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The spatio-temporal distribution of *Oncomelania hupensis* along Yangtze river in Jiangsu Province, China after implementation of a new, integrated schistosomiasis control strategy

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Abstract

This study concerns an integrated strategy of schistosomiasis control, focusing on the management and elimination of the main transmission cycles and reservoirs along Yangtze river, Jiangsu Province (China), instituted in 2004. Our analysis, including mapping, spatial autocorrelation and spatio-temporal scanning, was implemented between 2001 and 2013 to explore the changes in the distribution of *Oncomelania hupensis*, the intermediate host of *Schistosoma japonicum*. Two high-density snail locations in the upper and middle reaches of the river were observed along with one high-risk area due to infected snails in the upper reaches at the beginning of the study period. The number of high-density snail habitats declined sharply after 2004 and infected snails disappeared completely by 2010. Global spatial autocorrelation showed spatial clustering of snails in general, as well as of infected ones when snail densities were relatively high, while local spatial autocorrelation showed the number of specific clusters declining and switching spatially from the upper to the middle reaches of the Yangtze river in Jiangsu Province during the study period. The integrated snail control strategy was found to be effective, but the middle reaches of the river will require continued strong control resources.

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Introduction

Infection by *Schistosoma japonicum,* the parasitic flatworm that causes human schistosomiasis, is still a significant cause of morbidity in China and even more so in the Philippines (Zhou *et al*., 2009). The snail *Oncomelania hupensis* is the only intermediate host of *S. japonicum* in China. From the environmental point of view, the endemic areas fall into three main types: the marshlands and lakes region, the hilly and mountainous region, and the plains with water networks. The development of snails is not only affected by their own growth rhythm (Wilke *et al*., 2000), but also by the prevailing socio-economic situation as well as by environmental variables, such as hydrological characteristics, vegetation type, weather, elevation, *etc*. (Yang *et al*., 2005; Seto *et al*., 2008; Wu *et al*., 2008; Zhang *et al*., 2008; Yang *et al*., 2011).

Jiangsu Province comprises an area of 102,600 km^2 located downstream Yangtze River in the eastern part of China, where the marchlands, plains and hilly areas amount to 69, 17 and 14%, respectively. Historically (in 1949), with close to 2.5 million schistosomiasis patients and 1473 km^2 of snail habitats, Jiangsu province ranked fourth for snail-infested areas in the country and was also the most seriously affected province (Hong *et al*., 2011; Zhou *et al*., 2007). By 1976, however, the snail habitats had declined to less than 2% of what they once covered, but after the catastrophic floods of 1998 the schistosomiasis epidemic rebounded and the snail habitats increased significantly (Chen *et al*., 2002; Yang *et al*., 2012b). In 2004, a new comprehensive control strategy focusing on the management and elimination of the main transmission cycles and reservoirs was announced by the Ministry of Health of China (Wang *et al*., 2009; Collins *et al*., 2012). Based on this adjustment, the Government of Jiangsu province announced new medium- and long-term goals for its schistosomiasis control programme in 2005. The new approach included snail control, chemotherapy of both infected humans and livestock, improved sanitation, health education and targeted interruption of the schistosomiasis transmission cycle through environmental and behavioural modification (Yang *et al*., 2008; Hong *et al*., 2011; Liang *et al*., 2012). After the integrated control strategy had taken hold, the snail habitats started to decline, reaching 28 km^2 in 2013 (Lei *et al*., 2014). To follow up what was happening, we decided to apply spatio-temporal models to study the dynamic change of the snail habitats and evaluate the integrated control strategy in order to provide leads for a scientific basis for both snail and schistosomiasis control.

Materials and Methods

Study area

The study was centred on the part of Jiangsu province that is divided into a northern and southern part by the lower reach of Yangtze river. This area covers around 27,000 km^2 and includes seven cities (Nanjing, Zhenjiang, Yangzhou, Changzhou, Taizhou and Nantong). All snail habitats along Yangtze River in Jiangsu Province were selected. A digital map was downloaded from the national basic geographic map database of the National Basic Geographic Information Centre in China (http://www.ngcc.cn/). This map included all provincial and county-level administrative boundaries and rivers (Figure 1).

The snail survey database

Snail surveys were performed annually in March and April based on mechanical sampling using 0.1 m^2 frames of iron wire, placed about 10 m from each other (Agresti, 1991) in the snail habitats marked in Figure 1. All snails within the frame were collected, enumerated, crushed and microscopically examined to find out if they contained any *S. japonicum* sporocysts. The number of survey frames investigated along with the total number of live snails found per frame and the number of infected ones were counted. All areas where live snails were found were defined as snail-infested. The snail density was calculated as the number of snails per frame divided by the total number of frames used for the survey; the corresponding density of infected snails was calculated in the same way.

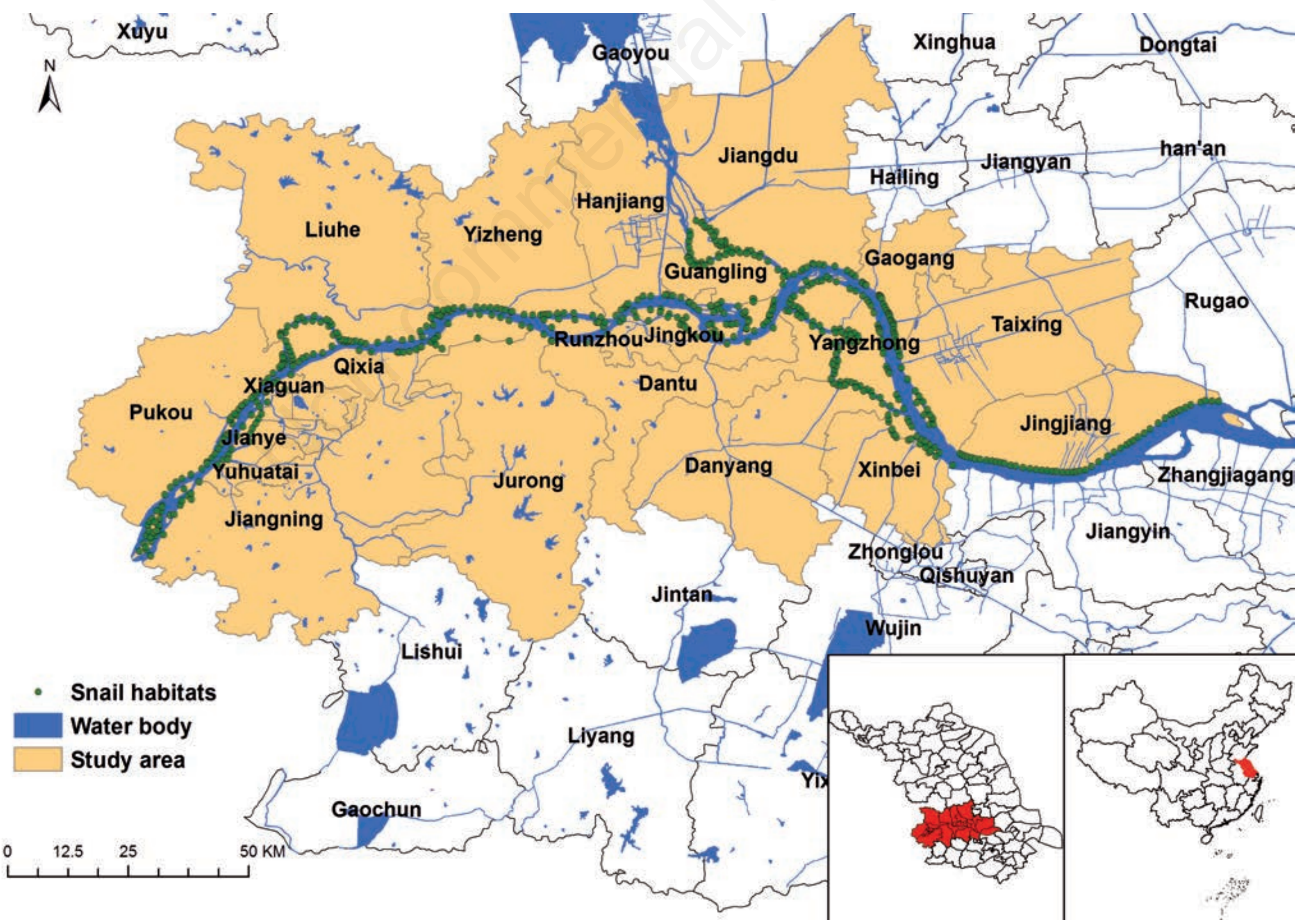

Figure 1. The study region along Yangtze River in Jiangsu Province, China.

The spatial snail database

The geographical coordinates of the surveillance sites were recorded with a global positioning systems receiver (Garmin Map76; Garmin, Lenexa, KS, USA). Based on these measurements, we recorded the changes in snail densities and habitats from 2001 to 2013. Then, we plotted the data using Google Earth® (Google, v. 7.1; Google, Mountain View, CA, USA) saving this information as keyhole markup language files (Sun *et al*., 2011; Yang *et al*., 2012a). These files were finally transferred into ArcGIS software v. 10.0 (ESRI, Redlands, CA, USA), thereby establishing a spatial survey database.

Descriptive analysis

The snail data from the different types of snail habitat in Jiangsu Province from 2001 to 2013 were downloaded from the survey database (Table 1). Classification was carried out using Excel (Microsoft Office, v. 2013) comparing the annual changes from 2001 to 2013 with respect to area, snail density and environmental type. The snail density was classified as belonging to one of six levels, namely: 0-0.1; 0.1-0.5; 0.5-1; 1-5; 5-10; and 10-∞snails per 0.1 m^2 frame. We recorded the total number of live snails and those found to be infected separately.

The chi-square test was used to explore statistically significant differences in snail density and habitat coverage. The linear-by-linear association test by SPSS (IBM, v. 19.0) was used to examine if the ranked data had a linear association (Agresti, 1991; Yaniv *et al*., 2011). Total snail densities and those of infected snails were mapped in ArcGIS and displayed as circles of different colours and sizes (Figure 2).

Spatial autocorrelation

Global and local spatial autocorrelation were used to describe the spatial snail distributions at different scales. The former was applied for the spatial distribution at the provincial scale and the latter for the

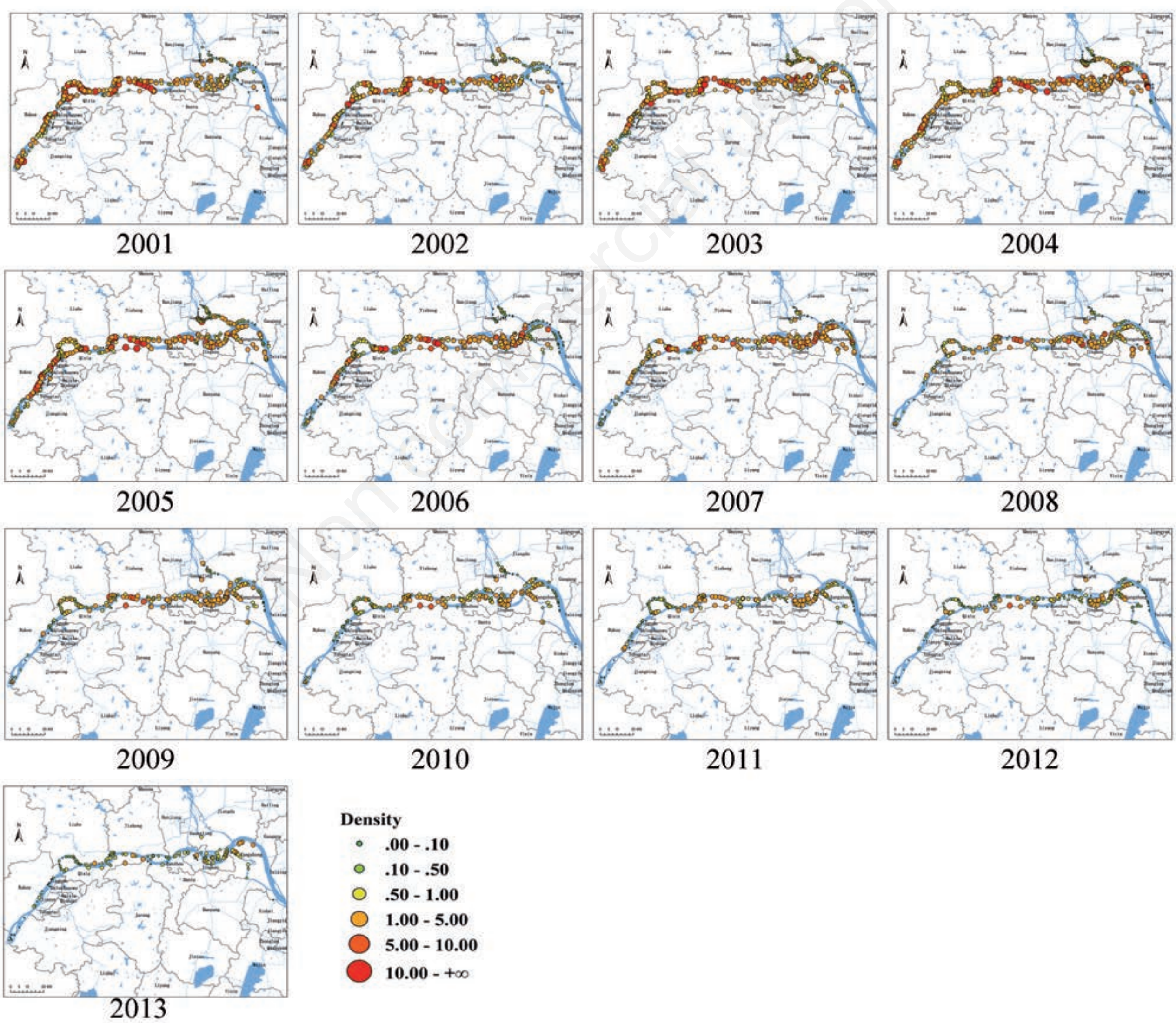

Figure 2. Snail densities along Yangtze River in Jiangsu Province (China), 2001-2013.

detection of local hotspots and/or coldspots using Gi* index analysis (Ord and Getis, 1995).

Global Moran's I varies between -1 and +1 with positive values indicating positive spatial autocorrelations, negative values negative ones and zero representing a random pattern. This approach was used to detect whether the snail densities (total and infected) had a global spatial autocorrelation at the provincial scale using the formulation:

$$I = \frac{n \sum_{i=1}^{n} \sum_{j=1}^{n} w_{ij}(x_i - \bar{x})(x_j - \bar{x})}{\sum_{i=1}^{n} \sum_{j=1}^{n} w_{ij} \sum_{i=1}^{n} (x_j - \bar{x})^2} \quad \text{(eq. 1)}$$

where n is the number of spatial units; x_i and x_j the observed density values (x) in the spatial i and j units; and W_{ij} the weight of the spatial relationship. The Z test (Ward and Carpenter, 2000) was used to find cluster trends with Z>1.96 indicating such a situation, while Z<-1.96 represents a discrete distribution.

Getis-Ord G statistics (Ord and Getis, 1995) is more sensitive for localised clusters and the Gi* index is useful for the identification of hotspots or cold spots, *i.e.* increased or decreased snail densities, since significantly high values are surrounded by other high values and low values are surrounded by low values (Truong and Somenahalli, 2011). The mathematical notations are:

$$G_i^* = \frac{\sum_{j=1}^{n} w_{ij} x_j - \bar{X} \sum_{j=1}^{n} w_{ij}}{S \sqrt{\frac{\left[n \sum_{j=1}^{n} w_{ij}^2 - \left(\sum_{j=1}^{n} w_{ij}\right)^2\right]}{n-1}}} \quad \text{(eq. 2)}$$

$$\bar{X} = \frac{\sum_{j=1}^{n} x_j}{n} \quad \text{(eq. 3)}$$

$$S = \sqrt{\frac{\sum_{j=1}^{n} x_j^2}{n} - \bar{X}^2} \quad \text{(eq. 4)}$$

where x_i and x_j are the observed snail density values (the i and j spatial total and infected) in units and W_{ij} the weight of the spatial relationship. As for the Moran's I investigation, the Z test was used to detect the significance of the spatial autocorrelation found.

Cluster analysis

SaTScan™ (v. 9.4; http://www.satscan.org/) was used to detect clusters of high and low snail numbers by the space-time permutation model, which is defined by a cylindrical window constrained to clusters with both the proportion of the population at risk (for infected snails) and study periods less than 50% (Coleman *et al.*, 2009). Relative risk (RR), *i.e.* the estimated risk within the cluster compared to the estimated risk outside the cluster, was calculated for each cluster. The mathematical notation is:

$$RR = \frac{n_{i,r}/\mu_{i,r}}{(N - n_{i,r})/(N - \mu_{i,r})} \quad \text{(eq. 5)}$$

where r is the radius of observed cases within the cluster; i the code of observed cases; $n_{i,r}$ the observed number of cases within the cluster; $m_{i,r}$ the expected number of observed cases; and N the total number of cases in the dataset. Monte Carlo simulations (999 times) were used for testing the significance at the 0.05 P level.

Results

Overall, the descriptive statistics demonstrated significant annual improved values after the new strategy had been instituted in 2004, both with respect to snail numbers in general and to those infected.

Table 1. Coverage and proportion of the three types of snail habitats in Jiangsu Province (China), 2001-2013.

Year	Marshlands (km^2, %)	Plains and canals (km^2, %)	Hills and mountains (km^2, %)	Total area (km^2)
2001	63.8-93.4	3.5-5.1	1.0-1.5	68.3
2002	67.5-94.1	3.4-4.7	0.9-1.2	71.8
2003	71.0-94.3	3.5-4.6	0.8-1.1	75.3
2004	74.0-93.9	4.0-5.1	0.8-1.0	78.8
2005	73.5-93.9	4.2-5.4	0.6-0.8	78.3
2006	57.2-93.8	3.4-5.5	0.4-0.7	61.0
2007	44.1-95.7	1.7-3.6	0.3-0.7	46.1
2008	38.5-94.5	1.9-4.7	0.4-0.9	40.8
2009	42.2-94.4	2.0-4.5	0.5-1.1	44.7
2010	41.7-94.5	2.0-4.4	0.5-1.1	44.2
2011	36.5-94.4	1.8-4.6	0.4-1.0	38.7
2012	36.4-94.4	1.8-4.6	0.4-1.0	38.6
2013	26.3-93.8	1.5-5.3	0.3-0.9	28.1

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Table 2. The value of Moran's *I* and its statistical significance of snail habitats along Yangtze river in Jiangsu province (China), 2001-2013.

Year	Density of the overall number of snails°			Density of infected snails#		
	Moran's *I*	*Z*	P	Moran's *I*	*Z*	P
2001	0.22	10.52	0	0.15	7.48	0
2002	0.27	9.53	0	*0.03*	*1.12*	*0.26*
2003	0.27	15.07	0	0.15	8.45	0
2004	0.22	13.58	0	0.12	6.72	0
2005	0.14	8.63	0	0.18	10.01	0
2006	0.17	8.89	0	0.13	7.11	0
2007	0.23	6.63	0	0.10	5.15	0
2008	0.13	3.98	0	0.03	0.83	0.41
2009	*0.15*	*1.54*	*0.12*	*0.15*	*15.2*	*0.13*
2010	0.25	2.50	0.01	-	-	-
2011	0.30	2.24	0.02	-	-	-
2012	0.24	19.5	0.05	-	-	-
2013	*0.13*	*0.77*	*0.44*	-	-	-

°Note the absence of clusters in 2009 and 2013 (in italics); #note the absence of clusters in 2002 and 2008-2009 (in italics).

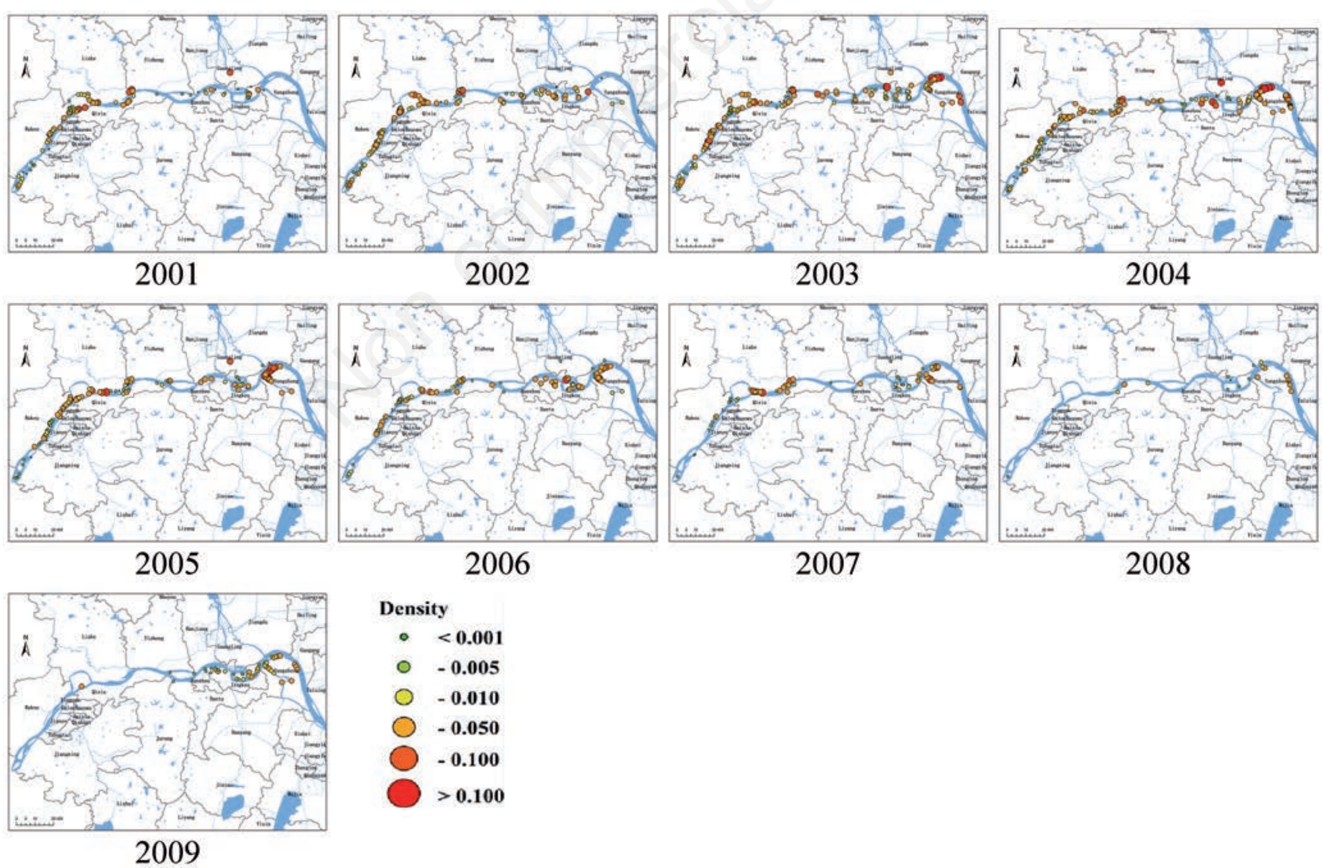

Figure 3. Densities of infected snails along Yangtze River in Jiangsu Province (China), 2001-2009. Note the ongoing, continuous disappearance of infected snail habitats over the period 2001-2009.

The total snail-infested areas increased significantly in the first 5 years (before the change took place), reaching a peak in 2005 before turning into a consistent, downward trend. Although, there were fluctuations, the overall trend was generally downward.

The snail densities found along Yangtze River are displayed as circles of different colours and sizes on the map in Figure 2. Green colour and small size indicate low densities, red and large size high densities with yellow and amber representing intermediate values (Figure 2). The average snail density declined from 2.0512 snails/0.1 m^2 in 2001 to 0.3739 snails/0.1 m^2 in 2013 (a reduction of 81.8%), while the density of infected snails declined from 0.0027 snails/0.1 m^2 in 2001 to 0.0006 snails/0.1 m^2 in 2009 (Figure 3). The chi-square test showed that the snail density in general (χ^2=493.573, P<0.01), as well as that of infected snails (χ^2=71.647, P<0.01), had declined significantly. The linear-by-linear association test also showed a linear downward trend of snail densities, for all snails (χ^2=247.752, P<0.01) as well as for those infected (χ^2=20.615, P<0.01).

The total area of snail habitats along Yangtze River declined from 57.7 km^2 in 2001 to 25.4 km^2 in 2013, while the area harbouring infected snails along Yangtze River was 16.3 km^2 in 2001, after which there was a downward trend ending with total elimination of infected snail habitats in 2010 (Figure 4). Although the proportion of snail-infested marshlands in Jiangsu Province made up more than 90% of all areas, the number of all snail habitats declined from 390 in 2001 to 151 in 2013 (a reduction by 61.3%). The number of infected snail habitats in these regions was even more strongly reduced and these habitats disappeared completely by 2010. The maps also show that the density of infected snail habitats in the marshlands along Yangtze River lingered the longest in the downstream areas of the river.

Spatial autocorrelation

At the provincial level, global autocorrelation indicated annual, statistically significant spatial clusters of snail density (P<0.05) during the entire study period with exception of the years 2009 and 2013 (Figure 5 and Table 2). However, as can be seen in the table, local clusters were observed in 2001 and from 2003 to 2007 (P<0.05) when investigating the presence and density of infected snails, No infected snails existed after 2009 and the distribution was random in the other years (2002 and 2008-2009).

When investigating local autocorrelation with the Gi* method, it was found that the snails in the period 2001-2007 were mainly concentrated in Nanjing, Yangzhou and other places along the upper reaches of the Yangtze River, while hotspots began to appear downstream, *e.g*. in Zhenjiang in 2008, and continued to do so until the end of the study period in 2013 (Figure 6). With regard to infected snails, the hotspots primarily clustered in two regions of Nanjing and Zhenjiang from 2001 to 2003. They did not appear in later years in Nanjing, but remained in Zhenjiang until 2009 (Figure 7). Table 3 shows that high levels of spatial clustering existed during most of the 13-year long study period, both of snails in general and infected snails (however, the latter only up to 2007). The RR of the two snail clusters was 1.19 (Table 3). From 2001 to 2005, the centre of east area was in Jingkou District, Zhenjiang City (E119.67°, N 32.26°) with a radius of 14.5 km, which included the entire city of Nanjing as well as three districts of Yangzhou City (Jiangdu, Guangling and Yangzhong) and two districts of Zhenjiang City (Jingkou and Dantu). The other centre existed from 2001 to 2006 and was centred in Yizheng District, Yangzhou City (E119.08°, N 32.25°). The radius was 39.9 km, including the districts of Hanjiang and Yizheng in Yangzhou City, the districts of Liuhe, Qixia, Pukou and Jiangning in Nanjing City and the districts of Runzhou, Dantu and Jingkou in Zhenjiang City (Figure 8). Areas at risk due to infected snails covered the whole of Nanjing City

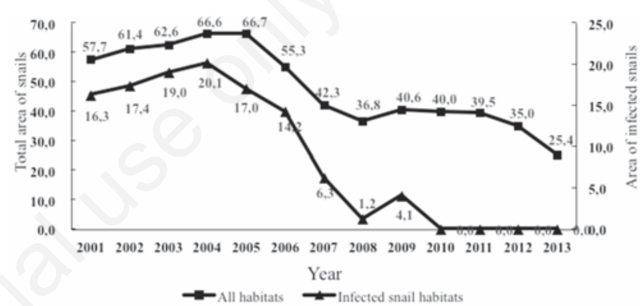

Figure 4. Areas covered by snail habitats along Yangtze River in Jiangsu Province (China), 2001-2013. Measurement in km^2.

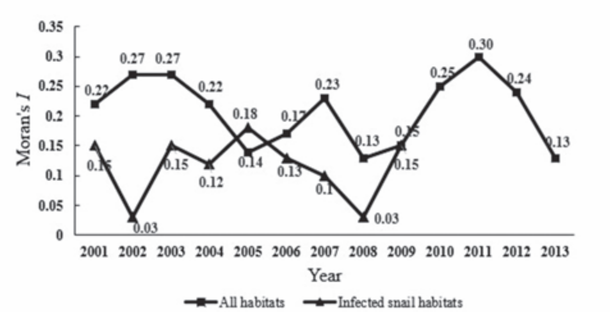

Figure 5. Moran's *I* applied to snail habitat densities along Yangtze River in Jiangsu Province (China), 2001-2013.

Table 3. Significant clusters found by the SaTScan™ for snail habitats along Yangtze River in Jiangsu Province (China), 2001-2013.

	No.	Cluster area			Cluster years	RR	P
		Latitude (N)	Longitude (E)	Radius (km)			
All live snails	1	32.26	119.67	14.46	2001-2005	1.19	0
	2	32.25	119.08	39.85	2001-2006	1.19	0
Infected snails	1	32.09	118.71	37.81	2002-2007	3.00	0

RR, relative risk.

from 2002 to 2007 with a radius of 37.8 km^2 centred on Xiaguan district (Figure 9).

Discussion

Previous studies have shown beyond doubt that flooding by the Yangtze River and other connected hydrological features are the main reasons for the spread of snails in the marshlands lining the river (Zhou *et al*., 2002). This makes it clear that an effective way to prevent the transmission of schistosomiasis would be to control the number of snails in these areas, which are frequented by both humans and domestic animals. Although the completion of the Three Gorges Dam has contributed to lower snail counts in general, since the water levels have dropped and flooding has been avoided (Li *et al*., 2013; Seto *et al*., 2008; Zhu *et al*., 2008), the chi-square and linear-by-linear association tests demonstrate that the change of control strategy in 2004 produced statistically verified improved results with respect to the snail numbers that have continued to diminish towards the end of the study period and beyond. This piece of information fills the long-standing gap of understanding how various control approaches work. We conclude thus that the Jiangsu Department of Schistosomiasis, thanks to its scientific planning and snail control strategy, has succeeded in controlling the intermediate snail host and thus the spread of schistosomiasis. It should be noted, however, that although all types of snail habitat have had a downward trend, only the marshlands data were used for the analysis presented here since this type of area dominates completely in

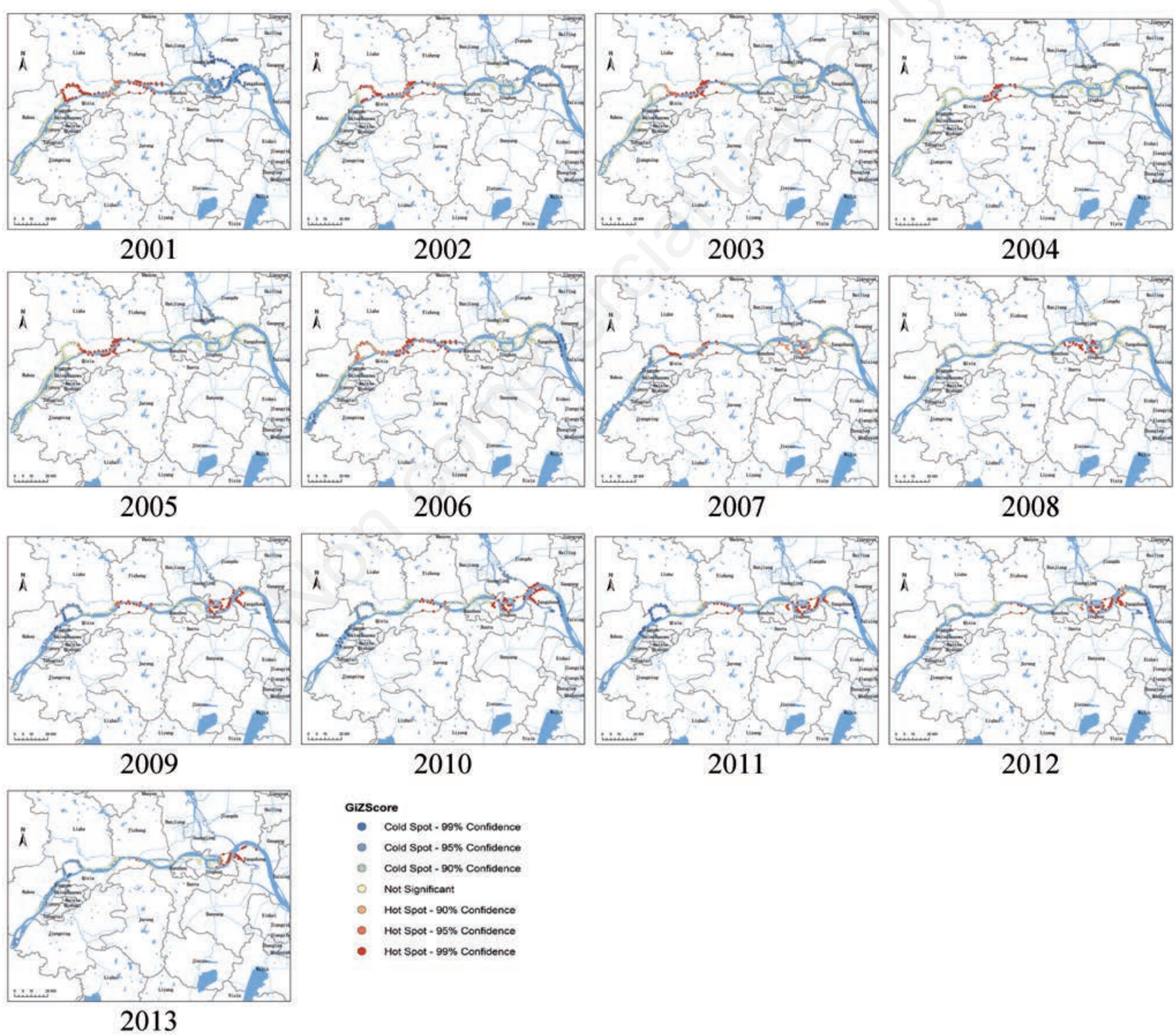

Figure 6. General distribution of snail habitats along Yangtze River in Jiangsu Province, (China) 2001-2013.

Jiangsu province (at least 90% of all snail-infested areas in the province).

Reflecting the degree of autocorrelation in the region, global Morans'*I* provided essential information on the spatial pattern of the snail distribution in the entire study area, and the Gi* index revealed the relevance of this property for each and adjacent spatial units (Sokal and Oden, 1978). Cluster formation at the provincial level, seen in most of the study years, indicated that some area(s) may include undetected high-density snail habitats. However, the disappearance of clusters of infected snails in the years before they were eliminated, and the declining cluster trend of snails in general in recent years, support the goal of eliminating schistosomiasis in China in the next decade (Tambo *et al*., 2014). The declining trend of hotspots and the change of local clusters from upstream to midstream of Yangtze river, as indicated by the Gi* index, are signs of the difference between snail control activities in different cities. This important finding indicates that some places located midstream of the Yangtze River in Jiangsu province need to pay more attention to the schistosomiasis problem and institute better snail control. The noted move of local clusters from low latitudes to high latitudes is of interest and requires further study to find out whether it is associated with environmental change as suggested by Zhou *et al*. (2008).

Two clusters of snail presence were found at the upstream and midstream of the Yangtze River in Jiangsu Province using spatio-temporal scanning. Time-wise, these clusters were almost identical to those that occurred in 2001-2006 and 2001-2005. Unlike the Gi* index, no clusters were discovered by SaTScan after 2006, while the Gi* index indicated continued existence of hotspots. The reason may be related to the different principles used by these two statistical approaches. Local spatial autocorrelation uses the spatial properties of one unit for the estimation of adjacent units indicating hotspots and cold spots by the statistically significance of property difference (Flahaut *et al*., 2003; Viladomat *et al*., 2014). The hotspots of infected snails showed statistical significance in the midstream location. The absence of clusters in this area by SaTScan method could be due to the fact that SaTScan calculates the relative likelihood ratio with non-clustering area under different radii by Monte-Carlo iterative simulation (Chong *et al*., 2013; Luo, 2013; Sherman *et al*., 2014). The snail density clearly decreased significantly and it was eventually hard to find a specific area showing a cluster phenomenon. Although differences between the two methods were recorded, the bottom line is that the integrated control strategy instituted in 2004 in Jiangsu province has had a good effect.

Apart from incurring at least some loss of information by the transfer of density data from actual measurement to numeration, the main limitation of this study is that it was only based on two variables, *i.e.* space and time. The effect of the many different environmental factors, which influence the spread and growth of the snail, could not be

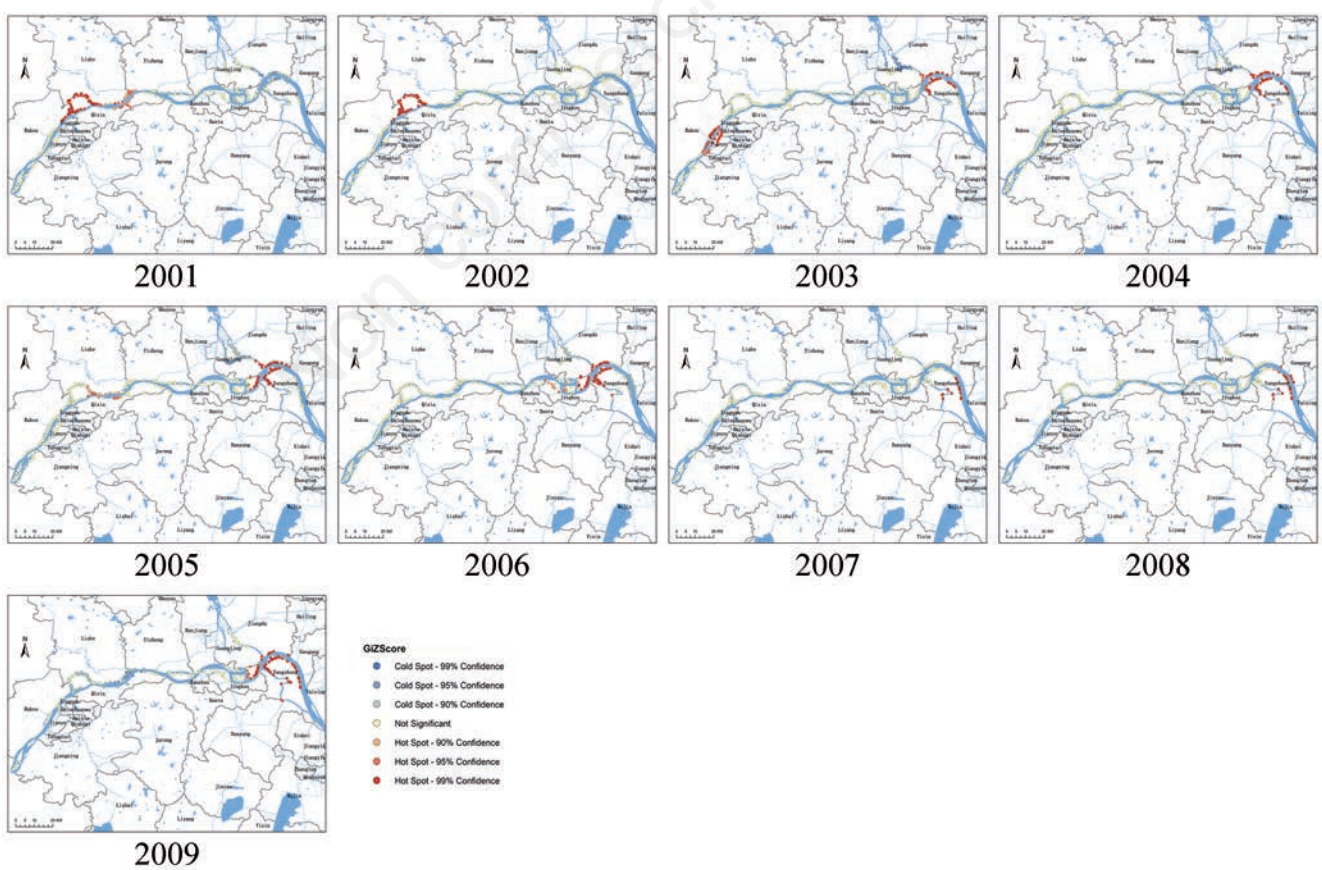

Figure 7. Distribution of infected snail habitats along Yangtze River in Jiangsu Province, (China) 2001-2013.

Figure 8. Spatio-temporal centres of snail habitats along Yangtze River in Jiangsu Province, (China) 2001-2013. The biggest cluster had a radius of 39.9 km and existed from 2001 to 2006 with its centre in Yizheng district, Yangzhou City, while the smaller one had a radius of 14.5 km and existed from 2001 to 2005 with its centre in Jingkou District, Zhenjiang City.

Figure 9. Spatio-temporal centre of infected snails along Yangtze River in Jiangsu Province, (China) 2001-2013. The total area at risk covered the whole Nanjing City from 2002 to 2007 with a radius of 37.8 km centred on Xiaguan District.

taken into account, partly since we focused on the marchlands only. Indeed, the inclusion of such factors and application of Bayesian spatio-temporal modelling would be the next step for a more detailed analysis of which factors and changes have strongest effect.

Conclusions

Statistically significant differences among the years of the study period were observed after the institution of an integrated strategy, even if the effect of the spread and growth of the intermediate *S. japonicum* host snails are difficult to pin down. By using a long-time evaluation, a clear reference for a sustained, downward trend was found with respect to the total number of snails in the endemic areas studied, including the elimination of infected snails. This finding supports the need for the implementation of an integrated snail control strategy to reach elimination of schistosomiasis in the next 5-10 years.

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