International Journal of Hygiene and Environmental Health 219 (2016) 709–723

Contents lists available at ScienceDirect

International Journal of Hygiene and Environmental Health

journal homepage: www.elsevier.com/locate/ijheh

Review

Assessing the impact of sanitation on indicators of fecal exposure along principal transmission pathways: A systematic review☆

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ARTICLE INFO

Article history:
Received 29 July 2016
Received in revised form
30 September 2016
Accepted 30 September 2016

Keywords:
Sanitation
Fecal contamination
Fecal-oral transmission
Water quality

ABSTRACT

Objective: Fecal-oral transmission of enteric and other pathogens due to poor sanitation is a major cause of morbidity and mortality, especially in low- or middle-income settings. Few studies have investigated the impact of sanitation on indicators of transmission, a prerequisite to achieving health gains. This review attempts to summarize the literature to date.

Methods: We searched leading databases to identify studies that address the effect of sanitation on various transmission pathways including fecal pathogens or indicator bacteria in drinking water, hand contamination, sentinel toys, food, household and latrine surfaces and soil, as well as flies and observations of human feces. This also included studies that assessed the impact of fecal contamination of water supplies based on distance from sanitation facilities. We identified 29 studies that met the review's eligibility criteria.

Results and conclusion: Overall, the studies found little to no effect from sanitation interventions on these transmission pathways. There was no evidence of effects on water quality (source or household), hand or sentinel toy contamination, food contamination, or contamination of surfaces or soil. There is some evidence that sanitation was associated with reductions in flies and a small effect on observations of feces (Risk Difference −0.03, 95%CI −0.06 to 0.01). Studies show an inverse relationship between the distance of a water supply from a latrine and level of fecal contamination of such water supply. Future evaluations of sanitation interventions should include assessments of effects along transmission pathways in order to better understand the circumstances under which interventions may be effective at preventing disease.

Contents

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https://doi.org/10.1016/j.ijheh.2016.09.021

1. Introduction

An estimated 2.4 billion people lack access to improved sanitation (UNICEF and WHO, 2015). Most of these individuals (71%) live in rural areas, as do more than 90% of the 1.1 billion who still practice open defecation; nearly all reside in developing countries, primarily in South and Southeast Asia and Sub-Saharan Africa (UNICEF and WHO, 2015).

Poor sanitation is associated with a heavy burden of disease. Diarrhea accounts for the largest share of that burden, causing an estimated 1.4 million deaths annually (Lozano et al., 2012; Prüss-Üstün et al., 2014) or 19% of all under-5 deaths in low-income settings (Boschi-Pinto et al., 2008). Soil-transmitted helminth infections, schistosomiasis, and trachoma are also primarily caused by poor sanitation. There is also evidence linking poor sanitation with stunting, environmental enteropathy and impaired cognition – long-term conditions that also aggravate poverty and impair economic development (Guerrant et al., 2013).

More than a half-century ago, Wagner and Lanoix (1958) described the principal pathways for fecal-oral transmission in terms of the five-F's: fluids, fingers, food, fields and flies. Historically, however, research around the impact of sanitation interventions has mainly focused on health outcomes, such as diarrhea or infection with specific pathogens such as soil-transmitted helminths. Comparatively few studies have actually assessed the direct impact of sanitation on these pathways of fecal exposure. Without knowing to what extent sanitation has interrupted one or more of these pathways, it can be difficult to interpret the effect of sanitation interventions on health—especially when the findings show little or no impact as in several recent trials (Arnold et al., 2010; Briceño et al., 2015; Clasen et al., 2014; Patil et al., 2014; Pickering et al., 2015). Understanding the impact of sanitation on fecal exposure pathways also provides important guidance on the sources of transmission that may dominate and thus could be targeted in an effective intervention.

As part of its effort to develop a set of guidelines on sanitation and health, the World Health Organization (WHO) commissioned this systematic review to assess the effectiveness of sanitation and sanitation interventions on fecal-oral transmission pathways, specifically – fecal pathogens or indicator bacteria in drinking water, hand contamination, sentinel toys, food, household and latrine surfaces and soil, as well as flies and observations of human feces. All study designs and settings were eligible. This review is part of a series of systematic reviews that also examine the impact of sanitation on coverage and use (Garn et al., submitted), sanitation-related infectious diseases and nutritional status (Freeman et al., submitted), and other outcomes such as school absenteeism, childhood cognition and aspects of personal wellbeing (Sclar et al., unpublished results).

2. Methods

2.1. Search strategy

We conducted a systematic review of the literature in order to identify relevant studies that address the impact of sanitation on the transmission pathway of fecal pathogens (see Supplemental Text S1 for protocol and Supplemental Text S2 for PRISMA Checklist). We included studies published in English, Spanish, Portuguese, French, German or Italian with any publication status (published, unpublished, in press, grey literature, etc.) written between 1950 and December 2015. We conducted our search in English and utilized the following generic search string: ((feces OR faeces) AND sanitation) AND (pathogen OR contamination). We searched the following databases: British Library for Development Studies, Campbell Library, clinicaltrials.gov, Cochrane Library, EMBASE, EBSCO (CINHAL, PsychInfo), LILACS, POPLINE, ProQuest, PubMed, Research for Development, Sanitary Engineering and Environmental Sciences (REPIDISCA), Social Science Research Network (SSRN), Sustainability Science Abstracts (SAS), Web of Science, and 3ie International Initiative for Impact Evaluation. We also searched the following organizations' conference proceedings and websites: Carter Center, Center for Disease Control and Prevention Global WASH, International Water Association, Menstrual Hygiene Management in WASH in Schools Virtual Conference, Stockholm Environment Institute, Stockholm World Water Week Conference, University of North Carolina Water and Health Conference, UNICEF Water, Sanitation and Hygiene, UNICEF WASH in Schools, USAID Environmental Health Project, WASHplus, World Bank Water and Sanitation Program. We hand searched references of other review papers that came out of the database and website searches of all included studies. Finally, we included relevant studies that were found during the database search of the other sanitation systematic reviews (Freeman et al., submitted; Garn et al., submitted; Sclar et al., unpublished results).

2.2. Study eligibility & extraction

Our review incorporated both experimental and observational study designs as defined by The Cochrane Handbook for

Systematic Reviews: randomized controlled trials (RCTs), quasi-RCTs, non-randomized controlled trials, controlled before-and-after, interrupted-time-series, historically controlled, case-control, cohort, case series and cross-sectional studies. All study settings and populations were eligible. Studies had to include sanitation as an exposure and fecal pathogens, indicators, or mechanical vectors as an outcome. In observational studies, the sanitation exposure could be measured as the presence or use of sanitation facilities or practice of open defecation, while in experimental studies it was measured as exposure to an intervention aimed at improving the safe disposal of human feces. We accepted hardware and software sanitation interventions as well as sanitation interventions that were combined with other interventions such as improvements to water supply or water quality or promotion of hygiene. Outcomes of interest encompassed the presence or quantity of fecal bacteria, viruses or parasites or indicators thereof (e.g. *E. coli*, fecal coliforms, thermotolerant coliforms and others) on hands, sentinel objects, food, fomites, household drinking water, household source water, latrine or household surfaces or surrounding soils. We also included mechanical vectors of fecal pathogens (e.g., synanthropic flies) and the presence or quantity of visible feces in latrine or household surroundings, be it animal or human feces.

One reviewer screened titles and two reviewers independently examined abstracts to determine if studies fell within the inclusion criteria for the review. Where a title or abstract could not be rejected with certainty, both reviewers screened the full text. The abstract screenings were compared and when the eligibility decision differed, a third reviewer made the final decision. The full text was then obtained for the selected studies and again screened for eligibility by two independent reviewers. We contacted authors of studies when additional data that was not reported was needed to assess eligibility for inclusion. The eligibility decisions were compared and a third reviewer again resolved any disagreements. Finally, two reviewers independently extracted data from the finalized list of eligible studies using a piloted data extraction form (see Supplemental Text S3). For studies with missing data, we attempted to contact authors to supply the necessary information. In cases of a discrepancy between the two extraction forms, the two reviewers discussed and reached agreement or deferred to a third reviewer. One reviewer then entered the data into Excel for analysis.

2.3. Assessment of bias & quality of evidence

Two reviewers independently assessed risk of bias and then one reviewer subsequently used the GRADE approach to assess quality of evidence. We used an adapted version of the Liverpool Quality Appraisal Tool (LQAT) for assessing risk of bias because of the tool's flexibility in creating exposure and outcome assessments specific to our diverse set of sanitation and transmission studies (Pope et al., unpublished). We assessed bias in only the experimental studies that examined sanitation interventions; we did not use the tool with respect to observational studies as they inherently present multiple sources of potential bias and were thus automatically determined to have very serious risk of bias. Our adapted LQAT tool examined eight different areas of bias: selection bias, response rate bias, allocation bias, follow-up bias, bias in exposure assessment, bias in outcome assessment, bias in ascertainment, and confounding in analysis.

To assess the overall quality of the body of evidence for each finding, we followed the GRADE guidelines and examined inconsistency, indirectness, lack of precision, publication bias and risk of bias through LQAT scores (Guyatt et al., 2011a). The body of evidence could be downgraded up to 2 points for each assessment component. Due to the difference in the LQAT assessment, the intervention studies for each finding were assessed separately from the observational studies, resulting in two GRADE scores for a given

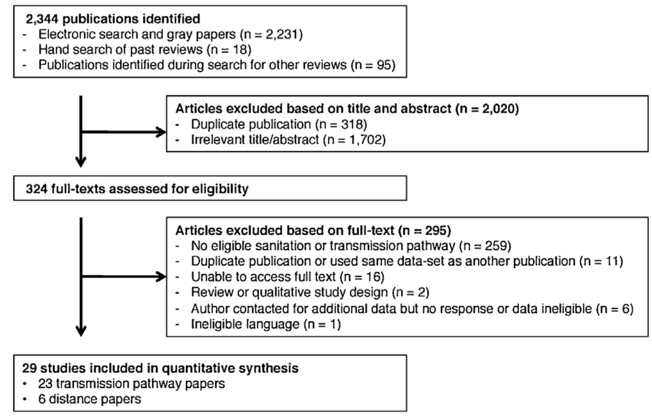

Fig. 1. PRISMA flow diagram of publications considered for the review.

finding. We assessed inconsistency, or heterogeneity, by looking across the effect estimates and determining if they showed the same direction of effect (i.e. protective vs. harmful). Indirectness refers to the lack of generalizability of the evidence to the review's specific research question of interest. However, since this review had a broad scope that considered any population and setting, we determined that none of the evidence should be downgraded for indirectness. We assessed imprecision by examining whether or not each effect estimate's confidence interval overlapped with the null and was thus not statistically significant. Finally, we did not downgrade for publication bias for several reasons. The database search was exhaustive, including both published and unpublished sources and non-English journals, and the research topic is well established making "lag bias" unlikely (Guyatt et al., 2011b). Moreover, lack of funnel plots, due to the variety of reported effect estimates, made it difficult to examine publication bias through the use of study results. The total number of downgrades for a given finding was then translated into a GRADE rating of Very Low, Low, Moderate or High quality of evidence.

2.4. Data synthesis

For studies reporting on the measure of effect on the transmission pathway, we extracted the measure reported by the study, whether it be risk ratio, odds ratio, mean difference or risk difference and, in one case (Clasen et al., 2014), a rate ratio. We also extracted the reported 95% confidence intervals (CI) around the effect estimate. We calculated these effect estimates and 95% CI when only raw numbers, beta coefficients or p-values were available. For continuous variables, the mean differences or the standardised mean differences (SMD) were reported.

Except in the case of observations of feces, we determined that a meta-analysis of the results was not justified due to substantial heterogeneity in the way studies measured and characterized the transmission pathway. While we allowed for a broad set of outcomes including fecal pathogens, indicators and mechanical vectors, these outcomes greatly varied in how they were measured, where they were measured and the type of measure of effect reported. For the meta-analysis of observed feces, we converted the corresponding measures of effect onto the risk difference scale using reported raw numbers when necessary. We used a random-effects model to estimate a pooled risk difference between the intervention/enhanced sanitation conditions compared to controls/participants without the condition. The meta-analysis was done using STATA 13 (StataCorp. 2013. College Station, TX, USA).

3. Results

3.1. Description of studies

3.1.1. Search results

Execution of the search strategy yielded 2344 titles and abstracts. After screening, two reviewers examined the full text of 324 studies for further assessment. Of these, 29 studies met the review's eligibility criteria (Fig. 1).

3.1.2. Study settings and participants

Except for Wedgworth and Brown (2013), which was conducted in the rural United States, all the studies were conducted in low-income countries (Tables 2 and 3). These included Bangladesh (Alam et al., 2015; Ashraf et al., 2012; Ashraf et al., 2011; Escamilla et al., 2013; Opisa et al., 2012), Brazil (Moura et al., 2010), Egypt (Afifi et al., 1998), The Gambia (Emerson et al., 2004), India (Clasen et al., 2014; Collinet-Adler et al., 2015; Eshcol et al., 2009; Harikumar and Chandran, 2013; Heijnen et al., 2015; Patil et al., 2014; Rajgire, 2013), Indonesia (Park et al., 2015), Kenya (Greene et al., 2012; Knappett et al., 2011), Mali (Pickering et al., 2015), Nigeria (Jinadu et al., 2007; Nwuba and Philips, 2015), Philippines (Barrios, 2008), Tanzania (Briceño et al., 2015; Exley et al., 2015; Mattioli et al., 2014; Pickering et al., 2010, 2012), and Uganda (Howard et al., 2003). Collectively, the included studies covered a total of 49,407 samples, be it water samples, hand rinses, household latrines observed, etc. Most (15) studies were conducted in rural settings; others were conducted in urban areas including slums (10) or in both rural and urban settings (3). Except for Greene et al. (2012), which was conducted in a school setting, all the studies investigated sanitation at the household or community level.

3.1.3. Study designs

Included studies followed a full range of study designs, including randomized controlled trials (Alam et al., 2015; Briceño et al., 2015; Clasen et al., 2014; Emerson et al., 2004; Greene et al., 2012; Jinadu et al., 2007; Patil et al., 2014; Pickering et al., 2015), quasi- and non-randomized controlled trials (Barrios, 2008; Park et al., 2015), cohort studies (Ashraf et al., 2012), and cross-sectionals studies (Afifi et al., 1998; Ashraf et al., 2011; Collinet-Adler et al., 2015; Escamilla et al., 2013; Eshcol et al., 2009; Exley et al., 2015; Harikumar and Chandran, 2013; Heijnen et al., 2015; Howard et al., 2003; Knappett et al., 2011; Mattioli et al., 2014; Moura et al., 2010; Nwuba and Philips, 2015; Opisa et al., 2012; Pickering et al., 2010; Pickering et al., 2012; Rajgire, 2013; Wedgworth and Brown, 2013).

3.1.4. Sanitation interventions and conditions

All included studies investigated the effect of some type of enhanced sanitation condition or intervention compared to a control or other counterfactual. Most interventions involved latrine promotion or construction, including the use of community led total sanitation (CLTS), either alone or in combination with another WASH activity such as sanitation marketing, a subsidized sanitation program such as India's Total Sanitation Campaign (TSC), or some unspecified approach (Table 2). Some studies compared individual household latrines with shared latrines (Exley et al., 2015; Heijnen et al., 2015). In some cases, the sanitation intervention only involved promotion of disposal of child feces (Jinadu et al., 2007), including the provision of devices such as potties or sanitary scoops (Ashraf et al., 2012), or behavior change promotion plus devices to improve latrine hygiene in shared sanitation settings (Alam et al., 2015). Latrines varied between unimproved latrines (compared with open defecation), improved pit latrines, pour flush latrines, latrines emptying into septic systems or unspecified latrines (Tables 2 and 3).

3.1.5. Study outcomes

In this review, study outcomes consisted of endpoints used to assess the impact of sanitation along fecal transmission pathways. Numerous studies used microbiological assays to quantify the effect of sanitation on indicators of fecal contamination (*E. coli*, fecal coliforms, thermotolerant coliforms and others) on water samples collected at drinking water sources (Clasen et al., 2014; Escamilla et al., 2013; Harikumar and Chandran, 2013; Howard et al., 2003; Knappett et al., 2011; Nwuba and Philips, 2015; Opisa et al., 2012; Park et al., 2015; Patil et al., 2014; Pickering et al., 2015), or stored drinking water in the home (Clasen et al., 2014; Heijnen et al., 2015; Mattioli et al., 2014; Patil et al., 2014; Pickering et al., 2015; Wedgworth and Brown, 2013) (Table 2). Other studies used similar microbiological methods to assess contamination on hands of children or caretakers (Clasen et al., 2014; Greene et al., 2012; Heijnen et al., 2015; Mattioli et al., 2014; Pickering et al., 2010), food (Afifi et al., 1998), soil from the latrine floor (Pickering et al., 2012) or household compound (Moura et al., 2010) or latrine hand contact surfaces (Exley et al., 2015). Some studies assessed the impact of the intervention on exposure by observing the presence of flies in latrines (Briceño et al., 2015; Exley et al., 2015; Heijnen et al., 2015; Pickering et al., 2015) or counting flies caught in food preparation sites (Clasen et al., 2014; Collinet-Adler et al., 2015), or in the case of a trachoma trial, caught on or around eyes (Emerson et al., 2004). Other studies made observations on the presence of feces in or around the compound (Alam et al., 2015; Ashraf et al., 2012, 2011; Barrios, 2008; Briceño et al., 2015; Heijnen et al., 2015; Jinadu et al., 2007; Patil et al., 2014; Pickering et al., 2015). Six studies that measured fecal contamination of drinking water also measured distance between the sanitation facilities and the drinking water source (Escamilla et al., 2013; Harikumar and Chandran, 2013; Howard et al., 2003; Knappett et al., 2011; Nwuba and Philips, 2015; Opisa et al., 2012) (Table 3).

3.2. Effects of sanitation

The main results of this review are summarized in Table 1. With some exceptions, studies that assessed the impact of sanitation on indicators of fecal contamination generally found no effect. The results are discussed in further detail in this section.

3.2.1. Water quality

One study following a cross-sectional design reported a protective effect on source water in open defecation free (ODF) villages compared to non-ODF villages in India (Rajgire, 2013); another non-RCT design reported household latrines to reduce contamination of household well water (Park et al., 2015). Two trials in India found no effect on source drinking water from latrines provided under the Total Sanitation Program (Clasen et al., 2014; Patil et al., 2014); another trial in Mali also found no effect of CLTS on source water quality (Pickering et al., 2015). With respect to stored drinking water in the home, six studies found no effect from sanitation (Clasen et al., 2014; Eshcol et al., 2009; Heijnen et al., 2015; Patil et al., 2014; Pickering et al., 2015; Wedgworth and Brown, 2013) except for one comparison that found a protective effect for *E. coli*, but not *Bacteroidales* (Mattioli et al., 2014).

3.2.2. Hand and sentinel object contamination

One RCT in Kenya that evaluated a comprehensive WASH in schools intervention reported the hand rinses from children in the intervention schools to be more contaminated than those in control schools (Greene et al., 2012). Four other studies, including one RCT (Clasen et al., 2014) and three cross-sectional studies (Heijnen et al., 2015; Mattioli et al., 2014; Pickering et al., 2010), found no difference in the level of hand contamination from sanitation interventions or improved sanitation conditions. Clasen et al. (2014) also

Table 1
Summary of findings by outcome.

Outcome	Total No. Studies (Interventions)	Effects from Sanitation	GRADE
Water quality	9	No effect	Very Low
	(3)	No effect	Very Low
Hand contamination	5	No effect	Very low
	(2)	No effect	[a]Very Low
Sentinel object (toys)	1	No effect	NA
	(1)	No effect	NA
Food contamination	1	No effect	NA
	(0)	NA	NA
Surfaces and soil contamination	3	Mixed effects	Very Low
	(0)	NA	NA
Flies	7	Reduced fly counts where sanitation achieved high levels of coverage and use	Very Low
	(4)		[a]Low
Observations of feces	10	Some evidence of slight reduction in levels of feces present (Risk Difference −0.03, 95% CI: −0.06–0.01)	Very Low
	(7)		[a]Very Low
Contamination of water supply by distance to latrine	6	Inverse relationship between distance of water supply from a latrine and the level of contamination of such water supply	Low
	(0)		NA

[a] Where GRADE scores were between two ratings, the lower rating was selected.

found no effect of latrine construction under the Indian TSC on contamination of toys provided to children as sentimental objects for child exposure.

3.2.3. *Food contamination*

Only one cross-sectional study reported on the effect of sanitation (whether or not households had an indoor latrine) on food contamination (Afifi et al., 1998). This study found that lack of an indoor latrine was associated with an increased risk of *B. cereus* and *E. coli* in food samples.

3.2.4. *Surfaces and soil contamination*

Three cross-sectional studies found mixed effects of sanitation on soil samples. Moura et al. (2010) reported household soil samples to be more highly contaminated among households with bathrooms compared to households without bathrooms, but reported no effect when comparing households that used the bathrooms versus those that did not use them. Pickering et al. (2012) found no differences in fecal indicator bacteria in soil samples from latrine floors of households using a pit latrine with a concrete slab versus those with an earthen floor. In a cross sectional study from Tanzania, samples from high contact latrine surfaces were less fecally contaminated in improved versus unimproved latrines and pour flush latrines versus pit latrines without slabs (Exley et al., 2015). However, Exley et al. (2015) also reported higher levels of contamination on surfaces of improved household latrines versus shared sanitation and pour flush latrines versus pit latrines with slabs, but the results were not statistically significant.

3.2.5. *Flies*

The seven reporting on the association between sanitation and the presence of flies also reported mixed effects (Briceño et al., 2015; Clasen et al., 2014; Collinet-Adler et al., 2015; Emerson et al., 2004; Exley et al., 2015; Heijnen et al., 2015; Pickering et al., 2015). Of the four RCTs, one reported a reduction in flies in latrines in an evaluation of CLTS in Mali (Pickering et al., 2015). The other three RCTs reported no effect on fly counts in food preparation areas from latrines constructed in rural India (Clasen et al., 2014), around eyes from the construction of latrines in The Gambia (Emerson et al., 2004), and another or observed in latrines in Tanzania (Briceño et al., 2015). However, a cross-sectional study by Collinet-Adler et al. (2015) did find a reduction in flies trapped in food preparation areas when comparing households that use an indoor latrine and those who do not. In a cross-sectional study, Exley et al. (2015) reported that individual improved latrines versus shared latrines and also pour flush latrines versus pit latrines with slabs were associated with lower odds of flies being caught on traps in latrines; however, there was no difference in odds of flies trapped in improved versus unimproved latrines or pour flush versus pit latrines without slabs. In urban slums in India, Heijnen et al. (2015) also found lower odds for the presence of flies in individual household latrines compared to shared latrines.

3.2.6. *Observations of feces*

Two RCTs of sanitation interventions—one consisting of an evaluation of CLTS in Mali (Pickering et al., 2015) and the other evaluating a program to promote safe disposal of child feces and hygiene (Jinadu et al., 2007)—reported significantly lower observations of feces from the intervention arm. A third RCT assessing the TSC in India (Patil et al., 2014) found no effect of the intervention on observations of feces in the household compound or latrine floor. A fourth RCT assessing CLTS in rural Tanzania reported no effect on observations of feces outside the latrine from an intervention involving CLTS plus sanitation marketing; however, when the intervention was combined with hand washing promotion, it reduced observations of feces outside the latrine but increased observations of feces inside the household compound (Briceño et al., 2015). The authors concluded generally that the intervention changed behavior but not enough to reduce open defecation and thus the presence of feces in the environment. One RCT actually reported increased observations of feces among intervention households that received behavior change messaging on use of shared latrines plus products to enhance latrine cleanliness, a condition the authors suggested may be attributable to attitudes about the landlord's responsibility for maintenance (Alam et al., 2015). A quasi-RCT study assessing a program to promote hygiene and safe disposal of child feces in rural Philippines (Barrios, 2008) and a cohort study assessing a sanitation scoop, potties and hygiene education in Bangladesh (Ashraf et al., 2012) found no effects on the presence of feces in the yard or compound. However, a non-RCT reported fewer positive responses to a survey question asking about the presence of feces around the home among members of a latrine intervention arm (Park et al., 2015). A cross-sectional study in urban slums in India found fewer observations of feces in individual household latrines compared to shared latrines (Heijnen et al., 2015). Finally, a cross-sectional study in rural Bangladesh found no effect on observations of feces in the household compound when comparing hygienic versus non-hygienic latrines and shared versus individual household latrines, but did find lower levels of observed feces among households with hygienic latrines versus no latrine (Ashraf et al., 2011). The pooled risk difference of sanitation on observations of feces was −0.03 (95% CI: −0.06 to 0.01), providing some evidence of a slight reduction in

Table 2
Summary of studies assessing impact of sanitation on fecal-oral transmission pathways.

Study Reference	Setting	Study Design	Sanitation Condition/Intervention	Sanitation Coverage	Indicator Measured	Measure Description	Sample Size N	Effect Estimate (95% CI)	Estimate Type
A. Microbiological Indicators									
Afifi et al. (1998)	Egypt, rural	Cross-sectional	Household (HH) has indoor latrine vs. does not	89% of HHs had an indoor latrine (11% do not)	*B. cereus*	Sample of food prepared for infant	300	0.38 (0.22, 0.68)	RR
					E. coli	Sample of food prepared for infant	300	0.67 (0.44, 1.00)	RR
			Latrine used by children vs. not	29% of HHs the children used the latrine (71% did not)	*B. cereus*	Sample of food prepared for infant	300	0.38 (0.14, 1.00)	RR
					E. coli	Sample of food prepared for infant	300	0.67 (0.49, 0.91)	RR
Clasen et al. (2014)	India, rural	RCT	TSC (pour-flush latrine) intervention HHs vs. control HHs	63% of HHs in intervention villages had a functional latrine (12% for control villages)	Thermotolerant coliforms (TTC)	Sample of household drinking water	4911	1.06 (0.89, 1.24)	OR
					TTC	Sample of source water	3868	1.08 (0.90, 1.30)	OR
					TTC	Hand rinse of mother	352	0.88 (0.49, 1.58)	OR
					TTC	Hand rinse of child <5	339	0.85 (0.47, 1.55)	OR
					TTC	Rinse of children's toys	326	0.83 (0.50, 1.40)	OR
Eshcol et al. (2009)	India, slums	Cross-sectional	HH has improved and hygienic toilet vs. other	22% of HHs had improved toilet (all HHs had some kind of toilet)	Fecal coliform	Sample of stored household drinking water	50	1.67 (0.39, 6.73)	OR
Exley et al. (2015)	Tanzania, rural and urban	Cross-sectional	Improved latrine vs. unimproved	30% of sampled latrines were improved (23% unimproved)	*E. coli* (per 100 ml)	Swab of high contact latrine surfaces	182	−119.4 (−122.32, −116.48)	MD
			Improved latrine vs. shared	30% of sampled latrines were improved (47% shared)	*E. coli* (per 100 ml)	Swab of high contact latrine surfaces	262	8.50 (6.50, 10.50)	MD
			Pour flush latrine vs. pit without slab	46% of samples latrines were pour flush (21% pit without slab)	*E. coli* (per 100 ml)	Swab of high contact latrine surfaces	229	−137 (−139.62, −134.38)	MD
			Pour flush latrine vs. pit with slab	46% of samples latrines were pour flush (33% pit with slab)	*E. coli* (per 100 ml)	Swab of high contact latrine surfaces	269	9.40 (7.36, 11.44)	MD
Greene et al. (2012)	Kenya, schools	RCT	Comprehensive school WASH vs. control schools	30 pupils/latrine in comprehensive WASH schools at follow-up (49 pupils/latrine in control schools)	*E. coli*	Hand rinse of schoolchildren	419	1.61 (0.86, 3.01)	RR
					High *E. coli* levels	Hand rinse of schoolchildren	416	3.69 (1.08, 12.60)	RR

			Comprehensive school WASH vs. Hand-washing promotion and Water treatment only schools	30 pupils/latrine in comprehensive WASH schools at follow-up (55 pupils/latrine in HP + WT only schools)	*E. coli*	Hand rinse of schoolchildren	330	1.63 (1.43, 1.85)	RR
					High *E. coli* levels	Hand rinse of schoolchildren	312	2.20 (1.84, 2.63)	RR
Heijnen et al. (2015)	India, slums	Cross-sectional	Private HH latrine vs. shared	58% of HHs had private latrine (42% shared)	Thermotolerant coliform	Hand-rinse of both hands of primary household caregiver	570	1.30 (0.93, 1.83)	OR
						Sample of household drinking water	570	1.22 (0.86, 1.71)	OR
Mattioli et al. (2014)	Tanzania, rural and urban	Matched case-control	Use of improved sanitation infrastructure vs. other/unimproved	38% of HHs had improved sanitation (51% had access to a private latrine)	*E. coli virulence gene*	Hand rinses of female head of household	256	0.74 (0.43, 1.30)	OR
					E. coli virulence gene	Sample of household stored water	276	0.58 (0.34, 0.98)	OR
					Enteric virus	Hand rinses of female head of household	258	1.17 (0.60, 2.26)	OR
					Enteric virus	Sample of household stored water	267	0.50 (0.09, 2.75)	OR
					Bacteroidales	Hand rinses of female head of household	258	1.34 (0.78, 2.30)	OR
					Bacteroidales	Sample of household stored water	267	1.51 (0.64, 3.59)	OR
Moura et al. (2010)	Brazil, rural	Cross-sectional	Presence of bathroom in HH vs. absent	75% of HHs had a bathroom	Variety of parasites	Soil sample from household compound	40	1.55 (1.46, 1.65)	RR
			Use of bathroom by residents vs. not used	80% of HHs used the bathroom	Variety of parasites	Soil sample from household compound	40	0.98 (0.92, 1.04)	RR
Park et al. (2015)	Indonesia, urban	Non-RCT	HH latrine vs. no latrine	50.2% of HHs had a latrine (one village was provided latrines and the other was not)	*E. coli*	Sample of household well water	106	0.01 (0.00, 0.23)	OR
					High *E. coli* levels	Sample of household well water	106	0.02 (0.01, 0.06)	OR
					Low *E. coli* levels	Sample of household well water	106	4.37 (1.46, 13.13)	OR
Patil et al. (2014)	India, rural	RCT	TSC (pour-flush latrine) intervention HHs vs. control HHs	44.1% of HHs had an individual latrine	*E. coli*	Sample of household drinking water	807	−0.03 (−0.10, 0.04)	RD
					E. coli	Sample of household source water	511	−0.02 (−0.18, 0.15)	RD

Table 2 (*Continued*)

Study Reference	Setting	Study Design	Sanitation Condition/Intervention	Sanitation Coverage	Indicator Measured	Measure Description	Sample Size N	Effect Estimate (95% CI)	Estimate Type
Pickering et al. (2010)	Tanzania, urban	Cross-sectional	Improved (private or shared) vs. other (private or shared latrine without septic tank or pit lining)	All HHs had access to a latrine be it private or shared (50% had improved)	*E. coli*	Hand rinses of mother and child	2041	−0.07 (−2.03, 1.89)	RD
					Fecal streptococci	Hand rinses of mother and child	2041	−0.34 (−0.50, −0.18)	RD
Pickering et al. (2012)	Tanzania, urban	Cross-sectional	Private improved pit latrine with concrete slab vs. private unimproved pit latrine with earthen floor	All HHs had pit latrines (50% had a pit latrine with concrete slab)	*E. coli* *(Log CFU/g)*	Soil sample from latrine floor	200	−0.8 (−1.86, 0.26)	MD
					Enterococci *(Log CFU/g)*	Soil sample from latrine floor	200	−0.3 (−1.12, 0.52)	MD
Pickering et al. (2015)	Mali, rural	RCT	CLTS villages vs. control villages	64.8% of HHs had access to a private latrine in the intervention villages at follow-up (34.6% in control villages)	*E. coli* *(Log MPN/100* ml*)*	Sample of source household water	357	−0.24 (−0.58, 0.10)	MD
						Sample of stored household drinking water	889	−0.15 (−0.40, 0.009)	MD
Rajgire (2013)	India, rural	Cross-sectiona	ODF village vs. OD not free village	Not reported	Thermotolerant coliform	Sample of household source water	211	0.16 (0.07, 0.35)	OR
Wedgworth and Brown (2013)	United States, rural	Cross-sectional	On-site septic tank vs. no or unknown sanitation	65.6% of HHs had an on-site septic tank (34.4% had no or unknown sanitation)	Fecal coliform	Sample of household drinking water	305	0.92 (0.41, 2.10)	OR
B. Flies									
Briceño et al. (2015)	Tanzania, rural	RCT	CLTS + sanitation marketing villages vs. control villages	87% of HHs had access to improved sanitation at baseline across all villages	Flies	# flies observed around latrine	2974	−0.02 (−0.09, 0.05)	RD
			CLTS + sanitation marketing + handwashing promotion w/tippy taps villages vs. control villages		Flies	# flies observed around latrine	2974	0.02 (−0.05, 0.09)	RD
Clasen et al. (2014)	India, rural	RCT	TSC (pour-flush latrine) intervention HHs vs. control HHs	63% of HHs in intervention villages had a functional latrine (12% for control villages)	Flies	# flies caught in food preparation site during 3 consecutive nights	572	0.73 (0.46, 1.16)	Rate Ratio

Collinet-Adler et al. (2015)	India, rural and urban	Cross-sectional	Family uses indoor latrine vs. does not	75% of HHs used an indoor latrine	Flies	# flies caught in food preparation site over the course of 1–15 days during 2 separate months	234	0.61 (0.45, 0.82)	RR
Emerson et al. (2004)	The Gambia, rural	RCT	Latrine construction intervention villages vs. control villages	100% of HHs in the intervention villages had a latrine (32.1% of HHs in control)	Flies (*musca domestica*)	# flies caught with hand-net In 15 min – fly had to touch eyes of volunteer child	192	0.04 [a]not significant	MD
					Flies (*musca sorbens*)	# flies caught with hand-net In 15 min – fly had to touch eyes of volunteer child	192	−0.56 [a]not significant	MD
Exley et al. (2015)	Tanzania, rural and urban	Cross-sectional	Improved latrine vs. unimproved	30% of sampled latrines were improved (24% unimproved)	Flies	Flies caught on sticky paper in latrine	173	0.82 (0.45, 1.51)	OR
			Improved latrine vs. shared	30% of sampled latrines were improved (46% shared)	Flies	Flies caught on sticky paper in latrine	244	0.35 (0.21, 0.60)	OR
			Pour flush latrine vs. pit without slab	45% of samples latrines were pour flush (22% pit without slab)	Flies	Flies caught on sticky paper in latrine	214	1.25 (0.70, 2.23)	OR
			Pour flush latrine vs. pit with slab	45% of samples latrines were pour flush (33% pit with slab)	Flies	Flies caught on sticky paper in latrine	251	0.45 (0.27, 0.76)	OR
Heijnen et al. (2015)	India, slums	Cross-sectional	Private household latrine vs. shared	58% of HHs had private latrine (42% shared)	Flies	Presence of flies in latrine cubicle (some or many vs. none)	764	0.13 (0.08, 0.22)	OR
Pickering et al. (2015)	Mali, rural	RCT	CLTS villages vs. control villages	64.8% of HHs had access to a private latrine in the intervention villages at follow-up (34.6% in control villages)	Flies	# flies observed in latrine	3178	−0.12 (−0.20, −0.03)	RD

Table 2 (*Continued*)

Study Reference	Setting	Study Design	Sanitation Condition/Intervention	Sanitation Coverage	Indicator Measured	Measure Description	Sample Size N	Effect Estimate (95% CI)	Estimate Type
C. Observations of Feces									
Alam et al. (2015)	Bangladesh, slums	RCT	Behavior change messaging on use and cleanliness of shared toilets + provision of flushing bucket, water storage bucket and waste bin vs. control	All HHs had access to shared sanitation	Observed feces	Feces coming out from septic tank, pit or from connected line	1214	0.02 (−0.01, 0.05)	RD
					Observed feces	Feces visible outside pan	1795	−0.01 (−0.04, 0.02)	RD
					Observed feces	Feces visible on path leading up to toilet	1214	0.02 (−0.02, 0.05)	RD
Ashraf et al. (2011)	Bangladesh, rural	Cross-sectional	HH has 'feces isolating' hygienic latrine vs. no access to hygienic latrine	15.8% of HHs had access to a hygienic latrine (82.5% had an unhygienic latrine and 1.7% did not have a latrine)	Observed feces	Human feces visible in household compound	1430	−0.22 (−0.41, −0.03)	RD
			HH has 'feces isolating' hygienic latrine vs. unhygienic latrine		Observed feces	Human feces visible in household compound	1406	−0.04 (−0.08, −0.00)	RD
			Latrine owned by HH vs. latrine shared	46.5% of HHs owned their latrine	Observed feces	Human feces visible in household compound	1406	0.01 (−0.02, 0.04)	RD
Ashraf et al. (2012)	Bangladesh, rural	Cohort (pre vs. post)	Saniscoop, potty and hygiene education intervention vs. control	Not reported	Observed feces	Human feces visible in household compound	200	.04 (−0.06, 0.15)	RD
Barrios (2008)	Philippines, rural	quasi-RCT	Promotion of safe disposal of child feces and hygiene vs. control	99% of adults reported defecating in a latrine	Observed feces	Feces visible in yard	248	0.10 (−0.02, 0.22)	OR
Briceño et al. (2015)	Tanzania, rural	RCT	CLTS + sanitation marketing villages vs. control villages	87% of HHs had access to improved sanitation at baseline across all villages	Observed feces	Feces visible outside latrine	2896	0.01 (−0.03, 0.06)	RD
					Observed feces	Feces visible inside household	3583	0.01 (−0.02, 0.04)	RD
			CLTS + sanitation marketing + handwashing promotion w/tippy taps villages vs. control villages		Observed feces	Feces visible outside latrine	2896	−0.04 (−0.08, −0.00)	RD
					Observed feces	Feces visible inside household	3583	0.08 (0.04, 0.12)	RD

Heijnen et al. (2015)	India, slums	Cross-sectional	Private HH latrine vs. shared	58% of HHs had private latrine (42% shared)	Observed feces	Feces visible in latrine cubicle	764	−0.22 (−0.27, −0.16)	RD
Jinadu et al. (2007)	Nigeria, rural	RCT	Promotion of latrine improvements, safe disposal of child feces and handwashing with soap vs. control	100% of HHs had access to a pit latrine (only 5.4% had a 'sanitary' pit latrine)	Observed feces	Feces visible in household compound	295	−0.29 (−0.37, −0.20)	RD
Park et al. (2015)	Indonesia, urban	Non-RCT	HH latrine vs. no latrine	50.2% of HHs had a latrine (one village was provided latrines and the other was not)	Observed feces	Self-reported Y/N to "Often see feces around the house?"	804	−0.07 (−0.12, −0.03)	RD
Patil et al. (2014)	India, rural	RCT	TSC (pour-flush latrine) intervention HHs vs. control HHs	44.1% of HHs had an individual latrine	Observed feces	Human/animal feces visible in household compound	3012	−0.02 (−0.07, 0.03)	RD
Pickering et al. (2015)	Mali, rural	RCT	CLTS villages vs. control villages	64.8% of HHs had access to a private latrine in the intervention villages at follow-up (34.6% in control villages)	Observed feces	Feces visible on latrine floor	3178	0.00 (−0.05, 0.05)	RD
					Observed feces	Human feces visible in household compound	39	−0.06 (−0.09, −0.02)	RD

[a] Unable to calculate the confidence interval for the mean difference but since the confidence intervals for the individual means of the intervention and control arm overlap the finding is not significant.

Table 3
Summary of studies assessing the impact of onsite sanitation on water quality by distance from water supply.

Study Reference	Setting	Study Design	Sanitation Distance Measure	Fecal Exp. Measured	Measure Description (Sample Size N)	Findings
Escamilla et al. (2013)	Bangladesh, rural	Cross-Sectional	Latrines and latrine-polluted ponds within × distance of tube well	*E. coli*	Water samples from tube wells (92)	*E. coli* levels during late monsoon season were positively correlated with the number of latrines and latrine-polluting ponds within 60–70 m away from tube wells (unsanitary latrines became significant starting at 30 m and sanitary latrines at 55m)
Harikumar and Chandran (2013)	India, urban	Cross-Sectional	Wells located >7.5 m from latrines vs. <7.5 m from latrine	*E. coli*	Water samples from dug wells (24)	Wells located <7.5 m from latrines had 6.25 greater odds of being contaminated than wells located >7.5m
Howard et al. (2003)	Uganda, urban	Cross-Sectional	Latrines × distance uphill from protected spring	Thermotolerant coliform and fecal streptoccoci	Water samples from protected springs (35)	Thermotolerant coliform and fecal streptococci contamination of protected springs (at levels >0 to >50 cfu/100 ml) was not significantly associated with proximity to latrines located <30 to <50 m uphill.
Knappett et al. (2011)	Kenya, slums	Cross-Sectional	Number of latrines within × distance of pond	Cultured *E. coli*, molecular measured *mE. coli*, Bacteroidales, and adenovirus	Water samples from pond water (43)	Cultured *E. coli* levels were significantly correlated with the number of latrines within 20–80 m of a pond (number of unsanitary latrines became significant within 15–80 m and sanitary latrines within 40–70m). *mE.coli* and Bacteroidales were significantly correlated with the number of unsanitary latrines within 80–100 m of a pond while adenovirus was not significantly correlated at any distance to any latrine type. The number of latrines at an optimal distance of 60 m was found to be significantly correlated to all three fecal bacteria (cultured *E. coli*, *mE.coli*, and Bacteroidales).
Nwuba and Philips (2015)	Nigeria, urban	Cross-sectional	Septic tank × distance from well	Total coliform	Water samples from wells (31)	A decrease in total coliform count was correlated with an increase in distance from well to septic tank. This correlation was stronger during the rainy season ($r = -0.58$, $P < 0.05$) compared to the dry season ($r = -0.51$, $P < 0.01$).
Opisa et al. (2012)	Bangladesh, rural	Cross-Sectional	Latrines × distance from well	*E. coli*	Water samples from protected and unprotected wells (53)	*E. coli* coliform density in wells was significantly negatively associated with lateral distance to pit latrines

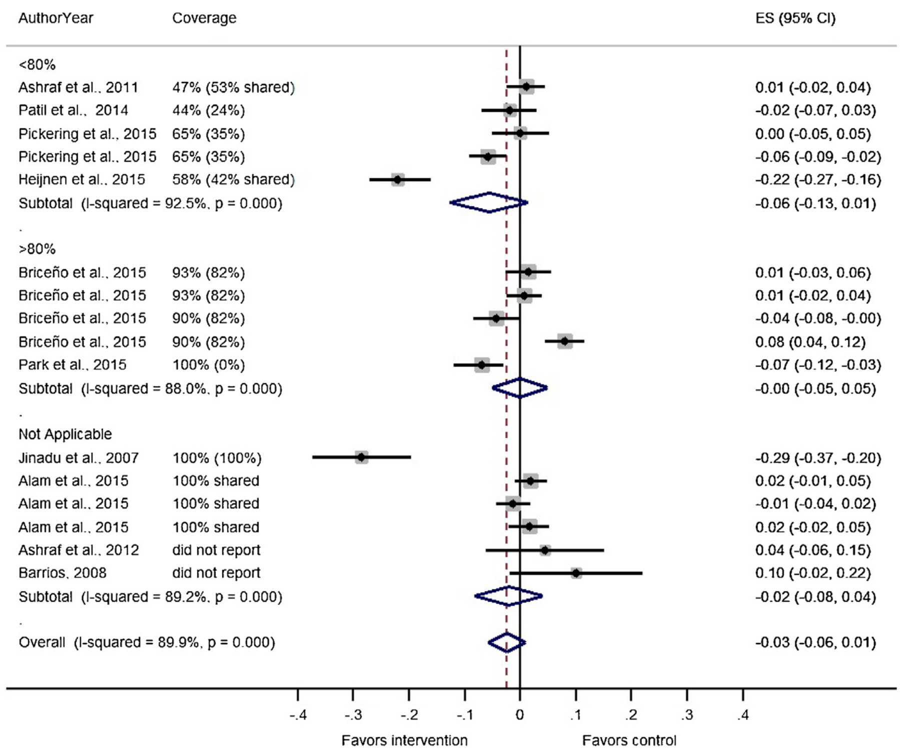

Fig. 2. Forest plot showing effect of sanitation on observation of feces, stratified by coverage. The measure of effect was risk difference between households with the intervention or other enhanced sanitation condition compared to controls or those without. Coverage subgrouping is by the percent of the study population in the intervention or enhanced sanitation condition group with access to a private latrine. The percent coverage for the control group is in parentheses. Studies that did not report a coverage measure, focused solely on shared sanitation, or had 100% coverage in both intervention and control groups were categorized as 'not applicable'.

levels of feces present albeit not statistically significant. Subgrouping on the level of sanitation coverage (at 80% cut point) provides some evidence that sanitation interventions are more effective at reducing levels of observed feces when coverage starts at a lower threshold and there is a greater difference in coverage between the intervention and control arm (see Fig. 2). The pooled risk difference for the <80% coverage subgroup was −0.06 (95% CI: −0.13, 0.01) while the >80% coverage subgroup had no risk difference pooled estimate of −0.00 (95% CI: −0.05, 0.05), suggesting more prominent detection of reduction in observed feces for studies with lower coverage thresholds. Moreover, the <80% coverage subgroup studies showcased greater difference in coverage between their intervention and control arms than the >80% coverage subgroup. The only point estimate from the >80% coverage subgroup that indicated significant reduction in feces present came from Patil et al. (2014) where there was a dramatic 100% difference in coverage between the intervention and control arm.

3.2.7. *Contamination of water supply by distance to latrine*

Findings on the association between fecal contamination of water and the distance between water supply and on site sanitation facilities are summarized in Table 3. In general, studies show an inverse relationship between the distance of a water supply from a latrine and the odds, risk or level of fecal contamination of such water supply. Results from these studies also suggest that the effects may not only depend on distance but also seasons (Escamilla et al., 2013) and latrine density (Knappett et al., 2011). However, all the studies were cross-sectional and thus only measured the effects on the distances actually present in the study setting; none of the studies experimented with the effect of distance keeping other potentially important co-variants constant. Given the effects of hydrology, gradients, soil conditions, seasons, fecal load, pathogens present and other factors on the migration of pathogens in the soil (Graham and Polizzotto, 2013), it is not clear from current evidence whether these results can be generalized to other settings.

3.3. *Risk of bias and GRADE*

The intervention studies scored relatively high on the LQAT assessment with an average risk of bias score of 8 out of 12 (range of 5–11), with 12 being no detection of bias in the study. In general, studies scored poorly on selection bias, response rate bias, and exposure assessment bias. Selection bias was a common issue in larger trials as they assessed transmission outcomes in convenient sub-groups of the study population. In other studies, selection of participants and response rate were simply not reported and thus bias was assumed possible. In many cases, exposure assessment bias was present because of the possibility of spillover due to the nature of the sanitation interventions.

The risk of bias assessment in GRADE was based on the averaged LQAT score for the set of intervention studies included in a given finding. We determined downgrade cut offs where an averaged score of 8 or below indicated serious or very serious risk of bias in the studies while a score of 9 or above indicated relatively low risk of bias. Most findings were only downgraded by 0.5 or not at all for the risk of bias assessment.

Overall, the different transmission pathway findings received a GRADE rating of low or very low. This was primarily because of the inconsistency found in the direction of the effect where some studies suggested a protective effect of sanitation while others suggested a harmful effect. Findings were also downgraded for imprecision, as many effect estimates were not statistically significant. However, it is interesting to note that while the observational studies automatically started at a GRADE rating of low, the distance papers maintained this rating and were not further downgraded like the other observational studies. This was due to the consistent finding across the distance papers that well contamination is negatively correlated with distance from a latrine and almost all six studies were statistically significant.

4. Discussion

The transmission pathways for oral-fecal exposure represented by the "five F's"—fingers, flies, food, fluids, fields—were first described over six decades ago (Wagner and Lanoix, 1958). To our knowledge, however, this review represents the first effort to assemble evidence on the effects of sanitation on the transmission pathways of fecal exposure. This may be partly due to the increase in research on sanitation generally, and more specifically on the number of studies that have measured the effects of sanitation on exposure pathways as an intermediate outcome in trying to assess sanitation interventions. Insofar as interrupting transmission is a necessary condition to reducing exposure and preventing diseases, understanding the impact of sanitation on these transmission pathways is often vital in explaining why an intervention did or did not have a health impact.

Overall, these studies showed only mixed effects of sanitation on most transmission pathways. Among the microbiological indicators on water (fluids), hands (fingers), fomites (toys), food, and soil/surfaces (fields), most studies found no effect. This was particularly true for the higher quality studies that followed experimental study designs. A non-RCT did report that improved sanitation reduced fecal contamination of drinking water (Park et al., 2015). However, even cross-sectional studies found little or no protective effects of sanitation on microbiological indicators along these transmission pathways. One of four RCTs found sanitation to reduce fly counts (Pickering et al., 2015); the other three trials assessing effects on flies from programmatically-delivered interventions showed no effects. A single cross-sectional study (Exley et al., 2015) reported reductions in flies from moving up the sanitation ladder (individual household latrines (versus shared)) and pour flush latrines (versus pit latrines) but not from other steps (improved versus unimproved latrines or pour flush versus pit latrines without slabs) (UNICEF and WHO, 2015).

Observations of feces around the home have long been known as a predictor of adverse health outcomes from sanitation-related diseases, including diarrhea (Bartlett et al., 1992; Traoré et al., 1994). Pooled estimates found a slight protective effect from sanitation on this indicator, though the overall results were not significant. One trial assessing a CLTS intervention (Pickering et al., 2015) and another trial assessing a combined intervention promoting sanitation, safe disposal of child feces and hygiene (Jinadu et al., 2007) reported reductions in observations of feces around the home or in the latrine. So did one observational study comparing 'feces isolating' hygienic latrines, including pour-flush, pit latrines with slab, and composting latrines whether shared or private, with no sanitation or non-hygienic latrines (Ashraf et al., 2011). However, another trial of CLTS (Briceño et al., 2015) and other studies of sanitation reported little or no effect on observations of feces. Subgrouping on the level of sanitation coverage provided some evidence that sanitation interventions are more effective at reducing levels of observed feces when coverage starts at a lower threshold and there is a greater difference in coverage between the intervention and control arm.

Results also suggest that coverage may impact the fly transmission pathway. In the four RCTs assessing the impact of the intervention on flies, for example, the one trial that found a significant reduction in flies reported full access (combining latrines owned or shared with neighbors) and high levels of use (Pickering et al., 2015). This is in contrast to two other RCTs that found no impact on flies, both of which reported lower levels of coverage and use (Briceño et al., 2015; Clasen et al., 2014). However, the remaining trial that found no impact on flies had 100% coverage and 98% use (Emerson et al., 2004).

4.1. Limitations

This review has two major limitations. Chief among these is the quality of the evidence. As noted above, most included studies are of poor methodological quality. Even conclusions that include studies using randomized study designs are only low quality of evidence or very low due to downgrading based on GRADE criteria. At the same time, we note that environmental health research in low-income settings is often subject to more challenges and have fewer financial resources or shorter time scales when compared to clinical trials in other settings for which many of the meta-analysis and systematic review methods were originally developed. Thus, the expectation of the degree of rigor found in the literature may differ, and the GRADE ratings and LQAT scores may be skewed lower for the entire field of research. The second major limitation is the inclusion of studies that are fundamentally heterogeneous. While all the studies assessed the impact of sanitation on pathways of fecal exposure in human populations, they varied significantly in ways that could explain their differences in results. This includes differences in study settings and populations, ambient conditions, population density, types of sanitation investigated, levels of coverage achieved, levels of adoption and use, pathways investigated, methods of assessing impact, indicators used, methods of analysis, and outcome measures of effect. This heterogeneity made a meta-analysis inappropriate for most comparisons covered by the review. It also suggests caution in any comparison of the results across studies.

5. Conclusions

Notwithstanding these limitations, this review suggests major deficiencies in sanitation efforts in low-income countries to mitigate the effects of fecal-oral transmission along well-known pathways. This may be explained in many cases by evidence that sanitation interventions often fail to achieve universal coverage or use (Garn et al., submitted). The failure of sanitation to mitigate exposure through these pathways may also explain differences in health impacts from sanitation interventions (Freeman et al., submitted). This review also demonstrates the need for any assessment of sanitation to carefully investigate the impact of the intervention on multiple transmission pathways. This should include rigorous approaches using more standardized methods that allow for comparisons across studies. As reducing exposure is a condition to preventing disease, the impact of the intervention on health—and the mechanism of action—can be better understood by documenting effects on these intermediate environmental outcomes.

Funding source

The World Health Organization provided funding for this review. WHO funding as made possible through contributions from the Department for International Development, UK and the Bill and Melinda Gates Foundation.

Acknowledgements

We are grateful to the following who contributed to the review: Darcy Anderson, Sophie Boisson, Patrick Brooks, Henrietta Lewis, Amrita Mahtani, Kate Medlicott, Divya Narayanan, Eva Rehfuess and Rachel Stelmach. We also acknowledge funding support for this review from the World Health Organization.

Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at http://dx.doi.org/10.1016/j.ijheh.2016.09.021.

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