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Potential schistosomiasis foci in China: A prospective study for schistosomiasis surveillance and response

Ying-Jun Qian[a], Shi-Zhu Li[a,1], Jing Xu[a], Kun Yang[b], Yi-Xin Huang[b], Zhi-Guo Cao[c], Feng Miu[d], Hui Dang[a], Li-Juan Zhang[a], Li Zhang[a], Qiang Wang[a], Robert Bergquist[e], Xiao-Nong Zhou[a,*]

[a] National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention, Key Laboratory of Parasite and Vector Biology, Ministry of Health, Shanghai 200025, China
[b] Jiangsu Institute of Schistosomiasis, Wuxi, Jiangsu, China
[c] Anhui Provincial Institute of Parasitic Diseases, Wuhu, Anhui, China
[d] Shandong Institute of Parasitic Diseases, Jining, Shandong, China
[e] Ingerod 407, Brastad, Sweden

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ABSTRACT

Schistosomiasis japonica was endemic in 12 provinces (including municipalities and autonomous regions) in the People's Republic of China (PR China). Despite the tremendous decrease of schistosomiasis incidence after almost 60 years of control, the distribution of snail-breeding sites has not been reduced significantly. In order to verify current transmission risks and identify the potential establishment of new foci of schistosomiasis driven by environmental changes, we conducted surveillance in selected risk areas of three provinces: Jiangsu, Anhui and Shandong from 2008 to 2010 in addition to routine snail surveillance. We investigated populations and possible reservoirs in sentinel sites and report that the total number of new acute cases did not diminish further in spite of ongoing control activities. In Anhui Province the local count compared to the national count was 43% (19/44) in 2008, 33% (25/75) in 2009 and 40% (17/42) in 2010. In all, 31.58 km^2 areas of snail breeding sites were newly detected nationwide through the year 2008–2010, of which the proportion of Anhui was 42% (5.03/11.98) in 2008, 95% (8.39/8.79) in 2009 and 79% (8.52/10.81) in 2010. Sentinel surveillance showed eight, nine and five confirmed cases of acute schistosomiasis in mobile populations (fishermen, migrant workers) in 2008, 2009 and 2010, respectively. All these cases were detected in Chaohu County, which must therefore be deemed an area at risk. We conclude that continuous surveillance with an emphasis on snails must be enhanced in potential risk areas in PR China.

1. Introduction

Schistosomiasis japonica continues to be a public health problem in the People's Republic of China (PR China). Thanks to political commitment and strong control efforts in the past, the endemic areas have been greatly reduced. Indeed, the lowest levels of infection in both human and cattle in history have been reached in the last decade (Li et al., 2009b; Utzinger et al., 2005; Wang et al., 2008; Zheng et al., 2012b; Zhou et al., 2005). Based on the "National Criteria for Control and Elimination of Schistosomiasis", jointly issued in 2006 by the General Administration of Quality Supervision, Inspection and Quarantine of PR China and the Standardization Administration of PR China (Zhang et al., 2007), transmission has been interrupted in five provinces, i.e. Shanghai (1985), Guangdong (1985), Guangxi (1988), Fujian (1987), Zhejiang (1995) and controlled in three: Sichuan (2008), Yunnan (2009) and Jiangsu (2010) (Deng et al., 2007; Jiang et al., 2007; Li et al., 2009a; Wen et al., 2006; Zhang et al., 2009; Zhou et al., 2012). However, some areas related to marshes and lakes in Anhui, Jiangxi, Hubei and Hunan provinces remain endemic (Zheng et al., 2012b; Zhou et al., 2012) (Fig. 1). Of all 454 previously endemic counties (including districts and cities), 60% (274) achieved the criterion of transmission interruption, with 23% (103) reaching transmission control and 17% (77) morbidity control. The number of patients was reduced by 30.5% from 412,927 in 2008 to 286,836 in 2011. By the end of 2011, only three local acute cases were reported. Compared to 57 reports in 2008, a reduction of 95% was achieved. A total number of 5146 infected cattle was reported in 2011 with an incidence rate of 0.7% against 9988 with 1.3% new infections in 2008. Nevertheless, a total of 1637 km^2 of

* Corresponding author at: National Institute of Parasitic Diseases, Shanghai 200025, China. Tel.: +86 021 64746458; fax: +86 021 64746458.
E-mail addresses: xiaonongzhou1962@gmail.com, ipdzhouxn@sh163.net (X.-N. Zhou).
[1] Co-first author.

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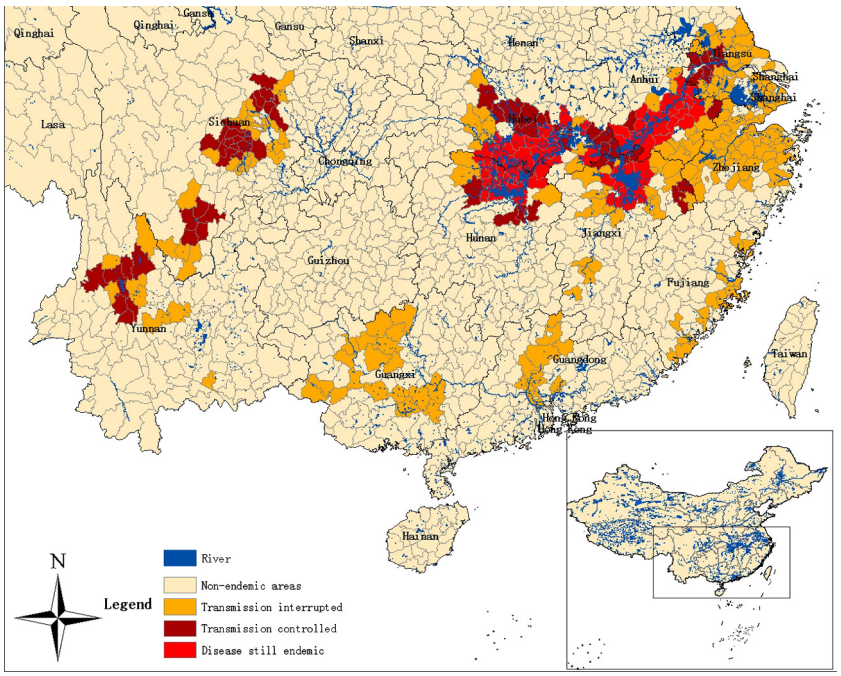

Fig. 1. Geographic distribution of schistosomiasis japonica based on the catalogues of the control programme in PR China in 2011.

snail breeding sites was surveyed in 2011, of which 12 km^2 were found to be newly infested. These numbers are close to that of in 2008 (1484 and 12 km^2), respectively (Zheng et al., 2012b).

In 2004, PR China upgraded schistosomiasis control together with the control of HIV/AIDS and tuberculosis to the highest priority level for communicable diseases (Engels et al., 2005; Zhou et al., 2012). Since then, fighting schistosomiasis has received unprecedented investments from the Government. The State Council issued the medium and long-term (2004–2015 in total) plan for prevention and control of schistosomiasis marking the shift from morbidity control to an integrated control strategy (Collins et al., 2012; Lin et al., 2007; Wang et al., 2008, 2009). Under the leadership of the Ministry of Health (MOH), interventions were put in place by removing cattle from the snail-infested areas, providing farmers with mechanized farm equipments, institution of environmental management geared at snail elimination, improving sanitation and access to clean water, providing boats with faecal containers among the major mobile population and strengthening surveillance and case management and implementing an intensive health education programme. Apart from the MOH, this new strategy involves a number of governmental sectors such as those dealing with agriculture, forestry, water conservancy, environment, education and others as needed (Yu et al., 2006). This approach proved successful and has added value beyond control of schistosomiasis, e.g. concomitant reduction of the prevalence of soil-transmitted helminth infections was also observed (Li et al., 2009b, 2012; Wang et al., 2009; Zheng, 2009).

Although great progress of schistosomiasis control was made in the past decades (Zheng et al., 2012b; Zhou et al., 2005), the potential risk of re-emerging transmission in controlled areas, or the appearance of new foci in sensitive areas, was recognized (Wang et al., 2004; Wu et al., 2005, 2008; Xu et al., 2011; Zheng et al., 2012a). In some areas, where transmission had been interrupted or was already well-controlled, progress levelled off resulting in enlarged snail-infested areas here and there (Huang et al., 1992; Wang et al., 2011; Xu et al., 2011). Following increases in snail densities and infection rates, re-emergence of schistosomiasis was reported with new infected cases attributable to environmental and social changes (Chen, 2005; Wang et al., 2004).

A recent discussion at the World Health Organization (WHO) indicates that a 2 °C temperature rise in PR China would result in the potential increase of 50–100% of the geographic distribution of snails (WHO, 2011a). Hence, the potential transmission of schistosomiasis in previously non-endemic areas would endanger the lives of tens of millions of people. Different mathematical models show that schistosomiasis is likely to extend northward due to the potential expansion of snail habitats (Liao, 2011; Yang et al., 2006a, 2006b; Yu et al., 2004; Zhou et al., 2008). This increase of endemic areas would primarily strike the provinces of Anhui and Jiangsu as well as the southern parts of Shandong and Henan. Water resource developments, i.e. the South-to-North Water Diversion Project (SNWDP) and the Three Gorges Dam (TGD), pose an additional challenge for the control of schistosomiasis (Wang et al., 2007; Yang et al., 2006b; Zhou et al., 2003), as seen in a potential scenario supported by snail experiments in Shandong and Jiangsu (Cao et al., 2007; Wang et al., 2010; Zheng et al., 2009). The 0–1 °C January isotherm, considered as the geographic limit for *Schistosoma japonicum* transmission as reflected by the temperature limit for snail survival, shifted from 33°15′ N to 33°41′ N, expanding the potential transmission area by 41,335 km^2 (Yang et al., 2005). A recent study of the impact of climate change on schistosomiasis predicts that schistosomiasis would potentially extend far northward already by the 2030s and more so in the 2050s and thus include the southern parts of the Shandong and Henan provinces (Zhou et al., 2008). Apart from the environmental impacts, another concern of schistosomiasis rebound is population movement that may transfer the disease from endemic areas to non-endemic places. In particular, those dealing with fishery, on-water construction, and boat dwellers are high-risk population due to the nature of their work (Liang et al., 2008).

Given the risks of increase of snail breeding sites as well as rebound of schistosomiasis, it is time to identify the high-risk areas in the context of a changing environment. According to the findings and the current surveillance system for schistosomiasis in China, we selected several high-risk areas to carry out on-site monitoring

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in humans, snails and reservoirs of the disease during 2008–2010 to verify the prediction of potential new foci in those areas and make recommendations for response where needed.

2. Materials and methods

2.1. Routine surveillance for human acute cases and snails

Data from 2008 to 2010 (calender year) emanating from rountine surveillance, based on the national guideline (MOH, 2005), were obtained from the annual national information system for schistosomiasis in the 12 endemic provinces.

2.2. Pilot surveillance

2.2.1. Site selection

A number of counties were selected as sentinel sites (Fig. 2), based on the following criteria:

1. Areas currently non-endemic for schistosomiasis but predicted to become endemic due to climate change.
2. Areas situated in close proximity to the SNWDP project.
3. Availability of local capacity to carry out surveillance.

Based on these criteria, we selected the two counties of Hongze and Xuyu in Jiangsu Province, Weishan County in Shandong Province and Chaohu County in Anhui Province for study. The former 2 counties are non-endemic areas but adjacent with endemic areas, Weishan county is not endemic but connecting to Jiangsu province, and Chaohu county where transmission has been interrupted. However, the study sites were not endemic in those selected areas. In all four sentinel sites, local income was mainly based on agriculture and other work outside the house. Tractor-ploughed, rice cultivation was the major activity. Tap-water and simple lavatories were generally available. All sites were relatively close to marches or lakes where the potential risk for snail-breeding sites is enhanced. Mobile populations exist in both Hongze and Chaohu (Fig. 2).

2.2.2. Case detection

Local residents, aged between 6 and 65, were selected for serologic testing by simple randomized sampling in the sentinel counties: in Hongze, Xuyu, Chaohu in 2008 and in Weishan in 2010. The indirect haemagglutination assay (IHA) followed by stool examination was used (MOH, 2000). According to MOH guidelines, the sera were tested at the dilutions 1:5, 1:10, 1:20 and 1:40. Those testing positive at 1:10 or at higher dilutions were followed up by parasitological diagnosis by Kato-Katz (Katz et al., 1972) with three slides for each stool specimen or the hatching test based on eggs captured in a nylon-tissue bag according to the national criteria (of 2006) for mobile populations, i.e. fishermen, boatmen or immigrants from other parts of the country staying for one month or longer. People at the sentinel sites were tested, except in Weishan, where no mobile populations were present during the study period. In total, 2204 local residents attended IHA, among whom 11 were conducted stool tests. For the mobile population, a total of 3746 were tested IHA while of them 78 were tested for confirmation by stool examination.

2.2.3. Snail investigations

From April to October in the period 2008–2010, the presence of snails in each sentinel site is monitored using routine surveillance or more vigilant approach. Routine surveillance is generally implemented in areas connecting to lakes, rivers or other water bodies where there is a potential risk of introducing snails. Snail vigilance, on the other hand, means active detection of snails in environments

Fig. 2. Location of the four pilot study areas (Hongze and Xuyu located in Jiangsu Province, Weishan located in Shandong Province, and Chaohu located in Anhui Province, all sentinel sites are marked in red star on the map).

where there are mobile populations, ships, or plant matter in the water that would favour snails from outside getting a foothold.

Routine snail surveillance was carried out in 3 potential snail infested areas in each of the 4 sentinel sites to search snails by using systematic sampling and detect their infections by microscopy during April to May, 2008–2010. Snails were captured in a frame equidistantly placed along in study sites. Snail vigilance was conducted to search for the snails attached in the floating debris and the straw of plan hanging into the water, in one area connecting to known snail habitats or otherwise in waterways where debris and aquatic plants were common (Xu et al., 2012) from April to October during the three-year study period. This approach included the shores where ships from suspected snail-breeding sites anchored.

2.2.4. Reservoir surveillance

From 2008 to 2010, surveys of free-roaming livestock (where available) were carried out each year. A total of 30 heads per each sentinel site were randomly selected to examine for the infection with *S. japonicum*, using the hatching method, followed the operational manual of schistosomiasis 3rd edition (MOH, 2000). Briefly, the faeces sample of one livestock (50 g per cattle, 30 g per sheep and 10 g per dog) was stirred with clean water of pH 7.2–7.6 and transferred into a plastic container through a sieve with holes (25.4 mm diameter). The supernatant was poured out after doing this twice spending about 20 min each time. Clean water was added to the top of the container, after which a plastic cover with a hole was added to the top of the container. Finally, a cubicle of water was rapidly backed off on the mouth of the plastic cover (Fig. 3). The filled cup is then transferred to an incubator and kept at $25 \pm 3\,^{\circ}C$ for observation after 1, 3 and 5 h to see if there is any miracidium. A final observation is made after 12 h.

2.3. Data analysis

A database resulting from the snail survey, population survey and animal reservoir survey was established using Microsoft Excel

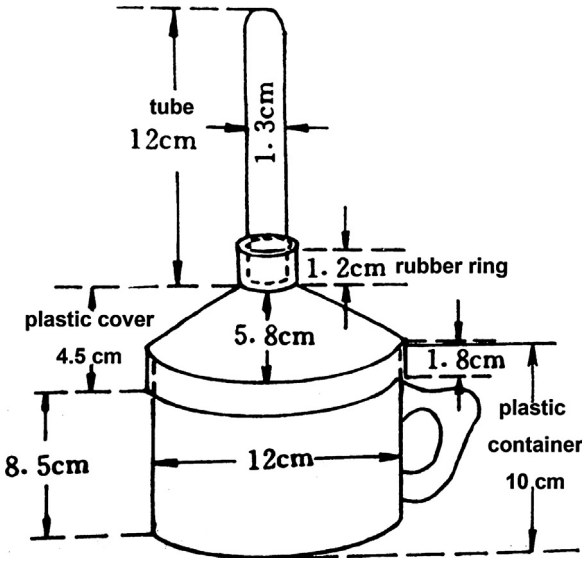

Fig. 3. Diagram for facility in egg hatching test for diagnosis of reservoir hosts (MOH, 2000).

2007. The raw data were verified for completeness and accuracy before entering into a computer, followed by cross-checking by a different staff. Description of the results from the cleaned data was done by descriptive statistics such as proportions and rates.

3. Results

3.1. Acute human cases and snails

A total of 161 acute human schistosomiasis cases were reported, among which Anhui Province accounted for 43% (19/44), 33% (25/75) and 40.5% (17/42) of the total number of cases in 2008, 2009 and 2010, respectively. Among them, small numbers were immigrants, e.g. there were four in 2008 (one from Jiangsu and three from other parts of the country), four in 2009 (two from Jiangsu and two from other parts of the country) and two cases in 2010, both from Jiangsu Province (Hao et al., 2009, 2010; Lei et al., 2011).

3.2. Active case detection

From 2008 to 2010, a total of 2204 local residents aged 6–65 were screened by serological test and 11 were found to be positive. However, none of these subjects was confirmed when parasitological diagnosis was done (Table 1). Among people in the three sentinel sites from the mobile populations, tested in 2008, 2009 and 2010, out of 3746 cases detected, 78 were positive by IHA with the overall serological positive rate of 1.7, 2.1 and 3.8%, respectively. Out of these 78 cases, eight, nine, and five were parasitologically confirmed in Chaohu alone in 2008, 2009 and 2010 (Table 2). Twelve of these 22 confirmed cases came from endemic areas, while the other 9 were people who had been working outside the county.

The total area of newly detected snail breeding sites declined by almost 10% from 12 km^2 in 2008 to 11 km^2 in 2010. However, the proportion of newly detected areas in Anhui increased from 42% (5/12) in 2008 to 79% (8/11) in 2010 (Fig. 4). Of these newly detected snail areas in Anhui in 2010, all were found in just three counties, i.e. Anqing, Xuancheng and Chaohu, accounting for 62% (5/8), 25% (2/8) and 12% (1/8) of the increase, respectively.

Taking the whole period 2008–2010 into account, a total of seven counties (Wuhu, Ma'anshan, Tongling, Anqing, Xuancheng, Chaohu and Chizhou) in Anhui were found to have newly detected snails-infested areas. Among all the counties, the newly detected

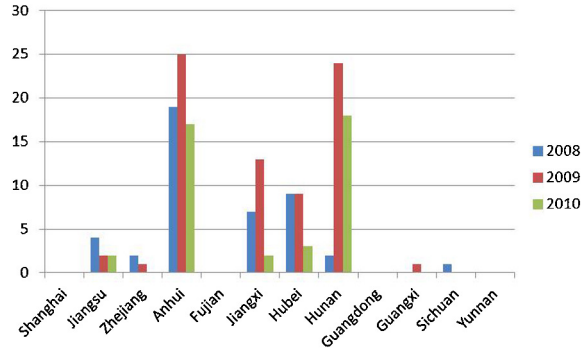

Fig. 4. Number of detected acute schistosomiasis in each province during 2008–2010.

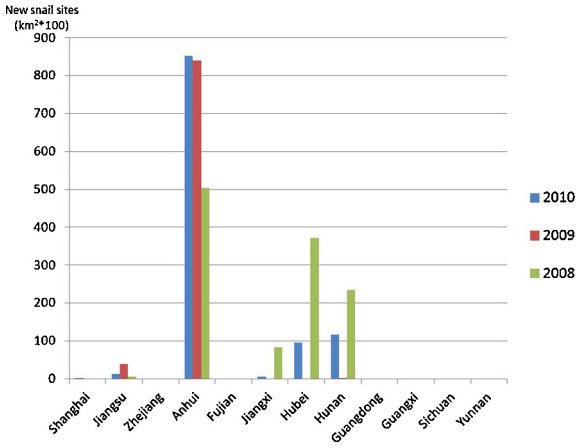

Fig. 5. New snail-infested areas based on annual survey data during 2008–2010.

areas in Anqing accounted for 62% (5/8), 71% (6/8), and 90% (4/5) in 2010, 2009 and 2008, respectively. In 2010, Xuancheng (25%) was the second largest new snail area, followed by Chaohu (12%) (Fig. 5).

3.3. Snail investigation

In the three years of the study period, a total of 0.39 and 0.41 km^2 areas were surveyed with 1593, 1662 and 1654 frames through routine surveillance, respectively (Table 3). No snails were found in any of these sites, neither were any snail detected (only empty shells) in the areas subjected to monitoring for floating debris for vigilance (Table 4).

3.4. Reservoir surveillance

A total of 91 heads of livestock (including cattle and pigs) were investigated in Chaohu county each year during the study period. No positive animals were found.

4. Discussion

Due to the reliance of an intermediate snail host and other biological attributes, the pattern of schistosomiasis distribution relies heavily on the status of the immediate outdoor surroundings and the large-scale geographical characteristics of the countryside. Temperature and the changing pattern of the water systems (canals, rivers and lakes) are the main drivers of the shifting pattern of the distribution of the disease. Transmission was observed to re-emerge in some areas after achieving interruption (Carlton et al., 2011; Shaoji and Dandan, 2002; Wu et al., 2005, 2008; Xu et al., 2011; Zhou et al., 2004). According to the predicted results

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Table 1
Results of local resident surveillance in sentinel sites 2008–2010.

Province	County	Serological test			Parasitological test	
		No. tested	No. positive	Infection rate (%)	No. tested	No. positive
Jiangsu	Hongze[a]	514	3	0.58	3	0
	Xuyu[a]	1035	6	0.58	6	0
Anhui	Chaohu[a]	301	0	0.00	0	0
Shandong	Weishan[b]	354	2	0.56	2	0
Total		2204	11	0.50	11	0

[a] Data collected in 2008.
[b] Data collected in 2010.

Table 2
Results of mobile population surveillance in sentinel sites 2008–2010.

Province	County	2008		2009		2010	
		Serological positive (%)	No. of stool positive	Serological positive (%)	No. of stool positive	Serological positive (%)	No. of stool positive
Jiangsu	Hongze	1.09 (7/642)	0 (0/1)[a]	1.37 (8/582)	0 (0/0)[a]	3.5 (21/600)	0 (0/21)
	Xuyu	0.99 (3/304)	0 (0/3)	0 (0/306)	0 (0/0)	5.09 (17/334)	0 (0/17)
Anhui	Chaohu	3.43 (11/321)	8 (8/10)[a]	4.97 (18/362)	9 (9/18)	3.05 (9/295)	5 (5/8)[a]
Shandong	Weishan	–	–	–	–	–	–
Total		1.66 (21/1267)	8	2.08 (26/1250)	9	3.82 (47/1229)	5

'–' indicates data not available.
[a] Those who were serological positive but did not attend stool test.

Table 3
Results of snail survey in sentinel sites 2008–2010.

Province	County	2008		2009		2010	
		Areas surveyed (km^2)	No. of frames surveyed	Areas surveyed (km^2)	No. of frames surveyed	Areas surveyed (km^2)	No. of frames surveyed
Jiangsu	Hongze	0.0067	317	0.0204	374	0.0204	380
	Xuyu	0.0554	372	0.0669	604	0.0669	617
Anhui	Chaohu	0.3260	904	0.3260	634	0.3260	606
Shandong	Weishan	–	–	0.0010	50	0.0010	51
Total		0.3881	1593	0.4143	1662	0.4143	1654

'–' indicates data not available

due to climate change and water transfer projects of PR China, there is an increasing risk that snails move into some of the currently non-endemic areas, for example triggering transfer of the disease to the northern part in the country through the SNWDP transfer (Peng et al., 2006; Yang et al., 2005; Yu, 2011). In particular the Hongze and Chaohu counties, which are situated along the route of the SNWDP, are at high risk when considered in the context of climate change (Zhou et al., 2003). The TGD area is also at risk for introduction of schistosomiasis and snails in the dam above the power station by migrants and plant transportation. In addition, mobile population is another important contribution to the transmission of schistosomiasis due to lack of awareness, inadequate access to health service, poor management, etc. We conducted active case detection, snail and reservoir surveillance address the ongoing transmission risks of *S. japonicum* in selected sites in Jiangsu, Anhui, and Shandong provinces in China under the overarching changing environment during 2008 to 2010. Two separate sources of data were involved, reports on human infections and snail populations from the national information system were maintained by MOH and data from a subset of counties were selected for targeted sentinel studies.

The fact that no cases were found in the local population, while the mobile population continued to produce confirmed cases in Chaohu County each year of the study period suggests that this county is a highly and confirmed risk area for schistosomiasis transmission, with the potential to spread. However, as many serological

Table 4
Results of floating debris survey in sentinel sites 2008–2010.

Province	County	2008			2009			2010		
		No. of sites	Weight of debris (kg)	No. of shells captured	No. of sites	Weight of debris (kg)	No. of shells captured	No. of sites	Weight of debris (kg)	No. of shells captured
Jiangsu	Hongze	–	–	–	1	307	256	1	254	117
	Xuyu	–	–	–	1	309	263	1	309	341
Anhui	Chaohu	1	46.3	274	9	166	260	4	66	24
Shandong	Weishan	1	0.37	31	1	0.19	0	–	–	–
Total		2	46.67	305	12	782.19	779	6	629	482

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positive cases did not attend the microscopy follow-up (see Table 2, where the numerator represents the number of positive cases, and the denominator the number of people attending the test), in particular people belonging to the mobile populations, the real level of risk may be underestimated.

The historical 0–1 °C January isotherm of the distribution of *O. hupensis* in China was considered as the approximate northern limit of *S. japonicum* transmission. Climate change, which may result in moving northward of the isotherm, coupled with water resource developments in China, may pose additional challenges for the control of schistosomiasis (Yang et al., 2005). Under the warming climate, this isotherm is moving northward which may pose a threat to those sentinel sites. Therefore, the increasing snail breeding areas, especially in Anhui, are of great concern. The finding that these areas continue to grow, as was shown over the study period, underlines the potential for the establishment of a new high-risk focus. For pilot surveillance, although no snails were detected in any of the four sentinel sites, the possible new foci driven by the seemingly ongoing change to a warmer climate cannot be ruled out. Importantly, not all risk areas predicted by climate change were covered, which limits the large-scale implications of this study.

This study emphasizes that we are reaching the limits of detection of current direct diagnostic techniques. These tools served us well in previous time when most infections were of high intensity but they are incapable of detecting all current infections in the present low-transmission settings, which most probably means that the results reported here are underestimations of the real situation (Lin et al., 2011; Spear et al., 2011). Moreover, the relative small size of the monitoring sites also limited the power of the final results. Surveillance of potentially snail-infested water would be helpful to further identify the risks; reference here is made to sentinel mice surveillance (Xie et al., 2005; Zheng et al., 2012a), which focuses on the infection status of mice living near lake areas suitable for snail habitats. In 2010, the positive results of sentinel mice infections in key water regions, where no infected snails were detected, suggests it could be used as a forecast tool that would be more sensitive than traditional surveillance (Zheng et al., 2012a). This seems an effective and promising surveillance approach to identify high risk areas for schistosomiasis transmission.

Some recent studies have indicated a lower possibility of snails spreading to the North (Huang et al., 2009, 2012), or that the possibility could be reduced through appropriate interventions (Liang et al., 2012). These results were based on statistic models of climatic factors, snail areas and incidence in special regions using historical data. To get a better, more convincing result, it would be helpful to integrate also factors other than temperature in the research on the potential for re-emergence and further spread of schistosomiasis.

The regional action plan for neglected tropical diseases (NTDs) in the Western Pacific area (2012–2016) was endorsed in the 63rd session of the Regional Committee for the Western Pacific Regional Office (WPRO) of the WHO (WHO, 2011b). This document indicates that elimination of schistosomiasis in PR China would be possible by 2016 as a result directly emanating from the successful implementation of the current control strategy. In 2010, Li Keqiang, Vice-Premier of PR China, put forward the new target to achieve transmission interruption by 2020 (Zhou et al., 2012). Additionally, it is obvious that surveillance and response serve as essential tools for disease control and elimination (Zhou et al., 2013). With the outcome of this study, we conclude that in order to achieve this goal, sustainable surveillance and response should be carried out and extended to all risk areas, while sustaining the current strategy of integrated control serving as a component of the early warning system (EWS) of schistosomiasis if the target of schistosomiasis elimination is to be met in the context of the ever changing environment.

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Competing interests

The authors have no competing interests.

Authors' contributions

QYJ, LSZ and XJ participated in the initial design of the paper, literature review and contributed equally to the writing. YK, HYX, CZG, MF, DH and ZLJ did the data collection and figure drawing. ZL and WQ helped data checking, verification and input. LSZ and WQ helped perfect the figures. WQ, QYJ, LSZ and XJ participated in the writing of the paper. RB and ZXN reviewed the first draft and edited. All authors reviewed and approved the final version.

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