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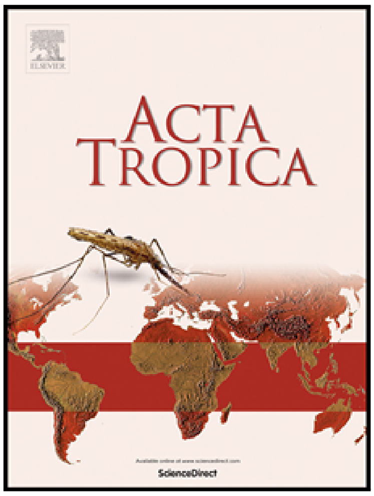

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Effectiveness of a community-based integrated strategy to control soil-transmitted helminthiasis and clonorchiasis in the People's Republic of China

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Abstract

Soil-transmitted helminthiases (STHs) are caused by a group of intestinal nematode infections due to poor hygiene and environments, and clonorchiasis is a food-borne trematode (FBT) infection caused by ingestion of raw freshwater fish. Both are endemic in the People's Republic of China. To explore a suitable control strategy, integrated interventions were applied between 2007 and 2009 in ten pilot counties (eight for the STHs and two for clonorchiasis). Drug administration was used for treatment and complementary efforts to improve the situation based on health education, provision of clean water and sanitation were carried out. Significant achievements were gained as reflected by a drastic decrease in prevalence these infections were demonstrated. The overall prevalence of STHs and clonorchiasis decreased from 35.9% to 7.8% and from 41.4% to 7.0%, respectively. The reduction of prevalence and high cost-effectiveness were documented supporting large-scale application of this integrated intervention in China and elsewhere.

Keywords: Soil-transmitted helminths, clonorchiasis, community-based strategy, integrated intervention, China

1. **Introduction**

Soil-transmitted helminthiases (STHs) are caused by a group of intestinal nematodes that includes an estimated 1.22 billion cases with *Ascaris lumbricoides*, 0.74 billion with hookworms (*Ancylostoma duodenale* and *Necator americanus*) and 0.80 billion with *Trichuris trichiura* (Bethony, et al.,2006; WHO, 2010), corresponding to the loss of many millions of disability-adjusted life years (DALYs) (Murray et al., 2012). The STHs are environmentally contagious infections with a global distribution that may cause nutritional impairment, cognitive impairment and even conditions requiring surgical interventions(WHO, 2010). Clonorchiasis is caused by ingesting raw freshwater fish harbouring infective metacercariae of *Clonorchis sinensis*(Lun et al., 2005). *C. sinensis* infection leads to diverse complications, such as cholecystitis, cholangitis and cholangiocarcinoma, causing premature loss of life(Sripa et al.,2012; Qian et al., 2011) . More than 15 million people are thought to be infected in East Asia causing 275 370 DALYs(Fürst et al., 2012); however, it is felt that that the risk posed by this infection is strongly underestimated(Sripa et al., 2012). Between 2001 and 2004, a total of 129 million people were estimated to be infected with STHs in the People's Republic of China (P.R. China): 85.9 million with *A. lumbricoides*, 39.3 million with hookworms and 29.1 million with *T. trichiura*(Chen et al., 2008). Another 12.5 million were found to be infected with *C. sinensis* in P.R. China(Chen et al., 2012; Qian et al., 2012; Qian et al., 2013). Due to the prevailing environmental conditions and lower level of social development, the STHs are predominantly endemic in western and southern areas(Chen et al., 2008), while clonorchiasis is mainly distributed in the south-eastern and north-eastern areas of the country because of the local habit of consuming raw fish(Chen et al., 2012; Qian et al., 2012; Qian et al., 2013). With STHs and clonorchiasis endemic in P.R. China, several national surveys of parasitic diseases have been carried out(Chen et al., 2008; Chen et al., 2012).

The high prevalence of STHs and clonorchiasis impede social and economic development in the less developed areas of P.R. China, and contributes to difficulties in the reduction of poverty implemented by the central government. The document "National Program for Control of Major Parasitic Diseases during 2006-2015" was issued by Ministry of Health in 2006 with the aim of accelerating the control of important parasitic diseases including STHs and clonorchiasis(Ministry of Health, 2013). Two major factors challenge the achievement of the goal set by the national control program: (i) the variable prevalence of the STHs and clonorchiasis in different regions due to differences in socioeconomic and environmental factors, a fact that shows that one strategy does not fit all; and (ii) the local knowledge of disease control aimed at STH and clonorchiasis is limited directly affecting available resources for their control. To succeed, it is essential to apply a strategy tailored to local settings considering local socioeconomic developments and institute collaboration with the different sectors existing at the county level. This paper describes the developments and results around the country with respect to these diseases.

2. Methods

2.1. Study sites

Pilot areas with varied prevalence at the county level were established in collaboration with local community and county governments in ten provinces to explore the integrated strategy for controlling STHs and clonorchiasis in the period 2006-2009. Tables S1 and S2 presents the provinces and counties selected for the study with their geographical and economic characteristics, while Figure 1. shows where they are geographically. A total of 3 527 600 inhabitants lived in the ten pilot areas in 2006 and the annual net income per capita ranged from RBM 2 171 to 4 100 (USD 304 - 574) with an average of RMB 3 361 (USD 470). The main income source is agricultural production of various kinds. All STH pilot areas were selected from counties situated south of 33° North Latitude with annual 1 000 - 2 000 mm rainfall; thus they are characterized by a warm and moist climate. The two clonorchiasis pilot areas were chosen from counties located in south-eastern and north-eastern P.R. China. No systematic interventions for parasitic diseases had been implemented in any of the pilot area during the previous 10 years.

< Figure 1 + Tables S1 and S2 near here>

2.2. Design and selection of pilot areas

The ten pilot areas were selected based on a previous national survey carried out between 2001 and 2004, out of which eight counties for STH and two for clonorchiasis. A baseline survey was carried out in each pilot area in 2006 followed by integrated interventions implemented from 2007 to 2009 in each pilot area based on drug administration followed by health education and provision of clean water while improving sanitation. A cost-effectiveness evaluation was carried out in late 2009 paying attention to prevalence in relation to changes in knowledge and behaviour.

The counties were classified as various strata based on the prevalence results from the baseline survey. For the STHs, the areas were referred to as either Stratus A = >50%; Stratus B = 20-50%; or Stratus C = <20% prevalence. For clonorchiasis the strata were only two: one with prevalence ≥40% (Stratus A) and one with prevalence <40% (Stratus B).

2.3. Baseline survey

Stratified random sampling was applied. Firstly, each pilot area was divided into five sub-areas based on location and named the eastern, western, southern, northern and central area, respectively. Secondly, one administrative village (which usually contains one or more natural villages) was randomly sampled from each area. Thirdly, one natural village was selected from each administrative village. Fourthly, about 500 villagers were selected at random from each village. Thus, a total of about 2 500 villagers were included in each pilot study.

The Kato-Katz method (Katz et al., 1972) was applied for distinguishing and counting helminth eggs. Briefly, one stool specimen was collected from each participant and one smear prepared for each specimen and examined under a light microscope. Meanwhile, questionnaires were administrated to capture individual knowledge and behaviour, i.e. asking for the cause of STHs or clonorchiasis, the harm and clinical presentations, how to treat the infections as well as which approaches known to prevent these infections. With regard to behaviour we enquired about the villagers' living habits such as occupation and dietary preferences as well as their compliance in taking anthelmintic drugs.

2.4. An integrated intervention

Diverse strategies must be employed to control helminthiases, e.g. health education, chemotherapy, provision of clean water and sanitation. However, as each approach on its own is insufficient, all these components were selected and integrated into one control methodology.

2.4.1. Drug administration

Either albendazole or mebendazole was applied for the STHs, both taken as a single dose of 400mg for adults and 200mg for children. Against clonorchiasis, we used either praziquantel or albendazole, the former taken at a single dose of 18.75mg/kg, twice a day for 2 consecutive days, and the latter as a single dose of 8mg/kg, twice a day for 4 consecutive days(Hotez et al., 2007).

For the STHs pilot areas, mass chemotherapy was carried out twice at the first year and once in the second and third year in Stratus A and given once a year for 3 consecutive years in Stratus B. Selective chemotherapy was instituted for the population at risk (children and adults engaged in barefoot farm work) once a year for 3 consecutive years in Stratus C. In the clonorchiasis pilot areas, mass chemotherapy was given once a year for 3 consecutive years in Stratus A, while selective chemotherapy targeting population at risk (habitants habitually eating raw freshwater fish) was implemented once a year for 3 consecutive years in Stratus B.

2.4.2. Health education

The contents of the education comprise the cause of these diseases including symptoms and clinical presentation, treatment and measures preventing infection. Villages were also advised to abandon unhealthy habits with regard to infection. The approaches included 1) discussions and training courses for health workers; 2) propaganda through mass media (radio, television and newspapers); 3) posters and hanging charts displayed at public places; 4) disseminating leaflets to households; especially housewives; and 5) teaching students through school platforms.

2.4.3 Sanitation

New village elements, such as provision of clean water and improved sanitation were implemented in all pilot areas. Clean water and sanitation for the households were provided by the local government. However, financial capacity limited activities in some places and thus the provision of clean water and sanitation varied somewhat in different pilot areas.

2.5. Assessment and quality control

The same sampling technique as that in baseline survey was adopted in evaluation survey in 2009. As 200 villages were selected from each of the five natural villages in each pilot area, a total of 1 000 villagers were selected from each pilot area. The examination technique was same as that used in the baseline survey, and so was the questionnaire investigation. Data on provision of clean water and construction of clean toilets between 2006 and 2009 were collected.

To guarantee quality during all activities mentioned above, several measurements were performed. Firstly, one general coordinating group, consisting of health department and experts, was set up at the beginning in order to supervise progress. Meanwhile, another technical guide group of experts from related areas was established to provide technical support. Thirdly, a standard operation protocol for drug administration was issued to guarantee the safety and effectiveness. Fourthly, many training courses were held at different levels before implementation of each technical activity. The staff was trained how to collect faecal samples and conduct questionnaire surveys, how to carry out health education at different occasions. Technical training for laboratory examination were specially emphasized, including preparation of Kato-Katz smears and how to do differential diagnosis between diverse helminth eggs.

2.6. Statistical analysis

Analysis was run in SPSS for Windows (version11.0; SPSS Institute, Inc., Chicago, IL, USA). Pearson x^2 test or Fisher's exact test when appropriate was used to assess the association between category variables. Statistical significance was given at *p*=0.05. Cost-effectiveness analyses were done by calculating the average cost for reduction of one infected case and the average cost for reduction of 1% prevalence in 10 000 persons.

3. Ethical clearance

The study was approved by the Ethics Committee of the National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention in Shanghai, P.R. China (NIPD/China CDC). The objectives, procedures and potential risks were orally explained and informed to all participants. A written consent form was also obtained from each participant with signature of him or his proxy.

4. Results

4.1. Baseline survey

In the STH pilot areas, a total of 20 408 villagers examined resulting in 7 322 persons found infected with an average prevalence of 35.9% (Figure 1). The prevalence ranged from 19.1% (XY_Yunnan) to 57.1% (DL_Sichuan). In the two clonorchiasis pilot areas, 2 162 out of 5 218 villagers were found to have *C. sinensis* eggs with an average prevalence of 41.4%. The prevalence was 67.5% and 14.0% in ZY_Heilongjiang and YS_Guangdong, respectively.

< Figure 1 near here>

Among the STH pilot areas, two were classified into Stratus A, i.e. TC_Hainan (54.6%) and DL_Sichuan (57.1%), five into Stratus B including TC_Anhui (31.8%), GX_Jiangxi (31.8%), YY_Hunan (32.0%), RX_Guangxi (30.1%) and KY_Guizhou (30.3%), and one into Stratus C, namely XY_Yunnan (19.1%). In the two clonorchiasis pilot areas, ZY_Heilongjiang (67.5%) was sorted as Stratus A and YS_Guangdong (14.0%) as Stratus B

4.2. Integrated Interventions

<u>4.2.1. Drug administration</u>

Over the three study years, 7 045 312 treatment doses in total were delivered in the study area (Table 1). The coverage rate in the eight pilot areas for STHs ranged from 61.0% to 96.1% in 2007, from 65.4 % to 97.8% in 2008 and from 69.4% to 98.5% in 2009, while for clonorchiasis it varied between 41.6% and

65.2% in 2007, 58.2% and 80.3% in 2008 and 44.7% and 83.9% in 2009. As can be seen in the table, the average coverage increased from 84.5% to reach 78.7% over the three-year period.

Owing to strict control of potential contraindications and dosage, only one case showed an allergic reaction to praziquantel and was cured after prompt treatment.

< Table 1 near here>

4.2.2. Health education

The times a person received health education (person-times) in the ten pilot areas between 2007 and 2009 amounted to 5 042 900. Health education was mentioned 659 times in mass media, 103 176 posters were put up, 4.0 million leaflets distributed and 5 965 demonstration boards issued. Additionally, 541 advocacy meetings were held. This is summarized in Table S3.

< Table S3 near here>

4.2.3. Sanitation

Including the addition of 979 913 persons since 2006, a total of 3 656 083 had access to safe water supply in the ten pilot areas by 2009, a 37.0% increase (Table 2). By 2009, a total of 773 693 sanitary lavatories had been built, 267 360 of which after 2006 (Table 3). As seen in the table, the overall coverage rate reached 50.0%, increasing by 47.0% compared to that in 2006 (34.0%).

< Table 2 and Table 3 near here>

4.2.4. Knowledge and practice

As can be seen in Table 4, three years of health education had provided acceptable knowledge with regard to the risk for STH and clonorchiasis to an average 96.0% of the population; the highest in ZY_Heilongjiang (100.0%) and the lowest in XY_Yunnan (87.0%). Compared to the baseline survey, knowledge had increased by 113.0% on average; the highest in TC_Anhui (221.0%) and the lowest in RX_Guangxi (18.0%).

An average proportion of correct practise in relation to the risk of infection had reached a very high level (99.0%) reaching 100.0% in TC_Anhui, TC_Hainan and KY_Guizhou and 96.0% in YY_Hunan (Table 4). Compared to the baseline survey, correct behaviour with regard to the risk of infection increased by 79.0% on average, with the highest in TC_Anhui (173.0%) and the lowest in RX_Guangxi (33.0%).

< Table 4 near here>

4.3. Prevalence change

In 2009, out of 8 204 persons examined, 636 were found with STH infections in the eight STH pilot areas, with an average prevalence of 8.0%. The highest prevalence was found in TC_Hainan (17.1%) and the lowest in TC_Anhui (2.0%). The average prevalence in three different strata were 13.6%, 6.4% and 2.5%, respectively (χ^2=2.48 , P>0.05).

Compared to 2006, the prevalence of STHs in 2009 had decreased by 78.0% on average, 75.6%, 79.5% and 87.1% in the three different strata, respectively. The reduction rate ranged from 58.5% in RX_Guangxi to 94.0% in TC_Anhui.

The prevalence in males decreased on average from 35.1% in 2006 to 7.4% in 2009, a decrease of 78.8%, while the prevalence in females on average decreased correspondingly from 36.6% to 8.1%, an overall decrease of 79.9%. The prevalence in the children decreased on average from 34.2% in 2006 to 6.9% in 2009 (78.8%).

4.3.1. *A. lumbricoides* infection

The prevalence of *A. lumbricoides* infection in 2009 in eight pilot areas varied from 0.1% to 7.4%, with an average of 2.5%. The average prevalence was 1.6%, 3.0% and 2.1% in three different strata, respectively (χ^2=12.23, P<0.05). The prevalence in the males and females was 2.7% and 2.3%, respectively (χ^2=1.22, P>0.05). The prevalence in children vis-à-vis adults was 2.7% and 2.4%, respectively (χ^2=0.48, P>0.05). The reduction rate of *A. lumbricoides* infection from 2006 to 2009 ranged from 63.8% to 99.0%, with an average of 85.8%. The prevalence decreased by 92.2%, 81.8% and 88.9% in three strata, respectively. The prevalence in males and females decreased by 84.5% and 87.1%, respectively, while the prevalence in the children and adults decreased by 87.1% and 85.6%, respectively.

4.3.2. Hookworm infection

The prevalence of hookworm infection in 2009 in the eight pilot areas ranged from 0.1% to 14.6%, with an average of 4.4%. The prevalence was 11.0%, 2.5% and 0.3% in three strata, respectively (χ^2=307.43, P<0.05). The prevalence in males and females was 4.1% and 4.7%, respectively (χ^2=1.32, P>0.05). The prevalence in children and adults was 2.8% and 4.9%, respectively (χ^2=14.18, P<0.05). The reduction of hookworm infections from 2006 to 2009 ranged from 59.0% to 96.7%, with an average of 76.6%. The prevalence in Stratus A and Stratus B decreased by 73.4% and 81.5%, respectively. The prevalence in males and females decreased by 77.3% and 75.9%, respectively, while the prevalence in children and adults decreased by 75.4% and 76.6%, respectively.

4.3.3. *T. trichiura* infection

The prevalence of *T. trichiura* infection in 2009 in the pilot areas ranged from 0.1% to 2.2%, with an average of 1.1%. The prevalence was 1.5%, 1.1% and 0.2% in the three strata, respectively (χ^2=10.62, P<0.05). The prevalence in males and females was 0.8% and 1.4%, respectively (χ^2=6.62, P<0.05). The prevalence in children and adults was 1.4% and 1.0%, respectively (χ^2=2.45, P>0.05). The reduction rate of *T. trichiura* infection from 2006 to 2009 ranged from 65.8% to 90.0%, with an average of 79.6%. The prevalence decreased by 86.2%, 72.7% and 74.0% in three strata, respectively. The prevalence in male and females decreased by 85.6% and 73.6%, respectively, while the prevalence in children and adults decreased by 82.4% and 78.5%, respectively.

4.3.4. Clonorchiasis

When 2 073 persons from the two clonorchiasis pilot areas were examined in 2009, 145 persons tested positively for *C. sinensis* eggs, an average prevalence of 7.0%. The prevalence in the strata A and B was 7.1% and 6.9%, respectively (χ^2=0.05, P>0.05), and the prevalence in males and females 8.8% and 4.9%, respectively (χ^2=11.83, P<0.05). The difference in prevalence between children and adults was small, i.e. 6.6% and 7.0%, respectively (χ^2=0.05, P>0.05). The overall prevalence reduction from 2006 to 2009 was 89.5% and 51.0% in strata A and B, respectively, with an average of 83.1%. With regard to males and females the decrease was 80.0% and 87.4%, respectively, while the prevalence in the children and adults declined by 72.6% and 84.6%, respectively.

5. Cost-effectiveness

A total of RMB 17 879 200.0 (USD 2 503 088.0) supported this study, using RMB 982 400.0 (USD 137 536.0) for training, RMB 1 863 000.0 (USD 260 820.0) for health education, RMB 1 041 200.0 (USD 145 768.0) for special surveys, RMB 9 162 600.0 (USD 1 282 764.0) for purchasing drugs, RMB 1 538 800.0 (USD 215 432.0) for labour service in delivering drugs, RMB 2 692 000.0 (USD 376 880.0) for meetings and supervisions and RMB 599 200.0 (USD 83 888.0) for miscellaneous expenses (Table 5).

< Table 5 near here>

The direct input for the eight pilot areas for STHs was RMB 11 449 100.0 (USD 00000), curing 709 000 persons, while that for the two clonorchiasis areas was RMB 6 430 100.0 (USD 900 214.0), curing 254 000 cases (Table 5). The average cost for STH treatment per person in the study period was RMB 16.2 (USD 2.3), and that for 1% prevalence reduction in 10 000 persons was RMB 1 450.0 (USD 205.0). The corresponding figures for clonorchiasis was RMB 25.3 (USD 3.5) and RMB 2 370.00

(USD 332.0).

< Table 5 near here>

6. Discussion

Both STHs and clonorchiasis are internationally recognized as NTDs(WHO, 2010; China CDC, 2010), which also corresponds to the current situation in P.R. China(Chen et al., 2008; Chen et al., 2012; Qian et al., 2012; Qian et al., 2013; Yang et al., 2013). Although great achievements in social and economic development have taken place in this country, STHs and clonorchiasis still constitute significant infection burden, especially in remote and/or less developed areas(Yang et al., 2013). The success realized in the pilot areas should be attributed to multi-sectoral cooperation and efforts from local governments at all levels leading to a community-based integrated strategy with specific targeting based on prevalence strata, with health education plying a leading role for sustaining the progress made for the long term.

Political will and the role of governments at all levels are important for successful NTD control (Stein et al.,2007) and political effort was taken into account in this pilot study. Indeed, these efforts played a key role in promoting community involvement in the control activities assuring cost-effectiveness of the work in the pilot areas. The governments responsible for the pilot areas took strong action in most cases, such as (i) creating general coordinating groups consisting of support staff and experts from the health department and other sectors; and (ii) establishing a lead group for each pilot area consisting of department heads, e.g., of Health, Education, Broadcasting, Water Resource and Agriculture, generally headed by the local Vice Mayor.

The lessons learnt by our pilot study provide a foundation for scaling up programmes for control and elimination of the NTDs. The evidence supplied clearly shows that significant achievements were obtained: (i) better than 75% reduction of STH and *Clonorchis* infections over the three study years; (ii) combined intervention measures with different chemotherapy approaches depending on the level of prevalence classification demonstrated high cost-effectiveness; and (iii) a community-based integrated strategy including health education, drug administration and provision of improved sanitation elements that proved feasible. The latter is particularly suited to rural areas characterized by minimal socioeconomic development as shown by the comparatively low cost RMB (16.2 - USD 2.3 for STHs and RMB 25.3 - USD 3.5 for clonorchiasis) for keeping a person cured for three years, which represents a good return on investment leading to lower transmission and better health, particularly in children.

Provision of clean water and construction of toilets were undertaken in accordance with the slogans "*Constructing a new village style*" and "*Establishment of healthy towns*", that served to even out imbalances of social and economic development. Furthermore, considering cultural differences, diverse approaches in health education were adopted. Both albendazole and mebendazole were applied for treatment of STHs here, which is consistent to the recommendation of World Health Organization (WHO) (WHO, 2002; Keiser et al., 2008). We used both praziquantel and albendazole for the treatment of clonorchiasis. In accordance with previous Chinese studies (Liu et al., 1994; Fang et al., 1995; Department of health of Guangdong province, 2013) it was demonstrated albendazole is as effective against *C. sinensis* but with less side effects compared to praziquantel which is the drug recommended by WHO (WHO, 2002).

Increased knowledge and change from hazardous habits was seen to benefit the sustainability of control activities(Ziegler et al., 2011; Bieri et al., 2013; Qian et al., 2013; Xayaseng et al., 2013), this health education is of crucial importance for the control of STHs and clonorchiasis. It also raised compliance with regard to participation in control activities and willingness to accept repeated chemotherapy. In our study, health education was initiated at the beginning in this study, which promoted smooth implementation of mass chemotherapy. As seen in Table S3, there was a high number of times (5 042 900) somebody received some form of health education (person-times), and this translated into a significant increase of knowledge and behaviour change.

Important lessons learnt from the pilot study serve to set the goal for the future national control programme, and how to sustain the achievements gained in those pilot areas. As the stage in control of parasitic diseases achieved influences the choice of intervention (Utzinger et al., 2012), significant reduction of the infections burden can only be obtained by selecting different approaches. Morbidity control should be the target in high-prevalence areas, where chemotherapy undoubtedly must play the core role (Utzinger et al., 2012; Prichard et al., 2012; Bockarie et al., 2013). For instance, high- frequency mass chemotherapy was applied in strata with over 20% STH and 40% *Clonorchis* infection, while selective chemotherapy was adopted where the prevalence was lower than that. This kind of differential chemotherapy not only benefits smooth implementation, but also increases cost-effectiveness. Experience also tells us that it is important to formulate a standard operation protocol for drug administration, particularly when carried out at large scale, such as spending 7 045 300 person-times deworming over three years as was done in our pilot areas.

Re-infection remains an important issues in the control of NTDs (Jia et al., 2012), and this is due to the resistance of local people to change their style of living (WHO,2002; Ziegler et al., 2011; Qian et al., 2013). However, our pilot studies show that construction clean water and toilets significantly promotes the sustainability of STH control(Ziegelbauer et al., 2012), and this lead should be taken up where uneven social development makes it a challenge to complete interruption of transmission through full coverage of improved sanitation.

Several limitations in this study were noted. Firstly, at the baseline surveys, 2 500 persons were enrolled but only 1 000 persons were included because of limited funding. Secondly, only prevalence data were provided, while intensity of infections should be evaluated to further demonstrate the effectiveness of the programme. Thirdly, only one slide were examined for one stool sample due to the limitation of field work, and better sensitivity would be obtained if more slides or more samples were examined.

In conclusion, the community-based integrated strategy used for control of STH infections and clonorchiasis has been demonstrated as a cost-effective approach. It would not only contribute positively to the Chinese national control program, but deserves to be considered for introduction in other endemic countries.

Since 2006, 22 national surveillance spots for STHs were established nationwide in combination with the work of pilot areas(Chen et al., 2013). After 2016, the national surveillance of STHs and clonorchiasis were both supported by the government and the range of surveillance were greatly expanded, with the prevalence greatly decreased(Zhu et al.,2019; Chen et al., 2019; Qian et al., 2018).

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Competing Interests:

The authors have declared that no competing interests exist.

Author contributions

Conceptualization, original draft writing, editing, resources, supervision: Ying-Dan Chen. Conceptualization, validation and supervision: Hua-Zhong Li. Conceptualization, resources and supervision: Long-Qi Xu. Formal analysis: Men-Bao Qian. Investigation: Hong-ChunTian, Yue-Yi Fang , Zhuo Ji and Meng Tang . Investigation and resources: Chang-Hai Zhou. Funding acquisition and editing : Qun Li, Zi-Jian Feng and Yu Wang. Editing: Robert Bergquist. Review and editing, supervision and project administration :Xiao-Nong Zhou.

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Table 1. Drug administration with coverage rates for each pilot area

Pilot area (county and province)	2007			2008			2009		
	No. of persons targeted for deworming	No. of persons dewormed	Coverage rate (%)	No. of persons targeted for deworming	No. of persons dewormed	Coverage rate (%)	No. of persons targeted for deworming	No. of persons dewormed	Coverage rate (%)
Zhaoyuan (ZY), Heilongjiang	327 384	147 120	41.6	327 968	190 991	58.2	327 968	146 644	44.7
Yangshan (YS), Guangdong	45 356	29 558	65.2	16 779	13 469	80.3	13 890	11 635	83.9
Tongcheng (TC), Anhui	489 200	470 000	96.1	56 743	37 500	66.1	487 450	445 000	91.3
Guixi (GX), Jiangxi	356 896	289 573	81.1	383 686	289 724	75.5	383 686	266 392	69.4
Yueyang (YY), Hunan	402 325	357 906	89.0	494 785	354 785	71.7	468 601	364 717	77.8
Rongxian (RX), Guangxi	570 492	416 826	73.1	611 604	498 852	81.6	611 604	503 001	82.2
Tunchang (TC), Hainan	221 526	270 340	61.0	220 872	144 388	65.4	223 584	159 208	71.2
Danling (DL), Sichuan	94 899	164 600	76.7	94 821	81 625	86.9	94 084	88 454	94.0
Kaiyang (KY), Guizhou	338 562	295 174	87.9	313 086	282 167	90.1	321 225	300 561	93.6
Xiangyun (XY), Yunnan	110 200	106 027	96.2	135 800	132 762	97.8	114 800	113 083	98.5
Total	**3 101 849***	**2 620 354***	**84.5***	**2 656 144**	**2 026 263**	**76.3**	**3 046 892**	**2 398 695**	**78.7**

Clonorchis trial areas highlighted in green and STH trial areas highlighted in blue.
Only selective chemotherapy was carried out in TC Anhui in 2008, where mass chemotherapy should have been carried out according to the design.
*These numbers include STH treatment in Yangshan (YS), Guangdong (145 009 target persons and 73 230 dewormed with a 50.5% coverage) that was not planned originally.

Table 2. Provision of clean water for each pilot area made since 2006

Pilot area (county and province)	2006		2007		2008		2009		Total	
	No. of persons with access to clean water	Benefit rate (%)	No. of persons with access to clean water	Benefit rate (%)	No. of persons with access to clean water	Benefit rate (%)	No. of persons with access to clean water	Benefit rate	Added numbers with access to clean water*	Rate of increase (%)
Zhaoyuan (ZY), Heilongjiang	68 968	18.6	107 864	28.9	158 324	42.1	232 674	61.8	163 706	232.9
Yangshan (YS), Guangdong	333 543	72.3	352 367	76.4	355 717	75.6	359 077	75.8	25 534	4.8
Tongcheng (TC), Anhui	443 000	69.1	638 809	99.3	631 000	98.2	630 387	97.2	187 387	43.7
Guixi (GX), Jiangxi	366 238	86.1	404 367	94.7	423 411	97.8	428 279	98.9	62 041	65.4
Yueyang (YY), Hunan	308 480	49.8	389 880	70.2	461 598	80.2	553 578	95.0	245 098	71.4
Rongxian (RX), Guangxi	691 500	99.9	692 100	99.9	692 200	99.9	692 300	100.0	800	0.1
Tunchang (TC), Hainan	138 900	61.9	139 700	62.2	150 400	66.3	150 669	66.3	11 769	15.5
Danling (DL), Sichuan	15 624	11.8	29 151	22.1	42 778	32.5	112 711	85.7	97 087	623.9
Kaiyang (KY), Guizhou	195 637	52.0	207 637	58.8	272 937	76.0	347 637	96.3	152 000	28.3
Xiangyun (XY), Yunnan	114 280	27.4	121 200	28.9	133 599	31.8	148 771	35.3	34 491	64.7
Total	**2 676 170**	**61.4**	**3 083 075**	**72.0**	**3 321 964**	**76.75**	**3 656 083**	**84.1**	**979 913**	**37.0**

Clonorchis trial areas highlighted in green and STH trial areas highlighted in blue.

Table 3. Provision of sanitation in each pilot area since 2006

Pilot area (county and province)	2006			2007			2008			2009		
	Total no. of households	No. of households with toilets	Coverage rate (%)	Total no. of households	No. of households with toilets	Coverage rate (%)	Total no. of households	No. of households with toilets	Coverage rate (%)	Total no. of households	No. of households with toilets	Cov ra
Zhaoyuan (ZY), Heilongjiang	146 000	200	0.1	153 538	500	0.3	158 393	1 000	0.6	164 091	1 000	
Yangshan (YS), Guangdong	124 768	65 173	52.2	126 775	70 887	55.9	131 433	71 428	54.4	132 650	72 100	
Tongcheng (TC), Anhui	203 176	14 947	7.4	206 150	96 047	46.6	207 847	102 959	49.5	209 181	104 355	
Guixi (GX), Jiangxi	156 712	56 571	36.1	158 878	85 937	54.1	154 851	89 837	58.0	154 851	92 437	
Yueyang (YY), Hunan	234 003	116 040	49.6	218 578	148 605	68.0	224 168	168 139	75.0	230 863	196 248	
Rongxian (RX), Guangxi	252 133	139 201	55.2	257 397	139 267	54.1	262 106	145 759	55.6	269 905	145 802	
Tunchang (TC), Hainan	64 351	21 850	34.0	64 932	24 520	37.8	65 846	25 720	39.1	65 918	25 840	
Danling (DL), Sichuan	46 996	9 258	19.7	46 996	13 644	29.0	47 028	16 022	34.8	47 022	18 052	
Kaiyang (KY), Guizhou	1 22 517	77 628	63.4	125 994	89 398	71.0	123 434	95 972	77.8	133 271	108 335	
Xiangyun(XY), Yunnan	126 209	5 464	4.3	127 463	6 925	5.4	127 710	8 311	6.51	130 420	9 523	
Total	**1 476 865**	**5 06 332**	**34.3**	**1 486 701**	**675 730**	**45.5**	**1 5022 816**	**725 147**	**48.25**	**1 538 172**	**773 692**	

Clonorchis trial areas highlighted in green and STH trial areas highlighted in blue.

Table 4. Improvement of knowledge and practice in each pilot area

Pilot area (county and province)	2006					2009					Increase (%)	
	Total no. of persons investigated	Knowledge		Practice		Total no. of persons investigated	Knowledge		Practice			
		Number	Rate (%)	Number	Rate (%)		Number	Rate (%)	Number	Rate (%)	Knowledge	Practice
Zhaoyuan (ZY), Heilongjiang	247	110	44.5	96	38.9	203	203	100.0	202	99.5	124.6	156.0
Yangshan (YS), Guangdong	-	-	-	-	-	225	218	96. 9	221	98.2	-	-
Tongcheng (TC), Anhui	210	65	31.0	77	36.7	198	197	99.5	198	100.0	221.5	172.7
Guixi (GX), Jiangxi	-	-	-	-	-	201	186	92.5	200	99.5	-	-
Yueyang (YY), Hunan	244	112	45.9	126	51.6	200	194	97.0	192	96.0	111.3	85.9
Rongxian (RX), Guangxi	215	178	82.8	158	73.5	200	195	97.5	196	98.0	17.8	33.4
Tunchang (TC), Hainan	285	128	44.9	188	66.0	210	203	96.7	210	100.0	115.2	51.6
Danling (DL), Sichuan	199	68	34.2	127	63.8	207	206	99.5	206	99.5	191.2	55.9
Kaiyang (KY), Guizhou	507	224	44.2	300	59.2	220	206	93.6	220	100.0	111.9	69.0
Xiangyun(XY), Yunnan	250	88	35.2	120	48.0	207	180	87.0	201	97.1	147.0	102.3
Total	**2 157**	**973**	**45.1**	**1 192**	**55.3**	**2071**	**1 988**	**96.0**	**2 046**	**98.8**	**112.8**	**78.8**

Clonorchis trial areas highlighted in green and STH trial areas highlighted in blue.

No data for Guixi, Jiangxi and Yangshan, Guangdong in 2006.

Table 5. Direct financial input for each pilot area intervention

Pilot area (county and province)	***Medical drugs used***	***Service charge for drug delivery***	***Health education***	***Training***	***Special survey***	***Meetings and supervision***	***Miscellaneous costs***
Zhaoyuan (ZY), Heilongjiang	541 2500	371 44	143 528	127 419	25 056	112 562	32 359
Yangshan (YS), Guangdong	108 162	101 602	124 256	88 657	121 165	230 314	38 093
Tongcheng (TC), Anhui	662 000	0	124 516	139 301	117 562	60 903	57 449
Guixi (GX), Jiangxi	450 000	70 080	195 000	127 251	53 436	65 492	207 373
Yueyang (YY), Hunan	532 384	517 500	190 000	79 600	475 40	40 000	0
Rongxian (RX), Guangxi	709 340	425 603	208 534	70 343	46 097	51 128	34 675
Tunchang (TC), Hainan	336 000	50 140	141 420	71 410	142 880	37 970	3 950
Danling (DL), Sichuan	331 662	115 922	119 690	57 262	17 473	24 518	24 006
Kaiyang (KY), Guizhou	445 500	181 145	219 349	122 030	72 110	105 232	45 302
Xiangyun (XY), Yunnan	175 080	39 700	146 700	89 100	97 900	48 900	0
Ministry of Health	0	0	100 000	0	0	541 000	0
China CDC	0	0	150 000	10 000	300 000	450 000	0
NIPD*	0	0	0	0	0	924 000	156 000
Total	**9 162 627**	**1 538 838.3**	**1.862 993.0**	0	0	**2 692 020**	**599 207**

Clonorchis trial areas highlighted in green and STH trial areas highlighted in blue.
All figures expressed in RMB (= 0.14 USD);. *National Institute of Parasitic Diseases, China CDC

Figure 1. Map of China with the pilot areas (provinces and counties) marked out