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Assessing effect of sanitation and water supply coverage thresholds on STH parasitology

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Abstract

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By Graeme C. Prentice-Mott

Based on current evidence, it may be challenging to eliminate soil-transmitted helminths (STH) through preventative chemotherapy (PC) alone. There is reason to believe combining water, sanitation, and hygiene (WASH) interventions with PC may be the next step towards STH elimination. We conducted secondary analysis of impact evaluation data collected by the Kenya Medical Research Institute (KEMRI) from January to May 2018 in schools participating in a national PC program (N = 9,400 students from 100 schools). Stool samples were analyzed using the Kato-Katz technique and household WASH conditions were recorded based on student reports. We used mixed-effects log-binomial and negative binominal hurdle models to assess associations between STH prevalence/infection intensity and WASH access in school-clusters. We found increased infection intensity for hookworms for those with a private household latrine (IRR 2.00; 95% CI: 1.05, 3.81). Prevalence of STH was also highest in students for whom 60-79.9% of classmates had access to a private household latrine (PR 5.59; 95% CI: 2.13, 14.68). While estimates were imprecise, among students with a private household latrine, having at least 80% of classmates who also had a private household latrine was associated with lower infection intensity for *T. trichiuria* and hookworms (IRR_{trichiuris} 0.15; 95% CI: <0.01, 4.78 – IRR_{hookworms} 0.23; 95% CI: 0.02, 2.68). We also found prevalence of *A. lumbricoides* was lower for students if at least 67% of classmates had household water access (PR 0.05; 95% CI: 0.02, 0.19). Our findings indicate that STH reductions following PC might not be observed in communities with increased latrine access, however the study may have limitations.

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Table of Contents

Introduction	1
Methods	5
Study Design	5
Outcomes	6
Predictors	6
Community Coverage Assessment	7
Control Variables	8
Data Analysis	9
Results	13
Descriptive Statistics for STH, sanitation, and water	13
Figure 1	14
Table 1	14
Table 2	15
Multivariable Analyses	15
Table 3	16
Table 4	17
Figure 2	18
Table 5	19
Figure 3	20
Discussion	20
Strengths	23
Limitations	25
Conclusion	25
Works Cited	27
Appendix	31
A1	31
A2	31
A3	32
A4	32
A5	32
A6	33
A7	33

Introduction

Estimates from 2010 set the number of individuals infected with at least one species of Soil-Transmitted Helminth (STH) at 1.45 billion worldwide [1]. While this represents a substantial decrease from the worldwide prevalence in 1990, sub-Saharan Africa has experienced only a moderate decrease in prevalence of less than 5% [1]. Precipitated by the London Declaration on Neglected Tropical Diseases (NTD) and by large commitments from the pharmaceutical sector toward STH morbidity control, preventative chemotherapy treatment for STH was delivered in 2016 within the Africa region to 185 million pre-school-age children (pre-SAC) and school-age children (SAC) out of 273 million requiring treatment [2]. This achievement meets the target of 50% treatment coverage by 2015 and is on track to meet the 2020 target of 75% treatment coverage for SAC and pre-SAC in all target countries set forth in the WHO global NTD strategy [3].

Preventative chemotherapy (PC) using anthelmintic treatment has almost exclusively targeted SAC, in consideration for the developmental impacts STH infection presents for these age groups. The negative impacts of STH infection on child nutritional well-being and physical development have been long understood [4,5], and a recent systematic review, despite varying measures of educational performance from included studies, found evidence to suggest an association between cognitive impairments in school children and STH infection [6]. However, findings from infectious disease modelling have raised issue with STH control strategies that exclude adult populations. Unless treatment coverage is high, frequent, and includes adults, the interruption of transmission

cannot be achieved, leading to persistent morbidity control [7]. Given the incompletely understood complexities of transmission-relevant contact patterns between SAC and pre-SAC and communities at large, school-based PC alone may be unable to lead to adequate control of STH transmission [8]. This argument is supported by evidence of rapid re-infection in endemic areas following PC programs, determined largely by pre-treatment infection levels, indicating PC may be unable to alter underlying transmission factors [9]. In addition, expanding treatment beyond SAC to other at-risk groups presents challenges and has so far lagged behind [10]. The importance of expanding PC may be clearer following a trial currently underway to assess the feasibility of STH transmission interruption through community-wide PC [11]. However, when considering minimum coverages for STH control programs, additional disease modeling suggests that elimination may be achieved without total community treatment if transmission intensity remains sufficiently low, achieved through behavioral and sanitation strategies [12].

Such strategies are supported by an accumulation of evidence linking improved access to water, sanitation, and hygiene (WASH) with reductions in STH. A systematic review examining the association between STH infection and WASH found that availability and use of latrines was associated with lower odds of any STH infection, as well as for both *A. lumbricoides* and *T. trichiuria* [13]. In addition to sanitation access, water treatment through filtration or boiling, along with access or use of handwashing soap, were both found to be associated with lower odds of STH infection. In terms of specific STH species, use of piped water was found to be associated with lower likelihoods of *A. lumbricoides* and *T. trichiuria*, and handwashing before eating and after defecation was

found to be associated with lower odds of *A. lumbricoides* infections [13]. A further review and meta-analysis found sanitation use or access, when compared to no sanitation, was protective for all species of STH, though few studies were conducted in schools and no associations were found when analysis was limited to sanitation interventions [14]

In recognition of the potential of WASH efforts, the World Health Organization (WHO) issued guidance recommending complementary preventative chemotherapy programs that include WASH interventions to prevent STH infection [3]. However, there are no commonly recognized WASH intervention designs or monitoring practices across STH programs [15], and there is an incomplete evidence base for the effectiveness of combining these measures alongside PC programs or which WASH interventions should be established for STH control [16]. In support of complementary programs, the recent WASH Benefits randomized control trial found that, following three rounds of albendazole treatment, the risk of re-infection with *A. lumbricoides* was substantially lower for students in schools which received a comprehensive WASH intervention compared to students in schools with no intervention, but no such reductions were observed for other STH species [17]. The WASH for Worms (W4W) randomized control trial involving PC naïve populations in East Timor, which assessed the effect of combining a community-integrated WASH program with PC, found no differences in *A. lumbricoides* or *N. americanus* (hookworm) infection or associated morbidity between trial arms, despite recording higher latrine use and lower open defecation rates in the intervention arm compared to the control arm [18]. Through mathematical modeling, researchers have argued the lack of difference in the W4W study was due to the relatively

slower impact of WASH remaining undetectable throughout the course of a trial alongside the strong, immediate impact of PC, even though models showed certain WASH programs to have substantial long-term impacts in the years after PC had been stopped [19].

Contrary to the findings in the W4W trial, increased proportions of households with accessible latrines would be expected to play an important role regarding the presence of infective STH eggs in the environment. *A. lumbricoides* eggs, for example, require embryonic gestation in the environment before becoming infective, meaning that expelled eggs are not immediately infective but, after becoming infective, can remain so for several months [20,21]. Given the transmission dynamics of STH, the reinfection of school children who have undergone anthelmintic treatment may well depend on the proportion of households in the child's community that are able to separate fecal waste from the environment through use of latrines. In support of the importance of this type of community sanitation access, recent evidence assessing trachoma and stunting suggest community coverage thresholds for sanitation are more important than individual household sanitation for these outcomes [22,23].

In this study, we used cross-sectional data collected in 2018 from 100 schools in Kenya to quantify associations between STH infection and community and household-level water and sanitation coverage. We hypothesized that with this type of community WASH access, and in particular sanitation, we would observe reduced levels of STH infection for individuals where community WASH access was high.

Methods

Study Design

We utilized data collected from schools within the Kenyan National School-Based Deworming Programme (KNSBDP), which, since 2012, has provided albendazole treatment for STH infection to all school-age children within targeted sub-counties based on the prevalence and intensity of infection [24]. Detailed methods for the data collection and stool microscopy can be found elsewhere [25]. The program is implemented by the Kenyan Ministry of Education, Science and Technology and the Kenyan Ministry of Health with integration into existing Kenyan national policy [26]. The Kenyan Medical Research Institute (KEMRI) has conducted monitoring and evaluation (M&E) of the program concerning its target to reduce prevalence of moderate to heavy infection to below 1.0%. From the period of 2012 to 2017, repeated cross-sectional surveys were carried out in a sample of schools participating in KNSDP, originally selected with two-stage sampling from within districts stratified by geography and anticipated endemicity [25,27]. In 2018, KEMRI began a new phase of M&E, surveying 100 schools purposively selected based on endemicity in year 5 of M&E. From within each school, 18 children were randomly sampled, 9 girls and 9 boys, from each of six classes, including Early Childhood Development (ECD) class and classes 2-6. For most schools, sampling totaled approximately 108 children [25,27]. Data collected in 2018 from these 100 schools were used for all analyses in this study.

Outcomes

Stool samples were collected from selected children in each school, from which duplicate slides were examined by separate microscopy technicians who characterized STH infection intensity using the Kato-Katz thick smear technique with a 41.7 mg template [27]. Eggs per gram (epg) were then recorded as the product of eggs counted on the slide and a standard conversion factor of 24 [27]. For this study, STH intensity for each species was estimated using the average epg count of both slides. This was accomplished by summing the counts of both slides and including an offset term equal to the log number of slides in all count models. The presence of any STH for prevalence measures was classified as an unconverted egg count greater than zero from either slide for any STH species.

Predictors

In order to obtain information about WASH conditions in children's homes, trained enumerators administered a survey questionnaire to sampled children at school. These interviews included questions regarding the presence of a latrine in the child's home, whether the latrine was private or shared, as well as the child's usual defecation location and whether a latrine was used for the child's most recent defecation. The child was also asked to characterize the main drinking water source in his/her home from a list of options including piped/tap, borehole/well, various surface water options, and bottled water. The enumerator also recorded whether the child was wearing shoes on the day of the survey visit, whether the child reported having taken anthelmintic treatment in the

past year, and whether the child reported soil-eating behavior. The enumerator conducted spot observations at school of WASH conditions, characterizing whether latrines were usable or not and noting their number, the availability of drinking water on the day of the survey visit, the main source of drinking water for students, and whether handwashing stations were available for students to use near the latrines.

Community Coverage Assessment

Variables for community-level sanitation and water were created following the design in Garn et al [22]. For each individual child, a value was assigned for the proportion of classmates sampled from the same school who reported having access to either household water supply or household sanitation, as defined below. For a given child, aggregation of these community-level estimates excluded that child, because inclusion would produce artificial correlation between individual-level and community-level variables.

A high proportion of children reported having a latrine accessible at home; however, many of these latrines were shared with other households. Current evidence suggests sharing latrines may be associated with increased diarrheal disease [28,29]. Furthermore, sharing sanitation facilities has been identified as a factor associated with both *A. lumbricoides* infection [30] and increased open defecation among household members [31]. In Kenya, location of a household's latrine off premise has been associated with increased STH infection [32]. This may be due to shared sanitation acting as an environmental reservoir for STH, which would support arguments that shared sanitation can increase transmission [33]. Additionally, based on the range of estimates for

community-level sanitation inclusive of shared latrines, it was determined there was too little variation among sampled participants, and so focus was limited to community-level access to private household sanitation.

Community-level sanitation coverage was then defined as the proportion of a child's classmates who had a private household latrine, excluding classmates who reported any open defecation, and community-level household water supply coverage was defined as the proportion of a child's classmates with household access to either piped/tap or borehole/well water. To determine meaningful thresholds for community-level water and sanitation coverage variables, locally estimated scatterplot smoothing was fitted to STH egg counts and binary STH presence with community coverage proportions as continuous predictors, with local linearity and a smoothing parameter of 0.7 to determine the distance between points to be fit together (A1). This produced graphical representations of the level of STH prevalence or egg count across values for community water/sanitation coverage, from which were discerned visual trends representing potential non-linear threshold effects. According to these discerned trends, cut-points values for community-level coverage were selected to create four different levels of community coverage, with consideration for maintaining adequate sample size within each level (A2, A3).

Control Variables

Fully adjusted models included variables for enumerator-observed shoe-wearing and child-reported soil-eating behavior. Control of school-level WASH characteristics included school-level variables for whether the students had access to water from a

piped/tap or borehole/well source, and whether the school met the Kenya specific pupil to usable latrine ratio for both girls and boys, 25:1 and 30:1, respectively. County-level population density was acquired from an online source available through UNICEF and entered into models categorically, and STH endemicity in Kenya was controlled for as high versus low by county level based on STH mapping [34].

Data Analysis

All multi-variable and adjusted analyses were carried out in R, version 3.5.2 [35], with use of statistical mixed modeling packages lme4 [36] and glmmTMB [37]. Estimates of STH infection intensity using epg counts are understood to follow a negative binomial distribution [21], and so negative binomial mixed models with random intercepts for each school were used, with estimates expressed as incident rate ratios (IRR). For STH prevalence overall and by species, log-binomial mixed models with random intercepts for each school were used, with estimates expressed as prevalence ratios (PR). For both STH prevalence and infection intensity by species, full models were constructed in order to characterize the combined effects of community- and household-level water/sanitation. Specified levels of community coverage were parameterized using indicator variables for each level above the reference lowest level. Following this parameterization, interaction effects were modeled using a δ term for the product of household water/sanitation access and each level of community water/sanitation access. Assessment of these interaction terms was then performed using likelihood ratio tests comparing full models and models without interaction terms, first jointly for water and sanitation together, and then, if significant, separately for both (A5, A6). For each modeled outcome y , the full model

with combined interaction effects can be expressed as follows, with b_{0i} representing random intercepts at each school and q and p representing the separate levels of community water/sanitation:

$$\begin{aligned} \ln(y) = & (\beta_0 + b_{0i}) + \beta_1 HH \text{ san} + \beta_2 HH \text{ wat} + \sum_{q=2}^Q \beta_q \text{ Com. san} + \sum_{p=2}^P \beta_p \text{ Com. wat} \\ & + \sum_{q=2}^Q \delta_q \text{ HH san} * \text{ Com. San} + \sum_{p=2}^P \delta_p \text{ HH wat} * \text{ Com. wat} \\ & + \sum_{r=1}^R \gamma_r \text{ confounders} \end{aligned}$$

Interaction terms found to be significant were then examined at each level of community water/sanitation coverage by observing the estimated marginal means and associated default 95% confidence intervals when holding the values of household water/sanitation constant. This allowed for the observation of the effect of community sanitation, for example, among both those with a household latrine and among those without a household latrine.

Correlation and multicollinearity were assessed prior to constructing full models since community water and sanitation coverage estimates were created directly from other specified predictors. This was done by first examining the r^2 value of linear models regressing on both community level water and sanitation coverages as continuous response variables. In all cases, r^2 values were below 0.01, indicating little correlation.

Secondly, a log-binomial model was fit to binary presence of STH with community coverages as continuous predictors in order to examine variance inflation factors, which in all cases were low enough to proceed with full modeling.

Most standard negative binomial statistical regression accounts for over-dispersion in count data by introduction of a clustering parameter, where the variance of an estimated mean is a function of this added parameter. Large frequencies of zeros may also contribute to over-dispersion in count data. In order to address this, zero-truncated hurdle modeling techniques have been developed, which use mixing probability distributions to model the probability of zero counts and the conditional probability of greater-than-zero counts jointly in the same model [38]. Because STH prevalence varied greatly among schools, with prevalence estimates of less than 1% observed in some schools and as much as 30.6% observed in one school (Table 1), models were fit with zero-truncation for comparison with other models. Using mixed-effects across models, and for each species, negative binomial hurdle models fit the data according to AIC values better than either a Poisson, negative-binomial, or Poisson hurdle model (A4). This model type was used for analyses of epg count throughout, which effectively allowed for the assessment of associations between WASH characteristics and STH infection intensity, among those infected. The zero-truncated probability used for modeling epg count at the i^{th} observation within the j^{th} school is represented below:

$$p(Y_{ij} = y_{ij} | u_{ij}, \alpha, \pi_{ij}) = \begin{cases} \pi_{ij}, & y_{ij} = 0 \\ (1 - \pi_{ij}) \frac{f_i(y_{ij} | u_{ij}, \alpha)}{1 - f_i(y_{ij} | u_{ij}, \alpha)}, & y_{ij} > 0 \end{cases}$$

In the two-part model above, π_{ij} represents the logistic probability of zero at the i^{th} observation within the j^{th} school. Conditional on being greater than zero, $f_i(y_{ij}|\mu_{ij}, \alpha)$ must be scaled on the remaining probability, $1 - \pi_{ij}$, in order for probabilities from the separate distributions to sum to 1 [38,39]. Additionally, $f_i(y_{ij}|\mu_{ij}, \alpha)$ is represented by the negative binomial probability with μ_{ij} mean and α dispersion parameter for the overall model.

$$p(Y_{ij} = y_{ij}|u_{ij}, \alpha) \frac{\Gamma(\alpha^{-1} + y_{ij})}{\Gamma(\alpha^{-1})y_{ij}!} \left(\frac{\alpha\mu_{ij}}{1 + \alpha\mu_{ij}} \right)^{y_{ij}} \left(\frac{1}{1 + \alpha\mu_{ij}} \right)^{\frac{1}{\alpha}}$$

The linear equations of the logistic component of hurdle models mirrored those specified in the conditional negative binomial component within a given model as described above. While inclusion of such terms improved fit only negligibly, this model specification allowed for estimation of the zero-prevalence odds ratio given an exposure pattern of interest, effectively comparing odds of *not* having the binary STH outcome. In conditions of low prevalence, the prevalence odds ratio can approximate the prevalence ratio [40]. Following this assumption, the corresponding reciprocals of zero-prevalence odds ratios were verified against prevalence ratios estimated using log-binomial models (A7).

Results

Descriptive Statistics for STH, sanitation, and water

The final dataset used in all analyses comprised 9,400 students aged 1-21 years from 100 schools and 20 counties (Figure 1). Of these 9,400 students, 12.3% had an infection with at least one species of STH. The overall mean epg was highest for *A. lumbricoides* at 2,505.5 (SE = 6.4), followed by *T. trichiuria* and then hookworms, both with much lower overall mean epg at 126.2 (SE = 4.1) and 95.5 (SE = 4.4), respectively (Table 1).

Prevalences of STH varied dramatically across counties, with some counties exhibiting prevalence below 0.01%, and at least one county exhibiting prevalence as high as 30.6%. Of the 9,400 students, 61.2% reported access to a household latrine not shared beyond the household or compound, 31.2% reported access to a household latrine that was shared beyond the household or compound, and only 2.7% reported no access to any household latrine (Table 2). Additionally, 48.3% of students reported household access to either piped/tap or borehole/well water (Table 2).

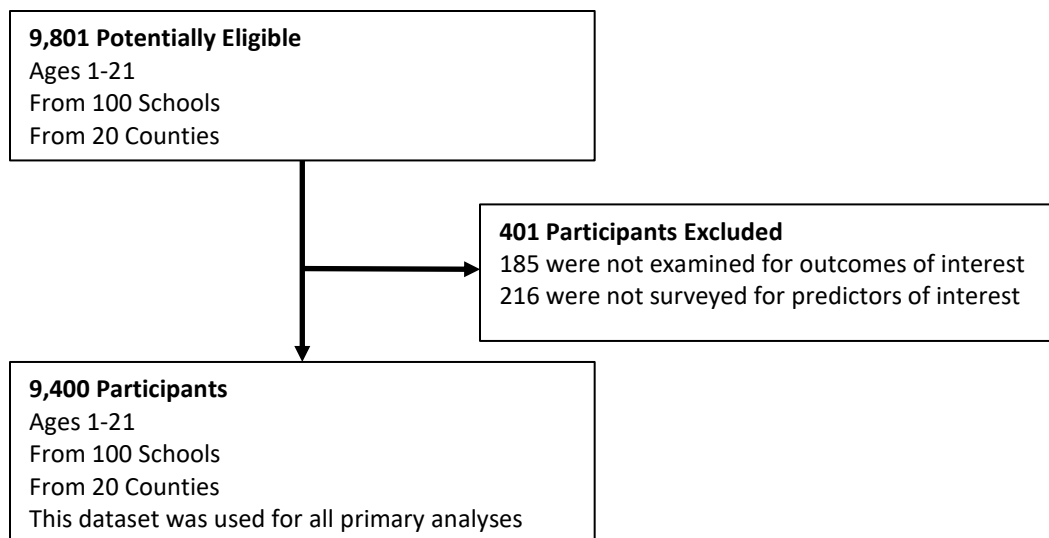


Figure 1. Study flow diagram

Table 1: Mean* EPG Count and Prevalence of Soil-Transmitted Helminth Infection by Species

Group	Students (n)	Schools (n)	STH Prevalence (%)	Treatment Coverage (%)	<i>A. lumbricoides</i>	<i>T. trichiuria</i>	Hookworms
Overall***	9,400	100	12.3	85.4	2,505.5 (6.4)	126.2 (4.1)	95.5 (4.4)
By County							
Bomet	530	5	23.4	89.2	1,687.2 (6.1)	105.1 (5.4)	<0.05
Bungoma	500	5	5.0	87.8	1,323.3 (3.9)	<0.05	36.0 (1.0)
Busia	523	5	23.5	94.3	3,518.1 (3.1)	180.2 (3.2)	72.3 (1.5)
Garissa	112	5	0.0	96.4	<0.05	<0.05	<0.05
Homabay	528	5	19.5	83.9	1,584.4 (6.7)	36.0 (2.8)	41.4 (4.4)
Kakamega	526	5	23.8	99.2	3,029.4 (5.9)	52.5 (2.9)	133.6 (1.7)
Kericho	529	5	16.8	89.8	2,250.8 (5.2)	59.9 (3.5)	110.0 (2.3)
Kilifi	491	5	3.1	96.9	12.0 (1.0)	63.3 (5.5)	36.0 (1.0)
Kisii	505	5	21.4	96.4	3,714.0 (5.7)	48.2 (3.3)	259.6 (2.4)
Kisumu	530	5	1.9	80.4	1,716.8 (33.6)	35.2 (2.8)	192.0 (1.0)
Kitui	536	5	0.0	19.8	<0.05	<0.05	12.0 (1.0)
Kwale	488	5	6.1	98.6	<0.05	253.8 (2.6)	254.8 (3.1)
Makueni	508	5	0.6	58.7	<0.05	<0.05	74.6 (1.9)
Migori	529	5	1.7	90.7	227.8 (10.0)	238.8 (13.9)	119.5 (5.0)
Mombasa	477	5	2.1	82.2	44,544.1 (1.3)	76.3 (5.6)	138.6 (1.4)
Narok	492	5	23.6	83.5	1,263.9 (8.6)	178.3 (4.3)	<0.05
Nyamira	496	5	22.4	97.0	2,810.3 (5.4)	118.7 (7.9)	10,417.8 (1.2)
Taita T.	472	5	0.2	87.7	14,208.0 (1.0)	<0.05	<0.05
Vihiga	517	5	30.6	98.3	4,521.4 (5.4)	130.6 (3.0)	151.8 (1.9)
Wajir	111	5	0.0	100.0	<0.05	<0.05	<0.05

*Mean and standard deviation are presented as the geometric mean and standard deviation, exclusive of zero values

***A. Duodenale* and *N. Americanus* are commonly grouped together as they are indistinguishable with microscopy detection methods

***Data collected by KEMRI in year 6 of M&E program of KNSBDP

Table 2: Household WASH Characteristics

Group	Private HH Latrine (%)*	Shared HH Latrine (%)	No HH Latrine (%)	Drinking Water (%)**	Handwashing Available (%)***
Overall****	61.2	36.2	2.7	48.3	62.1
By County					
Bomet	70.8	28.9	0.4	55.7	14.5
Bungoma	87.2	10.6	2.2	21.4	95.6
Busia	53.4	46.5	0.2	70.6	52.4
Garissa	15.2	83.9	0.9	72.3	92.0
Homabay	74.8	12.5	12.7	36.2	19.3
Kakamega	79.7	19.8	0.6	15.4	91.4
Kericho	86.8	12.9	0.4	58.2	5.1
Kilifi	82.9	10.0	7.1	99.0	97.8
Kisii	31.9	67.1	1.0	0.0	85.7
Kisumu	59.4	35.1	5.5	77.7	12.3
Kitui	4.7	90.7	4.7	61.2	98.9
Kwale	85.7	8.2	6.2	96.7	96.9
Makueni	25.4	72.1	2.6	40.4	94.5
Migori	33.8	64.3	1.9	10.6	79.0
Mombasa	76.7	22.4	0.8	99.0	52.4
Narok	86.4	12.4	1.2	27.9	17.5
Nyamira	27.6	71.8	0.6	6.9	69.2
Taita Taveta	67.0	32.4	0.6	78.2	30.9
Vihiga	81.4	18.6	0.0	4.8	94.8
Wajir	64.0	36.0	0.0	100.0	93.7

*Household access to latrine not shared by another household/compound

**Household access to either piped/tap or borehole/well water

***Bin/container available in household to wash hands after defecation which has water at least some of the time

****Data collected by KEMRI in year 6 of M&E program of KNSBDP

Multivariable Analyses

In the results from fully adjusted models, there were few associations between STH and household-level access to water or sanitation, with the exception of hookworms, where increased epg counts among students with hookworm infection were associated with household access to sanitation (IRR 2.00; 95% CI: 1.05, 3.81) and household access to water (IRR 2.34; 95% CI: 1.00, 5.50) (Table 3).

Table 3: Overall association between household latrine/water access and STH prevalence and infection intensity, conditional on infection, by species

Household Latrine Access*			Household Water Access**		
	PR (95% CI)	IIR (95% CI)		PR (95% CI)	IIR (95% CI)
Prevalence (Any)					
Without Access	1		Without Access	1	
With Access	0.99 (0.88, 1.12)		With Access	1.08 (0.94, 1.25)	
Ascaris					
Without Access	1	1	Without Access	1	1
With Access	0.92 (0.79, 1.06)	0.90 (0.72, 1.13)	With Access	1.14 (0.96, 1.36)	0.86 (0.64, 1.16)
Trichuris					
Without Access	1	1	Without Access	1	1
With Access	1.21 (0.98, 1.51)	0.76 (0.53, 1.10)	With Access	0.99 (0.79, 1.25)	0.87 (0.58, 1.30)
Hookworm					
Without Access	1	1	Without Access	1	1
With Access	1.27 (0.78, 2.06)	2.00 (1.05, 3.81)	With Access	1.31 (0.74, 2.32)	2.34 (1.00, 5.50)

*Household access to latrine not shared by another household/compound

**Household access to either piped/tap or borehole/well water

Overall associations between community water and sanitation coverages, estimated using fully-adjusted models, were unexpected. The prevalence of any STH infection was higher in students within areas of increased community sanitation coverage in comparison to students within the group of lowest community sanitation coverage, where less than 40% of a student's classmates had household sanitation access. This difference was greatest in students for whom 60-79% of classmates had household sanitation access (PR 5.59; 95% CI: 2.13, 14.68) (Table 4). Similarly, for both *A. lumbricoides* and *T. trichiuria*, prevalence was higher in areas of increased sanitation coverage, with the greatest difference in the 3rd coverage level (PR_{ascaris} 5.72; 95% CI: 1.80, 18.12) (PR_{trichuris} 15.05; 95 CI: 2.69, 84.32) (Table 4). In contrast to sanitation, students in groups with increased community water coverage had lower prevalence of any STH compared to students within the reference group, for whom less than 25% of classmates had household water access. In students for whom over 67% of classmates had household water access, prevalence of any STH was 84% lower compared to students in the reference group, for whom less than 25% of classmates had household water access (PR 0.16; 95% CI: 0.06,

0.45) (Table 4). This difference was also true for the prevalence of *A. lumbricoides* specifically (PR_{ascaris} 0.16; 95% CI: 0.06, 0.45) (Table 4). Estimates of the overall association between community water/sanitation coverages and STH infection intensity among students with infections were characterized by large confidence intervals that in most cases included estimates of null association. However, students infected with hookworms in the second community water coverage group, for whom 25-47.9% of classmates had household water access, had increased infection intensity in comparison to students from the lowest coverage group (IRR_{hookworm} 7.86; 95% CI: 1.35, 45.71) (Table 4). This association reversed in the group of highest community water coverage, given that infection intensity was lower for students with hookworm infection for whom over 67% of classmates had household water access (IRR_{hookworm} 0.16; 95% CI: 0.02, 1.09) (Table 4).

Table 4: Association between community-level water/sanitation access and STH prevalence and infection intensity, conditional on infection, by species

Community Sanitation Coverage*			Community Water Coverage**		
	PR (95% CI)	IRR (95% CI)		PR (95% CI)	IRR (95% CI)
Prevalence (Any)					
<39.9%	1		<24.9%	1	
40-59.9%	3.76 (1.22, 11.61)		25-47.9%	0.32 (0.11, 0.92)	
60-79.9%	5.59 (2.13, 14.68)		48-66.9%	0.37 (0.13, 1.09)	
80-100%	5.53 (2.17, 14.14)		67-100%	0.16 (0.06, 0.45)	
Ascaris					
<39.9%	1	1	<24.9%	1	1
40-59.9%	3.25 (0.83, 12.75)	1.63 (0.83, 3.17)	25-47.9%	0.26 (0.08, 0.88)	2.00 (0.98, 4.08)
60-79.9%	5.72 (1.80, 18.12)	1.51 (0.82, 2.77)	48-66.9%	0.33 (0.10, 1.11)	1.56 (0.80, 3.07)
80-100%	5.14 (1.66, 15.90)	1.34 (0.72, 2.49)	67-100%	0.05 (0.02, 0.19)	2.09 (0.91, 4.79)
Trichuris					
<39.9%	1	1	<24.9%	1	1
40-59.9%	11.73 (1.89, 72.85)	1.15 (0.16, 8.07)	25-47.9%	0.58 (0.12, 2.84)	0.77 (0.17, 3.42)
60-79.9%	15.05 (2.69, 84.32)	0.56 (0.08, 3.96)	48-66.9%	0.13 (0.02, 0.84)	0.41 (0.07, 2.59)
80-100%	6.89 (1.35, 35.27)	0.70 (0.08, 5.74)	67-100%	0.29 (0.07, 1.31)	1.59 (0.34, 7.48)
Hookworm					
<39.9%	1	1	<24.9%	1	1
40-59.9%	1.73 (0.33, 9.13)	4.06 (0.70, 23.50)	25-47.9%	0.64 (0.14, 2.87)	7.86 (1.35, 45.71)
60-79.9%	4.65 (0.98, 22.13)	1.05 (0.23, 4.92)	48-66.9%	0.30 (0.05, 1.92)	0.74 (0.18, 3.12)
80-100%	2.85 (0.59, 13.79)	0.80 (0.13, 5.03)	67-100%	0.31 (0.07, 1.39)	0.16 (0.02, 1.09)

*Percentage of classmates with household access to latrine not shared by another household/compound

**Percentage of classmates with household access to either piped/tap or borehole/well water

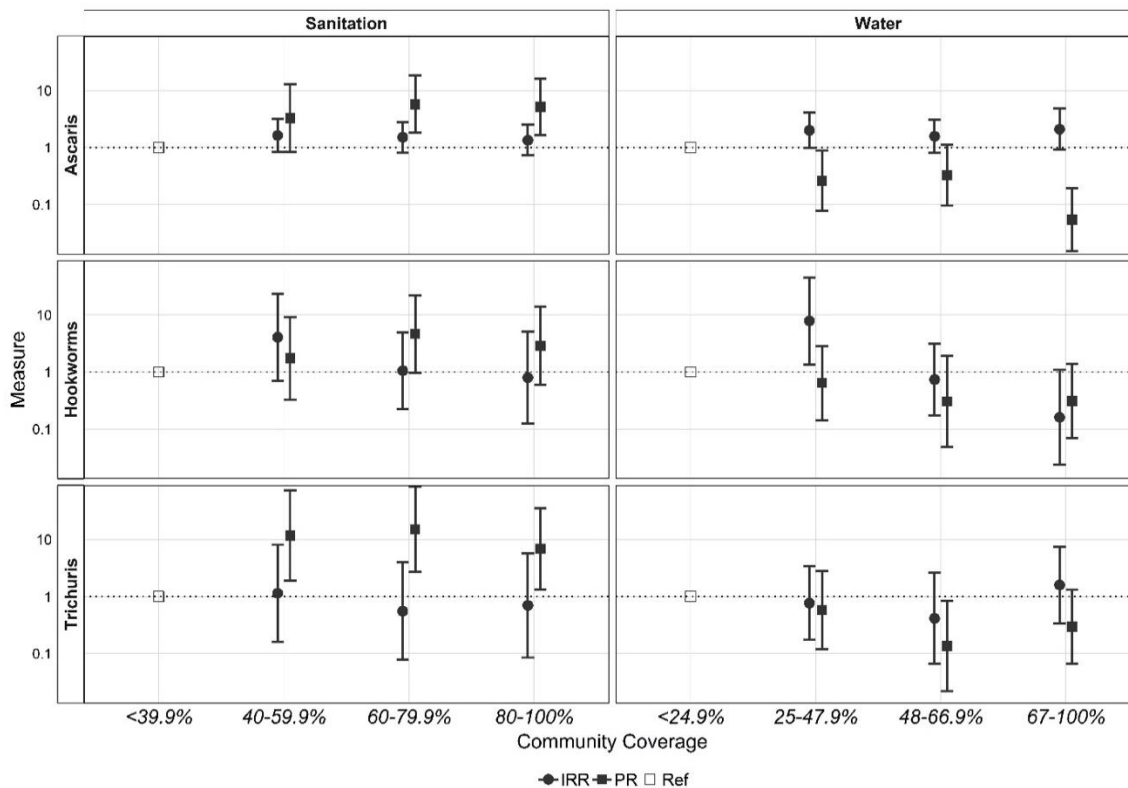


Figure 2: Overall multi-variable association between community-level water/sanitation access and STH prevalence and infection intensity, conditional on infection, by species. PR is the Prevalence Ratio with 95% CI for the prevalence of STH, and IRR is the Incident Rate Ratio with 95% CI for the infection intensity, conditional on STH infection. Reference group is students for whom less than 40% of classmates have access to household latrine, or for whom less than 25% of classmates have access to household water

The results of likelihood ratio tests of interaction terms between community and household sanitation access, and between community and household water access, indicated that both of these interaction terms contributed to the model fit when included in models for *T. trichiuria* and hookworms (A4, A5). However, estimates of the association between infection intensity and any one specific community water/sanitation coverage, when considered among individuals with or without water/sanitation access, were also characterized by wide confidence intervals that included estimates of null association.

Table 5: Association between community-level water/sanitation access and STH prevalence and infection intensity, conditional on infection, by species, among both students with household water/sanitation access and among students without household water/sanitation access

Community Sanitation Coverage*		Community Water Coverage**	
IRR (95% CI)		IRR (95% CI)	
<i>T. Trichiuria</i>			
With HH Latrine		With HH Water	
<39.9%	Ref	<24.9%	Ref
40-59.9%	0.24 (0.01, 6.08)	25-47.9%	2.84 (0.45, 18.02)
60-79.9%	0.12 (<0.01, 3.47)	48-66.9%	0.45 (0.05, 4.31)
80-100%	0.15 (<0.01, 4.78)	67-100%	4.34 (0.74, 25.55)
Without HH Latrine		Without HH Water	
<39.9%	Ref	<24.9%	Ref
40-59.9%	3.21 (0.31, 33.02)	25-47.9%	0.82 (0.18, 3.78)
60-79.9%	0.81 (0.08, 8.23)	48-66.9%	1.56 (0.16, 14.84)
80-100%	2.86 (0.18, 44.36)	67-100%	2.71 (0.40, 18.30)
<i>Hookworm</i>			
With HH Latrine		With HH Water	
<39.9%	Ref	<24.9%	Ref
40-59.9%	1.02 (0.09, 11.45)	25-47.9%	31.71 (2.94, 342.49)
60-79.9%	0.27 (0.03, 2.43)	48-66.9%	1.36 (0.13, 14.00)
80-100%	0.23 (0.02, 2.68)	67-100%	0.25 (0.02, 2.66)
Without HH Latrine		Without HH Water	
<39.9%	Ref	<24.9%	Ref
40-59.9%	24.76 (2.80, 218.95)	25-47.9%	1.38 (0.22, 8.79)
60-79.9%	6.12 (1.01, 37.14)	48-66.9%	0.88 (0.21, 3.72)
80-100%	2.97 (0.23, 37.66)	67-100%	0.30 (0.01, 8.64)

*Percentage of classmates with household access to latrine not shared by another household/compound

**Percentage of classmates with household access to either piped/tap or borehole/well water

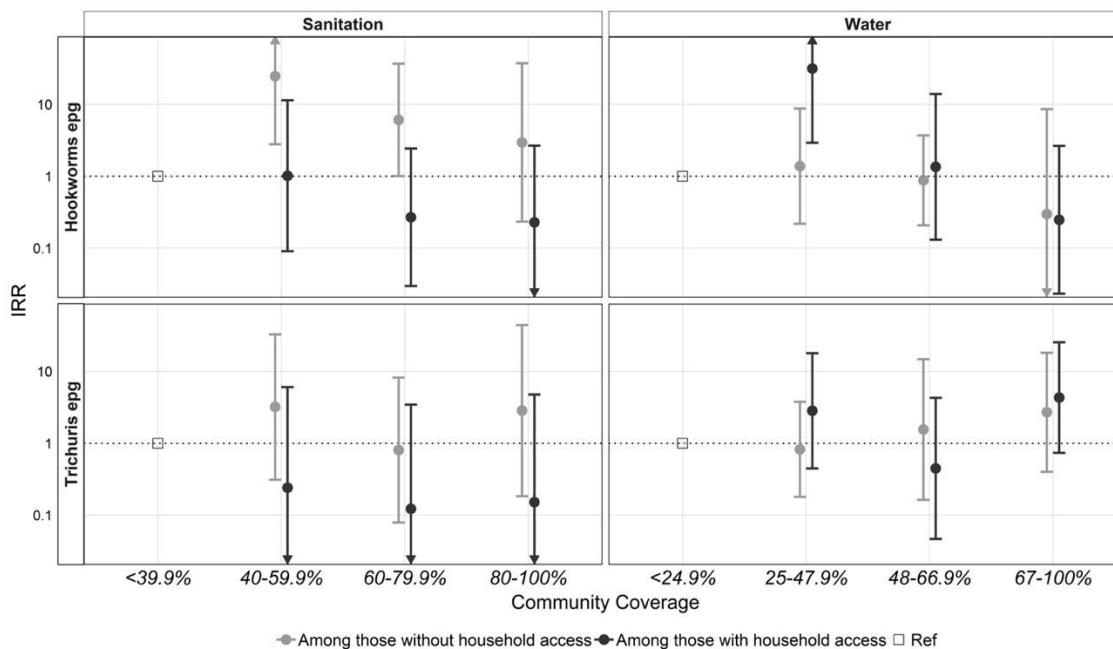


Figure 3: Multi-variable association, expressed as Incidence Rate Ratio with 95% CI, of community-level water/sanitation access and STH infection intensity, conditional on infection, for *T. trichiuria* and hookworms. Reference group is students for whom less than 40% of classmates have access to household latrine, or for whom less than 25% of classmates have access to household water

Discussion

Our findings suggest the association between STH infection and increased access to private household latrines may be complex and that, under certain conditions, communities undergoing PC where private household latrines are more common may have increased STH infection. However, where private household latrines may be a source of STH contamination, those with such latrines may benefit from having a high proportion of community members who also have private latrines for *T. trichiuria* and hookworms. On the contrary, communities where more dwellings have access to piped water supply may have reduced *A. lumbricoides* infection.

While there were few associations between STH and household-level sanitation access, those observed ran contrary to expectations. For students with hookworm infection, intensity of infection was higher in those with a household latrine not shared among other household/compounds (IRR 2.00; 95% CI: 1.05, 3.81) (Table 3). Increased STH infection was also observed in students who had a higher proportion of classmates with access to private household sanitation. The overall prevalence of any STH was higher at each community sanitation coverage threshold compared to the lowest level of access, this difference being highest for the 3rd threshold level (PR 5.59; 95% CI: 2.13, 14.68) (Table 4). Prevalences of *A. lumbricoides* and *T. trichiuria* were also higher within increased community sanitation coverage levels (Table 4). These findings may be consistent with evidence that, in rural Kenya, soil found at the entrance of household latrines is commonly contaminated with eggs of *A. lumbricoides* and *T. trichiuria* [41]. This may explain associations with STH infection and access to private latrines, given the soil around such latrines may be contacted more frequently by household members than soil surrounding shared latrines or soil at other areas used for defecation. It must also be considered that the proportion of households with private latrines may have been too high to detect any benefits of sanitation access for many school-communities in this study. A study nested within the WASH Benefits trial concluded that baseline sanitation coverages were already too high for the sanitation component of the intervention to meaningfully reduce STH contamination of soil sampled at households, given STH endemicity [42]. If such were the case in this study, any hypothesized benefit of increased proportions of household sanitation may have been too small to counteract uncontrolled confounders,

such as the presence of household animals, environmental conditions, or the conditions of the latrines themselves, none of which were available for analysis in this study.

In this study, given that household latrines were associated with increased STH prevalence and infection intensity, this association may have been somewhat mitigated by living in a community with increased proportions of household latrine access, even given the higher overall prevalence in such communities. While estimates for the association between infection intensity and community sanitation coverages among binary categories of household private latrine access were characterized by wide confidence intervals, there was a notable difference between those with and those without private household latrines. For students with a private household latrine, having at least 80% of classmates who also had private household latrine was associated with lower epg counts for both *T. trichiuria* and hookworms, compared to those for whom less than 40% of classmates had a private household latrine (IRR_{trichuris} 0.15; 95% CI: <0.01, 4.78 – IRR_{hookworms} 0.23; 95% CI: 0.02, 2.68). While the estimates themselves have wide confidence intervals, these estimates contributed to the fit of models when evaluated using likelihood ratio tests. This provides support for the argument that it may be inappropriate only to consider household-level effects of sanitation on STH. In the case of acute diarrhea and active trachoma, household latrines in poor condition may not confer the expected benefit [22,43], which may also be the case for STH. However, individuals infected with STH who have access to private household latrines may limit their contamination of environmental soil to within their household, and the benefit of this may be more

important for STH species that remain infective in the environment for shorter periods of time than *A. lumbricoides*.

Findings that prevalence of *A. lumbricoides* was lower in students for whom more classmates had household access to piped or borehole water may be consistent with evidence compiled in a systematic review of WASH and STH [13]. If at least 67% of classmates had household water access, students' prevalence of *A. lumbricoides* was greatly reduced in comparison to students for whom less than 25% of classmates had household access to water (PR 0.05; 95% CI: 0.02, 0.19).

On the whole, the direction and strength of association of both prevalence and egg count estimates were closely aligned with one another for a given specification of WASH access, with the notable exception of *A. lumbricoides* in the highest community water access coverage threshold (Table 4). Instances where estimates of prevalence are relatively low but estimates of infection intensity are relatively high might provide some indication of when reinfection is possible for populations with low prevalence. This potential for discordant estimates may support arguments for studies to report estimates of STH infection intensity in addition to prevalence.

Strengths

To our knowledge, there have been few experimental studies assessing the impact of complementing school-based PC with WASH programs, and results have so far been mixed [17,18]. Additional evidence could better inform policies of complementary

WASH interventions for STH control [16] and contribute to the establishment of WASH standards for STH control [15]. At least one experimental study underway will include secondary analyses assessing how WASH factors within study sites might impact reductions of STH following PC, however this is not a primary aim for this study [11]. Given that such studies are both time and resource intensive, observational studies can play a role in increasing evidence bases. To our knowledge, this study represents a novel analysis of community-level WASH access within the context of school-based PC. Household WASH conditions were recorded for students in 100 schools, which provided an opportunity to assess what associations water and sanitation access have with STH infection among 9,400 students, both on household and community levels, along with potential interactions between these levels.

When assessing STH within a population, in addition to prevalence, it is important to consider infection intensity, as this measure may be more relevant to transmission dynamics [12], and because STH-associated morbidity depends to some degree on the burden of worms present in a host [44]. Through use of mixed-effects negative binomial hurdle models, we were able to assess STH infection intensity among those infected. This statistical modeling technique may be a useful method for assessing STH infection intensity in populations where a large number of individuals do not have STH infection [13].

Limitations

This study had some limitations. While Kato-Katz smear slides were examined in duplicate, which adds rigor to the diagnostic process [45], this method can have limitations when used to assess multiple STH infections in the same sample and can result in false negative detections for hookworms if too much time transpires between slide preparation and examination [46]. This study was powered to detect differences in the overall prevalence of STH among all students, however it was not powered to detect cluster-level differences. An increased number of school-clusters with greater heterogeneity could improve the precision of estimates within specified community water and sanitation coverage levels, as well as allow for analysis of narrower, pre-defined intervals of these coverage levels. Additionally, student-reported household WASH conditions may be subject to limited accuracy. Ascertainment of STH epg counts was made independently of student-reported household WASH conditions. However, in this type of study, validation of student-reported conditions could be achieved through objective observation of household conditions within a sub-sample to determine if STH infection might lead to differences in student reporting accuracy. Lastly, the use of purposive sampling of schools after a 5-year course of PC may result in bias if schools which had higher baseline prevalence had been targeted for more intensive PC treatment.

Conclusion

Evidence from this study represents a point in time following several years of PC. Given also that our findings run contrary to previous studies linking latrine access and STH reductions, interpretation of these findings may have limitations. Assessment of

community level latrine access and STH outcomes following PC may require more objective characterization of household WASH access and data from a multiple year timespan including baseline data from before PC initiation. This study can be useful in designing further analyses of community WASH access using impact evaluation data from school-based PC.

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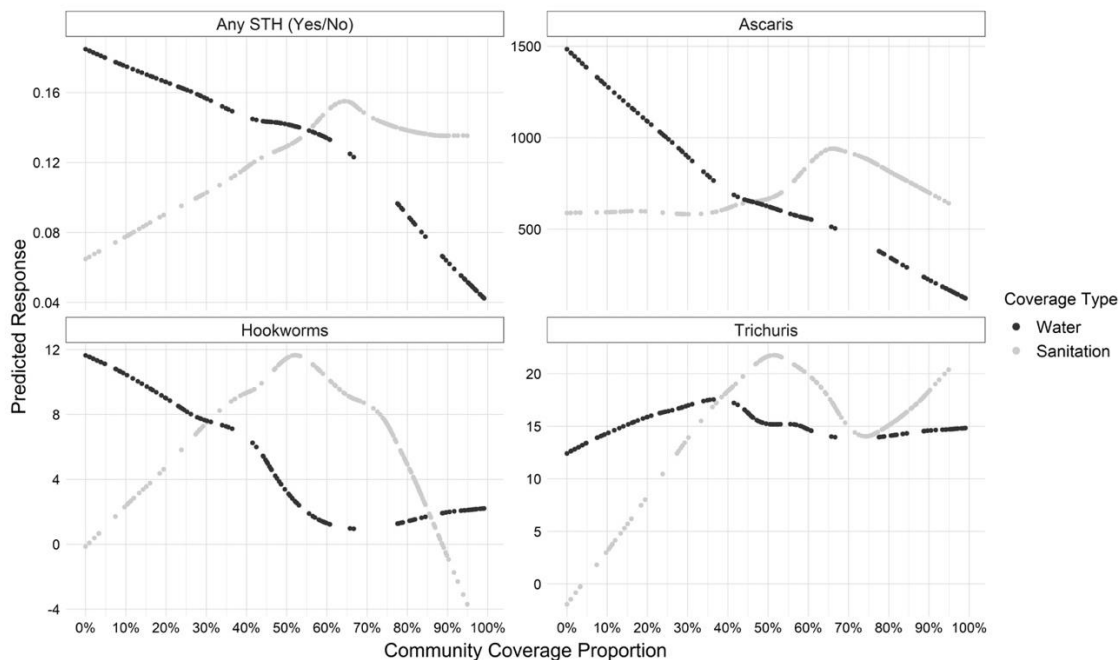
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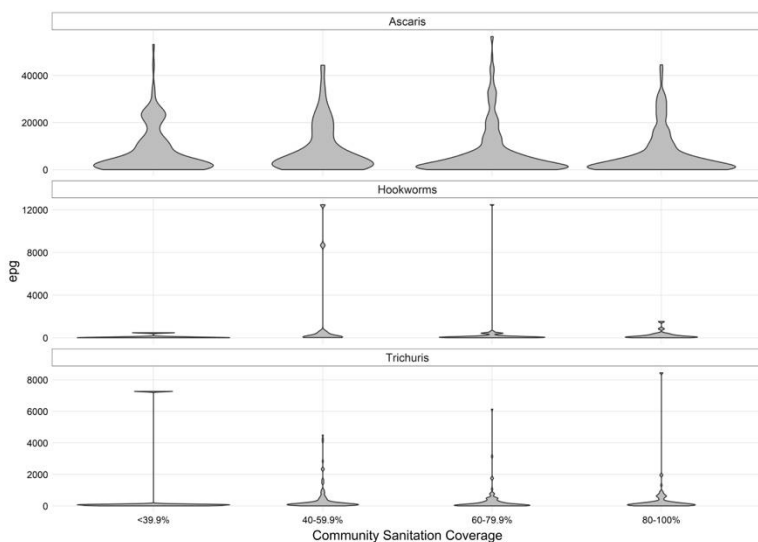
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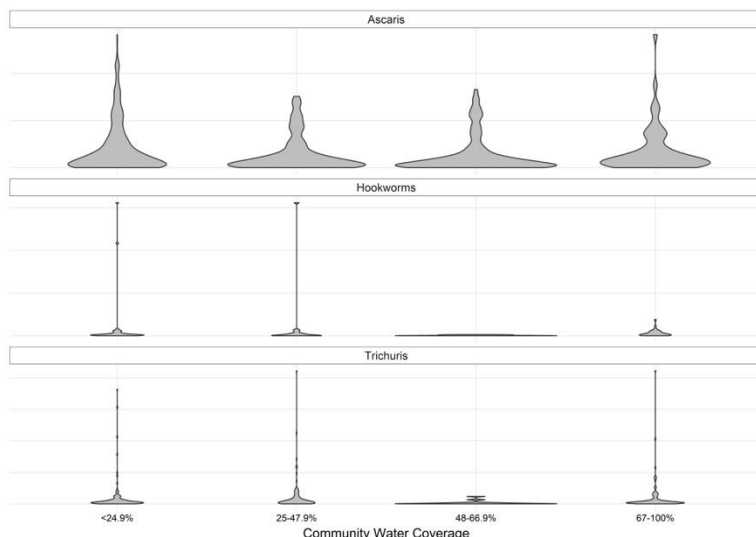
Appendix



A1. Loess smoothing of STH prevalence and epg count by species across community-level water/sanitation coverage percentages. Each point represents a summary measure of STH within a cluster of observations with similar community coverage values, and cluster closeness is determined by the specified smoothing parameter.



A2. Zero-truncated epg count by STH species across community sanitation coverage levels



A3. Zero-truncated egg count by STH species across community water coverage levels

A4. Difference in AIC comparing Poisson, negative binomial, Poisson hurdle, and negative binomial hurdle multi-level models of egg count by species

A. Lumbricoides			T. Trichiuria			Hookworm		
Model	Diff. AIC	DF	Model	Diff. AIC	DF	Model	Diff. AIC	DF
Hurdle	0	47	Hurdle	0	47	Hurdle	0	48
NegBin			NegBin			NegBin		
NegBin	1,578	24	NegBin	732	24	NegBin	118	25
Hurdle	15,665,260	46	Hurdle	360,764	46	Hurdle	78,741	47
Poisson			Poisson			Poisson		
Poisson	56,884,715	23	Poisson	1,527,363	23	Poisson	638,310	24

A5. Likelihood ratio tests of interaction terms for both community water/sanitation coverage

Model	Df	logLik	Deviance	Chisq	Chi Df	Pr (>Chisq)
Prevalence Reduced	17	-2927.6	5855.1			
Prevalence Full	23	-2922.4	5844.8	10.4	6	0.110
Ascaris Prevalence Reduced	17	-2351.2	4702.5			
Ascaris Prevalence Full	23	-2345.6	4691.2	11.3	6	0.080
Trichuris Prevalence Reduced	17	-1048.8	2097.6			
Trichuris Prevalence Full	23	-1039.4	2078.7	18.8	6	0.004
Hookworm Prevalence Reduced	17	-462.0	924.0			
Hookworm Prevalence Full	23	-460.5	920.9	3.1	6	0.794
Ascaris epg Reduced	35	-11937.9	23875.8			
Ascaris epg Full	47	-11929.9	23859.7	16.1	12	0.187
Trichuris epg Reduced	35	-3506.7	7013.4			
Trichuris epg Full	47	-3484.4	6968.8	44.5	12	<0.01
Hookworm epg Reduced	36	-1106.0	2211.9			
Hookworm epg Full	48	-1092.0	2184.1	27.8	12	0.006

In reduced models, interaction terms have been removed for both community water ~ household water and community sanitation ~ household sanitation

A6. Likelihood ratio tests of interaction terms for both community water/sanitation coverage

Model	Df	logLik	Deviance	Chisq	Chi Df	Pr(>Chisq)
Trichiuria epg Reduced (Water)	41	-3496.0	6992.0			
Trichiuria epg Full	47	-3484.4	6968.8	23.1	6	0.001
Hookworm epg Reduced (Water)	42	-1100.4	2200.7			
Hookworm epg Full	48	-1092.0	2184.1	16.6	6	0.011
Trichiuria epg Reduced (Sanitation)	41	-3494.7	6989.3			
Trichiuria epg Full	47	-3484.4	6968.8	20.5	6	0.002
Hookworm epg Reduced (Sanitation)	42	-1098.7	2197.4			
Hookworm epg Full	48	-1092.0	2184.1	13.3	6	0.038

In reduced models, interaction terms have been removed for either community water ~ household water or community sanitation ~ household sanitation

A7: Zero-prevalence odds ratio estimated from logistic component of negative binomial hurdle model, its reciprocal, and prevalence ratio estimated from log-binomial model, by STH species

	Household/Community Latrine Access				Household/Community Water Access			
	ZPOR*	P Value	Reciprocal	PR	ZPOR*	P Value	Reciprocal	PR
<i>Ascaris</i>								
No HH Access	Ref			Ref	No HH Access	Ref		Ref
HH Access	1.09	0.40	0.92	0.92	HH Access	0.80	0.06	1.25 1.14
<i>Trichuris</i>								
No HH Access	Ref			Ref	No HH Access	Ref		Ref
HH Access	0.72	0.04	1.40	1.21	HH Access	1.00	0.99	1.00 0.99
<i>Hookworm</i>								
No HH Access	Ref			Ref	No HH Access	Ref		Ref
HH Access	0.78	0.34	1.28	1.27	HH Access	0.74	0.33	1.34 1.31
<i>Ascaris</i>								
<39.9%	Ref			Ref	<24.9%	Ref		Ref
40-59.9%	0.28	0.04	3.58	3.25	25-47.9%	4.70	0.01	0.21 0.26
60-79.9%	0.16	<0.01	6.35	5.72	48-66.9%	3.28	0.04	0.30 0.33
80-100%	0.17	<0.01	6.03	5.14	67-100%	25.48	0.00	0.04 0.05
<i>Trichuris</i>								
<39.9%	Ref			Ref	<24.9%	Ref		Ref
40-59.9%	0.07	<0.01	13.42	11.73	25-47.9%	1.75	0.44	0.57 0.58
60-79.9%	0.06	<0.01	16.09	15.05	48-66.9%	8.44	0.01	0.12 0.13
80-100%	0.14	0.01	7.13	6.89	67-100%	3.74	0.05	0.27 0.29
<i>Hookworm</i>								
<39.9%	Ref			Ref	<24.9%	Ref		Ref
40-59.9%	0.58	0.44	1.73	1.73	25-47.9%	1.58	0.48	0.63 0.64
60-79.9%	0.21	0.02	4.75	4.65	48-66.9%	3.35	0.12	0.30 0.30
80-100%	0.35	0.12	2.86	2.85	67-100%	3.37	0.06	0.30 0.31

*Zero-prevalence odds ratio; reciprocal = 1/ZPOR

**Prevalence ratio estimated from log-binomial model