Perspectives

Malaria Elimination in China and Sustainability Concerns in the Post-elimination Stage

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ABSTRACT

The World Health Organization (WHO) certified China as officially malaria-free on June 30, 2021. Looking back at the public health history in China, malaria elimination has been a product of complex social engineering. Here, we summarized our experience and lessons, and found that malaria control and elimination in China is mainly attributed to governmental leadership, consistent efforts, technological innovations, and adaptive approaches. We also raised that vigilance should focus on imported cases through strengthening surveillance and response systems in order to prevent any re-establishment of transmission after elimination. China should continue to maintain its laboratory, clinical and field epidemiology capabilities. Continuous policy and financial support, multi-sectoral cooperation, and innovative strategies and approaches will remain essential. By integrating these, a malaria-free status can become sustainable.

INTRODUCTION

Malaria is a dangerous infection caused by parasites transmitted to humans through the bites of *Anopheles* mosquitoes. About half of the world's population is endangered by malaria, particularly those in under-developed countries. According to the latest World Malaria Report by the World Health Organization (WHO), there were an estimated 241 million malaria cases and a death toll of up to 627,000 globally in 2020 (*1*). While the gains in reducing global malaria cases and deaths to date have been impressive, the challenges remain substantial. The rate of progress that characterized the scale-up of interventions from 2000 to 2010 has not kept pace. In particular, the reductions in cases and deaths needed to achieve the 2030 targets for morbidity and mortality reduction from the WHO Global Technical Strategy for Malaria (2016–2030) have not been met over the last several years. Malaria case incidence and mortality rates continue to decline slower than needed. These facts highlight the need for continued efforts to reduce the toll of disease and approach the aggressive goal of being malaria-free globally.

Malaria has been eliminated in China since 2021. However, China should conscientiously implement the principles of "Consider prevention as a high-priority approach; Use scientific control strategies; Take adaptive measures; Comply with the classified guidance" and the working mechanism of "governmental leadership, multi-sectoral cooperation, and whole-society participation" to remain malaria-free. This study overviews malaria elimination in China and raises sustainability concerns about the post-elimination stage. These illustrations and encounters from China's success during malaria elimination will be significant references for nations focusing on elimination.

A BRIEF HISTORY OF MALARIA ELIMINATION IN CHINA: KEY STRATEGIES, METRICS, AND ACHIEVEMENTS

Malaria is an ancient disease with records that can be traced back to more than 3,500 years ago in oracle-bone inscriptions in China. The past centuries have witnessed several disasters by malaria-caused mortality and morbidity. In the early years after the founding of the People's Republic of China, approximately 80% of the population was under malaria threat, and the disease was prevalent in nearly 70% of counties (*2*–*5*). In 1954, 6.97 million malaria cases represented a national incidence rate of 12.29 per 1,000 estimated (Figure 1). There were still more than 24 million cases in 1970 (*6*). In China's malaria control campaign, concerted efforts for generations have led to an unprecedented descending incidence from 122.9/10,000 (6.97 million cases) in 1954 to 0.06/10,000 (7,855 cases) in 2010 (Figure 1). In

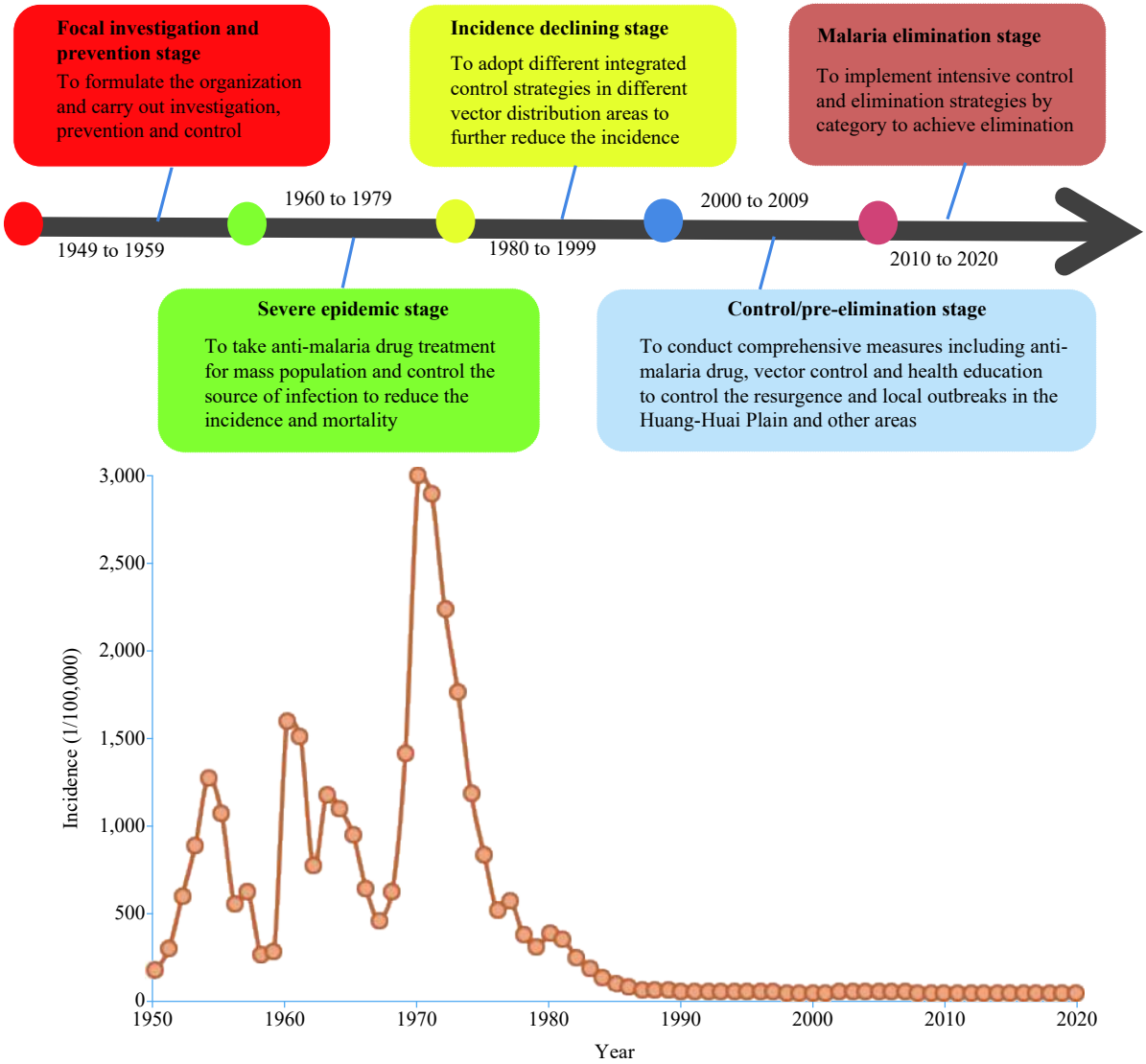

FIGURE 1. Malaria incidence in different periods and corresponding primary strategies in China.
Note: Focal investigation and prevention stage (1949–1959); Severe epidemic stage (1960–1979); Incidence declining stage (1980–1999); Control/pre-elimination stage (2000–2009); Malaria elimination stage (2010–2020).

response to the global malaria eradication initiative prompted by the Millennium Development Goals, China issued the National Action Plan for Malaria Elimination in China (2010–2020) in 2010: laying down the main objectives as eliminating malaria in most counties by 2015 and over the whole territory by 2020. In 2016, China was included by the WHO in the Elimination-2020 (E-2020) initiative as one of the 21 potential countries to reach malaria elimination by 2020. In 2017, for the first time, China reached the critical milestone of zero indigenous malaria cases (7). Zero indigenous transmission has been maintained for 4 consecutive years, achieving the goal proposed in the E-2020 initiative and the National Malaria Elimination Action Plan. Ultimately, on June 30, 2021, China was officially certified malaria-free by the WHO.

During the focal investigation and prevention stage (1949–1959), in light of high morbidity and mortality, lack of professional agencies, and lack of baseline data, China instituted professional agencies nationally and conducted baseline investigations and field trials for the national malaria control program. Notably, China defined malaria as a notifiable disease in 1956, which highlighted the hazards and importance of the disease for the first time.

The severe epidemic stage (1960–1979) was characterized by vivax malaria pandemics in central China. Therefore, China conducted mass drug administration (MDA) with prophylactic and radical

medications and initiated intranational cooperation mechanisms where the epidemic was unstable and endemic.

Through the comprehensive strategies in remote areas with severe outbreaks during the incidence declining stage (1980–1999), combined with prevention and control measures adopted in an earlier stage, malaria incidence declined continuously.

During the control/pre-elimination stage (2000–2009), despite case decline, China still faced severe issues in combating malaria: serious underreporting and high transmission in the Yunnan and Hainan provinces of southern China, and resurgence and outbreaks in central China. In response, China strengthened blood tests, early diagnosis, and appropriate treatment to solve these problems. Free mass distribution of long-lasting insecticide-treated nets (LLINs), health education, and monitoring and evaluation were also conducted with the support from the Global Fund, which offered important stimuli towards malaria elimination. More importantly, China established a timely, web-based reporting system and conducted targeted MDA in central China, which substantially reduced incidence to a record low: indicating the feasibility of eliminating malaria (*5*,*7*–*8*).

When China entered the malaria elimination stage (2010–2020), many institutions at the provincial or county levels still followed previously-used strategies. As a result, they overlooked the changes in concepts and methods necessary during the transition from the control to elimination stages. Consequently, the adaptation of alternative strategies at these governance levels was urgently needed. This involved setting priorities and operationalization based on local malaria epidemiology and robustness of the health system. These transitions required tailored responses, including an adaptive case- and focus-oriented comprehensive strategy and "1-3-7" approach, constructing and reinforcing elimination reporting systems, and implementing a diagnosis-reference laboratory network (*7*,*9*). Based on the successful experience of previous pilot trials on malaria control and elimination, Yunnan Province put forward and carried out a defensive 3-pronged strategy, as well as a "3+1" strategy (+1 was an extended buffer zone in Laiza City of Myanmar with a length of 20.5 km and a width of 2.5 km), in border areas to guarantee universal surveillance coverage and rapid response to any re-establishment of transmission (*9*–*10*).

In addition, regarding the management of imported malaria cases, an effective malaria detection and management system for migrant populations is essential: especially through multi-sectoral cooperation. Various capacity building and maintenance of malaria detection, diagnosis, treatment, and response are a fundamental components of keeping vigilance and the key to achieving elimination. Through these initiatives, China has continuously scaled up its efforts to realize its malaria-free status. Integrated cooperation, efficient information sharing, and action coordination between sectors, regions, and provinces fueled the progress in the last mile towards elimination in China.

SUSTAINABILITY CONCERNS IN THE POST-ELIMINATION STAGE

Despite the fact that China has obtained enormous success in its national malaria elimination program since 2010, there is still a long way to go for consolidating the achievements gained. Given that imported cases (which act as a source of infection) are detected almost daily, and that structural malaria vectors still exist, China still faces a possible long-term risk of experiencing re-established, indigenous malaria transmission. Moreover, there are complex multivariate ecological factors along border areas neighboring 4 Southeast Asian countries that complicate the matter even further (*11*–*12*). In recent years, imported cases from Africa or Southeast Asia accounted for a substantial proportion of total reported cases: caused by increasing numbers of laborers and business people returning from malaria-endemic areas. Strong multi-sectoral collaboration is needed to improve the management of imported cases (Figure 2), especially between the customs, health, and education sectors. Moreover, international cooperation between countries with endemic malaria, such as the Yunnan-Myanmar and China-Africa cooperation, is highly recommended.

The inadequate capacity to diagnose malaria in communities where malaria cases seldom or never occur is also a big challenge in maintaining malaria-free status in China (Figure 2). Constant capacity building of medical workers on malaria detection, diagnosis, treatment and response is required to avoid delayed case detection. In addition, alternative approaches, such as rapid detection tests (RDTs), should be prepared as supplementary tools, especially at the township level in rural areas.

Resistance to antimalarial drugs is also alarming. Various studies reported *Plasmodium falciparum*

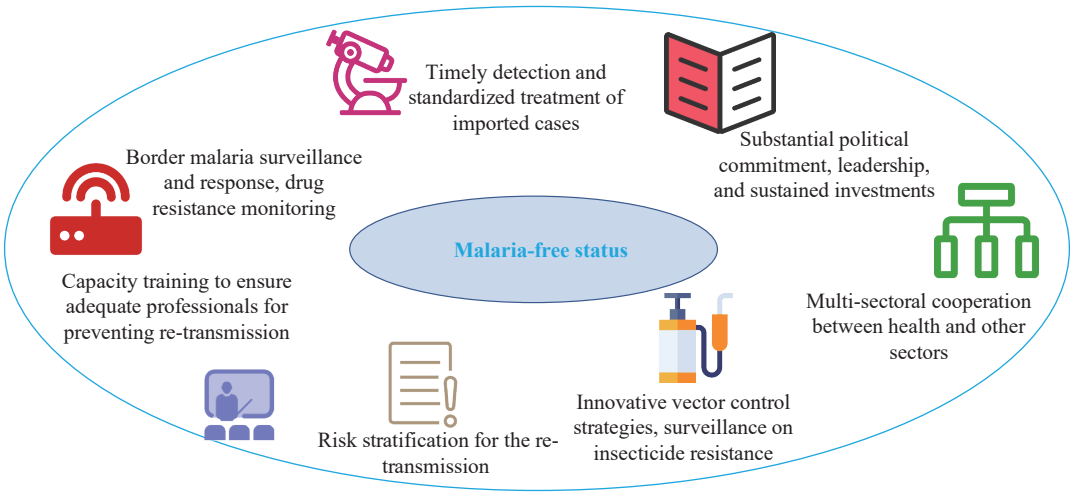

FIGURE 2. Key interventions needed to maintain malaria-free in the post-elimination stage.
Note: Countries that have achieved at least 3 consecutive years of zero indigenous cases are eligible to apply for a WHO certification of malaria-free status.

resistance to artemisinin, as well as *P. vivax* resistance to chloroquine, antifolate, and other therapies. To gather solid evidence on this issue, China has evaluated the prevalence of various drug-resistance genes in imported parasite isolates in past decades. Synonymous and nonsynonymous mutations in *pfmdr1, Pfdhfr*, *Pfdhps* and *Pfkelch13* were observed, indicating the presence and potential risk of multiple-drug resistance in imported malaria cases from both Africa and Southeast Asia isolates. The resistant parasite strains could contribute to the spread of drug resistance worldwide. Cases of imported malaria are increasing, and it is critical to conceive the approaches to surveillance, prevention and management of antimalarial drug resistance.

Also of importance, insecticide resistance has become a major obstacle to malaria control and elimination. The question of how to delay the spread of insecticide resistance is critical for developing and deploying effective vector control strategies and tools. Insecticide surveillance on primary malaria vectors in China indicated the spread of pyrethroid resistance among *An. sinensis* populations in a wide range of provinces including Yunnan and Hainan (*13*–*14*). Meanwhile, widespread and severe resistance to organophosphate insecticides in the southeastern region has also been reported. It is worth noting that some mosquito populations have evolved multi-resistance to applied insecticides such as pyrethroids, organophosphates, carbamates, and organochlorines.

To ensure the sustainability of a malaria-free status, it is necessary 1) to provide policy support, even after reaching the malaria-free milestone. Substantial political commitment and leadership, as well as sustained investments, are essential for deploying timely diagnosis, treatment, and effective prevention; 2) to maintain the continuity of sensitive and time-bound malaria surveillance-response systems so that all cases could be monitored promptly. Meanwhile, the corresponding response to foci could be delivered to prevent outbreaks or the reintroduction of malaria; 3) to improve reference laboratory and technical training, and to build and maintain the professional teams which can implement various measures; 4) to continue the multi-sectoral collaboration between the public health sector and other sectors such as commerce, tourism, and customs, and to strengthen closer international collaboration between malaria-endemic countries sharing a border with China. It will be more effective to perform joint and active surveillance and response by deploying prioritized activities through collaborations; 5) to invent active ingredients and integrate surveillance and monitoring of insecticides in addition to the core vector control approaches; 6) to monitor antimalarial drug resistance, especially through well-established antimalarial drug resistance markers and integrated drug efficacy surveillance (iDES), while conducting routine surveillance of imported malaria cases.

In addition, as SARS-CoV-2 spreads throughout the world, potential impacts on malaria incidence, mortality and service coverage have not been fully characterized. Thus, how to sustain China's malaria-free status once an outbreak or emergence of a novel

infectious disease, like coronavirus disease-19 (COVID-19), is also an important issue. Interventions to mitigate these challenges should strengthen communications and information sharing between malaria diagnosis and COVID-19 detection to avoid exposing malaria cases to COVID-19 (*15*). The focus on COVID-19 reduces or overwhelms malaria messages from the health community, which interrupts the timely deployment of interventions. Home-based malaria management, such as RDT and artemisinin-based combination therapy prescription drugs, should be recommended in such conditions.

CONCLUSION

China's malaria elimination was hard-earned and came only after decades of sustained investment and effort. Although China has eliminated malaria, various challenges and barriers threatening its malaria-free status still exist. Robust surveillance and response, constant capacity building, demand-oriented scientific research, and multi-channel cooperation are further needed to sustain China's malaria-free status in the future.

Conflicts of interest: No conflicts of interest.

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REFERENCES

1. WHO. World malaria report 2020: 20 years of global progress & challenges. https://www.who.int/teams/global-malaria-programme/reports/world-malaria-report-2020. [2022-3-22].
2. Tang L. Progress in malaria control in China. Chin Med J (Engl) 2000;113(1):89-92. https://pubmed.ncbi.nlm.nih.gov/11775219/.
3. Feng XY, Xia ZG, Feng J, Zhang L, Yan H, Tang LH, et al. The contributions and achievements on malaria control and forthcoming elimination in China over the past 70 years by NIPD-CTDR. Adv Parasitol 2020;110:63 – 105. http://dx.doi.org/10.1016/bs.apar.2020.03.005.
4. Feng XY, Xia ZG, Vong S, Yang WZ, Zhou SS. Surveillance and response to drive the national malaria elimination program. Adv Parasitol 2014;86:81 – 108. http://dx.doi.org/10.1016/B978-0-12-800869-0.00004-4.
5. Zhou XN, Xia ZG, Wang RB, Qian YJ, Zhou SS, Utzinger J, et al. Feasibility and roadmap analysis for malaria elimination in China. Adv Parasitol 2014;86:21 – 46. http://dx.doi.org/10.1016/B978-0-12-800869-0.00002-0.
6. Yin JH, Yang MN, Zhou SS, Wang Y, Feng J, Xia ZG. Changing malaria transmission and implications in China towards National Malaria Elimination Programme between 2010 and 2012. PLoS One 2013;8(9):e74228. http://dx.doi.org/10.1371/journal.pone.0074228.
7. Feng J, Zhang L, Huang F, Yin JH, Tu H, Xia ZG, et al. Ready for malaria elimination: zero indigenous case reported in the People's Republic of China. Malar J 2018;17(1):315. http://dx.doi.org/10.1186/s12936-018-2444-9.
8. Feng XY, Levens J, Zhou XN. Protecting the gains of malaria elimination in China. Infect Dis Poverty 2020;9(1):43. http://dx.doi.org/10.1186/s40249-020-00661-y.
9. Xu JW, Lin ZR, Zhou YW, Lee R, Shen HM, Sun XD, et al. Intensive surveillance, rapid response and border collaboration for malaria elimination: China Yunnan's "3 + 1"strategy. Malar J 2021;20(1):396. http://dx.doi.org/10.1186/s12936-021-03931-8.
10. Lin ZR, Li SG, Sun XD, Guo XR, Zheng Z, Yang J, et al. Effectiveness of joint 3 + 1 malaria strategy along China-Myanmar cross border areas. BMC Infect Dis 2021;21(1):1246. http://dx.doi.org/10.1186/s12879-021-06920-z.
11. Zhang Q, Sun JL, Zhang ZK, Geng QB, Lai SJ, Hu WB, et al. Risk assessment of malaria in land border regions of China in the context of malaria elimination. Malar J 2016;15(1):546. http://dx.doi.org/10.1186/s12936-016-1590-1.
12. Zhou S, Li ZJ, Cotter C, Zheng CJ, Zhang Q, Li HZ, et al. Trends of imported malaria in China 2010-2014: analysis of surveillance data. Malar J 2016;15:39. http://dx.doi.org/10.1186/s12936-016-1093-0.
13. Yang HL, Baloch Z, Xu JW, Sun XD, Lin ZR, Zhou YW, et al. Malaria: elimination tale from Yunnan Province of China and new challenges for reintroduction. Infect Dis Poverty 2021;10(1):101. http://dx.doi.org/10.1186/s40249-021-00866-9.
14. Qin Q, Li YJ, Zhong DB, Zhou N, Chang XL, Li CY, et al. Insecticide resistance of *Anopheles sinensis* and *An. vagus* in Hainan Island, a malaria-endemic area of China. Parasit Vectors 2014;7:92. http://dx.doi.org/10.1186/1756-3305-7-92.
15. Teboh-Ewungkem MI, Ngwa GA. COVID-19 in malaria-endemic regions: potential consequences for malaria intervention coverage, morbidity, and mortality. Lancet Infect Dis 2021;21(1):5 – 6. http://dx.doi.org/10.1016/S1473-3099(20)30763-5.