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Control of soil-transmitted helminthiasis in Yunnan province, People's Republic of China: Experiences and lessons from a 5-year multi-intervention trial

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ABSTRACT

The current global strategy for the control of soil-transmitted helminthiasis emphasises periodic administration of anthelminthic drugs to at-risk populations. However, this approach fails to address the root social and ecological causes of soil-transmitted helminthiasis. For sustainable control, it has been suggested that improvements in water, sanitation and hygiene behaviour are required. We designed a 5-year multi-intervention trial in Menghai county, Yunnan province, People's Republic of China. Three different interventions were implemented, each covering a village inhabited by 200–350 people. The interventions consisted of (i) initial health education at study inception and systematic treatment of all individuals aged ≥2 years once every year with a single dose of albendazole; (ii) initial health education and bi-annual albendazole administration; and (iii) bi-annual treatment coupled with latrine construction at family level and regular health education. Interventions were rigorously implemented for 3 years, whilst the follow-up, which included annual albendazole distribution, lasted for 2 more years. Before the third round of treatment, the prevalence of *Ascaris lumbricoides* was reduced by only 2.8% in the annual treatment arm, whilst bi-annual deworming combined with latrine construction and health education resulted in a prevalence reduction of 53.3% ($p < 0.001$). All three control approaches significantly reduced the prevalence of *Trichuris trichiura* and hookworm, with the highest reductions achieved when chemotherapy was combined with sanitation and health education. The prevalence of *T. trichiura* remained at 30% and above regardless of the intervention. Only bi-annual treatment combined with latrine construction and health education significantly impacted on the prevalence of *Taenia* spp., but none of the interventions significantly reduced the prevalence of *Strongyloides stercoralis*. Our findings support the notion that in high-endemicity areas, sustainable control of soil-transmitted helminth infections necessitates measures to reduce faecal environmental contamination to complement mass drug administration. However, elimination of soil-transmitted helminthiasis will not be achieved in the short run even with a package of interventions, and probably requires improvements in living conditions, changes in hygiene behaviour and more efficacious anthelminthic drugs and treatment regimens.

1. Introduction

Mass drug administration (MDA), more recently phrased "preventive chemotherapy" by the World Health Organization (WHO), refers to the periodic administration of anthelminthic drugs to populations at risk of morbidity and is the cornerstone of the current global strategy to control soil-transmitted helminthiasis and other neglected tropical diseases (WHO, 2006, 2010).

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Soil-transmitted helminthiasis is caused by chronic infection with the nematode worms *Ascaris lumbricoides*, hookworm (*Ancylostoma duodenale* and *Necator americanus*) and *Trichuris trichiura* (Bethony et al., 2006; Hotez et al., 2008; Knopp et al., 2012). Morbidity is associated with the intensity of infection (commonly expressed as eggs per 1 g of stool (EPG)), the duration of infection and the degree of multiparasitism (Ezeamama et al., 2005; Hall et al., 2008; Steinmann et al., 2010). Hence, the primary goal of MDA is a reduction of the infection intensity with the aim of eliminating moderate and especially heavy infections among school-aged children, women of childbearing age and other vulnerable groups (WHO, 2006). However, the high reproductive capacity of soil-transmitted helminths means that in the absence of additional interventions to break the transmission cycle, transmission usually is not interrupted even if the infection intensity is greatly reduced (Jia et al., 2012).

Promising interventions to interrupt transmission include the provision and use of adequate sanitation to end open defecation, improved personal and food hygiene behaviour and access to clean water (Albonico et al., 2006). Recent systematic reviews and meta-analyses have shown the pivotal importance of water, sanitation and hygiene (WASH) interventions for sustainable control of soil-transmitted helminthiasis (Strunz et al., 2014; Ziegelbauer et al., 2012). However, few studies have endeavoured to demonstrate the feasibility and community-effectiveness of different interventions for the control of soil-transmitted helminthiasis, and longitudinal data spanning several years are scarce.

The People's Republic of China (P.R. China) has made huge investments towards expanding safe water supply and sanitation. In 2012, for example, 98% of the population in urban areas had access to both an improved water source and sanitation according to official data, while in rural areas, the respective coverage rates were 85% and 70% (WHO/UNICEF Joint Monitoring Programme, 2014). Although open defecation has officially been ceased throughout the country (WHO/UNICEF Joint Monitoring Programme, 2014), this unhygienic behaviour persists in remote rural and marginalised communities, including those where the current study has been implemented (Steinmann et al., 2008a). In P.R. China, the great progress made in WASH indicators over the past two decades—in 1990, 33% of the total population had no access to safe water and 69% used unimproved sanitation facilities–have certainly contributed to the impressive reductions in the prevalence of soil-transmitted helminths that have been documented through nation-wide surveys. Indeed, the first national survey undertaken between 1988 and 1992 found prevalences of 47%, 19% and 17% for *A. lumbricoides*, *T. trichiura* and hookworm (Yu et al., 1994), while the second national survey, completed in 2004, found respective prevalences of 13%, 5% and 6% (Ministry of Health, 2005). These declines are confirmed by a recent systematic review of soil-transmitted helminth surveys across P.R. China and geostatistical meta-analysis (Lai et al., 2013). Undoubtedly, MDA-based control programmes contributed to the reduction of soil-transmitted helminthiasis, although there is still no national control programme pertaining to soil-transmitted helminthiasis in P.R. China (Montresor et al., 2008).

High levels of soil-transmitted helminth infections and rapid reinfection patterns resulting in pervasive intestinal multiparasitism have been documented in villages in the south-west of Yunnan province that are inhabited by the Bulang ethnic minority (Steinmann et al., 2008a; Yap et al., 2012a, 2013). Our previous research in this area has prompted local interest in designing, rigorously implementing and evaluating different anthelminthic treatment regimens and intervention packages for the control of soil-transmitted helminthiasis that might guide regional control interventions. Three intervention packages were tested based on epidemiological considerations and existing national guidelines for soil-transmitted helminthiasis control, with each intervention implemented in one community. The objective of this 5-year prospective community-based intervention study was to establish the feasibility and long-term community-effectiveness of different soil-transmitted helminthiasis control strategies in high endemicity settings.

2. Materials and methods

2.1. Ethics statement

The study was an integral part of a post-doctoral project for which ethical clearance was granted by the academic board of the National Institute of Parasitic Diseases, Chinese Center for Disease Control and Prevention (IPD, China CDC; Shanghai, P.R. China). The study was approved by village leaders and doctors of each study village. Written or oral informed consent to join the study was obtained during the baseline cross-sectional survey and again prior to the first drug administration, as appropriate: adults signed an informed consent declaration, while parents or legal guardians signed on behalf of minors who had assented orally.

2.2. Rationale and interventions

The design of the different interventions targeting soil-transmitted helminthiasis was guided by the following considerations and hypotheses: (i) the current standard approach to control soil-transmitted helminthiasis in P.R. China is annual MDA to the entire population in heavily endemic communities; (ii) regular MDA reduces the prevalence and intensity of soil-transmitted helminth infections, but fails to suppress rapid re-infection; (iii) reductions in the prevalence and intensity of infection correlate with the frequency of MDA; (iv) the provision of locally acceptable latrines reduces open defecation, translating into a direct impact on the transmission of soil-transmitted helminthiasis; and (v) the frequency of drug administration can be lowered once incidence rates have decreased considerably.

The following three intervention packages were developed and rigorously implemented during the first 3 years of the study (phase 1): (A) initial health education at study inception and annual administration of a single 400 mg oral dose of albendazole to all individuals aged 2 years and above; (B) initial health education at study inception and bi-annual administration of albendazole; and (C) construction of an improved latrine for each interested family, regular health education and bi-annual administration of albendazole. In a second phase, lasting for 2 more years, annual MDA replaced the more intensive control efforts specified above and was implemented in all three communities.

2.3. Study area and design

The study was implemented in three villages (Nanwen upper, Nanwen lower and Mangguo new) in the mountainous part of Menghai county, Yunnan province, in the south-western part of P.R. China. The three study villages are situated within a few kilometres of each other on the slope of a mountain and share important geographic and infrastructure characteristics, are inhabited exclusively by the Bulang ethnic minority group and the socioeconomic conditions are comparable. Nanwen upper village (geographical coordinates 21°46′02.15″N latitude, 100°23′50.61″E longitude; elevation about 1650 m above sea level; intervention (A)) is a community of about 80 households with approximately 320 residents. Nanwen lower village (21°46′34.02″N, 100°23′56.89″E; elevation about 1500 m; intervention (B)) consists of about 60 households with 240 residents. Mangguo new village (21°45′09.01″N,

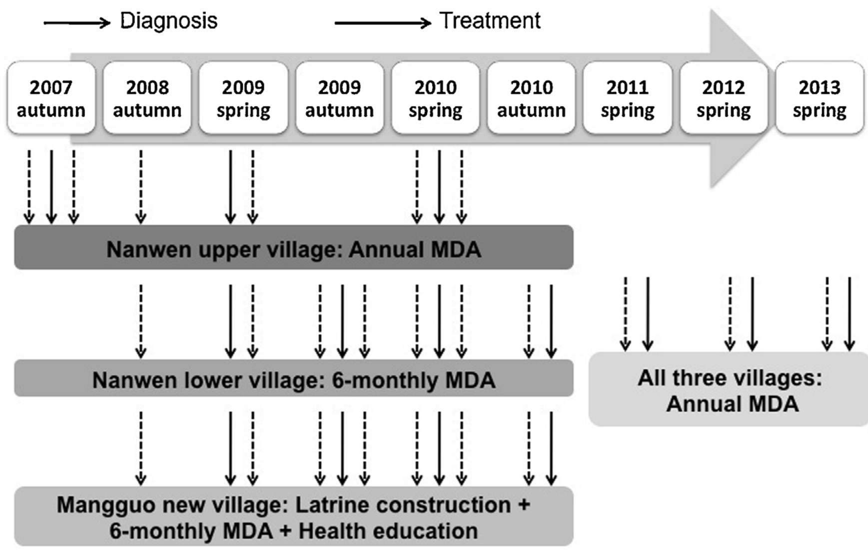

Fig. 1. Type of intervention implemented in the three study villages in Menghai county, Yunnan province, P.R. China at different time points throughout the study period.

100°18′47.20″E; elevation about 1300 m; intervention (C)) is inhabited by approximately 200 residents in 30 households. At the onset of our study, all households in the three intervention villages had access to running water and most were connected to the power grid, but no latrines were available, except a community latrine at the local primary schools. Farming is the only source of income in all three villages, with tea and sugar cane as main crops. Animal husbandry is limited to pigs and chicken.

In Nanwen upper village, activities were launched in spring 2007, within the frame of another study (Steinmann et al., 2008b). In the two remaining villages, baseline data were collected in autumn 2008 and interventions commenced in spring 2009. From 2007 to 2010, all interventions were implemented by the study team with the help of local village doctors and leaders, allowing direct supervision of drug administration and proper ingestion. This approach permitted rigorous evaluation of the effect of the different control strategies on the prevalence and intensity of soil-transmitted helminth infections over time. Starting in 2011 and until study completion in 2013 (Fig. 1), single-dose albendazole was offered annually to all inhabitants aged 2 years and above of the three villages. The latrines in Mangguo new village of course remained available. The study team no longer played an active role in the administration of treatments, which was organised by village doctors instead, nor did the study team provide health education messages or engage in active promotion of latrine use. This follow-up period thus allowed determination of the long-term community-effectiveness of MDA (Nanwen upper and lower villages) and MDA coupled with improved sanitation (Mangguo new village).

2.4. Anthelminthic drugs, health education and latrine construction

Single-dose albendazole (Sino-American Tianjin SmithKline and French Laboratories Ltd.) at a standard dose of 400 mg was offered to all inhabitants of the study villages aged 2 years and above together with bottled water to facilitate swallowing of the drug. According to local treatment guidelines, pregnant women (status verbally assessed) and individuals with acute or chronic diseases were not treated. An appropriate number of treatments was provided to a family representative (usually an adult female) or the village doctor to treat family members who were absent at the time of drug distribution.

Health education activities implemented in all three villages (in Nanwen upper and lower only at study inception and in Mangguo new village upon each evaluation of the intervention effectiveness) included putting up posters with pictorial and written explanations of parasite life cycles and basic hygiene advice in conspicuous locations and on latrine walls, explaining the posters in the local language, and showing ethanol-preserved helminth specimens to interested individuals. In Mangguo new village educational movies produced by the National Institute for Parasitic Diseases in Shanghai were screened at the local primary school upon completion of the latrines.

The latrines were constructed by a local company according to relevant government guidelines. The floor space of the latrines was approximately 1.5 × 1.5 m and walls were 2 m high, with openings below the corrugated iron roof for illumination and ventilation. The latrines had brick walls and a cement floor with a ceramic floor-level toilet bowl. A large two-partition cement chamber to store faecal matter was located behind the latrine, covered by a thick cement slab and connected to the bowl via a wide tube. A bucket and scoop for flushing the toilet were also provided.

2.5. Parasitological procedures

In each of the three study villages, about 100 stool samples were collected from randomly selected individuals of all ages at baseline and again before each round of MDA. During the first phase of the study, stool samples were also collected 3 weeks after MDA, from another random sample of 100 individuals (Fig. 1). Stool samples were transferred to a nearby laboratory and processed on the day of collection according to standard parasitological procedures.

First, samples were visually inspected for *Taenia* spp. proglottids and *A. lumbricoides* adult worms. Second, duplicate (except for baseline and evaluation of first treatment in Nanwen upper village, where a single slide was prepared) 41.7 mg Kato–Katz thick smears were prepared from each sample (Katz et al., 1972). Within 45 min, the slides were examined under a microscope by experienced laboratory technicians. Helminth eggs were counted and recorded for each helminth species separately. A longer clearing time was allowed in case of cold weather, carefully considering that hookworm eggs were not overcleared (Martin and Beaver, 1968). During the first phase, the Baermann technique and the Koga agar plate test were also conducted to detect *Strongyloides stercoralis*

Table 1
Baseline and follow-up prevalence in 2010 and 2013 of soil-transmitted helminths and *Taenia* spp. in three study villages in Menghai county, Yunnan province, P.R. China that were subjected to different control interventions, along with absolute and relative prevalence reductions (95% confidence interval).

Species		Nanwen upper village	Nanwen lower village	Mangguo new village	χ^2	*p*-Value
A. lumbricoides	Baseline	70.4 (63.5–76.6)	72.6 (62.8–80.9)	71.0 (61.2–79.0)	0.12	0.940
	Prevalence in 2010[*]	67.6 (57.8–76.4)	36.2 (26.5–46.7)	17.7 (11.2–26.0)	57.33	<0.001
	Reduction	2.8 (−9.4–15.0)	36.4 (23.4–49.4)[***]	53.3 (42.2–64.4)[***]		
	Relative reduction	4.0	50.1	75.0		
	Prevalence in 2013	51.0 (40.6–61.4)	77.4 (67.0–85.8)	44.9 (35.2–54.8)		<0.001
	Reduction	19.4 (5.8–33.0)[**]	−4.8 (−17.2–7.6)	26.1 (13.3–38.9)[***]		
T. trichiura	Baseline	87.0 (81.4–91.3)	71.6 (61.8–80.1)	63.6 (53.5–72.3)	16.55	<0.001
	Prevalence in 2010[*]	62.9 (52.9–72.1)	57.5 (46.8–67.6)	37.2 (28.3–46.8)	16.03	<0.001
	Reduction	24.1 (13.0–35.2)[***]	14.1 (0.8–27.4)[*]	26.4 (13.7–39.1)[***]		
	Relative reduction	27.7	19.7	41.5		
	Prevalence in 2013	45.8 (35.6–56.3)	51.2 (40.0–62.3)	25.2 (17.3–34.6)		<0.001
	Reduction	41.2 (29.1–53.3)[***]	20.4 (6.6–34.2)[**]	38.4 (26.1–50.7)[***]		
Hookworm	Baseline	56.5 (49.1–63.3)	67.7 (57.7–76.6)	86.0 (78.3–92.1)	23.11	<0.001
	Prevalence in 2010[*]	3.8 (1.0–9.5)	10.6 (5.2–18.7)	23.9 (16.4–32.8)		<0.001[a]
	Reduction	52.7 (42.9–62.5)[***]	57.1 (46.1–68.1)[***]	62.1 (51.9–72.3)[***]		
	Relative reduction	93.3	84.3	72.7		
	Prevalence in 2013	1.0 (0.0–5.7)	6.0 (2.0–13.3)	10.3 (5.2–17.7)		0.013[a]
	Reduction	55.5 (45.3–65.7)[***]	61.7 (51.3–72.1)[***]	75.7 (66.9–84.5)[***]		
S. stercoralis	Baseline	13.0 (8.7–18.6)	7.8 (3.4–14.9)	3.7 (1.0–9.1)		0.044[a]
	Prevalence in 2010[*]	8.7 (4.0–15.6)	3.2 (0.7–9.0)	3.5 (1.0–8.8)		0.184[a]
	Reduction	4.3 (−3.9–12.5)	4.6 (−1.7–10.9)	0.2 (−4.7–5.1)		
	Relative reduction	33.1	59.0	5.4		
	Prevalence in 2013	5.2 (1.7–11.7)	7.1 (2.7–14.9)	0.0 (N.A)		0.010[a]
	Reduction	7.8 (−0.3–15.9)	0.7 (−6.9–8.3)	3.7 (0.1–7.3)[**]		
Taenia spp.	Baseline	14.8 (10.0–20.3)	13.7 (7.7–22.0)	29.0 (21.0–38.8)	10.03	0.007
	Prevalence in 2010[*]	6.7 (2.7–13.3)	10.6 (5.2–18.7)	11.5 (6.3–18.9)	1.63	0.443
	Reduction	8.1 (0.0–16.2)	3.1 (−6.0–12.2)	17.5 (7.1–27.9)[*]		
	Relative reduction	54.7	22.6	60.3		
	Prevalence in 2013	1.0 (0.0–5.7)	7.1 (2.7–14.9)	3.7 (1.0–9.3)		0.106[a]
	Reduction	13.8 (6.4–21.2)[***]	6.6 (−2.0–15.2)	25.3 (16.0–34.6)[***]		

[*] Before last treatment of the year.
[**] $p < 0.05$ and $p \geq 0.001$.
[***] $p < 0.001$.
[a] Fisher's exact test.

and hookworm (the latter only on Koga agar plates) larvae (Koga et al., 1991; Yap et al., 2012b).

2.6. Statistical analysis

The prevalence of the various soil-transmitted helminth species and *Taenia* spp. was determined based on all available results from the different diagnostic tests, in order to maximise diagnostic sensitivity (Knopp et al., 2008; Steinmann et al., 2008a). Differences between villages were explored using the Pearson's χ^2 test or Fisher's exact test, as appropriate. Changes in helminth prevalence over time were attributed to interventions, and were evaluated using a 2-sided 2-sample test of proportions. The arithmetic mean number of EPG was calculated, and EPG values stratified into light, moderate and heavy infection intensity classes according to the cut-offs recommended by WHO.

3. Results

The intended sample size of about 100 individuals per village and stool sample collection campaign was met throughout the study. Over the course of the study, stool samples from 3121 individuals were collected and subjected to parasitological diagnosis.

3.1. Baseline prevalence and intensity of helminth infections

The baseline prevalence of *A. lumbricoides* was comparable in all three study villages (range: 70.4–72.6%, $p = 0.940$), but differed significantly between the villages for the other helminth species (Table 1). In brief, the hookworm prevalence ranged between 56.5% (Nanwen upper village) and 86.0% (Mangguo new village). With regard to *T. trichiura*, the highest prevalence was observed in Nanwen upper village (87.0%), while the lowest prevalence was noted in Mangguo new village (63.6%). Considerably lower prevalences were recorded for *Taenia* spp. (ranging between 13.7% in Nanwen lower village and 29.0% in Mangguo new village) and *S. stercoralis* (ranging between 3.7% in Mangguo new village and 13.0% in Nanwen upper village).

With the exception of *A. lumbricoides* in Nanwen upper village, where most infections were of moderate intensity (5000–49,999 EPG), the microscopic examination of the initial set of Kato–Katz thick smears revealed mainly light-intensity infections for *A. lumbricoides*, hookworm and *T. trichiura* in the three study villages. Heavy infection intensities were rarely encountered (Table 2).

3.2. Effect of control interventions (2007/2008–2010)

The three intervention packages all showed an immediate effect on the observed prevalence and intensity of *A. lumbricoides*, hookworm and *T. trichiura*. However, reinfection occurred rapidly. A clear trend towards a stronger effect in response to more intensive control efforts was observed in the case of *A. lumbricoides* (Table 1). While the prevalence of this species was reduced by only 2.8% between 2008 and 2010 in the village subjected to annual deworming (non-significant difference), bi-annual treatment coupled with continued health education and latrine construction cut the prevalence by more than half (−53.3%, $p < 0.001$). In the absence of concurrent latrine provision, deworming every 6 months resulted in a lower, but still highly significant prevalence reduction (−36.4%, $p < 0.001$). The relative prevalence reduction within the first 2 years of interventions was between 4.0% and 75.0% in the three study villages.

The three control schemes all resulted in significant reductions of the *T. trichiura* prevalence; the highest absolute (26.4%) and

Table 2
Median infection intensity (median eggs per 1 g of faeces (EPG) among the infected) of common soil-transmitted helminths at baseline, in 2010 and in 2013 in three study villages in Menghai county, Yunnan province, P.R. China that were subjected to different control interventions.

Species		Nanwen upper village	Nanwen lower village	Mangguo new village
A. lumbricoides	Baseline median EPG	6018	4338	2988
	2010 median EPG*	3084	5676	978
	2013 median EPG	8652	8256	768
T. trichiura	Baseline median EPG	252	144	84
	2010 median EPG*	66	108	36
	2013 median EPG	60	96	48
Hookworm	Baseline median EPG	192	96	312
	2010 median EPG*	0	48	78
	2013 median EPG	264	108	48

* Before last treatment of the year.

relative (41.5%) prevalence reductions were recorded following bi-annual treatment complemented by health education and latrine construction. The absolute reduction in hookworm prevalence also increased as a function of the intensity of intervention (52.7–62.1%, all $p < 0.001$). However, in relative terms, the opposite trend was observed; in Nanwen upper village, where annual chemotherapy was dispensed, the relative hookworm prevalence was reduced by 93.3%, while in Mangguo new village that was subjected to the most intensive control efforts, the relative prevalence reduction was considerably lower (72.7%).

While the three interventions showed an effect on the prevalence of *S. stercoralis*, none of the recorded reductions were of statistical significance. Only bi-annual chemotherapy combined with health education and latrine construction resulted in a significant reduction of the prevalence of *Taenia* spp. infection; the absolute prevalence was reduced from 29.0% to 11.5% ($p < 0.05$) in Mangguo new village, while smaller, statistically non-significant reductions were observed in the other two villages.

In Nanwen upper village, most of the *A. lumbricoides* infections were of moderate intensity before the second treatment. One year later, after study participants had received two rounds of treatment, the proportion of moderate-intensity infections had declined to about one third, but a small number of heavy infections remained. In Nanwen lower village, the proportion of moderate-intensity *A. lumbricoides* infections declined from 40% (baseline) to 20% (1-year follow-up) and 30% (2-year follow-up). In Mangguo new village that was subjected to the most intense control efforts, 35% of the *A. lumbricoides* infections were of moderate intensity at study inception, while the respective proportion of moderate-intensity infections had declined to 15% and 5% at the 1-year and the 2-year follow-up surveys, respectively.

While a few moderate-intensity *T. trichiura* infections were observed in both Nanwen upper and Nanwen lower villages before the third round of treatment, moderate-intensity *T. trichiura* infections had disappeared in Mangguo new village already at the 1-year follow-up. After the first round of treatment, moderate- and heavy-intensity hookworm infections were only found in Nanwen lower village. Thereafter, remaining hookworm infection intensities were all classified as light.

3.2.1. Long-term effect of interventions under programmatic conditions (2007/2008–2013)

While the incidence of *A. lumbricoides* remained quite high in the three study villages, the extent differed as a function of the intensity and mix of interventions (Fig. 2 and Table 2). Indeed, after three rounds of interventions, the prevalence of *A. lumbricoides* in Mangguo new village was reduced to a very low level (from 17.7% before to 1.6% after MDA) and incidence rates between MDA cycles were insufficient to counter the impact of treatment. Bi-annual treatment also had a clear, yet less pronounced effect against *A. lumbricoides*. However, a relaxation of intervention efforts after year 3 immediately translated into a rise in the *A. lumbricoides* prevalence in the three intervention villages. At study completion in 2013, Mangguo new village still had the lowest prevalence of *A. lumbricoides* (44.8%), but the prevalence and intensity in the other two villages had bounced back to or even exceeded pre-intervention levels. The highest prevalence at study completion was found in Nanwen lower village (77.4%).

The prevalence and intensity of *T. trichiura* slowly declined in response to the interventions, initially in all three villages but then reached a plateau at around 40–60% in Nanwen lower village, while in Nanwen upper village and Mangguo new village, the slow decline persisted even beyond the relaxation of intervention efforts (Fig. 3 and Table 2). In the village where MDA was accompanied by latrine construction, the decline was more pronounced and quicker than in the other two villages where deworming once or twice a year was the primary intervention. The integrated control approach also appeared to almost completely prevent new infections with *T. trichiura*. In the remaining two villages, there were clear signs of on-going transmission.

All interventions had a pronounced and lasting effect on the prevalence of hookworm infection (Fig. 4). In Nanwen upper village, only few new cases were seen after the first round of treatment and then the prevalence continuously declined. In the two remaining villages, new cases were noted after each round of treatment, but the prevalence of hookworm remained much lower than at study initiation even after transition to more programmatic control conditions after 3 years. At the end of our study in 2013, the highest prevalence of hookworm was noted in Mangguo new village (11%). Of note, the median infection intensity in Mangguo new village was the highest among the three study villages at study inception but declined the most and was the lowest at study completion (Table 2).

The effect of an integrated control approach (i.e. bi-annual MDA coupled with regular health education and latrine construction) *versus* annual deworming with only some initial health education on the local transmission of intestinal helminths is evident from a direct comparison between Mangguo new village and Nanwen lower village. The integrated control package resulted in greater prevalence reductions compared to annual deworming alone. Of note, in the presence of latrines, the rebound in the *A. lumbricoides* prevalence was less pronounced compared to the situation where no latrines were available, and *S. stercoralis* appeared to completely disappear from Mangguo new village (Fig. 5). With regard to infection intensity, within the first 3 years of interventions, the integrated control approach had an obvious impact on the three common soil-transmitted helminth species. Of note, MDA alone was only effective in reducing the intensity of hookworm infections, while the intensity of *A. lumbricoides* infection was barely affected and that of *T. trichiura* was only slightly lower than at baseline (Fig. 6). At the end of the second phase in 2013, the infection intensities generally followed the trends in prevalence;

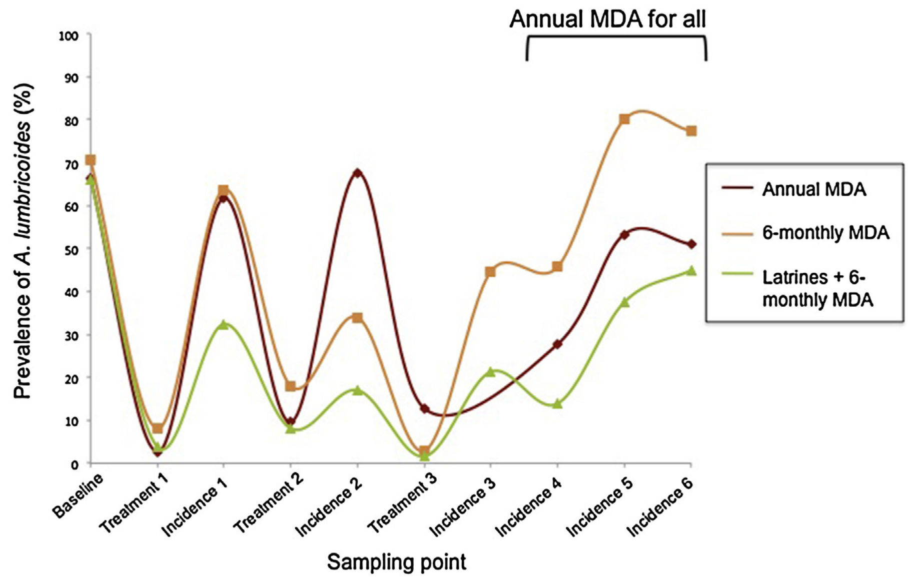

Fig. 2. Prevalence of *A. lumbricoides* in three study villages in Menghai county, Yunnan province, P.R. China that were subjected to different control interventions at various sampling points.

the intensity of *A. lumbricoides* infections even decreased further in the village where latrines were concurrently implemented. The intensity of *T. trichiura* infection remained stable, while that of hookworm varied considerably without any clear trend.

4. Discussion

Based on biological considerations and social-ecological contexts, coupled with practical experience and mathematical modelling, it has long been argued that sustainable control of soil-transmitted helminthiasis and other helminthiases requires integrated approaches, including the provision of clean water, adequate sanitation and appropriate hygiene behaviour in addition to MDA targeting specific at-risk groups or entire population at high coverage levels (Strunz et al., 2014; Truscott et al., 2014; Utzinger et al., 2009, 2011). However, data on the long-term effects of different strategies for the control of soil-transmitted helminthiasis are scarce, and only very few longitudinal studies with different intervention mixes tested in parallel in comparable settings have been published.

The present study offers new evidence for the incremental benefits of more frequent MDA (i.e. biannually rather than annual deworming), as well as the concurrent provision of sanitation and continuous health education in a high-endemicity setting of P.R. China. We found that the provision of sanitation coupled with regular health education and bi-annual administration of anthelminthic drugs resulted in higher *A. lumbricoides* prevalence and infection intensity reductions than 6-monthly chemotherapy alone. Annual MDA only showed a limited effect. Similar trends were observed with regard to *T. trichiura*, but changes were slower and less pronounced. After 5 years of interventions; the community prevalence was still around 30–60% in the study villages with no further declines in one of the villages in the second phase of the study. This finding might be explained by the considerably lower efficacy of single-dose albendazole against *T. trichiura* compared to *A. lumbricoides* and hookworm (Keiser and Utzinger, 2008).

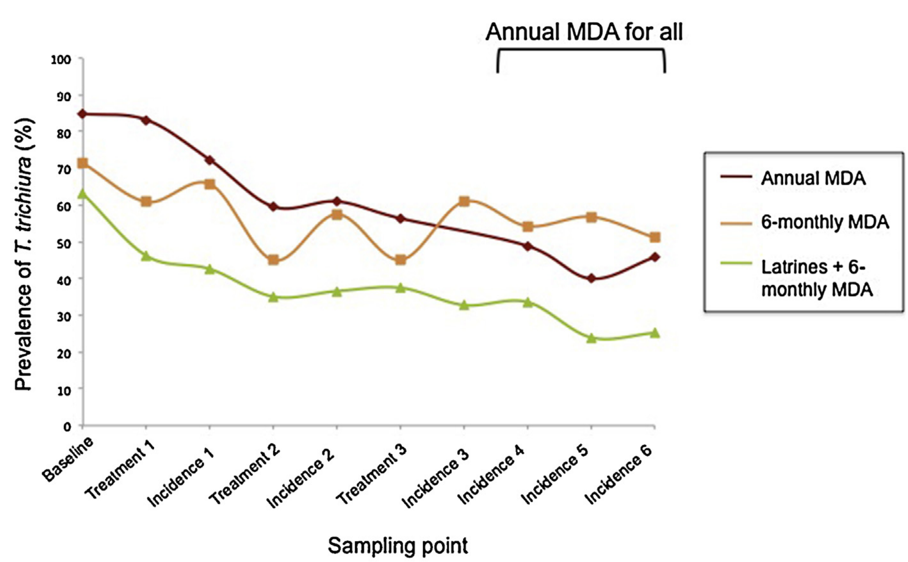

Fig. 3. Prevalence of *T. trichiura* in three study villages in Menghai county, Yunnan province, P.R. China that were subjected to different control interventions at various sampling points.

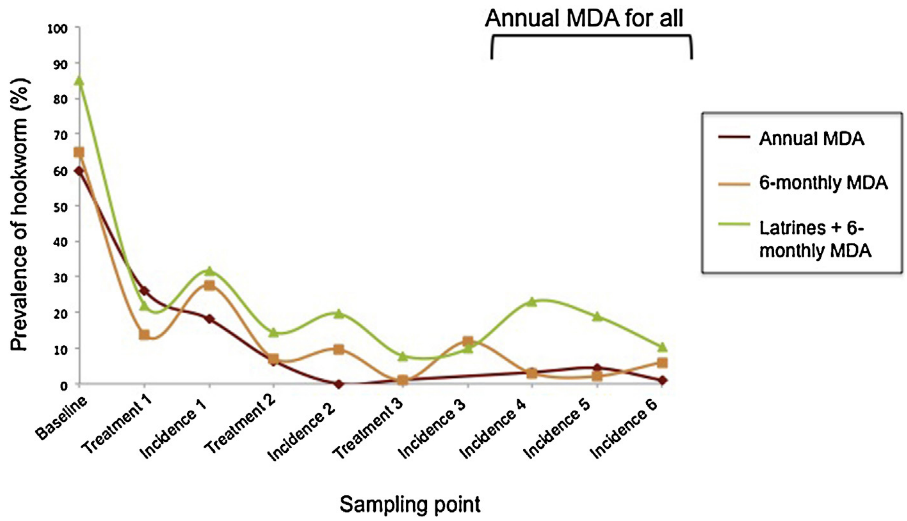

Fig. 4. Prevalence of hookworm in three study villages in Menghai county, Yunnan province, P.R. China that were subjected to different control interventions at various sampling points.

Arguably, a more efficacious drug regimen would be needed in order to accelerate the control of trichuriasis, such as repeated dosing of albendazole or mebendazole, combination therapy (e.g. mebendazole combined with ivermectin) or administration of oxantel pamoate, ideally combined with albendazole (Knopp et al., 2010; Speich et al., 2014; Steinmann et al., 2011). Interestingly, a similar level of residual *T. trichiura* infection after many years of intensive single-dose MDA was found in recent studies conducted on the islands of Zanzibar (Knopp et al., 2009; Speich et al., 2014). Hookworm incidence appeared to be low and even the least intensive intervention package had a pronounced effect on the prevalence of this intestinal parasite, suggesting that in our study area, each of the tested interventions would likely succeed in eliminating hookworm if it were implemented over several more years. Our finding of markedly slower reinfection patterns of hookworm compared to *A. lumbricoides* and *T. trichiura* is in line with a recent systematic review and meta-analysis (Jia et al., 2012). Of note, the lowest hookworm baseline prevalence and the steepest decline in community prevalence was observed in Nanwen upper village, where initial health education and annual MDA was implemented. From an ecological point of view, this village is the highest with regard to altitude (1650 m above sea level). The impact of the interventions was more limited in the lowest-lying Mangguo new village (1300 m above sea level) despite the concurrent installation of sanitation facilities and regular health education. However, a much more marked decline in the median infection intensity among the infected was noted in this village compared to the other villages. Marginal effects of improved sanitation on hookworm prevalence have been documented before. It must also be considered that the health education stressed basic hygiene behaviour, particularly hand-washing, but did not focus on barefoot walking. Information, education and communication (IEC) pertaining to the control of soil-transmitted helminthiasis in P.R. China should benefit from a novel approach that has been developed as the study was ongoing and is currently undergoing extensive field testing in the study area: a cartoon-based educational video, phrased “The

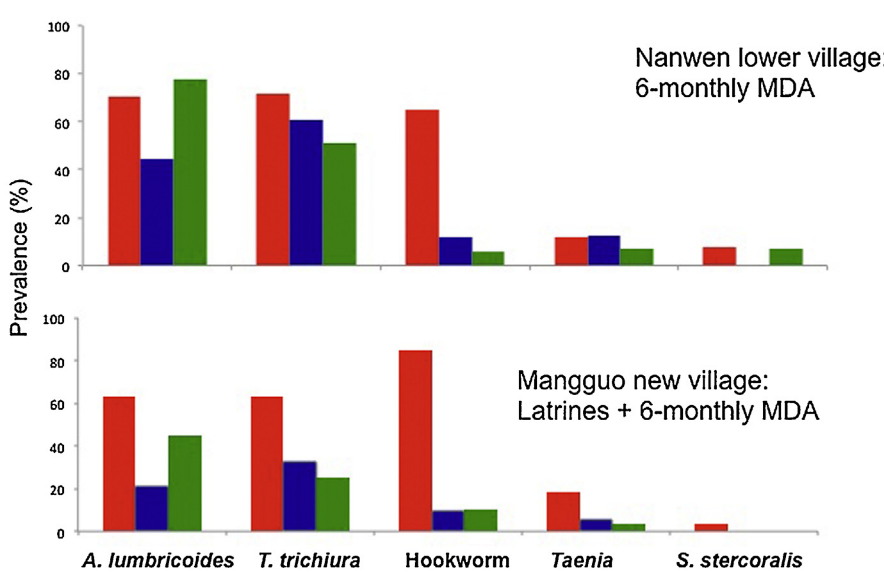

Fig. 5. Prevalence of intestinal helminths in two study villages in Menghai county, Yunnan province, P.R. China that were subjected to different control interventions at baseline (red bars), 2010 autumn (blue bars) and 2013 spring (green bars) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.).

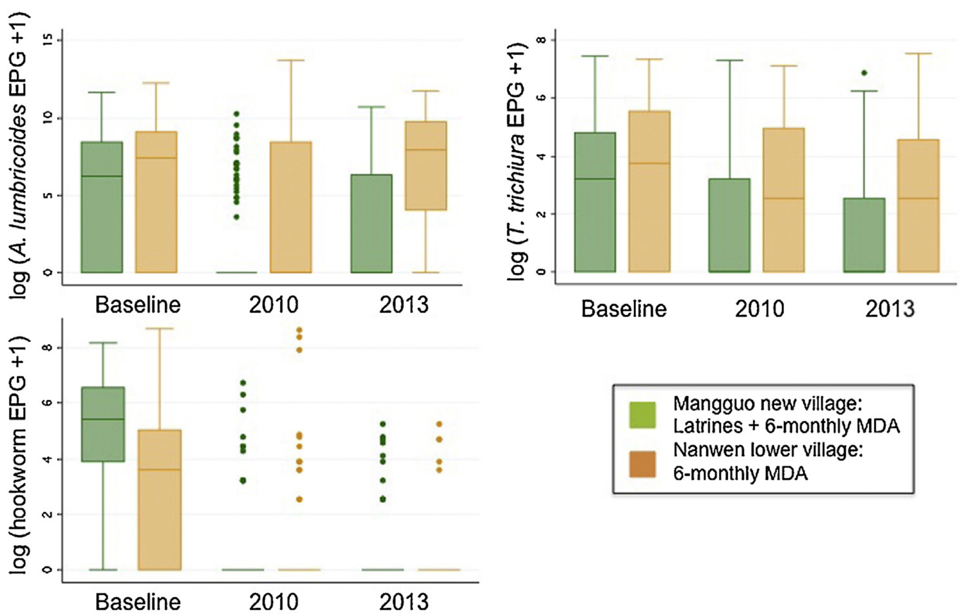

Fig. 6. Infection intensity of soil-transmitted helminths in two study villages in Menghai county, Yunnan province, P.R. China that were subjected to different control interventions at baseline, 2010 autumn and 2013 spring.

Magic Glasses" (Bieri et al., 2013). Promising results, particularly in terms of reduced *A. lumbricoides* incidence, had been achieved when a first version of the video was tested in Hunan province.

The results of our study must be interpreted with caution for a number of reasons. First, the sample size was small as each intervention was implemented in only one village, and while these showed similar demographic, ecological and socioeconomic characteristics, subtle differences resulted in slightly different soil-transmitted helminth prevalences at baseline and likely influenced incidence and reinfection patterns. Second, treatment compliance could not be systematically determined as posttreatment surveys of treatment compliance proofed unreliable. Third, the combination of interventions into packages and their application to single villages makes it impossible to determine the efficacy of individual interventions (e.g. latrine construction alone). Finally, the longitudinal follow-up of a defined cohort instead of a random sample at each sampling point might have provided more accurate information on the dynamics of infection, interventions and re-infection patterns.

In the frame of the current study, the effect of different interventions on two intestinal parasites not commonly targeted by helminthiasis control programmes was also investigated; namely, *S. stercoralis* and *Taenia* spp. A trend towards lower *Taenia* spp. prevalence over time and depending on the intensity and the mix of control interventions was observed. Some activity of albendazole against both parasites has been documented before (Marti et al., 1996; Steinmann et al., 2008b). It must also be noted that in parallel to the construction of latrines, pig sheds were constructed in Mangguo new village as a part of a community development programme. This initiative boosted smallholder pig husbandry since piglets were given to each family, but also provided for better separation of pigs from human faeces and thus a reduced risk for porcine cysticercosis. The improved sanitation conditions in the village should also translate into a lower risk of human cysticercosis. No case of cysticercosis has been diagnosed in any of the three villages over the course of the study. The limitations with regard to the content of health education messages mentioned for hookworm also apply in the case of *S. stercoralis*, as both nematodes share the same mode of transmission.

The declared aim of the global strategy for the control of soil-transmitted helminthiasis is morbidity control rather than local elimination, with infection intensity expressed in terms of egg counts used as surrogate marker for morbidity (Gabrielli et al., 2011; WHO, 2006). A marked effect on infection intensity was achieved in the case of hookworm and in that of *A. lumbricoides* in the village where intensive MDA was coupled with latrine construction and health education. In the same village, only a limited effect was observed against *T. trichiura*. Of note, the baseline intensity of *A. lumbricoides* infections was mostly moderate, while that of *T. trichiura* and hookworm was low.

Treatment coverage rates were typically around 80–90% of the eligible population during the first phase of the study (2007/2008–2010). However, the persistence of a few medium and even heavy intensity infections suggests that certain individuals consistently missed or deliberately avoided treatment. The second phase of the study (2011–2013) simulated a situation more representative of a large-scale control programme and, predictably, the community-effectiveness of the intervention declined and started to deviate from the clear pattern observed during the first 3 years of interventions where strong efforts were in play. Potential explanations most probably included the lower frequency of MDA and uneven dedication of local authorities and village doctors in ensuring high treatment coverage. Population growth meant that new households did not have proper latrines in Mangguo new village unless they built them with their own resources. Encouragingly, the use of available latrines appeared to have been solidly entrenched by the start of the second phase and their impact on local parasite transmission was still apparent at the end of the study. This indicates that the provision of latrines is a sustainable intervention in the project area and that it is an important addition to MDA-based efforts to control soil-transmitted helminthiasis.

Subsidising latrines is highly controversial as it results in a feeling of entitlement and can stymie independent latrine construction with own funds (Harvey, 2011). Some sanitation projects involving subsidised latrines have also failed due to poor acceptance of the provided latrines, misappropriation of latrine buildings, wanting maintenance or other problems (Harvey, 2011). To improve community ownership of the intervention and diminish funding needs, a community-led total sanitation (CLTS) approach has been developed and is now being implemented in several countries (Kar and Chambers, 2008; Schmidlin et al., 2013). Alternative strategies have also been successful, including social marketing of sanitation (Evans et al., 2014). The rather high cost of about US$ 300 per latrine in the present project, not least caused by the use of a professional construction company and commercial materials including a ceramic toilet bowl, may be unsustainable in countries other than P.R. China where the government routinely heavily subsidises local infrastructure development, particularly in the frame of demonstration projects. Furthermore, the incentives for households to build latrines independently have certainly been compromised by the provision of free latrines at study inception through the local government. This deterrent would be countered by the clear benefits in terms of comfort that villagers perceived getting from latrines and probably also the status and prestige that come with latrines, all of which might be convincing arguments for other households to invest in latrines on their own. During functionality checks it was observed that lighting and water pipes for showering had been installed, and informal exchanges with villagers and their leaders indicated that people in Mangguo new village found it increasingly embarrassing to practice open defecation. The construction of latrines also had another effect on the community, namely an increased sense of responsibility for the community environment that manifested itself in additional activities such as organised waste disposal and road pavement.

5. Conclusions

The impact of standard interventions for the control of soil-transmitted helminthiasis, including MDA, latrine construction and health education depends on the socioeconomic context, local ecological conditions, intensity and mix of the intervention tools, the rigorousness with which it is implemented and the parasite species that is considered for impact evaluation. In a high-prevalence setting, even intensive efforts are not sufficient to sustainably suppress the transmission of *A. lumbricoides* and eliminate *T. trichiura*, while annual MDA alone can greatly reduce the prevalence of hookworm infection. Besides regular deworming, strengthening sanitation infrastructure plays a crucial role in soil-transmitted helminthiasis control programmes, and should be matched with setting-specific IEC. All interventions must be adapted to local needs and conditions, and be implemented rigorously and consistently to be effective. The impact of specific interventions and their combinations should be evaluated in the frame of larger, cluster-randomised controlled trials.

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