

# Community-wide versus school-based targeted deworming for soil-transmitted helminth control in school-aged children in Vietnam: the CoDe-STH cluster-randomised controlled trial



Clare E. F. Dyer,<sup>a,l</sup> Dinh Ng-Nguyen,<sup>b,l</sup> Naomi E. Clarke,<sup>a,l</sup> Sze Fui Hii,<sup>c</sup> Hieu Quoc Nguyen,<sup>b</sup> Van-Anh Thi Nguyen,<sup>b</sup> Thai Van Nguyen,<sup>b</sup> Trong Van Nguyen,<sup>b</sup> Tam Thi Ngo,<sup>d</sup> H. M. P. Dilrukshi Herath,<sup>c</sup> Handan Wand,<sup>a</sup> Luc E. Coffeng,<sup>e</sup> Justine C. Marshall,<sup>a</sup> Darren J. Gray,<sup>f,g</sup> Roy M. Anderson,<sup>h</sup> Archie C. A. Clements,<sup>ij,k</sup> John M. Kaldor,<sup>a</sup> Rebecca J. Traub,<sup>c</sup> and Susana Vaz Nery<sup>a,\*</sup>



<sup>a</sup>The Kirby Institute, University of New South Wales, Sydney, NSW, Australia

<sup>b</sup>Faculty of Animal Sciences and Veterinary Medicine, Tay Nguyen University, Dak Lak, Vietnam

<sup>c</sup>Faculty of Science, Melbourne Veterinary School, The University of Melbourne, Melbourne, Vic, Australia

<sup>d</sup>Centers for Disease Control and Prevention, Dak Lak, Vietnam

<sup>e</sup>Department of Public Health, Erasmus MC, University Medical Center Rotterdam, Rotterdam, the Netherlands

<sup>f</sup>Research School of Population Health, Australian National University, Canberra, ACT, Australia

<sup>g</sup>QIMR Berghofer Medical Research Institute, Brisbane, Australia

<sup>h</sup>Faculty of Medicine, School of Public Health, Imperial College London, London, United Kingdom

<sup>i</sup>Faculty of Health Sciences, Curtin University, Perth, WA, Australia

<sup>j</sup>Telethon Kids Institute, Perth, WA, Australia

<sup>k</sup>Peninsula Medical School, University of Plymouth, Plymouth, United Kingdom

## Summary

**Background** Soil-transmitted helminth (STH) infection control programs typically consist of school-based preventive chemotherapy (PC) targeted to school-aged children. STH reservoirs in untreated community members contribute to ongoing transmission in children. The CoDe-STH (Community Deworming against STH) trial, conducted in Dak Lak province, Vietnam, between October 2019 and November 2020, aimed to determine whether community-wide mass drug administration (MDA) is more effective than school-based targeted PC in reducing STH prevalence and intensity in children.

**Methods** In this two-arm cluster randomised controlled trial, 64 primary schools were randomly assigned 1:1 to receive either school-based targeted PC (“school arm”) or community-wide MDA (“community arm”). A single dose of albendazole 400 mg was used for deworming. The primary outcome was hookworm prevalence in schoolchildren, measured using quantitative real-time PCR. We also measured infection intensity for *Necator americanus* only, using qPCR cycle threshold (Ct) values converted into eggs per gram of faeces (EPG). Analysis was by intention to treat. The trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12619000309189).

**Findings** The analysis included 4955 children in the school arm and 5093 children in the community arm. *N. americanus* was the dominant STH species. The relative reduction in hookworm prevalence was not significantly different between the school arm (30.1%, 95% confidence interval [CI] 20.5–36.9) and the community arm (34.6%, 95% CI 19.9–49.4). Due to lower baseline prevalence than expected, the study was underpowered to detect a difference in prevalence reduction between the study arms. The community arm showed significantly greater relative reduction in *N. americanus* infection intensity (56.0%, 95% CI 39.9–72.1) compared to the school arm (3.4%, 95% CI –24.7 to 31.4). The community arm also showed greater relative reduction in prevalence of moderate-to-heavy intensity ( $\geq 2000$  EPG) *N. americanus* infections (81.1%; 95% CI 69.7–92.6) compared to the school arm (39.0%, 95% CI 13.7–64.2).

**Interpretation** Although no impact was seen on overall prevalence, community-wide MDA was more effective in lowering *N. americanus* infection intensity in schoolchildren compared to school-based targeted PC, measured 12 months after one round of albendazole deworming with high coverage.

DOI of original article: <https://doi.org/10.1016/j.lanwpc.2023.100913>

\*Corresponding author. The Kirby Institute, University of New South Wales, Level 6, Wallace Wurth Building High Street, Kensington, NSW 2052, Australia.

E-mail address: [snery@kirby.unsw.edu.au](mailto:snery@kirby.unsw.edu.au) (S. Vaz Nery).

<sup>l</sup>Joint first authors.

The Lancet Regional Health - Western Pacific 2023;41: 100920

Published Online xxx  
<https://doi.org/10.1016/j.lanwpc.2023.100920>

**Funding** National Health and Medical Research Council, Australia (APP1139561).

**Copyright** © 2023 The Authors. Published by Elsevier Ltd. This is an open access article under the CC BY-NC-ND license (<http://creativecommons.org/licenses/by-nc-nd/4.0/>).

**Keywords:** Soil-transmitted helminths; Hookworm; Deworming; Mass drug administration; Targeted preventive chemotherapy

### Research in context

#### Evidence before this study

Soil-transmitted helminth (STH) control programs typically focus on deworming school- and preschool-aged children using school-based targeted preventive chemotherapy (PC). Mathematical modelling studies suggest that expanding to community-wide mass drug administration (MDA), whereby all age groups receive deworming, will lead to additional reductions in STH infections in children as well as in the community as a whole. A large systematic review and meta-analysis found that mass deworming led to greater STH prevalence reduction among children than targeted deworming. The TUMIKIA trial in Kenya showed that community-wide deworming with albendazole was more effective in reducing prevalence and intensity of hookworm infection among all ages compared to school-based targeted deworming. However, there are no large-scale clinical trials comparing the impact of mass deworming and targeted deworming with a focus specifically on school-aged children, considered the group at highest risk of morbidity.

#### Added value of this study

The CoDe-STH trial was a large cluster-randomised controlled trial conducted in 64 primary schools and their surrounding communities, in Dak Lak province, Vietnam. We found that community-wide MDA using albendazole led to a greater reduction in hookworm infection intensity among school-

aged children, compared to school-based targeted PC. Community-wide MDA also led to a greater reduction in the prevalence of moderate-to-heavy intensity hookworm infection compared to school-based targeted PC. Our trial used quantitative real-time polymerase chain reaction (qPCR), a highly sensitive diagnostic technique, to detect and quantify hookworm infections.

#### Implications of all the available evidence

The results from the CoDe-STH trial are consistent with mathematical modelling and meta-analysis that suggested a greater impact of community-wide MDA on reducing STH infections specifically in school-aged children, a group considered at high risk of STH-associated morbidity. Our results also complement findings from the TUMIKIA RCT in Kenya that showed improved STH control across all age groups following community-wide deworming. Our findings add to the growing evidence base that the optimal design of STH control programs includes community-wide MDA, particularly in settings of high hookworm burden, and also provide support for the wider scale use of qPCR as a diagnostic technique for STH infections. Community-wide MDA can also allow for integration with control strategies for other neglected tropical diseases, reflecting one of the key cross-cutting targets in the World Health Organization's NTD road map for 2021–2030.

## Introduction

Soil-transmitted helminth (STH) infections are the most widespread neglected tropical disease (NTD) and are caused by parasitic intestinal worms including *Ascaris lumbricoides*, *Trichuris trichiura*, hookworms (*Necator americanus*, *Ancylostoma duodenale*, and *Ancylostoma ceylanicum*) and *Strongyloides stercoralis*. Primarily affecting poor and marginalised populations in low- and middle-income countries, STHs infect around one billion people globally, causing loss of almost two million disability-adjusted life years annually.<sup>1,2</sup> Morbidity associated with STH infections is greatest in children.<sup>3</sup>

The core strategy to achieve STH control, as recommended by the World Health Organization (WHO), is regular school-based targeted preventive chemotherapy (PC) of preschool- and school-aged children using albendazole or mebendazole.<sup>4</sup> The WHO's most recent

road map for NTDs sets a target to eliminate STHs as a public health problem in 96% of endemic countries by 2030, with elimination as a public health problem defined as <2% prevalence of moderate-to-heavy STH infections.<sup>4,5</sup>

STH prevalence often returns to pre-treatment levels within six months of deworming,<sup>6</sup> meaning that school-based targeted PC needs to be repeated for multiple years. Ongoing transmission among children following school-based targeted PC is attributable to STH reservoirs in untreated community members, particularly for hookworm, given that up to 80% of hookworm infections are found in people aged 15 years and older.<sup>7</sup> These reservoirs sustain parasite transmission in the context of ongoing environmental contamination in the absence of improved water, sanitation and hygiene (WASH).<sup>8</sup> As a result, school-based targeted PC is unlikely to interrupt STH transmission, particularly for

hookworm.<sup>7–10</sup> It has been suggested that community-wide mass drug administration (MDA), where whole communities are treated with anthelmintics, may be an effective alternative to school-based targeted PC that can achieve improved STH control and potentially interrupt STH transmission. Community-wide MDA has been used successfully to control other NTDs including trachoma, onchocerciasis, and lymphatic filariasis.<sup>11</sup>

A recently completed cluster randomised controlled trial (RCT) in Kenya found that community-wide MDA was more effective than school-based targeted PC in reducing hookworm prevalence and infection intensity, assessed by the Kato–Katz diagnostic technique, in community members of all ages.<sup>12</sup> The multicentre large-scale DeWorm3 trial, in progress in Benin, India, and Malawi, looks to assess whether bi-annual community-wide MDA can achieve interruption of STH transmission.<sup>13</sup>

Existing anthelmintic drug donations, through which many countries obtain drugs for deworming programs, are insufficient to allow community-wide MDA for STH control. Generating evidence to quantify the health benefits of community-wide MDA versus school-based targeted PC is essential to inform policy refinement and advocacy for additional drug donations and/or consistent supply at reduced costs.

Here we report the results of the CoDe-STH cluster-randomised controlled trial that took place in Dak Lak province, Vietnam, where school-based targeted PC has been implemented routinely since 2007, with a one-year interruption in 2018. This is the first clinical trial comparing the impact of community-wide MDA and school-based targeted PC on STH infections specifically in school-aged children. We hypothesise that deworming entire communities will lead to additional reductions in STH infections among school-aged children, compared to deworming school-aged children only.

## Methods

### Study design

The CoDe-STH trial was a two-arm cluster RCT conducted in Dak Lak Province, Vietnam between 28 October 2019 and 16 November 2020.<sup>14</sup> The trial was conducted in 64 primary schools, and in surrounding communities (“hamlets”) where children attending the primary schools resided. Each cluster was composed of a single primary school and its surrounding catchment hamlets. The study consisted of two rounds of data collection, conducted at baseline (November 2019, immediately prior to intervention delivery), and 12 months following intervention delivery.

This study received ethical approval from the Human Research Ethics Committees at the University of New South Wales (HC190136) and Tay Nguyen University (1804-QĐ-ĐHTN-TCCB). The published study protocol contains a full description of the trial methodology.<sup>14</sup>

### Participants

Primary schools, which include grades one to five, were eligible to participate in the study if they had between 200 and 450 students enrolled (due to sample size requirements and operational constraints), and were located in a rural, remote, or very remote area, as defined by the Department of Education and Training.<sup>14</sup> From the list of 129 eligible schools, 64 schools were randomly selected, stratified by district proportionally to the number of schools in each of the 13 rural districts.

For each study school, we designated a group of “participating hamlets”, starting with the hamlet that had the largest number of children attending the school, and continuing sequentially until the selected hamlets (typically between two and four hamlets per school) collectively included at least 70% of children enrolled in the school. This process allowed us to define a distinct catchment area for each school. To ensure that no study schools shared hamlets in their catchment areas, no more than one school was selected from a given commune. A total of 216 hamlets (103 in the school arm and 113 in the community arm) were included, consisting of 39,553 households (20,058 in the school arm and 19,495 in the community arm).

Participants in data collection were children who attended study schools, lived in a participating hamlet, and were in grade one to four at study baseline. Children in grade five did not participate in data collection because they were no longer in primary school at the time of the follow up data collection.

Participants in the study intervention (deworming with albendazole) were all children attending study schools, and all people who lived in participating hamlets in the community arm.

Verbal consent was obtained from school headmasters of participating schools, and from hamlet leaders in the community arm. Written informed consent was obtained from parents or caregivers of children who were eligible to participate in data collection. Consent was not required for children to receive albendazole at school, because school-based deworming is usual practice in Vietnam.

### Randomisation and masking

The 64 study schools were randomised 1:1 to the school and community arms of the study (32 schools per arm), stratified by district. Randomisation was performed by an independent statistician, using a computerised random number generator. The participants and the research team, who recruited participants and delivered study interventions, were aware of the allocated study arm; blinding was not possible given the nature of the interventions. The laboratory staff who assessed study outcomes were blinded to participant allocations.

### Procedures—data collection

Data collected from study participants at baseline included a questionnaire and a parasitological survey. The parasitological survey was repeated 12 months following the study intervention.

Questionnaires were administered at baseline to children for whom informed consent had been obtained, and their parent or caregiver. These were delivered in interview format by the research team and data were entered using electronic tablets via REDCap electronic data capture software hosted at UNSW Sydney. Questions focused on participants' defecation and hygiene practices, household water and sanitation access, socioeconomic status, and home environment. A full list of questionnaire variables is included in the [Appendix \(Web Text 1\)](#).

Parasitological surveys involved collection and analysis of one stool sample from each child whose parents provided informed consent. Early morning stool samples were brought to school by participating children, with 3 g aliquots preserved by the field team in 5% (w/v) potassium dichromate and kept on ice until refrigerated. Stool samples were sent to the University of Melbourne for analysis by qPCR as described previously.<sup>16,17</sup> Due to budget constraints, qPCR analysis was limited to 120 randomly selected stool samples per school at both study time points. At baseline, these samples were selected randomly, while at follow-up samples from children whose stool sample was analysed at baseline were purposefully selected. Where these numbered fewer than 120, additional stool samples to make up the 120 sample size were selected randomly.

Following washing and beating steps, DNA extraction was performed using the Maxwell® RSC PureFood GMO and Authentication Kit on a Maxwell® RSC 48 Instrument (Promega Corporation). Multiplex PCR assays were then used to detect and quantify *N. americanus*, *A. duodenale*, and *A. ceylanicum*, *Ascaris* spp., *Trichuris* spp. and *Strongyloides* spp., using Equine Herpes Virus 4 and human DNA as qPCR internal and DNA extraction controls, respectively.<sup>15,17,18</sup> Infection intensity was determined using previously published linear regression equations derived from faeces seeded with helminth eggs, to convert qPCR cycle threshold (Ct) values obtained from qPCR into eggs per gram of faeces (EPG).<sup>15,16</sup> As samples were found to be embryonated following transportation, conversion equations derived for embryonated eggs were used; these were available only for *N. americanus* ( $EPG = 10^{((Ct-32.657)/-3.878)}$ ), *Ascaris* spp. ( $EPG = 10^{((Ct-30.048)/-3.2804)}$ ), and *Trichuris* spp. ( $EPG = 10^{((Ct-31.888)/-4.048)}$ ).<sup>16-18</sup>

### Procedures—study interventions

In both study arms, one round of deworming with 400 mg albendazole (Alzental, Shingpoon Pharmaceuticals) was offered to all children attending each study school immediately following baseline data collection.

Albendazole was delivered and directly observed by the research team at the school, assisted by school teachers. For children who were absent on the day of albendazole distribution, doses were left at the school for the teacher to administer when they returned to school in the subsequent week, along with a register for teachers to record these doses. Treatment coverage was recorded by the research team at the school, and by registers provided by teachers for any doses provided at a later date for children who were absent. All deworming at schools conducted in the study was delivered as part of the routine national school-based deworming program. The study team worked closely with the Ministry of Education, Ministry of Health, and relevant local authorities to ensure that trial activities were synchronised with the national program.

In the community arm, deworming was offered in all participating hamlets. The research team conducted house-to-house visits with the assistance of village health staff in eligible hamlets, and 400 mg albendazole was offered to all household members (excluding children aged under one year of age, women in their first trimester of pregnancy, and children who reported already receiving albendazole at school).<sup>19</sup> Treatment coverage was recorded by the research team. All recorded doses were directly observed; albendazole doses were not left behind for household members who were not present at the time of intervention delivery.

### Outcomes

The primary outcome was prevalence of hookworm infection (unspicated) in school-age children, detected using qPCR, 12 months after albendazole distribution.<sup>14</sup> Secondary outcomes were prevalence of *N. americanus*, *A. duodenale*, *A. ceylanicum* (species-specific hookworm infections), *Ascaris* spp., and *Trichuris* spp.; mean intensity of hookworm infection (in EPG); treatment coverage with albendazole (i.e., the proportion of eligible schoolchildren and community members who receive albendazole); and adverse events following albendazole distribution.

In a change from the published study protocol, arithmetic mean intensity of hookworm infection (the average number of eggs per gram of faeces) was assessed only for *N. americanus* because infection intensity in EPG could not be calculated for other hookworm species due to absence of published conversion formulae. Additionally, prevalence of moderate-to-heavy *N. americanus* infection, defined using WHO thresholds as  $\geq 2000$  EPG,<sup>20</sup> was added as a secondary outcome, given the focus on reducing moderate-to-heavy intensity infections in the recently published WHO road map.<sup>4</sup>

Treatment coverage was defined for school-based deworming as the number of albendazole doses delivered as a proportion of the number of students enrolled at the school; and for community-based deworming as the number of albendazole doses delivered to eligible

hamlet residents, excluding children dewormed at school, as a proportion of the population of each hamlet, obtained from the hamlet leader.

Adverse events were recorded using passive monitoring. Following deworming, school staff, village health staff, and hamlet health staff were asked to record anyone who reported a possible adverse event following drug delivery. The research team returned to each school and hamlet one week after albendazole administration to collect information about adverse events from the village and hamlet health staff and school teachers.

### Statistical analysis

Full details of sample size calculations are provided in the published study protocol.<sup>14</sup> We assumed a baseline hookworm prevalence of 20% based on a pre-baseline prevalence survey conducted in 2018, and a relative hookworm prevalence reduction of 79% after community-wide MDA and 45% after school-based targeted PC at 12 months' follow-up.<sup>10</sup> We assumed an average cluster size of 120 children and, based on a prior study conducted in a similar prevalence setting in Timor-Leste,<sup>21</sup> an intra-cluster correlation coefficient of 0.12, with a power of 80%. The required sample size was 32 primary schools in each study arm. The study was not powered to detect differences in prevalence for *A. lumbricoides* or *T. trichiura*.

In order to collect data and stool samples for 120 children in each cluster, we aimed to recruit at least 180 participants per cluster to allow for 30% loss to follow-up and failure to provide stool samples.<sup>14</sup> Intention to treat analyses were performed, including all participants who had a stool sample analysed at baseline and/or follow-up, and regardless of whether albendazole was taken at baseline. We described the cohort using counts and percentages of demographic variables at the individual level, by trial arm.

We used generalised linear mixed models (GLMMs) to compare the impact of the study interventions on hookworm prevalence, infection intensity, and prevalence of moderate-to-heavy infections.<sup>20</sup> The school was included as a random effect, and an interaction term for study arm (control or intervention) and timepoint (baseline or follow-up) used to quantify the additional impact of the community arm compared to the school arm. Analysis of prevalence reduction used a logistic regression approach, while analysis of infection intensity reduction used arithmetic means to better capture variation and a negative binomial regression approach for the analysis.<sup>22</sup> All analyses included age and sex as fixed effects and the interaction term for study arm and timepoint.

An additional set of GLMMs were run to compare the impact of the study intervention, adjusted for WASH and sociodemographic variables collected during the baseline questionnaires. These analyses only

included children for whom both child and caregiver questionnaires were completed. The analyses were conducted using a domain-based approach, which has been described previously<sup>23</sup> and is summarised in the [Supplementary Web Files \(Web Text 2\)](#).

Because the baseline hookworm prevalence in some schools was lower than expected, we conducted post-hoc sensitivity analyses excluding schools where baseline hookworm prevalence was <5%; this resulted in the exclusion of seven schools in the school arm and 11 schools in the community arm.

A post-hoc secondary cluster-level analysis of the data was also carried out, as another method to compare the impact of the study interventions on prevalence outcomes.<sup>24</sup> Briefly, the observed differences in hookworm prevalence, and moderate-to-heavy hookworm prevalence, were calculated as proportions in each cluster at baseline and follow-up periods for school and community arms separately. The estimated mean difference between the baseline and follow-up were calculated and presented for school and community arms. The 95% confidence intervals (CIs) were presented by incorporating any variability due to the variation between clusters by using t-test in the cluster-period proportions.<sup>24</sup>

All analyses were performed using Stata version 17 (College Station, TX, USA).<sup>25</sup> The trial was registered with the Australian New Zealand Clinical Trials Registry (ACTRN12619000309189).

### Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

### Results

A total of 13,989 children were eligible for inclusion in data collection, and informed consent was obtained for 12,842 children. Overall, across the two study time points, 4955 children were included in the school arm and 5093 in the community arm ([Fig. 1](#)).

[Table 1](#) shows selected baseline characteristics of the study population; the full list of characteristics is provided in [Web Table 1](#). There was an approximately even split between males and females in the study population and an even distribution across school grades. At baseline, over a third of participants (1322/3797) in the school arm and nearly 50% (1761/3838) in the community arm were Kinh ethnicity (considered the ethnic majority in Vietnam).

Hookworm prevalence at baseline was 16.7% (95% CI 12.1–22.7; 635/3797) in the school arm and 11.7% (95% CI 7.8–17.3; 450/3838) in the community arm. The vast majority of infections were *N. americanus*, with

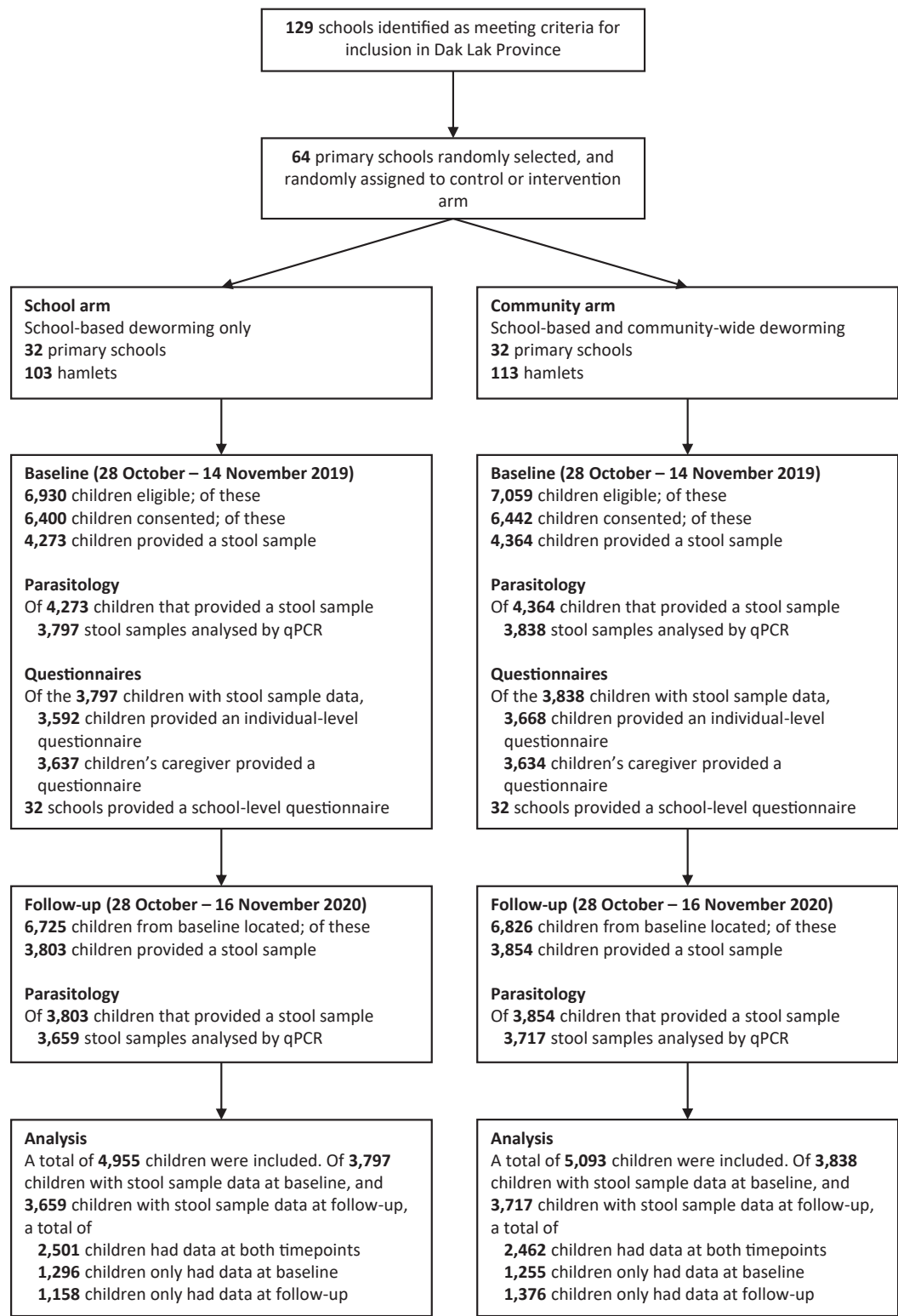


Fig. 1: Flow diagram detailing number of schools and hamlets in each study arm, and number of participants at each study timepoint and in final analysis.

	School arm n (%; 95% CI)	Community arm n (%; 95% CI)
Demographic characteristics <sup>a</sup>	N = 3797	N = 3838
Grade 1	1012 (26.7, 24.4–29.0)	991 (25.8, 23.8–27.9)
Grade 2	1041 (27.4, 26.0–28.9)	1057 (27.5, 25.6–29.5)
Grade 3	895 (23.6, 21.7–25.5)	939 (24.5, 22.5–26.6)
Grade 4	849 (22.4, 20.2–24.7)	851 (22.2, 20.0–24.6)
Male	1819 (47.9, 45.7–50.2)	1910 (49.8, 48.1–51.5)
Female	1978 (52.1, 49.8–54.3)	1928 (50.2, 48.5–51.9)
Kinh ethnicity	1322 (34.8, 22.5–49.5)	1761 (45.9, 33.0–59.4)
Ede ethnicity	1461 (38.5, 24.3–55.0)	720 (18.8, 10.0–32.5)
Other ethnicity	1014 (26.7, 15.5–42.0)	1357 (35.4, 24.0–48.6)
Household characteristics <sup>b</sup>	N = 3637	N = 3634
Household has improved water source	3077 (84.6, 79.2–88.8)	3098 (85.3, 81.1–88.6)
Mother's highest education level		
Never attended/did not finish primary school	931 (25.6, 19.6–32.7)	717 (19.7, 16.1–24.0)
Completed primary but not secondary school	1174 (32.3, 29.4–35.3)	1128 (31.0, 28.1–34.1)
Completed secondary school	1077 (29.6, 25.5–34.0)	1308 (36.0, 32.0–40.2)
Further education after secondary school	308 (8.5, 6.3–11.2)	350 (9.6, 7.5–12.3)
Occupation of main income earner		
Farmer	3327 (91.5, 88.2–93.9)	3307 (91.0, 88.4–93.1)
Household income (annual)		
<20 M VND	1625 (44.7, 41.0–48.4)	1643 (45.2, 39.3–51.2)
20 M–50 M VND	918 (25.2, 21.3–29.7)	976 (26.9, 22.2–32.1)
50 M–200 M VND	218 (6.0, 4.4–8.2)	297 (8.2, 5.3–12.4)
>200 M VND	16 (0.4, 0.2–0.8)	30 (0.8, 0.5–1.4)
Individual characteristics <sup>c</sup>	N = 3592	N = 3668
Sanitation access and behaviour		
Household has latrine	2658 (74.0, 64.7–81.5)	2805 (76.5, 68.7–82.8)
Always use household latrine	2179 (82.0, 77.6–85.6)	2203 (78.5, 73.2–83.0)
Usual place of defecation at home		
Household toilet/latrine	2651 (73.8, 64.9–81.2)	2859 (77.9, 69.9–84.3)
Shared toilet/latrine	48 (1.3, 0.9–1.9)	45 (1.2, 0.7–2.2)
Open defecation	838 (23.3, 16.5–32.0)	731 (19.9, 13.9–27.8)
Ever practice open defecation at home	863 (24.0, 21.2–27.2)	910 (24.8, 20.7–29.4)
Usual place of defecation at school		
School toilet/latrine	3269 (91.0, 85.2–94.7)	3324 (90.6, 83.1–95.0)
Open defecation	156 (4.3, 2.0–9.2)	240 (6.5, 2.9–14.0)
Ever practice open defecation at school	296 (8.2, 6.1–11.1)	328 (8.9, 5.8–13.5)
Hygiene access and behaviour		
Handwashing station available at home	3223 (89.7, 82.2–94.3)	3362 (91.7, 88.0–94.3)
Soap available for handwashing	2399 (66.8, 59.3–73.5)	2594 (70.7, 64.3–76.4)
Always wash hands after defecating	2124 (59.1, 52.4–65.5)	2217 (60.4, 52.6–67.8)
Always wash hands before eating	1868 (52.0, 45.2–58.8)	1882 (51.3, 43.9–58.6)
Always wear shoes outside	2652 (73.8, 68.0–78.9)	2598 (70.8, 62.6–77.9)
Always wear shoes when defecating	2416 (67.3, 61.8–72.3)	2443 (66.6, 61.1–71.7)

All proportions adjusted for school clustering. CI = confidence interval. <sup>a</sup>N refers to number of children with stool sample data at baseline (individual-level data). <sup>b</sup>N refers to number of children with stool sample data and caregiver questionnaire data at baseline (individual-level data). <sup>c</sup>N refers to number of children with stool sample data and individual questionnaire data at baseline (individual-level data).

**Table 1: Selected baseline characteristics of study population.**

a baseline prevalence of 16.2% (95% CI 11.6–22.2; 617/3797) in the school arm and 11.3% (95% CI 7.5–16.9; 435/3838) in the community arm. All other STH species had a baseline prevalence of <1% (Web Table 2). At

baseline the arithmetic mean intensity of *N. americanus* infections was similar in the school arm (1678.8 EPG; 95% CI 1370.4–2056.6) and community arm (1699.4 EPG; 95% CI 1426.9–2023.9). The prevalence of

moderate-to-heavy *N. americanus* infections was also similar in the school arm (3.6%; 95% CI 2.3–5.6; 136/3797) and community arm (3.0%; 95% CI 1.8–4.9; 115/3838).

At follow-up, the prevalence of hookworm was 11.7% (95% CI 8.1–16.6; 428/3659) and 7.7% (95% CI 5.3–11.0; 285/3717) in the school and community arms, respectively, corresponding to a relative reduction in prevalence of 30.1% (95% CI 20.5–39.6) and 34.6% (95% CI 19.9–49), respectively (Table 2). GLMM analyses adjusted for age and sex showed no statistically significant difference in the relative hookworm prevalence reduction between school and community arms (0.93; 95% CI 0.70–1.24;  $p = 0.636$ ) (Table 3).

As shown in Table 4, at follow-up there was a much lower *N. americanus* mean infection intensity in the community arm (747.7 EPG; 95% CI 545.2–1025.4) compared to the school arm (1622.0 EPG; 95% CI 955.7–2752.9). The relative reduction in intensity between baseline and follow-up was 3.4% (95% CI –24.7 to 31.4) in the school arm and 56.0% (95% CI 39.9–72.1) in the community arm. The difference in relative reduction of infection intensity between study arms was statistically significant in the GLMM adjusted for age and sex (0.36; 95% CI 0.17–0.73;  $p = 0.005$ ) (Table 3). This means that community-wide MDA led to a 64% greater reduction in the mean infection intensity of *N. americanus* than school-based targeted PC.

As shown in Table 5, at follow-up the prevalence of moderate-to-heavy *N. americanus* infections was lower in the community arm (0.6%; 95% CI 0.3–1.0; 21/3717) compared to the school arm (2.2%; 95% CI 1.2–4.0; 80/3659). The relative reduction in moderate-to-heavy *N. americanus* infections between baseline and follow-up was 39.0% (95% CI 13.7–64.2) in the school arm and 81.1% (95% CI 69.7–92.6) in the community arm. This difference in relative reduction between study arms was statistically significant in the GLMM adjusted for age and sex (0.30; 95% CI 0.14–0.62;  $p = 0.001$ ). This indicates that community-wide MDA led to a 70% greater reduction in the prevalence of moderate-to-heavy *N. americanus* infections compared with school-based targeted PC.

The intra-cluster correlation coefficient for hookworm infection at baseline was 0.138.

Albendazole coverage of children at school was 96.8% (95% CI 96.4–97.1) in the school arm and 95.3% (95% CI 94.9–95.7) in the community arm. Treatment coverage of community members was 89.9% (95% CI 89.7–90.1). No adverse events were recorded.

Post-hoc GLMM analyses excluding schools where baseline prevalence was <5% gave similar results (Table 3) as did the GLMMs additionally adjusted for WASH and sociodemographic variables (Web Table 3). Findings obtained in the cluster level analysis for prevalence of hookworm (absolute risk difference = –0.04; 95% CI –0.30 to 0.22;  $p = 0.772$ ) were also not

statistically significant (Web Table 4). However, the finding that community-wide MDA led to a greater reduction in the prevalence of moderate-to-heavy *N. americanus* infections compared with school-based targeted PC was supported by the cluster-level analysis (absolute risk difference = –0.42; 95% CI –0.84 to 0.01;  $p = 0.047$ ) (Web Table 4).

Web Tables 5–7 show factors associated with hookworm infection, *N. americanus* infection intensity, and moderate-to-heavy *N. americanus* infection. Older age, being in an ethnic group other than Kinh, having a *Strongyloides* spp. co-infection, defecating outdoors at school, having an unimproved household water supply, and having a primary caregiver who never attended school or did not complete primary school were associated with increased odds of *N. americanus* infection (Web Table 5). Older age, being in an ethnic group other than Kinh, having a *Strongyloides* spp. co-infection, practising open defecation at home, and having a primary caregiver who never attended school or did not complete primary school were associated with higher *N. americanus* infection intensity (Web Table 6) as well as increased odds of moderate-to-heavy *N. americanus* infection (Web Table 7). The full baseline risk factor analysis has been published separately.<sup>26</sup>

## Discussion

The CoDe-STH trial compared the impact of school-based targeted PC and community-wide MDA on the prevalence and intensity of hookworm infections among school-aged children.<sup>14</sup> Although the study demonstrated no additional impact of community-wide MDA on hookworm prevalence reduction, several key secondary outcomes showed a significant difference between study arms. We found that 12 months after deworming with albendazole, community-wide MDA led to a significantly greater reduction in the mean *N. americanus* infection intensity among school-aged children, as well as a greater reduction in moderate-to-heavy intensity infections, compared to school-based targeted PC. Indeed, after just one round of deworming, community-wide MDA reduced the prevalence of moderate-to-heavy intensity hookworm infection below the WHO target of 2%, while this was not achieved following targeted PC in the school arm. These findings relate to the role adults play in sustaining hookworm infection in communities if left untreated.<sup>7</sup> Without deworming of adults in the school arm, the worm burden in the population—and therefore environmental contamination with infective stages—remains high. Children are at greater risk of infection in their communities, and as a result, population-level infection intensity returns to pre-deworming levels within 12 months, as demonstrated in the school arm of this trial. Following community-wide MDA, the worm burden is reduced in adults as well as children, and therefore the



	Baseline (%, 95% CI)		Follow-up (%, 95% CI)		Relative reduction in prevalence (%, 95% CI)	
	School (N = 3797)	Community (N = 3838)	School (N = 3659)	Community (N = 3717)	School	Community
Overall	16.7 (12.1–22.7)	11.7 (7.8–17.3)	11.7 (8.1–16.6)	7.7 (5.3–11.0)	30.1 (20.5–39.6)	34.6 (19.9–49.4)
By sex						
Male	19.2 (13.6–26.5)	13.6 (8.6–19.8)	12.5 (8.4–18.2)	8.5 (5.8–12.3)	35.0 (25.5–44.6)	37.0 (20.6–53.4)
Female	14.4 (10.4–19.7)	9.9 (6.4–15.0)	11.0 (7.6–15.7)	6.9 (4.6–10.2)	23.4 (11.9–34.9)	30.8 (14.7–46.9)
By age at study baseline <sup>a</sup>						
6 years	14.8 (10.3–20.9)	8.4 (5.3–13.2)	8.9 (5.5–14.1)	5.0 (2.6–9.6)	39.9 (20.9–58.9)	40.5 (12.8–68.1)
7 years	13.5 (9.3–19.3)	9.4 (5.8–14.7)	8.7 (5.7–13.1)	6.1 (3.9–9.5)	35.5 (20.2–50.8)	35.0 (9.6–60.4)
8 years	14.6 (9.8–21.1)	10.9 (6.5–17.7)	10.8 (7.1–16.2)	6.7 (4.0–10.8)	25.6 (10.1–41.1)	38.6 (20.2–57.0)
9 years	18.4 (11.1–25.2)	13.3 (9.4–18.5)	13.3 (8.8–19.8)	10.3 (6.9–15.2)	27.4 (14.1–40.7)	21.9 (1.1–42.8)
10 years	23.8 (17.9–30.8)	18.8 (12.2–27.9)	19.0 (13.9–25.3)	10.6 (7.4–15.1)	20.3 (0.9–41.5)	43.6 (20.5–66.7)
11 years	62.3 (46.2–76.0)	34.1 (22.2–48.4)	46.2 (28.2–65.2)	17.5 (7.9–34.4)	25.9 (4.4–47.3)	48.7 (15.4–81.9)
By ethnic group						
Kinh	2.4 (1.5–4.0)	2.8 (1.8–4.4)	1.2 (0.7–2.0)	1.7 (0.9–3.1)	49.9 (21.4–78.4)	39.3 (1.6–80.2)
Ede	24.8 (19.3–31.4)	18.5 (14.5–23.3)	16.5 (12.6–21.3)	16.1 (12.1–21.1)	33.5 (23.5–43.4)	12.8 (8.0–33.5)
Other	23.7 (14.3–36.6)	19.7 (11.5–31.7)	17.8 (9.7–30.4)	11.2 (7.1–17.2)	24.8 (7.5–42.1)	43.5 (27.8–59.3)

<sup>a</sup>Eight children (two in the school arm and six in the community arm) were not included in the overall analysis as they were older than 11 years.

**Table 2: Prevalence of hookworm at study baseline and follow-up.**

level of environmental contamination with infective stages is also reduced. As a result, children are infected at a lower rate, leading to lower infection intensity levels.

As mentioned above, the trial hypothesis that hookworm prevalence would decrease more following community-wide MDA versus school-based targeted PC was not supported. In part this is due to the negative binomial distribution of infection intensity within the community, which is typical for all helminth infections of humans.<sup>27</sup> With this distribution where most individuals harbour no or low infection burdens, and a few people harbour high infection burdens, large changes in the mean intensity of infection are typically linked to relatively small changes in prevalence. Our findings are consistent with mathematical modelling studies of helminth transmission and control impact that assume parasites are negatively binomially distributed in the human population, and have shown that one

year after treatment, the prevalence of hookworm in school-aged children reduces much less than the mean intensity of infection, regardless of the deworming approach.<sup>7</sup> It is only in the longer term when mean intensity reaches very low levels that the effects of the different strategies on prevalence reduction are evident.<sup>7</sup>

Elimination of lymphatic filariasis, onchocerciasis, and trachoma has been achieved in many countries globally through a community-wide MDA strategy.<sup>11</sup> The main limiting factor for adopting a community-wide MDA approach for STH control is drug availability and cost implications. STH infections are so widespread globally that donations of anthelmintic drugs and/or supply at affordable cost would need to increase drastically to enable community-wide MDA in all at-risk areas and operational costs would be large.<sup>7</sup> However, modelling predicts that in the long term, overall costs would be lower than repeating school-based targeted PC

	Adjusted for age and sex			
	N <sup>a</sup>	Point estimate <sup>b</sup>	95% CI	p value
All study schools included				
Hookworm infection	15,011	0.93	0.70–1.24	0.636
<i>N. americanus</i> infection intensity (EPG)	15,011	0.36	0.17–0.73	<b>0.005</b>
Moderate-to-heavy <i>N. americanus</i> infection	15,011	0.30	0.14–0.62	<b>0.001</b>
Schools excluded if baseline prevalence <5%				
Hookworm infection	10,800	0.90	0.65–1.23	0.493
<i>N. americanus</i> infection intensity (EPG)	10,800	0.35	0.17–0.73	<b>0.005</b>
Moderate-to-heavy <i>N. americanus</i> infection	10,800	0.30	0.14–0.63	<b>0.002</b>

Results in bold indicate significance at p < 0.05 level. EPG = eggs per gram of faeces. <sup>a</sup>Observations included in regression models. <sup>b</sup>Relative difference in reduction between trial arms.

**Table 3: Difference between study arms (school versus community arm) in prevalence and infection intensity reduction.**

	Baseline Arithmetic mean EPG (95% CI <sup>a</sup> )		Follow-up Arithmetic mean EPG (95% CI <sup>a</sup> )		Relative reduction % (95% CI)	
	School arm N = 617	Community arm N = 435	School arm N = 416	Community arm N = 268	School arm	Community arm
Overall	1678.8 (1370.4–2056.6)	1699.4 (1426.9–2023.9)	1622.0 (955.7–2752.9)	747.7 (545.2–1025.4)	3.4 (–24.7 to 31.4)	56.0 (39.9–72.1)
By sex						
Male	1673.9 (1289.1–2058.8)	1566.0 (1232.6–1899.6)	1951.7 (1275.9–2627.4)	624.6 (421.9.8–924.9)	–16.6 (–66.0 to 32.8)	60.1 (41.4–78.8)
Female	1684.9 (1290.8–2078.9)	1884.7 (1388.0–2381.5)	1319.6 (902.9–1736.4)	884.3 (575.2–1359.6)	21.7 (–9.6 to 53.0)	53.1 (26.7–79.4)
By age at study baseline <sup>b</sup>						
6 years	993.6 (660.5–1494.7)	1246.8 (768.3–2023.3)	1189.4 (573.0–2468.9)	430.5 (253.4–731.4)	–19.7 (–132.8 to 93.4)	65.5 (36.5–94.4)
7 years	1445.6 (1059.0–1973.2)	1489.5 (1003.91–2209.9)	1970.7 (937.0–4144.7)	335.9 (210.9–535.1)	–36.3 (–136.8 to 64.2)	77.4 (63.3–91.6)
8 years	1736.5 (1150.9–2620.2)	1262.7 (909.6–1752.9)	1535.9 (855.3–2758.1)	971.1 (436.5–2160.6)	11.6 (–42.5 to 65.6)	23.1 (–36.1 to 82.3)
9 years	1760.7 (1186.1–2613.7)	1912.5 (1444.4–2532.4)	1631.3 (971.7–2738.5)	855.9 (486.5–1505.8)	7.4 (–40.3 to 55.0)	55.2 (24.9–85.6)
10 years	1792.0 (1273.1–2522.5)	2402.1 (1662.7–3470.1)	1882.2 (833.6–4249.7)	1017.4 (449.0–2305.2)	–5.0 (–90.4 to 80.4)	57.6 (15.1–100.2)
11 years	3293.4 (1588.8–6826.9)	3023.8 (1411.8–6476.3)	937.3 (330.3–2660.2)	684.9 (314.2–1492.9)	71.5 (32.3–110.7)	77.4 (44.2–110.5)
By ethnic group						
Kinh	710.0 (302.5–1666.7)	694.7 (286.9–1682.2)	859.4 (487.9–1513.7)	446.3 (249.8–797.4)	–21.0 (–759.2 to 717.1)	35.8 (–96.1 to 167.7)
Ede	1767.4 (1388.6–2249.7)	1879.9 (1457.2–2425.2)	1252.6 (777.1–2019.2)	709.1 (408.7–1230.3)	29.1 (–0.3 to 58.3)	62.3 (38.3–86.2)
Other	1652.2 (1175.3–2322.7)	1788.3 (1427.3–2240.5)	2157.6 (952.8–4885.8)	837.4 (551.8–1270.9)	–30.6 (–85.4 to 24.2)	53.2 (29.5–76.8)

This table includes only those who had *N. americanus* infection. CI = confidence interval; EPG = eggs per gram of faeces. <sup>a</sup>Based on a negative binomial distribution around the mean. <sup>b</sup>Values for children aged >11 years omitted (two children in school arm; six children in community arm).

**Table 4: Infection intensity (arithmetic mean EPG) of *N. americanus* at baseline and follow-up.**

indefinitely, given that community-wide MDA could be stopped after achieving transmission interruption.<sup>7</sup> The DeWorm3 trial is underway, aiming to identify whether STH elimination is possible with community-wide deworming.<sup>13</sup> Community-wide MDA also provides greater opportunity for potential integration with treatment for other NTDs, reflecting one of the key cross-cutting targets in the WHO’s NTD road map for 2021–2030.<sup>4</sup>

To our knowledge, the CoDe-STH trial is the largest trial conducted to date using quantitative real-time PCR (qPCR), a more sensitive diagnostic technique that allows for differentiation of hookworm species and more accurate detection of light-intensity infections compared to conventional diagnostic methods such as Kato–Katz. Whilst qPCR has been established for some time as a sensitive diagnostic tool for STHs, the use of conversion equations to convert Ct values to egg counts is still novel, with only a few published studies utilising this

approach.<sup>15–18</sup> WHO thresholds for determining light, moderate and heavy infection intensity categories are based on egg counts obtained using the conventional Kato–Katz approach, whereas this trial utilised egg counts derived from qPCR Ct values. We recognise that the quantification of STH infections using Ct values produces results that are different to EPG results from Kato–Katz. Previous studies have shown that egg counts derived from qPCR Ct values are often higher than those obtained using microscopy.<sup>15,28</sup> While this has no impact on the results within this trial because both trial arms used the same diagnostic method, it does limit comparisons to prevalence measurements in other studies derived from other diagnostic methods, and the relationship between infection intensity measurements in this study and the WHO targets. Additional studies are required to further understand the relationship between qPCR-derived egg counts to those derived from Kato–Katz and other microscopy-based techniques, and

	Baseline % (95% CI)		Follow-up % (95% CI)		Relative reduction in prevalence % (95% CI)	
	School arm N = 3797	Community arm N = 3838	School arm N = 3659	Community arm N = 3717	School arm	Community arm
Heavy	2.0 (1.3–3.3)	1.4 (0.9–2.3)	1.2 (0.6–2.6)	0.3 (0.1–0.6)	39.4 (2.3–76.3)	79.0 (64.3–93.6)
Moderate	1.6 (1.0–2.5)	1.6 (0.9–2.9)	1.0 (0.5–1.7)	0.3 (0.1–0.5)	38.4 (18.2–58.7)	83.1 (68.8–97.4)
Light	12.7 (9.2–17.2)	8.3 (5.6–12.3)	9.2 (6.4–12.9)	6.6 (4.5–9.7)	27.5 (17.7–37.3)	20.3 (0.1–40.4)
Moderate-to-heavy	3.6 (2.3–5.6)	3.0 (1.8–4.9)	2.2 (1.2–4.0)	0.6 (0.3–1.0)	39.0 (13.7–64.2)	81.1 (69.7–92.6)

CI = confidence interval.

**Table 5: Prevalence of heavy, moderate, and light intensity *Necator americanus* infection.**

therefore to the WHO thresholds and targets. However, quantitative PCR is rapidly emerging as the gold standard for STH diagnostics, with additional benefits including its ability to differentiate between hookworm species and detect *Strongyloides* spp.<sup>15</sup> Using a highly-sensitive diagnostic technique also becomes increasingly important as communities approach STH transmission interruption, where detection of light-intensity infections is crucial.

There were several limitations of this study. We observed imbalances in baseline hookworm prevalence (but not infection intensity) between study arms, which arose by chance and was accounted for in the statistical analysis. There was a round of deworming conducted by the national program six months prior to study baseline, which reduced the baseline hookworm prevalence, contributing to a lower-than-expected impact of the intervention, and resulting in the study being underpowered to detect the primary outcome. Due to low baseline prevalence of other STH species, we were limited to studying the impact of the intervention on hookworm, which was the dominant STH in the region.

It was not feasible to provide deworming to every catchment hamlet for schools in the intervention arm. As such, children attending intervention arm schools, but who lived in hamlets that did not receive deworming, may have had an increased risk of STH infection in their communities, which could contribute to increased transmission in the school environment. Any impact of this would bias results towards the null.

CoDe-STH is the first large-scale trial comparing community-wide MDA and school-based targeted PC for STH control in South-East Asia, and the first to demonstrate the additional benefits of community-wide deworming specifically for school-aged children. The only other published trial comparing the impact of school-based targeted PC and community-wide MDA reported a higher prevalence reduction across all age groups in the MDA arm.<sup>12</sup> As hookworm prevalence increases with age<sup>7</sup> and whole communities do not typically receive deworming, a large prevalence reduction at community level would be expected after a community-wide deworming intervention when previously high burden adults receive effective treatment. The CoDe-STH study investigated the impact of community-wide MDA specifically on school-aged children, demonstrating enhanced benefits for this high-risk group as a result of reducing overall community STH burden.

The greater reduction in moderate-to-heavy intensity hookworm infections achieved a year after a single round of albendazole deworming is an important finding as countries aim to reach the WHO elimination target of <2% prevalence of moderate-to-heavy intensity infection. These findings may also be translated to a greater reduction in morbidity in this vulnerable

population and are particularly relevant in settings where regular school-based PC has failed to achieve control targets, even with high reported treatment coverage.

The results of this cluster RCT contribute to the growing evidence base that the optimal design of STH control programs includes community-wide MDA, particularly in settings with high hookworm burden. These are important findings, the implications of which must be considered by policy makers as the push to control and eliminate neglected tropical diseases intensifies. Further research is required to assess the cost-benefit aspects of expanded treatment and, in this context, the role of more sensitive diagnostics in targeting treatment.

#### Contributors

CEFD: investigation, project administration, data curation, formal analysis, visualisation, writing - original draft.

DN: investigation, project administration, supervision, writing - review and editing.

NEC: methodology, investigation, project administration, data curation, visualisation, writing - original draft, writing - review and editing.

SFH, HMPDH: investigation, validation, writing - review and editing.

HQN, VTH, ThVN, TrVN, TTN: investigation, supervision.

HW: methodology formal analysis, writing - review and editing.

LEC: funding acquisition, methodology, formal analysis, writing - review and editing.

JCM: writing - review and editing.

DJG, RMA, ACAC: funding acquisition, methodology, writing - review and editing.

RJT: conceptualisation, funding acquisition, methodology, resources, supervision, writing - review and editing.

JMK: methodology, writing - review and editing.

SVN: conceptualisation, funding acquisition, methodology, resources, supervision, writing - original draft, writing - review and editing.

#### Data sharing statement

De-identified participant data are available on reasonable request addressed to the corresponding author under certain conditions (with the consent of all participating centres and with a signed data access agreement).

#### Declaration of interests

The authors declare no competing interests.

#### Acknowledgements

The authors would like to thank all members of the research field team as well as all of the village and hamlet health staff and hamlet leaders for their tireless work in data collection and intervention implementation. We also thank Dr Tuyen Kim Thi Nguyen, Dr Hoa Thu Thi Pham, and Dr Hoa Thi Nguyen from the Centres for Disease Control and Prevention in Dak Lak, Vietnam, and Ms Xoan Thi Mai and A/Prof Trong Van Phan from Tay Nguyen University, Dak Lak, Viet Nam. We are grateful to Dr Patsy Zendejas-Heredia for her work in developing the qPCR Ct to EPG conversion equations. Finally, we acknowledge all of the teachers, headmasters, parents and children who participated in this study.

The trial was funded by the National Health and Medical Research Council, Australia (APP1139561). LEC acknowledges funding from the Dutch Research Council (NWO, grant 016.Veni.178.023).

#### Appendix A. Supplementary data

Supplementary data related to this article can be found at <https://doi.org/10.1016/j.lanwpc.2023.100920>.

## References

- 1 Global burden of disease (GBD) study 2019. *Intestinal nematode infections*; 2019. [https://www.healthdata.org/results/gbd\\_summaries/2019/intestinal-nematode-infections-level-3-cause](https://www.healthdata.org/results/gbd_summaries/2019/intestinal-nematode-infections-level-3-cause). Accessed May 5, 2022.
- 2 Montresor A, Mupfasoni D, Mikhailov A, et al. The global progress of soil-transmitted helminthiases control in 2020 and World Health Organization targets for 2030. *PLoS Negl Trop Dis*. 2020;14(8):e0008505.
- 3 Hotez PJ, Bundy DAP, Beegle K, et al. Helminth infections: soil-transmitted helminth infections and schistosomiasis. In: Jamison DT, Breman JG, Measham AR, et al., eds. *Disease control priorities in developing countries*. Washington (DC): The International Bank for Reconstruction and Development/The World Bank/Oxford University Press; 2006.
- 4 WHO. *Ending the neglect to attain the sustainable development goals: a road map for neglected tropical diseases 2021–2030*. 2020.
- 5 Casulli A. New global targets for NTDs in the WHO roadmap 2021–2030. *PLoS Negl Trop Dis*. 2021;15(5):e0009373.
- 6 Jia T-W, Melville S, Utzinger J, King CH, Zhou X-N. Soil-transmitted helminth reinfection after drug treatment: a systematic review and meta-analysis. *PLoS Negl Trop Dis*. 2012;6(5):e1621.
- 7 Anderson RM, Turner HC, Truscott JE, Hollingsworth TD, Brooker SJ. Should the goal for the treatment of soil transmitted helminth (STH) infections be changed from morbidity control in children to community-wide transmission elimination? *PLoS Negl Trop Dis*. 2015;9(8):e0003897.
- 8 Anderson RM, Truscott JE, Pullan RL, Brooker SJ, Hollingsworth TD. How effective is school-based deworming for the community-wide control of soil-transmitted helminths? *PLoS Negl Trop Dis*. 2013;7(2):e2027.
- 9 Coffeng LE, Bakker R, Montresor A, de Vlas SJ. Feasibility of controlling hookworm infection through preventive chemotherapy: a simulation study using the individual-based WORMSIM modelling framework. *Parasit Vectors*. 2015;8(1):541.
- 10 Clarke NE, Clements ACA, Doi SA, et al. Differential effect of mass deworming and targeted deworming for soil-transmitted helminth control in children: a systematic review and meta-analysis. *Lancet*. 2017;389(10066):287–297.
- 11 WHO. *Crossing the billion: lymphatic filariasis, onchocerciasis, schistosomiasis, soil-transmitted helminthiases and trachoma: preventive chemotherapy for neglected tropical diseases*. 2017.
- 12 Pullan RL, Halliday KE, Oswald WE, et al. Effects, equity, and cost of school-based and community-wide treatment strategies for soil-transmitted helminths in Kenya: a cluster-randomised controlled trial. *Lancet*. 2019;393(10185):2039–2050.
- 13 Ásbjörnsdóttir KH, Ajjampur SSR, Anderson RM, et al. Assessing the feasibility of interrupting the transmission of soil-transmitted helminths through mass drug administration: the DeWorm3 cluster randomized trial protocol. *PLoS Negl Trop Dis*. 2018;12(1):e0006166.
- 14 Clarke NE, Ng-Nguyen D, Traub RJ, et al. A cluster-randomised controlled trial comparing school and community-based deworming for soil transmitted helminth control in school-age children: the CoDe-STH trial protocol. *BMC Infect Dis*. 2019;19(1):822.
- 15 Hii SF, Senevirathna D, Llewellyn S, et al. Development and evaluation of a multiplex quantitative real-time polymerase chain reaction for hookworm species in human stool. *Am J Trop Med Hyg*. 2018;99(5):1186–1193.
- 16 Zendejas-Heredia PA, Colella V, Hii SF, Traub RJ. Comparison of the egg recovery rates and limit of detection for soil-transmitted helminths using the Kato-Katz thick smear, faecal flotation and quantitative real-time PCR in human stool. *PLoS Negl Trop Dis*. 2021;15(5):e0009395.
- 17 Le B, Clarke N, Hii SF, et al. Using quantitative PCR to identify opportunities to strengthen soil-transmitted helminth control in Solomon Islands: a cross-sectional epidemiological survey. *PLoS Negl Trop Dis*. 2022;16(5):e0010350.
- 18 Dyer CEF, Clarke NE, Nguyen D, et al. Assessing the efficacy of albendazole against hookworm in Vietnam using quantitative PCR and sodium nitrate flotation. *PLoS Negl Trop Dis*. 2022;16(10):e0010767.
- 19 WHO. *Preventive chemotherapy to control soil-transmitted helminth infections in at-risk population groups*. 2017.
- 20 Montresor A, Crompton DW, Hall A, Bundy D, Savioli L, World Health Organization. *Guidelines for the evaluation of soil-transmitted helminthiasis and schistosomiasis at community level: a guide for managers of control programmes*. World Health Organization; 1998.
- 21 Nery SV, McCarthy JS, Traub R, et al. A cluster-randomised controlled trial integrating a community-based water, sanitation and hygiene programme, with mass distribution of albendazole to reduce intestinal parasites in Timor-Leste: the WASH for WORMS research protocol. *BMJ Open*. 2015;5(12):e009293.
- 22 Vercruyse J, Behnke JM, Albonico M, et al. Assessment of the anthelmintic efficacy of albendazole in school children in seven countries where soil-transmitted helminths are endemic. *PLoS Negl Trop Dis*. 2011;5(3):e948.
- 23 Aw JYH, Clarke NE, McCarthy JS, et al. Giardia duodenalis infection in the context of a community-based deworming and water, sanitation and hygiene trial in Timor-Leste. *Parasit Vectors*. 2019;12(1):491.
- 24 Hayes RJ, Moulton LH. *Cluster randomised trials*. Chapman and Hall/CRC; 2017.
- 25 StataCorp. *Stata statistical software: release 17*. College Station, TX: StataCorp LLC; 2021.
- 26 Hughes A, Ng-Nguyen D, Clarke NE, et al. Epidemiology of soil-transmitted helminths using quantitative PCR and risk factors for hookworm and *Necator americanus* infection in school children in Dak Lak province, Vietnam. *Parasit Vectors*. 2023;16(1):213.
- 27 Anderson RM, May RM. *Infectious diseases of humans: dynamics and control*. Oxford University Press; 1992.
- 28 Bartlett AW, Traub R, Amaral S, et al. Comparison between quantitative polymerase chain reaction and sodium nitrate flotation microscopy in diagnosing soil-transmitted helminth infections. *Am J Trop Med Hyg*. 2021;105(5):1210–1213.