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The Impact of Water, Sanitation, and Hygiene (WaSH) in the Presence of Suboptimal Adherence and Complex Interdependencies

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An abstract of
A dissertation submitted to the Faculty of the
James T. Laney School of Graduate Studies of Emory University
in partial fulfillment of the requirements for the degree of
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Abstract

The Impact of Water, Sanitation, and Hygiene (WaSH) in the Presence of Suboptimal Adherence and Complex Interdependencies

By Joshua Val Garn

The health and educational impacts of school-based water, sanitation, and hygiene (WaSH) are not well established. Suboptimal adherence to WaSH – either to individual technologies and behaviors, or to complementary WaSH combinations – adds complexity to estimating these effects. We performed three studies, each relating to WaSH access and adherence. In our first two studies, we characterize the effects of WaSH in school settings where there was suboptimal adherence and complex adherence patterns. We hypothesized that increased adherence to relevant WaSH combinations would be associated with prevention of infectious diseases. For our final study we sought to understand factors associated with suboptimal adherence, specifically the sanitation component of WaSH.

Our first study used data from a cluster randomized trial that took place in 185 Kenyan schools. There was sub-optimal implementation of WaSH at many schools (i.e. poor school-level adherence), which may have led to intention-to-treat results that were different from what might have been observed under hypothetical conditions of good adherence. We used an instrumental variable analysis to estimate the effects of school-level WaSH adherence on diarrheal illness and on soil-transmitted helminth (STH) infection. We observed that for several outcomes, the preventive effects of WaSH were stronger among schools with better adherence.

For our second study, we characterized the associations between *A. lumbricoides* reinfection and children's WaSH exposures at school and home, for pupils attending 51 Kenyan schools. There was evidence that some WaSH exposures are independently associated with *A. lumbricoides* reinfection, but that others depended upon adherence to combinations of WaSH. Estimates were sometimes more pronounced with adherence at both school and home. Counterintuitively, increased access to school latrines was associated with higher reinfection.

In our final study, we used data from 60 Kenyan schools, and characterized the associations between school sanitation conditions and pupils' use of sanitation facilities. A variety of school sanitation conditions were associated with pupils' toilet use, including pupil to toilet ratio, toilet type, toilet age, the number of toilets in a block, and facility cleanliness.

Taken together, these three studies help to characterize the complex role of WaSH adherence in improving child health.

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WASH

Water, sanitation, and hygiene (WaSH) interventions generally target the introduction of sufficient quantities of clean and safe water, the facilities and means to have appropriate sanitary disposal of excreta, and the behavioral hygiene training to facilitate good health. There are a variety of technologies and behaviors that are all parts of WaSH, and WaSH interventions may focus on some or many of these technologies and behaviors. For instance, clean water interventions may focus on bringing in new clean water (e.g. drilling boreholes, or clean water rain systems, piped water), on the safe storage of water, or on the treatment of water (e.g. chlorination). Sanitation interventions may focus on increasing latrine availability (e.g. building of improved latrines), on improving latrine quality (e.g. providing cleaning supplies for latrines), or on behavioral components of sanitation (e.g. encouraging use of latrines). Hygiene interventions might provide soap, handwashing stations, or behavioral training on handwashing. Throughout the paper the term ‘WaSH component’ or ‘WaSH domain’ is occasionally used to loosely to refer to one of the separate parts of WaSH (e.g. water, sanitation, or hygiene) by itself. These domains, in reality, consist of a variety of technologies and behavioral interventions, which are both individually important and interdependent in preventing a variety of infectious disease outcomes.

We often measure access by using the terms ‘improved water’ or ‘improved sanitation’ as defined by the WHO/UNICEF Joint Monitoring Programme (JMP) for Water Supply and Sanitation.[1] Improved sanitation should adequately divide excreta from human contact, and may include a "flush toilet, piped sewer system, septic tank, flush/pour flush to pit latrine, ventilated improved pit latrine, pit latrine with slab, composting toilet, or special case." Improved water is defined as either water that is "piped into the dwelling, piped into the yard/plot, public tap or standpipe, tubewell or borehole, protected dug well, protected spring, or rainwater."

In spite of WaSH having a relatively long public health history and even being so accepted publicly, for much of the world access to basic services has been strikingly slow.[2] In industrialized countries nearly all people have access to improved sanitation, whereas in developing countries, many of which are located in Asia or Sub-Saharan Africa, only about half have access to improved sanitation facilities and within these developing countries.[3] Around 768 million people worldwide lack improved water sources, and 2.5 billion are lacking improved sanitation facilities.[1] Improved sanitation is barely keeping pace with increases in populations.[3] Furthermore, a large portion of the world does not even have access to an improved water source, and sanitary practices such as defecation in the open further complicate this public health problem.[1,3] In spite of the lack of significant progress, the challenges presented in improving water, sanitation, and hygiene are not insurmountable, as current interventions are highly cost-effective, and generally found to be effective in reducing the disease burden.[2,4]

We use the terms WaSH adherence throughout this paper to loosely mean access and use of WaSH. Suboptimal WaSH adherence – either to individual WaSH technologies and behaviors, or to varying WaSH combinations – plays an important role in increasing exposure to pathogens, and is a focal point of this paper.

WASH AND DISEASE

Public health benefits of clean water, sanitation, and hygiene have been documented for over 150 years, with John Snow, the father of modern epidemiology first discovering the importance of clean water and sanitation in relation to cholera, and Ignas Semmelweis demonstrating the benefits of handwashing in obstetric clinics. In spite of this longstanding history, the burden of disease due to worldwide WaSH inadequacies is striking. In 2002, it was estimated that inadequate WaSH led to approximately 4.0% of all deaths and 5.7% of the total disease burden worldwide.[5] More recent estimates are that safe water, improved sanitation, and appropriate hygiene would prevent approximately 2.4 million deaths worldwide (4.2% of all deaths), and 6.6% of the global burden of disease.[6,7] Most of the deaths that are associated with unimproved hygiene, sanitation, and unsafe/insufficient water are among children, often under the age of five. In fact, 19% of the child mortality worldwide is attributed to poor water, sanitation, and hygiene.[2,6,7] WaSH deficiencies are known to lead to increased mortality and morbidity via a number of mechanisms, both pathogenic (e.g. bacteria, viruses, soil-transmitted helminths, etc.)[4,5,8] and environmental (arsenic, copper, fluoride, lead, and nitrate).[4]

The focus of this dissertation will be on WaSH and its relation to diarrheal illness and soil-transmitted helminth infection, as these are two major causes of public health burden in terms of morbidity and mortality, particularly in developing countries. We also further discuss the importance of WaSH in primary school settings, as each of our studies are based in Kenyan primary schools.

Diarrheal illness

Diarrheal illness is one of the leading causes of mortality in children under 5. More recent, and estimates are that it leads to 700,000 deaths per year among children under the age of five.[9] The mortality associated with diarrheal disease is highest in Africa and Southeast Asia, and the majority of these deaths take place in only 15 high-burden countries.[9,10]

A variety of viral, bacterial, and parasitic organisms may contribute to diarrhea related morbidity and mortality. A recent systematic review assessed 13 pathogens as potential causes of diarrhea related mortality, including: "Rotavirus, enteropathogenic *Escherichia coli,* enterotoxigenic *Escherichia coli, Salmonella spp.* (excluding *Salmonella typhi*), *Shigella spp.*, *Campylobacter spp.*, *Vibrio cholerae* 01 and 0139, *Giardia lamblia*, *Cryptosporidium spp.*, *Entamoeba hystolitica*, human Caliciviruses (genogroup I and II norovirus and sapovirus) or astrovirus, coronavirus, and enteric adenovirus." They found that over half of the serious diarrhea episodes could be attributed to a small number of pathogens (i.e. rotavirus, EPEC, calcivirus, and ETEC). It is not always possible to identify a specific cause of diarrhea, either because no pathogens are identified or because multiple pathogens are identified. Regardless, for most pathogens that cause diarrhea, disease is transmitted primarily through a fecal-oral mechanism, and so transmission should be preventable by improvements to WaSH technologies and behaviors as shown below.

WaSH and diarrhea in developing countries: In developing countries many of the WaSH technologies and behaviors, implemented as either as single component interventions or as complete packages (e.g. water, sanitation and hygiene interventions) have shown small to moderate improvements in the reduction of diarrheal illness. Meta-analytic results aiming to quantify the effects of separate WaSH components on diarrheal illness have shown protective effects of hygiene interventions (RR = 0.63, 95% CI 0.52 – 0.77), sanitation interventions (RR = 0.68, 95% CI 0.53 – 0.87), water supply interventions (RR = 0.75, 95% CI 0.62 – 0.91), and water quality interventions (RR = 0.69, 95% CI 0.53 – 0.89).[11] A more recent meta-analysis suggests that the efficacy of sanitation interventions and of water interventions depends heavily on the quality and permanence of the upgrade.[12] When using meta-analysis to study multiple interventions in developing countries, comprehensive WaSH (interventions assessing multiple WaSH components) also reduced diarrheal illness levels significantly (pooled RR of 0.67; 95% CI 0.59 – 0.76).[11]

WaSH and diarrhea in developed countries: Decreasing diarrhea due to WaSH interventions depends in part on baseline economic conditions.[11] In market economies hygiene interventions have been shown to significantly decrease diarrheal disease with a pooled risk ratio estimate from meta-analysis of 0.58 (95% CI 0.48 – 0.71), but very few studies have addressed the individual effects of sanitation, water supply, or water quality, as these WaSH components are probably already sufficient in most places in market economies.[11]

Soil-Transmitted Helminth infection

It has been estimated that over 1 billion people throughout the world are infected with STHs. Chronic STH infections particularly impact school-aged children, leading to anemia,[13] slowed physical and/or cognitive development,[14] and STH infections account for over 5 million disability adjusted life years annually.[15] The primary STHs or interest are roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*) and hookworms (*Necator americanus* or *Ancylostoma duodenale*).[16-18] Each of these adult worms reside in the intestines, and their eggs are passed with feces into the environment. The transmission mechanism of *A. lumbricoides* and *T. Trichiura* are primarily through the ingestion of eggs. The transmission mechanism of hookworm is different, with eggs developing into infective larvae outside of the body, and these larvae are then able to penetrate the skin. For each of the three STHs, newly passed eggs are not immediately infective, and require several weeks, optimally in warm, moist, shaded conditions, to develop into infective eggs (or for hookworm, infective larvae).

Once infected, one can easily be treated using anthelminthic drugs, such as Albendazole or Mebendazole.[19] Mass deworming programs, targeted to either school children or the overall community, are being implemented throughout the world to reduce the prevalence of STHs and their associated morbidity.[20,21] While, mass deworming does a good job of eliminating these parasites from individuals, without improvements in WaSH, and the benefits of drug administration are not sustained.[22] For example, one study found that even though deworming had a very high cure rate, *A. lumbricoides* returned to pretreatment levels within six months.[23] Another problem of this mass-deworming approach, is that without careful monitoring, soil-transmitted helminths may develop resistance to anti-helminthic drugs over time.[24]

WaSH on STH infection: A number of studies have focused on the protective effects of sanitation, against STH infection.[25-27] A recent meta-analysis of 36 studies found that sanitation protected against STHs infection, with an OR 0.54 (95% CI: 0.28–1.02) for *T. trichiura*, 0.63 (95% CI: 0.37–1.05) for hookworm, and 0.78 (95% CI: 0.60–1.00) for *A. lumbricoides*.[26] Studies including water supply or hygiene components have also found some protective effects.[25,28]

However, there are several gaps in the literature. Most studies have assessed WaSH only in the home setting, rather than in schools, or both at home and at school. Also, little is known in how individual WaSH technologies and behaviors work both individually and in concert in protecting against helminth reinfection.

WASH IN SCHOOLS

The problem of WaSH access is particularly important in schools.[29] In these schools, WaSH facilities are often either inadequate in both quality or quantity.[29] Children, the group at highest risk of WaSH related morbidity and mortality, spend large amounts of time at school in close personal contact with many other children, making it an environment that can increase transmission of disease. School WaSH is may serve as a locus to learn and practice WaSH, which may also spill into home WaSH practices.

Jasper et al. performed a systematic review of 47 papers, most of which were observational research, and found both health and non-health benefits associated with WaSH in schools.[30] Evidence was found that school WaSH may increase pupils' water intake, and attendance; and that it may decrease diarrheal and gastrointestinal diseases.[30]

Appropriate sanitation is of particular importance in the school environment, as open defecation creates an unsanitary school environment. However, unclean toilets also may present a vehicle for transmitting a wide range of infectious agents.[31] We address school sanitation in greater detail, as this topic will serve as a foundation for our third paper.

Sanitation in Schools: The problem of inadequate sanitation is important for school-aged children, who experience over 2.8 billion cases of diarrhea annually,[32] and who bear much of the burden of STH morbidity.[17] Inadequate sanitation has been associated with a number of health problems, including stunted growth,[33,34] diarrheal illness,[35-37] and even death.[6,7] Equitable access to school sanitation is of particular concern. Data are scarce, but recent estimates suggest that only 45% of schools in low income countries have adequate sanitation facilities.[38]

The health and educational benefits of increasing the number of latrines in schools are still not well understood. To our knowledge, no trial assessing only the benefit of additional latrines in schools has been conducted, likely because implementing sanitation without hygiene is not seen as best practice and may not be policy relevant.[39] The only comprehensive school WASH trial that also included latrine provisions found decreased pupil absence, increased enrollment, and decreased diarrheal illness, but only among certain subsets of the study population,[40,41] and found reduced STH infection rates for the *A. lumbricoides* worm, but not other helminths.[28] Furthermore, pupils attending schools in an arms that received latrine provisions received little benefit compared to pupils in otherwise similar intervention arms but without latrine provisions[40,41] and latrine provisions were even associated with increased pupil hand contamination.[42] These results suggest that other factors, besides simply providing school latrines, are important to the success of school sanitation interventions at scale.

One possibility for the mixed success of this previous trial is that while the number of latrines increased, latrine dirtiness could actually increase pupils' exposure to disease.[31] For instance, studies have found that dirty school sanitation facilities are associated with increased bacterial pathogens throughout the bathroom,[43] and with increased incidence of diarrhea,[31] vomiting,[31] and dysentery outbreaks.[44] Decreasing the pupil to latrine ratio in a school is hypothesized to improve the overall latrine use in that school,[40,45] but for this increase in latrine use to improve public health, it must also coincide with a net reduction in pupils' exposures to pathogens.

Another possibility for the mixed success of this previous trial relates to the actual use of the latrines. There has been considerable attention to the child-centered design of sanitation facilities in schools,[46,47] however little empirical data exist on how the type, design, and maintenance of facilities affect behavior or health. Provisions of toilets at schools do not guarantee that those toilets are well maintained, or that they will even be used by pupils. When latrines are available, children may choose to use the latrines or urinals, to openly defecate or urinate in or around the school grounds, or to hold their use until they can access a preferable toilet or openly defecate outside of school.[48] Open defecation, which affects pupil health by increasing exposure to fecal pathogens, has been observed in lower resource schools even when school toilets are present.[49] Toilet avoidance behavior also occurs,[50-53] and can affect pupil health by causing personal discomfort and even bowel or urinary problems.[51,52] However, no rigorous studies have quantified how characteristics of toilets might lead to improved use.

There are a number of factors that are thought to be important to pupils actually using school latrines. One is toilet or latrine access, which in the school setting is most often measured using the pupil to toilet or pupil to latrine ratio. International guidelines set forth by the World Health Organization for low cost settings are that there should be one latrine per 25 girls, and one latrine per 50 boys plus one urinal.[29] In Kenya – the setting of the studies in this dissertation – the goal put forth by the government is to have a pupil to latrine ratio of 25:1 for girls, and 30:1 for boys,[54] although this standard is not currently being obtained. It is not well understood how pupil to latrine ratio affects actual toilet use in this setting.

Besides toilet availability, pupils have self-reported a number of other factors that they perceive to affect their toilet use. In these studies, some of the self-reported barriers inhibiting school toilet use include restricted access to toilets (e.g. only allowed to use during break), privacy concerns (e.g. insecurity of being heard), lack of locks, fear of getting locked in because of old locks, lack of access to toilet paper, dirtiness of facilities, bullying, physical appearance, and smell.[50-53,55] It should be noted that many of these concerns are easily addressable by focusing on better constructing and maintaining facilities. It has been noted that in terms of health benefits, maintenance and cleaning may be equally as important (or even more) than the pupil to latrine ratio.[31] These studies have taken place primarily in Europe, and rely heavily on pupil reported measures. Our study is the first to rigorously quantify the relationships between toilet characteristics and use in lower resource schools. An increased understanding of how school sanitation conditions are associated with pupils' use will facilitate the development and implementation of appropriate of sanitation in schools throughout the world, and lead to improved health and educational outcomes for children.

STUDY AIMS

Study 1

Because adherence to WaSH in trials is often poor, it can lead to intention-to-treat results that are very different than what would have been seen under optimal adherence. In spite of the strong biological plausibility and long-standing history of epidemiologic studies supporting the preventive effects of WaSH on health in non-school settings,[35,36,56,57] the positive effects of school WaSH on health and educational outcomes in recent trials has shown mixed results. For example, the only comprehensive school WASH trial that also included latrine provisions found decreased pupil absence, increased enrollment, and decreased diarrheal illness, but only among certain subsets of the study population,[40,41] and found reduced STH infection rates for the *A. lumbricoides* worm, but not other helminths.[28] Furthermore, pupils attending schools in an arms that received latrine provisions received little benefit compared to pupils in otherwise similar intervention arms but without latrine provisions[40,41] and latrine provisions were even associated with increased pupil hand contamination.[42] One possible reason for these results is poor implementation by schools of WaSH (i.e. school-level adherence). For our **Aim 1** we used an instrumental variable analysis (within the structural nested model framework) to understand the causal effects of actual WaSH adherence on pupil health outcomes. Specifically, we used a weighted generalized structural nested mean model to obtain the effect of observed WaSH adherence (compared to a referent) among schools that adhered to WaSH (i.e. the effect of treatment on the treated).[58] This will supplement previously reported ITT analyses,[28,40,41,59] and lead to a fuller understanding of how to best utilize resources to improve health.

Study 2

Characterizing the relationship between WaSH and STH reinfection is important, although it presents some methodological complexities in epidemiologic studies. First, WaSH is a multi-faceted exposure containing several primary domains (e.g. water, sanitation, & hygiene), each of which is composed of many different technologies and behaviors that vary between the school and home environments. Most prior WaSH studies have not attempted to model individual WaSH technologies and behaviors simultaneously, in the multi-level school and home contexts in which they actually exist. Further, while these WaSH technologies and behaviors have the potential to be individually important, they are also interdependent and interact in complex pathways to reduce pathogen exposure (e.g. a pupil's handwashing behavior depends on soap and water availability). Little has been done to characterize the complex interactions between WaSH technologies and behaviors, and their relationship to STH reinfection. Our study uses data from year two of a longitudinal study led by The Kenya Medical Research Institute (KEMRI), which was designed to assess pupils' STH reinfection following yearly MDA.[60] The objectives of this particular study were to **(Aim 2)** characterize how pupils' school and home WaSH exposures were associated with *A. lumbricoides* reinfection, and specifically to characterize how combinations of behaviors and technologies interact in the prevention of helminth reinfection.

Study 3

While much work has been done to increase the raw numbers of new sanitation facilities (e.g. latrines) worldwide, it is also vital to make sure that these interventions are being implemented in a way so that latrines are actually being used. Our final study makes important contributions to this effort. For **Aim 3**, we focused specifically on ascertaining which school sanitation conditions are associated with pupils' use of sanitation facilities in 60 primary schools in Kenya. We characterized how varying pupil to toilet ratio was associated with the overall use of toilets at schools. We also characterized how toilet conditions, such as toilet cleanliness, age, type, and structure were associated with pupils' use at specific facilities.

SUMMARY

Although there is ever growing evidence supporting WaSH for a number of outcomes, the burden of disease due to worldwide disparities in WaSH is still striking. Without a better understanding of the complexities that drive adherence to WaSH, the appropriate implementation of WaSH worldwide may be thwarted. Our research will play an important role in gaining an understanding of how WaSH adherence affects trial estimates and specifically how increased adherence and access to WaSH interventions might mitigate diarrheal illness reduction and helminth infection. We also seek an understanding of the interdependence of the different WaSH components, hoping to gain insights into how to best focus our public health efforts in implementing multiple component interventions. For our final question, we focus specifically on sanitation, and on ascertaining which factors might be most important in improving use in school latrine facilities.

CHAPTER 2: Methods to deal with non-adherence in trials

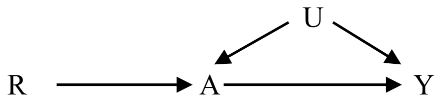
OVERVIEW

The overall goal for our first study was to measure the effect of school level WaSH adherence on a number of pupil health outcomes. Here we discuss commonly used analyses, including the intention-to-treat, as-treated, per-protocol, endogenous regressor, principal stratification, and the structural nested model analyses. We summarize their strengths and limitations as they relate to our WaSH trial and to our specific study goals. For accessibility and illustrative purposes, we present most of these analyses in the context of a simple two armed randomized trial with individual-level adherence and a dichotomous outcome. In reality, our WaSH trial has a number of added complexities, including it being a cluster randomized trial with a complex sampling scheme, cluster-level adherence, multiple study arms, and various types of outcomes. The robustness of the structural nested model allows us to overcome many of these complexities. We introduce the structural nested model framework, which is the methodology we will use in our first paper as it allows us to account for the added complexities of our WaSH trial.

RANDOMIZED CONTROLLED TRIALS

Randomized controlled trials (RCTs), randomly assign an exposure to individuals so as to decrease the possibility of confounding by unknown or unmeasured confounders. Figure 2.1 below shows a simple causal diagram that illustrates the issue of adherence (often termed compliance in the literature) in RCTs.[61,62] In this simple example, participants are randomized to an intervention (R=1 or R=0), their adherence to the assigned intervention is measured (A=1 or A=0), and the outcome (Y=1 or Y=0) is compared between intervention groups. U is a measure of confounders, variables that both affect adherence and the outcome, and may be either unknown, measured or unmeasured. The causal directed acyclic graph below depicts the ideal scenario (double-blind, placebo controlled, well-measured exposure/outcome, etc.), and assumes no other causal effects represented by other arrows exist.

Figure 2.1. Directed acyclic graph from simple double-blind, placebo controlled randomized controlled trial.[62]



INTENTION-TO-TREAT ANALYSIS

The intention to treat analysis (ITT) is the most commonly used analysis in trials, and measures the average causal effect of randomization, R, on the outcome, Y, regardless of adherence to the intervention.[61] The DAG shows that even in the presence of poor adherence, R is not confounded by U. The ITT analysis has become the analysis of choice in randomized trials, primarily because it, on average, accounts for confounding, including confounding by unknown or unmeasured confounders.

When researchers are interested in the effectiveness of an intervention, or in other words the ability of that specific intervention to produce results under real-world conditions,[63] the ITT analysis is ideal, as produces a valid causal estimate of the effect of the intervention. However, when researchers are interested in efficacy – or ability to produce intended results under ideal conditions[63] – of a drug or intervention, the ITT estimator may be a distorted measure of the treatment itself when adherence to the intervention is poor.[64] As adherence decreases, the ITT effect will tend to differ from the effect of actual adherence to the treatment**.**[61] In other words, in the case of non-adherence the ITT estimand does not necessarily measure the actual biological or practical effect of the exposure.

Another way to understand the effects of non-adherence, is to use potential outcomes. The potential outcomes model we use was first introduced by Neyman in 1923,[65] and has been further developed by Rubin and others.[64,66,67] Throughout this section on the ITT analysis, and the following sections on the as-treated, per-protocol, and principal stratification analyses, we show several examples and use some of the notation similar to those in a review by Little and Rubin.[64] We continue to consider the simple case of a two arm trial where individuals are randomized (R) to either an intervention (r=1) or a control (r=0), and where we have observed the actual treatment (A). Their binary adherence to the intervention leads to four unique compliance types: 1) never takers – those who would not ever receive the intervention even when assigned to the intervention group, 2) defiers – those who would always do the opposite of their assigned treatment, 3) compliers – those who would always comply with their assigned treatment regardless of treatment assignment, and 4) always-takers – those who would always take the intervention regardless of their assigned treatment. We show the distribution of these compliance types, in the context of a simple randomized trial in Table 2.1. We point out that these four compliance types are incompletely observed.[64] We used A(1) to denote the actual treatment (1 or 0) when randomized to r=1, and A(0) to denote the treatment when randomized to r=0. Similarly, Y(1) represents the outcome when the participant was randomized to the intervention arm, and Y(0) represents the outcome when the participant was randomized to the control arm.

Table 2.1. Distribution of participants in a hypothetical randomized controlled trial, based on their randomization, adherence, outcome, and compliance types.

r=1				r=0		
	A(1)=1	A(1)=0			A(0)=1	A(0)=0
Y(1)=1	always-takers, compliers;	never-takers, defiers;		Y(0)=1	always-takers, defiers;	compliers, Never-takers;
Y(1)=0	always-takers, compliers;	never-takers, defiers;		Y(0)=0	always-takers, defiers;	compliers, never-takers;

Using this notation, the estimand for the ITT analysis is E(Y(1) - Y(0)).[64] This is well-defined, in that it compares always-takers, compliers, never-takers, and defiers in the treatment arm, to always-takers, compliers, never-takers, and defiers in the control arm. Because we randomized, there is on average balance of these adherence types in both intervention arms of the study. However, it is also easy to see that the ITT estimand is not measuring the practical or biological effect of the exposure of interest (A) on disease (Y).

AS-TREATED ANALYSIS

A widely used analysis (often as either a secondary or alternative analysis) is the "as-treated" analysis which compares the actual received treatment (A) and ignores randomization.[64] In the as-treated analysis individuals are classified based on their adopted treatment (A), and the randomization variable (R) is irrelevant to this analysis. It is clear by the DAG shown in Figure 2.1 that when measuring the effect of A→Y in the presence of poor compliance, that there is the potential of confounding by either measured or unmeasured U. If adherence were perfect (A always equals R), or if there were no confounders, simple comparisons would lead to an unbiased measure. Even if confounders existed but could be measured, regression could be used to make appropriate comparisons. The problem is that if there are any unmeasured or unknown confounders, the resulting estimate of A on Y may be biased.

Table 2.2. Distribution of participants in an as-treated analysis

	A=1	A=0
Y=1	always-takers, compliers, defiers	never-takers, compliers, defiers
Y=0	always-takers, compliers, defiers	never-takers, compliers, defiers

To illustrate this issue using the potential outcomes model from this same hypothetical randomized trial, we collapsed table 2.1 on A to create Table 2.2. In the as-treated analysis, the estimand is $E(Y|A=1) – E(Y|A=0)$. This comparison is not consistent with a valid individual level causal effect – the exposed group consists of always-takers, compliers, and defiers, which are compared to never-takers, compliers, and defiers in the unexposed group.[64] This imbalance is likely to coincide with imbalances in important confounders among the different compliance types. Without further assumptions, the as-treated analysis does not produce a valid causal effect.[68]

PER-PROTOCOL ANALYSIS

Another widely used analysis (often supplementary) is the "per-protocol analysis" which compares only those participants who took the treatment as they were randomized, and differs from the as-treated analysis in that participants who did not follow their treatment assignment are dropped from the analysis.[64] Table 2.3 illustrates the per-protocol analysis using the potential outcomes model from this same hypothetical randomized trial, and is different from Table 2.1 in that participants who did not follow their treatment assignment are dropped from the analysis. In the per-protocol analysis, the estimand is E(Y|A=1,R=1) – E(Y|A=0,R=0). This compares the risk of disease among always-takers and compliers in the intervention arm to the risk of disease among compliers and never-takers in the control arm.[64] As with the as-treated analysis, and for similar reasons, the per-protocol analysis also creates a comparison that is not consistent with a valid individual level causal effect, and is likely to produce biased estimates.[69] If researchers had the ability to account for all confounders (U), appropriate causal effects could be ascertained for either the as-treated or per-protocol effects, but it is impossible to know if one has accounted for all unknown confounders.

Table 2.3. Distribution of participants in a per-protocol analysis

r=1				r=0		
	A=1	~~A=0~~			~~A=1~~	A=0
Y=1	always-takers, compliers;	~~never-takers, defiers;~~		Y=1	~~always-takers, defiers;~~	compliers, Never-takers;
Y=0	always-takers, compliers;	~~never-takers, defiers;~~		Y=0	~~always-takers, defiers;~~	compliers, never-takers;

Limitations of the ITT, per-protocol and as-treated analyses relating to our WaSH trial: Even in the setting of a simple randomized trial, each of the three methods have clear limitations and these limitations also translate to our more complex WaSH studies. The ITT analysis measures the effect of randomization that is on average unconfounded, but does not measure the efficacy (a biological or practical type effect) of the treatment in the presence of non-adherence. The per-protocol and as-treated methodologies attempt to ascertain the biological or practical effect of a drug or treatment, but when adherence is imperfect, the comparisons are likely to suffer from confounding.

INSTRUMENTAL VARIABLE ANALYSES

When adherence is poor in randomized trials, the ITT estimator may be a distorted measure of the causal effect of the actual exposure (e.g. WaSH) itself, and may merit supplementing the ITT analysis with a valid causal effect measuring adherence on the outcome.[70,71] The randomized assignment variable can be used as an instrument to control for unmeasured confounding and obtain a valid causal effect. The instrumental variable analysis may help us to overcome some of the aforementioned inadequacies associated with the ITT, per-protocol, and as-treated analyses, and allows for an estimate of the treatment or intervention on the outcome while accounting for unknown or unmeasured confounding.

The IV analysis is dependent on the instrument meeting certain assumptions, which may change depending on the framework one is using. Generally the assumptions are: 1) *the instrument* has a causal effect on the actual treatment, 2) the instrument has a causal effect on the outcome only through the actual treatment (i.e. no direct effect, also known as the exclusion restriction), and 3) that the instrument does not share common causes with the outcome (i.e. no confounding of the instrument on the outcome).[61] In the field of observational epidemiology the instrumental variable analysis is not often used because it would be difficult to meet (or even assess) these assumptions in most observational studies, but in the context of a double-blind, placebo controlled randomized trial it is easy to imagine how the randomization variable could serve as an instrument and easily meet all three conditions.[61]

I will discuss in detail below three common instrumental variable frameworks: 1) the principal stratification framework, 2) The regression with an endogenous variable framework, and 3) the structural nested model framework.

Principal stratification framework

The Principal stratification framework is based upon potential outcomes and is based on the idea that under each of the treatments for which one could be randomized, there are a number of potential adherence outcomes, and these categories based on these potential outcomes are called principal strata (see Table 2.1).[68] Principal strata are assumed to be like any other baseline covariates in that they are not affected by treatment assignment. Stratification by these principal strata adjusts for imbalances in covariates (both known and unknown) that may have confounded the relationship between the adherence variable and the outcome. Comparisons that are made between two treatments within a principal stratum would be comparing individuals with similar potential outcomes, and therefore produce valid causal effects.[68]

CACE: One type of a causal effect that is calculated within the principal stratification framework is the complier average causal effect, or CACE, and is the treatment effect for "compliers" (i.e. those who would comply when assigned to either treatment).[68,72,73] Using the notation from Table 2.2, the CACE might be written as $E(Y(1)|\text{compliers}) – E(Y(0)|\text{compliers})$, or alternatively can be written $E(Y(1)|A(1)=1,A(0)=0) – E(Y(0)| A(1)=1,A(0)=0)$. The comparison being made is between "compliers" in the intervention arm, and "compliers" in the control arm.[64] It is the effect that would have been observed if we had done the ITT analysis among only the compliers.

This comparison appears problematic because these principal stratum are unobserved for each individual, as individuals are only assigned to one of the treatments.[64,68,74] Even though these principal strata are unobserved, the principal stratification framework is still useful for several reasons. Certain study designs, especially randomized studies, can facilitate acceptable assumptions that allow for the estimation of valid causal effects by using averages over groups of respondents.[64] We cover this in detail in the following section. It is also possible to infer latent principle strata based on their baseline covariates through modeling.[74] Finally, at the very least, a theoretical utilization of this framework allows us to better define and understand causal effects, and to whom they might apply in a given study.

Within the principal stratification framework, the CACE can be estimated directly without modeling by employing a number of assumptions which are often feasible in randomized, placebo-controlled studies. The assumptions are[64,72]

1) Ignorability of the instrument: Ignorability means that the potential outcomes are independent of the R, conditioning on confounding covariates. Successfully randomized experiments need not condition on pre-treatment variables, as they trivially satisfy ignorability.[74]

2) The stable unit treatment value assumption (SUTVA): SUTVA consists of two sub assumptions, the first relates to independence – that each participant's treatment assignment doesn't impact other participant's outcome – and the second is consistency – that each participant's potential outcome is linked to the observed outcome, meaning that under a given treatment assignment the outcome does not change even if the administration of the intervention varies.[75]

3) Exclusion restriction: The exclusion restriction means that there is no direct effect of randomization, R, on the outcome.

4) Nonzero denominator: This assumption is simply that the study population has at least some compliers.

5) Monotonicity: Monotonicity is the formal name of an assumption that simply means there are no "defiers," or participants who would always do the opposite of their assigned treatment.[76]

If these potential outcomes are well-defined for each person, we can conceptualize that the overall ITT effect from a randomized controlled trial is a weighted average of the effect of treatment for each of the four compliance potential outcome types:[74]

(equation 2.1) $ITT = p_c(ITT_c) + p_{nt}(ITT_{nt}) + p_{at}(ITT_{at}) + p_d(ITT_d)$, where p the represents the prevalence of each compliance type, and the subscripts for compliers, never-takers, always-takers, and defiers, respectively. The ITT effects on the right side of the equation are the ITT effects that would have been observed had the study been done on individuals only of a specific compliance type. With the monotonicity (i.e. no-defier) assumption – an assumption that is justifiable if the treatment isn't available to the control group – the last term becomes zero because p_d is zero. Randomization effectively will balance covariates – including the potential outcome compliance types – in the treatment arm and control arm implying that ITT_{at} and ITT_{nt} will always be equal to zero. We are left with:

(equation 2.2) $ITT = p_c(ITT_c) = p_c(CACE)$, and therefore the $CACE = ITT / p_c$.

Note above that the "ITT_c" is equivalent to the "CACE." Even though the prevalence of 'compliers' is unobserved, an unbiased estimate of the proportion of compliers can be obtained given the previous assumptions. We observe the proportion of participants in the treatment arm who used the assigned treatment (compliers and always-takers = p(A=1|R=1)), and we know the proprtion in the control arm who used the treatment (always-takers = p(A=1|R=0)), and the difference in these two proportions is an unbiased estimate of the proportion of compliers.[64] This is called the IV estimator (sometimes called the Wald estimator) of the CACE:[64,72,74]

(equation 2.3) $\widehat{CACE} = ITT / \hat{p}_c = E(Y(1) - Y(0)) / [p(A=1|R=1) - p(A=1|R=0)]$.

More complicated approaches, such as Bayesian and likelihood approaches, have also been used to calculate the CACE, and are required for more complex trial settings (e.g. multiple randomization arms). These methods use models to infer principle strata, based on their baseline covariates, and once the latent compliance types are identified, effect estimates are produced by conditioning on the latent principle stratum.[77] These approaches require many of the same assumptions as the instrumental variable estimator approach we previously discussed and also have many of the same limitations.

Limitations of the principal stratification framework relating to our WaSH trial: A primary limitation of the principal stratum framework which precludes us from using it for our WaSH trial is that this framework becomes increasingly difficult to use with multiple study arms, because the number of principal strata for which a single individual can belong increases exponentially for each additional study arm (from 4 principal strata for a 2 arm trial to 27 principal strata for a three arm trial)[78] and the underlying assumptions to identify the CACE and other estimands are not sufficient.[78,79] Another important problem of this framework is that these principal stratum are unobserved for each individual.[64] Another difficulty in using the principal stratification framework for our WaSH trial, is that control schools in our study may have access to different WaSH components, and when the control group has access to the treatment there is the real possibility of all four compliance types existing, making the monotonocity assumption (no-defiers) unlikely and further concealing who the observed 'compliers' really are.

Regression with an endogenous variable framework

We continue to use the notation from above as we present the endogenous regressor framework,[72,80] where R is the instrument, A is the adherence variable, Y is the outcome variable, and U represents all known and unknown confounders. For simplicity, we continue to omit subscripts indexing individuals. We might write the model of interest as,

(equation 2.4) $Y = \beta_0 + \beta_1 A + \varepsilon$,

where our interest is in the true effect of adherence to the intervention, A, and ε represents that portion of the outcome that is not explained by A. In this situation, the estimate of β_1 would be biased because the error (ε) is correlated with the outcome Y due to confounding. A is called an endogenous regressor because changes in A are associated not only with changes in Y but also with the error. In the epidemiologic literature we might say that A is confounded by U (unknown and/or known confounders) as U is a cause of both A and Y, and that if all U variables were included in the model, it might allow for an unbiased estimate of β_1. However, it is impossible to know if all unmeasured confounders were included.

The IV analysis can be easily applied through two-stage-least-squares analysis, (2SLS). In the first stage, A is decomposed into a part that is causal and a part that is not by using ordinary least squares (OLS) to regress the endogenous adherence variable A on the instrumental variable R. The predicted value of A (i.e. $\widehat{A}$) is produced for each observation. For example,

(equation 2.5) $\widehat{A} = \widehat{\beta}_0 + \widehat{\beta}_1 R + \tau_1$.

In the second stage, OLS is again used, but to regress Y on the estimate produced above, and produces an unbiased estimate of the effect of A on Y. The second stage is shown as,

(equation 2.6) $Y = \beta_0 + \beta_1 \widehat{A}_j + \varepsilon^*$.

By using the estimate $\widehat{A}$ as the regressor we are only using the portion of A that is correlated with the outcome through its effects on the first stage (and not correlated with ε in equation 2.4).

The assumptions for this framework are that the instrumental variable has a causal effect on treatment, the instrument can affect the outcome only through treatment (i.e. the exclusion restriction), and that the instrument does not share common causes with the outcome. However, for a causal and precise interpretation of the effect, the framework implicitly requires the assumption that there are no effect modifiers.[58]

Limitations of the endogenous regressor framework relating to our WaSH trial: The endogenous regressor framework is limited in that it is not clear, without making further assumptions, to what groups effect estimates might apply. This limitation is resolved by other frameworks that are based on potential outcomes.

Structural nested modeling framework

The structural nested model framework, which was first developed by Robins[81] and has since been generalized by others,[58,82,83] provides a robust framework allowing it to be used in complex trial designs like ours, which has multiple intervention arms, cluster-level randomization, complex sampling schemes, and a variety of outcome types. The structural nested model's effects are also easily interpreted based on potential outcomes, with the premise that potential outcomes are independent of the randomization variable.[77] The structural nested modeling framework shares a similarity with the principal stratification framework, in that it is based on potential outcomes, but is also different in that the structural nested modeling framework conditions on *observed adherence* – the effect of actually receiving treatment – whereas the principal stratification framework conditions on a latent principal stratum that is unobserved. The framework is used to produce the effect of observed adherence compared to a counterfactual reference level of adherence, both conditional on the observed adherence level. This effect is often known as the effect of the treatment among the treated. The SNM, relevant notation, and estimation algorithm as they relate to our study are shown below.[58] The SNM is[58]

(equation 2.7) $h(E^{W1}(Y_{ij}(a)|A_i=a, R_i)) - h(E^{W1}(Y_{ij}(0)|A_i=a, R_i)) = a_v\xi$,

where $Y_{ij}(a)$ represents the potential outcome for the j^th^ pupil in the i^th^ school at some observed adherence level a. A_i represents either a multinomial or continuous school-level adherence variable. For example, in the water available schools where we have three study arms we let $A_i=0$

when the i^{th} school adequately adhered to zero of the three WaSH components, let A_i=1 when the i^{th} school adequately adhered to one or two components, and we let A_i=2 when the i^{th} school adequately adhered to all three components. a_v represent a vector for the multinomial adherence variable. R_i represents a multinomial school-level randomization variable. For example, we let R_i represent a multinomial variable denoting randomization to one of the three study arms in the water available group. E^{W1} represents a weighted expectation, which accounts for individual-level confounders using the weight W_{ij1}. h represents a link function (e.g. $h(p) = p$; $h(p) = \log(p)$; $h(p) = \log(p/(1-p))$). ξ represents a causal effect – for example a RD, logRR, or logOR corresponding to the link function that was used to transform the left parts of the model.

Note that only $Y_{ij}(a)$ is actually observed, whereas the potential outcome $Y_i(0)$ is not observed but is a counterfactual that is modeled. Asymptotically unbiased estimators of ξ are able to be produced based on the premise that the potential outcomes are independent of the randomization variables, given the study assumptions are met.[77] The structural nested model framework is used to produce the effect of observed adherence compared to a counterfactual reference level of adherence, both conditional on the observed adherence level. This effect is also known as the effect of the treatment on the treated in less complex settings.

Structural Nested Model Assumptions: We show a DAG (Figure 2.2) to facilitate description of the SNM study assumptions, as they relate to our WaSH study. The validity of the estimate, including the ability of the structural nested model to account for unknown/unmeasured school-level confounding, is dependent upon meeting a number of study assumptions that are described below, and also described in greater detail elsewhere.[58]

1) We assume the exclusion restriction is met, which is that there are no direct effects of randomization assignment on the outcome (as shown in the bottom of the Figure 2.2 DAG). This assumption requires that randomization of a school to receive WaSH does not directly prevent (or cause) diarrheal illness/STH infection except through adherence to WaSH.

2) We make the consistency assumption, which is that the outcomes that we observe are the potential outcomes.[84] In our specific study, this means that when we observe school-level adherence at a given level (e.g. a=3), that this observed adherence is intrinsically linked to a well-defined potential outcome.

3) We assume that individual-level potential outcomes are independent of randomization, conditional upon individual-level confounders. We used weights, as discussed earlier, to remove the association between individual-level confounders and randomization. In the Figure 2.2 DAG, this weighting would remove the arrow from the individual-level confounders to randomization.

4) We assume our data follow a structural nested mean model: $h(E^{W1}(Y_{ij}(a)|A_i=a, R_i)) = h(E^{W1}(Y_{ij}(0)|A_i=a, R_i)) + a\xi$, where h represents a link function (e.g. $h(p) = p$; $h(p) = \log(p)$; $h(p) = \log(p/(1-p))$) and where ξ corresponds to a causal effect (e.g. RD, logRR, or logOR , respectively). Implied in the above model is a no interaction assumption, which is illustrated in the Figure 2.2 DAG. If there are effect modifiers in the population the assumption may still be valid if either there is no imbalance in these effect modifiers across adherence levels, or if the causal effect due to adherence is the same for each level of R_i in spite of an imbalance. Furthermore, if there are known effect modifiers, the assumption can be satisfied by stratifying.

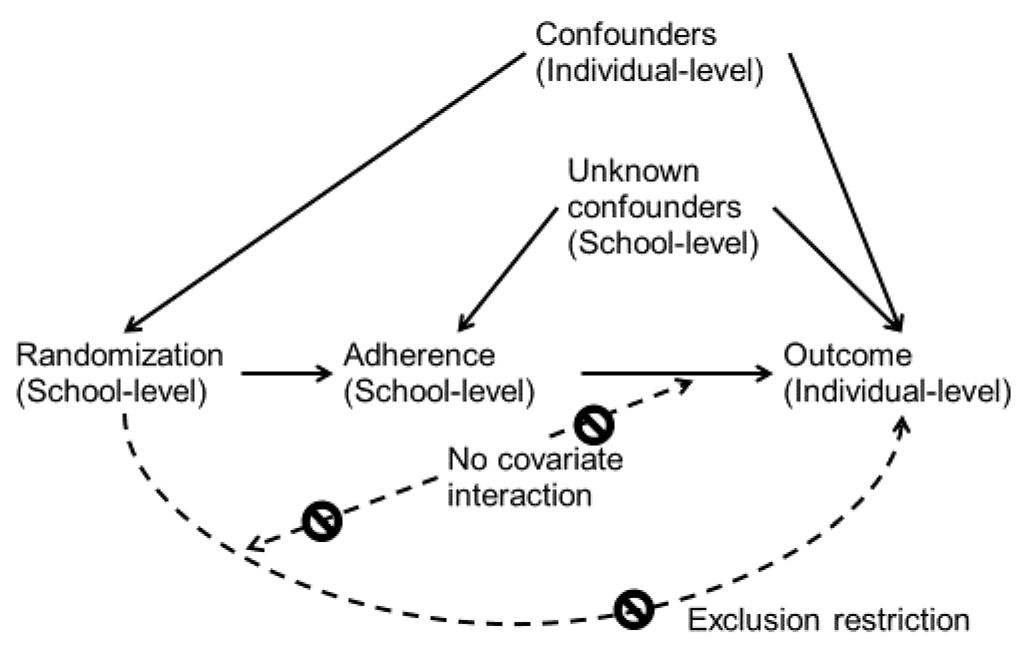


Figure 2.2. Directed acyclic graph describing study assumptions.[75]

Structural nested model estimation

We must first produce the overall weights (W_{ij}). W_{ij} is the product of confounding weight (W_{ij1}) and the sampling weights (W_{ij2}). W_{ij1} is the weight that is used to remove the association between individual-level confounders and randomization. W_{ij2} is the inverse of the probability of selection of each pupil into the study, and is necessary here because our study used a complex sample design. W_{ij1} and W_{ij} are produced as shown:

```
proc surveylogistic data=diarrheal_illness;
        class pupil_grade;
        model R = pupil_grade / link=glogit;
        output out=invweights predicted=predprobs;
        weight Wij2;
        strata stratum;
        cluster psu;
run;

data weights;
```

```
        set invweights;
        Wij1 = .;
        Wij1 =1/predprobs;
        Wij = Wij1* Wij2;
        if _LEVEL_ = R;
run;
```

To estimate the parameters of interest in the structural nested mean model, we used an iterative algorithm which applies Newton's method to solve the two estimating equations below.

(equation 2.8) $\sum_i \sum_j W_{ij} D_i^T [Y_{ij} - \mu (A_i, R_i; \eta)] = 0$, and

(equation 2.9) $\sum_i \sum_j W_{ij} R_{vi}^T [h^{-1} (h(\mu(A_i, R_i; \eta)) - A_{vi}\xi) - \alpha] = 0$,

where η represents the $E^{W1}(Y_{ij} | A_i, R_i)$, α represents the $E^{W1}(Y_{ij}(0))$, ξ represents the causal effect of adherence on the outcome given A_i and R_i, and D is a function of A_i and R_i, defined as $(A_{vi}, R_{vi}, A_i{*}R_i)^T$, R_{iv} is a vector of dummy variables representing randomization to one of three arms, and all other variables are as previously defined. A SAS program which was designed for a three armed trial with two strata was obtained from Brumback,[58] and was slightly modified to allow for variation in either the number of strata or the number of study arms. Generally, the steps to solving these estimating equations are as follows.

Step 1. We first solve the estimating equation (equation 2.8) using a fully parameterized model, to obtain an estimate of η for each participant. For instance, if our outcome followed a binomial distribution, we might use PROC GENMOD as shown:

```
proc genmod data=sim.data0;
        model Y= A1 A2 R1 R2 A1*R1 A1*R2 A2*R1 A2*R2/dist= bin link=logit;
        weight Wij;
        output out=sim.xbeta xbeta=linpred;
run;
```

Step 2. Letting $h^{-1}(.) = g(.)$, substitute $\hat{\eta}$ from the first equation (equation 2.8), for η in the second equation (equation 2.9). Using Newton's method, we linearize $g(D_i \hat{\eta} - A_{vi}\xi)$ about an initial (or current) estimate of ξ, ξ^t, where t indexes the iteration number. Equation 2 reduces to:

(equation 2.9a) $\sum_i \sum_j W_{ij} R_{vi}^T [g(D_i \hat{\eta} - A_{vi}\xi) - \alpha] = 0$

$g(D_i \hat{\eta} - A_i\xi)$ is approximated by $(Y_i^* - A_{vi}^*\xi^t)$, where Y_i^* and A_{vi}^* are derived using Taylor series approximation. For instance, for the logistic structural nested model, $g(x) \equiv \exp(x)/(1+\exp(x))$, and we let $Y_i^* \equiv g(D_i \hat{\eta} - A_{vi}\xi^t) + A_{vi}^*\xi^t$, and $A_{vi}^* \equiv A_{vi} g(D_i \hat{\eta} - A_{vi}\xi^t)(1 - g(D_i \hat{\eta} - A_{vi}\xi^t))$. Equation (equation 2.9) further reduces to:

(equation 2.9b) $\sum_i \sum_j W_{ij} R_{vi}^T [Y_i^* - A_{vi}^*\xi - \alpha] = 0$

For example, when using the logistic structural nested model Y_i^* and A_{vi}^* can be calculated within a data step in SAS using the linear predictor (output in step 1), the adherence variables (A_{vi}), the outcome variable (Yi), and an initial estimate of the causal effect (ξ^t) using the code:

```
lp=linpred-A1*squig1 - A2*squig2;
expitlp=exp(lp)/(1+exp(lp));
Ystar = expitlp + (A1*squig1 + A2*squig2)*expitlp*(1-(expitlp));
Astar1 = (A1*expitlp)*(1-(expitlp));
Astar2 = (A2*expitlp)*(1-(expitlp));
```

If we were instead using the log structural nested model, we would let $g(x) \equiv \exp(x)$, and we let $Y_i^* \equiv g(D_i \hat{\eta} - A_{vi}\xi^t) + A_{vi}^*\xi^t$, and $A_{vi}^* \equiv A_{vi} g(D_i \hat{\eta} - A_{vi}\xi^t)$. Y_i^* and A_{vi}^* would then be calculated using the following code within a SAS data step:

```
lp=linpred-A1*squig1 - A2*squig2;
```

```
        explp=exp(lp);
        Ystar = explp*(1+ A1*squig1 + A2*squig2);
        Astar1 = A1*explp;
        Astar2 = A2*explp;
```

Step 3. Solve equation 2.9b using instrumental variable software using Y_i* as the response variable, R_i as the instrument, and A_i* as the endogenous regressor, and obtain updated estimates of ξ^t. For example, using SAS's PROC SYSLIN:

```
proc syslin data=sim.iv 2sls;
        endogenous Astar1 Astar2;
        instruments R1 R2;
        model Ystar =Astar1 Astar2;
        weight Wij;
run;
```

Step 4. Update the initial estimate of ξ^t.

Step 5. Repeat steps 2 to 4 iteratively, until all parameters converge on a fixed value.

Step 6. Calculate the RR(a)= $(E^{W1}(Y_{ij}(a)|A_i=a)) / E^{W1}(Y_{ij}(0)|A_i=a))$. The numerator of the RR(a), $(E^{W1}(Y_{ij}(a)|A_i=a))$, is observed in the data and therefore easily calculated regressing Y_{ij} on A_i from the observed data while using the overall analysis weights (e.g. W_{ij}). Given the study assumptions are met and that the first estimating equation is specified correctly (e.g. by using a fully saturated model), then in the final iteration of $(Y_i^* – A_i^*\xi^t)$, that is $Y_i(0)$, represents true potential outcome had that participant's school been assigned to the control arm (had R_i been equal to 0). The denominator $(E^{W1}(Y_{ij}(0)|A_i=a))$ can therefore be estimated by regressing $E^{W1}(Y_i(0))$, from the final iteration in step 5, on our observed adherence variable, A_i.

Step 7. To estimate the variance, we use the jackknife estimator of the variance. This is a method where we systematically delete each primary sampling unit (school) and estimate the parameter of interest without that individual school, following steps 1-6 above repeatedly for all schools. The variance is then estimated by measuring the sum of the squared differences of each estimate from the initial parameter estimate, which is multiplied by a correction factor that accounts for the stratification. The jackknife estimator is:

$$\hat{\text{var}}(\hat{\theta}) = \sum_{h=1}^{H}((C_h - 1)/C_h) \sum_{c=1}^{C_h}(\hat{\theta}^{hc} - \hat{\theta})^2,$$

where $\hat{\theta}$ represents the overall parameter estimate and $\hat{\theta}^{hc}$ represents the paramater estimate deleting the c$^{\text{th}}$ school which is in the h$^{\text{th}}$ stratum (district).

Limitations of the structural nested model framework relating to our WaSH trial: As with all of the instrumental variable methods, the assumptions are not always testable, and off concern for us, is our inability to blind WaSH interventions (which may affect our ability to meet the exclusion restriction assumption) and our inability to detect important effect modifiers. In spite of these limitations, we believe this framework provides the best opportunity to answer our question, and obtain unconfounded estimates for the effect of school-level adherence on individual-level health outcomes.

CHAPTER 3: Using structural nested models to estimate the effect of school WaSH on pupil diarrhea and STH infection

Article type: Original Article

Running head:

School WaSH adherence on diarrheal illness and STH infection

ABSTRACT

Background: We conducted a cluster randomized water, sanitation, and hygiene (WaSH) trial in 185 schools in Nyanza province, Kenya (2007–2009). There was sub-optimal implementation (i.e. poor school-level adherence) at many schools, which may have led to intention-to-treat results that were different from what would have been observed under hypothetical conditions of good adherence. The primary goal of this study was to estimate causal effects of school-level adherence to WaSH on several different pupil health outcomes.

Methods: The schools were separated into water availability groups, based their access to an improved water source. Schools from each group were randomized into one of several WaSH intervention arms or a control arm, and this randomization variable was used as an instrumental variable. School-level adherence to WaSH was defined by the number of school WaSH components (i.e. water, latrines, soap) that had been adequately implemented. The outcomes of interest were pupil diarrhea, STH reinfection, and STH infection intensity (eggs per gram of feces). We used a weighted generalized structural nested mean model to calculate risk ratios, and used the jackknife estimator of the variance to calculate 95% confidence intervals.

Results: In the water scarce group, there was evidence of decreased diarrheal illness for pupils attending schools that adhered to two or to three of the WaSH components (RR for two = 0.26, 95% CI: 0.10, 0.68; RR for three = 0.086, 95% CI: 0.0026, 2.8), compared to what the potential risk would have been in these same schools had they not adhered to any WaSH components. In the water available group, no decreases in diarrheal illness were observed with better WaSH adherence. For the helminth outcomes, with increasing WaSH adherence we observed imprecisely measured decreases in helminth reinfection and helminth intensity for several worms, but primarily among girls and not boys.

Conclusions: Our analysis yielded point estimates that suggested protective effects with increased adherence, although many effects were imprecisely measured.

INTRODUCTION

There are thought to be a number of health and non-health benefits associated with water, sanitation, and hygiene (WaSH) in schools, including increased water intake, increased pupil attendance, and possibly decreased diarrheal and gastrointestinal diseases.[30] In spite of biological plausibility and a long-standing history of epidemiologic studies supporting the preventive effects of WaSH on health (e.g. John Snow),[35,36,56,57] the results from some rigorous school-based WaSH trials have been mixed.[28,30,41] For example, we conducted a cluster randomized WaSH trial in 185 schools in Nyanza province, Kenya (2007–2009), and the intention-to-treat (ITT) results showed decreased incidence of diarrheal illness, but only among the most water scarce schools that also received a water provision;[41] and reduced STH infection rates, but primarily among girls and primarily for the *Ascaris lumbricoides* worm but not other helminthes.[28] However, there was sub-optimal implementation (i.e. poor school-level adherence) at many schools, which may have contributed to these trial results.

As in our trial, most trials report the intention-to-treat (ITT) effect – the average causal effect of randomization on the outcome – regardless of adherence to the intervention.[61] However, if implementation of the intervention at the school-level was poor, the ITT results may be very different from what would have been observed under hypothetical conditions of good school-level adherence. In our study, because implementation of the intervention was suboptimal, the

ITT estimator may be a distorted measure of the causal effect of WaSH itself, and may merit supplementing the ITT analysis with a valid causal effect measuring adherence on the outcome.[70,71] The public health significance of understanding the effect of adherence on the outcome, is that if one could pinpoint that negative or mixed trial results as being due to suboptimal adherence, then it might lead researchers to focus simply on improving adherence rather than on finding alternative interventions.

There are several methodologies we could use to estimate the effect of WaSH adherence, as opposed to the effect of randomization, on our outcomes. Commonly used approaches such as the 'as-treated' and 'per-protocol' analyses are likely to suffer from unmeasured confounding.[64] Another alternative for measuring the effect of adherence is to use an instrumental variable (IV) analysis. The IV analysis produces an effect for adherers, and uses the randomized assignment variable as an instrument to control for confounding, even for unknown or unmeasured confounders. There are a number of instrumental variable frameworks, although some present difficulties for our trial design.[58] The endogenous regressor framework[85] presents difficulties of interpretation.[58] The principal stratification framework is easily interpretable as it is based on potential outcomes, but in trials with multiple intervention arms it becomes increasingly complex to identify principal strata.[58,86] The structural nested model framework, which was first developed by Robins[81] and has since been generalized by others,[58,82,83] provides a robust framework allowing it to be used in complex trial designs like ours, which has multiple intervention arms, cluster-level randomization, complex sampling schemes, and a variety of outcome types. The structural nested model's effects are also easily interpreted based on potential outcomes, with the premise that potential outcomes are independent of the randomization variable.[77] Due to its robustness and interpretability, we used the structural nested model for our study.

We performed an instrumental variable analysis to adjust for unmeasured confounders, and estimate the causal effects of school-level adherence to WaSH on several pupil-level health outcomes, including pupil diarrhea, pupil STH reinfection, and STH infection intensity measured in eggs per gram of feces. We hypothesized that the preventive effects of WaSH would be more pronounced among schools with better adherence to the intervention. This study will help us gain an understanding of the important public health implications of poor adherence to school WaSH.

METHODS

Our data are from a cluster-randomized trial that was designed to assess the impact of school-based WaSH interventions on health and educational outcomes.[28,40,41,59] The study took place between 2007 and 2009 in 185 rural primary schools in what were formerly four districts of Nyanza Province, Kenya – Rachuonyo, Suba, Nyando, and Kisumu. Student absence was the primary outcome of the original trial, and both the ITT results and the IV results have been reported elsewhere for this outcome.[40,58] The ITT results along demographic information can be found elsewhere for each of the pupil health outcomes – diarrheal illness among pupils,[41] pupil helminth reinfection,[28] and intensity of pupil STH infection.[28] Here we supplement these previously reported ITT analyses with IV analyses.

Data collection: Data were collected by trained enumerators from the Great Lakes University of Kisumu. School WaSH characteristics, including WaSH adherence, were collected both by direct observation and by structured interviews with head teachers. Pupils were interviewed about their WaSH knowledge, attitudes and practices, and about self-reported health and education outcomes. Interviews with teachers were conducted in English while interviews with pupils were conducted in the Dholuo language. There was a baseline data collection that took place between February and March of 2007. Following implementation of the interventions, data for the first follow-up were collected between September and October of 2008 for the diarrheal illness study, and in April of 2008 for the Helminth study. Enumerators visited the schools unannounced on a randomly selected day of the week within the study period.

School selection: All selection criteria were determined in collaboration with implementing partners and the Kenyan Government. An initial survey was sent out to all primary schools in the geographic area (n=1,084) to asses WaSH conditions; 83% of the surveys were returned. Schools in certain administrative divisions and schools with pupil to latrine ratios that already meet the Government of Kenya standard (25:1 for girls and 30:1 for boys) were ineligible for the study, leaving 289 eligible schools.[54] Schools were divided into two groups based on whether or not they had an improved water source within one kilometer during the dry season. 135 ‘water available’ schools and 50 ‘water scarce’ schools were randomly allocated into study arms using a random number generator, with the allocation stratified by geographic district (Rachuonyo, Suba, and Nyando/Kisumu). The STH study was nested within the larger trial, and took place among only a randomly selected subset of 39 schools from Rachuonyo and Nyando/Kisumu that were already taking part in the water available group of the larger study (Table 3.1). Randomization and implementation of the interventions took place immediately after a baseline assessment and before the first follow-up visit.

Pupil selection: For both the diarrheal illness and helminth outcomes, a systematic random sampling scheme was used to select pupils from the school registers, sampling by sex and grade. Different pupils were surveyed at baseline and follow-up due to high turnover of pupils. A summary of the study design for each of the pupil health outcomes is shown in Table 3.1.

For the diarrheal illness outcome, at each of the 185 schools, 25 pupils grades 4–8 were randomly selected and surveyed in regards to their recent diarrheal history, their WaSH history, and to ascertain important demographic and covariate information. For the STH outcomes, at each of the 39 primary schools, 25 pupils, grades 4–8 were randomly selected and surveyed (independently from the selection that took place in the diarrhea study), and provided stool specimens which were analyzed for common helminth parasites.

Interventions/randomization: The schools were divided into two separate groups based on water availability (whether or not a school had a water source within one kilometer of the school), and schools in these two groups were then randomized separately. In the water available group,135 schools were randomly allocated into *three* study arms of equal size: 1) the water available control arm; 2) the hygiene promotion and water treatment arm; and 3) the hygiene promotion and water treatment, plus sanitation improvement arm. In the water scarce group, 50 schools were randomly allocated into two study arms of equal size: 1) the water scarce control arm; and 2) the hygiene promotion and water treatment, plus sanitation, plus water supply improvement arm.

All schools that received hygiene promotion received a three-day training directed to teachers on the importance of handwashing with soap, a provision of water containers with taps, and instruction on behavior change methods. Schools were also encouraged to purchase soap (though it was not provided). Schools that received water treatment improvements were given a one-year supply of WaterGuard – a 1.2% chlorine-based point-of-use water disinfectant promoted by Population Services International – and were also given narrow-mouthed containers with taps for drinking water storage. These interventions were based on systems pioneered by the CDC.[87] Schools that received sanitation improvements were given enough latrines so that they attained the government standard of pupil to latrine ratio (up to a maximum of seven latrines). All the water scarce schools that received water supply improvements were given either a drilled borehole with piped access to the school (n = 12) or a 60m^3 rainwater harvesting system (n = 13). All control schools received the interventions at the end of the study.

All of the interventions were implemented by CARE and Water.org. It was not possible to mask the schools, the data collectors, or the pupils to the intervention arm to which the school had been randomized. However, some of the intervention components, such as teacher training or chlorination of water, may not have been apparent to the pupils.

Outcomes: For the diarrheal illness outcome, our outcome of interest was pupil-reported diarrhea (binary), defined as three or more loose or watery stools over any 24 hour period in the previous week.[88]

For the STH outcomes, all sampled pupils provided a stool specimen that was analyzed for *Ascaris lumbricoides*, for *Trichuris trichiura*, and for any species of hookworm using the

Kato-Katz method.[89,90] The outcomes of interest were STH reinfection (binary), and also intensity of infection which was measured as eggs per gram of feces (a count). We assessed helminth reinfection and intensity of STH infection by individual worm species, and also by any STH. All children attending any of the 185 schools received yearly deworming (400mg of Albendazole).

Adherence: We measured adherence to three separate school-level WaSH components on the day of the study visit: 1) soap availability, 2) safe water availability, and 3) latrine acceptability.[58] Soap availability was defined as the school having handwashing soap near the latrines for pupil use. Safe water availability was defined as the school either having available water from an improved water source, or having available water with detectable chlorine from any source. Latrine acceptability was based on the school having an adequate number of latrines that were maintained and structurally intact.

In a traditional 'as-treated' analysis, one could theoretically produce an estimate for all eight possible combinations of the above WaSH components and compare each combination to schools that adhered to zero components, ignoring randomization. Beyond the problem of unmeasured confounding with this analysis, the as-treated analysis was problematic because not all of these potential WaSH combinations existed. There are also constraints in how we define our adherence variable when using an instrumental variable analysis, specifically, that we should only have as many effect estimates as instruments.[58] However, within this constraint we do have flexibility to define adherence either continuously or categorically. Due to these constraints, in each of our analyses we define adherence by the number of WaSH components to which each school adhered. We created a composite, 4-level variable that is the sum of whether or not there was soap available (yes=1, no=0), safe-water available (yes=1, no=0), and acceptable latrines at the school (acceptable=1, not acceptable=0). This four-level adherence variable can be used as either a continuous variable or can be categorized.

Safety, and confidentiality: IRB approval was obtained from The Emory University Institutional Review Board (Atlanta, GA, USA). Permission to conduct the trial was also granted by the Government of Kenya Ministries of Health, Water and Irrigation, and Education. Oral assent was obtained from all participants, and approval was also obtained by head teachers of each school in *loco parentis*. All results, at the individual, and school level are anonymous, so as to keep the confidentially of participants.

Analysis

Weights: Because this trial was cluster randomized, individual-level balance of covariates is not guaranteed by randomization, so we also produced weights which we call W_{ij1} that were used to remove the association between individual-level confounders and randomization.[58] For our diarrhea study, we used weights to control for pupils' grade (as a proxy for age). For our helminth study, we used weights to control for pupils' age, pupils' shoe-wearing behavior (important for hookworm), and for geophagy (a soil-eating practice). Sampling weights were also produced to account for the unequal probability of selection of individuals into the study. These weights, which we call W_{ij2}, are simply the inverse of the probability of selection of each pupil into the study. We will call the product of these two separate weights W_{ij}, which is an overall weight that accounts simultaneously for the complex sampling of pupils and for confounding by individual covariates.[58] It was this overall weight, W_{ij}, which was used for parameter estimation of the structural nested mean model. Further details on the calculations of each of these weights are shown in Appendix 3.

Structural nested models: We used a weighted generalized structural nested mean model for parameter estimation.[58] The structural nested modeling framework is based on potential outcomes, and conditions on observed adherence – the effect of actually receiving treatment. The structural nested model is:

$$h(E^{W1}(Y_{ij}(a)|A_i=a, R_i)) - h(E^{W1}(Y_{ij}(0)|A_i=a, R_i)) = a_v\xi,$$

where $Y_{ij}(a)$ represents the potential outcome for the jth pupil in the ith school at some observed adherence level a, A_i represents either a multinomial or continuous school-level adherence variable, R_i represents a multinomial school-level randomization variable, E^{W1} represents a weighted expectation (e.g. using the weight W_{ij1} from above), *h* represents a link function (e.g. *h*(p) = p; *h*(p) = log(p); *h*(p) = log(p/(1-p))), and ξ represents a causal effect – for example a RD, logRR, or logOR corresponding to the link function that was used to transform the left parts of the model. The subscript v (e.g. a_v) denotes a vector function, perhaps when adherence is multinomial. Note that only $Y_{ij}(a)$ is actually observed, whereas the potential outcome $Y_i(0)$ is not observed but is a counterfactual that is modeled. Asymptotically unbiased estimators of ξ are able to be produced based on the premise that the potential outcomes are independent of the randomization variables, given the study assumptions are met.[77] The structural nested model framework is used to produce the effect of observed adherence compared to a counterfactual reference level of adherence, both conditional on the observed adherence level. This effect is also known as the effect of the treatment on the treated in less complex settings.

Details on both parameter estimation and variance estimation are summarized in Appendix 3 and elsewhere.[58] We were not able to find any statistical software to automate the estimation process. We modified a SAS program written by Brumback et al.,[58] greatly simplifying parameter estimation for this cluster-randomized design.

Structural Nested Model Assumptions: We show a DAG (Figure 3.1) to facilitate description of these study assumptions. The validity of the estimate, including the ability of the structural nested model to account for unknown/unmeasured school-level confounding, is dependent upon meeting a number of study assumptions that are described below, and also described in greater detail elsewhere.[58]

1) We assume the exclusion restriction is met, which is that there are no direct effects of randomization assignment on the outcome (as shown in the bottom of the Figure 3.1 DAG). This

assumption requires that randomization of a school to receive WaSH does not directly prevent (or cause) diarrheal illness/STH infection except through adherence to WaSH.

2) We make the consistency assumption, which is that the outcomes that we observe are the potential outcomes.[84] In our specific study, this means that when we observe school-level adherence at a given level (e.g. a=3), that this observed adherence is intrinsically linked to a well-defined potential outcome.

3) We assume that individual-level potential outcomes are independent of randomization, conditional upon individual-level confounders. We used weights, as discussed earlier, to remove the association between individual-level confounders and randomization. In the Figure 3.1 DAG, this weighting would remove the arrow from the individual-level confounders to randomization.

4) We assume our data follow a structural nested mean model: $h(E^{W1}(Y_{ij}(a)|A_i=a, R_i)) = h(E^{W1}(Y_{ij}(0)|A_i=a, R_i)) + a\xi$, where h represents a link function (e.g. $h(p) = p$; $h(p) = \log(p)$; $h(p) = \log(p/(1-p))$) and where ξ corresponds to a causal effect (e.g. RD, logRR, or logOR , respectively). Implied in the above model is a no interaction assumption, which is illustrated in the Figure 3.1 DAG. If there are effect modifiers in the population the assumption may still be valid if either there is no imbalance in these effect modifiers across adherence levels, or if the causal effect due to adherence is the same for each level of R_i in spite of an imbalance. Furthermore, if there are known effect modifiers, the assumption can be satisfied by stratifying. For example, in the previously reported helminth ITT trial, the preventive effect of WaSH on helminth reinfection was observed primarily among girls.[28] Due to this apparent effect modification and to better meet assumption 4 above, we chose to stratify each of the helminth analyses by sex.

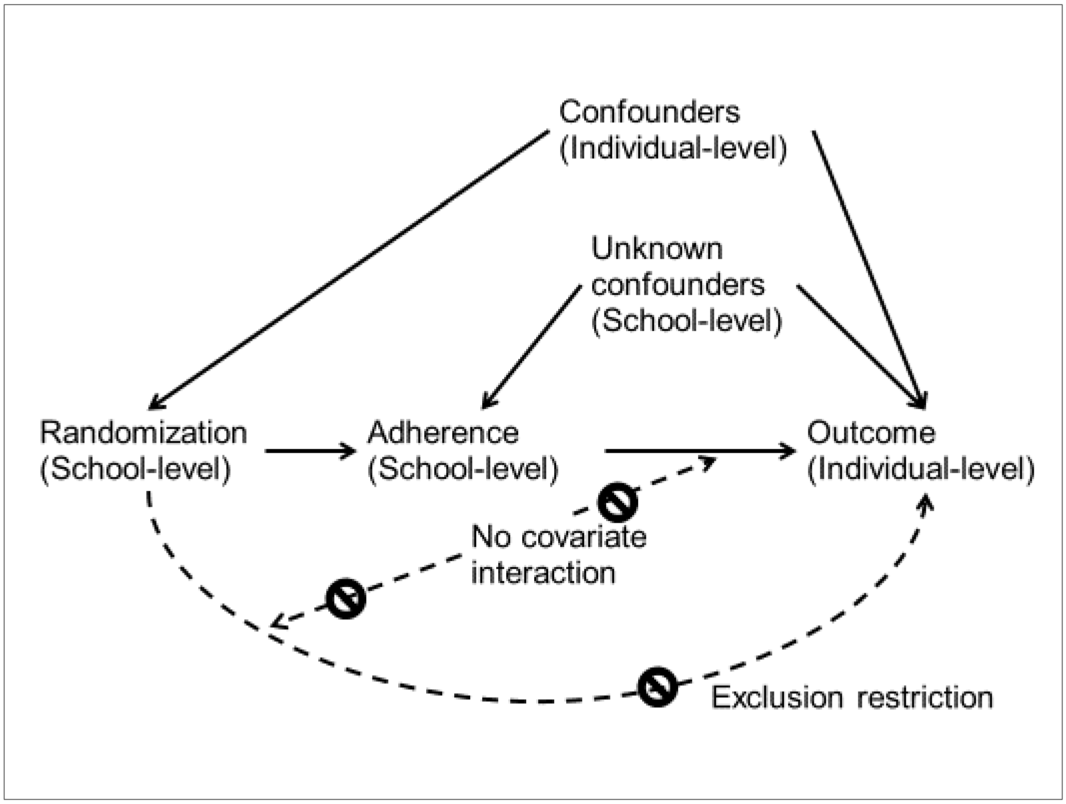


Figure 3.1. Directed acyclic graph describing study assumptions.[75]

IV analyses: The primary goal of our study was to estimate well-defined causal effects of school-level WaSH adherence on individual-level outcomes. SAS programs for the log, logistic, and linear structural nested model were obtained from Brumback et al.[58] These programs were designed for a three armed trial with two strata, and were modified to allow for variations in the number of strata and study arms in our study.

The effects of interest for the diarrheal illness outcome and helminth reinfection outcomes study were the risk ratios comparing the probability of disease among adherers to what the probability of disease would have been had this same group not adhered: RR(a)= $(E^{W1}(Y_{ij}(a)|A_i=a)) / E^{W1}(Y_{ij}(0)|A_i=a))$. The numerator, $E^{W1}(Y_{ij}(a)|A_i=a)$, is the observed probability of disease among adhering schools, and is easily calculated without any modeling. The denominator, the $E^{W1}(Y_{ij}(0)|A_i=a)$, can be estimated by regressing $E^{W1}(Y_i(0))$ on observed A_i, where $E^{W1}(Y_i(0))$ is modeled using the instrument and represents the true potential outcome had a participant's school counterfactually not adhered to the intervention.

The risk ratio can be produced with either the log, logistic, or linear structural nested model. We chose to use the logistic structural nested model for the diarrheal illness outcome and helminth reinfection outcome. We report the observed numerator, the modeled denominator, and the risk ratios.

The effect of interest for the helminth intensity of infection outcome (a count), was the prevalence ratio comparing the egg count among pupils in adhering schools to what the egg count would have been had these same schools not adhered. For this outcome we used the log-linear structural nested model. We report the observed numerator, the modeled denominator, and the risk ratios.

For all IV analyses, we use the jackknife estimator of the variance to estimate 95% confidence intervals.[91] This variance estimation procedure was also built into the program that was provided to us.[58]

ITT analyses: The RRs that were produced from the IV analyses for each outcome were then compared to RRs using the ITT analysis. Estimates for the diarrheal illness,[41] and STH infection[28] outcomes, have been previously reported. However, ORs (not RRs) were reported, and more complex longitudinal and/or adjusted analyses were sometimes used. We recalculate the unadjusted ITT RR for each outcome at follow-up one. We used the following model to estimate the RR for the three-armed trial:

$$g(\mu_{ij}) = \alpha_0 + \beta_1 \text{Intervention1}_i + \beta_2 \text{Intervention2}_i$$

μ_{ij} is the expectation of the response variable – either binary diarrheal illness, binary helminth reinfection, or a count of helminth eggs per gram – where we let $g(\mu_{ij})$ equal $\log(\mu_{ij})$

for both the binary and count outcomes. The school-level WaSH interventions are represented by dummy variables corresponding to each of the two intervention arms, with the control arm as the referent. In the two armed trial, only β_1 would be included in the model. The variance estimates were produced using survey software and reflect disproportionate sampling of pupils within schools, the clustering of pupils within schools, and the stratified randomization by geographical districts.

RESULTS

WaSH adherence: We assessed the strength of our instrument (i.e. in the Figure 3.1 DAG that there is an arrow from school-level randomization to school-level adherence). In each of the three study groups we observed a significant effect of randomization on adherence (p<0.01; Table 3.2). In the water scarce group, 16 of the 25 *control* schools did not have access to any WaSH components, and the other nine control schools had access to only a single WaSH component (through a different mechanism), whereas in the water scarce *intervention* arm the majority of the schools adhered to two or three WaSH components. We also observed a similar increase in adherence in the water available intervention arms. Although we observed an increase in the level of adherence in all intervention arms across the study, we also observed that only 29 schools across the entire study were observed to have fully adhered to all three WaSH components at this follow-up visit.

Diarrheal illness: When using the continuous adherence variable, we observed that pupils attending schools that adhered to two of the WaSH components, had decreased diarrheal illness compared to their potential risk had these same schools not adhered to any WaSH components (RR = 0.26, 95% CI: 0.10, 0.68; Table 3.3). The point estimate for a three unit change in adherence also suggested a strong protective effect, although it was imprecisely measured (RR = 0.086, 95% CI: 0.0026, 2.8). Using the categorical adherence variable, we observed that pupils attending schools that adhered to two or more WaSH components had a decreased risk of diarrheal illness compared to their potential risk had these same schools not adhered to WaSH (RR = 0.27, 95% CI: 0.10, 0.74; Table 3.3). For comparison, the ITT effect, which compares all water scarce intervention schools to all water scarce control schools without regard to WaSH adherence was RR=0.38 (95% CI: 0.20, 0.73).

In the water available schools, we had two instruments due to having three randomization arms, so we were able to produce two adherence effects using a single model. We observed that the two adherence risk ratios were in opposite directions, with the RR for pupils in schools that adhered to all three WaSH components being in the preventive direction (RR=0.75, 95% CI: 0.052, 11), and the RR for pupils in schools adhering to either one or two WaSH components being in the harmful direction (RR=1.5, 95% CI: 0.11, 22) although both effects had wide confidence intervals (Table 3.3).

Helminth reinfection: All of the ITT and IV effects for WaSH and helminth reinfection had confidence intervals that included one (Tables 3.4a). We did observe that all of the IV point estimates among girls were in the preventive direction; the point estimates for *A. lumbricoides* (RR=0.23, 95% CI: 0.045, 1.2) and hookworm (RR=0.26, 95% CI: 0.055, 1.2) were particularly strong, although imprecise. For boys, the hookworm IV point estimate among fully adherent schools was also strong (RR=0.25, 95% CI: 0.41, 1.5)) and nearly identical to the IV point estimate that we observed for girls. For boys, the *A. lumbricoides* and *T. trichiura* IV point estimates among fully adherent schools were both similar to the ITT result, which was slightly above the null.

Helminth intensity: All of the ITT and IV effects for WaSH and helminth intensity had confidence intervals that included one (Tables 3.4b). The direction and strength of the prevalence ratios for most of the helminth intensity outcomes matched the pattern that we observed for the helminth reinfection outcomes, although the confidence intervals were always much wider for the helminth intensity outcomes.

DISCUSSION

We found that school WASH adherence was sub-optimal at many schools. Our instrumental variable results from the water scarce schools suggested a very strong preventive effect of adherence to WaSH on reducing pupils' diarrheal illness, whereas results were less clear in water available schools and in the helminth subset of schools. For several of our outcomes, we observed that IV point estimates were often much further from the null than ITT point estimates.

Sub-optimal WaSH adherence may be one reason why this and other previous school WaSH trial results have been underwhelming, at least considering the strong biological plausibility and long-standing history of WaSH in epidemiologic studies in non-school settings.[35,36,56,57] The strong preventive point estimates that we often observed lend to the theory that adherence may be an important factor in previous trial results. However, our estimates were often imprecisely measured and sometimes we even observed point estimates in the harmful direction, and so there are probably also a number of other factors besides adherence that are important in reducing these infectious disease outcomes.

It is not clear why our results were different in water scarce versus water available schools. One possibility is that the WaSH interventions in the water scarce schools were more comprehensive, notably including a *community-level* water source. It may be that access to water is the final sufficient component to allow individuals to practice WaSH both at school, and possibly also at home and elsewhere in the community.

Our study was a cluster-randomized design, with multiple intervention arms, and with a complex sampling scheme, and we were able to produce causal effects for both count and binary outcomes using several different adherence structures. The robustness of this methodology may be useful as a supplemental analysis in other types of complex trials, when adherence is poor.

In both the diarrheal illness and the STH infection outcomes, we assumed balance in the baseline prevalence of the outcomes in each arm, due to randomization. For the diarrheal illness outcome we did not have the ability to asses this assumption, as the baseline data were not available.[41] For the helminth outcomes, some minor imbalances were observed for some worms at baseline *pre-deworming*,[28] however the mass deworming should have equalized these imbalances between randomization arms. We used the terminology ‘reinfection’ throughout, as opposed to ‘prevalence.’ However, our measure is may not truly be cumulative incidence as there is the possibility that pupils were absent[40] the day the drugs were administered or that the deworming drugs eliminated some worms incompletely.[92]

The methodology used in our study is not without limitations. We do believe that the study assumptions could be plausibly met, however, these assumptions are also not testable. In particular, our inability to blind WaSH interventions and our need to reduce the dimensionality of adherence could theoretically affect our ability to meet the exclusion restriction assumption. In the helminth study, we stratified by sex to better attempt to meet the no interaction assumption (i.e. assumption 4), as differential effects had been observed by sex.[28] Stratifying, while possibly satisfying this assumption, exaggerates the problem of wide confidence intervals that is already common to this and most IV analyses.[93,94] While the assumptions of our analysis were not testable, it is sometimes possible to falsify assumptions,[94] however, in our analyses we did not find any evidence that would guarantee that one or more of the assumptions were not met.

While we were able to produce effects for either categorical or continuous adherence structures, the method had difficulty producing solutions or producing precise confidence intervals when we tried different adherence categorizations. We observed that the iterative algorithm was more likely to converge when using a continuous adherence structure compared with categorical adherence structures, especially when categories became small or the outcomes were rare. However, while convergence may improve with continuous adherence, this may be problematic if the relationship between adherence and the outcome is not linear on the logit or log scale.

CONCLUSIONS

We found that school WASH adherence was sub-optimal at many schools. Our instrumental variable results from the water scarce schools suggests a very strong preventive effect of adherence to WaSH on reducing pupils' diarrheal illness. We also observed that the instrumental variable point estimates for several of the outcomes were notably further from the null than ITT point estimates, although the IV results were often imprecise. Our results show the utility of supplementing ITT results with an instrumental variable analysis, and give an example of applying IV analyses in a complex setting.

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Table 3.1. Number of schools and pupils at follow-up one (2008) of cluster-randomized WaSH trial in Nyanza Province Kenya.

	Water available schools[*]			**Water scarce schools**[*]	
	Control	HP&WT[‡]	HP&WT + San[‡]	Control	HP&WT + Wat + San[‡]
Pupil diarrhea					
N schools	45[§]	45[§]	45	25	25
n pupils sampled at follow-up	1127	1156	1134	606	622
Pupil STH infection					
N schools	19	N/A	20[c]	N/A	N/A
n pupils sampled at follow-up	465	N/A	490	N/A	N/A

[*] Schools without a water source within 1 kilometer during the dry season were classified as 'water scarce' and all other schools were classified as 'water available.' [‡] HP&WT = hygiene promotion and water treatment; san = sanitation; water = water supply. [§] We didn't have complete adherence data on one of these schools, so it was not included in the final IV analyses.

Table 3.2. Adherence by water availability group and outcome type at follow-up one.

	Water available schools[*]				Water scarce schools[*]		
	Control	HP&WT[‡]	HP&WT + San[‡]	***p***[§]	Control	HP&WT + Wat + San[‡]	***p***[§]
Pupil diarrhea							
N schools with complete data[‖]	44	44	45		25	25	
Adherence level 0[¶]	23 (52%)	3 (7%)	4 (9%)	<0.01	16 (64%)	1 (4%)	<0.01
Adherence level 1	21 (48%)	17 (39%)	8 (18%)		9 (36%)	10 (40%)	
Adherence level 2	0 (0%)	15 (34%)	17 (38%)		0 (0%)	10 (40%)	
Adherence level 3	0 (0%)	9 (20%)	16 (36%)		0 (0%)	4 (16%)	
None	23 (52%)	3 (7%)	4 (%)		16	1 (4%)	
Latrines	20 (45%)	5 (11%)	4 (%)		9	5 (20%)	
Safe water	1 (2%)	12 (27%)	4 (%)		0 (0%)	5 (20%)	
Soap	0 (0%)	0 (0%)	0 (0%)		0 (0%)	9 (36%)	
Latrines + Safe water	0 (0%)	9 (20%)	12 (%)		0 (0%)	0 (0%)	
Latrines + Soap	0 (0%)	1 (2%)	0 (%)		0 (0%)	0 (0%)	
Safe water + Soap	0 (0%)	5 (11%)	5 (%)		0 (0%)	1 (3%)	
Latrines + Safe water + Soap	0 (0%)	9 (20%)	16 (%)		0 (0%)	4 (16%)	
Pupil STH infection							
N schools with complete data[‖]	19	-	19				
Adherence level 0[¶]	8 (42%)	-	3 (16%)	<0.01	-	-	-
Adherence level 1	11 (58%)	-	5 (26%)		-	-	
Adherence level 2	0 (0%)	-	6 (32%)		-	-	
Adherence level 3	0 (0%)	-	5 (26%)		-	-	
None	8 (42%)	-	3 (16%)		-	-	
Latrines	11 (58%)	-	2 (11%)		-	-	
Safe water	0 (0%)	-	3 (16%)		-	-	
Soap	0 (0%)	-	0 (0%)		-	-	
Latrines + Safe water	0 (0%)	-	3 (16%)		-	-	
Latrines + Soap	0 (0%)	-	0 (0%)		-	-	
Safe water + Soap	0 (0%)	-	3 (16%)		-	-	
Latrines + Safe water + Soap	0 (0%)	-	5 (26%)		-	-	

[*] Schools without a water source within 1 kilometer during the dry season were classified as 'water scarce' and all other schools were classified as 'water available.' [‡] HP&WT = hygiene promotion and water treatment; san = sanitation; water = water supply. [§] Comparing control and intervention schools using the Mann-Whitney U-test. [‖] Schools missing adherence were not included in the final instrumental variable analyses. [¶] Adherence was defined by the number of WaSH components (i.e. soap availability, safe water availability, and latrine acceptability) to which each school adhered.

Table 3.3. ITT and IV risk ratios for school WaSH adherence and pupil diarrheal illness.

Outcome group	**Model**	**Numerator risk**[*, ‡]	**Denominator risk**[*, ‡]	**RR (95% CI)**
Pupil diarrhea				
Water scarce[§]	ITT model:[*]			
	HP&WT +Wat + San[‖] vs. control arm	0.034	0.089	0.38 (0.20-0.73)
	Continuous adherence IV model: [‡, ¶]			
	Adherence to 2 components vs. 0 components	0.038	0.14	0.26 (0.10-0.68)
	Adherence to 3 components vs. 0 components	0.015	0.18	0.086 (0.0026-2.8)
	Categorical adherence IV model: [‡, ¶]			
	Adherence to ≥ 2 components vs. 0 or 1 components	0.038	0.14	0.27 (0.10-0.74)
Water available[§]	ITT model:[*]			
	HP&WT[‖] vs. control arm	0.064	0.061	1.1 (0.66-1.7)
	HP&WT + San[‖] vs. control arm	0.058	0.061	0.95 (0.60-1.5)
	Categorical adherence IV model 2: [‡, ¶]			
	Adherence to 1 or 2 components vs. 0 components	0.066	0.043	1.5 (0.11-22)
	Adherence to 3 components vs. 0 components	0.050	0.066	0.75 (0.052-11)

[*] The ITT estimate compares all intervention schools to all control schools. The numerator is the pupil's risk in intervention schools and the denominator is the pupil's risk in control schools. [‡] The IV estimate compares pupil's risk in schools that adhered at a given level, compared to their potential risk had these same schools not adhered to WaSH. The numerator is the observed pupil risk in a given subset of schools adhering at a given level, and the denominator is the pupil's potential risk *in those same schools* had the schools adhered at the referent level. Adherence was defined by the number of WaSH components to which each school adhered. [§] Schools without a water source within 1 kilometer during the dry season were classified as 'water scarce' and all other schools were classified as 'water available.' [‖] HP&WT = hygiene promotion and water treatment; san = sanitation; water = water supply. [¶] The two-arm trial has a single instrument, so we are constrained to produce a single estimate per model. The three arm trial has 2 instruments so we can calculate two estimates using a single model.

Table 3.4a. ITT and IV risk ratios for school WaSH adherence and pupil helminth reinfection.

		Girls[*]			Boys[*]		
Outcome	**Model**	**Numerator risk[‡, §]**	**Denominator risk[‡, §]**	**RR (95% CI)**	**Numerator risk[‡, §]**	**Denominator risk[‡, §]**	**RR (95% CI)**
A. lumbricoides reinfection	ITT model:[‡]						
	HP&WT + San[‖] vs. control arm	0.040	0.10	0.39 (0.14-1.1)	0.075	0.071	1.1 (0.50-2.2)
	Continuous adherence IV model:[§]						
	Adherence to 2 vs. 0 components	0.054	0.16	0.33 (0.082-1.3)	0.084	0.072	1.2 (0.34-3.9)
	Adherence to 3 vs. 0 components	0.048	0.20	0.23 (0.045-1.2)	0.099	0.081	1.2 (0.22-6.9)
	Categorical adherence IV model:[§]						
	Adherence to ≥ 2 vs. 0 or 1 components	0.046	0.14	0.33 (0.08-1.3)	0.098	0.084	1.2 (0.31-4.3)
Hookworm reinfection	ITT model:[‡]						
	Model 0: HP&WT + San[‖] vs. control arm	0.082	0.15	0.56 (0.27-1.2)	0.11	0.16	0.66 (0.31-1.4)
	Continuous adherence IV model:[§]						
	Adherence to 2 vs. 0 components	0.097	0.24	0.40 (0.14-1.1)	0.11	0.27	0.40 (0.11-1.4)
	Adherence to 3 vs. 0 components	0.077	0.29	0.26 (0.055-1.2)	0.077	0.31	0.25 (0.41-1.5)
	Categorical adherence IV model:[§]						
	Adherence to ≥ 2 vs. 0 or 1 components	0.082	0.20	0.42 (0.14-1.2)	0.081	0.19	0.42 (0.12-1.5)
T. trichiura reinfection	ITT model:[‡]						
	Model 0: HP&WT + San[‖] vs. control arm	0.053	0.071	0.74 (0.17-3.3)	0.055	0.052	1.1 (0.45-2.4)
	Continuous adherence IV model:[§]						
	Adherence to 2 vs. 0 components	0.064	0.088	0.73 (0.058-9.2)	0.050	0.047	1.1 (0.24-4.9)
	Adherence to 3 vs. 0 components	0.067	0.10	0.64 (0.020-20)	0.049	0.044	1.1 (0.10-13)
	Categorical adherence IV model:[§]						
	Adherence to ≥ 2 vs. 0 or 1 components	0.076	0.10	0.75 (0.08-6.9)	0.067	0.062	1.1 (0.29-3.9)

[*] We stratified by sex because sex was observed to be an effect modifier. [‡] The ITT estimate compares all intervention schools to all control schools. The numerator is the pupil's risk in intervention schools and the denominator is the pupil's risk in control schools. [§] The IV estimate compares pupil's risk in schools that adhered at a given level, compared to their potential risk had these same schools not adhered to WaSH. The numerator is the observed pupil risk in a given subset of schools adhering at a given level, and the denominator is the pupil's potential risk *in those same schools* had the schools adhered at the referent level. Adherence was defined by the number of WaSH components to which each school adhered. [‖] HP&WT = hygiene promotion and water treatment; san = sanitation; water = water supply.

Table 3.4b. ITT and IV prevalence ratios for school WaSH adherence on pupil helminth intensity in eggs per gram (EPG) of feces.

		Girls[*]			Boys[*]		
Outcome	**Model**	**Numerator EPG[‡, §]**	**Denominator EPG[‡, §]**	**Egg prevalence ratio (95% CI)**	**Numerator EPG[‡, §]**	**Denominator EPG[‡, §]**	**Egg prevalence ratio (95% CI)**
A. lumbricoides EPG	ITT model:[‡]						
	Model 0: HP&WT + San[‖] vs. control arm	260	851	0.31 (0.07-1.3)	630	550	1.1 (0.32-4.0)
	Continuous adherence IV model:[§]						
	Adherence to 2 vs. 0 components	424	1530	0.28 (0.039-2.0)	750	589	1.3 (0.12-13)
	Adherence to 3 vs. 0 components	322	2144	0.15 (0.00062-36)	968	706	1.4 (0.052-37)
	Categorical adherence IV model:[§]						
	Adherence to ≥ 2 vs. 0 or 1 components	344	1286	0.27 (0.03-2.1)	956	746	1.3 (0.13-13)
Hookworm EPG	ITT model:[‡]						
	Model 0: HP&WT + San[‖] vs. control arm	31	47	0.66 (0.14-3.0)	34	47	0.73 (0.24-2.2)
	Continuous adherence IV model:[§]						
	Adherence to 2 vs. 0 components	42	79	0.53 (0.018-15)	37	81	0.45 (0.18-11)
	Adherence to 3 vs. 0 components	42	98	0.43 (0.0043-43)	31	95	0.33 (0.0024-45)
	Categorical adherence IV model:[§]						
	Adherence to ≥ 2 vs. 0 or 1 components	44	69	0.64 (0.03-14)	30	54	0.56 (0.05-7.0)
T. trichiura EPG	ITT model:[‡]						
	Model 0: HP&WT + San[‖] vs. control arm	12	8	1.5 (0.31-6.9)	7	4	1.5 (0.52-4.4)
	Continuous adherence IV model:[§]						
	Adherence to 2 vs. 0 components	13	8	1.6 (0.059-45)	5	3	1.8 (0.022-150)
	Adherence to 3 vs. 0 components	17	9	1.9 (0.025-150)	5	1	4.8 (0.0021-11000)
	Categorical adherence IV model:[§]						
	Adherence to ≥ 2 vs. 0 or 1 components	18	12	1.5 (0.15-15)	8	4	1.8 (0.11-28)

[*] We stratified by sex because sex was observed to be an effect modifier. [‡] The ITT estimate compares all intervention schools to all control schools. The numerator is the mean EPG of feces in intervention schools and the denominator is the EPG of feces in control schools. [§] The IV estimate compares the mean EPG of feces in schools that adhered at a given level, compared to the potential EPG of feces had these same schools not adhered to WaSH. The numerator is the observed EPG of feces in a given subset of schools adhering at a given level, and the denominator is the potential EPG of feces *in those same schools* had the schools adhered at the referent level. Adherence was defined by the number of WaSH components to which each school adhered. [‖] HP&WT = hygiene promotion and water treatment; san = sanitation; water = water supply.

CHAPTER 4: Pupils' school and home water, sanitation, and hygiene exposures on *Ascaris lumbricoides* reinfection

TITLE: Pupils' school and home water, sanitation, and hygiene exposures on *Ascaris lumbricoides* reinfection following school-based deworming: a cross-sectional study in Kenya

SHORT TITLE: WaSH exposure and *Ascaris lumbricoides* reinfection

ABSTRACT

Introduction: Water, sanitation, and hygiene (WaSH) technologies and behaviors are interdependent and interact in complex ways in disease prevention. However, little has been done to understand these complex relationships. The purpose of this particular study was to characterize how pupils' school and home WaSH exposures were associated with *A. lumbricoides* reinfection, and to characterize relevant interactions between separate WaSH technologies and behaviors.

Methods: We conducted a study on 4,404 children attending 51 primary schools in Kenya. We observed school WaSH conditions and also used structured interviews to further ascertain pupils' access and use of WaSH both at school and home. Our outcome of interest was binary *A. lumbricoides* reinfection since the previous annual school-wide deworming. Our primary exposures of interest were pupils' access to an improved water source, access to sanitation, and practice of handwashing, both at school and at home, but we also assessed other WaSH technologies and behaviors. We used multivariable mixed effects logistic regression to characterize how each WaSH exposure was associated with reinfection in separate models that either ignored or that considered interactions between different WaSH technologies and behaviors.

Results: The majority of our variables of interest were not associated with *A. lumbricoides* reinfection, but several were, including shoe wearing, school sanitation access, and handwashing. The association between handwashing and *A. lumbricoides* depended upon the school also having access to an improved water source that reliably produced water, and was notably stronger for pupils that washed their hands at *both* school *and* home. Counterintuitively, increased access to latrines at school was associated with increased reinfection; a finding possibly due to increased use at unhygienic sanitation facilities.

Conclusions: This study contributes to a further understanding of the impact of WaSH on *A. lumbricoides* infection, and the importance of accounting for interdependencies between different WaSH technologies and behaviors.

Keywords: School WaSH; Soil-transmitted helminths; *Ascaris lumbricoides*, Kenya

INTRODUCTION

It has been estimated that more than 1 billion people throughout the world are infected with soil-transmitted helminths (STHs), primarily roundworm (*Ascaris lumbricoides*), whipworm (*Trichuris trichiura*) and hookworms (*Necator americanus* or *Ancylostoma duodenale*).[18] STH infections can lead to anemia,[13] and slowed physical and cognitive development.[14] School-aged children bear much of the burden of STH morbidity,[17] which accounts for over 5 million disability adjusted life years annually.[15]

Mass drug administration (MDA) programs that administer anthelminthic drugs such as Albendazole or Mebendazole at either the school or community level[19] are being implemented throughout the world to reduce the prevalence of STHs and their associated morbidity.[20,21] While, MDA greatly reduces parasite loads, deworming does not prevent transmission or re-infection.[22] MDA efficacy varies depending on worm species and the type of deworming drug being used,[92] but even when cure rates are high, STH prevalences often return to near pretreatment levels within 6 months due to reinfection.[23]

STH infection occurs most frequently through ingestion of eggs found in fecal material or in the case of hookworm directly through the skin. As such, it has been shown in many studies that transmission is preventable through environmental improvements and improved hygienic behaviors, specifically access to microbiologically safe water, improved sanitation, and handwashing with soap (WaSH).[25-28] While preventive effects of WaSH on STH infection have generally been observed, there is noted heterogeneity across studies, with both a diversity of previous study designs and a variety of WaSH behaviors and technologies under study.[25-28]

Characterizing the relationship between WaSH and STH reinfection is important, although it presents some methodological complexities in epidemiologic studies. First, WaSH is a multi-faceted exposure containing several primary domains (e.g. water, sanitation, & hygiene), each of which is composed of many different technologies and behaviors that vary between the school and home environments. Most prior WaSH studies have not attempted to model individual WaSH technologies and behaviors simultaneously, in the multi-level school and home contexts in which they actually exist. Further, while some WaSH technologies and behaviors have the potential to be individually important, many are likely interdependent and interact in complex pathways to reduce pathogen exposure (e.g. a pupil's handwashing behavior depends on soap and water availability). Little has been done to characterize the complex interactions between WaSH technologies and behaviors, and their relationship to STH reinfection.

Our study uses data from year two of a longitudinal study led by The Kenya Medical Research Institute (KEMRI), which was designed to assess pupils' STH reinfection following yearly MDA.[60] The objectives of this particular study were to characterize how pupils' school and home WaSH exposures were associated with *A. lumbricoides* reinfection, and specifically to characterize how combinations of behaviors and technologies interact in the prevention of helminth reinfection. This study will help us to gain an understanding of which individual and combinations of WaSH technologies and behaviors are most likely to reduce exposure to infective eggs and to prevent *A. lumbricoides* reinfection.

METHODS

Study context: In 2011, the Children's Investment Fund Foundation provided five years of funding to support national school-based-deworming in Kenya, where Albendazole would be provided to school-children annually in efforts to reduce the overall prevalence of STHs and their associated morbidity.[60] The design of the study is shown in Figure 4.1. Predictive mapping was originally used to identify 66 endemic districts,[95,96] and from these 66 districts, 20 districts were randomly selected with a selection probability proportional to the population size.[60] Six districts were selected each from Nyanza and Western Provinces, five districts from Coast Province, and three districts from Rift Valley Province. The M&E had three tiers of monitoring. In the first tier, 200 schools were randomly selected from the 20 districts mentioned above, and all of these schools would undergo long term follow-up in years 3 and 5. Of these 200 schools, 60 were randomly selected for a second tier of additional monitoring, where they would be surveyed annually for 5 years, both before yearly treatment of Albendazole (to ascertain the helminth prevalence), and 3-5 weeks after the treatment (to evaluate the efficacy of the treatment in reducing eliminating STHs). In the third tier of monitoring, 10 different schools undergo follow-up assessments in years 3 and 5, which included the administration of surveys at four time points over the course of the year, along with also receiving the same pre-and post-treatment surveys which were given to the 60 schools in the second tier. Within this national school-based-deworming program, we developed tools and protocols for surveillance of WaSH conditions among this subset of 70 schools that received yearly deworming. The survey instruments were based on tools developed as part of a school-based WaSH trial previously administered in Nyanza Province Kenya.[28] At each visit, approximately nine boys and nine girls were randomly sampled from each grade (2 to 6) using random number tables, and individual exposure and outcome data were collected.

Study population: Our research in this paper takes place among the schools participating in the 2nd and 3rd tier of the M&E, and during year three of the M&E program. We had aimed to include all 70 of these schools but due to logistical difficulties in scaling up the deworming program in Coast Province, the 19 schools from Coast Province were not included in our study. Our final sample included 51 schools; 21 from Western Province, 10 from Rift Valley Province, and 20 from Nyanza Province. We had 4,404 pupil respondents from grades 2-6, weighted to represent 15,960 total pupils, with an equivalent proportion of girls and boys (50%).

Data collection and follow-up timeline: At baseline and at each of the follow-ups, school WaSH conditions were observed, pupils' WaSH histories were collected, and pupils' stool samples were gathered (both pre- and post-deworming) and tested for the presence of common helminth eggs. The baseline surveys and initial deworming took place between January and April of 2012. The first follow-up took place in the second year of the M&E, in 2013. During the second year, there were several limitations, including that fewer pupils were interviewed per school, only an abridged version of the WaSH survey was administered, and the WaSH exposure history was, by mistake, not administered until several months after the measurement of the outcome making temporality a concern, and that the survey was administered on paper surveys, instead of being collected electronically, and due to this had more missing data and transcription errors. Furthermore, the ten high-frequency schools were not included, by design.

Data presented the current study was collected during the third year of the M&E (the second follow-up round), in attempts to ameliorate each of the above limitations. The second follow-up took place two years after baseline, and one year after the second mass deworming, between May and June of 2014. Preceding the data collection, in February of 2014 we piloted a revised paper version of the surveys in order to better capture each student's entire WaSH history and the school's observed WaSH conditions. The final versions of these paper surveys are shown in the Appendix 4.1. In early May of 2014 we piloted a mobile version of the survey using Open Data Kit (ODK) Collect on mobile *Android devices.* All school and pupil surveys from the 2014 follow-up were collected by enumerators using ODK Collect on mobile *Android devices*, and all surveys were conducted in the pupil's native language(s) by trained KEMRI staff.

Outcome: Stool samples were collected from each pupil, prepared on two separate slides, and the slides were analyzed independently for presence and intensity of STH species using the Kato Katz method.[89] The outcome of interest for this study was pupil reinfection by *A. lumbricoides* (yes vs. no). We used the term 'reinfection' throughout, as is commonly found in the literature, although the infection may not always truly be a "re" infection as in a second infection, and although it is not quite cumulative incidence due to the possibility of the deworming program incompletely eliminating the parasite from all individuals during the previous follow-up.

Exposures: We administered a pupil survey to ascertain pupils' access to and use of different WaSH technologies and behaviors both at school and at home (Appendix 4.1). The school survey was also administered to collect both teacher-reported and observed school WaSH conditions.

Our primary exposures of interest were access to an improved water source, access to sanitation, and practice of handwashing, with separate variables for each of these primary exposures at both school and at home. We observed the water source at each school, and categorized these sources as improved or unimproved as defined by the WHO/UNICEF Joint Monitoring Program (JMP) for Water Supply and Sanitation.[1] Because water availability was so variable at schools, we further constrained our definition of an improved school water source by whether water was reliably available throughout the year, with water availability being teacher reported. The pupil's home water source was self-reported, and was then categorized as either improved or unimproved as defined by the JMP. Access to school sanitation for each pupil was defined by whether or not that pupil's school had met the World Health Organization pupil to latrine ratio recommendations for each sex of pupils (25:1 for girls, and 50:1 + one urinal for boys).[29] Access to home sanitation was pupil reported, and was categorized as either having a personal sanitation facility in their compound, having a shared facility with other households, or not having access to a toilet facility at home. Both school and home handwashing were assessed by self-report, and we compared pupils who reported always washing their hands after defecation to pupils who reported washing their hands only sometimes or never.

We also had interest in a number of other WaSH technologies and behaviors. School-level factors included the enumerator-observed presence of visible feces inside sanitation facilities (percentage of all school latrines with visible feces), and the enumerator-observed presence of visible feces outside of the sanitation facilities at the school (yes vs. no). Individual or home-level factors included the pupil-reported type of anal cleansing materials used (water, paper products, leaves/rocks/nothing), pupil-reported floor type at home (earth vs. other), pupil's shoe wearing as observed by the enumerator during the visit (closed shoe, sandal, no shoes), and pupil's reported practice of eating soil (yes vs. no) – a practice common in some areas of Kenya.[97]

We produce individual estimates for each WaSH variable of interest. We also have the ability to contrast various combinations of WaSH variables in meaningful ways. We had specific interest in understanding the effect of having access to an improved water source *both* at school and at home, of having access to sanitation *both* at school and at home, and of practicing handwashing *both* at school and at home, and so we also show these relevant contrasts.

We had originally considered the possibility that the proportion of pupils in the school that wash their hands could potentially affect helminth reinfection through group-level adherence, even in the absence of an individual pupil's adherence, for example through herd protection.[98,99] We aggregated individual handwashing responses to the school level, and calculated the proportion of pupils in each school that always washed their hands. However, because school-level handwashing was poor at most schools (see Figure 4.2), the variable lacked the necessary heterogeneity to be able to include in our multivariable models. For example, in 44 of the 51 schools, fewer than 10% of the pupils reported always washing their hands after defecation.

The inclusion of each variable was chosen *a priori* based on biological plausibility and on the previous literature. Sometimes separate variables measured similar constructs, and in Appendix 4.2 we show correlations between these variables, and reasoning why we included specific variables in our models. We also perform several sensitivity analyses to ascertain the impact of choosing one variable over another, when two variables measured a similar construct.

Confounders: We controlled for the outcome prevalence at baseline at each school (e.g. pre-deworming in 2012) as this variable may affect the probability of person to person transmission for unaffected individuals in the population.[100,101] This is because infective *A. lumbricoides* eggs may persist in the environment for many years.[102] Other confounder variables that we included were mean annual temperature, mean annual precipitation (both were linked to school locations from http://www.worldclim.org/bioclim), and the former province where the schools were located (Western, Rift Valley, and Nyanza Province). We also controlled for other important risk factors, including the pupil's sex, grade, whether the pupil had siblings under age five at home, and the pupil's SES (using a continuous wealth index score constructed using principal component analysis).[103] We also considered that these potential confounders may act as effect modifiers of some of our WaSH variables of interest, which we discuss in the section below.

Interaction specification: We also had interest in how combinations of behaviors and technologies interact in the prevention of helminth reinfection. We determined *a priori* a number of interactions of interest and the potential interactions of interest, which are shown in Table 4.1. The decision to designate specific interaction terms was based upon biological plausibility, and focused on interactions with public health relevance (i.e. actionable). All of these potential effect modifiers were assessed using forward selection, and only those effect modifiers that produced estimates in that were meaningfully different (e.g. estimates in opposite directions or markedly different), would be retained in the final model. When considering the inclusion of each term, multicollinearity between terms (the presence of high condition indices with several high variance decomposition proportions)[104] and whether or not the model converged with the interaction terms of interest were also factors used to determine whether or not each term could be included in the model.

Safety and confidentiality: Ethical approval was obtained by The Kenya Medical Research Institute (KEMRI) ethics committee. Emory researchers received de-identified data, and so it was determined by the Emory University institutional review board that IRB review was not required as the study did not meet the definitions of research with "human subjects."

Data analysis: For descriptive statistics, we used the sampling weights and the complex sample design to present percentages that were representative of all pupils in grades 2-6 from these schools. These descriptive statistics were carried out in SAS-Callable SUDAAN version 11.0.1. All of our bivariable and multivariable analyses were carried out in SAS version 9.4 (Cary, NC, USA).

We used multilevel mixed effects regression models to quantify the relationship between individual WaSH technologies and behaviors, and *A. lumbricoides* reinfection (yes vs. no). We first modeled the bivariate associations between each exposure of interest, and the *A. lumbricoides* reinfection, accounting only for clustering of pupils within schools. We then used multivariable models to account for WaSH technologies and behaviors simultaneously, along with the confounders and effect modifiers as discussed above, and a random intercept to account for the correlation of pupils within schools. The final model resembled the form of the general model:

$$\mathrm{logit}(\mu_{ij}) = \alpha_0 + \sum_{p=1}^{P} \beta_p \mathrm{WaSH} + \sum_{q=1}^{Q} \gamma_q \ \mathrm{Confounder} + \sum_{p=1}^{P}\sum_{q=1}^{Q} \delta_{pq} \ \mathrm{WaSH} * \mathrm{Confounder} + \sum_{p=1}^{P}\sum_{p=1}^{P} \delta_{pp} \ \mathrm{WaSH} * \mathrm{WaSH} + u_{0j}$$

where μ_{ij} represents the probability of *A. lumbricoides* reinfection on the ith student within the jth school. The WaSH variables are both individual-level variables (ij), and school-level variables (j), but subscripts i and j have been suppressed for simplicity. Because interaction is an important component to our study question, we assessed many WaSH*confounder, and WaSH*WaSH variables but only those interaction terms that produced odds ratio estimates that were meaningfully different (e.g. estimates in opposite directions or markedly different) were retained in the final model. u_j represents a random intercept which is included to account for clustering, or that observations within the jth school are correlated.

RESULTS

WaSH: School-level access and adherence to WaSH was suboptimal in many schools. Around half of the schools (49%) had handwashing facilities near the toilets, but only 12% of the schools had soap available at the handwashing facilities (Table 4.2). Only 4% of pupils reported always washing their hands with soap after defecation (Table 4.3). Regarding water access at school, 53% of schools had an improved water source, and 57% had drinking water reliably available year round; 20% of the schools had both an improved water source that produced water year round. Observations of sanitation facilities showed that 16% of the schools met the WHO pupil to latrine standards for girls, and 26% met the WHO pupil to latrine standards for boys.

Home WaSH conditions were also suboptimal, although somewhat better than at school (Table 4.3). Of our primary exposures of interest, only 8% of pupils reported always washing their hands with soap, 51% reported having an improved water source for drinking, and 55% of pupils had a personal latrine in their compound.

A. lumbricoides prevalence: The *A. lumbricoides* prevalence among pupils attending the 51 schools was 17% (pre-deworming during the follow-up in 2014; data not shown). One year earlier at the 2013 follow-up, we had worm prevalence data on 45 of these schools – those monitored in the 2nd tier of the M&E program – and the post-deworming *A. lumbricoides* prevalence was 2%. We also had worm prevalence data on 50 of these schools at baseline in 2012 (preceding both the baseline and first follow-up dewormings), and at that time the *A. lumbricoides* prevalence was 24%. Other parasite data, including prevalences of other worms, and STH prevalences in all 200 schools are described elsewhere.[60]

Wash and A. lumbricoides reinfection: In bivariate analyses, a number of several WaSH characteristics were associated with *A. lumbricoides* reinfection (Table 4.4, column 1). Pupils who reported always washing their hands *at school* had a lower odds of *A. lumbricoides* reinfection (OR = 0.59, 95% CI: 0.35-1.01; *p*=0.05). Having access to an improved water source that reliably produced water *at school* was not significantly associated with *A. lumbricoides* reinfection (OR = 1.14, 95% CI: 0.58-2.21; *p*=.071). Pupils attending schools that met the WHO pupil to latrine ratio recommendations (25:1 for girls and 30:1 for boys + one urinal) had higher reinfection compared to schools that did not meet these guidelines (OR = 1.89, 95% CI: 1.22–2.9; *p*=<0.01). None of these three primary WaSH exposures *at home* were significantly associated with *A. lumbricoides* reinfection. However, pupils with an earth/sand floor at home had higher *A. lumbricoides* reinfection compared to pupils with cement/wood/iron sheet floors (OR = 1.28, 95% CI: 1.02-1.62; *p*=0.36), and pupils who were wearing shoes and pupils who were wearing sandals, each had lower odds of STH infection, compared to pupils who were shoeless (shoes OR = 0.60, 95% CI: 0.48–0.74; *p*=<0.01; sandals OR = 0.58, 95% CI: 0.45–0.74; *p*=<0.01).

In the multivariable regression analyses, several of the associations, and most notably the association between handwashing and *A. lumbricoides*, were attenuated towards the null. Pupils attending schools that met the WHO pupil to latrine ratio recommendations had higher reinfection compared to schools that did not meet these guidelines (OR = 1.55, 95% CI: 1.01-2.38; *p*=0.04). Wearing closed toed shoes or sandals was again associated with lower helminth reinfection (shoes OR = 0.68, 95% CI: 0.55–0.85; *p*=<0.01; sandals OR = 0.63, 95% CI: 0.49–0.81; *p*=<0.01).

We explored the data for meaningful variable interactions among a number of *a priori* potential interaction terms (Table 4.1). The only meaningful interaction terms that were found and that persisted in our final model were the school and home terms between handwashing and having access to an improved water source. These interactions between handwashing and improved water source access were observed at school (*p* <0.01; Table 4.5.a) and also to a much lesser degree at home (*p* =0.30; Table 4.5.b). For example, pupils' handwashing at school was associated with lower helminth reinfection in schools that had an improved water source that reliably produced water, (OR = 0.46, 95% CI: 0.23-0.89; *p*=0.02), but not in schools with an unimproved water source (OR = 2.14, 95% CI: 0.81-5.69; *p*=0.13). This general pattern between handwashing and having an improved water source was also seen at home, although to a lesser degree. The ORs for all of the other variables were similar (within 10%) to those from the fully-adjusted, no-interaction model, and are shown in Appendix 4, Table A4.3.

We contrasted relevant WaSH combinations to obtain the effects of each of the three WaSH domains at *both* school and home together (Table 4.6). Using the no-interaction model, each of the odds ratios were null for each of the three WaSH domains. Using the interaction model, the OR for handwashing at *both* school and at home among pupils that also had access to an improved water source was 0.38 (95% CI: 0.18-0.83; *p*=0.01), compared to handwashing at neither place.

We performed sensitivity analyses to assess the robustness of this association by including either a different handwashing variable (last WaSH in place of always washing), or a different water source variable (improved water source in place of improved water source that reliably produced water). In both models this interaction persisted, although the ORs were closer to the null. For example the OR for *always* handwashing among pupils with an improved water source *not accounting for water reliability* was 0.59 (95% CI: 0.33-1.07) and the OR for washing after the *last* defecation among pupils with an improved *water source that reliably produced water* was 0.68 (95% CI: 0.44-1.1).

DISCUSSION

This study is one of the first to assess the associations between *A. lumbricoides* reinfection following deworming and different WASH technologies and behaviors – both individually and interacting in concert –among pupils attending Kenyan schools. We found that some WaSH behaviors and technologies were independently associated with *A. lumbricoides* reinfection, whereas others were interdependent upon combinations with other variables. For example, the association between handwashing and *A. lumbricoides* depended upon the school's access to an improved water source that reliably produced water. We also found strong preventive estimates when we considered handwashing both at school and at home, compared to at neither place. Other results were unintuitive or inconsistent in their support of WaSH, such as our finding that pupils in schools that met the WHO pupil to latrine ratio guidelines had higher *A. lumbricoides* reinfection.

Our findings suggests that a school's access to an improved water source that reliably produces water is important for the success of handwashing interventions. Our models had the capacity to capture the effects of WaSH simultaneously at school and at home, and we observed an especially strong association between of handwashing and *A. lumbricoides*, but again depending on presence of an improved water source both at school and at home. These results may shed light on results from a recent study in Kenya, which found reductions in enrollment, and diarrheal illness but *only in those schools that were also provided a water source.*[41,105] Other school WaSH studies, including meta-analyses, often consider either water or sanitation or hygiene without considering their codependence,[26,27] but this may overlook valuable information. Another hypothesis for why we might have observed this interaction between handwashing and an improved water source, may have little to do with water quality. It is possible that some pupils were not truthfully answering about handwashing behavior, and that by including this interaction term, pupils who reported always handwashing but sometimes lacked the capacity to do so would be moved into a separate 'stratum' from those individuals who reported always handwashing and also had the capacity to do so, allowing the handwashing estimates to differ by differing levels of adherence. Other handwashing variable constructs that we used in sensitivity analyses showed similar results, indicating robustness across measures.

While our findings from our interaction model – that handwashing requires water – are seemingly obvious, the co-dependence of these separate WaSH domains is an important message when trying to implement handwashing worldwide. Even though we did not observe other pre-hypothesized interactions in this population, there may still be merit to assessing these interactions in other populations. One possibility for why we did not observe more interactions is that our analyses may have only been adequately powered to detect the strongest interactions, and that other weaker interactions may have been overlooked. WaSH conditions, especially access to and practice of handwashing, were poor throughout all schools, and an increased number of pupils who practiced WaSH would have improved the power of our analyses.

Meta-analyses, primarily from non-school settings, have found decreased STH infection with improved sanitation access.[26,27] One possibility for our finding of higher *A. lumbricoides* reinfection among pupils in schools that met the WHO pupil to latrine ratio guidelines is that latrine dirtiness may increase pupils' exposure to disease[31]. This is supported by other studies that have found latrine provisions to be associated with increased pupil hand contamination,[42] or that have found associations between dirty latrines and bacterial pathogens throughout the bathroom,[43] diarrhea,[31] vomiting,[31] and dysentery.[44] A lower pupil to latrine ratio has been found to be associated with increased latrine use[106] which could further propagate pupils' exposure to pathogens. We assessed the interaction between this latrine access variable and latrine cleanliness and did not find a meaningful interaction. The observation of increased *A. lumbricoides* reinfection among pupils with better latrine access adds to evidence simply that meeting international coverage targets, in the absence of uptake or of a reduction in exposures, may be insufficient to improve health.[107,108]

Shoe-wearing was strongly associated with *A. lumbricoides* reinfection in each analysis, and floor type was associated with *A. lumbricoides* in the unadjusted analysis. These may work through a common mechanism, although it is unclear how the eggs would be ingested. Shoe-wearing has been associated with decreased STH infection in other studies, although usually with hookworm,[27] as hookworm can be contracted through the skin. It is also possible that this may be related to SES, although we included variables that control for household wealth.

We focused solely on *A. lumbricoides* for several reasons. First, a higher endline prevalence of *A. lumbricoides* (17%) provided an adequately powered analysis whereas the prevalence of hookworm and *T. trichiura* were low (2% and 5%, respectively; data not shown). Second, Albendazole is known to be more effective in the elimination of *A. lumbricoides* than both *T. trichiura* and hookworm,[92] allowing us to more closely approximate cumulative incidence since the previous deworming and thereby strengthening our study design. A final reason to focus on *A. lumbricoides* is that progress for eliminating this worm might depend more heavily on WaSH, because ingestion is the infection mechanism and the long infective period of *A. lumbricoides* eggs in soil (up to 10 years).[102] Suboptimal WaSH access and adherence in these schools may be a reason that *A. lumbricoides* prevalence has only changed from 24% percent in 2012 (data not shown) to 17% in 2014, following two cycles of mass deworming. In contrast, hookworm prevalence – which has a different mechanism of infection (through the skin) and has a shorter infective period of the larvae – has gone from 16% to 2% over the same time period.[109]

There are several potential limitations of our study. There is still the possibility of confounding by unknown or unmeasured variables, although we did control for many confounders in our analyses. Our exposures were primarily self-reported, however, we were able to observe some observed variables, and to calculate correlations between variables measuring similar constructs. We also observed a low prevalence of several exposures such as handwashing, suggesting that over-reporting of these might have been rare. We only used a single day of observations to capture pupils' sometimes-time-varying WaSH histories, however, we performed sensitivity analyses to compare pupils' 'last' behavior and what they reported 'always' doing. Our results will be most generalizable to populations undergoing similar mass-deworming programs. Our outcome is not truly 'reinfection' due to the possibility of incomplete coverage or effectiveness of the deworming drugs. However, Albendazole is known to have a high cure rate for elimination of *A. lumbricoides.*[92] Furthermore, one year before our study, we had worm prevalence data on pupils from 45 of these schools, and the post-deworming *A. lumbricoides* prevalence was 2%, suggesting that our outcome prevalence of 17% may approximately reflect reinfection.

CONCLUSIONS

This study is one of the first to assess the associations between *A. lumbricoides* infection and different WASH technologies and behaviors – both individually and in interacting in concert – among pupils attending Kenyan primary schools. Our study shows the importance of accounting for interdependencies between different WaSH technologies and behaviors. We found several associations between WaSH behaviors and technologies and *A. lumbricoides* reinfection, including for shoe wearing behavior, for school sanitation access, and for handwashing, but the association between handwashing and *A. lumbricoides* depended upon the school also having access to an improved water source that reliably produced water. We also found stronger preventive estimates, when we considered adherence to handwashing both at school and at home. Results were sometimes counterintuitive or inconsistent in their support of WaSH, such as our finding that pupils in schools that met the WHO pupil to latrine ratio guidelines had higher *A. lumbricoides* reinfection.

Acknowledgements

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Table 4.1. Potential interactions of interest.

Interaction of interest	Retained*
Effect modification between *A. lumbricoides* **and**…	
handwashing at school, by the type of school water source‡	yes
handwashing at home, by the type of home water source‡	yes
handwashing at school, by the type of anal cleansing materials	no
handwashing at home, by the type of anal cleansing materials	no
handwashing at home, by baseline worm prevalence	no
handwashing at school, by baseline worm prevalence	no
the type of school water source,‡ by baseline worm prevalence	no
the type of school water source,‡ by baseline worm prevalence	no
latrine access at home, by baseline worm prevalence	no
latrine access at school, by baseline worm prevalence	no
open defecation at home, by any of the climate	no
open defecation at home, by baseline worm prevalence	no
visible feces in the open at school, by baseline worm prevalence	no
visible feces in the open at school, by any of the climate	no
visible feces in the open at school, by shoe wearing	no
visible feces in latrines at school, by baseline worm prevalence	no
visible feces in latrines at school, by any of the climate	no
visible feces in latrines at school, by shoe wearing	no
a natural floor at home, by shoe wearing	no
soil eating behavior, by baseline worm prevalence	no
The interactions between...	
school and home handwashing practice	no
school and home latrine access	no
school and home water access	no

*All of these potential effect modifiers were assessed using forward selection, and only those effect modifiers that produced estimates in that were meaningfully different (e.g. estimates in opposite directions or markedly different), would be retained in the final model. ‡Improved versus unimproved, as defined by the WHO/UNICEF Joint Monitoring Program (JMP) for Water Supply and Sanitation.[1]

Table 4.2. Observed and teacher reported WaSH conditions among 51 Kenyan primary schools.

	N	%
Total number of schools	51	100%
School Hygiene		
Handwashing facilities near the toilets	25	49%
Water in handwashing facilities	30	58%
Soap available at the handwashing facilities	6	12%
School Water		
Improved water source for drinking[§]	27	53%
Drinking water reliably available year round	29	57%
Improved water source that reliably produced water	10	20%
School Sanitation		
Meets the WHO pupil to latrine ratio standards for girls*	8	16%
Meets the WHO pupil to latrine ratio standards for boys*	13	26%
Latrines clean in school[¶]	11	22%
Feces visible on grounds outside of the latrines	16	31%

*There was one all-boys school and one all-girls school, so the denominator for this variable is 50 schools. [‡]The World Health Organization pupil to latrine ratio recommendations are 25:1 for girls, and 50:1 + one urinal for boys.[29] [§]As defined by the WHO/UNICEF Joint Monitoring Program (JMP) for Water Supply and Sanitation.[1] [¶] No visible feces inside any of the latrines.

Table 4.3. Pupil- reported WaSH conditions by 4,404 respondents, weighted to represent 15,960 pupils from grades 2-6 in 51 Kenyan primary schools.

	n or %*	SE*
Total number of pupil respondents	4,404	
Weighted population size	15,960	
School Hygiene		
School provides a handwashing place	62.8%	0.8
Water always available at that place	19.9%	0.9
Soap always available at that place	1.0%	0.2
Handwashed with soap and water the last time they defecated	12.3%	0.8
Always handwashes with soap and water after defecating	3.8%	0.4
School Water		
Water always available for drinking	21.0%	0.9
School Sanitation		
Usually defecate in the latrine/toilet at school	99.4%	0.1
Used a latrine/toilet at school last time they defecated	97.5%	0.3
Think their friends always defecate in the latrine/toilet at school	75.7%	1.0
Home Hygiene		
Have a handwashing place	49.7%	1.0
Water always available at that place	18.9%	0.8
Soap always available at that place	10.3%	0.6
Handwashed with soap and water the last time they defecated	33.1%	1.0
Always handwashes with soap and water after defecating	8.1%	0.5
Home Water		
Have an improved water source for drinking§	50.65%	1.08
Water always available for drinking	85.0%	0.9
Home Sanitation		
Have a personal toilet/latrine in your home/compound?	55.0%	1.0
Have a shared toilet/latrine in your home/compound?	42.0%	1.0
No toilet/latrine in your home/compound	2.9%	0.3
Usually defecate in the latrine/toilet at home	98.6%	0.2
Used a latrine/toilet at home last time they defecated	96.8%	0.3

* Weighted % and SE both use the sampling weights and the complex sample design. §As defined by the WHO/UNICEF Joint Monitoring Program (JMP) for Water Supply and Sanitation.[1]

Table 4.4. ORs comparing WaSH technologies and behaviors with *A. lumbricoides* reinfection among 4,404 pupils in 51 Kenyan primary schools.

	Unadjusted/bivariate models		Adjusted no interaction model[‡]	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
School WaSH variables				
Always handwash after defecation		0.05		0.14
Yes	0.59 (0.35-1.01)		0.66 (0.38-1.15)	
No	referent		referent	
Improved water source that reliably produced water		0.71		0.56
Yes	1.14 (0.58-2.21)		1.15 (0.71-1.89)	
No	referent		referent	
Pupil:latrine ratio acceptable		<0.01		0.04
Yes	1.89 (1.22-2.91)		1.55 (1.01-2.38)	
No	referent		referent	
Visible feces on latrine floor/walls		0.67		0.47
All latrines have feces	1.26 (0.44-3.62)		1.40 (0.57-3.43)	
No latrines have feces	referent		referent	
Feces visible outside latrines		0.28		0.38
Yes	1.48 (0.73-2.98)		1.27 (0.74-2.18)	
No	referent		referent	
Anal cleansing with		0.99		0.39
Water	1.04 (0.62-1.75)		0.85 (0.42-1.70)	
Leaves/rocks/nothing	referent		referent	
Paper product	1.01 (0.80-1.28)		1.14 (0.89-1.46)	
Home WaSH variables				
Always handwash after defecation		0.68		0.97
Yes	0.94 (0.69-1.28)		0.99 (0.71-1.39)	
No	referent		referent	
Improved water source		0.94		0.56
Yes	0.94 (0.77-1.16)		1.07 (0.86-1.33)	
No	referent		referent	
Toilet is		0.85		0.66
Shared	1.06 (0.86-1.32)		1.11 (0.88-1.40)	
No toilet	0.99 (0.57-1.69)		0.98 (0.57-1.70)	

Personal	referent		referent	
Anal cleansing with		0.36		0.30
Water	1.23 (0.77-1.98)		1.60 (0.84-3.05)	
Leaves/rocks/nothing	referent		referent	
Paper product	0.91 (0.74-1.11)		0.98 (0.77-1.24)	
Other WaSH variables				
Shoe wearing		<0.01		<0.01
Closed shoes	0.60 (0.48-0.74)		0.68 (0.55-0.85)	
Sandals	0.58 (0.45-0.74)		0.63 (0.49-0.81)	
No shoes	referent		referent	
Type of floor in home		0.036		0.71
Earth/sand	1.28 (1.02-1.62)		1.06 (0.77-1.45)	
Cement/wood/iron sheets	referent		referent	
Student eats soil (geophagy) *		0.45		0.38
Yes	1.14 (0.82-1.58)		1.16 (0.83-1.62)	
No	referent		referent	
Confounders‡				
Grade		0.10		0.24
2	1.44 (1.10-1.89)		1.35 (1.03-1.79)	
3	1.30 (0.99-1.72)		1.26 (0.95-1.67)	
4	1.21 (0.92-1.61)		1.17 (0.88-1.56)	
5	1.14 (0.87-1.52)		1.10 (0.83-1.47)	
6	referent		referent	
Sex		<0.01		<0.01
Male	1.45 (1.22-1.73)		1.32 (1.11-1.60)*	
Female	referent		referent	
Data not shown for other confounders‡	Data not shown‡	Data not shown‡	Data not shown‡	Data not shown‡

*Geophagy is a soil eating practice common in some parts of Kenya.[97] ‡Both adjusted models controlled for all of the variables in this table, and also confounders which are not shown here, including whether pupils had siblings under age 5, household wealth score, the baseline *A. lumbricoides* prevalence at each school, the mean annual temperature, annual precipitation, and province. All three models accounted for clustering of pupils within schools. § ¶

Table 4.5.a Interaction between pupil handwashing at school, and type of water source at school among 4,404 pupils in 51 Kenyan primary schools.

	Always handwash		Never handwash		Adjusted ORs (95% CI)[*] for handwashing within strata of water source
	N with / without Ascaris	Adjusted OR (95% CI)[*]	N with / without Ascaris	Adjusted OR (95% CI)[*]	
Improved water source	16/139	0.55 (0.25-1.22); *p*=0.14	364/1570	1.20 (0.74-1.96); *p*=0.46	0.46 (0.23-0.89); *p*=0.02
Unimproved water source	8/37	2.14 (0.81-5.69); *p*=0.13	351/1919	1.00; referent	2.14 (0.81-5.69); *p*= 0.13
Adjusted ORs (95% CI)[*] for an improved water source within strata of handwashing		0.26 (0.075-0.87); *p*=0.03		1.20 (0.74-1.96); *p*=0.46	
Measure of effect modification on multiplicative scale: ratio of ORs (95% CI) = 0.21 (0.067-0.68); *p* = <0.01.					

[*] Model includes handwashing*water interaction terms. All ORs are adjusted for all of the variable in Table 4.4 and additionally controlled for whether pupils had siblings under age 5, household wealth score, the baseline *A. lumbricoides* prevalence at each school, the mean annual temperature, annual precipitation, and province.

Table 4.5.b Interaction between pupil handwashing at home, and type of water source at home among 4,404 pupils in 51 Kenyan primary schools.

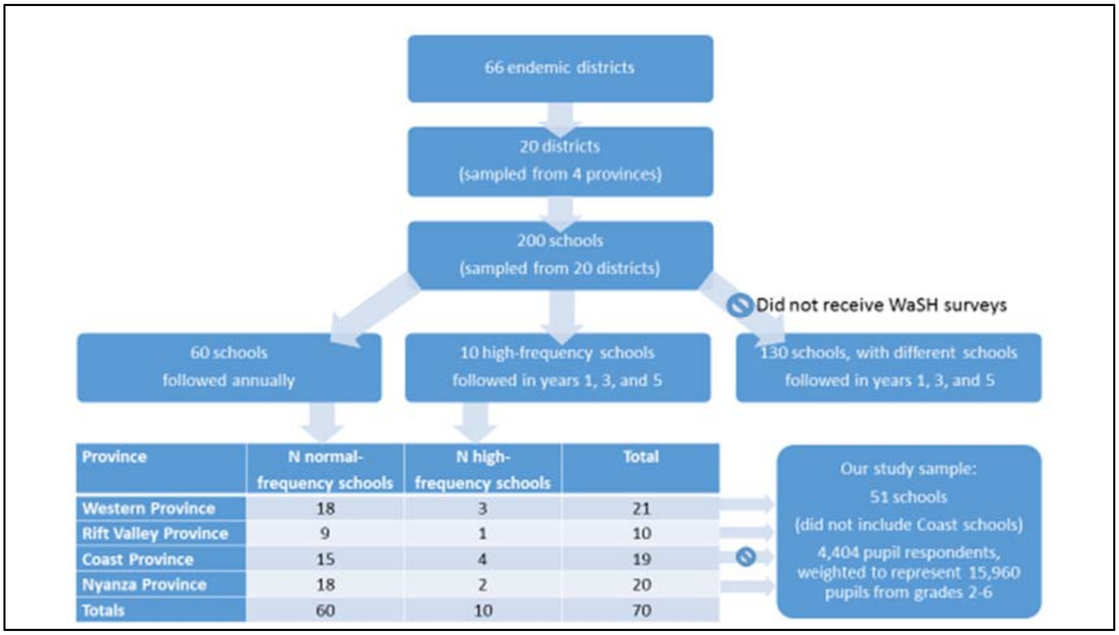
	Always handwash		Never handwash		Adjusted ORs (95% CI)[*] for handwashing within strata of water source
	N with / without Ascaris	Adjusted OR (95% CI)[*]	N with / without Ascaris	Adjusted OR (95% CI)[*]	
Improved water source	30/237	0.92 (0.57-1.50); *p*=0.75	232/1497	1.09 (0.87-1.38); *p*=0.42	0.84 (0.52-1.36); *p*=0.48
Unimproved water source	38/110	1.17 (0.75-1.83); *p*=0.47	439/1821	1.00; referent	1.17 (0.75-1.8); *p*=0.47
Adjusted ORs (95% CI)[*] for an improved water source within strata of handwashing		0.78 (0.42-1.45); *p*=0.44		1.09 (0.87-1.38); *p*=0.42	
Measure of effect modification on multiplicative scale: ratio of ORs (95% CI) = 0.71 (0.38-1.35); *p* = 0.30					

[*] Model includes handwashing*water interaction terms. All ORs are adjusted for all of the variable in Table 4.4 and additionally controlled for whether pupils had siblings under age 5, household wealth score, the baseline *A. lumbricoides* prevalence at each school, the mean annual temperature, annual precipitation, and province.

Table 4.6. Additional OR contrasts using the no interaction model and the interaction model from Tables 4.4 and 4.5, respectively.

	OR (95% CI)	*p*-value
No interaction model[*]		
Always handwash		
at school *and* home	0.66 (0.35-1.21)	0.18
at neither place	referent	
Access to an improved water source		
at school *and* home	1.24 (0.73-2.10)	0.43
at neither place	referent	
Increased latrine access at school and at home		
at school *and* home	1.58 (0.79-3.19)	0.20
at neither place	referent	
Interaction model[‡]		
	Among those with an improved water source	
Always handwash		
at school *and* home	0.38 (0.18-0.83)	0.01
at neither place	referent	
	Among those with an unimproved water source	
Always handwash		
at school *and* home	2.52 (0.85-7.44)	0.21
at neither place	referent	
	Among those who always handwash	
Access to an improved water source		
at school *and* home	0.20 (0.051-0.78)	0.02
at neither place	referent	
	Among those who did not handwash	
Access to an improved water source		
at school *and* home	1.32 (0.78-2.25)	0.30
at neither place	referent	
Increased latrine access at school and at home	**Among everybody**	
at school *and* home	1.56 (0.78-3.16)	0.21
at neither place	referent	

[*] All ORs are adjusted for all of the variable in table 4.4 and additionally controlled for whether pupils had siblings under age 5, household wealth score, the baseline *A. lumbricoides* prevalence at each school, the mean annual temperature, annual precipitation, and province. [‡] Model includes handwashing*water interaction terms and controls for the same variables as the above model.



Province	N normal-frequency schools	N high-frequency schools	Total
Western Province	18	3	21
Rift Valley Province	9	1	10
Coast Province	15	4	19
Nyanza Province	18	2	20
Totals	60	10	70

Figure 4.1. Design of this WaSH study nested within the monitoring and evaluation program.

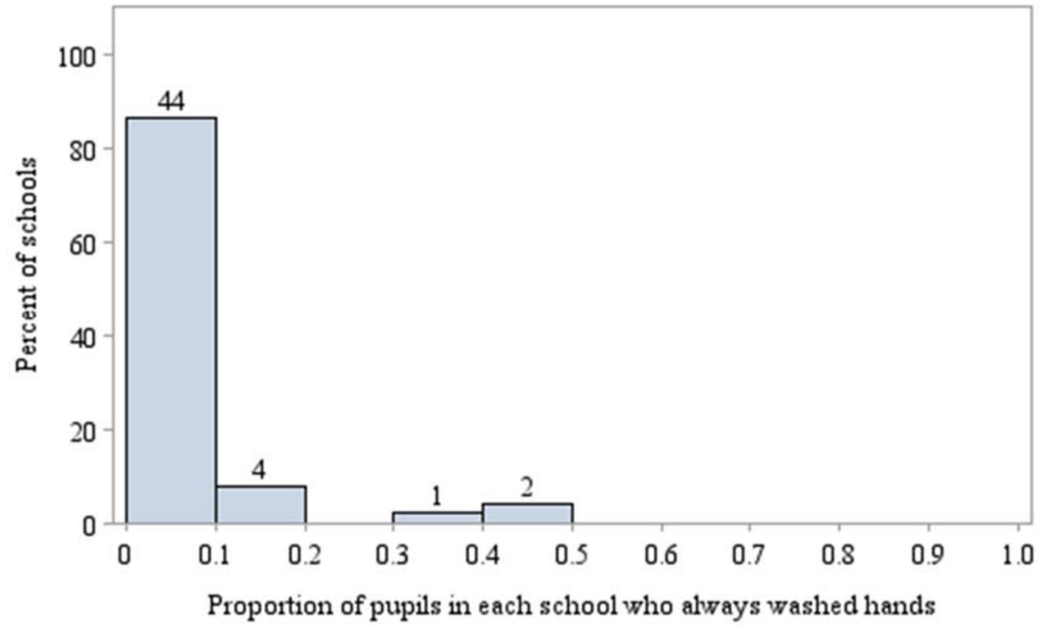


Figure 4.2. Histogram of school-level handwashing.

CHAPTER 5: Factors associated with pupil toilet use in Kenyan primary schools

TITLE: Factors associated with pupil toilet use in Kenyan primary schools

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Abstract: The purpose of this study was to quantify how school sanitation conditions are associated with pupils' use of sanitation facilities. We conducted a longitudinal assessment in 60 primary schools in Nyanza Province, Kenya, using structured observations to measure facility conditions and pupils' use at specific facilities. We used multivariable mixed regression models to characterize how pupil to toilet ratio was associated with toilet use at the school-level and also how facility conditions were associated with pupils' use at specific facilities. We found a piecewise linear relationship between decreasing pupil to toilet ratio and increasing pupil toilet use ($p < 0.01$). Our data also revealed significant associations between toilet use and newer facility age ($p < 0.01$), facility type ($p < 0.01$), and the number of toilets in a facility ($p < 0.01$). We found some evidence suggesting facility dirtiness may deter girls from use ($p = 0.06$), but not boys ($p = 0.98$). Our study is the first to rigorously quantify many of these relationships, and provides insight into the complexity of factors affecting pupil toilet use patterns, potentially leading to a better allocation of resources for school sanitation, and to improved health and educational outcomes for children.

Keywords: sanitation; school sanitation; latrine use; toilet use; pupil to latrine ratio; pupil to toilet ratio; cleanliness; Kenya

INTRODUCTION

The problem of inadequate sanitation is important for school-aged children, who experience over 2.8 billion cases of diarrhea annually,[32] and who bear much of the burden of soil-transmitted helminth morbidity.[17] Inadequate sanitation can lead to a number of health problems, including stunted growth,[33,34] diarrheal illness,[35,36] and even death.[6,7] Equitable access to school sanitation is of particular concern. Data are scarce, but recent estimates suggest that only 45% of schools in low income countries have adequate sanitation facilities.[38]

The health and educational benefits of increasing the number of latrines in schools are still not well understood. To our knowledge, no trial assessing only the benefit of additional latrines in schools has been conducted, likely because implementing sanitation without hygiene is not seen as best practice and may not be policy relevant.[39] The only comprehensive school WASH trial that also included latrine provisions found decreased pupil absence, increased enrollment, and decreased diarrheal illness, but only among certain subsets of the study population,[40,41] and found reduced STH infection rates for the *Ascaris lumbricoides* worm, but not other helminths.[28] Furthermore, pupils attending schools in an arms that received latrine provisions received little benefit compared to pupils in otherwise similar intervention arms but without latrine provisions[40,41] and latrine provisions were even associated with increased pupil hand contamination.[42] These results suggest that other factors, besides simply providing school latrines, are important to the success of school sanitation interventions at scale.

One possibility for the mixed success of this previous trial is that while the number of latrines increased, latrine dirtiness could actually increase pupils' exposure to disease.[31] For instance, studies have found that dirty school sanitation facilities are associated with increased bacterial pathogens throughout the bathroom,[43] and with increased incidence of diarrhea,[31] vomiting,[31] and dysentery outbreaks.[44] Decreasing the pupil to latrine ratio in a school is hypothesized to improve the overall latrine use in that school,[40,45] but for this increase in latrine use to improve public health, it must also coincide with a net reduction in pupils' exposures to pathogens.

Another possibility for the mixed success of this previous trial relates to the actual use of the latrines. There has been considerable attention to the child-centered design of sanitation facilities in schools,[46,47] however little empirical data exist on how the type, design, and maintenance of facilities affect behavior or health. Provisions of toilets at schools do not guarantee that those toilets are used or are well maintained. When latrines are available, children may choose to use the latrines or urinals, to openly defecate or urinate in or around the school grounds, or to hold their use until they can access a preferable toilet or openly defecate outside of school.[48] Open defecation, which affects pupil health by increasing exposure to fecal pathogens, has been observed in lower resource schools even when school toilets are present.[49] Toilet avoidance behavior also occurs,[50-53] and can affect pupil health by causing personal discomfort and even bowel or urinary problems.[51,52] However, no rigorous studies have quantified how characteristics of toilets that lead to improved use.

The purpose of this study was to quantify how school sanitation conditions are associated with pupils' use of sanitation facilities in 60 primary schools in Kenya. We characterize how varying pupil to toilet ratio was associated with the overall use of toilets at schools. We also characterize how toilet conditions, such as toilet cleanliness, age, type, and structure were associated with pupils' use at specific facilities.

METHODS

This study took place in 60 schools (17,564 pupils at baseline) from the Rachuonyo (N=33), and Kisumu East/Nyando (N=27) Districts in Nyanza Province, Kenya. Our study uses data gathered during a trial that was designed to understand if low-cost and easily implemented latrine cleaning supply and handwashing interventions decreased school absence.[106] Schools were randomized into three different arms: 1) a latrine cleaning arm, which received soap for handwashing, cleaning supplies for latrines, and training on maintenance, 2) a handwashing arm, which received soap only, and 3) a control arm, which received no intervention. All of the inputs in the intervention arms were provided after the baseline visit. Depleted or missing supplies were replenished to intervention schools as needed during the surveillance period, starting after the August school break and continuing to just prior to the final data collection. Upon completion of the study, the control arm received all the same inputs as the latrine cleaning arm. We used the data that were gathered in an observational setting, considering the toilet facility's actual cleanliness (and other facility characteristics) without regard to whether or not a school was randomized to receive or actually had latrine cleaning supplies.

Data collection

All data for this study were collected by trained enumerators from the Great Lakes University of Kisumu. Data collection was conducted from late May 2010 through early November 2010.

At each of five study rounds, enumerators observed sanitation conditions at each latrine and each urinal immediately upon arrival at the school in the morning. School visits were unannounced and on a randomly selected day during a given week within the study round period. These data were recorded using Syware Visual CE v10 software (Cambridge, MA) on Dell Axim x51 (Round Rock, TX) personal digital assistants. Enumerators recorded the latrine's or urinal's cleanliness (i.e. 'clean,' 'slightly dirty,' 'very dirty), the presence of visible feces (i.e. 'no visible feces,' 'small amounts of visible feces,' 'feces very visible) or visible urine (i.e. 'no visible urine,' 'small amounts of visible urine,' 'urine puddling'), the smell (i.e. 'minimal smell,' 'strong smell inside,' 'strong smell inside and outside'), the presence of flies (i.e. 'none,', 'some flies inside,' 'many flies inside'), and the presence of functioning shutters. The above three-level variables were re-categorized with the worst category being compared to the combined moderate and best category. This categorization was used in all analyses, and was chosen for simplicity of model interpretation. Because these variables were subjective to the enumerators, baseline measures were independently collected from two different enumerators at each toilet on the same day, and the inter-rater reliability was calculated (Appendix 5, Table A5.1). Only those variables with substantial inter-rater agreement, as defined by Landis and Koch to mean a Cohen's kappa statistic of over 0.6[110] were included in the final analyses. Although we collected data on sanitation conditions at the toilet-level, for most analyses we aggregated the variables to the level of the "block" or "toilet facility," in order to better relate these predictors to pupils' use of facilities. We use the terms "block" and "toilet facility" synonymously to mean a structure that contains any number of conjoined, similarly constructed toilets, which is typically assigned to either boys or girls for use.

Pupils' use of toilet facilities was also observed at these corresponding five school visits. Observations of toilet use always took place during the 30-minute morning break, between 11:00 and 11:30 AM across all schools, and always took place after the observation of toilet facilities. Pupils' toilet use was recorded on paper surveys by two trained enumerators who, from a discrete distance, tallied the number of pupils who approached and/or entered the block during the break period. It was not possible to observe the actual entrance into every individual toilet, because entrances were often on opposite sides of a given block. For this reason, toilet use was tallied at the block-level, rather than at the individual toilet-level; when the block only had one latrine – which was observed 36% of the time – then the block-level was also the toilet-level. However, the block-level is of interest, as it is the level of implementation of newly built groups of latrines or urinals. Because old, out-of-use toilets often remain standing, we limited all analyses to toilets that were actually used by pupils in grades 1-8, or indicated as in use by teachers at the school.

The type of toilet facility was recorded on paper at the first and final round only. Enumerators recorded whether the toilet was a traditional latrine, a ventilated improved pit latrine (VIP: a latrine with a pipe from the pit to the top of the latrine, which is covered with a fly screen at the top of the outlet), a prefabricated plastic latrine, an above ground vault composting latrine, or a urinal. There was substantial agreement between measures at the two visits (kappa=.76), with the primary source of disagreement being between VIP latrines and traditional latrines that were classified differently at the two visits (probably due to a missing fly screen or broken pipe). Above ground vaults were uncommon (1%). We created an 'uncertain/other' category for the previously mentioned toilets that were either difficult to categorize across the two visits or uncommon. During the first and final visit, the enumerators also observed whether or not the toilet was installed by the SWASH+ trial—a trial that installed many new toilets between 2007 and 2008—and this information was used as a proxy for newer toilet age. We do not have any other information on whether other new latrines were constructed besides those built by SWASH+.

Total and sex disaggregated school enrollment were collected during the first and final rounds using school records, and these enrollment totals, along with the number of working latrines and urinals, were used to calculate the pupil to toilet ratios, separately for boys and girls. We calculated the pupil to toilet ratio at each time point, allowing for slight changes if either the enrollment or if the number of in use toilets varied over time. We also used the enrollment numbers to create a school enrollment variable, where we categorized schools into enrollment quartiles.

To further capture important confounders, we collected data on community characteristics in the areas around each school. Enumerators conducted interviews with the heads of household at 25 systematically sampled households in the catchment area of each school. Enumerators collected both observed and head-of-household-reported information on wealth, and WASH conditions in the household. These data were then aggregated for use as community-level variables in our analyses. We used latrine coverage (percent of households with a latrine), and the wealth index score (a continuous variable constructed using principal component analysis)[103] as markers of latrine availability outside of school and of socio economic status, respectively.

Analysis

School and facility characteristics: We show descriptive statistics for the schools and toilet facilities under study. School-level data were aggregated across the five time points by taking the mean of the five follow-up values for a given school. Using this aggregated data, we report the mean and distribution among all 60 schools. Facility-level data are shown at the baseline visit. We show toilet use at both the school, and facility level.

Pupil to toilet ratio and school-level toilet use: We used a multivariable logistic mixed effects model with a binomial outcome to characterize the relationship between pupil to toilet ratio and toilet use. The effect of pupil to toilet ratio was modeled as piecewise linear, with the locations of the knots (i.e. breakpoints) being determined during exploratory graphical analyses (Appendix 5, Figure A5.1). Pupils' toilet use was measured as the total pupil uses at a school during the 30 minute break divided by the number of pupils at the school, by sex. Pupil to toilet ratio, calculated separately for each sex, was our primary predictor variable of interest. We report the adjusted odds ratio (aOR) comparing the odds of toilet use at various levels of pupil to toilet ratio, controlling for all the other variables in the model. Confounders were chosen *a priori* based on biological plausibility and from the very small existing literature on this topic. In preliminary analyses, interaction between sex and pupil to toilet ratio was assessed by including product terms in the model. However, we had predetermined that only interaction terms that were statistically significant with a p-value *(p)* of < 0.1 would persist in the final model, and by this criterion all interaction terms were excluded from our final model.

Specifically, the model that we used was

$$\begin{aligned}\text{logit}(\mu_{it}) = \alpha_0 + \beta_1 \text{Pupil to latrine ratio}_{it} + \beta_2(&\text{Pupil to latrine ratio}_{it} \\ &- 25)\text{X}_{it} + \sum_{q=1}^{Q} \gamma_q \text{ Confounders}_{it} + \text{u}_{0i}\,,\end{aligned} \qquad 1)$$

where μ_{it} is the expectation of the response variable (school toilet use). The outcome and predictors were observed at the t^{th} round, in the i^{th} school for each sex attending the school. β_1 represents the change in the log-odds of toilet use for each one unit increase in pupil to toilet ratio for schools with a pupil to toilet ratio of $\leq 25:1$ (adjusting for all the other variables in the model). X_{it} is a dummy variable that equals zero if the pupil to toilet ratio is ≤ 25 and equals one if pupil to toilet ratio is > 25. $\beta_1 + \beta_2$ represents the change in the log-odds of toilet use for each one unit increase in pupil to toilet ratio for schools with a pupil to ratio of $> 25:1$. u_{0j} represents a random intercept for each school. Confounders included sex, toilet coverage in the surrounding community, school enrollment quartiles, wealth index score, geographic district, and study round.

We used this model to predict the increase in toilet use given the theoretical addition of one or more toilets at a school of a given enrollment size. We assume a variety of initial pupil to toilet ratios but, for simplicity, we always assumed an enrollment of 150 boys and 150 girls—

numbers markedly similar to the population averages of our study population. The results might be interpreted as *if we were to add one sex-specific toilet to a school with a given sex-specific pupil to toilet ratio (e.g. 150:1, 75:1, 25:1, etc.) and with enrollment of 150 pupils of that sex, then the relative odds of toilet use would increase by 'aOR' times.*

We used the logistic link (which produces an odds ratio), because models did not converge with the log link (which produces a risk ratio). We did not use linear regression, as it is suboptimal to model proportions that have values near zero, where the relationship is not linear. We used a simple linear spline with a single breakpoint due to its simple interpretation and as it fit the data well (Figure 5.1; Appendix 5, Figure A5.1).

For all of our regression models, we accounted for correlation of the repeated measures over time and for correlation of observations within schools.[104] All analyses were performed in SAS 9.3 (SAS Institute, Cary NC). We accounted for the correlation between repeated measures by specifying the R correlation matrix using the GLIMMIX procedure. We chose a compound symmetric covariance structure and also verified that this was an appropriate option using the robust 'empirical' option. Observations within schools were also correlated, and we accounted for this correlation by including a random intercept for school.

Toilet facility characteristics associated with facility-level toilet use: We used a multivariable negative binomial mixed effects model to characterize the relationship between different toilet facility characteristics and the count of uses at specific facilities. The unit of analysis was the block or facility—a group similarly constructed and conjoined latrines/urinals. Pupils' use, measured at the facility, was the dependent variable, and that block's characteristics were the predictors. We report the adjusted incidence rate ratio (aIRR) for each predictor. The aIRR compares the count of pupil uses during the 30-minute break between a toilet facility with the risk category and a toilet facility with the referent category, all other variables in the model being held constant. Interaction between sex and each of the other primary exposures of interest was assessed by including product terms in the model. Interaction between facility shutters and toilet type (urinal vs. latrine) was also assessed, as urinals are often built purposefully without shutters and were hypothesized to be different than latrines. We predetermined that only interaction terms that were statistically significant with a *p* of < 0.1 would persist in the final model.

The general form of our adjusted model was

$$\log\left(\mu_{ijt}\right) = \alpha_0 + \sum_{p}^{P} \beta_p \text{ Facility characteristics}_{ijt} + \sum_{q=1}^{Q} \gamma_q \text{ Confounders}_{ijt} + \sum_{r=1}^{R} \delta_r \text{ Interaction terms}_{ijt} + u_{0j}\,, \qquad 2)$$

where μ_{ijt} is the expectation of the response variable (count of uses at facilities). The outcome and predictors were observed at the t^{th} round, on the i^{th} toilet facility, which is in the j^{th} school. The facility characteristics included the facility's cleanliness, age, presence of many flies, presence of shutters, number of toilets (using indicator variables), and type (VIP latrines, prefabricated plastic latrines, uncertain/other latrines, urinals, and traditional latrines as the referent,). Confounders included sex designation of the block, pupil to toilet ratio at the school, toilet coverage in the surrounding community, school enrollment quartiles, wealth index score, geographic district, and study round. Only the sex*cleanliness and the shutters*toilet type interaction terms met the criterion to be included in our final model. u_{0j} represents a random intercept for each school. We accounted for correlated data by specifying the working correlation matrix using the GLIMMIX procedure, as discussed previously.

RESULTS

School and toilet facility characteristics

We aimed to collect observations at 60 schools over five time points (300 observations), but due to school sporting events and holidays, we only collected complete data on 290 school observations (97%). An average of 301 pupils were enrolled per school, 48.6% of whom were girls. The mean number of toilets at each school was 9.8—5.0 of these being designated for boys and 4.8 being designated for girls. The median pupil to toilet ratio was 29 for boys (range: 11-129) and 30 for girls (range: 8-159). 60.6% of the schools reported having a water source, 88.3% had water available for cleaning, and 25.2% had supplies available for toilet cleaning. Surveys of households in the catchment areas around the schools revealed that on, average, 58.3% of the households had a working latrine.

The cleanliness variable captures several important aspects of pupils' exposure to human excrement. For example, 98.2% of the time when a latrine block was observed to have the 'most feces' and 80.5% of the time when a latrine block was observed to have 'puddles of urine,' that latrine block was also marked as being 'very dirty' (data not shown). Because the substantial correlation between these variables, only the cleanliness variable was used in adjusted analyses. On average during each of the five rounds, 635 pupils across the 60 schools used a toilet facility that was observed as being very dirty during the break (data not shown).

At each round, we observed an average of 258 toilet facilities and 594 latrines/urinals. Each block had an average of 2.3 toilets (range: 1-10; Table 5.2). Sanitation facilities varied in type, with 17.9% being traditional pit latrines, 39.5% ventilated improved latrines, 19.4% prefabricated plastic latrines, 14.0% were classified as uncertain or other types of latrines, and 8.5% were urinals. As for toilet conditions, 31.8% of the latrine facilities were observed to be very dirty, 12.8% had feces that were very visible, 8.9% had puddling urine, 19.4% had no shutter on the majority of toilets in the block, 10.0% had many flies inside, and 25.6% were had a strong smell both inside and outside the facility.

On average, 15.7% of the pupils within each school used a toilet during the break; use was similar for boys (15.0%) and girls (16.6%; Table 5.1). The average toilet facility was used 8.1 (SD 8.5) times per 30-minute break (Table 5.2). We did not observe use at the individual toilet-level, but knowing the total uses per school and the number of latrines per school we were able to calculate that each latrine was used on average by four pupils during the 30-minute break.

Factors associated with latrine use

Pupil to toilet ratio and school-level toilet use: As pupil to toilet ratio increases (becomes worse) there is a linear decrease in pupil toilet use with a natural breakpoint (change in slope) at a pupil to toilet ratio of 25:1 (Figure 5.1.a). However, as pupil to toilet ratio increases, the number of average uses per toilet also increases linearly up until a pupil to toilet ratio of 100:1 (Figure 5.1b), after which the average number of uses per toilet plateaus at between 9 and 10 uses per toilet (i.e. each toilet being used about once every 3-4 minutes throughout the entire 30 minute break). In adjusted analyses, the predicted change in the log-odds of a pupil using a toilet for each one unit increase in pupil to toilet ratio was -0.030 (95% confidence interval (CI): -0.045, -0.014, $p < 0.01$), and that slope persisted up to a pupil to toilet ratio of 25:1, after which the slope (i.e. $\beta_1 + \beta_2$) was -0.005 (95% CI: -0.007, -0.003, $p < 0.01$).

We used our model based estimates to predict the increase in school toilet use given the theoretical addition of one or more sex-specific toilets, at a school of an initial sex-specific pupil to latrine ratio and enrollment size (Table 5.3). Although we previously found the slope between use and pupil to toilet ratio to be flatter for pupil to toilet ratios ≥ 25, the predicted relative increase in the odds of toilet use from adding one, or several, toilets is much greater for the schools with a lower initial pupil to toilet ratio. For example, the aOR from hypothetically adding one toilet for a given sex of pupils is 1.45 (95% CI: 1.21-1.74) in a school with a starting pupil to toilet ratio of 150:1, whereas it is only 1.04 (95% CI: 1.02-1.06) in a school with a starting pupil to toilet ratio of 15:1. The predicted odds of toilet use increases 2.61 fold (95% CI: 1.91-3.57) by hypothetically adding ten toilets for a given sex of pupils in a school with an initial sex-specific pupil to toilet ratio of 150:1. A number of other contrasts of policy interest are also shown.

Toilet facility characteristics associated with facility-level toilet use: A number of facility characteristics were associated with toilet use (Table 5.4). We found an interaction in how dirty toilet facilities were used, based on whether the facility was designated for boys or girls (*p* =

0.10), and there was some evidence, although our estimate was imprecisely measured, that dirtiness may be a deterrent to toilet facility use for girls (aIRR=0.84, 95% CI: 0.71-1.01, p = 0.06), but not for boys (aIRR=1.00, 95% CI: 0.88-1.14, p = 0.98). We also found a significant interaction in how facilities with missing shutters were used, based on whether the facility contained urinals or latrines (p < 0.01). *Urinal* facilities that didn't have a shutter had increased use (aIRR=1.49, 95% CI: 1.13-1.96), whereas *latrine* facilities that didn't have a shutter had little change in use (aIRR=0.89, 95% CI: 0.73-1.08), each compared to their counterpart with shutters. Urinal facilities without shutters were designated for primarily for boys (94%). We also observed increased use at newer facilities compared to older ones (aIRR=1.16, 95% CI: 1.05-1.29).

The toilet type and structure also played an important role in facility use. We observed increased use at urinals without shutters (aIRR=1.86, 95% CI: 1.50-2.32), and decreased use at prefabricated plastic latrines (aIRR=0.67, 95% CI: 0.52-0.86), each compared to traditional pit latrines. Increasing number of toilets in a block was associated with increased use at that block, however, use did not increase to the degree expected, given the added capacity of the block (Figure 5.2).

DISCUSSION

The purpose of this study was to characterize how a school's pupil to toilet ratio, and a toilet facility's characteristics are each associated with toilet use patterns. This is the first study to rigorously characterize many of these relationships, and as such, provides important insights into how to improve pupils' toilet use and resource allocation for school sanitation.

Our data support the importance of lower pupil to toilet ratios, and quantify the benefits of following guidelines such as those set by the World Health Organization (25:1 for girls, and 50:1 + one urinal for boys) [29] and the Kenyan government (25:1 for girls, and 30:1 for boys) .[54] We also observed increased use of urinals, compared to traditional pits, which is further support for the current WHO guidelines, of including a urinal for boys. The greatest increases in toilet use was seen among schools that easily superseded these guidelines (e.g. <15:1). However, we show that schools with worst ratios, are most likely to benefit, in terms of increased toilet use, from the addition of even a small number of toilets.

In our fully adjusted model, we found some evidence suggesting facility dirtiness may deter girls from toilet use, but not boys. The finding that many pupils are not discriminating which facilities they used based on toilet cleanliness is an important one, as facility cleanliness may be equally, or even more important for pupils' health and attendance than the pupil to toilet ratio.[31] This finding is also different from previous studies, which detected both a meaningful and statistically significant associations between toilet cleanliness and toilet use for both boys and girls.[50,55] However, our study offers the methodological improvement of control for a number of potential confounders. To replicate these previous studies we performed an unadjusted sub-analysis (data not shown) and were also able to find a statistically significant association, however as we added necessary confounders into the model, this association dissipated. Another important difference between our study and previous studies is that we were able to use observed measures of facility characteristics rather than pupil-reported measures. It is possible that our *observed* measure of cleanliness were different from how pupils actually *perceive* and self-report toilet cleanliness. For example, our enumerators were trained to denote the toilet as dirty based on the presence of dirt, trash, feces, or urine on the floor or walls of the toilet, whereas it is possible that pupils judge toilet cleanliness based on these, but also other factors such as the toilet's age, structure, or type, which we captured using other variables.

The number of toilets in the block was an important factor for use. However, we found that increasing the number of toilets in a block does not increase the use proportional to its increased capacity (e.g. doubling the number of toilets does not double pupil use at that block; Figure 5.2). There are a number of possibilities as to why children may avoid using blocks with more toilets. In other studies, children have reported a number of deterrents to toilet use, including privacy concerns (e.g. insecurity of being heard),[50,51,53] teasing and bullying,[50-52] and smell,[50,51,53] each of which is probably exacerbated by concentrating toilets into larger blocks.

The amount of privacy required for urination may be different than the amount of privacy required for defecation. This is reflected in our observation that *urinal* facilities that didn't have a shutter had increased use, whereas *latrine* facilities that didn't have a shutter had a point estimate reflecting decreased use although the 95% CI included the null. However, our finding of increased use in urinals without doors is implicitly sex-specific, as 94% of these urinals were actually designated for boys.

Our study has several limitations. Our study is observational, and therefore has the potential for unmeasured confounding. However, we are able to control for many conceivable confounders. Furthermore our results are biologically plausible and confirm many long-standing, yet untested beliefs. It would also be difficult, and possibly unethical, to randomize some of our exposures of interest, and so observational studies may be the design of necessity. A second limitation is that we were not able to obtain toilet-level pupil use, or the exact reasons for a pupil using a block (e.g. urination, defecation, menstrual hygiene management, etc.). We were, however, able to develop valid models that predict block level visits, controlling for the number of toilets within a block. Aggregating latrine-level data, allowed us to observe the relationship between our latrine-level predictors and facility-level use, however, these relationships should be interpreted with care, because when facilities contain several toilets, latrine-level decisions may not always be reflected in what is observed at the block-level (i.e. ecological correlations do not necessarily represent individual correlations). Finally, our results should be generalized carefully. Our study coincided with a 'light-touch intervention' trial that provided intervention schools cleaning supplies, and it is not clear what we would have observed had those intervention schools not received any cleaning supplies (e.g. toilets being even dirtier). Our results are most generalizable to similar schools; for example rural, low-resource schools in sub-Saharan African countries.

CONCLUSIONS

There are a number of factors that play important roles in pupils' use of school toilets, including pupil to toilet ratio, toilet type, toilet age, and number of toilets in the toilet block, and possibly cleanliness. Cleanliness is of particular interest, as it is likely related to pupils' exposure to human excrement. This study provides important insights into how to more effectively improve pupil toilet use in schools in developing countries, potentially leading to a better allocation of resources for school sanitation, and to improved health and educational outcomes for children.

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Author Contributions

Bethany Caruso, Matthew Freeman, and Richard Rheingans were involved in the design of the initial trial. Bethany Caruso participated in the data collection. Joshua Garn, Carolyn Drews-Botsch, Michael Kramer, Babette Brumback, and Matthew Freeman each contributed to the methodologic design of this study, and Joshua Garn performed and takes responsibility for all analyses. Joshua Garn drafted the manuscript. All authors participated in the editing of the manuscript, and in the approval of the final manuscript.

Conflicts of Interest

The authors declare no conflict of interest.

Table 5.1. School demographics (N=60 schools), aggregating 5 follow-up measures.*

Variable	**Mean or % (SD)**
Pupils enrolled per school‡	301.4 (166.7)
Percentage of girls per school	49% (4)
Pupil to toilet ratio for boys‡	37.0 (24.0)
Pupil to toilet ratio for girls‡	36.6 (24.6)
Number of toilets per school	9.8 (3.9)
Number of designated boy toilets per school	5.0 (2.0)
Number of designated girl toilets per school	4.8 (2.4)
Percentage of households in surrounding community with working latrines	58% (20)
Percentage of schools with a water source	61% (38)
Percentage of schools with water available for toilet cleaning	88% (20)
Percentage of schools with supplies for latrine cleaning	25% (33)
Percentage of pupils in school that used a toilet during the 30 minute break	16% (6)
Percentage of boys in school that used a toilet	15% (6)
Percentage of girls in school that used a toilet	17% (7)

*The 5 follow-up values were averaged together for each school, and the distributions of those average school-values are shown here. ‡Data are skewed. Median enrollment was 258.8 (range: 94.2-830.4). Median pupil to toilet ratio for boys was 29 (range:11-129) and median pupil to toilet ratio for girls was 30 (range: 8-159).

Table 5.2. Toilet facility conditions at baseline visit.

Variable	N (%) or mean (SD)
Total number of toilet facilities	258 (100%)
Mean toilets per facility*	2.3 (1.4)
Mean pupil use per toilet facility*	8.1 (8.5)
Toilet facility conditions[‡]	
'Very dirty'	82 (31.8%)
'Feces very visible'	33 (12.8%)
'Most visible urine'	23 (8.9%)
'Many flies inside'	27 (10.5%)
'No shutter'	50 (19.4%)
'Strong smell inside and outside'	66 (25.6%)
Newer age[§]	128 (49.6%)
Number of toilets per facility	
1 toilet	92 (35.7%)
2 toilets	76 (29.5%)
3 toilets	46 (17.8%)
4 toilets	27 (10.5%)
5 toilets	6 (2.3%)
6 or more toilets	11 (4.3%)
Type of toilet facility	
Traditional latrine	45 (17.9%)
Ventilated improved pit latrine	102 (39.5%)
Prefabricated plastic latrines	50 (19.4%)
Uncertain/other[‖]	36 (14.0%)
Urinal	22 (8.5%)
Facilities assigned to girls	117 (46.6%)

*Data were skewed. Median latrines per block was 2 (range: 1-10). Median use per block was 6 (range: 0-55). [‡]The worst category is shown, and the combined moderate and best category are the reciprocal. [§]Whether the toilet facility was from SWASH+ served as a proxy for newer toilet age. [‖]The uncertain/other category primarily consists of VIP latrines that were not easily categorized (e.g. missing a fly screen/broken pipe).

Table 5.3. Contrast of adjusted odds ratio for school toilet use and school pupil to toilet ratio, given one additional toilet is added to a school.*

Starting sex-specific pupil:toilet ratio	Hypothetical addition of toilets, for a given sex of pupils	New sex-specific pupil:toilet ratio*	Predicted increase in use. aOR‡ (95% CI)
15:1	+ 1 toilet	13.6:1	1.04 (1.02-1.06)
25:1	+ 1 toilet	21.4:1	1.11 (1.05-1.18)
50:1	+ 1 toilet	37.5:1	1.06 (1.03-1.10)
75:1	+ 1 toilet	50:1	1.13 (1.07-1.20)
150:1	+ 1 toilet	75:1	1.45 (1.21-1.74)
25:1	+ 5 toilets	13.6:1	1.40 (1.18-1.67)
50:1	+ 5 toilets	18.8:1	1.36 (1.23-1.51)
75:1	+ 5 toilets	21.4:1	1.43 (1.27-1.61)
150:1	+ 5 toilets	25:1	1.86 (1.38-2.51)
150:1	+ 10 toilets	13.6:1	2.61 (1.91-3.57)

*Assuming a school enrollment size of 150 boys/girls. The aOR compares the odds of school toilet use during the 30-minute break between schools with varying pupil to toilet ratios, all other variables in the model being held constant. ‡Model adjusts for sex, school enrollment quartiles, toilet coverage in the community, wealth index score, geographic district, and study round (also accounts for correlation between repeated measures and clustering within schools).

Table 5.4. Adjusted incidence rate ratio for facility use for each predictor of interest.*

	aIRR[‡]	95% CI	*p*
Toilet facility conditions[§]			
'Very dirty'[‖]	-		
Dirty facility for girls	0.84	0.71-1.01	0.06
Dirty facility for boys	1.00	0.88-1.14	0.98
'Many flies inside'	1.03	0.89-1.20	0.69
'No shutter'[‖]	-	-	
No shutter for urinals	1.49	1.13- 1.96	<0.01
No shutter for all other latrines	0.89	0.73-1.08	0.22
Newer age[¶]	1.16	1.04-1.29	<0.01
Type of toilet facility			
Traditional pit latrine	referent		
Ventilated improved pit latrine	1.12	0.94-1.33	<0.01
Prefabricated plastic latrine	0.67	0.52-0.86	
Uncertain/other**	1.04	0.87-1.23	
Urinal[‖]	-		
Urinals without shutters	1.86	1.50-2.32	<0.01
Urinals with shutters	1.11	0.78-1.60	0.56
Number of toilets per block			
1 toilet	referent		
2 toilets	1.14	0.97-1.34	<0.01
3 toilets	1.46	1.21-1.75	
4 toilets	1.89	1.55-2.29	
5 toilets	1.94	1.36-2.79	
6 or more toilets	2.67	2.15-3.33	

*aIRR compares the count of pupil uses during the 30-minute break between a block with the risk category and a block with the referent category, all other variables held constant. [‡]Model controlled for each of the variables shown in this table, and also the sex designation of the block, the pupil to toilet ratio at the school, latrine coverage in the surrounding community, school enrollment quartiles, wealth index score, geographic district, and study round. The model also accounts for correlation between repeated measures and clustering within schools. [§]Each of these is a binary variable, where the inverse serves as the referent. [‖]Significant interactions were detected so subgroup specific aIRRs are reported. [¶]Whether the toilet facility was from SWASH+ served as a proxy for newer toilet age. **The uncertain/other category primarily consists of VIP latrines that were not easily categorized (e.g. missing a fly screen, or a broken pipe).

Figure 5.1. (**a**) Proportion of pupils who used a toilet at each school as a function of pupil to toilet ratio. (**b**) Average uses per toilet at each school as a function of pupil to toilet ratio. Pupil to toilet ratio was calculated separately for boys and girls. Both figures were fit with a piecewise trend line.

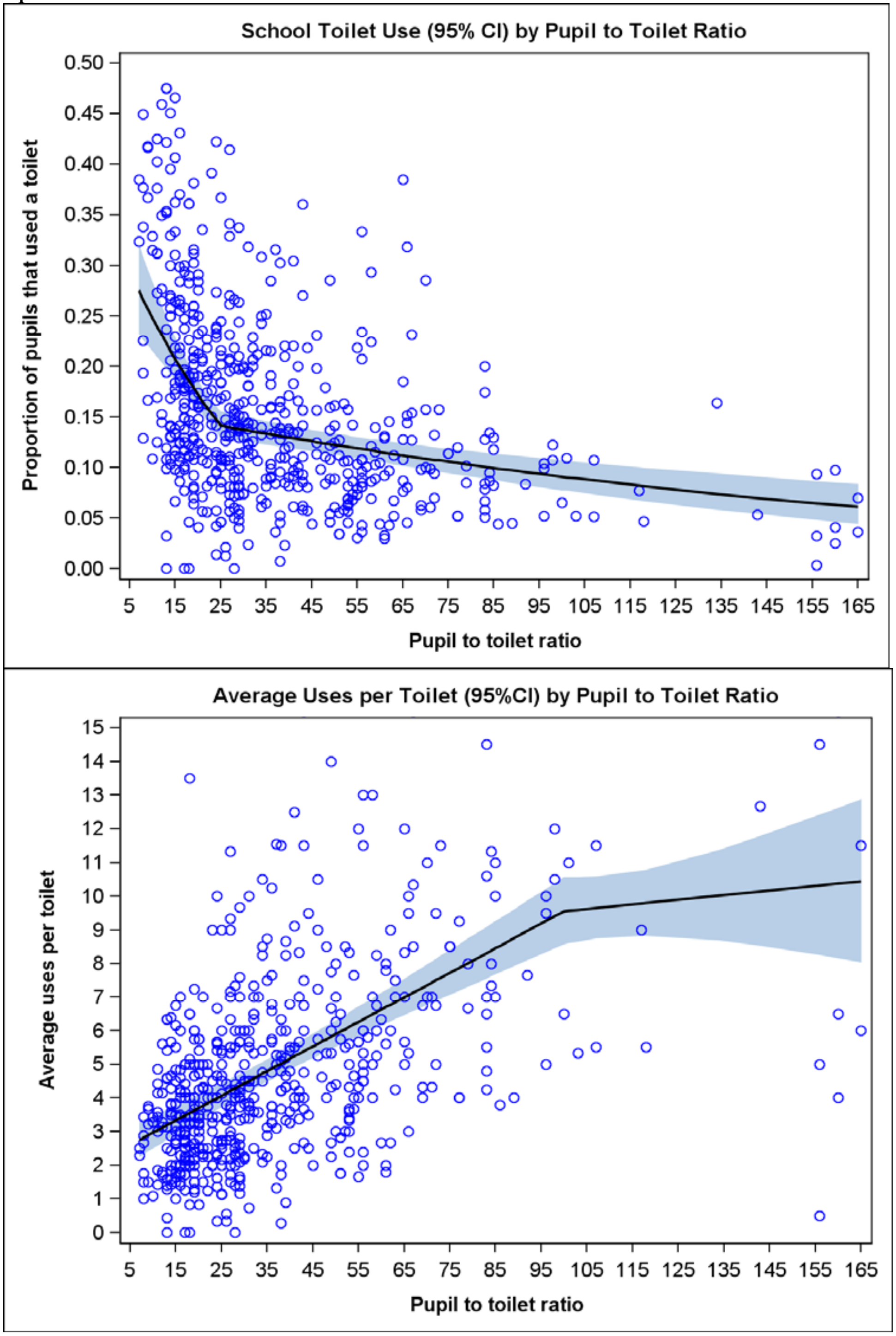
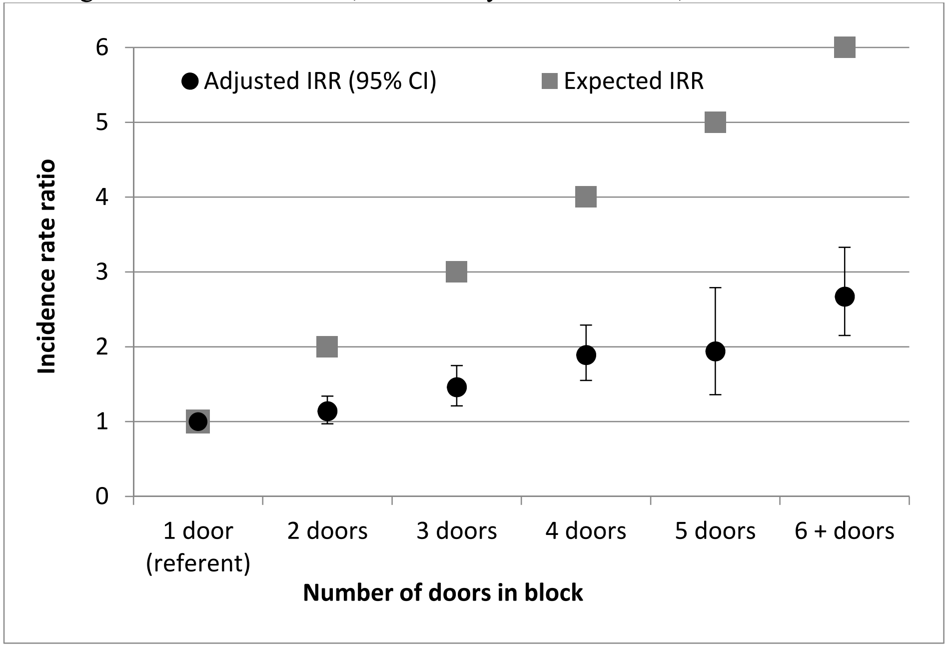


Figure 5.2. Adjusted IRR and expected IRR comparing the count of pupil uses in a facility with a given number of toilets, to a facility with one toilet, all other variables held constant.



CHAPTER 6: Conclusions and future directions

Prior to this dissertation, little had been done to understand how suboptimal adherence to WaSH and the complex interdependencies between different WaSH components impacts infectious disease outcomes. Each of our three studies addressed different, yet complimentary aspects of WaSH adherence, and contributes to a further understanding of the impact of WaSH on pupil health in Kenya. For our first study, we performed an instrumental variable analysis to estimate causal effects of school-level WaSH adherence on several pupil-level health outcomes. For our second study, we characterized how WaSH exposures were associated with *A. lumbricoides* reinfection, emphasizing the interactions and complementarity between different WaSH technologies and behaviors. For our final study, we characterized how school sanitation conditions were associated with pupils' use of sanitation facilities.

In both of our first two studies there were indications that adherence to WaSH was beneficial for several of the outcomes, among either the more adherent schools or among adherent subsets of pupils. Specifically, our instrumental variable analysis revealed that among the water scarce schools there was a strong preventive effect of decreased diarrheal illness with increased school-level WaSH adherence. For this outcome and several of the STH outcomes we observed that IV point estimates were further from the null than ITT point estimates, suggesting an increased preventive effect with increasing school-level adherence. In our second study, we observed that *A. lumbricoides* reinfection was lower among those individuals who always practiced handwashing *and* also had an improved water source that reliably produced water. We also observed that these handwashing effects were stronger when handwashing was practiced both at school and at home, rather than at just one or the other. Our second study is suggestive that adherence to unique WaSH combinations may be important for reducing exposure to pathogens and *A. lumbricoides* reinfection. For example, the model that considered interactions between handwashing and having an improved water source showed the strong interdependence of these two WaSH exposures.

The results from our study suggest that there may be a natural hierarchy of interdependence between different WaSH technologies and behaviors. In our first two studies, a common finding was the dependence upon a quality water source. In the first study, the most compelling results were observed among the water scarce schools – the group of schools that received a community water source. In the second study, handwashing was only associated with decreased *A. lumbricoides* reinfection among pupils with access to a quality water source. Both studies are suggestive that a quality water source may be an important component for WaSH to prevent these infectious diseases. Sanitation provisions, or at least having more latrines in a school, didn't notably prevent diarrheal illness in study one and was even associated with increased STH infection in study two. It is possible that latrine dirtiness may have increased pupils' exposure to disease.[31] We later found in our third study, that lower pupil to latrine ratio is associated with increased latrine use[106] and this situation of increased latrine use among schools with better latrine coverage could possibly propagate pupils' exposure to pathogens; especially if latrines were dirty. Sanitation should play a positive role in the prevention of STH infection and diarrheal illness, but our studies suggest that just having access to latrines may not be sufficient. This is supported by similar null findings from a large recent trial in India.[107] It is possible that variations in latrine cleanliness, latrine use, and handwashing after latrine use must additionally all play important roles in order to reduce exposure to pathogens and to reduce these illnesses.

For our third paper we characterized factors associated with pupils' use of sanitation facilities.[106] We found a number of factors were associated with pupils' use of school toilets, including pupil to toilet ratio, toilet type, toilet age, the number of toilets in the toilet block, and possibly cleanliness. This was the first study to our knowledge to rigorously characterize these associations between sanitations conditions and use, and serves as a logical step towards finding ways to improve pupils' use of toilet facilities. The actual *use* of sanitation facilities – and also of each of the other WaSH components – is a critical component that is often ignored in studies. Our study will be useful to bridging this gap, and may be informative for policy makers as they determine how to most effectively allocate resources for sanitation.

While there is a continued push to increase worldwide access to WaSH,[1,111] this needs to be done in a way that also increases the appropriate *use* of WaSH. Our studies are only a beginning, in understanding how suboptimal adherence to WaSH and complex interdependencies between different WaSH technologies and behaviors impact infectious disease outcomes. Our studies also make a significant contributions to the literature. For example, a lesson from our first study where we observed stronger effects among adhering schools, might be that implementers spend more time and resources implementing interventions (rather than finding new technologies to implement). Potential lessons from our second study, might be that researchers should assess complex interactions, and that future interventions might be comprehensive enough to satisfy interdependencies between different WaSH technologies and behaviors, such as the interdependence of handwashing on water. A potential lesson from our third study, is that various factors might contribute to adherence, and that policy makers and researchers might use this information to develop interventions that optimize adherence. Future studies should consider and implement WaSH interventions that might improve adherence, they should consider the natural hierarchy and interdependencies between different WaSH technologies and behaviors, and they should monitor the efficacy of interventions *in regards to adherence*. As an intermediate outcome, improved adherence will certainly have downstream effects and play an important role in improving pupils' health.

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APPENDIX

Appendix 3.

Appendix 3.1 Structural nested model estimation.

The SNM, relevant notation, and estimation algorithm are shown below:[58]

$h(E^{W1}(Y_{ij}(a)|A_i=a, R_i)) - h(E^{W1}(Y_{ij}(0)|A_i=a, R_i)) = a_v\xi$

$Y_{ij}(a)$ represents the potential outcome for the jth pupil in the ith school at some observed adherence level a. A_i represents either a multinomial or continuous school-level adherence variable. For example, in the water available schools where we have three study arms we let $A_i=0$ when the ith school adequately adhered to zero of the three WaSH components, let $A_i=1$ when the ith school adequately adhered to one or two components, and we let $A_i=2$ when the ith school adequately adhered to all three components. a_v represent a vector for the multinomial adherence variable. R_i represents a multinomial school-level randomization variable. For example, we let R_i represent a multinomial variable denoting randomization to one of the three study arms in the water available group. E^{W1} represents a weighted expectation, which accounts for individual-level confounders using the weight W_{ij1}. h represents a link function (e.g. $h(p) = p$; $h(p) = \log(p)$; $h(p) = \log(p/(1-p))$). ξ represents a causal effect – for example a RD, logRR, or logOR corresponding to the link function that was used to transform the left parts of the model.

We must first produce the overall weights (W_{ij}). W_{ij} is the product of confounding weight (W_{ij1}) and the sampling weights (W_{ij2}). W_{ij1} is the weight that is used to remove the association between individual-level confounders and randomization. W_{ij2} is the inverse of the probability of selection of each pupil into the study, and is necessary here because our study used a complex sample design. W_{ij1} and W_{ij} are produced as shown:

```
proc surveylogistic data=diarrheal_illness;
        class pupil_grade;
        model R = pupil_grade / link=glogit;
        output out=invweights predicted=predprobs;
        weight Wij2;
        strata stratum;
        cluster psu;
run;

data weights;
        set invweights;
        Wij1 = .;
        Wij1 =1/predprobs;
        Wij = Wij1* Wij2;
        if _LEVEL_ = R;
run;
```

To estimate the parameters of interest in the structural nested mean model, we used an iterative algorithm which applies Newton's method to solve the two estimating equations below.

(1) $\sum_i \sum_j W_{ij} D_i^T [Y_{ij} - \mu (A_i, R_i; \eta)] = 0$, and
(2) $\sum_i \sum_j W_{ij} R_{vi}^T [h^{-1} (h(\mu(A_i, R_i; \eta)) - A_{vi}\xi) - \alpha] = 0$,

where η represents the $E^{W1}(Y_{ij} | A_i, R_i)$, α represents the $E^{W1}(Y_{ij}(0))$, ξ represents the causal effect of adherence on the outcome given A_i and R_i, and D is a function of A_i and R_i, defined as $(A_{vi}, R_{vi}, A_i{*}R_i)^T$, R_{iv} is a vector of dummy variables representing randomization to one of three arms, and all other variables are as previously defined. A SAS program which was designed for a three armed trial with two strata was obtained from Brumback,[58] and was slightly modified to allow for variation in either the number of strata or the number of study arms. Generally, the steps to solving these estimating equations are as follows.

Step 1. We first solve the estimating equation (1) using a fully parameterized model, to obtain an estimate of η for each participant. For instance, if our outcome followed a binomial distribution, we might use PROC GENMOD as shown:

```
proc genmod data=sim.data0;
        model Y= A1 A2 R1 R2 A1*R1 A1*R2 A2*R1 A2*R2/dist= bin link=logit;
        weight Wij;
        output out=sim.xbeta xbeta=linpred;
run;
```

Step 2. Letting $h^{-1}(.) = g(.)$, substitute $\hat{\eta}$ from equation (1), for η in equation (2). Using Newton's method, we linearize $g(D_i \hat{\eta} - A_{vi}\xi)$ about an initial (or current) estimate of ξ, ξ^t, where t indexes the iteration number. Equation 2 reduces to:

(2a) $\sum_i \sum_j W_{ij} R_{vi}^T [g(D_i \hat{\eta} - A_{vi}\xi) - \alpha] = 0$

$g(D_i \hat{\eta} - A_i\xi)$ is approximated by $(Y_i^* - A_{vi}^* \xi^t)$, where Y_i^* and A_{vi}^* are derived using Taylor series approximation. For instance, for the logistic structural nested model, $g(x) \equiv \exp(x)/(1+\exp(x))$, and we let $Y_i^* \equiv g(D_i \hat{\eta} - A_{vi}\xi^t) + A_{vi}^* \xi^t$, and $A_{vi}^* \equiv A_{vi} g(D_i \hat{\eta} - A_{vi}\xi^t)(1 - g(D_i \hat{\eta} - A_{vi}\xi^t))$. Equation (2) further reduces to:

(2b) $\sum_i \sum_j W_{ij} R_{vi}^T [Y_i^* - A_{vi}^* \xi - \alpha] = 0$

For example, when using the logistic structural nested model Y_i^* and A_{vi}^* can be calculated within a data step in SAS using the linear predictor (output in step 1), the adherence variables (A_{vi}), the outcome variable (Yi), and an initial estimate of the causal effect (ξ^t) using the code:

```
        lp=linpred-A1*squig1 - A2*squig2;
        expitlp=exp(lp)/(1+exp(lp));
        Ystar = expitlp + (A1*squig1 + A2*squig2)*expitlp*(1-(expitlp));
        Astar1 = (A1*expitlp)*(1-(expitlp));
        Astar2 = (A2*expitlp)*(1-(expitlp));
```

If we were instead using the log structural nested model, we would let $g(x) \equiv \exp(x)$, and we let $Y_i^* \equiv g(D_i \hat{\eta} - A_{vi}\xi^t) + A_{vi}^* \xi^t$, and $A_{vi}^* \equiv A_{vi} g(D_i \hat{\eta} - A_{vi}\xi^t)$. Y_i^* and A_{vi}^* would then be calculated using the following code within a SAS data step:

```
        lp=linpred-A1*squig1 - A2*squig2;
        explp=exp(lp);
        Ystar = explp*(1+ A1*squig1 + A2*squig2);
        Astar1 = A1*explp;
```

```
Astar2 = A2*explp;
```

Step 3. Solve equation (2b) using instrumental variable software using Y_i* as the response variable, R_i as the instrument, and A_i* as the endogenous regressor, and obtain updated estimates of ξ^t. For example, using SAS's PROC SYSLIN:

```
proc syslin data=sim.iv 2sls;
        endogenous Astar1 Astar2;
        instruments R1 R2;
        model Ystar =Astar1 Astar2;
        weight Wij;
run;
```

Step 4. Update the initial estimate of ξ^t.

Step 5. Repeat steps 2 to 4 iteratively, until all parameters converge on a fixed value.

Step 6. Calculate the RR(a)= $(E^{W1}(Y_{ij}(a)|A_i=a)) / E^{W1}(Y_{ij}(0)|A_i=a))$. The numerator of the RR(a), $(E^{W1}(Y_{ij}(a)|A_i=a))$, is observed in the data and therefore easily calculated regressing Y_{ij} on A_i from the observed data while using the overall analysis weights (e.g. W_{ij}). Given the study assumptions are met and that the first estimating equation is specified correctly (e.g. by using a fully saturated model), then in the final iteration of $(Y_i^* – A_i^*\xi^t)$, that is $Y_i(0)$, represents true potential outcome had that participant's school been assigned to the control arm (had R_i been equal to 0). The denominator $(E^{W1}(Y_{ij}(0)|A_i=a))$ can therefore be estimated by regressing $E^{W1}(Y_i(0))$, from the final iteration in step 5, on our observed adherence variable, A_i.

Step 7. To estimate the variance, we use the jackknife estimator of the variance. This is a method where we systematically delete each primary sampling unit (school) and estimate the parameter of interest without that individual school, following steps 1-6 above repeatedly for all schools. The variance is then estimated by measuring the sum of the squared differences of each estimate from the initial parameter estimate, which is multiplied by a correction factor that accounts for the stratification. The jackknife estimator is:

$$\hat{\mathrm{var}}(\hat{\theta}) = \sum_{h=1}^{H}((C_h - 1)/C_h) \sum_{c=1}^{C_h}(\hat{\theta}^{hc} - \hat{\theta})^2,$$

where $\hat{\theta}$ represents the overall parameter estimate and $\hat{\theta}^{hc}$ represents the paramater estimate deleting the c^th^ school which is in the h^th^ stratum (district).

Appendix 4.

Appendix 4.1. Child and school WaSH questionnaires.

CHILD QUESTIONNAIRE

NOTE: Samples must be taken for every child, which means the information above must be completed for all children selected to be examined and surveyed in each school. For every other child (half of the total children selected), complete the full child questionnaire on the next page.

If the pupil is selected for the full questionnaire you might start by introducing yourself and trying to help them feel comfortable. If it hasn't been done already, give a brief background, and tell why the survey is important. Explain to the pupil that there aren't any right or wrong answers to any question, and that we really appreciate their honesty. Explain to the pupil that they don't have to answer any question that they don't want to answer. Ask the pupil if they would like to participate.

CHILD INFORMATION	
Primary school code: |_____|_____|_____|_____|_____|_____|	**District Code:** |____|____|____|
Round: ☐ **1** ☐ **2** ☐ **3** ☐ **4** ☐ **5**	**Pre or post deworming treatment:** ☐ **pre** ☐ **post**
Child ID |___|___|___|___|___|___|___|___|___|	
Age: |_____|_____| **years** **Class:** |_____|_____|	**Gender:** ☐ **Male** ☐ **Female**

CHILD QUESTIONNAIRE

KENYA NATIONAL DEWORMING PROGRAMME

RESIDENCE
"Now I would like to ask you a few questions about your home and family."
A1. What is the name of the village you reside in now? ________________________________
FAMILY AND SIBLINGS
B1.How many people live in your household? (e.g. share a cooking pot)………..…………………………... [___]
B2. How many brothers and sisters do you have?... [___]
B3.How many of these siblings attend school? …………………………………………………….…...... [___]
B4.How many of these siblings are under 5 years old?... [___]
HOUSEHOLD WEALTH INFORMATION
C1. Who is the head of household? **Read out options, only enter one answer**………………………………………………………………… [__] 1 = Father; 2 = Mother; 3 = Grandparent; 4 = Sibling; 5 = Other *specify* [_____________________]
C2. What is the highest level of education attained by the household head? **Read out options, only enter one answer**………………………………………………………………… [__] 1 = No formal education; 2 = some primary; 3 = Primary complete; 4 = Secondary complete or above; 5 = Don't know
C3. What type of walls does your house have? **Read out options, only enter one answer**………………………………………………………………… [__] 1=Stone or bricks or cement; 2=Clay or mud; 3=Wood; 4=Iron sheets; 5=Other *specify* [_______________]

C4. What type of floors does your house have?
Read out options, only enter one answer……………………………… [__]
1=Cement or tiles or linoleum; 2=Wooden planks; 3=Earth or sand; 4=Iron sheets;
5=Other *specify* [____________________]

C5. What type of roof does your house have?
Read out options, only enter one answer……………………………… [__]
1=Tiles; 2=Iron sheets; 3=Grass or thatch; 4=Makuti; 5=Other (*specify*) [____________________]

C6. In your house, are there any of the following? **Read out and fill with 1= Yes; 2 = No:**
Car……………………………… [__]
Motorbike……………………………… [__]
Bicycle……………………………… [__]
Mobile phone……………………………… [__]
Radio……………………………… [__]
Television……………………………… [__]
Sofa set……………………………… [__]
Electricity……………………………… [__]

DEWORMING USE

"Now I would like to ask you about previous deworming."

D1. Have you received treatment for worms in the last year? ……………………………… [__]
Read out options, only enter one answer
1 = Yes; 2 = No; 3 = Don't know

D2. **If yes to D1,** Where did you receive treatment? ……………………………… [__]
Read out options, only enter one answer
1 = School**;** 2 = Health centre; 3 = Home; 4 = Community programme; 5 = Shop; 6= Others *specify* [________]

D3. **If yes to D1,** How many tablets were you given?
Enter number ……………………………… [__|__|__]
Enter if 999, if Don't know

D4. **If yes to D1,** What colour were the tablets?
Enter one answer ……………………………… [__]
1 = White; 2 = Yellow; 3 = Blue; 4 = Don't know; 5 = Others **…***specify* [__________________]

HOUSEHOLD WASH INFORMATION

"Now I would like to ask you a few questions about your access and use of water, sanitation, and hygiene at home." Note: If the student attends a boarding school, these questions relate where they sleep (and not their family's household).

E1. Do you have a toilet/latrine in your home/compound?……………………………… [__]
1=Yes; 2=No

E2. **If yes to E1,** Is that toilet/latrine shared with other households/compounds?……………………………… [__]
1=Yes; 2=No

E3. At home, where do you usually go to urinate……………………………… [__]
Read out options, only enter one answer
1=In my latrine/toilet; 2=In a latrine outside compound; 3=Around/outside compound (e.g. in the bush); 4=In the bathroom/shower

E4. At home, where do you usually go to take a long call (defecate)?……………………………… [__]
Read out options, only enter one answer
1=In my latrine/toilet; 2=In a latrine outside compound; 3=Around/outside compound (e.g. in the bush)

E5. Last time you took a long call **at home**, did you use a latrine/toilet?……………………………… [__]
1=Yes; 2=No

E6. At home, do you have something to use for cleaning up after a long call always, sometimes, or never? .... [__]
1=Always; 2=Sometimes; 3=Never

E7. What do you usually use to clean up after taking a long call when at home?……………………………… [__]
Read out options, only enter one answer
1=Tissue paper; 2=Water; 3=Newspaper; 4=Books; 5=Leaves; 6=Rocks; 7= Nothing

E8. Is there a place (e.g. container, basin, sink) at home for you to wash your hands after you take a long call?[__]
1=Yes; 2=No

E9. **If yes to E8,** Is water available for washing your hands at that place always, sometimes, or never?........... [__]
1=Always; 2=Sometimes; 3=Never

E10. **If yes to E8,** Is handwashing soap available at that place always, sometimes, or never?.......................... [__]
1=Always; 2=Sometimes; 3=Never

E11. **If yes to E8,** Did you wash your hands with **soap and water** at this place the last time you took a long call at home?.. [__]
1=Yes; 2=No

E12. At home, do you wash your hands with soap and water after taking a long call always, sometimes, or never?.. [__]
1=Always; 2=Sometimes; 3=Never

E13. What is the <u>main</u> source of water for drinking in your home? ……………………………….[__]
Read out options, only enter one answer
1=Piped/tap water; 2=Borehole or well; 3=Rain water; 4=Stream, lake or river; 5=Bottled water

E14. When you are at home, do you use this water source for drinking water always, sometimes, or never? ..... [__]
1=Always; 2=Sometimes; 3=Never

SCHOOL WASH INFORMATION

"Now I would like to ask you a few questions about your access and use of water, sanitation, and hygiene at school."

F1. At school, where do you usually go to urinate?.. [__]
Read out options, only enter one answer
1=Latrine/toilet at school; 2=To a latrine near the school; 3=Around/outside school compound (e.g. in the bush); 4=I wait/hold it until school is over

F2. At school, where do you usually go to take a long call?.. [__]
Read out options, only enter one answer
1=Latrine/toilet at school; 2=To a latrine near the school; 3=Around/outside school compound (e.g. in the bush); 4=I wait/hold it until school is over

F3. When your friends have to take a **long call** at school, do you think they use a latrine always, sometime, or never?..[__]
1=Always; 2=Sometimes; 3=Never

F4. Last time you took a **long call** at school, did you use a latrine/toilet? ....[__]
1=Yes; 2=No

F5. Does the school provide something to use for cleaning up after a long call always, sometimes, or never? ... [__]
1=Always; 2=Sometimes; 3=Never

F6. What do you usually use to clean up after a long call when at school?.. [__]
Read out options, only enter one answer
1=Tissue paper; 2=Water; 3=Newspaper; 4=Books; 5=Leaves; 6=Rocks; 7= Nothing

F7. Does the school provide a place (e.g. container, basin, sink), for you to wash your hands after taking a long call?.. [__]
1=Yes; 2=No

F8. **If yes to F7**, is soap available at that place always, sometimes, or never?.. [__]
1=Always; 2=Sometimes; 3=Never

F9. **If yes to F7,** Is water available at that place always, sometimes, or never?.. [__]
1=Always; 2=Sometimes; 3=Never

F10. **If yes to F7,** did you wash your hands with soap and water **at this place** the last time you took a long call at school?.. [__]
1=Yes; 2=No

F11. At school, do you wash your hands with soap and water after taking a long call always, sometimes, or never? (can even be with own soap)………………………………... [__]
1=Always; 2=Sometimes; 3=Never

F12. Is there water available for drinking at school always, sometimes, or never?.. [__]
1=Always; 2=Sometimes; 3=Never

F13. **If always or sometimes to F13**, When you are at school, do you use the school water source for drinking always, sometimes, or never?.. [__]
1=Always; 2=Sometimes; 3=Never

OTHER INFORMATION

G1.In the past 5 school days, how many days did you miss?..[__]
Only enter one answer:
Zero days=0; One day=1; Two days=2; Three days=3; Four days=4; Five days= 5

G2. Do you ever eat soil or clay? ……………………………………[__]
1=Yes; 2=No

G3. Observe: What sort of shoes is the child wearing? ……………………………………..[__]
1=Closed shoes; 2=Sandals; 3=No shoes

KENYA NATIONAL SCHOOL DEWORMING SURVEY 2012

SCHOOL INFORMATION AND DEMOGRAPHICS

District code: |_____|_____|_____|

School code: |_____|_____|_____|

GPS Longitude: |__|__| : |__|__|__|__|__|

GPS Latitude: |__|__| : |__|__|__|__|__|
(N/S)

Negative ☐ Positive ☐ (tick as appropriate)

Date of visit:
|____|____|/|____|____|/|____|____|
day month year

Start of school term:
|____|____|/|____|____|/|____|____|
day month year

School type: Day ☐ Boarding ☐

Gender of pupils: Mixed☐ Boys☐ Girls☐

A. SCHOOL DEMOGRAPHICS	**ECD**	**P1**	**P2**	**P3**	**P4**	**P5**	**P6**	**P7**	**P8**
A1.Total boys enrolled:									
A2. Total girls enrolled:									
A3. Total boys present today:									
A4. Total girls present today:									
A5. Total male teachers:									
A6. Total female teachers:									

WATER and SANITATION FACILITIES

B1. Does the school have any of the following? Ask to see. ***Enter 1 =Yes and 2 = No***

Unlocked and accessible separate toilets for boys and girls………………………...………[__]
Handwashing facilities near the toilets…………………………………………………...[__]
Water in handwashing facilities………………………………………………..[__]
Soap is available at the handwashing facility……………………………………[__]
Water available for drinking today……………………………………………..[__]
First Aid kit……………………………………………………………………...………..[__]
If yes, what does it contain? [____]

B2. If the school has handwashing facilities near the toilets, what type are they?
Only enter one answer…………………………………………………………………...[__]
1 = tap water; 2 = handwash basin; 3 = leaky tins; 4 = Others (Specify) […………………..]

B3. What is the <u>main</u> source of water for drinking for pupils in this school?
Only enter one answer ………………………………………………………………..[__]
1=Piped/tap water; 2=Borehole or well; 3=Rain water; 4=Stream, lake or river; 5=Bought; 6=Bottled water;
7=Others……………………………………………… *specify* [_____________________]

B4. How many months of the year does the school **not** have water available for pupils to drink? .... No. months[__]

B5-B17: **Fill out latrine worksheet on final page**

SCHOOL HEALTH ACTIVITIES and IEC MATERIAL

C1. In the last 12 months, was the school involved in any of the following school health activities? ***Enter 1 =Yes and 2 = No***

School feeding programme……………………..……………………………………………[__]

If yes, is handwashing practiced before feeding?...[__]

Water and sanitation programme………………………………………………...……….[__]

School deworming programme……………………………………………...……………[__]

If yes, who did the deworming [______________ ___________ _____________________]

If yes, which deworming drugs were used:

☐ Bilhazia/Schistosomiasis ☐ Lymphatic Filariasis ☐ STH

Were any teachers at this school trained for school-based deworming in the past 6 months…..[__]

If yes, who did the training [___________________________________]

Any other programme, please specify [____]

Please provide details of the above programmes:

C2. Does the school have any of the following? ***Enter 1 =Yes and 2 = No***

Deworming IEC posters on display in the classrooms……………………..……………[__]

Deworming IEC posters on display in the headteachers office………………..…………...[__]

Deworming IEC booklets in the school library………………………………..………...[__]

Other deworming IEC material, please specify [___________________________________]

Please provide further details of the above:

Instructions: Fill out the worksheet below. Each line represents a latrine block (a natural grouping of latrines). If a block has one side for boys and one side for girls then enter it in as two separate blocks (one line for boys and one line for girls). If a single block has both latrines and urinals, then enter it in as two separate blocks (one line for latrines and one line for urinals). For B6 through B17 only enter data for **usable** latrines (ignore teacher latrine blocks, locked latrines, and latrines with full pits).

School Code:________________

B5 Number of latrines in block	B6 Number of **usable** latrines in block	B7 Assigned to: 1. Girls 2. Boys 3. Shared	B8 For grades: 1=All non-ECD 2=ECD 3=P1-P4 4=P5-P8 5=special needs	B9 Type of latrine 1=Water bourne 2=VIP latrine 3=Ordinary pit 4=Urinal	B10 Number of usable latrines with doors that close	B11 Number of usable latrines with doors that lock from the inside	B12 Number of usable latrines with visible feces inside	B13 Number of usable latrines with visible feces outside or around	B14 Number of usable latrines with excessive bad smell	B15 Number of usable latrines with excessive flies	B16 Number of usable latrines with good structure (slab, walls & roof)	B17 Number of usable latrines that are clean

Appendix 4.2. Variable specification procedures.

Because there were many WaSH technologies and behaviors of interest, we used a number of guiding criterion during the variable specification and model specification:

We first aggregated variables to the correct levels based on causal hypotheses of how they might affect the outcome. Some variables were collected at the pupil-level, although they are intrinsically school-level variables, and were therefore aggregated these to the school-level.

We assessed the homogeneity of variables to see if they have enough variation to be included in the analyses. We also assessed that there were sufficient numbers in cells of categorical variables, and when we observed small cell counts we considered the possibility of combining similar categories in order to resolve the problem.

Although access to WaSH is important, we generally assumed that pupils' helminth reinfection could be affected only through *use* of WaSH, and not through access alone. For example, the presence of a handwashing station can only affect pupil health through handwashing. However, we allow for the possibility that pupils' helminth reinfection may be affected through group-level adherence, even in the absence of individual-level adherence, for example through herd protection. For example, school-level handwashing behavior may have an effect on individual-level reinfection, for example by herd protection, even among individuals who do not WaSH their hands.

We sometimes had more than one variable that measured a similar construct. We assessed the correlations between variables with similar constructs. We show this information in the table below. We also assessed collinearity of variables in the full model and eliminated terms that were collinear (measured by the presence of high condition indices with several high variance decomposition proportions).[112]

Our primary exposures of interest were access to an improved water source, access to sanitation, and practice of handwashing, with separate variables for each of these at school and at home. We also had interest in a number of other WaSH technologies and behaviors. We attempted to control for a number of important confounders, and to include relevant interactions between variables. The inclusion of each variable was chosen *a priori* based on biological plausibility and on the previous literature. Sometimes separate variables measured similar constructs, and in the table below we show correlations between these variables, and the reasons why chose to include specific variables in our models. Further details on each variable of interest are also discussed in the text of chapter 4.

Appendix 4.2. Variable specification procedures.

Variables	Type	Level	Included	Variable notes
School Hygiene				
School provides a handwashing place	Pupil reported	Aggregated to school-level	No, only adherence is relevant	Handwashing only functions through adherence, so having access alone was not important to our models. We considered a Mokken scale for all of these variables, and they were highly scalable: Loevinger H coefficient = 0.70.* However, the scale overemphasized access and underemphasized actual adherence. The correlation coefficient between last HW and always HW was 0.45 (*p*=<0.01). We used the always HW variable in our primary analysis as it represented the public health ideal, but we used the last HW variable in a sensitivity analysis as it is less prone to recall bias.
Water always available at that place	Pupil reported	Aggregated to school-level.	No, only adherence is relevant	
Soap always available at that place	Pupil reported	Aggregated to school-level	No, only adherence is relevant	
Handwashed with soap and water the last time they defecated	Pupil reported	Pupil-level	No, redundant	
Always handwashes with soap and water after defecating	Pupil reported	Pupil-level	Yes	
Handwashed with soap and water the last time they defecated (same as above, but aggregated)	Pupil reported	Aggregated to school-level	No, homogenous	We had originally considered the possibility of group-level, or herd protection. However, because individual-level and school-level handwashing was poor at most schools (see table 4.3 and Figure 4.2), the variable lacked the necessary heterogeneity to be able to include in our multivariable models.
Always handwashes with soap and water after defecating (same as above, but aggregated)	Pupil reported	Aggregated to school-level	No, homogenous	
Handwashing facilities near the toilets	Observed	School-level	No, only adherence to HW is relevant	We assumed that access to handwashing supplies could only improve health through actual use (i.e. washing ones hands). These variables assessing access alone were therefore not included in our models.
Water in handwashing facilities	Observed	School-level	No, only adherence to HW is relevant	
Soap available at the handwashing facilities	Observed	School-level	No, only adherence to HW is relevant	

School Water				
Water always available for drinking	Pupil reported	Aggregated to school-level	No, redundant	Pupil reported water availability and teacher reported availability were measured with different questions; the correlation coefficient between these original continuous variables was 0.35 (*p*=<0.01). We believed the teacher reported value would be less prone to reporting errors and so we used a categorized version of this variable (always available vs. not). For our primary analysis, we collapsed this variable with the improved water source variable. We used the other variables with similar constructs in sensitivity analyses.
Improved water source for drinking§	Observed	School-level	No, redundant.	
Drinking water is reliably available	Teacher reported	School-level	No, redundant.	
Improved water source that reliably produced water	Multiple sources	School-level	Yes	
School Sanitation				
Usually defecate in the latrine/toilet at school	Pupil reported	Aggregated to school-level	No, homogenous, redundant	The construct we wanted to measure was contamination by open defecation at the school. Many of these variables were too homogenous to use. We used the observed variable (i.e. whether or not there were feces visible on the grounds), as it was sufficiently heterogenous and was the most direct measure.
Used a latrine/toilet at school last time they defecated	Pupil reported	Aggregated to school-level	No, homogenous, redundant	
Think their friends always defecate in the latrine/toilet at school	Pupil reported	Aggregated to school-level	No, redundant	
Feces visible on grounds outside of the latrines	Observed	School-level	Yes	
Meets the WHO pupil to latrine ratio standards for girls	Observed	School-level	Yes	This was derived from the pupil to latrine ratio variable.
Meets the WHO pupil to latrine ratio standards for boys	Observed	School-level	Yes	This was derived from the pupil to latrine ratio variable.
Latrines clean at school	Observed	School-level	No, redundant	These are intrinsically latrine-level variables, but latrine-level analysis were not possible for our study. The correlation coefficient between these variables was -0.93 (*p*=<0.01). We used
Feces visible in latrines at school	Observed	School-level	Yes	

				the visible feces variable as it was more relevant to the fecal-oral transmission mechanism. The variable was defined as the percentage of latrines in the school with no visible feces inside any of the latrines.
Anal cleansing at school	Pupil reported	Pupil-level	Yes	This variable was recategorized as a three-level variable (water vs. leaves/rocks/nothing vs. nothing) due to small cell counts.
Home Hygiene				
Have a handwashing place	Pupil reported	Pupil-level	No, only adherence to HW is relevant	Handwashing only functions through adherence, so having access alone was not important to our models. We considered a Mokken scale for all of these variables, and they were highly scalable: Loevinger H coefficient = 0.77.* However, the scale overemphasized access and underemphasized actual adherence. The correlation coefficient between last HW and always HW was 0.29 (*p*=<0.01). We used the always HW variable in our primary analysis as it represented the public health ideal, but we used the last HW variable in a sensitivity analysis as it is less prone to recall bias.
Water always available at that place	Pupil reported	Pupil-level	No, only adherence to HW is relevant	
Soap always available at that place	Pupil reported	Pupil-level	No, only adherence to HW is relevant	
Handwashed with soap and water the last time they defecated	Pupil reported	Pupil-level	No, redundant.	
Always handwashes with soap and water after defecating	Pupil reported	Pupil-level	Yes	
Home Water				
Have an improved water source for drinking	Pupil reported	Pupil-level	Yes	We used the improved water source variable. Pupils reported that water was generally available for drinking at home.
Water always available for drinking	Pupil reported	Pupil-level	No, homogenous.	
Home Sanitation				
Have personal toilet/latrine in home	Pupil reported	Pupil-level	Yes	This variable was collected using two questions, and was later categorized into a single variable (personal vs. shared vs. none).
Have shared toilet/latrine in home	Pupil reported	Pupil-level		
No toilet/latrine in home	Pupil reported	Pupil-level		

Usually defecate in the latrine/toilet at home	Pupil reported	Pupil-level	No, homogenous	These both measured a similar construct, but were very homogenous, so we didn't use either of them.
Used a latrine/toilet at home last time they defecated	Pupil reported	Pupil-level	No, homogenous	
Anal cleansing at home	Pupil reported	Pupil-level	Yes	This variable was recategorized as a three-level variable (water vs. leaves/rocks/nothing vs. nothing) due to small cell counts.
Other WaSH variables				
Shoe wearing	Observed	Pupil-level	Yes	This variable was observed, but may not reflect long-term shoe wearing behavior.
Type of floor in home	Pupil reported	Pupil-level	Yes	This variable was recategorized as a binary variable (earth/sand vs. cement/wood/iron sheets) due to small cell counts.
Student eats soil (Geophagy)	Pupil reported	Pupil-level	Yes	This was a binary variable (yes vs. no), and may not reflect long-term practices.
Confounders				
Grade	Pupil reported	Pupil-level	Yes	Categorical variables, grades 2-6.
Sex	Observed uniforms	Pupil-level	Yes	Male vs. female.
Siblings under 5	Pupil reported	Pupil-level	Yes	This count variable was recategorized as a binary variable (yes vs. no).
Wealth score	Pupil reported	Pupil-level	Yes	This variable was derived from many different household asset variables, using PCA.[103]
Baseline *A. lumbricoides* prevalence	Measured	Aggregated to school-level	Yes	Pupil STH infection was measured at the baseline visit.
Mean annual temperature	Measured	School-level	Yes	Linked to school locations from http://www.worldclim.org/bioclim.
Annual precipitation	Measured	School-level	Yes	
Province	Observed	Province-level	Yes	This was used as a proxy of geography. Former province was used instead of county because of the large number of counties.

* Mokken suggested that a Loevinger H coefficient of ≥ .5 denoted a strong scale.[113]

Table A4.1. Comprehensive table of school WASH conditions among 51 Kenyan primary schools.

	N	%
Total number of schools	51	100
Province		
Western	21	41.2
Rift Valley	10	19.6
Nyanza	20	39.2
School Sanitation		
Does the school meet the WHO pupil to latrine ratio standards for girls?*		
Yes	8	16.0
No	42	84.0
Does the school meet the WHO pupil to latrine ratio standards for boys?*		
Yes	13	26.0
No	37	74.0
Are there feces visible anywhere outside of the latrines		
Yes	16	31.4
No	35	68.6
N of schools with no visible feces inside of the latrine	11	21.6
School Hygiene		
Does the school have handwashing facilities near the toilets?		
Yes	25	49.0
No	26	51.0
Does the school have water in handwashing facilities?		
Yes	30	58.8
No	21	41.2
Soap is available at the handwashing facility?		
Yes	6	11.8
No	45	88.2
If the school has handwashing facilities near the toilets, what type are they?		
Tap water	4	7.8
Handwash basin	11	21.6
Leaky tins	21	41.2
Other	2	3.9
N/A, doesn’t have	13	25.5
School Water		
Does the school have water available for drinking today?		
Yes	28	54.9
No	23	45.1
What is the main source of water for drinking for pupils in this school?		
Piped/tap water	5	9.8
Borehole or well	20	39.2
Rain water	16	31.4
Stream, lake or river	8	15.7
Bought	0	0.0
Bottled water	0	0.0
Other	2	3.9
Does the school have an improved water source for drinking?		
Yes	27	52.9
No	24	47.1

How many months of the year does the school **not** have water available for pupils to drink?		
0	29	56.9
1-3	11	21.6
4-6	7	13.7
7 or more	4	7.8
Does the school have drinking water available year round?		
Yes	29	56.9
No	22	43.1
Does the school have an improved water source *that has water year round* for drinking?		
Yes	10	19.6
No	41	80.4

*There was one all boys school, and one all girls school, so the denominator reflects 50 schools.

Table A4.2. Comprehensive table showing WaSH characteristics for 4,404 respondents, weighted to represent 15,960 pupils from grades 2-6 in 51 Kenyan primary schools.

	Weighted %	SE of %
Home Sanitation		
Do you have a toilet/latrine in your home/compound?		
Yes	97.1	0.3
No	2.9	0.3
Is that toilet/latrine shared with other households/compounds?		
Yes	42.0	1.0
No	55.0	1.0
N/A (there is no toilet/latrine)	3.0	0.3
At home, where do you usually go to urinate?		
In my latrine/toilet	87.4	0.5
In a latrine outside compound	6.8	0.4
Around/outside compound (e.g. in the bush)	7.4	0.4
In the bathroom/shower	0.0	0.0
At home, where do you usually go to take a long call (defecate)?		
In my latrine/toilet	92.6	0.4
In a latrine outside compound	6.0	0.4
Around/outside compound (e.g. in the bush)	1.4	0.2
Last time you took a long call **at home**, did you use a latrine/toilet?		
Yes	96.8	0.3
No	3.2	0.3
At home, do you have something to use for cleaning up after a long call		
Always	48.9	1.0
Sometimes	45.3	1.0
Never	5.9	0.5
What do you usually use to clean up after taking a long call when at home?		
Tissue paper	39.7	1.0
Water	3.3	0.2
Newspaper	22.1	0.8
Books	5.1	0.4
Leaves	28.6	1.0
Rocks	0.0	0.0
Nothing	1.2	0.2
Home Hygiene		
Is there a place (e.g. container, basin, sink) at home for you to wash your hands after you take a long call?		
Yes	49.7	1.0
No	50.3	1.0
Is water available for washing your hands **at that place**		
Always	18.9	0.8
Sometimes	30.3	1.0
Never	0.5	0.1
N/A (there is no place)	50.3	1.0
Is handwashing soap available **at that place**		
Always	10.3	0.6
Sometimes	32.9	0.9
Never	6.5	0.4

N/A (there is no place)	50.3	1.0
Did you wash your hands with **soap and water** at this place the last time you took a long call at home?		
Yes	33.1	1.0
No	16.6	0.8
N/A (there is no place)	50.3	1.0
At home, do you wash your hands with soap and water after taking a long call		
Always	8.1	0.5
Sometimes	57.7	1.0
Never	34.2	1.0
Home Water		
What is the main source of water for drinking in your home?		
Piped/tap water	16.5	0.9
Borehole or well	30.6	1.0
Rain water	3.4	0.4
Stream, lake or river	49.3	1.1
Bottled water	0.1	0.1
When you are at home, do you use this water source for drinking water		
Always	85.0	0.9
Sometimes	14.3	0.9
Never	0.7	0.1
School Sanitation		
At school, where do you usually go to urinate?		
Latrine/toilet at school	97.6	0.3
To a latrine near the school	0.5	0.1
Around/outside school compound (e.g. in the bush)	1.8	0.3
I wait/hold it until school is over	0.0	0.0
At school, where do you usually go to take a long call?		
Latrine/toilet at school	99.4	0.1
To a latrine near the school	0.3	0.1
Around/outside school compound (e.g. in the bush)	0.2	0.1
I wait/hold it until school is over	0.1	0.1
When your friends have to take a **long call** at school, do you think they use a latrine		
Always	75.7	1.0
Sometimes	24.2	1.0
Never	0.1	0.1
Last time you took a **long call** at school, did you use a latrine/toilet?		
Yes	97.5	0.3
No	2.5	0.3
Does the school provide something to use for cleaning up after a long call		
Always	9.7	0.6
Sometimes	3.2	0.3
Never	87.1	0.6
What do you usually use to clean up after a long call when at school?		
Tissue paper	16.0	0.9
Water	3.8	0.3

Newspaper	14.7	0.8
Books	43.5	1.2
Leaves	18.2	0.9
Rocks	0.0	0.0
Nothing	3.8	0.4
School Hygiene		
Does the school provide a place (e.g. container, basin, sink), for you to wash your hands after taking a long call?		
Yes	62.8	0.8
No	37.2	0.8
Is soap available **at that place**		
Always	1.0	0.2
Sometimes	5.4	0.4
Never	56.4	0.8
N/A (school does not provide a place)	37.2	0.8
Is water available **at that place**		
Always	19.9	0.9
Sometimes	42.3	0.9
Never	0.7	0.1
N/A (school does not provide a place)	37.2	0.8
Did you wash your hands with soap and water **at this place** the last time you took a long call at school?		
Yes	12.3	0.8
No	50.5	0.9
N/A (school does not provide a place)	37.2	0.8
At school, do you wash your hands with soap and water after taking a long call		
Always	3.8	0.4
Sometimes	27.9	0.9
Never	68.2	1.0
School Water		
Is there water available for drinking at school		
Always	21.0	0.9
Sometimes	49.0	1.0
Never	29.9	0.8
When you are at school, do you use the school water source for drinking		
Always	20.2	0.8
Sometimes	47.1	0.9
Never	2.8	0.4
N/A (as they said ‘never’ in previous question)	29.9	0.8
Other WaSH related Helminth Risk Factors		
What type of floors does your house have?		
Cement or tiles or linoleum	23.6	1.0
Wooden planks	0.2	0.0
Earth or sand	78.1	1.0
Iron sheets	0.3	0.1
Observed: What sort of shoes is the child wearing?		
Closed shoes	42.6	1.0
Sandals	17.7	0.8
No shoes	39.7	1.0

Other non-WaSH covariates		
Do you ever eat soil or clay?		
Yes	8.0	0.5
No	92.0	0.5
Sex		
Male	50.0	0.5
Female	50.0	0.5
Grade		
2	19.0	3.0
3	19.9	3.2
4	20.6	3.3
5	20.3	3.2
6	20.2	3.3
Are there siblings under 5 at home		
Yes	47.2	0.9
No	52.8	0.9

Table A4.3. Unadjusted and adjusted odds ratios comparing WaSH technologies and behaviors with *A. lumbricoides* reinfection among pupils in 51 Kenyan primary schools

	Interaction model adjusted OR (95% CI)[§]	
School WaSH variables		
Always HW after defecation	Among improved WS[‖]	Among unimproved WS[‖]
Yes	0.46 (0.23-0.89)[*]	2.1 (0.81-5.7)
No	referent	referent
Improved WS that reliably produced water	Among HW[‖]	Among non-HW[‖]
Yes	0.26 (0.075-0.87)[*]	1.2 (0.74-2.0)
No	referent	referent
Anal cleansing with		
Water	0.67 (0.35-1.3)	
Leaves/rocks/nothing	0.88 (0.69-1.1)	
Paper product	referent	
Pupil:latrine ratio acceptable		
Yes	1.6 (1.0-2.4)[*]	
No	referent	
Visible feces on latrine floor/walls		
All latrines have feces	1.4 (0.55-3.3)	
No latrines have feces	referent	
Feces visible outside latrines		
Yes	1.3 (0.75-2.2)	
No	referent	
Home WaSH variables		
Always HW after defecation	Among improved WS[‖]	Among unimproved WS[‖]
Yes	0.84 (0.52-1.4)	1.2 (0.75-1.8)
No	referent	referent
Improved water source (WS)	Among HW	Among non-HW
Yes	0.78 (0.42-1.5)	1.1 (0.87-1.4)
No	referent	referent
Anal cleansing with		
Water	1.6 (0.83-2.9)	
Leaves/rocks/nothing	1.0 (0.80-1.3)	
Paper product	referent	
Toilet is		
Shared	1.1 (0.89-1.4)	
No toilet	0.99 (0.572-1.7)	
Personal	referent	
Other WaSH variables		
Shoe wearing		
Closed shoes	0.68 (0.55-0.85)[*]	
Sandals	0.63 (0.49-0.82)[*]	
No shoes	referent	
Type of floor in home		
Earth/sand	1.1 (0.78-1.5)	
Cement/wood/iron sheets	referent	
Student eats soil (Geophagy)[¶]		
Yes	1.1 (0.82-1.6)	
No	referent	

Confounders[§]	
Grade	
2	1.4 (1.0-1.8)[*]
3	1.3 (0.96-1.7)[‡]
4	1.2 (0.89-1.6)
5	1.1 (0.84-1.5)
6	Referent
Sex	
Male	1.3 (1.1-1.6)[*]
Female	referent
Data not shown for other confounders[§]	Data not shown[§]

[*] 95% CI does not include one. [‡] 90% CI does not include one. [§] Both adjusted models controlled for all of the variables in this table, and also confounders which are not shown here, including whether pupils had siblings under age 5, household wealth score, the baseline *A. lumbricoides* prevalence at each school, the mean annual temperature, annual precipitation, and province. All three models accounted for clustering of pupils within schools. [‖] Interactions were detected so subgroup specific ORs are reported. [¶] Geophagy is a soil eating practice common in some parts of Kenya.[97]

Appendix 5.

Table A5.1. Inter-rater reliability for the subjective latrine measures.*

	Three level variables		Two level variables‡
	kappa	Weighted kappa	kappa
In use	-	-	.89
'No shutter'	-	-	.88
'Worst smell'	.52	.59	.57
'Feces very visible'§	.70	.76	.79
'Most visible urine'§	.45	.51	.63
'Very dirty'§	.57	.64	.70
'Many flies inside'	.47	.51	.63

*We only used the variables in analysis if there was substantial agreement, defined by Landis and Koch to mean a Cohen's kappa statistic of over 0.6.[110] ‡Each of the above three-level variables was later categorized for simplicity of model interpretation, with the worst category being compared to the combined moderate and best category. §The feces and urine variables were not used in our primary analyses; we chose to use the cleanliness variable instead, which also captures many aspects of a pupil's exposure to human excrement.

Figure A5.1. (**a**) Proportion of pupils who used a toilet at each school as a function of pupil to toilet ratio, fit with an ordinal pupil to toilet ratio variable. (**b**) Proportion of pupils who used a toilet at each school as a function of pupil to toilet ratio, fit with a piecewise quadratic spline (knots shown by vertical lines).