CHAPTER SIX

Engagement of the National Institute of Parasitic Diseases in control of soil-transmitted helminthiasis in China

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Contents

Abstract

Soil-transmitted helminthiases (STHs) have been widely transmitted in China and the control of STHs was initiated by NIPD-CTDR since its foundation. Three national surveys on STHs have been carried out in China, and the infection rate has dropped from 53.58% in the first national survey (1988–92) to 4.49% in the third national survey (2014–16)

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due to strong interventions including mass drug administration, health education and environment improvement. National surveillance of STHs started in 2006 and has been implemented successively until now, which allows to understand the endemic status and trends of STHs prevalence in China. Surveillance has been expanded to 30 provinces of China since 2016. Integrated pilot programmes have been implemented between 2006 and 2009, in which an integrated strategy, with health education and control of infection sources as key components, was adopted. Since 2019, new control pilots have been started, which will be continued for five successive years to further explore appropriate control strategies in the current "new era". With the decline of infection rate of STHs, China is approaching the elimination stage for STHs. In order to achieve this final target, poverty alleviation programmes should be integrated with precise control measures, according to real situations.

1. Introduction

Soil-transmitted helminths (STHs) are nematodes that do not require intermediate hosts for their development. Their eggs or larvae have the capacity to infect the human body directly from the environment (mainly soil). Soil-transmitted helminths include hookworm, *Ascaris lumbricoides* and *Trichuris trichiura* (Jourdan et al., 2018; Tang et al., 2012). Infections due to STHs cause serious harm to human health, especially in children, as it retards their growth and development, leading to malnutrition and developmental disorders (Bethony et al., 2006; Brooker et al., 2008). STHs account for the largest number of infections among neglected tropical diseases (NTDs), with a disease burden of 3.38 million disability-adjusted life years (DALYs), out of which the disease burdens of hookworm, *A. lumbricoides* and *T. trichiura* infections are 1.76 million, 1.08 million and 0.54 million, respectively (GBD 2015 DALYs and HALE Collaborators, 2016). These important parasitic diseases are mainly endemic in the developing regions of Asia, Africa and Latin America (Chammartin et al., 2013; Karagiannis-Voules et al., 2015; Silver et al., 2018). An updated national survey was implemented in China in 2015, which was coordinated by the National Institute of Parasitic Diseases at China CDC and Chinese Center for Tropical Diseases Research (NIPD-CTDR). The results of the survey estimated that about 29.12 million people were infected with STHs in the country, out of which 16.97 million, 8.83 million and 6.60 million people were infected with hookworm, *A. lumbricoides* and *T. trichiura*, respectively (Zhou, 2018).

STHs have been prevalent in China for a long time, but no detailed investigation was carried out until 1950 by the Eastern-China Branch of

the Chinese Academy of Medicine, by then the main institute for parasitic disease control in China and a predecessor of NIPD-CTDR. Thereupon the central government, prioritized hookworm control as of 1956 onwards with the announcement of the "National Program for Agricultural Development from 1956 to 1967 (draft)" in which hookworm was listed as one of the five important parasitic diseases for urgent control efforts. The Hookworm Disease Research Laboratory was established by the Institute of Parasitic Diseases (IPD) at the Chinese Academy of Medical Sciences in the beginning of 1958, but research work on hookworm disease was also carried out by the Pathogen Biology Research Laboratory and the Pharmacology Research Laboratory of the IPD. Between 1983 and 2001, the IPD went through two developmental stages, i.e. the IPD at Chinese Center for Preventive Medicine and the IPD, Chinese Academy of Preventive Medicine. These were the stages before the institutes name was officially changed to the NIPD under the Chinese Center for Disease Control and Prevention in 2002. The name of Chinese Center for Tropical Diseases Research was added in 2017 (hereinafter referred to as "NIPD-CTDR"). The department of soil- and food-borne parasitic diseases was established and entrusted with the responsibility of effective prevention and control of soil-transmitted and food-borne parasitic diseases in cooperation with other departments in NIPD-CTDR (Yu and Zhou, 2013).

This paper summarizes the activities and progress made on STH prevention and control in NIPD-CTDR, so as to provide references to optimize STH control efforts in the future.

2. Epidemiological surveys and national surveillance system

2.1 National survey on soil-transmitted helminthiasis

Three national surveys have been carried out in China, in the 1990s, 2000s and 2010s, respectively, in which STHs were all included.

2.1.1 The national survey on distribution of human parasites

In 1986, the former Ministry of Health issued a "Notice on the National Survey of Human Parasites Distribution". The national survey on distribution of human parasites (hereinafter referred to as "the first national survey") were implemented between 1988 and 1992 under the leadership of the former Ministry of Health (Yu et al., 1994a). Investigations were carried out in 30 provinces, autonomous regions and municipalities

(hereinafter referred to as "provinces") in mainland China and 1,477,742 persons were investigated.

Stratified cluster random sampling was employed in situations with large number of parasite species, large sample sizes, various local conditions that enhance STHs transmission, and areas with no prior survey reports. Three steps random sampling was strictly followed in the sampling process and control measures were designed to reduce sampling errors.

Great achievements were made in the first national survey. The main species, distribution and prevalence of human parasites were ascertained in China. Overall STH infection rate was 53.58% and the estimated number of infected populations was 536 million. The infection rates of *A. lumbricoides*, hookworm and *T. trichiura* were 47.00%, 17.17% and 18.80%, with estimated infected populations of 531 million, 194 million and 212 million, respectively. High endemic areas were mainly distributed in the eastern and southern parts of China (Fig. 1). The survey also revealed

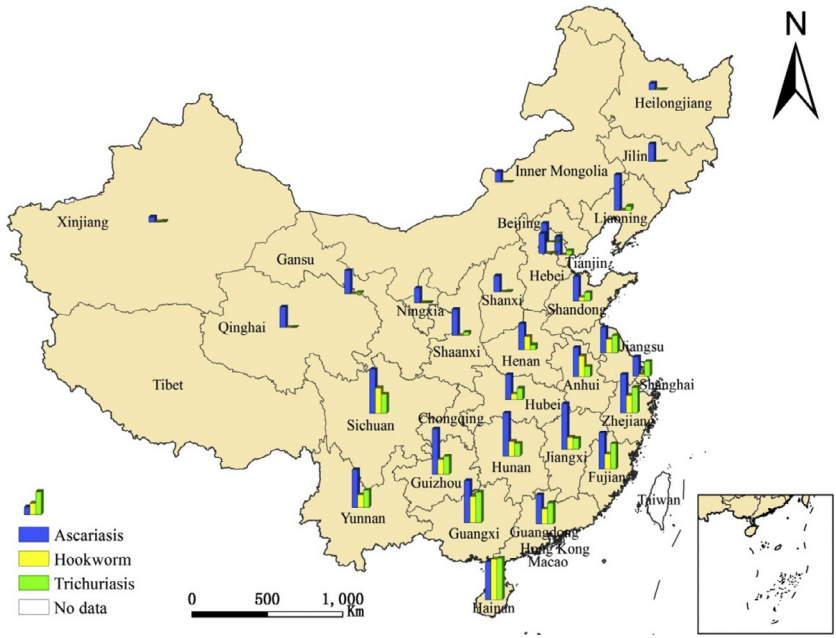

Fig. 1 Distribution of STHs in China according to the first national survey. *Data source: according to data from literature Yu S.H., Xu L.Q., Jiang Z.X., Xu S.H., Han J.J., Zhu Y.G., Chang J., Lin J.X., Xu F.N., 1994a. Report on the first nationwide survey of the distribution of human parasites in China. 1. Regional distribution of parasite species. Chin. J. Parasitol. Parasit. Dis. 12(4), 241–247.*

that mixed infections of the two hookworm species (*Necator americanus* and *Ancylostoma duodenale*) occurred in most regions of China, but with varying proportions across regions. Generally, *A. duodenale* was distributed in the northern region whereas *N. americanus* dominated the southern region (Tang et al., 2012; Xu et al., 2000). It was also discovered during the national survey that STHs infections varied in different climatic and geographical zones in China. The tropical region showed the highest infection rate, followed by subtropical zones, warm temperate zones, special temperature zones, intermediate temperate zones and cold temperate zones. Also, infection rates were highest in wet areas, followed by semi-humid areas, while the infection rate in semi-arid and arid areas was low. Finally, the STH prevalence trend in China was revealed with the implementation of the national survey. The first national survey created a significant pathway that led to effective prevention and control in China, which was reflected in the following aspects.

The results obtained from the survey, provided evidence-based references to the development of the "Strategic Target of Preventive Health Care in China (2000)", the "National Eighth Five-Years Programme (1995–2000)", the "National Ninth Five-Years Programme (2001–10)", and the "National Tenth Five-Years Programme (2011–15)" on parasitic diseases control and the National Control Programme on Key Parasitic Diseases (2016–2020). The range of control work was successively expanded and infection rates of STHs decreased from 1995 to 2016. During this period the tasks for parasitic diseases control were always listed in the national control programme by the National Health Commission of China.

Control strategies and recommendations were put forward based on the findings from the first national survey, which helped to develop the "Implementation Plan on Control of Common Helminthiasis" by the former Ministry of Health, and promote the national parasitic disease control programmes. Through the national parasitic diseases control programme initiated in 1992, a total of 120 million people received anthelmintic treatment in 1994, 80% of the patients had a reduction in intensity of infection, and more than 14 million people were cured.

Children were considered as the key targets in the national parasitic diseases control programme, according to the results from the first national survey. The number of infections with *A. lumbricoides*, hookworm and *T. trichiura* was 190 million, 70 million and 40 million, respectively, among 310 million children under 14 years old in China. In view of this situation, a document entitled "National Control Program for Student's Helminth

Infection" was jointly issued by the former Ministry of Health and the former National Education Commission, and collective deworming in the students from elementary and middle school was conducted nationwide since 1992. STHs infection rates in school-age children have decreased significantly following 10 years of effective deworming programme.

The parasitic control institutions in the country became more established with high-quality professionals. Before the first national survey, the specialized institutions for parasitic diseases control in the southern regions were tending to reduce staff, or even to abolish few of these institutions, which prompted professionals to consider changing career paths following the control of schistosomiasis, malaria, or filariasis. The timely implementation of this survey prompted local governments to retain or strengthen capacities in specialized institutions for parasitic disease control in each province in southern China. In addition, capacities of staff were enhanced by putting them through adequate training while pilot surveys were implemented. A total of 7404 professional technicians across the country were enrolled for 504 training courses to improve their knowledge on STH epidemiology and control. This strategy provided a platform to train considerable number of professionals, and many senior and middle-level professionals have updated their knowledge and mastered new technologies through training, which prompted parasitic control accordingly.

Also, in-depth development of scientific research was promoted through the execution of the survey, which provided insights to raise many research questions and led to many proposed research projects. Pharmaceutical companies and other health service providers that envisioned huge market opportunities from the survey invested heavily in developing new drugs and diagnostic tools for the prevention and treatment of parasitic diseases both domestic and abroad.

Finally, effective implementation of the survey and the national parasitic diseases control programmes have further enhanced China's reputation globally. This has also increased both domestic and international cooperation and exchanges, which prompted knowledge sharing and transferring. The article of the "National survey of human parasitic diseases in China" was published as a special report in the Southeast Asian Journal of Tropical Medicine and Public Health (Yu et al., 1994b), and was appraised highly by this journal in term of the huge sampling size and quality of the survey. The journal opined that it might be difficult to achieve similar objective elsewhere around the world. The wealth of information contained in the report have been crucial in making informed decisions and

this with other notable achievements have enhanced Chinas reputation in the global health community.

In addition, the first national survey received the "First Prize of the Major Medical Science and Technology Award by Ministry of Health in 1994" and the "Second Prize of the National Science and Technology Progress Award in 1995". Also, the book entitled "Color Atlas of Human Parasitology" (Yu and Xu, 1992) was compiled and published by experts using samples obtained from the survey, and has become an important reference book for staff in disease control and teaching agencies. A large amount of data was obtained from the survey and an important review titled "Distribution and pathogenic impact of human parasites in China" (Xu et al., 2000) was published. This book was one of the most cited books in parasitology for 10 years after its publication. Moreover, a special edition of Chinese Journal of Parasitic Diseases was published based on survey of many provinces (special edition on Survey of Human Parasites, 1991).

The first national survey initiated a new era in China's STH control and research. In 2010, WHO's first Global Report on Neglected Tropical Diseases (NTDs) classified 17 types of diseases as NTDs, including 14 soil-borne, food-borne or arbo-parasitic disease (WHO, 2010). The results of the first national survey led China to prioritize "NTDs" 15 years before WHO.

2.1.2 Survey on the status of human key parasitic diseases in China

The national survey on the status of human key parasitic diseases in China (hereinafter referred to as "the second national survey") was implemented between 2001 and 2004, covering 31 provinces across China (Hong Kong, Macao and Taiwan not included) (Xu et al., 2005). NIPD-CTDR was responsible for organizing the survey and also summarizing the survey report for the second national survey, in which a total of 356,629 people were investigated.

Findings from the second national survey indicated that STHs infection rate was 19.56% and the estimated population infected was 129 million. The infection rate of hookworm, *A. lumbricoides* and *T. trichiura* was 6.12%, 12.72% and 4.63%, while the estimated population infected was 39.3 million, 85.93 million and 29.09 million, respectively (Wang, 2008). Highly endemic areas were mainly distributed in the south and southeast part of China (Fig. 2).

This survey was of great significance because STHs prevalence and distribution characteristics were updated. The survey showed that parasite

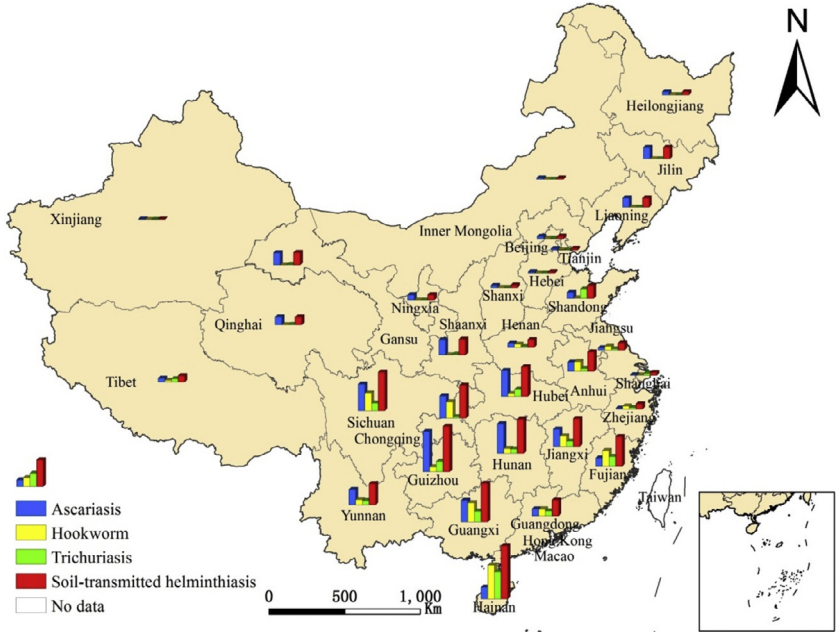

Fig. 2 Distribution of STHs in China according to the second national survey. *Data source: according to data from literature Xu, L.Q., Chen, Y.D., Sun, F.H., Cai, L., Fang, Y.Y., Wang, L.P., Liu, X., Li, L.S., Feng, Y., Li, H., 2005. A national survey on current status of the important parasitic diseases in human population. Chin. J. Parasitol. Parasit. Dis. 23, 332–340.*

infections were most severe in the western part of China, with high infection rates among women and children. Compared with the first national survey, the infection rate of hookworm, *A. lumbricoides* and *T. trichiura* has decreased significantly, and the number of infected persons also declined appreciably. The second survey also helped stakeholders to evaluate the effectiveness of STHs prevention and control in the past 10 years. Compared with the first national survey, the infection rate, number of infected persons and the number of STHs multi-species infections have all decreased significantly, indicating the success of 10 years' massive deworming in elementary and middle school in rural areas, together with the integrated control measure of health education, improved access to potable water sources and sanitary facilities. Lastly, the severity of STHs was objectively evaluated during the second survey. Findings indicated the proportion of hookworm and *A. lumbricoides* infection in fatality among hospitalized patients with parasitic diseases was 0.17% and 0.60%, respectively. Misdiagnosis of STHs remained very high, which caused high burden.

This survey provided the basis to optimize the strategies and develop effective prevention and control measures. To further promote the control on STHs in China, the establishment of a national surveillance network for STHs started. In 2006, a total of 22 national surveillance spots were established by the former Ministry of Health. Meanwhile, provincial surveillance spots were set up by many provinces, thus leading to the establishment of STHs surveillance network in China. STHs control strategies were proposed based on the prevalence of each endemic area. These included, (i) implementation of collective deworming for areas with infection rate >20% in prevalence, to reduce infection rate and intensity; (ii) adoption of counter-measures such as deworming of key populations to reduce infection rate in areas with 5–20% in prevalence; (iii) selective deworming for areas with <5% in prevalence. The National Control Plan for Major Parasitic Diseases (2006–15) was initiated by the former Ministry of Health during the 12th Five-Year Plan following the second survey. Fourthly, the infection rate of *A. lumbricoides* was first included in the evaluation index system for national hygiene in city (town) by the National Patriotic Health Campaign Committee in 2005. In addition, STHs epidemic status and control implementation were included in the National Health Statistics Survey System for the first time. Comprehensive STHs demonstration plots were established. In 2006, the "Working Plan for parasitic diseases comprehensive demonstration plots" was established by the former Ministry of Health, and eight STHs comprehensive demonstration plots were set up in highly endemic areas. Finally, this survey paved the way for the development and use of technology in control, thereby, making up for shortage of technical staff for parasitic disease control.

2.1.3 National survey on current status of major human parasitic diseases

The former National Commission for Health and Family Planning organized the third National Survey on Current Status of Major Human Parasitic Diseases (hereinafter referred to as the "the third national survey") between 2014 and 2016. The survey covered 31 provinces in mainland of China (Hongkong, Macao and Taiwan not included), and 484,210 people from rural areas were investigated.

Findings from the third national survey indicated that STHs infection rate was 4.49%, with an estimated population of 29.12 million under infection. The prevalence of hookworm was 2.62%, *A. lumbricoides* 1.36% and *T. trichiura* 1.02%. Correspondingly, the population under infection was 16.97 million, 8.82 million and 6.60 million, respectively

(Karagiannis-Voules et al., 2015). Highly endemic areas were still distributed in the south and southwest part of China (Fig. 3).

The endemic status of STHs in the new era was revealed by the third national survey. Results showed that STHs infection rates in rural areas have dropped to 4.49%, yet areas with high endemicity still existed. Low endemic or sporadic status was shown in most areas and endemic areas were evidently shrunk. Yet, STHs infection rate in some provinces or regions were still high, even up to 20%. Also, dominant species in STHs were altered due to control effort as indicated in the results obtained. The order of dominant species in this survey were hookworm, *A. lumbricoides* and *T. trichiura*, with infection rates of 2.62%, 1.36% and 1.02%, respectively. The order of dominance was *A. lumbricoides* (47.00%), *T. trichiura* (18.80%) and hookworm (17.17%), while the order in second survey was *A. lumbricoides* (12.57%), hookworm (6.08%) and *T. trichiura* (4.56%). Moreover, the regional distribution has been illustrated. Meso-endemic areas with infection rate >5% and hyper-endemic areas >20% were mainly

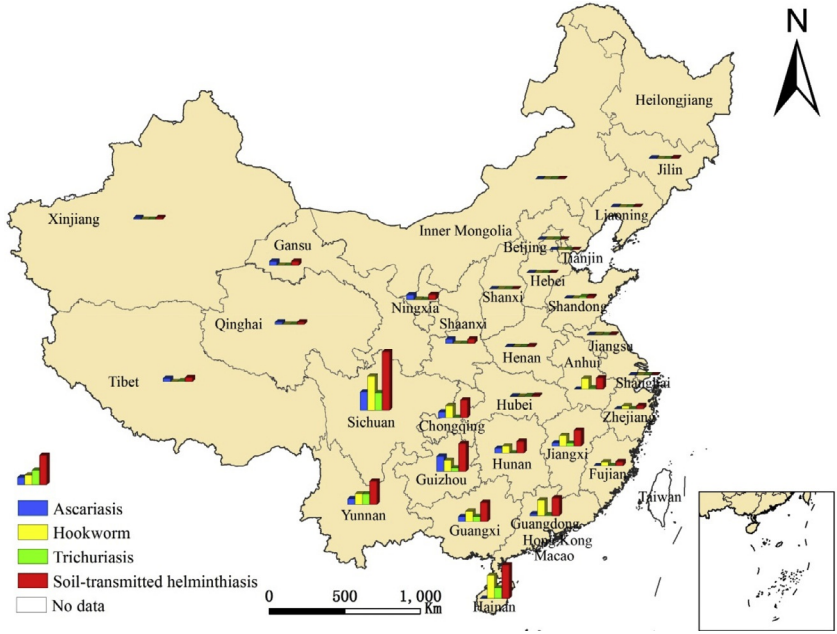

Fig. 3 Distribution of STHs in China according to the third national survey. *Data source: according to data from literature Zhou X.N., 2018. Report on the National Survey of Important Human Parasitic Diseases in China (2015). People's Medical Publishing House, Beijing.*

distributed in the southern and southwestern parts of China including Sichuan, Hainan, Guizhou, Yunnan, Chongqing, Guangxi, Guangdong and Jiangxi. The third national survey also revealed that the population infected with STHs was still huge. Hence, the disease burden could not be neglected.

Suggestions for the next STHs control stages were proposed following execution of the third national survey. It was opined that prevention and control efforts should be maintained, while the control plan for major parasitic diseases should be further implemented. Also, multi-sectoral co-operation was to be strengthened and comprehensive measures to be implemented. Furthermore, prevention and control key points should be emphasized, and precise control measures be adequately implemented. Lastly, there was a need to improve the comprehensive surveillance system and also pursue regular execution of the national survey to adequately inform decisions for control plan and implementation.

The third national survey played an important role in promoting STHs prevention and control in the new era. This survey did not only provide detailed information for the "National Control Program for Major Parasitic Diseases (2006–15)" evaluation, but also helped to lay a solid foundation for the implementation of the "National Control Program for Echinococcosis and other Important Parasitic Diseases (2016–2020)"; This also enhanced the effectiveness of the national surveillance system in the country. The STH national surveillance system was greatly expanded from 22 surveillance spots in 22 provinces to more than 200 surveillance spots in 30 provinces after the survey (Chen and Zang, 2013). Lastly, new national STHs control pilots were established based on this survey, and 12 STHs pilots have been being conducted in 9 provinces since 2019.

2.2 Establishment and improvement of the national surveillance system on soil-transmitted helminthiasis

STHs surveillance was included in the national surveillance system for key infectious diseases and vectors by China CDC in 2006, while the national surveillance programme for STHs was issued by the former Ministry of Health (Chinese Center for Disease Control and Prevention, 2006). This led to the establishment of 22 national surveillance spots of STHs, which monitors STHs endemic status and environmental transmission factors. The drafting of the national surveillance programme for STHs, staff training, annual checks, data analysis and surveillance report were all undertaken by NIPD-CTDR. In addition, an "Operation Manual for STHs

National Surveillance Program" was also provided to ensure surveillance quality (Chinese Center for Disease Control and Prevention, 2011).

In total, 1000 people were investigated at each surveillance spot, and more than 20,000 people were investigated nationally every year. The results showed that STHs infection rates from 2006 to 2010 were 20.88%, 18.93%, 16.59%, 13.30% and 11.25% respectively, which indicated a year-by-year declining pattern. The surveillance programme was revised in 2011 following the surveillance situation and the operation manual was modified accordingly (Chinese Center for Disease Control and Prevention, 2014). STHs infection rates at the national surveillance spots from 2011 to 2015 were 9.67%, 6.90%, 3.12%, 4.49%, and 4.95% respectively (Chen and Zang, 2013; Chinese Center for Disease Control and Prevention, 2015; Zhu et al., 2019), indicating continuing decline in the endemic trends. Establishment of provincial surveillance spots were promoted by the 22 national surveillance spots, and 158 provincial surveillance spots were set up by the end of 2015 (Zhu et al., 2019). People's awareness on parasitic disease control was improved through the implementation of the surveillance work.

STHs surveillance was included in the "Central Transfer Payment for control of Malaria and Other important Parasitic Disease" in 2016 by the former National Health and Family Planning Commission. All the provinces in mainland of China were required to conduct STHs surveillance, and in each P/A/M, the number of surveillance spots (counties) implemented each year should be more than 10% of all counties. STHs surveillance spots were more than 200 annually from 2016 to 2018 (Zhu et al., 2019), and the surveillance range has been continuously expanded. Surveillance results obtained between 2016 and 2018 showed that STHs infection rates were 2.46% 1.78%, 1.29% respectively, and this is the lowest point ever achieved in the history of STHs control efforts in China (Chinese Center for Disease Control and Prevention, 2016, 2018; Zhu et al., 2019).

Since 2017, data from national surveillance has been reported through the "Information Management System for Parasitic Diseases". This system is of great significance for the management of surveillance data, and it has been successively improved through usage, with faster report speed and more restrict logistic limitation. In addition, the annual surveillance together with the national competition on parasitic disease control had provided opportunities for professionals at provincial, city and county levels. Training and selection were carried out every year, and a proportion of grass-roots professionals were trained, thus improving their skills, thereby, becoming backbones of grass-root disease control agencies.

3. Control pilots and new strategy development

After the first national survey, the large-scale population-based deworming was implemented in China according to the high endemic status of STHs in China revealed, and the infection rate of STHs was significantly decreased. After the second national survey, the comprehensive control strategy of "health education as leadership, control of infection source as priority" explored by demonstration plots were carried out (Fig. 4).

In 2006, the "Work Program for Comprehensive demonstration plots of Parasite Diseases" was initiated by the former Ministry of Health to speed up control implementation in highly endemic areas, and eight comprehensive demonstration plots for STHs were established (Disease control agency of the Ministry of Health, China CDC, 2010) (Figs. 5 and 6). This control initiative was implemented for three successive years and completed in 2009. All tasks regarding control implementation including baseline investigation, selection of deworming drugs, drawing deworming plan, quality control, mid-term and final evaluation, data collection and data analysis were undertaken by NIPD-CTDR.

The control strategies of "health education as leadership, control of infection source as priority" and the control measures of "improving water,

Fig. 4 Control strategies of STHs in different stages of China.

Fig. 5 Sample examination in comprehensive demonstrating zones of STHs.

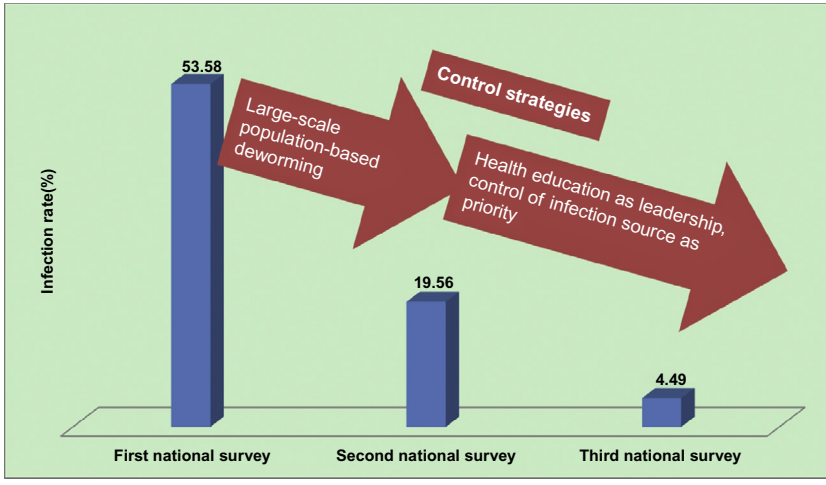

Fig. 6 Drug dispensing in comprehensive demonstrating zones of STHs.

lavatory and hygiene in conjunction with behavioural changes and drug administration" were implemented in the demonstration plots. Under the above guidelines, health education activities of various forms and contents were carried out in all comprehensive demonstrating plots. Mass media of radio, television, newspapers and internet were utilized, and seminars, training, school lectures, door-to-door propaganda, and posters in public places

were also used for public education, the harm, transmission routes, and prevention measures of STHs were all publicized. Professionals at all levels were also trained in the way of cascade training. Also, drug administration was implemented according to the prevalence level in comprehensive demonstrating plots from 2006 to 2008. In towns with prevalence more than 50%, mass drug administration was implemented twice in 2006, and once in 2007 and 2008 respectively; In towns with prevalence between 20% and 50%, the masses were guided to deworm voluntarily once a year in 2006–08; In towns with prevalence between 10% and 20%, high risk population were guided to deworm voluntarily once a year in 2006–08, other people were encouraged to have voluntary examination and treatment; In towns with prevalence less than 10%, all people were encouraged to have voluntary examination and treatment. Moreover, the water, lavatory and hygiene of environment were improved in the comprehensive demonstrating plots under the leadership of government.

In 2010, the final evaluation of the 3 years control implementation on demonstration plots was assessed by NIPD-CTDR. From 2006 to 2009, deworming drug was administrated to 6.43 million person-times, and health education was given to 4.23 million person-times while the control initiative lasted. STHs infection rates in demonstration plots, Class I, II, and III were 55.85%, 31.16%, and 19.14% and was reduced by 75.63%, 79.52% and 87.08%, respectively. The outcome of control efforts exceeded the original targets. Meanwhile, living conditions of people and sanitary facilities in demonstration plots were significantly improved. Also, water and toilet reforms have been strengthened, with enhanced public's awareness to imbibe strong personal hygiene culture and improved knowledge on STHs parasites transmission routes to curtail transmission (Zhang et al., 2011).

Driven by the achievements made with the demonstration plots control initiative, a total of 99,761,380 person-times of health education were conducted nationwide, 97,658,472 person-times of STHs deworming were carried out and 390,506 person-times of professionals were trained at all levels. Decline in STHs infection rates in 23 provinces reached the target of the National Control Program for Key Parasitic Disease (2006–15) target, that is, provinces with infection rates $\geq$20%, 20% > infection rate $\geq$ 5%, and <5% according to the second national survey decreased by more than 80%, 70% and 60%, respectively (Chen et al., 2019).

The successful experience of the comprehensive demonstration plots has explained the control strategies of "health education as leadership, control of

infection source as priority" for effectively controlling STHs in China, and health education was one of the most important measures deployed to achieve this feat. A series of health education activities popular with the masses was carried out by making full use of the available resources in various places to enhance people's awareness on disease prevention and treatment, improve their compliance, thus making control efforts more effective. Experts were organized to develop a promotion plan for the propagation of the demonstrating plots control initiative experiences (Wang, 2011).

Experts from NIPD-CTDR participated in the formulation of the "Technical Plan for the Prevention and Control of STHs" in 2009, adopting "health education as leadership, control of infection source as priority" and the control measures of "improving water, lavatory and hygiene in conjunction with behavioural changes and drug administration" strategies in the demonstration plots. The endemic areas were divided into three categories in terms of STHs parasites infection rates such as hookworm, and drug administration plan was determined accordingly. In areas predominantly endemic with hookworm, knowledge of "footwears when farming and no use of fresh manure as fertilizer" was propagated in health education, and the tribendimidine, independently produced by NIPD-CTDR, was listed in the priority drugs.

The National Program for Prevention and Control of Key Parasitic Diseases (2016–2020) proposed the establishment of 1–2 control pilots in each of the key endemic provinces to achieve the planned targets. With implementation of the Poverty alleviation Project in China, the living conditions of people in poverty-stricken areas were improving, yet the prevalence of STHs in many areas were still high. So it was decided that the control of STHs be combined with the poverty alleviation project. The main purpose of the control pilots was to explore and establish sustainable control mechanisms and efforts in local endemic settings to gradually reduce parasitic diseases infection rates, so as to ensure that the programme goals are achieved, and the achievements on disease control and poverty alleviation were expanded and consolidated. The criteria for the selection of pilot areas include high STHs endemicity, poor or underdeveloped county, need for improvement on access to good water sources and lavatory, and zeal by the local government to achieve parasitic disease control objectives. Based on the result of the third national survey and the poverty alleviation process in each county, 12 counties (cities) from 9 provinces were determined as the new control pilots of STHs by NIPD-CTDR, which were all poverty-stricken areas with high prevalence of STHs.

The control pilots (counties) commenced in 2019 with 5 years completion target, and new areas for control pilots will be selected 5 years later. Following the success achieved with STHs control in demonstration plots between 2006 and 2009 with the experiences gained using combinations of control strategies. Control efforts have been strengthened. Specifically, the following aspects will be implemented in the new control pilots: in-depth health education, effective patient investigation and treatment, comprehensive improvement of water and toilet, strengthening capacity building for disease control, and enhancing information management.

4. Applied research on diagnostics and drugs

4.1 Applied research on diagnosis

4.1.1 Improved Kato-Katz thick smear method

In 2018, experts in NIPD-CTDR formulated the health industry standard (WS/T 570-2017) patent of "Detection of intestinal helminths-The Kato-Katz method for Intestinal Worm Detection", which was issued in 2017 but officially implemented on 1 February 2018. Moreover, "Diagnosis of hookworm disease" (WS 439-2013) was officially implemented on 1 December 2013. Similarly, Diagnosis of enterobiasis (WS 469-2015) and "Diagnosis of ascariasis" (WS/T 565-2017) were formally implemented on 1 September 2015 and 1 February 2018, respectively.

4.1.2 Little tube counting method

Experts from NIPD-CTDR established the little tube counting method other than the commonly used saturated saline flotation method and the modified Kato-Katz staining smear method. This method was compared with the Hong's and Stoll's method using 13 positive stools samples, and results obtained showed that there was no significant difference in the three methods in terms of total number of eggs, but the fluctuation range in the little tube counting method (33.3%$\sim$281.5%) was smaller than the others. Infection intensity was divided into light infection (number of eggs: 0–399), moderate infection (400–2999) and heavy infection (above 3000), according to the Kato-Katz method, while 30 stool samples with light infection, 58 with moderate infection, and 18, with heavy infection were counted by the little tube counting method and Hong's method respectively. The number of eggs detected by the little tube counting method was 143.5% ($P<0.05$) compared with Hong's method, and there was no significant difference between these two methods with the moderate and heavy

infected faecal samples. Therefore, the little tube counting method was not only accurate in counting hookworm eggs, but also easy to carry. The quantity of saturated saline and faecal samples required are much less than those in Hong's method, saving 1/3–1/2 of the examination time (Wang and Chen, 1959).

4.1.3 Isolation of hookworm larvae and autogenous nematodes

Faecal samples collected from manure pit are often mixed with autogenous nematodes (nematodes that live in the pit), which affects the counting accuracy of hookworm larvae. Therefore, it is necessary to devise a method to kill the autogenous nematodes without affecting hatching and development of hookworm larvae. Through multiple experiments, it was found that the double-layer cotton paper is best for separating hookworm larvae, with a formaldehyde concentration of 0.7%, and the effects were best if the samples were prepared in 6% salt water or treated in 6% formaldehyde solution for 30 min before cultivation (Yu and Zhou, 2013).

4.1.4 New methods for isolation of hookworm larvae

Isolate hookworm larvae from the soil are important to understand the source of hookworm infection and, also assess the effectiveness of hookworm disease control. In the past, the method of separating hookworm larvae was difficult to apply because of the complicated operations and heavy equipment needed. To solve this problem, experts from NIPD-CTDR developed a new method. The operation steps are as follows; soil samples were place on a cotton paper in a separating device, and the separating device was loaded in a container, then salt water with temperature 42–48 °C and 4.8–5.2% concentration were added to the soil without passing the surface of the cotton paper, then, the load container was placed in an incubator and kept in 42–48 °C for 1.5–2 h. Thereafter, the separating device was taken out, and the liquid in the container was decanted. Natural sedimentation was obtained by decanting the supernatant after 15–20 min. This new method was commonly used in the national surveillance of STHs (Chinese Center for Disease Control and Prevention, 2011; Yu and Zhou, 2013).

4.1.5 Quantitative method for hookworm larvae culture with glass tube and filter

The glass tube filter paper method is often required in parasites investigation and drug efficacy assessment to culture hookworm larvae for identification

and counting. Repeated tests had shown that the detection rate of glass tube filter paper method developed by NIPD-CTDR is higher than that of Hong's method. The glass tube filter paper method can determine the degree of infection and identify the parasites species with convenient operation and high accuracy (Hookworm Research Laboratory, Shanghai Institute of Parasitic Diseases, 1977). It was widely used in national epidemiological investigation and drug efficacy evaluation for a long time.

4.2 Research on drugs application

Between the 1960s and mid-1970s, pyrantel, levamisole, albendazole and mebendazole were developed abroad successively. These drugs were then synthesized in China and, after pharmacological and toxicological tests, used in clinical treatment of intestinal helminth infections (Xiao, 2009a; Xiao et al., 1990, 2002; Zhang et al., 2019). Other than that, in the mid-1980s, researchers in NIPD-CTDR independently synthesized the new drug tribendimidine and conducted a series of acute and subacute toxicity tests (Xiao et al., 2004, 2005). It was found that in treating *Nippostrongylus brasiliensis*, *Ancylostoma caninum* and *Necator americanus*, smaller dose and shorter courses of treatment were needed for tribendimidine when compared with mebendazole and pyrantel pamoate (Xiao et al., 2004). Also, through pharmacokinetics, tribendimidine was shown to have stable chemical properties, a wide deworming spectrum, a fast deworming effect, a low dose required and low toxicity for the effective dose, as advantages. It was therefore recommended for clinical use (Xiao et al., 2005, 2013). In 2004, the new drug certificates and production licences for tribendimidine was issued by State Food and Drug Administration (SFDA) (Zhang et al., 2019), and then clinical trials were conducted by the NIPD-CTDR (Xiao et al., 2007, 2013; Zhang et al., 2008, 2019). From 2005 to 2007, a clinical experiment was carried out on 1292 cases infected with intestinal nematodes in Hainan, Sichuan and Guizhou, and the effectiveness and safety of tribendimidine on hookworm disease and ascariasis were evaluated. The result showed that under the used dosage for expanding treatment in larger sample of patients with various ages and infected with *A. duodenale*, *A. lumbricoides* and other helminths, tribendimidine enteric coated tablet is safe with satisfactory efficacy (Zhang et al., 2008). Also, from 2006 to 2007, an open and multi-centre clinical trial was conducted in the provinces of Hainan, Sichuan and Guizhou to evaluate the efficacy and safety of tribendimidine in treatment of children with hookworm and

A. lumbricoides infections. A total of 899 children aged 4–14 years were enrolled in the study. The results showed that tribendimidine gave at a single dose of 200 mg exhibits lower adverse effect rate and potential efficacy in the treatment of children with hookworm and *A. lumbricoides* infections (Xiao et al., 2007).

5. Future perspectives

STH prevention and control in China has evolved over nearly 70 years and the control strategy has developed from large-scale population-based deworming to comprehensive control strategy explored by demonstration plots (Fig. 4). Through the implementation of effective control efforts STHs infection rate in China has dropped from 53.58% in the first national survey to 4.49% in the third national survey. Also, we achieved the lowest STHs infection rate in the country's history, and infected population has been greatly reduced, meanwhile, majority of the population are implicated with mild infections. Hence, STHs control has achieved a remarkable feat.

STHs epidemic also shows new features in the new period. Firstly, its epidemic is characterized by regionalization. Results obtained from national surveillances and surveys indicated that >5% infection rate are mainly distributed in the southern and southwestern parts of China. Climate condition in these areas is warm and humid, and most of the areas are underdeveloped. Vegetable farms are still common in rural areas, making them suitable for STHs (such as hookworm) transmission. Secondly, the distribution characteristics of population are significant. Data showed that STHs infection rates (hookworm, *A. lumbricoides* and *T. trichiura*) were all higher in female than that of male, and was highest in age group 60 years and above than in any other age groups. These age group are mainly engaged in agricultural production in rural areas, and their hygiene and habits while on their farms could hardly be changed through simple health education. Thirdly, the dominant STH species have changed. Currently, hookworm infection rate are higher than that of *A. lumbricoides* and *T. trichiura*, making it dominant STH species in China. There is need to prioritize targeting the elderly who are actively involved in agricultural practices in rural areas for STHs prevention and control activities.

Despite the achievements made with control efforts in China, STHs transmission risk remains. The national surveillance on STHs in 2018 showed that 11 of 24 provinces conducted soil pollution surveillance and

detected hookworm larval contamination, with 2.48% average detection rate by households. Detection rate in the most polluted provinces was 25.49%. Similarly, contamination of soil with *A. lumbricoides* eggs was detected in 16 out of 24 provinces, with detection rate of 5.23%, and the detection rate of the most polluted provinces was 26.00% (Chinese Center for Disease Control and Prevention, 2018). This suggest that the use of fresh manure as fertilizer still exists in rural areas, and there are some shortcomings with the management of harmless toilets. This, therefore, indicate that STHs transmission risk still exists.

In view of the recent STH endemicity characteristics in China, strategies developed for effective disease prevention and control are as follows.

In the new era, the "National Control Program on Key Parasitic Diseases" target will be achieved by combining control efforts with the health poverty alleviation project. Findings from the third national survey indicated that STHs (hookworm, *A. lumbricoides* and *T. trichiura*) infection rates decreased with improved economic situation and standard of living because the infection rate positively correlated with the poverty level. Among the 436 counties (cities/districts) surveyed, 145 were poverty-stricken counties, and infection rates were higher than counties with good standard of living (Zhou, 2018). Therefore, STHs control efforts should be carried out by the local government authorities in conjunction with the National Health Poverty alleviation Project.

It is therefore necessary for stakeholders to improve the national surveillance mechanisms to further enhance its efficiency and quality. There is also, need to strengthen the capacities of professionals at all levels including provincial, city, and county levels to improve their performances in disease diagnosis, data analysis and reporting by engaging in workshop programmes, training exchanges and competitions. Also, in-depth application of the data management system for national surveillance should be promoted by completing the archives, making it a large platform for parasitic disease surveillance, and data sharing, thus, providing data support for formulation and implementation of control strategies.

Lastly, it is imperative to target accurate control plan and precise implementation of control strategies due to STH transmission dynamics and distribution characteristics in different areas across the country. Women, adolescents, children, middle-aged and elderly people involved in agricultural practices in rural areas should be prioritized for effective monitoring and encouraged to adhere to information passed onto them using health education materials and other control platforms. Control strategies of

"health education as leadership, control of infection source as priority" and the control measures of "improving water, lavatory and hygiene in conjunction with behavioural changes and drug administration" should be implemented in hyper- and meso-endemic areas to improve people's awareness on imbibing good personal hygiene culture. While health education should be implemented areas with in low endemicity and the pursuit of improved compliance to STHs examination and treatment should be enhanced. People in endemic areas should be adequately enlightened to cooperate with the government to actively promote the construction of harmless toilets and standardize their use in rural areas targeted for control.

6. Conclusions

STHs control in China has achieved remarkable accomplishments (Table 1), and this giant stride has not gone unnoticed globally (Qian et al., 2013, 2019; Song et al., 2018; Wang et al., 2016). Owing to establishment of the "National Control Plan of Key Parasitic Disease (2016–2020)" and the initiation of the "Criteria for transmission control and interruption of soil-transmitted nematodiasis" in 2018 (National Health Commission of the People's Republic of China, 2018), efforts will be geared towards eliminating STHs in the country. To achieve the elimination goals, experiences should be summed up and shared, new strategies should be implemented accordingly, control implementation should be standardized and poverty alleviation programme should be integrated in order to lay a solid foundation for effective control and elimination of STHs in China.

Table 1 Main achievements made by the NIPD-CTDR.

Type of achievements	Name	Main accomplisher/ author	Achievements
National surveys	The national survey on distribution of human parasites	Yu Senhai, Xu Longqi, Jiang Zexiao, Xu Shuhui[a], Han Jiajun[a], Zhu Yuguang[a], Chang Jiang[a], Lin Jinxiang[a], Xu Funiu[a]	First Prize of the Major Medical Science and Technology Award by Ministry of Health in 1994 Second Prize of the National Science and Technology Progress Award in 1995

Table 1 Main achievements made by the NIPD-CTDR.—cont'd

Type of achievements	Name	Main accomplisher/ author	Achievements
	Survey on the status of human key parasitic diseases in China	Wang Longde[a], Qi Xiaoqiu[a], Wang Yu[a], Hao Yang[a], Yang Weizhong[a], Tang Linhua, Xu Longqi, Feng Zheng	Survey report by People's medical publishing house in 2008
	National survey on current status of major human parasitic diseases	Zhou Xiaonong, Li Shizhu, Li Zhongjie[a], Chen Yingdan, et al.	Survey report by People's medical publishing house in 2018
Control strategies	Control strategies and application effectiveness of soil- and food-borne parasitic diseases	Chen Yingdan, Li Huazhong[a], Xu Longqi, Yang Weizhong[a], Tian Hongchun[a], et al.	Third Prize of Science and Technology by Chinese Preventive Medicine Association in 2013
Publications	Colour atlas of human parasitology	Yu Senhai, Xu Longqi	Published by China Science and Technology Press in 1992
	Distribution and pathogenic impact of human parasites in China	Yu Senhai, Xu Longqi, Xu Shuhui	Published by People's medical publishing house in 2000
	Series books of human parasitic disease for grass-roots staff: soil-borne parasitic diseases	Zhou Xiaonong	Published by People's medical publishing house in 2011
	Illustrated parasitology and parasitoses (two volumes)	Xu Longqi	Published by China Science and Technology Press in 2016

Continued

Table 1 Main achievements made by the NIPD-CTDR.—cont'd

Type of achievements	Name	Main accomplisher/ author	Achievements
Health industrial standards	Diagnosis of ascariasis	Chen Yingdan, Zhou Changhai, Xu Longqi, Tian Hongchun[a], Yao Linong[a], Yang Yichao[a], Cai Li[a], Zhou Xiaonong, Zheng Bin, Zang Wei, Zhu Huihui	Chinese health industry standards, issued in 1 February 2018 (WS/T 565—2017)
	Detection of intestinal helminths-the Kato-Katz method	Chen Yingdan, Zhu Tingjun, Zhou Changhai, Xu Jing, Zheng Bin, Li Shizhu, Xiao Ning, Zhou Xiaonong, Zeng Xiaojun[a], Liu Hongkun[a]	Chinese health industry standards, issued in 1 February 2018 (WS/T 570—2017)
	Criteria for transmission control and interruption of soil-transmitted nematodiasis	Chen Yingdan, Zhou Xiaonong, Zhou Changhai, Li Shizhu, Zhu Tingjun, Xu Yili[a], Xu Longqi, Zheng Bin, Cai Li[a], Li Huazhong[a], Sun Fenghua[a]	Chinese health industry standard, issued in 1 April 2018 (WS/T 629—2018)
Patents	Enteric-coated tablet of tribendimidine for deworming	Yao Runhua, Gao Hongfei, Ren Hainan, Qiang Huiqin, Chen Yaoqing, Hu Ling, Sun Yi[a], Zhang Jun[a]	Invention Patent in 2002 (96116469.7) National certificate of class I new drug in 2004
	Special quantitative board of Kato-Katz thick smear method	Xu Longqi, Chen Yingdan, Zhou Changhai	Certificate of Utility Model Patent in 2011 (ZL 2011 20025026.3)

Table 1 Main achievements made by the NIPD-CTDR.—cont'd

Type of achievements	Name	Main accomplisher/ author	Achievements
	Device for separating hookworm larva from soil	Wang Jujun, Zhou Changhai, Wang Guofei, Chen Yingdan	Certificate of Utility Model Patent in 2013 (ZL 2013 20092966.3)
	Anal swab for detection of *Enterobius vermicularis*	Chen Yingdan, Zhou Changhai, Wang Jujun, Zhu Tingjun, Zang Wei, Zhu Huihui	Certificate of Utility Model Patent in 2015 (ZL 2014 20707045.8)
	Immuno-chromatographic test strip for rapid detection of hookworm disease and its preparation	Wang Junyun, Shi Feng, Yang Yuetao, Gao Chunhua, Yang Yi, Zhu Huihui, Chen Yingdan	Invention Patent in 2015 (ZL 2015 10405625.0)

[a]Accomplishers not from the NIPD-CTDR.

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Competing interests

The authors declare that they do not have competing interests.

Authors' contributions

H.-H.Z., M.-B.Q., Y.-D.C., S.-Z.L., and X.-N.Z. conceived the study; H.-H.Z., M.-B.Q., and Y.-D.C. wrote and revised the manuscript; H.-H.Z., C.-H.Z., M.-Z.Z., J.-L.H., T.-J.Z., M.-B.Q., Y.-D.C., S.-Z.L., and X.-N.Z. revised the manuscript and gave approval of the version to be published. All the authors read and approved the final version of the manuscript.

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