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Viewpoint

China's new strategy to block *Schistosoma japonicum* transmission: experiences and impact beyond schistosomiasis

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Summary Despite sustained efforts for its control made over the past 50+ years, the re-emergence of schistosomiasis in China was noted around the turn of the new millennium. Consequently, a new integrated strategy was proposed to stop the contamination of schistosome eggs to the environment, which emphasizes health education, access to clean water and adequate sanitation, mechanization of agriculture and fencing of water buffaloes, along with chemotherapy. Validation of this integrated control strategy in four pilot counties in the provinces of Anhui, Hubei, Hunan and Jiangxi revealed significant reductions in the rate of *Schistosoma japonicum* infection in humans and intermediate host snails. Importantly, this strategy showed an impact on diseases beyond schistosomiasis, signified by concomitant reductions in the prevalence of soil-transmitted helminth infections. In view of China's new integrated strategy for transmission control of schistosomiasis showing an ancillary benefit on other helminthic diseases, we encourage others to investigate the scope and limits of integrated control of neglected tropical diseases.

keywords *Schistosoma japonicum*, soil-transmitted helminths, transmission, control, environmental management, water and sanitation, integration, China

Introduction

The Government of China recognized the public-health, social and economic importance of schistosomiasis early on (Maegraith 1958; Utzinger *et al.* 2005; Zhou *et al.* 2005). Hence, a national control programme was established as early as in the mid-1950s. This programme has been implemented until this day, including periodic policy reviews to keep the control strategy in line with field realities and to adapt the approaches to the changing economic, epidemiological and socio-political conditions (Wang *et al.* 2008). As a result, the prevalence of *Schistosoma japonicum* among humans has been reduced by more than 90% (Zhou *et al.* 2007). In parallel, a significant reduction of the *S. japonicum* prevalence in domestic animals (water buffalo are the key reservoir host) has been achieved, along with a reduction of the area infested with the intermediate host snail, *Oncomelania hupensis* (Utzinger *et al.* 2005; Zhou *et al.* 2005, 2007). However, with the termination of the 10-year World Bank Loan Project (WBLP) for schistosomiasis control in 2001 (Chen *et al.* 2005), the steady reduction in the prevalence of, and morbidity due to *S. japonicum* in humans came to a halt, and there were signs of re-emergence of the disease in certain areas (Liang *et al.* 2006). Thus, there was growing concern that the national control programme would not reach its ultimate goal – the elimination of the disease from China – and that schistosomiasis control efforts would be cut back due to a spurious perception that the disease is under complete control with no particular risk posed to the public any longer. The latter notion stems from the increasing concentration of cases in poor and marginalized rural communities, and the fading of the disease from public discourse in the wake of the cessation of mass mobilizations for schistosomiasis control.

In 2004, in a move contrasting with the global status of schistosomiasis as a so-called neglected tropical disease (Hotez *et al.* 2006), China classified schistosomiasis together with HIV/AIDS, tuberculosis and hepatitis B as the top priority in the control of communicable diseases (Wang *et al.* 2008). The declared goals were to reduce the infection prevalence among humans in all endemic counties to <5% by 2008, and then to below 1% by 2015 (Wang *et al.* 2009). Importantly, a new integrated control strategy was seen as a necessary step to achieving these targets. It was felt that the set targets could not be reached by chemotherapy and snail control alone, particularly in the lake and marshland regions, where >80% of today's human infections are concentrated (Wang *et al.* 2009).

In this viewpoint, we briefly review the succession of schistosomiasis control approaches employed in China with an emphasis on the latest developments: the design, implementation and validation of a new integrated strategy aimed at transmission control and interruption. We then put forward a preliminary assessment of the potential impact of this strategy beyond the target disease schistosomiasis, placing emphasis on soil-transmitted helminthiasis. Our assessment is based on data from various locations where the new strategy had been rolled out and its effectiveness monitored.

Schistosomiasis control in China: the historical context

Human schistosomiasis must have been a problem in China for thousands of years. Indeed, the first confirmed cases date back more than 2000 years (Chen & Feng 1999), while the discovery of *S. japonicum* eggs in a patient had to wait until 1905 (Logan 1905). The impact of the disease has been vividly described in the poem 'Farewell, God of Plague' by Chairman Mao Zedong (Bundy & Gottlieb 1999; Utzinger *et al.* 2005). His aspiration to eliminate the disease, and the call for action to get rid of schistosomiasis, were also described in this poem.

In the mid-1950s, the national control programme was launched. Within five decades, the number of people infected with *S. japonicum* in China had declined from an estimated 11.6 millions to approximately 726 000 (Zhou *et al.* 2007). This success can be attributed to the recognition of the public-health importance of the disease, sustained commitment of the central government to supporting control, and sufficient flexibility to revise and adapt the employed control strategy in the light of new evidence and the changing nature of control needs (Utzinger *et al.* 2005; Wang *et al.* 2008).

Initially, and up to the mid-1980s, activities focused on transmission control, an approach in line with the global control strategy at the time (WHO 1985). By integrating snail control with the agricultural production system, the *O. hupensis* habitats could be reduced by more than two-third. By the end of the 1980s, the disease had been eliminated in four of the 12 formerly endemic provinces, and the number of residual human infections was reduced to an estimated 1.64 million cases (Utzinger *et al.* 2005; Zhou *et al.* 2005). However, morbidity remained a serious problem with more than 20 000 cases of advanced schistosomiasis.

With the introduction of the antischistosomal drug praziquantel, the global schistosomiasis control strategy shifted from transmission control to morbidity control. The strong reliance on praziquantel-based morbidity control during the 10-year WBLP in China, complemented with health education and continued snail control, is a typical example. In the mid-1990s, schistosomiasis had been eliminated in a fifth province and, at the turn of the new millennium, the number of people infected with *S. japonicum* in China dropped below 1 million cases for the first time, along with a further reduction in the proportion of sampled sites with infected *O. hupensis* (Utzinger *et al.* 2005; Zhou *et al.* 2005). However, the diminished funding after the WBLP, in connection with wider demographic, environmental and socio-economic transformations and changes in the health sector, including cost escalation and declining quality and availability of primary health care and preventive care, contributed to the re-emergence of schistosomiasis in certain parts of the country (Bian *et al.* 2004; Liang *et al.* 2006; Zhou *et al.* 2008).

The current situation

Despite great efforts and major achievements, schistosomiasis is still endemic in seven Chinese provinces. According to the 2004 national survey, the highest human prevalences were found in the provinces of Hunan (4.2%), Hubei (3.8%), Jiangxi (3.1%) and Anhui (2.2%). Stratification by eco-epidemiological settings showed that the lake and marshland regions were most severely affected; the overall human prevalence in these areas was 3.8% (Zhou *et al.* 2007). The pivotal role of these settings for the public-health challenge of schistosomiasis as a whole in China is evident from the following points:

- more than 80% of infected humans live in the central wetlands (Wang *et al.* 2009);
- over 80% of all areas with infected snails are located in this region (Zhou *et al.* 2007);
- an increasing number of acute human infections are seen in urban settings connected with the Yangtze River (Wang *et al.* 2004; Chen *et al.* 2007);
- the bovine infection rate is higher in this eco-zone than in any other region (Zhou *et al.* 2007); and
- a positive correlation between the average human and bovine infection rates was noted after surveying 202 sites ($r = 0.42$, $P < 0.001$; Wu *et al.* 2007).

The social and economic transition in China has resulted in strong economic growth, particularly in the cities and in the East, while the gap between urban and rural areas, as well as the economic difference between the western and eastern regions of the country has widened (Han *et al.* 2008; Tang *et al.* 2008). Although mechanization of farming is the stated ultimate goal it has not been widely achieved, reflecting the uneven development across economic sectors. Continued reliance on water buffaloes in many places constitutes a major risk factor for schistosomiasis since bovines have been shown to contribute 80% or more to the local transmission in certain areas (Wang *et al.* 2005; Gray *et al.* 2007). The central government is aware of these problems, and directions have been given to build a 'new socialist countryside' (Huang & Zhang 2007). Health and well-being, including the control of communicable and parasitic diseases such as schistosomiasis, are key components of the new initiative.

An integrated control strategy

A revised integrated strategy for schistosomiasis control in China had been proposed in recognition of the challenges posed by the re-emergence of the disease. The immediate goal of this strategy is to effectively suppress the re-emergence of schistosomiasis, while ultimately striving for its elimination. This strategy takes environmental and socio-economic factors into account and is based on the understanding that the epidemiology of schistosomiasis is influenced not only by human demography and social connectivity (Gurarie & Seto 2009), but also strongly affected by the presence and movement of livestock (Huang & Manderson 2005; McManus *et al.* 2009). According to the underlying rationale, which builds on previous experience gained with schistosomiasis control, the main emphasis has shifted back to transmission control, whilst praziquantel-based morbidity control is further consolidated. This re-targeting of the control approach is based on the understanding that whenever the environmental contamination with *S. japonicum* eggs from humans and domestic animals can be reduced or even eliminated, the production of cercariae in *O. hupensis* will diminish, since the lifespan of infected snails is shorter than one year (Zhou *et al.* 2005; Yang *et al.* 2007). After careful considerations, the following set of technical measures was successfully tested in two pilot sites of Jiangxi province (Wang *et al.* 2009):

- reduction of the infection source by mechanization of agriculture, facilitated by the replacement of water buffaloes with tractors;
- improved access to clean water, facilitated by supplying tap water at home;
- improved sanitation, facilitated by constructing lavatories and latrines;
- livestock management by fencing of pastures to stop the indiscriminate environmental contamination with schistosome eggs from buffalo faeces; and
- faeces management for certain sectors of the population, e.g. provision of on-board containers for collection of human faeces from high-risk groups such as fishermen and boatmen, and the safe disposal of collected faeces in newly constructed latrines on-shore.

Figure 1 depicts these five key technical measures. Supplementary measures include enhanced information, education and communication (IEC) activities targeting high-risk groups such as school-aged children, boatmen and fishermen (Figure 2). The key IEC message is that it is essential to isolate cattle from the grasslands where this is infested with intermediate host snails, and to improve sanitation for villagers, since bovine and human faeces are the main sources of *S. japonicum* infection in snails. In areas where *O. hupensis* are particularly widespread, additional control measures are considered such as focal mollusciciding and environmental management.

This revised integrated control strategy therefore relies on an array of improved transmission control measures, coupled with the consolidation of ongoing praziquantel-based human and bovine treatments. This control approach holds promise for adaptation to different eco-epidemiological settings due to its modular design.

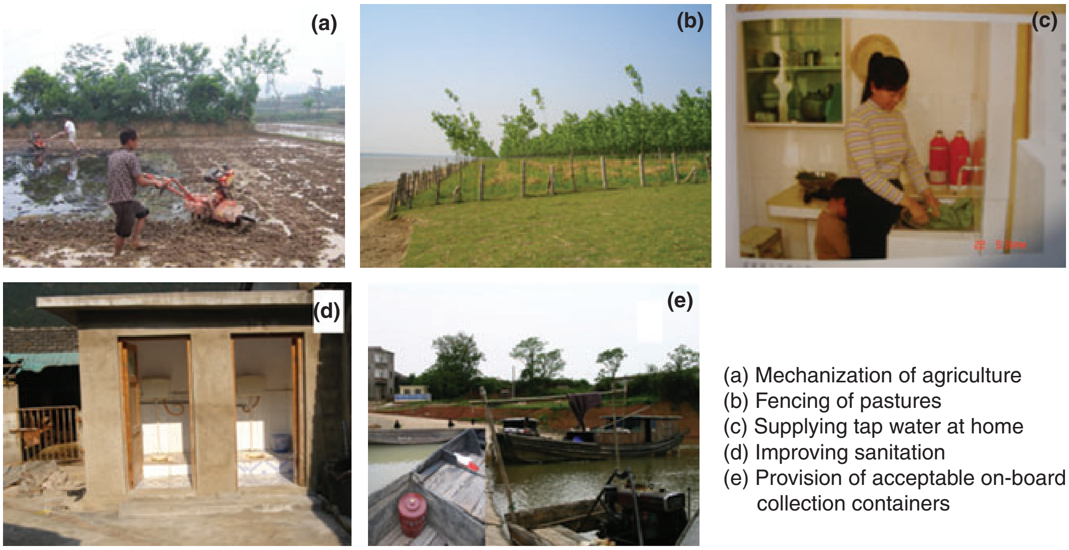

Figure 1 The key technical measures of the revised integrated schistosomiasis control strategy in China.

Figure 2 Health education billboard in China that should enhance IEC for transmission control of schistosomiasis targeted at high-risk groups such as school-aged children, boatmen and fishermen.

First experiences

Four pilot sites at county level (i.e. one each in Jinxian county in Jiangxi province, Anxian county in Hunan province, Hanchuan county in Hubei province and Guichi county in Anhui province), were selected in 2005, to monitor the effects of this revised integrated control approach on the prevalence of *S. japonicum* infection in humans and intermediate host snails. Table 1 summarizes which packages of the key technical measures were implemented in the respective pilot sites, showing the modular character of the new control strategy. Figure 3 shows the implementation of the key technical measures in relation to *S. japonicum* transmission, and the timing when human infections were examined and snail surveillance carried out.

The first initiated study was implemented in two pilot villages of Jinxian county in the Poyang Lake area, and the results obtained with this revised integrated control approach over a 30-month period have been presented elsewhere, along with the tools and techniques used for their evaluation (Wang *et al.* 2009). In brief, changes in *S. japonicum* infection rates in humans and snails, and infectivity of lake water were utilized as primary outcome measures. After three transmission seasons, the prevalence of *S. japonicum* in humans was reduced to <1%. In addition, a significant reduction in the number of infected *O. hupensis* snails in the sampling sites became apparent, and the general risk for infection from the lake water had been significantly decreased. The costs for the various

Table 1 Implementation of key technical measures pertaining to the revised integrated schistosomiasis control strategy in China in the four pilot sites in the lake and marshland regions of the Yangtze River valley

	Pilot site			
Key technical measures implemented	Jinxian county, Jiangxi province	Anxian county, Hunan province	Hanchuan county, Hubei province	Guichi county, Anhui province
Mechanization of agriculture	√	√	√	√
Improving access to clean water	√	–	–	√
Improving sanitation	√	–	–	√
Fencing of pastures	√	√	√	–
Provision of on-board collection containers	√	–	–	–

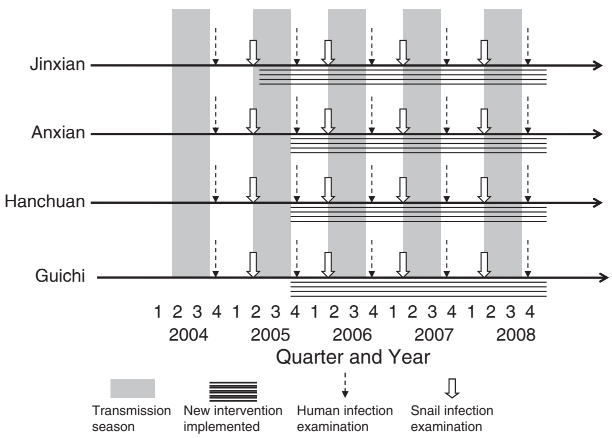

Figure 3 Diagram depicting the implementation of key technical interventions and surveillance activities (humans and snails) in the four pilot sites.

interventions were recorded and will, together with the effectiveness data, allow subsequent cost-effectiveness analyses.

Data collected in the other sites during the pilot phase of the new integrated control strategy highlight the strengths of the revised approach, while also revealing challenges and potential future stumbling blocks. Interventions were implemented and data collected as described by Wang *et al.* (2009). Table 2 shows the annual number of individuals (residents aged 5–65 years) surveyed and the percentage of people found positive for *S. japonicum* eggs by stool examination. A two-pronged diagnostic approach was employed (Zhu 2005; Balen *et al.* 2007). All individuals aged between 5 and 65 years were first screened using antibody-based immunological tests (Zhu 2005; Wang *et al.* 2006). Those found positive (i.e. those with schistosome-specific antibodies) were invited for stool examination, using the Kato-Katz technique (Katz *et al.* 1972). From each individual, one stool sample was obtained and three Kato-Katz thick smears were prepared and examined under a light microscope by experienced laboratory technicians. The already low human infection prevalence observed in Jinxian in 2007 (0.5%) further decreased in 2008 to a level as low as 0.08%. In the other pilot sites, after three or four transmission seasons, the human infection prevalence had dropped from 11.2% to 0.9% in Anxian, from 13.3% to 1.8% in Hanchuan and from 4.7% to 1.5% in Guichi (Figure 4a). At the unit of individual infection rates, these reductions were all highly statistically significant (all $P < 0.001$ except for the first year in Hanchuan). The *O. hupensis* infection rates were also reduced significantly (all $P < 0.05$ except for the last year when the infection rate reached 0) (Table 3, Figure 4b).

Impact beyond the target disease schistosomiasis

An important feature of the Kato-Katz technique is that it allows not only the quantification of *S. japonicum* (and *S. mansoni* when used in Africa and the Americas) but gives also information regarding other helminth infections (Bergquist *et al.* 2009). Of particular note are the common soil-transmitted helminths (*Ascaris lumbricoides*, hookworm and *Trichuris trichiura*; Bethony *et al.* 2006) and the food-borne trematodes (e.g. *Clonorchis sinensis*; Keiser & Utzinger 2009), which are all endemic in China. In the Jinxian pilot site, the prevalence of *A. lumbricoides* and *T. trichiura* in humans was monitored since the onset of interventions in 2005. As shown in Figure 4c, the prevalence of both *A. lumbricoides* and *T. trichiura* decreased gradually over time. Within 3 years, the prevalence of *A. lumbricoides* had dropped from 27.6% to 3.8% ($\chi^2 = 259.5$; $P < 0.001$) and that of *T. trichiura* had declined from 62.0% to 7.5% ($\chi^2 = 788.9$; $P < 0.001$). It is conceivable that similar drops in infection rate occurred for hookworm, but such data are not available since the Kato-Katz technique is not suitable for hookworm diagnosis when the slides are not examined promptly (e.g. within 30–90 min; Martin & Beaver 1968). For diagnosis of *S. japonicum* (and *S. mansoni*), however, reading of

Table 2 The *S. japonicum* infection rate among humans (village residents, aged 5–65 years) between 2004 and 2008 in the four pilot sites

Year of survey	Jinxian county, Jiangxi province				Anxian county, Hunan province				Hanchuan county, Hubei province				Guichi county, Anhui province			
	No. of people examined	Infection rate (%)	χ^2	*P*	No. of people examined	Infection rate (%)	χ^2	*P*	No. of people examined	Infection rate (%)	χ^2	*P*	No. of people examined	Infection rate (%)	χ^2	*P*
2004	1093	9.3			2342	11.2			180	13.3			–	–		
2005	1224	3.7	29.6	<0.001	2956	7.4	22.4	<0.001	123	13.8	0.002	0.96	6223	4.7		
2006	1213	0.9	85.6	<0.001	2984	4.6	81.4	<0.001	5431	1.6	117.2	<0.001	6542	1.6	98.2	<0.001
2007	1211	0.5	97.9	<0.001	3045	2.0	199.5	<0.001	6903	2.6	68.2	<0.001	4235	1.8	59.8	<0.001
2008	1272	0.08	118.1	<0.001	2915	0.9	259.8	<0.001	5844	1.8	104.7	<0.001	3780	1.5	68.9	<0.001

For Jinxian, Anxian and Hanchuan counties, *P* values are calculated with reference to the infection rates in 2004, while in Guichi county, the year of reference is 2005.

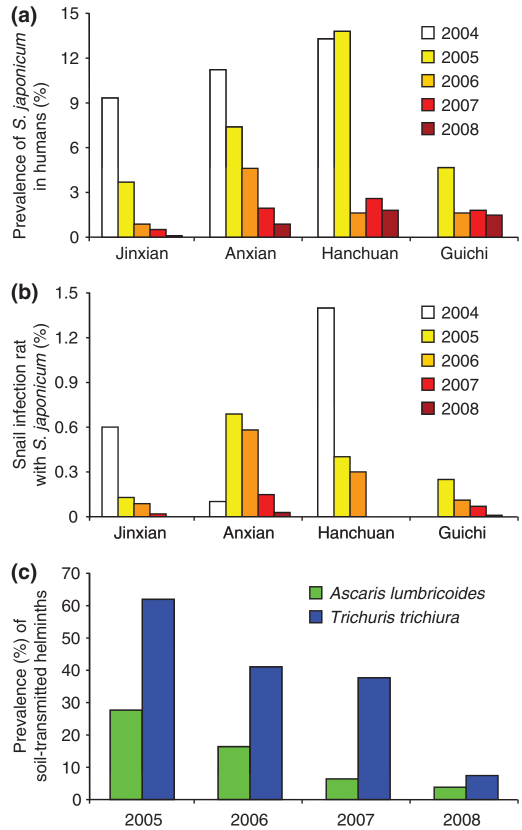

Figure 4 Effect of the revised integrated schistosomiasis control strategy in China on the prevalence of *Schistosoma japonicum* in humans (a), *S. japonicum* in intermediate host snails (b) and the soil-transmitted helminths *Ascaris lumbricoides* and *Trichuris trichiura* in humans (c).

Kato-Katz thick smears are usually done several hours (or days) after slide preparation to facilitate accurate quantification of schistosome eggs (Bergquist *et al.* 2009). Still, the highly significant decreases in the prevalence rates of *A. lumbricoides* and *T. trichiura* are a clear sign that the integrated control programme has an impact beyond the target disease schistosomiasis. In this context, it should be noted that sanitation and IEC activities of the control programme are the likely components of the package of interventions responsible for the observed reductions in the prevalence of soil-transmitted helminths.

Scope and limits of the new integrated control strategy

The Chinese schistosomiasis control programme can serve as a role model for helminth control interventions in contemporary times, similar to the integrated helminth

Table 3 The *S. japonicum* infection rate of *O. hupensis* snails between 2004 and 2008 in the four pilot counties

	Jinxian county, Jiangxi province				Anxian county, Hunan province				Hanchuan county, Hubei province				Guichi county, Anhui province			
Year of survey	No. of snails examined	Infection rate (%)	χ^2	*P*	No. of snails examined	Infection rate (%)	χ^2	*P*	No. of snails examined	Infection rate (%)	χ^2	*P*	No. of snails examined	Infection rate (%)	χ^2	*P*
2004	3620	0.6			2886	1.07			2283	1.4			–	–		
2005	4458	0.13	11.7	<0.001	10 244	0.69	3.8	0.05	6237	0.4	23.7	<0.001	19 987	0.25		
2006	5292	0.09	17.2	<0.001	10 362	0.58	7.2	0.007	2270	0.3	15.0	<0.001	22 043	0.11	10.9	<0.001
2007	4274	0.02	21.1	<0.001	3884	0.15	24.3	<0.001	2304	0	30.5	<0.001	15 478	0.07	15.5	<0.001
2008	753	0	3.4	0.06	2863	0.03	26.5	<0.001	2445	0	32.4	<0.001	18 889	0.01	40.2	<0.001

For Jinxian, Anxian and Hanchuan counties, *P* values are calculated with reference to the infection rates in 2004, while in Guichi county, the year of reference is 2005.

control programme one hundred years ago in the southern United States (Stiles 1939). The renewed emphasis on transmission control and ultimately transmission interruption, by implementing a diversity of interventions in an integrated fashion proved feasible and effective in the lake and marshland areas of China. As shown in the pilot sites, significant reductions were achieved not only in the prevalence of *S. japonicum* in humans and the intermediate host snails, but also in the prevalence of soil-transmitted helminths. This is an important finding in view of growing attention paid to integrating control efforts targeting many different parasitic diseases (Hotez *et al.* 2006, 2007; Utzinger *et al.* 2009).

All key technical measures of the proposed strategy are in line with the 'new socialist countryside' initiative in China (Huang & Zhang 2007). Moreover, as new tools become available (e.g. a veterinary schistosomiasis vaccine; McManus & Loukas 2008), these can be further integrated into the current scheme because of its modular design. We feel that this revised integrated schistosomiasis control strategy can be implemented elsewhere in the endemic areas of the lake and marshland regions, and that it will have an ancillary impact on soil-transmitted helminthiasis and, possibly, also food-borne trematodiasis. To ensure the long-term success of schistosomiasis control, it is imperative that the necessary means for infrastructure development and control interventions are made available for an extended period of time. In addition, infrastructures (e.g. latrines and safe water supply) must be properly maintained and gradually improved, and behavioural changes become permanent. This can only be achieved through continued commitment by the relevant authorities, supported by local resources for control and ownership of the programme. Moreover, communities must dispose the means for necessary investment, and a sense of stewardship, so that responsibility can be built among the local population (Aagaard-Hansen *et al.* 2009).

The following limitations are offered for consideration. First, the highly significant reductions in human *S. japonicum* and soil-transmitted helminth infection prevalences and the infection level of intermediate host snails are based on individual-level data. In case the analyses were made at the unit of pilot intervention sites, the strengths of the evidence is reduced. Second, detailed cost-effectiveness analyses are needed as this new integrated control approach is resource intensive, which might jeopardize broader-scale application, particularly in the wake of a global economic downturn. On the effectiveness side, the impact on diseases other than schistosomiasis needs to be considered. Third, whether or not this new integrated control strategy can be adapted for specific conditions in the mountainous areas of Sichuan and Yunnan provinces needs to be determined. In this connection, it is important to note that the transmission of schistosomiasis in the mountainous areas of China is characterized by distinct ecological, economic, epidemiological and socio-cultural conditions (Spear *et al.* 2004; Gurarie & Seto 2009). Given the modular design of the control interventions, it should be possible though. It is further hoped that experiences and expertise gained in China could stimulate integrated control of schistosomiasis and other helminth diseases elsewhere.

An aside, but an important one, is the resulting greenhouse 'footprint' of the revised control strategy. In this way, the new initiative will have an impact far beyond schistosomiasis as it aims at profound shifts in agricultural techniques. Counter-intuitively, the overall greenhouse effect of all relevant gases released might decrease rather than increase since the shift from biological to mechanical workforce not only entails the introduction of fuel-burning machines but also the demise of a large number of water buffaloes which are an important source of methane, a far more potent greenhouse gas than carbon dioxide.

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