1 **Integrating water, sanitation, handwashing, and nutrition interventions to reduce child soil-**

2 **transmitted helminth and *Giardia* infections: a cluster-randomized controlled trial in rural**

3 **Kenya**

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26 **Short title: Integrated WASH and child parasite infections**

27 **Trial registration:** ClinicalTrials.gov NCT01704105,

28 https://clinicaltrials.gov/ct2/show/NCT01704105

29   **Abstract**

30   **Background.** Helminth and protozoan infections affect >1 billion children globally. Improved

31   water, sanitation, handwashing, and nutrition could be more sustainable control strategies for

32   parasite infections than mass drug administration (MDA), while providing other quality of life

33   benefits.

34   **Methods and Findings.** We enrolled geographic clusters of pregnant women into a cluster-

35   randomized controlled trial that tested six interventions: disinfecting drinking water(W),

36   improved sanitation(S), handwashing with soap(H), combined WSH, improved nutrition(N), and

37   combined WSHN. We assessed intervention effects on parasite infections by measuring *Ascaris*

38   *lumbricoides, Trichuris trichiura*, hookworm, and *Giardia duodenalis* among individual children

39   born to enrolled mothers and their older siblings (ClinicalTrials.gov NCT01704105). We collected

40   stool specimens from 9077 total children in 622 clusters, including 2346 children in control,

41   1117 in water, 1160 in sanitation, 1141 in handwashing, 1064 in WSH, 1072 in nutrition, and

42   1177 in WSHN. In the control group, 23% of children were infected with *Ascaris lumbricoides*,

43   1% with *Trichuris trichuria,* 2% with hookworm and 39% with *Giardia duodenalis*. After two

44   years of intervention exposure, *Ascaris* infection prevalence was 18% lower in the water

45   treatment arm (95% confidence interval (CI) 0%, 33%), 22% lower in the WSH arm (CI 4%, 37%),

46   and 22% lower in the WSHN arm (CI 4%, 36%) compared to control. Individual sanitation,

47   handwashing, and nutrition did not significantly reduce *Ascaris* infection on their own*,* and

48   integrating nutrition with WSH did not provide additional benefit. *Trichuris* and hookworm were

49   rarely detected, resulting in imprecise effect estimates. No intervention reduced *Giardia*.

50   Reanalysis of stool samples by quantitative polymerase chain reaction (qPCR) confirmed the

51   reductions in *Ascaris* infections measured by microscopy in the WSH and WSHN groups. Lab

52   technicians and data analysts were blinded to treatment assignment, but participants and

2

53   sample collectors were not blinded. The trial was funded by the Bill & Melinda Gates Foundation

54   and USAID.

55   **Conclusions.** Our results suggest integration of improved water quality, sanitation, and

56   handwashing could contribute to sustainable control strategies for *Ascaris* infections,

57   particularly in similar settings with recent or ongoing deworming programs. Water treatment

58   alone was similarly effective to integrated WSH, providing new evidence that drinking water

59   should be given increased attention as a transmission pathway for *Ascaris*.

60

61   **Key words:** water, sanitation, handwashing, nutrition, intestinal worms, protozoa, low-income

62   countries

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64

65   **Introduction**

66   Intestinal soil-transmitted helminth (STH) infections, including *Ascaris lumbricoides*, *Trichuris*

67   *trichiura*, and hookworm, and the protozoa *Giardia duodenalis* are common parasitic infections

68   among children in low-resource settings and neglected tropical diseases. Globally, STH are

69   estimated to affect 1.45 billion people(1), while *Giardia* has been cited as the most common

70   enteropathogen in low-income countries(2). STH and *Giardia* infections can result in poor

71   absorption of nutrients and weight loss(3,4). There is some evidence that STH and *Giardia*

72   infections, even when asymptomatic, may contribute to growth faltering and impaired cognitive

73   development(5-8). Longitudinal cohort studies in Bangladesh and Brazil have identified early

74   infection with *Giardia* as a risk factor for stunting among children(7,9). In Peru, children with

75   multiple *Giardia* infections per year during the first two years of life had lower cognitive function

76   scores at age 9 than children with one or fewer *Giardia* infections(10). The effect of child STH

77   infections on child growth, cognitive development, and school performance has been mixed and

78   strongly debated by experts, with some suggesting additional evidence is needed(5,6,11).

79

80   School-based mass drug administration (MDA) campaigns have been the cornerstone of the

81   global strategy to control STH infections; however, high reinfection rates limit the ability of MDA

82   to achieve sustained reduction in STH infection prevalence(12). *Ascaris, Trichuris*, *Giardia,* and

83   *Ancylostoma duodenale* are primarily transmitted through the fecal-oral ingestion route,

84   although *Ancylostoma duodenale* as well as *Necator americanus* can be transmitted

85   transdermally. A meta-analysis of studies from settings with medium-to-high endemic STH

86   prevalence identified an average reinfection rate for *Ascaris* at 12 months at 94% of baseline

87   prevalence, while the average 12-month reinfection rates for *Trichuris* and hookworm were 82%

4

88   and 57%, respectively(13). To achieve elimination of STH transmission, it has been suggested

89   that MDA control efforts may need to be integrated with improved water, sanitation, and

90   handwashing(14). Control of *Giardiasis* has historically relied on drug treatment after diagnosis

91   as well as exposure prevention by water treatment and improved sanitation, but zoonotic

92   transmission can complicate exposure prevention(15). Recent systematic reviews suggest that

93   improved water, sanitation, and handwashing can reduce the odds of STH and *Giardia*

94   infections, though the quality of the evidence base remains poor and consists almost exclusively

95   of observational analyses(16,17).

96

97   An individual's susceptibility to STH and *Giardia* infection is influenced by exposure and immune

98   response. A recent systematic review concluded that there was some evidence that nutritional

99   supplementation decreases the risk of infection or reinfection with STH, but studies have been

100   of low quality(18). Plausible mechanisms by which nutrition might reduce STH or *Giardia*

101   infection are through improvements in effective immune response including repair of cell

102   damage caused by parasite infection, and through changes to the gut microbiome(19,20).

103

104   We conducted a cluster-randomized controlled trial in rural Kenya to assess the effects of water,

105   sanitation, handwashing, and nutrition interventions delivered alone and in combination on

106   child parasite infections. STH and *Giardia* infections were pre-specified as trial outcomes before

107   the trial began(21). In a separate paper, we reported the effects of the interventions on child

108   growth and diarrhea(22). The trial's nutrition intervention was the only component that

109   improved child growth, but none of the interventions reduced diarrhea(22). Here, we report

110   intervention effects on *Ascaris, Trichuris,* hookworm, and *Giardia* infections measured after two

111   years of intervention exposure.

112

113   **Materials and Methods**

114

115   *Study design*

116   The trial protocol and detailed methods are published(21). The trial was registered at

117   ClinicalTrials.gov, identification number: NCT01704105. The study protocol was approved by the

118   Committee for the Protection of Human Subjects at the University of California, Berkeley

119   (protocol number 2011-09-3654), the Institutional Review Board at Stanford University (IRB-

120   23310), and the Scientific and Ethics Review Unit at the Kenya Medical Research Institute

121   (protocol number SSC-2271). Innovations for Poverty Action (IPA) enrolled participants,

122   implemented the intervention delivery, and collected the data. Mothers provided written

123   informed consent for themselves and their children.

124

125   Clusters of eligible pregnant women each were randomized by geographic proximal blocks into

126   one of eight study arms: chlorine treatment of drinking water (W); improved sanitation

127   including provision of toilets with plastic slabs and hardware to manage child feces (S);

128   handwashing with soap (H); combined WSH; infant and young child feeding counseling plus

129   small-quantity lipid-based nutrient supplements (N); combined WSHN; a double-sized active

130   control, and a passive control arm. Children in the passive control arm were purposively

131   excluded from parasitology measurement (Figure 1).

132

133   We conducted a cluster-randomized trial because components of the intervention promotion

134   activities were at the community level and there could have been behavior and infectious

135   disease interactions between neighboring households. Villages were eligible for selection into

136   the study if they were rural, the majority of the population lacked access to piped water

137   supplies, and there were no other ongoing WSH or nutrition programs. Within selected villages,

138   a census was conducted to identify eligible pregnant women in their second or third trimester

139   that planned to continue to live at their current residence for the next year. Since interventions

140   were designed to reduce child exposure to pathogens through a cleaner environment and

141   exclusive breastfeeding, we enrolled pregnant women to allow time for intervention delivery to

142   occur prior to or as close to birth as possible. Clusters were formed from 1-3 neighboring villages

143   and had a minimum of six pregnant women per cluster after the enrollment survey. Children

144   born to enrolled pregnant mothers were considered "index" children. Outcomes were assessed

145   after two years of intervention exposure among index children, including twins, as well as

146   among one older child in the index child's compound to understand the effect of the

147   interventions on both preschool aged and school aged children. The older child was selected by

148   enrolling the youngest available child within the age range of 3-15 years old, with priority for a

149   sibling in the index child's household.

150

151   *Baseline survey*

152   A survey at enrollment measured household socioeconomic characteristics and demographics

153   (maternal age, maternal education, electricity access, type of floor, number of people in the

154   household), as well as water, sanitation, and handwashing infrastructure and behaviors (type of

155   water source, reported water treatment, defecation location, type of toilet, presence of water

156   and soap at a handwashing station). In addition, at study enrollment we measured *Giardia,*

157   *Entamoeba histolytica* and *Cryptosporidium spp.* among children residing in study compounds

158   between 18 and 27 months of age (the projected age range for index children at the end of the

159   study) to assess baseline prevalence of these pathogens. STH were not measured at enrollment

160   among these proxy children because it was not logistically feasible to deworm infected children

161   at baseline. We also collected 100ml samples from primary drinking water sources accessed by

162   study households and household stored drinking water (if available). We transported the

163   samples on ice to field labs and enumerated *Escherichia coli* in each sample by membrane

164   filtration followed by culture on MI media.

165

166   *Randomization and blinding*

167   A few weeks after enrollment, clusters were randomly assigned to intervention arms at the

168   University of California, Berkeley by an investigator independent of the field research team

169   (BFA) using a random number generator. Groups of nine, geographically adjacent clusters were

170   block-randomized into the six intervention arms, the double-sized active control arm, and the

171   passive control arm (the passive control arm was not included in the parasite assessment).

172   Participants and other community members were informed of their intervention group

173   assignment after the baseline survey. Blinding (masking) participants was not possible given the

174   nature of the interventions. Data and stool sample collectors were not informed of the cluster

175   intervention assignment, but could have inferred treatment status by observing intervention

176   hardware. Lab technicians were blinded to intervention status. Two authors (AJP and JS)

177   independently replicated the statistical analyses while blinded to intervention status.

178

179   *Intervention delivery*

180   Intervention delivery began <3 months after enrollment. In the water intervention arms (W,

181   WSH, WSHN), community health promoters encouraged drinking water treatment with chlorine

182   (liquid sodium hypochlorite) using either manual dispensers installed at the point-of-collection

183   (community water source) in study villages or using bottled chlorine provided directly to

184   households every 6 months. In the sanitation arms (S, WSH, WSHN), households received new

185   latrines or existing latrines were upgraded and improved by installing a plastic slab that included

186   a lid. All households in sanitation arm study compounds were provided with a child potty for

187   each child <3 years as well as a "sani-scoop" to remove animal and human feces from the

188   compound. In the handwashing arms (H, WSH, WSHN), households were provided with two

189   handwashing stations—near the latrine and the cooking area. Stations included dual foot-pedal

190   operated jerry cans that could be tipped to dispense either soapy water or rinse water.

191   Households were responsible for keeping the stations stocked with rinse water, and community

192   health promoters refilled soap regularly. In the nutrition arms (N, WSHN), small quantity lipid-

193   based nutrient supplements (LNS) were provided to children from 6-24 months of age. Children

194   received monthly rations of LNS for addition to complementary foods twice per day. Nutrition

195   messaging included promoting dietary diversity during pregnancy and lactation, early initiation

196   of breastfeeding, exclusive breastfeeding from 0-6 months, continued breastfeeding through 24

197   months, timely introduction of complementary foods, dietary diversity for child feeding, and

198   child feeding during illness.

199

200   Community health promoters were nominated by mothers in the community and trained to

201   provide intervention-specific behavior change activities and instructions on hardware use or

202   provision of nutrition supplements. They were also trained to measure child mid-upper arm

203   circumference to identify and provide referrals for potential cases of severe acute malnutrition.

204   Each intervention consisted of a comprehensive behavior change package of key messages;

205   visual aids in the form of flip charts, posters, and reminder cue cards; interactive activities with

206   songs, games, or pledges to commit to practice target behaviors; and the distribution of arm-

207   specific hardware, products, or supplements. Households in the active control group received

9

208 visits from promoters to measure child mid-upper arm circumference and provide malnutrition

209 referrals, but did not receive any intervention related hardware or messaging. Promoters were

210 instructed to visit households monthly. Key messages and promoter materials are available at

211 https://osf.io/fs23x/.

212

213 Adherence to the interventions was measured during unannounced household visits after one

214 year and two years of intervention exposure (see SI).

215

216 *Measurement of parasite infections*

217 We measured parasite infections approximately 27 months post-enrollment (which equates to a

218 minimum of 24 months of intervention exposure since intervention hardware was delivered <3

219 months of enrollment). Stool samples were collected from index children and older children in

220 sterile containers and transported on ice to the closer of two central field labs located in

221 Kakamega or Bungoma. Field staff revisited households up to 3 times to collect stool samples.

222 *Ascaris lumbricoides, Trichuris trichiura*, and hookworm eggs were immediately enumerated

223 (same day) by double-slide Kato Katz microscopy with 41.7 mg templates. Both slides created

224 from each stool sample were counted by a trained parasitologist, and two different

225 parasitologists counted each slide from the same sample. A supervisor with expertise in STH egg

226 identification reviewed 10% of all slides and any discrepancies were corrected. STH egg counts

227 were averaged for analysis if both slides from one stool sample were positive. Two aliquots of

228 stool (one mixed with ethanol) were transported on dry ice to the Eastern and Southern Africa

229 Centre of International Parasite Control laboratory at KEMRI in Nairobi, Kenya for further

230 analysis.

231

232   One aliquot was analyzed by monoclonal enzyme-linked immunosorbent assay (ELISA) assay

233   (*Giardia II^TM,* Alere International Limited, Galway, Ireland) for the presence or absence of *Giardia*

234   *duodenalis* cysts. Samples were measured by ELISA in duplicate; if there was a discrepancy

235   between duplicates, the sample was re-run. DNA was extracted from the other aliquot

236   (preserved in ethanol) for stool samples collected from children in the control, WSH, and WSHN

237   groups. Four qPCR assays were run in duplicate on each sample to detect the following targets:

238   *Necator americanus, Ancylostoma duodenale, Trichuris trichiura,* and *Ascaris lumbricoides* (see

239   SI for further details)(23)*.*

240

241   *Outcomes*

242   STH and *Giardia* infections were pre-specified outcomes in the parent WASH Benefits trial prior

243   to the start of data collection; see Figure 3 in Arnold and others (21). Parasite infections were

244   measured two years after the start of intervention activities. The main indicators of parasite

245   infections were prevalence of each individual STH infection, any STH infection, and the

246   prevalence of *Giardia* infection among index and older children from the same compound.

247   Additional indicators of parasite infections included intensity of *Ascaris, Trichuris*, and

248   hookworm measured in eggs per gram (epg) of feces; intensity binary category of *Ascaris*

249   infection measured as low intensity (1-5000 epg) or moderate/high intensity (>5000 epg)

250   infection following World Health Organization (WHO) cutoffs; prevalence of co-infection with

251   two or three STH; and prevalence of co-infection with *Giardia* and any STH. The trial's original

252   protocol included *Entamoeba histolytica* and *Cryptosporidium spp*. as additional protozoan

253   endpoints. At enrollment, *Giardia* prevalence was 40% among 535 children 18-27 months old in

254   study compounds, while *Cryptosporidium Spp.* prevalence was 1% and *E. histolytica* prevalence

255   was 0%. We determined the extremely low prevalence made these trial endpoints futile due to

256   limited statistical power, and since each required a separate assay on the ELISA platform, the

257   study's steering committee decided to not test for them at follow-up.

258

259   *Sample size calculations*

260   All households in all clusters enrolled into the main trial were invited to participate in the

261   measurement of parasite infections. The main trial was powered for a minimum detectable

262   effect of 0.15 in length-for-age *Z* score and a relative risk of diarrhea of 0.7 or smaller for a

263   comparison of any intervention with the double-sized control group, assuming a type I error (α)

264   of 0·05 and power (1–β) of 0.8, a one-sided test for a two-sample comparison of means, and

265   10% loss to follow-up. This led to a planned design of 100 clusters per arm and 10 index children

266   per cluster. Given this design and a single, post-intervention measure, we estimated that the

267   trial's sample size would be sufficient at 80% power with a two-sided α of 0.05 to detect a

268   relative reduction of 18% in infection prevalence of any parasite. Our minimum detectable

269   effect calculations assumed 50% prevalence in the control arm, a village intraclass correlation

270   (ICC) of 0.14, two children measured per enrolled household (index child plus an older sibling),

271   and 70% successful stool collection and analysis.

272

273   *Statistical analysis*

274   All statistical analyses and comparisons between arms (W, S, H, WSH, N, WSHN compared to

275   active-control) were pre-specified prior to unblinding of investigators and published with a time-

276   stamp on the Open Science Framework (OSF) (https://osf.io/372xf/). Replication scripts and

277   data are also provided at the same link. Our alternative hypothesis for all comparisons was that

278   group means were not equal (two-sided tests). We estimated unadjusted and adjusted

279   intention-to-treat effects between study arms using targeted maximum likelihood estimation

12

280   (TMLE) with influence curve-based standard errors that treated clusters as independent units

281   and allowed for outcome correlation within clusters(24,25). Our parameters of interest for

282   dichotomous outcomes were prevalence ratios. Our parameter of interest for helminth intensity

283   was the relative fecal egg count reduction. We calculated the relative reduction using both

284   geometric and arithmetic means. We did not perform statistical adjustments for multiple

285   outcomes to preserve interpretation of effects and because many of our outcomes were

286   correlated(26). We estimated adjusted parameters by including variables that were associated

287   with the outcome to potentially improve the precision of our estimates. We pre-screened

288   covariates (see SI for full list) to assess whether they are associated (P-value <0.2) with each

289   outcome prior to including them in adjusted statistical models. We conducted subgroup

290   analyses to explore effect modification on *Ascaris* and *Giardia* infection presence for the

291   following factors: index child status, consumed deworming medicine in past 6 months (*Ascaris*

292   only), consumed soil in past week (index children only), >8 people in compound, and if

293   defecation occurred on the same day as stool collection. Statistical analyses were conducted

294   using R version 3.3.2 (www.r-project.org).

295

296   **Results**

297

298   *Enrollment*

299   Pregnant women were enrolled into the cluster-randomised controlled trial from Kakamega,

300   Bungoma, and Vihiga counties in Kenya's western region. Enrollment occurred between

301   November 2012 - May 2014; 8246 pregnant women were enrolled. Clusters with an average of

302   12 eligible pregnant women each were randomized by geographic proximal blocks into one of

303   eight study arms: chlorine treatment of drinking water (W); improved sanitation including

304   provision of toilets with plastic slabs and hardware to manage child feces (S); handwashing with

305   soap (H); combined WSH; infant and young child feeding counseling plus small-quantity lipid-

306   based nutrient supplements (N); combined WSHN; a double-sized active control, and a passive

307   control arm. Children in the passive control arm were purposively excluded from parasitology

308   measurement (Figure 1). Parasite infections were measured among children born to enrolled

309   pregnant mothers (index children) as well as their older siblings.

310

311   Enrollment characteristics of the study population were similar between arms (Table S1). Most

312   households accessed springs or wells as their primary drinking water source. In the control

313   group, 24% of households accessed unprotected water sources, such as springs, dug wells, and

314   surface water. The microbial quality of drinking water was very poor, as has been reported

315   previously for this study area(27); 96% (n=1829) of source water samples and 94% (n=5959) of

316   stored drinking water samples contained *Escherichia coli* contamination. Most (82%) households

317   owned a latrine, but only 15% had access to a latrine with a slab or ventilation pipe (Table S1).

318   Soap and water availability for handwashing at a designated handwashing location was low

319   (<10%).

320

321   *Indicators of intervention uptake*

322   After one year of intervention, 89-90% of households that received the sanitation intervention

323   had access to an improved latrine (compared to 18% in active-control arm) and 79-82% of these

324   had access to an improved latrine after two years of intervention. In the water intervention

325   arms, 40-44% of households had a detectable chlorine residual in their stored drinking water at

326   the one-year follow up (compared to 3% of control households) and 19-23% had chlorine

327   detected after two years. 76-78% of households that received the handwashing intervention

14

328   had soap and water available at a handwashing station (compared to 12% in the control arm)

329   after one year and this decreased to 19-23% at year two. Consumption of LNS sachets by

330   children in the nutrition arms was 95-96% of the expected two sachets per day at the one-year

331   follow up and 114-116% of expected at the 2-year follow up (>100% is possible because

332   additional LNS packets were delivered in case of future delivery delays) (Tables S2 & S3).

333

334   *Infection prevalence*

335   Soil-transmitted helminth and *Giardia* infections were measured after two years of exposure to

336   the interventions. We collected stool specimens from 9077 children aged 2-15 years old at the

337   two-year survey during January 2015 – July 2016; including 4928 index children (median age in

338   years: 2.0, interquartile range (IQR): 1.9, 2.1) and 4149 older children (median age in years: 5.0,

339   IQR: 4.2, 6.4) residing in an index child's compound (Figure 1). A total of 2346 children in 158

340   control clusters, 1117 children in 77 water clusters, 1160 children in 77 sanitation clusters, 1141

341   children in 77 handwashing clusters, 1064 children in 76 WSH clusters, 1072 children in 78

342   nutrition clusters, and 1177 children in 79 WSHN clusters provided stool specimens. Stool

343   specimens were successfully collected from 95% (4928 of 5202) of available index children and

344   from 93% (4149 of 4484) of available older children two years after intervention delivery (Figure

345   1 shows number of children not available due to no live birth, death, refusal, or absent; Table S7

346   shows characteristics of children lost to follow up). In the control group 22.6% of children were

347   infected with *Ascaris* (ICC: 0.10), 2.2% with hookworm (ICC: 0.04), 1.2% with *Trichuris* (ICC: 0.07)

348   (measured by Kato-Katz microscopy)*,* and 39% with *Giardia* (measured by enzyme-linked

349   immunosorbent assay)(Table S4). *Ascaris* infection prevalence was similar for index children

350   (22.8%) and older children (22.3%) in the control group (Table S6). Caregivers reported that 39%

351   of index children and 10% of older children had consumed soil in the past 7 days.

15

352

353   *Effect of interventions on parasite infection prevalence*

354   Infection prevalence of each STH, any STH, and *Giardia* was compared between each

355   intervention group (W, S, H, WSH, WSHN) and the double-sized active control group (C); see

356   methods for further details of the analysis. Compared to the control group, *Ascaris* infection

357   prevalence was 18% lower in the water arm (Prevalence Ratio [PR]: 0.82, 95% Confidence

358   Interval [CI] 0.67, 1.00), 22% lower in the combined WSH arm (PR: 0.78, 95% CI 0.63, 0.96), and

359   22% lower in the WSHN arm (PR: 0.78, 95% CI 0.64, 0.96) (Figure 2, Table S4). Sanitation,

360   handwashing, and nutrition did not significantly reduce *Ascaris* infection on their own (Figure 2).

361   The combined WSH intervention reduced infection with any STH by 23% (PR: 0.77, 95% CI 0.63,

362   0.95) and the combined WSHN intervention reduced infection with any STH by 19% (PR: 0.81,

363   95% CI 0.66, 0.98) (Table S4). No interventions significantly reduced the prevalence of

364   hookworm and *Trichuris,* though the low prevalence in the control arm meant that any

365   reduction due to intervention would be difficult to detect in the trial (Table S4). No interventions

366   reduced *Giardia* prevalence (Figure 2).

367

368   We re-analyzed all stool samples collected from children enrolled in the control, combined WSH,

369   and WSHN arms by quantitative polymerase chain reaction (qPCR) to validate our estimates

370   based on microscopy measurements. These three arms were selected for the qPCR subset

371   analysis prior to unblinding of investigators to results and were chosen based on the hypothesis

372   that these arms would be the most likely to have low-intensity STH infections if any of the

373   interventions were effective. qPCR analyses resulted in almost identical intervention effect

374   estimates to those based on microscopy (Figure 3, Table S8). Compared to the control group,

375   *Ascaris* infection prevalence was 21% lower (PR: 0.79, 95% CI 0.64, 0.97) in the WSN group and

16

376   23% lower (PR: 0.77, 95%CI 0.64, 0.93) in the WSHN group. We also did not detect any

377   significant effects of the interventions on *Trichuris* or hookworm infections using qPCR data

378   (Table S8).

379

380   *Effect of interventions on infection intensity*

381   *Ascaris* infection intensity was lower in children in the water arm (fecal egg count reduction with

382   geometric means [FECR]: -16%, 95% CI -32%, -1%), the WSH arm (FECR: -19%, 95% CI -33%, -5%),

383   and the WSHN arm (FECR: -18%, 95% CI -32%, -4%) compared to the control arm; FECR with

384   arithmetic means showed similar results (Table 1). The prevalence of heavy/moderate intensity

385   *Ascaris* infections was 10.0% in the water arm, 10.9% in WSH, and 10.3% in WSHN compared to

386   12.7% in the control arm; these differences were not statistically significant at the 95%

387   confidence level (Table S4).

388

389   The FECR with arithmetic means indicated that children in the WSH arm had lower intensity

390   infections with hookworm (3 eggs per gram [epg] *vs.* 11 epg in control) (Table 1). In addition, the

391   FECR with arithmetic means indicated lower *Trichuris* infection intensity in the WSH (0 epg *vs.* 6

392   epg in control), nutrition (2 epg), and the WSHN (1 epg) arms. Children that received the WSHN

393   intervention had 27% lower prevalence of coinfection with STH and *Giardia* compared to the

394   control group (PR: 0.73, 95% CI 0.56, 0.97)(Table S4). STH coinfection was rare (<2% in control

395   arm) and at similarly low levels in interventions arms (Table S4).

396

397   *Adjusted models and subgroup analyses*

398   Adjusted effect estimates were similar to unadjusted effects (Table S4). Subgroup analyses of

399   intervention effects stratified by child age, reported soil consumption (index children only),

17

400   number of people living in the compound, deworming (*Ascaris* only), and time since defecation

401   did not show any strong effect modification (Table S6).

402

403   **Discussion**

404

405   This study provides new evidence on the effect of improved water, sanitation, handwashing in

406   the household, and nutrition interventions, alone and in combination, on the prevalence of

407   infection with STH and *Giardia*. Our findings demonstrate that an integrated water, sanitation,

408   and handwashing intervention targeting the household environment in rural Kenya reduced

409   *Ascaris* infection prevalence by 22%, while a water treatment intervention reduced *Ascaris*

410   infection by 18%. Almost identical effect estimates generated by analyzing stool samples with

411   microscopy and qPCR in a subset of arms leant additional credibility to the overall results (Figure

412   3). In addition, we found that improved nutrition did not enhance the effectiveness of the WSH

413   intervention. *Trichuris* and hookworm prevalence were too low to precisely assess intervention

414   impact in this setting, and *Giardia* was unaffected by the interventions. Although the integrated

415   WSH intervention did not succeed in improving child growth or reducing symptomatic diarrhea

416   in this trial(22), our findings confirm that WSH can effectively interrupt environmental helminth

417   transmission.

418

419   A limited number of randomized controlled trials (RCTs) have previously analyzed the effect of

420   WSH interventions on STH infection. Two RCTs in rural India found no impact of community

421   sanitation interventions on helminth infections; however, both studies reported low usage rates

422   of toilets among intervention households(28,29). Several school-based RCTs combining

423   deworming with handwashing promotion have reported significant reductions in *Ascaris*

18

424   reinfection prevalence in China, Ethiopia, and Peru(17,30). A school-based integrated WSH

425   intervention combined with deworming in rural Kenya also reduced the odds of *Ascaris*

426   reinfection(31). While previous RCTs demonstrate the success of school-based deworming

427   combined with hygiene promotion, our results contribute new evidence from a large, cluster-

428   randomized trial that improving WSH in the household environment can reduce *Ascaris*

429   infections in a rural, low-income setting.

430

431   We did not detect an effect of the single sanitation intervention on STH infection prevalence.

432   One potential explanation for the lack of impact may be that transitioning households from

433   using traditional pit latrines to pit latrines with slabs may not have a measurable impact on STH

434   transmission. A shift from households practicing open defecation to using latrines might be

435   more likely to reduce STH transmission, with little additional benefit from improving latrine

436   quality. A recent trial in Cote d'Ivoire reported greater reduction in hookworm infection

437   prevalence among communities that received a community-led total sanitation intervention

438   (designed to reduce open defecation levels) integrated with community-wide MDA compared to

439   community-wide MDA alone (32). A second explanation may be that sanitation interventions are

440   more effective at interrupting environmental transmission of pathogens when they are

441   implemented at the community level(33), whereas our intervention only improved sanitation

442   access in compounds with enrolled pregnant women.

443

444   The reductions in *Ascaris* prevalence in the combined arms could have resulted from improved

445   water quality alone; *Ascaris* prevalence was 18% lower in the single water intervention arm than

446   the control, a similar magnitude to the 22% reduction in the integrated intervention arms. Near

447   identical reductions in *Ascaris* infection across all three water intervention arms suggests that

19

448 water could have been an important transmission pathway in this population, which was

449 interrupted by chlorine treatment. However, we cannot rule out contribution to reductions from

450 other interventions in the combined arms; *Ascaris* prevalence was lower (20%) in each of the

451 single sanitation, handwashing, and nutrition intervention arms, compared to 23% prevalence in

452 the control arm. Chlorine is not known to inactivate *Ascaris* eggs, but one experimental study

453 did find that chlorine can delay egg development and infectivity(34); it's possible that delayed

454 egg infectivity could reduce the risk of consuming an infective egg through drinking water. The

455 proportion of households using jerry cans (a plastic water container with a narrow capped

456 opening) to safely store drinking water was slightly higher in the water intervention arms than

457 other arms (Tables S2 & S3). Our findings indicate that water is an understudied transmission

458 pathway for *Ascaris*. We believe drinking water treatment should be further investigated as an

459 STH control strategy, and that chlorine should be further explored as a method for inhibiting

460 *Ascaris* egg development in drinking water supplies*.

461

462 The combined WSHN intervention was similarly effective to WSH in reducing *Ascaris* prevalence,

463 and improved nutrition did not reduce STH or *Giardia* infection on its own. Together, these

464 results suggest that improved nutrition intervention did not reduce parasite infection in this

465 population. Trials investigating the impact of micronutrient supplementation on STH infection or

466 reinfection have reported mixed results(18). Our results are consistent with a Kenyan trial that

467 found no effect of school-based micronutrient supplementation on reinfection with *Ascaris*(35).

468 Considering interventions in this trial did not include treatment with antiparasitic drugs, further

469 research would be valuable to understand if LNS supplementation could prevent parasite

470 infections after drug treatment.

471

472   *Giardia* prevalence was unaffected by any of the interventions in this trial. Our results stand in

473   contrast to results from the parallel WASH Benefits trial conducted in Bangladesh(36), which

474   detected reductions in *Giardia* infection prevalence in the handwashing, sanitation, combined

475   WSH, and combined WSHN arms(37). One potential explanation for lack of intervention effects

476   in this trial is that water could be the primary transmission pathway for *Giardia* in this study

477   setting, and *Giardia* is highly resistant to chlorination. The majority of households in the WASH

478   Benefits Bangladesh trial accessed protected tubewells providing water with lower levels of

479   fecal contamination compared to the springs and shallow wells accessed by households in this

480   trial(27,38). Another potential explanation is that handwashing rates with soap were not high

481   enough at the time of measurement to interrupt *Giardia* transmission; presence of soap and

482   water at a handwashing station decreased from 78% at year one to 19% at year two among

483   households in the WSH arm (Tables S2 & S3). *Giardia* is also zoonotic(4); exposure to avian and

484   ruminant fecal contamination in the household environment could mitigate the effect of

485   improved sanitation on transmission. Animal feces management was not a targeted behavior of

486   the intervention packages.

487

488   This trial had some limitations. Chlorination does not inactivate protozoa, but was selected as

489   the most appropriate water treatment intervention for the study context considering previous

490   local acceptability, affordability, and effectiveness against bacterial and viral enteric pathogens.

491   We measured parasite infections two years after intervention delivery; measurement among

492   the study population at one year could have produced different results because of higher

493   intervention adherence at that time (Table S2) and different child age-related exposures (e.g.

494   younger children may be more likely to consume soil). We were unable to blind study

495   participants due to the nature of the interventions; however, our outcomes were objective

21

496   indicators of infection analyzed by blinded laboratory technicians, and blinded analysts

497   replicated the data analysis.

498

499   During our trial, Kenya implemented a national school-based mass drug administration (MDA)

500   program to reduce STH prevalence(39); and 43% of study children reported consuming

501   deworming medication in the past 6 months (Table S6). Reported consumption of deworming

502   medicine was similar across study arms, suggesting no systematic differences in program

503   coverage or intensity between arms (Table S10). We observed similar *Ascaris* prevalence among

504   study index children (23%, median age 2 years) and older children (22%, median age 5 years),

505   suggesting that school-based MDA could be missing a key reservoir of infection among young,

506   preschool aged children. Moreover, an environmental survey conducted during the national

507   deworming program in our study region reported common detection of STH eggs in soil

508   collected from the entrance to homes, with *Ascaris* eggs detected in soil in 19% of

509   households(40). Taken together, these findings suggest additional control strategies beyond

510   school-based deworming might be necessary to fully interrupt environmental STH transmission.

511

512   In contrast to most previous trials evaluating the effect of WSH or nutrition on STH infection,

513   administering deworming medication was not included with our intervention. Our findings

514   represent the potential impact of WSH and nutrition interventions in the context of exposure to

515   a deworming program implemented at national scale. Although the magnitude of *Ascaris*

516   prevalence reduction observed in the WSH and water intervention arms may be lower than

517   what could be achieved by drug treatment in the short term, reduced STH infection after two

518   years of intervention exposure indicates sustained impact. Our results support the proposal that

519   improved WSH complement chemotherapy in the global effort to eliminate STH transmission.

22

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References

1. Pullan RL, Smith JL, Jasrasaria R, Brooker SJ. Global numbers of infection and disease burden of soil transmitted helminth infections in 2010. Parasites & Vectors. Parasites & Vectors; 2014 Jan 21;7(1):1–19.

2. Rogawski ET, Bartelt LA, Platts-Mills JA, Seidman JC, Samie A, Havt A, et al. Determinants and Impact of Giardia Infection in the First 2 Years of Life in the MAL-ED Birth Cohort. J Pediatric Infect Dis Soc. Oxford University Press; 2017 Jun 1;6(2):153–60.

3. Bethony J, Brooker S, Albonico M, Geiger SM, Loukas A, Diemert D, et al. Soil-transmitted helminth infections: ascariasis, trichuriasis, and hookworm. The Lancet. 2006 May;367(9521):1521–32.

4. Certad G, Viscogliosi E, Chabé M, Cacciò SM. Pathogenic Mechanisms of Cryptosporidium and Giardia. Trends in Parasitology. Elsevier Ltd; 2017 Mar 20;:1–16.

5. Dickson R, Awasthi S, Williamson P, Demellweek C, Garner P. Effects of treatment for intestinal helminth infection on growth and cognitive performance in children: systematic review of randomised trials. BMJ. 2000 Jun 24;320(7251):1697–701.

6. Taylor-Robinson DC, Maayan N. Deworming drugs for soil-transmitted intestinal worms in children: effects on nutritional indicators, haemoglobin and school performance. … Database Syst Rev. 2012.

7. Donowitz JR, Alam M, Kabir M, Ma JZ, Nazib F, Platts-Mills JA, et al. A Prospective Longitudinal Cohort to Investigate the Effects of Early Life Giardiasis on Growth and All Cause Diarrhea. Clinical Infectious Diseases. 2016 Aug 24;63(6):792–7.

8. Simsek Z, Zeyrek FY, Kurcer MA. Effect of Giardia infection on growth and psychomotor development of children aged 0-5 years. J Trop Pediatr. 2004 Apr;50(2):90–3.

9. Prado MS, Cairncross S, Strina A, Barreto ML, Oliveira-Assis AM, Rego S. Asymptomatic giardiasis and growth in young children; a longitudinal study in Salvador, Brazil. Parasitology. Cambridge University Press; 2005 Jul 1;131(1):51–6.

10. Berkman DS, Lescano AG, Gilman RH, Lopez SL, Black MM. Effects of stunting, diarrhoeal disease, and parasitic infection during infancy on cognition in late childhood: a follow-up study. The Lancet. 2002;359(9306):564–71.

11. Owada K, Nielsen M, Lau CL, Clements ACA, Yakob L, Soares Magalhaes RJ. Measuring the Effect of Soil-Transmitted Helminth Infections on Cognitive Function in Children: Systematic Review and Critical Appraisal of Evidence. Advances in Parasitology. 2017 Jan 1.

12. Clarke NE, Clements ACA, Doi SA, Wang D, Campbell SJ, Gray D, et al. Differential effect of mass deworming and targeted deworming for soil-transmitted helminth control in children: a systematic review and meta-analysis. The Lancet. 2017 Jan;389(10066):287–

569   97.

570   13.   Jia T-W, Melville S, Utzinger J, King CH, Zhou X-N. Soil-Transmitted Helminth Reinfection
571   after Drug Treatment: A Systematic Review and Meta-Analysis. Cooper PJ, editor. PLoS
572   Negl Trop Dis. 2012 May 8;6(5):e1621.

573   14.   Campbell SJ, Nery SV, McCarthy JS, Gray DJ, Magalhães RJS, Clements ACA. A Critical
574   Appraisal of Control Strategies for Soil-Transmitted Helminths. Trends in Parasitology.
575   Elsevier; 2016 Feb 1;32(2):97–107.

576   15.   Savioli L, Smith H, Thompson A. Giardia and Cryptosporidium join the "Neglected
577   Diseases Initiative." Trends in Parasitology. 2006 May;22(5):203–8.

578   16.   Speich B, Croll D, Fürst T, Utzinger J, Keiser J. Effect of sanitation and water treatment on
579   intestinal protozoa infection: a systematic review and meta-analysis. The Lancet
580   Infectious Diseases. Elsevier; 2016 Jan 1;16(1):87–99.

581   17.   Strunz EC, Addiss DG, Stocks ME, Ogden S, Utzinger J, Freeman MC. Water, Sanitation,
582   Hygiene, and Soil-Transmitted Helminth Infection: A Systematic Review and Meta-
583   Analysis. Hales S, editor. PLoS medicine. Public Library of Science; 2014 Mar
584   25;11(3):e1001620–38.

585   18.   Yap P, Utzinger J, Hattendorf J, Steinmann P. Influence of nutrition on infection and re-
586   infection with soil-transmitted helminths: a systematic review. Parasites & Vectors.
587   BioMed Central; 2014 May 19;7(1):229.

588   19.   David LA, Maurice CF, Carmody RN, Gootenberg DB, Button JE, Wolfe BE, et al. Diet
589   rapidly and reproducibly alters the human gut microbiome. Nature. Nature Publishing
590   Group; 2015 Apr 9;505(7484):559–63.

591   20.   Glendinning L, Nausch N, Free A, Taylor DW, Mutapi F. The microbiota and helminths:
592   sharing the same niche in the human host. Parasitology. 2014 Sep;141(10):1255–71.

593   21.   Arnold BF, Null C, Luby SP, Unicomb L, Stewart CP, Dewey KG, et al. Cluster-randomised
594   controlled trials of individual and combined water, sanitation, hygiene and nutritional
595   interventions in rural Bangladesh and Kenya: the WASH Benefits study design and
596   rationale. BMJ Open. 2013 Aug 1;3(8):e003476–6.

597   22.   Null C, Stewart CP, Pickering AJ, Global HDTL, 2018. Effects of water quality, sanitation,
598   handwashing, and nutritional interventions on diarrhoea and child growth in rural Kenya:
599   a cluster-randomised controlled trial. The Lancet Global Health. 2018.

600   23.   Pilotte N, Papaiakovou M, Grant JR, Bierwert LA, Llewellyn S, McCarthy JS, et al.
601   Improved PCR-Based Detection of Soil Transmitted Helminth Infections Using a Next-
602   Generation Sequencing Approach to Assay Design. Albonico M, editor. PLoS Negl Trop
603   Dis. Public Library of Science; 2016 Mar;10(3):e0004578.

604   24.   Gruber S, van der Laan MJ. tmle: An R Package for Targeted Maximum Likelihood
605   Estimation. Journal of Statistical Software. 2012 Nov 6;:1–35.

606 25. Balzer LB, van der Laan MJ, Petersen ML. Adaptive pre-specification in randomized trials
607   with and without pair-matching. Statistics in Medicine. Wiley-Blackwell; 2016 Nov
608   10;35(25):4528–45.

609 26. Schulz KF, Grimes DA. Multiplicity in randomised trials I: endpoints and treatments.
610   Lancet. Elsevier; 2005 May;365(9470):1591–5.

611 27. Pickering AJ, Arnold BF, Dentz HN, Colford JM, Null C. Climate and Health Co-Benefits in
612   Low-Income Countries: A Case Study of Carbon Financed Water Filters in Kenya and a Call
613   for Independent Monitoring. Environ Health Perspect. National Institute of
614   Environmental Health Science; 2017 Mar;125(3):278–83.

615 28. Patil SR, Arnold BF, Salvatore AL, Briceno B, Ganguly S, Colford JM, et al. The Effect of
616   India's Total Sanitation Campaign on Defecation Behaviors and Child Health in Rural
617   Madhya Pradesh: A Cluster Randomized Controlled Trial. Hunter PR, editor. PLoS
618   medicine. Public Library of Science; 2014 Aug 26;11(8):e1001709.

619 29. Clasen T, Boisson S, Routray P, Torondel B, Bell M, Cumming O, et al. Effectiveness of a
620   rural sanitation programme on diarrhoea, soil-transmitted helminth infection, and child
621   malnutrition in Odisha, India: a cluster-randomised trial. The Lancet Global Health.
622   Elsevier; 2014 Nov 1;2(11):e645–53.

623 30. Mahmud MA, Spigt M, Bezabih AM, Pavon IL, Dinant G-J, Velasco RB. Efficacy of
624   Handwashing with Soap and Nail Clipping on Intestinal Parasitic Infections in School-Aged
625   Children: A Factorial Cluster Randomized Controlled Trial. Bhutta ZA, editor. PLoS
626   medicine. 2015 Jun 9;12(6):e1001837–16.

627 31. Freeman MC, Clasen T, Brooker SJ, Akoko DO, Rheingans R. The Impact of a School-Based
628   Hygiene, Water Quality and Sanitation Intervention on Soil-Transmitted Helminth
629   Reinfection: A Cluster-Randomized Trial. American Journal of Tropical Medicine and
630   Hygiene. The American Society of Tropical Medicine and Hygiene; 2013 Nov 6;89(5):875–
631   83.

632 32. Hürlimann E, Silué KD, Zouzou F, Ouattara M, Schmidlin T, Yapi RB, et al. Effect of an
633   integrated intervention package of preventive chemotherapy, community-led total
634   sanitation and health education on the prevalence of helminth and intestinal protozoa
635   infections in Côte d'Ivoire. Parasites & Vectors. BioMed Central; 2018 Feb 27;11(1):115.

636 33. Harris M, Alzua ML, Osbert N, Pickering A. Community-Level Sanitation Coverage More
637   Strongly Associated with Child Growth and Household Drinking Water Quality than
638   Access to a Private Toilet in Rural Mali. Environmental Science & …. American Chemical
639   Society; 2017 Jun 1;51(12):7219–27.

640 34. Oh K-S, Kim G-T, Ahn K-S, Shin S-S. Effects of Disinfectants on Larval Development of
641   Ascaris suum Eggs. Korean J Parasitol. 2016 Feb;54(1):103–7.

642 35. Olsen A, Thiong'o FW, Ouma JH, Mwaniki D, Magnussen P, Fleischer Michaelsen K, et al.
643   Effects of multimicronutrient supplementation on helminth reinfection: a randomized,
644   controlled trial in Kenyan schoolchildren. Transactions of the Royal Society of Tropical

26

645   Medicine and Hygiene. 2003 Jan;97(1):109–14.

646 36. Luby SP, Rahman M, Arnold BF, Unicomb L, Ashraf S, Winch PJ, et al. Effects of water
647   quality, sanitation, handwashing and nutritional interventions on diarrhoea and child
648   growth in rural Bangladesh: A cluster randomized trial. The Lancet Global Health.

649 37. Lin A, Ercumen A, Benjamin-Chung J, Arnold BF, Das S, Haque R, et al. Effects of water,
650   sanitation, handwashing, and nutritional interventions on child enteric protozoan
651   infections in rural Bangladesh: A cluster-randomized controlled trial. Clin Infect Dis. 3rd
652   ed. 2018 Apr 13;16:87.

653 38. Pickering AJ, Ercumen A, Arnold BF, Kwong LH, Parvez SM, Alam M, et al. Fecal Indicator
654   Bacteria along Multiple Environmental Transmission Pathways (Water, Hands, Food, Soil,
655   Flies) and Subsequent Child Diarrhea in Rural Bangladesh. Environmental Science &
656   Technology. American Chemical Society; 2018 Jun 14;52(14):7928–36.

657 39. Okoyo C, Nikolay B, Kihara J, Simiyu E, Garn JV, Freeman MC, et al. Monitoring the impact
658   of a national school based deworming programme on soil-transmitted helminths in
659   Kenya: the first three years, 2012 – 2014. Parasites & Vectors. BioMed Central; 2016 Jul
660   25;9(1):408.

661 40. Steinbaum L, Njenga SM, Kihara J, Boehm AB, Davis J, Null C, et al. Soil-Transmitted
662   Helminth Eggs Are Present in Soil at Multiple Locations within Households in Rural Kenya.
663   Aroian RV, editor. PLoS ONE. Public Library of Science; 2016;11(6):e0157780.

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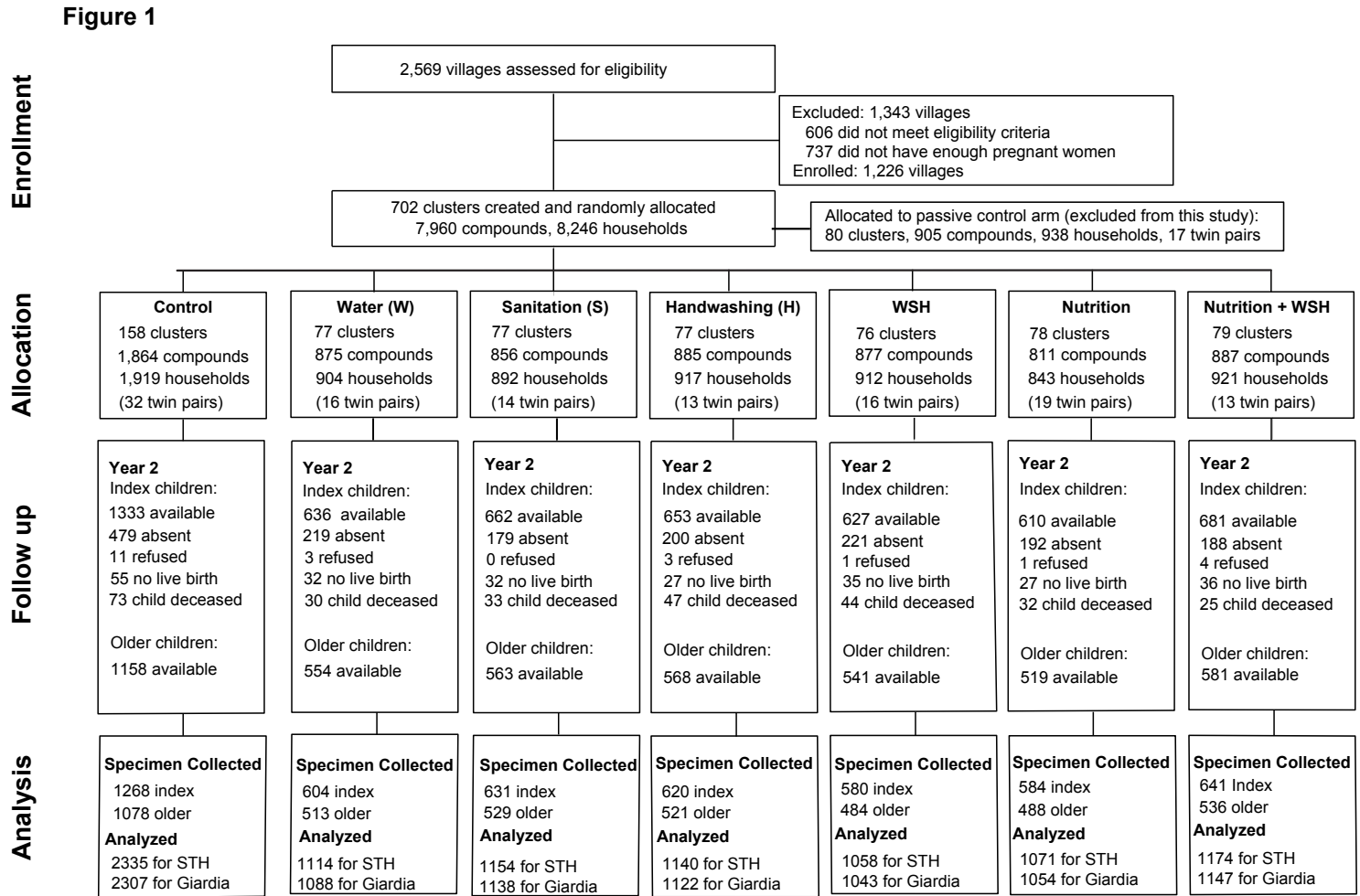**FIGURES**

Figure 1. Trial profile.

Figure 1

Figure 2. Effect of the interventions on infection with *Ascaris* and *Giardia.* Prevalence ratios estimated by targeted maximum likelihood estimation. Error bars show 95% confidence intervals for the prevalence ratios.
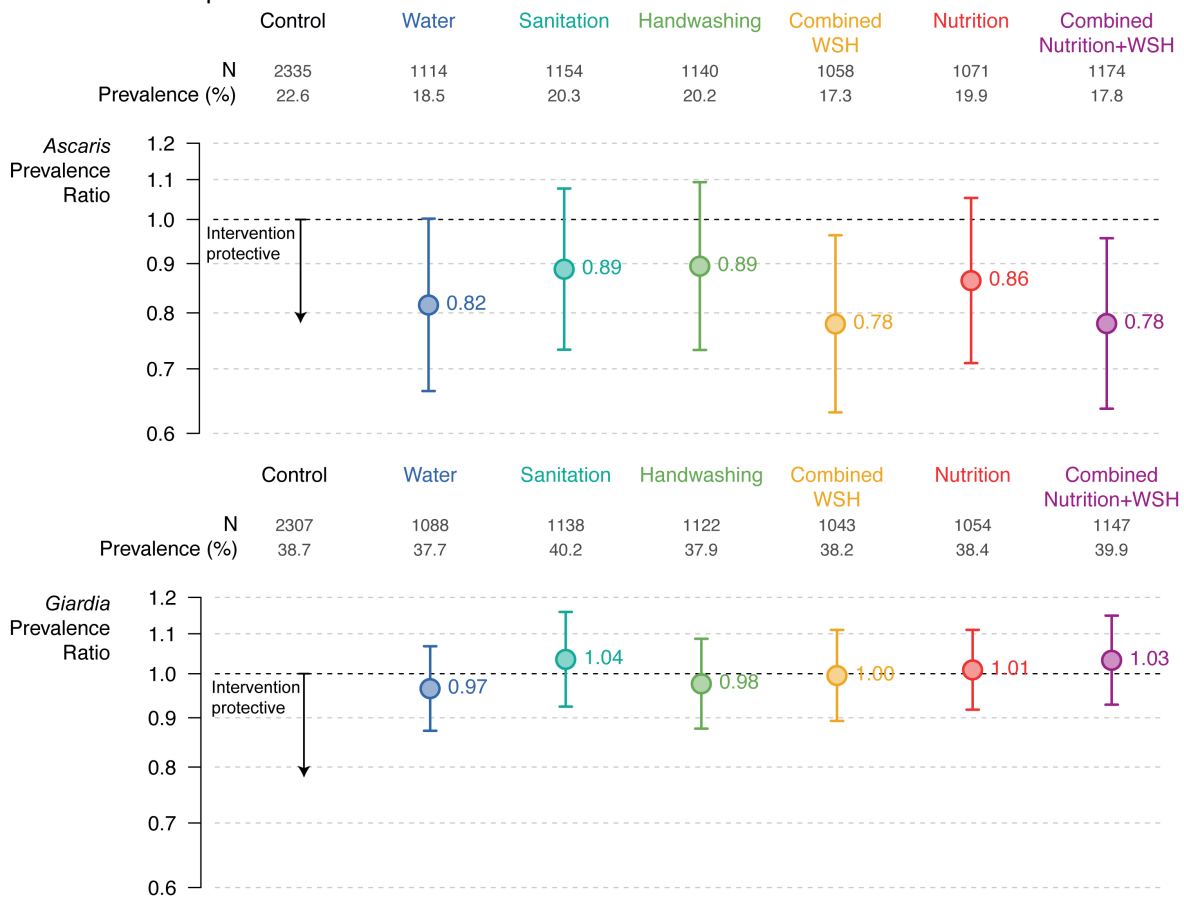
Figure 3. Effect of the combined interventions on infection with *Ascaris* estimated with Kato-Katz microscopy (left) and by qPCR (right). Prevalence ratios estimated by targeted maximum likelihood estimation. Error bars show 95% confidence intervals for the prevalence ratios.
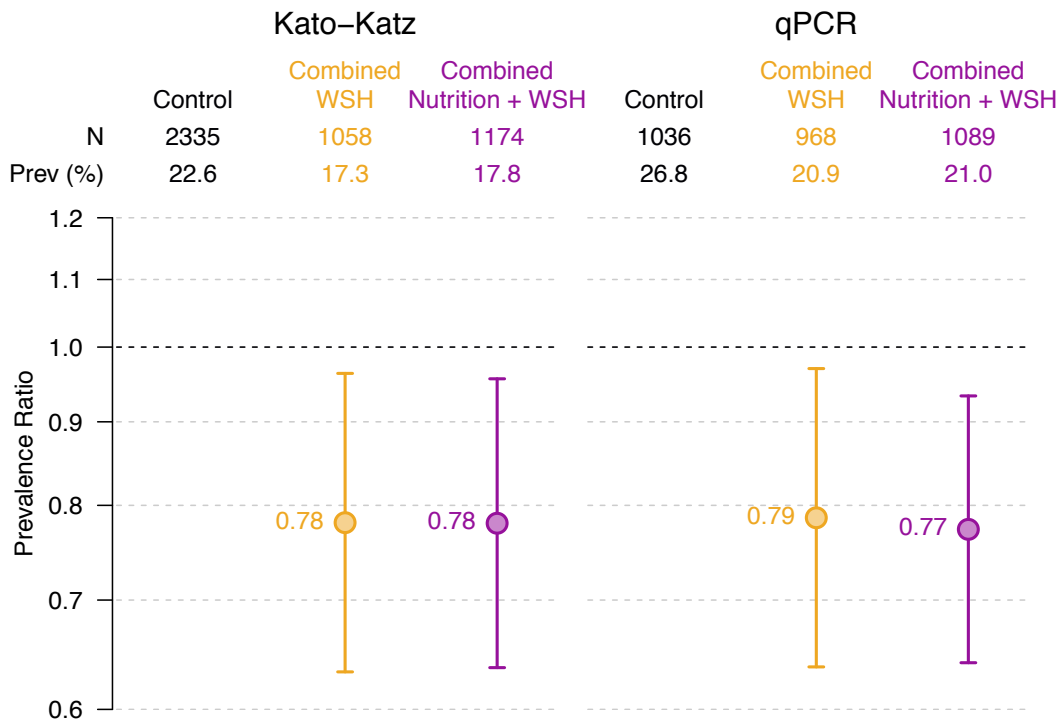
Table 1. Effect of the interventions on infection intensity, measured by fecal egg count reduction (FECR) with arithmetic and geometric means in eggs per gram (epg). FECR estimated by targeted maximum likelihood estimation. Bold indicates p<0.05. *Values of 0.5 epg substituted for samples below the detection limit to calculate log-transformed mean

| | | | Arithmetic mean | | | | Geometric mean | | | |
Ascaris FECR	N	Arithmetic mean, epg	FECR	95% CI		P-value	Log10 mean*, epg	FECR	95% CI		P-value
Control	2335	3641					0.60				
Water	1114	2682	**-0.26**	**-0.52**	**-0.01**	**0.04**	0.40	**-0.16**	**-0.32**	**-0.01**	**0.04**
Sanitation	1154	3443	-0.04	-0.32	0.23	0.75	0.50	-0.09	-0.25	0.07	0.27
Handwashing	1140	3386	-0.03	-0.34	0.28	0.85	0.50	-0.08	-0.25	0.08	0.31
WSH	1058	2571	**-0.27**	**-0.52**	**-0.02**	**0.03**	0.40	**-0.19**	**-0.33**	**-0.05**	**0.01**
Nutrition	1071	3303	-0.11	-0.34	0.12	0.35	0.50	-0.10	-0.25	0.04	0.16
Nutrition + WSH	1174	2927	-0.21	-0.46	0.03	0.09	0.40	**-0.18**	**-0.32**	**-0.04**	**0.01**
Hookworm FECR											
Control	2335	12					-0.25				
Water	1114	10	-0.20	-0.84	0.44	0.54	-0.23	0.02	-0.02	0.05	0.37
Sanitation	1154	10	-0.16	-0.90	0.57	0.67	-0.24	0.01	-0.02	0.04	0.42
Handwashing	1140	23	0.93	-1.39	3.25	0.43	-0.21	0.03	0.00	0.07	0.08
WSH	1058	3	**-0.74**	**-0.91**	**-0.58**	**0.00**	-0.26	-0.02	-0.04	0.01	0.18
Nutrition	1071	12	0.16	-1.17	1.50	0.81	-0.23	0.03	-0.01	0.06	0.14
Nutrition + WSH	1174	24	1.02	-1.87	3.91	0.49	-0.23	0.02	-0.01	0.06	0.22
Trichuris FECR											
Control	2335	6					-0.27				
Water	1114	6	0.04	-1.91	1.98	0.97	-0.27	0.00	-0.03	0.03	0.92
Sanitation	1154	4	-0.19	-1.49	1.11	0.78	-0.27	0.00	-0.03	0.02	0.77
Handwashing	1140	6	0.03	-1.40	1.46	0.97	-0.26	0.01	-0.02	0.04	0.46
WSH	1058	0	**-0.91**	**-1.07**	**-0.75**	**0.00**	-0.29	-0.02	-0.04	0.00	0.06
Nutrition	1071	2	**-0.64**	**-1.22**	**-0.05**	**0.03**	-0.28	-0.02	-0.04	0.01	0.18
Nutrition + WSH	1174	1	**-0.81**	**-1.15**	**-0.47**	**0.00**	-0.29	-0.02	-0.05	0.00	0.10