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Systematic Review

Non-clinical interventions for acute respiratory infections and diarrhoeal diseases among young children in developing countries

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Abstract

OBJECTIVE To assess the effectiveness of non-clinical interventions against acute respiratory infections and diarrhoeal diseases among young children in developing countries.
METHODS Experimental and observational impact studies of non-clinical interventions aimed at reducing the incidence of mortality and/or morbidity among children due to acute respiratory infections and/or diarrhoeal diseases were reviewed, following the Cochrane Handbook for Systematic Reviews of Interventions and the PRISMA guidelines.
RESULTS Enhancing resources and/or infrastructure, and promoting behavioural changes, are effective policy strategies to reduce child morbidity and mortality due to diarrhoeal disease and acute respiratory infections in developing countries. Interventions targeting diarrhoeal incidence generally demonstrated a reduction, ranging from 18.3% to 61%. The wide range of impact size reflects the diverse design features of policies and the heterogeneity of socio-economic environments in which these policies were implemented. Sanitation promotion at household level seems to have a greater protective effect for small children.
CONCLUSION Public investment in sanitation and hygiene, water supply and quality and the provision of medical equipment that detect symptoms of childhood diseases, in combination of training and education for medical workers, are effective policy strategies to reduce diarrhoeal diseases and acute respiratory infections. More research is needed in the countries that are most affected by childhood diseases. There is a need for disaggregation of analysis by age cohorts, as impact effectiveness of policies depends on children's age.

keywords health policy, respiratory infections, diarrhoeal diseases, children, developing countries, systematic review

Introduction

Children have been at the centre of recent global efforts to improve health conditions in developing countries. Notable strides have been made towards reducing child mortality. Over the last 20 years, child mortality rates worldwide have fallen considerably, from 87 to 51 deaths per 1000 live births. In absolute terms, this represents a reduction from 12 to 6.9 million children dying every year (Unicef 2012). Despite this progress, more than 19 000 children still die every day, many from preventable and treatable infectious diseases such as acute respiratory infections (ARI) and diarrhoeal diseases (DD).

Currently, child mortality rates in developing countries are approximately eight times as high as those observed in developed countries. These deaths are highly concentrated, with about half occurring in five countries: India, Nigeria, Democratic Republic of the Congo, Pakistan and China (Black *et al*. 2010). India and Nigeria alone account for more than one-third of the child deaths worldwide. The fact that a large proportion of child deaths are caused by preventable and treatable infectious diseases is symptomatic of dysfunctional policy strategies and health systems in the developing world. Assessing 'what works' in tackling child morbidity and mortality is thus critical for future policy actions.

Acute respiratory infections – notably pneumonia – and diarrhoeal diseases are the first and second leading causes of death among young children, causing 1.6 and 1.3 million child deaths per year, respectively (Black *et al*. 2010). Young children are particularly vulnerable to the negative health implications of diarrhoeal infections. Prolonged periods of diarrhoea can cause micronutrient deficiencies that increase the risk of contracting pneumonia while impairing growth and development of children (World Health Organization 2003; EPH 2004). Early malnutrition is also linked to poor cognitive functioning and learning capacity (Scrimshaw 1998; Worobey *et al.* 2006), which in the long term leads to lower labour productivity and poverty (Wagstaff & Watanabe 1999; Grosse & Roy 2008; Hoddinott *et al.* 2008).

Clinical interventions for diarrhoea and respiratory infections such as antibiotics, probiotics and zinc have been implemented and assessed under various environmental settings (Das *et al.* 2010, 2012; Soares-Weiser *et al.* 2010; Theodoratou *et al.* 2010; Traa *et al.* 2010; Lazzerini & Ronfani 2011; Dennehy 2012; Dinleyici *et al.* 2012). In contrast, non-clinical interventions including education and training programmes, and/or improved sanitation, water supply and quality, and nutrition are comparatively under-studied.

Earlier reviews on non-clinical interventions for diarrhoeal diseases have had a different focus to this study. For instance, one review focused only on successful interventions and included articles which measured outcomes such as adherence to intervention aspects and/or reduction in risk behaviours among adults (Khanal *et al.* 2013). Moreover, that review is rather limited in scope and coverage, including only four studies from 1990 to 2011. Another review focused on clinical and non-clinical interventions against diarrhoea (Shah *et al.* 2012). Although the latter group of interventions may overlap with those included in this study, that review covered interventions in high-income countries and outcomes for all ages rather than children exclusively. This study is the first extensive systematic review on non-clinical interventions to reduce morbidity and mortality due to ARI and DD among young children in developing countries.

The study contributes to the existing literature in two important respects. First, it focuses on policies that have been tested in a developing country context, and which specifically target and measure the impact on children. Second, it builds a theory of change in which non-clinical interventions are understood to both complement and serve as channels through which *preventive* clinical innovations (e.g. vaccine immunizations) and *treatment* clinical innovations (e.g. zinc supplements, oral rehydration salts and antibiotic treatment of pneumonia) are enhanced.

Study design

We conducted a systematic review following the Cochrane Handbook for Systematic Reviews of Interventions (Higgins & Green 2008) and the PRISMA guidelines (Moher *et al.* 2009) of the following databases: Medline, Embase, Global Health, IBSS, Web of Science and Econlit. The search was conducted on 10 July 2012 with no start date limit. The following terms were included as follows: 'measles' or 'morbilli' or 'rubeola' or 'polio*' or 'infantile paralysis' or 'pneumon*' or 'diarrhoea*' or 'diarrhea*' or 'rotavirus' or 'escherichia coli' or 'gastroenteritis' or 'pertussis' or 'whooping cough' combined with the terms 'develop* countr*' or 'low middle income', and 'child*' or 'adolescen*' or 'teen*' or 'youth' or 'young', and 'program*' or 'project' or 'vaccine*' or 'policy' or 'strategy' or 'intervention' or 'immuniz*' or 'immunis*' or campaign*' or 'rehydrate* solution*' or 'antibiotic*' or 'treatment' or 'medicat*' or 'zinc therap*'. Where available, filters on age range, language and document type were applied to exclude articles that focused on adults. The resulting articles were refined by excluding editorials and biographies, and those set in developed countries. Previous systematic reviews were also included via the search strategy. Thus, any systematic review published on or before July 10, 2012 on the topic would have been captured by our search. A follow-up search conducted on October 15, 2014 containing identical search terms and databases to our original search, as well as a search of the Cochrane database reconfirmed the uniqueness of our study.

Studies were included if they evaluated non-clinical interventions aimed at reducing child mortality or morbidity in a developing country due to either diarrhoeal or respiratory diseases. These included education and training programmes for mothers and health workers; sanitation interventions that provided latrines, soap and animal corrals; water supply and quality policies; and nutritional interventions.

The link between poor nutrition and childhood diseases and death is well-established (Langford *et al.* 2011). Malnutrition has been implicated as an underlying cause of death in over half of deaths of children aged 4 and under in developing countries, due to the synergy between poor nutrition and other health problems such as diarrhoeal diseases and respiratory infections (Pelletier *et al.* 1995). Interventions against malnutrition typically involve educational programmes for mothers and supporting health and nutrition workers in introducing feeding recommendations (Bhandari *et al.* 2004).

Non-clinical interventions focused on education and training programmes are also under-studied. For instance, a recent review of training programmes for health professionals to improve care of seriously ill newborns in developing countries identified only two studies for inclusion (Opiyo & English 2010). Existing studies tend to focus on all age groups rather than young children specifically (Esrey *et al.* 1985, 1991; Fewtrell *et al.* 2005), or on children living in developed countries (Rabie & Curtis 2006). Whilst such training programmes may be considered 'clinical' interventions insofar as health professionals are taught how to administer vaccines and treatments, the thrust of such programmes is education to health workers (non-clinical), rather than actual administration of medicines or vaccines (firmly within the realm of clinical interventions). Hence, we classify such interventions as non-clinical rather than clinical. Nonetheless, we acknowledge both the overlap between health intervention types and the lack of consensus pertaining to definitions of clinical *vs.* non-clinical interventions.

Ecological, case-controlled, retrospective cohort, non-blind randomized and non-randomized quasi-experimental studies, including interrupted time series, were included. Our inclusion criteria reflect guidelines on systematic literature reviews in public health, which recommend the inclusion of study designs such as non-experimental, on the basis that the interventions being reviewed dictate which study designs are included (not vice versa) (Jackson & Waters 2005). Although the evidence yielded through randomized control trials has stronger internal validity than observational studies, they are not always feasible due to of ethical and logistic considerations. Furthermore, recent evidence suggests that there are little effect estimate differences between observational studies and randomised control trials, regardless of the specific observational study design (Anglemyer *et al.* 2014). Therefore, we include in the review both observational and experimental studies.

Slightly different definitions of 'children' were used during the search, as dictated by existing age categories in search databases. Studies which presented data on children aged five or younger were included. Other units of analysis beyond individuals, such as households or neighbourhoods, were also included if they presented data on children specifically. Figure 1 presents the systematic review's flow diagram with inclusion and exclusion criteria, and the number of records and papers reviewed.

Non-clinical interventions comprised educational or training programmes regarding hygiene, sanitation, nutrition, and case management, and infrastructure enhancements regarding water quality and supply, and latrine access. Selected studies described and evaluated one or more of the above interventions. The main outcome measures were childhood mortality and morbidity due to diarrhoeal and respiratory diseases, although studies frequently contained additional outcomes such as quality of treatment provided, admissions to hospital and hygiene behaviours. Grey literature was included to lessen publication bias. In cases of studies yielding two or more articles based on the same sample or intervention, the main or latest article was included and all secondary articles were excluded.

Four thousand six hundred thirty six abstracts were screened, resulting in 82 full texts assessed for eligibility. Twenty one articles were included after considering the inclusion criteria described above. A hand search of the reference lists of these 21 articles resulted in the inclusion of 20 additional relevant articles. The final sample included 41 studies. The following data were extracted from each study: type and setting of intervention, year of publication, year(s) of data collection, research methodology, sample size, outcome measures, impact size and summary of main findings. The included articles were synthesized according to a theory of change model presented in Figure 2.

Results

A summary of the characteristics of included studies is provided in Table A1 in the Appendix. A variety of sample unit types were observed among the studies, including children (Azurin & Alvero 1974; Khan 1982; Mtango & Neuvians 1986; Sircar *et al.* 1987; Stanton & Clemens 1987; Alam *et al.* 1989; Han & Hlaing 1989; Pandey *et al.* 1989, 1991; Aziz *et al.* 1990; Greenwood *et al.* 1990; Tonglet *et al.* 1992; Ahmed *et al.* 1993; Bang *et al.* 1994; Haggerty *et al.* 1994; Bateman *et al.* 1995; Hoque *et al.* 1996; Lye *et al.* 1996; Shahid *et al.* 1996; English *et al.* 1997; Semenza *et al.* 1998; Froozani *et al.* 1999; Quick *et al.* 1999; Roberts *et al.* 2001; Jensen *et al.* 2003; Nanan *et al.* 2003; Reller *et al.* 2003; Sobsey *et al.* 2003; Clasen *et al.* 2004; Luby *et al.* 2004, 2006; Oberhelman *et al.* 2006; Garrett *et al.* 2008; Kolahi *et al.* 2009; Rana 2009; Langford *et al.* 2011), health facility admissions (Daniels *et al.* 1990), households (Lockwood *et al.* 2001) and municipality (Rasella *et al.* 2010). Of those studies where the exact number of children could be ascertained, sample sizes varied from 51 to 17 101 children aged 5 or younger for interventions for diarrhoeal diseases and 11 291 to 83 233 for interventions for ARI.

We identified two main drivers of change: first, policies that aim at *enhancing supply-side capabilities* in the area of material resources and infrastructure and second, policies that aim at *promoting behavioural change*, primarily through information and education. The 41 articles included in the review belong to one of these two drivers of change. The majority of studies (27) assessed the efficacy of interventions primarily focused on enhancing resources or infrastructure, while 14 focused on

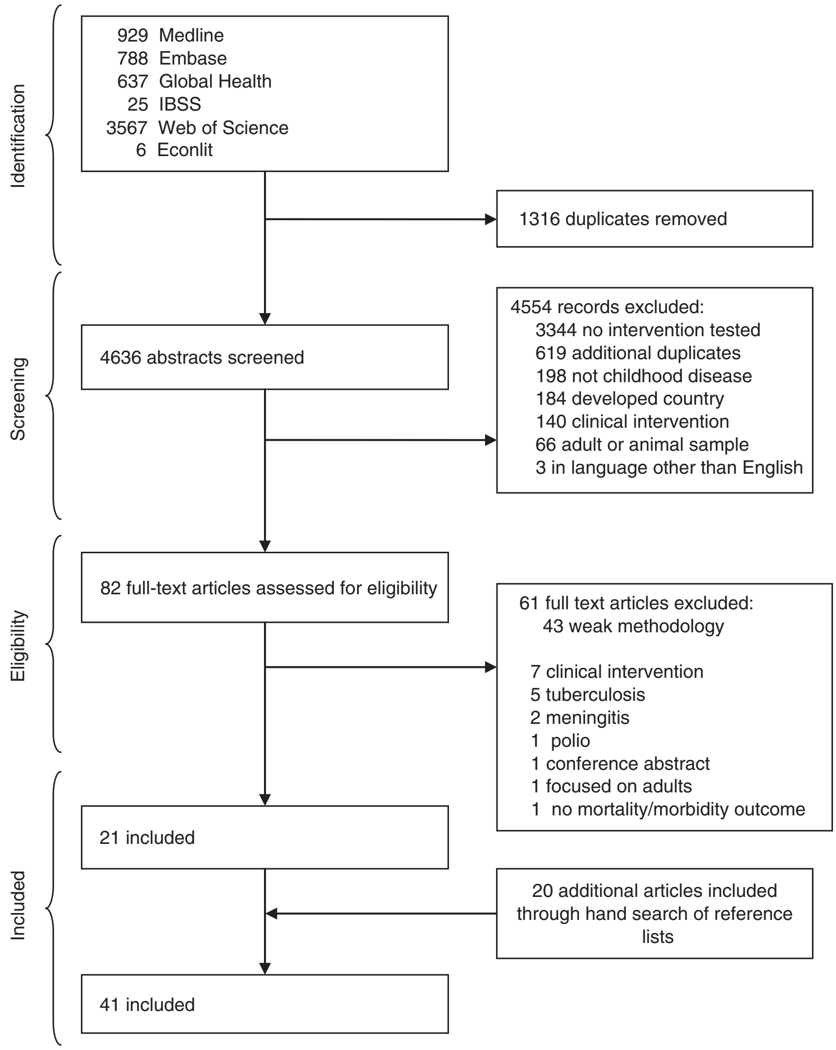

Figure 1 Systematic review flow diagram.

interventions promoting behavioural change among child caregivers and health workers.

Enhancing supply-side capabilities

This type of non-clinical interventions is depicted in the first column on the left-hand side of Figure 2. Examples include the installation of hand pumps in communities to improve water distribution or connection of households to municipal water sources (Tonglet *et al.* 1992; Semenza *et al.* 1998; Kolahi *et al.* 2009). Water quality interventions involve the removal of microbial contaminants, either at the source or at the household level. Such interventions were frequently paired with the provision of improved water storage vessels. Graf *et al.* (Graf *et al.* 2010) assessed an innovation to improve water quality through solar disinfection, while others focused on the provision of safe water storage containers (Roberts *et al.* 2001), ceramic water filters and chlorine or other water disinfectants (Semenza *et al.* 1998; Jensen *et al.* 2003; Reller *et al.* 2003; Sobsey *et al.* 2003; Clasen *et al.* 2004). The majority of these studies focused on individual children as their unit of analysis. The findings of two studies, which focused instead on the household (Lockwood *et al.* 2001) and municipality (Rasella *et al.* 2010) levels, are reported separately at the end of this section.

Sanitation interventions assessed the impact of excreta disposal, usually via latrine ownership. Daniels *et al.* (Daniels *et al.* 1990) found that children from households with a latrine experienced 24% fewer diarrhoeal episodes than children from households without a latrine (OR = 0.76, 95% CI = 0.58–1.01).

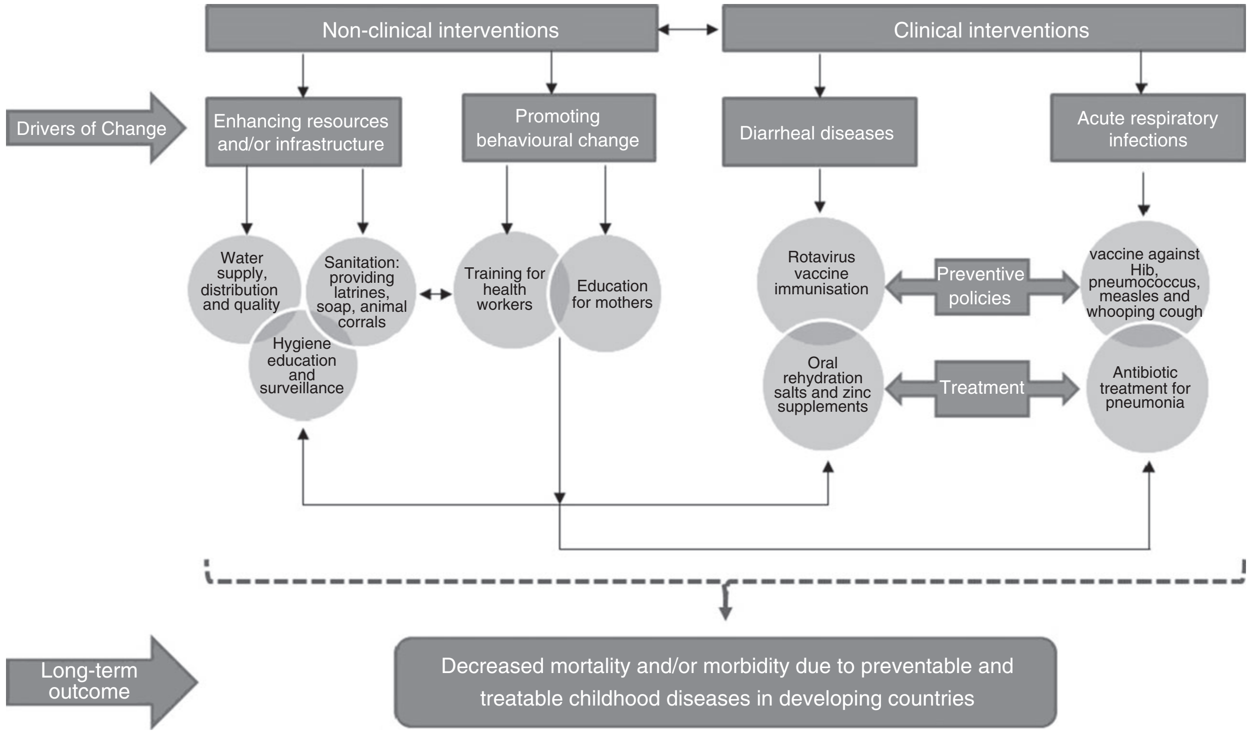

Figure 2 Theory of change flow diagram.

Water supply interventions included the provision of new or improved water supplies, or improved distribution. One study assessed the impact of peri-urban access to a metropolitan sewerage system (Kolahi *et al.* 2009), while another analysed water improvement involving the installation of a piped water network (Tonglet *et al.* 1992).

Semenza *et al.* (Semenza *et al.* 1998) compared diarrhoeal incidence between a group who had access to a piped municipal water system to a group without access, further dividing the latter into a control and intervention group. The intervention group received chlorination and safe water equipment. The diarrhoeal rates for children were 84.4 per 1000 per month for households with piped water; 127.7 per 1000 children per month for households without piped water and the intervention and 42.2 per 1000 children per month for households without piped water but with intervention.

Tonglet *et al.* (Tonglet *et al.* 1992) found that children living in villages with a piped water source and who lived less than a five-minute walk from the water source, and those in households which used more than 50 l of water per day, experienced half the incidence of diarrhoea of other children in the intervention village. Similar results are reported by (Aziz *et al.* 1990) and (Hoque *et al.* 1996). These findings demonstrate the impact of relative accessibility to improved water supply facilities *within* communities.

Studies that explored differences within intervention groups, or contained two intervention groups, add nuance to these findings (Azurin & Alvero 1974; Aziz *et al.* 1990; Nanan *et al.* 2003). Azurin and Alvero (Azurin & Alvero 1974) found that the rate of diarrhoea incidence was markedly less in the intervention group which received both improved waste disposal and improved water supply (193 per 1000) than intervention groups which received only improved water supply or only improved waste disposal (213.7 and 321.1 per 1000, respectively) and a control group which received neither (542.2 per 1000).

A number of multipronged interventions supplemented resource improvements with an educational component targeting child caregivers (Azurin & Alvero 1974; Khan 1982; Alam *et al.* 1989; Aziz *et al.* 1990; Bateman *et al.* 1995; Hoque *et al.* 1996; Quick *et al.* 1999; Nanan *et al.* 2003; Garrett *et al.* 2008). Han and Hlaing (Han & Hlaing 1989) provided mothers and children with soap and instructions to wash their hands after defecation and before handling and eating their meals. The intervention yielded a 30% reduction of diarrhoeal incidence among

0–4 year olds, 31% among those younger than two and 33% among those aged two or older.

A more extensive intervention that consisted of augmented water supply through hand pumps and health education for mothers show that the use of hand pump water for drinking and washing, removal of child's faeces from the yard, and maternal hand washing before handling food and after defecation, resulted in a decreased yearly diarrhoea incidence in children by more than 40% compared to children living in households where none or only one of these practices was promoted (Alam *et al.* 1989). Hand washing promotion and plain soap have an impact on the incidence of diarrhoea among children aged 5 and younger on the order of 39–42%, depending on the level of malnourishment of children (Luby *et al.* 2004).

Diarrhoea prevalence is also found to be consistently lower among infants and children aged 1–2 years who live in neighbourhoods that received one of the following: diluted bleach and a water vessel, soap and hand washing promotion messages, flocculent-disinfectant water treatment and a water vessel, disinfectant water treatment and soap and hand washing promotion (Luby *et al.* 2006). However, the differences in prevalence between these were not statistically significant and yielded extremely large confidence intervals.

A similar study assessed the effect of improved drinking water supply, sanitation facilities, and awareness and practices about hygiene behaviour (Nanan *et al.* 2003). It found that children in control villages had a 33% higher adjusted odds ratio for having diarrhoea than children living in intervention villages (adjusted odds ratio, 1.331; $P < 0.049$) (Nanan *et al.* 2003). Within their intervention group, boys had 25% lower odds of having diarrhoea than girls (adjusted odds ratio, 0.748; $P < 0.049$).

A large-scale intervention comprising point-of-use treatment of contaminated source of water with disinfectant, safe storage of treated water and community education reported that households in intervention areas had 44% fewer diarrhoea episodes than those in the control area ($P = 0.002$), with significantly less diarrhoea among infants <1 year old (Quick *et al.* 1999).

Other policies have combined sanitation, hygiene, education and water supply. For example, Rana (Rana 2009) assessed an initiative that included promotional activities for installation of sanitary latrines and tube wells, along with extensive health and sanitation education. A significant reduction in point prevalence of waterborne diseases (including diarrhoea, dysentery, jaundice, worm infections and typhoid fever) was observed among under-five children, ranging from 22 to 13% ($P < 0.001$).

Although most studies discussed above find improved outcomes from health interventions, a few did not. Jensen *et al.* (Jensen *et al.* 2003) report that the incidence of diarrhoea among children in an intervention village that received water through a chlorinated water supply scheme did not differ statistically from a neighbouring village that used water from a non-chlorinated water supply. Also, a programme that instructed mothers and children how to wash their hands after defecation and before handling and eating their meals was found to have no impact on dysentery rates among older children (Han & Hlaing 1989).

Mixed findings were also reported by Reller *et al.* (Reller *et al.* 2003), who found that an intervention group which received disinfectant for drinking water plus a storage vessel was the only group to experience a significant decline in diarrhoeal episodes among children aged one or younger. Other intervention groups, including those who received water disinfectant only, bleach only or bleach plus a storage vessel did not experience a significant reduction of diarrhoeal episodes among children compared with the control group.

Two studies assessed the impact of an intervention at a national level. For instance, an integrated approach introduced in Nicaragua improved (i) water supply and sanitation infrastructure; (ii) knowledge about hygiene; and (iii) policy sustainability at community, institutional and national levels (Lockwood *et al.* 2001). The interventions were associated with a 7% decrease in the incidence of diarrhoeal diseases. Rasella *et al.* (Rasella *et al.* 2010) report outcomes from Brazil's Family Health Programme. Mortality rates due to diarrhoeal diseases for children under 5 years fell from 0.81 to 0.46 per 1000 live births, as did mortality from lower respiratory infections (from 1.39 to 0.96 per 1000 live births).

Promoting behavioural change

The promotion of behavioural change has been a major driver in non-clinical interventions aimed at reducing child mortality and morbidity (Figure 2). Policies designed to tackle diarrhoeal diseases have extensively focused on mothers of young children, while those designed against respiratory infections have also included health worker training and education components.

The intervention described by Haggerty *et al.* (Haggerty *et al.* 1994) featured educational messages instructing the disposal of animal faeces, hand washing after defecation and before meal preparation and disposal of children's faeces. The study found an 11% reduction in reported diarrhoea among children in the intervention group, compared with controls ($P < 0.025$). Results of similar interventions are reported in Stanton and Clemens (Stanton & Clemens 1987).

Ahmed *et al.* (Ahmed *et al.* 1993) found that an intervention consisting of educational messages and household surveillance regarding hygiene practices led to a decrease in the prevalence of diarrhoea in intervention *vs.* control groups, but for only 4 of the 6 month intervention period. Whether the difference in prevalence was statically different was not reported. Moreover, these results are hindered by significant differences between the control and intervention groups at baseline.

A project that promoted hand washing through the provision of soap and education showed no difference in the rates of diarrhoea or dysentery among children under age five; however, the rates of dysentery were lower among children aged five and older (Sircar *et al.* 1987). In contrast, Quick *et al.* (Quick *et al.* 1999) found that infants aged <1 year experienced a 53% reduction in diarrhoeal episodes after hand washing, although no significant effect was observed among children aged one through 1 years. Similar results are reported in (Shahid *et al.* 1996), (Luby *et al.* 2006) and (Langford *et al.* 2011).

Bateman *et al.* (Bateman *et al.* 1995) tested two policy designs: Model 1 was based on education sessions with tube well caretakers, their spouses and tube well users, whereas Model 2 added additional outreach activities such as school programmes, child-to-child activities and activities with key community members. Findings show a two-thirds reduction of diarrhoea in the intervention areas *vs.* the control groups, together with the smaller differences between Model 1 and Model 2. This suggests that the key elements of a successful hygiene behavioural change were associated with the similar components in both models.

Froozani *et al.* (Froozani *et al.* 1999) assessed an educational programme promoting breastfeeding among new mothers in Iran. The mean number of days of diarrhoea among infants in the intervention group was significantly lower than in the control group ($P \leq 0.004$).

Regarding ARI, English *et al.* (English *et al.* 1997) implemented a nutrition improvement programme. The treatment group showed a significant reduction in the incidence of respiratory infections, from 49.5% to 11.2%, and in diarrhoeal infections, from 18.3% to 5.1% ($P < 0.00001$). Khan *et al.* (Khan *et al.* 1990) examined a project that trained community-based health workers to recognize signs of pneumonia and differentiate between cases requiring treatment with antibiotics at home or referral to hospital. The results showed that the acute lower respiratory infection (ALRI)-specific mortality rate among children under age five was 6.3 deaths per 1000 children per year vis-à-vis 14.4 in control villages ($P = 0.0001$).

Lye *et al.* 1996 studied a training programme targeting mothers of children under age five in addition to health staff. The results showed a reduction in the incidence of severe ARI cases over a 62-week period of the intervention. Mtango and Neuvians (Mtango & Neuvians 1986) implemented a health service outreach programme featuring regular home visits by health workers. Within a two-year period, the total under-five mortality rates fell from 40.1 to 29.2 per 1000 children. Bang *et al.* (Bang *et al.* 1994) report a 44% decline ($P < 0.01$) in the neonatal mortality rate due to pneumonia following the implementation of a training programme for paramedical workers, village health workers and traditional birth attendants.

Two training programmes were implemented by Pandey *et al.* (Pandey *et al.* 1989, 1991) in rural Nepal. The intervention in the first study was associated with a 69% decrease ($P < 0.01$) in the ARI-specific death rate between baseline and 2-year follow-up (Pandey *et al.* 1989). Interestingly, there was an increase in the number of ARI episodes, which was likely due to mothers being better able to identify ARI episodes in years following the intervention. The second intervention, which featured the training of indigenous community health workers to detect and treat pneumonia, led to a 28% reduction in the risk of death from all causes (beyond pneumonia) by the third year since implementation (RR: 0.72, 95% CI: 0.63–0.82) (Pandey *et al.* 1991). A similar intervention in The Gambia aimed at decreasing morbidity and mortality due to both diarrhoea and ARI reported less striking results, with children in the intervention group experiencing less gastroenteritis and ARI, although the difference was not statistically significant (Greenwood *et al.* 1990).

Discussion

Most of the evidence reviewed in this study supports the proposition that enhancing resources and/or infrastructure, and promoting behavioural change, are effective policy strategies to reduce child morbidity and mortality due to diarrhoeal disease and ARI in developing countries.

However, not all diarrhoeal interventions led to a decrease in diarrhoeal occurrence. For instance, an intervention which chlorinated the public water supply in a Pakistani village did not yield a reduction in diarrhoea incidence among children (Jensen *et al.* 2003). The lack of effect may stem from other causes of diarrhoea in the sample, for instance, waterborne parasites resistant to chlorine, contamination in the home due to storage practices and supplementing the (scheduled) public water supply with other sources such as hand pumps. Other factors, such as living in overcrowded and poor-quality environments, also promote the spread of disease, potentially obscuring the impact of the chlorination program. Further, the authors note that the intervention and control village were not comparable at baseline regarding water quality, and that their sample size was rather limited (Jensen *et al.* 2003).

The study by Reller *et al.* (Reller *et al.* 2003) with four intervention groups also yielded unexpected results. For children under 1 year of age, the only intervention to have an impact on incidence of diarrhoea was the disinfectant plus storage vessel group. However, a high degree of inconsistent adherence to the interventions may have lessened the overall impact. While even inconsistent adherence appeared to yield positive results for the adult portions of the samples, younger children with less developed immune and gastrointestinal systems may derive less benefit from inconsistent adherence (Reller *et al.* 2003).

Successful interventions targeting diarrhoeal incidence demonstrated a reduction ranging from 18.3% (Roberts *et al.* 2001) to 61% (Rana 2009). This wide range of impact size seems to reflect the diverse types of policy designs, along with the heterogeneity of socio-economic environments in which these interventions were implemented. The findings regarding the impact of water sanitation initiatives is well supported by previous reviews, albeit focused on general populations rather than on children in developing countries (Esrey *et al.* 1985, 1991).

Findings are mixed when looking at impact size by different age cohorts. Whilst some studies show greater impacts among infants and very young children (Quick *et al.* 1999), others find greater effect among older children (Sircar *et al.* 1987; Aziz *et al.* 1990; Luby *et al.* 2006), with infants and children aged 2–5 benefitting more than those aged 1–2 (Shahid *et al.* 1996). Although age seems to influence the degree of policy effectiveness, age-disaggregated research demand further attention to determine more precisely the impact of age-specific and combined interventions.

A number of studies, especially those concerned with reducing diarrhoeal disease, feature a multifaceted approach. Although there is evidence to suggest that interventions that include several components yield more successful outcomes than single interventions (Azurin & Alvero 1974; Bateman *et al.* 1995; Reller *et al.* 2003; EPH 2004), another study concluded that multiple interventions were not necessarily more effective than interventions with a single focus (Fewtrell *et al.* 2005). Therefore, further research is needed to shed light on whether multifaceted interventions are more effective than those of single focus.

Some interventions, including sanitation promotion among households, have a greater protective impact for infants as they may come into more frequent contact with surfaces including faeces-contaminated floors in and around dwellings than adults and older children. Infants and very young children also rely on others to wash their hands for them, which certainly influences the efficacy of hand washing promotion interventions.

Although almost half of deaths globally among young children occur in India, Nigeria, Democratic Republic of the Congo, Pakistan and China (Black *et al.* 2010), only a third of the studies included in this review were based in one of these countries. Pakistan was fairly well represented, with five studies (Khan *et al.* 1990; Jensen *et al.* 2003; Nanan *et al.* 2003; Luby *et al.* 2004, 2006), while two studies each were set in India (Sircar *et al.* 1987; Bang *et al.* 1994) and Zaire (Tonglet *et al.* 1992; Haggerty *et al.* 1994). Surprisingly, no rigorous studies were identified in the context of Nigeria or China. The results of this review show a relative dearth of studies on respiratory infections (six studies) compared to those on diarrhoeal diseases (32 studies), with three covering both diseases. The limited knowledge base on non-clinical interventions on reducing respiratory infections is surprising given the global burden of disease and the effectiveness of some policy initiatives (Rabie & Curtis 2006).

As articles in languages other than English were excluded, we may have missed out some evidence. However, given that most relevant studies are published in English, we believe the magnitude of the bias is contained. The degree to which publication bias impacts the overall findings is difficult to estimate. In a departure from the PRISMA checklist, we did not carry out an assessment of risk of bias within and across studies. However, the fact that the grey literature was included in the review, and that some peer-review studies (Han & Hlaing 1989; Jensen *et al.* 2003; Reller *et al.* 2003) did report null or negative findings, seems to indicate that publication bias is minimal. Nevertheless, we do not rule out the possibility of a degree of bias in our results.

This systematic review identified several non-clinical interventions in the fight against diarrhoeal diseases and respiratory infections that kill approximately 3 million children in developing countries every year (Black *et al.* 2010). Public investment in sanitation and hygiene, water supply and quality, along with training and education for medical workers, can under certain conditions be effective instruments to reduce diarrhoeal diseases and acute respiratory infections in developing countries.

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Appendix

Table A1 Study characteristics of included articles

Study	Setting	Study design	Sample	Intervention	Outcome
(a) Enhancing resources and/or infrastructure					
Alam *et al.*	Bangladesh (rural)	Non-blind RCT	623 children aged 6–23 months.	Enhanced water supply and quality through handpumps, and health education for mothers.	The intervention decreased yearly diarrhoea incidence in children by more than 40% compared with children living in control households. Children in the intervention area had, on average, 3.4 diarrhoea episodes in a year *vs.* 4.1 among children in the control area ($P < 0.01$).
Aziz *et al.*	Bangladesh (rural)	Non-blind RCT	Five villages with a total population of approximately 9600 inhabitants (number of children unknown)	Water, sanitation and hygiene education.	Children in the intervention area experienced 25% fewer episodes of diarrhoea than those in the control area. An impact on diarrhoea was seen in each age group except for those aged 0–5 months. The incidence density ratios showed that the impact appeared to increase with age, with the greatest effect in the 36–59 months age group.

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Azurin and Alvero	Philippines (peri-urban)	Non-blind RCT	527 children aged 0–4.	Safe water and sanitary facilities for human waste disposal.	Improvement of either water supply or toilet facilities or both was effective in significantly reducing the incidence of cholera in intervention communities compared with control. The greatest improvement was observed in the community in which both water supply and toilets were improved than in the communities in which either water or toilets were improved. The rate of cholera infection among those aged 0–4 was 193.1 per 1000 in the group which received toilets and water, 213.7 per 1000 in the group which received improved water, 321.1 per 1000 in the group which received toilets, and 542.2 per 1000 in the group which received no intervention.
Clasen *et al.*	Bolivia (rural)	Non-blind RCT	32 children aged 0–4, drawn from 50 households	Household-based ceramic water filters	Risk of diarrhoea was reduced by 83% (estimated OR 0.17, 95 per cent CI 0.06, 0.49, p 0.001). The risk of diarrhoea decreased by 0.97 (95 per cent CI 0.96, 0.99, $P < 0.02$) for each year of life. Diarrhoea prevalence was reduced by 72%.

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Daniels *et al*.	Lesotho (rural)	Case–control	A total of 1604 health facility admissions of children aged 0–4	The Rural Sanitation Pilot Project (RSPP), which promoted and constructed ventilated improved pit latrines and provided health education directed at improving standards of personal and domestic hygiene practices.	Cases were significantly less likely than controls to come from latrine-owning houses ($P < 0.01$, OR = 0.76, 95% CI = 0.62–0.93). Children under the age of five from households with a latrine may experience 24% fewer episodes of diarrhoea than such children from households without a latrine (OR = 0.76, 95% CI = 0.58–1.01). The impact of latrines on diarrhoea was greater in those households that used more water, practised better personal hygiene, and where mothers had a higher level of education or worked outside the home.
Garrett *et al*.	Kenya (rural)	Quasi-experimental non-blind RCT	960 children aged 0–4	The Safe Water System: point-of-use chlorination, safe water storage, sanitation and rainwater harvesting.	Living in an intervention village was associated with lower diarrhoea risk (RR: 0.31, 95% CI: 0.23–0.41)
Graf *et al*.	Cameroon (urban)	Non-blind RCT	738 and 2193 randomly selected households (Number of children not reported)	Solar water disinfection.	A decrease in diarrhoea prevalence among children under the age of five was observed in the intervention group, from 34.4% prior to the intervention to 22.8% after the intervention (x2 = 19.18, $P = 0.001$, OR = 1.77).

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Han and Hlaing	Myanmar/ Burma (urban)	Non-blind RCT	494 children aged 0–4	Handwashing promotion	The diarrhoeal incidence among children in intervention households was significantly lower than that among those in the control households (IDR = 0.70, 95% CI = 0.54–0.92). The percentage reductions in diarrhoea incidence for the 0–4, younger than 2, and 2 or > 2 age groups were 30, 31 and 33, respectively. Although there was a 40 reduction in dysentery incidence (IDR = 0.58, 95% CI = 0.22–1.55) in children under 2 years, there was no impact in older children (IDR = 1.2, 95% CI = 0.52–2.80).
Hoque *et al.*	Bangladesh (rural)	Cross sectional survey follow-up of earlier non-blind RCT	645 children aged 0–4	Water, sanitation and hygiene education.	The percentage reporting a diarrhoea attack in their intervention area was 6% *vs.* 10% in the control area (RR = 1.96; 0.96 < RR<2.78; Mantel-Haenszel x2 test = 3.28; P < 0.07.
Jensen *et al.*	Pakistan (rural)	Non-blind RCT	226 children aged 0–4	Chlorination of drinking water.	The intervention was not associated with a decrease in the incidence diarrhoea.
Khan	Bangladesh (unknown)	Non-blind RCT	199 children aged 0–4	Handwashing with soap intervention. Individuals were provided with soap and water pitchers, only water pitchers, only soap or neither.	Just over 10% of children in the intervention group which received soap and water pitchers subsequently became infected with shigellosis after a family member was diagnosed, compared with over 50% of children in the control group (those who received no soap or water).
Kolahi *et al.*	Iran (urban)	Nonrandomized control trial	4179 children aged 0–4	Household access to an urban sewerage system.	The incidence of diarrhoea among children decreased.

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Lockwood *et al.*	Nicaragua (rural)	Quasi-experimental interrupted time series design	1183 individual households drawn from 8 departments of the country and 37 municipalities	Nicaragua Rural Water Supply, Sanitation, and Environmental Health Programme, which improved access to safe sources of drinking water and excreta disposal facilities, promoted hygiene and conducted capacity-building activities.	The percentage of households where children aged four or under have had diarrhoea during the 2 weeks prior to the survey was 20 at baseline, 20 at the first follow-up survey and then dropped to 15 and then 13 in the second and third follow-up surveys, respectively.
Luby *et al.*	Pakistan (urban)	Cluster RCT	4691 children	The Karachi Soap Health Study, a handwashing promotion intervention.	Infants living in households that received handwashing promotion and plain soap had 39% fewer days with diarrhoea (95% CI, −61% to −16%) *vs.* infants living in control neighbourhoods. Severely malnourished children (weight for age z score, −3.0) living in households that received handwashing promotion and plain soap had 42% fewer days with diarrhoea (95% CI, −69% to −16%) *vs.* severely malnourished children in the control group. Similar reductions in diarrhoea were observed among children in households receiving antibacterial soap.

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Luby *et al.*	Pakistan (urban)	Cluster RCT	1323 households (number of children unreported)	Point-of-use water disinfectant treatment, along with handwashing with soap promotion.	Diarrhoea prevalence was consistently lower among infants and children 1–2 years old who lived in intervention neighbourhoods compared with control neighbourhoods. However, the magnitude of the reductions were less than the overall reduction for all ages, and many of the individual age and intervention specific reductions were not statistically significant. Infants < 1 year old in the 'bleach water treatment' experienced a diarrhoea prevalence of 8.30% (20% less than control), 'soap and handwashing promotion' a prevalence of 7.86% (24% less than control), 'flocculent-disinfectant water treatment' a prevalence of 6.20% (40% less than control), and 'flocculent-disinfectant plus soap' 6.48% (38% less than control). However, none of these differences are statistically significant and yielded extremely large confidence intervals.
Nanan *et al.*	Pakistan (rural)	Case control study	803 children aged 0–5	Water and sanitation extension programme (WASEP) project, aimed at improving potable water supply, sanitation facilities, and awareness and practices about hygiene behaviour.	Children in control villages had a 33% higher AOR for having diarrhoea than children in intervention villages (AOR, 1.331; $P < 0.049$).

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Oberhelman *et al.*	Peru (peri-urban)	Non-blind RCT	137 children aged 0–4	Corralling free-range chickens	For children aged three and under, the intervention group experienced 3.16 episodes per person per year, compared with 2.61 episodes per person per year in the control group. The difference was not significant in a student's *t*-test. The intervention had little impact, which suggests that diarrhoea incidence among this sample is due to infections acquired outside the home.
Quick *et al.*	Bolivia (peri-urban)	Non-blind RCT	160 children aged 0–4	Point-of-use treatment of contaminated water with disinfectant, safe storage of treated water and community education.	Infants < 1 year old had significantly less diarrhoea than control children ($P = 0.05$ and 0.01, respectively). Diarrhoeal incidence was reduced 53% among infants. However, the intervention had an insignificant effect on diarrhoeal episodes for children aged one through four.
Rana	Bangladesh (rural)	Interrupted time series experimental study	17 101 children aged 0–4	Promotional activities including the installation of tube wells and sanitary latrines, and health education for improving hygienic behaviour.	Among under-five children, the incidence of waterborne diseases was reduced from 22% to 13% ($P < 0.001$).
Rasella, Aquino and Barreto	Brazil (unknown)	Ecological study	2601 Brazilian municipalities.	The Family Health Programme (FHP), a strategy for reorganization of primary health care in Brazil.	Mortality rates for diarrhoeal diseases decreased from 0.81 to 0.46 per 1000 live births (a 43% reduction), as did mortality from lower respiratory infections (from 1.39 to 0.96 per 1000 live births, a 31% reduction). Reductions of 31% (95% CI: 20–40%) and 19% (95% CI: 8–28%) in mortality rates due to diarrhoeal diseases and lower respiratory infections, respectively, were observed in municipalities with the highest FHP coverage.

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Reller *et al.*	Guatemala (rural)	Non-blind RCT	1145 children aged 0–4	Household-based drinking water disinfectant and a storage vessel.	Children in households which received flocculant disinfectant and a storage vessel experienced significantly fewer episodes of diarrhoea than the control group (AOR = 0.69, 95% CI = 0.50–0.95). Infants in households who received flocculant disinfectant plus a storage vessel had 30% fewer episodes of diarrhoea compared with infants who received flocculant disinfectant alone. Children < 5 years of age who lived in households with water treatment had fewer episodes of severe diarrhoea than controls, but they did not have fewer episodes of prolonged diarrhoea.
Roberts *et al.*	Malawi (refugee camp)	Non-blind RCT	500 Mozambican refugee households	Water storage improvement programme.	There was 31% less diarrhoeal disease ($P = 0.06$) in children under 5 years of age in the intervention group.
Semenza *et al.*	Uzbekistan (urban)	Cluster randomized intervention study	344 children aged 0–4	Home chlorination of drinking water for a sample lacking access to piped water.	The relative risk of diarrhoea among children in the intervention rather than control (no access to piped water received no intervention) was 0.33 (95% CI = 0.19–0.57). The relative risk of children who received the intervention *vs.* those who received piped water was 0.50 (95% CI = 0.29–0.84). The relative risk of children in the control group *vs.* those who received piped water was 1.5 (95% CI = 1.05–2.13).
Shahid *et al.*	Bangladesh (peri-urban)	Non-blind RCT	77 children aged 0–11 months, 46 aged 12–23 months, and 147 aged 24–59 months.	Handwashing and education programme	Diarrhoea incidence was reduced 61% among those aged 0–11 months, 47% among those aged 12–23 months, and 56% among those aged 24–59 months in the intervention area.

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Sircar *et al.*	India (urban)	Non-blind RCT	340 children aged 0–4	Handwashing promotion and education programme	The difference in the incidence of diarrhoea and between those younger than the age of five in study and control groups was not significantly different. This was due to the inability to enforce handwashing practices in this younger age group.
Sobsey *et al.*	Bangladesh and Bolivia (peri-urban)	Non-blind RCT	Approximately 140 households in Bolivia and about 275 households in Bangladesh.	Chlorination and safe storage of household drinking water	In Bangladesh, the mean diarrhoea incidence rates for children <5 years of age were significantly lower ($P = 0.029$, *t*-test) in intervention households (20.8 episodes/1000 days) than in control households (24.3 episodes/1000 days). However, in Bolivia, the mean rates in children <5 years of age were only slightly lower in the intervention group (0.77) than in the control group (0.81).
Tonglet *et al.*	Zaire (rural)	Non-blind concurrent cohort study	906 children aged < 4 at the commencement of the study	Installation of a piped water network.	Median diarrhoea incidence per 2 weeks was significantly lower in the two intervention villages (0.084 and 0.088) than in the control village (0.091) ($P < 0.05$).
(b)Promoting behavioural change					
Ahmed *et al.*	Bangladesh (rural)	Non-blind control trial	370 households with children aged 0–18 months.	Educational messages to improve hygiene practices, surveillance of households in the intervention areas to assess household cleanliness and adherence to hygiene messages.	Mid-way through the intervention the prevalence of diarrhoea in the intervention site was consistently lower than that of the control site. At the end of the intervention, the difference between the sites in diarrhoeal rates disappeared.
Bang *et al.*	India (rural)	Non-blind RCT	83 233 individuals (number of children unreported)	Educational intervention training paramedical workers, village health workers and traditional birth attendants to diagnose and treat childhood pneumonia.	Neonatal mortality due to pneumonia was reduced by 44% in the intervention *vs.* control area ($P < 0.001$). Post-intervention, the total neonatal mortality rates were 78.7 and 62.8 per 1000 in the control and intervention areas, respectively ($P < 0.01$).

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Bateman *et al.*	Bangladesh (rural)	Non-blind cluster trial	400 children aged 0–4	Model 1: Education sessions with the tube well caretakers, their spouses and tubewell users. Model 2: Model one intervention plus outreach activities including school programmes, child-to-child activities, and activities with key influencers in the community.	In both Models, there is a dramatic reduction in diarrhoea in the intervention areas compared with control areas, with an overall reduction of about two-thirds in the former. The per cent of children with diarrhoea within the 2 weeks before the survey are 23 *vs.* 65 for Model 1 intervention and control, and 20 *vs.* 57 for Model 2 intervention and control groups, respectively.
English *et al.*	Vietnam (unknown)	Non-blind RCT	Approximately 720 children aged 0–5	Nutrition improvement programme based on household food production and nutrition education.	The project commune showed a significant reduction ($P < 0.00001$) in the incidence of respiratory infections (from 49.5% to 11.2%) and diarrhoeal infections (18.3% to 5.1%). The incidence of pneumonia and severe pneumonia was also significantly reduced in the intervention commune ($P < 0.0001$). There was no significant change in the incidence and severity of respiratory disease or the incidence of diarrhoeal disease in the control commune.
Froozani *et al.*	Iran (urban)	Quasi-experimental non-blind RCT	120 infants	Educational intervention to promote breastfeeding.	The mean number of days of diarrhoea in the study group was significantly lower ($P \leq 0.004$) than in the control group.

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Greenwood *et al.*	The Ganbia (rural)	Non-blind RCT	Approximately 2500 children aged 0–4	Introduction of primary health care consisting of an educational intervention to train village health workers and traditional birth attendants to recognize and treat chronic diarrhoea, acute gastroenteritis, respiratory infection and other diseases.	Children in the intervention village had fewer deaths due to gastroenteritis and acute respiratory infection than children in control villages. However, the differences were not statistically significant, and there were no differences in the proportion of deaths from diarrhoea/ malnutrition. There were differences regarding morbidity. Children in intervention villages had less prevalence of the following symptoms: mild and severe respiratory, and diarrhoea and vomiting.
Haggerty *et al.*	Zaire (rural)	Non-blind RCT	Approximately 300 families (number of children unreported)	Hygiene education.	During the post-intervention period, diarrhoeal morbidity was greatly reduced relative to the previous year among all children in both intervention and control groups. Diarrhoeal incidence rates declined by approximately 50% in each group, and the reductions were highly significant within each age category in both groups (SND tests, $P < 0.0001$ in every case). One year after baseline, overall, children in intervention sites had a reported mean of 0.85 episodes of diarrhoea, while children in control sites had 0.90 episodes (NS). There was no discernible evidence of a trend towards fewer episodes of diarrhoea in intervention compared with control children after the intervention. Nevertheless, proportionately fewer children in intervention sites were reported to have diarrhoea than at control sites.

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Khan *et al.*	Pakistan (rural)	Cluster non-blind RCT followed by a time-interrupted series study.	Children aged 0–5 residing in 38 villages (population, 37 245) (number of children unreported)	Case management by village-level community health workers, backed up by local health centre staff, engaging in active case-finding and providing maternal health education.	The ALRI-specific mortality rate among children <5 years old in intervention villages was 6.3 deaths per 1000 children per year, compared with 14.4 in seven control villages ($P = 0.0001$), a difference of 56%. Within 1 year of the interventions being extended to the control villages, the ALRI-specific mortality rate in these villages dropped by 55% to 6.5 per 1000 children per year ($P = 0.06$). The ALRI-specific infant (< 1 year old) mortality rate in the intervention villages was 15.5 per 1000 live births per year in 1985–86, compared with 32.5 per 1000 per year in the control villages, a 52% difference ($P = 0.006$). After interventions began in the control villages in 1987, the ALRI-specific infant mortality rate dropped to 15.0 per 1000 per year ($P = 0.12$).
Langford *et al.*	Nepal (urban)	Non-blind RCT	88 infants aged 3–12 months	Soap distribution and handwashing education for mothers	Children from the intervention group reported fewer episodes of diarrhoea (3.0 vs. 4.33 episodes for intervention and control, respectively, $P = 0.049$). Intervention children experienced 31% fewer episodes of diarrhoea, and 41% fewer days of diarrhoea, than children in the control group.
Lye *et al.*	Malaysia (unspecified)	Non-blind RCT	Approximately 2500 children aged 0–4	Health education and training.	The reduction in the incidence of severe acute respiratory infection cases in the intervention area was significantly greater than in the control area ($P < 0.05$).

Table A1 (*Continued*)

Study	Setting	Study design	Sample	Intervention	Outcome
Mtango and Neuvians	Tanzania (rural)	Cluster non-blind RCT	16 126 children aged 0–4 in the first year of the intervention, 19 014 in the second year	Health service outreach programme consisting of Village Health Workers visiting households and providing education and treatment for acute respiratory infections.	The total under-five mortality was reduced by 27.2% from 40.1 to 29.2 per 1000 children. The disease-specific mortality rate for pneumonia was reduced by 30.1% from 14.3 to 10.0 per 1000 children per year, contributing 40% to the overall mortality reduction.
Pandey *et al.*	Nepal (rural)	Quasi-experimental interrupted time series design.	1019 children aged 0–4	Health education for mothers and other family members to recognize symptoms of ARI, along with immunization and supportive measures such as the encouragement of breastfeeding, and the training and deployment of community health workers to recognize and treat ARI.	There was a 59% reduction in the ARI-specific death rate between baseline and 1 year into the program, and a further 25% reduction 2 years into the programme, a total drop of 69%. This reduction is statistically significant ($P < 0.01$). There was an increase in the number of ARI episodes, which was likely due to mothers being better able to identify ARI episodes in years following the intervention.
Pandey *et al.*	Nepal (rural)	Quasi-experimental interrupted time series design.	13 404 children aged 0–4	Indigenous community health workers in Jumla district were trained to detect and treat pneumonia.	The programme led to a 28% reduction in the risk of death from all causes by the third year since implementation (relative risk: 0.72, 95% CI: 0.63–0.82). There was a significant trend towards lower mortality with the greater duration of the programme (Mantel–Haenszel chi-square for trend = 5.4, $P < 0.02$).
Stanton and Clemens	Bangladesh (urban)	Non-blind RCT	51 communities	Educational intervention promoting hygienic behaviour.	During the 6 months after the intervention, the rate of diarrhoea in children aged five and under was 4.3 per 100 in the intervention communities and 5.8 in the control communities, yielding a protective efficacy of 26% ($P < 0.0001$).