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Jai K. Das
Yousaf Bashir Hadi
Rehana Salam
Mehar Hoda
Zohra S. Lassi

See next page for additional authors

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Fly control to prevent diarrhoea in children

Jai K Das¹, Yousaf Bashir Hadi², Rehana A Salam¹, Mehar Hoda¹, Zohra S Lassi³, Zulfiqar A Bhutta⁴

¹Division of Women and Child Health, Aga Khan University Hospital, Karachi, Pakistan. ²Department of Internal Medicine, West Virginia University, Morgantown, West Virginia, USA. ³The Robinson Research Institute, The University of Adelaide, Adelaide, Australia. ⁴Centre for Global Child Health, The Hospital for Sick Children, Toronto, Canada

Contact address: Zulfiqar A Bhutta, Centre for Global Child Health, The Hospital for Sick Children, Toronto, ON, M5G A04, Canada. zulfiqar.bhutta@sickkids.ca, zulfiqar.bhutta@aku.edu.

Editorial group: Cochrane Infectious Diseases Group.


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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 We did not apply any filters for language, publication status (published, unpublished, in press, and ongoing), or publication date.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.
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 setting 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.

Fly control to prevent diarrhoea in children (Review)

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### Summary of Findings for the Main Comparison

Interventions to control disease spread from the housefly compared with no intervention for childhood diarrhoea

**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

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Illustrative comparative risks* (95% CI)</th>
<th>Relative effect (95% CI)</th>
<th>Number of participants (studies)</th>
<th>Certainty of the evidence (GRADE)</th>
<th>Comments</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>Assumed risk</td>
<td>Corresponding risk</td>
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<tr>
<td></td>
<td>No intervention</td>
<td>Infections to control disease spread from the housefly</td>
<td></td>
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</tbody>
</table>
| Incidence of diarrhoea  | 7.1 mean episodes of diarrhoea per child-year in first year  
6.5 mean episodes of diarrhoea per child-year in second year | 6.3 mean episodes of diarrhoea per child-year in first year of intervention  
4.4 mean episodes of diarrhoea per child-year in first year of intervention | RaR 0.77 (0.67 to 0.89) | 491 participants (one study) | ⬤⬜️⬜️ due to risk of bias and indirectness  
Insecticide spraying may decrease diarrhoea incidence compared to no intervention |
|                         | 5.1 mean episodes of diarrhoea per child-year  
5.8 mean episodes of diarrhoea per child-year | 5.8 mean episodes of diarrhoea per child-year in first year of intervention | RaR 1.15 (0.90 to 1.47) | 491 participants (one study) | ⬤⬜️⬜️ due to risk of bias and indirectness  
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**

<table>
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<tr>
<th>Grade</th>
<th>Description</th>
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<tr>
<td>High certainty</td>
<td>further research is very unlikely to change our confidence in the estimate of effect.</td>
</tr>
<tr>
<td>Moderate certainty</td>
<td>further research is likely to have an important impact on our confidence in the estimate of effect and may change the estimate.</td>
</tr>
<tr>
<td>Low certainty</td>
<td>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.</td>
</tr>
<tr>
<td>Very low certainty</td>
<td>we are very uncertain about the estimate.</td>
</tr>
</tbody>
</table>

*a* Downgraded by 1 due to serious risk of bias: one RCT but lacked allocation concealment and blinding.

*b* No serious inconsistency.

*c* Downgraded 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.

*d* No 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.

**Housefly Control Measures**
- Elimination of fly breeding sites
- Reduction of sources that attract houseflies
- Prevention of contact between flies and disease-causing organisms
- Protection of people, food and food utensils from contact with flies

**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-
Impact 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/)
- 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 fulfill 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).
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 as 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.

### 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.

### 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, 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.

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

### 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, 118 in unsprayed villages, and 88 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.

Acknowledgements

The Academic Editor of this review is Dr Michael Eisenhut. The editorial base of the Cochrane Infectious Diseases Group is funded by UK aid from the UK government for the benefit of low- and middle-income countries (project number 300342-104). The views expressed do not necessarily reflect the UK government’s official policies.

References

References to studies included in this review

Chavasse 1999 [published data only]

References to studies excluded from this review

Abdel-Gawaad 1972 [published data only]

Armstrong 1914 [published data only]

Barreto 2011 [published data only]

References to studies included in this review

Butt 2015 [published data only]
Butt T, Von Seidlein L. A systematic review of the impact of improved housing interventions on health in low and middle income tropical settings. Conference: ISPOR 18th Annual European Congress Milan Italy var. pagings, 2015; Vol. 18:A564.

Clasen 2014 [published data only]

Burgess 2015 [published data only]

Butt 2015 [published data only]
Butt T, Von Seidlein L. A systematic review of the impact of improved housing interventions on health in low and middle income tropical settings. Conference: ISPOR 18th Annual European Congress Milan Italy var. pagings, 2015; Vol. 18:A564.

Clasen 2014 [published data only]

References to studies excluded from this review

Abdel-Gawaad 1972 [published data only]

Armstrong 1914 [published data only]

Barreto 2011 [published data only]

Burgess 2015 [published data only]

Butt 2015 [published data only]
Butt T, Von Seidlein L. A systematic review of the impact of improved housing interventions on health in low and middle income tropical settings. Conference: ISPOR 18th Annual European Congress Milan Italy var. pagings, 2015; Vol. 18:A564.

Clasen 2014 [published data only]
Fly control to prevent diarrhoea in children (Review)

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Emerson 2004 [published data only]


Emerson 1999 [published data only]

Emerson 2004 [published data only]


Heijnen 2015 [published data only]

Inder Singh 1971 [published data only]

Inder Singh 1973 [published data only]

Jung 2016 [published data only]

Lindsay 2015 [published data only]

McCabe 1957 [published data only]

Meiffert 1967 [published data only]

Overgaard 2016 [published data only]

Parvez 2017 [published data only]

Schmidt 2016 [published data only]

Sehgal 1970 [published data only]

Skogvård 2004 [published data only]

Songe 2017 [published data only]

Srinivasan 2003 [published data only]
Terry 1913  [published data only]

Tilak 2007  [published data only]

Tilak 2010  [published data only]

Vasiliev 1970  [published data only]

Vlppo 1950  [published data only]

Watt 1948  [published data only]
Watt J, Lindsay DR. Diarrheal disease control studies; effect of fly control in a high morbidity area. *Public Health Reports* 1948;63(1):1319–33. PUBMED: 18885786

Weir 1952  [published data only]

West 2006  [published data only]

Zakharaova 1977  [published data only]

Additional references

Abu-Rayyan 2010

Baker 1947

Bhutta 2013

Chavasse 1994

Chavasse 1996

Chompook 2006

Derbeneva-Uhova 1966

Egger 1997

Farag 2013

GRADEpro GDT 2015  [Computer program]

Guyatt 2008

Harbord 2006

Higgins 2011

Hogsett 1999
Jinadu 2004

Keiding 1975

Lazarus 1989

Levine 1991

Lindsay 2012

Lou 1990

Peter 1997

Rego 2005

Rego 2007
Rego RF, Barreto ML, Santos R, de Oliveira NF, Oliveira S. Rubbish index and diarrhoea in Salvador, Brazil.

*Indicates the major publication for the study*
## Characteristics of included studies  
*ordered by study ID*

**Chavasse 1999**

<table>
<thead>
<tr>
<th>Methods</th>
<th>Cluster-randomized controlled trial</th>
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</thead>
<tbody>
<tr>
<td>Participants</td>
<td>491 children under 5 years of age in study villages in Pakistan</td>
</tr>
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</table>
| Interventions | Flies controlled through insecticide spraying in 6 intervention villages and 2 control villages  
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  
2 villages did not receive any treatment throughout the intervention duration and were control villages |
| Outcomes | Incidence of diarrhoea: mean episodes per child year  
Mean number of flies caught per sticky paper in 24 hours |
| Notes | None |

### Risk of bias

<table>
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<tr>
<th>Bias</th>
<th>Authors’ judgement</th>
<th>Support for judgement</th>
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<td>Random sequence generation (selection bias)</td>
<td>Low risk</td>
<td>Randomization of villages was done by picking numbers out of a hat at a meeting</td>
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<tr>
<td>Allocation concealment (selection bias)</td>
<td>Low risk</td>
<td>No allocation concealment was done but it is unclear how it could affect the study outcome</td>
</tr>
</tbody>
</table>
| 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 |
### Selective reporting (reporting bias)

<table>
<thead>
<tr>
<th>Study</th>
<th>Selective reporting (reporting bias)</th>
<th>Risk</th>
<th>Description</th>
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<tbody>
<tr>
<td>Chavasse 1999</td>
<td>Low risk</td>
<td>No protocol was available but the expected outcomes were reported</td>
<td></td>
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</tbody>
</table>

### Other bias

<table>
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<tr>
<th>Study</th>
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<th>Description</th>
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<tr>
<td></td>
<td>Low risk</td>
<td>No other sources of bias identified. The following criteria specific to cluster-randomized trials were assessed in addition:</td>
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</tr>
<tr>
<td></td>
<td></td>
<td>(i) recruitment bias: low risk (comment: individuals were not recruited to the trial after the clusters had been randomized</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(ii) baseline imbalance: low risk (comment: baseline characteristics were similar in the intervention and control clusters</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iii) loss of clusters: low risk (comment: there was no loss of complete clusters)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(iv) incorrect analysis: low risk (comment: analysis accounted for the effect of clustering)</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>(v) comparability with individually randomized trials: unclear risk (comment: there was no other individually randomized trial included in the analysis)</td>
<td></td>
</tr>
</tbody>
</table>

### Characteristics of excluded studies [ordered by study ID]

<table>
<thead>
<tr>
<th>Study</th>
<th>Reason for exclusion</th>
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</thead>
<tbody>
<tr>
<td>Abdel-Gawaad 1972</td>
<td>No population of interest</td>
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<tr>
<td>Armstrong 1914</td>
<td>Study design does not fulfil the inclusion criteria</td>
</tr>
<tr>
<td>Barreto 2011</td>
<td>No original data</td>
</tr>
<tr>
<td>Burgess 2015</td>
<td>No outcomes of interest</td>
</tr>
<tr>
<td>Butt 2015</td>
<td>Review article</td>
</tr>
<tr>
<td>Clasen 2014</td>
<td>Intervention was latrine construction and promotion. Decrease in diarrhoea cannot be attributed to fly control only</td>
</tr>
<tr>
<td>Cohen 1991</td>
<td>Study population was soldiers aged 18 to 22.</td>
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<tr>
<td>Collinet-Adler 2015</td>
<td>No intervention of interest</td>
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<td>Corbo 1951</td>
<td>No outcomes of interest</td>
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<tr>
<td>Emerson 1999</td>
<td>Study design does not fulfil the inclusion criteria</td>
</tr>
<tr>
<td>Reference</td>
<td>Outcome Details</td>
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<tr>
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<td>----------------------------------------------------------------------------------</td>
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<tr>
<td>Emerson 2004</td>
<td>No diarrhoea related outcomes</td>
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<tr>
<td>Gorbatow 1951</td>
<td>Observational study</td>
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<tr>
<td>Heijnen 2015</td>
<td>No intervention of interest</td>
</tr>
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<td>Inder Singh 1971</td>
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<td>Inder Singh 1973</td>
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</tr>
<tr>
<td>Jung 2016</td>
<td>Study protocol only</td>
</tr>
<tr>
<td>Lindsay 1953</td>
<td>Outcomes not available for our population of interest</td>
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<tr>
<td>Lindsay 2013</td>
<td>No outcome of interest</td>
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<tr>
<td>McCabe 1957</td>
<td>Study on excreta disposal</td>
</tr>
<tr>
<td>Meifert 1967</td>
<td>Study focuses on fly density only, with no mention of diarrhoea</td>
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<tr>
<td>Overgaard 2016</td>
<td>No intervention of interest</td>
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<tr>
<td>Parvez 2017</td>
<td>No intervention of interest</td>
</tr>
<tr>
<td>Schmidt 2016</td>
<td>No intervention of interest</td>
</tr>
<tr>
<td>Sehgal 1970</td>
<td>Outcomes not available for our population of interest</td>
</tr>
<tr>
<td>Skovgård 2004</td>
<td>No outcomes of interest: study focused on cattle and pig farms</td>
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<tr>
<td>Songe 2017</td>
<td>No intervention of interest</td>
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<td>Srinivasan 2003</td>
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<td>Terry 1913</td>
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<td>Tilak 2007</td>
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</tr>
<tr>
<td>Tilak 2010</td>
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<td>Vasiliev 1970</td>
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<td>Vlippo 1950</td>
<td>Outcomes not available for our population of interest</td>
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<td>Watt 1948</td>
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<td>Weir 1952</td>
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Appendix 1. 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

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<td>23 17 and 22</td>
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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
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12 randomized controlled trial/
13 randomization/ or randomization.mp.
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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]
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21 10 and 20

PubMed

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Fly control to prevent diarrhoea in children (Review)

Copyright © 2018 The Authors. Cochrane Database of Systematic Reviews published by John Wiley & Sons, Ltd. on behalf of The Cochrane Collaboration.
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</tr>
<tr>
<td>#3</td>
<td>Search housefly OR houseflies OR fly</td>
<td></td>
</tr>
<tr>
<td>#2</td>
<td>Search “Houseflies”[Mesh]</td>
<td></td>
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</tbody>
</table>

**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)

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<th>#</th>
<th>Query</th>
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<tbody>
<tr>
<td>S3</td>
<td>S1 AND S2</td>
</tr>
<tr>
<td>S2</td>
<td>TX diarrh* OR TX gastroenteritis OR TX dysenter* OR TX shigella OR TX vibrio OR TX cholera OR TX rotavirus OR TX giardi*</td>
</tr>
<tr>
<td>S1</td>
<td>TX fly OR TX “house fly” OR TX flies OR TX houseflies OR TX musca OR TX chrysomya OR TX muscid</td>
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### 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.

### Sources of Support

**Internal sources**
- Division of Women and Child Health, Aga Khan University, Karachi, Pakistan.
- Liverpool School of Tropical Medicine, UK.

**External sources**
- Department for International Development (DFID), UK.
  Project number 300342-104
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