

1 **Domains of transmission and association of community, school, and household sanitation**
2 **with soil-transmitted helminth infections among children in coastal Kenya**

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21 **Abstract**

22 Introduction - Few studies have simultaneously examined the role of sanitation conditions at
23 the home, school, and community on soil-transmitted helminth (STH) infection. We examined
24 the contribution of each domain that children inhabit (home, village, and school) and
25 estimated the association of sanitation in each domain with STH infection.

26 Methods - Using data from 4,104 children from Kwale County, Kenya, who reported attending
27 school, we used logistic regression models with cross-classified random effects to calculate
28 measures of general contextual effects and estimate associations of village, school, and
29 household sanitation with STH infection.

30 Findings - We found reported use of a sanitation facility by households was associated with
31 reduced prevalence of hookworm infection but not with reduced prevalence of *T. trichiura*
32 infection. School sanitation coverage > 3 toilets per 100 pupils was associated with lower
33 prevalence of hookworm infection. School sanitation was not associated with *T. trichiura*
34 infection. Village sanitation coverage > 81% was associated with reduced prevalence of *T.*
35 *trichiura* infection, but no protective association was detected for hookworm infection.

36 General contextual effects represented by residual heterogeneity between village and school
37 domains had comparable impact upon likelihood of hookworm and *T. trichiura* infection as
38 sanitation coverage in either of these domains.

39 Conclusion - Findings support the importance of providing good sanitation facilities to support
40 mass drug administration in reducing the burden of STH infection in children.

41 **Author Summary**

42 Infection by whipworm and hookworm results from either ingestion of eggs or larvae or
43 through skin exposure to larvae. These eggs and larvae develop in suitable soils contaminated
44 with openly-deposited human faeces. Safe disposal of faeces should reduce transmission of
45 these soil-transmitted helminths (STH), yet evidence of the impact of sanitation on STH
46 transmission remains limited. We used data collected during a large, community-wide survey
47 to measure prevalence of STH infections in coastal Kenya in 2015 to examine the relationship
48 between sanitation conditions at home, school, and village and the presence of STH infection
49 among 4,104 children who reported attending schools. We found that sanitation access at
50 home and school sanitation coverage, but not the overall level of village sanitation coverage,
51 was protective against hookworm infection. In contrast, only high village sanitation coverage,
52 but not home or school sanitation, was protective against whipworm infection. Current STH
53 control strategies emphasise periodic deworming through mass drug administration (MDA) of
54 at-risk populations, including school-age children. Our findings highlight the need for
55 continued efforts, alongside MDA, to extend access to good sanitation facilities at homes,
56 schools, and across communities.

57

58 **Introduction**

59 In 2016, it was estimated that world-wide more than 1.5 billion people were infected with at
60 least one species of soil-transmitted helminth (STH)(1). Infection by roundworm, *Ascaris*
61 *lumbricoides*, and whipworm, *Trichuris trichiura*, results from ingestion of embryonated eggs,
62 and the hookworms, *Necator americanus* and *Ancylostoma duodenale*, infect humans through
63 skin exposure to or ingestion of larvae (*A. duodenale*) that develop in warm, moist soils from
64 eggs in openly-deposited human faeces (2, 3). Preventing human contact with excreta through
65 consistent safe disposal of faeces should reduce STH transmission, yet evidence of the impact
66 of sanitation on STH remains limited (4-6). The concept of private and public domains of
67 transmission for STH has been described previously (7, 8), but to our knowledge few studies
68 have simultaneously examined the role of sanitation conditions at the home, school, and
69 community on STH infection (9-11).

70

71 Multilevel statistical models provide a means to estimate effects of individual factors, using
72 measures of association. They can simultaneously assess general contextual effects upon
73 individual health outcomes, using measures of within-unit clustering and between-unit
74 heterogeneity (12, 13). Such models provide a useful complement to mathematical modelling
75 of transmission dynamics for examining specific effects and possible areas for intervention
76 (14). Identifying effects of sanitation within each of the domains that a child inhabits will
77 contribute to evidence for the prioritization of sanitation promotion activities alongside the
78 regular deworming of at-risk populations, including school-aged children, recommended by
79 the World Health Organization (15, 16).

80

81 Employing multilevel modelling, we investigate the relative importance of household, village
82 and school domains and estimate the association of sanitation in each domain on STH
83 infection among Kenyan children who attend school.

84

85 **Methods**

86 *Study Population*

87

88 The study took place in Kwale County on the south Kenyan coast. Data were collected during
89 a cross-sectional parasitological survey conducted between March-May 2015 as the baseline
90 for TUMIKIA, a randomised, controlled trial to evaluate the impact and cost-effectiveness of
91 school-based versus community-wide deworming on STH transmission (NCT02397772,
92 www.clinicaltrials.gov).

93

94 Study design, baseline findings, and impact have been described previously (17, 18) (Halliday
95 KE, Oswald WE, Mcharo C, Beaumont E, Gichuki PM, Kepha S, et al. Community-level
96 epidemiology of soil-transmitted helminths in the context of school-based deworming:
97 Baseline results of a cluster randomised trial on the coast of Kenya. In Press). For the baseline
98 survey, 225 households were randomly selected within 120 community units (CUs) of
99 approximately 1000 households comprising 2 to 7 villages. Among consenting households, a
100 structured questionnaire was conducted with the head of household or primary caregiver to

101 collect information on demographics, ownership of key assets, and sanitation, hygiene, and
102 water conditions. One household member (aged ≥ 2 years) was randomly selected to provide
103 a stool sample. A questionnaire was then conducted with individuals who provided samples
104 or their caregiver to collect information on deworming within the last year and observe their
105 footwear. School facility surveys were conducted across Kwale County in June 2015 and July
106 2016. During visits, student enrolment was recorded from school registers, and sanitation
107 conditions were assessed using structured observations. All data were collected on
108 smartphones running the Android operating system (Google, Mountain View, CA, USA) using
109 SurveyCTO (Dobility, Inc., Cambridge, MA, USA). Records from school and household surveys
110 were linked based on the school each child reported attending. Geographic coordinates
111 (based on WGS84 datum) were systematically collected at each household and school using
112 the smartphones' global positioning systems. Missing coordinates for 4 schools were obtained
113 from Google Maps (Google, Mountain View, CA, USA). Children were excluded *a priori* if they
114 lived in villages or attended schools in semi-arid areas unsuitable for STH transmission
115 (Halliday KE, Oswald WE, Mcharo C, Beaumont E, Gichuki PM, Kepha S, et al. Community-level
116 epidemiology of soil-transmitted helminths in the context of school-based deworming:
117 Baseline results of a cluster randomised trial on the coast of Kenya. In Press). Children were
118 eligible if they were sampled in the 2015 TUMIKIA baseline parasitological survey, aged 5 to
119 14 years, and reported attending school.

120

121 *STH infection*

122

123 Kato-Katz microscopy was used to enumerate STH eggs (*A. lumbricoides*, *T. trichiura*, and
124 hookworm) per gram of stool. For both hookworm and *T. trichiura*, our outcome was a
125 dichotomous indicator for the presence of > 0 eggs in stool samples (i.e. prevalence). *A.*
126 *lumbricoides* was not examined in detail since few cases were detected. STH infection was also
127 classified based on categories of infection intensity (19), and frequencies were tabulated
128 across categories of household, community, and school sanitation as detailed below.

129

130 *Sanitation measures*

131

132 The measure for household sanitation access was combined from reported use of a toilet
133 facility on or off the household's compound. Using all households sampled per village for the
134 TUMIKIA baseline survey, this measure of household sanitation was aggregated for village
135 sanitation coverage, as the percentage of households with reported access to sanitation.
136 During structured observations at schools, the number of latrines considered usable (not
137 assigned to teachers, locked, or with full pits) was quantified, excluding urinals, for both girls
138 and boys. School sanitation coverage was calculated as the number of usable toilets per
139 enrolled pupil, in contrast to the indicator of students per toilet (20). Village and school
140 sanitation coverage were categorised based on estimated quartiles to explore possible non-
141 linear relationships during modelling.

142

143 *Covariates*

144

145 Information on covariate specification and creation of household socioeconomic status
146 measure is described elsewhere (Halliday KE, Oswald WE, Mcharo C, Beaumont E, Gichuki PM,
147 Kepha S, et al. Community-level epidemiology of soil-transmitted helminths in the context of
148 school-based deworming: Baseline results of a cluster randomised trial on the coast of Kenya.
149 In Press). One school surveyed in 2015 was missing total enrolment, so 2016 enrolment was
150 used. For 51 schools attended by children for which we had no 2015 data, enrolment and
151 sanitation conditions from the 2016 survey were used. Environmental and sociodemographic
152 conditions hypothesized to influence STH transmission and sanitation coverage were
153 assembled in a geographic information system using ArcGIS 10.5 (ESRI, Redlands, CA, USA),
154 and values were extracted for each school and household (Halliday KE, Oswald WE, Mcharo C,
155 Beaumont E, Gichuki PM, Kepha S, et al. Community-level epidemiology of soil-transmitted
156 helminths in the context of school-based deworming: Baseline results of a cluster randomised
157 trial on the coast of Kenya. In Press). We aggregated mean continuous and mode categorical
158 values per village, using all households sampled per village.

159

160 *Ethical Approval*

161

162 The TUMIKIA trial protocol was approved by the Kenya Medical Research Institute and
163 National Ethics Review Committee (SSC Number 2826) and the London School of Hygiene &
164 Tropical Medicine (LSHTM) Ethics Committee (7177). Written informed consent was sought

165 from the household head or adult answering the household-level questionnaire and from the
166 individual selected to provide the stool sample and complete the individual-level
167 questionnaire. Parental consent was sought for individuals aged 2 to 17 years and written
168 assent was additionally obtained from children aged 13 to 17 years. All information and
169 consent procedures were conducted in Kiswahili.

170

171 *Statistical analyses*

172

173 We estimated associations between sanitation conditions in the domains of interest and
174 presence of hookworm and *T. trichiura* infection, separately, using logistic regression models
175 with cross-classified (non-nested) random effects to account for membership of children
176 within village of residence and school attended.

177

178 We fit a series of generalised mixed models (with logit link), excluding observations with
179 missing outcome or covariate information, which assumes the probability of having complete
180 data is independent of the outcome after adjusting for included covariates. First, we fit an
181 intercept-only model containing school- and village-specific random effects to quantify
182 between school and between village variation in STH infection. Next, we fit models with fixed
183 effects for sanitation conditions in each domain separately and then together in a combined
184 unadjusted model. Finally, we fit a model containing all sanitation effects, adjusting for
185 potential confounders. Confounders were selected based on existing knowledge and encoding

186 possible causal relationships in directed acyclic graphs. We then implemented d-separation in
187 DAGitty to identify minimal sufficient sets of available covariates to control to estimate effects
188 of sanitation on both hookworm (S2 Supporting Information) and *T. trichiura* infections (S3
189 Supporting Information)(21, 22). Estimation used Hamiltonian Monte Carlo sampling to
190 improve mixing and reduce auto-correlation (23). We conducted a sensitivity analysis
191 excluding outliers in and missingness of distance from child's home to reported school
192 attended.

193

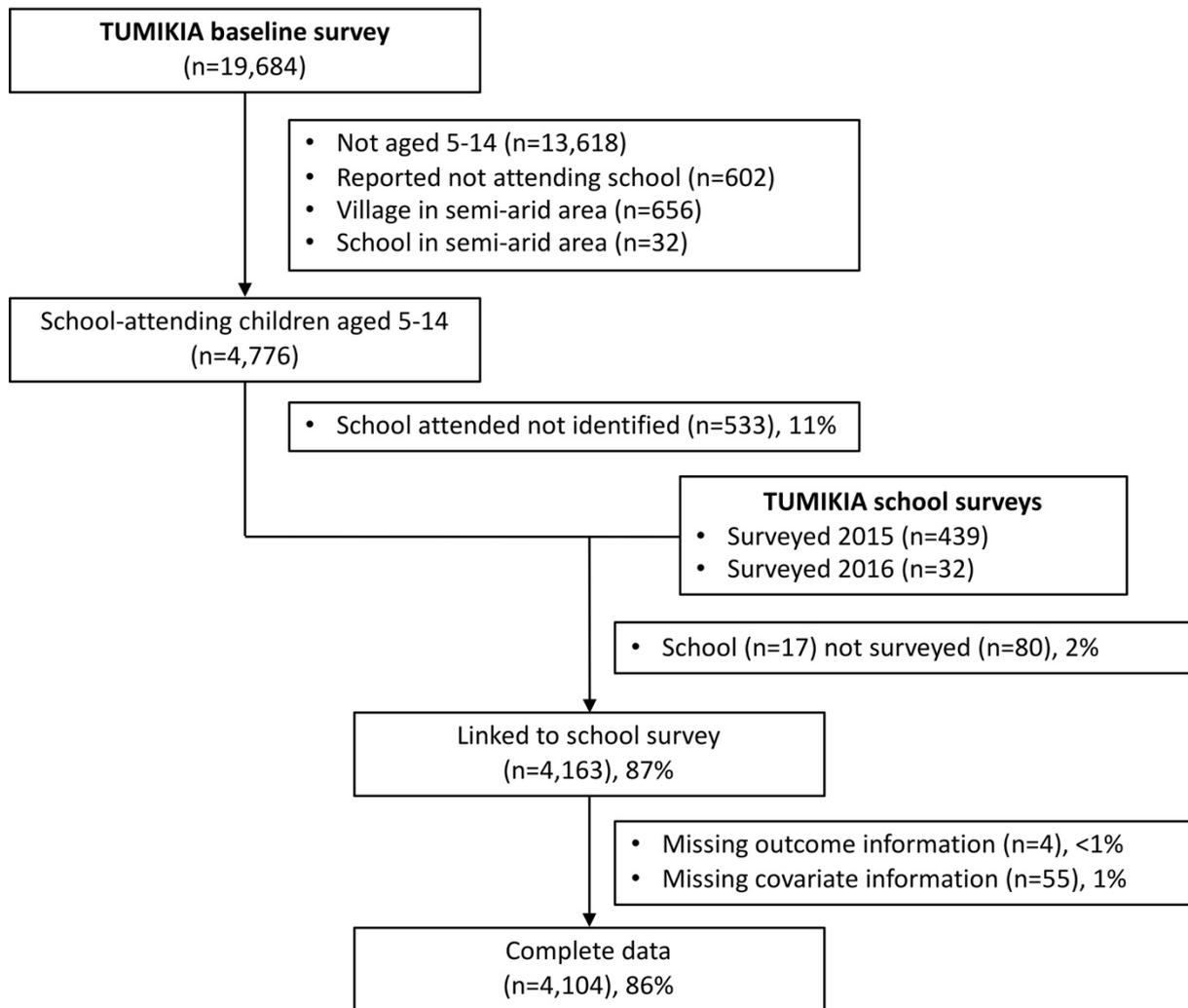
194 We report prevalence odds ratios (PORs) with 95% credible intervals (CIs) as fixed effects for
195 sanitation in each domain. We also calculated measures to quantify general contextual effects
196 on individual infection (13). Proportion of total observed individual variation in the outcome
197 attributable to between-school and between-village variation, or intraclass correlation
198 coefficient (ICC), was calculated using the latent variable method. This method converts
199 individual variance to the logistic scale from the probability scale and assumes an underlying
200 continuous propensity for infection following a logistic distribution with individual variance of
201 $\pi^2/3$ (24). We calculated median odds ratios (MORs), as measures of residual heterogeneity
202 on the odd ratio scale. MORs are always greater than or equal to 1 (MOR = 1 if there is no
203 variation between areas) and interpreted as the median value of the odds ratios between
204 comparable individuals drawn randomly from high and low risk areas. MORs are useful as they
205 measure how much individual infection is determined by domain membership and are directly
206 comparable to fixed effects (24). The ICC is recommended, however, for estimating general
207 contextual effects as a measure of clustering that incorporates both between- and within-area

208 variance (12). We calculated 80% interval odds ratios (80% IORs) for village and school
209 sanitation fixed effects. This measure does not reflect the estimate's precision but instead is
210 recommended to consider residual variation in the interpretation of fixed effects (25). A wider
211 interval indicates greater unexplained between-area variation, and the inclusion of 1 indicates
212 between-area variance is large compared to the specific fixed effect. Analyses were conducted
213 in Stata 15 (StataCorp LP, College Station, TX, USA) and in R 3.5 (r-project.org) using the 'brms'
214 package.

215

216 **Results**

217 Of 6,066 school-aged children with matched samples in the survey, 602 (10%) reported not
218 attending school, and 688 (11%) reported attending school but resided in a village or were
219 linked to a school in a semi-arid area (Figure 1). Among these excluded children, prevalence
220 of infection was 3% (22/688), < 1% (4/688), and 0% (0/688) for hookworm, *T. trichiura* and *A.*
221 *lumbricoides*, respectively. Of 4,776 eligible children, the school reported to be attended was
222 identified for 4,243 children (89%) and school survey data was available for 4,163 children
223 (87%). Eligible children without school information were younger, more often being boys, less
224 likely to have been dewormed, and less poor (S4 Table). Data were available for 4,104 eligible
225 children (86%).



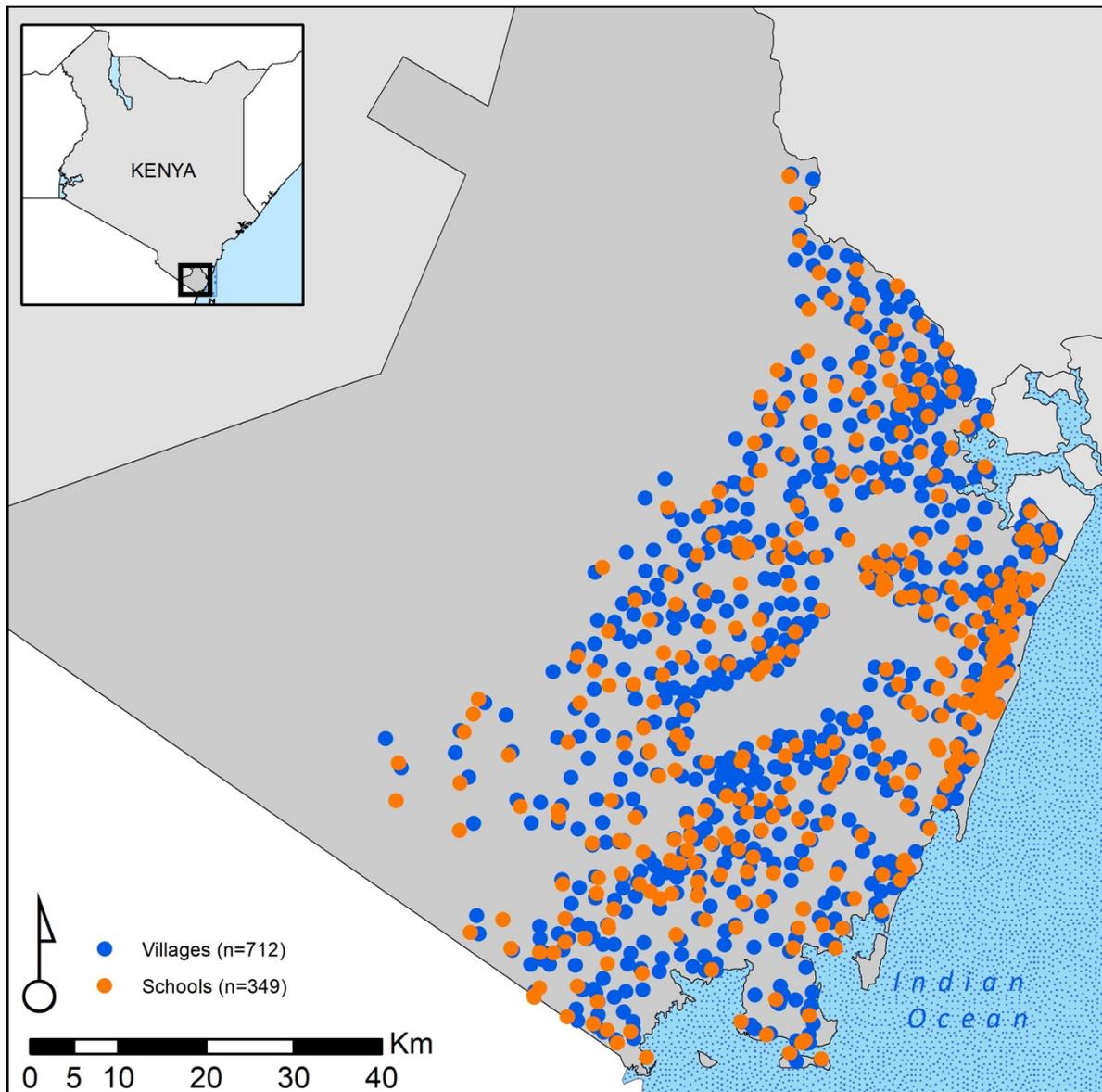
226

227 Figure 1. Flow chart of participants in the TUMIKIA baseline survey who were included in the
228 current analysis. Eligible sample included children aged 5-14 years who reported attending
229 school and not residing in villages or attending schools in semi-arid areas. The proportion of
230 eligible subjects with complete data is 86% (4,104/4,776).

231

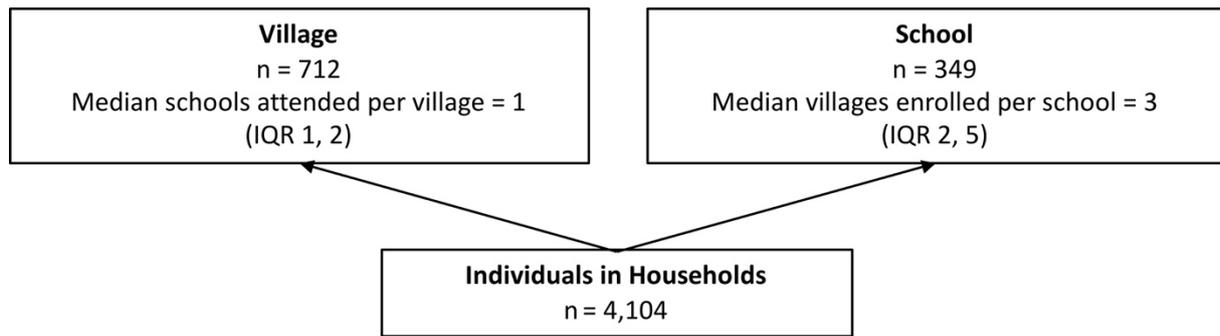
232 Participants resided in 712 villages (median sampled per village 4, range 1, 38) and reported
233 attending 349 schools (median sampled per school 9, Range 1, 49) (Figure 2). Figure 3
234 describes the structure of the data. In half of all villages, resident children reported attending

235 the same school (range 1 to 8 schools per village). Included schools enrolled children from 1
236 up to 13 villages. Table 1 describes individual, household, and village characteristics of
237 included children.



238

239 Figure 2. Village of residence and attended schools among 4,104 school-attending children
240 aged 5-14 years in Kwale County, Kenya, 2015.



241

242 Figure 3. Diagram for the classification model of individuals, villages, and schools.

243

244 **Table 1. Summary characteristics for 4,104 school-attending children in coastal Kenya, 2015**

Characteristics	No. or Mean	% or SD
Individual level (n=4104)		
Age (years)	9.46	2.65
Being girls	2,129	51.88
Observed wearing shoes	1,443	35.16
Reported deworming in past year	2,219	54.07
Reported household access to toilet	2,255	54.95
Reported improved water source	2,216	54.00
Missing	13	0.32
Time to fetch water, < 30 min	3,344	81.48
Missing	14	0.34
Covered floor	833	20.30

Household wealth quintile			
	Most poor, 1	1,190	29.00
	2	2,158	52.58
	Least poor, 3	756	18.42
	Distance to school (km) (n=3906)	2.25	5.82
Village level (n=712)			
	Proportion reporting toilet access	0.53	0.31
Urbanization			
	Rural	545	76.54
	Periurban	141	19.80
	Urban	26	3.65
Aridity index			
	Dry sub-humid (> 0.5--0.65)	284	39.89
	Humid (> 0.65)	428	60.11
	Soil sand content \geq 62%	256	35.96
School level (n=349)			
	Usable toilets per pupil	0.03	0.02
	Pupils per usable toilet	57.79	47.35
	Total enrolment	479.47	270.67
Urbanization			

Rural	234	67.05
Periurban	84	24.07
Urban	31	8.88
Aridity index		
Dry sub-humid (> 0.5--0.65)	130	37.25
Humid (> 0.65)	219	62.75
Soil sand content \geq 62%	126	36.10

245

246 Overall prevalence of any detected infection was 17.8% and 6.0% for hookworm and *T.*
247 *trichiura*, respectively, and most infections were classified as light (Table 2). Comparing
248 median odds ratios in tables 3 and 4, school attended had greater impact than village of
249 residence upon hookworm infection (School MOR 2.73, 95% CI 2.50, 2.98; Village MOR 2.09,
250 95% CI 1.74, 2.38). School and village membership had comparable impacts on *T. trichiura*
251 infection (School MOR 2.92, 95% CI 2.40, 3.43; Village MOR 2.78, 95% CI 2.28, 3.29). Calculated
252 ICC showed similar results. Including measures for sanitation in household, school, and village
253 domains in separate models did not meaningfully change measures of variance and
254 heterogeneity (S5 Table). Including all domain sanitation measures in the same model, we saw
255 no change in calculated MOR and ICC values for hookworm or *T. trichiura* (Tables 3 and 4).
256 Adjusting for potential confounders, residual heterogeneity between schools decreased for *T.*
257 *trichiura* and, to a lesser extent, hookworm infection, but residual heterogeneity between
258 villages was unchanged.

259

260 **Table 2. Intensity and any presence of STH infections by household, school, and village**
 261 **sanitation conditions among 4,104 school-attending children in coastal Kenya, 2015.**

		Intensity					
		None	Light	Moderate	Heavy	Any	
Infection		N	%	%	%	%	
Hookworm	Overall	4,104	82.21	16.91	0.56	0.32	17.79
	Household						
	sanitation access						
	Y	2,255	84.12	15.25	0.40	0.22	15.88
	N	1,849	79.88	18.93	0.76	0.43	20.12
	School sanitation						
	coverage (per 100)						
	< 1.49	1,182	81.30	17.77	0.68	0.25	18.70
	1.49 - 2.17	1,181	80.10	19.14	0.68	0.08	19.90
	2.18 - 3.13	1,077	83.84	15.51	0.46	0.19	16.16
	> 3.13	664	84.94	13.70	0.30	1.05	15.06
	Village sanitation						
	coverage						

		≤ 0.25	792	83.59	15.53	0.63	0.25	16.41
		0.26 - 0.54	1,123	82.37	16.92	0.53	0.18	17.63
		0.54 - 0.81	1,130	77.88	20.71	0.88	0.53	22.12
		> 0.81	1,059	85.65	13.88	0.19	0.28	14.35
<i>T. trichiura</i>	Overall		4,104	94.05	5.43	0.49	0.02	5.95
	Household							
	sanitation access							
		Y	2,255	94.10	5.54	0.35	0.00	5.90
		N	1,849	94.00	5.30	0.65	0.05	6.00
	School sanitation							
	coverage (per 100)							
		< 1.49	1,182	92.89	6.35	0.68	0.08	7.11
		1.49 - 2.17	1,181	95.17	4.40	0.42	0.00	4.83
		2.18 - 3.13	1,077	94.15	5.48	0.37	0.00	5.85
		> 3.13	664	93.98	5.57	0.45	0.00	6.02
	Village sanitation							
	coverage							
		≤ 0.25	792	94.19	4.80	1.01	0.00	5.81
		0.26 - 0.54	1,123	94.57	5.08	0.36	0.00	5.43

0.54 - 0.81	1,130	93.27	6.28	0.35	0.09	6.73
> 0.81	1,059	94.24	5.38	0.38	0.00	5.76

A. lumbricoides Overall 4,104 99.32 0.41 0.24 0.02 0.68

262 Hookworm intensity categories (epg=eggs per gram): none 0 epg; light <2,000 epg; moderate

263 2,000-<4,000 epg; heavy ≥4,000 epg

264 *T. trichiura* intensity categories (epg=eggs per gram): none 0 epg; light <1,000 epg; moderate

265 1,000-<10,000 epg; heavy ≥10,000 epg

266 *A. lumbricoides* intensity categories (epg=eggs per gram): none 0 epg; light <5,000 epg;

267 moderate 5,000-<50,000 epg; heavy ≥50,000 epg

268

269 **Table 3. Sanitation and contextual effects on presence of hookworm infection among 4,104**

270 **school-attending children in coastal Kenya**

Fixed Effects	Intercept-Only		Unadjusted		Adjusted ¹		80% IOR
	POR	(95% CI)	POR	(95% CI)	POR	(95% CI)	
Household							
Sanitation access	--	--	0.63	(0.51, 0.79)	0.76	(0.61, 0.95)	--

Sanitation and STH in coastal Kenya

2

School sanitation

coverage (per 100)

1.49 - 2.17	--	--	0.89	(0.55, 1.42)	0.79	(0.51, 1.21)	(0.14, 4.52)
2.18 - 3.13	--	--	0.86	(0.54, 1.36)	0.64	(0.40, 0.98)	(0.11, 3.66)
> 3.13	--	--	0.58	(0.35, 0.98)	0.51	(0.31, 0.83)	(0.09, 2.94)

Village sanitation

coverage

0.26 - 0.54	--	--	1.28	(0.89, 1.86)	1.40	(0.96, 2.08)	(0.33, 6.06)
0.54 - 0.81	--	--	1.52	(1.01, 2.29)	1.86	(1.22, 2.86)	(0.43, 8.01)
> 0.81	--	--	1.21	(0.75, 1.92)	1.40	(0.86, 2.34)	(0.33, 6.06)

Contextual Effects

School

Variance	1.11	(0.92, 1.31)	1.12	(0.93, 1.32)	0.93	(0.74, 1.14)	--
Median Odds Ratio	2.73	(2.50, 2.98)	2.74	(2.51, 2.99)	2.51	(2.27, 2.77)	--
ICC	0.22	(0.20, 0.24)	0.22	(0.20, 0.24)	0.19	(0.17, 0.21)	--

Village

Variance	0.60	(0.34, 0.83)	0.61	(0.34, 0.85)	0.65	(0.41, 0.89)	--
Median Odds Ratio	2.09	(1.74, 2.38)	2.11	(1.74, 2.41)	2.16	(1.84, 2.46)	--
ICC	0.12	(0.07, 0.15)	0.12	(0.07, 0.16)	0.13	(0.09, 0.17)	--

271 POR = Prevalence Odds Ratio; CI = Credible Interval; IOR = Interval Odds Ratio; ICC =
 272 Intraclass Correlation Coefficient
 273 ¹Adjusted for age (centred at 9), being female, reported deworming in past year, observed
 274 shoe-wearing, household floor covered, village high soil sand content, village aridity index
 275 (scaled 100x), village urban/periurban/rural, school high soil sand content, school aridity
 276 index (scaled 100x), school urban/periurban/rural

277

278 **Table 4. Sanitation and contextual effects on presence of *T. trichiura* infection among 4,104**
 279 **school-attending children in coastal Kenya**

Fixed Effects	Intercept-Only		Unadjusted		Adjusted ¹		80% IOR
	POR	(95% CI)	POR	(95% CI)	POR	(95% CI)	
Household							
Sanitation access	--	--	0.95	(0.66, 1.38)	1.00	(0.68, 1.46)	--
School sanitation coverage (per 100)							
1.49 - 2.17	--	--	0.75	(0.36, 1.51)	1.23	(0.70, 2.23)	(0.29, 5.26)
2.18 - 3.13	--	--	0.85	(0.42, 1.70)	1.07	(0.60, 1.93)	(0.25, 4.57)
> 3.13	--	--	0.81	(0.36, 1.73)	1.06	(0.56, 1.95)	(0.25, 4.53)

Village sanitation

coverage

0.26 - 0.54	--	--	1.00	(0.51, 1.92)	0.59	(0.30, 1.15)	(0.09, 4.05)
0.54 - 0.81	--	--	1.57	(0.79, 3.16)	0.82	(0.41, 1.62)	(0.12, 5.57)
> 0.81	--	--	0.84	(0.37, 1.90)	0.30	(0.14, 0.68)	(0.04, 2.07)

Contextual Effects

School

Variance	1.26	(0.84, 1.67)	1.34	(0.92, 1.78)	0.64	(0.11, 1.10)	--
Median Odds Ratio	2.92	(2.40, 3.43)	3.02	(2.50, 3.57)	2.14	(1.37, 2.72)	--
ICC	0.22	(0.17, 0.26)	0.23	(0.18, 0.27)	0.13	(0.03, 0.19)	--

Village

Variance	1.15	(0.75, 1.56)	1.17	(0.77, 1.59)	1.12	(0.75, 1.51)	--
Median Odds Ratio	2.78	(2.28, 3.29)	2.81	(2.31, 3.33)	2.74	(2.28, 3.23)	--
ICC	0.20	(0.15, 0.24)	0.20	(0.15, 0.24)	0.22	(0.18, 0.26)	--

280 POR = Prevalence Odds Ratio; CI = Credible Interval; IOR = Interval Odds Ratio; ICC =

281 Intraclass Correlation Coefficient

282 ¹Adjusted for household SES category, village high soil sand content, village aridity index
283 (scaled 100x), village urban/periurban/rural, school high soil sand content, school aridity
284 index (scaled 100x), school urban/periurban/rural

285

286 Reported presence of household sanitation access reduced odds of hookworm infection by
287 37%, compared to no household sanitation access (POR 0.63, 95% CI 0.51, 0.79), among
288 children in villages and schools with similar sanitation conditions. Adjusting for potential
289 confounders, this association was attenuated towards null (POR 0.76, 95% CI 0.61, 0.95).
290 School sanitation coverage in the two highest quartiles (> 2.17 toilets per 100 students) was
291 associated with lower hookworm prevalence, compared to the lowest coverage quartile (<
292 1.49 toilets per 100 students), adjusting for potential confounders and household and village
293 sanitation (POR 0.64, 95% CI 0.40, 0.98; POR 0.51, 95% CI 0.31, 0.83). No evidence of
294 association of household or school sanitation with *T. trichiura* infection was detected. Children
295 in villages where 54 to 81% of households had sanitation access, compared to children in
296 villages with \leq 25% sanitation coverage, had 1.86 times the odds of hookworm infection (POR
297 1.86, 95% CI 1.22, 2.86). Children in villages where > 81% of households had sanitation access,
298 compared to children in villages with \leq 25% sanitation coverage, had 70% lower odds of *T.*
299 *trichiura* infection (POR 0.30, 95% CI 0.14, 0.68). Results were robust to the exclusion of 199
300 children without household coordinates and 197 reporting attending a school > 6.5 km from
301 their house.

302

303 Calculated 80% IORs from adjusted models for hookworm and *T. trichiura* were wide and
304 included one for both village and school sanitation measures, indicating sanitation was less

305 important for explaining individual infection, compared to residual variation between these
306 domain levels. For example, comparing children with identical characteristics but drawn from
307 either a village with sanitation coverage $\leq 25\%$ or a village with sanitation coverage $> 81\%$,
308 odds of *T. trichiura* infection will be between 0.04 and 2.07 in 80% of such comparisons.

309

310 **Discussion**

311 In this analysis of baseline data from the TUMIKIA trial, we found notable differences between
312 two species of STH in the relationship between sanitation availability and prevalence of
313 infection within different domains among school-attending children in coastal Kenya.
314 Reported use of a sanitation facility by households was associated with reduced prevalence
315 of hookworm infection but was not associated with reduced prevalence of *T. trichiura*
316 infection. Meanwhile, village sanitation coverage $> 81\%$ was associated with reduced
317 prevalence of *T. trichiura* infection, but no protective association was detected for hookworm
318 infection. School sanitation coverage > 3.13 toilets per 100 pupils was associated with lower
319 prevalence of hookworm infection. This coverage level, corresponding to a pupil:toilet ratio
320 of 32:1, supports the minimum ratios (25:1 for girls and 35:1 for boys) currently recommended
321 by the Kenyan government (26). School sanitation was not associated with *T. trichiura*
322 infection, however. We found that general contextual effects, represented by residual
323 heterogeneity between village and school domains, had comparable impact upon likelihood
324 of hookworm and *T. trichiura* infection as sanitation coverage in either of these domains.

325

326 Three published meta-analyses record considerable heterogeneity in estimates of the effect
327 of sanitation access on hookworm and *T. trichiura* infection. Ziegelbauer et al. found that
328 sanitation was protective against both hookworm and *T. trichiura* infection (5). Strunz et al.
329 found no association of sanitation access with hookworm infection, but it was protective
330 against *T. trichiura* (4). Freeman et al., in the most recent review, found no association of
331 sanitation access with *T. trichiura* infection but sanitation access was protective against
332 hookworm (6). Our findings for household and school sanitation are consistent with these
333 latter results, while adjusting for village and school sanitation coverage plus potential
334 confounders and conditional on village and school membership. Freeman et al. concluded
335 that the lack of an association of sanitation access with *T. trichiura* may result from sanitation's
336 expected long-term impact on infection compared to a shorter-term impact on reinfection (6).
337 Our findings would support this conclusion. Albendazole, the medication used for Kenya's
338 National School-Based Deworming Programme (NSBDP), is less effective against *T. trichiura*,
339 compared to hookworm and *A. lumbricoides* (27). Observed associations of household and
340 school sanitation with lower hookworm prevalence in this population of school-attending
341 children could reflect impacts of sanitation in these domains on reinfection, following school-
342 based deworming, rather than a reduction in infection, which might only be observable for *T.*
343 *trichiura* over a longer time period.

344

345 The meta-analyses described above did not distinguish between sanitation access at home or
346 at school. We estimated the independent effects of sanitation access at both the household
347 and school on STH infection. We also expanded upon previous work to estimate the effect of
348 village sanitation coverage (9, 10). The protective association of village sanitation coverage

349 against *T. trichiura* may reflect longer-term impacts of sanitation and a possible community-
350 wide (herd) effect at access levels > 80%, independent of household sanitation access and
351 other factors. In contrast, we found no consistent pattern between village sanitation coverage
352 and hookworm infection. We may not have observed an association because many of the
353 included villages with the lowest sanitation coverage were also in the most arid environments,
354 limiting their suitability for transmission.

355

356 Our results clearly show the large contextual effects of village and school domains relative to
357 the estimated fixed effects. The 80% IOR does not indicate precision but provides an interval
358 around our estimated village and school sanitation effects that incorporates unexplained
359 variability between these domains. This result, coupled with the calculated ICCs and MORs,
360 indicates that sanitation coverage in these domains is not a strong predictor of hookworm or
361 *T. trichiura* infection in this setting, though some protective associations were observed.
362 Others have also reported that village membership alone has a large impact on the likelihood
363 of hookworm or *T. trichiura* infection (28), and that heterogeneity of prevalence is associated
364 with multiple environmental and socioeconomic factors (29). Adjusting for potential
365 individual, village and school level confounders in our models did not meaningfully explain
366 further heterogeneity in hookworm infection between villages or schools but did explain some
367 heterogeneity in *T. trichiura* infection between schools.

368

369 Though our general contextual effects indicate that village is a relevant context for analysis,
370 the representativeness of village measures is a limitation of the current study. We aggregated
371 village measures from all households sampled for the baseline survey. Because sampling for

372 TUMIKIA was based on CUs, the number of units sampled per village varied. We assumed that
373 included units were representative, but our sample may not have adequately characterised
374 village conditions. Village membership was based on an administrative rather than geographic
375 grouping, so it may also not represent sanitation conditions in the area surrounding study
376 households. While useful for implementation purposes, village may not be the most suitable
377 scale at which to assess community-wide sanitation effects. Future studies could use varying
378 spatial buffers with complete household samples to examine community-wide effects of
379 sanitation coverage on STH infection and identify target thresholds (30). Our household
380 sanitation measure was based on a reported measure and may not reflect actual consistent
381 usage and faeces disposal by household members or faecal contamination levels in the area.
382 Our outcome measure was based on a single stool sample, which may also have
383 underestimated prevalence (31).

384

385 In the current study, sanitation conditions, as measured, explained little of the heterogeneity
386 in transmission between villages and schools. Further studies should examine the role of
387 sanitation in different domains against STH infections within the context of school- and
388 community-based mass drug administration. We found evidence of a protective effect of
389 sanitation access at the household against hookworm infection and a sanitation coverage
390 threshold at which a community-wide effect against *T. trichiura* was observed. We also found
391 evidence in support of current school sanitation coverage guidelines towards the control of
392 hookworm infection. In summary, our findings highlight the need for continued efforts,
393 alongside mass drug administration, to extend access to good sanitation facilities at homes,
394 schools, and across communities.

395 **Data sharing statement**

396 Individual participant data (after de-identification) that underlie the results reported in this
397 paper will be made available on LSHTM Data Compass. The data will be available at the time
398 of publication and researchers can request access through the Data Compass portal. Requests
399 for release of the data will be reviewed by the relevant institutional review boards.

400

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407 **References**

- 408 1. GBD Compare Data Visualization [Internet]. Institute for Health Metrics and Evaluation,
409 University of Washington. 2016 [cited July 19, 2018]. Available from:
410 <http://vizhub.healthdata.org/gbd-compare>.
- 411 2. Brooker S, Clements AC, Bundy DA. Global epidemiology, ecology and control of soil-
412 transmitted helminth infections. *Adv Parasitol*. 2006;62:221-61.
- 413 3. Feachem RG, Bradley DJ, Garelick H, Mara DD. Sanitation and disease: Health aspects of
414 excreta and wastewater management. . Bank W, editor. New York, NY: John Wiley & Sons; 1983.
- 415 4. Strunz EC, Addiss DG, Stocks ME, Ogden S, Utzinger J, Freeman MC. Water, sanitation,
416 hygiene, and soil-transmitted helminth infection: a systematic review and meta-analysis. *PLoS Med*.
417 2014;11(3):e1001620.
- 418 5. Ziegelbauer K, Speich B, Mausezahl D, Bos R, Keiser J, Utzinger J. Effect of sanitation on soil-
419 transmitted helminth infection: systematic review and meta-analysis. *PLoS Med*.
420 2012;9(1):e1001162.
- 421 6. Freeman MC, Garn JV, Sclar GD, Boisson S, Medicott K, Alexander KT, et al. The impact of
422 sanitation on infectious disease and nutritional status: A systematic review and meta-analysis. *Int J*
423 *Hyg Environ Health*. 2017;220(6):928-49.
- 424 7. Brooker S, Alexander N, Geiger S, Moyeed RA, Stander J, Fleming F, et al. Contrasting
425 patterns in the small-scale heterogeneity of human helminth infections in urban and rural
426 environments in Brazil. *Int J Parasitol*. 2006;36(10-11):1143-51.
- 427 8. Cairncross S, Blumenthal U, Kolsky P, Moraes L, Tayeh A. The public and domestic domains in
428 the transmission of disease. *Trop Med Int Health*. 1996;1(1):27-34.
- 429 9. Freeman MC, Chard AN, Nikolay B, Garn JV, Okoyo C, Kihara J, et al. Associations between
430 school- and household-level water, sanitation and hygiene conditions and soil-transmitted helminth
431 infection among Kenyan school children. *Parasites & vectors*. 2015;8:412.
- 432 10. Garn JV, Mwandawiro CS, Nikolay B, Drews-Botsch CD, Kihara JH, Brooker SJ, et al. *Ascaris*
433 *lumbricoides* Infection Following School-Based Deworming in Western Kenya: Assessing the Role of
434 Pupils' School and Home Water, Sanitation, and Hygiene Exposures. *Am J Trop Med Hyg*.
435 2016;94(5):1045-54.
- 436 11. Gass K, Addiss DG, Freeman MC. Exploring the relationship between access to water,
437 sanitation and hygiene and soil-transmitted helminth infection: a demonstration of two recursive
438 partitioning tools. *PLoS Negl Trop Dis*. 2014;8(6):e2945.
- 439 12. Austin PC, Merlo J. Intermediate and advanced topics in multilevel logistic regression
440 analysis. *Stat Med*. 2017;36(20):3257-77.
- 441 13. Merlo J, Wagner P, Austin PC, Subramanian SV, Leckie G. General and specific contextual
442 effects in multilevel regression analyses and their paradoxical relationship: A conceptual tutorial.
443 *SSM Popul Health*. 2018;5:33-7.
- 444 14. Diez Roux AV, Aiello AE. Multilevel analysis of infectious diseases. *J Infect Dis*. 2005;191 Suppl
445 1:S25-33.
- 446 15. Freeman MC, Ogden S, Jacobson J, Abbott D, Addiss DG, Amnie AG, et al. Integration of
447 water, sanitation, and hygiene for the prevention and control of neglected tropical diseases: a
448 rationale for inter-sectoral collaboration. *PLoS Negl Trop Dis*. 2013;7(9):e2439.
- 449 16. WHO. Guideline: preventive chemotherapy to control soil-transmitted helminth infections in
450 at-risk population groups. Geneva: World Health Organization; 2017.
- 451 17. Brooker SJ, Mwandawiro CS, Halliday KE, Njenga SM, McHaro C, Gichuki PM, et al.
452 Interrupting transmission of soil-transmitted helminths: a study protocol for cluster randomised trials
453 evaluating alternative treatment strategies and delivery systems in Kenya. *BMJ Open*.
454 2015;5(10):e008950.

- 455 18. Pullan RL, Halliday KE, Oswald WE, McHaro C, Beaumont E, Kepha S, et al. Effects, equity, and
456 cost of school-based and community-wide treatment strategies for soil-transmitted helminths in
457 Kenya: a cluster-randomised controlled trial. *The Lancet*. 2019.
- 458 19. Montresor A, Crompton DWT, Hall A, Bundy DAP, Savioli L. Guidelines for the evaluation of
459 soil-transmitted helminthiasis and schistosomiasis at community level. Geneva, Switzerland: World
460 Health Organization; 1998. Report No.: WHO/CTD/SIP/98.1.
- 461 20. WHO/UNICEF. Core questions and indicators for monitoring WASH in Schools in the
462 Sustainable Development Goals. Geneva, Switzerland: World Health Organization; 2016.
- 463 21. Rothman KJ, Greenland S, Lash TL. *Modern Epidemiology*, 3rd Ed. Philadelphia, PA:
464 Lippincott, Williams, & Wilkins; 2008.
- 465 22. Textor J, Hardt J, Knuppel S. DAGitty: a graphical tool for analyzing causal diagrams.
466 *Epidemiology*. 2011;22(5):745.
- 467 23. Burkner P. Advanced Bayesian Multilevel Modeling with the R Package brms: r-project.org;
468 2018 [cited 2018 August 21]. Available from: [https://cran.r-](https://cran.r-project.org/web/packages/brms/vignettes/brms_multilevel.pdf)
469 [project.org/web/packages/brms/vignettes/brms_multilevel.pdf](https://cran.r-project.org/web/packages/brms/vignettes/brms_multilevel.pdf).
- 470 24. Merlo J, Chaix B, Ohlsson H, Beckman A, Johnell K, Hjerpe P, et al. A brief conceptual tutorial
471 of multilevel analysis in social epidemiology: using measures of clustering in multilevel logistic
472 regression to investigate contextual phenomena. *J Epidemiol Community Health*. 2006;60(4):290-7.
- 473 25. Larsen K, Merlo J. Appropriate assessment of neighborhood effects on individual health:
474 integrating random and fixed effects in multilevel logistic regression. *Am J Epidemiol*.
475 2005;161(1):81-8.
- 476 26. KMOH. Kenya Environmental Sanitation and Hygiene Policy 2016-2030. Nairobi, Kenya:
477 Republic of Kenya Ministry of Health; 2016.
- 478 27. Keiser J, Utzinger J. Efficacy of current drugs against soil-transmitted helminth infections:
479 systematic review and meta-analysis. *JAMA*. 2008;299(16):1937-48.
- 480 28. Benjamin-Chung J, Nazneen A, Halder AK, Haque R, Siddique A, Uddin MS, et al. The
481 Interaction of Deworming, Improved Sanitation, and Household Flooring with Soil-Transmitted
482 Helminth Infection in Rural Bangladesh. *PLoS Negl Trop Dis*. 2015;9(12):e0004256.
- 483 29. Bisanzio D, Mutuku F, Bustinduy AL, Mungai PL, Muchiri EM, King CH, et al. Cross-sectional
484 study of the burden of vector-borne and soil-transmitted polyparasitism in rural communities of
485 Coast Province, Kenya. *PLoS Negl Trop Dis*. 2014;8(7):e2992.
- 486 30. Fuller JA, Villamor E, Cevallos W, Trostle J, Eisenberg JN. I get height with a little help from
487 my friends: herd protection from sanitation on child growth in rural Ecuador. *Int J Epidemiol*.
488 2016;45(2):460-9.
- 489 31. Knopp S, Mgeni AF, Khamis IS, Steinmann P, Stothard JR, Rollinson D, et al. Diagnosis of soil-
490 transmitted helminths in the era of preventive chemotherapy: effect of multiple stool sampling and
491 use of different diagnostic techniques. *PLoS Negl Trop Dis*. 2008;2(11):e331.

492

493 **Supporting Information Legends**

494 **S1 Checklist. STROBE Checklist**

495 **S2 Supporting Information. Sanitation and hookworm infection model code (dagitty.net)**

496 **S3 Supporting Information. Sanitation and *Trichuris trichiura* infection model code**

497 **(dagitty.net)**

498 **S4 Table. Characteristics of school-attending children in non-arid areas by linked to school**

499 **survey information status**

500 **S5 Table. Unadjusted sanitation exposures and contextual effects on presence of hookworm**

501 **and *T. trichiura* infection among 4104 school-attending children in coastal Kenya**