


# Effectiveness of Deworming with Single-Dose Albendazole for Preschool-Aged Children in the Dominican Republic

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## Abstract

**Background.** The World Health Organization recommends biannual deworming with single-dose albendazole for all children over 1 year in regions where soil-transmitted helminths (STH) are endemic. There are limited data from the Dominican Republic (DR) on the effectiveness of deworming programs. **Methods.** Between January and June 2019, we enrolled 63 preschool-aged children at a community clinic in the DR. Participants received albendazole at enrollment. Stool samples were collected and examined for parasites at enrollment, 2 to 4 and 12 to 16 weeks post-albendazole. Caregivers were surveyed on home hygiene practices and children's symptoms. **Findings.** At enrollment, 1 or more parasites were noted in 89% of samples. *Ascaris lumbricoides* (68%) was the most common species, followed by *Entamoeba histolytica* (35%) and *Giardia intestinalis* (8%). Two-to-four weeks post-albendazole, fewer than half of those with *A. lumbricoides* infections at baseline had cleared the infection. STH symptoms significantly improved between enrollment and 2 to 4 weeks. By 12 to 16 weeks after treatment, *A. lumbricoides* infections were as high as baseline. **Interpretation.** Although limited by size and available technology, our study contributes data on STH in the DR. Single-dose deworming with albendazole did not reduce *Ascaris lumbricoides* infections in our sample. As STH are the most common neglected tropical diseases and negatively impact children's health globally, further studies on both effective deworming programs and interventions to prevent STH are needed.

## Keywords

soil-transmitted helminthiases, preventive chemotherapy, *Ascaris lumbricoides*, DR, Caribbean, Latin America

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## Lay Summary

Soil-transmitted helminthiases (STH) are one of the most common parasitic infections in the world. In the short term, STH cause gastrointestinal and systemic symptoms and in the long-term they may negatively impact children's growth and development. The World Health Organization recommends regular deworming of children over 1 year of age who live in endemic areas. Data on STH in the Dominican Republic are limited although STH are common among children in Latin

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America and the Caribbean. We studied the effectiveness of a deworming program for low-income, preschool-aged children in Dominican Republic using a single dose of albendazole. We examined stool samples and symptoms on enrollment, and then at 2 to 4 weeks and 12 to 16 weeks post-albendazole. Almost 90% of participants had 1 or more parasites in their stool on enrollment. The most common parasite identified was *A. lumbricoides*, a soil-transmitted helminth. There was no decrease in *A. lumbricoides* infections following albendazole therapy, although symptoms of STH did improve. Our findings suggest that STH and other intestinal parasite infections are very common among low-income children in Dominican Republic and that effective prevention, control, and eradication measures are still needed.

## Introduction

Soil-transmitted helminthiasis (STH) are the most common neglected tropical diseases, impacting an estimated 1.5 billion people globally.<sup>1</sup> STH are spread through human feces, and their persistence is intimately linked with poverty and inadequate water and sanitation infrastructure in low- and lower-middle income countries (LMIC).<sup>1-3</sup> The global burden of STH fell 42% between 1990 and 2010, but these gains were disproportionately experienced by upper-middle-income countries, and by wealthier households within LMIC.<sup>4,5</sup> The World Health Organization (WHO) recently published updated targets for elimination of STH as a public health concern over the next decade.<sup>6</sup>

Children are at particular risk for STH, and the proposed roles of STH in anemia, poor growth, and impaired neurocognitive development among infected children are the topic of ongoing investigation and debate.<sup>1,7-9</sup> School-based deworming programs are a common prevention and control strategy globally but exclude at-risk preschool children.<sup>10</sup> Results of a recent meta-analysis and large Kenyan randomized controlled trial suggest that mass (ie, community-wide) deworming is more effective in treating STH in children than targeted or school-based programs.<sup>11,12</sup>

Current WHO guidelines recommend annual or biannual deworming with single-dose albendazole or mebendazole for children ages 12 to 60 months in endemic areas.<sup>1</sup> Single-dose albendazole therapy has proven effective in reducing *Ascaris lumbricoides* infections in studies from multiple regions.<sup>13-16</sup> However, the emergence of anti-helminthic drug resistance, especially in settings where parasites are under selection pressure due to deworming programs, remains a concern.<sup>17</sup> The WHO recommends assessing the effectiveness of on-going deworming programs if chemotherapy appears

ineffectual, or when a program has operated for 4 or more years.<sup>18</sup> Even when effective, rapid reinfection after treatment is the norm.<sup>19,20</sup>

Despite the high regional prevalence of STH in Latin American and the Caribbean, studies from the Dominican Republic (DR) are few.<sup>21,22</sup> Limited data suggest STH are very common among children in the DR.<sup>22</sup> A global study of equity in deworming programs indicated that lower-income DR households, where the need is greatest, are under-accessed.<sup>5</sup> To our knowledge, there have been no published studies on the efficacy of deworming programs in the DR. We present here the results of our prospective cohort study on STH in preschool-aged Dominican children from low-income neighborhoods. We aimed to identify the primary species responsible for STH in our cohort, and to determine the effectiveness of our biannual deworming program.

## Methods

### Study Design and Enrollment

We consecutively enrolled children between 24 and 60 months of age who presented to the *Niños Primeros en Salud* (NPS) clinic in Consuelo, San Pedro de Macoris Municipality, Dominican Republic between January and June 2019. NPS provides free primary care, including nutritional monitoring and support, to all children under the age of 5 years who live in the 8 most impoverished Consuelo neighborhoods.<sup>23</sup> Any child within the aforementioned age range who presented for care at NPS or was visited as part of routine community-based health check-ups, had no chronic medical conditions, and was not ill enough to warrant immediate referral to a higher level of care, was eligible. No children screened during enrollment were deemed ineligible. On enrollment, every child provided a stool sample and then received a single dose of albendazole. Study staff surveyed the child's primary caregiver regarding the child's participation in prior deworming programs and the presence of current symptoms that could be attributable to STH infection (ie, diarrhea, abdominal pain, malnutrition, malaise, and stunted development). The surveys also asked about access and practices related to household and personal hygiene.<sup>24</sup> A nurse collected anthropometric data for every participant and nutrition status was classified per WHO definitions (WHO weight-for-age z-score < -2, WHO height-for-age z-score < -2, WHO weight-for-height z-score < -2).<sup>25,26</sup> Children provided follow-up stool samples approximately 2 to 4 weeks and 12 to 16 weeks after receiving albendazole. Caregivers were asked about children's symptoms at both follow-up visits.

## Stool Sample Collection and Examination

Participants' caregivers were given a sterile receptacle to collect stool either at the clinic or at home; stool collected at home was returned to the clinic by the caregiver shortly after collection. One sample was collected per participant at each time point. Clinic laboratory staff without knowledge of participants' symptoms prepared a slide with a sample of stool mixed with Lugol solution, and then used a light microscope to examine the slide for adult parasites, larvae, and amoeba and giardia cysts.

## Treatment of Parasite Infections

Children received 1 dose of albendazole (400 mg, per WHO guidelines) on enrollment.<sup>1</sup> Albendazole was administered under direct observation by a clinic nurse. Metronidazole was prescribed for any child with amoebiasis (35 mg/kg/day every 8 hours for 7 days) or giardiasis (25 mg/kg/day every 8 hours for 5 days) at any time point.

## Statistical Analysis

STH and symptoms were compared across time points using chi-squared tests unless cell sizes were <5, for which Fisher's exact test was used. All analyses were performed in Stata SE version 14.2.

## Ethical Approval

Approval for this study was provided by the Servicio Nacional de Salud Hospital Infantil Dr. Robert Reid Cabral, Santo Domingo, República Dominicana.

## Results

### Participant Characteristics and Home Hygiene Practices

We enrolled 63 (39%) of 161 eligible children. All eligible families who did not enroll reported difficulty collecting stool for the baseline assessment. Stool samples were available for all participants at enrollment, 68% at 2 weeks, and 89% at 12 weeks. Median time to follow up between enrollment and the second study visit (Week 2-4) was 25.5 days (IQR 18, 33); median time to follow up between enrollment and the third study visit (Week 12-16) was 112 days (IQR 104.5, 122.5). Table 1 summarizes enrolled participants' demographic variables and home hygiene practices. The median age at enrollment was 39 months and 54% were female. Approximately 10% were underweight, 8% were stunted, and 10% were wasted. All participants old enough to be eligible for NPS's deworming program prior to enrollment had

**Table 1.** Demographic Characteristics and Home Hygiene Practices.<sup>a</sup>

Characteristics	N=63
Age in months, median (IQR)	39 (32.48)
Female sex, No. (%)	34 (54)
Underweight, <sup>b</sup> No. (%)	6 (10)
Stunted, <sup>c</sup> No. (%)	5 (8)
Wasted, <sup>d</sup> No. (%)	6 (10)
Child received albendazole for deworming previously, No. (%)	61 (97)
Household drinking water source, No. (%) <sup>e</sup>	
Bottled water only	59 (94)
Bottled and unboiled tap water	4 (6)
Caregiver washes hands with soap, No. (%)	61 (97)
Before preparing food	58 (92)
After using the toilet	53 (84)
After washing child/changing child's diaper	60 (95)
Child's feces disposed in:	
Toilet	39 (62)
Latrine	3 (5)
Open air	1 (2)
Unknown <sup>f</sup>	20 (32)

Abbreviation: IQR, interquartile range.

<sup>a</sup>All hygiene practices per caregiver report.

<sup>b</sup>WHO weight-for-age z-score < -2.

<sup>c</sup>WHO height-for-age z-score < -2.

<sup>d</sup>WHO weight-for-height z-score < -2.

<sup>e</sup>Almost 70% of caregivers purchased bottled water of the same brand. No differences in infection prevalence based on bottled water brands were noted.

<sup>f</sup>Data available for all participants. "Unknown" includes "bedpan" and "diaper" as these responses do not indicate location of final disposal.

received albendazole at least annually. Most caregivers reported bottled water as their household's only drinking water source, with almost 70% purchasing bottled water from the same local distributor; 6.4% also reported consuming unboiled tap water. More than 80% of caregivers reported washing their hands with soap prior to cooking, after using the toilet, and after changing a child's diaper. Clear information about fecal disposal was available for 68% of participants. Of those, almost 62% of caregivers reported that their child used a flush toilet, with only 1 reporting open air defecation.

### STH Infections

Table 2 summarizes the number and type of parasite infections at each time point. At enrollment, 89% of participants had parasite-positive stool. *A. lumbricoides* (68%) was the most common species identified, followed by *Entamoeba histolytica* (35%) and then *Giardia intestinalis* (8%). More than 22% of participants had co-infection with both *A. lumbricoides* and either *E. histolytica* or *G. intestinalis*. There was no significant

**Table 2.** Soil-Transmitted Helminthiasis and Other Parasite Infections by Time Point and Species, No. (%)<sup>a</sup>

	Enrollment (N=63)	Week 2-4 <sup>b</sup> (N=46)				Week 12-16 <sup>c</sup> (N=58)	
	Total (%)	Cleared	New	Persistent	Unavailable	Re-infected	Total (%)
None	7/63 (11)	—	3	—	2/7 (29)	—	5/58 (9)
<i>Ascaris lumbricoides</i>	43/63 (68)	9/43 (21)	14	22/43 (51)	12/43 (28)	6/9 (67)	40/58 (69)
<i>Entamoeba histolytica</i>	22/63 (35)	11/22 (50)	8	5/22 (23)	6/22 (27)	1/11 (9)	16/58 (28)
<i>Giardia intestinalis</i>	5/63 (8)	4/5 (80)	—	0/5 (0)	1/5 (20)	1/4 (25)	4/58 (7)
<i>Hymenolepis nana</i>	—	—	—	—	—	—	1/58 (2)
Co-infection with $\geq 2$ species	14/63 (22)	1/14 (7)	5	1/14 (7)	4/14 (29)	0/1 (0)	10/58 (17)

<sup>a</sup>Enrollment vs week 2 total infections compared using Fisher's exact test for any comparison where cell-size was  $< 5$  and chi-squared for all other comparisons; no comparisons had  $P < 0.05$ .

<sup>b</sup>Co-infections were defined as cleared only if all species were cleared; for 9 co-infection cases on enrollment, only 1 species was cleared by Week 2 to 4. Unavailable indicates cases in which data was available at enrollment but not at Week 2 to 4.

<sup>c</sup>Some participants who provided Week 2 to 4 samples did not provide Week 12 to 16 samples and vice-versa thus clearance/new/persistent infection cannot be clearly summarized at week 12 to 16. Reinfection is defined as the presence of parasites at Week 12 to 16 for individuals for whom complete data is available and who cleared their stool between Enrollment and Week 2 to 4.

**Table 3.** Caregiver-Reported Symptoms by Time Point, No. (%).

	Enrollment				Week 2-4			
	Ascaris only (N=29)	Amoeba/ <i>Giardia</i> only (N=13)	Co-infection (N=14)	None (N=7)	Cleared Ascaris (N=9)	Cleared Amoeba/ <i>Giardia</i> (N=15)	Persistent infection (N=37)	New infection (N=5)
Asymptomatic	5 (17)	1 (8)	1 (7)	1 (14)	3 (33)	8 (13)	11 (30)	1 (20)
Fever	9 (31)	5 (39)	2 (14)	1 (14)	1 (11)	0 (0)	4 (11)	0 (0)
Vomiting	4 (14)	2 (15)	0 (0)	1 (14)	0 (0)	0 (0)	0 (0)	0 (0)
Anorexia	13 (45)	7 (54)	3 (21)	1 (14)	4 (44)	3 (20)*	11 (30)	3 (60)
Abdominal pain	3 (10)	3 (23)	5 (36)	2 (29)	2 (22)	1 (7)	6 (16)*	1 (20)
Abdominal distension	8 (28)	5 (39)	3 (21)	2 (29)	1 (11)	3 (20)	8 (22)*	2 (40)

Enrollment totals vs week 2 to 4 totals compared using Fisher's exact test for any comparison where cell-size was  $< 5$  and chi-squared for all other comparisons.

\* $P < 0.05$ .

Only 1 subject cleared both co-infection species between Week 0 and Week 2 to 4.

difference in the proportion of stools showing *A. lumbricoides* infections 2 to 4 weeks after albendazole therapy. Only 20% of those with *A. lumbricoides* at enrollment who provided stool at week 2 to 4 had cleared their stool following albendazole therapy. Half of those with *E. histolytica* and all with *G. intestinalis* who provided stool at week 2 to 4 cleared those species following metronidazole therapy. At week 2 to 4 there were 14 new *A. lumbricoides* and 8 new *E. histolytica* infections. By week 12 to 16, a third of those who had cleared parasites following therapy were re-infected. No participants remained parasite-free throughout the study.

### Participant Symptoms

Table 3 summarizes caregiver-reported symptoms associated with STH infection. The most common symptom

reported across time points was anorexia. Caregivers reported significantly less anorexia, and abdominal distension 2 to 4 weeks after therapy. Anorexia improved specifically in children who cleared amoebiasis or giardiasis with metronidazole. Abdominal pain and abdominal distension improved in children with persistent parasite infections at Week 2 to 4.

### Discussion

In this prospective cohort study of preschool-aged, Dominican children from a low-income community receiving biannual preventive chemotherapy for STH with single-dose albendazole, we did not find that deworming sustainably reduced the prevalence of *A. lumbricoides* infections. With fewer than half of patients with *A. lumbricoides* clearing this parasite from their



stool at 2 to 4 weeks post treatment, both albendazole resistance and rapid re-infection are possible. Our findings expand the limited data currently available on STH in the DR. To our knowledge, ours is the first study to evaluate the effectiveness of an active deworming program in the DR. The findings suggest that such programs may be less successful than hoped. Our participants are members of a key population that STH eradication efforts must reach to meet WHO targets over the next decade: impoverished children in low- and lower-middle-income countries.<sup>4-6</sup>

We did not have a large enough group of initially uninfected children to allow us to identify household hygiene practices that may be protective in this setting. Prevalence of parasite infections commonly transmitted through contaminated food, water, and environmental contamination was high in our cohort despite equally high reports of appropriate handwashing, access to flush toilets, and access to bottled water. NPS nurses and community health workers provide free public health education to the community and caregivers' answers to our questions on this topic may have been subject to social desirability bias. Water bottled and packaged for sale in the DR may not be sufficiently purified or chemically treated, and this could have contributed to parasite infections in our cohort.<sup>27</sup> Nearly 70% of caregivers reported purchasing bottled water from the same local distributor, and there were no differences in infection prevalence between consumers of different bottled water brands. Geophagia, on which we did not survey caregivers, is commonly observed among young children in Consuelo and is another likely source of parasites.

The relative prevalence of parasite species identified in our sample is similar to a prior community survey in Verón, DR, with *A. lumbricoides*, *E. histolytica*, and *Giardia* species accounting for the majority of infections.<sup>22</sup> In contrast to the Verón study, we did not identify any cases of *Enterobius vermicularis*. The apparent poor response of *A. lumbricoides* to albendazole therapy in our sample is inconsistent with findings from other studies of single-dose albendazole efficacy.<sup>13-16</sup> Albendazole resistance is still a possible explanation for the limited response to deworming in our study. Although albendazole resistance has not been documented in the DR or neighboring Haiti, regular deworming of children in both countries does place *A. lumbricoides* under considerable selection pressure.

We employed the stool processing methods available to staff at a community clinic in a low-resource setting (ie, light microscopy of unconcentrated stool) and were unable to measure ova density in eggs per gram of stool,

the preferred standard for assessing anti-helminth drug efficacy.<sup>18</sup> It is possible that parasite loads were high and that albendazole lowered the load without eliminating the infection in children with persistent infections. Our inability to measure parasite load is a major limitation of our study and raises important questions about how to best assess deworming programs at the community level.

The timescale for reinfection suggested by the literature is on the order of months, not weeks, suggesting that lack of clearance of parasites likely played a bigger role than reinfection in the sustained high rates of *A. lumbricoides* seen at the 2 to 4 week timepoint.<sup>19,20</sup> Some STH symptoms were responsive to therapy in our cohort, even in children who did not clear their infection after therapy. Although coinfection with other parasites was common and metronidazole seemed to be more effective at clearing susceptible parasites, clearance of amoebiasis and giardiasis did not fully explain the improvement in symptoms. Albendazole may have been successful at reducing the burden of parasites, and thus reducing symptoms, which our stool analysis methods may not have been sensitive enough to capture. Our conclusions regarding infection clearance and symptomatic relief following therapy are also limited by incomplete stool and symptom data at Week 2 to 4, and incomplete stool data at Week 12 to 16. Many families reported difficulty collecting the stool samples.

## Conclusions

In this small, prospective cohort study of preschool-aged Dominican children from a low-income community, parasite infections were identified in nearly all children. *A. lumbricoides*, *E. histolytica*, and *G. intestinalis* were the most common organisms identified. Deworming with single-dose albendazole had limited effectiveness at clearing *A. lumbricoides* infections, although symptoms did improve in the month following treatment. Further study is needed on STH prevention in endemic areas and on integrated eradication strategies for low-income households in particular.

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## Author Contributions

IJ: contributed to conception and design; contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy; AC: contributed to acquisition; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy; BA: contributed to acquisition, analysis, and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy; RO: contributed to analysis and interpretation; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy; RC: contributed to conception and design; contributed to acquisition; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy; AD: contributed to conception and design; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy; JC: contributed to conception and design; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy; MRH: contributed to analysis and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy; APS: contributed to conception and design; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy. EDL: contributed to conception and design; contributed to analysis and interpretation; drafted manuscript; critically revised manuscript; gave final approval; agrees to be accountable for all aspects of work ensuring integrity and accuracy.

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