Effect of water, sanitation and hygiene interventions on pathogens in the environment: Individual participant data meta-analysis

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# Abstract

(to write)

# Background

Water, sanitation and hygiene (WASH) improvements aim to reduce childhood enteric infections, subsequent diarrheal disease and growth faltering by reducing child exposure to fecal-orally transmitted pathogens in the environment. Until recently, trials of WASH interventions have primarily focused on documenting health outcomes such as caregiver-reported diarrhea without quantifying intermediate outcomes along the causal chain, such as detection of pathogens in environmental samples and in human biological specimens. Without measuring these causal intermediates, trials are limited to a “black box” understanding, where underlying mechanisms of interventions are unknown and investigators can only speculate about reasons for intervention success or failure. Inspecting the causal chain is especially important given the small or null effects on child diarrhea and growth achieved in recent well-conducted trials of WASH interventions.1,2,**humphreyIndependentCombinedEffects2019a?**

Additionally, studies that have collected environmental samples to date have primarily focused on drinking water (and, to a smaller extent, hands and food) while other pathways such as soil and surfaces in the domestic environment have received less attention.3 Furthermore, most studies have relied on measuring indicator organisms in the environment as a proxy for pathogens; these indicators can originate from non-fecal sources,4 cannot differentiate between human vs. animal fecal contamination,5 and correlate poorly with the presence of pathogen.6 Recent advances in DNA-based diagnostics now allow detection of a range of enteropathogens in human biological specimens and environmental samples,7 as well as distinction between human vs. animal fecal sources through molecular source tracking (MST) markers.8

(Add a paragraph on existing studies on WASH intervention effects on MST markers that weren’t included)

We aimed to assess the effect of WASH interventions on specific pathogens, pathogen types (viruses, bacteria, protozoa, helminths) and human vs. animal MST markers in the environment. We conducted a systematic review of WASH intervention studies that have measured pathogens and/or MST markers in environmental samples, and we conducted an individual participant data (IPD) meta-analysis of WASH trials that have measured pathogens and/or MST markers in the environment to explore causal relationships between WASH interventions and pathogen and MST presence and abundance in the environment.

# Methods

We conducted a systematic literature search to identify WASH intervention trials and quasi-experimental (matched cohort or controlled before-and-after) studies that have measured pathogens and/or MST markers in environmental samples as well as at least one of the health outcomes of interest (caregiver-reported diarrhea, child growth or pathogens in stool). We developed a search strategy from a two-step process. First, the known studies meeting out inclusion criteria were examined for keywords and Medical Subject Heading (MeSH) terms relating to each of the following categories of terms comprising our search string: WASH interventions; microbial source tracking and environmental contamination; enteric infection; diarrhea; and child growth and development. Next, we performed an initial search using these terms and extracted other relevant terms and synonyms from relevant articles in the search results. Search terms are listed in Supplementary Table 1. We queried the following databases for relevant studies: PubMed, Embase, CAB Direct Global Health, Agricultural & Environmental Science Database, Web Of Science, Scopus. We only included English language publications published in 2000 or after so that only studies with more recently developed pathogen detection methods were included. We included studies meeting the following inclusion criteria: 1) Randomized controlled trial or quasi-randomized study (i.e., matched cohort, controlled before-and-after study) of water, sanitation or hygiene intervention, 2) measure pathogens and/or MST markers in environmental samples, and 3) measured at least one health outcome of interest: pathogens in stool, self-reported diarrhea, or child anthropometry. The third criteria was needed to examine the hypothesized causal pathway from WASH intervention to child health through reduced environmental contamination, and the analysis is presented in a companion paper (Mertens et al. 2021).

* Prescreening
* Clustering
* Handling multiple rounds
* OSF link

# Results

* Covidence details (search terms, number returned, studies with no response)
* Studies included

Date of search: 1/19/2021 Returned 3,376 results. 3,253 were excluded as irrelevant in the abstract screening stage, and of the 125 remaining studies, 15 met the inclusion criteria after full text screening by two authors. The 15 publications identified included multiple publications from the same intervention studies, and 6 unique intervention studies were identified by the systemtic review.

1. The WASH Benefits Bangladesh trial9
2. The WASH Benefits Kenya trial9
3. The MapSan trial in Mozambique10
4. The Gram Vikas matched cohort study in India11
5. The Total Sanitation Campaign trial in India12
6. The CHoBI7 Trial in Bangladesh (Add citation)

Data was shared by the primary investigators of the first 5 studies, but the authors of the CHoBI7 Trial declined to share the data.  
-Note village level WQ data in Odisha

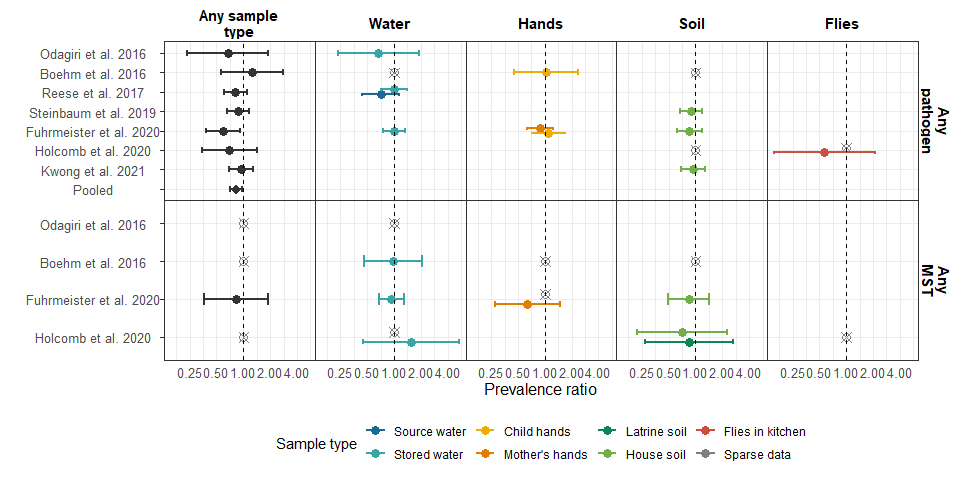
-Note subsidies within the WASH Benefits Bangladesh trial

* Data from each study (Targets, methods of ascertainment, number of sample types, number of samples)
* Number of outcomes for each study, number of samples
* Prevalences for primary outcomes
* PR’s
* Abundance results

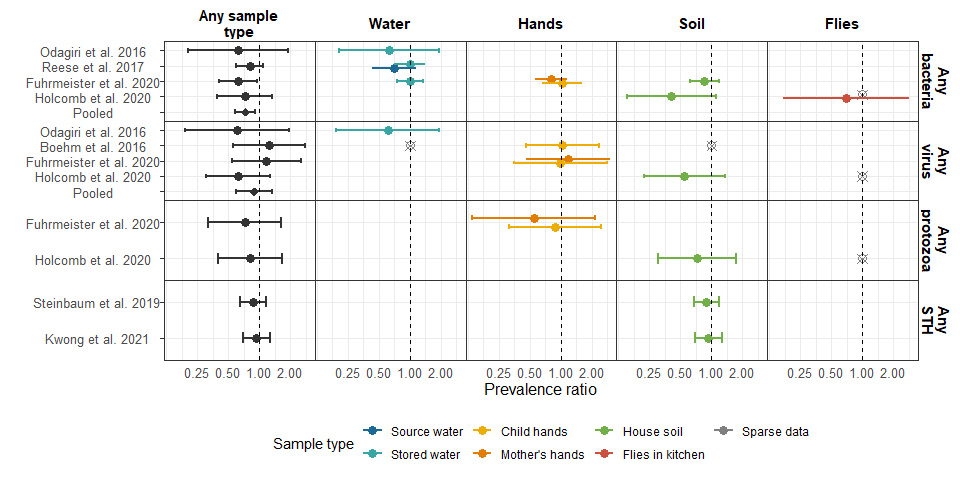
# Discussion

* Discuss significant results and any consistencies across studies.
* Discuss differences in interventions across studies
* Differences in adjusted vs. unadjusted estimates
* Limitations \* Sparse in many categories \* Abundance imputation \* Look at primary manucript discussions
* Future research needs?

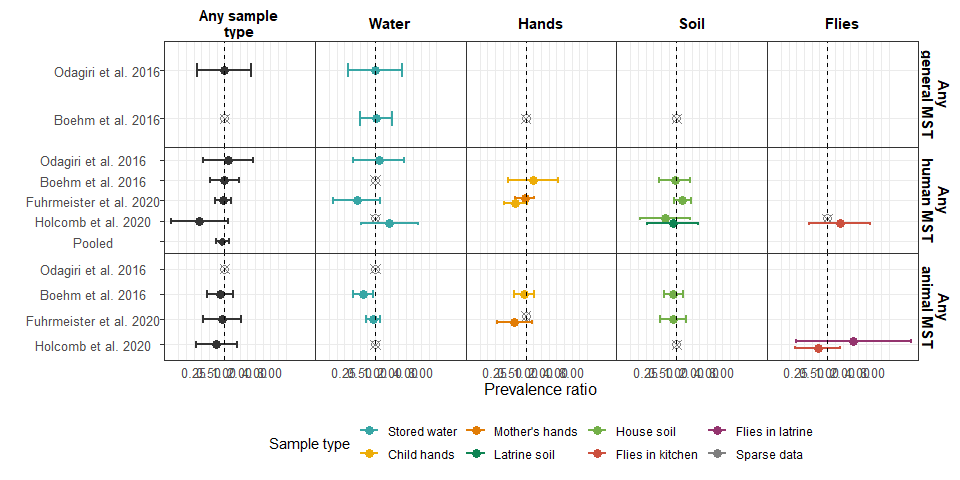
# Figures



**Figure 1.** Forest plots of intervention effects on any enteropathogen, and any MST markers in different types of environmental samples. Pooled estimates are presented when there are four or more study-specific estimates for a specific sample and target combination. Empty, grey, crossed points denote contrasts where data existed but with either too low or too high a prevalence to estimate a prevalence ratio. All estimated are adjusted for potential confounders.



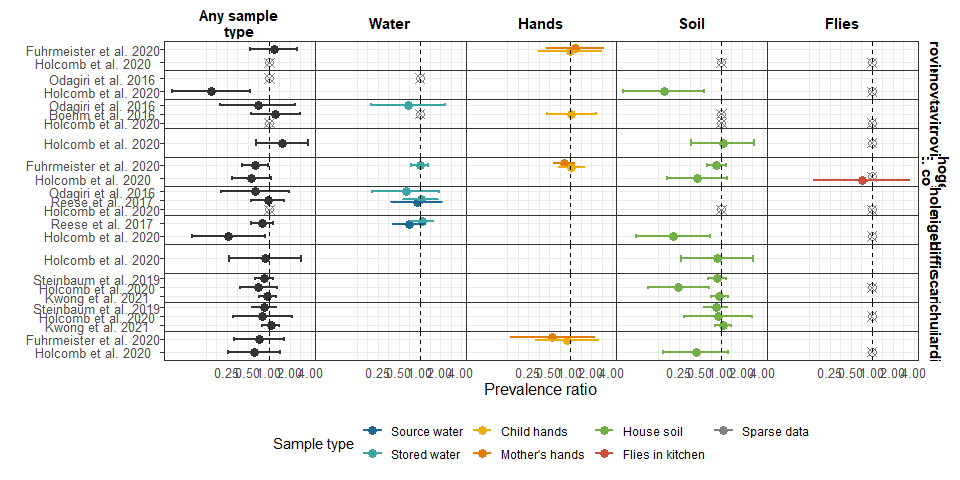
**Figure 2.** Forest plots of intervention effects on any virus, any bacteria, any protozoa and any STH prevalences in different types of environmental samples.



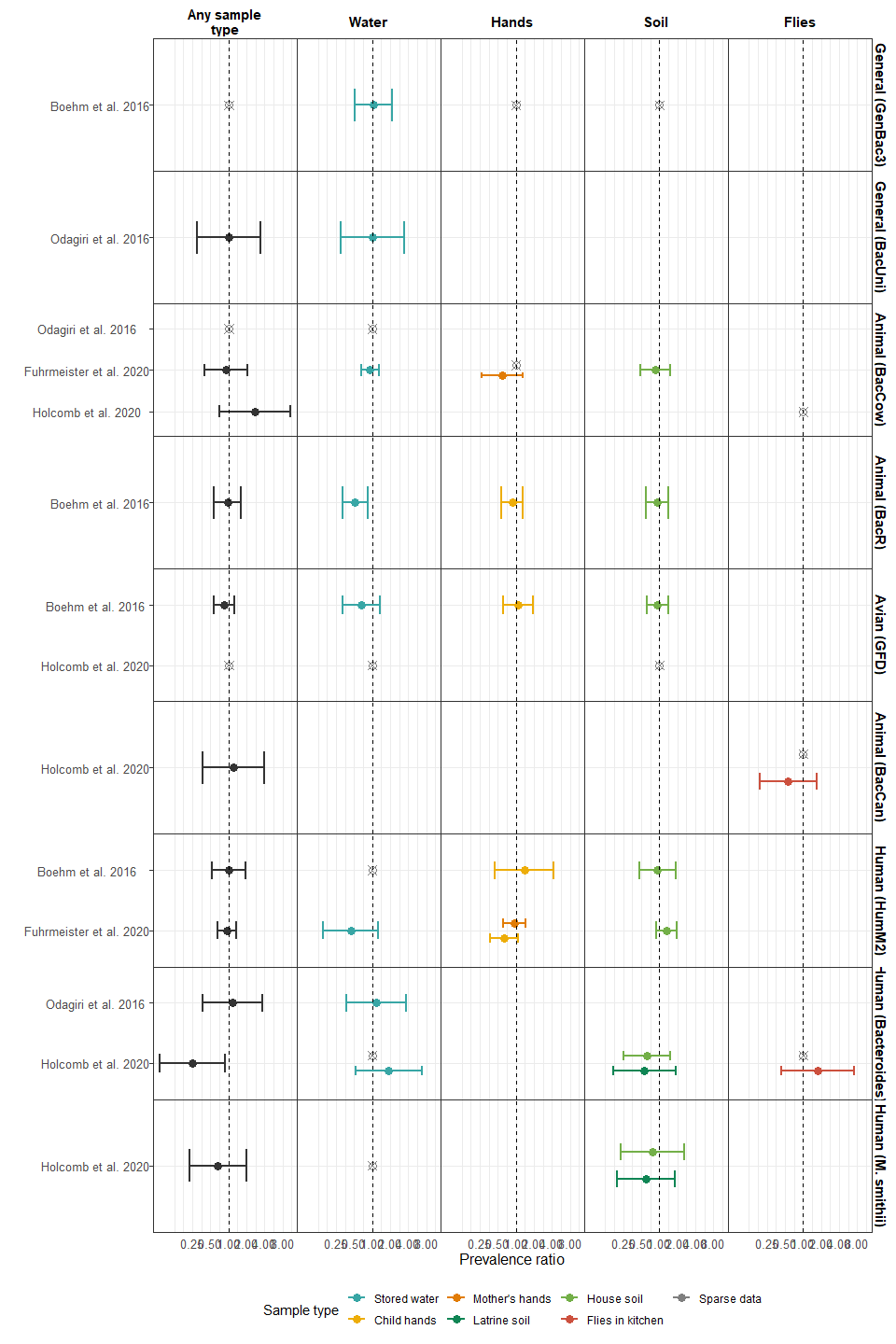
**Figure 3.** Forest plots of intervention effects on any general, human and animal MST markers in different samples of environmental samples.

# Tables

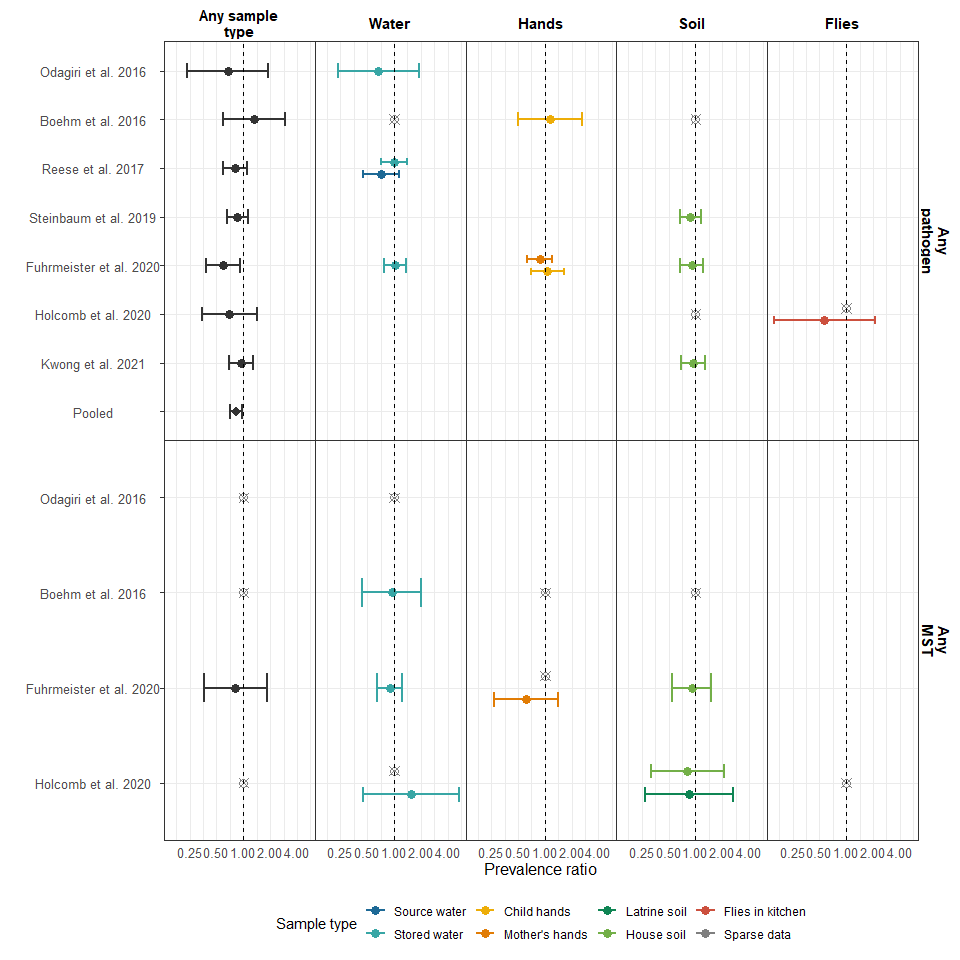
# Supplimentary Figures



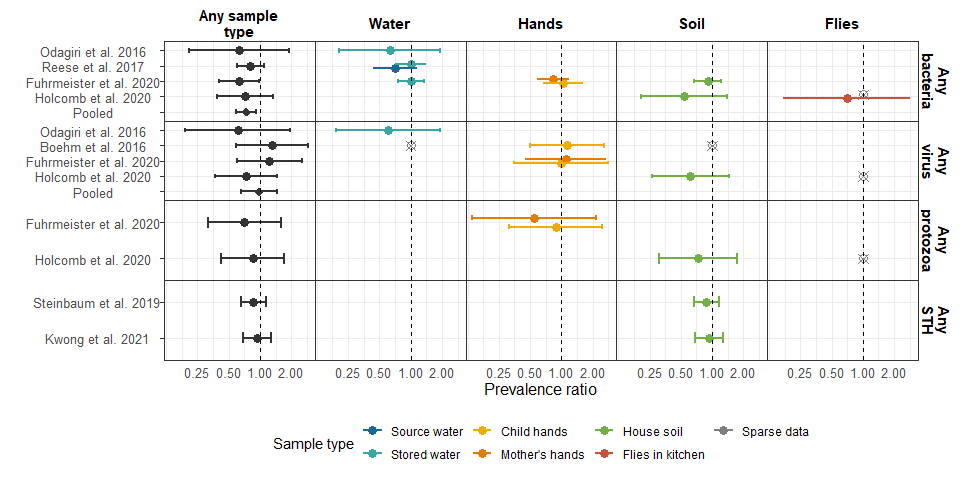
**Supplimentary Figure 1.** Prevalence of specific pathogens



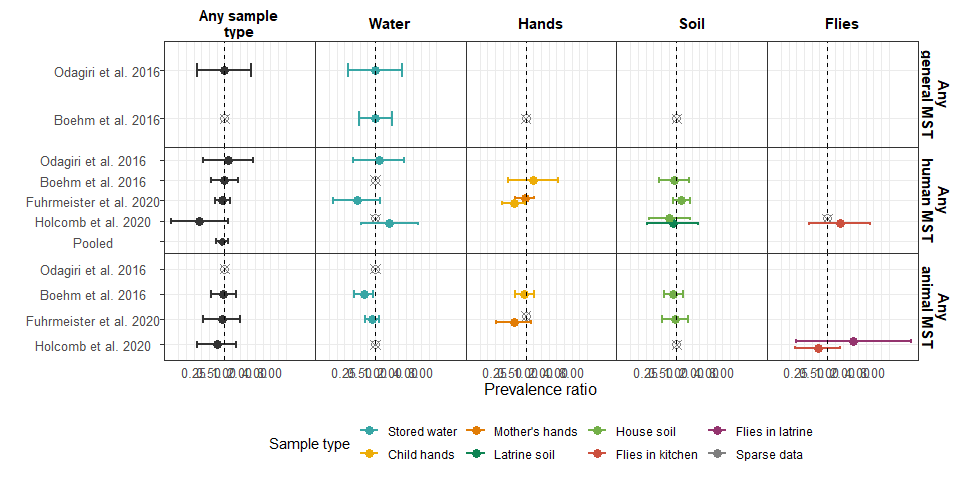
**Supplimentary Figure 2.** Prevalence of specific MST markers



**Supplimentary Figure 3.** Forest plots of unadjusted intervention effects on any enteropathogen, and any MST markers in different types of environmental samples. Pooled estimates are presented when there are four or more study-specific estimates for a specific sample and target combination. Empty, grey, crossed points denote contrasts where data existed but with either too low or too high a prevalence to estimate a prevalence ratio. All estimated are adjusted for potential confounders.



**Supplimentary Figure 4.** Forest plots of unadjusted intervention effects on any virus, any bacteria, any protozoa and any STH prevalences in different types of environmental samples.



**Supplimentary Figure 5.** Forest plots of unadjusted intervention effects on any general, human and animal MST markers in different samples of environmental samples.

# Supplimentary Tables

# References

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