ORIGINAL ARTICLE

A Strategy to Control Transmission of *Schistosoma japonicum* in China

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ABSTRACT

BACKGROUND

Schistosoma japonicum causes an infection involving humans, livestock, and snails and is a significant cause of morbidity in China.

METHODS

We evaluated a comprehensive control strategy in two intervention villages and two control villages along Poyang Lake in the southeastern province of Jiangxi, where annual synchronous chemotherapy is routinely used. New interventions, implemented from 2005 through 2007, included removing cattle from snail-infested grasslands, providing farmers with mechanized farm equipment, improving sanitation by supplying tap water and building lavatories and latrines, providing boats with fecal-matter containers, and implementing an intensive health-education program. During the intervention period, we observed changes in *S. japonicum* infection in humans, measured the rate of infection in snails, and tested the infectivity of lake water in mice.

RESULTS

After three transmission seasons, the rate of infection in humans decreased to less than 1.0% in the intervention villages, from 11.3% to 0.7% in one village and from 4.0% to 0.9% in the other (P<0.001 for both comparisons). The rate of infection in humans in control villages fluctuated but remained at baseline levels. In intervention villages, the percentage of sampling sites with infected snails decreased from 2.2% to 0.1% in one grassland area and from 0.3% to no infection in the other (P<0.001 for both comparisons). The rate of infection in mice after exposure to lake water decreased from 79% to no infection (P<0.001).

CONCLUSIONS

A comprehensive control strategy based on interventions to reduce the rate of transmission of *S. japonicum* infection from cattle and humans to snails was highly effective. These interventions have been adopted as the national strategy to control schistosomiasis in China.

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During the past five decades, the Chinese government has placed a high priority on the control of schistosomiasis and has carried out many control programs.[1-3] These efforts have resulted in a substantial reduction in the prevalence of infection with *Schistosoma japonicum* in humans, from approximately 11.6 million cases in the mid-1950s to 726,000 cases in 2004.[4] The number of provinces in which this disease is endemic has been reduced from 12 to 7. In spite of these achievements, progress in the control of this disease appeared to be stagnating.[5,6] National surveys of schistosomiasis in China showed that the prevalence of schistosomiasis infection in humans in areas in which it is endemic had not substantially changed from 1995 (4.9%) to 2004 (5.1%).[4,7,8] More than 80% of current cases are found in the lake and marshland regions of Hunan, Hubei, Jiangxi, Anhui, and Jiangsu provinces, and elimination of transmission has proved difficult to achieve.[8]

Past efforts to control snail populations through the use of chemical molluscicides or alteration of their habitats have resulted in environmental pollution and damage.[9,10] The use of synchronous chemotherapy for humans and domestic animals has been only temporarily effective. Studies have shown high rates of reinfection in both humans and domestic animals.[11,12] Other factors that have complicated recent efforts to control schistosomiasis have included ecologic changes in the environment, frequent flooding, and population movement.[13-17] As a result, the habitats of oncomelania snail species have increased, and more infections in humans have occurred.[1,17-19]

In 2004, the State Council of China established two targets for the National Schistosomiasis Control Program. First, by 2008, the goal was to reduce the rate of infection in humans in all counties in which *S. japonicum* is endemic to less than 5%, including 110 counties that had a prevalence exceeding 5%. Second, by 2015, the program aimed to reduce the rate of infection in humans to less than 1%.[4,6,20] To reach these targets, the Ministry of Health recognized an urgent need to develop a new schistosomiasis control strategy for China. On the basis of studies identifying cattle as the primary source of *S. japonicum* infection for the oncomelania snails and the limited life span of infected snails,[10,21] we developed a comprehensive control strategy aimed at reducing the roles of cattle and humans as sources of infection for snails.[21] In this report, we describe the implementation of this strategy in an endemic area during a 30-month period from 2005 through 2007. We also provide an assessment of the effectiveness of the strategy and discuss the adoption of this approach as a national strategy to control transmission of *S. japonicum*.

METHODS

ANALYSIS OF THE STUDY AREA

Poyang Lake, with an area of 4350 km² in the flooding season and 3500 km² in the dry season, is the largest freshwater lake in China. It is located along the mid-to-lower reaches of the Yangtze River in the southeastern province of Jiangxi.[5,22] We carried out the study in four villages in which *S. japonicum* is endemic around Poyang Lake: two intervention villages (Aiguo, with a human infection rate of at least 10%, and Xinhe, with a human infection rate of 5 to 10%, both in Jinxian County) and two control villages (Ximiao and Zhuxi of Xingzhi County, both with human infection rates of 5 to 10%).[23]

Aiguo and Xinhe lie along the embankment of the grasslands of Liuling and Niuzhou, next to Poyang Lake (Fig. 1). Residents of Aiguo and Xinhe perform their farming activities in the grasslands and carry out fishing and boating activities in lake water adjacent to the grasslands. The grasslands are infested with the oncomelania snails. Snails are infected by miracidia (the larval stage of *S. japonicum* hatched from eggs deposited by human or bovine feces).[22] Humans and cattle are infected when they come into contact with such water.[24] Although infection can occur at any time from March through November, it peaks during the flooding season (June through September) when the water level in the lake rises and much of the grasslands is under water.[22,25] Villagers come into contact with the infected water primarily through daily activities such as fishing, cultivating crops, cutting weeds, washing clothes, and swimming. Cattle are the only domestic animals in the grasslands.

INTERVENTIONS TO CONTROL INFECTION

Before the initiation of our study, activities had been undertaken in the intervention and control villages to control *S. japonicum* infection. These interventions included synchronous chemotherapy with praziquantel for all villagers and their cattle

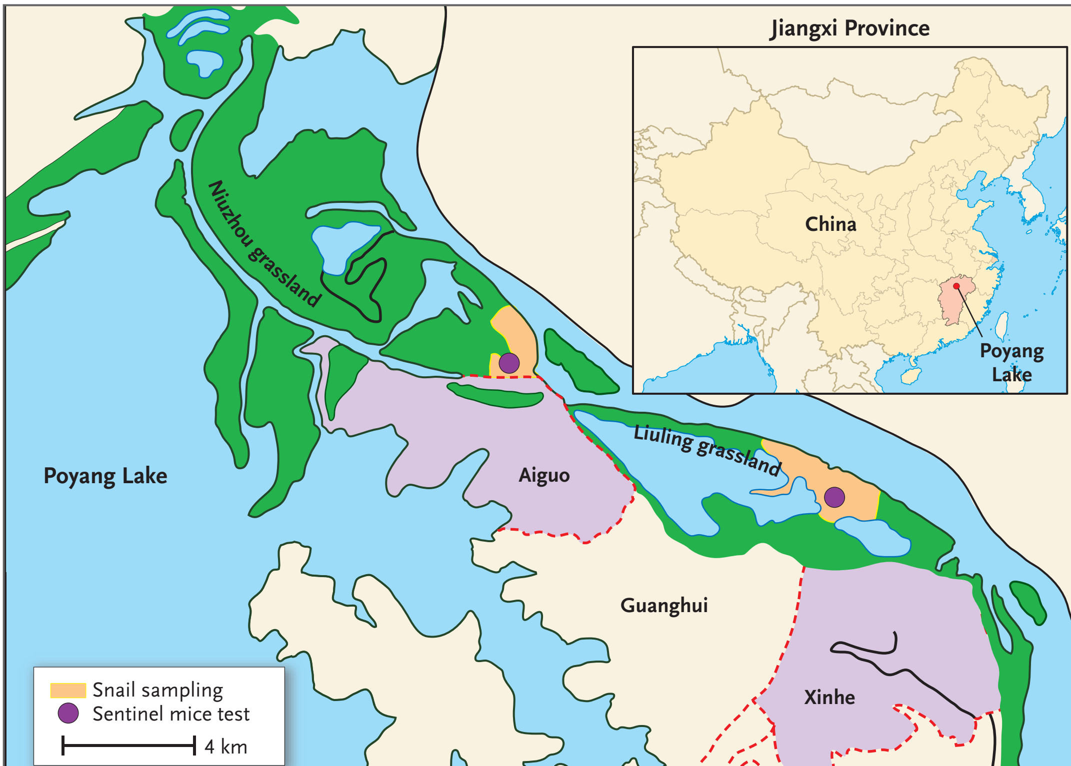

Figure 1. Location of Study Area in Jinxian and Xingzhi Counties, Jiangxi Province.
In China's Jiangxi Province, the grassland areas surrounding Poyang Lake are largely covered by water during the flooding season near the two control villages, Ximiao and Zhuxi (not shown), and the two intervention villages, Aiguo and Xinhe. Investigators sampled snail populations and studied the level of water infectivity (with the use of sentinel mice) in grassland areas in which *Schistosoma japonicum* infection is endemic.

and health education focusing on avoidance of snail-infested areas and associated lake water.[26,27] These activities continued during the study period in all four villages.

During the study period from May 2005 through November 2007, we implemented additional interventions with the aim of controlling the sources of *S. japonicum* infection. The study and its interventions were reviewed and approved by the human subject research committee of the Jiangxi Provincial Institute of Parasitic Diseases.

First, we implemented interventions to eliminate cattle as a source of infection to snails. In May 2005, we implemented regulations prohibiting the grazing of cattle in the grasslands. To replace cattle, we purchased 316 small farm machines and trained farmers to use them.

Second, from May 2005 through August 2005, we implemented interventions to reduce humans as a source of infection in snails. These interventions were aimed at reducing transmission by improving sanitation. We supplied tap water to 662 households by building two public wells and 215 household wells. In addition, we constructed 643 home lavatories, 7 public latrines with three-cell septic tanks, 189 household marsh-gas (methane) pools, and 2 public, medium-to-large marsh-gas pools. The gas pools were built so that biogas from the septic tanks could be collected and used as fuel by villagers. We provided all boats with fecal-matter containers so that human feces could be disposed of on land instead of directly into the lake. By September 2005, all of the residents had access to tap water and 95% had access to lavatories or latrines.

Third, an intensified health education program was carried out. The central message was the need to isolate cattle from the grasslands and to improve sanitation for villagers because bovine and human feces are sources of *S. japonicum* infection in snails, which in turn cause infection in humans and cattle. In addition to presenting this information on billboards, a special effort was made to seek out fishermen and other residents with regular access to the lake and to make sure they understood the message. Additional health education sessions were provided to schoolchildren.

To implement the new interventions, the government provided funding to remove cattle from the grasslands and build public latrines, public marsh-gas pools, and public wells. The government also provided subsidies to purchase mechanized farm equipment and construct home lavatories, household marsh-gas pools, and household wells.

ASSESSMENT OF INTERVENTIONS

Infection in Humans

After the transmission season of each year (usually in October or November), we carried out an annual survey of human *S. japonicum* infection in the intervention and control villages. In Aiguo, Ximiao, and Zhuxi, we started the annual survey in 2002; in Xinhe, we started in 2004 (Fig. 2). During the survey, a team went from house to house and collected stool samples from the first 300 to 350 residents between the ages of 5 and 65 years. Fecal examination with three thick smears for each person was performed with the use of the Kato–Katz technique.[28]

Infection in Snails

We systematically sampled oncomelania snails on the Niuzhou and Liuling grasslands[10] before the start of the transmission season in April of 2005, 2006, and 2007 (Fig. 2). Sampling was carried out in an area in which most of the farming and cattle grazing took place — the area most frequently used by villagers (Fig. 1). We calculated the percentage of snails that were infected with *S. japonicum* and the proportion of sampling sites with infected snails. The same area of grassland was used in all studies.

Assessment of Lake Water

We assessed the extent to which cercariae of *S. japonicum* infest the lake water, using exposure tests with mice during the height of the transmission season in August of 2005, 2006, and 2007 (Fig. 2). The mice were exposed to lake water with the use of the sentinel mice technique for 1.5 hours each time, twice a day, for 3 consecutive days. The mice were euthanized 40 days after exposure and checked for the presence of adult worms of *S. japonicum* in their mesenteric veins. (Additional information on the study area, preexisting interventions, and assessment of effectiveness of study interventions is available in the Supplementary Appendix, available with full text of this article at NEJM.org.)

STATISTICAL ANALYSIS

We prespecified the following outcome measurements: the rate of infection of humans with *S. japonicum*, the rate of infection of snails with *S. japonicum*, the percentage of sampling sites with infected snails, and the percentage of mice infected with *S. japonicum*. All data were entered and checked with the use of FoxPro, version 6.0

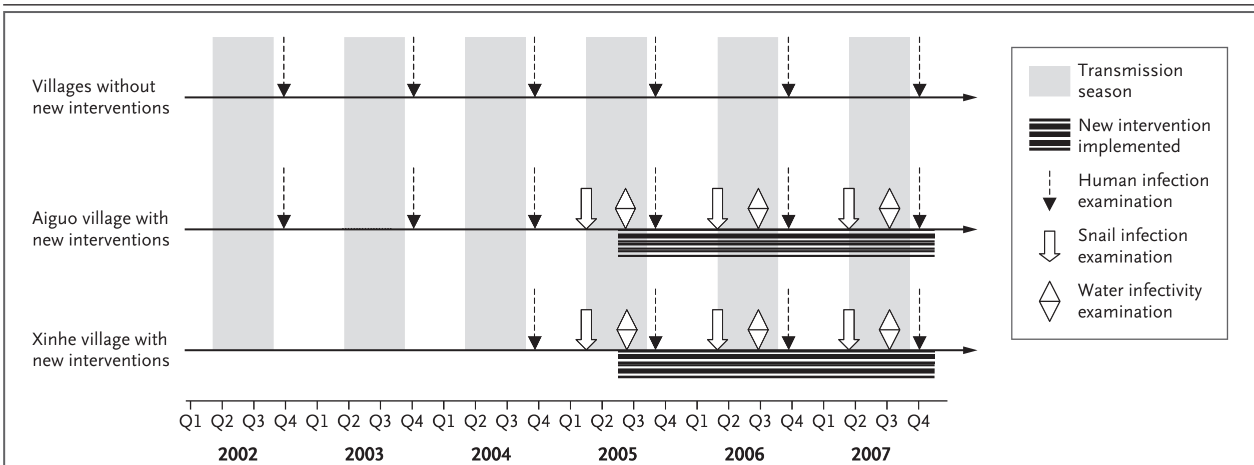

Figure 2. Quarterly Timeline of Interventions and Assessments in Control and Intervention Villages.

(Microsoft), and statistical analyses were performed with the use of SPSS software, version 13.0. We used the chi-square test, including testing for trend when appropriate, to examine any change in proportions over time. Two-sided P values were calculated for all comparisons without adjustment for multiple testing.

RESULTS

INFECTION IN HUMANS

After the implementation of new interventions to control the source of *S. japonicum* infection, the percentage of villagers with such infections declined to less than 1% in both Aiguo and Xinhe (Table 1 and Fig. 3). In Xinhe, this low level of infection was evident for 3 years, beginning in October 2005. In Aiguo, infections in humans decreased by 35.5%, 84.5%, and 94.1% after one, two, and three transmission seasons, respectively ($P=0.02$, $P<0.001$, and $P<0.001$). In Xinhe, infections in humans decreased by 78.8%, 86.0%, and 77.0% after one, two, and three transmission seasons, respectively ($P=0.007$, $P=0.002$, and $P=0.01$). During the most recent survey in the autumn of 2008, the rate of infection in humans in the study areas remained below 1%.

By contrast, in the two control villages, there was no sustained decline in the rate of infection during the 6-year period. In addition, there were substantial year-to-year variations in the levels of infection. In Ximiao, an acute outbreak of *S. japonicum* infection in 2005 resulted in a temporary increase in the proportion of residents who were infected. In Zhuxi, there was a temporary decline in the level of infection during 2005 and 2006 but a resurgence of infection in 2007, in which the rate of infection returned to the pre-2005 level.

INFECTION IN SNAILS

During the two transmission seasons after the implementation of new interventions to control the sources of *S. japonicum* infection, the percentage of sampling sites with infected snails in Niuzhou and Liuling grasslands decreased by 95% ($P<0.001$) and 100% ($P=0.07$), respectively (Table 2). The percentage of snails infected with *S. japonicum* in Niuzhou and Liuling grasslands decreased by 93% ($P<0.001$) and 100% ($P=0.001$), respectively. During the most recent survey in the spring of 2008, no snail infection was reported.

Table 1. Identification of *Schistosoma japonicum* Infection by Fecal Examination among Residents of Villages around Poyang Lake.*

Month and Year	Control Villages†				Intervention Villages			
	Ximiao		Zhuxi		Aiguo		Xinhe	
	no. of persons examined	*no. (%) with infection*	*no. of persons examined*	*no. (%) with infection*	*no. of persons examined*	*no. (%) with infection‡*	*no. of persons examined*	*no. (%) with infection§*
October 2002	300	21 (7.0)	878	51 (5.8)	300	41 (13.7)	ND	ND
November 2003	300	17 (5.7)	922	47 (5.1)	330	36 (10.9)	ND	ND
November 2004	300	21 (7.0)	936	59 (6.3)	793	90 (11.3)	300	12 (4.0)
October 2005	344	80 (23.3)	572	20 (3.5)	519	38 (7.3)	353	3 (0.8)
November 2006	299	39 (13.0)	549	9 (1.6)	512	9 (1.8)	359	2 (0.6)
October 2007	375	30 (8.0)	234	13 (5.6)	447	3 (0.7)	325	3 (0.9)

* ND denotes not done.

† As compared with 2002, there was a significant change in the rate of infection only in 2005 and 2006, when the annual rates increased in Ximiao ($P<0.02$ for both comparisons) and decreased in Zhuxi ($P<0.05$ for both comparisons).

‡ In Aiguo, there was no significant change in the rate of infection from 2002 through 2004 ($P=0.37$), but there was a significant decline from 2005 through 2007 ($P<0.001$).

§ In Xinhe, there was a significant decline in the rate of infection from 2004 through 2007 ($P<0.001$).

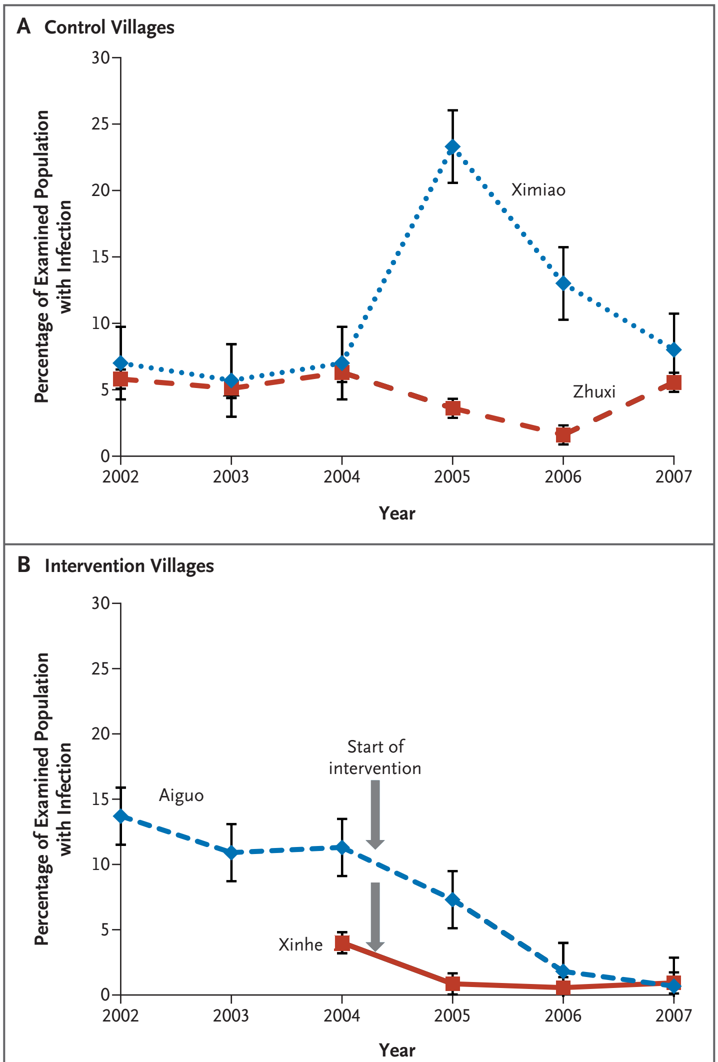

Figure 3. **Rates of Infection with *Schistosoma japonicum* in Humans in Control and Intervention Villages from 2002 through 2007.**

Rates of infection were assessed at the end of the transmission season for each year in the two control villages, Ximiao and Zhuxi, and in the two intervention villages, Aiguo and Xinhe. The I bars represent 95% confidence intervals.

INFECTIVITY OF LAKE WATER

In August 2005, during the early phase of implementation of the new control strategy, 46 of 58 mice (79%) were infected with *S. japonicum*. In August 2006, only 1 of 45 mice (2%) was infected. The infectivity of lake water had decreased by 97% ($P<0.001$). In August 2007, after more than 2 years of implementation of the control strategy, none of 61 mice were infected ($P<0.001$).

COST OF INTERVENTIONS

The cost of implementing the new interventions totaled $373,200 (in U.S. dollars). The government provided $263,500 (71%) of the funding, including full funding to remove cattle from the grasslands ($102,600) and to build public latrines ($15,400), public marsh-gas pools ($2,500), and public wells ($6,400). These funds included payments of $85 to farmers for each head of cattle removed. In addition, the government also provided subsidies to villagers to purchase mechanized farm equipment ($68,200, or 40% of the cost) and to build home lavatories ($52,900, or 75% of the cost), household marsh-gas pools ($15,400, or 62% of the cost), and household wells ($14,100, or 82% of the cost). Among the $109,700 provided by villagers, $75,700 (69%) went to the purchase of mechanized farm equipment.

DISCUSSION

In our study, we found that the burden of schistosomiasis in humans can be rapidly reduced to less than 1% in an endemic area by applying a comprehensive strategy to reduce the roles of humans and cattle as sources of *S. japonicum* infection in snails. A substantial reduction in the rate of human *S. japonicum* infection was observed within half a year. After 30 months (including three transmission seasons), the rate of infection in humans declined by more than 90% in a village with a high rate of infection and by more than 75% in a village with a medium rate of infection.

Three lines of evidence support a causal relationship between the control strategy and a reduction in the rate of infection in humans. First, a decline in the rate of infection to less than 1% occurred after the implementation of new interventions and only in the intervention areas. Second, in our intervention areas, the decline in the percentage of infected snails paralleled the decline in infected humans. After two transmission seasons, the percentage of snails infected by *S. japonicum* declined by 93 to 100%, and the percentage of sampled grassland areas with infected snails declined by 95 to 100%. Third, during the peak transmission period, the infectivity of lake water — as measured by the ability to infect mice with *S. japonicum* — was reduced by 97% after two transmission seasons and by 100% after three transmission seasons.

Taken together, these results suggest that a strategy to reduce the transmission of *S. japonicum* infection from humans and cattle to snails led to a dramatic reduction in the number of infected snails in their natural habitat.[29,30] This reduction,

Table 2. Infection with *Schistosoma japonicum* in Snails in Grasslands.

Grassland Area	Survey Period	Sampling Sites	Sampling Sites with Infected Snails	Snails Examined	Infected Snails
		no.	*no. (%)*	*no.*	*no. (%)*
Niuzhou	April 2005	1054	23 (2.2)	3944	41 (1.0)
	April 2006	1067	10 (0.9)	2519	10 (0.4)
	April 2007	917	1 (0.1)*	1429	1 (0.1)*
Liuling	April 2005	2171	6 (0.3)	922	6 (0.7)
	March 2006	1822	3 (0.2)	1968	3 (0.2)
	April 2007	1171	0†	1383	0‡

* P<0.001 for the comparison with the 2005 value.
† P=0.07 for the comparison with the 2005 value.
‡ P=0.001 for the comparison with the 2005 value.

in turn, virtually eliminated lake water as a source of infection in humans. Therefore, even though people continued to come into contact with snails and with lake water, the rate of infection in humans declined to a relatively low level.

The study suggests that China's targets of reducing the level of infection in all endemic counties to less than 5% by 2008 and to less than 1% by 2015 can be achieved if this new strategy is rapidly and broadly implemented. As a result of these data, the Chinese government has adopted the interventions used in our study as the national strategy for the control of schistosomiasis. The interventions to control human and bovine sources of *S. japonicum* infection in snails are now part of the recently introduced Schistosomiasis Prevention and Control Regulations.[20,31] The Chinese government has rapidly expanded this program to more than 90 counties in five endemic provinces.

Past approaches to reduce the rate of schistosomiasis infection in humans focused on providing praziquantel as chemotherapy to humans and cattle.[5,32,33] In endemic areas, this approach reduced the prevalence of infection in humans to 1 to 5% but did not eradicate such infection. This is because chemotherapy reduces disease prevalence only at the time of its administration and does not prevent reinfection. It has been determined that a high proportion of cases of schistosomiasis are due to reinfection.[6,27,29,34,35] Therefore, we did not rely on chemotherapy as our main control intervention. Instead, given that 80% of all snail infections originate from cattle,[8] our approach focused on removing cattle from the grasslands where the snails reside. This is probably the most important aspect of our control strategy. In addition, we reduced the human source of snail infection by improving sanitation, thereby decreasing the amount of human excreta discharged into the lake and grasslands.

The main limitation in our study was that we included only a small number of villages, which were not selected in a random manner. Therefore, the magnitude of effect from this set of interventions could be different if applied to other endemic areas. In spite of this factor, we believe that the new national strategy can substantially reduce the burden of schistosomiasis in China.

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