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# Effects of Annual Mass Treatment with Ivermectin for Onchocerciasis on the Prevalence of Intestinal Helminths

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# **ABSTRACT**

We evaluated the effect of annual ivermectin (IV) distribution for onchocerciasis on the prevalence of soil transmitted helminth (STH) infections in school-aged (SAC) and preschool-aged (PAC) children by comparing children in villages that had received treatment for 13 years to those from socioeconomically similar villages in untreated areas. We enrolled 1,031 SAC and 211 PAC for Kato Katz examinations. Treated areas had a lower prevalence of *Ascaris* (SAC: 3% versus 12%, P < 0.0001; PAC: 3% versus 10%, P = 0.012; PAC: 1% versus 8%, P = 0.019), but not hookworm (SAC: 38% versus 42%, P = 0.20; PAC: 21% versus 27%, P = 0.30). The prevalence of *Ascaris* or *Trichuris* in treated areas was below the WHO threshold for mass antihelminthic treatment (MDA), but not for hookworm. We conclude that benzimidazole MDA in IV treatment areas is indicated to effectively control hookworm.

# INTRODUCTION

The soil transmitted helminths (STH), primarily *Ascaris lumbricoides*, hookworms (*Necator americanus*, and *Ancyclostoma duodenale*), and *Trichuris trichiura*, are highly prevalent in Nigeria, as in most of sub-Saharan Africa<sup>.1–4</sup> They are responsible for significant morbidity and mortality worldwide, causing an estimated loss of 39 million disability adjusted life years (DALYs). This disability burden is greater than that due to malaria (35.7 million DALYs), the comparison, STH are among the most neglected of the "neglected tropical diseases." The STH infections disproportionately affect those living in the most resource poor settings, where the infections' effects contribute to the continued cycle of poverty. Although the ultimate goal involves elimination of STH infections through improved hygiene and sanitation, achieving this goal will take time and considerable resources. In the meantime, reductions in morbidity and mortality can be achieved through mass treatment programs, similar to those in place for onchocerciasis and lymphatic filariasis. Treatment of intestinal helminths has been shown to have beneficial effects on growth and nutrition, child mortality, and school performance. 8-10

The most recently published World Health Organization (WHO) guidelines (2006) recommend treatment of all school-aged children (SAC) twice a year in communities where the prevalence of infection exceeds 50% in a sample of SAC, and once a year if the prevalence is 20–50%. With a prevalence of less than 20%, treatment on a case by case basis is recommended. The guidelines also recommend treatment of preschool-aged children (PAC) but do not give guidance on how often. The Global Target put forth by the World Health Assembly Resolution 54.19 in 2001 is that at least 75% of all school-aged children at risk of morbidity from schistosomiasis and STH should be regularly reached and treated by the year 2010. As we have reached this deadline, it is imperative to look at how current programs aimed at other tropical diseases, such as onchocerciasis, may be helping to meet this goal.

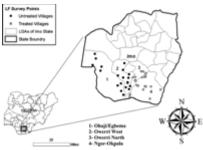
Ivermectin (IV) causes paralysis and death of many nematode parasites. <sup>12</sup> It is the drug of choice for onchocerciasis and is routinely used as a mass treatment agent in onchocerciasis and lymphatic filariasis treatment programs, supplied by a generous donation from Merck & Co. Ivermectin was included in the list of WHO recommended drugs<sup>11</sup> for treatment of STH (except hookworms) in 2002, but has since been replaced on the list by the benzimidazole class of anthelmintics. <sup>13</sup> A few studies in humans have shown ivermectin to be efficacious against *Ascaris* (cure rates 78.4–100%)<sup>14-17</sup> and *Strongyloides* (cure rates 83–84%),<sup>15, 18</sup> but have had mixed results for the treatment of *Trichuris* (cure rates 11%, 35.2%, 85%)<sup>14, 15, 17, 19</sup> and hookworm (cure rates from 0% to 42%). <sup>15-17, 19, 20</sup> Previously published studies have shown an initial decrease in prevalence of STH infection immediately following therapy with IV or albendazole, with a gradual rise in prevalence of infection back to baseline over several months to a year. <sup>14, 21</sup> A study by Ranque and colleagues<sup>22</sup> using quarterly IV therapy for a year found a significant decrease in the prevalence of STH infection after the first round of therapy, with no subsequent additional decrease. Moncayo and colleagues<sup>23</sup> studied the impact of

twice per year IV therapy in northeastern Ecuador on STH. However, no studies have been done to look at the effect on the prevalence of STH following annual mass drug administration (MDA) with IV for onchocerciasis that occurs at approximately 40 million treatments per year in Africa. <sup>24</sup>

The use of annual IV distribution to prevent morbidity caused by onchocerciasis began in Imo state, Nigeria, in 1993 and reached statewide in 1995 following a national onchocereciasis assessment survey that showed high prevalence of onchocerciasis throughout much of southeastern Nigeria. <sup>6, 25</sup> This program was begun as a combined effort of the State Ministry of Health, the Lions Clubs, and the River Blindness Foundation. For a time it also received support from the African Program for Onchocerciasis Control (APOC). The distribution program is now run by the State Ministry of Health in conjunction with The Carter Center. Imo State is composed of 27 districts known as local government areas (LGAs). On the basis of the 1995 disease mapping for onchocerciasis, 18 of the 27 LGAs in Imo state receive annual IV therapy because onchocerciasis is a public health problem there. In affected villages, all village members taller than 90 cm are treated annually with a dose (based on height) of approximately 150 mg/kg. 11 The remaining nine LGAs were determined not to have sufficient onchocerciasis prevalence to warrant mass ivermectin treatment. There is no mass treatment programs with benzimidazoles in Imo State directed specifically for STH. Therefore, Imo state provides an ideal setting in which to evaluate the effect of long-term (13 year) annual therapy with ivermectin on the prevalence of STH infections. The important programmatic question to be answered is whether a benzimidazole needs to be added in areas where the African IV-based annual MDA program for onchocerciasis is active to more effectively control STH.

# **METHODS**

**Sampling methodology.** From July to August, 2008, we performed a cross-sectional survey of STH prevalence in Imo state, Nigeria. We used a stratified sampling procedure to choose 40 villages, 20 treated and 20 untreated villages (Figure 1). We first selected four LGAs of similar ecology (SES, rainfall, soil type); two (Owerri North and Ngor-Okpala) from the areas where all village members taller than 90 cm are offered treatment annually, and two (Ohaji-Egbema and Owerri West) from areas where no systematic antiparasitic therapy is given, matching villages to be sampled as closely as possible for those factors likely to affect STH prevalence. We selected villages that were rural and poor, having the greatest likelihood of high STH prevalence and being the most similar one to another. In the untreated areas we used a random sampling procedure to select 10 villages in each LGA to be surveyed. There are no school based or mass treatment programs with either IV or benzimidazoles in these villages. In the treated areas, we used the IV treatment coverage figures for the last several years to choose 10 villages in each LGA with the highest ivermectin coverage. Coverage in treated villages averaged 65% of total population (range 24–89%) over the period from 2001 to 2005, improving to 81% (range 73–92%) from 2006 to 2008. In these villages, IV is distributed only by community directed distributors; no school-based distribution programs exist.



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FIGURE 1. Imo State Nigeria, showing treated and untreated local government areas (LGAs) and villages <u>Table 1</u>. Demographic characteristics of untreated and treated children.

**Subject enrollment.** Two groups of children were enrolled: 1) school-aged children (SAC) from 10 to 16 years of age and 2) preschool-aged children (PAC) who were over 2 years of age and less than 90 cm, to ensure that they had never been treated. Collection cups were distributed to 25–30 SAC to allow (after attrition) for a minimum sample of 25 SAC. Collection cups were distributed up to 10 PAC from each village who fulfilled the enrollment criteria (over 2 years and less than 90 cm); generally, fewer than 10 children meeting these criteria were available. The SAC were accepted for enrollment if they were in primary school grades 4, 5, or 6, or junior secondary (JS) school grades 1, 2, or 3 (equivalent to grades 7, 8, 9). The SAC were excluded from the study if they were less than 10 years or greater than 16 years of age or if they were pregnant. Only one SAC and one PAC from a given household were enrolled. Each child who received a cup had

his/her name recorded. The child or child's guardian was instructed to put a walnut sized amount of feces (size showed with a rock) of his or her stool from the next morning into the collection cup using a wooden stick, which was provided. The child/guardian was also instructed to wash his/her hands with soap and water afterwards (noting that this should always be done after defecation). The specimen cups were collected the following day, at which time data were recorded on the survey participant's gender, age, whether the child had taken ivermectin in the previous year, history of passing worms, latrine use, and whether they wore shoes regularly. Height was recorded by measurement against a calibrated pole, weight was recorded using a scale, and mid-arm circumference was measured with a tape measure. All children who returned with stool collection cups were enrolled; those who did not return were called using the previous day's list. If less than 25 children of those who originally received cups failed to deliver samples, additional cups were distributed to those who thought they could provide "on the spot" delivery of fecal specimens until we had collected at least 25 samples from the village. If children did not know their age, it was estimated based on school grade (children entering grade 4 were estimated at 10 years, grade 5 at 11 years, etc. Children who had completed JS3 were estimated at 15 years).

**Laboratory methods.** The samples were placed in a box with ice packs and returned immediately to the laboratory located at The Carter Center Southeastern Program Office Headquarters in Owerri, Nigeria. Samples were processed by the modified Kato-Katz method<sup>26</sup> within 10 hours of collection, and slides were read within 60 minutes of processing by one of five experienced laboratory technicians by light microscopy (400x). Three slides were prepared from each sample, to increase the likelihood of detecting light infections. Egg counts for Ascaris, hookworm, Trichuris, and Schistosoma mansoni were recorded quantitatively and expressed as eggs per gram (epg) by multiplying the egg counts by 24. The presence of other intestinal helminths was documented qualitatively for each slide. The egg count for each species of parasite was read only from the first slide on which that parasite was found. For quality control, all positive slides were immediately confirmed as positive by a second technician. At the end of the day, slides from 20% of patients were reread by a second technician. The technician performing the quality control at the end of the day was blinded to the results of the first reader. There was never more than 10% difference in egg counts between the first and second reader, and no slides were identified as positive by one reader but negative by the other. Intensity of infection was defined per WHO guidelines. <sup>27</sup> Infection with *Ascaris* was considered light with < 5,000 epg, moderate with 5.000–49.999 epg, and heavy with ≥50.000 epg. Infection with Trichuris was considered light with < 1,000 epg, moderate with 1,000– 9,999 epg, and heavy with≥10,000 epg. Infection with hookworm was considered light with < 2,000 epg, moderate with 2,000–3,999 epg, and heavy with  $\geq$ 4,000 epg.

**Treatment.** All infected children identified during the survey process were treated with 400 mg of albendazole. One child was infected with *S. mansoni* and was treated with praziquantel.

**Statistical methods.** Data were analyzed with EpiInfo for Windows (CDC, Atlanta, GA) and SAS (version 9.1, Cary, NC). Egg count data were not normally distributed, but were

skewed toward low egg counts. For this reason, logarithmic transformation and geometric means were calculated for fecal egg density using antilog-1 where x = number of eggs/gram feces and n the number of persons tested. The non-parametric Kruskal Wallis test was used to test whether the difference in geometric means was significant. For univariate analyses statistical significance was determined using  $\chi^2$  test. Multivariate logistic regression was performed using generalized estimating equations and an exchangeable working correlation structure to adjust for correlation within villages. The results of the multivariate logistic regression were reported as odds ratios (OR) and Wald  $\chi^2$  P values. Multivariate models for infection with each type of infection were adjusted for gender, residence in a treatment area, playing barefoot, and reported presence of latrine. Data were considered statistically significant with P value < 0.05. Sensitivity, the ability of a test to correctly identify diseased individuals, and specificity, the ability of a test to correctly identify individuals without disease, were calculated for indicators of disease reported by the children.

# RESULTS

A total of 1,031 school-aged children and 211 preschool-aged were enrolled: 537 school-aged and 109 preschool-aged from the untreated areas and 494 school-aged and 102 preschool-aged from the treated areas. There was no statistically significant difference in the percent of males in treated and untreated groups. There was no difference in the mean age, height, weight, or arm circumference of the two groups (Table 1). Overall, 46% of surveyed children in the untreated area were infected with intestinal helminths, whereas only 40% of children in the treated areas were infected; this difference was statistically significant (P = 0.024) (Table 2).

View this table:	TABLE 1				
[in a new window]	Demographic characteristics of untreated and treated children*				

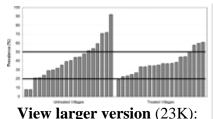
View this table:	TABLE 2			
[in a new window]	Prevalence of infection in children in untreated and treated			
	villages			

**School-aged children.** Among school-aged children, there was a significant difference in the prevalence of infection with *Ascaris* and *Trichuris* in the treated compared with untreated areas (Table 2). There was no difference in the prevalence of hookworm infection (Table 2). The geometric mean egg count per gram stool was also significantly higher in untreated versus treated MDA samples for *Ascaris* and *Trichuris*, but not for hookworm (*Ascaris*: 1.42 [95% CI 0.97–1.97] versus 0.17 [95% CI 0.08–0.28], *P* < 0.0001; *Trichuris*: 0.56 [95% CI 0.39–0.76] versus 0.27 [95% CI 0.16–0.38], *P* = 0.01; hookworm: 7.48 [95% CI 5.76–9.62] versus 5.84 [95% CI 4.43–7.62], *P* = 0.18). The range of *Ascaris* eggs per gram of stool in untreated versus treated areas was 0–20,760 eggs per gram (epg) compared with 0–5,664 epg, 0–5,208 epg versus 0–312 epg for *Trichuris*, and 0–6,888 versus 0–7,944 for hookworm. In all groups, most of the infections were of light intensity; heavy infections were seen only with hookworm infection. Only one child infected with *Ascaris* had a moderate intensity infection in the treated area (6.7%), compared with 18 (26.9%) with moderate intensity infections in the

untreated area (P = 0.07). Only light intensity *Trichuris* infections were seen in the treated areas, whereas 3 children (5.7%) had moderate intensity infections in the untreated area (P = 0.55). Heavy infections with hookworm occurred in 3.2% and 1.8% of children in the treated and untreated area, and moderate intensity infections occurred in 2.1% and 2.7% of children in the treated and untreated area (P = 0.77). Only one child was found to be infected with *S. mansoni*, none were infected with *Schistosoma hematobium*.

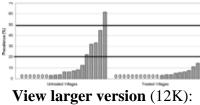
**Preschool-aged.** Among preschool-aged children, who had never received IV even in treated areas, there was a significant difference in the prevalence of infection with *Trichuris* in the treated (1%) compared with untreated areas (8%) (P = 0.019). The difference in the prevalence of Ascaris infection approached statistical significance (3% versus 10%, P = 0.051). There was no difference in the prevalence of hookworm infection (21% versus 27%, P = 0.30). Geometric mean egg counts per gram of stool among all children 2–4 years of age were higher in untreated versus treated MDA; this difference was significant for Ascaris and Trichuris but not for hookworm (Ascaris: 0.91 [95% CI 0.30–1.83] versus 0.24 [95% CI 0–0.59], *P* = 0.04; *Trichuris*: 0.39 [95% CI 0.12–0.73] versus 0.05 [95% CI 0–0.14], P = 0.01; hookworm: 2.44 [95% CI 1.30–4.14] versus 1.74 [95% CI 0.82–3.12], P = 0.36). The range of eggs per gram of stool in untreated versus treated areas was 0-18,648 for Ascaris, compared with 0-6,000 in the treated region, 0–312 versus 0–96 for *Trichuris*, and 0–624 versus 0–1,632 for hookworm. Three children had Ascaris infection of moderate intensity; one in the treated and two in the untreated areas, respectively (P = 1). The infections with *Trichuris* and hookworm were all of light intensity. There was one case of infection with S. mansoni.

Effects of ivermectin on the need for community treatment. From a community perspective, nearly all the villages required at least school-based therapy for hookworm; six of the untreated and four of the treated villages had prevalence of infection > 50% and so qualified for MDA for the entire community (P = 0.597) (Figure 2). None of the treated villages, however, qualified for MDA for either Ascaris or Trichuris, whereas five and four of the untreated villages qualified for MDA for Ascaris and Trichuris, respectively (P = 0.047 for Ascaris and P = 0.106 for Trichuris, Ascaris data shown in Figure 3). Of these, one village qualified for community-wide MDA for a prevalence of *Ascaris* > 50%.



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FIGURE 2. Prevalence of hookworm infection among school-aged children by village. This graph shows the prevalence of hookworm infection by village. The black lines indicate the WHO recommended thresholds for school-aged (20%) and community-wide treatment (50%). There was no statistically significant difference in the number of villages requiring mass drug administration (MDA) for hookworm between treated and untreated areas.



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FIGURE 3. Prevalence of *Ascaris* infection among school-aged children by village. This graph shows the prevalence of Ascaris infection by village. The zeros represent villages with no infections. The black lines indicate the WHO recommended thresholds for school-aged (20%) and communitywide treatment (50%). The difference in number of villages requiring mass antihelminthic treatment (MDA) between treated and untreated areas was statistically significant.

**Factors contributing to infection.** Among SAC, untreated children had a statistically significant increase in the OR for infection for Ascaris (P = 0.001) and Trichuris (P = 0.001)0.024) but not for hookworm (P = 0.5) in univariate analysis (Table 3). Playing barefoot was not associated with a statistically significant change in the OR for any of the infections. There was a slightly higher prevalence of latrines in the treated community, however, this was not found to be statistically different from the untreated communities. Living in a house where there was no latrine was associated with an increased risk of hookworm infection, but not Ascaris or Trichuris infection. Children who reported always using the latrine had a lower risk of infection with hookworm and Trichuris than did children who lived in a house where there was no latrine. Children who reported using the latrine sometimes were similarly protected against hookworm, whereas children who lived in a house with a latrine but reported never using it had no protection from hookworm infection (Table 3). Latrine usage was not associated with a change in infection with Ascaris. Similar results were seen when multivariate analysis was used to control for community level similarities (Table 3).

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#### TABLE 3

[in a new window] Univariate and multivariate analysis of factors contributing to infection among SACs

Among untreated PAC, living in a treatment area resulted in a statistically significantly decreased OR for infection for Ascaris and Trichuris, but not for hookworm, in both univariate and multivariate analysis (Table 4). Among PAC, neither gender nor living in a house with a latrine was significantly associated with infection. Because of the small number of cases of Trichuris, we were unable to include the absences of latrine as a factor in the model. Because of the extremely high percent of children who played barefoot (> 95% in all groups), we were unable to model this risk factor for any of the infections.

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#### TABLE 4

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Univariate and multivariate analysis of factors contributing to infection among PACs

**History of worms.** A history of passing worms was associated with an increased risk of infection, both overall and for each specific type of infection. However, it was neither a sensitive nor specific marker of infection. Overall, sensitivity was 48% and specificity was 67% for detecting any infection; sensitivity was higher when only the untreated group was considered (sensitivity 58%, specificity 63%), but lower in the treated group (sensitivity 35%, specificity 72%). Sensitivity was highest for Ascaris infection (sensitivity 64%, specificity 63%). Sensitivity for detection of hookworm and *Trichuris* was similar: for hookworm sensitivity was 48% and specificity was 66%, for *Trichuris* sensitivity was 51% and specificity was 62%. Similar results were obtained if the PACs were excluded.

# DISCUSSION

We evaluated the effect of annual IV distribution to prevent morbidity caused by onchocerciasis on the prevalence of STH infections in SAC and PAC by comparing STH prevalence in areas that had received annual treatment of 13 years to untreated areas. Annual community-wide MDA with ivermectin was associated with a decreased prevalence and intensity of infection of both *Ascaris* and *Trichuris* infection in both SAC and PAC, but did not decrease the prevalence or intensity of hookworm infection in either age group. This is in line with previous data showing a poor efficacy of ivermectin against hookworm. <sup>10-14</sup> Although IV treatment did not completely rid the communities of *Ascaris* or *Trichuris*, the prevalence of infection was lowered sufficiently so that all the treated communities were below the WHO recommended threshold for treatment of these parasites. It is interesting to note that MDA clearly affected the force of transmission, because even the PACs, who would never have received IV, had a lower prevalence of infection in the treated areas.

This study showed that hookworm infection remains a public health problem in rural Nigerian communities being treated with IV MDA for onchocerciasis. Annual IV MDA was insufficient to decrease community-wide prevalence of hookworm below WHO mass treatment thresholds. On the basis of our findings, the addition of a benzimidazole to annual IV therapy appears indicated. In addition, an expanded benzimidazole MDA program is needed in areas that are not currently receiving IV MDA for onchocerciasis. Single-dose therapy with albendazole is more effective (72%) than mebendazole (15%) against hookworm. In areas where annual distribution of ivermectin is ongoing, "piggybacking" an additional albendazole tablet into the program would increase the cost per person by the cost of a tablet of albendazole, 27, 29, 30 and costs related to importation and transports to intervention areas. However, expanding coverage to new areas where piggybacking with other MDA programs could not occur would have a much higher incremental cost as the cost of drug delivery would need to be considered. Twice per year treatments in communities where STH prevalence is > 50% (per WHO recommendations) would dramatically increase costs in both areas.

Moncayo and colleagues<sup>23</sup> conducted a similar study to this one in northeastern Ecuador in areas where IV had been distributed largely on a 6 month (semiannual) schedule as an intervention for onchocerciasis for 15 to 17 years. Their study showed a significant impact only on the prevalence and intensity of infection of *Trichuris*, finding no effect on either *Ascaris* or hookworm infection. This is curious because several studies have shown ivermectin to be efficacious against *Ascaris* (cure rates 78.4–100%). They too noted an effect even among PACs who were ineligible for IV therapy, and called, as do we, for the addition of albendazole to the onchocerciasis IV MDA program to enhance impact against STH.

Although other studies have found a significant impact of STH infections on growth and development, <sup>19, 31-33</sup> we were unable to show a significant difference in mean height, weight, mid-upper arm circumference, or body mass index (BMI) in the treated versus

untreated groups. Although we found a significant impact of ivermetin on the prevalence of *Ascaris* and *Trichuris*, there was no difference in the prevalence or intensity of infection with hookworm in the treated versus untreated areas. The lack of efficacy against hookworm, the STH most associated with causing anemia and intestinal inflammation, explains the lack of difference in growth parameters.

The current WHO guidelines advocate STH treatment of PACs, but provide no specific recommendations as to how often this treatment should be given. In addition, treatment of PACs is not addressed in the World Health Assembly Resolution. Although school-aged children typically have a higher worm burden than preschool-aged children, PACs are still at risk for infection, as shown in our study and others. <sup>3, 34-36</sup> Very few studies have been done looking at the negative effects on growth and development in the PAC age group. However, given the rapid rate of development it is conceivable that infections in this age may be more deleterious to subsequent growth and cognitive development than infections suffered in later childhood. The available data shows that deworming of STH-infected PAC improves their health and allows them to reach their cognitive potential. <sup>34</sup>, Although treatment of SAC may decrease the prevalence in the rest of the community, including in PAC, treatment in this age still appears warranted if age appropriate antihelminthic preparations can be manufactured.

Although intermittent chemotherapy provides a useful tool to combat STH infections, long-term control and eradication of STH infections will require significant improvements in hygiene and sanitation. Reporting consistent latrine use was associated with a decreased rate of infection with both hookworm and *Trichuris*, although not with *Ascaris*. This is in keeping with a study by Sorensen and others, <sup>38</sup> which also found that latrine ownership had more impact on hookworm infection than on *Trichuris* or *Ascaris*. Nguyen and others <sup>39</sup> also found that hookworm infection, but not *Ascaris* or *Trichuris*, was associated with lack of a closed latrine (OR = 2.0). Other studies have found improved sanitation alone to be an insufficient control measure for intestinal helminth infections, but have not noted a differential effect with different intestinal parasites. <sup>40, 41</sup>

Reported use of shoes was not associated with a lower prevalence of hookworm infection; although this has previously been reported to be protective against hookworm infection. <sup>42</sup> However, so few children reported shoe use that this finding is probably not noteworthy. In addition, those wearing shoes used "flip-flops," which do not provide much protection from soil, especially in the rainy season.

A history of passing worms was associated with an increased risk of infection, both overall and for each specific type of infection. However, it was neither a sensitive nor specific marker of infection. This suggests that questioning children regarding passing of worms should not be used in place of stool examinations to determine whether villages are in need of treatment of STH.

A weakness of this study was that the baseline level of STH infection in these villages was not obtained before initiating MDA. Although the villages sampled were matched as closely as possible for factors that would be likely to influence the prevalence of STH

infection, we cannot be sure that the treated villages had the same initial prevalence and intensity of STH as the untreated villages. However, given the similar hookworm findings between areas, and the known properties of ivermectin against the STHs, we think our assumption that *Ascaris* and *Trichuris* levels were similar before IV interventions began is reasonable.

Further studies are indicated to determine if annual IV and albendazole will suffice to control STHs in IV-treated onchocerciasis areas where STH prevalence is > 50%, so averting the need to invest in an additional treatment round. In addition, preschool-aged children are at risk for STH infections and better studies and age appropriate drug preparations are needed to guide recommendations for STH treatment in this age group.

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