Spatio-Temporal Heterogeneity of Schistosomiasis in China Based on Multi-stage, Continuous Downscaling of Sentinel Monitoring

Yan-Feng Gong
National Institute of Parasitic Diseases
Jia-Xin Feng
NIPD: National Institute of Parasitic Diseases
Zhuo-Wei Luo
NIPD: National Institute of Parasitic Diseases
Jing-Bo Xue
NIPD: National Institute of Parasitic Diseases
Zhao-Yu Guo
NIPD: National Institute of Parasitic Diseases
Li-Juan Zhang
NIPD: National Institute of Parasitic Diseases
Shang Xia
NIPD: National Institute of Parasitic Diseases
Shan Lv
NIPD: National Institute of Parasitic Diseases
Jing Xu
NIPD: National Institute of Parasitic Diseases
Shizhu Li (lisz@chinacdc.cn)
Chinese Center for Disease Control and Prevention

Research

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Abstract

Background: There is a continuous decline in the prevalence of schistosomiasis and the number of *Schistosoma japonicum* infections in humans and livestock in China. However, there are a large number of factors that have not been resolved and which may contribute to future transmission of schistosomiasis. These include a range of sources for *S. japonicum* infection, difficulty in management of *S. japonicum* sources of infection, frequent emergence and re-emergence of *Oncomelania hupensis* snail habitats, and the problematic elimination of snail habitats. These factors challenge progress towards the elimination of schistosomiasis in 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 spatio-temporal 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 spatial distribution of schistosomiasis. Further, spatio-temporal clusters of *S. japonicum* infections in humans, livestock, and *O. hupensis* were evaluated by Poisson model.

Results: The prevalence of *S. japonicum* human infections was reduced from 2.06% to zero based on the national schistosomiasis surveillance sites of China during the period 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*. The decline in prevalence of *S. japonicum* infections in humans, livestock, and *O. hupensis* was statistically significant from 2005 to 2019 ($P < 0.01$). There was an exception to the decline in *S. japonicum* infections in livestock during the period from 2008 to 2012. Using an SDE tool, 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 found to be highly consistent with clusters of *S. japonicum* infections in livestock and *O. hupensis*. These clusters were in the five 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 two 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, and the hilly regions in the middle of Sichuan Province.

Conclusions: This study demonstrate a significant spatio-temporal heterogeneity of schistosomiasis in China. A remarkable decline in endemic schistosomiasis was observed between 2005 and 2019. However, there continues to be a long-term risk of schistosomiasis transmission in local areas, with high-risk areas primarily located in the Poyang Lake and Dongting Lake regions, with frequent acute *S. japonicum* infections. Using a One Health approach, further reinforcement of an integrated schistosomiasis control strategy, with an emphasis on the sources of *S. japonicum* infection, is required to facilitate the elimination of schistosomiasis in China by 2030.

Background

Schistosomiasis is prevalent in 78 countries or territories across Asia, Africa, and South America. Currently, more than 200 million people are estimated to have the disease and more than 800 million are at risk for infection. The global disability-adjusted life years (DALYs) due to schistosomiasis is 70 million [1]. This infectious disease was once hyper-endemic in southern China, with 11.6 million schistosomiasis patients and 1.2 million bovine infections with *Schistosoma japonicum*. There were 14.2 billion m^2 snail habitats at the founding of the People's Republic of China [2]. The national schistosomiasis control strategy in China has shifted three times. The first was a snail control-based integrated strategy (from the founding of the People's Republic of China to the early 1980s), followed by a morbidity control strategy based on synchronous chemotherapy for humans and bovines (from the middle 1980s to 2003). The third was an integrated strategy based on control of the source of *S. japonicum* infections (from 2004 to present) [3]. With these concerted efforts, endemic schistosomiasis has continuously declined in both prevalence and numbers of *S. japonicum* infections in humans and livestock. Of the 450 Chinese counties endemic for schistosomiasis, 337 counties (74.89%) eliminated schistosomiasis, 97 (21.56%) achieved transmission interruption, and 16 (3.55%) achieved transmission control by the end of 2020 [4]. 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, a high degree of 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 [5]. Further, currently available tools do not meet the requirements of the national schistosomiasis elimination program, which impedes the elimination of schistosomiasis from China [6].

Large-scale schistosomiasis surveillance programs have been launched to facilitate the national schistosomiasis elimination program in China [7]. Data captured from the national schistosomiasis surveillance programs will provide insight into endemic schistosomiasis, an understanding of the prevalence of *S. japonicum* infections in humans and livestock, as well as the endemic foci of *Oncomelania hupensis* in China [8, 9]. The focus of currently available surveillance data is on the description of spatial, temporal, and population distribution of schistosomiasis. However, knowledge of the spatio-temporal heterogeneity of schistosomiasis in China is lacking. Spatial epidemiology effectively quantifies spatial distribution and provides disease mapping, cluster analysis, and risk factor identification. Spatial epidemiology provides insights into disease control, prevention, and health resource allocation [10]. Recently, Li and colleagues [11] used both global Moran's *I* and Anselin's local Moran's *I* statistics (LISA) 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. The model was based on annual snail survey data. Pinheiro and colleagues [12] 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 for the development of a schistosomiasis control strategies. Based on multi-stage downscaling and continuous sentinel monitoring data, the aim of this study was 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.

Methods

Data collection

Schistosomiasis surveillance data were provided by the National Institute of Parasitic Diseases, 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 endemic province of China [13]. 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 [8,9]. The miracidium hatching test was used to detect *S. japonicum* infections in livestock [8,9]. Snail surveys were conducted in snail habitats and in suspected snail-infested habits by systematic sampling and environmental sampling at national schistosomiasis surveillance sites. All captured snails were assessed for viability and *S. japonicum* infection [8,9]. 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.

Data processing

County-based schistosomiasis surveillance data were captured from national schistosomiasis surveillance sites in China from 2005 to 2014 that included the number of; those tested for *S. japonicum* infection using sero-diagnostic assays, seropositive individuals, individuals tested for *S. japonicum* infections using parasitology testing, egg-positive individuals, livestock tested for *S. japonicum* infection, egg-positive livestock, living *O. hupensis* snails, and *O. hupensis* snails with *S. japonicum* infection. The sero-prevalence and prevalence of *S. japonicum* infection in humans, livestock, and *O. hupensis* were calculated using the following formulas:

Sero-prevalence of *S. japonicum* human infections = number of sero-positives/number of individuals with serological screening for *S. japonicum* infection × 100%.

Parasitology infection rate of sero-positives = number of egg-positive/number of individuals tested for *S. japonicum* infection with parasitology tools × 100%.

Prevalence of *S. japonicum* human infection = sero-prevalence of *S. japonicum* human infections × parasitological infection rate of sero-positives × 100%.

Prevalence of *S. japonicum* infections in livestock = number of egg-positive livestock/number of livestock tested for *S. japonicum* infection × 100%.

Prevalence of *S. japonicum* infections in *O. hupensis* = number of *O. hupensis* with *S. japonicum* infections/number of living snails × 100%.

Trend analysis of schistosomiasis

All schistosomiasis surveillance data captured from national schistosomiasis surveillance sites of China during the period from 2005 to 2014 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 [14].

Annual percent change (APC) from 2005 to 2014 was estimated. A Joinpoint model, based on an algorithm, was used to assess significant change in schistosomiasis trends.

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 disease [15]. The long and short axes of an ellipse indicate the direction of major and minor trends in spatial distribution of a disease. The size of the long and short axes identifies the degree of deviation from center for the spatial distribution of schistosomiasis in major and minor trend directions [15]. In this study, an SDE tool was used to determine the central tendency and dispersion of spatial distributions for schistosomiasis.

Temporal-spatial cluster analysis

Temporal-spatial clusters of *S. japonicum* infections were identified in humans, livestock, and *O. hupensis* from 2015 to 2019 using a Poisson model and SaTScan version 9.4.2 [16]. 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 (*LLR*), 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 [17]. In China, the national schistosomiasis control program was implemented in counties, with the endemic status of schistosomiasis assigned to an administrative village as a national schistosomiasis surveillance site. In this manner the overall prevalence of schistosomiasis in a county was determined. In this study, we used the schistosomiasis clusters in an administrative village to define the cluster of schistosomiasis in a county.

Results

Trends in prevalence of schistosomiasis

The prevalence of *S. japonicum* infection trended toward continuous decline in humans, bovines, 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% to zero and from 0.26% to zero 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 ($P < 0.01$). There was an exception to the decline in prevalence of *S. japonicum* infections in livestock during the period from 2008 to 2012. The greatest reduction was seen in the prevalence of *S. japonicum* infections in livestock, with APCs of 41.4% for 2005–2008 (95% *CI*, –46.8% to –35.4%), and 67.2% for 2012–2019 (95% *CI*, –79.7% to –46.8%), followed by the prevalence of human infections, with APCs of 10.65% for 2005–2019 (95% *CI*, –53.45% to –35.81%), and APCs of *O. hupensis* infections at 14.07% (95% *CI*, –21.89% to –5.47%) for 2005–2019 (Table 1, Figure 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, directional 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 for *S. japonicum* human infections based on the national schistosomiasis surveillance sites from 2005 to 2014 (Figure 3), 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. In 2014, the SDE covered the schistosomiasis-endemic foci of four provinces (Hubei, Hunan, Anhui, and Jiangxi), indicating a yearly reduction in the size of schistosomiasis-affected regions from 2005 to 2014. The endemic foci were comprised of the five provinces of Hunan, Hubei, Jiangxi, Anhui, and Jiangsu within the lake region.

Figure 4 shows change in the weighted centers and SDE of *S. japonicum* human infections for the five 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 a 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.

Temporal-spatial clusters of schistosomiasis transmission risk

At the county level, space-time scan analysis identified six clusters of *S. japonicum* human infections across five provinces in lake areas (*RR*: 1.77 to 12.6) and five clusters in two mountainous provinces of Sichuan and Yunnan (*RR*: 6.5 to 9.19) based on the national schistosomiasis surveillance sites from 2005 to 2019. The six clusters covered 32 counties in five province lake areas. There were 13 counties in Hunan, 13 in Hubei, four in Jiangxi, and three in Anhui. The clusters were primarily in: Yueyang City (5), Yiyang City (3), and Changde City (4) of the Hunan Province; Jingzhou City (7) of the Hubei Province; and Shangrao City (3) of the Jiangxi Province accounting for 68.75% (22/32) of all clusters (Figure 5, Table 2). In addition, the five clusters in the two mountainous provinces covered two counties in the Yunnan Province and seven in the Sichuan Province. The clusters were primarily in the Liangshan Prefecture (2) and Meishan City (3) of the Sichuan Province, accounting for 55.56% (5/9) of all clusters (Figure 5, Table 2).

At the county level, space-time scan analysis identified four clusters of *S. japonicum* livestock infections across five provinces in lake areas (*RR*: 3.01 to 9.04) and two clusters in two provinces of Sichuan and Yunnan (*RR*: 3.4 to 7.32) based on the national schistosomiasis surveillance sites from 2005 to 2019. The four clusters covered 32 counties across five provinces in lake areas, including nine counties in Hunan, nine in Hubei, nine in Jiangxi, and seven in Anhui. The clusters were primarily in: Jingzhou City (7) of the Hubei Province; Changde City (4) and Yueyang City (4) of the Hunan Province; Jiujiang City (4) and Nanchang City (3) of the Jiangxi Province; and Anqing City (4) and Chizhou City (2) of the Anhui Province accounting for 82.35% (28/34) of all clusters (Figure 6, Table 3). In addition, two clusters in the mountainous regions covered two counties in the Yunnan Province, including Weishan County and Eryuan County (Figure 6, Table 3).

At a county level, space-time scan analysis identified seven clusters of *S. japonicum* infections in *O. hupensis* across five provinces in lake areas (*RR*: 3.18 to 53.48) and two clusters in two provinces of Sichuan and Yunnan (*RR*: 8.75 to 23.26) based on the national schistosomiasis surveillance sites from 2005 to 2019. The seven clusters covered 18 counties across five provinces in lake areas including 11 counties in Hunan, six in Jiangxi, two in Hubei, two in Jiangsu, and three in Anhui. The clusters were mainly in: Yueyang City (4), Changde City (5), and Yiyang City (3) of the Hunan Province; Nanchang City (3) and Shangrao City (2) of Jiangxi Province; Zhenjiang City (2) of Jiangsu Province; and Anqing City (3) of the Anhui Province accounting for 91.67% (22/24) of all clusters (Figure 7, Table 4). In addition, two clusters in the two mountainous provinces covered two counties in Yunnan Province and one in Sichuan Province including Eryuan County and Dali County of the Yunnan Province, and Dechang City of the Sichuan Province (Figure 7, 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 five 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 two mountainous provinces were predominantly in the northwestern portion of Yunnan Province and the Daliangshan Mountain area in the south of Sichuan Province and in the hilly regions within the middle of Sichuan Province (Figure 8). There were eight counties with clusters of *S. japonicum* infections in humans, livestock, and *O. hupensis* in; Huarong, Anxiang, Jinshi, Hanshou, Yuanjiang, Huangzhou, Yugan, and Eryuan (Figure 8).

Discussion

The transmission of schistosomiasis involves multiple cycles and a large number of factors, which affect disease transmission. Following the termination of the World Bank Loan Project for 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 [18]. In 2005, there were 27,285 individuals and 33,736 bovines with *S. japonicum* infections and 3.863 billion m^2 of snail habitat in China [19]. 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, night soil management, and cementing of ditches [20]. Based on the principle of “prevention first, scientific control, highlighting key points and classified guidance”, this integrated strategy reinforced schistosomiasis examination and therapy for humans and livestock, as well as snail survey and control. By 2019, there were two individuals and seven bovines with S. japonicum infections and 3.624 billion m^2 of snail habitat in China [21].

Understanding factors that affect schistosomiasis transmission and awareness of endemic status alterations are prerequisites for preventive disease control. During the period from 2005 through 2014, a total of 80 national schistosomiasis surveillance sites were established in China. These included; fork beach, islet without embankment, islet with embankment, inner embankment, plateau, mountain, hill, and waterway networks. Data from the national schistosomiasis surveillance sites identified the main types of schistosomiasis-endemic foci as well as trends in the prevalence of *S. japonicum* infections in China [8, 13]. To further understand the potential transmission risk for schistosomiasis, a total of 454 national schistosomiasis surveillance sites were established during the period from 2015 through 2019. The sites covered all schistosomiasis-endemic counties as well as four counties in the Three Gorges Reservoir area. Surveillance included case monitoring, transmission factors, and transmission risk [9]. From 2015 to 2019, the prevalence of *S. japonicum* infections reduced from

2.0682% 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. Joinpoint regression analysis showed; the APC of *S. japonicum* infections in livestock to be 41.4% from 2005–2008 and 67.2% from 2012–2019; an APC of 10.65% for *S. japonicum* human infections from 2005–2013 and 20.83% from 2013–2019; and an APC of 14.07% for *S. japonicum* infections in *O. hupensis* from 2005–2019. 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, a number of factor lead to occult infections such as contact with low-intensity *S. japonicum* cercariae in low-endemic areas and the difficulty of low-intensity infection diagnosis, results in an underestimation of the prevalence of *S. japonicum* infection [22]. Currently, schistosomiasis is weakly endemic in China, with the prevalence of *S. japonicum* infections in humans, livestock, and *O. hupensis* approaching zero in all national schistosomiasis surveillance sites. However, it is likely that this is an underestimate of schistosomiasis because of the insensitivity of diagnostic assays.

In this study we found a yearly reduction in the schistosomiasis-affected regions of China from 2005 to 2014. By weighted SDE, the affected areas were predominantly located in endemic foci of four provinces; Hunan, Hubei, Jiangxi, and Anhui. These foci were concentrated in Poyang and Dongting Lake regions. These results are similar to the national report on schistosomiasis in China [23, 24] and to high-risk areas for schistosomiasis based on modeling [25, 26]. 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 serve as reservoirs for *S. japonicum* [27]. There is an increased possibility of exposure to snail-infested sites and *S. japonicum*-infested waters for local residents who fish, pasture, and farm. Further, the residents are typically in boats and release their feces directly into lakes, resulting in long-term and extensive infections [28]. In marshlands and lake areas, local residents breed and pasture their animals, which makes elimination of schistosomiasis difficult[29]. Currently, livestock and fishermen frequent snail-infested areas, with risk of *S. japonicum* infection a persistent threat [30].

Because of the life cycle and transmission pattern of the parasite, no changes in high-risk environments are possible and as a consequence there is a high risk for schistosomiasis transmission in local Chinese regions [31]. Poisson analysis identified eleven clusters of *S. japonicum* human infections, six clusters of livestock infections, and nine 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 [21]. 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* are widespread and concentrated in marshland and lake areas, associated with widespread snail habitats, with large numbers of floating boatmen and fishermen, as well as livestock management difficulties [32, 33]. While the clusters of *S. japonicum* infection were relatively small and dispersive in the two mountainous provinces, they were associated with the block- or dot-like distribution of snails [34, 35]. These findings provide an 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 likely lead to a rebound in schistosomiasis. Surveillance for *S. japonicum* infection and *O. hupensis* needs to be intensified in marshlands, lake areas, and mountainous regions. Further, reinforcement of an integrated schistosomiasis control strategy that emphasizes consideration of; the sources of *S. japonicum* infection, human *S. japonicum* infections, livestock infections, wild animal infections, and *O. hupensis* infections are recommended for elimination of schistosomiasis in China [36]. A surveillance-response system using a One Health approach is appropriate.

This study has limitations. First, the spatio-temporal analysis of *S. japonicum* infections in humans, livestock, and *O. hupensis* was based at the county level. Future studies at a finer scale (at a village or individual scale) are needed. Second, natural and socio-economic factors were not considered with regard to the spatio-temporal heterogeneity of *S. japonicum* infections in humans, livestock, or *O. hupensis*. Further analysis of climate, geography, and social developments at a finer scale would provide important insights into precision control of schistosomiasis.

Conclusions

In summary, the results of this study demonstrate significant spatio-temporal heterogeneity for schistosomiasis in China. Based on the multi-stage downscaling of continuous sentinel monitoring data, a remarkable decline was seen in endemic schistosomiasis in China during the period from 2005 through 2019, with markedly reduced disease. 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, where frequent acute *S. japonicum* infections occur. Using a One Health approach, reinforcement of an integrated schistosomiasis control strategy with emphasis on the sources of *S. japonicum* infection, and on the inclusion of human, livestock, wild animal, and *O. hupensis S. japonicum* infections will provide an effective surveillance-response system that will insure elimination of schistosomiasis in China by 2030.

Abbreviations

Oncomelania hupensis O. hupensis

standard deviational ellipse SDE

disability-adjusted life years DALYs

Annual percent change APC

log likelihood ratio LLR

relative risk RR

Declarations

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Authors' contributions

Yanfeng Gong: Writing - Original Draft, Methodology, Formal analysis and Software.

Jia-Xin Feng, Zhuowei Luo: Validation and Formal analysis.

Jingbo Xue, Zhaoyu Guo: Investigation, Formal analysis.

Li-Juan Zhang, Shang Xia: Data curatuion.

Shan Lv, Jing Xu: Review and Conceptualization.

Shizhu Li: Study Design, Conceptualization, Writing - Review & Editing, and Project administration.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Ethics approval and consent to participate

This paper was based on an analysis of routinely collected surveillance data from national institute of parasitic diseases, China CDC. No individual information was revealed.

Consent for publication

Not applicable

Competing interests

The authors declare that they have no competing interests.

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Tables

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

Parameter	Time period	*t* value	*P* value	Annual percent change	Lower limit of 95% *CI*	Upper limit of 95% *CI*
Prevalence of *Schistosoma japonicum* infection in humans	2005–2019	–8.12	< 0.01	−45.35	−53.45	−35.81
Prevalence of *Schistosoma japonicum* infection in livestock	2005–2008	–13.00	< 0.01	−41.40	−46.80	−35.40
	2008–2012	–2.10	0.07	−17.10	−32.80	2.4
	2012–2019	–5.50	< 0.01	−67.20	−79.70	−46.80
Prevalence of *Schistosoma japonicum* infection in snails	2005–2019	–3.43	< 0.01	−14.07	−21.89	−5.47

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 number	Time period	Cluster center		Radius (km)	Observed number	Expected number	*RR*	*LLR*	*P* value	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.

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 number	Time period	Cluster center		Radius (km)	Observed number	Expected number	*RR*	*LLR*	*P* value	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.

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 number	Time period	Cluster center		Radius (km)	Observed number	Expected number	*RR*	*LLR*	*P* value	No. of counties clustered
			Longitude	Latitude							
Five provinces in marshland and lake regions	1	2006–2010	28.91°	111.98°	92.7	698	128.9	7.32	691.5	<0.01	10
	2	2005–2007	29.47°	113.01°	0.00	162	21.60	7.99	190.4	<0.01	1
	3	2005–2009	28.55°	115.95°	78.48	235	75.39	3.36	113.4	<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	23.7	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.

Figures

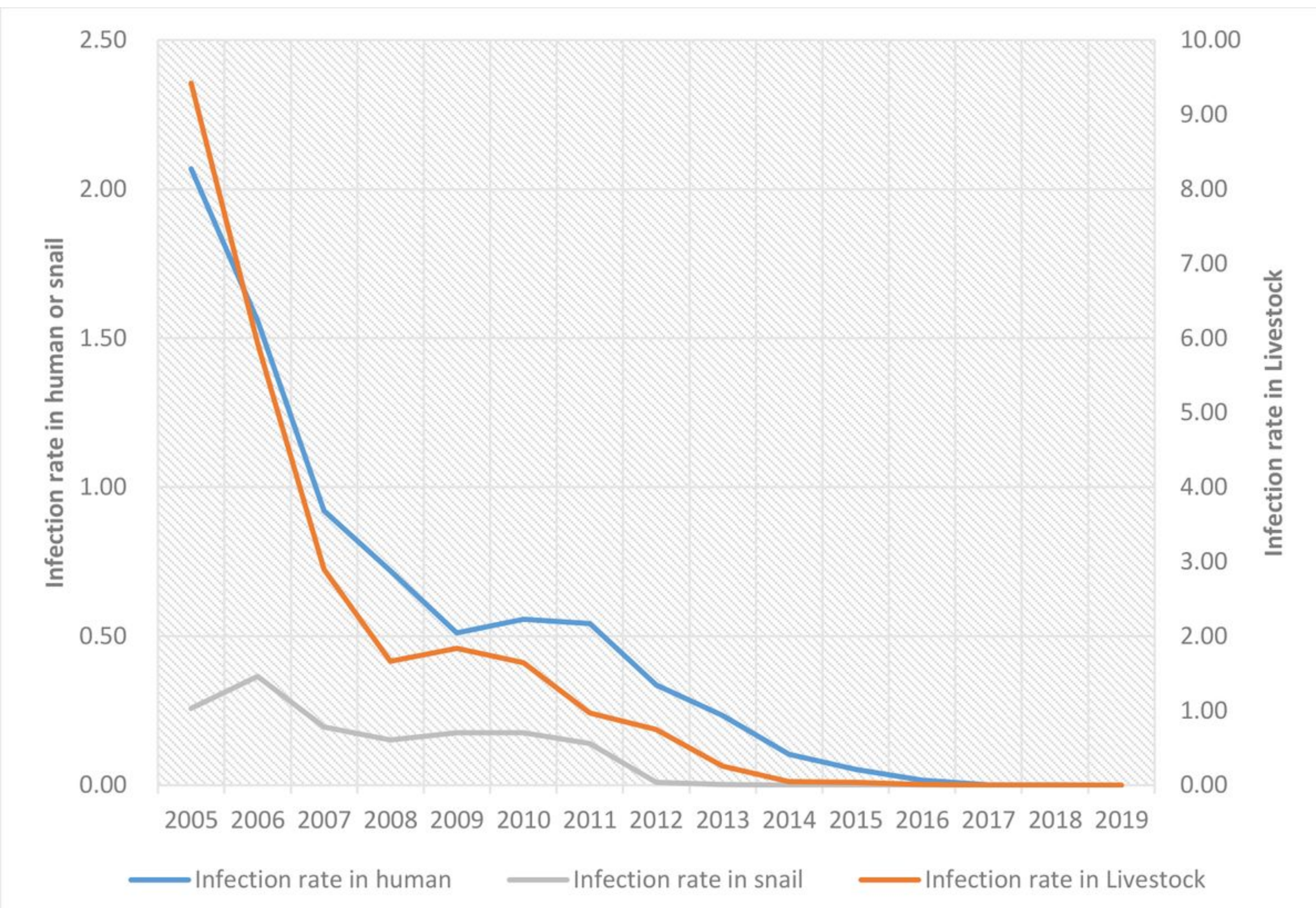

Figure 1

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

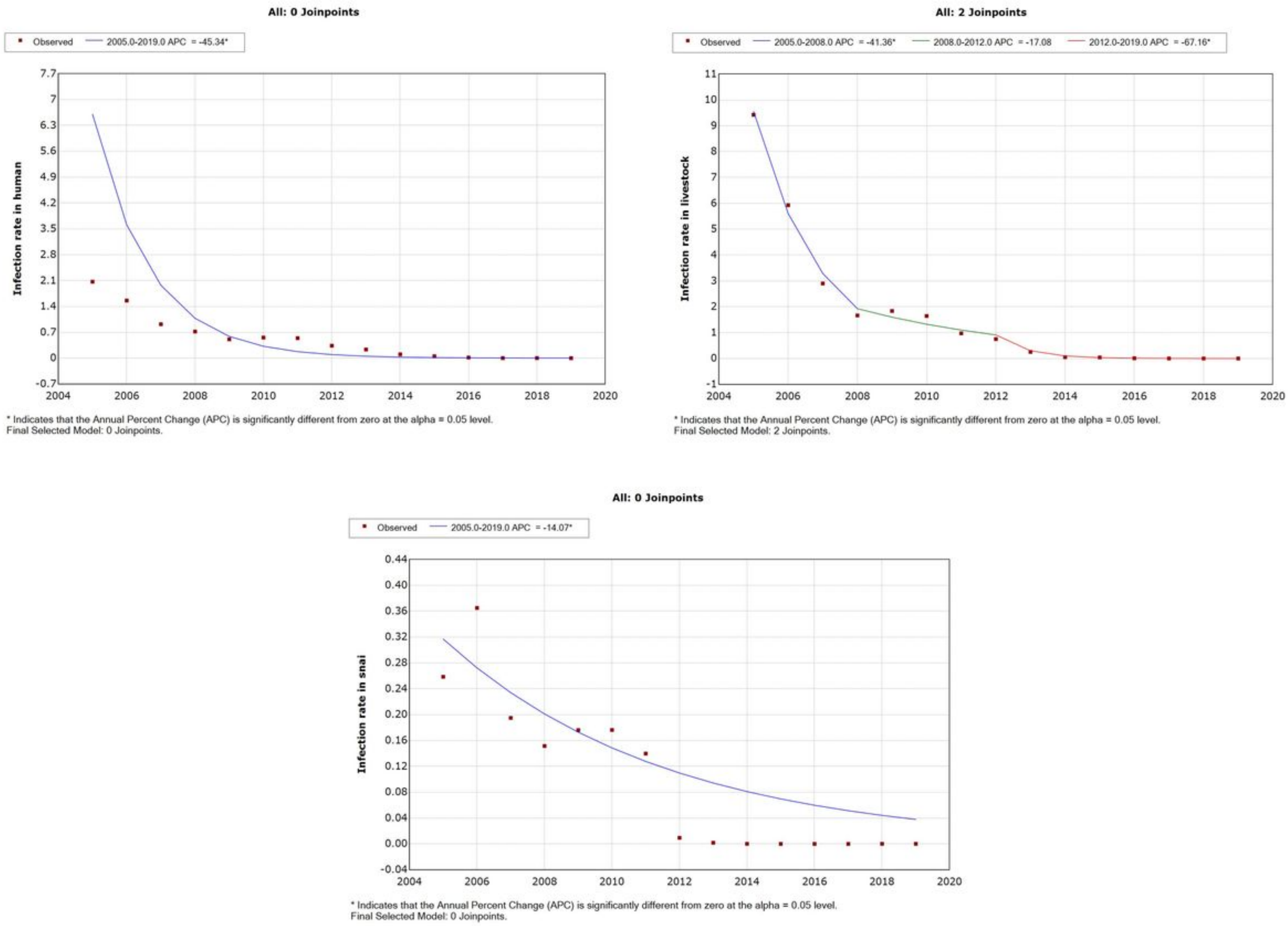

Figure 2

Trend changes in the prevalence of Schistosoma japonicum infection in humans, livestock, and Oncomelania hupensis based on the national schistosomiasis surveillance sites of China from 2005 to 2019. a, Trend changes in the prevalence of Schistosoma japonicum infections in humans; b, trend changes in the prevalence of Schistosoma japonicum infections in livestock; c, trend changes in the prevalence of Schistosoma japonicum infections in Oncomelania hupensis.

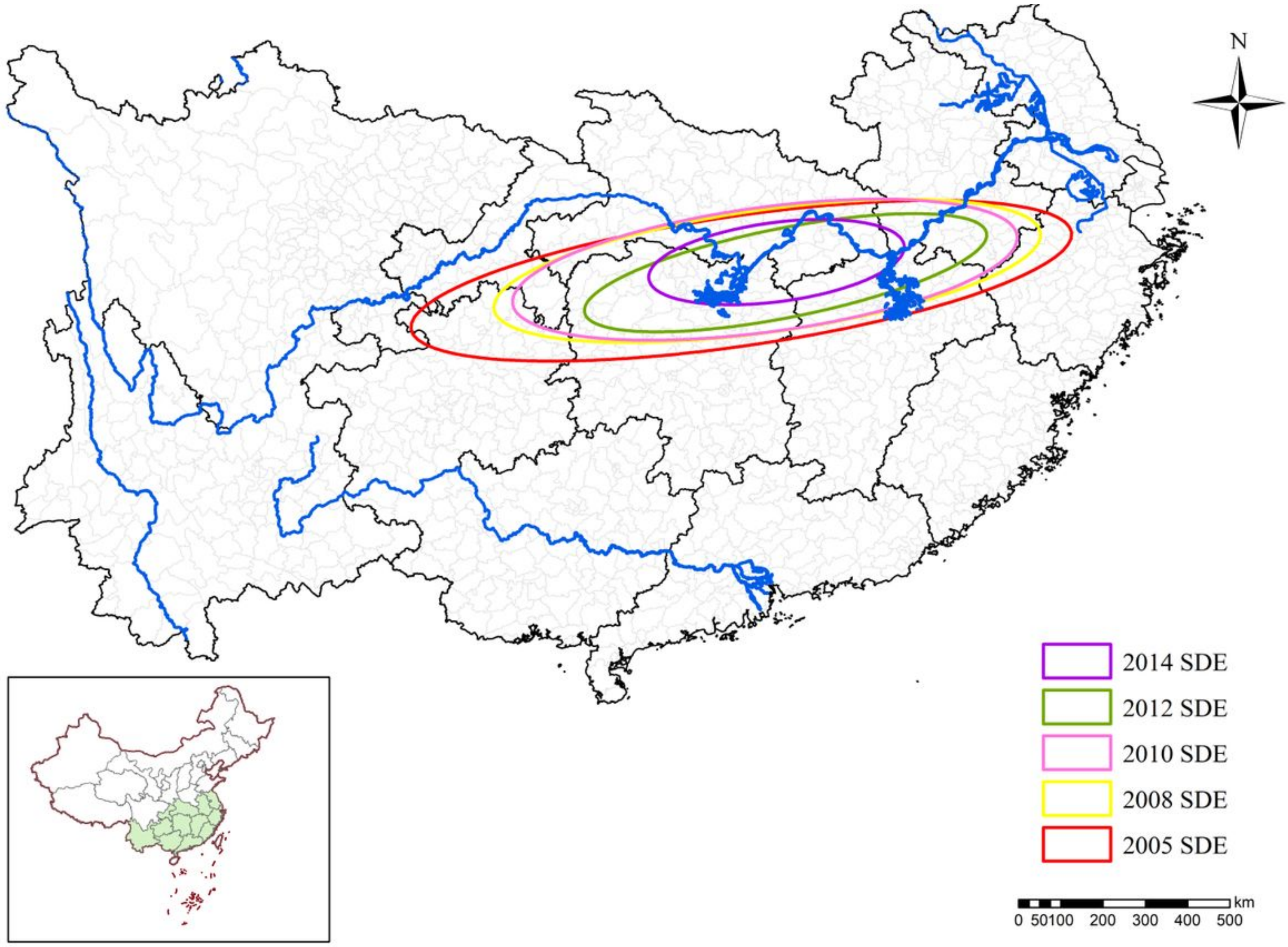

Figure 3

Discrete trend changes in the prevalence of human schistosomiasis based on the national schistosomiasis surveillance sites of China from 2005 to 2014.

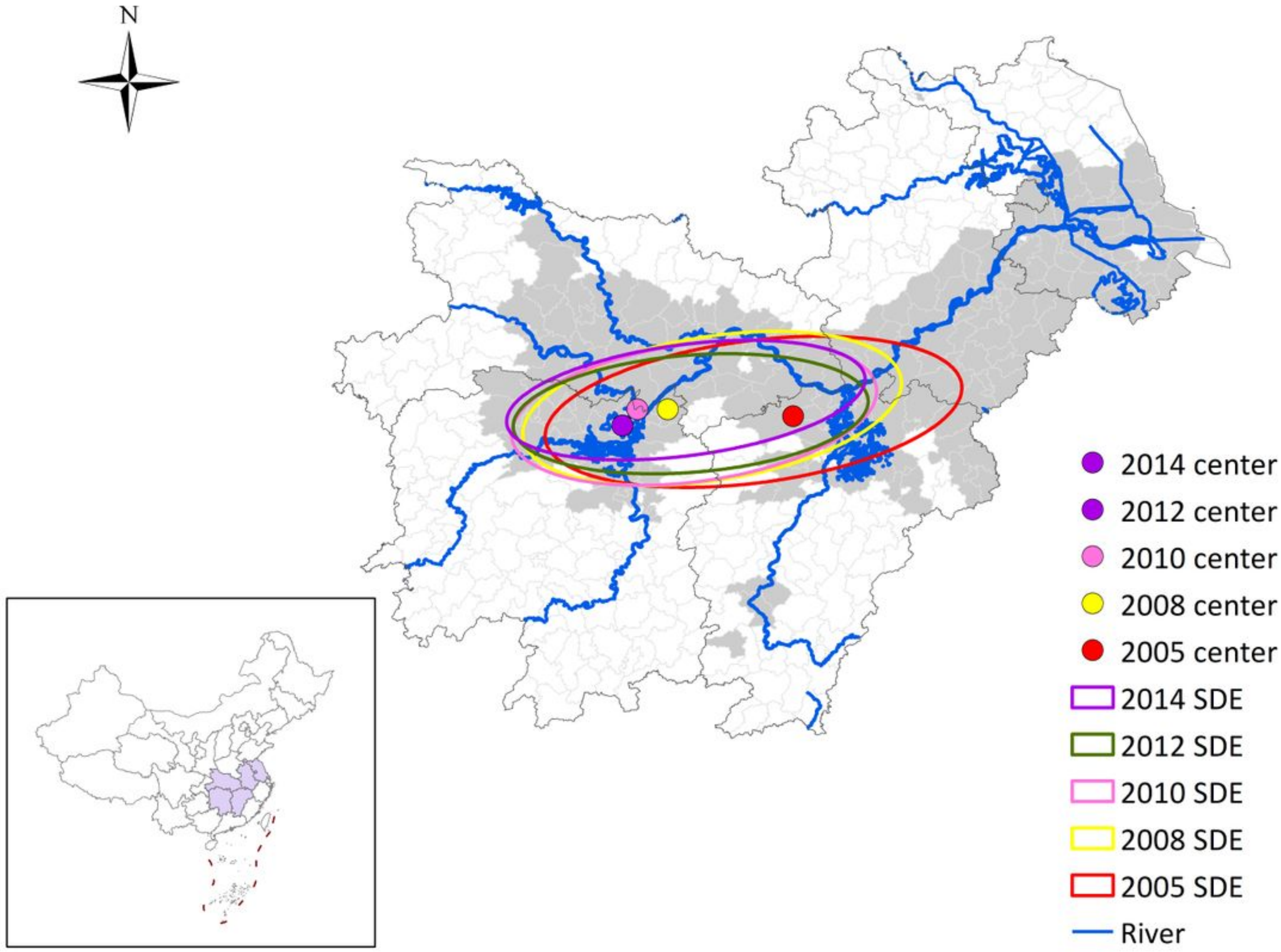

Figure 4

Central and discrete trend changes in schistosomiasis cases in five Chinese provinces; Hunan, Hubei, Anhui, Jiangxi, and Jiangsu from 2005 to 2014.

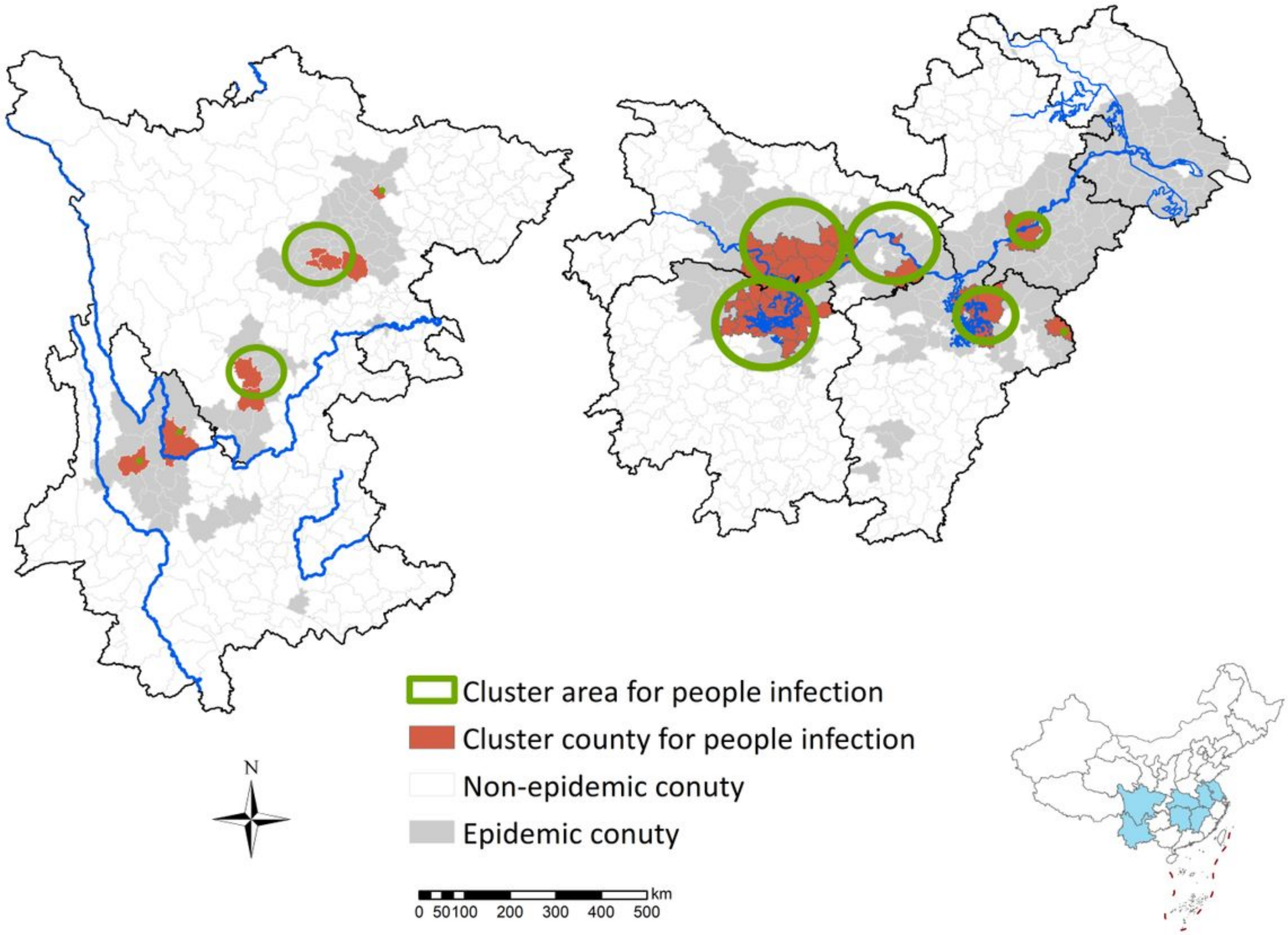

Figure 5

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

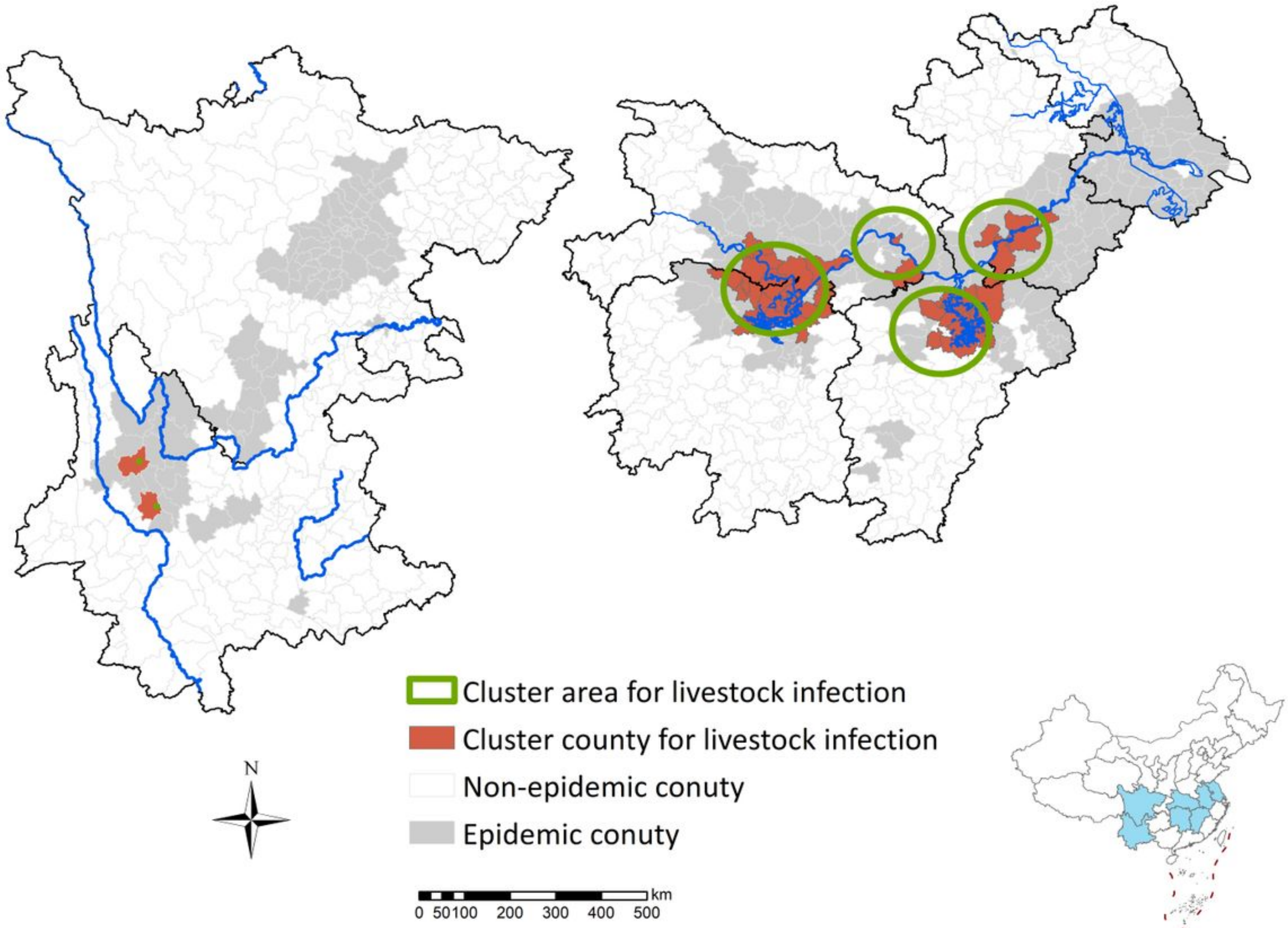

Figure 6

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

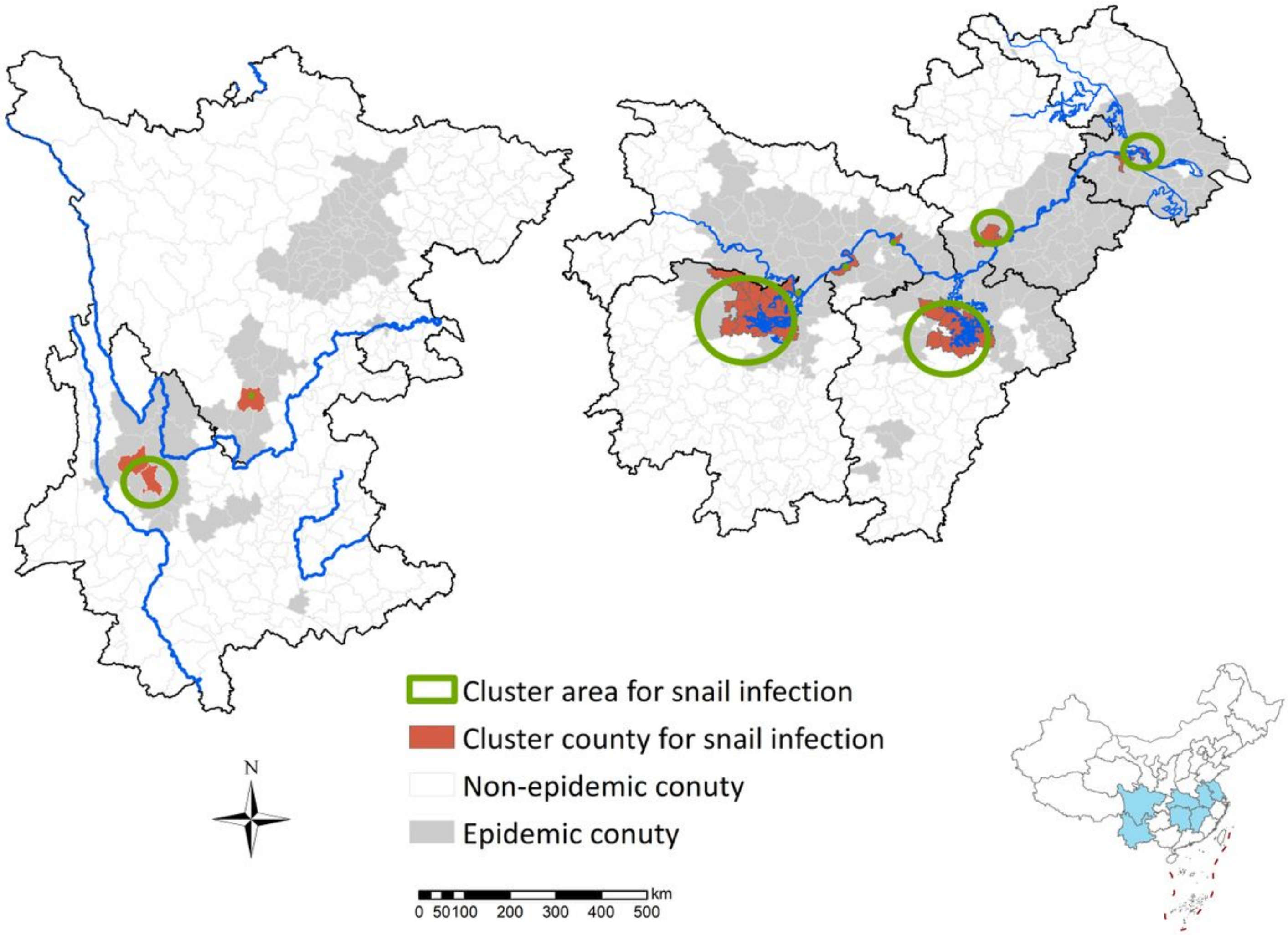

Figure 7

Spatio-temporal cluster distributions of Schistosoma japonicum infections in Oncomelania hupensis based on the national schistosomiasis surveillance sites of China from 2005 to 2019.

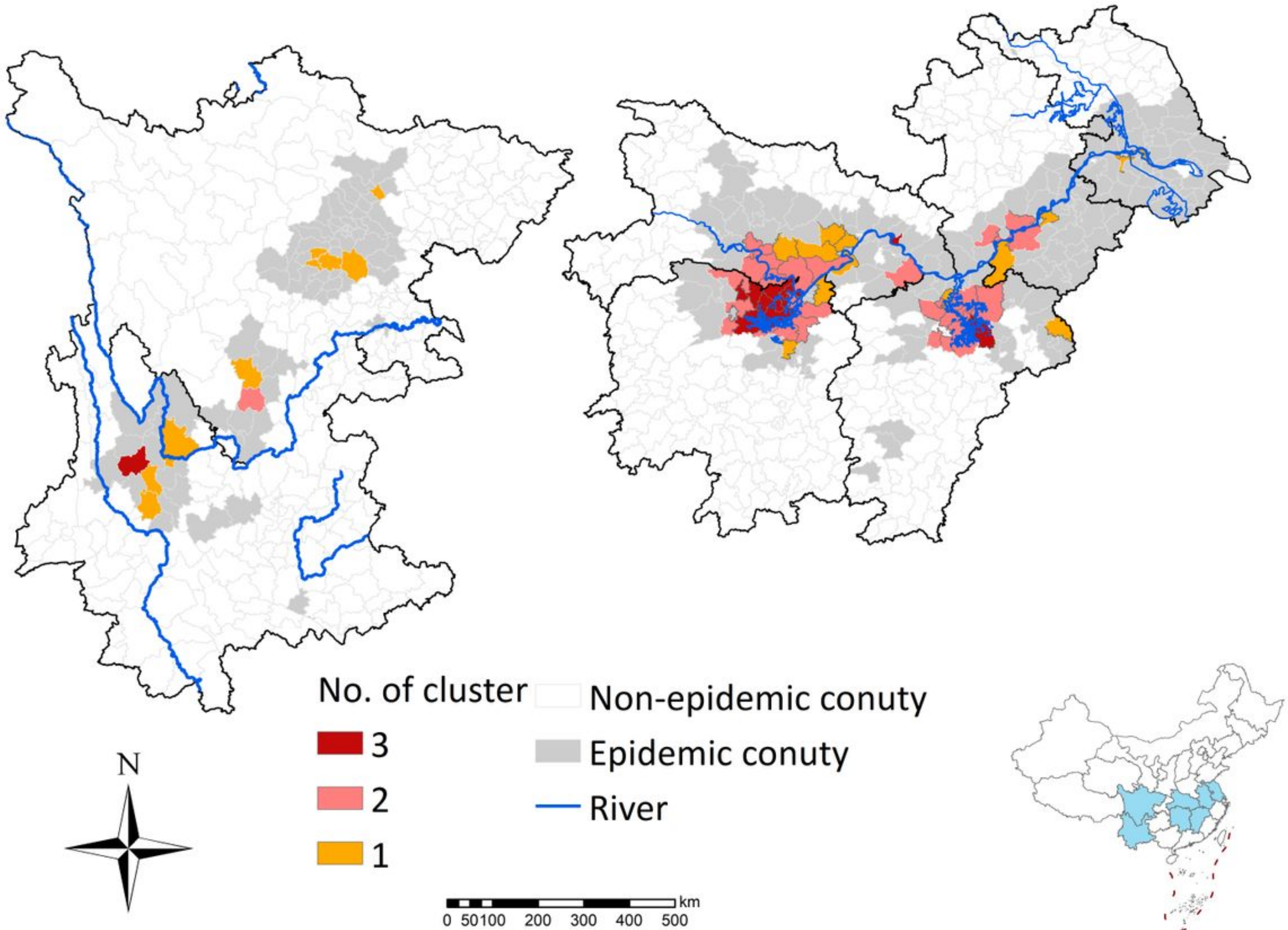

Figure 8

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.

Supplementary Files

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- Graphical.jpg