CHAPTER THREE

Lessons from Malaria Control to Elimination: Case Study in Hainan and Yunnan Provinces

Zhi-Gui Xia[1,#], Li Zhang[1,#], Jun Feng[1], Mei Li[1], Xin-Yu Feng[1], Lin-Hua Tang[1], Shan-Qing Wang[2], Heng-Lin Yang[3], Qi Gao[4], Randall Kramer[5], Tambo Ernest[6], Peiling Yap[7], Xiao-Nong Zhou[1,*]

[1]National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention; Key Laboratory of Parasite and Vector Biology, MOH; WHO Collaborating Centre for Malaria, Schistosomiasis and Filariasis, Shanghai, People's Republic of China
[2]Hainan Provincial Center for Disease Control and Prevention, Haikou, People's Republic of China
[3]Yunnan Provincial Institute of Parasitic Diseases, Pu-er, People's Republic of China
[4]Jiangsu Provincial Institute of Parasitic Diseases, Wuxi, People's Republic of China
[5]Duke Global Health Institute, Duke University, Durham, NC, USA
[6]Centre for Sustainable Malaria Control, Faculty of Natural and Environmental Science; Center for Sustainable Malaria Control, Biochemistry Department, Faculty of Natural and Agricultural Sciences, University of Pretoria, Pretoria, South Africa
[7]Department of Epidemiology and Public Health, Swiss Tropical and Public Health Institute, Basel, Switzerland; University of Basel, Basel, Switzerland
*Corresponding author: E-mail: zhouxn1@chinacdc.cn

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[#] Contributed equally to this paper.

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Abstract

Reduction patterns of *Plasmodium falciparum and P. vivax* malaria transmission and the role of an integrated strategy of case management and vector control are compared between different ecological zones. The epidemiology of malaria in Hainan and Yunnan provinces was disparate, even though distinct malaria control strategies have been adapted to different situations based on risk group, vector behaviours, local health infrastructure, and environmental conditions. The island Hainan appears to be victorious in eliminating malaria. However, there is still a long way to go to prevent the reintroduction of malaria in Hainan province and eliminating malaria in the border areas of Yunnan province. This review of the experiences and challenges from malaria control to elimination in Hainan and Yunnan provinces of southern China will provide a basis for the future elimination of malaria in the whole country.

1. INTRODUCTION

Malaria is an important parasitic disease that has severely damaged the Chinese people's life safety and health and slowed the country's economic and social development in the early years of last century. (Chen, 2014). Since the establishment of the People's Republic of China (P.R. China) in 1949, malaria prevention and control in the country has made remarkable achievements with governmental support at all levels. The epidemic area has been greatly reduced, with the number of malaria cases decreasing from more than 24 million in the early 1970s to tens of thousands by the end of the 1990s (Tang, 1999a).

P. falciparum malaria has been eliminated from all areas by 2000, except for the provinces of Yunnan and Hainan (Bi et al., 2013; Tang, 1999a; Tang et al., 2012a).

Due to the complexity of risk factors, the spread of malaria is fast and capricious. Since 2000, the epidemic situation of malaria in P.R. China has become more severe, with outbreaks occurring regularly in some regions (Zhang et al., 2008b; Zhou et al., 2008). This can be mainly explained by weakened prevention and control systems, inadequate fund investments in some regions, and the influence of the mobile population and high endemic situations in some of the neighbouring countries on the border areas of southern China (Zheng et al., 2013; Zofou et al., 2014). Malaria prevalence in the country reached its peak in 2006, when the number of malaria cases was more than 60,000, and the incidence was up to around 5 per 100,000. Due to the presence of geographical conditions naturally suited for transmission, multi-drug resistant *P. falciparum* and highly efficient vectors of *Anopheles minimus* and *An. dirus*, both Hainan and Yunnan are provinces with high malaria transmission, where *P. falciparum and P. vivax* malaria are epidemic throughout the year (Liu, 2014; Zhou et al., 2007).

To accelerate the process for efficient malaria prevention and control in light of the changing malaria situation in China, to ensure people's health and promote social-economic development in epidemic areas, and to position China as the leading developing country in achieving malaria elimination, the *National Malaria Control programme (NMCP) in 2006–2015* was formulated and issued by the Ministry of Health with the following goals (China, 2006):

1. By 2010, malaria will be under control in all counties, except for the border counties of Yunnan and the mountainous counties of central and southern part of Hainan, and 70% of the counties will have achieved basic elimination of malaria.
2. By 2015, malaria will be under control in the border counties of Yunnan and in mountainous counties of central and southern part of Hainan, while the other previously epidemic counties will have achieved basic elimination of malaria, and Hainan province will have eliminated falciparum malaria.

Through implementing the NMCP from 2006 to 2015, the central and local governments have increased support of and investments in malaria control, causing the rising in the number endemic counties to be effectively controlled. By 2009, the number of malaria patients dropped to about 14,000; the incidence in more than 95% of the counties dropped to below 1 per 10,000. To further protect the health of China's population, promote

coordinated development of the economy and society, and respond to the Millennium Development Goals on the eradication of malaria globally, the Chinese Ministry of Health, together with the other 12 central governmental sectors, jointly issued the *Chinese Malaria Elimination Action Plan (2010–2020)* that was a sign of launching the National Malaria Elimination Programme (NMEP) in P.R. China (China, 2010). Based on the malaria situation reported in 2006–2008, all the counties of P.R. China were divided into the following four types:

Type 1: There were local malaria infections during those 3 years, and the incidence rate of each year was greater than or equal to 1 per 10,000.

Type 2: There were local infections during those 3 years, and the incidence rate was less than 1 per 10,000 for at least a year.

Type 3: No local infection was reported in three consecutive years.

Type 4: Nonendemic area of malaria.

The following goals were set for the different types of malaria transmission:

1. All Type 3 counties are to achieve malaria elimination by 2015.
2. All Type 2 counties and Yunnan Type 1 counties located outside the border area are to achieve no local malaria infection by 2015 and attain elimination by 2018.
3. Type 1 counties in the border region of Yunnan should have their malaria incidence drop to below 1 per 10,000 by 2015, achieve no local malaria infection by 2017, and attain elimination by 2020.

According to the *Chinese Malaria Elimination Action Plan (2010–2020)*, there were 10 Type 1 counties and 8 Type 2 counties in Hainan province and 19 Type 1 counties, 55 Type 2 counties and 55 Type 3 counties in Yunnan province. In 2012, after nearly 3 years of implementation, there was no local malaria infection for 1 year, no local *P. falciparum* malaria infection for 3 consecutive years, and only 13 imported malaria cases were reported that year in Hainan province. On the other hand, Yunnan province reported 853 malaria cases, but with only 133 indigenous cases that were distributed in 20 counties, and the county incidence rates were lower than 1 per 10,000 in 2012 (Xia et al., 2013).

Because both Hainan and Yunnan are the most serious provinces for malaria transmission in P.R. China before launching the NMEP, their progress in elimination has a significant impact on the overall malaria situation of the country. Therefore, this paper aims to analyse the changing characteristics of *P. falciparum* and *P. vivax* malaria transmission in both provinces, review the successful experiences of malaria control, and identify the risks and challenges for the future. Distillation of such knowledge will not only benefit further malaria elimination in these two provinces but also the whole country.

2. BACKGROUND OF TWO PROVINCES

2.1 Geography, population and health system

Hainan Island, the southernmost province of China, is located at north latitude 18°10′–20°10′ and east longitude 108°37′–111°03′. The region has an area of 33,900 square kilometres with 20 counties and a population of 8.87 million in 2012. The province is characterized by mountains, hills, plateaus and plains. The tropical monsoon and marine climates jointly produce a generally warm temperature, with an annual temperature change of less than 15 °C (59 °F) and rich rainfall of average annual precipitation between 1500 mm and 2000 mm (Wen et al., 2011; Xiao et al., 2010, 2012). Owing to its tropical climate, Hainan's economy is predominantly agricultural, and the island is cultivated extensively with paddy rice, coconuts, palm oil, sisal, tropical fruits, black pepper, coffee, tea and rubber trees. Hainan's health system is composed of hospitals, centres for disease control and prevention, and blood collection centres at different levels. These health and medical institutions play a huge part in malaria control, both historically as well as currently. In Hainan province, the counties are directly under the jurisdiction of provincial authority without a prefecture level. Unlike Yunnan province, almost all the counties are in close proximity with each other and can be reached by car within 3 h from the provincial capital of Hainan.

Yunnan province is located in southwestern China, it includes 129 counties and borders Myanmar, Lao People's Democratic Republic (Lao PDR) and Vietnam, spanning approximately 394,000 square kilometres, with a population of 46.59 million in 2012. It has similar monsoon climates as Hainan province and lowland tropical rain forest vegetation. Temperatures regularly exceed 30 °C (86 °F) in the warmer half of the year in most areas and average annual rainfall ranges from 600 mm to 2300 mm. Yunnan is one of China's relatively underdeveloped provinces with more poverty-stricken counties than the other provinces (Bi & Tong, 2014). However, due to its special geographical location, the province has comparative advantages in exporting agricultural and mineral resources (Feng et al., 2012; Hao et al., 2013; Meng et al., 2010). Health systems, including hospitals, centres for disease control and prevention as well as blood collection centres in Yunnan province at all levels play a key role in dealing with all types of public health threats, including malaria. At the provincial level, the Yunnan Provincial Institute of Parasitic Diseases is responsible for malaria control in the whole province.

2.2 Natural factors for malaria transmission

Hainan province, located in the tropics, has been one of the main malaria transmission areas in P.R. China. Its climate and environment are within the suitable range for the breeding of *An. dirus* and *An. minimus*. Geographically, malaria cases in Hainan province were mainly distributed in patches in the southwest region of the island, while fewer cases were sparsely distributed in the northeast area. Such distributions are largely related to the natural environment of the different counties. The temperature is hotter and the humidity of the mountainous areas is higher in the southwest than in the northeast, making the southwest region more suitable for the growth of anopheline mosquitoes and the transmission of malaria (Wang et al., 2012a; Wang and Cai, 1996).

Yunnan borders Myanmar, Lao PDR and Vietnam, which are highly endemic for malaria. Influenced by the Indian Ocean, the Pacific monsoon climate and its special landforms, Yunnan is well suited for malaria transmission under various climates and special human landscapes (Yang, 2001; Yang et al., 1988). Due to a complex interplay of all these factors, Yunnan has become the most endemic province for malaria in P.R. China, rendering it the most difficult for malaria control in the country. Geographically, complicated malaria distribution and numerous *Anopheles* species are the characteristics of malaria epidemiology in Yunnan province. In the high-risk border area, where the number of malaria cases is largely dependent on climatic conditions, including temperature, relative humidity and rainfall (Bi et al., 2013), the main vector is *An. minimus*. While in the rice-growing area, *An. sinensis* is the main vector; in the high-altitude mountains of the northwest, it is *An. kunmingensis*; and in the valley areas of the northeast, it is *An. anthropophagus* (Dong, 2000).

2.3 Social-economic factors for malaria transmission

In Hainan province, some scholars have found that the culture, malaria knowledge and health organisation conditions at the grassroots level of Li and Miao minorities in high malaria-endemic mountainous areas had a positive effect on local malaria control. Health care service was the main social factor, and carrying out health education and improving the capacities of grassroots health organization in malaria diagnosis and treatment were the critical elements for effective malaria control (Cai et al., 1995; Chen et al., 1995, 1996).

On the other hand, studies in Yunnan province have demonstrated that the main factors for local malaria transmission were mountainous lodging,

usage of mosquito nets, house structure, and per capita income of local people (Chen et al., 1998).

2.4 Behavioral factors for malaria transmission

Rubber planting is the main source of family income for Hainan middle-west residents; by having to go to the mountains for such work, they stand a greater chance of contracting malaria. Other studies in Nan-qiao Township of Wan-ning County showed that mountain lodging was the main source of malaria infections, especially *P. falciparum* malaria, and infections from the mountains were highly common in Hainan province (Cai and Weng, 2013). Workers in the mountains had to engage in labour-intensive jobs, lived in dilapidated conditions near anopheline mosquito breeding sites, and lacked access to mosquito nets and health care, making them a high-risk population to be targeted in the NMCP in Hainan (Wu et al., 1995).

In border and minority areas of Yunnan province, residents have relatively low educational levels, special living habits, and frequent movement across the border. The border minority populations lag behind in awareness for malaria, with a lower proportion of people seeking diagnosis within 48 h of fever or using of insecticide-treated mosquito nets, making them the main targeted group for local malaria control (Chen et al., 1998; Cheng et al., 1997).

3. MALARIA TRANSMISSION PATTERNS, PARTICULARLY IN 2004–2012

The epidemiological data of malaria reported through the web-based case reporting system and annual malaria statistics reporting system from 2004 to 2012 were collected and analysed with the following main results.

3.1 Overview of malaria prevalence

An average of 26,674 malaria cases per year were reported nationwide in 2004–2012 (excluding Hong Kong, Macau and Taiwan). From 2004 to 2006, malaria cases increased, with about 38,000 cases each in 2004 and 2005 and around 60,000 cases in 2006. From 2007 to 2012, malaria was effectively controlled in the country, as the reported number of cases and incidence rate declined at an average annual rate of 40.7% and 40.0%, respectively.

Hainan province reported an annual average of 2650 malaria cases in 2004–2012, and its yearly contribution to the total number of cases nationally has declined to 0.4% in 2012, when only 13 cases were reported.

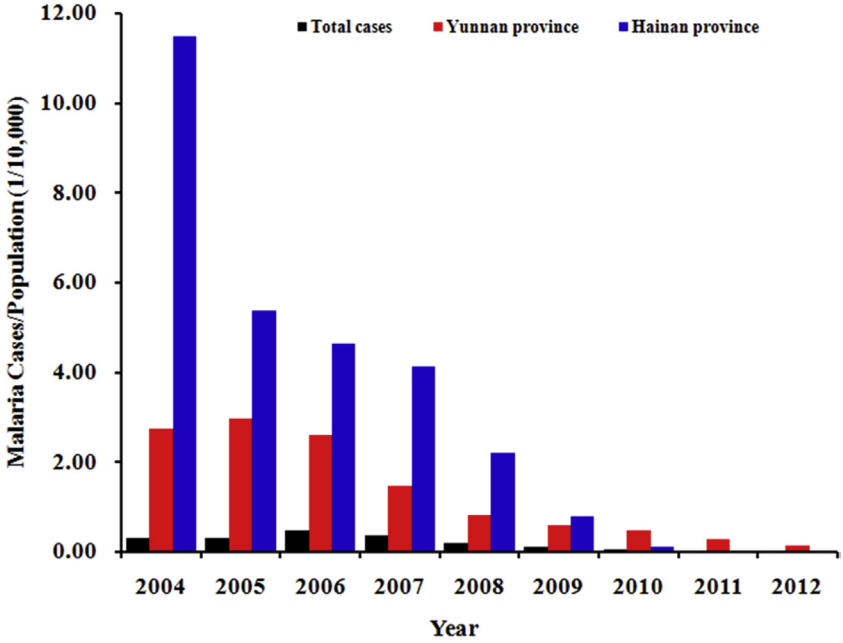

Figure 3.1 Reported malaria cases per population in 2004–2012 of Yunnan, Hainan and nationwide.

Yunnan province reported an annual average of 5984 malaria cases in 2004–2012. The yearly number of cases has been on the decline since 2005. The lowest proportion of malaria infections, accounting for 13.9% of the total number of cases nationwide in 2008, and has since risen to 25.5% in 2012, when a total of 635 cases were reported (Figure 3.1).

3.2 Cases by *Plasmodium* species

In Hainan province, a total of 12,225 (51.3%) *P. vivax* malaria cases, 2061 (8.6%) *P. falciparum* malaria cases and 9567 (40.1%) unclassified malaria cases were reported from 2004 to 2012. The *P. vivax, P. falciparum* and unclassified malaria cases declined each year, with average annual rates of 53.3%, 14.3% and 24.9%, respectively. Unfortunately, the proportion of *P. falciparum* malaria saw an increase since 2009. In 2012, the proportion of *P. vivax* and *P. falciparum* malaria stood at 30.0% and 70.0%, respectively.

In the same period, a total of 39,471 (73.3%) *P. vivax* malaria cases, 10,987 (20.4%) *P. falciparum* malaria cases and 3402 (6.3%) unclassified malaria cases were reported, including 108 malaria deaths, in Yunnan province. The *P. vivax, P. falciparum* and unclassified malaria cases declined, with average annual rates of 28.6%, 25.7% and 34.3%, respectively. In 2012, the *P. vivax,*

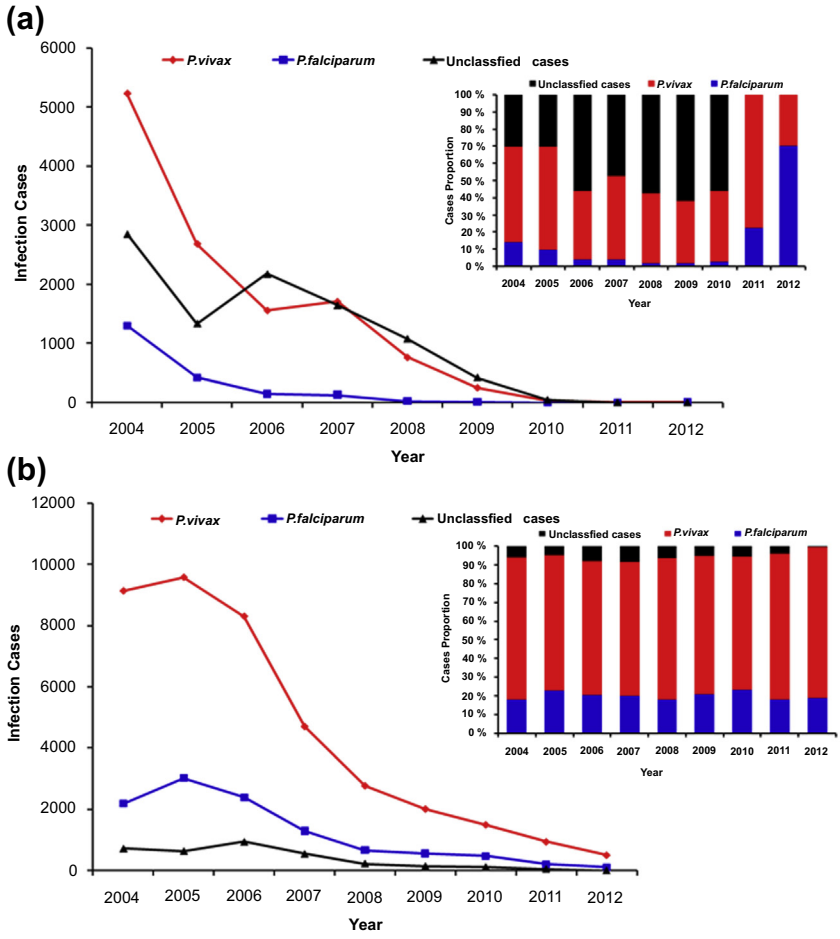

Figure 3.2 Reported malaria cases in 2004–2012 of Hainan (a) and Yunnan (b) provinces by *plasmodium* species.

P. falciparum and unclassified malaria cases accounted for 80.6%, 19.1% and 0.3%, respectively. The highest numbers of total cases, *P. vivax* cases and *P. falciparum* malaria cases from this province were all reported in 2005, accounting for 33.1%, 31.3% and 80.7% of the national figures, respectively (Figure 3.2).

3.3 Spatiotemporal distribution

Geographically, the reported *P. vivax* malaria cases in Hainan province were mainly distributed in the counties of Qiong-zhong (14.9%), Dong-fang (13.8%), Bai-sha (12.4%), Le-dong (11.9%) and Wan-ning (10.2%). The *P. falciparum* malaria cases were mainly found in counties of Dong-fang (29.1%), San-ya (21.6%), Le-dong (15.1%), Ling-shui (8.2%) and Bai-sha (6.3%).

In Yunnan province, the reported *P. vivax* malaria cases were mainly distributed in the prefectures of Bao-shan (29.3%), De-hong (26.2%), Lin-cang (8.2%), Hong-he (7.6%) and Pu-er (7.0%). The *P. falciparum* malaria cases were mainly reported from the prefectures of De-hong (55.7%), Bao-shan (41.2%), Lin-cang (6.6%), Pu-er (5.5%) and Hong-he (4.5%).

Both the geographical distribution and numbers of *P. vivax* and *P. falciparum* malaria cases reported in Hainan and Yunnan provinces have shrunk, but this phenomenon was more significant in Hainan province. There are still many reported malaria cases in areas of Yunnan province, particularly those areas of bordering other malaria endemic countries, such as Myanmar (Figure 3.3 and Figure 3.4).

With regard to seasonal distribution, the reported *P. vivax* and *P. falciparum* malaria cases in Hainan province occurred mainly from May to September, accounting for 48.2% and 61.9%, respectively, of all cases in a year. The cases peaked in August, when the reported numbers of the two species were 13.9% and 14.7%, respectively. These seasonal characteristics of malaria distribution were more obvious from 2004 to 2007 and less evident recently as malaria transmissions were reduced to a very low level and most cases were imported.

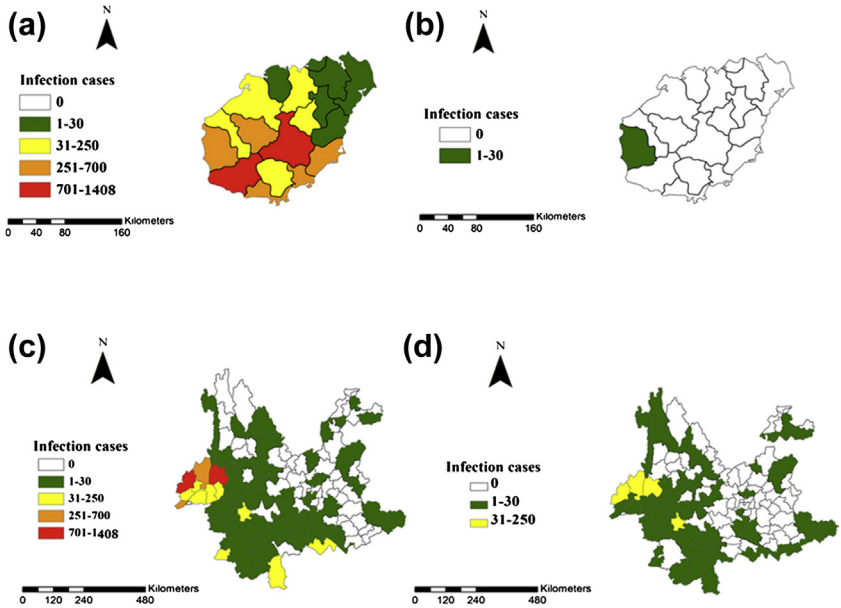

Figure 3.3 Geographical distribution of reported *P. vivax* malaria cases in Hainan province in 2004 (a) and 2012 (b) and Yunnan province in 2004 (c) and 2012 (d), classified by the number of malaria cases in each county.

In Yunnan province, the reported *P. vivax* and *P. falciparum* malaria cases occurred mainly in April to August. The top-five months for *P. vivax* malaria occurrence were June (13.0%), July (12.5%), May (12.3%), August (11.1%) and September (9.1%). For *P. falciparum* malaria cases, these months were May (16.2%), June (14.7%), April (11.2%), July (10.2%) and November (8.5%). Likewise, the seasonal characteristics were also less evident recently in this province (Figure 3.5).

3.4 Demographical characteristics

Among *P. vivax* malaria cases reported from Hainan province between 2004 and 2012, a total of 761 (6.2%) cases were in the age group of <10 years, 7985 (65.3%) cases were in the 10- to 34-year group, 3207 (26.2%) cases were reported for 35–60 years, and 272 (2.2%) cases were for >60 years. In particular, the number of young and middle-aged patients was 3.6 times higher than older patients. Similarly, the number of male patients was 3.4 times higher than that of the females. For *P. falciparum* infections, 178 (8.6%) cases were in the age group of <10 years, 1361 (66.0%) cases were for 10–34 years, 484 (23.5%) cases for 35–60 years, and 38 (1.8%) cases for >60 years. In particular, the number of young and middle-aged

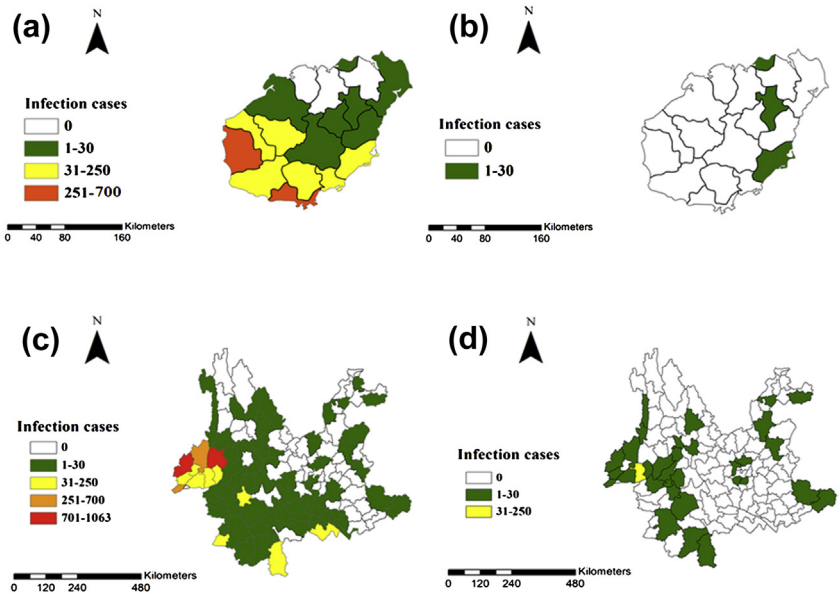

Figure 3.4 Geographical distribution of reported *P. falciparum* malaria cases in Hainan province in 2004 (a) and 2012 (b) and Yunnan province in 2004 (c) and 2012 (d), classified by the number of malaria cases in each county.

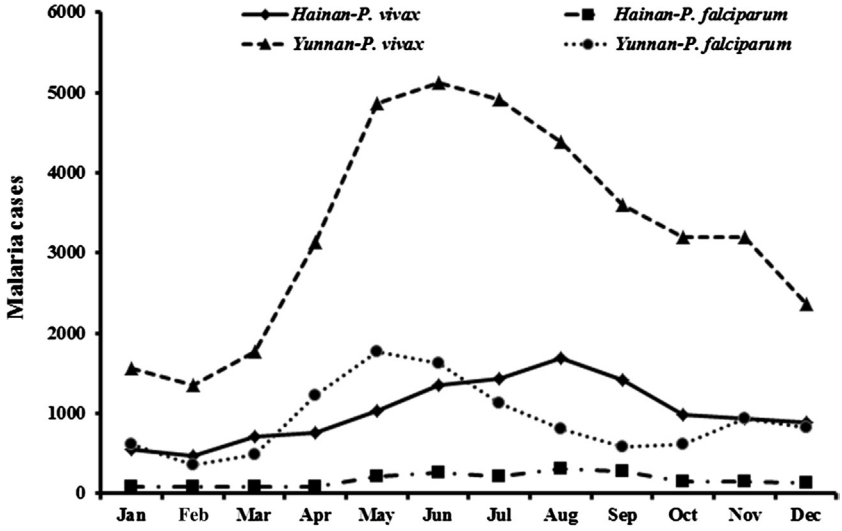

Figure 3.5 The patterns of the number of the reported *P. vivax and P. falciparum* malaria cases in 2004–2012 of Hainan and Yunnan provinces by month.

patients was 3.7 times higher than that of older patients, and the number of male patients was 3.3 times higher than that of the females.

For *P. vivax* malaria cases in Yunnan province, a total of 3080 (7.8%) cases were reported in the age group of <10 years, 26,968 (68.3%) cases in 10–34 years, 8786 (22.3%) cases in 35–60 years, and 637 (1.6%) cases in >60 years. The number of young and middle-aged patients was 3.7 times higher than that of older patients. The number of male patients was also 3.4 times higher than that of female patients. With regards to *P. falciparum* infections, 662 (6.0%) cases were in the age group of <10 years, 7595 (69.1%) cases in 10–34 years, 2594 (23.6%) cases in 35–60 years, and 136 (1.2%) cases in >60 years. The number of young and middle-aged patients was 5.0 times higher than that of older patients. The number of male patients with *P. falciparum* malaria was 4.5 times higher than that in the females (Figure 3.6).

Stratification of *P. vivax* malaria cases in Hainan province from 2004 to 2012 according to occupation revealed that infections occurred mainly in farmers (53.1%), followed by migrant peasant labourers (14.4%), students (12.0%) and workers (11.5%). *P. falciparum* malaria cases were also mainly distributed in farmers (54.5%), followed by students (13.8%), migrant peasant labourers (12.1%) and workers (8.6%).

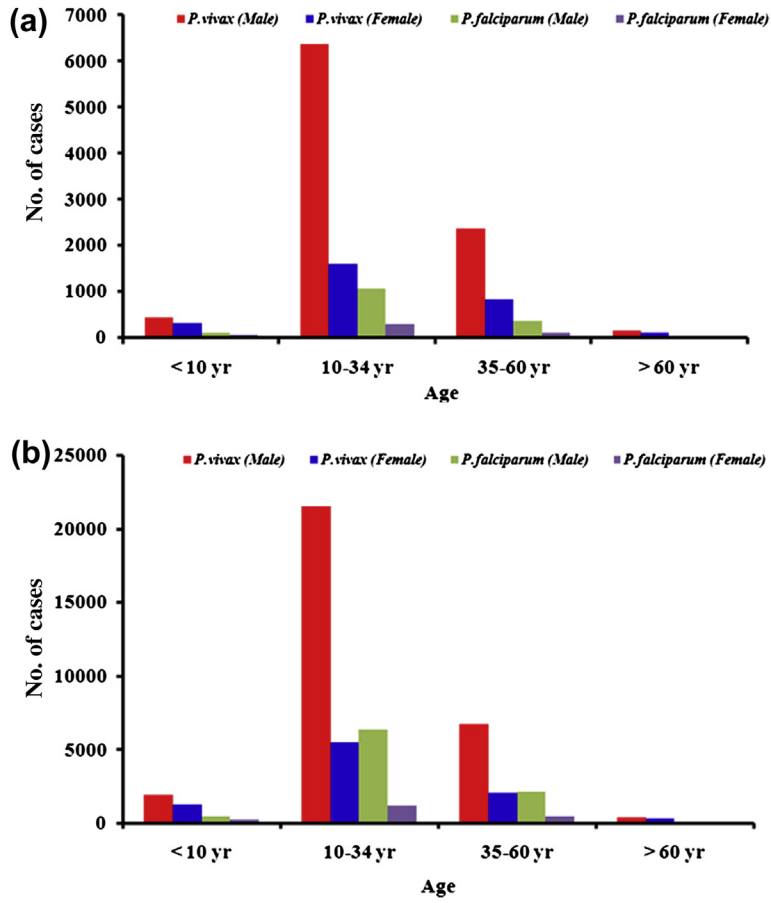

Figure 3.6 The number of the reported *P. vivax and P. falciparum* malaria cases in 2004–2012 of Hainan (a) and Yunnan (b) provinces by age group and gender.

In Yunnan province, *P. vivax* malaria cases were highly prevalent in farmers (53.6%), followed by migrant peasant labourers (23.8%), students (8.2%) and workers (3.3%). A similar distribution was observed for *P. falciparum* malaria cases in farmers (54.7%), migrant peasant labourers (26.1%), students (5.6%), and workers (3.6%).

3.5 Cases by acquisition

From 2004 to 2012, a total of 12,210 (99.9%) indigenous and 15 (0.1%) imported *P. vivax* malaria cases were reported in Hainan province. The imported *P. vivax* cases were from Cambodia (5 cases), Myanmar (3 cases),

Pakistan (4 cases) and Indonesia (3 cases). For *P. falciparum* malaria, there were 2046 (99.3%) indigenous cases and 15 (0.7%) imported cases, including 10 cases from Africa, 3 cases from southeast Asia and 2 cases with unclear sources information. There has been no local transmission of *P. falciparum* malaria since 2010 and no local malaria transmission since 2012. Most current cases were imported and only sporadic cases occurred recently in this province (Figure 3.7).

In Yunnan province, a total of 27,411 (69.5%) indigenous and 12,060 (30.6%) imported *P. vivax* malaria cases were reported; the imported cases were mainly from Myanmar (6832 cases, 56.7%). For *P. falciparum* malaria,

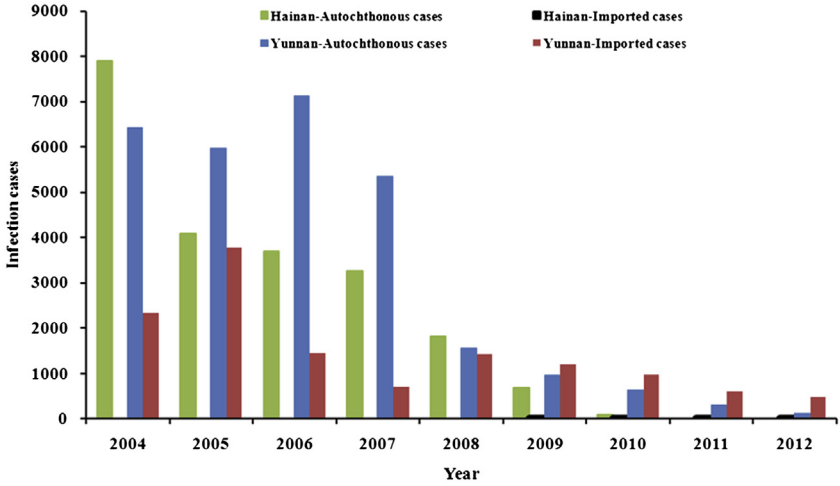

Figure 3.7 The number of the reported *P. vivax* malaria cases in 2004–2012 of Hainan and Yunnan provinces by acquisition.

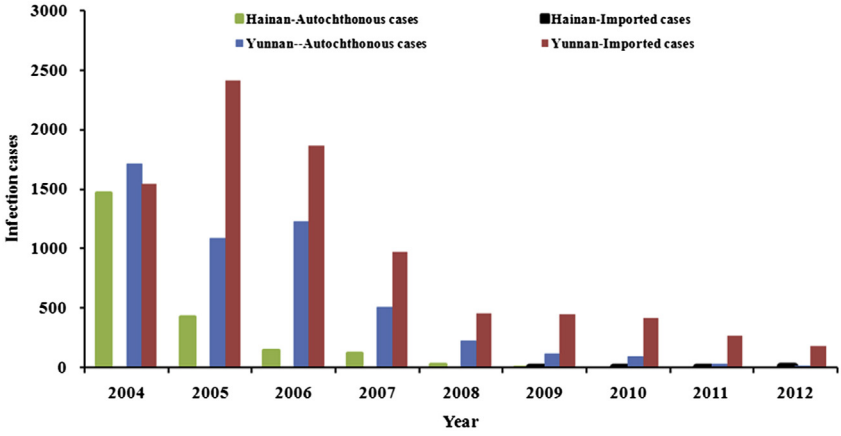

Figure 3.8 The number of the reported *P. falciparum* malaria cases in 2004–2012 of Hainan and Yunnan provinces by acquisition.

there were 5018 (45.7%) indigenous cases and 5969 (54.3%) imported cases; 79.2% of the imported cases were from Africa, including Nigeria (12.3%) and the Republic of Congo (12.3%). The highest proportion (77.7%) of indigenous malaria cases occurred in 2007, and then an increasing proportion of the imported malaria was observed (Figure 3.8). In contrast, a total of 679 imported malaria cases were reported in 2012, accounting for 79.6% of the total number of cases.

4. HISTORY OF MALARIA CONTROL

The history of malaria control in Hainan province can be divided into five stages in the past 60 years (Tang et al., 2012a; Wang, 2000). The first was the stage of investigation and pilot control in 1951–1958, when epidemiological investigations and key control trials were carried out by the National Malaria Research Station and Hainan Malaria Control Dispensary. The second stage in 1959–1966 consisted of comprehensive control, exterminating *An. minimus* and reducing the prevalence of malaria cases. As large-scale malaria campaigns were performed in this stage, using mass chemoprophylaxis and comprehensive insecticide spraying integrated with environmental improvement to control the vectors of *Anopheles* spp., *An. minimus* was basically wiped out by 1964 and a dramatic decline of malaria incidence rate was observed in Hainan Island. Although some success was achieved, this strategy was still slow to proceed as high-quality performance was needed, and the sustainability of such a strategy proved to be difficult.

The third stage, conducted in 1967–1983, relied mainly on vector control and highlighted the containment of chloroquine-resistant *P. falciparum*. The main countermeasures were to strengthen control and research of chloroquine-resistant *P. falciparum*, control infectious sources with mass or targeted drug administration, control vectors with insecticidal nets, and carry out blood tests in fever patients to detect and treat malaria cases. The fourth stage was a point-to-area, joint and comprehensive control stage in 1984–2000. The strategies were to intensify the regular malaria management, keep the former effective interventions, consolidate and enlarge the joint efforts in control of malaria, adopt mass or targeted drug administration to control infectious sources in the high endemic areas, control vectors with insecticidal nets, identify malaria with microscopy and treat febrile patients, carry out malaria surveillance and control among uphill and external mobile populations, establish integrated malaria control trials, and remove the focal zones of malaria.

The fifth stage was carried out in 2001–2012, with further reduced malaria incidence rates; infectious source control was the dominant

intervention. The main strategies were to carry out comprehensive and regular malaria management, fulfil blood tests among febrile patients, discover and treat malaria infections and foci in a timely manner, strengthen mobile population management, and implement surveillance on parasitaemia rate in population, antimalarial drug resistance and mosquito vectors. After strong efforts for more than half a century, remarkable achievements have been obtained in Hainan. Annual morbidity of malaria decreased continuously and endemic areas shrunk substantially, such that no high- or super-risk areas exist. Currently, malaria infections are only confined to remote forest zones in some counties of south-central Hainan. The annual incidence of malaria has fallen from 9890.21 per 100,000 in 1995 to 0.11 per 100,000 in 2012, and no malaria deaths were found in eight consecutive years since 2005 (Du, 2001; Huang et al., 2010; Liu et al., 2012; Zeng et al., 2013).

The history of malaria control in Yunnan province can be illustrated in four stages (Li and Wu, 2009; Tang et al., 2012b; Yang, 1995). The first stage in the 1950s was to establish a control system. Prevention teams were orgnized to mobilize the communities to participate in control of malaria and vectors, the malaria control institutions was established to carried out malaria control trials and to explore experiences and methods for control in large areas. The second stage in 1960–1979 was performed to control malaria incidence and decrease malaria mortality with mass preventions and treatments. This included comprehensive and equally important interventions of infectious source control and vector extermination, delivering treatment and antirelapse treatment of malaria patients, and conducting mass chemoprophylaxis in the transmission seasons of endemic areas.

The third stage in 1980–1999 saw the implementation of integrated measurements. Emphasis was placed on prevention of key areas and protection of key populations, highlighting the surveillance of infectious sources and vectors, carrying out blood tests in febrile patients with a testing rate of no less than 5% at the county level and a coverage rate of more than 80% at the village level, identifying and treating malaria patients, eliminating the focal zone, intensifying the management of mobile populations to prevent the import and spread of infectious sources, and establishing vector surveillance sites. The fourth stage in 2000–2012 was conducted to consolidate the achievements of malaria control and improve the surveillance in border areas. It focused on mobile populations and mountainous residents, who were targeted according to the malaria situation and vector distribution in different periods and areas. Integrated strategies of infectious source managements and vector control were applied to further decrease malaria cases and deaths

and shrink malaria endemic areas, especially *P. falciparum* malaria, and malaria surveillance and the treatment disposal of imported case were strengthened.

5. MALARIA INTERVENTIONS FROM CONTROL TO ELIMINATION

5.1 Case detection

Blood testing in febrile patients as part of malaria surveillance is the most effective method for the detection of malaria cases. There are some differences in the blood testing procedures from the two provinces. In Hainan province, the malaria microscopy centre in each county's Center for Disease Control and Prevention (CDC) and the malaria microscopy station in each township hospital provided blood test for *Plasmodium* spp. for suspected outpatients with fever. Health workers in villages and farms in malaria endemic areas sampled blood from febrile patients and sent them to health facilities at a higher level at regular intervals for *Plasmodium* detection (Huang et al., 2010; Wang et al., 2003). From 2002 to 2012, a total of 17,32,823 blood tests were done in the province, resulting in a testing rate of 10.2%. A total of 17,522 persons were confirmed with malaria infections, with a positive rate of 0.8%.

In Yunnan province, blood testing was carried out in all medical organizations capable of conducting malaria microscopic examinations, and rapid diagnostic tests (RDTs) for *Plasmodium* antigen detection were used in some qualified medical organizations or village clinics. Active case investigations were done by county CDCs in the transmission seasons in areas including administrative villages with a malaria morbidity of more than 20 per 10,000, and natural villages reporting indigenous cases where no local infections appeared in the past 3 years. Household investigations were used to understand the local malaria situation, and patients with fever or with a history of fever in the past 2 weeks were registered and blood tests were performed on them. From 2002 to 2012, a total of 59,45,383 blood tests were conducted, leading to a testing rate of 1.7%. A total of 74,763 malaria patients were subsequently confirmed, with a positive rate of 1.3% (Figure 3.9).

5.2 Antimalarial drug administration

The first choice of treatment for *P. vivax* malaria infection is chloroquine phosphate (0.6 g single dose for the first day, 0.3 g daily for the next 2 days, total 1.2 g/3 days) combined with primaquine phosphate (22.5 mg single dose/day for 8 days, total 180 mg/8 days) tablets, and antirelapse treatment using primaquine (180 mg, divided into eight doses, one dose daily) given during the nontransmission season for reducing malaria reservoirs entering into the

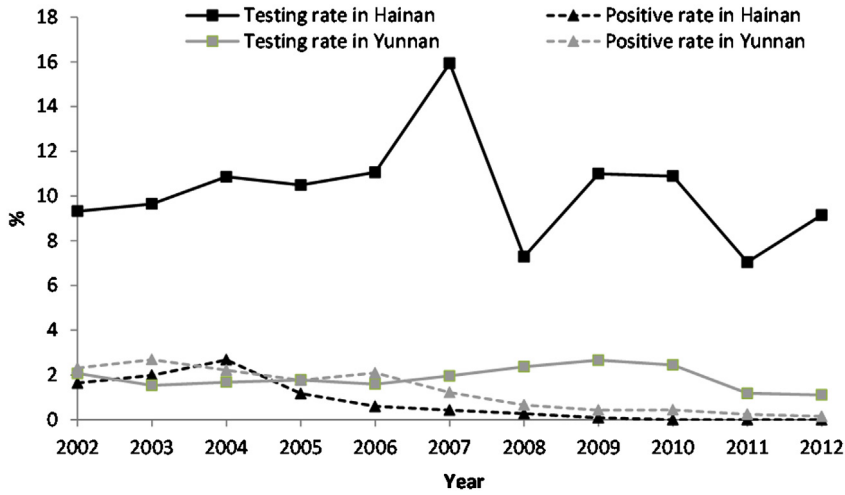

Figure 3.9 Annual blood testing rate in febrile patients and their positive rate in 2002–2012 of Hainan and Yunnan provinces.

transmission season (Chen, 2014). For *P. falciparum* malaria, artemisinin-based combination therapy (ACT) was applied for treatment of uncomplicated cases, while injectable artesunate or artemether is the first choice for severe malaria.

In addition, mass drug administration is one of the interventions in the two provinces for reducing malaria transmission. From 2002 to 2012, a total of 77,206 people in Hainan province received a dose of chloroquine plus primaquine during malaria transmission seasons; in Yunnan province, 14,50,175 doses were administered. For administration of antimalarials in nontransmission seasons, a total of 6,55,287 persons received treatment in Hainan province and 6,62,498 persons in Yunnan province were treated (Figure 3.10 and figure 3.11).

5.3 Vector control

Since the mid-1950s, indoor residual spraying (IRS) had been performed comprehensively 1–2 times per year, mainly using pesticides (dichloro-diphenyl-tricgloroethane or hexachlorocyclohexane) in the province of Hainan. After the 1970s, IRS and distribution of insecticide treated bed-net s(ITN) were focused on key areas or villages using deltamethrin. ITN was implemented once a year before the peak of malaria transmission season, where the bed nets of each natural village or residential group were collected and treated by the professional teams (Cui, 2003). After the 1990s, in order to achieve further reduction of human exposure and vectorial

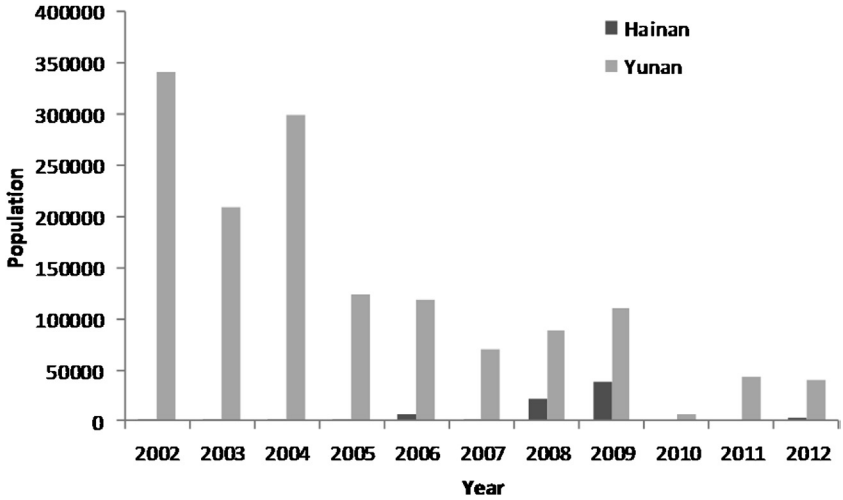

Figure 3.10 Number of chemoprophylaxis doses administered in transmission season in 2002–2012 of Hainan and Yunnan provinces.

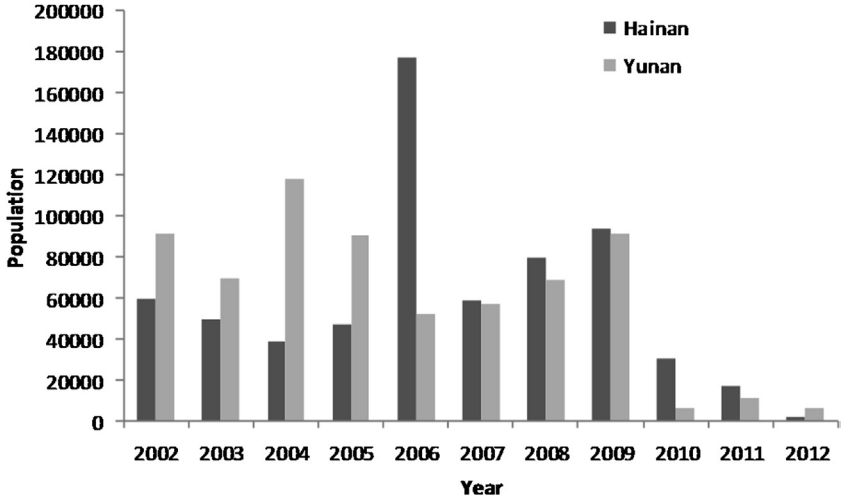

Figure 3.11 Number of patients consuming antimalarials in nontransmission season in 2002–2012 of Hainan and Yunnan provinces.

capacity, the use of bed nets was strengthened through free distribution integrated with health education for residents. From 2002 to 2008, Hainan province distributed 5,68,936 INTs, protecting a population of 9,96,246. In addition, IRS on a total area of 36,64,083 m^2 was performed, protecting a population of 1,72,828 (Cai and Weng, 2013).

In Yunnan province, IRS was performed 1–2 times at three-monthly intervals in the transmission season using pyrethroid and organophosphate insecticides; their continuous use was limited to no more than 3 years. The first round of IRS was 1 month ahead of the local peak of the transmission season, and the second round was decided based on the locality during the malaria-transmission season. In 2002–2010, a total of 1,68,03,115 and 33,89,998 people were protected by IRS and ITNs, respectively, in the province of Yunnan.

In both Yunnan and Hainan provinces, the Patriotic Health Campaign was combined with the New Rural Communities Construction, where targeted environmental improvements were conducted. Action items included the removal of stagnant water, clearance of ditches, intermittent irrigation, and other measures. Campaigns were used to promote improved indoor ventilation conditions and to change outdoor sleeping habits. Where possible, fish and other biological agents were also used in rice fields, ditches, ponds, and other major water bodies to control the breeding of mosquito larvae (Yang, 2001).

5.4 Pilot studies

In 1991, Hainan translated the successful experience of malaria control in the pilot Mao-yang Township of Wu-zhi-shan County to another 10 townships, each selected from 10 high malaria endemic counties. Besides the increase in equipment and investments such as manpower, materials and financial resources, Hainan formulated unified plans for malaria control and programme management and adopted integrated interventions, such as improving grass-roots health organizations and strengthening control efforts. Through 20 consecutive years of operation, promising results were obtained, providing experience for malaria control in high transmission areas, especially against *P. falciparum* malaria in tropical forest areas (Wang et al., 2012b). In the years of 1995–1997, Hainan started another pilot programme in Nan-qiao Township of Wan-ning County. A strategy of controlling the source of infection combined with health education was adopted. The villages and populations at high risk for malaria were targeted; interventions on health education and behavioural changes were performed in those high-risk villages as well as middle and primary schools to improve local knowledge on malaria transmission and self-protection methods. Mass chemoprophylaxis was also administered to residents living in high-risk villages and mountainous lodging, and the treatment of each malaria patient was monitored. Finally, this pilot study achieved the desired effect and provided new experiences for further malaria control in the Hainan mountains (Chen et al., 1996; Chen et al., 1999b). All of these positive pilot experiences solidified

the evidence base for effective design and implementation of malaria control strategies and interventions (Hu et al., 2013).

Yunnan also actively explored alternative strategies in malaria control through pilot studies. Malaria prevalence and economic development in Cang-yuan county, which borders Myanmar, were directly affected by malaria epidemics occurring in the border regions of Myanmar. To reduce malaria transmission from the original source, a protection zone on the border was established. Under the support of the Chinese Ministry of Health and the UK Health Unlimited, the pilot project of *Joint Malaria Control on the China–Myanmar Border* was officially launched in 2007 in Cang-yuan county of Yunnan province and six townships of Meng-mao county, as well as Bang-kang and Nan-deng under Wa State in Myanmar, to explore a novel mode of joint malaria control in border areas. Gradually, this mode was expanded to 25 border counties of Yunnan province, and the mechanism was eventually established for joint malaria control on the China-Myanmar border with an aim to reduce malaria morbidity and mortality, which included technical cooperation, information exchange, bilateral training, health education, sharing epidemic information, and providing nets for people in the border areas (Chen et al., 2011; Tang, 1999b).

5.5 Partnership

Hainan has cooperated with relevant research institutes and universities nationwide to carry out a number of malaria studies, due to access to ministerial and provincial awards. In 1990s, Hainan also received funds from the Special Programme for Research & Training in Tropical Diseases (TDR), World Health Organisation (WHO) for health system strengthening and Japan's National Institute of Environmental Sciences. Dozens of domestic and foreign experts and scholars visited Hainan for collaborative research and local malaria control, thus accelerating the process of malaria control in this province. From 2003 to 2012, Hainan conducted three rounds of malaria programmes supported by the Global Fund to Fight AIDS, Tuberculosis and Malaria (GFATM), effectively complementing the local malaria control efforts (Yang et al., 2012).

From 2003 to 2013, Yunnan conducted five rounds of malaria programmes supported by the GFATM. Yunnan province strengthened malaria control in the border region in 2004 and 2005 with support from WHO in six counties, namely Yan-jin, Xin-ping, Yuan-jiang, Hong-he, Yuan-yang and Mo-Jiang, where malaria incidence was high, through provision of standardized malaria management, equipment, antimalarial drugs, health education,

technical training and the establishment of a malaria information platform. These activities improved local capacity in malaria control, health education and information delivery. In 2010, Yunnan carried out a WHO-supported malaria control programme to roll back malaria in four counties of Xi-meng, Rui-li, Teng-chong and Cang-yuan. This generated a great breakthrough in malaria control programme management and facilitated the exchange of epidemic information in cross-border regions (Tang et al., 2012b).

5.6 Surveillance

Malaria surveillance is an important component of malaria control and eventual elimination. According to the *National Malaria Surveillance Scheme in 2005–2010* and the *National Surveillance Scheme for Malaria Elimination* in P.R. China, both Hainan and Yunnan provinces set up sentinel sites based on the geographical distribution of malaria incidence and vectors. In 2005–2010, malaria surveillance for the control phase was implemented. Subsequently, malaria surveillance for the elimination phase was initiated. In the control phase, the main purposes of surveillance were to understand the epidemic situation and its influencing factors, master the epidemic patterns and trends, and provide a scientific basis for effective development and evaluation of strategies for malaria control. In the elimination stage, the main purposes of surveillance are to detect malaria cases as well as possible transmission and its influencing factors in a timely manner, assess the control effects and potential risks of malaria transmission, and provide reference and basis for the malaria elimination programme.

Results from the Malaria Information System in 2013 showed that the key indicators for the implementation of the NMEP all reached 100% in Hainan province, including the case reporting rate within 1 day after diagnosis, the case laboratory testing rate, the case laboratory-confirmed rate, the epidemiological case investigation rate within 3 days after diagnosis, and malaria foci clear-up rate within 7 days after case diagnosis. In Yunnan province, only the epidemiological case investigation rate within 3 days after diagnosis was lower than 88%, while all other indicators were above 90%.

6. CHALLENGES FOR MALARIA ELIMINATION

6.1 Challenges in Hainan province

6.1.1 Management of the mobile population

Since reforms on the national economic systems in 1988, malaria control among the mobile population became the focal efforts in Hainan province.

Years of comprehensive malaria prevention and control measures for the Hainan mobile population have achieved good results, as seen through the yearly decline of malaria incidence. Studies have shown that the positive rate of blood tests among the migrant population presenting with fever was higher than not only that of nonmigrant febrile patients, but also the overall positive rate of the province. This suggests that malaria control in Hainan should still have a strong emphasis on the mobile population and efforts should not be reduced in intesity. Malaria control of the mobile population is crucial to prevent the spread of malaria epidemics, develop effective strategies and consolidate antimalarial achievements (Cai, 2002; Lin et al., 2009; Wang et al., 1996). Most mobile populations are from nonimmune communities in nonmalaria endemic areas, have big movement radiuses and relatively weak awareness of self-protection against infectious diseases, and are engaged in agricultural activity in remote and originally high malaria endemic areas, where it is difficult to obtain an early diagnosis and appropriate treatment. All of these factors have brought about a series of difficulties and challenges for successful malaria control and elimination. Therefore, the strengthening of malaria management of the migrant population, especially in the originally high malaria endemic areas of central and southern Hainan, remains the focus for malaria elimination at present and in the future. Consolidation of achievements relating to decades of malaria control in the province might provide new insights on how to solve current challenges (Xu et al., 2007).

6.1.2 Prevention of malaria reintroduction

Hainan has made remarkable achievements in malaria control and elimination. To consolidate the existing achievements and prevent malaria reintroduction and resurgence, the province will adhere to comprehensive strategies of infection source management in combination with vector control and vulnerable population protection. To prevent malaria transmission and outbreaks, the strengthening of monitoring and protection of high-risk groups, including the mobile population, should be continued, and any possible malaria foci should be discovered and eliminated in a timely manner. In the spring and autumn every year, chemoprophylaxis should be provided in a targeted way to reach groups in malaria endemic areas. Routine malaria management should be enhanced through standardized, scientific and institutionalized ways. Finally, it is imperative for all levels of governments to maintain their investments in the abovementioned prevention strategies so as to sustain the malaria-free status of Hainan province (Wang et al., 2012a).

6.2 Challenges in Yunnan province

6.2.1 High malaria transmission on the China–Myanmar border

Yunnan malaria cases occur mainly in the border region, which is the highest area for the malaria transmission intensively, and the major transmission area of *P. falciparum* in P.R. China. Yunnan has 4,061 km of borderline, and malaria is heavily transmitted in the border areas close to Myanmar. High malaria prevalence in the neighbour countries, frequent movement of the border population and suitable natural settings for malaria transmission are major causes for more severe malaria in the Yunnan border areas. These areas have proved to be more difficult for control than other areas of P.R. China.

There are several specific challenges of malaria control on the China–Myanmar border (Chen et al., 1999a; Li et al., 2011; Yang, 1998; Zhou and Pongsa, 2002). First, it is very difficult to monitor and manage the frequent movement of the local people. According to records in some studies, more than 6,00,000 people cross the Yunnan border annually. With the development of a subeconomic region in Lan-cang and the Mekong River area, the number of mobile individuals and their movement radius will continue to expand. Because the parasitaemia positive rate among border migrants is significantly higher than that of local residents, such movement could result in the constant importation of malaria reservoir into P.R. China. However, there is currently no effective way to manage this population flow. Second, the existence of multiresistant *P. falciparum,* complex malaria vectors and insecticide resistance have made cross-border malaria control more difficult. Third, there is a serious shortage of funding, rendering it difficult to implement normal antimalarial activities. Fourth, there is inadequate awareness of the importance of having and maintaining teams proficient in malaria control at base level. Because malaria control and elimination involves long-term and hard work, many professionals have become weary of the difficulties and challenges ahead. This fatigue, alongside a general trend of decreased malaria burden, has caused unconscious on malaria control among professionals. Facing similar issues, other countries of the Greater Mekong subregion should definitely seek domestic support and international cooperation.

6.2.2 Heterogeneity and complexity of malaria epidemiology and vectors

Malaria control in Yunnan province is more difficult because the vectors are numerous and widely distributed, making the patterns of malaria transmission more complex. Owning to the special terrain and

complicated habitats, Yunnan is known for having a three-dimensional climate, housing more *Anopheles* species than the rest of P.R. China. In Yunnan province, the species of *An. minimus*, *An. sinesis*, *An. lesteri* (or *An. anthropophagus*), *An. kunmingensis*, *An. dirus*, *An.jeyporiensis* and *An. nigerrimus* are recognized as being naturally infected by *Plasmodium parasites*. *An. minimus* is the main malaria vector in the valley, reservoir and semi-mountainous areas at altitudes less than 1400 m, south of 27° north latitude. *An. sinesis* and *An. lesteri* are important malaria vectors in the low thermal valley around Jin-sha River, north of 27° north latitude. *An. kunmingensis* is the main malaria vector north of 24° north latitude at altitudes more than 1560 m (Gong et al., 2012). A study showed that the anopheline community on the China–Myanmar border comprises 13 species; *An. minimus* is the dominant species with a high human blood index (Yu et al., 2013). However, the distributions and malaria transmission roles of all the above-mentioned vectors across the border areas are still not clear and require further investigation.

6.2.3 Management of the mobile population

In Yunnan province, there are 12 national ports of first class, eight of second class, 90 border passageways and 103 free points for trade. None of these entry points include a natural barrier or difficult access. Every year, tens of millions of people from Yunnan or other provinces go to the border area for business, construction, mining and other activities. The large size of the mobile population brings great difficulties to malaria control and management (Li, 2006).

At present, the problems in malaria management of mobile populations are as follows. First, there is no specific organization responsible for the task on management of cross-border mobile population, resulting in unstandardized management. Basic demographic and border crossing data are not of high quality. At the same time, local populations focus mainly on economic benefits of mobility, lacking awareness of disease prevention and antimalarial knowledge. Second, rural doctors are not well remunerated, causing them to be less active in the management of mobile populations. Third, the low-quality housing common to the area and poor equipment of the medical teams have proved to be an obstacle to the management of mobile populations. In most rural hospitals, blood tests cannot be carried out. In some hospitals, even though microscopy can be carried out, professionals have limited skills with microscopic examination, so the confirmation rate of malaria is not high. All of these factors could delay the treatment of exogenous malaria, which usually results in the accumulation and spread of infectious source among the mobile

populations. The lack of awareness of imported malaria in medical staffs in township hospitals and village clinics, and the insufficient or delayed treatment provided, can result in second or even third generations of malaria cases.

Fourth, unsatisfactory effect and passive position of the overall management of mobile populations were due to insufficient campaigns as well as lack of attention paid by the government, especially to the supervision and urgency for malaria management of mobile populations, which could lead to reduced performance of health professionals. Fifth, networks of joint malaria control are not in place, causing diagnosis and treatment of some mobile patients to be delayed. In short, malaria management in migrant populations, as one of main measures for malaria control, involves complex social system engineering. It is very hard to rely solely on malaria professionals and other health personnel. Strong support from the government and full cooperation of different sectors are definitely required (Tong et al., 2007; Xiong et al., 2009).

6.2.4 Capability building at the ground level

In the stage of malaria elimination, the level of core knowledge on malaria among medical staff at the ground level will directly affect their abilities in discovering, diagnosing and treating the imported malaria cases timely and correctly. In Yunnan province, a relatively sound structure for malaria control system across different levels above the township was established, and in quite a few counties health centres responsible for medical and health care at the village level have also been established through integration of townships and villages. However, the reduced number and aging of technical personnel, increased mobility of staff to other disease areas and the lack of investment from government have led to weakness in malaria control, particularly at levels below provincial levels (Su et al., 2005; Yang, 2001). Therefore, more attention and input should be paid to capacity building at the grassroots level, not only to increase health infrastructure but also improve professional knowledge. Professional and technical trainings should be strengthened and can be performed in batches. The training content should be enriched, and the effectiveness of training must be ensured to improve the capacity of local staffs.

6.2.5 Prevention of malaria reintroduction

Remarkable achievements in malaria prevention and control have been obtained in Yunnan province with the support of domestic and international funds. The incidence of malaria decreased from 249.38 per 10,000

in 1953 to 0.138 per 10,000 in 2012. To achieve the goal of eliminating malaria in Yunnan province by 2020 according to the Chinese NMEP's goal (2010–2020), the following strategies should be further employed on the basis of consolidating previous control results. First, it is necessary to strengthen malaria control and stabilize the malaria epidemic situation in areas having local transmission or high transmission potential. Second, it is to keep malaria rates low in border areas, prevent malaria outbreaks in natural villages, and reduce malaria death cases. Third, it is to actively execute malaria surveillance and response during the postelimination stage, including strengthening of malaria management among mobile populations and treating endogenous and exogenous malaria cases in time, to prevent cases of secondary generation and the re-establishment of malaria transmission (Gao, 2011).

6.2.6 Monitoring of antimalarial drug resistance

In Yunnan province, the scope and degree of *P. falciparum* resistance to antimalarial drugs increased since the 1970s, when a chloroquine-resistant *P. falciparum* strain was found in the Meng-ding township of Geng-ma county. According to some surveys since the 1990s, *P. falciparum* in the border region has produced resistance to chloroquine, amodiaquine, piperaquine, and the sensitivity to artesunate and pyronaridine is less than that observed in the 1980s (Yang, 2001; Zhang et al., 2008a). Due to resistance or reduced sensitivity of *P. falciparum* to a variety of antimalarial drugs, patients infected with *P. falciparum* may not be well treated. Recrudescence and retransmission is an urgent issue for significant control and elimination of *P. falciparum* transmission in the border areas of Yunnan province. The resistance of *P. falciparum* to antimalarial drugs has limited the application of mass drug administration. To control and eliminate malaria effectively, medication should be targeted and combined to delay the emergence of drug resistance.

Artemisinin-based drugs, including ACT, are currently the most effective drugs against *P. falciparum* malaria and have been recommended for worldwide use by WHO. However, because of the irregular application and the cross-resistance of other drugs, the sensitivity of *P. falciparum* to artemisinin has decreased in the border areas of Thailand and Cambodia, and has been spreading to the surrounding countries, such as Vietnam and Myanmar. This has caused great concerns among international academics and disease control agencies (WHO, 2012). Although no ACT-tolerant parasite of *P. falciparum* have been found on the China–Myanmar border (Huang et al., 2012; Wang et al., 2012c), China is facing the risks of introduction

and spread of ACT-resistant strains, which will have negative influence on malaria elimination in P.R. China. Therefore, monitoring and surveillance of possible artemisinin resistance through therapeutic efficacy studies under network cooperation of the Great Mekong subregion need to be strengthened.

7. CONCLUSIONS

Owning to their unique natural geographical features, social-economic environments and culture, Hainan and Yunnan have been the provinces most suffered from malaria in P.R. China. The epidemiology of the disease was extremely variable, and different situations required distinct malaria control strategies, which have been adapted to risk groups, vector behaviours, local health infrastructure, and environmental conditions. The building of a preventive and antiepidemic infrastructure and health care system, combined with the training of personnel, have allowed the government to use techniques of mass mobilization to launch programmes of vector control and mass therapy. Provinces and counties were also organized into the regional alliances to facilitate malaria control and surveillance. There was evidence for the efficacy and cost-effectiveness of malaria interventions and a significant increase in funding from all levels of government and the GFATM (2003–2012).

Specifically, the following strategies through the national programmes have played key roles in malaria control:

1. To ensure access to early and accurate diagnosis, followed by prompt, effective and safe treatment through public and private sectors, such as providing qualified microscopy, RDTs and ACTs
2. To ensure full coverage of the population at risk with appropriate vector control measures, such as Long-lasting insecticide-treated nets and IRS
3. To strengthen malaria health education, promotion, and community mobilization efforts and change behaviour, particularly in maximizing utilization of malaria control and elimination services
4. To ensure comprehensive coverage of vulnerable, poor and marginalized populations at high risk for malaria with appropriate malaria interventions
5. To strengthen the malaria surveillance system by improving case reporting, passive and active case detection, entomological and antimalarial resistance monitoring, and ensuring adequate outbreak response capability

6. To provide effective programme management, based on firm leadership commitment, so as to allow high-quality implementation of strategies from malaria control to elimination

With decades of efforts, great progress has been made in these two provinces. In 2012, there was no local infectious malaria for 1 year and no local *P. falciparum* infections for 3 consecutive years in Hainan province. Only 13 malaria cases were reported in that year, all of which were imported. Yunnan province had reported 853 malaria cases, with only 133 local infections in 20 counties, and most of the county incidence rates were lower than 1 per 10,000. However, there is still a long way to go for preventing reintroduction in Hainan province and eliminating malaria in the border areas of Yunnan province.

In recent years, with a growing economy and increasing international exchanges, the number of the imported cases have increased in P.R. China. For example, Hainan province, which is now being developed as an international tourism island, is especially important to solidify the existing malaria elimination efforts on the basis of strengthening the capacity of surveillance and response among mobile population.

The area on the China-Myanmar border is one of the least developed areas, and the population is comprised of ethnic minority groups who are at the highest risk for *P. falciparum* infections because they are often mobile due to their occupations. Control work in the border areas is often hindered by inadequate infrastructure for service delivery, shortages of trained health workers, interruptions in the procurement and delivery of health products, and limited investments in health. It is important to improve living conditions and work opportunities for poor people in their places of residence and to address population movements across borders. Furthermore, people need to be educated about preventive measures and the availability of diagnostic and treatment services, and policies should be reinforced in both public and private health care facilities. There is also a need for adequate coverage with good quality laboratory and clinical services for malaria detection, reporting and surveillance. Also, there should be collaboration between neighbouring countries and organizations to decrease malaria transmission and monitor the therapeutic efficacy of antimalarial drugs in endemic areas of the neighbouring countries (Xu and Liu, 2012). Civil society organizations or non-government organizations (NGOs) present a potentially valuable resource with which to help tackle the growing problem in Great Mekong subregions. These organizations are often able to exercise greater flexibility in accessing hard-to-reach areas, tracking migrants, and implementing cross-border approaches. This enables them to

play important roles in assisting the extension, strengthening and community uptake of government health systems and reaching populations that would otherwise be missed. Through these cooperative efforts, malaria can be eliminated in Yunnan province. However, even after local transmission is interrupted, efforts should be maintained to prevent reintroduction and reestablishment of local malaria transmission via the imported cases.

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