kui, L. (2019). Epidemic situation of malaria in Qingdao City from 2012 to 2017. *Chinese Journal of Schistosomiasis Control* **30**: 664-668. https://doi.org/10.16250/j.32.1374.2018014

Tatarsky, A., Aboobakar, S., Cohen, J.M., Gopee, N., Bheecarry, A., Moonasar, D., Phillips, A.A., Kahn, J.G., Moonen, B., Smith, D.L. *et al*. (2011). Preventing the reintroduction of malaria in Mauritius: a programmatic and financial assessment. *PLoS One* **6**: e23832. https://doi.org/10.1371/journal.pone.0023832

Walter, K. & John, C.C. (2022). Malaria. *JAMA* **327**: 597. https://doi.org/10.1001/jama.2021.21468

Wang, D.Q., Liang, X.H., Lu, S.N., Ding, W., Huang, J., Wen, X., Lv, S., Xiao, N., Husain, L. & Zhou, X.N. (2022a). China's long march to malaria elimination: a case of adaptive management. *Malaria Journal* **21**: 38. https://doi.org/10.1186/s12936-021-04038-w

Wang, T., Fan, Z.W., Ji, Y., Chen, J.J., Zhao, G.P., Zhang, W.H., Zhang, H.Y., Jiang, B.G., Xu, Q., Lv, C.L. *et al*. (2022b). Mapping the distributions of mosquitoes and mosquito-borne arboviruses in China. *Viruses* **14**: 691. https://doi.org/10.3390/v14040691

WHO. (2022). World Malaria Report 2022. Geneva: World Health Organization. https://www.who.int/publications/i/item/9789240064898. Accessed 19 January 2024.

Willey, S. (2014). Malaria: The Story of Struggle, Suffering, and Eradication. *Honors Projects* 140. https://scholarworks.bgsu.edu/honorsprojects/140.

Yong-Liang, Y., Kang-Ming, L., Sheng-Rong, W. & Chuan-Jin, Z. (2015). Analysis of epidemic situation of malaria in Longlin various nationalities autonomous county in Guangxi from 1951 to 2014. *Chinese Journal of Schistosomiasis Control* **28**: 185-188. https://doi.org/10.16250/j.32.1374.2015173

Yu, T., Fu, Y., Kong, X., Liu, X., Yan, G. & Wang, Y. (2020). Epidemiological characteristics of imported malaria in Shandong Province, China, from 2012 to 2017. *Scientific Reports* **10**: 7568. https://doi.org/10.1038/s41598-020-64593-1

Zhou, X.N. (2021). China declared malaria-free: a milestone in the world malaria eradication and Chinese public health. *Infectious Diseases of Poverty* **10**: 98. https://doi.org/10.1186/s40249-021-00882-9

Zhu, G. & Cao, J. (2023). Regular assessment is an effective approach to maintaining the capacity of prevention of re-establishment from imported malaria in China. *Chinese Journal of Schistosomiasis Control* **35**: 113-115. https://doi.org/10.16250/j.32.1374.2023049