Independent and combined effects of nutrition and sanitation interventions on enteric pathogen carriage and child growth in rural Cambodia: a factorial cluster-randomised controlled trial

Amanda Lai[1,2], Irene Velez[3], Ramya Ambikapathi[4], Krisna Seng[3], Karen Levy[5], Erin Kowalsky[1,2], David Holcomb[1], Konstantinos T. Konstantinidis[2], Oliver Cumming[6], Joe Brown[1*]

[1] Department of Environmental Sciences and Engineering, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
[2] School of Civil and Environmental Engineering, Georgia Institute of Technology, Atlanta, Georgia, USA
[3] MSI, A Tetra Tech Company, Arlington, Virginia, USA
[4] Department of Public Health, Purdue University, West Lafayette, Indiana, USA
[5] Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, Washington, USA
[6] Department of Disease Control, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK

* Corresponding author: Joe Brown, joebrown@unc.edu

Summary

Background

Childhood exposure to enteric pathogens associated with poor sanitation contributes to undernutrition, associated with adverse effects later in life. This trial assessed the independent and combined effects of nutrition and sanitation interventions on child growth outcomes and enteric pathogen infection in rural Cambodia, where the prevalence of childhood stunting remains high.

Methods

We conducted a factorial cluster-randomised controlled trial of 4,015 households with 4,124 children (1-28 months of age at endline) across three rural provinces in Cambodia. Fifty-five communes (clusters) were randomly assigned to a control arm or one of three treatments: a nutrition-only arm, a sanitation-only arm, and a combined nutrition and sanitation arm receiving both treatments. The primary outcome was length-for-age Z-score (LAZ); other outcomes included weight-for-age Z-score (WAZ), weight-for-length Z-score (WLZ), stunting, wasting, underweight, and caregiver-reported diarrhoea. We assayed stool specimens from a subset of all children (n = 1,620) for 27 enteric pathogens (14 bacteria, 6 viruses, 3 protozoa, and 4 soil-transmitted helminths) and estimated effects of interventions on enteric pathogen detection and density. Analysis was by intention-to-treat. The trial was pre-registered with ISRCTN Registry (ISRCTN77820875).

Findings

Self-reported adherence was high for the nutrition intervention but uptake was low for sanitation. Compared with a mean LAZ of -1.04 (SD 1.2) in the control arm, children in the nutrition-only arm (LAZ +0.08, 95% CI -0.01-0.18) and combined nutrition and sanitation arm (LAZ +0.10, 95% CI 0.01-0.20) experienced greater linear growth; there were no measurable differences in LAZ in the sanitation-only arm (LAZ -0.05, 95% CI -0.16-0.05). We found no effect of any intervention (delivered independently or combined) on either enteric pathogen frequency or pathogen load in stool. Compared with a mean WAZ of -1.05 (SD 1.1) in the control arm, children in the nutrition-only arm (WAZ +0.10, 95% CI 0.00-0.19) and combined intervention arm (WAZ +0.11, 95% CI 0.03-0.20) were heavier for their age; there was no difference in WAZ in the sanitation-only arm. There were no differences between arms in prevalence of stunting, wasting, underweight status, one-week period prevalence of diarrhoea, pathogen prevalence, or pathogen density in stool.

Interpretation

Improvements in child growth in nutrition and combined nutrition and sanitation arms are consistent with previous efficacy trials of combined nutrition and sanitation interventions. We found no evidence that the sanitation intervention alone improved child growth or reduced enteric pathogen detection, having achieved only modest changes in access and use.

Funding

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Introduction

Childhood undernutrition is associated with higher susceptibility to infectious disease, reduced cognitive function, and various adverse outcomes later in life[1]. Growth faltering is an effect of chronic undernutrition and tends to manifest in a child's first two years[2]. Many studies have focused on improving infant and child nutrition to achieve better growth outcomes[3,4]. However, nutrition interventions alone have not been successful in eliminating stunting, suggesting that broader interventions addressing other important factors are needed alongside exclusive breastfeeding and improved nutritional intake[5].

Reducing early childhood exposure to enteric pathogens through safe water, sanitation, and hygiene (WASH) may complement other interventions by reducing diarrhoeal diseases and environmental enteric dysfunction (EED)[6]—both of which can impact early childhood growth and development[7]. Observational studies have found strong associations between child growth faltering and poor access to sanitation[8]. However, recent randomised controlled trials (RCTs) in Zimbabwe[9], Bangladesh[3], and Kenya[4] that delivered standalone household-level sanitation interventions (not coupled with other nutrition or hygiene interventions) were not found to improve child growth.

The community-led total sanitation (CLTS) framework is an approach to ending open defecation (OD) through behavioural change and collective action rather than through the provision of hardware and materials. CLTS and other rural promotion-based interventions shift the focus from individual and household sanitation practices to a community-level concern over OD by triggering collective behaviour change through powerful emotional drivers such as shame and disgust, as well as positive motivators such as improved health, dignity, and pride. Observational studies in Cambodia[10] and Ecuador[11] found higher community-level sanitation coverage to be associated with reduced prevalence of stunting. Despite this, recent RCTs employing promotion-based interventions have found mixed effects on child growth. One trial was found to be successful in improving child growth in Mali[12], but this effect was not observed in other trials elsewhere[13,14].

This study contributes to a growing body of literature on the impact of combined nutrition and sanitation interventions on early child growth, caregiver-reported diarrhoea, and detection and quantification of enteric pathogens in stool as a proxy for enteric infection. While diarrhoea has been widely used as a primary outcome measure in WASH studies[3,4,12,15], recent studies have used stool-based detection of enteric pathogens[15] and anthropometry measurements[3,4,9] as primary outcomes that are more objectively measurable and may also broadly indicate health status by capturing cumulative effects of exposures via EED[6]. We used a factorial cluster-randomised controlled trial (cRCT) to assess the independent and combined effects of nutrition and sanitation interventions delivered in the context of a large-scale, USAID-funded rural nutrition and sanitation/hygiene program in Cambodia. We hypothesised that children receiving both sanitation and nutrition interventions would have increased linear growth compared with children from control areas lacking these interventions. We further hypothesised that combined nutrition and sanitation interventions would lead to synergistic improvements in linear growth beyond what was realised in either standalone intervention arm. The hypothesised pathway for

these effects, consistent with secondary outcome measures, was reduced enteric pathogen frequency and enteric pathogen load in stools (Figure 1).

Methods

Study design and participants

We implemented a two-by-two factorial cRCT in rural communes in three provinces in Cambodia: Battambang, Pursat, and Siem Reap. The communes targeted by the program were selected based on two criteria: communes where at least 30% of the population was living below the poverty line according to the 2011 Cambodia Ministry of Planning's Commune Database; and communes where latrine subsidies were not then in place. This study is reported per the Consolidated Standards of Reporting Trials (CONSORT) guideline (see Supplementary Material for CONSORT checklist).

Randomisation and masking

In 2015, prior to the start of project activities, we randomly assigned communes to one of three treatment arms (nutrition only, sanitation/hygiene only, combined nutrition and sanitation/hygiene) or control arm using a random number generator with reproducible seed in Stata 13 (Stata, College Station, TX). Randomisation was conducted at the commune level to limit the risk of contamination between study arms and all villages within each commune received the assigned intervention. Following randomisation, three communes were dropped from the trial due to objections from the local governments of overlap with other current programming. This resulted in 55 communes with treatment arms of different sizes: 11 communes in nutrition-only arm; 13 in sanitation-only arm; 12 in combined-intervention arm; and 19 in control arm (Figure 2). The trial enrolled primary caregivers with a child who was born after intervention implementation began (up to 28 months prior) and who had lived in the commune during the child's entire life, resulting in a participant population of children 1-28 months old. Neither participants nor field staff were masked to treatment status due to the nature of the interventions, but data collection teams were blinded to the arm assignment and number of treatment arms.

Procedures

The interventions were delivered in the 36 intervention communes over the course of two years, between 2015-2017, while the remaining 19 control communes were unexposed to the programmes. Two international non-governmental organizations—Save the Children and SNV—provided programmatic implementation and coordinated activities with local governments. The nutrition interventions included complementary feeding activities and education through community-based growth promotion sessions; caregiver groups; home visits; and conditional cash transfers (CCTs) linked to the utilization of key health and nutrition services focusing on first 1,000 days of life. The sanitation interventions consisted primarily of CLTS as it was delivered here, latrine vouchers coupled with supply-side support for sanitation and hygiene products, and social behaviours change communications (SBCC). Intervention activities and frequency are summarized in Table 1, and additional details about the interventions are described in the Supplementary Material.

The survey was communicated in the Khmer language to assess household and child-level risk factors of children under 28 months of age. Enumerators completed in-home interviews with the

primary caregiver of children in the household about basic household member information; breastfeeding and nutrition of children up to age 28 months; number of pregnancies and child births of the caregiver; intervention exposure and participation; household WASH conditions and practices; and household assets/characteristics to construct wealth scores (excluding WASH variables). We also documented process evaluation (PE) indicators based on self-reported receipt of, and participation in, intervention activities to assess intervention fidelty and adherence, respectively. We attempted to collect a stool sample from each child and randomly selected a subset of stools for analysis by reverse-transcription quantitative polymerase chain reaction (RT-qPCR) of 30 enteric pathogen genes using a custom-developed TaqMan Array Card (TAC; ThermoFisher Scientific, Waltham, VA), as described in the Supplementary Material.

Outcomes

The primary outcome was length-for-age Z-score (LAZ). For children 1-24 months in age, we measured recumbent length; for children 24-28 months in age, we measured standing height. Herein, "length" will be inclusive of both recumbent length and standing height. Secondary outcomes included weight-for-age Z-score (WAZ); weight-for-length Z-score (WLZ); proportion of children stunted (LAZ<-2), underweight (WAZ<-2), and wasted (WLZ<-2); caregiver reported diarrhoea; all-cause mortality; and enteric pathogen detection and quantification in stool. Child length and weight were measured by trained paired enumerators following guidelines from the National Health and Nutrition Examination Survey (NHANES)[16]. Final measurements took place in August 2019, 28 months after the end of the roll-out period. Data collection was completed by KHANA Centre for Population Health Research, with oversight and support from Management Systems International (MSI). Data collection details, measurement protocols, and PE indicators are further described in Supplementary Material.

We assessed enteric pathogens as the prevalence of individual gene targets, the number of co-detected pathogens, and enteric pathogen-associated gene copies per gram of stool based on PCR quantification cycle (Cq) and standard curves. *E.coli* pathotypes were defined as: EAEC (*aaiC*, or *aatA*, or both), atypical EPEC (*eae* without *bfpA*, *stx1*, and *stx2*), typical EPEC (*bfpA*), ETEC (*STh*, *STp*, or *LT*), and STEC (*eae* without *bfpA* and with *stx1*, *stx2*, or both). Details on nucleic acid extraction and molecular assaying are described in Supplementary Material.

Statistical analysis

We performed an intention-to-treat (ITT) analysis for all outcomes using generalised estimating equations (GEE) with robust standard errors to account for clustering at the village level. We did not consider pre-intervention covariate balance[17] but present secondary analyses adjusted for pre-specified pre-intervention covariates in the Supplementary Material. Outcomes in each treatment arm were compared to the control arm and between standalone treatment arms and the combined treatment arm. We used linear regression to estimate mean differences in LAZ, WAZ, WLZ, and $\log_{10}$-transformed pathogen gene target densities and used log-linear Poisson regression to estimate the prevalence ratio (PR) between arms for nutritional status (stunting, wasting, and underweight), diarrhoea, and overall mortality. Enteric pathogen gene outcomes were dichotomised, with positive detections defined by a Cq <35[18], and Poisson regression was used to estimate PRs for individual pathogens detected in stool. We further estimated the incidence rate ratio (IRR) of co-detected pathogens (total and in subgroups by bacteria, viruses, protozoa, and STHs) using negative binomial regression. We did not adjust for multiple comparisons for

growth, diarrhoea, or mortality outcomes[3,19], but we did apply the Benjamini-Hochberg procedure to control the false discovery rate within analyses of multiple enteric pathogen outcomes[20]. Details on power calculations are included in Supplementary Material.

Ethics

The study received approval from the National Ethics Committee for Health Research in the Cambodian Ministry of Health, Georgia Institute of Technology, and New England Institutional Review Board. Prior to any data collection, the trial was explained to participants in the Khmer language. Written and verbal consent were obtained prior to administering the surveys and anthropometry measurements. The trial was pre-registered with ISRCTN Registry (ISRCTN77820875).

Results

Among 82 presumptively eligible communes, the provincial governments in 27 declined to participate. Ultimately, the evaluation included 55 communes randomly assigned to one of three treatment arms (n=36 communes) or control arm (n=19 communes); the control arm was relatively oversized to enhance statistical efficiency of multiple hypothesis testing[21]. Figure 2 shows the trial profile by intervention subgroups. 4,015 households participated in endline surveys; 4,005 households were included in these analyses (10 were excluded due to incomplete surveys), and 4,124 children had anthropometry measures taken.

Household and caregiver characteristics were mostly similar across treatment and control groups (Table 2). Primary caregivers in the control group reported lower levels of primary school attendance compared to the treatment groups, but paternal primary school attendance was similar. Households in the nutrition-only and sanitation-only groups had higher wealth index scores compared to households in the combined intervention and control groups. The control group had a higher prevalence of improved water source as their main source of drinking water compared to the treatment groups.

Nutrition intervention fidelity was high, with households in the nutrition-only and combined-intervention arms reporting significantly higher participation in these activities compared to the sanitation-only and control groups (Table 3). Approximately 60% of households in the nutrition-only and combined-intervention arms reported participating in at least four of the eight nutrition intervention activities, compared to 4% in the sanitation-only and control arms. Conversely, sanitation intervention fidelity was very low, with only 6% of households in the sanitation-only and control arms reporting participation in any CLTS activity, compared to 14% of households in the nutrition-only arm and 25% in the combined-intervention arm.

More households in the control arm (70%) had an improved water source as their main source of drinking water, an indicator of nutrition intervention adherence, compared to other arms (approximately 60% in other arms; Table 4). The combined intervention arm had greater access to improved sanitation facilities (61%) compared to the nutrition-only (55%), sanitation-only (51%), and control (52%) arms. OD (self-reported) was practiced less in the combined intervention arm (7%) compared to the nutrition-only (14%), sanitation-only (16%), and control (16%) arms. Notably, the sanitation-only arm experienced a significantly larger increase in sanitation coverage (+25 percentage points [pp]) compared to all other arms (+14pp in nutrition-

only arm, +19pp in combined and control arms), though sanitation gains across all arms were evident in the intervention period, reflecting a strong secular trend of sanitation expansion that has been widely documented in rural Cambodia[8,10,22,23]. Additional intervention adherence indicators related to environmental hygiene are reported in the Supplementary Material.

Primary and secondary outcomes

Mean LAZ in the control arm was -1.04 (SD 1.20). Compared with control, children in the nutrition-only arm were longer by a mean of 0.08 LAZ (95% CI -0.01, 0.18), and children in the combined-intervention arm were longer by 0.10 LAZ (95% CI 0.01, 0.20), although these differences were not observed in the adjusted analyses (

Table 5, Figure 3, Supplementary Material). Children in the nutrition-only arm and combined-intervention arm were heavier than children in the control arm by a mean of 0.10 WAZ (95% CI 0.00, 0.19) and 0.11 (95% CI 0.03, 0.20), respectively. These differences were slightly attenuated in the adjusted analyses (

Table 5, Supplementary Material). No differences were observed between the control arm and intervention arms in terms of WLZ. Children in the combined intervention arm were also longer and heavier, on average, than children in the sanitation-only arm by 0.16 LAZ (95% CI 0.04, 0.27) and 0.10 WAZ (95% CI 0.01, 0.20), respectively. LAZ and WAZ were similar between children in the nutrition-only and combined intervention arms.

Compared with the control arm, none of the intervention arms differed in the prevalence of children who experienced stunting, wasting, diarrhoea (7-day recall), or mortality (Table 6). However, the combined intervention reduced underweight prevalence by 18% (PR 0.82, 95% CI 0.68, 0.99) relative to the control arm. Although the combined intervention did not significantly impact stunting prevalence compared with the control arm or the nutrition-only arm, the sanitation-only arm was associated with a 20% increase (PR 1.2, 95% CI 1.0, 1.5) in the prevalence of both stunting and underweight status when compared to the combined intervention. All associations with stunting and underweight were attenuated in adjusted analyses (Supplementary Material).

Enteric pathogen results

We assessed enteric pathogen-associated gene targets in 1,620 randomly selected stools that demonstrated acceptible amplification (of 4,114 stools total, see Supplementary Material): 305 from the nutrition arm, 333 from the sanitation arm, 438 from the combined-intervention arm, and 544 from the control arm. We detected at least one bacterial gene in 87% of all samples, at least one viral gene in 49% of samples, at least one protozoan gene in 20% of samples, and at least one STH gene in 2% of samples. Enteroaggregative *E. coli* (EAEC), enteric pathogenic *E. coli* (EPEC), enterovirus, *Campylobacter* spp., and enterotoxigenic *E. coli* (ETEC) were the most prevalent pathogens (Table 7). We detected a mean 2.2 bacterial genes (out of 9), 0.59 viral genes (out of 6), 0.21 protozoan genes (out of 4), and 0.03 STH genes (out of 4) in each sample. We found no differences in the rate of bacterial, viral, protozoan, or STH gene co-detection between the control arm and any treatment arm or between the combined arm and the standalone intervention arms (Table 8). Prevalence increased with age for many pathogens (aEPEC, ETEC, *Shigella*/EIEC (*ipah*), STEC, adenovirus, *Giardia*), while prevalence peaked for children 9-17 months for other pathogens (*Campylobacter* spp., *C.diff*, EAEC, *Salmonella* spp.; Supplementary Material).

Examining prevalence of specific targets compared to the control arm, the nutrition-only arm demonstrated increased prevalence of any bacterial gene (PR 1.06, 95% CI 1.01, 1.11), adenovirus (PR 1.88, 95% CI 1.41, 2.51) and heat-labile/heat-stable ETEC (PR 2.00, 95% CI 1.19, 3.36) and reduced prevalence of EIEC/*Shigella* spp. (PR 0.60, 95% CI 0.39, 0.94). Children in the sanitation-only arm had less EPEC (PR 0.88, 95% CI 0.78, 1.00) compared to control. In the combined-intervention arm, atypical-EPEC prevalence decreased (PR 0.85, 95% CI 0.73, 0.98) while the prevalence increased for heat-stable ETEC (PR 1.42, 95% CI 1.01, 2.00), heat-labile/heat-stable ETEC (PR 1.74, 95% CI 1.06, 2.86), and any viral gene (PR 1.16, 95% CI 1.02, 1.31). We found similar mixed effects when comparing pathogen gene prevalence in individual treatment arms compared to the combined arm; there was slightly lower combined prevalence of any bacterial target (PR 0.96, 95% CI 0.91, 1.02) and enterovirus (PR 0.82, 95% CI 0.67, 1.00) in the sanitation-only arm, and we found higher prevalence of adenovirus (PR 1.42, 95% CI 1.07, 1.87) in the nutrition-only arm (Table 9).

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305 Generally, differences in mean gene quantities were consistent with prevalence differences
306 (Table 9;

Table 10). We detected lower concentrations of pathogen-associated genes in the nutrition-only and sanitation-only arms compared with the control arm; children in the nutrition-only arm carried lower quantities of STEC (-1.46 $\log_{10}$-copies, 95% CI -2.97, 0.06) and *Giardia* (-1.73 $\log_{10}$-copies, 95% CI -3.02, -0.44), and children in the sanitation-only arm carried lower quantities of EPEC (-0.54 $\log_{10}$-copies, 95% CI -1.17, 0.09) and STEC (-1.71 $\log_{10}$-copies, 95% CI -3.07, -0.34). There was no measurable difference in mean gene quantities between the combined and control arm. There was no significant difference in quantity of pathogen genes between treatment arms after adjusting for multiple comparisons[20].

Discussion

We found a modest effect on growth from the nutrition-only intervention and a greater effect in the combined intervention arm that was likely attributable to the nutrition intervention alone. By contrast, the sanitation intervention alone was not associated with growth improvements, relative to control conditions, and demonstrated significantly poorer growth than the combined intervention arm. The similar impacts on linear growth between the nutrition-only and combined intervention arms were consistent with the observed linear growth improvements being attributable primarily to the nutrition intervention alone, further suggesting that the addition of this sanitation intervention to the nutrition intervention did not produce synergistic effects. Intermediate outcomes of meal frequency and dietary diversity were similar between arms, so the observed effects may have been attributable to other elements of the nutrition or combined intervention not captured by these measures. We observed no meaningful differences between arms with respect to secondary outcome measures of WAZ, WLZ, stunting, wasting, underweight status, diarrhoea, mortality, pathogen prevalence, pathogen co-detection rate, or pathogen gene copy quantity. Although molecular detection of a specific pathogen in stool does not necessarily signal active enteric infection, potential for disease, or direct effects on the individual, it does unambiguously indicate prior exposure to that pathogen. Our specific pathogen targets were selected *a priori* based on a range of globally observed enteric pathogens and may not fully capture the relevant enteric pathogens in rural Cambodia; however, the consistently high pathogen prevalence across all treatment arms suggests the suite of interventions assessed in this trial did not prevent environmental exposure to enteric pathogens.

Our findings are consistent with results from several recent randomised factorial WASH and nutrition efficacy trials reporting protective effects of combined/integrated interventions and null effects of WASH alone on child growth outcomes[3,4,9]. A small number of experimental trials[24] and many observational studies[8,10] have reported increases in child growth and reductions in stunting prevalence with improvements in sanitation coverage and commensurate reductions in OD; among the latter, unmeasured confounding is a likely explanation for observed effects[24].

While gains in the proportion of the population self-reporting access to sanitation were highest in the sanitation only arm (+25 pp), these were only modestly higher than the gains for the control (+19 pp) and nutrition arms (+14 pp); furthermore, sanitation coverage gains for the combined intervention matched the control arm at +19 pp. Comparable secular trends of increasing sanitation coverage in Cambodia have been documented previously: the percentage of children younger than five years of age with access to an improved sanitation facility increased from 5% in 2000 to 17% in 2005, 29% in 2010, and 54% in 2014, the most recent nationally representative DHS survey[8,23]. Correspondingly swift improvements have been documented

specifically in rural areas, where access to any sanitation facility increased from 30% in 2010 to 44% in 2014 and improved sanitation coverage rose from 27% to 43%[8,23]. The rapid pace of WASH development in rural Cambodia makes it challenging to measure the impact of specific programs. However, the lack of differences in other sanitation intervention adherence indicators suggests low overall uptake of the sanitation intervention and only modest increases in sanitation coverage attributable to the intervention, which were likely insufficient to reduce community exposure and transmission. Zoonotic transmission from domestic animals, for instance, was not addressed by this or many other WASH trials, as indicated by nearly 80% of households across all treatment arms lacking access to an area free of animals for children to safely play[25].

The frequency and intensity of contact from program promoters was much greater in the nutrition intervention than the sanitation intervention. Recipients of the nutrition intervention participated in monthly activities, whereas the sanitation intervention consisted of one triggering session with infrequent follow-up visits. The lower contact frequency may explain the discrepancy in intervention adherence. Both arms receiving the nutrition programming reported higher levels of participation in the key intervention activities—including sanitation intervention activities—suggesting higher adherence to the nutrition intervention than the sanitation intervention. Self-reported CLTS participation rates were equally low in both the sanitation-only and control arms at 6%, while 14% of nutrition-only recipients and 25% of combined intervention recipients reported CLTS participation. The comparatively elevated CLTS participation in the nutrition-only arm may reflect biases embedded in the self-reporting process; given the 28+ months that had elapsed since the initial CLTS triggering session and the infrequency of CLTS follow-up visits, households that only received the sanitation intervention may have been less likely to recall programming of any kind than households that participated in the more frequent and intense nutrition intervention activities. Furthermore, the "Growth Together" SBCC campaign, which promoted 13 core health, nutrition, sanitation, and hygiene practices, was fully incorporated into all intervention activities across the three intervention arms, meaning households receiving the higher intensity nutrition programming also encountered the associated SBCC sanitation messaging much more frequently than households in the sanitation-only arm. The SBCC campaign was also promoted nationally on television, such that households in the control arms may have been nearly as exposed to its content as sanitation-only households, while the nutrition-only and combined intervention arms received substantial in-person promotion of the SBCC campaign messaging.

Due to the nature of the interventions and resource considerations, all trial outcomes were assessed during a single survey round conducted 28 months after initiating the intervention programming, which introduced some limitations. Growth and pathogen outcomes were assessed in children from one to 28 months of age, meaning that older children received the treatments for a longer duration but were initially exposed to less mature intervention conditions than the younger children born later. The timing of outcome ascertainment also precluded detecting effects that may only be realized later in childhood, such as potentially rapid catch-up growth after 24 months of age that may reverse earlier growth faltering[26]. While a focus on the first 1,000 days is justified[2], investigation of growth and growth-promoting factors after this window may provide additional insight on improved WASH practices and their role in supporting long-term development and health.

While molecular detection of a specific pathogen in stool unambiguously indicates prior exposure to that pathogen, our data do not necessarily indicate active enteric infection, potential for disease, or direct effects on the individual. We were limited by the suite of pathogen targets selected on our custom TAC assay; we selected these targets *a priori* based on a range of globally observed enteric pathogens, but we cannot know whether these were the most important enteric pathogens in rural Cambodia. There is also evidence that the *invA* gene, which was selected for *Salmonella* spp. detection, is not specific to *Salmonella enterica* and suggest the consideration of other genes, such as *ttrA/C*, for reliable detection of *S. enterica*[27].
It is highly plausible that this sanitation intervention simply failed to sufficiently reduce environmental exposure to enteric pathogens. For example, only 22% of households in our survey were observed to have a child play environment free of animals, with little difference between treatment and control arms; this is a transmission pathway that our trial and many other WASH trials have not addressed[25]. The trial design is predicated on the theory that gains in sanitation coverage may lead to improved growth outcomes in children via reductions in the transmission of enteric infection and disease, though links between sanitation coverage and specific outcomes are poorly understood in high-burden settings. The change in community coverage in this trial was limited and likely insufficient to reduce community exposure and transmission.

There are a few key observations from this study that should be considered in future interventions and effectiveness trials of comparable interventions. Increased frequency, duration, and intensity of CLTS programming could have resulted in greater uptake of sanitation in target communes. Despite the sanitation coverage gains observed in the sanitation-only arm, much of which may have been as a result of the sanitation intervention, we are unable to attribute beneficial effects—i.e., measurable differences in prespecified outcomes—to the sanitation intervention due to the high sanitation gains also observed in the control arm. There may have been other benefits of sanitation gains that were not measured, including in safety and broader measures of well-being[28]. Future trials may also include additional objective outcome measures, including intermediate measures of environmental contamination that are on the causal pathway between interventions and exposures.

Our work is consistent with a growing body of research reporting high prevalence of enteric pathogen exposure in early childhood, which may lead to long-term effects on health[15,18,29,30]. Reducing these exposures in high-burden settings requires transformative interventions that have the potential to dramatically reduce direct and indirect contact with all faeces, including animal faeces[24], across multiple pathways.

Other Information

Trial Registry

The trial is registered with ISRCTN Registry (ISRCTN77820875).

Protocol

The National Ethics Committee for Health Research in the Cambodian Ministry of Health reviewed and approved the protocols (NECHR #110) prior to the start of data collection. The study also received approvals from the Institutional Review Board at Georgia Institute of Technology (Ref: H19286) and from New England IRB (IRB#: 120190186).

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Author contributions

Conceptualisation	IV, OC, JB
Data Curation	IV, KS, AL
Formal Analysis	AL, RA, IV
Funding Acquisition	IV, JB
Investigation	AL, KS, IV, JB
Methodology	AL, IV, OC, JB
Project Administration	IV, KS, JB
Resources	IV, JB
Software	N/A
Supervision	IV, KS, OC, JB
Validation	N/A
Visualisation	N/A
Writing – Original Draft Preparation	AL
Writing – Review & Editing	AL, IV, RA, EK, DH, KS, OC, JB, KL

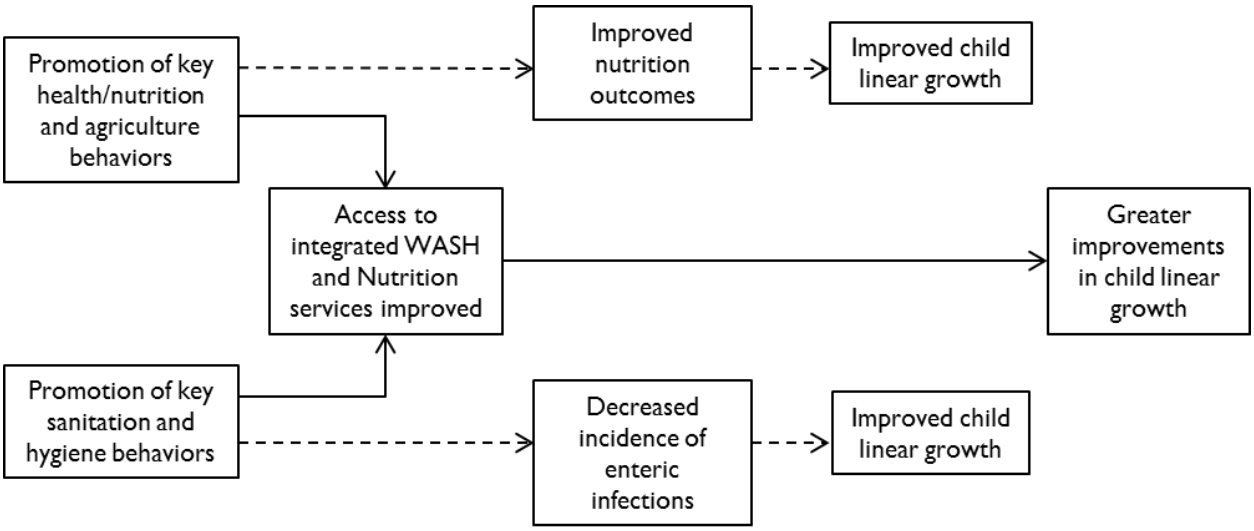

Figure 1: Theory of change diagram

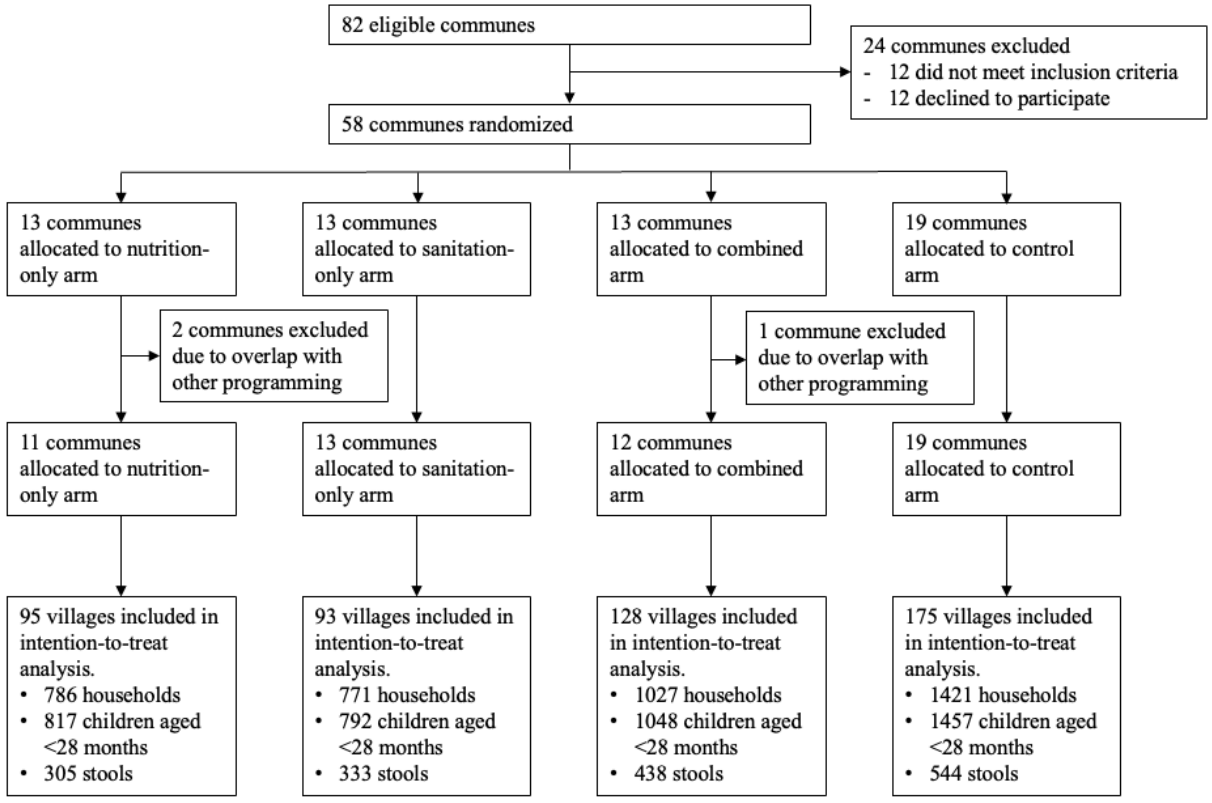

Figure 2: Trial profile

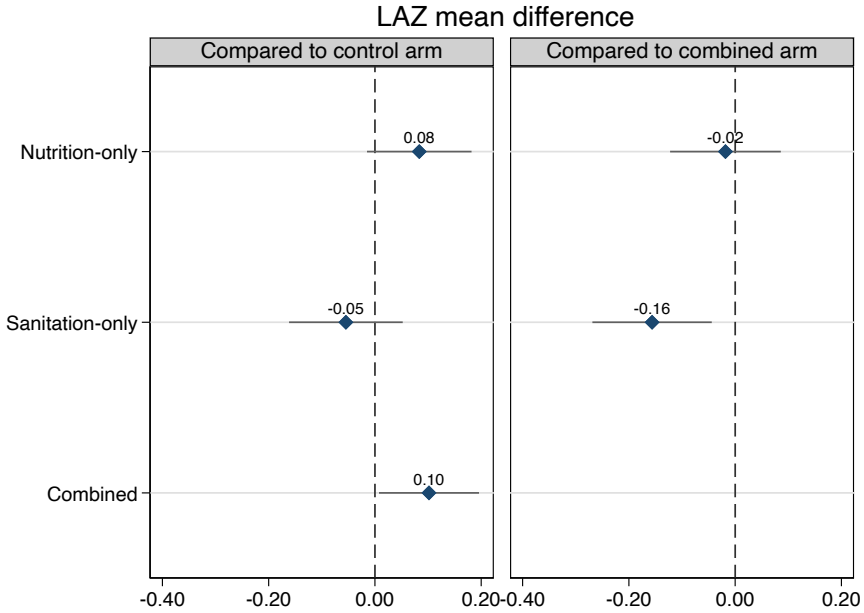

Figure 3: Unadjusted intervention effects on LAZ. Estimates are mean differences (point) with 95% CIs (line)

468 **Figure 4: Impact of interventions on unadjusted prevalence ratio of individual pathogens.**
469 **Point estimates and 95% confidence intervals were determined using log-linear Poisson**
470 **models with generalized estimating equations.**

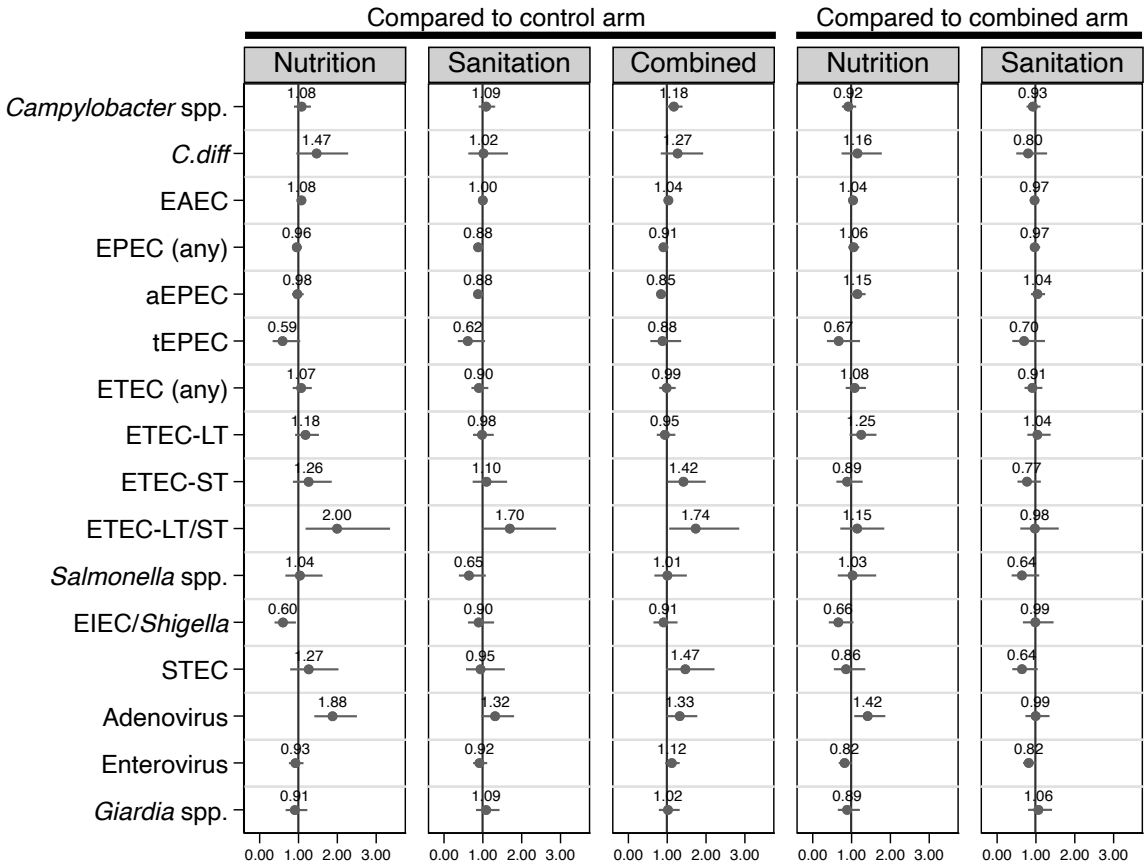

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Table 1: Summary of intervention activities

	Intervention activity	Frequency
Nutrition-only		
	Community dialogues led by village chief and VHSG to support children's growth	Quarterly
	Caregiver group sessions led by local women trained by staff to promote 13 key stunting prevention behaviours	Monthly
	GMP sessions led by VHSGs to monitor growth and refer children who were sick or not growing well to health centers	Monthly
	Home visits to pregnant women, caregivers of children 9-11 months old, and caregivers of children not growing well to promote childcare and feeding, home hygiene, and handwashing	Monthly
	Village fair help twice per year to offer hands-on learning experiences (health/nutrition, WASH and agricultural using games, latrine marketing and sales	Twice per year
	CCT (cash for antenatal and postnatal care visits and adherence to handwashing stations), vouchers for water filters and food baskets	Up to six payments over first 1,000 days of child life
Sanitation-only		
	CLTS triggering session	Once
	Door-to-door visits to provide information about sanitation/latrines	At least five times per village
	Latrine vouchers to subsidise poor households in villages that reached 75% sanitation coverage to achieve sufficient open defecation free (ODF) coverage	Once, as needed
	Promoted supply-side support by connecting small- and medium-sized enterprises (SMEs) with communes after triggering event	Continuously
Combined		
	All activities described in NUTR and SAN groups above	See above
Control		
	None	N/A

Table 2: Household and caregiver characteristics

	Nutrition-only		Sanitation-only		Combined		Control	
	Mean	95% CI	Mean	95% CI	Mean	95% CI	Mean	95% CI
Buddhist	0.98	(0.97, 0.99)	0.97	(0.96, 0.98)	0.96	(0.95, 0.97)	0.99	(0.98, 0.99)
Married or living together	0.95	(0.93, 0.96)	0.94	(0.92, 0.95)	0.94	(0.92, 0.95)	0.95	(0.94, 0.96)
Maternal age (years)	32.0	(31.2, 32.7)	31.1	(30.4, 31.9)	31.9	(31.2, 32.5)	31.0	(30.5, 31.5)
Primary caregiver has attended primary school	0.87	(0.85, 0.89)	0.87	(0.84, 0.89)	0.88	(0.85, 0.89)	0.81	(0.79, 0.83)
Spouse has attended primary school	0.90	(0.88, 0.92)	0.86	(0.83, 0.88)	0.87	(0.85, 0.89)	0.87	(0.85, 0.89)
Household size	5.63	(5.48, 5.78)	5.54	(5.40, 5.69)	5.36	(5.24, 5.47)	5.52	(5.42, 5.62)
Number of children in HH	2.61	(2.52, 2.70)	2.61	(2.51, 2.70)	2.43	(2.36, 2.50)	2.43	(2.37, 2.49)
Has electricity	0.73	(0.70, 0.76)	0.74	(0.71, 0.77)	0.76	(0.73, 0.78)	0.75	(0.72, 0.77)
Owns a mobile phone	0.93	(0.92, 0.95)	0.90	(0.88, 0.92)	0.87	(0.85, 0.89)	0.90	(0.89, 0.92)
Has a finished floor [1]	0.92	(0.90, 0.94)	0.93	(0.91, 0.95)	0.96	(0.94, 0.97)	0.96	(0.95, 0.97)
Wealth index score, excluding WASH variables	0.06	(-0.06, 0.19)	0.19	(0.05, 0.33)	-0.02	(-0.14, 0.09)	-0.12	(-0.21, -0.03)
Improved drinking water source [2]	0.59	(0.56, 0.62)	0.56	(0.52, 0.59)	0.61	(0.58, 0.64)	0.70	(0.68, 0.72)
Has water source on site	0.68	(0.64, 0.71)	0.58	(0.55, 0.61)	0.60	(0.57, 0.63)	0.65	(0.62, 0.67)
Water source is <5 min, roundtrip	0.20	(0.16, 0.25)	0.23	(0.19, 0.28)	0.24	(0.19, 0.29)	0.34	(0.29, 0.39)
Reported minutes to fetch water, roundtrip	12.42	(10.6, 14.2)	14.14	(12.5, 15.8)	14.50	(13.1, 15.9)	13.56	(12.3, 14.8)

[1] Finished floor defined as floor made of wood plans, palm/bamboo, parquet or polished wood, vinyl or asphalt strips, ceramic tiles, cement tiles, or cement. Floor materials were classified by enumerator observation. [2] Improved sources of drinking water include: piped water into dwelling/yard/plot, public tap or standpipe, tube well or borehole, protected dug well, protected spring, bottled water, and rainwater.

Table 3: Intervention fidelity indicators

	Nutrition-only			Sanitation-only			Combined			Control		
Nutrition	N	n	%	N	n	%	N	n	%	N	n	%
Participated in any "First 1,000 Days" type activity [1]	817	615	75%	792	145	18%	1,055	813	77%	1,460	383	26%
Participated in any GMP	817	641	78%	792	181	23%	1,055	935	89%	1,460	482	33%
Received home visit VHSG	817	518	63%	792	227	29%	1,055	661	63%	1,460	490	34%
Enrolled in any CCT program for health and nutrition [2]	817	224	27%	792	19	2%	1,055	228	22%	1,460	31	2%
Received any voucher for food basket [3]	817	440	54%	792	1	0%	1,055	554	53%	1,460	6	0%
Received any voucher for water filter [3]	817	41	5%	792	40	5%	1,055	149	14%	1,460	100	7%
Aware of *Grow Together* campaign [4]	817	353	43%	792	93	12%	1,055	471	45%	1,460	149	10%
Participation in nutrition intervention activities: none (0 of 8)	817	65	8%	792	404	51%	1,055	44	4%	1,460	585	40%
Participation in nutrition intervention activities: low (1-3 of 8)	817	262	32%	792	359	45%	1,055	367	35%	1,460	809	55%
Participation in nutrition intervention activities: med (4-6 of 8)	817	387	47%	792	29	4%	1,055	501	47%	1,460	65	4%
Participation in nutrition intervention activities: high (7-8 of 8)	817	103	13%	792	0	0%	1,055	143	14%	1,460	1	0%
Sanitation												
Any CLTS participation [5]	817	115	14%	792	46	6%	1,055	261	25%	1,460	81	6%
Received any voucher to build latrine [6]	817	66	8%	792	51	6%	1,055	123	12%	1,460	84	6%

[1] "First 1,000 Days" activities were administered in nutrition-only and combined arms and include: community dialogues, caregiver group education sessions, and village fairs. [2] CCT program ended in Jan 2019 and the Government of Cambodia started a new CCT program in July 2019 across study area. CCT program administered in nutrition-only and combined arms only. [3] Vouchers for water filter and food baskets were targeted subsidies distributed to CCT participants in nutrition-only and combined arms. [4] *Grow Together* campaign was part of the nutrition programming (nutrition-only and combined arms). However, three TV spots were seen across all four arms. [5] In sanitation-only and combined arms, the Ministry of Rural Development confirmed that the project was the only CLTS campaign active in those areas. [6] Latrine vouchers were targeted subsidies given to households in villages that reached 75% sanitation coverage in sanitation-only and combined arms.

Table 4: Intervention adherence indicators (28-months after intervention)

	Nutrition-only			Sanitation-only			Combined			Control		
Nutrition	N	n or mean	% or SD	N	n or mean	% or SD	N	n or mean	% or SD	N	n or mean	% or SD
Visited health facility for at least four antenatal care check-ups	697	632	91%	712	646	91%	910	819	90%	1,257	1116	89%
Brought child for monthly GMP at community or health center	817	641	78%	792	181	23%	1,055	935	89%	1,460	482	33%
Breastfeeding exclusively for children <6 months	171	109	64%	161	110	68%	205	140	68%	272	182	67%
Ever breastfed (all children)	817	797	98%	792	765	97%	1,048	1021	97%	1,457	1420	97%
Solid and semi-solid foods eaten for children >6 months	646	609	94%	631	611	97%	843	792	94%	1,185	1134	96%
Dietary diversity score (0-7)	817	2.24	1.61	792	2.19	1.58	1,048	2.20	1.62	1,457	2.33	1.59
Achieved minimum dietary diversity	817	202	25%	792	177	22%	1,048	247	24%	1,457	350	24%
Achieved minimum meal frequency	817	537	66%	792	518	65%	1,048	680	65%	1,457	977	67%
Achieved minimum acceptable diet	817	170	21%	792	159	20%	1,048	205	20%	1,457	310	21%
Treated drinking water	817	548	67%	792	471	59%	1,055	765	73%	1,460	1,037	71%
Treated drinking water with filter	817	151	18%	792	160	20%	1,055	302	29%	1,460	548	40%
Sanitation												
Had improved sanitation facility [1]	816	452	55%	791	400	51%	1,054	638	61%	1,459	759	52%
Open defecation (OD)	817	112	14%	792	126	16%	1,055	73	7%	1,460	231	16%
Used shared toilet	817	252	31%	791	264	33%	1,054	343	33%	1,459	468	32%
Caregiver reported adults in HH openly defecating	697	92	13%	658	116	18%	973	118	12%	1,208	213	18%
Time to get to toilet, one way (minutes)	171	4.22	4.11	166	3.92	3.83	219	4.74	8.17	291	5.05	8.27
Reported latrine built as a result of CLTS activity	115	51	44%	46	15	33%	261	91	35%	81	28	35%
Reported latrine built using latrine voucher	50	10	20%	15	4	27%	91	37	41%	28	12	43%
Main reason for not constructing latrine: lack of funds	20	17	85%	18	14	78%	60	55	92%	14	14	100%
Main reason for construction latrine: privacy	51	7	14%	15	6	40%	91	6	7%	28	7	25%
Main reason for construction latrine: security	51	10	20%	15	2	13%	91	20	22%	28	4	14%
Main reason for construction latrine: hygiene	51	17	33%	15	5	33%	91	43	47%	28	10	36%
Main reason for construction latrine: OD is harmful	51	5	10%	15	1	7%	91	9	10%	28	5	18%

Child stools properly disposed of [2]	817	581	71%	792	515	65%	1,055	781	74%	1,460	993	68%
Community-level open defecation before intervention	817	28%	27%	792	41%	33%	1,055	28%	28%	1,460	32%	31%
Community-level open defecation after intervention	817	14%	21%	792	16%	21%	1,055	9%	17%	1,460	13%	20%
Environmental hygiene												
Child stools left in the open	817	147	18%	792	170	21%	1,055	160	15%	1,460	315	22%
Child play environment observed to be free of animals	817	182	22%	792	187	24%	1,055	261	25%	1,460	294	20%
Child play environment observed to be free of garbage/HH waste	817	298	36%	792	290	37%	1,055	419	40%	1,460	567	39%
Child play environment observed to be free of sharp objects	817	449	55%	792	427	54%	1,055	639	61%	1,460	818	56%
Child play environment observed to be free of faeces	817	313	38%	792	304	38%	1,055	448	42%	1,460	555	38%
[1] Improved sanitation facilities include: flush/pour flush toilet to a piped sewer system, septic tank or pit latrine, a ventilated improved pit latrine, a pit latrine with slab, and a composting toilet. [2] Proper disposal of children faeces consist of putting or rinsing stool into a sanitation facility or burying it; improper disposal of children faeces includes putting or rinsing stool into a drain or ditch, throwing it into garbage or leaving it in the open.												

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Table 5: Effects of interventions on length and weight (Primary outcome (LAZ) and secondary outcomes (WAZ, WLZ)), comparing intervention arms to control and single intervention arms to combined intervention

				Unadjusted mean difference (95% CI)	
	N	Mean	SD	Compared to control arm	Compared to combined intervention arm
LAZ					
Nutrition-only	798	-0.95	1.16	0.08 (-0.01, 0.18)	-0.02 (-0.12, 0.09)
Sanitation-only	777	-1.09	1.23	-0.05 (-0.16, 0.05)	-0.16 (-0.27, -0.04)
Combined	1037	-0.94	1.16	0.10 (0.01, 0.20)	--
Control	1443	-1.04	1.20	--	--
WAZ					
Nutrition-only	815	-0.95	1.29	0.10 (0.00, 0.19)	-0.02 (-0.12, 0.08)
Sanitation-only	792	-1.04	1.13	0.01 (-0.07, 0.09)	-0.10 (-0.20, -0.01)
Combined	1044	-0.94	1.11	0.11 (0.03, 0.20)	--
Control	1452	-1.05	1.10	--	--
WLZ					
Nutrition-only	814	-0.60	1.04	0.06 (-0.03, 0.15)	-0.02 (-0.12, 0.08)
Sanitation-only	790	-0.59	0.98	0.06 (-0.02, 0.14)	-0.02 (-0.11, 0.07)
Combined	1043	-0.58	1.03	0.08 (0.00, 0.16)	--
Control	1452	-0.65	0.98	--	--

Table 6: Effects of intervention on child health outcomes, comparing intervention arms to control and single intervention arms to combined intervention.

				Compared to control arm	Compared to combined-intervention arm
	N	Mean	SD	PR (95% CI)	PR (95% CI)
Stunted					
Nutrition-only	801	0.15	0.36	0.84 (0.69, 1.03)	0.93 (0.74, 1.15)
Sanitation-only	782	0.21	0.40	1.12 (0.94, 1.33)	1.23 (1.02, 1.49)
Combined	1046	0.17	0.37	0.91 (0.76, 1.09)	--
Control	1449	0.18	0.39	--	--
Wasted					
Nutrition-only	815	0.07	0.26	0.87 (0.65, 1.17)	1.12 (0.80, 1.57)
Sanitation-only	790	0.07	0.26	0.84 (0.62, 1.14)	1.08 (0.76, 1.53)
Combined	1052	0.07	0.25	0.78 (0.58, 1.04)	--
Control	1457	0.08	0.28	--	--
Underweight					
Nutrition-only	816	0.15	0.35	0.85 (0.71, 1.03)	1.04 (0.84, 1.29)
Sanitation-only	792	0.17	0.38	1.00 (0.85, 1.19)	1.22 (1.00, 1.49)
Combined	1053	0.14	0.35	0.82 (0.68, 0.99)	--
Control	1457	0.17	0.38	--	--
Diarrhoea (7-day recall)					
Nutrition-only	788	0.19	0.39	0.89 (0.74, 1.06)	0.95 (0.78, 1.14)
Sanitation-only	752	0.21	0.41	0.99 (0.84, 1.17)	1.05 (0.88, 1.25)
Combined	1018	0.20	0.40	0.94 (0.80, 1.11)	--
Control	1411	0.21	0.41	--	--
All-cause mortality					
Nutrition-only	1574	0.03	0.16	1.55 (0.71, 3.39)	1.61 (0.68, 3.82)
Sanitation-only	1636	0.03	0.16	1.09 (0.50, 2.40)	1.13 (0.48, 2.68)
Combined	1932	0.03	0.16	0.96 (0.44, 2.10)	--
Control	2688	0.03	0.16	--	--

499 **Table 7: Enteric pathogen gene prevalence among treatment arms**

	All samples (N=1620)	Nutrition-only (N=305)	Sanitation-only (N=333)	Combined (N=438)	Control (N=544)
Bacteria					
Campylobacter spp.	551 (34%)	104 (34%)	114 (34%)	162 (37%)	171 (31%)
Clostridium difficile	139 (9%)	33 (11%)	25 (8%)	41 (9%)	40 (7%)
EAEC	1029 (64%)	204 (67%)	207 (62%)	281 (64%)	337 (62%)
EPEC	899 (55%)	172 (56%)	173 (52%)	234 (53%)	320 (59%)
aEPEC	703 (43%)	139 (46%)	137 (41%)	173 (39%)	254 (47%)
tEPEC	109 (7%)	15 (5%)	17 (5%)	32 (7%)	45 (8%)
ETEC	422 (26%)	86 (28%)	79 (24%)	114 (26%)	143 (26%)
ETEC-LT	342 (21%)	75 (25%)	68 (20%)	86 (20%)	113 (21%)
ETEC-ST	194 (12%)	39 (13%)	37 (11%)	63 (14%)	55 (10%)
ETEC-LT/ST	114 (7%)	28 (9%)	26 (8%)	35 (8%)	25 (5%)
Salmonella spp.	134 (8%)	28 (9%)	19 (6%)	39 (9%)	48 (9%)
Shigella spp.	186 (11%)	24 (8%)	39 (12%)	52 (12%)	71 (13%)
STEC	132 (8%)	27 (9%)	22 (7%)	45 (10%)	38 (7%)
Vibrio cholerae	10 (1%)	1 (0%)	6 (2%)	1 (0%)	2 (0%)
At least 1 bacterium detected	1410 (87%)	276 (90%)	282 (85%)	386 (88%)	466 (86%)
Mean number of bacteria detected	2.48 (2.42, 2.55)	2.46 (2.32, 2.60)	2.43 (2.28, 2.57)	2.51 (2.39, 2.63)	2.51 (2.40, 2.62)
Viruses					
Adenovirus	287 (18%)	77 (25%)	59 (18%)	78 (18%)	73 (13%)
Astrovirus	7 (0%)	2 (1%)	1 (0%)	3 (1%)	1 (0%)
Enterovirus	558 (34%)	97 (32%)	105 (32%)	169 (39%)	187 (34%)
Norovirus	54 (3%)	8 (3%)	9 (3%)	20 (5%)	17 (3%)
Rotavirus	17 (1%)	2 (1%)	2 (1%)	6 (1%)	7 (1%)
Sapovirus	24 (1%)	4 (1%)	5 (2%)	9 (2%)	6 (1%)
At least 1 virus detected	788 (49%)	152 (50%)	157 (47%)	231 (53%)	248 (46%)
Mean number of viruses detected	1.20 (1.17, 1.23)	1.25 (1.17, 1.33)	1.15 (1.09, 1.21)	1.23 (1.17, 1.30)	1.17 (1.12, 1.23)
Protozoa					
Cryptosporidium	17 (1%)	4 (1%)	1 (0%)	6 (1%)	6 (1%)
Entamoeba	13 (1%)	1 (0%)	1 (0%)	8 (2%)	3 (1%)
Giardia	306 (19%)	52 (17%)	68 (20%)	84 (19%)	102 (19%)
At least 1 protozoan detected	328 (20%)	56 (18%)	69 (21%)	93 (21%)	110 (20%)
Mean number of protozoa detected	1.02 (1.01, 1.04)	1.02 (0.98, 1.05)	1.01 (0.99, 1.04)	1.05 (1.01, 1.10)	1.01 (0.99, 1.03)
STH					
Ascaris lumbricoides	3 (0%)	0 (0%)	0 (0%)	3 (1%)	0 (0%)
Trichuris trichiura	3 (0%)	1 (0%)	1 (0%)	0 (0%)	1 (0%)
Ancylostoma duodenale	17 (1%)	0 (0%)	4 (1%)	4 (1%)	9 (2%)
Necator americanus	20 (1%)	3 (1%)	6 (2%)	5 (1%)	6 (1%)
At least 1	37 (2%)	4 (1%)	10 (3%)	9 (2%)	14 (3%)
Mean number of STH detected	1.16 (1.04, 1.29)	1.00 (1.00, 1.00)	1.10 (0.90, 1.30)	1.33 (1.00, 1.67)	1.14 (0.95, 1.34)

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Table 8: Unadjusted incidence rate ratios of co-detected bacteria, viruses, protozoa, and STHs, comparing intervention arms to control and single intervention arms to combined intervention.

		Compared to control arm			Compared to combined arm	
	N	Nutrition-only	Sanitation-only	Combined	Nutrition-only	Sanitation-only
Bacteria	1620	1.04 (0.95, 1.13)	0.96 (0.87, 1.05)	1.03 (0.95, 1.12)	0.01 (-0.08, 0.10)	-0.07 (-0.17, 0.02)
Viruses	1620	1.16 (0.99, 1.37)	1.02 (0.86, 1.19)	1.22 (1.05, 1.41)	-0.04 (-0.21, 0.12)	-0.18 (-0.34, -0.02)
Protozoa	1620	0.92 (0.68, 1.23)	1.03 (0.79, 1.35)	1.10 (0.85, 1.41)	-0.18 (-0.48, 0.12)	-0.06 (0.66, -0.34)
STHs were omitted because <5% of samples had detectable STH genes.						

Table 9: Unadjusted prevalence ratios (PR) of detected bacteria, viruses, protozoa, and STHs, comparing intervention arms to control and single intervention arms to combined intervention.

	Compared to control arm			Compared to combined arm	
	Nutrition-only	Sanitation-only	Combined	Nutrition-only	Sanitation-only
Any bacterium	1.06 (1.00, 1.11)	0.99 (0.93, 1.05)	1.03 (0.98, 1.08)	1.03 (0.98, 1.08)	0.96 (0.91, 1.02)
Camploybacter spp.	1.08 (0.89, 1.32)	1.09 (0.90, 1.32)	1.18 (0.99, 1.40)	0.92 (0.76, 1.12)	0.93 (0.76, 1.12)
C.diff	1.47 (0.95, 2.28)	1.02 (0.63, 1.65)	1.27 (0.84, 1.93)	1.16 (0.75, 1.78)	0.80 (0.50, 1.29)
EAEC	1.08 (0.97, 1.20)	1.00 (0.90, 1.12)	1.04 (0.94, 1.14)	1.04 (0.94, 1.16)	0.97 (0.87, 1.08)
EPEC	0.96 (0.85, 1.08)	0.88 (0.78, 1.00)	0.91 (0.81, 1.02)	1.06 (0.93, 1.20)	0.97 (0.85, 1.11)
aEPEC	0.98 (0.84, 1.14)	0.88 (0.75, 1.03)	0.85 (0.73, 0.98)	1.15 (0.97, 1.37)	1.04 (0.88, 1.24)
tEPEC	0.59 (0.34, 1.05)	0.62 (0.36, 1.06)	0.88 (0.57, 1.37)	0.67 (0.37, 1.22)	0.70 (0.39, 1.24)
ETEC	1.07 (0.85, 1.35)	0.90 (0.71, 1.15)	0.99 (0.80, 1.22)	1.08 (0.85, 1.38)	0.91 (0.71, 1.17)
ETEC-LT	1.18 (0.92, 1.53)	0.98 (0.75, 1.29)	0.95 (0.74, 1.21)	1.25 (0.95, 1.65)	1.04 (0.78, 1.38)
ETEC-ST	1.26 (0.86, 1.86)	1.10 (0.74, 1.63)	1.42 (1.01, 2.00)	0.89 (0.61, 1.29)	0.77 (0.53, 1.13)
ETEC-LT/ST	2.00 (1.19, 3.36)	1.70 (1.00, 2.89)	1.74 (1.06, 2.86)	1.15 (0.71, 1.85)	0.98 (0.60, 1.59)
Salmonella spp.	1.04 (0.67, 1.62)	0.65 (0.39, 1.08)	1.01 (0.67, 1.51)	1.03 (0.65, 1.64)	0.64 (0.38, 1.09)
EIEC/*Shigella* spp.	0.60 (0.39, 0.94)	0.90 (0.62, 1.29)	0.91 (0.65, 1.27)	0.66 (0.42, 1.05)	0.99 (0.67, 1.46)
STEC	1.27 (0.79, 2.03)	0.95 (0.57, 1.57)	1.47 (0.97, 2.22)	0.86 (0.55, 1.36)	0.64 (0.39, 1.05)
Any virus	1.09 (0.95, 1.26)	1.03 (0.89, 1.20)	1.16 (1.02, 1.31)	0.94 (0.82, 1.09)	0.89 (0.77, 1.03)
Adenovirus	1.88 (1.41, 2.51)	1.32 (0.96, 1.81)	1.33 (0.99, 1.78)	1.42 (1.07, 1.87)	0.99 (0.73, 1.35)
Enterovirus	0.93 (0.76, 1.13)	0.92 (0.75, 1.12)	1.12 (0.95, 1.32)	0.82 (0.67, 1.01)	0.82 (0.67, 1.00)
Any protozoa	0.91 (0.68, 1.21)	1.02 (0.78, 1.34)	1.05 (0.82, 1.34)	0.86 (0.64, 1.16)	0.98 (0.74, 1.29)
Giardia	0.91 (0.67, 1.23)	1.09 (0.83, 1.43)	1.02 (0.79, 1.33)	0.89 (0.65, 1.22)	1.06 (0.80, 1.42)
Gene targets with <5% prevalence were omitted from PR analyses: *V.cholera*, astrovirus, norovirus, rotavirus, sapovirus, *Cryptosporidium*, *Entamoeba,* and all STHs (*Ascaris, Trichuris, Ancylostoma,* and *Necator*).					

Table 10: Mean difference in log_{10}-transformed gene copy estimates, comparing intervention arms to control and single intervention arms to combined intervention.

	Compared to control arm			Compared to combined arm	
	Nutrition-only	Sanitation-only	Combined	Nutrition-only	Sanitation-only
Bacteria					
CAMP	0.22 (-0.60 - 1.03)	-0.40 (-1.27 - 0.48)	-0.24 (-1.00 - 0.53)	0.45 (-0.37 - 1.28)	-0.16 (-1.05 - 0.73)
CDIF	0.31 (-1.14 - 1.75)	-0.37 (-1.92 - 1.19)	0.19 (-1.16 - 1.54)	0.11 (-1.29 - 1.52)	-0.56 (-2.08 - 0.96)
EAEC_aaic	-0.38 (-1.35 - 0.60)	0.35 (-0.52 - 1.22)	-0.28 (-1.08 - 0.52)	-0.10 (-1.11 - 0.92)	0.63 (-0.28 - 1.54)
EAEC_aata	-0.36 (-1.26 - 0.53)	-0.24 (-1.05 - 0.56)	0.12 (-0.69 - 0.93)	-0.48 (-1.43 - 0.47)	-0.36 (-1.24 - 0.51)
EPEC_bfpa	-1.08 (-3.47 - 1.31)	-1.13 (-3.16 - 0.89)	1.15 (-0.38 - 2.67)	-2.23 (-4.57 - 0.11)	-2.28 (-4.24 - -0.32)
EPEC_eae	-0.12 (-0.80 - 0.56)	-0.54 (-1.17 - 0.09)	0.24 (-0.33 - 0.82)	-0.37 (-1.05 - 0.32)	-0.78 (-1.41 - -0.15)
ETEC_LT	-0.62 (-1.64 - 0.40)	-0.47 (-1.56 - 0.61)	-0.03 (-1.06 - 1.00)	-0.59 (-1.65 - 0.47)	-0.44 (-1.57 - 0.68)
ETEC_stp	0.13 (-1.73 - 1.98)	1.29 (-0.61 - 3.20)	0.87 (-0.97 - 2.71)	-0.75 (-2.61 - 1.11)	0.42 (-1.49 - 2.33)
SALM	1.42 (-0.04 - 2.87)	0.27 (-0.97 - 1.52)	0.80 (-0.33 - 1.93)	0.62 (-0.93 - 2.17)	-0.53 (-1.89 - 0.83)
IPAH	0.22 (-1.33 - 1.77)	-0.28 (-1.68 - 1.13)	1.17 (0.07 - 2.26)	-0.95 (-2.43 - 0.53)	-1.44 (-2.77 - -0.11)
STEC1	-1.46 (-2.97 - 0.06)	-1.71 (-3.07 - -0.34)	-0.00 (-1.49 - 1.49)	-1.46 (-2.84 - -0.07)	-1.70 (-2.92 - -0.49)
STEC2	-0.20 (-1.45 - 1.04)	0.09 (-1.20 - 1.37)	0.72 (-0.47 - 1.91)	-0.92 (-2.06 - 0.22)	-0.63 (-1.82 - 0.56)
Viruses					
ADEV	0.50 (-0.48 - 1.49)	0.67 (-0.32 - 1.67)	0.48 (-0.42 - 1.38)	0.03 (-0.96 - 1.02)	0.20 (-0.80 - 1.20)
ENTV	-0.40 (-1.09 - 0.28)	-0.35 (-0.97 - 0.26)	-0.26 (-0.77 - 0.24)	-0.14 (-0.84 - 0.56)	-0.09 (-0.72 - 0.54)
Protozoa					
GIAR	-1.73 (-3.02 - -0.44)	0.23 (-1.16 - 1.62)	-0.14 (-1.47 - 1.18)	-1.58 (-3.06 - -0.11)	0.37 (-1.19 - 1.93)
Gene targets with <5% prevalence were omitted from PR analyses: *V.cholera*, astrovirus, norovirus, rotavirus, sapovirus, *Cryptosporidium*, *Entamoeba,* and all STHs (*Ascaris, Trichuris, Ancylostoma,* and *Necator*).					

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Supplementary Material

Independent and combined effects of nutrition and sanitation interventions on enteric pathogen infection and child growth in rural Cambodia: a factorial cluster-randomised controlled trial

Amanda Lai[1,2], Irene Velez[3], Ramya Ambikapathi[4], Krisna Seng[3], Karen Levy[5], Erin Kowalsky[1,2], David Holcomb[1], Konstantinos T. Konstantinidis[2], Oliver Cumming[6], Joe Brown[1*]

[1] Department of Environmental Sciences and Engineering, Gillings School of Global Public Health, University of North Carolina at Chapel Hill, Chapel Hill, North Carolina, USA
[2] School of Civil and Environmental Engineering, Georgia Institute of Technology, Atlanta, Georgia, USA
[3] MSI, A Tetra Tech Company, Arlington, Virginia, USA
[4] Department of Public Health, Purdue University, West Lafayette, Indiana, USA
[5] Department of Environmental and Occupational Health Sciences, University of Washington, Seattle, Washington, USA
[6] Department of Disease Control, Faculty of Infectious and Tropical Diseases, London School of Hygiene and Tropical Medicine, London, UK

* Corresponding author: Joe Brown, joebrown@unc.edu

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S1: Intervention procedures

Nutrition Interventions

The nutrition interventions consisted primarily of complementary feeding activities and education through community-based delivery platforms, and conditional cash transfers, vouchers, and social and behavioural change (SBCC) linked to the adoption and utilization of key health and nutrition practices, services, and products.

The Community Nutrition component used evidence-based integrated nutrition interventions for the "first 1,000 days" of life. Village Health Support Groups (VHSGs), supervised by health workers and Commune Councils for Women and Children (CCWC), sought to improve childcare and development at multiple levels: individual, family, and community. Five core activities comprised the community initiative designed to prevent malnutrition:

1) Community Dialogues: This activity was led quarterly by the Village Chief and VHSGs. The community gathered to talk, decide, and take action together to support all children to grow healthy. Communities reviewed progress of creating a healthy environment, discussed one key action to jointly address challenges, and decided together how everyone can come together to achieve this action.
2) Caregiver Group Education Sessions: Caregiver Groups were peer-led groups of women who use a 13- session experiential learning manual following each of the key behaviours promoted by the program implementers. Program staff trained two members per group to facilitate monthly sessions for their group, with support from elder women in the community and trained Community Agents.
3) Growth Monitoring and Promotion: VHSGs monitored every child every month. Children who were sick or not growing well were referred to health centres or referral hospitals, as appropriate, and followed up at home after treatment.
4) Home visits: VHSGs and Mother Support Group (MSG) members provided tailored interpersonal communication during home visits to promote childcare and feeding practices, home hygiene, and proper use of latrines and handwashing stations. Home visits were conducted for pregnant women, caregivers of children 9-11 months old and caregivers of children not growing well.
5) Village Fairs: This activity was held twice a year for each village. Village fairs offered women and their families' hands-on learning experiences that bring together health/nutrition, WASH and agriculture using games, demonstrations and practice, interactive discussions and latrine marketing and sales by local participating sanitation suppliers.

CCT acted as a social safety net mechanism for poor "first 1,000 days" families, serving as an incentive for women to access services, practice specific behaviours, and overcome constraints related to poverty. Eligible families (based on poverty status) could receive up to six payments, for a total of $65 over the first 1,000 days of a child's life, which were transferred directly into women's bank accounts after completed use of health and nutrition services.

1) First transfer: $12.50 at 1 month postpartum. Conditions: At least four antenatal care visits, delivery in a health centre, and at least two postnatal care visits.
2) Remaining five transfers: $10 for the second to fifth transfers and $12.50 for the last transfer over the next 23 months postpartum. Conditions: Monthly monitoring of

children's growth through Growth Monitoring and Promotion (GMP) at the health centres or in the community, and handwashing station at home.

Vouchers served as another mechanism to encourage demand and overcome access constraints related to poverty. Vouchers were distributed to poor "first 1,000 days" families in communes where the CCT is implemented and is redeemable for discounts on water filters ($5 co-payment) and two food baskets ($5 co-payment). Vouchers were only distributed in combined intervention groups.

SBCC consisted of media and materials to promote key behaviours in health/nutrition, sanitation/hygiene, and agriculture. The project's SBCC framework was grounded in evidence of what works in social and behaviour change and foundational work done by program implementers the year before the start of the study. On the nutrition side, SBCC supported all the Community Nutrition activities, described above, and was implemented by community change agents (VHSGs and caregiver peer groups).

1) Grow Together: The campaign focused on 13 key stunting prevention behaviours (Figure below) spanning health, nutrition, WASH, and agriculture to stimulate relevant actions for children to grow and reach their full potential. It was not possible to exclude the WASH messaging from the Grow Together campaign, so caregivers received information on all 13 behaviours as part of the nutrition programming.

2) To complement the print materials, the SBCC media plan included three television spots including the foundational Grow Together TV spot, latrine construction and Small Fish Powder; 13 "soundbites"; an advocacy package for local leaders; and more than 20 print materials carrying the same "look and feel" to link to core values and motivations to take action.

3) The “first 1,000 days” family SBCC package was centered on a Family Commitment Card enumerating the critical practices and allowing families to prioritize behaviours and visualize successes and gaps. As the Family Card filled with accomplishments, the family was recognized as a growth champion with a child book and other incentives to mark its accomplishment. A behaviour wheel checklist to guide home visits showing health/nutrition and sanitation/hygiene practices supplemented the Family Card.

Sanitation Interventions

The sanitation interventions consisted primarily of community-led total sanitation (CLTS), coupled with supply-side support for sanitation and hygiene products, latrine vouchers, and SBCC on hygiene practices.

CLTS aimed to achieve sustained behaviour change through the process of community “triggering” leading to spontaneous and long-term abandonment of open defecation practices. This one-time triggering event was conducted in collaboration with the Ministry of Rural Development and provincial and district departments of rural development. In alignment with national Open Defecation Free certification guidelines, CLTS covered entire villages to minimize the risk of fecal-oral contamination for all children. Following CLTS triggering, program staff monitored the commitments of families and communities through door-to-door visits. These visits took place at least 5 times per village and were used to also raise awareness and create demand for sanitation/latrines.

Latrine vouchers were a targeted subsidy to poor households in villages that reached 75% sanitation coverage. Vouchers were redeemable for a discount on latrine materials ($15 co-payment). In the combined-intervention villages, latrine vouchers were initially linked to the CCT program, and so were only offered to those beneficiaries. However, this requirement was phased out and latrine vouchers were eventually available to all poor households in eligible villages.

Supply-side support consisted of collaborating with private and public sector actors to develop locally sensitive market-oriented approaches for the integrated business service centres around “first 1,000 days” products and services. Program staff encouraged knowledge sharing across small- and medium-sized enterprises (SMEs) as well as utilized existing resource centres and agencies to develop the capacity of SMEs for effective service delivery and to increase their outreach to poor and relatively remote areas. Program staff identified a number of successful businesses within or outside the project area and organized interfaces between new and existing businesses to give mutual learning opportunities between SMEs and develop linkages for possible collaboration. In addition, suppliers were linked to communes where CLTS triggering had occurred so they could follow-up with households that committed to purchasing or building latrines.

SBCC on the sanitation side consisted of sanitation campaigns in primary schools to ensure children become agents of change and carry new behaviours home. As change agents, children have the potential to convince their families to construct latrines or purchase a handwashing station, and to use them.

Additional notes on intervention procedures

There were differences in frequency and intensity of contact from program promoters across intervention arms, possibly resulting in reduced impact of the relatively light-touch sanitation intervention. Arms receiving nutrition intervention participated in monthly activities, whereas arms receiving sanitation intervention participated in one triggering session with few and infrequent follow-up visits. Thirteen core health/nutrition and sanitation/hygiene behaviours were promoted as part as the "Growth Together" SBCC campaign. The campaign was broadcasted on television indiscriminately across the country – and subsequently across treatment and control arms. The core behaviours were also promoted during all intervention activities, resulting in higher intensity of programming (including promotion of sanitation and hygiene practices) in the nutrition arms. The lower frequency in contact may explain the discrepancy in intervention adherence. The nutrition arms reported higher levels of participation in the key intervention activities, suggesting higher adherence of the nutrition intervention compared to the sanitation intervention. Similarly, those in the sanitation-only arm reported CLTS participation rates no different from the control arm (6% and 6%), compared with self-reported CLTS participation in the nutrition and combined arms (14% and 25%; **Error! Reference source not found.**; **Error! Reference source not found.**). The high self-reported CLTS participation in the nutrition-only arm compared to the control arm may reflect biases embedded in the self-reporting process, especially when considering the time elapsed since the initial CLTS interventions took place (28+ months prior) and how infrequently CLTS contact occurred relative to nutrition intervention. Households that already had access to sanitation may not have engaged with the CLTS programming, the survey respondent may not have been aware of or may not recall specific activities, or other reporting biases could have played a role. The greater frequency and intensity of contact between the interventions and the respondents in the nutrition arms may have resulted in greater apparent recall of programming of any kind in this arm, possibly increasing reporting and observer biases; participants were not masked to intervention status due to the nature of the interventions. It is also possible that there were other nutrition- and/or WASH-related outreach efforts from actors external to the intervention program. We included observable indicators in addition to self-reported measures as indicators of intervention adherence, which included direct observations of sanitation facilities and domestic hygiene status (e.g., faeces in the play environment of children).

S2: Data collection

A primary survey, based mainly on validated Cambodia DHS questionnaires and piloted in adjacent districts to the study area, was conducted to assess household and child-level risk factors of children under 28 months of age.

Enumerators completed in-home interviews, in the Khmer language, with the primary caregiver of children between 1 to 28 months of age in the household. Field staff asked caregivers questions about basic household member information; breastfeeding, health, and diet of the target children; hygiene, water and sanitation practices; pregnancies and child births of the caregiver; intervention exposure and participation; household WASH conditions; and household assets/characteristics to construct wealth scores. Child height and weight were measured by trained paired enumerators following guidelines from the Food and Nutrition Technical Assistance project (FANTA)[1].

For nutrition-related data collection, we included the infant and young children feeding indicators suggested by the World Health Organisation (WHO), which include minimum dietary diversity, minimum meal frequency, and minimum adequate diet[2]. WHO dietary diversity score consists of categorising solid foods into seven food groups, including: grains, legumes/nuts, dairy, flesh meat, eggs, vitamin-A-rich fruits and vegetables, and other fruits and vegetables. To suit the Cambodian context, the evaluation team asked additional questions on the types of fish and other wild animals consumed, which are included in the flesh meat group. The dietary diversity score is on a scale from 0 – 7 and determined based on the number of food groups the caregiver reported to have fed the child in the last 24 hours; minimum dietary diversity is defined as having received food from four or more food groups (or a dietary diversity score greater than or equal to four). Minimum meal frequency is defined by the frequency of solid and semi-solid foods received based on a child's age and whether the child is breastfed. The minimum number of times breastfed children should receive solid, semi-solid, or soft foods varies with age (2 times if 6–8 months and 3 times if 9–23 months). The minimum number of times non-breastfed children should receive solid, semi-solid, or soft foods, including milk, is 4 times for all children 6–23 months.

For sanitation-related data collection, we included household WASH indicators and environmental hygiene indicators. Household WASH indicators included drinking water source, access, and treatment; handwashing station access; sanitation facilities access; and disposal of child stools. Environmental hygiene indicators included presence of human stools, animal faeces, animals, and garbage in child's play environment.

As part of a supplemental analysis to assess the effects of key community-level WASH indicators (sanitation coverage and rates of open defecation), a secondary survey was conducted in households randomly selected in the same areas (three households per village) and irrespective of whether there was a child living in the household. Given the oversampling of households with children under 28 months of age, post-stratification weights were used to get a representative sample of the population. Sampling weights were calculated as follows: first, we estimated the proportion of households with children under 28 months of age at the village-level by creating a list of eligible children with the village chief and VHSG. This estimate was then divided by the proportion of sampled households with children under 28 months of age at each village to yield

the sampling weight for each household from the main sample. For the three additional households, the sampling weights were calculated by dividing the remaining proportion of total households at the village level by the proportion of sampled households at each village. This resulted in underweighting the households with children under 28 months of age and overweighting the supplemental households.

S3: Sample size and power calculations

Sample size was chosen to balance the size of the study and the minimum detectable difference between arms. Increased allocation of eligible communes to the control arm was stipulated to enhance statistical efficiency of multiple hypothesis testing, resulting in 19 communes assigned to the control arm (one-third of the total) and 13 to each intervention arm[3]. Power calculations used α=0.05, power=0.8, mean LAZ estimate (prior to intervention rollout) of -0.96 with a standard deviation of 1.19, intra-cluster correlation of 0.014 on the LAZ outcome measure at the commune level, and a two-sided test for a two-sample comparison of means. LAZ calculations used a standard equation assuming a single, post-treatment measurement at 2 years, resulting in a total of 4,015 households consisting of 73 observations per commune. These sample size calculations suggest that this study had sufficient power to detect a minimum detectable effect size (MDES) of 0.19 for differences in the LAZ scores between treatment arms and a MDES of 0.18 for differences between each treatment arm and the control arm, similar to other trials[4]. An MDES of 0.19 translates to a 23.4% change in LAZ score between treatment arms; an MDES of 0.18 translates to a 22.2% change in LAZ scores between treatment and control arms[5]. While empirical evidence to serve as an adequate basis for the MDES was limited, another large factorial WASH and nutrition trial targeted a similar LAZ MDES of 0.18 between treatment arms and a MDES of 0.15 in mean LAZ scores between treatment and control arms[6,7].

The following sample size calculations for the primary outcome, difference in mean HAZ scores between treatment groups, were conducted based on different ICC scenarios. This is revised to account for a drop of three treatment communes after randomization occurred. Power calculations assume α=0.05, power=0.8, mean baseline HAZ estimate of -1.637 with a standard deviation of 1.286, and a two-sided test for a two-sample comparison of means. HAZ calculations use a standard equation assuming a single, post-treatment measurement at 2 years.

MDES between treatment groups	Subjects per cluster (commune)	Estimated total number of subjects required (all 4 arms)
	ICC=0.01	
0.15	155	8,525
0.16	115	6,325
0.17	90	4,950
0.18	**73**	**4,015**
0.19	61	3,355
0.2	52	2,860
	ICC=0.015	
0.15	690	37,950
0.16	268	14,740
0.17	162	8,910
0.18	114	6,270
0.19	87	4,785
0.2	70	3,850
	ICC=0.02	

0.15	NA	NA
0.16	NA	NA
0.17	876	48,180
0.18	268	14,740
0.19	155	8,525
0.2	107	5,885

For the supplemental analysis on community-level WASH indicators, the required sample size was calculated based on a conventional approach for proportions to collect reliable point-estimates of sanitation coverage at the group level, at the 95 percent confidence level with a margin of error of +/-5 percent.

$$N = p(1-p) * \left[\frac{Z}{ME}\right]^2 * 4 = 0.408(1-0.592) * \left[\frac{1.96}{0.05}\right]^2 * 4 = 1{,}024$$

where:
$p =$ proportion of sanitation coverage of 0.408, estimated using DHS 2014 data
$Z = 1.96$ (for 95% confidence level)
$ME =$ margin of error of +/-5%

Given the 491 villages, sample size was rounded up to three additional randomly selected households per village, for a target total of 1,473 additional households, as shown in the table below.

Required Sample Size

Provinces	**Communes**	**Villages**	**HHs Main Sample**	**HHs Secondary Sample**
Battambang	22	180	1,606	540
Pursat	6	83	438	249
Siem Reap	27	228	1,971	684
Total	**55**	**491**	**4,015**	**1,473**

S4: Anthropometry protocols

Anthropometric measurement is comprised of weight and length. Weight was measured using Uniscale (UNICEF recommended scale) in Kilogram with precision to one decimal point. Length was measured using a length board (UNICEF / WFP recommended) in Centimetre with precision to one decimal point. Two data measurements were required, one from the measurement taker and another one from an assistant. The measurement procedure followed FANTA Guidelines:

- Weight measurement:
    - *Preparation*: Ensure enough material is available for measurement (scale, battery, pen, tissue, record form, and age calculation form) with proper function. Ensure that the scale is positioned in a plate and smooth surface. Measurement taker is on the right hand of mother/caregiver while assistant is in front of mother/caregiver. Ensure that children dress light clothes with no cap or shoes. Assistant helps mother/caregiver in carrying the child and asks mother/caregiver to go on to the scale after proper functioning.
    - *During Measurement*: Request mother/caregiver to stand on the scale, inform the measurement result loudly, press button to measure child, hand the child to mother/caregiver after scale functioning, read weight of child out loud so that assistant can record the measurement.
    - *Second Measurement*: Request mother/caregiver to step off the scale. Repeat the measurement steps. Record second measurement.
- Length measurement:
    - *Preparation*: Prepare length board on a plate and smooth surface. Ensure length board stability, take off shoe and cap from child. Check measurement level on the length board, and ensure the record form.
    - *During Measurement*: Lay child on his back on the board, check head, eye, shoulder, hand, buttock, knees and heel. Make sure body is in proper position and still. Measurement must be read to the nearest of 0.1 cm. Repeat the measurement one more time to ensure accuracy of reading. If the two measurements are different by more than 1.0 cm, then a third measurement is taken.
- Following the weighing and length measurements, any child who is classified as severely malnourished is referred to the health clinic.
- Training: The enumerators were trained on the protocols to follow and how to calibrate equipment. Tested on accurate recording of length measurements. Hands-on practice in pairs and then we did a standardization exercise where the entire team is tested on their ability to measure child length accurately and precisely. Measurers had to meet the accuracy and precision threshold to pass and be hired as enumerators for data collection.
- Field supervision: The anthropometry specialist was present in the field during the entire baseline phase, accompanying enumerators to ensure proper technique with the height and weight measurements and recording.

S5: Nucleic acid extraction and PCR procedures

Stool samples were collected and preserved in duplicate using Zymo DNA/RNA Shield buffer (Zymo Research, Irvine, CA) at 1:1 by volume and stored in -20°C until extraction. A subset of stool samples were randomly selected for extraction and molecular analysis. Our extraction protocol was adapted from the xTAG Gastrointestinal Pathogen Panel (GPP; Luminex Molecular Diagnostics, Toronto, ON, Canada) protocol for pre-treatment and the QIAamp 96 Virus QIAcube HT (Qiagen, Germany) protocol for remaining extraction procedures[8]. Briefly, 200 mg solid (or 200 uL if liquid) preserved stool was combined with 1000 uL of Buffer ASL (Qiagen, Germany) in an SK38 soil grinding tube (Bertin, Rockville, MD), vortexed for 5 minutes (Vortex Genie 2, Scientific Industries, Bohemia, NY), incubated at room temperature for 10 minutes, and centrifuged at 12,000g for 2 minutes (Eppendorf, Enfield, CT). 200 uL of supernatant was used for total nucleic acid extraction following the QIAamp 96 Virus QIAcube HT protocol. We assayed total nucleic acids using a custom-developed TaqMan Array Card (TAC; ThermoFisher Scientific, Waltham, VA) – a compartmentalised probe-based quantitative real-time polymerase chain reaction (PCR) assay for 30 enteric pathogen genes using individual assays validated in previously published literature in TAC format[9,10]. PCR cycling conditions were also adapted from previous work[9,10]. Details on specific targets, assays, assay validation, and other analytical metadata are included in Supporting Information.

We collected 4,114 stools in totla and assessed enteric pathogen-associated gene targets in 1,745 for molecular analysis using multiple-target PCR for presence of gene targets associated with key enteric pathogens (bacteria, viruses, protozoa, and STH). We omitted 125 samples due to lack of amplification of one or more of three controls (phHPV as DNA control; MS2 as RNA control; manufacturer internal positive control) or due to unstable noise in amplification curves. 1,620 samples were included in the final dataset.

S6: TaqMan Array Card performance and standard curve parameters

Target	Target gene	Slope	Y-intercept	R2	Efficiency	LLOD (GC/rxn)*
Enteric bacterial 16S	16S	-3.613	42.29	0.960	89%	10
pan-Adenovirus	hexon	-3.372	38.58	0.994	98%	10
Ancylostoma duodenale	*ITS2*	-3.506	41.68	0.994	93%	10
Ascaris lumbricoides	*ITS1*	-3.479	40.72	0.992	94%	10
Astrovirus	capsid	-3.337	37.89	0.997	99%	10
Campylobacter jejuni	cadF	-3.562	40.22	0.999	91%	10
Clostridium difficile	tcdB	-3.427	38.25	1.000	96%	10
Cryptosporidium parvum	*LIB13*	-3.505	40.17	0.999	93%	10
Cryptosporidium hominis	*LIB13*	-3.433	39.49	0.999	96%	10
EAEC (aaic)	*aaic*	-3.342	36.18	0.997	99%	1
EAEC (aata)	*aata*	-3.221	35.10	0.987	104%	1
Entamoeba histolytica	18S rRNA	-3.406	40.42	0.993	97%	10
Enterovirus	5'UTR	-3.396	38.94	0.999	97%	10
EPEC (bfpa)	*bfpa*	-3.380	37.81	0.994	98%	10
EPEC (eae)	*eae*	-3.391	38.20	0.995	97%	10
ETEC (LT)	LT	-3.591	39.38	0.988	90%	1
ETEC (STh)	STh	-3.428	38.46	0.996	96%	10
ETEC (STp)	STp	-3.377	37.75	0.994	98%	10
Giardia spp.	18S rRNA	-3.412	40.17	0.999	96%	10
EIEC/*Shigella* spp.	*ipaH*	-3.332	38.14	0.999	100%	10
Necator americanus	*ITS2*	-3.434	40.55	0.994	96%	10
Norovirus GI	ORF1-2	-3.457	39.85	1.000	95%	10
Norovirus GII	ORF1-2	-3.387	38.53	0.999	97%	10
Rotavirus	NSP3	-3.624	41.79	0.998	89%	10
Salmonella spp.	*invA*	-3.446	40.67	0.996	95%	10
Sapovirus I	RdRp	-3.392	39.22	0.998	97%	1
Sapovirus IV	RdRp	-3.384	39.00	0.998	97%	10
STEC	*stx1*	-3.397	38.49	0.998	97%	1
STEC	*stx2*	-3.396	38.53	0.997	97%	1
Trichuris trichiura	18S rRNA	-3.307	40.31	0.999	101%	100
Vibrio cholerae	*hlyA*	-3.418	41.00	0.999	96%	100

*Lower limit of detection estimated by assuming Cq cutoff of 35[11]

S7: List of primers and probes in custom-TAC.
All sequences were based on cited references.

	Organism	Target gene	Forward Sequence #1 (5'-3')	Reverse Sequence #1 (5'-3')	Probe Sequence #1 (5'-3')	References
Virus	Astrovirus	capsid	CAGTTGCTTGCTGCGTTCA	CTTGCTAGCCATCACACTTCT	CACAGAAGAGCAACTCCATCGC	[1]
	Enterovirus	5'UTR	CCCTGAATGCGGCTAATCC	GCGATTGTCACCATWAGCAG	CCGACTACTTTGGGWGTCCGT	[2]
	Norovirus GI	ORF1-2	CGYTGGATGCGNTTYCATGA	CTTAGACGCCATCATCATTYAC	TGGACAGGAGATCGC	[2]
	Norovirus GII	ORF1-2	CARGARBCNATGTTYAGRTGGATGAG	TCGACGCCATCTTCATTCACA	TGGGAGGGCGATCGCAATCT	[1]
	Sapovirus	RdRp	GAYCAGGCTCTCGCYACCTAC	CCCTCCATYTCAAACACTA	CYTGGTTCATAGGTGGTRCAG	[1]
		RdRp	TTTGAACAAGCTGTGGCATGCTAC	CCCTCCATYTCAAACACTA	CAGCTGGTACATTGGTGGCAC	[1]
	pan-Adenovirus	hexon	GCCACGGTGGGGTTTCTAAACTT	GCCCCAGTGGTCTTACATGCACATC	TGCACCAGACCCGGGCTCAG	[1]
	Rotavirus	NSP3	ACCATCTWCACRTRACCCTCTATGAG	GGTCACATAACGCCCCTATAGC	AGTTAAAAGCTAACACTGTCAAA	[1]
Bacterium	*Campylobacter jejuni*	cadF	CTGCTAAACCATAGAAATAAAATTTCTCAC	CTTTGAAGGTAATTTAGATATGGATAATCG	CATTTTGACGATTTTTGGCTTGA	[1]
	Clostridium dificile	tcdB	GGTATTACCTAATGCTCCAAATAG	TTTGTGCCATCATTTTCTAAGC	CCTGGTGTCCATCCTGTTTC	[1]
	EAEC	aaiC	ATTGTCCTCAGGCATTTCAC	ACGACACCCCTGATAAACAA	TAGTGCATACTCATCATTTAAG	[1]
		aatA	CTGGCGAAAGACTGTATCAT	TTTTGCTTCATAAGCCGATAGA	TGGTTCTCATCTATTACAGACAGC	[1]
	STEC1	*stx1*	ACTTCTCGACTGCAAAGACGTATG	ACAAATTATCCCCTGWGCCACTATC	CTCTGCAATAGGTACTCCA	[1]
	STEC2	*stx2*	CCACATCGGTGTCTGTTATTAACC	GGTCAAAACGCGCCTGATAG	TTGCTGTGGATATACGAGG	[1]
	EPEC	eae	CATTGATCAGGATTTTTCTGGTGATA	CTCATGCGGAAATAGCCGTTA	ATACTGGCGAGACTATTTCAA	[1]
	ETEC	bfpa	TGGTGCTTGCGCTTGCT	CGTTGCGCTCATTACTTCTG	CAGTCTGCGTCTGATTCCAA	[1]
		LT	TTCCCACCGGATCACCAA	CAACCTTGTGGTGCATGATGA	CTTGGAGAGAAGAACCCT	[1]
		STh	GCTAAACCAGYAGRGTCTTCAAAA	CCCGGTACARGCAGGATTACAACA	TGGTCCTGAAAGCATGAA	[1]
		STp	TGAATCACTTGACTCTTCAAAA	GGCAGGATTACAACAAAGTT	TGAACAACACATTTTACTGCT	[1]

	Shigella/EIEC	*ipaH*	CCTTTTCCGCGTTCCTTGA	CGGAATCCGGAGGTATTGC	CGCCTTTCCGATACCGTCTCTGCA	[1]
	Salmonella enterica	*invA*	TCGGGCAATTCGTTATTGG	GATAAACTGGACCACGGTGACA	AAGACAACAAAACCCACCGC	[2]
	Vibrio cholerae	*hlyA*	ATCGTCAGTTTGGAGCCAGT	TCGATGCGTTAAACACGAAG	ACCGATGCGATTGCCCAA	[2]
Protozoa	*Cryptosporidium hominis*	*LIB13*	TCCTTGAAATGAATATTTGTGACTCG	AAATGTGGTAGTTGCGGTTGAAA	CTTACTTCGTGGCGGCGT	[2]
	Cryptosporidium parvum	*LIB13*	TCCTTGAAATGAATATTTGTGACTCG	TTAATGTGGTAGTTGCGGTTGAAC	TATCTCTTCGTAGCGGCGTA	[2]
	Giardia spp.	18S rRNA	GACGGCTCAGGACAACGGTT	TTGCCAGCGGTGTCCG	CCCGCGGCGGTCCCTGCTAG	[1]
	Entamoeba histolytica	18S rRNA	ATTGTCGTGGCATCCTAACTCA	GCGGACGGCTCATTATAACA	TCATTGAATGAATTGGCCATTT	[1]
Helminth	*Ascaris lumbricoides*	*ITS1*	GCCACATAGTAAATTGCACACAAAT	GCCTTTCTAACAAGCCCAACAT	TTGGCGGACAATTGCATGCGAT	[2]
	Trichuris trichiura	18S rRNA	TTGAAACGACTTGCTCATCAACTT	CTGATTCTCCGTTAACCGTTGTC	CGATGGTACGCTACGTGCTTACCATGG	[1]
	Necator americanus	*ITS2*	CTGTTTGTCGAACGGTACTTGC	ATAACAGCGTGCACATGTTGC	CTGTACTACGCATTGTATAC	[2]
	Ancylostoma duodenale	*ITS2*	GAATGACAGCAAACTCGTTGTTG	ATACTAGCCACTGCCGAAACGT	ATCGTTTACCGACTTTAG	[2]
Control	MS2	*MS2g1*	TGGCACTACCCCTCTCCGTATTCAC	GTACGGGCGACCCCACGATGAC	CACATCGATAGATCAAGGTGCCTACAAGC	[1]
	bacterial 16S		TGCAAGTCGAACGAAGCACTTTA	GCAGGTTACCCACGCGTTAC	CGCCACTCAGTCACAAA	[2]

[1] Liu, J. et al. A Laboratory-Developed TaqMan Array Card for Simultaneous Detection of 19 Enteropathogens. J. Clin. Microbiol. 51, 472 LP – 480 (2013).
[2] Liu, J. et al. Optimization of Quantitative PCR Methods for Enteropathogen Detection. PLoS One 11, e0158199 (2016).
[3] Narayanan, J. et al. Quantitative Real-Time PCR Assays for Detection of Human Adenoviruses and Identification of Serotypes 40 and 41. Appl. Environ. Microbiol. 71, 3131–3136 (2005).

S8: qPCR assay validation

We tested preserved stools using a custom-developed TaqMan Array Card (TAC; ThermoFisher Scientific, Waltham, VA) – a compartmentalised probe-based quantitative polymerase chain reaction (qPCR) assay for enteric pathogen genes using individual assays validated in previously published literature in TAC format[9,10]. qPCR cycling conditions were also adapted from previous work[9,10] We further validated targets using synthetic nucleic acids (GeneArt, ThermoFisher Scientific) as positive controls (PCs). PC material for each individual assay was combined to a concentration of 10^{10} gene copies (GC)/uL. Two serial dilutions were run on the custom TAC: a high-concentration 10-fold dilution series (10^{9} GC/uL to 10^{2} GC/uL) was used to determine range of the limit-of-quantification (LOQ) to order of magnitude; subsequently, a low-concentration 2-fold dilution series diluted within the determined LOQ range was used to estimate the delta-Rn threshold for each assay's LOQ.

S9: Process evaluation indicators

We documented process evaluation (PE) indicators to assess fidelty and adherence of intervention activities 28 months after the end of intervention roll-out. Fidelity was measured based on self-reported receipt of intervention activity, which included eight key nutrition activities: community dialogues (quarterly); caregiver group education course (monthly); village fairs (bi-annually); growth monitoring program (monthly); home health visits from VHSG (monthly); CCT with rolling enrolment (disbursed payments as participants met the various conditions); food vouchers (delivered once to CCT participants); and water filter vouchers (delivered once to CCT participants). Adherence was measured based on self-reported participation of intervention activities, which included household WASH practices and child nutrition behaviours.

S10: Intervention adherence

We assessed four key caregiver behaviours related to environmental hygiene: drinking and use of clean water, handwashing with soap and water at critical times, proper disposal of children's stools, and provision of safe play environments for children. Implementation programming encouraged safe handwashing behaviours as part of the "First 1,000 Days" activities and the nutrition CCT. Those in the nutrition-only arm (7%) and combined-intervention arm (9%) had greater awareness of critical handwashing times compared to those in the sanitation-only arm (4%) and control arm (4%), though levels were still low. There was a slightly higher prevalence of soap and water observed at handwashing stations in the combined-intervention (72%) and control (76%) arms than the nutrition-only (69%) and sanitation-only (70%) arms. We defined proper disposal of children's stools as discarding into a toilet/latrine or burying and considered discarding faeces into a drain, garbage or other solid waste, or leaving in the open to be improper disposal practices. Nutrition-only and combined intervention arms reported higher levels of proper disposal (71% and 74%, respectively) compared to the sanitation-only and control arms (65% and 68%, respectively). Few households were found to have safe play environments, defined as being free of observed human faeces, animal faeces, garbage/household waste, and sharp objects/other harms. 25% of households in the combined intervention arm had child play environments free of faeces observed by enumerators at the time of the household visit, compared to 21% in the nutrition-only, sanitation-only, and control arms. More households in the nutrition-only (78%) and combined-intervention (89%) arms brought children to health centres for monthly GMP visits than sanitation-only (23%) and control (33%) arms. There were no differences in breastfeeding behaviours between intervention and control arms, with 60-70% of each arm reporting continuous breastfeeding for children for the first two years. There were no statistically meaningful differences in dietary diversity score, minimum dietary diversity, and minimum meal frequency across the four arms.

S11: Adjusted analyses

Covariates were considered as potential confounders using a "common cause" approach[14] and based on the conceptual framework of literature-supported variables associated with diet and WASH conditions or nutritional status[15]. We also considered covariates that were found to be both associated with primary outcome measures and imbalanced across treatment arms before intervention delivery, of which only pre-intervention village-level sanitation coverage met the inclusion criteria. We calculated household wealth using an asset-based wealth index using methodology provided by the Demographic and Health Survey (DHS)[16], constructed using principal component analysis excluding WASH assets[17]. In the adjusted analyses, we included the following covariates, identified *a priori*: child sex (dichotomous), child age (continuous, in months), maternal age (continuous, in years), maternal education (ordinal, based on mother's highest level of education attended), number of household members (continuous), household wealth index quintile (ordinal), and community-level open defecation (OD) measured at prior to intervention rollout (continuous).

Effects of interventions on height/length and weight (Primary outcome (LAZ) and secondary outcomes (WAZ, WHZ)), comparing intervention arms to control and single intervention arms to combined intervention

				Compared to control arm		Compared to combined intervention arm	
	N	Mean	SD	Unadjusted mean difference (95% CI)	Adjusted mean difference (95% CI)	Unadjusted mean difference (95% CI)	Adjusted mean difference (95% CI)
LAZ							
Nutrition-only	798	-0.95	1.16	0.08 (-0.01, 0.18)	0.09 (-0.01, 0.19)	-0.02 (-0.12, 0.09)	0.01 (-0.09, 0.11)
Sanitation-only	777	-1.09	1.23	-0.05 (-0.16, 0.05)	-0.05 (-0.15, 0.05)	-0.16 (-0.27, -0.04)	-0.13 (-0.23, -0.02)
Combined	1037	-0.94	1.16	0.10 (0.01, 0.20)	0.08 (-0.01, 0.17)	--	--
Control	1443	-1.04	1.20	--	--	--	--
WAZ							
Nutrition-only	815	-0.95	1.29	0.10 (0.00, 0.19)	0.10 (0.01, 0.20)	-0.02 (-0.12, 0.08)	0.01 (-0.08, 0.11)
Sanitation-only	792	-1.04	1.13	0.01 (-0.07, 0.09)	0.01 (-0.07, 0.09)	-0.10 (-0.20, -0.01)	-0.08 (-0.17, 0.00)
Combined	1044	-0.94	1.11	0.11 (0.03, 0.20)	0.09 (0.01, 0.17)	--	--
Control	1452	-1.05	1.10	--	--	--	--
WHZ							
Nutrition-only	814	-0.60	1.04	0.06 (-0.03, 0.15)	0.06 (-0.02, 0.15)	-0.02 (-0.12, 0.08)	0.00 (-0.09, 0.09)
Sanitation-only	790	-0.59	0.98	0.06 (-0.02, 0.14)	0.05 (-0.03, 0.13)	-0.02 (-0.11, 0.07)	-0.01 (-0.10, 0.08)
Combined	1043	-0.58	1.03	0.08 (0.00, 0.16)	0.06 (-0.02, 0.14)	--	--
Control	1452	-0.65	0.98	--	--	--	--
Covariates in adjusted analyses include: child sex, child age, maternal age, maternal education, number of household members, household wealth index quintile, and community-level OD measured prior to intervention delivery							

Effects of intervention on child health outcomes, comparing intervention arms to control and single intervention arms to combined intervention.

				Compared to control arm		Compared to combined-intervention arm	
	N	Mean	SD	PR (95% CI)	aPR (95% CI)	PR (95% CI)	aPR (95% CI)
Stunted							
Nutrition-only	801	0.15	0.36	0.84 (0.69, 1.03)	0.83 (0.68, 1.02)	0.93 (0.74, 1.15)	0.90 (0.72, 1.12)
Sanitation-only	782	0.21	0.40	1.12 (0.94, 1.33)	1.11 (0.94, 1.31)	1.23 (1.02, 1.49)	1.20 (0.99, 1.46)
Combined	1046	0.17	0.37	0.91 (0.76, 1.09)	0.92 (0.77, 1.10)	--	--
Control	1449	0.18	0.39	--	--	--	--
Wasted							
Nutrition-only	815	0.07	0.26	0.87 (0.65, 1.17)	0.85 (0.63, 1.14)	1.12 (0.80, 1.57)	1.09 (0.78, 1.52)
Sanitation-only	790	0.07	0.26	0.84 (0.62, 1.14)	0.83 (0.61, 1.13)	1.08 (0.76, 1.53)	1.06 (0.75, 1.51)
Combined	1052	0.07	0.25	0.78 (0.58, 1.04)	0.78 (0.58, 1.05)	--	--
Control	1457	0.08	0.28	--	--	--	--
Underweight							
Nutrition-only	816	0.15	0.35	0.85 (0.71, 1.03)	0.84 (0.69, 1.02)	1.04 (0.84, 1.29)	0.99 (0.80, 1.24)
Sanitation-only	792	0.17	0.38	1.00 (0.85, 1.19)	1.00 (0.85, 1.17)	1.22 (1.00, 1.49)	1.18 (0.97, 1.44)
Combined	1053	0.14	0.35	0.82 (0.68, 0.99)	0.84 (0.70, 1.01)	--	--
Control	1457	0.17	0.38	--	--	--	--
Diarrhoea (7-day recall)							
Nutrition-only	788	0.19	0.39	0.89 (0.74, 1.06)	0.90 (0.76, 1.08)	0.95 (0.78, 1.14)	0.96 (0.80, 1.16)
Sanitation-only	752	0.21	0.41	0.99 (0.84, 1.17)	0.98 (0.83, 1.16)	1.05 (0.88, 1.25)	1.05 (0.87, 1.25)
Combined	1018	0.20	0.40	0.94 (0.80, 1.11)	0.94 (0.79, 1.11)	--	--
Control	1411	0.21	0.41	--	--	--	--
All-cause mortality							
Nutrition-only	1574	0.03	0.16	1.55 (0.71, 3.39)	--	1.61 (0.68, 3.82)	--
Sanitation-only	1636	0.03	0.16	1.09 (0.50, 2.40)	--	1.13 (0.48, 2.68)	--
Combined	1932	0.03	0.16	0.96 (0.44, 2.10)	--	--	--
Control	2688	0.03	0.16	--	--	--	--
Covariates in adjusted analyses include: child sex, child age, maternal age, maternal education, number of household members, household wealth index quintile, and community-level OD measured prior to intervention delivery							

Adjusted mean difference of detected bacteria, viruses, protozoa, and STHs, comparing intervention arms to control. Adjusted analyses controlled for the following covariates: child age, child sex, maternal age, maternal education, number of household members, household wealth quintile.

		Compared to control arm			Compared to combined arm	
	N	Nutrition-only	Sanitation-only	Combined	Nutrition-only	Sanitation-only
Bacteria	1406	-0.04	-0.09	0.02	-0.07	-0.11

		(-0.22, 0.13)	(-0.27, 0.09)	(-0.15, 0.19)	(-0.25, 0.12)	(-0.30, 0.08)
Viruses	786	0.08 (-0.01, 0.17)	-0.01 (-0.09, 0.07)	0.06 (-0.02, 0.15)	0.02 (-0.08, 0.12)	-0.07 (-0.16, 0.01)
Protozoa	327	0.01 (-0.03, 0.05)	0.01 (-0.03, 0.04)	0.05 (-0.01, 0.11)	-0.04 (-0.10, 0.03)	-0.04 (-0.10, 0.02)
STH	37	0.01 (-0.31, 0.32)	-0.10 (-0.42, 0.22)	0.13 (-0.25, 0.52)	-0.13 (-0.43, 0.18)	-0.23 (-0.62, 0.16)

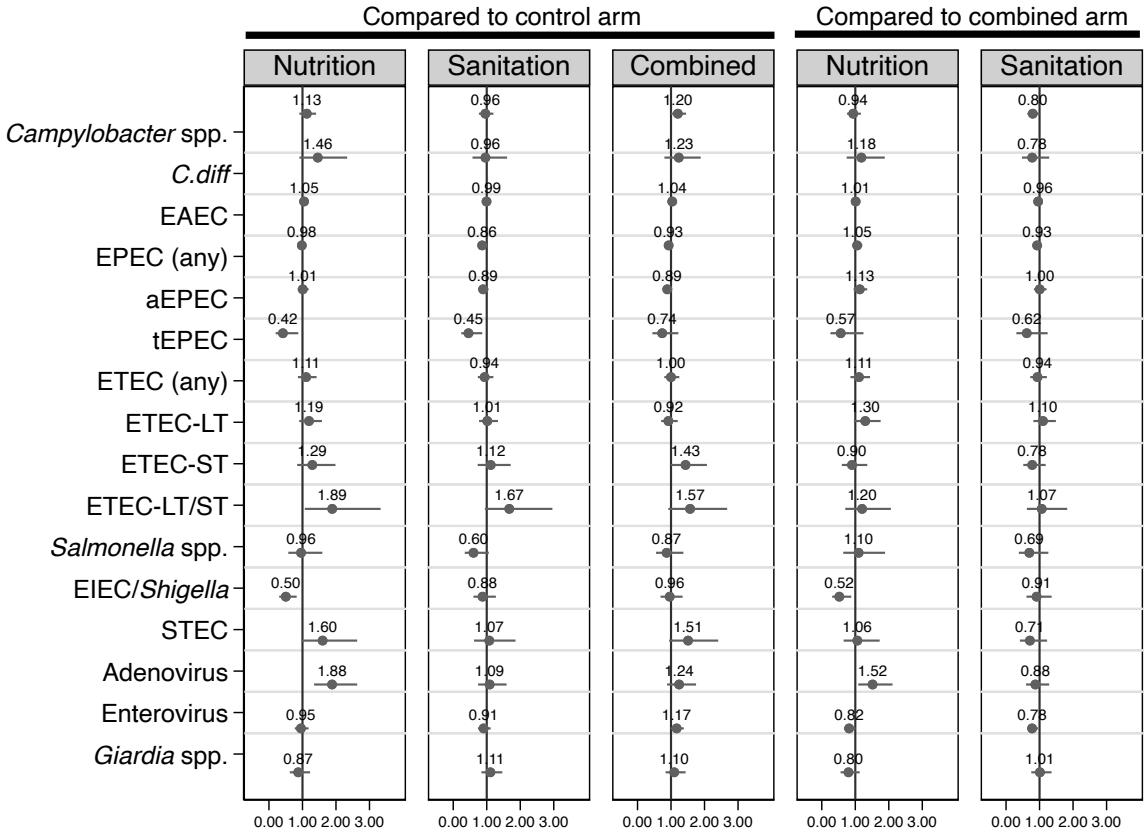
Adjusted prevalence ratios (aPR) of detected bacteria, viruses, protozoa, and STHs, comparing intervention arms to control. Adjusted analyses controlled for the following covariates: child age, child sex, maternal age, maternal education, number of household members, household wealth quintile

	Compared to control arm			Compared to combined arm	
	Nutrition-only	Sanitation-only	Combined	Nutrition-only	Sanitation-only
Any bacterium	1.06 (1.01, 1.11)	0.99 (0.93, 1.04)	1.05 (1.00, 1.10)	1.01 (0.96, 1.06)	0.94 (0.89, 1.00)
Camploybacter spp.	1.10 (0.90, 1.35)	1.10 (0.91, 1.34)	1.20 (1.01, 1.43)	0.92 (0.75, 1.12)	0.92 (0.76, 1.11)
C.diff	1.43 (0.92, 2.22)	0.98 (0.60, 1.59)	1.21 (0.80, 1.83)	1.18 (0.76, 1.83)	0.81 (0.51, 1.29)
EAEC	1.09 (0.98, 1.21)	1.01 (0.90, 1.12)	1.05 (0.96, 1.16)	1.03 (0.93, 1.15)	0.96 (0.86, 1.07)
EPEC	0.95 (0.84, 1.07)	0.87 (0.77, 0.99)	0.94 (0.84, 1.04)	1.01 (0.89, 1.15)	0.93 (0.81, 1.07)
aEPEC	0.96 (0.83, 1.12)	0.87 (0.75, 1.02)	0.87 (0.75, 1.00)	1.11 (0.94, 1.31)	1.01 (0.85, 1.20)
tEPEC	0.61 (0.34, 1.08)	0.59 (0.34, 1.00)	0.94 (0.60, 1.47)	0.65 (0.36, 1.18)	0.62 (0.36, 1.10)
ETEC	1.06 (0.84, 1.33)	0.89 (0.70, 1.12)	1.01 (0.82, 1.25)	1.05 (0.83, 1.33)	0.88 (0.69, 1.12)
ETEC-LT	1.18 (0.91, 1.52)	0.97 (0.75, 1.26)	0.97 (0.76, 1.25)	1.21 (0.92, 1.59)	1.00 (0.75, 1.32)
ETEC-ST	1.20 (0.82, 1.76)	1.06 (0.71, 1.57)	1.42 (1.01, 2.00)	0.84 (0.59, 1.21)	0.74 (0.51, 1.09)
ETEC-LT/ST	1.89 (1.13, 3.16)	1.62 (0.95, 2.77)	1.74 (1.07, 2.84)	1.08 (0.68, 1.73)	0.93 (0.57, 1.52)
Salmonella spp.	1.08 (0.69, 1.70)	0.67 (0.40, 1.13)	1.00 (0.65, 1.53)	1.09 (0.68, 1.73)	0.68 (0.40, 1.16)
EIEC/*Shigella* spp.	0.56 (0.36, 0.86)	0.86 (0.60, 1.22)	0.95 (0.68, 1.32)	0.59 (0.37, 0.92)	0.90 (0.61, 1.32)
STEC	1.22 (0.76, 1.94)	0.92 (0.55, 1.52)	1.46 (0.96, 2.22)	0.83 (0.53, 1.31)	0.63 (0.38, 1.03)
Any virus	1.08 (0.93, 1.24)	1.03 (0.89, 1.20)	1.16 (1.02, 1.32)	0.93 (0.80, 1.07)	0.89 (0.77, 1.03)
Adenovirus	1.80 (1.35, 2.40)	1.30 (0.95, 1.78)	1.36 (1.02, 1.83)	1.32 (1.00, 1.74)	0.95 (0.70, 1.30)
Enterovirus	0.93 (0.76, 1.13)	0.94 (0.77, 1.14)	1.12 (0.94, 1.32)	0.83 (0.68, 1.02)	0.84 (0.69, 1.02)
Any protozoa	0.90 (0.68, 1.20)	1.01 (0.78, 1.30)	1.14 (0.90, 1.45)	0.79 (0.59, 1.06)	0.88 (0.67, 1.16)
Giardia	0.91 (0.68, 1.23)	1.07 (0.82, 1.39)	1.13 (0.88, 1.46)	0.81 (0.59, 1.09)	0.95 (0.72, 1.25)
Gene targets with <5% prevalence were omitted from PR analyses: *V.cholera*, astrovirus, norovirus, rotavirus, sapovirus, *Cryptosporidium*, *Entamoeba,* and all STHs (*Ascaris, Trichuris, Ancylostoma,* and *Necator*).					

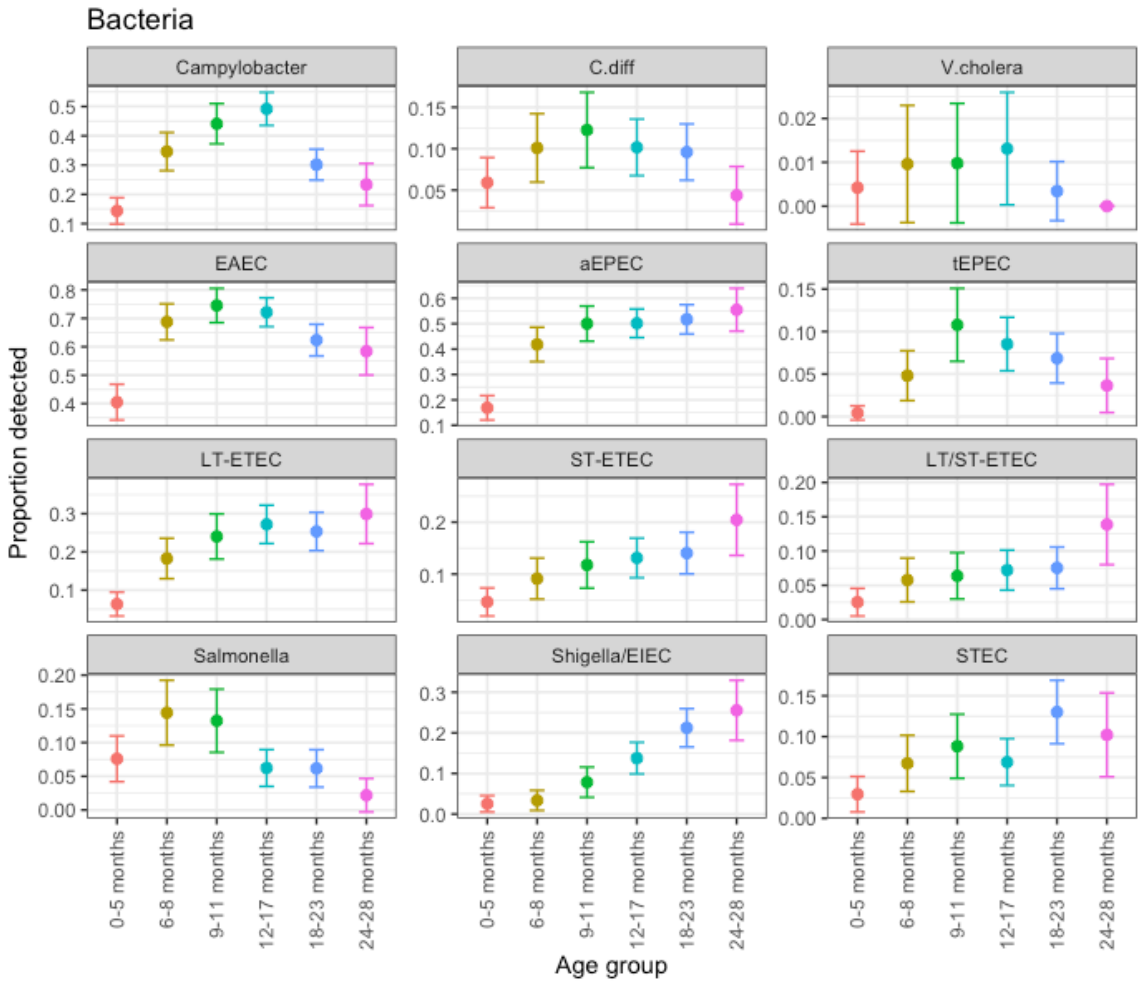
Limitations

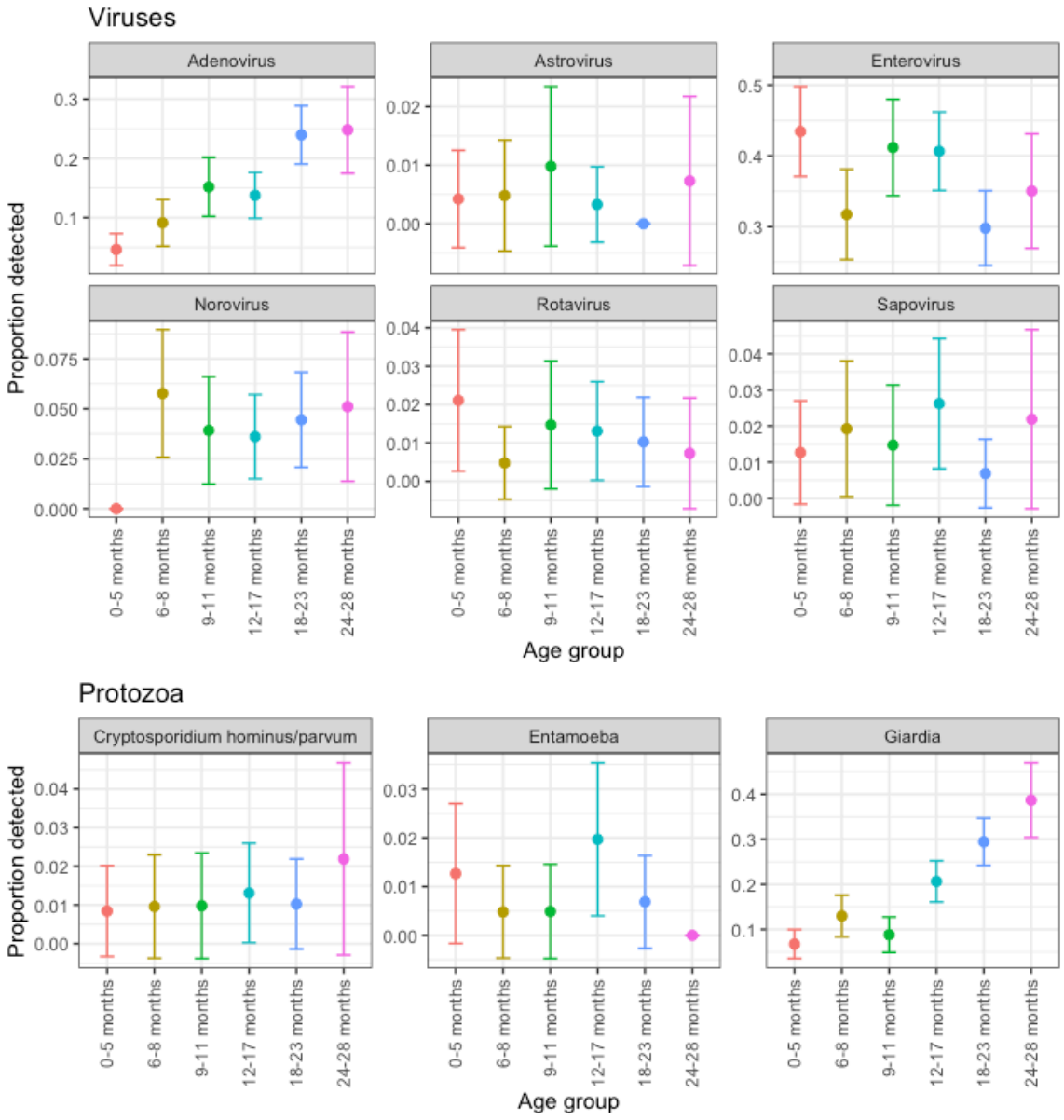
This trial was limited in its capacity to measure intervention impacts due to our use of a single cross-sectional survey to retrospectively assess interventions delivered over the previous 28 months. This study included children born from 28 months before up to one month before the final measurement, with the primary outcome variable of age-adjusted linear growth on a continuous scale. As a result, children were exposed to varying levels of "maturity" of the interventions to which they are exposed.

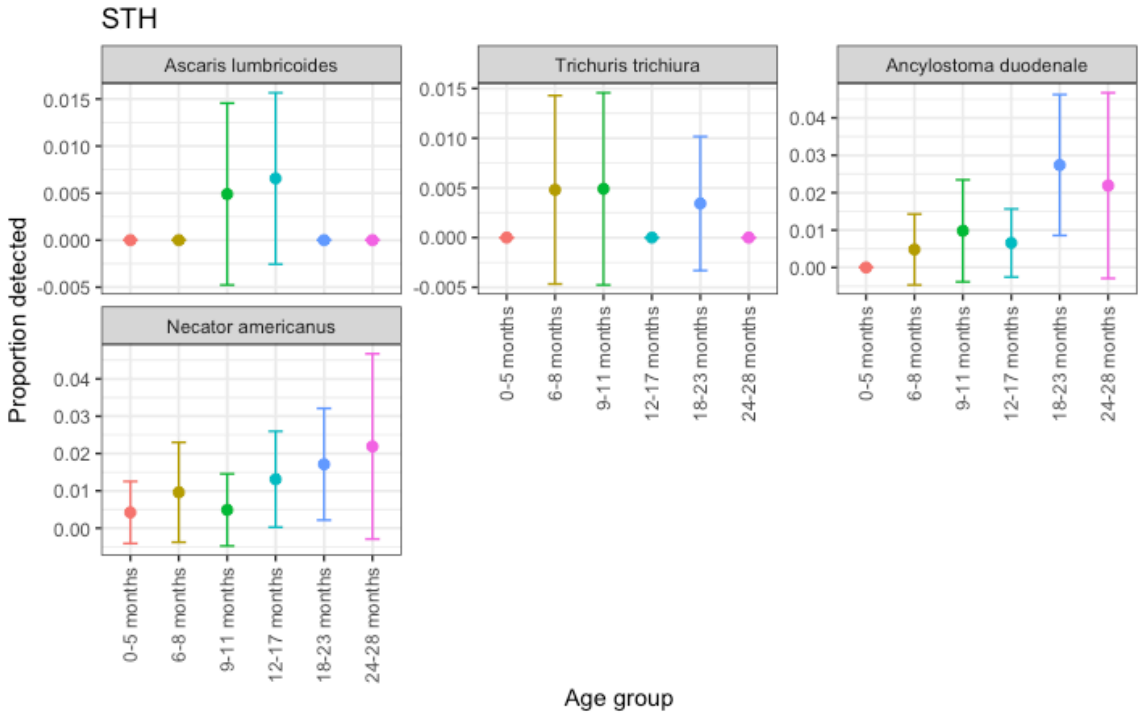
Impact of interventions on adjusted prevalence ratio of individual pathogens. Point estimates and 95% confidence intervals were determined using generalised log-linear Poisson models adjusting for covariates associated with each pathogen outcome: child age, child sex, maternal age, maternal education, number of household members, household wealth quintile.



S12: Age-stratified pathogen prevalence




Viruses
Adenovirus
Astrovirus
Enterovirus
Norovirus
Rotavirus
Sapovirus
Proportion detected
0-5 months
6-8 months
9-11 months
12-17 months
18-23 months
24-28 months
Age group
Protozoa
Cryptosporidium hominus/parvum
Entamoeba
Giardia
Proportion detected
0-5 months
6-8 months
9-11 months
12-17 months
18-23 months
24-28 months
Age group


STH
Ascaris lumbricoides
Trichuris trichiura
Ancylostoma duodenale
Necator americanus
Proportion detected
Age group
0-5 months
6-8 months
9-11 months
12-17 months
18-23 months
24-28 months

S13: Pre-intervention sanitation coverage

Treatment	Commune	% of households with improved drinking water source	% of households with access to improved sanitation facilities	% of households reporting open defecation practices	% of households with shared sanitation facilities	% of households reporting safe disposal of child stools
Nutrition	Chhnal Moan	52%	38%	24%	89%	46%
Nutrition	Preah Phos	67%	41%	48%	85%	58%
Nutrition	Prey Tralach	86%	29%	43%	55%	53%
Nutrition	Robas Mongkol	80%	69%	23%	92%	67%
Nutrition	Samraong	67%	48%	33%	84%	48%
Nutrition	Sangvaeuy	83%	33%	42%	73%	50%
Nutrition	Sdau	75%	54%	25%	88%	63%
Nutrition	Ta Krei	87%	60%	23%	100%	61%
Nutrition	Ta Pon	80%	80%	7%	92%	75%
Nutrition	Ta Pung	86%	76%	0%	100%	89%
Nutrition	Thipakdei	94%	64%	21%	91%	65%
Sanitation	Basak	60%	20%	73%	75%	18%
Sanitation	Chrouy Neang Nguon	90%	62%	19%	87%	71%
Sanitation	Khnar Sanday	95%	43%	50%	100%	41%
Sanitation	Lvea Krang	89%	33%	44%	75%	40%
Sanitation	Pou Treay	80%	0%	80%	100%	0%
Sanitation	Preaek Chik	85%	50%	35%	91%	47%
Sanitation	Ruessei Krang	48%	27%	58%	90%	25%
Sanitation	Srae Nouy	72%	36%	53%	87%	46%
Sanitation	Ta Meun	97%	73%	0%	79%	84%
Sanitation	Ta Yaek	89%	37%	44%	77%	80%
Sanitation	Traeng	100%	54%	33%	87%	71%
Sanitation	Varin	81%	48%	48%	91%	27%
Sanitation	Yeang	93%	27%	20%	40%	67%
Combined	Hab	75%	75%	15%	100%	71%
Combined	Kaev Poar	83%	54%	17%	76%	93%
Combined	Kakaoh	79%	46%	21%	79%	71%
Combined	Kampong Preang	94%	83%	6%	94%	70%
Combined	Kanhchor	44%	31%	53%	92%	56%
Combined	Khnat	92%	67%	6%	92%	73%
Combined	Mukh Paen	100%	39%	33%	70%	50%
Combined	Prey Chruk	100%	42%	27%	82%	63%
Combined	Slaeng Spean	90%	40%	44%	85%	47%

Combined	Srae Sdok	75%	37%	35%	74%	49%
Combined	Svay sa	81%	62%	14%	81%	80%
Combined	Ta Lou	90%	48%	27%	81%	53%
Control	Anlong Reab	85%	31%	38%	71%	88%
Control	Ballangk	100%	25%	75%	100%	27%
Control	Chan Sar	84%	44%	18%	64%	68%
Control	Chob Ta Trav	100%	40%	60%	100%	36%
Control	Doun Ba	95%	59%	27%	93%	81%
Control	Kantuot	67%	17%	83%	100%	0%
Control	Kdei Run	100%	43%	33%	82%	46%
Control	Khnar Pou	79%	63%	13%	83%	65%
Control	Lveaeng Ruessei	90%	44%	31%	82%	52%
Control	Mukh Reah	76%	33%	38%	70%	53%
Control	Ou Ta Paong	80%	48%	26%	79%	61%
Control	Prey Khpos	100%	80%	7%	96%	90%
Control	Reaksmei Sangha	70%	30%	26%	58%	71%
Control	Roung Kou	96%	26%	56%	70%	21%
Control	Ruessei Lok	71%	33%	50%	80%	33%
Control	Run Ta Aek	86%	24%	38%	63%	44%
Control	Snuol	96%	26%	52%	70%	54%
Control	Spean Tnaot	84%	62%	7%	82%	71%
Control	Ta Loas	100%	67%	15%	78%	70%

S14: CONSORT checklist for RCTs

CONSORT 2010 checklist of information to include when reporting a randomised trial*

Section/Topic	Item No	Checklist item	Reported on page No
Title and abstract			
	1a	Identification as a randomised trial in the title	1
	1b	Structured summary of trial design, methods, results, and conclusions (for specific guidance see CONSORT for abstracts)	1, 2
Introduction			
Background and objectives	2a	Scientific background and explanation of rationale	3
	2b	Specific objectives or hypotheses	3,4
Methods			
Trial design	3a	Description of trial design (such as parallel, factorial) including allocation ratio	4
	3b	Important changes to methods after trial commencement (such as eligibility criteria), with reasons	4, Supplementary Material
Participants	4a	Eligibility criteria for participants	4, Supplementary Material
	4b	Settings and locations where the data were collected	4
Interventions	5	The interventions for each group with sufficient details to allow replication, including how and when they were actually administered	4, Supplementary Material
Outcomes	6a	Completely defined pre-specified primary and secondary outcome measures, including how and when they were assessed	5
	6b	Any changes to trial outcomes after the trial commenced, with reasons	n/a
Sample size	7a	How sample size was determined	5, Supplementary Material
	7b	When applicable, explanation of any interim analyses and stopping guidelines	n/a
Randomisation:			
Sequence generation	8a	Method used to generate the random allocation sequence	4
	8b	Type of randomisation; details of any restriction (such as blocking and block size)	4
Allocation concealment mechanism	9	Mechanism used to implement the random allocation sequence (such as sequentially numbered containers), describing any steps taken to conceal the sequence until interventions were assigned	4
Implementation	10	Who generated the random allocation sequence, who enrolled participants, and who assigned participants to interventions	4

Blinding	11a	If done, who was blinded after assignment to interventions (for example, participants, care providers, those assessing outcomes) and how	4
	11b	If relevant, description of the similarity of interventions	n/a
Statistical methods	12a	Statistical methods used to compare groups for primary and secondary outcomes	5
	12b	Methods for additional analyses, such as subgroup analyses and adjusted analyses	5, Supplementary Material
Results			
Participant flow (a diagram is strongly recommended)	13a	For each group, the numbers of participants who were randomly assigned, received intended treatment, and were analysed for the primary outcome	6
	13b	For each group, losses and exclusions after randomisation, together with reasons	6
Recruitment	14a	Dates defining the periods of recruitment and follow-up	4
	14b	Why the trial ended or was stopped	n/a
Baseline data	15	A table showing baseline demographic and clinical characteristics for each group	Table 2
Numbers analysed	16	For each group, number of participants (denominator) included in each analysis and whether the analysis was by original assigned groups	6
Outcomes and estimation	17a	For each primary and secondary outcome, results for each group, and the estimated effect size and its precision (such as 95% confidence interval)	6-8, Figure 3, Figure 4, Tables 6-10
	17b	For binary outcomes, presentation of both absolute and relative effect sizes is recommended	Tables 6-10
Ancillary analyses	18	Results of any other analyses performed, including subgroup analyses and adjusted analyses, distinguishing pre-specified from exploratory	Supplementary Material
Harms	19	All important harms or unintended effects in each group (for specific guidance see CONSORT for harms)	n/a
Discussion			
Limitations	20	Trial limitations, addressing sources of potential bias, imprecision, and, if relevant, multiplicity of analyses	9-10
Generalisability	21	Generalisability (external validity, applicability) of the trial findings	10-11
Interpretation	22	Interpretation consistent with results, balancing benefits and harms, and considering other relevant evidence	9-11
Other information			
Registration	23	Registration number and name of trial registry	12
Protocol	24	Where the full trial protocol can be accessed, if available	12
Funding	25	Sources of funding and other support (such as supply of drugs), role of funders	12

*We strongly recommend reading this statement in conjunction with the CONSORT 2010 Explanation and Elaboration for important clarifications on all the items. If relevant, we also recommend reading CONSORT extensions for cluster randomised trials, non-inferiority and equivalence trials, non-pharmacological treatments, herbal interventions, and pragmatic trials. Additional extensions are forthcoming: for those and for up to date references relevant to this checklist, see www.consort-statement.org.

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