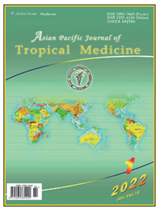

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Spatiotemporal heterogeneity of schistosomiasis in mainland China: Evidence from a multi−stage continuous downscaling sentinel monitoring

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ABSTRACT

Objective: To determine the spatiotemporal distribution of *Schistosoma* (*S.*) *japonicum* infections in humans, livestock, and *Oncomelania* (*O.*) *hupensis* across the endemic foci of China.

Methods: Based on multi-stage continuous downscaling of sentinel monitoring, county-based schistosomiasis surveillance data were captured from the national schistosomiasis surveillance sites of China from 2005 to 2019. The data included *S. japonicum* infections in humans, livestock, and *O. hupensis*. The spatiotemporal trends for schistosomiasis were detected using a Joinpoint regression model, with a standard deviational ellipse (SDE) tool, which determined the central tendency and dispersion in the spatial distribution of schistosomiasis. Further, more spatiotemporal clusters of *S. japonicum* infections in humans, livestock, and *O. hupensis* were evaluated by the Poisson model.

Results: The prevalence of *S. japonicum* human infections decreased from 2.06% to zero based on data of the national schistosomiasis surveillance sites of China from 2005 to 2019, with a reduction from 9.42% to zero for the prevalence of *S. japonicum* infections in livestock, and from 0.26% to zero for the prevalence of *S. japonicum* infections in *O. hupensis*. Analysis using an SDE tool showed that schistosomiasis-affected regions were reduced yearly from 2005 to 2014 in the endemic provinces of Hunan, Hubei, Jiangxi, and Anhui, as well as in the Poyang and Dongting Lake regions. Poisson model revealed 11 clusters of *S. japonicum* human infections, six clusters of *S. japonicum* infections in livestock, and nine clusters of *S. japonicum* infections in *O. hupensis*. The clusters of human infection were highly consistent with clusters of *S. japonicum* infections in livestock and *O. hupensis*. They were in the 5 provinces of Hunan, Hubei, Jiangxi, Anhui, and Jiangsu, as well as along the middle and lower reaches of the Yangtze River. Humans, livestock, and *O. hupensis* infections with *S. japonicum* were mainly concentrated in the north of the Hunan Province, south of the Hubei Province, north of the Jiangxi Province, and southwestern portion of Anhui Province. In the 2 mountainous provinces of Sichuan and Yunnan, human, livestock, and *O. hupensis* infections with *S. japonicum* were mainly concentrated in the northwestern portion of the Yunnan Province, the Daliangshan area in the south of Sichuan Province,

Significance

There are still a large number of factors associated with the transmission of schistosomiasis in China such as difficulty in the management of *Schistosoma japonicum* sources, frequent emergence and re-emergence of snail habitats. This study reveals a long-term risk of transmission in local areas, with the highest-risk areas primarily in Poyang Lake and Dongting Lake regions, requiring to focus on vigilance against the rebound of the epidemic.

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and the hilly regions in the middle of Sichuan Province.

Conclusions: A remarkable decline in the disease prevalence of *S. japonicum* infection was observed in endemic schistosomiasis in China between 2005 and 2019. However, there remains a long-term risk of transmission in local areas, with the highest-risk areas primarily in Poyang Lake and Dongting Lake regions, requiring to focus on vigilance against the rebound of the epidemic. Development of high-sensitivity detection methods and integrating the transmission links such as human and livestock infection, wild animal infection, and *O. hupensis* into the surveillance-response system will ensure the elimination of schistosomiasis in China by 2030.

KEYWORDS: Schistosomiasis; Sentinel surveillance; Spatiotemporal heterogeneity; China

1. Introduction

Schistosomiasis is a chronic and debilitating disease, remaining a major public health problem across Africa, South America, and Asia[1]. According to the Institute for Health Metrics and Evaluation (IHME) at the University of Washington in Seattle, WA, USA, there were around 140 million cases of schistosomiasis in the world in 2019, which corresponds to 1.64 million disability-adjusted life years (DALYs) in 2019[2].

However, the World Health Organization (WHO) estimates that there are 800 million people at risk for schistosomiasis with around 240 million infected, which would correspond to a slightly higher DALY score[3]. The infectious disease was once hyper-endemic in southern China, with 11.6 million schistosomiasis patients and 1.2 million bovine infections with *Schistosoma* (*S.*) *japonicum*. There were 14.2 billion m^2 snail habitats at the founding of the People's Republic of China[4]. With concerted efforts, of the 450 Chinese counties endemic for schistosomiasis, 337 counties (74.89%) eliminated schistosomiasis, 97 (21.56%) achieved transmission interruption, and 16 (3.56%) achieved transmission control by the end of 2020[5,6]. However, there are still a large number of factors associated with the transmission of schistosomiasis in China including a wide range of *S. japonicum* sources of infection, difficulty in the management of *S. japonicum* sources of infection, frequent emergence and re-emergence of snail habitats, and the problematic nature of snail habitat elimination[7,8].

Large-scale schistosomiasis surveillance programs have been launched to facilitate the national schistosomiasis elimination program in China[9]. Data captured from the national schistosomiasis surveillance programs will provide insights into endemic schistosomiasis, an understanding of the prevalence of *S. japonicum* infections in humans and livestock, as well as the endemic foci of *Oncomelania* (*O.*) *hupensis* in China[10,11]. The focus of currently available surveillance data is on the description of spatial, temporal, and population distribution of schistosomiasis. However, knowledge of the spatiotemporal heterogeneity of schistosomiasis in China is scarce. Spatial epidemiology provides insights into disease control, prevention, and health resource allocation[12]. Recently, Li *et al.*[13] used both global Moran's I and Anselin's Local Moran's I statistics to construct a retrospective space-time permutation model for identification of the spatial and temporal distributions of emerging snail-infested sites in the Hunan Province from 1949 to 2016. Pinheiro *et al.*[14] employed spatial epidemiological summaries to determine the spatial-temporal distribution of schistosomiasis-related mortality in Brazil from 2003 to 2018. Spatial analysis has considerable potential for the assessment of schistosomiasis transmission risk and the development of schistosomiasis control strategies. Based on multi-stage downscaling and continuous sentinel monitoring data, this study aimed to determine the spatial-temporal distribution of *S. japonicum* infections in humans, livestock, and *O. hupensis* across the endemic foci of China. In this manner, those areas in need of schistosomiasis control will be identified. Further, results will provide insight into schistosomiasis management and surveillance during the elimination stage of the program.

2. Materials and methods

2.1. Data collection

Schistosomiasis surveillance data were provided by the National Institute of Parasitic Diseases, the Chinese Center for Disease Control and Prevention. According to the epidemiological profile of schistosomiasis, a stratified method was used to assign national schistosomiasis surveillance sites within the endemic province of China[15]. Permanent residents aged 6 to 65 years underwent serological screening at national schistosomiasis surveillance sites for *S. japonicum* infection, as well as measurements of antibody titers for *S. japonicum*. Seropositive individuals were tested for parasites by the Kato-Katz technique and by the miracidium hatching test[10,11]. The miracidium hatching test was used to detect *S. japonicum* infections in livestock[10,11]. Snail surveys were conducted in snail habitats and suspected snail-infested habitats through systematic sampling and environmental sampling at national schistosomiasis surveillance sites. All captured snails were assessed for viability and *S. japonicum* infection[10,11]. Field schistosomiasis surveillance was conducted by local schistosomiasis control institutions. Annual schistosomiasis surveillance data were reported to the National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention.

2.2. Data processing

County-based schistosomiasis surveillance data were captured from national schistosomiasis surveillance sites in China from 2005 to 2019. It mainly includes the number of serological tests, the number of positive serological tests, the number of pathogenic tests, the number of positive pathogenic tests, the number of livestock tests, the number of livestock pathogenic tests positive, the number of live *O. hupensis* snails, and the number of infectious *O. hupensis* snails detected.

The formula are calculated as follows:

Seroprevalence in humans=the number of positive serological tests/the number of serological tests×100%

Positive rate of pathogenic tests=the number of positive pathogenic tests/the number of pathogenic tests×100%

Prevalence in humans=seroprevalence in humans×positive rate of pathogenic tests×100%

Prevalence in livestock=the number of livestock pathogenic tests positive/the number of livestock tests×100%

Prevalence in *O. hupensis*=the number of infectious *O. hupensis* detected/the number of live *O. hupensis*×100%

2.3. Trend analysis of schistosomiasis

All schistosomiasis surveillance data captured from national schistosomiasis surveillance sites of China during the period from 2005 to 2019 were entered into Microsoft Excel 2019 (Microsoft Corporation, Redmond, WA, USA). Prevalence trends for *S. japonicum* infection in humans, livestock, and *O. hupensis* were estimated using Joinpoint regression analysis with the Joinpoint Regression Program version 4.6.0.0[16]. The annual percent change from 2005 to 2019 was calculated. A Joinpoint model, based on an algorithm, was used to assess significant change in schistosomiasis trends.

2.4. Central tendency and dispersion analysis

A standard deviational ellipse (SDE) tool, also termed a directional distribution tool, was used to identify the spatial distribution of the disease[17]. The long and short axes of an ellipse indicate the direction of major and minor trends in the spatial distribution of the disease. The size of the long and short axes identifies the degree of deviation from the center for the spatial distribution of schistosomiasis in major and minor trend directions[17]. In this study, an SDE tool was used to determine the central tendency and dispersion of spatial distributions for schistosomiasis.

2.5. Temporal-spatial cluster analysis

Temporal-spatial clusters of *S. japonicum* infections were identified in humans, livestock, and *O. hupensis* between 2005 and 2019 using a Poisson model and SaTScan version 9.4.2[18]. The space-time permutation scan statistic allows a dynamic scan using a cylindrical window in dimensions of time scales and geographical location. A log-likelihood ratio, a statistic that tests the difference between the observed number and the expected number in and outside the window, was estimated and relative risk (*RR*) calculated. The Monte Carlo method was used for the permutation test, which identified high-prevalence clusters[19].

3. Results

3.1. Trends in the prevalence of schistosomiasis

The prevalence of *S. japonicum* infection trended toward a continuous decline in humans, livestock, and *O. hupensis* based on the national schistosomiasis surveillance sites of China from 2005 to 2019 (Figure 1). There was a reduction in human infections from 2.06% in 2005 to zero in 2019. For livestock, the reduction was from 9.42% in 2005 to zero in 2019 and from 0.26% in 2005 to zero in 2019 for *O. hupensis* (Table 1). Joinpoint regression analysis revealed a statistically significant decline in the prevalence of *S. japonicum* infections in humans, livestock, and *O. hupensis* based on the national schistosomiasis surveillance sites from 2005 to 2019 (P<0.01) except that the decline in the prevalence of *S. japonicum* infections in livestock during 2008 and 2012 was not significant (Table 1).

Table 1. Joinpoint trend analysis for the change in the prevalence of *Schistosoma japonicum* in humans, livestock, and *Oncomelania hupensis* based on the national schistosomiasis surveillance sites of China from 2005 to 2019.

Prevalence	Time period	*t*	*P*	Annual percent change	Lower limit of 95% *CI*	Upper limit of 95% *CI*
Humans	2005-2019	−8.12	<0.01	−45.35	−53.45	−35.81
Livestock	2005-2008	−13.00	<0.01	−41.40	−46.80	−35.40
	2008-2012	−2.10	0.07	−17.10	−32.80	2.40
	2012-2019	−5.50	<0.01	−67.20	−79.70	−46.80
Oncomelania hupensis	2005-2019	−3.43	<0.01	−14.07	−21.89	−5.47

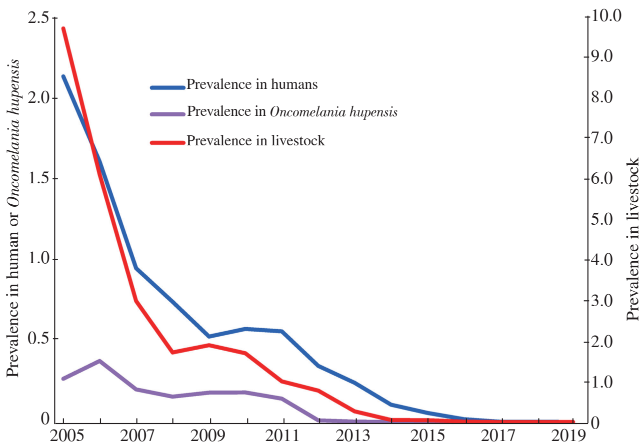

Figure 1. Changes in the prevalence of *Schistosoma japonicum* in humans, livestock, and *Oncomelania hupensis* based on the national schistosomiasis surveillance sites of China from 2005 to 2019.

3.2. Central tendency and dispersion in spatial distributions of schistosomiasis

Since there were few egg-positive individuals identified at the national schistosomiasis surveillance sites since 2015, spatial dispersion analysis may result in bias. We, therefore, determined the central tendency and dispersion of spatial distributions for schistosomiasis using an SDE tool for the years 2005 to 2014.

For the weighted SDE of *S. japonicum* human infections based on the national schistosomiasis surveillance sites from 2005 to 2014 (Figure 2A), the long axis of the weighted SDE identified a similar direction for the Yangtze River each year from 2005 to 2014, with a yearly reduced standard deviation in both long and short axes. From 2005 to 2014, the spatial dispersion of the epidemic became smaller. By the year 2014, the SDE covered part of the schistosomiasis-endemic foci of four provinces (Hubei, Hunan, Anhui, and Jiangxi),

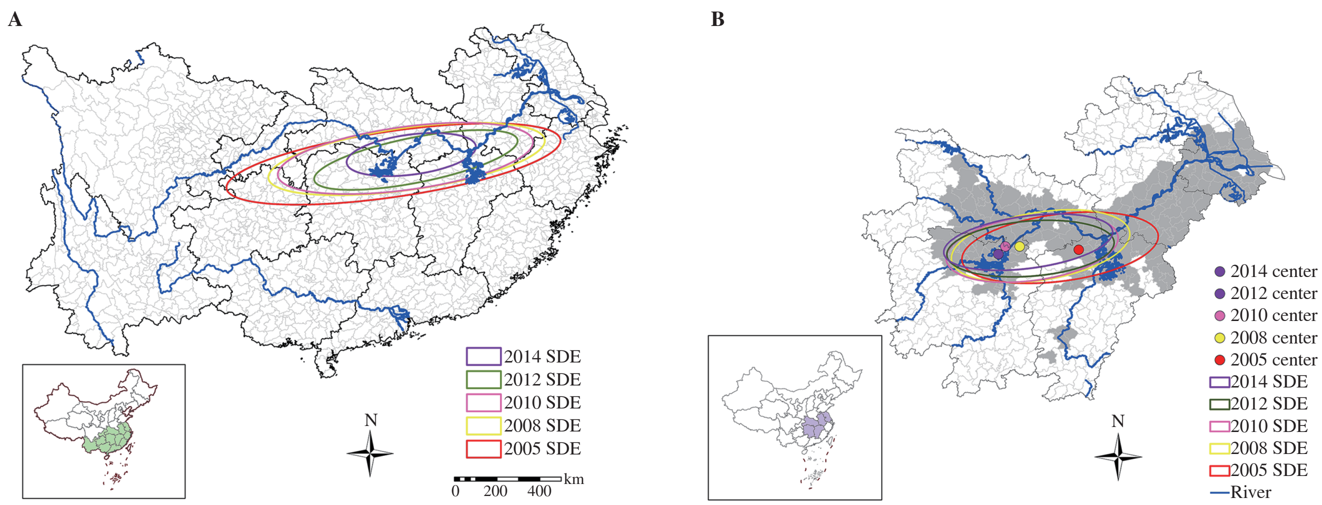

Figure 2. Central and discrete trend changes in the prevalence of human schistosomiasis (A: in the Yangtze River Basin and its southern provinces; B: in five Chinese provinces: Hunan, Hubei, Anhui, Jiangxi, and Jiangsu)

Table 2. Spatio-temporal cluster analysis of human *Schistosoma japonicum* infections based on the national schistosomiasis surveillance sites of China from 2005 to 2019.

Environmental type	Cluster circle	Time period	Cluster center		Radius (km)	Observed number	Expected number	*RR*	LLR	*P*	No. of counties clustered
			Longitude	Latitude							
Five provinces in marshland and lake regions	1	2005-2006	29.01	116.71	56.91	442	39.14	12.55	698.51	<0.01	3
	2	2005-2009	28.85	112.36	96.35	1012	294.51	4.25	604.86	<0.01	13
	3	2005-2009	30.44	114.89	83.12	327	85.39	4.08	204.95	<0.01	3
	4	2005-2006	30.69	117.57	33.28	158	33.64	4.85	121.99	<0.01	2
	5	2005-2007	30.41	112.91	94.45	311	181.64	1.77	40.07	<0.01	10
	6	2005-2007	28.69	118.25	0.00	64	29.37	2.13	13.83	<0.01	1
Two provinces in mountainous regions	1	2005-2007	26.12	99.97	0.00	78	10.56	9.18	95.59	<0.01	1
	2	2005-2006	30.20	103.51	64.36	75	11.10	8.29	85.70	<0.01	4
	3	2005-2006	27.88	102.28	53.43	53	6.65	9.19	66.91	<0.01	2
	4	2005-2006	26.69	100.76	0.00	50	11.17	5.05	38.40	<0.01	1
	5	2005-2006	26.69	100.76	0.00	19	3.06	6.50	19.11	<0.01	1

RR: relative risk; LLR: log likelihood ratio. Five provinces in marshland and lake regions refer to Hunan, Hubei, Anhui, Jiangxi and Jiangsu provinces; Two provinces in mountainous regions refers to Yunnan and Sichuan Provinces.

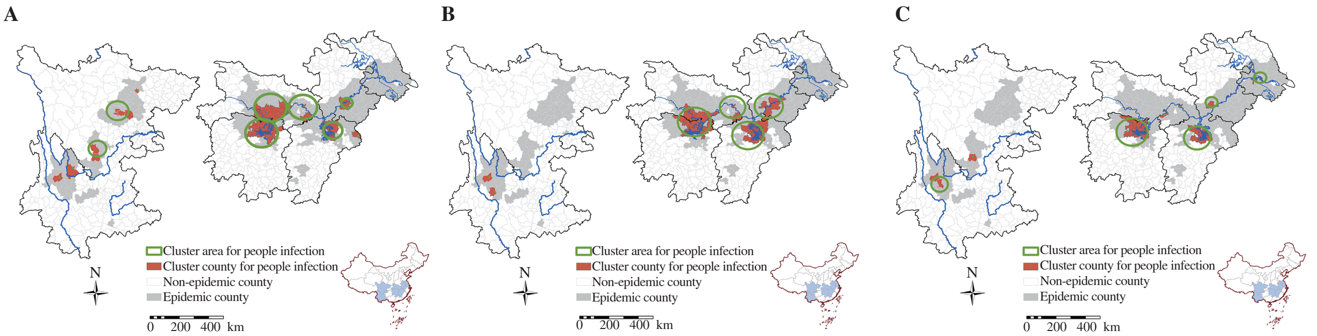

Figure 3. Spatio-temporal cluster distributions of schistosomiasis based on the national schistosomiasis surveillance sites of China from 2005 to 2019. (A: *Schistosoma japonicum* infections in humans; B: *Schistosoma japonicum* infections in livestock; C: *Schistosoma japonicum* infections in *Oncomelania hupensis*.

Table 3. Spatio-temporal cluster analysis of *Schistosoma japonicum* infections in livestock based on the national schistosomiasis surveillance sites of China from 2005 to 2019.

Environmental type	Cluster circle	Time period	Cluster center		Radius (km)	Observed number	Expected number	*RR*	LLR	*P*	No. of counties clustered
			Longitude	Latitude							
Five provinces in marshland and lake regions	1	2005-2006	29.54	112.55	97.47	268	47.35	7.83	277.76	<0.01	18
	2	2005-2006	30.52	117.10	82.98	82	17.41	5.11	65.08	<0.01	7
	3	2005-2006	30.44	114.89	74.40	47	5.47	9.04	60.62	<0.01	2
	4	2005-2006	28.70	115.82	93.25	77	27.25	3.01	31.78	<0.01	9
Two provinces in mountainous regions	1	2005-2006	25.23	100.31	0.00	221	69.87	7.32	157.99	<0.01	1
	2	2005-2006	26.12	99.97	0.00	29	9.08	3.40	14.38	<0.01	1

RR: relative risk; LLR: log likelihood ratio; Five provinces in marshland and lake regions refer to Hunan, Hubei, Anhui, Jiangxi and Jiangsu provinces; Two provinces in mountainous regions refers to Yunnan and Sichuan Provinces.

indicating a yearly reduction in the size of schistosomiasis-affected regions from 2005 to 2014. The endemic foci were comprised of the five provinces (Hunan, Hubei, Jiangxi, Anhui, and Jiangsu) within the lake region (Dongting Lake area and Poyang Lake area).

Figure 2B shows the change in the weighted centers and SDE of *S. japonicum* human infections for the 5 lake region provinces during the period from 2005 to 2014. The centers of *S. japonicum* human infection were Dongting and Poyang Lake areas, with a tendency for a shift westward. The long axis of the SDE showed a similar direction toward the Yangtze River, with a reduced standard deviation in the long axis and a minor alteration in the standard deviation for the short axis, indicating shrinkage in coverage by the SDE. In 2014, the SDE mainly covered the northern portion of Hunan Province, the southern portion of Hubei Province, the northern portion of Jiangxi Province, and the southwestern portion of Anhui Province.

3.3. Temporal–spatial clusters of schistosomiasis transmission risk

At the county level, space-time scan analysis identified 6 clusters of *S. japonicum* human infections across 5 provinces in lake areas (*RR* 1.77 to 12.55) and five clusters in two mountainous provinces of Sichuan and Yunnan (*RR* 5.05 to 9.19) based on the national schistosomiasis surveillance sites from 2005 to 2019. The 6 clusters covered 32 counties in 5 provinces of lake areas including 13 counties in Hunan, 13 in Hubei, 4 in Jiangxi, 2 in Anhui 0 in Jiangsu. The 6 clusters were primarily in: Yueyang City (5), Yiyang City (3), Changde City (4) and Changsha City (1) of Hunan Province; Jingzhou City (7), Xiaogan City (1), Qianjiang City (1), Xiantao City (1), Huanggang City (1), Huangshi City (1) and Wuhan City (1) of Hubei Province; Shangrao City (3), Jiujiang City (1) of Jiangxi Province; Chizhou City (1) and Anqing City (1) in Anhui province (Figure 3A, Table 2). In addition, the 5 clusters in the 2 mountainous provinces covered 2 counties in Yunnan Province and 7 in the Sichuan Province. The clusters were mainly in the Liangshan Prefecture (2), Meishan City (3), Mianyang City (1), and Chengdu City (1) of Sichuan Province; Lijiang City (1) and Dali Prefecture (1) of Yunnan Province (Figure 3A, Table 2).

At the county level, space-time scan analysis identified 4 clusters of *S. japonicum* livestock infections across 5 provinces in lake areas (*RR* 3.01 to 9.04) and 2 clusters in 2 provinces of Sichuan and Yunnan (*RR* 3.40 to 7.32) based on the national schistosomiasis surveillance sites from 2005 to 2019. The 4 clusters covered 36 counties across 5 provinces in lake areas, including 11 counties in Hunan, 9 in Hubei, 9 in Jiangxi, 7 in Anhui, and 0 in Jiangsu. The clusters were primarily located in: Changde City (4), Yueyang City (5) and Yiyang City (2) of Hunan Province; Jingzhou City (7), Huanggang City (1) and Huangshi City (1) in Hubei; Jiujiang City (4), Shangrao (2) and Nanchang City (3) of Jiangxi Province; Anqing City (4), Tongling City (1) and Chizhou City (2) of

Table 4. Spatio-temporal cluster analysis of *Oncomelania hupensis* infections based on the national schistosomiasis surveillance sites of China from 2005 to 2019.

Environmental type	Cluster	Time period	Cluster center		Radius (km)	Observed number	Expected number	*RR*	LLR	*P*	No. of counties clustered
			Longitude	Latitude							
Five provinces in marshland and lake regions	1	2006-2010	28.91	111.98	92.70	698	128.90	7.32	691.50	<0.01	10
	2	2005-2007	29.47	113.01	0.00	162	21.60	7.99	190.40	<0.01	1
	3	2005-2009	28.55	115.95	78.48	235	75.39	3.36	113.40	<0.01	6
	4	2006-2007	32.24	119.80	36.08	160	52.78	3.18	72.81	<0.01	2
	5	2005-2007	29.98	113.95	0.00	17	0.32	53.48	50.90	<0.01	1
	6	2005-2009	30.44	114.89	0.00	33	4.41	7.58	38.00	<0.01	1
	7	2005-2006	30.74	116.84	35.08	35	6.00	5.91	32.93	<0.01	3
Two provinces in mountainous regions	1	2005-2006	25.70	100.17	50.88	55	5.21	23.70	97.29	<0.01	2
	2	2005	27.41	102.18	0	12	1.54	8.75	14.76	<0.01	1

RR: relative risk; LLR: log likelihood ratio; Five provinces in marshland and lake regions refer to Hunan, Hubei, Anhui, Jiangxi and Jiangsu provinces; Two provinces in mountainous regions refer to Yunnan and Sichuan Provinces.

Anhui Province (Figure 3B, Table 3). In addition, 2 clusters in the mountainous regions covered 2 counties in Yunnan Province, including Weishan County and Eryuan County (Figure 3B, Table 3).

At a county level, space-time scan analysis identified 7 clusters of *S. japonicum* infections in *O. hupensis* across 5 provinces in lake areas (*RR* 3.18 to 53.48) and 2 clusters in 2 provinces of Sichuan and Yunnan (*RR* 8.75 to 23.70) based on the national schistosomiasis surveillance sites from 2005 to 2019. The 7 clusters covered 24 counties across 5 provinces in lake areas including 11 counties in Hunan, 6 in Jiangxi, 2 in Hubei, 2 in Jiangsu, and 3 in Anhui. The clusters were mainly in Yueyang City (3) Yiyang City (3) and Changde City (5) of Hunan Province; Shangrao City (1), Nanchang City (2) and Jiujiang City (2) of Jiangxi Province; Xianning City (1) and Huanggang City (1) in Hubei province; Zhenjiang City (2) of Jiangsu Province, and Anqing City (3) of the Anhui Province (Figure 3C, Table 4). In addition, 2 clusters in the 2 mountainous provinces covered 2 counties (Dali and Eryuan) in Yunnan and 1 (Dechang) in Sichuan (Figure 3C, Table 4).

These results identify clusters of *S. japonicum* infections in humans, livestock, and *O. hupensis* to be concentrated in the north of Hunan Province, south of Hubei Province, north of Jiangxi Province, and southwest of Anhui Province. Infections were across 5 provinces in lake areas, with clusters predominantly located around Poyang Lake, Dongting Lake, and along the middle and lower reaches of the Yangtze River. The clusters of *S. japonicum* infections in humans, livestock, and *O. hupensis* in the 2 mountainous provinces were predominantly in the northwestern portion of Yunnan Province and the Daliangshan Mountain area in the south of Sichuan Province and the hilly regions within the middle of Sichuan Province. There were 8 counties with clusters of *S. japonicum* infections in humans, livestock, and *O. hupensis* including Huarong, Anxiang, Jinshi, Hanshou, Yuanjiang, Huangzhou, Yugan, and Eryuan (Figure 4).

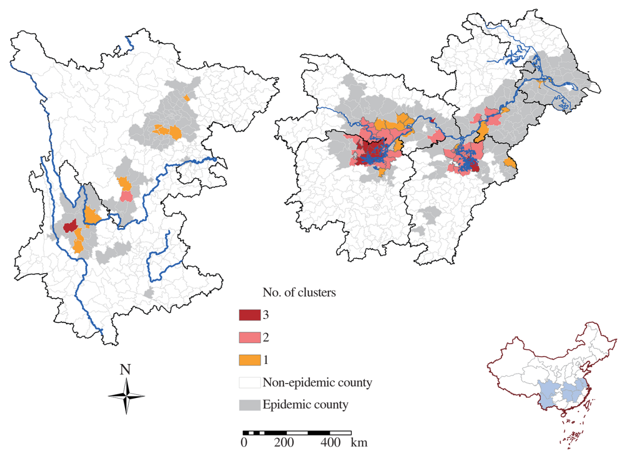

Figure 4. Overlapping cluster regions for *Schistosoma japonicum*-infected humans, livestock, and *Oncomelania hupensis* based on the national schistosomiasis surveillance sites of China from 2005 to 2019.

4. Discussion

Following the termination of the World Bank Loan Project for the Chinese Schistosomiasis Control Program in the early 1990s, there was a rebound and re-emergence of schistosomiasis in counties across China where transmission interruption or control had been achieved[20,21]. During the period from 2005 through 2019, an integrated strategy, with an emphasis on the management of the source of *S. japonicum* infections, was implemented for schistosomiasis control in China. The strategy included: expanded examination and therapy for schistosomiasis, raising livestock in pens, replacement of bovine with machines, improved sanitation, fecal management, and cementing of ditches[22].

During the period from 2005 to 2014, a total of 80 national schistosomiasis surveillance sites were established in China. To further understand the potential transmission risk for schistosomiasis, a total of 454 national schistosomiasis surveillance sites were established during the period from 2015 to 2019. The sites covered all schistosomiasis-endemic counties as well as 4 counties in the Three Gorges Reservoir area because the environment is suitable for the growth of *O. hupensis* due to the completion of the Three Gorges Dam, which is likely to lead to the epidemic of schistosomiasis. Surveillance included case monitoring, transmission factors, and transmission risk[11,23]. From 2005 to 2019, the prevalence of *S. japonicum* infections reduced from 2.07% to zero in humans, from 9.42% to zero in livestock, and from 0.26% to zero in *O. hupensis* based on the national schistosomiasis surveillance sites. These data demonstrate the remarkable effectiveness of the integrated strategy for schistosomiasis control, which included improved sanitation, protection of human health, and reductions in poverty due to endemic schistosomiasis foci. However, several factors leading to occult infections such as contact with low-intensity *S. japonicum* cercariae in low-endemic areas and the difficulty of low-intensity infection diagnosis, result in an underestimation of the prevalence of *S. japonicum* infection[24]. Currently, schistosomiasis is in a low epidemic state in China, with the prevalence of *S. japonicum* infections in humans, livestock, and *O. hupensis* approaching zero in all national schistosomiasis surveillance sites. However, this is likely to underestimate the risk of schistosomiasis due to the low sensitivity of diagnostic assays.

In this study, we found a yearly reduction in the schistosomiasis-affected regions of China. The affected areas were predominantly located in endemic foci of 4 provinces including Hunan, Hubei, Jiangxi, and Anhui. The foci were concentrated in Poyang and Dongting Lake regions, which were consistent with the areas with more cases and a wide area of *O. hupensis* reported from the national report on schistosomiasis[25,26] and as high-risk areas for schistosomiasis based on modeling prediction[27,28]. There are widespread marshlands around the Dongting and Poyang Lake areas, with many *O. hupensis* infested sites and a large number of livestock that can be reservoirs for *S. japonicum*[29]. There is still an increased possibility of exposure to infected snail and *S. japonicum* for residents who fish, pasture, and farm in the waters. Further, the residents typically live in the boats and release their feces directly into lakes, resulting in long-term and extensive infections[30]. The residents breed and pasture their animals in marshlands and lake areas, which makes the elimination of schistosomiasis more difficult[31]. Livestock and fishermen frequent snail-infested areas, with the risk of *S. japonicum* infection a persistent threat[32].

Due to the unique life cycle and transmission characteristics of schistosomiasis, there is still a high risk for schistosomiasis transmission in local regions[33]. The Poisson analysis identified 11 clusters of *S. japonicum* human infections, 6 clusters of livestock infections, and 9 clusters of *O. hupensis* infections. The clusters of human infection were highly consistent with those of livestock and *O. hupensis* infection. The clusters were mainly located around the Poyang and Dongting Lake areas, Jianghan Plain areas, the middle and lower reaches of the Yangtze River, the northwestern part of Yunnan Province, the Dalianshan Mountain area in the south of Sichuan Province, and the hilly regions in the middle of Sichuan Province. In addition, clusters of schistosomiasis transmission risk identified by hotspot analysis were essentially consistent with schistosomiasis transmission-controlled counties and the neighboring transmission interrupted areas[23]. Our findings indicate a high risk of schistosomiasis transmission in these clustering areas, with the possibility of a rebound in schistosomiasis requiring close attention.

The clusters of *S. japonicum* infection in humans, livestock, and *O. hupensis* in marshland and lake areas are widespread and concentrated, associated with widespread snail habitats, large numbers of floating boatmen, and fishermen, as well as livestock management difficulties[34,35]. While the clusters of *S. japonicum* infection were relatively small and dispersive in the 2 mountainous provinces, associating with the dot-like distribution of snails[36,37]. These findings provide extensive coverage of high-risk areas for schistosomiasis in marshland and lake areas, where rebound of schistosomiasis requires careful attention during the elimination stage. Although there is limited schistosomiasis transmission risk in mountainous areas, socio-economic under-development and complex natural environments will also likely lead to a rebound in schistosomiasis. Therefore, Surveillance for *S. japonicum* infection and *O. hupensis* needs to be intensified both in marshland and lake areas and mountainous regions[38].

This study analyzed the temporal and spatial heterogeneity of the prevalence of schistosomiasis in humans, livestock, and snails in China from 2005 to 2019. It covers a long time of 15 years and wide distribution of all schistosomiasis endemic counties in China. This study was subject to some limitations: diagnostic tests used in China are the Kato-Katz technique and the miracidium hatching test, thus the figures reported in this paper are based on these tests. The problem with those tests is that they are not sufficiently sensitive for the low levels of worm burdens in China today. There are more sensitive techniques available, such as PCR, LAMP, and the circulating cathodic antigen, which would give slightly higher levels of infection if applied.

Given all of that, a remarkable decline in the disease prevalence of *S. japonicum* infection was observed in endemic schistosomiasis in China during the period between 2005 and 2019. However, there remains a long-term risk of transmission in local areas, with the highest-risk areas primarily in Poyang Lake and Dongting Lake regions, requiring to focus on vigilance against the rebound of the epidemic. Development of high-sensitivity detection methods and integrating the transmission links such as human and livestock infection, wild animal infection, and *O. hupensis* into the surveillance-response system will ensure the elimination of schistosomiasis in China by 2030.

Conflict of interest statement

The authors declare that they have no competing interests.

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Authors' contributions

YFG: writing original draft, methodology, formal analysis, and software; JXF, ZWL: validation and formal analysis; JBX, ZYG: investigation, formal analysis; LJZ, SX: data curatuion; SL, JX: review and conceptualization; SZL: study design, conceptualization, writing, review, editing, and project administration.

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