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Fly control to prevent diarrhoea in children

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[Intervention Review]

Fly control to prevent diarrhoea in children

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ABSTRACT

Background

Diarrhoeal disease accounts for millions of child deaths every year. Although the role of flies as vectors of infectious diarrhoea has been established, fly control is not often mentioned as an approach to decrease childhood diarrhoea. Theoretically, fly control for decreasing diarrhoea incidence can be achieved by intervening at four different levels: reduction or elimination of fly breeding sites; reduction of sources that attract houseflies; prevention of contact between flies and disease-causing organisms; and protection of people, food, and food utensils from contact with flies.

Objectives

To assess the impact of various housefly control measures on the incidence of diarrhoea and its related morbidity and mortality in children under five years of age.

Search methods

We searched electronic databases including the Cochrane Central Register of Controlled Trials (CENTRAL) in the Cochrane Library, MEDLINE, Embase, CINAHL, and LILACS, from database inception to 24 May 2018. We also searched trial registries for relevant grey literature and ongoing trials. We checked the references of the identified studies and reviews. We did not apply any filters for language, publication status (published, unpublished, in press, and ongoing), or publication date.

Selection criteria

We planned to include randomized controlled trials (RCTs), quasi-RCTs, and controlled before-and-after studies that studied the effect of fly control on diarrhoea in children under five years of age.

Data collection and analysis

Two review authors extracted the data and independently assessed the risk of bias in the included study. We planned to contact study authors for additional information, where necessary. We assessed the certainty of the evidence using the GRADE approach.

Fly control to prevent diarrhoea in children (Review)

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Main results

We included one cluster-RCT (491 participants) conducted in Pakistan that evaluated insecticide spraying in the first two years and baited fly traps in the third year. Insecticide spraying reduced the fly population (house index) in the intervention group during the four months of the year when both flies and cases of diarrhoea were more common, but not at other times. On average, this was associated with a reduction in the incidence of diarrhoea in the first year (illustrative mean episodes per child-year in the intervention group was 6.3 while in the control group was 7.1) and second year of the intervention (illustrative mean episodes per child-year in the intervention group was 4.4 while in the control group was 6.5; rate ratio (RaR) 0.77, 95% confidence interval (CI) 0.67 to 0.89, low-certainty evidence). In the third year of the intervention, the baited fly traps did not demonstrate an effect on the fly population or on diarrhoea incidence (RaR 1.15, 95% CI 0.90 to 1.47, low-certainty evidence).

Authors' conclusions

The trial, conducted in a setting where there were clear seasonal peaks in fly numbers and associated diarrhoea, shows insecticide spraying may reduce diarrhoea in children. Further research on whether this finding is applicable to other settings is required, as well as work on other fly control methods, their effects, feasibility, costs, and acceptability.

PLAIN LANGUAGE SUMMARY

Fly control to prevent diarrhoea in children

What is the aim of this review?

To find out if controlling flies can prevent diarrhoea in children under the age of five years.

Key messages

The results of this review are limited as we included only a single study, which suggested fly control through insecticide spraying may reduce diarrhoea in children during 'fly seasons' when both flies and diarrhoea incidence peak. Further research on the effects in other settings is required, as well as research on fly control methods, their implementation, effects, costs, and acceptability.

What was studied in the review?

Diarrhoea is a common cause of death in poor countries. Although we know that flies transmit diarrhoea-causing agents, the effects of fly control programmes are not part of most health-promotion programmes.

Cochrane researchers searched for available studies up to 24 May 2018 and included one study (491 children under five years of age). This study was conducted in eight villages in Pakistan and tested the effects of insecticide spraying and baited fly traps on fly populations, and diarrhoeal incidence in children.

What are the main results of the review?

Insecticide spraying almost eliminated the flies and there were 23% fewer cases of diarrhoea in children residing in the sprayed villages when compared to unsprayed villages. This was due to an effect on the incidence of diarrhoea during fly seasons but not in the non-fly season (low-certainty evidence). Baited fly traps may have been ineffective in controlling flies and diarrhoea compared to villages with no fly traps (low-certainty evidence).

How up to date is this review?

The review authors searched for available studies up to 24 May 2018.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON *[Explanation]*

Interventions to control disease spread from the housefly compared with no intervention for childhood diarrhoea						
<p>Patient or population: children under 5 years of age Settings: community settings (Pakistan) Intervention: interventions to control disease spread from the housefly (insecticide spraying and fly traps) Comparison: no intervention</p>						
Outcome	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk	Corresponding risk				
	No intervention	Interventions to control disease spread from the housefly				
Incidence of diarrhoea	7.1 mean episodes of diarrhoea per child-year in first year	6.3 mean episodes of diarrhoea per child-year in first year of intervention	RaR 0.77 (0.67 to 0.89)	491 participants (one study)	⊕⊕○○ LOW ^{a-d} <i>due to risk of bias and indirectness</i>	Insecticide spraying may decrease diarrhoea incidence compared to no intervention
	6.5 mean episodes of diarrhoea per child-year in second year	4.4 mean episodes of diarrhoea per child-year in first year of intervention				
	5.1 mean episodes of diarrhoea per child-year	5.8 mean episodes of diarrhoea per child-year	RaR 1.15 (0.90 to 1.47)	491 participants (one study)	⊕⊕○○ LOW ^{a-c} <i>due to risk of bias and indirectness</i>	Baited fly traps may have little or no effect on diarrhoea incidence compared to no intervention

* The basis for the **assumed risk** (for example, the median control group risk across studies) is provided in footnotes. The **corresponding risk** (and its 95% CI) is based on the assumed risk in the comparison group and the **relative effect** of the intervention (and its 95% CI).
Abbreviations: CI: confidence interval; RaR: rate ratio.

GRADE Working Group grades of evidence

High certainty: further research is very unlikely to change our confidence in the estimate of effect.

Moderate certainty: further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.

Low certainty: further research is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Very low certainty: we are very uncertain about the estimate.

^aDowngraded by 1 due to serious risk of bias: one RCT but lacked allocation concealment and blinding.

^bNo serious inconsistency.

^cDowngraded by 1 due to indirectness: the study evaluated insecticide sprays and traps for fly control to assess the impact on diarrhoea. However, other biological or social factors might lead to substantial differences in the magnitude of effect.

^dNo serious imprecision.

BACKGROUND

Diarrhoea is defined by the World Health Organization (WHO) as the passage of three or more liquid or loose stools per day (or more frequent passage than is normal for the person) (WHO/UNICEF 2013). Continued diarrhoea leads to loss of fluid and electrolytes, and may become life-threatening, especially in young children and people who are immunosuppressed or malnourished. Millennium Development Goal (MDG) 4 was set up with a target to reduce deaths of children under five years of age by two-thirds from the 1990 baseline by the year 2015. There has been a decline in child mortality but it did not meet the MDG 4 targets, with diarrhoea contributing to around a tenth of all child deaths (UNICEF 2013). The mortality rate for children under five years of age globally was 43 deaths per 1000 live births in 2015, which represents a 44% reduction since 2000 (United Nations 2017). However, diarrhoea continues to be a major cause of morbidity and mortality in young children, especially in low- and middle-income countries and a lot still has to be done if the child health targets of the United Nations Development Programme's Sustainable Development Goals (SDG) are to be achieved. An estimated 2% of all worldwide diarrhoeal episodes progress to severe disease, with the incidence and case-fatality ratios being much higher in low-income countries than in middle- and high-income countries (Walker 2013). Diarrhoea is the second leading cause of death in children under five years of age and is accountable for around 525,000 deaths among children under five each year; thus control of diarrhoea is essential if the world desires to achieve SDG for child health.

Several strategies have been employed to reduce the morbidity and mortality associated with diarrhoea. The Global Action Plan for Diarrhoea and Pneumonia has identified the need for improvements in water, sanitation, and hygiene facilities, breastfeeding practices, vitamin A supplementation, and a rotavirus vaccine as a priority for the prevention, or reduction in severity, of diarrhoea; as well as the need for continued and improved use of oral rehydration salts (ORS), zinc, and antibiotics for some bacterial strains

for effective treatment (Bhutta 2013). There is strong circumstantial evidence that flies are vectors of infectious diseases, especially diarrhoea (Emerson 1999). The impact of controlling houseflies in preventing infectious diarrhoea in community settings has long been under question (Chavasse 1994; Chavasse 1996), and vector control may be acquired by intervening at any of the following levels: reduction or elimination of fly breeding sites; reduction of sources that attract houseflies; and prevention of contact between flies and disease-causing organisms, food, food utensils, and people.

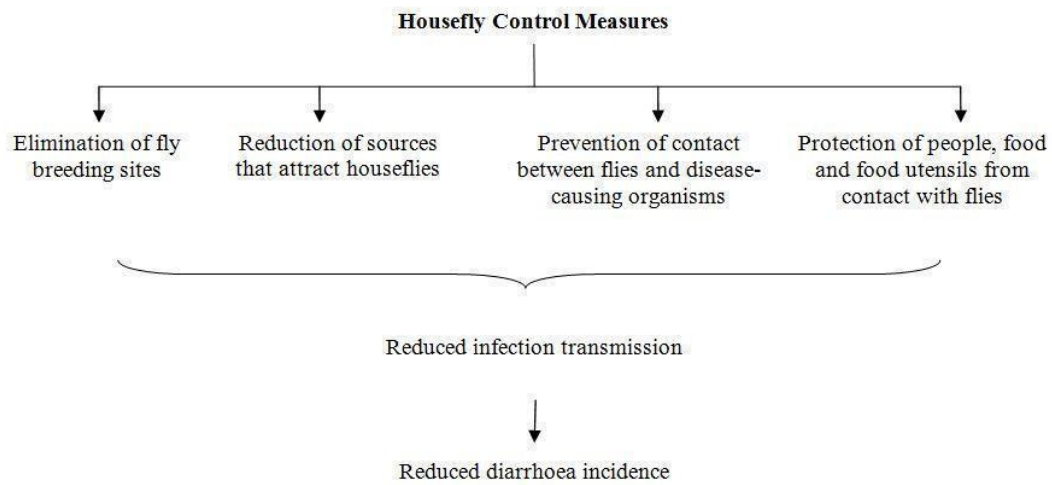
Description of the condition

The role of houseflies in acting as mechanical vectors for many diarrhoea-causing agents has been fairly well established in several settings (Chavasse 1999; Chompook 2006; Cohen 1991; Farag 2013; Levine 1991; Watt 1948). The common housefly, *Musca domestica*, is a vector for more than 100 serious pathogens including those causing typhoid, cholera, salmonellosis, shigellosis, dysentery, anthrax, and parasitic worms (Peter 1997). Flies can also transmit eye diseases, such as trachoma, and infect wounds and skin with diseases such as cutaneous diphtheria, mycoses, and yaws. Other fly species that can cause diarrhoea include other Muscidae and *Chrysomya* spp (for example, *Chrysomya putoria*) (Lindsay 2012). Larvae swallowed in food material sometimes survive in the human gut, causing intestinal myiasis, with symptoms of pain, nausea, and vomiting. Individual studies have shown a reduction in diarrhoea incidence in children following fly control measures (Chavasse 1999; Emerson 1999).

Description of the intervention

An intervention may be applied at one of many levels to control disease spread from the housefly to the child under five years of age (Figure 1), including the following.

Figure 1. Pathways for fly control and impact on diarrhoea incidence.



Reduction or elimination of fly breeding sites

One of the most common breeding sites for houseflies is animal manure. Composting of animal manure is the process of decomposing the organic matter to be used as a fertilizer and soil amendment. Reduction or elimination of fly breeding sites has been shown to effectively and economically decrease housefly populations (Abu-Rayyan 2010; Lazarus 1989). As houseflies complete their reproductive cycle in as little as seven days, improved manure removal practices, such as the recommended scheduled seven-day (or more frequent) removal can be essential in interrupting the life-cycle of the housefly. This method has emerged as an economical means of reducing housefly populations (Lazarus 1989). Killing adult flies may reduce the infestation, but elimination of breeding areas is necessary for comprehensive management.

Reduction of sources that attract houseflies

Infantile diarrhoea is associated with the presence of garbage in the environment (Rego 2005; Rego 2007). Housefly larvae feed on moist food rich in organic matter. Dumping of domestic waste in open spaces, especially close to residential areas, is an obvious attractant for flies and serves as a favourable breeding ground. Reduction of open waste disposal sites or using closed/sheltered sites will directly reduce the source that attract flies. Ordinarily, fly control from 1 to 2 kilometres around a municipality will prevent ingress of the house fly into a municipality (Bennett 2008). Relocation of dump sites to areas distant from residential areas can serve as an efficient means of reduction of sources.

Prevention of contact between flies and disease-causing organisms

Improvements in sanitation and excreta disposal, including the presence of ventilated pit latrines, prevents contact of flies with disease-causing organisms in human faeces; and establishment of proper excreta disposal facilities in rural areas has been associated with reduction in diarrhoeal incidence (Lou 1990). While a pit latrine may seem to attract flies with its odour, the ventilation mechanism prevents them from entering the latrine and coming in contact with faeces, and hence potentially diarrhoea-causing organisms (Jinadu 2004). This prevents flies from ready access to potential pathogens.

Protection of people, food, and food utensils from contact with flies

The use of insecticides or fly traps, or both, inside and outside homes, dairy farms, restaurants and schools can help prevent contact with flies. Spraying dichlorodiphenyltrichloroethane (DDT) and other insecticides has been successfully used in the past (Baker 1947), both individually in homes and country-wide. Alternative fly control strategies have emerged, including the use of biological control organisms (Hogsette 1999), due to ecological concerns and increasing housefly resistance to DDT (Derbeneva-Uhova 1966; Keiding 1975). The efficiency of fly traps has improved substantially over time and experimentation. Choice of insecticide, design and construction of the traps, and trap-placement tactics (site, relation to sunlight, wind direction) have been noted to have an im-

pact on trap efficacy. Yield from individual fly traps varies widely from over 700 flies per day to none at all (Chavasse 1999).

How the intervention might work

Targeting the housefly at multiple levels is a comprehensive means of controlling incidence of diarrhoea in young children. Measures include reducing the vector population, reducing contact of flies with disease-causing organisms, and contact of flies with humans and fomites (an object, such as clothing or furniture, that may itself be contaminated with infectious organisms and serve in their transmission to others). These measures would lower the chances of children coming in contact with disease-causing organisms and hence would lead to a reduction in diarrhoea incidence and its associated morbidity and mortality.

Why it is important to do this review

Diarrhoea contributes to a major share of morbidity and mortality in children under the age of five years globally. If there is evidence that housefly control measures could reduce the incidence of diarrhoea and consequent morbidity and mortality in children, these measures could play a part in reducing diarrhoea burden in low- and middle-income countries and could be a step towards achieving SDG 3 and beyond. There is no existing systematic review which assess the impact of fly control measures on infection control to date and this Cochrane Review systematically analyses the existing data to assist effective policy-making.

OBJECTIVES

To assess the impact of various housefly control measures on the incidence of diarrhoea and its related morbidity and mortality in children under five years of age.

METHODS

Criteria for considering studies for this review

Types of studies

We considered randomized controlled trials (RCTs), cluster RCTs, quasi-RCTs (qRCTs), and controlled before-and-after studies (CBA).

Types of participants

We planned to include studies that assessed the impact of housefly control measures on the incidence of diarrhoea and its related morbidity and mortality in children under the age of five years.

Types of interventions

We considered interventions at any one or more of the aforementioned four levels: interventions for reduction or elimination of fly breeding sites; reduction of sources that attract houseflies; prevention of contact between flies and disease-causing organisms; and protection of people and fomites from contact with flies. These specific interventions were compared to the control group.

Types of outcome measures

We examined the following primary and secondary outcomes. We proposed to include studies evaluating any fly outcomes if they also examined the impact of the intervention on children under the age of five years.

Primary outcomes

- Incidence of diarrhoea: number of episodes of diarrhoea (as defined by study authors) experienced by each child over a defined period.
- Clinic visits: number of outpatient clinic visits of children presenting with diarrhoea.
- Emergency department visits: number of visits of children to the emergency department presenting with diarrhoea.
- Hospital admissions: number of children admitted to a hospital with diarrhoea as a primary cause.
- Recurrent diarrhoea: repeat episodes of diarrhoea in a defined period (as mentioned by the study author).

Secondary outcomes

- Duration of hospitalization: mean number of days children were hospitalized due to diarrhoea as a primary cause.
- Diarrhoea-specific mortality: deaths due to diarrhoea as a primary cause or its consequences.
- House index: average number of flies caught over a defined period.
- Ovitrap index: average number of ovitraps with houseflies in a defined area.
- Fly density: average grid count of houseflies in a defined area.
- Adverse effects including insecticide resistance.

Search methods for identification of studies

We identified all relevant studies regardless of language, publication status (published, unpublished, in press, and ongoing) or publication date.

Electronic searches

We searched the following databases using the search terms and strategy described in [Appendix 1](#).

- The Cochrane Central Register of Controlled Trials (CENTRAL), published in the Cochrane Library (May 2018)
 - MEDLINE (PubMed; 1966 to 23 May 2018)
 - MEDLINE (OVID; 1946 to 23 May 2018)
 - Embase (OVID, 1947 to 23 May 2018)
 - CINAHL (EBSCOHost, 1981 to 23 May 2018)
 - LILACS (BIREME, 1982 to 23 May 2018)
 - PsycINFO (EBSCOHost, 1800 to 23 May 2018)
 - ERIC (EBSCOHost, 1966 to 23 May 2018)
 - Science Citation Index Expanded (SCI-EXPANDED) and Social Sciences Citation Index (SSCI; Web of Science, 1900 to 23 May 2018)
 - Conference Proceedings Citation Index- Science (CPCI-S) and Conference Proceedings Citation Index- Social Science & Humanities (CPCI-SSH; Web of Science, 1990 to 23 May 2018)

We also searched the following.

- The Cochrane Infectious Diseases Group Specialized Register
 - Global Index Medicus - AFRO (<http://indexmedicus.afro.who.int/>)
 - PAHO (Pan American Health Library, www.paho.org/hq/)
 - Dopher and TROPHI (EPPI centre, <https://eppi.ioe.ac.uk/webdatabases4/Intro.aspx?ID=9>)
 - 3ie Database of Impact Studies (www.3ieimpact.org/en/evidence/impact-evaluations/)
 - IMSEAR (Index Medicus for the South-East Asian Region (www.who.int/library/databases/searo/en/)
 - WHO Regional Office for the Eastern Mediterranean (EMRO, www.emro.who.int/index.html)
 - WHO Regional Office for the Western Pacific Region (WPRO, www.wpro.who.int/en/)

All the above were accessed on 23 May 2018, using the terms fly, flies, housefly, houseflies, musca.

We also searched the following sources for relevant grey literature and ongoing trials.

- System for Information on Grey Literature in Europe (SIGLE, www.opengrey.eu/)
- ClinicalTrials.gov
- Current Controlled Trials (www.controlledtrials.com/)
- the WHO International Clinical Trials Registry Platform (www.who.int/ictrp/search/en/)

These were also all searched on 23 May 2018, using the terms fly, flies, housefly, houseflies, musca.

Searching other resources

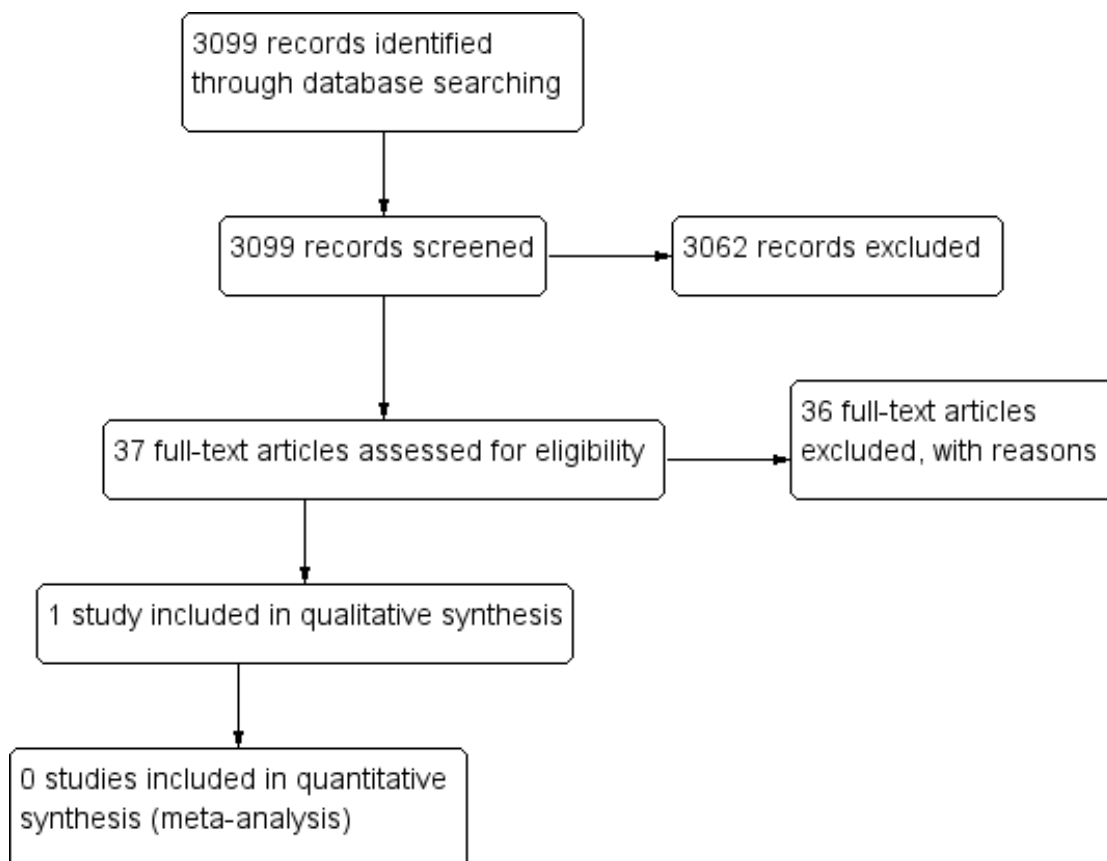
We examined the reference lists of included studies and relevant systematic reviews identified by the above methods for additional studies.

Data collection and analysis

Selection of studies

Two review authors (YBH and RAS) independently screened the literature search results by title and abstract for potentially relevant trials. We coded articles as either 'retrieve', if articles potentially fulfilled the inclusion criteria or if it was unclear whether the article fulfilled the inclusion criteria or not; or 'do not retrieve' for articles that did not fulfil the inclusion criteria. We obtained the full-text reports of potentially relevant trials. Two review authors (YBH and RAS) independently applied the inclusion criteria to the full reports using an eligibility form and scrutinized publications to ensure we included each trial in the review only once. We resolved disagreements through discussion with a third review author (JKD). We listed the studies excluded after full-text assessment and the reasons for exclusion in the 'Characteristics of excluded studies' table. We illustrated the study selection process in a PRISMA study flow diagram ([Figure 2](#)).

Figure 2. PRISMA diagram.



Data extraction and management

Two review authors (YBH and ZSL) extracted the data using a pre-designed data extraction form. We resolved discrepancies through discussion or, when required, by consulting a third review author (RAS). We entered the data into Review Manager 5 (RevMan 5) (Review Manager 2014), and checked for accuracy.

Assessment of risk of bias in included studies

Two review authors (JKD and RAS) independently assessed risk of bias for each study using the criteria outlined in Higgins 2011. We resolved any disagreement by discussion or by involving a third review author (ZSL).

Random sequence generation (checking for possible selection bias)

We assessed the method used to generate the allocation sequence for each included study in sufficient detail to allow an assessment

of whether it should produce comparable groups. We assessed the methods as at: low risk of bias, if a truly random process; high risk of bias, if non-random methods were used; or unclear.

Allocation concealment (checking for possible selection bias)

We assessed for each included study the method used to conceal allocation to interventions prior to assignment and assessed whether intervention allocation could have been foreseen in advance of, or during recruitment, or changed after assignment. We assessed the methods as at low risk of bias (for example, telephone or central randomisation, consecutively numbered sealed opaque envelopes); or high risk of bias (open random allocation, unsealed or non-opaque envelopes, alternation, date of birth); or unclear risk of bias.

Blinding of participants and personnel (checking for possible performance bias)

We assessed the methods used, if any, for each included study to blind study participants and personnel from knowledge of which intervention a participant received. We considered that studies were at low risk of bias if they were blinded, or if we judged that the lack of blinding would be unlikely to affect results. We assessed blinding separately for different outcomes or classes of outcomes. We assessed the methods as at low, high, or unclear risk of bias for participants; and low, high, or unclear risk of bias for personnel.

Blinding of outcome assessment (checking for possible detection bias)

We described for each included study the methods used, if any, to blind outcome assessors from knowledge of which intervention a participant received. We assessed blinding separately for different outcomes or classes of outcome. We assessed methods used to blind outcome assessment as at low, high, or unclear risk of bias.

Incomplete outcome data (checking for possible attrition bias due to the amount, nature, and handling of incomplete outcome data)

We described the completeness of data for each included study, and for each outcome or class of outcomes including attrition and exclusions from the analysis. We stated whether attrition and exclusions were reported and the numbers included in the analysis at each stage (compared with the total randomized participants), reasons for attrition or exclusion where reported, and whether missing data were balanced across groups or were related to outcomes. Where sufficient information was reported, or could be supplied by the study authors, we would have re-included missing data if we had undertaken any analyses. We assessed methods as at low risk of bias (for example, no missing outcome data; missing outcome data balanced across groups); high risk of bias (for example, numbers or reasons for missing data imbalanced across groups; 'as treated' analysis done with substantial departure of intervention received from that assigned at randomisation); or unclear risk of bias.

Selective reporting (checking for reporting bias)

We described for each included study how we investigated the possibility of selective outcome reporting bias. We assessed the methods as at low risk of bias (where it was clear that all of the study's prespecified outcomes and all expected outcomes of interest to the review have been reported); or high risk of bias (where not all the study's pre-specified outcomes were reported, one or more reported primary outcomes were not pre-specified, outcomes of interest were reported incompletely and so could not be used, or the study failed to include results of a key outcome that would have been expected to have been reported); or unclear risk of bias.

Other bias

We would have described any other bias if we had suspected it, for each study. We planned to assess whether each study was free of other problems that could put it at low, high, or other risk of bias.

Overall risk of bias

We intended to make explicit judgements about whether studies were at high risk of bias, according to the criteria given in [Higgins 2011](#). We assessed the likely magnitude and direction of the bias and whether we considered it likely to impact on the findings. If we had found any such bias, we would have explored the impact of the level of bias through undertaking sensitivity analyses. For cluster-randomized trials and qRCTs, we additionally assessed the following 'Risk of bias' criteria.

- Recruitment bias
- Baseline imbalance
- Loss of clusters
- Incorrect analysis
- Comparability with individually randomized trials

For CBA, we planned to use the Cochrane 'Risk of bias in non-randomized studies of interventions' (ROBINS-I) assessment tool to assess bias due to confounding, bias in selection of participants into the study, bias in classification of interventions, bias due to deviation from intended interventions, bias due to missing data, bias in measurement of outcomes, and bias in selection of the reported results.

Measures of treatment effect

Dichotomous data

We planned to present results as summary risk ratio or rate ratio with 95% confidence intervals (CIs) for dichotomous data.

Continuous data

We planned to use the mean difference if outcomes were measured in the same way between studies for continuous data, and use the standardized mean difference to combine studies that measured the same outcome, but used different methods.

Unit of analysis issues

We planned to include cluster-RCTs in the analyses along with individual RCTs, and the method of analysis is described in our protocol ([Das 2015](#)). However, we only included one cluster-RCT in the analysis.

If we had identified studies with more than two intervention groups (multi-arm studies), where possible we intended to combine groups to create a single pair-wise comparison or use the

methods set out in [Higgins 2011](#) to avoid double-counting study participants.

Dealing with missing data

We described missing data, including the number of participants lost to follow-up. Differential dropout rates can lead to biased estimates of the effect size, and bias may arise if the reasons for dropping out differ across groups. We assessed the reasons for loss to follow-up. If data were missing for some cases or if the reasons were not reported, we intended to contact the study authors. For included studies, we noted levels of attrition. We intended to explore the impact of including studies with high levels of missing data in the overall assessment of treatment effect by using sensitivity analysis.

Assessment of heterogeneity

We examined the included studies for clinical, methodological and statistical heterogeneity. We assessed clinical heterogeneity by comparing the distribution of important factors, such as the study participants, study setting, dose, assessment tools and duration of the intervention and co-interventions. We evaluated methodological heterogeneity on the basis of factors such as the method of sequence generation, allocation concealment, blinding of outcome assessment and losses to follow-up. We planned to assess statistical heterogeneity in each meta-analysis using the Tau², I² statistic, and Chi² statistic. We intended to regard heterogeneity as substantial if the I² statistic value was greater than 50%, and either Tau² was greater than zero or there was a low P value (< 0.10) in the Chi² test for heterogeneity. In case of absence of heterogeneity, we wished to perform pre-specified subgroup analysis.

Assessment of reporting biases

We would have investigated reporting biases (such as publication bias) using funnel plots if 10 or more studies were included in meta-analysis. For continuous outcomes, we intended to use the test proposed by [Egger 1997](#). For dichotomous outcomes, we intended to use the test proposed by [Harbord 2006](#). If we had detected asymmetry in any of these tests or it was suggested by a visual assessment, we would have performed exploratory analyses to investigate it.

Data synthesis

We planned to carry out statistical analysis using RevMan 5, but as only one study was included, we could not carry out a meta-analysis ([Review Manager 2014](#)). Our intended analysis is documented in [Das 2015](#).

We prepared 'Summary of findings' tables using the GRADE approach ([Guyatt 2008](#)), and GRADEpro GDT software ([GRADEpro GDT 2015](#)).

Preplanned sensitivity analysis based on risk of bias is outlined in our protocol ([Das 2015](#)).

RESULTS

Description of studies

See the 'Characteristics of included studies' table and the 'Characteristics of excluded studies' table.

Results of the search

We identified 3099 records through searches, of which we excluded 3062 after screening by title and abstract. We excluded 36 articles after full-text assessment and one study met the inclusion criteria. See [Figure 2](#) for details regarding the number of studies at different stages of the review.

Included studies

Only [Chavasse 1999](#) fulfilled the inclusion criteria.

Design

[Chavasse 1999](#) is a cluster-RCT.

Interventions

The intervention consisted of ultra-low-volume space spraying with insecticide (Aqua K-Othrine, a water-based formulation of deltamethrin) to control flies. Spraying was done twice a week between March and November of each year. The study also tested the use of fly baits as a second intervention but that was tested in a village in a separate year when the first intervention had already been tested.

Participants

The study included children less than five years old from a total of eight villages in Pakistan. The six intervention villages were randomly assigned to two groups: in intervention group A, flies were controlled through insecticide spraying for the first intervention year and group B served as control, while in the second intervention year group B received the intervention and group A served as a control. In the third year, a second intervention (baited fly traps) was given in group A as intervention and group B was a control. Two separate villages were observed as controls and did not receive any intervention throughout the three-year intervention duration. A total of 491 children under the age of five years were enrolled in the study during the initial survey, 214 in group A and 277 in group B. The median age of participants and the number

of families residing in each compound were similar. During the course of the study, the participants who reached the age of five years were successively removed from the data collection process and more children were recruited who moved into the intervention area or were born in the intervention villages. Daily diarrhoea profiles were compiled for a total of 810 children who, for all or some of the duration of study, were less than five years old.

Support or sponsorship

The study received financial support from Thrasher Research Fund, ODA, and Médecins Sans Frontières. The insecticide used in the study was donated by AgrEvo and sprayers were provided by Hudson (USA).

Baseline characteristics of participants

The baseline diarrhoea incidence during the month at the start of the study was 0.4 episodes per child per month in both groups.

Studied outcomes

The study monitored fly density with standard sticky fly-papers, which were hung in areas of the compounds where fly resting sites were either suspected or identified through faecal deposits. The number of flies stuck to the papers after 24 hours was noted as outcome. The study also reported the incidence of diarrhoea in children less than five years of age residing in the intervention and control villages. The study personnel conducted weekly interviews with mothers, who reported the days on which their child/children had diarrhoea during the week being studied. Diarrhoea incidence was derived by the authors from the daily diarrhoea data, and they considered two days free of diarrhoea as an indicator of the end of an episode.

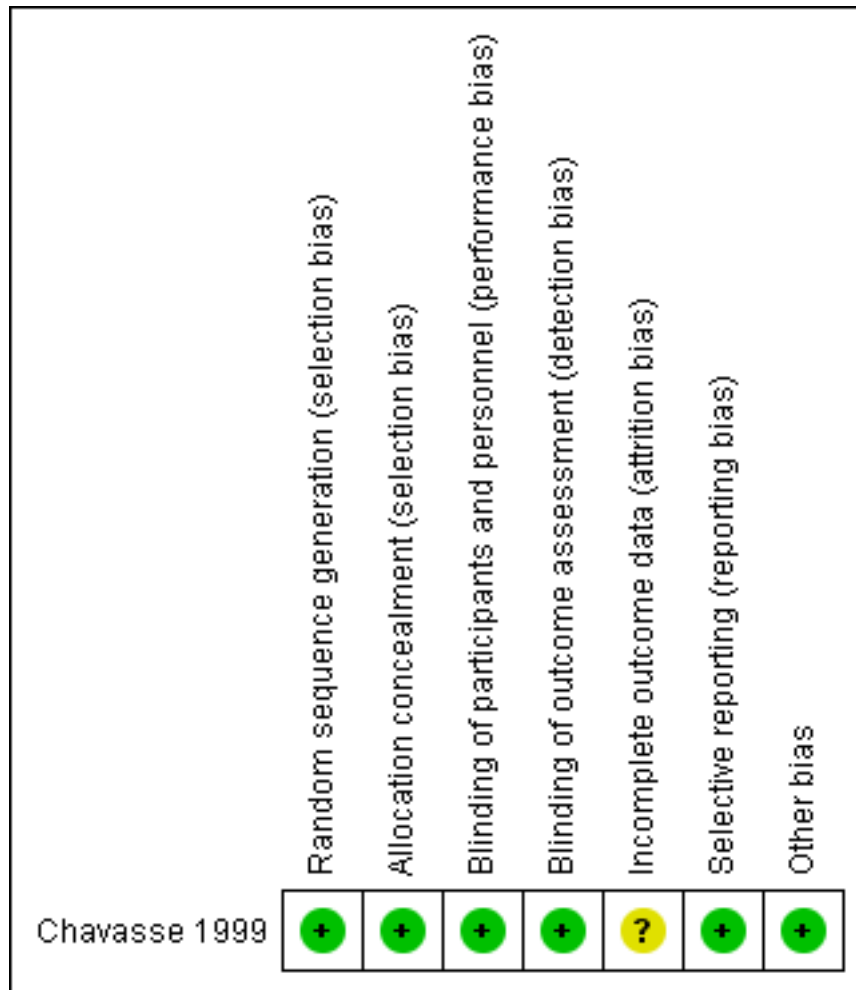
Excluded studies

We excluded 36 studies after full-text assessment for the reasons outlined in the '[Characteristics of excluded studies](#)' table.

Risk of bias in included studies

[Figure 3](#) shows a summary of the 'Risk of bias' assessments.

Figure 3. 'Risk of bias' summary: review authors' judgements about each 'Risk of bias' item for each included study.



Allocation

Randomization was done by picking names of villages from a hat during a meeting. There was no allocation concealment.

some other families moved into the villages and children were born. Due to the nature of the outcomes studied (diarrhoea in children was noted every week to calculate incidence), it is unclear how this may have biased the results.

Blinding

There was no blinding of the participants or the personnel. Due to the nature of the interventions and the outcomes, it is unclear how non-blinding could have biased the results.

Selective reporting

A published protocol was not available, but the expected outcomes were reported.

Incomplete outcome data

During the course of the study, 186 children reached five years of age, 24 died, and 145 moved away from the study area. Moreover,

Other potential sources of bias

No other potential sources of bias.

Effects of interventions

See: [Summary of findings for the main comparison](#) 'Summary of findings' table 1

We could not pool data or perform meta-analyses due to inclusion of just one study. We have provided a narrative synthesis of the Chavasse 1999 findings.

Primary outcomes

Incidence of diarrhoea

Diarrhoea incidence was lower in sprayed villages than in unsprayed villages in both year 1 (mean episodes per child⁻ year in the sprayed villages was 6.3 compared to 7.1 in the control villages)

and year 2 (mean episodes per child⁻ year in the sprayed villages was 4.4 compared to 6.5 in the control villages). When adjusted for year, the analysis of impact of fly control indicated a significant reduction in diarrhoea incidence associated with insecticide spraying (rate ratio (RaR) 0.77, 95% CI 0.67 to 0.89, $P = 0.007$), thus the reduction in diarrhoea incidence attributable to fly control through insecticide spraying was 23% (95% CI 11 to 33, $P = 0.007$). During months other than the fly season, no difference was detected between the two groups (RaR 1.03, 95% CI 0.84 to 1.27, $P = 0.70$). In the third year, when baited fly traps were used, there was no difference detected in diarrhoea rate between the two groups (RaR 1.15, 95% CI 0.90 to 1.47). The authors noted that when fly densities were low the two groups had similar diarrhoea incidence, while there was some carry-over effect of the insecticides on fly densities after the end of the fly season.

The study did not report on any of the other primary outcomes (clinic visits; emergency department visits; hospital admissions; and recurrent diarrhoea).

Secondary outcomes

House index

In the first year of fly season, the mean number of flies caught per paper per day was three in sprayed villages, 118 in unsprayed villages, and 88 in the control villages. In the second year, the mean number of flies caught per paper per day was two in sprayed villages, 57 in unsprayed villages, and 63 in the control villages. Thus spraying was highly effective in reducing flies in both years (house index). Baited fly traps were tested in the third year in one group only and mean number of flies caught in all three groups (89 in group with traps, 54 in group without traps, and 90 in the control group) was relatively similar.

None of the other secondary outcomes were reported (fly density; duration of hospitalization; diarrhoea-specific mortality; or ovitrap index). The study did not report any adverse effects.

DISCUSSION

Summary of main results

See [Summary of findings for the main comparison](#).

Fly control as an intervention for diarrhoea prevention has not been studied comprehensively. The limited data from one study suggests that insecticide spraying may reduce the incidence of diarrhoea in children less than five years of age residing in areas with high fly density during fly and wet seasons, while there was no difference during the non-fly season (low-certainty evidence). Baited fly traps may have no effect on the house index and diarrhoea incidence (low-certainty evidence).

Overall completeness and applicability of evidence

Overall, there is a scarcity of data on the subject. There is a need for robust evidence examining different pathways of transmission, in various settings, to provide a fair estimate of the effect and benefits of targeting flies to reduce the incidence of diarrhoea, which continues to present a challenge to child health globally.

Fly control has been linked to diarrhoea prevention. Given the scarcity of data and the research demonstrated by our review, it is noted that fly control has not been evaluated in a similar way to other preventive strategies that have been endorsed by the WHO and other funding and implementing organizations. We excluded most studies in the domain as they were either small-scale observational studies or other types of studies with very weak methodological quality, and did not report on our outcomes of interest. This suggests that this area of research has not been given its due attention and is broadly an ignored domain. Even the studies that did evaluate the intervention of interest did not look at diarrhoea and other morbidities as outcomes but were only focused on process outcomes. Hence, there is a need to conduct high-quality studies to evaluate the effectiveness of using fly control as a means for diarrhoea prevention in children less than five years of age.

Certainty of the evidence

This review summarizes findings from only one study with 491 participants. The study reported only one of the pre-specified primary outcomes, incidence of diarrhoea, and we judged the certainty of the evidence to be 'low'. The included study lacked allocation concealment and blinding. Further research in this domain is very likely to have an important impact on our confidence in the estimate of effect and is likely to change the estimate.

Potential biases in the review process

We did not identify any potential sources of bias regarding the review process. We conducted an extensive search of pre-specified electronic databases and screened all identified records. We followed the methods specified in the published protocol (Das 2015), and involved two review authors at each step. Only one study was eligible for inclusion and reported on only one pre-specified primary outcome (incidence of diarrhoea) and one pre-specified secondary outcome (house index).

Agreements and disagreements with other studies or reviews

To our knowledge, there are no other reviews or ongoing studies assessing the effectiveness of fly control interventions on childhood diarrhoea. We did not identify any disagreements with published data on the subject.

AUTHORS' CONCLUSIONS

Implications for practice

The findings of the one included study suggest that insecticide spraying reduces the incidence of diarrhoea in high fly-density

areas during fly and wet seasons. The evidence is not applicable to policy and practice because the existing evidence is scarce and has very limited generalizability.

Implications for research

Our review has identified a scarcity of interventional studies targeting fly control as a mechanism for diarrhoea prevention. Randomized controlled trials targeting various mechanisms of fly control should be conducted so that the effectiveness of each intervention can be assessed. Future studies should take into account the different cultural practices, local Musci species, socioeconomic factors, and hygiene-related practices among other variables, in order to develop an understanding of the circumstances in which fly control can be recommended as a viable intervention for diarrhoea prevention in children.

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* Indicates the major publication for the study

CHARACTERISTICS OF STUDIES

Characteristics of included studies [ordered by study ID]

Chavasse 1999

Methods	Cluster-randomized controlled trial	
Participants	491 children under 5 years of age in study villages in Pakistan	
Interventions	<p>Flies controlled through insecticide spraying in 6 intervention villages and 2 control villages</p> <p>Group A (3 villages) got the intervention (insecticide spraying) in 1995. Group B (3 villages) got the intervention (insecticide spraying) in 1996. A second intervention of fly traps was done in group A in 1997</p> <p>2 villages did not receive any treatment throughout the intervention duration and were control villages</p>	
Outcomes	<p>Incidence of diarrhoea: mean episodes per child- year</p> <p>Mean number of flies caught per sticky paper in 24 hours</p>	
Notes	None	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Randomization of villages was done by picking numbers out of a hat at a meeting
Allocation concealment (selection bias)	Low risk	No allocation concealment was done but it is unclear how it could affect the study outcome
Blinding of participants and personnel (performance bias) All outcomes	Low risk	No blinding was done. But due to the nature of the interventions and the outcomes, it is unclear how non-blinding could have biased the results
Blinding of outcome assessment (detection bias) All outcomes	Low risk	No blinding was done. But due to the nature of the interventions and the outcomes, it is unclear how non-blinding could have biased the results
Incomplete outcome data (attrition bias) All outcomes	Unclear risk	During the course of the study, 186 children reached the age of 5 years, 24 died, and 145 moved away from the study area. Moreover, some other families moved into the villages and increased the number of children studied. Due to the nature of the outcomes studied (diarrhoea in children was noted every week to calculate incidence), it is unclear how this may have biased the results

Chavasse 1999 (Continued)

Selective reporting (reporting bias)	Low risk	No protocol was available but the expected outcomes were reported
Other bias	Low risk	No other sources of bias identified. The following criteria specific to cluster-randomized trials were assessed in addition: (i) recruitment bias: low risk (comment: individuals were not recruited to the trial after the clusters had been randomized) (ii) baseline imbalance: low risk (comment: baseline characteristics were similar in the intervention and control clusters) (iii) loss of clusters: low risk (comment: there was no loss of complete clusters) (iv) incorrect analysis: low risk (comment: analysis accounted for the effect of clustering) (v) comparability with individually randomized trials: unclear risk (comment: there was no other individually randomized trial included in the analysis)

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Abdel-Gawaad 1972	No population of interest
Armstrong 1914	Study design does not fulfil the inclusion criteria
Barreto 2011	No original data
Burgess 2015	No outcomes of interest
Butt 2015	Review article
Clasen 2014	Intervention was latrine construction and promotion. Decrease in diarrhoea cannot be attributed to fly control only
Cohen 1991	Study population was soldiers aged 18 to 22.
Collinet-Adler 2015	No intervention of interest
Corbo 1951	No outcomes of interest
Emerson 1999	Study design does not fulfil the inclusion criteria

(Continued)

Emerson 2004	No diarrhoea related outcomes
Gorbatow 1951	Observational study
Heijnen 2015	No intervention of interest
Inder Singh 1971	No outcomes of interest
Inder Singh 1973	No outcomes of interest
Jung 2016	Study protocol only
Lindsay 1953	Outcomes not available for our population of interest
Lindsay 2013	No outcome of interest
McCabe 1957	Study on excreta disposal
Meifert 1967	Study focuses on fly density only, with no mention of diarrhoea
Overgaard 2016	No intervention of interest
Parvez 2017	No intervention of interest
Schmidt 2016	No intervention of interest
Sehgal 1970	Outcomes not available for our population of interest
Skovgård 2004	No outcomes of interest: study focused on cattle and pig farms
Songe 2017	No intervention of interest
Srinivasan 2003	No outcome of interest
Terry 1913	No population of interest
Tilak 2007	No outcomes of interest
Tilak 2010	No outcomes of interest
Vasiliev 1970	No diarrhoea outcomes
Vlppo 1950	Outcomes not available for our population of interest
Watt 1948	Outcomes not available for our population of interest
Weir 1952	No outcomes of interest

(Continued)

West 2006	No outcomes of interest
Zakharova 1977	No diarrhoea-related outcomes

APPENDICES

Appendix I. Search strategies

Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily, Ovid MEDLINE and Versions(R)

Search strategy

-
- 1 *Houseflies/
 - 2 (housefly or houseflies or fly).ti. or (housefly or houseflies or fly).ab.
 - 3 ("musca domestica" or musca or chrysomya or muscid*).ti. or ("musca domestica" or musca or chrysomya or muscid*).ab.
 - 4 Insect Vectors/
 - 5 "insect vector*".ti. or "insect vector".ab.
 - 6 "insect vectors".ti. or "insect vectors".ab.
 - 7 1 or 2 or 3 or 4 or 5 or 6
 - 8 Diarrhea/
 - 9 Diarrh*.ti. or Diarrh*.ab.
 - 10 gastroenteritis.ti. or gastroenteritis.ab.
 - 11 Gastroenteritis/
 - 12 (dysenter* or shigella or vibrio or cholera or rotavirus or giardi*).ti. or (dysenter* or shigella or vibrio or cholera or rotavirus or giardi*).ab.
 - 13 (density or index).ti. or (density or index).ab.
 - 14 8 or 9 or 10 or 11 or 12 or 13
 - 15 7 and 14
 - 16 (children or child or childhood or infant* or toddler* or pediatri* or paediatric*).ti. or (children or child or childhood or infant* or toddler* or pediatri* or paediatric*).ab.
 - 17 15 and 16
 - 18 randomized controlled trial/ or controlled clinical trial/
 - 19 (randomized or randomised or randomly or placebo or double-blind* or single-blind*).mp.)
 - 20 (before and after study).mp
 - 21 Controlled Before-After Studies/
 - 22 18 or 19 or 20 or 21
 - 23 17 and 22

Embase (OVID)

- 1 houseflies.mp. or house fly/

- 2 musca domestica.mp.
 3 (chrysomya or muscid*).mp.
 4 disease carrier/
 5 1 or 2 or 3 or 4
 6 diarrhea/
 7 diarrh*.mp.
 8 (gastroenteritis or dysenter* or shigella or vibrio or cholera or rotavirus or giardi*).mp.
 9 6 or 7 or 8
 10 5 and 9
 11 clinical trial/
 12 randomized controlled trial/
 13 randomization/ or randomization.mp.
 14 (single blind* or double blind*).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
 15 randomly allocated.mp.
 16 (before and after study).mp. [mp=title, abstract, subject headings, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword]
 17 prospective study/
 18 11 or 12 or 13 or 14 or 15 or 16 or 17
 19 10 and 18
 20 (children or child or childhood or infant* or toddler* or pediatr* or paediatr*).mp.
 21 10 and 20

PubMed

Search	Query
#29	Search (#28) AND #23
#28	Search (((#27) OR #26) OR #25) OR #24)
#27	Search "Controlled Before-After Studies"[Mesh]
#26	Search "before and after study" Field: Title/Abstract
#25	Search "Randomized Controlled Trial" [Publication Type] OR "Controlled Clinical Trial" [Publication Type]
#24	Search randomized OR placebo OR randomly OR groups OR trial Field: Title/Abstract
#23	Search (#21) AND #22
#22	Search child* OR infant* OR toddler* OR boys OR girls OR newborn* OR neonate*
#21	Search (#20) AND #10
#20	Search (((((#19) OR #18) OR #17) OR #15) OR #14) OR #12
#19	Search density OR index Field: Title/Abstract

(Continued)

#18	Search dysenter* OR shigella OR vibrio OR cholera OR rotavirus OR giardi* Field: Title/Abstract
#17	Search "Gastroenteritis"[Mesh]
#15	Search gastroenteritis Field: Title/Abstract
#14	Search diarrh* Field: Title/Abstract
#12	Search "Diarrhea"[Mesh]
#10	Search (((("Houseflies"[Mesh]) OR #3) OR #5) OR #6) OR #7) OR #9
#9	Search "Insect Vectors"[Mesh]
#7	Search insect vector* Field: Title/Abstract
#6	Search musca OR chrysomya OR muscid* Field: Title/Abstract
#5	Search musca domestica Field: Title/Abstract
#3	Search housefly OR houseflies OR fly Field: Title/Abstract
#2	Search "Houseflies"[Mesh]

Cochrane Library

ID Search

- #1 housefly or houseflies or fly
- #2 "musca domestica" or musca or chrysomya or muscid*
- #3 "insect vector*"
- #4 #1 or #2 or #3
- #5 MeSH descriptor: [Diarrhea] explode all trees
- #6 MeSH descriptor: [Gastroenteritis] explode all trees
- #7 diarrh* or gastroenteritis
- #8 dysenter* or shigella or vibrio or cholera or rotavirus or giardi*
- #9 #5 or #6 or #7 or #8
- #10 #4 and #9

Web of Science

TOPIC: (fly or "house fly" or flies or houseflies or musca or chrysomya or muscid*) AND TOPIC: (diarrh* OR gastroenteritis or dysenter* or shigella or vibrio or cholera or rotavirus or giardi*)
Indexes=SCI-EXPANDED, SSCI, CPCI-S, CPCI-SSH

LILACS

Search on : fly or "house fly" or flies or houseflies or musca or chrysomya or muscid\$ [Words] and diarrh\$ OR gastroenteritis or dysenter\$ or shigella or vibrio or cholera or rotavirus or giardi\$ [Words]

CINAHL, PsycInfo, ERIC (EBSCOHost)

#	Query
S3	S1 AND S2
S2	TX diarrh* OR TX gastroenteritis OR TX dysenter* OR TX shigella OR TX vibrio OR TX cholera OR TX rotavirus OR TX giardi*
S1	TX fly OR TX "house fly" OR TX flies OR TX houseflies OR TX musca OR TX chrysomya OR TX muscid

CONTRIBUTIONS OF AUTHORS

All authors contributed to writing this review, and read and approved the final manuscript.

DECLARATIONS OF INTEREST

JKD: none known.

YBH: none known.

RAS: none known.

MH: none known.

ZSL: none known.

ZAB: none known.

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- Liverpool School of Tropical Medicine, UK.

External sources

- Department for International Development (DFID), UK.
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DIFFERENCES BETWEEN PROTOCOL AND REVIEW

We amended the title from 'Interventions to control flies for preventing diarrhoea in children under five years of age' to 'Fly control to prevent diarrhoea in children'.

We planned to pool data and undertake meta-analysis. However, we could not perform this due to inclusion of only a single study.

INDEX TERMS

Medical Subject Headings (MeSH)

Diarrhea [epidemiology; *prevention & control]; Incidence; Insecticides; Mosquito Control [*methods]; Pakistan [epidemiology]

MeSH check words

Child, Preschool; Humans; Infant; Infant, Newborn