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Recollections

Accelerating the Control and Elimination of Major Parasitic Diseases in China — On World NTD Day 2024

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Neglected tropical diseases (NTDs) are a group of diseases associated with poverty that affect over 1 billion people worldwide (*1*). On May 31, 2021, the World Health Assembly (WHA) officially recognized January 30 as World Neglected Tropical Diseases Day through decision *WHA74(18)*. This designation aims to raise awareness about the severe impact of NTDs on disadvantaged populations and to mobilize support for control, elimination, and eradication efforts. The theme for World Neglected Tropical Diseases Day 2024 is "Unite, Act, Eliminate." In November 2020, the 73rd World Health Assembly endorsed the report "Ending the neglect to attain the Sustainable Development Goals: a road map for neglected tropical diseases 2021–2030" (*2*). This comprehensive report establishes global targets and milestones for the prevention, control, elimination, or eradication of 20 diseases and disease groups, aligned with the Sustainable Development Goals. Three primary pillars will guide global efforts in achieving these targets: 1) accelerating programmatic action, 2) intensifying cross-cutting approaches, and 3) promoting country ownership through changes in operating models and culture. The roadmap sets the elimination of schistosomiasis, visceral leishmaniasis (VL), and soil-transmitted helminthiases (STHs) as public health problems and outlines control measures for echinococcosis, foodborne trematodiases, and taeniasis/cysticercosis in China. In this paper, we review the progress and accomplishments in the control of major parasitic diseases in China over the past decade and analyze the ongoing challenges in achieving the elimination targets outlined in the World Health Organization (WHO) roadmap. We discuss the latest advancements, obstacles, and key tasks in the control of major parasitic diseases in China, aiming to provide insights into the realization of the targets outlined in the *WHO roadmap for neglected tropical diseases 2021–2030* and the *Outline of the Healthy China 2030 Plan*.

PROGRESS TOWARD THE CONTROL AND ELIMINATION OF MAJOR PARASITIC DISEASES

China, once heavily endemic for NTDs with a high disease burden, has made significant progress in disease control. The WHO declared lymphatic filariasis (LF) elimination in China in 2007, making it the first country to achieve this milestone (*3*). By the end of 2023, transmission interruption of schistosomiasis was achieved in all endemic areas of China (*4*). The number of schistosomiasis cases decreased from 240,597 in 2012 to 28,568 in 2022, representing an 88.13% decline, and no new local infections in humans, cattle, or snails have been reported since 2015 (*5–6*). After a national epidemiological survey of echinococcosis was conducted in 2012, integrated interventions focusing on controlling infection sources in endemic areas led to a continuous decline in prevalence (*7*). The prevalence rate of echinococcosis in endemic areas was 58.35 per 100,000 in 2022, marking a significant 79.29% reduction compared to the prevalence rate of 280 per 100,000 in 2012 (*8*). In most endemic areas of China, the prevalence of STHs and foodborne trematodiases has been maintained at a low level (*9*). Three national surveys on STHs have been conducted in China, and the infection rate has dropped from 53.58% in the first survey (1988–1992) to 4.49% in the third survey (2014–2016) due to strong interventions such as mass drug administration, health education, and environmental improvement (*10*). Data from national surveillance sites indicate that the prevalence of STH infection rate in China dropped from 2.46% in 2016 to 0.84% in 2020 (*11*). Additionally, the reported cases of VL decreased from 322 in 2016 to 239 in 2022. The overall prevalence of VL in humans remained low throughout China (*12–13*), although there were local areas where mountain-type zoonotic VL resurged (*14*). Overall, China is making significant strides toward achieving the 2030 targets outlined in the *Outline of Healthy*

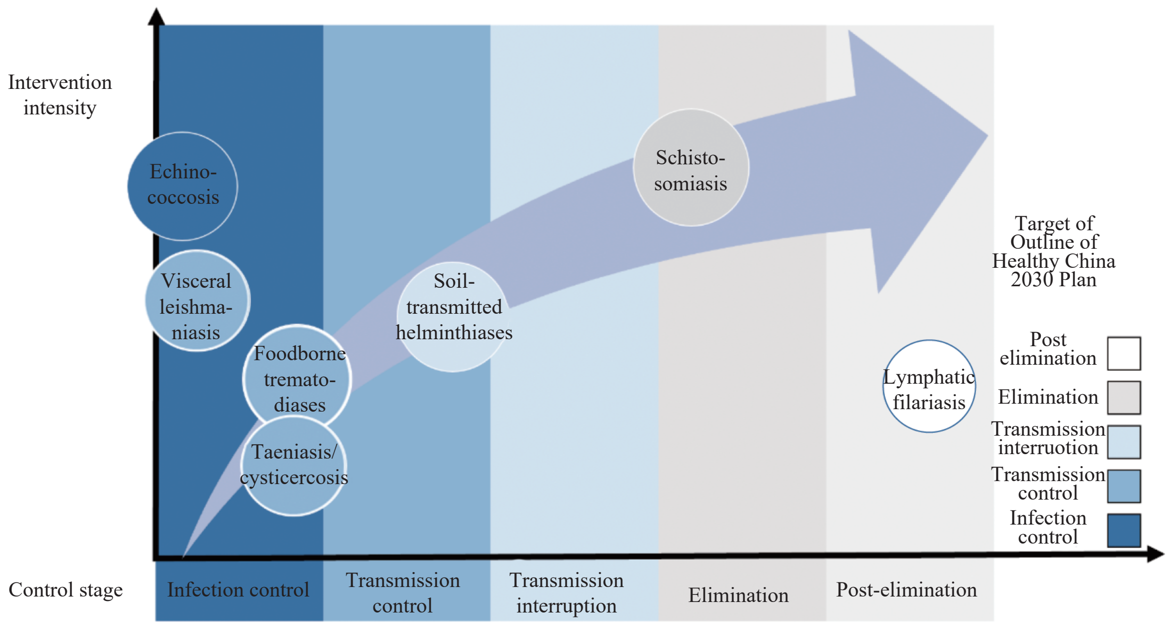

FIGURE 1. Progress and targets of major parasitic disease control programs in China.

China 2030 Plan (Figure 1).

EXPERIENCES LEARNED

Program Orientation — The First Cornerstone of the New Roadmap: Accelerating Program Action

In order to enhance the management and elimination of prevalent parasitic diseases, the Chinese government has developed disease control programs that take into account socioeconomic and epidemiological factors. These programs are designed to address specific diseases such as schistosomiasis, malaria, echinococcosis, soil-transmitted helminth infections (STHs), foodborne trematodiases, and VL. Targeted measures and technical guidelines have been implemented to ensure the sustainability of these programs. Regular evaluations have been carried out to assess the effectiveness of interventions and monitor the progress of disease control.

The *Outline of Healthy China 2030 Plan*, released by the Chinese government in 2016, set an ambitious goal of eliminating schistosomiasis and controlling echinococcosis in all disease-endemic counties by 2030. In June 2023, the *Action Plan to Accelerate the Achievement of Schistosomiasis Elimination Goal (2023–2030)* was jointly formulated by 11 ministries of the Chinese government. This plan provides detailed targets over three periods and emphasizes major countermeasures to eliminate schistosomiasis in China. These programs and action plans serve as the foundation for achieving the targets outlined in the new strategic plan.

Integrated Control — The Second Cornerstone of the New Roadmap: Improving the Development of Cross-Disciplinary Tools

An integrated strategy was implemented to control major parasitic diseases, focusing on the control of infection sources. This strategy employed classified guidance and scientific control principles, and involved multisectoral and multidisciplinary collaborations. Resources from the health, agricultural, forestry, water resource development, land resources, and education sectors were mobilized to implement various measures, including disease surveillance, management of animal reservoir hosts, environmental health treatment, safe water supply, vector control, and health education. These comprehensive efforts were aimed at effectively combating major parasitic diseases (*15*).

Based on the characteristics of transmission, integrated strategies have been implemented to control parasitic diseases. For the control and elimination of schistosomiasis, the agricultural sector has implemented measures such as replacing farming cattle with machines, confining domestic animals, and prohibiting grazing to regulate infection sources. The water conservancy and forestry sectors have employed engineering measures to control intermediate host snails by hardening ditches, modifying environments, and planting forests, suppressing snails' survival. To control echinococcosis, the agricultural sector has strengthened livestock enclosure measures and standardized slaughter practices to manage the infection source in animals. The public security department has intensified efforts to eliminate infected and stray dogs for VL control. In addition, the government has made active improvements in water supply systems and sanitation facilities to prevent and control soil-transmitted helminth infections. These countermeasures resulted in significant improvement in the supply of safe water, hygiene and sanitation of communities, a good social atmosphere supporting interventions, and interruption of schistosomiasis transmission.

Furthermore, collaborative efforts between universities and research institutions have led to the development of various innovative tools and techniques for the detection of parasites, including molecular detection assays, gene traceability techniques, vector characterization, and identification assays. Additionally, intelligent field control and surveillance-response systems have been implemented, along with the development of effective antiparasitic agents and molluscicides. These advancements have been integrated into national parasitic disease control programs, marking a significant milestone in our progress toward achieving the objectives outlined in the new road map (*16*).

Organization and Leadership — The Third Cornerstone of the New Roadmap: Changing the Operation Pattern and Cultivation

Since the establishment of the People's Republic of China, the control of parasitic diseases has been a top priority for the Chinese government. Measures include the development of annual governmental working plans that incorporate parasitic disease control programs, financial support from the central government, and the establishment of a comprehensive mechanism for government leadership, multisectoral collaborations, and joint prevention and control strategies. These efforts have included the allocation of human resources, as well as financial and material support, to enhance disease control capabilities. This has involved the establishment and improvement of disease surveillance networks in high-risk endemic areas, the development of a national-provincial-county level diagnostic laboratory network, and the implementation of major control and surveillance projects for parasitic diseases at a national level (*17*). In addition, the involvement of corporations, universities, institutions, and non-governmental organizations has been crucial in mobilizing collective efforts and creating an environment conducive to joint prevention and control. This collaborative approach has been instrumental in achieving the targets outlined in the new roadmap.

MAJOR CHALLENGES TO ACHIEVE THE TARGETS SET IN THE NEW ROADMAP

Despite the significant progress achieved in the implementation of major parasitic disease control programs in China, there are still numerous challenges that need to be addressed in accordance with the targets established by the WHO road map for neglected tropical diseases 2021–2030 and the *Outline of Healthy China 2030 Plan*. These challenges include global climate warming, ecological environmental deterioration, and unchanged living conditions and behaviors (*18*). First, the transmission of major parasitic diseases is influenced by a wide range of factors, and the progress of control programs for these diseases remains weak (*19*). Consequently, there have been occasional re-emergence or resurgences of major parasitic diseases. Second, the feasibility and effectiveness of interventions against different diseases vary across regions. For instance, implementing control activities against parasitic diseases in agricultural and pasture areas of western China poses difficulties, and the control and surveillance of taeniasis/cysticercosis, scabies, and other ectoparasitic diseases need improvement. Lastly, as China approaches the pre-elimination stage for major parasitic diseases, there is an increasing demand for precision control methods. Innovative strategies, interventions, and techniques are urgently required to expedite disease elimination.

PERSPECTIVES

In line with the *WHO road map for neglected tropical diseases 2021–2030* and the *Outline of Healthy China 2030 Plan*, targeted control programs for parasitic diseases are developed and executed with the guidance of the government. These programs involve collaboration across multiple sectors, integration with rural revitalization projects, and effective social governance. Additionally, tailored measures are implemented based on specific local conditions to effectively control and eliminate major parasitic diseases.

For each neglected tropical disease, specific strategies have been identified in national control programs implemented in endemic areas. While transmission interruption has been achieved for some diseases, the strategy for eliminating schistosomiasis has been updated to focus on infection source control and strengthening snail control in key environments, as outlined in the *Action Plan to Accelerate the Achievement of Schistosomiasis Elimination Goal (2023–2030)*. In endemic areas of echinococcosis, a comprehensive control strategy that prioritizes infection source management while integrating standardized investigation and treatment for patients, intermediate host prevention, and control is recommended to advance the control process. For VL, specific measures should be implemented based on different epidemiological characteristics. In endemic areas of the Mountainous Sub-type of Zoonotic VL, strategies should include dog regulation, vector control, and patient treatment. For Anthroponotic VL, emphasis should be placed on identifying and treating patients along with vector control. In the Desert Sub-type of Zoonotic VL, it is important to treat infected individuals and implement protective measures for the population, along with vector control. To control soil-transmitted helminthiases and foodborne parasitic diseases, a comprehensive control strategy should be adopted. This strategy should focus on health promotion as a guiding principle, along with infectious source management. It should involve implementing preventive measures such as health education campaigns, chemotherapy for humans and animals, improvements in water supply systems and sanitation facilities, and enhanced food safety management through national monitoring systems.

To effectively address the three major challenges in achieving the targets outlined in the new road map, we recommend actively promoting the application of the One Health concept (*20*). This concept encompasses Human, Animal, and Environmental health and aims to optimize support for control interventions and technical tools. By consolidating these three cornerstones, we can accelerate the elimination of major parasitic diseases in China.

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Preplanned Studies

Analysis of Epidemiological and Issues Encountered in Case Reports on Echinococcosis — China, 2022

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Summary

What is already known about this topic?

Echinococcosis is classified as a Class C infectious disease in China. It is endemic in 370 counties located in the agricultural and pastoral regions of western China.

What is added by this report?

This report provides a comprehensive overview of the cases of echinococcosis reported in China in 2022. Following a thorough evaluation conducted by provincial CDCs, it was identified that 105 new cases were not reported through the National Notifiable Disease Reporting System. Furthermore, there were 1,051 cases that were reported among patients who had been previously diagnosed with echinococcosis.

What are the implications for public health practice?

The reported cases of echinococcosis in non-endemic counties of provincial-level administrative divisions where the disease is endemic need to be given more attention, as there is a potential risk of it spreading within the non-endemic areas. Inadequate reporting practices by clinical medical institutions are hindering the subsequent investigations carried out by CDCs. It is important to implement enhanced health promotion efforts that focus on high-risk populations to address unhealthy lifestyles.

This article aims to analyze the reported cases of echinococcosis in China in 2022, providing insights into the distribution and epidemiological characteristics of the disease. The analysis will contribute to the development of effective prevention and control strategies. The data of reported cases were collected and analyzed using descriptive epidemiological methods. In 2022, a total of 2,711 cases were reported nationwide, including 105 cases that were not captured by the National Notifiable Disease Reporting System (NNDRS) and were subsequently reported by provincial CDCs after verification. Among the reported cases, 1,051 (39.33%) were re-visited in the epidemic provincial-level administrative divisions (PLADs), 39 cases (1.44%) were reported in 16 non-endemic PLADs, and 154 cases (5.76%) were reported in non-endemic counties within the epidemic PLADs. The reported cases of echinococcosis in China have consistently declined for three years until 2022. However, there are still challenges in the national program of echinococcosis control, necessitating continued reinforcement. It is important to reinforce the reporting of cases in non-endemic areas and remain vigilant about the potential for spread. The government should increase investments, enhance public health facilities, and elevate the standards of primary medical and healthcare services.

Echinococcosis, also known as hydatidosis, is a globally prevalent zoonotic parasitic disease caused by *Echinococcus* larvae. It poses significant threats to human health and life, while inflicting substantial economic losses on animal husbandry production (*1–3*). China is heavily affected by echinococcosis, with two types: alveolar echinococcosis and cystic echinococcosis. Echinococcosis is widespread in 370 counties within western agricultural and pastoral areas of China, threatening nearly 60 million people. This has a significant impact on public health and animal husbandry development in endemic areas (*4–5*). The Qinghai-Xizang Plateau is particularly affected, ranking first in the world in terms of epidemic scope, threatened population, and number of patients (*6–7*). According to the Chinese Law on the Prevention and Treatment of Infectious Diseases, echinococcosis is classified as a Class C infectious disease. Since 2004, it has been included in the NNDRS. Echinococcosis cases have also been reported in non-endemic PLADs for an extended period (*8–9*).

The echinococcosis cases reported by the NNDRS in 2022 were retrieved using the search criteria of a final review date between January 1, 2022, and December 31, 2022. Suspected and duplicate cases were excluded from the study. Echinococcosis cases from Hong Kong Special Administrative Region

(SAR), China; Macao SAR, China; and Taiwan, China, were not included. The cases were determined based on the Diagnostic Criteria for Echinococcosis (WS257-2006). The provincial CDCs reviewed the retrieval results and identified revisiting patients who had previously been diagnosed with echinococcosis and sought re-examination or drug dispensing at hospitals in 2022. Duplicate reported cases, where the same ID number was reported multiple times within the same month, were eliminated. Additionally, missing reported cases that were diagnosed by medical institutions according to WS257-2006 in 2022 but were not found in the retrieval results were included. For basic descriptive statistical analyses, Microsoft Excel (version 2016, Microsoft Corp., Redmond, USA) and SAS Software (version 9.4, SAS Institute Inc., NC, USA) were used. The statistical significance was determined using a two-tailed P-value <0.05.

In 2022, a total of 2,711 echinococcosis cases were reported across 25 PLADs, including cities and autonomous regions. Fortunately, there were no deaths reported. Of these cases, 1,051 were revisiting cases, and 105 cases were initially unreported but later confirmed. The majority of cases (98.56%, n=2,672) were reported in endemic PLADs. The three PLADs with the highest number of reported cases were Xinjiang Uygur Autonomous Region, Sichuan Province, and Qinghai Province. Additionally, there were 39 cases reported in 16 non-endemic PLADs, which is 14 cases fewer than in 2021.

In 2022, cases of echinococcosis were reported in various age groups in China. The median age in endemic PLADs was 48 years, with the majority falling within the age brackets of 50 and 40, accounting for 23.02% (624/2,672) and 20.91% (567/2,672), respectively. Non-endemic PLADs had an average age of 38.21±17.27 years, mainly concentrated in the age groups of 40 and 10, comprising 30.77% (12/39) and 15.38% (6/39), respectively. There was no statistically significant difference in the age distribution between endemic and non-endemic PLADs (χ^2=12.51, P=0.085). The male to female ratio was approximately 1:1.14 in endemic PLADs and 1:1.44 in non-endemic PLADs; however, this gender distribution difference did not reach statistical significance (χ^2=2.28, P=0.131) (Table 1).

In 2022, there were reported cases of echinococcosis observed in China among various population groups. In the endemic PLADs, the highest number of cases were reported by farmers (44.12%, 1179/2,672), followed by herdsmen (25.94%, 693/2,672), and houseworkers and unemployed individuals (6.96%, 186/2,672). In non-endemic PLADs, the primary reporting groups were farmers, commercial service personnel, students, as well as houseworkers and unemployed individuals, accounting for a total proportion of 79.49% (31/39) (Table 1).

In 2022, 77.03% (285/370) of the counties affected by the epidemic reported cases, comprising 92.88% (2,518/2,711) of the total reported cases in China. Among these counties, there were 65 with 10 or more cases, 66 with 5–9 cases, and 154 with less than 5 cases. Yining City in Xinjiang Uygur Autonomous Region (43 cases), Gande County in Qinghai Province (34 cases), Chabuchal County in Xinjiang Uygur Autonomous Region (32 cases), Dari County in Qinghai Province (31 cases), and Yining County in Xinjiang Uygur Autonomous Region (29 cases) had the highest number of reported cases after revisiting and removal of cases. Loss to follow-up accounted for 2.56% (1/39) of cases, and 5.13% (2/39) of cases were linked to overseas sources. Additionally, six non-endemic PLADs reported suspected local infections: Guizhou (3 cases), Shandong (3 cases), Hebei (2 cases), Heilongjiang (1 case), Hunan (1 case), and Liaoning (1 case). Further investigation in non-endemic PLADs found that 28.21% (11/39) of cases had no travel or living history in endemic areas, while 64.10% (25/39) had a travel or living history in endemic areas, with the majority (60%) originating from Xinjiang (Figure 1).

In 2022, there were a total of 154 reported cases in non-endemic counties within the epidemic PLADs, which accounted for 5.76% (154/2,672) of all reported cases in the epidemic PLADs. Specifically, Shaanxi, Inner Mongolia, and Yunnan had higher proportions of reported cases in non-endemic counties, with proportions of 84.62% (11/13), 37.14% (13/35), and 28.57% (8/28) respectively (Table 2). The counties with the highest number of reported cases in non-endemic counties within the epidemic PLADs were Xinshi District of Xinjiang (11 cases), Shaybak District of Xinjiang (10 cases), Chengzhong District of Qinghai (8 cases), Chengxi District of Qinghai (7 cases), and Tianshan District of Xinjiang (7 cases).

A total of 1,051 revisiting cases were identified in the epidemic PLADs across China in 2022, comprising 39.33% (1,051/2,672) of all reported cases in these PLADs. Among the PLADs, Sichuan had the highest proportion of revisiting cases, accounting for 81.88% (524/640), followed by Qinghai with 49.92% (299/599), Gansu with 41.11% (104/253), and Ningxia with 37.50% (51/136). Please refer to Table 2 for detailed information.

TABLE 1. Characteristics and distribution of reported echinococcosis cases in China, 2022.

Feature	Number of reported cases of endemic PLADs												Non-endemic PLADs	
	Inner Mongolia	Sichuan	Yunnan	Xizang	Shaanxi	Gansu	Qinghai	Ningxia	Xinjiang	XPCC	Total	Composition rate, %	Number of reported case	Composition rate, %
Age, years														
0–	0	11	0	4	0	0	9	1	53	3	81	2.99	2	5.13
10–	1	33	2	7	0	6	26	0	97	7	179	6.60	6	15.38
20–	1	71	0	18	0	5	66	1	49	5	216	7.97	5	12.82
30–	7	112	2	28	1	17	87	13	84	8	359	13.24	5	12.82
40–	7	152	4	29	3	37	149	19	159	8	567	20.91	12	30.77
50–	8	125	5	29	3	84	144	28	171	27	624	23.02	4	10.26
60–	3	71	12	10	4	48	56	33	89	3	329	12.14	3	7.69
70–	8	65	3	12	2	56	62	41	60	8	317	11.69	2	5.13
Occupation														
Nursery children	0	1	0	2	0	0	1	0	9	1	14	0.52	0	0
Scattered children	0	10	0	1	0	0	7	0	7	0	25	0.94	0	0
Students	1	19	2	4	0	3	16	1	125	10	181	6.77	7	17.95
Teachers	0	0	0	0	0	1	7	2	5	0	15	0.56	1	2.56
Household assistants and childcare providers	0	0	0	1	0	0	0	0	0	0	1	0.04	0	0
Service providers	0	1	0	0	0	0	0	0	1	0	2	0.07	0	0
Commercial service	3	3	0	1	2	4	2	1	32	2	50	1.87	7	17.95
Medical personnel	0	1	0	0	0	0	2	0	2	0	5	0.19	0	0
Workers	0	5	1	5	0	1	5	0	25	7	49	1.83	0	0
Peasants	8	291	17	55	7	195	140	102	344	20	1,179	44.12	12	30.77
Herdsmen	10	220	3	43	0	14	360	1	40	2	693	25.94	0	0
Seafarers and long-distance drivers	0	0	0	0	0	0	0	0	1	0	1	0.04	0	0
Staff	2	3	1	4	1	2	3	0	21	1	38	1.42	2	5.13
Retirees	3	6	2	8	3	10	13	9	55	10	119	4.45	0	0
Unemployed or at home	8	24	0	6	0	14	20	19	85	10	186	6.96	5	12.82
Religious professionals	0	31	0	0	0	2	13	0	0	0	46	1.72	0	0
Freelancers	0	0	1	0	0	0	1	1	3	0	6	0.22	0	0
Others	0	1	0	1	0	0	0	0	1	1	4	0.15	1	2.56
Unknown	0	24	1	6	0	7	9	0	6	5	58	2.17	4	10.26
Gender														
Male	17	256	13	65	10	126	269	54	405	36	1,251	46.82	23	58.97
Female	18	384	15	72	3	127	330	82	357	33	1,421	53.18	16	41.03
Total	35	640	28	137	13	253	599	136	762	69	2,672	100.00	39	100.00

Abbreviation: XPCC=Xinjiang Production and Construction Corps; PLADs=provincial-level administrative divisions.

DISCUSSION

The number of reported echinococcosis cases in China has shown a consistent decrease, declining from 6,800 cases in 2017 to 2,711 cases in 2022, which indicates that the epidemic in our nation has been

FIGURE 1. The Sankey diagram of exported PLADs and imported non-endemic PLADs of echinococcosis in China, 2022.
Abbreviation: XPCC=Xinjiang Production and Construction Corps; PLADs=provincial-level administrative divisions.

effectively contained. The data reveals that individuals in occupations such as farmers, herdsmen, houseworkers, unemployed individuals, and students are still at a high risk for echinococcosis infection. It is evident that there is a lack of awareness regarding the transmission risks of echinococcosis among certain individuals, particularly those living in non-endemic PLADs and regions. This lack of awareness has resulted in a deficiency of effective preventive measures. Some areas still suffer from inadequate public health facilities, including limited access to hand-washing facilities. Furthermore, certain regions continue to engage in practices such as consuming undercooked animal meat and drinking untreated water, which creates favorable conditions for the transmission of echinococcosis. The limited healthcare resources in these regions have also posed challenges to the national program for echinococcosis control.

During the data verification process, we encountered several challenges. These included instances of duplicated reporting of previous cases, as well as omissions of newly detected cases and statistical errors in certain disease-affected regions. After consulting with the staff of the primary CDCs, we discovered that some new cases had been identified during the screening of key groups conducted by CDCs in collaboration with medical institutions. However, due to potential delays in seeking hospital treatment, these individuals may have been unintentionally overlooked in the reporting process, despite being confirmed cases according to the diagnostic criteria established by

TABLE 2. Case composition reported in endemic PLADs.

PLADs	Number of reported cases (%)			
	Endemic county report	Non-endemic counties in the PLADs	Revisiting	Total
Inner Mongolia	18 (51.43)	13 (37.14)	4 (11.43)	35
Sichuan	80 (12.50)	36 (5.63)	524 (81.88)	640
Yunnan	19 (67.86)	8 (28.57)	1 (3.57)	28
Xizang	137 (100.00)	–	–	137
Shaanxi	2 (15.38)	11 (84.62)	0 (0)	13
Gansu	132 (52.17)	17 (6.72)	104 (41.11)	253
Qinghai	276 (46.08)	24 (4.01)	299 (49.92)	599
Ningxia	83 (61.03)	2 (1.47)	51 (37.50)	136
Xinjiang	654 (85.83)	43 (5.64)	65 (8.53)	762
XPCC	66 (95.65)	0 (0)	3 (4.35)	69
Total	1,467 (54.90)	154 (5.76)	1,051 (39.33)	2,672

Note: "–"=The prevalence of echinococcosis is endemic in all counties within Xizang; however, due to various limitations, it is not feasible to ascertain the precise number of re-diagnosed cases among those reported.
Abbreviation: XPCC=Xinjiang Production and Construction Corps; PLADs=provincial-level administrative divisions.

authorized physicians during the screening. Additionally, the available data does not specify whether the patient has cystic or alveolar echinococcosis, which is essential information. The non-standard reporting practices adopted by clinical medical institutions have significantly hindered the subsequent investigation efforts of the CDCs.

Echinococcosis, a parasitic disease that poses a significant threat to human health, requires increased attention and support through the implementation of the One Health approach. It is important to prioritize the standardization of the "Infectious Disease Report Card" filling process in primary medical institutions. The next step would be to plan a training course on relevant policies, or alternatively, prepare a work specification promptly and ensure its distribution among the relevant clinicians in order to enhance the quality of reporting. In addition, there is a need to intensify the dissemination of epidemic prevention and control measures, enhance public awareness of preventive practices, and guide individuals in adopting scientifically recommended personal hygiene habits, such as frequent handwashing and avoiding close contact with dogs. Moreover, it is crucial to discourage the consumption of undercooked animal meat or contaminated water sources and to avoid contact with marmots and other wild animals to minimize the risk of infection.

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Preplanned Studies

Laboratory and Semi-Field Evaluation on S-Methoprene Formulations Against *Anopheles sinensis* (Diptera: Culicidae) — Yuxi City, Yunnan Province, China

Wenbo Hu[1]; Yijin Chen[1]; Ying Liang[2]; Tianyun Su[3,#]; Qiyong Liu[2,#]; Xuewen Li[4]; Xiaobo Liu[2,5,6,#]

Summary

What is already known about this topic?

Anopheles sinensis (*An. sinensis*) is the predominant malaria vector in China. The impact of S-methoprene on the emergence process of mosquito larvae suggests its potential as a control method for vector mosquitoes. However, the efficacy of S-methoprene in controlling *An. sinensis* has not yet been demonstrated.

What is added by this report?

The effectiveness of S-methoprene against *An. sinensis* was assessed in laboratory and semi-field conditions in Yunnan Province.

What are the implications for public health practice?

These results offer valuable options and guidance for utilizing S-methoprene products in malaria reimportation prevention areas within Yunnan Province.

Malaria is an infectious disease transmitted by mosquitoes, specifically through the bite of *Anopheles* mosquitoes or by blood transfusion from an infected person. In 2021, there were approximately 247 million malaria cases reported in 84 countries endemic to malaria (*1*).

The most common mosquito species responsible for malaria transmission in China is *Anopheles sinensis (An. sinensis)* Wiedemann (*2*). Chemical control is currently a primary method for comprehensive vector management due to its simplicity, effectiveness, and ease of use. However, the emergence of pesticide resistance among malaria vector mosquitoes has become a significant concern. Yunnan Province, located in the Greater Mekong subregion (GMS), is particularly vulnerable as a malaria hotspot (*3*). Studies have demonstrated that *An. sinensis* mosquitoes in Yuxi City, Yunnan Province have developed resistance to traditional chemical insecticides like organophosphorus, carbamate, organochlorines, and pyrethroids (*4*).

In recent years, biological control has gained attention in the field of entomology and vector control as a potential solution to pesticide resistance. One notable biological insecticide is the juvenile hormone analogue S-methoprene, which has been used in the United States since the 1970s and is recognized for its efficacy against various vector species while maintaining environmental safety and non-target organism protection (*5*). Several formulations of S-methoprene, including emulsifiable concentrate, microcapsule suspensions, granules, pellets, water-soluble pouches, and briquets (*6*).

S-methoprene technical material and its products were tested in a laboratory against late-instar larvae of *An. sinensis*. Following this, an experimental site in Yuxi City, Yunnan Province (Figure 1) was selected to evaluate the impacts of different formulations of S-methoprene products on *An. sinensis* under semi-field conditions (Supplementary Material, available at https://weekly.chinacdc.cn/). The bioassays showed that the formulated products and technical material had similar efficacy in inhibiting adult emergence at three different IE levels. Under semi-field conditions, a 20% microcapsule suspension at a dosage of 0.025–0.1 mL/m^2 provided 100% efficacy for at least 3 days, while 1% granules at9.09 g/m^2 and 4.3% granules at 2.0 g/m^2 providedmore than 85% efficacy for at least 14 days. The results confirmed the strong biological activity and safety profile of S-methoprene, supporting its recommendation as a standard larvicidal tool for controlling *An. sinensis* in various habitats while adhering to local regulations.

In the concurrent bioassays, we tested the effectiveness of S-methoprene technical material, microencapsulated suspension, and two granules against *An. sinensis*. The results showed that all formulations exhibited high activity in inhibiting adult emergence. Interestingly, there were no significant differences observed between the formulated products and the pure S-methoprene technical material at three different application levels. This data is summarized in

TABLE 1. Laboratory bioassays on S-methoprene technical material and products against *Anopheles sinensis*.

Product	IE 10 (μg/L) (95% *CI*)	IE50 (μg/L) (95% *CI*)	IE 90 (μg/L) (95% *CI*)
Technical S-methoprene	0.055 (0.012–1.060)	0.220 (0.119–0.303)	0.883 (0.640–1.529)
microencapsulated suspension	0.046 (0.019–0.076)	0.236 (0.017–0.322)	1.199 (0.744–2.893)
1% granule	0.052 (0.009–1.065)	0.221 (0.116–0.331)	1.238 (0.885–3.840)

Note: Mortality data was corrected by factoring the mortality in untreated control (6.4%–8%) using Abbott formula (Abbott, 1925) before probit analysis.
Abbreviation: *CI*=confidence intervals; IE=inhibition of emergence.

Table 1.

During the testing period, the infection rate (IE) of *An. sinensis* against IE in untreated control (UTC) was as low as 0–4%. The experimental endpoint was considered achieved when the IE provided by the insecticidal preparations was less than 85%. There were dose-dependent and time-related effectiveness trends observed within the intended range of 0.025–0.1 mL/m^2. On the third day of the evaluation period, all three selected concentrations showed 100% efficacy. However, on the 7th day of assessment, the IE decreased to 48% at 0.025 mL/m^2 and 52% at 0.038 mL/m^2. For the highest concentration of 0.1 mL/m^2, assessments were conducted from day 14 until the experimental endpoint (Figure 2). The IE% showed a highly significant difference among the UTC and treatment groups (χ^2=193.2–250.0, *P*<0.001), as well as among the doses on days 3, 7/14 (χ^2=10.4–18.9, *P*<0.01).

Dose-dependent and time-related effectiveness trends were observed within the intended range of 1.60–9.09 g/m^2. On the third day of the evaluation period, all three selected concentrations demonstrated 100% efficacy. However, at a concentration of 1.60 g/m^2, the effectiveness persisted for less than 7 days. By the 14th day of assessment, the effectiveness decreased to 38% at 5.13 g/m^2 and 86% at 9.09 g/m^2. For the highest concentration of 9.09 g/m^2, assessments were continued from day 21 until the end of the experiment (Figure 2). The effectiveness percentage (IE%) showed significant differences among the UTC and treatment groups (χ^2=150.9–250.0, *P*<0.001), as well as among the different doses on days 3, 14–21 (χ^2= 9.33–11.27, *P*<0.01).

Dose-dependent and time-related trends in effectiveness were observed within the intended range of 0.4–2 g/m^2. By the third day of evaluation, all three selected concentrations showed 100% efficacy. At a concentration of 0.4 g/m^2, the duration of effectiveness was less than 7 days. On the 7th day of evaluation, all concentrations showed 100% efficacy. On the 21st day, the effectiveness decreased to 76% at 1.0 g/m^2 and 80% at 2.0 g/m^2. The effectiveness percentages were significantly different among the untreated control group and the various treatments (χ^2=145.7–250.0, *P*<0.001) and among the doses on days 3, 14–21 (χ^2=27.78–31.86, *P*<0.01).

A
B

FIGURE 1. Semi-field testing site in Yuxi City, Yunnan Province. (A) Microcosms; (B) Assembled sentinel cage.

DISCUSSION

The Greater Mekong Subregion (GMS), which includes Yunnan Province of China, Cambodia, Lao PDR, Myanmar, Thailand, and Vietnam, is a significant malaria hotspot. The introduction of the Mekong Malaria Program (MRP) by the World Health Organization (WHO) has led to notable improvements

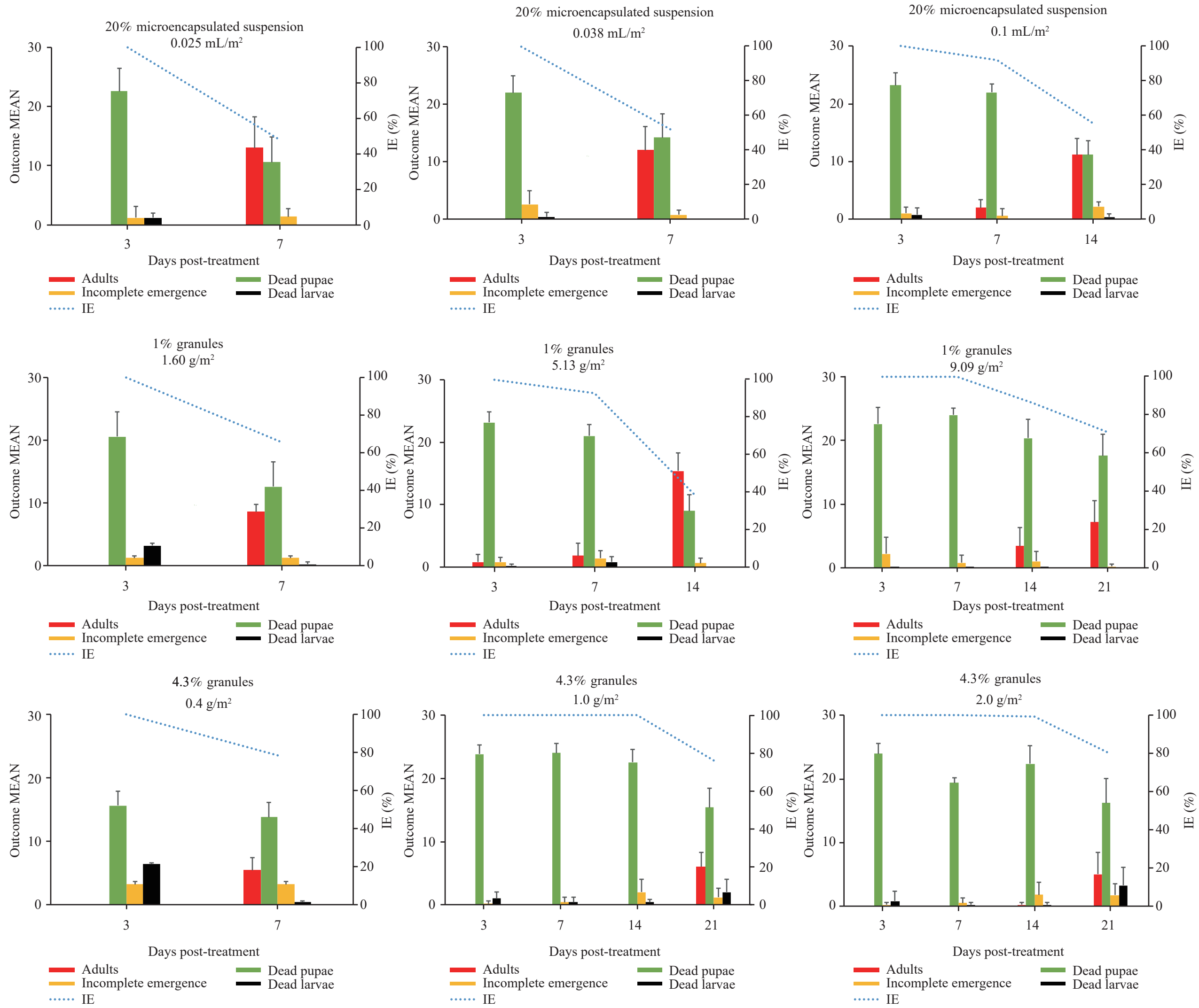

FIGURE 2. Inhibition of emergence (IE) against *Anopheles sinensis* by S-methoprene products with a water depth of 13.0 cm.

in malaria control in the region, with a consistent decrease in annual malaria incidence and deaths (*4*).

Integrated mosquito control, combining environmental management and targeted pesticide use, is essential for reducing mosquito populations and controlling mosquito-borne diseases. Larviciding, which targets the aquatic stages of mosquitoes, is a cost-effective approach in mosquito control compared to adulticiding, which targets adult mosquitoes.

For example, in a study by Zhou et al., it was found that *An. sinensis*, the malaria vector, has developed high resistance to conventional chemical insecticides such as beta-cypermethrin and propoxur in Yunnan Province (*7*).

Over the past 50 years, the USA has established the advantages of S-methoprene against economically significant pests in public health, livestock, stored goods, and agriculture (*6*). However, S-methoprene is rarely used in China, with only the Synergetica Life Science Changzhou company producing S-methoprene products. It rapidly degrades in soil, particularly under sunlight, with a half-life of 10–14 days. The primary microbial degradation product is carbon dioxide (*8*).

To cater to various application scenarios, S-methoprenate products have been developed in multiple forms, with granules and microencapsulated suspensions being the most popular. The milky white turbid microcapsule suspension, diluted with water, was utilized with spraying equipment. The granules used granulated as a natural carrier with a diameter of 1.0–2.0, which was doubled using a specialized binding technique. Both products were extensively evaluated against the index species, utilizing late fourth instar larvae in laboratory and field studies. These larvae, prior to pupation, exhibit high susceptibility to external JHAs due to low levels of internally present juvenile hormone III. The comparable efficacy of the formulations with the S-methoprene technical materials in bioassays justified further field evaluation for both the granules and microencapsulated suspensions.

The formulated S-methoprene product showed the desired initial and residual efficacy against *An. sinensis*. Microcapsules were used at concentrations of 0.025 mL/m^2, 0.038 mL/m^2, and 0.1 mL/m^2, effectively controlling *An. sinensis* for a minimum of 3 days at a water depth of 13 cm. Granules, on the other hand, exhibited longer persistence. The 1% granules provided over 85% control for at least 14 days at a concentration of 9.09 g/m^2. Similarly, at doses of 1.0 g/m^2 and 2.0 g/m^2, the 4.3% granules maintained at least 85% control for 14 days. It is worth noting that microencapsulated suspension and granules have distinct characteristics and are suited for different scenarios. The effectiveness observed can be attributed to the special carrier system, which ensures proper binding, preservation, and transport of the active ingredient. In the case of microcapsule suspension, the methoprene ester is coated within the capsule shell, providing protection against light damage and extending the effectiveness period (*9*). The granules, composed of fossilized diatoms, possess a high water absorption capacity and a large surface area, reducing exposure of the active ingredient to ultraviolet radiation and microbial activity in aquatic ecosystems (*10*).

This study has several limitations primarily due to the semi-field evaluation approach. First, the study excluded factors such as rainfall and sunlight exposure and instead created more controlled microcosms. Additionally, the capture of *An. sinensis* larvae in the field may introduce inevitable systematic errors, as less motile larvae are more likely to be captured.

There is an urgent need to find alternatives to conventional chemical pesticides to address the problem of mosquito resistance, specifically with larvicides that are effective and cost-efficient. S-methoprene has been shown to be safe for non-target organisms and environmentally friendly. Considering its proven performance against *An. sinensis* and its ability to adapt to different scenarios, it would be reasonable to recommend S-methoprene as a standard larvicidal tool for various mosquito habitats, while complying with local regulations.

Conflicts of interest: No conflicts of interest.

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SUPPLEMENTARY MATERIAL

The S-methoprene technical material used in this study was provided by Synergetica Life Science Changzhou Co., LTD. (Jiangsu, China). The S-methoprene 20% microencapsulated suspension (WP20210196 by China Ministry of Agriculture) was also used. The 1% and 4.3% granules used in the experiment were obtained from the same supplier. These granules are yellowish/brownish in color and have a diameter ranging from 1.0 to 2.0 mm, with various shapes including round and angular.

The mosquito species *An. sinensis*, a malaria vector, was obtained from the insectary of the National Key Laboratory of Intelligent Tracking and Forecasting for Infectious Diseases at the National Institute for Communicable Disease Control and Prevention, Chinese Center for Disease Control and Prevention. The insectary maintains a stable and susceptible population of this species. The *An. sinensis* larvae used in the field trial were collected from Yuanjiang County, Yuxi City, Yunnan Province. For laboratory bioassays and on-site insecticide efficacy evaluation, late 4th instar larvae, which were about to pupate, were selected.

Laboratory bioassays were conducted to validate the quality of microencapsulated suspension and granules, as well as the technical grades, using previously established techniques. The S-methoprene technical material was dissolved in pure acetone (Sinopharm Chemical Reagent Co., Ltd, China) and then serially diluted with the same solvent. The microencapsulated suspension was dissolved in dechlorinated water. The granules were powdered in a high-speed blender (Bear Electric Co., Ltd, China) at the maximum speed in interruption mode, and then suspended in tap water by vortexing for 3 minutes.

For the bioassay, five concentrations within the dose range that caused approximately 5%–95% cumulative mortality at adult emergence were used. Each concentration and the untreated control (UTC) were replicated three times. The UTC had the same conditions as the experimental group, except that no insecticide was added.

Each replicate consisted of 25 late 4th instar larvae placed in 200 mL of tap water in a 250 mL disposable Styrofoam cup. The insecticide was administered according to the planned concentration and continuously observed. To promote larval growth until pupation, approximately 150 mg of tropical fish food (Desai Limited, Germany) was added to each bioassay cup. The bioassays were carried out within a temperature range of 27.0 ℃–29.0 ℃.

The inhibition of emergence was recorded when all exposed larvae exhibited outcomes. The concentration-response data were analyzed using SPSS2020 and Probit regression to calculate the concentrations that caused 10%, 50%, and 90% inhibition of emergence (referred to as IE10, IE50, and IE90) respectively, along with their corresponding 95% confidence intervals. In the control group, if the IE was greater than 95%, no correction was performed. For values between 80% and 95%, Abbott's formula was used for correction. If the IE was less than 80%, the experiment was repeated.

The test site chosen for this study was located in Ganzhuang Street, Yuanjiang County, Yuxi City, Yunnan Province. In order to create microcosms, blue plastic boxes were placed in shaded areas. The microcosms measured 0.74 L × 0.54 W × 0.41 D meter. Sandy loam soil, approximately 1.5 cm deep, was added to the microcosms. This soil was collected from a nearby paddy field that had no history of pesticide or herbicide applications. To mimic the breeding environment, the water was maintained at a depth of 13 centimeters. Larval food, in the form of tropical fish food pellets, was added at a rate of approximately 6 grams per microcosm, both after flooding and on a weekly basis as organic enrichment. Daily records were kept for local temperature and humidity. To prevent oviposition by natural mosquito populations, primarily Culex spp., the microcosms were covered with window screens (1.4 mm) during non-sampling periods. Each treatment and UTC was replicated five times. Treatment was initiated on the fifth day after flooding, when the organic enrichment had properly fermented and the soil had settled. The microcapsule suspension was administered at dosages of 0.025 mL/m^2, 0.038 mL/m^2, and 0.100 mL/m^2. The 1% granules were applied at dosages of 1.60 g/m^2, 5.13 g/m^2, and 9.09 g/m^2. The 4.3% granules were applied at dosages of 0.4 g/m^2, 1.0 g/m^2, and 2.0 g/m^2.

In this study, late 4th instar larvae from *An. sinensis* colonies, previously reared in an insectary, were introduced into sentinel cages on days 3, 7, 14, 21, and 28 for testing. Each microcosm contained approximately 50 larvae (Table 1). The sentinel cage was a 1,000 mL square plastic tub with a 2×4 cm window on each of its four sides. The windows were covered with 0.3 mm screen to allow water to flow freely while retaining the larvae and pupae. The cage lid was perforated for ventilation and to prevent debris from entering. To serve as a floater, a plastic foam floater was attached underneath the rim of the cage. Two days after the introduction of larvae, 25 pupae were collected from each sentinel cage and placed in a 250 mL Styrofoam cup filled with 200 mL water from the same microcosm. The remaining larvae and pupae in the sentinel cages were disposed of properly. The cup containing pupae was covered with a window screen (1.4 mm) to confine emerged adults. Different outcomes, such as mortality (in the form of dead pupae mostly, and occasionally incompletely emerged adults with attached wings and/or legs) and successful emergence (only free pupal exuviae were considered), were recorded separately. Once recorded, the adult mosquitoes in the cup were disposed of properly.

The mean IE% for each treatment on each sample day was calculated as follows:

$$\text{IE\%} = 1 - \frac{\text{number of successfully emerged adults}}{\text{total number of pupae isolated}}$$

The statistical analysis used for determining the significance of the IE% among treatments and the UTC was the Chi-square test, with χ^2 values of 3.84 and 6.63 for the significance levels of *P*=0.05 and *P*=0.01, respectively.

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