Effects of sewerage on diarrhoea and enteric infections: a systematic review and meta-analysis

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Summary

Background **Sanitation is inadequate in most cities in developing countries, with major effects on infectious disease burden: in this situation, is piped sewerage an appropriate solution, or should efforts focus on systems based on onsite solutions, such as latrines? We reviewed the effects of the presence of sewerage systems on diarrhoeal disease and related outcomes. We included only observational studies because so far there have been no randomised controlled trials.**

Methods **We identified relevant studies by use of a comprehensive strategy including searches of Medline and other databases from 1966 to February, 2010. In studies that compared sewerage with one other sanitation category, we used relative risk (RR) estimates for sewerage versus the other category. When a single study made two or more comparisons, we calculated a weighted average RR value, and used this value in our meta-analysis. We used the most adjusted RR estimate provided by the authors; if no adjusted estimate was available, we used the crude estimate. To obtain pooled-effect estimates, meta-analyses were done by use of an inverse variance method—ie, the study-specific adjusted log ORs for case-control and cross-sectional studies, and log RRs for cohort studies, were weighted by the inverse of their variance to compute a pooled RR with 95% CI.**

Findings **25 studies investigated the association between sewerage and diarrhoea or related outcomes, including presence of intestinal nematodes. Pooled estimates show that sewerage systems typically reduce diarrhoea incidence by about 30% (RR 0·70, 95% CI 0·61–0·79), or perhaps as much as 60% when starting sanitation conditions are very poor. Studies with objective outcome measures showed even stronger pooled effect than studies that assessed diarrhoea incidence with interviews, while sensitivity analysis indicated that the effect remains even if we assume strong residual confounding.**

Interpretation **Sewerage interventions seem to reduce the incidence of diarrhoea and related outcomes. However, we urge cautious interpretation of these findings, because, in many contexts, sewerage might be less cost effective and sustainable than onsite alternatives.**

Funding **None.**

Introduction

Improvements in sanitation will likely lead to reductions in morbidity due to faeco-orally transmitted diseases. The sewerage-based sanitary revolution in 19th and early 20th century Britain is widely accepted to have had a massive public health effect,[1] but the evidence supporting the health benefits of sanitation in present-day developing contexts is sparse.[2]

One of the major expected health benefits of improved sanitation is reduced morbidity and mortality due to diarrhoeal diseases,[3] which remain a major contributor to general morbidity and mortality in middle-income and low-income countries worldwide.[4] Worldwide deaths from diarrhoea in children younger than 5 years are estimated at about 1·9 million every year, about 20% of total child deaths.[5] In developing countries, 10% of the total burden of disease is estimated to be attributable to poor water, sanitation, and hygiene, and about 60% of this is due to diarrhoeal diseases.[6]

We systematically review the effects of one particular sanitation solution, waterborne sewerage, on diarrhoeal disease and related outcomes. In waterborne sewerage systems, faecal wastewater from cistern-flush or pour-flush toilets (and often kitchen and washing wastewater) is piped out of the community for disposal elsewhere, ideally after treatment; common alternative solutions in lower-income contexts include pit latrines of diverse types, and pour-flush toilets discharging to septic tanks or to open drains. Additionally, many poor people living in urban environments do not have toilets in their own home, and use communal facilities or open defecation.[7,8] Related previous reviews[2,9–12] offer very useful analyses of water supply, sanitation, and hygiene education effects, but have generally analysed all types of sanitation solution together, without distinguishing sewerage or other specific solutions. Two of these reviews applied meta-analysis.[2,12] Fewtrell and co-workers[2] investigated the effects of sanitation on diarrhoeal disease, and included only four studies of the effects of sanitation interventions (none of them sewerage interventions). Since June 2003, the end-date for Fewtrell and co-workers' search of published work, several new studies of sewerage effects have been published. Additionally, our own search has identified several studies of the effects of sewerage not included in that study. Waddington and co-workers[12] investigated sanitation in general, but also more specifically sewerage and latrines; however, they include only four studies of the effects of sewerage in their analysis.

Whether or not to invest in sewerage (as opposed to onsite sanitation solutions such as latrines, septic tanks, or dry-composting toilets) is a practically relevant question for urban sanitation planners in developing countries.[13] Some authors suggest that sewerage, or low-cost variants thereof, is the solution of choice in dense urban settlements,[14,15] whereas others conclude that it is often too costly and no more effective than properly designed onsite sanitation.[16,17] Politicians in the developing world are often judged to favour sewerage excessively, at the expense of simpler solutions that might be more beneficial to poor people.[18] Recent estimates suggest that the proportion of urban households connected to sewers ranges from about 83% in west Asia, through 73% in north Africa, 62% in Latin America, 50% in east Asia, 24% in south Asia, 19% in sub-Saharan Africa, to just 9% in southeast Asia.[14] In most cities in low-income countries (notably in sub-Saharan Africa and southeast Asia), sewerage typically serves only the city's business centre, and indeed some major cities (eg, Lagos) have practically no functional sewerage system even in central districts.

Clasen and co-workers[19] have recently submitted a protocol to the Cochrane Collaboration for a review of the effect of excreta disposal interventions on all types of diarrhoea, including only randomised and quasirandomised controlled trials. So far, however, there have been no randomised controlled trials of sewerage provision. Indeed, there are formidable barriers to the randomisation of interventions of this type: notwithstanding the theoretical possibility of stepped-wedge designs,[20] in practice it would be extremely difficult for a major sewerage project to select its districts of intervention randomly and not on the basis of financial factors, social concerns, site topography, and network logic.

In our systematic review and meta-analysis we investigate the association between sewerage provision and diarrhoea and related outcomes, considering all relevant studies published so far. We report the participants, interventions, comparands, outcomes, and study design as outlined in the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.[21]

Methods

Search strategy and inclusion criteria

We searched databases from 1966 to end February, 2010, to identify all potentially eligible studies. For Medline, we applied the following algorithm both in Medical Subject Heading and in freetext words: ("sanitation" "or" "sewer*" or "excreta-disposal) and ("diarrhea*" or "diarrhoea*" or "cholera" or "shigell*" or "dysenter*" or "cryptosporid*" or "giardia*" or "escherichia" or "clostridium" or "campylobacter" or "vibrio" or "enteric" or "entamoeb*" or "norovirus" or "rotavirus" or "adenovirus" or "etec" or "parasitic" or "intestinal-parasites" or "nematode*" or "ascari*" or "trichuri*" or "hookworm" or "pinworm" or "cyclospora"). Similar strategies were used to search Embase (1980–2009), the Latin American and Caribbean Health Science Information database, and the Institute for Scientific Information Proceedings database. We also examined the references of every article retrieved and those of recent reviews of health effects of sanitation.[2,9–12] Unpublished studies were not included.

Studies were included if they presented original data from case-control or cohort studies, non-randomised trials, or cross-sectional studies; the outcome of interest was clearly defined as diarrhoea or presence of gastrointestinal pathogen; one of the exposure factors was sanitation type, and one of the levels of this factor was sewerage; and estimates were provided of odds ratio (OR), relative risk (RR), or longitudinal prevalence ratio (LPR; defined by Barreto and co-workers[22]) and its CIs, or enough data were provided to calculate them. After initial screening of titles and abstracts by GN, eligibility for inclusion was established independently by GN and BT; no disagreements arose. If data on the same population were duplicated in more than one study, the most complete study was included in the analysis. We included studies in children or adults in any region of the world; interventions were any piped sewerage intervention; comparisons were the pre-sewerage sanitation situation of the study's selected non-sewerage comparison situation; outcomes were diarrhoea or specified enteric infections including helminth infections.

Data extraction and quality assessment

Data were recorded in a standard data-recording form developed for this study. The standard data items included authors, year of publication, study location (country, city or cities), study periods, study design, sanitation levels, minimum and maximum age of people participating (years, months), sample size, control group selection characteristics, follow-up periods in cohort studies (mean, range), outcome, outcome measurement details, effect estimator (OR, RR, other), effect estimate, 95% CIs, and adjustment factors used. When further clarification was necessary (particularly of sanitation levels), we attempted to contact the authors. Risk ratios, LPRs, and case-control ORs are treated as equivalent RR estimates.

18 of 25 studies included in our review compared sewerage with one other sanitation category, most commonly flush toilets discharging to septic tanks or open drains. In these cases we used RR estimates for sewerage (sanitation level 1; L1) versus the other category (sanitation level 2; L2). When a single study made two or more comparisons (eg, sewerage *vs* septic tanks [L1 *vs* L2] and sewerage *vs* latrines [L1 *vs* L3]), we calculated a weighted average RR value, and used this value in our meta-analysis; additionally, specific subgroup analyses were done with the individual RR estimates for L1 versus L2 and L1 versus L3. We used the most adjusted RR

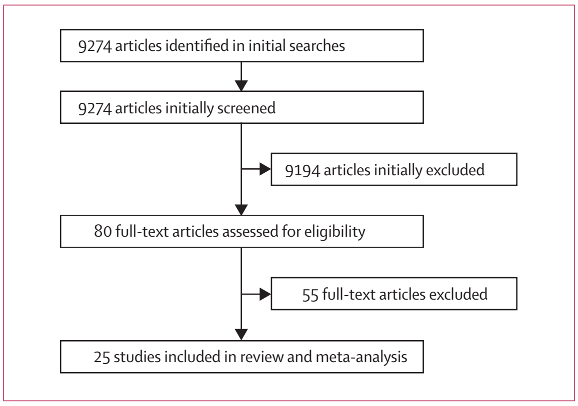

Figure 1: **Flow diagram of study selection**

estimate provided by the authors; if no adjusted estimate was available, we used the crude estimate.

Study quality was assessed by use of a five-point binary scale that we specifically developed for this study. The scale is based on the Newcastle-Ottawa scale[23] and the scale used by Fewtrell and co-workers[2] but with modifications in view of standard guidelines[24,25] and our own judgment. The first point assessed exposure, rating how clearly sanitation levels were defined: a score of one was given if all sanitation levels were described, and a score of zero for an insufficient description (eg, "non-sewered" without further clarification). The second point assessed outcome, rating whether the measurement was acceptable: a score of one was given for objective measures such as clinical diagnosis or stool analysis, or interviews with a guardian with clear definition of diarrhoea episode and a recall period of 2 weeks or less, and a score of zero if other or unspecified measures were used. The third point assessed comparison group, rating whether the selection of a control group was acceptable: for cohort studies a score of one was given if the people in the comparison group were drawn from the same source populations as the people in the sewerage group, and a score of zero was given if the people in the comparison group were drawn from different populations or the procedure was unspecified; for case-control studies a score of one was given if the people in the control group had confirmed absence of recent history of diarrhoea or similar diseases and a score of zero was given if the people in the comparison group might have had diarrhoea or similar diseases recently, or no information was available; for cross-sectional studies a score of one was given if the people in the comparison group were drawn from same source populations as the people in the sewerage group and a score of zero was given if the people in the comparison group were drawn from different populations, or if the procedure was unspecified. The fourth point assessed participation, rating whether participation or follow-up was acceptable: for cohort studies a score of one was given if loss to follow-up was less than 20% in all cohorts and a score of zero was given if loss to follow-up was greater or unspecified; for case-control studies a score of one was given if there was at least 80% participation in both groups and a score of zero was given if participation was lower or unspecified; for cross-sectional studies a score of one was given if actual sample size was at least 80% of the people initially approached and a score of zero was given if the sample size was lower or unspecified. The fifth point assessed confounding, rating whether adjustment, matching, and restriction were acceptable: a score of one was given if there was adjustment, matching, or restriction at least for age, and either household income or mother's educational level, and a score of zero was given if these criteria were not met or unspecified. Quality scoring was done by GN and BT independently, and the average score used in subsequent analyses. The proportion of agreement between the two raters ranged from 91% for point two to 100% for points one and four. Subgroup analyses done subsequently considering each of the five criteria separately, and considering the aggregate scores.

Statistical analysis

To obtain pooled effect estimates, meta-analyses were done by use of an inverse variance method—ie, the study-specific adjusted log ORs for case-control and cross-sectional studies, and log RRs for cohort studies, were weighted by the inverse of their variance to compute a pooled RR and its 95% CI. This method of pooling gives greater weight to large studies in the final pooled estimate. The presence of between-study heterogeneity was assessed using a parametric bootstrap version of the DerSimonian and Laird Q test, and heterogeneity was quantified as the proportion of total variance due to between-study variance (R_I).[26] Sources of heterogeneity were explored by visual examination of forest plots, and by analyses of subgroups of studies defined by characteristics including design, outcome variable, subject age, study location, and type of sanitation comparison. We present both fixed-effects and random-effects pooled estimates but use and report the latter when heterogeneity was present, as in our main analysis and most subgroup analyses: the randon-effects model is generally thought to give more reliable results than the fixed-effects model, including a more conservative (wider) CI, when the studies being considered show high heterogeneity.[25] Publication bias[27] was assessed using the Egger test for funnel-plot assymetry.[28] All analyses were done with the program HEpiMA version 2.1.3[29] and SPSS version 16.0 (SPSS, Inc, Chicago IL).

Results

9274 studies were identified in our initial searches, and after initial screening of titles and exclusion of repeat hits from different searches, 80 studies remained (figure 1). After review of abstracts, then of full texts and, where necessary, after communication with authors, 25 studies met the criteria for inclusion in our review (table 1). 11 studies were incidence-based (six cohort studies, four case-control studies, and one non-randomised trial), and 14 were cross-sectional.

The studies included in our review were done between 1980 and 2006, in ten countries. 14 studies were from Brazil;[22,32–36,38,45–51] the other studies were from Mexico,[31,43,44] Nicaragua,[52] Honduras,[53] Peru,[30] the USA,[37] Iran,[39] Syria,[40] Saudi Arabia,[41] and Australia.[42] Precise age ranges of the participants involved varied, but 21 of 25 studies were of children, with minimum ages between 0 and 12 months and maximum ages between 3 months and 14 years. The primary outcome was diarrhoea incidence in 17 studies, *Giardia* spp prevalence (in stool) in four studies, intestinal parasite prevalences (in stool) in three studies, and cryptosporidium seroprevalence in one study (table 1; full details in webappendix). All but one[34] of the incidence-based studies had diarrhoea as an outcome.

Figure 2 shows effect estimates from the individual studies. Table 2 lists the pooled effect estimates for all 25 studies and diverse subgroups. The pooled RR estimate from all 25 studies was 0·70 (95% CI 0·61–0·79), with high heterogeneity and no evidence of publication bias (Egger's test for funnel plot asymmetry p=0·21; figure 3). Heterogeneity remained high in most subgroup analyses (table 2), but was moderate among cross-sectional studies (R_i=0·56), studies in which sewerage was compared with septic-tank-only (R_i=0·50), and studies in which the outcome was not diarrhoea (ie, mostly helminth prevalence; R_i=0·49), and low among studies in regions other than Latin America (R_i=0·21) and non-child studies (R_i=0·05).

See Online for webappendix

	Design	Sample*	Outcome (outcome measure)	Assessment	Adjust†	Quality score
Barreto (2007)[22]	Cohort (after-before)‡	1007	Diarrhoea (longitudinal prevalence)	Reported in the past 3–4 days; twice weekly visits (3–8 months follow-up)	Yes	4·0
Checkley (2004)[30]	Cohort (single area)‡	110	Diarrhoea (incidence)	Reported in the past day; daily visits (35 months follow-up)	Yes	4·0
Macías-Carrillo (2005)[31]	Cohort (single area)	··	Diarrhoea (incidence)	Reported in the past 2 weeks; visits every 2 weeks (3 months follow-up)	Yes	2·5
de Melo (2008)[32]	Cohort (two districts)	42	Diarrhoea (incidence)	Reported in the past 2 days; visits every 2 days (12 months follow-up)	No	3·0
Moraes (2003)[33]	Cohort (three by three districts)‡	417	Diarrhoea (incidence)	Reported in the past week; weekly visits (12 months follow-up)	Yes	3·0
Mascarini-Serra (2010)[34]	Cohort (after-before)‡	890	Intestinal parasites (point prevalence)	Stool analysis	Yes	4·0
Ferrer (2008)[35]	Case-control	3040	Diarrhoea (incidence)	Diarrhoea reported by guardian as reason for consultation	Yes	2·5
Heller (2003)[36]	Case-control‡	··	Diarrhoea (incidence)	Diarrhoea diagnosis in clinic	Yes	2·0
Menon (1990)[37]	Case-control	80	Rotavirus diarrhoea (incidence)	Stool analysis	Yes	4·0
Sobel (2004)[38]	Case-control	736	Diarrhoea (incidence)	Diarrhoea diagnosis in clinic	Yes	3·0
Kolahi (2008)[39]	Trial (before-after)‡	1046	Diarrhoea (incidence)	Reported in past 2 weeks, two visits, before and after sewerage	No	1·5
Almerie (2008)[40]	Cross-sectional	1213	*Giardia* spp (point prevalence)	Stool analysis	Yes	3·0
Al-Shammari (2001)[41]	Cross-sectional	1347	Intestinal parasites (point prevalence)	Stool analysis	Yes	5·0
Boreham (1981)[42]	Cross-sectional (two districts)‡	130	*Giardia* spp (point prevalence)	Stool analysis	No	3·0
Cifuentes (2002)[43]	Cross-sectional	827	Diarrhoea (incidence)	Reported in the past 2 weeks	Yes	3·0
Cifuentes (2004)[44]	Cross-sectional	1581	*Giardia* spp (point prevalence)	Stool analysis	No	3·0
Gross (1989)[45]	Cross-sectional‡	52	Diarrhoea (incidence)	Reported in the past 2 weeks	No	3·0
Moraes (2004)[46]	Cross-sectional (three by three districts)‡	681	Intestinal parasites (point prevalence)	Stool analysis	Yes	3·0
Silva (2009)[47]	Cross-sectional	291	*Giardia* spp (point prevalence)	Stool analysis	Yes	3·0
Teixeira (2005)[48]	Cross-sectional	291	Diarrhoea (incidence)	Reported in the past 3 days	Yes	2·5
Teixeira (2007)[49]	Cross-sectional	66	*Cryptosporidium* spp seroprevalence (point seroprevalence)	Blood analysis	No	3·0
Vázquez (1999)[50]	Cross-sectional	··	Diarrhoea (incidence)	Reported in the past 2 weeks	No	3·0
Gutierres Arteiro (2007)[51]	Cross-sectional‡	279	Diarrhoea (incidence)	Recorded monthly by community health workers	No	2·0
Pradhan (2002)[52]	Cross-sectional‡	245	Diarrhoea (incidence)	Reported in the past month	Yes	2·0
Walker (1999)[53]	Cross-sectional‡	1072	Diarrhoea (incidence)	Reported in the past month	No	1·0

*The number of people in the sewerage group, not including the comparison groups; for case-control studies, this is the total number of cases and controls in the sewerage group; for details (including the number of cases of diarrhoea or other outcome in each group) see webappendix. †Did the study use appropriate procedures to match control districts or subjects, and apply appropriate adjustment for likely sociodemographic confounders? ‡Studies that specifically set out to assess sewerage effect; the other studies included sanitation level as one exposure factor among many.

Table 1: **Summary of the 25 studies included in the meta-analysis**

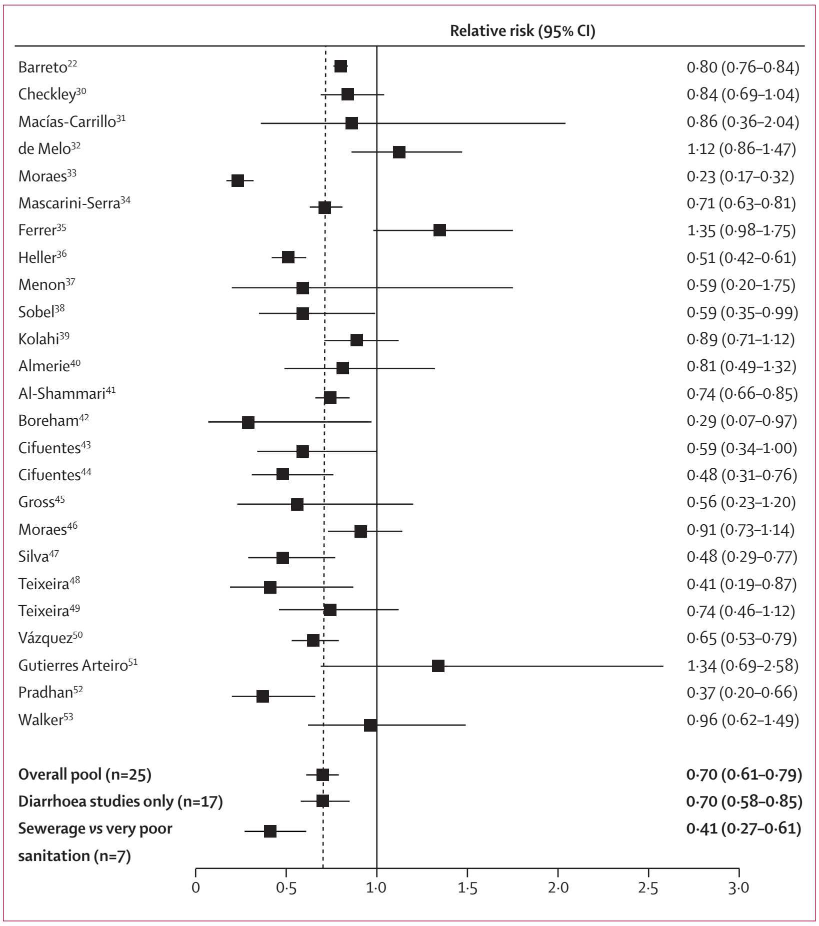

***Figure 2:* Study-specific relative risks (RRs) from the 25 studies of effect of sewerage on diarrhoea and related outcomes**

Three pooled estimates are also shown. The dotted line represents the overall pooled estimate. RR values of less than one suggest a protective effect of sewerage. The comparison of sewerage with very poor sanitation is a pool of the RR estimates for sewerage versus L3 only (table 3).

The pooled estimate of effect for studies in which the outcome was diarrhoea (RR 0·70, 95% CI 0·58–0·84) was very similar to that for studies in which the outcome was not diarrhoea (0·71, 0·62–0·82; table 2).

The pooled RR estimate for studies of incidence alone was 0·72 (0·59–0·88). The pooled RR estimate for studies that received a quality score of 3 or more was 0·67 (0·58–0·77).

As determined by the inclusion criteria, all studies included sewerage as one level of the sanitation factor. Although in two studies[35,50] sewerage and septic tanks were bundled into a single factor level; the pooled RR estimate excluding these studies was 0·67 (0·59–0·77), compared with 0·70 (0·61–0·79) for all 25 studies. The other sanitation levels varied (ie, the sanitation types with which sewerage was compared; see webappendix), but in most cases the main comparand was flush toilet discharging to septic tank or open drain.

Detailed comparison of sewerage with other specific sanitation solutions is not possible on the basis of the studies we reviewed, because few studies gave detailed information on the mix of sanitation solutions used in the comparison groups. For example, in many studies the comparand included flush toilets discharging to open drains, but this might mean at best piped discharge to concrete-lined stormwater drains, or at worst overground drainage to informal ditches in the street or in the plot itself. Nevertheless, some exploration of this question is possible. A subgroup analysis of the seven studies with a third “very poor” sanitation level (L3; table 3), estimates for sewerage versus L3 (table 3), suggests greater health effect (RR 0·41, 0·27–0·61; table 2) than the corresponding analysis of all 25 studies with the sewerage versus L2 estimates (0·73; 0·65–0·82; table 2). Furthermore, six of the seven studies in which sewerage was compared with two other sanitation levels noted the expected dose–response type effect—ie, disease burden was lowest with sewerage, and lower for the nominally next best sanitation level than for the nominally worst sanitation level. These results thus accord with the expectation that sewerage will have a greater health effect when the starting sanitation situation is especially poor. Also of interest is whether sewerage maintains its apparent beneficial effect when the starting sanitation situation is relatively good. Five studies specifically compared sewerage with septic tanks only (ie, all or nearly all households in the comparison group had septic tanks). However, a subgroup analysis of only these five studies gave a pooled RR estimate of 0·69 (0·54–0·89), not appreciably different from the pooled estimate of 0·71 (0·62–0·82) obtained for the remaining 20 studies.

Discussion

Our meta-analysis suggests that sewerage typically has a positive effect on enteric infectious disease burden. Considering all studies included in this review, pooled estimates suggest a reduction of about 30% (0·70, 0·61–0·79) in diarrhoea incidence and in other indicators of enteric disease burden; a similar reduction (34%) is obtained if we include only studies rated as high quality. These estimates are similar to Fewtrell and co-workers’[2] estimate of 32% (0·68, 0·53–0·87) derived from two studies of the effect of non-sewerage sanitation interventions on diarrhoea, and Waddington and co-workers’[12] estimate of 31% (0·69, 0·38–1·26) based on four studies of the effect of sewerage interventions on diarrhoea.

In our analysis we noted high between-study heterogeneity in effect size, for which there are several possible explanations, including geographical variation in the cause of enteric infection,[54] and between-study variation in the precise sanitation characteristics of the comparison groups (ie, the groups with which sewerage was compared). Nonetheless, most studies included in this review compared sewerage with a situation in which most households had flush toilets discharging either to septic tanks or open drains. This sanitation mix is typical of urban districts receiving sewerage in low-income and middle-income countries, where sewerage systems will usually be constructed only in communities that already have household-level piped water supply. Thus our pooled effect estimate is an approximate estimate of the likely effect of sewerage in typical intervention contexts in low-income and middle-income countries: where the existing sanitation situation is very poor we can expect a stronger effect (eg, where there is widespread reliance on open defecation, or on insanitary household or public latrines, or where there are many flush toilets discharging directly to the local environment); where onsite sanitation is functioning well, we might expect a weaker effect. But certainly, pooled effect estimates in this context are indicative rather than definitive.

Of the studies included in our meta-analysis, some compared districts with sewers with districts without, whereas others compared districts before and after construction of sewerage systems (table 1). In two studies,[22,39] districts that were classed as having sewerage systems had very low connection rates. Both the household's sewerage status (connected or not to the network) and the district's sewerage status (proportion of households connected) can be expected to affect disease risk, and both should ideally be taken into account in the multivariate analysis to estimate RRs, as done for example by Barreto and co-workers.[22] By contrast, none of the studies in which sanitation status was established at household level included any form of adjustment for district-level sewerage coverage (although it would certainly be possible to do so if this information were available).

Health-effect assessments of sanitation and similar interventions are plagued with methodological difficulties,[55,56] and some authors have expressed scepticism that observational studies and non-masked trials can ever produce valuable results in such contexts.[57] Major potential sources of effect-exaggerating error include: biases due to absence of masking,[58] biases related to recall error when diarrhoea incidence is assessed on the basis of mothers' reports, and biases due to absence of random allocation.

Masking of participants involved in the studies and interviewers is difficult or impossible in studies of large-scale infrastructure interventions, such as sewerage programmes, and this is a particular cause for concern when the outcome measure is a subjective report. In fact, appropriately assessed self-reported diarrhoea incidence (our second quality criterion) is probably better described as semi-objective than as subjective; nevertheless, this concern remains. But in our analysis the pooled RR estimate assessing only interview-based studies was similar to the pooled estimate for studies that were not based on interview (RR 0·73 *vs* 0·66), arguing against an important effect of courtesy bias (related to a respondent's desire to please the interviewer by reporting a positive effect of the intervention). Furthermore, the pooled RR estimate including only studies that specifically set out to assess the effect of sanitation on health (table 1) was much the same as the estimate for studies in which sanitation type was included as one among many exposure factors (0·69 *vs* 0·70)—this result again argues against influences of both courtesy bias and investigator bias (related to an investigator's belief that sewerage will have a positive effect).

When diarrhoea incidence is assessed on the basis of mothers' reports, recall error is a minor problem when

	Number of studies	Fixed effects pooled RR (95% CI)	Random effects pooled RR (95% CI)	R_i	Q test p value
All studies (sewerage *vs* other solutions)	25	0·76 (0·74–0·79)	0·70 (0·61–0·79)	0·87	<0·0001
Cohort+non-randomised trial	7	0·78 (0·75–0·82)	0·72 (0·57–0·90)	0·96	<0·0001
Case-control	4	0·69 (0·60–0·79)	0·72 (0·38–1·34)	0·94	<0·0001
Cohort+non-randomised trial+case-control	11	0·78 (0·74–0·81)	0·72 (0·59–0·88)	0·95	<0·0001
Cross-sectional	14	0·71 (0·65–0·78)	0·68 (0·58–0·79)	0·56	0·0100
All designs (sewerage *vs* septic-tank-only)	5	0·76 (0·67–0·86)	0·69 (0·54–0·89)	0·50	0·2950
All designs (sewerage *vs* L2 only)	25	0·78 (0·75–0·81)	0·73 (0·65–0·82)	0·82	<0·0001
All designs (sewerage *vs* L3 only)	7	0·39 (0·37–0·41)	0·41 (0·27–0·61)	0·98	<0·0001
Outcome diarrhoea	17	0·77 (0·74–0·81)	0·70 (0·58–0·84)	0·93	<0·0001
Outcome not diarrhoea	8	0·73 (0·67–0·79)	0·71 (0·62–0·82)	0·49	0·0840
Child studies	21	0·76 (0·73–0·79)	0·66 (0·57–0·77)	0·90	<0·0001
Non-child studies	4	0·79 (0·71–0·89)	0·80 (0·71–0·90)	0·05	0·3840
Studies in Latin America	20	0·76 (0·73–0·79)	0·68 (0·59–0·79)	0·91	<0·0001
Studies not in Latin America	5	0·77 (0·69–0·86)	0·77 (0·67–0·90)	0·21	0·3390

For most analyses (with high heterogeneity as shown by high between-study variance, R_i) the random-effects estimate of pooled effect is the appropriate estimate on which to base conclusions. RR=relative risk. L2 and L3 are non-sewerage sanitation levels; unless otherwise stated, comparison is of sewerage (L1) with other (L2, or L2-and-L3 for studies with a third sanitation level; see table 3 and webappendix).

Table 2: **Summarised results of meta-analyses of different subgroups of studies**

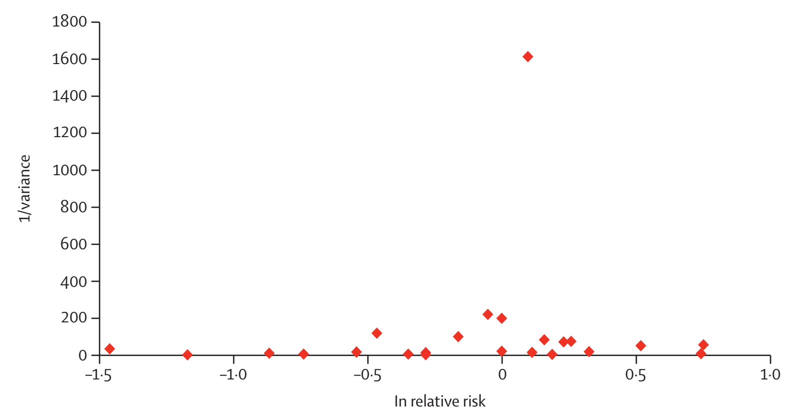

Figure 3: **Funnel plot of inverse variance of relative risk (RR) against ln RR for the 25 studies**
The study at the top of the plot, with very low variance, is Barreto et al (2007).[22] Lack of publication bias is indicated by the horizontal scatter about the lowest-variance studies.

Study	RR sewerage *vs* other*	RR sewerage *vs* L2 only†	RR sewerage *vs* L3 only†
Checkley (2004)[30]	0·84 (0·69-1·04)	0·85 (0·64-1·14)	0·84 (0·71-1·12)
Moraes (2003)[33]	0·23 (0·17-0·32)	0·34 (0·23-0·50)	0·12 (0·08-0·20)
Al-Shammari (2001)[41]	0·74 (0·66-0·85)	0·79 (0·69-0·90)	0·44 (0·29-0·67)
Cifuentes (2004)[44]	0·48 (0·31-0·76)	0·52 (0·31-0·89)	0·40 (0·17-0·93)
Gross (1989)[45]	0·56 (0·23-1·20)	0·73 (0·28-1·73)	0·46 (0·18-1·02)
Moraes (2004)[46]	0·91 (0·73-1·14)	0·94 (0·93-0·95)	0·38 (0·34-0·40)
Teixeira (2007)[49]	0·74 (0·46-1·12)	0·94 (0·50-1·78)	0·57 (0·30-1·09)

*Relative risk (RR) estimates for L1 versus (L2 and L3), as used in the main meta-analysis and in all subgroup analyses except analyses six, seven, and eight in table 2; these RR estimates are those shown for both studies in figure 2. †RR estimates for L1 versus L2 only, and L1 versus L3 only, where L3 is the poorest sanitation level: for example, Checkley (2004)[30] compared "sewerage" (L1) with "latrines or equivalent" (L2) and "no facility" (L3). The webappendix gives full details of sanitation levels in each study, and of the precise procedures used to obtain the RR estimate in each case.

***Table 3:* Relative risk estimates from the seven studies that compared sewerage with two other sanitation levels**

the incidence estimate is being used to compare risk between different groups, as long as it can reasonably be assumed that the size and direction of error does not differ between the groups compared (Schmidt WP, London School of Hygiene and Tropical Medicine, personal communication).

Possible biases due to non-random allocation of participants involved in the study to the different sanitation conditions are certainly a serious cause for concern. Sanitation project beneficiaries have usually been selected in some way.[59] This selection might be of wealthier or healthier people (through self-selection as a result of ability to pay connection and maintenance charges, or subsidy capture, or better education; or through an administrative decision to service wealthy central districts), or sometimes of poorer or unhealthier people (through an administrative decision to target poorer individuals or districts). Thus health status in districts or households with sewerage systems might be at least partly due to selection bias. Most studies included in our review used acceptable multivariate adjustment procedures (our fifth quality criterion), and inadequate adjustment does not seem to have been a cause of effect exaggeration: the pooled RR was 0·64 (0·53–0·77) when this criterion was met and 0·78 (0·63–0·97) when it was not met. Nevertheless, residual confounding might remain after routine adjustment for sociodemographic confounders. To explore this further, we did a sensitivity analysis as described by Greenland.[60] Let us assume the presence of an unidentified factor that halves the risk of diarrhoea (ie, RR disease with confounder=0·5) and that this factor is twice as prevalent among people with sewerage than among people without (ie, RR exposure with confounder=2). It is very unlikely that a factor so strongly associated with sewerage provision and diarrhoea remains undiscovered; however, even if it did, the adjusted RR for the effect of sewerage on diarrhoea would still be 0·78.

Our meta-analysis included cross-sectional designs, which are generally thought suboptimum for causal inference. However, our analysis shows no appreciable difference between the pooled estimate for cross-sectional studies and that for incidence studies.

A potential concern in the case of incidence studies with long follow-up periods is lack of correction for repeated measures. Few studies seem to have taken this into account; however, we think this is unlikely to have had a major effect on individual-study effect estimates, or on our pooled estimates. Notably, the very low variance in the study of Barreto and co-workers[22] (figure 3) might be partly attributable to non-correction for repeated measures, but excluding this study from the meta-analysis had little effect on the pooled estimate (0·68, 0·58–0·79), versus 0·70 (0·61–0·79) for all 25 studies.

We make no recommendations here about the design of future studies. We would however like to make a plea for clearer reporting. In particular, studies of sanitation effect should include careful descriptions of the different sanitation levels being compared. For example, if sewered districts are being compared with non-sewered districts, estimates would be helpful of the proportion of households in each district for which sanitation is sewer, flush to septic tank, flush to open drain, pit latrine, dry-composting toilet, or open defecation (or whatever the common categories are in the communities under study), as well as quantitative observational data on the surface presence of wastewater, and other relevant indicators of the quality (as opposed to type) of sanitation. In several of the studies we included in our review, the sanitation situation with which sewerage was compared was simply described as "no sewerage", with no further clarification. Even when some further clarification was provided, in most cases it was insufficient to provide a clear picture of the sanitation situation in the districts studied. Clear differentiation between sanitation solutions is, in our view, important in studies of this type, since it is sufficiently clear that improvement of sanitation has positive health effects: what is needed is ongoing comparative evaluation—based on health effects and other relevant determinants, including cost—of different types of sanitation solution.

The results of our review suggest that replacement of urban onsite sanitation with sewerage systems typically has a substantial positive effect on enteric disease burden. This is a biologically plausible finding—ie, we would expect health benefits from an urban sanitation system that pipes faecal wastes out of the populated area, as long as that system is functioning reasonably well. However, a positive health effect of sewerage does not imply that sewerage is necessarily the appropriate choice in cities in developing countries. We cannot be certain that the reductions in disease burden achieved in the cities studied so far (mostly in Latin America) can be achieved in other cities worldwide. Even if sewerage can achieve a genuine reduction in disease burden, it will not necessarily be cost effective—in many contexts a greater per-dollar reduction in disease burden might be achieved by improvement of onsite sanitation. Estimation of the life-cycle costs of different sanitation solutions in different contexts is complex, and beyond the scope of our review; however, the capital cost of a flush toilet and sewer connection will be substantially more than that of a well constructed onsite solution.[61] These cost concerns are especially relevant if financial resources are limited. Most studies included in our review have been from middle-income countries, such as Brazil and Mexico, as opposed to low-income countries in Africa and Asia where cost constraints are more severe and current institutional capacity to maintain sewerage systems is, in some countries, clearly inadequate. Concerns about whether sewerage interventions genuinely benefit poor people are also very relevant: most previous sewerage interventions in African cities have either not intended to provide coverage for the poorest communities or have aimed to do so but failed.[62] Clearly, a given sewerage intervention can only be thought appropriate if it is cost effective, sustainable in terms of both system maintenance and environmental impact, and genuinely of benefit to poor communities.

Contributors

GN was involved in the design of the study, the search of published work, the analysis and interpretation of data, and the writing of the paper. SP was involved in the design of the study and the interpretation of data. BT led the design of the study and did the statistical design, and was involved in the analysis and interpretation of data and the writing of the paper.

Conflicts of interest

We declare that we have no conflicts of interest.

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