Journal of Infection 91 (2025) 106528

Contents lists available at ScienceDirect

Journal of Infection

journal homepage: www.elsevier.com/locate/jinf

Parasites and Parasitic Diseases

Clonorchiasis in China: Geospatial modeling of the population infected and at risk, based on national surveillance

Men-Bao Qian [a,b,c,d,e,*,1], Ji-Lei Huang [a,b,c,d,1], Li Wang [f,1], Chang-Hai Zhou [a,b,c,d], Ting-Jun Zhu [a,b,c,d], Hui-Hui Zhu [a,b,c,d], Yun-Ting He [f], Xiao-Nong Zhou [a,b,c,d,e,**], Ying-Si Lai [f,***], Shi-Zhu Li [a,b,c,d,e,**]

[a] National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention (Chinese Center for Tropical Diseases Research), Shanghai, China
[b] NHC Key Laboratory of Parasite and Vector Biology, Shanghai, China
[c] WHO Collaborating Center for Tropical Diseases, Shanghai, China
[d] National Center for International Research on Tropical Diseases, Shanghai, China
[e] School of Global Health, Chinese Center for Tropical Diseases Research, Shanghai Jiao Tong University School of Medicine, Shanghai, China
[f] Department of Medical Statistics, School of Public Health, Sun Yat-sen University, Guangzhou, Guangdong, China

ARTICLE INFO

Article history:
Accepted 30 May 2025
Available online 3 June 2025

Keywords:
Bayesian geostatistical model
Clonorchiasis
Clonorchis sinensis
Surveillance

SUMMARY

Objectives: Clonorchiasis is highly endemic in China. The unavailability of fine-scale distribution of population with infection and at risk hinders the control.
Methods: This study established Bayesian geostatistical models to estimate age- and gender-specific prevalence of Clonorchis sinensis infection at high spatial resolution (5 × 5 km^2), based on the surveillance data in China between 2016 and 2021, together with socioeconomic, environmental and behavioral determinants. The population at risk and under infection, as well as chemotherapy need were then estimated.
Results: In 2020, population-weighted prevalence of 0.67% (95% Bayesian credible interval (BCI): 0.58%–0.77%) was estimated for C. sinensis infection in China, corresponding to 9.46 million (95% BCI: 8.22 million-10.88 million) persons under infection. High prevalence was demonstrated in southern areas, including Guangxi (8.92%, 95% BCI: 7.10%–10.81%) and Guangdong (2.99%, 95% BCI: 2.43%–3.74%). A conservative estimation of 99.13 million (95% BCI: 88.61 million-114.40 million) people were at risk of infection, of which 51.69 million (95% BCI: 45.48 million-57.84 million) need chemotherapy.
Conclusions: Clonorchiasis is an important public health problem in China, especially in southern areas, due to the huge population at risk and large number of people under infection. Implementation of chemotherapy is urged to control the morbidity.

Introduction

Clonorchiasis, belonging to food-borne trematodiasis, is caused by the ingestion of raw freshwater fish containing the infective metacercariae of *Clonorchis sinensis*.[1,2] Clonorchiasis causes diverse symptoms and morbidities, including gallstone, cholecystitis, and cholangitis.[3–6] In particular, *C. sinensis* is a definite carcinogen, leading to fatal cholangiocarcinoma.[7] Clonorchiasis is endemic in eastern Asia, including China, South Korea, northern Vietnam and far east of Russia.[8,9] Globally, a conservative estimation of 15 million persons are infected with *C. sinensis*.[8] The estimated population under infection in China was about 5 million in 1988–1992, 13 million in 2001–2004 and 6 million in 2014–2015, according to three national surveys.[10] An estimation of 15 million in 2010 was also argued based on a geostatistical modeling study.[11] The significant variation of number on the one hand is due to the change in prevalence, but on the other hand, it demonstrates the lack of high-quality and accurate epidemiological data for clonorchiasis.

* Correspondence to: National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention (Chinese Center for Tropical Diseases Research), No. 207 Rui Jin Er Road, Shanghai 200025, China.
** Corresponding authors at: National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention (Chinese Center for Tropical Diseases Research), Shanghai, China.
*** Corresponding author.
E-mail addresses: qianmb@nipd.chinacdc.cn (M.-B. Qian), zhouxn1@chinacdc.cn (X.-N. Zhou), laiys3@mail.sysu.edu.cn (Y.-S. Lai), lisz@chinacdc.cn (S.-Z. Li).
[1] These authors contributed equally to this work.

https://doi.org/10.1016/j.jinf.2025.106528
0163-4453/

World Health Organization (WHO) aims to intensify the global control of food-borne trematodiasis, including clonorchiasis, in the road map for controlling neglected tropical diseases (2021–2030).[12] Chemotherapy is the pillar for tackling clonorchiasis, because persistent damage could be exerted by *C. sinensis* due to its long survival in human beings, usually over 20 years.[12–14] However, the population at risk in China and corresponding chemotherapy needs have not yet been illuminated, which hinders the implementation of precise intervention.

Thus, accurate and fine-scale distributions are expected to be established for the population under infection as well as the population at risk and corresponding chemotherapy needs of clonorchiasis. We integrated the updated surveillance data of clonorchiasis in China and socioeconomic, environmental and behavioral determinants, and applied the geostatistical modeling technique to map the fine-scale infection distribution. Then, we estimated the number of population at risk and corresponding chemotherapy needs.

Methods

Study design

This study first estimated the national fine-scale infection distribution for clonorchiasis in China, through the geostatistical modeling technique, which integrated the epidemiological data and socioeconomic, environmental and behavioral determinants. Based on the prevalence distribution, the population under infection was captured. The high-resolution prevalence distribution was further aggregated at the county level, which was used to identify number of counties in different prevalence levels. The population at risk was estimated in two scenarios (A and B), in which a prevalence threshold of 1% and 0.1% at county level were respectively adopted to separate out the endemic areas. Corresponding to the two scenarios, the population need for chemotherapy was modeled under two strategies (A and B). Correspondingly, the number of drugs needed was also estimated.

Epidemiological data, and environmental, socioeconomic, and behavioral covariates

Age- and gender-specific prevalence of *C. sinensis* infection at village/community level and the behavior of ingesting raw freshwater fish locally between 2016 and 2021 was retrieved from the National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention (Chinese Center for Tropical Diseases Research). In each year, about 300 counties were surveyed. Each included county was divided into five parts based on its geography. One town was then sampled from each part and then one village/community was sampled from each town. About 200 persons from each village/community were included as participants. One fresh fecal sample was collected from each participant and then examined for *C. sinensis* eggs by the Kato-Katz method.[15] Two smears were prepared for each samples and the number of eggs was recorded quantitatively. The heads of the villages/communities were asked whether local persons having the behavior of ingesting raw freshwater fish.

Environmental factors included land surface temperature (LST), normalized difference vegetation index (NDVI), land cover, elevation, precipitation, distance to water bodies, climate zones, soil moisture, soil types, soil pH, and soil erosion, while socioeconomic factors contained GDP, nighttime lights, human influence index (HII), urban extents, travel time to the nearest big city, and travel time to healthcare (Table S1). In addition, the probability of local practice of ingesting raw freshwater fish was considered as a behavior factor, which was estimated at a 5 × 5 km^2 spatial resolution based on Bayesian geostatistical modeling of the survey data on heads of the villages/communities mentioned above (Method S1 and Fig. S1).

The study was approved by the Ethical Review Committee in National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention (Chinese Center for Tropical Diseases Research) (Reference No.: 2021006).

Statistical analysis

The participants in each village/community were divided into five age groups for both genders, namely 0–14, 15–29, 30–44, 45–59 and over 60 years old. More on the data process and variable selection procedure were shown in Method S2.

Prevalence of *C. sinensis* infection was modeled using Bayesian geostatistical logistic regression, incorporating both the fixed effects of the predictors and spatial random effects (Method S3).[16–18] A hurdle model was also employed to perform sensitivity analysis, as the observed data included a large number of zero results, referred as the zero-inflated issue (Method S4).[19] The model with the lowest mean absolute error (MAE) from 5-fold cross-validation was selected as the optimal one. Besides MAE, other evaluation metrics, including mean error (ME), the proportion of Bayesian credible interval (BCI) covering observed values and corresponding width of BCI were calculated to comprehensively assess the model's performance. This multi-metric approach ensured a thorough understanding of each model's accuracy and reliability. The risk of *C. sinensis* infection was estimated on a regular grid covering 557 549 pixels across China, with a spatial resolution of 5 × 5 km^2. The pixel-based age- and gender-specific risk maps were first established, and then, by projecting to the gridded population, the population-adjusted prevalence was estimated, either at pixel-level or aggregated administrative levels (e.g., county, provincial and national level).

To estimate the need for chemotherapy, the prevalence was categorized into five groups at the county level: ≥ 20%, 10%−20%, 1%−10%, 0.1%−1%, and < 0.1%. The study defined endemic areas as locations where the prevalence of *C. sinensis* infection met specific thresholds. Two scenarios (A and B) were estimated with a prevalence threshold of 1% and 0.1%, respectively. Correspondingly, two chemotherapy strategies (A and B) were analyzed (Table S2). Mass chemotherapy once a year was modeled for prevalence ≥ 10% in both strategies, following the WHO recommendation.[14] In areas with lower prevalence, selective chemotherapy was employed, namely selective chemotherapy targeting a prevalence of 1%−10% in Strategy A and a prevalence of 0.1%−10% in Strategy B. For selective chemotherapy, the individual with the behavior of ingesting raw freshwater fish was targeted. The positive and negative predictive values (PPV and NPV) of the behavior for selecting individuals for chemotherapy in the group of 1%−10% were 87.30% and 29.76%, while that in the group of 0.1%−1% were 23.81% and 3.24%, respectively.[20] Praziquantel, the drug recommended by WHO for clonorchiasis, was assumed to be administered at a dose of 75 mg/kg of body weight.[21] An average weight of 35 kg, 55 kg and 65 kg was adopted for children below 14, adult female (over 14) and adult male (over 14).[22] Each table of praziquantel was set as 200 mg.

R (version 4.2.3) was utilized for the complete statistical analysis, and the Bayesian geostatistical models were implemented using INLA package.[17] The maps were created using ArcGIS (version 10.1).

Results

Epidemiological profiles of observed data in the surveillance spots

Out of 1 873 668 participants from 31 provinces, 18 550 were detected with *C. sinensis* infection, yielding a crude prevalence of 0.99% (Fig. S2). Positive cases were detected in 19 provinces, with high crude prevalence in Guangxi (9.22%, 6740 out of 73 112),

Table 1
Observed and estimated prevalence, and estimated population under infection with *Clonorchis sinensis* by provinces in China.

Provinces	No. examined	No. positive	Proportion (%)	Prevalence (%) (median and 95% BCI)	Population under infection× 1000 (median and 95% BCI)
Anhui	91689	30	0.03	0.08 (0.05, 0.16)	47.50 (28.46, 93.29)
Beijing	12537	0	0.00	0.00 (0.00, 0.16)	0.51 (0.01, 44.42)
Chongqing	29182	1	0.00	0.04 (0.01, 0.20)	9.58 (2.78, 54.12)
Fujian	63199	109	0.17	0.06 (0.03, 0.14)	24.25 (12.14, 58.09)
Gansu	67907	1	0.00	0.02 (0.00, 0.21)	4.90 (0.90, 52.85)
Guangdong	108375	3546	3.27	2.99 (2.43, 3.74)	3712.13 (3008.68, 4635.63)
Guangxi	73112	6740	9.22	8.92 (7.10, 10.81)	4204.31 (3347.15, 5096.85)
Guizhou	53809	322	0.60	0.34 (0.23, 0.55)	115.65 (77.63, 184.73)
Hainan	14134	0	0.00	0.02 (0.00, 0.55)	1.84 (0.13, 55.69)
Hebei	93948	0	0.00	0.01 (0.00, 0.12)	7.46 (1.18, 94.33)
Heilongjiang	86762	3754	4.33	1.29 (1.04, 1.63)	510.75 (409.27, 644.44)
Henan	111687	1	0.00	0.02 (0.01, 0.12)	16.70 (5.12, 113.77)
Hubei	55885	0	0.00	0.02 (0.00, 0.19)	11.62 (2.10, 101.16)
Hunan	142219	942	0.66	0.17 (0.13, 0.25)	113.57 (84.04, 164.22)
Jiangsu	44392	18	0.04	0.07 (0.03, 0.18)	53.69 (25.05, 148.18)
Jiangxi	27515	112	0.41	0.17 (0.07, 0.52)	83.41 (34.17, 248.70)
Jilin	76779	2912	3.79	0.71 (0.52, 0.99)	194.87 (142.41, 271.23)
Liaoning	82100	14	0.02	0.02 (0.00, 0.13)	8.14 (2.17, 58.64)
Neimenggu	49997	0	0.00	0.04 (0.01, 0.31)	9.94 (2.71, 81.06)
Ningxia	21666	0	0.00	0.01 (0.00, 0.27)	0.38 (0.02, 19.55)
Qinghai	35842	0	0.00	0.00 (0.00, 0.17)	0.32 (0.03, 10.71)
Shaanxi	44883	0	0.00	0.02 (0.00, 0.20)	6.74 (0.74, 76.52)
Shandong	76591	9	0.01	0.04 (0.02, 0.15)	39.88 (15.33, 154.34)
Shanghai	11241	0	0.00	0.00 (0.00, 0.12)	1.13 (0.03, 37.28)
Shanxi	66278	1	0.00	0.01 (0.00, 0.17)	4.49 (0.67, 64.29)
Sichuan	102324	30	0.03	0.06 (0.03, 0.14)	50.38 (27.07, 109.53)
Tianjin	10098	0	0.00	0.00 (0.00, 0.08)	0.51 (0.01, 14.11)
Xinjiang	76995	6	0.01	0.05 (0.02, 0.25)	13.35 (4.47, 62.64)
Xizang	20836	0	0.00	0.02 (0.00, 0.57)	1.06 (0.07, 26.51)
Yunnan	70325	2	0.00	0.04 (0.01, 0.20)	20.31 (6.08, 97.90)
Zhejiang	51361	0	0.00	0.01 (0.00, 0.11)	8.41 (1.36, 69.94)
Total	1873668	18550	0.99	0.67 (0.58, 0.77)	9456.61 (8220.14, 10877.16)

Table 2
Observed and estimated prevalence, and estimated population under infection with *Clonorchis sinensis* by genders and age groups in China.

	No. examined	No. positive	Proportion (%)	Prevalence (%) (median and 95% BCI)	Population under infection × 1000 (median and 95% BCI)
Male					
0–14	217581	358	0.16	0.25 (0.20, 0.30)	323.83 (268.86, 400.18)
15–29	80538	660	0.82	0.86 (0.74, 1.00)	1154.96 (990.83, 1341.14)
30–44	162991	3115	1.91	1.15 (1.01, 1.30)	1918.87 (1682.77, 2176.90)
45–59	219738	5107	2.32	1.01 (0.89, 1.13)	1717.11 (1523.38, 1921.32)
60+	230911	2828	1.22	0.85 (0.75, 0.96)	1020.84 (899.40, 1145.47)
Subtotal	911759	12068	1.32	0.85 (0.75, 0.97)	6145.75 (5396.05, 6987.85)
Female					
0–14	193656	243	0.13	0.12 (0.10, 0.16)	133.75 (107.98, 173.81)
15–29	91132	445	0.49	0.46 (0.38, 0.55)	593.45 (493.97, 712.29)
30–44	182773	1644	0.90	0.63 (0.54, 0.74)	1003.96 (858.44, 1180.24)
45–59	247883	2549	1.03	0.57 (0.49, 0.65)	932.88 (800.85, 1070.77)
60+	246465	1601	0.65	0.53 (0.45, 0.61)	655.33 (555.57, 752.33)
Subtotal	961909	6482	0.67	0.48 (0.41, 0.56)	3319.75 (2817.86, 3879.39)
Total	1873668	18550	0.99	0.67 (0.58, 0.77)	9456.61 (8220.14, 10877.16)

Heilongjiang (4.33%, 3754 out of 86 762), Jilin (3.79%, 2912 out of 76 779), and Guangdong (3.27%, 3546 out of 108 375) (Table 1). Higher prevalence was demonstrated in male (1.32%, 12 068 out of 911 759) than in female (0.67%, 6482 out of 961 909) (Table 2). High prevalence was shown in the age groups older than 30 years.

Performance of models and important determinants

Both Bayesian logistic regression and hurdle model for prevalence exhibited reasonable and similar model performance (Table S3, Table S4, Fig. S3, and Fig. S4). The MAE was lower in the former compared to the latter (0.44% vs 0.60%). Although the 95% coverage was lower in the former than in the latter (81.46% vs 88.42%), the width in the former showed superiority than the latter (1.00% vs 3.42%). After further considering the relative simplicity, logistic regression modeling framework was finally adopted. The model identified nine factors as influencing factors, including age, gender, elevation, HII, nighttime lights, precipitation, distance to the nearest open water body, the probability of local practice of ingesting raw freshwater fish and NDVI (Table S3).

National prevalence

High infection risk distributed in southern and northeastern China, particularly in the northern, southwestern, and some eastern regions of Guangxi, the Pearl River Delta region in Guangdong, as well as in the northwestern regions of Jilin, the southwestern and northeastern regions of Heilongjiang (Fig. 1). The population-adjusted national prevalence was 0.67% (95% BCI: 0.58%–0.77%), while at provincial level, highest prevalence was demonstrated in Guangxi (8.92%, 95% BCI: 7.10%–10.81%), followed by Guangdong (2.99%, 95% BCI: 2.43–3.74), Heilongjiang (1.29%, 95% BCI: 1.04%–1.63%) and Jilin

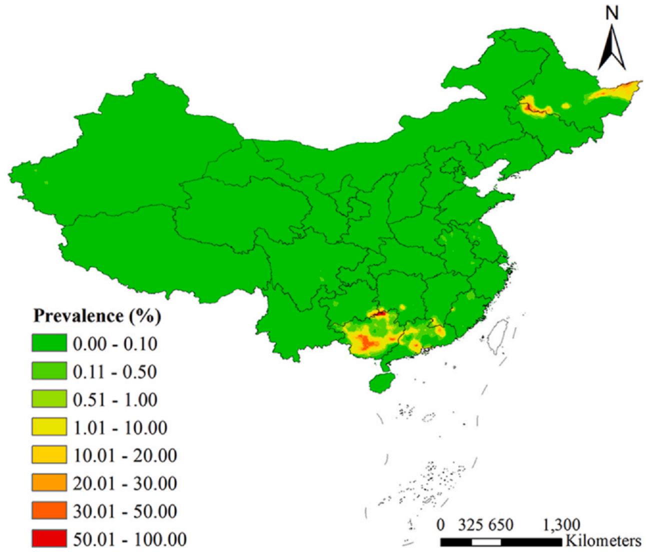

Fig. 1. Estimated prevalence of *Clonorchis sinensis* infection across China at 5×5 km^2 resolution.

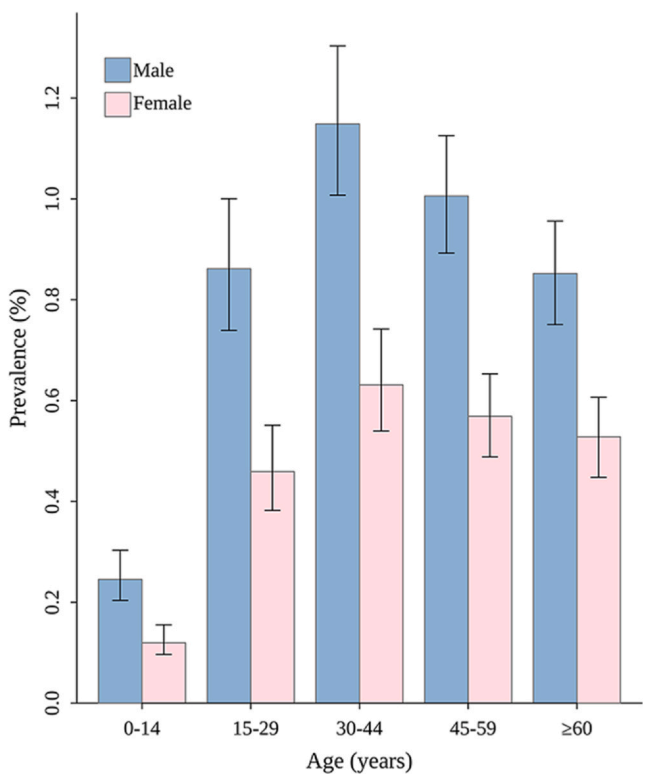

Fig. 2. Estimated prevalence of *Clonorchis sinensis* infection by genders and age groups in China.

(0.71%, 95% BCI: 0.52%–0.99%) (Table 1). The prevalence was higher in male (0.85%, 95% BCI: 0.75%–0.97%) than in female (0.48%, 95% BCI: 0.41%–0.56%) (Table 2, Fig. 2). And those aged 30–59 years old showed highest prevalence compared to other age groups (Table 2, Fig. 2).

Population under infection

Totally, 9.46 million (95% BCI: 8.22 million-10.88 million) people were estimated to be infected with *C. sinensis*, while Guangxi and Guangdong harbored the most, with a figure of 4.20 million (95% BCI: 3.35 million-5.10 million) and 3.71 million (95% BCI: 3.01 million and 4.64 million), respectively (Table 1). The estimated population under infection was 6.15 million (95% BCI: 5.40 million-6.99 million) in male and 3.32 million (95% BCI: 2.82 million-3.88 million) in female (Table 2). The number exceeded 1 million in those aged 30–44, 45–59, 15–29, and 60+ in male and aged 30–44 in female.

Population at risk and with chemotherapy needs

The number of counties with a prevalence over 20%, 10%–20%, 1%–10%, and 0.1%–1% was 22 (95% BCI: 15–28), 24 (95% BCI: 17–30), 121 (95% BCI: 103–143) and 336 (95% BCI: 283–395), respectively (Table 3). The corresponding population was 13.62 million (95% BCI: 8.54 million-17.37 million), 15.70 million (95% BCI: 8.14 million-21.73 million), 69.93 million (95% BCI: 58.45 million-85.49 million), and 179.99 million (95% BCI: 145.79 million-217.56 million). The estimated population at risk was 99.13 million (95% BCI: 88.61 million-114.40 million) under scenario A and 280.06 million (95% BCI: 244.00 million-320.33 million) under scenario B (Table 4). The population requiring chemotherapy was 51.69 million (95% BCI: 45.48 million-57.84 million) in strategy A and 57.60 million (95% BCI: 51.25 million-63.94 million) in strategy B (Table 4, Fig. S5 and Fig. S6), while the corresponding drugs needed in tablets was 1080.82 million (95% BCI: 948.48 million-1210.94 million) and 1203.91 million (95% BCI: 1068.79 million-1337.20 million) (Table S5, Fig. S7 and Fig. S8).

Discussion

This study demonstrated a heavy burden of clonorchiasis in China in terms of the huge population at risk and large number of individuals under infection. The prevalence was especially high in Guangxi and Guangdong in southern areas, while it was also high in Heilongjiang and Jilin in northeastern areas. Adult males were predominantly afflicted. Overall, this study explicitly urges the implementation of interventions to control the morbidity of clonorchiasis in China. The chemotherapy needs estimated at county level in this study also provide reference for precise intervention.

As neglected tropical diseases, epidemiology data for food-borne trematodiasis are very scarce.[23] In China, high-resolution epidemiological data are available for many parasitic diseases, e.g. village level for schistosomiasis and malaria and county level for echinococcosis.[24–26] However, only provincial-level data were available for clonorchiasis owing to several national surveys. On the other hand, spatial variation is high for clonorchiasis due to the differential distribution of determinants involved in the transmission, e.g., the distribution of the two intermediate hosts and the dietary habit of ingesting raw freshwater fish.[9,27] Thus, the unavailability of high-resolution distribution hinders the control of clonorchiasis.[23] In this study, we applied the geostatistical modeling techniques to establish high-resolution map for prevalence. Because the transmission of clonorchiasis is driven by the distribution of two intermediate hosts and individuals' dietary behavior, thus, any factor involved in the transmission could influence the distribution of clonorchiasis and subsequently be employed to model the endemicity. In this study, diverse determinants were found to be relevant to the prevalence. The ingestion of raw freshwater fish is of crucial importance, which is well demonstrated in many studies.[20,28] This dietary habit was differential in different genders and ages,[29] and thus, these two factors were included as important determinants. Economic status is relevant to the practice of ingesting raw freshwater fish at community and individual level, and thus HII is also included in the model.[28,30] The elevation, precipitation, distance to nearly water and NDVI are highly relevant to the distribution of intermediate hosts.[9,11] It is well documented that high elevation is associated with a low

Table 3
Number of counties by provinces and prevalence levels of *Clonorchis sinensis* infection in China.

Provinces	No. counties				
	< 0.1% (95% BCI)	0.1% - < 1% (95% BCI)	1% - < 10% (95% BCI)	10% - < 20% (95% BCI)	≥ 20% (95% BCI)
Anhui	84 (71, 93)	20 (11, 32)	0 (0, 3)	0 (0, 0)	0 (0, 0)
Beijing	16 (10, 16)	0 (0, 6)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Chongqing	35 (25, 38)	3 (0, 12)	0 (0, 2)	0 (0, 0)	0 (0, 0)
Fujian	67 (55, 75)	16 (8, 29)	1 (0, 4)	0 (0, 0)	0 (0, 0)
Gansu	83 (70, 87)	4 (0, 13)	0 (0, 4)	0 (0, 0)	0 (0, 0)
Guangdong	42 (33, 49)	40 (30, 50)	33 (26, 41)	7 (3, 10)	3 (0, 5)
Guangxi	5 (1, 10)	34 (26, 42)	45 (37, 55)	10 (5, 14)	16 (11, 21)
Guizhou	66 (49, 76)	19 (9, 35)	2 (0, 5)	1 (0, 2)	0 (0, 1)
Hainan	23 (13, 24)	1 (0, 9)	0 (0, 2)	0 (0, 0)	0 (0, 0)
Hebei	164 (140, 167)	3 (0, 21)	0 (0, 5)	0 (0, 0)	0 (0, 0)
Heilongjiang	77 (62, 87)	23 (13, 34)	17 (11, 24)	4 (2, 7)	2 (0, 4)
Henan	152 (130, 157)	5 (0, 25)	0 (0, 4)	0 (0, 0)	0 (0, 0)
Hubei	98 (81, 103)	5 (0, 19)	0 (0, 5)	0 (0, 0)	0 (0, 0)
Hunan	100 (87, 108)	18 (11, 31)	2 (2, 5)	1 (0, 1)	0 (0, 1)
Jiangsu	77 (62, 87)	19 (9, 32)	0 (0, 5)	0 (0, 0)	0 (0, 0)
Jiangxi	81 (63, 92)	15 (4, 30)	4 (1, 10)	0 (0, 1)	0 (0, 0)
Jilin	48 (39, 53)	6 (2, 15)	4 (3, 7)	1 (0, 2)	0 (0, 1)
Liaoning	96 (82, 100)	4 (0, 16)	0 (0, 3)	0 (0, 0)	0 (0, 0)
Neimenggu	94 (82, 101)	8 (2, 17)	1 (0, 6)	0 (0, 1)	0 (0, 0)
Ningxia	22 (16, 22)	0 (0, 5)	0 (0, 2)	0 (0, 0)	0 (0, 0)
Qinghai	45 (38, 45)	0 (0, 5)	0 (0, 2)	0 (0, 0)	0 (0, 0)
Shaanxi	102 (85, 107)	4 (0, 17)	0 (0, 5)	0 (0, 0)	0 (0, 0)
Shandong	122 (102, 133)	13 (3, 31)	0 (0, 4)	0 (0, 0)	0 (0, 0)
Shanghai	16 (10, 16)	0 (0, 6)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Shanxi	114 (94, 117)	3 (0, 20)	0 (0, 5)	0 (0, 0)	0 (0, 0)
Sichuan	154 (137, 169)	28 (14, 45)	1 (0, 5)	0 (0, 0)	0 (0, 0)
Tianjin	16 (12, 16)	0 (0, 4)	0 (0, 0)	0 (0, 0)	0 (0, 0)
Xinjiang	96 (86, 104)	10 (3, 19)	1 (0, 5)	0 (0, 1)	0 (0, 0)
Xizang	73 (65, 74)	1 (0, 8)	0 (0, 2)	0 (0, 0)	0 (0, 0)
Yunnan	118 (100, 126)	10 (3, 26)	1 (0, 6)	0 (0, 0)	0 (0, 0)
Zhejiang	87 (74, 90)	3 (0, 15)	0 (0, 3)	0 (0, 0)	0 (0, 0)
Total	2345 (2278, 2403)	336 (283, 395)	121 (103, 143)	24 (17, 30)	22 (15, 28)

Table 4
Population at risk of *Clonorchis sinensis* infection and corresponding chemotherapy needs by provinces in China.

Provinces	No. population at risk of infection (× 1000)		No. population with chemotherapy needs (× 1000)	
	Scenario A	Scenario B	Strategy A	Strategy B
Anhui	0.00 (0.00, 2249.04)	14165.02 (7481.20, 22004.24)	0.00 (0.00, 693.01)	486.69 (245.26, 1164.74)
Beijing	0.00 (0.00, 0.00)	0.00 (0.00, 10888.17)	0.00 (0.00, 0.00)	0.00 (0.00, 486.68)
Chongqing	0.00 (0.00, 1517.56)	2297.88 (0.00, 9327.11)	0.00 (0.00, 463.68)	77.45 (0.00, 708.65)
Fujian	255.55 (0.00, 1228.18)	5340.28 (1877.84, 13265.91)	78.31 (0.00, 383.73)	247.98 (81.36, 712.09)
Gansu	0.00 (0.00, 1209.78)	1132.35 (0.00, 5536.49)	0.00 (0.00, 411.40)	41.31 (0.00, 525.98)
Guangdong	46503.45 (38406.92, 55886.46)	85891.32 (78222.17, 95495.54)	24016.20 (18840.37, 29253.69)	25283.76 (20239.66, 30309.44)
Guangxi	32130.28 (29144.59, 35867.56)	45332.12 (42666.23, 46856.33)	19200.38 (17250.93, 21177.32)	19619.52 (17773.88, 21552.05)
Guizhou	854.24 (597.14, 2649.79)	8211.15 (3885.21, 14707.47)	637.22 (370.13, 1105.47)	861.24 (530.46, 1457.20)
Hainan	0.00 (0.00, 1276.90)	453.88 (0.00, 5073.21)	0.00 (0.00, 430.71)	14.80 (0.00, 527.27)
Hebei	0.00 (0.00, 2157.41)	1386.30 (0.00, 12461.55)	0.00 (0.00, 696.06)	47.28 (0.00, 1087.06)
Heilongjiang	7602.26 (6201.15, 9636.95)	15272.55 (11967.91, 20063.06)	3413.48 (2783.35, 4233.58)	3665.28 (3034.42, 4497.00)
Henan	0.00 (0.00, 2360.56)	3832.05 (0.00, 16442.62)	0.00 (0.00, 775.26)	130.44 (0.00, 1294.27)
Hubei	0.00 (0.00, 2113.45)	2405.34 (0.00, 11608.23)	0.00 (0.00, 707.77)	87.13 (0.00, 1048.18)
Hunan	1507.56 (1507.56, 2852.49)	10723.60 (6256.21, 18231.13)	637.67 (605.93, 1032.12)	973.99 (768.74, 1408.52)
Jiangsu	0.00 (0.00, 3465.91)	14841.15 (6692.74, 28093.45)	0.00 (0.00, 1064.42)	551.22 (218.73, 1766.13)
Jiangxi	1625.61 (721.80, 5137.90)	8877.11 (3247.78, 19096.44)	549.55 (223.22, 1916.24)	788.91 (405.99, 2143.31)
Jilin	2690.62 (2690.62, 4145.91)	6449.38 (3791.57, 10698.08)	1162.77 (883.37, 1701.78)	1292.63 (1002.56, 1909.90)
Liaoning	0.00 (0.00, 1519.06)	1830.75 (0.00, 8935.46)	0.00 (0.00, 471.00)	62.69 (0.00, 682.01)
Neimenggu	69.14 (0.00, 1955.19)	1989.39 (490.94, 5990.07)	21.04 (0.00, 669.39)	97.73 (16.36, 789.94)
Ningxia	0.00 (0.00, 578.67)	0.00 (0.00, 1840.67)	0.00 (0.00, 176.27)	0.00 (0.00, 253.76)
Qinghai	0.00 (0.00, 307.32)	0.00 (0.00, 1251.82)	0.00 (0.00, 99.35)	0.00 (0.00, 115.86)
Shaanxi	0.00 (0.00, 1922.76)	1371.30 (0.00, 9018.10)	0.00 (0.00, 610.32)	53.25 (0.00, 802.77)
Shandong	0.00 (0.00, 3738.30)	10216.59 (2342.19, 26461.10)	0.00 (0.00, 1244.31)	368.55 (76.56, 1837.21)
Shanghai	0.00 (0.00, 0.00)	0.00 (0.00, 12106.95)	0.00 (0.00, 0.00)	0.00 (0.00, 469.83)
Shanxi	0.00 (0.00, 1778.62)	847.42 (0.00, 8845.99)	0.00 (0.00, 550.44)	29.16 (0.00, 751.30)
Sichuan	159.09 (0.00, 2090.17)	12829.84 (5986.98, 22316.72)	52.88 (0.00, 735.17)	493.02 (196.60, 1169.28)
Tianjin	0.00 (0.00, 0.00)	0.00 (0.00, 4729.31)	0.00 (0.00, 0.00)	0.00 (0.00, 165.77)
Xinjiang	70.41 (0.00, 1284.39)	2934.71 (855.73, 5710.52)	21.83 (0.00, 429.83)	133.26 (30.95, 529.86)
Xizang	0.00 (0.00, 954.70)	280.75 (0.00, 1463.44)	0.00 (0.00, 299.44)	9.34 (0.00, 309.62)
Yunnan	151.81 (0.00, 2555.45)	4215.65 (882.64, 11294.60)	49.39 (0.00, 822.51)	191.51 (30.51, 995.45)
Zhejiang	0.00 (0.00, 2011.00)	1504.46 (0.00, 11507.53)	0.00 (0.00, 618.28)	54.74 (0.00, 835.96)
Total	99132.07 (88606.07, 114400.74)	280063.31 (243998.29, 320333.30)	51687.02 (45484.23, 57837.70)	57601.80 (51248.64, 63940.70)

prevalence of clonorchiasis and opisthorchiasis (another important liver fluke disease endemic in Southeast Asia), which is attributed to the habitant preference of snail hosts.[31,32] Precipitation determines the formation of water bodies. Especially, a lack of precipitation will increase the mortality of snails.[2] Nearing to the water increases the accessibility to freshwater fish.[33] It is interesting that two distant hotspots of clonorchiasis are distributed in southern and northeastern China. On the one hand, the suitable environments, e.g., low elevation and high precipitation in both southern and northeastern China, favor the survival and reproduction of intermediate hosts, especially snails. On the other hand, people in these two regions both prefer the ingestion of raw freshwater fish.[30,34,35]

The finding of 9.46 million persons under infection with *C. sinensis* demonstrates high endemicity of this disease in China. Taking consideration of the significant control and even elimination of many other parasitic diseases in China, clonorchiasis is becoming more and more important. It should be noticed that a significant variation of our finding with that of national survey in 2014–2015 in which 6 million were estimated. In that national survey, the investigation of clonorchiasis in rural areas was combined with that of soil-transmitted helminthiases, while a special survey was implemented for clonorchiasis in urban areas. A prevalence of 0.71% in urban areas and 0.23% in rural areas was demonstrated. Thus, it is argued that the sampling in rural areas targeting soil-transmitted helminthiases underestimated clonorchiasis.[10]

This study not only provided the accurate population under infection, but also estimated the population at risk. It is challenging to estimate the population at risk for clonorchiasis due to the difficulty in classifying endemic areas. The endemicity of clonorchiasis is determined by both the distribution of intermediate hosts, especially snails and the dietary habit of ingesting raw freshwater fish. On one hand, the existence of animal reservoirs could complete the circulation while people are not involved in if they don't hold the raw-fish-eating habit.[36] On the other hand, the transportation of freshwater fish spreads the transmission into areas where there are no intermediate snail hosts, especially in large cities.[30] Thus, this study reversely utilized the prevalence data to estimate the population at risk. It was argued that the cases detected in the areas with a very low prevalence probably consumed raw freshwater fish in high prevalent areas during their trip or earlier living there, which may not cause local transmission.[37,38] Because there was no availability of definite criteria, we adopted two scenarios with different prevalence thresholds (1% and 0.1%, respectively). WHO estimated that 265 million persons were at risk of clonorchiasis in China in 1990s,[39] while a number of approximate 600 million was estimated in 2000s in other study.[33] Our finding significantly increases the accuracy through the classification of county-level prevalence data, which will benefit the precise adoption of intervention.

This study has important implications for the control of clonorchiasis. First, clonorchiasis is becoming an important public health problem in China, compared to the significant control of other neglected tropical diseases. Furthermore, China harbors the largest cases in the globe, because the number of *C. sinensis* cases is estimated to be 1.42 million in South Korea and 1 million in Vietnam, respectively.[9] Thus, the adoption of intensified control is urged in China. Second, chemotherapy should be of crucial importance nowadays due to the high endemicity, especially in southern areas. Mass chemotherapy and selective chemotherapy are suggested based on the prevalence level. Third, the variations by populations should also be considered. Because of the high prevalence, adult males should be prioritized, in which a high coverage of chemotherapy is needed.[22] Fourth, the ingestion of raw freshwater fish is of crucial importance in clonorchiasis. Thus, education is advocated. Compared to adult males, females and children are more prone to avoiding or abandoning this practice and thus education for them could sustain the control effectiveness.[40] Finally, environments are important in the completion of *C. sinensis* infection, and thus environmental modification to block the contamination of feces into water should also be integrated to increase the sustainability.

This study has several limitations. First, we took the surveillance data of clonorchiasis between 2016 and 2021 as a cross-sectional study, which didn't illuminate the time trend. The surveillance spots in each year were not randomly sampled, which would lead to misunderstanding in time trend if data were analyzed by year. Especially, *C. sinensis* survives in human beings for over 20 years,[13] and no large-scale control has been implemented during this time. Additionally, both theoretical models and field observations demonstrate a high re-infection of clonorchiasis.[41,42] Thus, it is believed that the prevalence of clonorchiasis would not be changed significantly during the period. However, it is still valuable to establish temporal trends in the future through longitudinal designs and improved sampling strategies. Second, the data on the practice of ingesting raw freshwater fish was only qualitatively collected at the village/community level. This may affect the precision of the model's weight estimation for this risk factor. Future research is expected to collect more detailed data, such as individual-level consumption frequency and quantity. Third, high-quality distribution data for intermediate hosts, especially the first intermediate host-snails, will further increase the quality of the estimated distribution. However, this data is not available. Indeed, the inclusion of the environmental determinants indirectly reflected the contribution of the distribution of intermediate hosts. However, it is still expected to establish a national database for intermediate hosts in the future.

Conclusions

This study demonstrates the importance of clonorchiasis as a public health problem in China in terms of the huge population under infection. High prevalence is distributed in the southern areas, while adults, especially men, dominate the burden. Thus, intervention especially chemotherapy is needed to target these highly endemic areas and populations. The estimated population for chemotherapy at county level in this study could guide the adoption of precise intervention for clonorchiasis.

Funding

This work was supported by the National Natural Science Foundation of China (Grant No. 82373645), Shanghai Talent Program, National Key Research and Development Program of China (Grant Nos. 2021YFC2300800 and 2021YFC2300804), National Natural Science Foundation of China (Grant No. 82073665).

Author contributions

MBQ, XNZ, YSL, and SZL conceived and designed this study. MBQ, JLH, LW, CHZ, TJZ, HHZ, and YTH collected the data. MBQ, JLH, LW, YTH, and YSL performed the analysis. MBQ, LW, and YSL drafted the manuscript. XNZ, and SZL made critical revisions of the manuscript. All authors revised the manuscript and approved the final version before submission.

Data availability

Environmental and socioeconomic data are open access (Table S1 in Supplementary Information). Epidemiological and behavioral data are not publicly available but are available on reasonable request after review by the National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention (Chinese Center for Tropical Diseases Research).

Declaration of Competing Interest

The authors declare that they have no competing interests.

Acknowledgements

We thank all the staff from Center for Diseases Control and Prevention or Control Station of Parasitic Diseases at provincial, prefectural and county levels who participated in the field survey.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at doi:10.1016/j.jinf.2025.106528.

References

1. Qian MB, Utzinger J, Keiser J, Zhou XN. *Clonorchiasis. Lancet* 2016;**387**(10020):800–10.
2. Qian MB, Keiser J, Utzinger J, Zhou XN. *Clonorchiasis and opisthorchiasis: epidemiology, transmission, clinical features, morbidity, diagnosis, treatment, and control. Clin Microbiol Rev* 2024;**37**(1):e0000923.
3. Choi D, Lim JH, Lee KT, Lee JK, Choi SH, Heo JS, et al. *Gallstones and Clonorchis sinensis infection: a hospital-based case-control study in Korea. J Gastroenterol Hepatol* 2008;**23**(8 Pt 2):e399–404.
4. Kim MS, Lee JS, Rim HJ. *Studies on the clinical aspects of clonorchiasis in Korea. Korea Univ Med J* 1982;**19**(1):107–21.
5. Qiao T, Ma RH, Luo XB, Luo ZL, Zheng PM. *Cholecystolithiasis is associated with Clonorchis sinensis infection. PLoS One* 2012;**7**(8):e42471.
6. Qian MB, Li HM, Jiang ZH, Yang YC, Lu MF, Wei K, et al. *Severe hepatobiliary morbidity is associated with Clonorchis sinensis infection: the evidence from a cross-sectional community study. PLoS Negl Trop Dis* 2021;**15**(1):e0009116.
7. Bouvard V, Baan R, Straif K, Grosse Y, Secretan B, El Ghissassi F, et al. *A review of human carcinogens–Part B: biological agents. Lancet Oncol* 2009;**10**(4):321–2.
8. Qian MB, Chen YD, Liang S, Yang GJ, Zhou XN. *The global epidemiology of clonorchiasis and its relation with cholangiocarcinoma. Infect Dis Poverty* 2012;**1**(1):4.
9. Xiao HY, Chai JY, Fang YY, Lai YS. *The spatial-temporal risk profiling of Clonorchis sinensis infection over 50 years implies the effectiveness of control programs in South Korea: a geostatistical modeling study. Lancet Reg Health West Pac* 2023;**33**:100697.
10. Qian MB, Zhou CH, Zhu HH, Zhu TJ, Huang JL, Chen YD, et al. *From awareness to action: NIPD's engagement in the control of food-borne clonorchiasis. Adv Parasitol* 2020;**110**:245–67.
11. Lai YS, Zhou XN, Pan ZH, Utzinger J, Vounatsou P. *Risk mapping of clonorchiasis in the People's Republic of China: a systematic review and Bayesian geostatistical analysis. PLoS Negl Trop Dis* 2017;**11**(3):e0005239.
12. WHO. Ending the neglect to attain the Sustainable Development Goals—a road map for neglected tropical diseases 2021–2030; 2020.
13. Attwood HD, Chou ST. *The longevity of Clonorchis sinensis. Pathology* 1978;**10**(2):153–6.
14. WHO. Expert consultation to accelerate control of foodborne trematode infections, taeniasis and cysticercosis; 2017.
15. Ting-Jun Z, Chang-Hai Z, Long-Qi X, Bin Z, Yan-Hong X, Ying-Dan C. *Interpretation of detection of intestinal helminthes-the Kato-Katz method (WS/T 570-2017). Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi* 2018;**30**(5):575–7.
16. Rue H, Martino S, Chopin N. *Approximate Bayesian inference for latent Gaussian models by using integrated nested Laplace approximations. J R Stat Soc Ser B Stat Methodol* 2009;**71**(2):319–92.
17. Lindgren F, Rue H. *Bayesian spatial modelling with R-INLA. J Stat Softw* 2015;**63**:1–25.
18. Lindgren F, Rue H, Lindström J. *An explicit link between Gaussian fields and Gaussian Markov random fields: the stochastic partial differential equation approach. J R Stat Soc Ser B Stat Methodol* 2011;**73**(4):423–98.
19. Heilbron DC. *Zero-altered and other regression models for count data with added zeros. Biom J* 1994;**36**(5):531–47.
20. Qian MB, Jiang ZH, Ge T, Wang X, Zhou CH, Zhu HH, et al. *Rapid screening of Clonorchis sinensis infection: performance of a method based on raw-freshwater fish-eating practice. Acta Trop* 2020;**207**:105380.
21. Qian MB, Patel C, Palmeirim MS, Wang X, Schindler C, Utzinger J, et al. *Efficacy of drugs against clonorchiasis and opisthorchiasis: a systematic review and network meta-analysis. Lancet Microbe* 2022;**3**(8):e616–24.
22. Qian MB, Zhou CH, Zhu HH, Chen YD, Zhou XN. *Cost yield of different treatment strategies against Clonorchis sinensis infection. Infect Dis Poverty* 2021;**10**(1):136.
23. Qian MB, Zhou XN. *Human liver flukes in China and ASEAN: time to fight together. PLoS Negl Trop Dis* 2019;**13**(4):e0007214.
24. Zhang L, He J, Yang F, Dang H, Li Y, Guo S, et al. *Progress of schistosomiasis control in People's Republic of China in 2022. Zhongguo Xue Xi Chong Bing Fang Zhi Za Zhi* 2023;**35**(3):217–24.
25. Wang LY, Qin M, Liu ZH, Wu WP, Xiao N, Zhou XN, et al. *Prevalence and spatial distribution characteristics of human echinococcosis in China. PLoS Negl Trop Dis* 2021;**15**(12):e0009996.
26. Qian MB, Chen J, Bergquist R, Li ZJ, Li SZ, Xiao N, et al. *Neglected tropical diseases in the People's Republic of China: progress towards elimination. Infect Dis Poverty* 2019;**8**(1):86.
27. Zhu TJ, Chen YD, Qian MB, Zhu HH, Huang JL, Zhou CH, et al. *Surveillance of clonorchiasis in China in 2016. Acta Trop* 2020;**203**:105320.
28. Nguyen TTB, Dermauw V, Dahma H, Bui DT, Le TTH, Phi NTT, et al. *Prevalence and risk factors associated with Clonorchis sinensis infections in rural communities in northern Vietnam. PLoS Negl Trop Dis* 2020;**14**(8):e0008483.
29. Qian MB, Zhou CH, Jiang ZH, Yang YC, Lu MF, Wei K, et al. *Epidemiology and determinants of Clonorchis sinensis infection: a community-based study in southeastern China. Acta Trop* 2022;**233**:106545.
30. Jiang ZH, Wan XL, Lv GL, Zhang WW, Lin Y, Tang WQ, et al. *High prevalence of Clonorchis sinensis infection in Guangxi, southern China. Trop Med Health* 2021;**49**(1):6.
31. Li X, Chen Y, Huang G, Sun X, Mo G, Peng X. *Epidemiology and risk factors of Clonorchis sinensis infection in the mountainous areas of Longsheng County, Guangxi: insights from automated machine learning. Parasitol Res* 2025;**124**(3):26.
32. Wang YC, Feng CC, Sithithaworn P. *Environmental determinants of Opisthorchis viverrini prevalence in northeast Thailand. Geospat Health* 2013;**8**(1):111–23.
33. Keiser J, Utzinger J. *Emerging foodborne trematodiasis. Emerg Infect Dis* 2005;**11**(10):1507–14.
34. Deng ZH, Fang YY, Zhang QM, Mao Q, Pei FQ, Liu MR. *The control of clonorchiasis in Guangdong province, southern China. Acta Trop* 2020;**202**:105246.
35. Han S, Zhang X, Chen R, Wen J, Li Y, Shu J, et al. *Trends in prevalence of clonorchiasis among patients in Heilongjiang province, Northeast China (2009-2012): implications for monitoring and control. PLoS One* 2013;**8**(11):e80173.
36. Yang TT, Yao LN, Yao SR, Ruan W, Chen HL, Xia SR, et al. *Assessment of Clonorchis sinensis epidemic trends and its natural epidemic focus in northern area of Zhejiang province. Zhejiang Yu Fang Yi Xue* 2011;**23**(5):17–8.
37. He ZY, Wang XM, Wu WT, Li X, Ren HL, Li XY. *Surveillance and analysis of important human parasitic infections in Beijing during 2016—2020. Zhongguo Ji Sheng Chong Xue Yu Ji Sheng Chong Bing Za Zhi* 2021;**39**(4):557–60.
38. Wang ZY, Zhang YG, Ou HF, Wu HY, Ma XJ, Dai SM, et al. *Laboratory detection and traceability analysis of an imported case of clonorchiasis in Shanghai city. Re Dai Yi Xue Za Zhi* 2022;**22**(5):706–10.
39. WHO. *Control of foodborne trematode infections. Report of a WHO Study Group. World Health Organ Tech Rep Ser* 1995;**849**:1–157.
40. Qian MB, Zhou XN. *Children education for sustainable control of liver fluke infections. Infect Dis Poverty* 2022;**11**(1):119.
41. Huang XH, Qian MB, Zhu GH, Fang YY, Hao YT, Lai YS. *Assessment of control strategies against Clonorchis sinensis infection based on a multi-group dynamic transmission model. PLoS Negl Trop Dis* 2020;**14**(3):e0008152.
42. Li Z, Xin H, Qian MB, Sun J, Yang Y, Chen Y, et al. *Clonorchis sinensis reinfection rate and reinfection determinants: a prospective cohort study in Hengxian county, Guangxi, China. J Infect Dis* 2022;**225**(3):481–91.