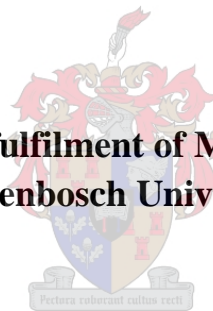# A Systematic Review of the Effects of Interventions to Inform or Educate Caregivers about Childhood Vaccination in Low and Middle-Income Countries

By

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A dissertation in partial fulfilment of MSc clinical epidemiology at Stellenbosch University

Supervisor: Professor Charles S Wiysonge

March 2016

Declaration

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Signature:

Name: Lungeni Auguy Lukusa

Date: March 2016

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Abstract

Background: Despite their proven effectiveness in reducing childhood infectious diseases, the uptake of vaccines remains suboptimal in low and middle-income countries. Identifying strategies for transmitting accurate vaccine information to caregivers would boost childhood vaccination coverage in these countries. The aim of this review was to assess the effects on vaccination coverage of interventions to inform or educate caregivers about childhood vaccination in low and middle-income countries, compared to standard immunisation practices. We chose only information and education because doing a review of all possible interventions for increasing coverage would take more time and resources.

Methods: In May 2015 we conducted a comprehensive search of both peer-reviewed and grey literature. We searched PubMed, Scopus, Cochrane Central Register of Controlled Trials, Web of Science, Cumulative Index of Nursing and Allied Health, prospective trial registries, and reference lists of relevant publications. We included only individual randomised controlled trials (RCTs). The systematic review is registered in the PROSPERO International Prospective Register of systematic reviews, registration number CRD42014010141

Results: Our search identified 963 records from which eight studies were considered potentially eligible. After assessment of eligibility, we included six studies and two studies were excluded. Four included studies were conducted in Pakistan, one in India, and one in Nepal.

The six studies reported immunisation status after community-based information or face-to-face education. Five studies reported coverage with three doses of the combined diphtheria-tetanus-pertussis vaccine (DTP3) and one reported coverage with at least one vaccine. Combining the data shows that information or education significantly improves vaccination coverage: risk ratio (RR) 1.36, 95 % Confidence interval (CI) 1.14 to 1.62. However, there was significant statistical heterogeneity: χ^2 (df=5) = 14.26; P=0.01, I^2=65 %. The heterogeneity could be explained, at least in part, by the type of intervention.

Three studies used community-based information. Two reported DTP3 coverage and one reported coverage with at least one vaccine. Combining data for the three studies shows that community-based information improves vaccination coverage (RR 1.61, 95%CI 1.19 to 2.18), with no significant statistical heterogeneity: χ^2 (df = 2) =3.18, P =.0.20, I^2=37%. Three studies used face-to-face education and reported DTP3 coverage. Combining data for the three studies shows that face-to-face education improves vaccination coverage (RR 1.24, 95% CI 1.01 to 1.53), with significant statistical heterogeneity: χ^2 (df = 2) =7.63, P = 0.02, I^2=74%. The differences between the subgroups (i.e. information versus education) were not significant: χ^2 (df = 1) =1.97, P=0.16, I^2=49.3%.

Conclusions: This review shows a significant improvement in childhood immunisation coverage that was observed in caregivers who received education or information on the importance of vaccines, compared to those who received standard health promotion messages only. The review demonstrates that providing vaccine-related education to caregivers in an effective manner may improve childhood immunisation coverage in low and middle-income country settings.

Keywords: Information, education, parents, caregivers, childhood vaccination, low and middle-income countries

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Background

The use of vaccines during childhood has been one of the most effective public health interventions for combating infectious diseases [1]. Vaccination is vital not only in averting infections, it also mitigates the severity of disease and prevents some cancers (for example, cancers of the cervix and liver) [1].The Expanded Programme on Immunisation (EPI), established in 1974 by the World Health Organization (WHO), has greatly reduced the global burden of poliomyelitis, measles, tetanus, viral hepatitis B, diphtheria, and other diseases [3]. However, vaccination coverage remains low in many low and middle-income countries (LMICs). As a consequence, millions of children in such countries still die from diseases that could have been prevented with vaccines [2].

Low immunisation coverage in LMICs has been attributed to several reasons, including family characteristics, parental attitudes and knowledge, and inadequate information and communication [4]. In particular, poor understanding of vaccines and vaccination schedules is associated with low immunisation coverage in LMICs [5]. A randomised controlled trial has suggested that caregiver concerns regarding childhood vaccines may be due to conflicting information parents receive about the safety and risks of vaccines [6]. Therefore, it is important that caregivers are directed to accurate information so that they can make informed decisions regarding vaccination of their childhood [6].

The use of messages that address caregivers' concerns and false beliefs may be an effective method for increasing compliance with vaccination schedules. Healthcare providers need strategies to successfully transfer vaccine-related information [7] and to deal empathically and effectively with caregivers who have been exposed to anti-vaccination rumours and question the need to vaccinate their children [8].

Communication between and among providers and recipients of healthcare services has been highlighted as an emerging field of importance within the healthcare landscape [9]. Active engagement and effective communication between healthcare providers and recipients are safe and efficient ways for improving a broad range of healthcare outcomes [10]. Informing and educating caregivers about the benefits of vaccination could empower them to undertake effective preventive health care in general, which in turn could increase vaccination coverage [11]. Therefore, it is important to identify relevant interventions for informing and educating caregivers about the importance of childhood vaccination in LMICs.

Objectives

The objective is to assess the effects of information/education of caregivers on childhood vaccination coverage.

Methods

Criteria for considering studies for this review

Types of studies

The synopsis for this systematic review protocol was registered in the International Prospective Register of Systematic Reviews (http://www.crd.york.ac.uk/PROSPERO), registration number CRD42014010141 [12].

We included randomised controlled trials (RCTs), with randomisation at either individual or cluster level. For cluster RCTs, we only included those with at least two intervention and two control clusters. We have included only studies conducted in low and middle-income countries, as defined by the World Bank [13].

Types of participants

The participants of interest were caregivers (defined as parents, legal guardians, or other persons assuming the parental role) to whom information or education about vaccination was given.

Types of interventions

This review focused on interventions to inform or educate caregivers about the importance of vaccination. These interventions included information sessions, group classes, oral presentations, slide shows, seminars, workshops, printed materials (pamphlets, posters, and brochures), audio or video recordings, and one-on-one education. These interventions could be delivered either face-to-face, by mail (email, letters, or postcards), or through phone calls or mobile phone text messaging. Interventions aimed at reminding caregivers about vaccination sessions for their children, or recalling caregivers who have missed vaccination

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visits, were outside the scope of the review and were excluded. We compared the information or educational interventions to no intervention or standard immunisation practices in the study setting.

Types of outcome measures

Primary outcomes

The primary outcomes for this review are children's immunisation status, defined as DTP3 coverage or other vaccination status as reported by the trial authors (if DTP3 coverage was not reported)

Secondary outcome

The secondary outcome is vaccination coverage with individual vaccines as reported by the trials authors.

Search methods for identification of studies

We developed a comprehensive search strategy for searching peer-reviewed and grey literature (See Appendix).

Electronic searches

Sources of peer-reviewed literature searched included PubMed (date of search 23 May 2015), Cochrane Central Register of Controlled Trials (CENTRAL) (date of search 27 May 2015), ISI Web of Science (Science Citation Index) (date of search 25 May 2015), Cumulative Index of Nursing and Allied Health (CINAHL) (date of search 25 May 2015), and PDQ Evidence (date of search 20 May 2015).

Searching other resources

In addition, we searched for ongoing trials in the WHO International Clinical Trials Registry Platform and Clinicaltrials.gov, and checked reference lists of relevant reviews and full-text articles assessed for eligibility . We included articles available on 31 May 2015.

Data collection and analysis

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Selection of studies

Two investigators (Lungeni Lukusa and Nyanyiwe Mbeye) independently screened the search outputs for potentially eligible studies. Full texts of selected studies were retrieved and the two investigators independently assessed them for eligibility against the study inclusion criteria. All potential eligible studies were published in English. Disagreements about the inclusion of studies were resolved through discussion and consensus. If disagreements were not resolved, a third investigator (Charles Wiysonge) was involved. Reasons for excluding potentially eligible studies are provided.

Data extraction and management

Two investigators (Lungeni Lukusa and Nyanyiwe Mbeye) independently extracted data using a pre-designed pilot-tested data collection form and compared their results, resolving discrepancies by consensus and arbitration by a third investigator as required. The data to be extracted included study design and methods, country setting (including income level as defined by the World Bank) and participant characteristics, intervention characteristics, study outcomes, and study funding sources. All eligible studies were From LMICs.

Assessment of risk of bias in included studies

The two investigators (Lungeni Lukusa and Nyanyiwe Mbeye) independently assessed the risk of bias in each included study using the following criteria: adequacy of random sequence generation and allocation concealment (for risk of selection bias); blinding of participants and personnel (for risk of performance bias); blinding of outcome assessors (for risk of detection bias); completeness of outcome data (for risk of attrition bias); and completeness of outcome reporting (for risk of reporting bias)[14] . For each domain, we have classified the risk of bias as "low" if the criterion was adequately addressed, "unclear" if the information provided was not sufficient to make an informed judgement or "high" if the criterion was not adequately addressed.

We then summarised the assessments and categorise the included studies into three levels of bias: low, moderate, and high risk of bias. Every study that is classified as low risk for all domains have considered to be at low risk of bias. Any study that has a high risk of selection,

detection or attrition bias are categorised as having a high risk of bias. All other studies are considered to have a moderate risk of bias.

Measures of treatment effect

We have conducted data analysis using the latest version of the Cochrane Collaboration Review Manager statistical software (http://ims.cochrane.org/RevMan). We have express the results of each study as a risk ratio (RR) and its 95% confidence interval (CI) for immunisation coverage [14].

Unit of analysis issues

We have included data from eligible cluster RCTs in relevant meta-analyses after controlling for the design effect, using the intra-cluster correlation coefficient (ICC) derived from the same or similar published cluster RCT[15,16].

Assessment of heterogeneity

Statistical heterogeneity in each meta-analysis are assessed using the chi-squared test of homogeneity and quantified using the Higgins' I-squared statistic. We have defined statistical heterogeneity at the 10% alpha level; and assessed the source of observed statistical heterogeneity using subgroup analyses (i.e. community-based information and face-to-face education).

Assessment of reporting biases

We would have used funnel plots to assess the possibility of publication bias across studies for every meta-analysis involving 10 or more studies [16]. Publication bias leads to funnel plot asymmetry; but when there are fewer than 10 studies in a meta-analysis, funnel plot tests are unreliable in differentiating between real asymmetry and the play of chance. Other causes of funnel plot asymmetry may include delayed-publication bias, location bias, selective outcome reporting, poor methodological design, inadequate analysis, fraud, and chance [16].

Data synthesis

We have pooled the RRs and 95 % CIs of studies with identical outcomes and interventions; using random-effects meta-analysis, because of observed significant statistical heterogeneity.

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We have included data from eligible cluster RCTs in relevant meta-analyses after controlling for the design effect, using the intra-cluster correlation coefficient (ICC) derived from the same or similar published cluster RCT[15,16].

We have used the GRADE approach to assess the certainty of the evidence for each outcome [17], and present data in forest plots and "Summary of Findings" tables [18]. We have written this review following the published protocol [21] and the grading following the GRADE guideline [19, 20].

Subgroup analysis and investigation of heterogeneity

We have conducted subgroup analysis for the primary outcome (i.e. vaccination coverage), with subgroups defined by type of intervention (information versus educational interventions). We have chosen the subgroup based on a specific hypothesis. Educational interventions (e.g. structured and interactive communication tools [15] may lead to a better understanding of the importance of immunisation by caregivers and thus be more effective at increasing vaccination coverage than mass information campaigns.

Sensitivity analysis

We planned to perform a sensitivity analysis to determine the robustness of the findings to risk of bias in any meta-analysis involving 10 or more studies. We did not have the required number of studies for this analysis [16].

Results

Description of studies

Results of the search

We initially identified a total of 963 records from the electronic databases; we removed duplicates and screened 932 records. After screening title and abstracts we excluded 924 records based on there are title and abstracts, and 8 studies were selected for the full test screening and assed for eligibility. We included 6 studies and 2 studies were excluded (see flow chart of study selection in Figure 1).
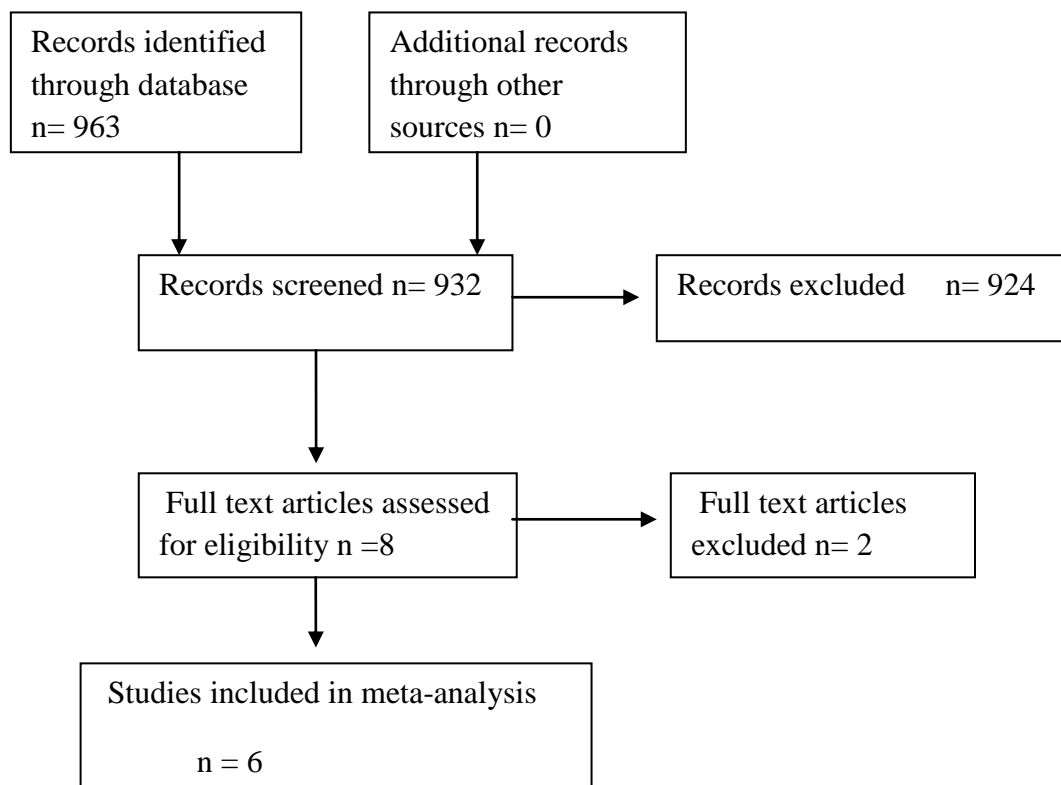
Figure 1: PRISMA flow chart of study selection for the review

Included studies

We included six studies: Andersson 2009[22], Bolam 1998[23], Owais 2011[5], Pandey 2007[24], Usman 2009[25], and Usman 2011[26].

Two cluster-randomised studies were included in this review [22, 24]: see Characteristics of included studies, both studies compared interventions aimed at communities to inform and/or educate about early childhood vaccination with routine immunisation. Owais 2011 was a multi-site community-based, randomized controlled educational intervention. Three studies compared single-session interventions [23, 25, 26]. The approach employed by Bolam 1998 included four arms which assessed both single-session and multi-session interventions. Participants in intervention groups A and B were given face to face education at their child's birth, with immunisation status assessed at three months after birth. The combination of groups A and B together was compared with groups C and D together as the control group (single-session intervention versus no intervention). After the three-month immunisation

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status assessment, groups A and C were given face to face education. Immunisation status was assessed again at six months after birth. Groups B and C (single- session intervention) and group A (considered a multi-session intervention at this time point with the intervention given twice, at birth and three months after birth) were compared with group D as the control group for both comparisons (single session intervention versus no intervention and multi-session intervention versus no intervention). The single-session interventions were face to face education delivered once in clinic settings. Bolam 1998 used 20-minute sessions delivered by a midwife or a community health worker. The other studies involved two- to three-minute education delivered by a data collector or study interviewer [25, 26,30].

Characteristics of studies

Table 1: Characteristics of included studies

1. Andersson 2009 [22]

Methods	Following a baseline survey of randomly selected representative census enumeration areas, a computer generated random number sequence assigned 18 intervention and 14 control clusters. The intervention comprised three structured discussions separately with male and female groups in each cluster. The first discussion shared findings about vaccine uptake from the baseline study; the second focussed on the costs and benefits of childhood vaccination; the third focussed on local action plans. Field teams encouraged the group participants to spread the dialogue to households in their communities. Both intervention and control clusters received a district-wide health promotion programme emphasizing household hygiene and prevention of diarrhoea in children.
Participants	Be part of the randomly selected 32 enumeration areas (EA) from Lasbela district population census among which the intervention group was thus 18 enumeration areas, each of four or five villages and including a total of 3166 children under the age of five years. The 14 control EA, also each of four or five villages, included a total of 2475 children.
Interventions	Three phase discussion : • In the first phase the community groups analysed the situation about child vaccination in their union council. They discussed the prevalence of measles among children and the proportion of children getting vaccinated in their own community, and the importance of childhood vaccinations. • The second phase discussed evidence on costs and benefits of vaccination from the baseline survey, including the costs of treating a child with measles in comparison with the costs of getting a child vaccinated against measles. The groups also discussed the complications of measles, and benefits and adverse effects of measles vaccination. • In the third phase the groups identified the specific challenges and barriers to child vaccination in their own communities and developed plans for actions they could take themselves to address some of these challenges. These

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	included methods for spreading the discussion about vaccination to other community members, as well as ways to increase access to vaccination services, such as sharing transport and helping with childcare. • Health education with messages particularly about household hygiene and prevention of diarrhoea in children.	
Outcomes	**Primary outcomes:** The primary outcome was uptake of measles and full DPT vaccination of 12-23 month olds, as reported by the main caregiver. **Secondary outcomes:** Secondary outcomes specified per protocol were the theory-based "cascada" of intermediate outcomes leading to vaccination uptake: conscious knowledge, attitudes about vaccination, subjective norms, intention to change, agency/self-efficacy, and discussion within the household.	

Risk of Bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (risk of selection bias)	Low risk	Random number generator allocated the baseline communities to 18 interventions and 14 control EAs.
Allocation concealment (risk of selection bias)	Low risk	The sequence was concealed and the intervention assigned centrally
Blinding of participants and providers (risk of performance bias)	Low risk	Blinding was not mentioned. Few people participated in the structured discussion groups but the intention was for these people to widen the discussion, so that most parents in each intervention cluster would know of the structured discussions. However the field co-ordinator for the surveys knew which clusters received the intervention but interviewers did not know.
Blinding of outcome assessors (risk of detection bias)	Unclear risk	The field coordinator for the household surveys (MB) knew which clusters had received the intervention but interviewers did not. We did not evaluate the success of this blinding.
Incomplete outcome data (attrition bias)	Low risk	The baseline survey contacted 538 children aged 12-23 months in intervention and 373 in control communities. The follow-up survey contacted 536 in intervention and 420 in control communities, the increase in the control communities being because of fuller access to one of the control communities, which was not possible in the base-line survey.
Selective reporting (reporting bias)	Low risk	The study protocol published[22] included all outcomes that were assessed in the published trial report
Other bias	Low risk	Willingness to travel to vaccinate was higher in intervention than control cluster (P value = 0.009) in the study [22], and was adjusted for in the analysis.

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2. Bolam 1998[23]

Methods	Randomised controlled trial with community follow up at 3 and 6 months post-partum by interview in Nepal were the estimated population of Kathmandu municipality is 500 000, with an annual urban growth rate of 7.4%.9 PrasutiGriha is the main government funded maternity hospital in Kathmandu, with 250 beds, 15 000 deliveries annually, and outpatient services for the local urban and surrounding populations. As there are no formal addresses in Kathmandu, a house to house survey of two communities was conducted before the study. Kirtipur is a peri urban area 5 km south west of the hospital that contains 3663 households with a total population of 21 368. It is a settled community of mainly wage labourers and farmers. Kalimati is an urban area of central Kathmandu situated 2 km from PrasutiGriha and containing 2467 households with a total population of 13 875.This is a mixed community of long term residents and recent migrants.
Participants	All pregnant women admitted to PrasutiGriha hospital for delivery residing in these two communities : Kirtipur is a peri urban area 5 km south west of the hospital that contains 3663 households with a total population of 21 368. It is a settled community of mainly wage labourer sand farmers. Kalimati is an urban area of central Kathmandu situated 2 km from PrasutiGriha and containing 2467 households with a total population of 13 875.This is a mixed community of long term residents and recent migrants.
Interventions	Mothers receiving health education immediately after birth and at 3 months post-partum (group A), health education at birth only (group B), health education at three months only (groupC), or no health educational (groupD). For outcomes at three months, we combined groups A and B as the intervention group and C and D as the control group. For the outcomes at 6 months, the groups were compared individually.
Outcomes	Primary outcomes were the duration of exclusive breast feeding; mothers' knowledge of important signs of pneumonia and appropriate management of diarrhoea (mothers were asked: "How do you know if your baby with cough has pneumonia?" and, "If your baby has diarrhoea how must you care for him?"); uptake of immunisation; and use of postnatal family planning services. A secondary outcome was infant nutritional status.

Risk of Bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (risk of selection bias)	Low risk	The unit of randomisation was the individual mother. Restricted randomisation was used in blocks of 20, each block consisting of a random ordering of the numbers 0-19. Numbers 0-4, 5-9, 10-14, and 15-19 were assigned to groups A to D respectively
Allocation concealment (risk of selection bias)	Low risk	The details of allocation to groups for consecutively recruited mothers were in sealed envelopes.
Blinding of participants and providers (risk of performance bias)	High risk	Clearly, the mothers recruited and the health educators were not blind to the assignment of mothers to different groups. The data analysts were not blind to the coding of the groups.
Blinding of outcome assessors (risk of detection bias)	Low risk	The outcome assessors were always blind to the assignment at both the 3 and 6 month follow up visits.
Incomplete outcome	High risk	They recruited 540 mothers, 135 to each of the four groups, and

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data (attrition bias)		followed up 403 (75%) to 3 months postpartum and 393 (73%) to 6 months. The main reason for loss to follow up was the mother moving back to her parental home as part of cultural tradition. Two mothers entered into the trial whose deliveries resulted in a stillbirth were withdrawn from the trial and received neither the intervention nor follow up.
Selective reporting (reporting bias)	unclear risk	Outcome at 3 months Table 2 shows the outcomes at 3 months postpartum. We compared mothers in groups A and B, who received health education at birth, with those in groups C and D, who received none. Mothers in groups A and B were slightly more likely to report tachypnoea as a sign of acute respiratory infection, but this did not quite reach statistical significance (odds ratio 1.48, 95% confidence interval 1.00 to 2.19, P=0.06).Also, 20% of mothers in groups A and B were using contraception compared with only 14% of those in groups C and D, but this difference was not significant. There were no differences for the other outcomes. Immunisation coverage was higher than we had hypothesised for both groups (85% in groups C and D, 87% in groups A and B): our sample size would have detected an increase to 93% coverage in groups A and B at 5% significance (one sided test) and 78% power. Outcome at 6 months Table 3 shows the outcomes at 6 months post-partum. We made two broad comparisons: groups A and B (health education at birth) compared with groups C and (no health education at birth),and groups A and C (health education at 3 months) compared with groups Band D(no health education at 3 months).The only significant difference we observed for all outcomes was an increase in uptake of family planning at 6 months in groups A and B (odds ratio 1.62, 95% confidence interval 1.06 to 2.5).To test for interactions, we compared outcomes by health education at birth stratified by whether health education was given at 3 months post-partum using tests for heterogeneity: we found no significant interactions. Post study calculations of the power of our study to detect a significant, one sided difference in exclusive breast feeding between groups (based on our hypothesis of 25% in mothers given no health education and 40% in those given education) were 67% (comparing group A with group D) and 84% (comparing groups A,B and C with group D)
Other bias	Low risk	The mothers were seen individually for the educational session, with indicating low risk of contamination.

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3. Owais 2011[5]

Methods	This was a multi-site community-based, randomized controlled educational intervention trial conducted at five low-income sites in Karachi. Among these, one community was urban, whereas the other four were peri-urban, located about 45 minutes travel outside of Karachi. The population in the study areas has low literacy, with only 24% of the population being literate. The total combined population of all five study sites is approximately 260,000, with high infant and maternal mortality rates. The major income generating activities include fishing and livestock rearing, or employment in local small industries (garment and leather).
Participants	All mothers living in the study areas (five low income sites in Karachi), and having a live child ≤ 6 weeks old, were eligible to be enrolled in the study. Each mother-infant pair, who consented to participate in the study, was assigned a unique study identification number.
Interventions	Easy- to-understand pictorial cards, using very simple language, to convey three key messages as part of the educational intervention were designed. The first key message highlighted how vaccines save children's lives. The second message provided logistic information about the address and location of the local vaccination centers. The third key message emphasized the significance of retaining immunization cards, and the role they could play at the time of the child's school admissions. These messages took about 5 minutes to impart, and were given by the trained CHWs to each participant at their household.
Outcomes	The study outcome in each study group was the immunization status of DPT-3/Hepatitis B at 4 months after enrolment (4 to 5 months of infant's age). Immunization rates of DPT-3/Hepatitis B vaccines for intervention and control groups were assessed by an investigator, and were divided into two categories: 1) Infants receiving all three doses of DPT/Hepatitis B vaccines (assessed through vaccination cards) were considered "DPT-3/Hepatitis B fully immunized". 2) Infants missing any dose of DPT/Hepatitis B or who had lost their vaccination cards were termed"DPT-3/Hepatitis B non-immunized".

Risk of Bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (risk of selection bias)	Low risk	Randomization lists, stratified for each of the five enrolment sites were generated by a computer and provided to the CHWs Upon consent, mother-infant pairs were assigned either to intervention or control arms through block randomization (n = 4), according to the computer-generated list.
Allocation concealment (risk of selection bias)	Low risk	Mother-infant pairs were assigned either to intervention or control arms through block randomization (n = 4), according to the computer-generated list.
Blinding of participants and providers (risk of performance bias)	High risk	As the intervention was educational, blinding of study staff and participants was not possible.
Blinding of outcome assessors (risk of detection bias)	Low risk	Outcome assessment was done by an investigator (BH) at each participant's house, four months after initial enrolment. The investigator was blinded to the exposure status of participants.
Incomplete outcome	Low risk	Four infants were lost to follow-up from the intervention group, and

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data (attrition bias)		five were lost to follow-up from the control group during the study period and were excluded from the analysis. Therefore, 179 enrolled infants were included in the analysis from the intervention group and 178 from the control group. The distribution of enrolled mother-infant pairs among the five study sites was weighted to represent population size in each area.
Selective reporting (reporting bias)	Unclear risk	Four infants were lost to follow-up from the intervention group, and five were lost to follow-up from the control group during the study period and were excluded from the analysis. No Claire explanation for missing participants.
Other bias	Low risk	The distribution of baseline characteristics of the participants in the intervention and control arms is summarized in Table 1. No significant differences were observed between the two groups, although the proportion of mothers who had received no formal education was higher in the control group compared to those in the intervention group (75% vs. 66%).

4. Pandey 2007[24]

Methods	Community-based, cluster randomized controlled trial conducted from May 2004 to May 2005 in 105 randomly selected village clusters in Uttar Pradesh state in India.
Participants	5 village clusters from the selection of 105 village clusters over 21 districts in Uttar Pradesh state in India.
Interventions	An information campaign was conducted in each intervention village cluster in June 2004 .The information campaign was conducted in 2 rounds in each village cluster, separated by a period of 2 weeks. Each round consisted of 2 to 3 meetings, as well as distribution of posters and leaflets .Each meeting lasted about an hour and consisted of a 15-minute audiotaped presentation that was played twice, opportunities to ask questions, and distribution of leaflets. • Health services information included the specific days and hours a nurse midwife is available in the village; the obligation of the nurse midwife to provide free prenatal and postnatal care, including tetanus vaccines and prenatal supplements for mothers and health care and vaccinations for infants; health centers available for more specialized care; and where to complain about quality or quantity of health services • Social services information included how much school fees are for low and mid to high-caste children, sources and oversight of education funds, obligations of oversight committees, requirements for semi-annual village governance meetings, organization and funding of village government and development work, right to obtain copies of village records, and where to complain about education or village governance problems.

Outcomes	Visits by nurse midwife; prenatal examinations, tetanus vaccinations, and prenatal supplements received by pregnant women; vaccinations received by infants; excess school fees charged; occurrence of village council meetings; and development work in villages.

Risk of Bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (risk of selection bias)	Low risk	From a comprehensive list of blocks and village clusters, we used a random number generator to randomly select 1 block within each district and then randomly select 5 village clusters within each block. We then randomly assigned districts to intervention and control arms.
Allocation concealment (risk of selection bias)	Low risk	By randomly selecting only 5 village clusters of about 1000 in each district, We spread the selection of 105 village clusters over 21districts to minimize any potential for contamination between intervention and control villages.
Blinding of participants and providers (risk of performance bias)	Low risk	At base line we did not tell the households that any informational meetings would be done later, nor did they know that they would be reinter viewed at 1 year.
Blinding of outcome assessors (risk of detection bias)	Unclear risk	Baseline survey participants were re- interviewed 12 months later by research assistants who had no knowledge of the intervention. To maintain this blinding, intervention group subjects were not asked whether they attended an informational meeting.
Incomplete outcome data (attrition bias)	Low risk	For 5 of 8 outcomes, comparing within-household changes from baseline to follow-up was not possible, be- cause households that reported those outcomes at base line were often not reporting on the same outcomes at 1year. For example, a household reporting on prenatal outcomes at baseline would no longer have a pregnant woman to report prenatal outcomes on at1year.For these we additionally conducted a multivariate regression comparing intervention to controlat1year, using a random-effects model in which random effects are at the village cluster level and standard errors are clustered at the village cluster level.
Selective reporting (reporting bias)	Unclear risk	Both parents from each household were asked several questions about access to health and social services. Health services questions included whether a nurse midwife had come to the village in the past 4weeks; whether there was a pregnant woman in the household within the past 12 months and, if so, whether she had received a prenatal examination, tetanus shots, and prenatal supplements (iron/folic acid tablets); and whether there was an infant younger than 1 year in the household and, if so, whether he or she had received any vaccinations. Social services questions included how many children went to primary school in the village for the previous academic year and how much in school fees they were charged, whether a village council meeting had occurred in the past 6months, and whether development work was performed in the village.
Other bias	Low risk	They spread the selection of 105 village clusters over 21districts to minimize any potential for contamination between intervention and control villages.

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5. Usman 2009[26]

Methods	This randomized controlled trial was conducted at EPI centers located in urban areas of Karachi city. One EPI center was selected from each of the five administrative districts of Karachi. These immunization centers were housed in government dispensaries and basic health units providing primary health care to the urban population in their catchment areas.
Participants	Consenting mother–child unit with children visiting the selected EPI centers for DPT1 immunization and residing in the same area for the last 6 months were eligible to participate in the study.
Interventions	Type of intervention: Intervention: In our study, we had three intervention groups [redesigned card (Group 1), center-based education (Group 2), and redesigned card with center-based education (Group 3)] -in Group 1, a trained data collector printed the upcoming DPT2 immunization date and day on both outer sides of the card and showed it to the mother. Mother was asked to hang the card at a frequently visible place in her home and to bring it along on the next immunization visit. Similarly at DPT2 visit, the date and day for DPT3 immunization visit was printed on both outer sides of the card while the date and day for the DPT2 visit was crossed out to avoid any confusion to the mothers • In Group 2, we designed a 2 –3minutes of center-based education session for mothers, emphasizing the importance of immunization schedule completion. The education session also included the information about potential adverse impact on child's health if the schedule was not completed. The education session was in simple local language • In Group 3 received both the redesigned card and center- based education in exactly the same way as described above.
Outcomes	The study outcome in each study group was the immunization status at the completion of 90-day follow-up after enrolment at DPT1 visit. The immunization status was categorized into those who completed both DPT2 and DPT3 (termed "DPT3 completed" or "completed DPT3") and all others, i.e. those who either did not complete both DPT2 and DPT3 or did not complete DPT3 only during the follow-up period (termed "DPT3 not completed").

Risk of Bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (risk of selection bias)	Low risk	The Principal Investigator provided a computer generated randomization list to each enrolment center. The randomization list indicated the study group against each study ID. Each enrolled mother–child unit received a study ID and was assigned to a study group as indicated on the randomization list.
Allocation concealment (risk of selection bias)	High risk	The randomization list indicated the study group against each study ID. Each enrolled mother–child unit received a study ID and was assigned to a study group as indicated on the randomization list.

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Blinding of participants and providers (risk of performance bias)	High risk	Owing to the nature of interventions, neither the study participants nor the data collectors enrolling the study participants and recording the study outcome were blinded to the type of intervention the study participants received.
Blinding of outcome assessors (risk of detection bias)	High risk	Owing to the nature of interventions, neither the study participants nor the data collectors enrolling the study participants and recording the study outcome were blinded to the type of intervention the study participants received.
Incomplete outcome data (attrition bias)	Unclear risk	No study participant was lost to follow-up since the study participants not returning for either DPT2 or DPT3 were considered DPT3 not completed. Child's age at DPT1 was not available for 39 (1.5%) children out of the total 1500. Out of 375 mother–child units in each study group, the data on 368 in Group 1, 369 in Group 2, 366 in Group 3, and 358 in Group 4 were used for the final model in multivariable analysis. This method may include participants who were vaccinated in other center.
Selective reporting (reporting bias)	Unclear risk	The published protocol was not mentioned, but All outcomes identified were reported on in the results.
Other bias	Unclear risk	The study did not specify information.

6. Usman 2011 [26]

Methods	Mother-child units were enrolled at DTP1 and randomized to four study groups: redesigned card, center-based education, combined intervention, and standard care. Each child was followed-up for 90 days to record the dates of DTP2 and DTP3 visits. The study outcome was DTP3 completion by the end of follow-up period in each study group.
Participants	All Mother-children pairs visiting the selected EPI centers for DTP1from all rural centers around Karachi based on the highest volume of children vaccinated for DTP1 immunizations in previous year, provided that the mother had been living in the area for last six months or more.
Interventions	Mother-child pairs were randomly allocated to three intervention and one standard care groups. At enrolment in the first intervention group ("Redesigned card"), a trained interviewer pasted the upcoming date and day of DTP2 immunization on both outer sides of the card and showed it to the mother. Mother was asked to hang the card in her home at a frequently visible place and requested that she bring the card along on her next immunization visit to the EPI center. At DPT2 visit, the interviewer crossed out the date and day for DTP2 visit to avoid any confusion to the mothers; pasted the date and day for the upcoming DTP3 immunization visit on both sides of the card: and showed the information to the mother. Mothers in the second intervention group ("Center-based education") received center-based education from trained study interviewers. Mothers in the third intervention group ("Combined intervention") received both the redesigned card and center-based education in exactly the same way as described above.

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Outcomes	The study outcome was the immunization status of each child at the end of day 90 post enrolment. The immunization status was dichotomized into completion of both DTP2 and DTP3 (termed "DTP3 completed") and all others (termed "DTP3 not completed").

Risk of Bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (risk of selection bias)	Low risk	The lead investigator provided a computer generated randomization list to each enrolment center. Each enrolled mother-child pair received an identification number (ID) from the randomization list and was assigned to the study group corresponding to the ID on the list.
Allocation concealment (risk of selection bias)	High risk	Each enrolled mother-child pair received an identification number (ID) from the randomization list and was assigned to the study group corresponding to the ID on the list.
Blinding of participants and providers (risk of performance bias)	High risk	Because of the overt nature of interventions, neither the study participants nor the interviewers enrolling the study participants and recording the study outcome were blinded to the type of intervention received by the study participants.
Blinding of outcome assessors (risk of detection bias)	High risk	Because of the overt nature of interventions, neither the study participants nor the interviewers enrolling the study participants and recording the study outcome were blinded to the type of intervention received by the study participants.
Incomplete outcome data (attrition bias)	Unclear risk	Since the study participants who had not returned to the centers within 90 days of their DPT1 visit were considered DTP3 not completed, no study participant was considered lost to follow-up. The study outcome was the immunization status of each child at the end of day 90 post enrolment. The immunization status was dichotomized into completion of both DTP2 and DTP3 (termed "DTP3 completed") and all others (termed "DTP3 not completed").
Selective reporting (reporting bias)	Unclear risk	The study outcome was the immunization status of each child at the end of day 90 post enrolment. The immunization status was dichotomized into completion of both DTP2 and DTP3 (termed "DTP3 completed") and all others (termed "DTP3 not completed).
Other bias	Unclear risk	The study reported some significant baseline differences between intervention and control groups across demographic feature.

Excluded studies

We excluded 2 studies after screening the full texts (see Characteristics of excluded studies). The main reasons for exclusions were that the location or study design used did not meet our inclusion criteria.

The reasons for the exclusion of the studies are given in Table 3.

Table 2: Characteristics of excluded studies

Study	Reasons for exclusion
Barreto 1992[27]	The study assessed effects of information campaigns on vaccination coverage in Brazil We excluded study because it is not a randomised controlled trial
De 2002[29]	The study assessed effects of information campaigns on vaccination coverage in India . We excluded study because it is not a randomised controlled trial

Risk of bias in included studies

For the outcome the assessments of risk of bias for the included studies are detailed in the studies table Characteristics of included studies and are summary (see Figure 2 and Figure 3). We have reported risk of bias across all outcomes for each study as we assessed that the risk of bias did not differ significantly across outcomes within the studies. We judged both the included studies to be of unclear to low risk of bias, since they had low risk of bias for sequence generation; low risk of bias for allocation concealment; and low[22] or unclear [24] risk of bias for selective outcome reporting. These were the factors that we had determined a priori to be the most important in influencing overall risk of bias [29]. Two studies confirmed that allocation was not concealed and were rated at high risk of this form of selection bias [25, 26]. One study described adequate allocation concealment methods [23] and so was at low risk of bias for this domain [30]. One study blinding of study staff and participants was not possible was rated at high risk bias [5].

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Figure 2: Risk of bias summary: review authors' judgements about each risk of bias item for each included study.
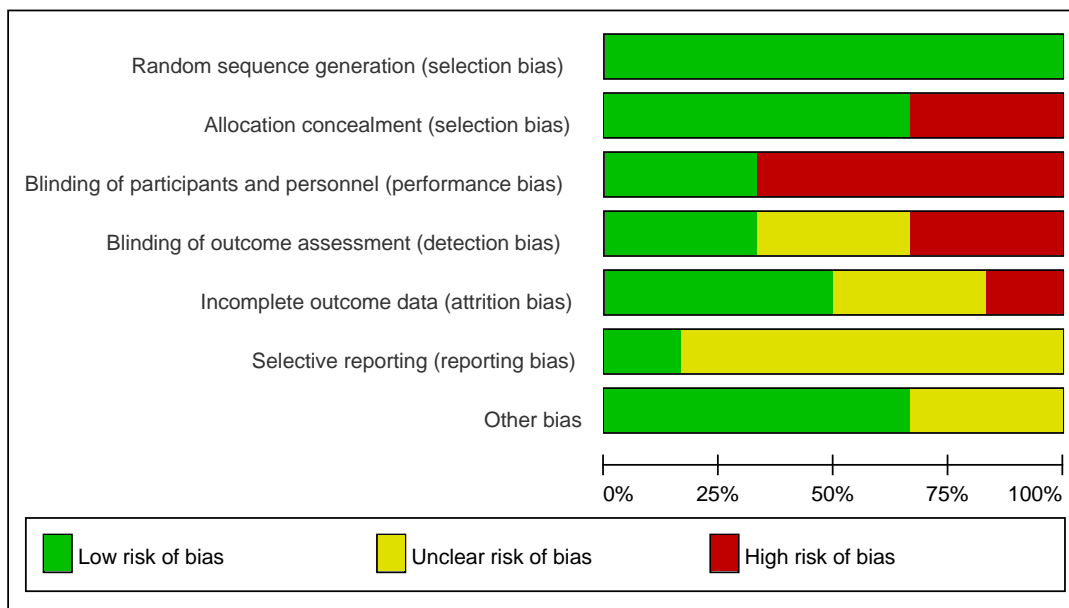
Figure 3: Risk of bias graph: review authors' judgements about each risk of bias item presented as percentages across all included studies.

Allocation (selection bias)

All studies were at low risk of bias for random sequence generation. A random number generator was used to select communities for assignment to intervention and control groups. Allocation concealment was adequately described in study [22, 23], but not mentioned in [24].

All studies were at low risk of bias for random sequence generation, describing adequate allocation to intervention groups by computer random number generator or by random numbers table.one study described adequate allocation concealment methods [23] and so was at low risk of bias for this domain, while two studies confirmed that allocation was not concealed and were rated at high risk of this form of selection bias [25, 26, 30].

Blinding (performance bias and detection bias)

For these interventions, it was not possible to blind participants in the intervention clusters to receipt of the intervention. However, the clusters were spread geographically, so the risk of contamination between the clusters was probably low. In both of the included studies the field co-ordinator for the surveys knew which clusters had received the intervention but the

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interviewers did not. The follow-up interviews were performed by a research assistant who had no knowledge of the intervention. We assessed the studies to be at low risk of bias for performance bias, but unclear risk of bias for detection bias. We assess it as unlikely that it was possible to maintain the blinding of the people who performed the analysis [22, 24, 29].

Due the nature of the interventions, blinding participants and personnel was not possible in the included study, and all was assessed as high risk of bias on this domain. Outcome assessors were adequately blinded in this study [23, 30]. As the intervention was educational, blinding of study staff and participants was not possible. The investigator was blinded to the exposure status of participants [5].

Incomplete outcome data (attrition bias)

We assessed the included studies [22, 24] to be at low risk for attrition bias. There was no loss of clusters in the [22] trial and all loss of households in [24] were accounted for by households having moved to another area prior to the final survey [29].

One study had a high risk of attrition bias [23]. The study authors excluded those lost to follow-up from the analysis, which accounted for 25% and 27% of the sample at three and six month follow-up, respectively. Two studies were judged as being at unclear risk of attrition bias. Analysis was reportedly on an intention-to treat-basis [25, 26], but there were several elements of concern. In two studies [25, 26], while the authors recorded no loss to follow-up, they classified all non-respondents as failing to meet the outcome (receipt of DTP3 vaccine). The impact of this approach to analysis is unclear, as it is possible that some non-respondent participants may have received vaccination elsewhere [30].

We assessed one study [5] to be low risk for attrition bias. Because four infants were lost to follow-up from the intervention group and five were lost to follow-up from the control group during the study period and were excluded from the analysis. The distribution of enrolled mother-infant pairs among the five study sites was weighted to represent population size in each area.

Selective reporting (reporting bias)

We assessed [22] as low risk as the published study protocol does not include any outcomes that were not assessed in the published trial report. For [26], we were not able to identify a published protocol and were therefore not able to assess if all outcomes were reported. This domain was therefore assessed to be at unclear risk of bias [29].

Four studies [5, 23, 25, 26] did not mention published protocols against which trials could be assessed, so it was not possible to determine whether selective reporting had been a factor in any included studies. All were rated as unclear risk of bias on this domain [30].

Other potential sources of bias

One study reported some significant baseline differences between intervention and control groups across demographic feature [26], for which it was rated as unclear risk of bias [23] was judged to be at low risk of bias due to low risk of contamination and comparability of groups at baseline. There was insufficient information to judge if other potential sources of bias were present in [25] and the study was rated at unclear risk of bias [30].

No significant differences were observed between the two groups [5], although the proportion of mothers who had received no formal education was higher in the control group compared to those in the intervention group (75 % versus 66 %), Baseline characteristics of study participants were compared using proportions and the study was rated at low risk of bias.

We assessed that the trials were at low risk for other sources of bias.

- Recall bias: information regarding the vaccination was obtained by interview. However, since any recall bias should have influenced both arms of the trial, we assessed the risk of bias to be low.
- Selective recruitment of participants: as the study clusters were scattered geographically, it is unlikely that the participants knew which villages were control or intervention clusters. We therefore assessed this risk of bias to be low.
- Groups comparable at baseline: there was a slightly uneven distribution of low-caste versus mid-to-high-caste households in one of the studies [24]. However, we assessed the risk of bias to be low because the baseline differences were small.

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Willingness to travel to vaccinate was higher in intervention than control cluster (P value = 0.009) in the other study [22], but this was adjusted for in the analysis and we assessed the risk of bias to be low.

Effects of interventions

See: Summary of findings for the main comparison. We have presented an outline of the main findings for each outcome in Summary of findings for the main comparison.

1. Vaccination coverage (DTP3 or as reported by authors)

Six studies reported immunisation status after community-based information [5, 22, 24] and face-to-face education [23, 25, 26], Five reported coverage with DTP3 [5, 22, 23, 25, 26] and one reported coverage with at least one vaccine [24]. Combining the data shows that information or education improves vaccination coverage (RR 1.36, 95 % CI 1.14 to 1.62). However, there was significant statistical heterogeneity: χ^2 (df = 5) = 14.26; P = 0.01, I^2 = 65 %. The heterogeneity could be explained, at least in part, by the type of intervention.

Three studies used community-based information. Two reported DTP3 coverage [5, 22] and one reported coverage with at least one vaccine [24]. Combining data for the three studies show that community-based information improves vaccination coverage (RR 1.61, 95 % CI 1.19 to 2.18), with no significant statistical heterogeneity: χ^2 (df =2) =3.18, P =.0.20, I^2 = 37 %.

Three studies used face-to-face education and reported DTP3 coverage [23, 25, 26]. Combining data for the three studies show that face-to-face education improves vaccination coverage (RR 1.24, 95 % CI 1.01 to 1.53), with significant statistical heterogeneity: χ^2 (df =2) =7.63, P =.0.02, I^2=74 %. (Results in figure 4)

The differences between the subgroups were not significant: : χ^2 (df =1) =1.97, P =0.16, I^2 = 49.3 %.

2. Vaccination coverage with individual vaccine

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2.1. DTP3

Two studies assessed Community-based information on DTP3 coverage [5, 22].

Children' s immunisation status was measured in the two studies[5, 22]. We considered the studies to be sufficiently clinically homogenous for pooling the data, Subtotal (95% CI): Risk Ratio 1.68, 95% (1.09, 2.59), the level of statistical heterogeneity was low (Tau² = 0.07; χ^2 = 3.11, df = 1 (P = 0.08); I² = 68 %) T; test for overall effect: Z = 2.04 (P = 0.04).

Owais 2011 showed that the intervention may improve vaccination for DPT3, compare to control group ((Risk Ratio 1.39, 95% (1.07, 1.81). For [22]: the intervention may improve vaccination for DPT3, compare to control group Risk Ratio 2.17, 95% (1.43, 3.29)

Three studies assessed face-to-face education versus control on DTP3 coverage [23, 25, 26], with the outcome measured three months after the delivery of the intervention. The interventions were assessed by [23] a study with low risk of bias and had shown no evidence of the effect, while studies [25, 26] with higher risk of bias and larger sample size have shown significant increases in DPT3 vaccine.

We considered the studies to be sufficiently clinically homogenous for pooling the data, The Subtotal (95% CI) Risk Ratio 1.24, 95% CI :1.01, 1.53), the level of statistical heterogeneity was low (Tau² = 0.02; : χ^2 = 7.63, df = 2 (P = 0.02); I² = 74%) ;Test for overall effect: Z = 2.04 (P = 0.04) , the pooled are presented results in figure 5

The results from [23] show no evidence of a significant effect (Risk Ratio 0.99, 95% CI: 0.71 to 1.38), while [25, 26] have shown statistically significant improvements in DPT3 vaccine for the intervention group when compared with control ((Risk Ratio 1.18; 95 % CI: 1.05, 1.33); Risk Ratio 1.50, 95 % CI: 1.27, 1.77)).

2.2. Measles vaccine

In [22] the intervention show moderate evidence in measles vaccine coverage, compare to control group (Risk Ratio 1.63, 95 % CI (1.03, 2.58). (Results presented in figure 6)

2.3. Received at least one vaccine

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In [24] the trail suggested that the intervention may make no improvements in receiving at least one vaccine, compare to control group Risk Ratio 1.43, 95% CI (0.72, 2.86) (results presented in figure7)

Table 3: Summary of effects of information or education for vaccination

Outcome or Subgroup	Studies	Participants	Statistical Method	Effect Estimate
1.1 Vaccination coverage	6		Risk Ratio (IV, Random, 95% CI)	1.36 [1.14, 1.62]
1.1.1 Community-based information	3		Risk Ratio (IV, Random, 95% CI)	1.61 [1.19, 2.18]
1.1.2 Face-to-face education	3		Risk Ratio (IV, Random, 95% CI)	1.24 [1.01, 1.53]
1.2 DTP3	5		Risk Ratio (IV, Random, 95% CI)	Subtotals only
1.2.1 Community-based information	2		Risk Ratio (IV, Random, 95% CI)	1.68 [1.09, 2.59]
1.2.2 Face-to-face education	3		Risk Ratio (IV, Random, 95% CI)	1.24 [1.01, 1.53]
1.3 Measles vaccine	1		Risk Ratio (IV, Random, 95% CI)	1.63 [1.03, 2.58]
1.4 Received at least one vaccine	1		Risk Ratio (IV, Random, 95% CI)	1.43 [0.72, 2.86]

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.1.1 Community-based information				
Andersson 2009	0.7734	0.2124	11.2%	2.17 [1.43, 3.29]
Owais 2011	0.3293	0.1355	17.9%	1.39 [1.07, 1.81]
Pandey 2007	0.3577	0.3536	5.3%	1.43 [0.72, 2.86]
Subtotal (95% CI)			34.5%	1.61 [1.19, 2.18]
Heterogeneity: Tau² = 0.03; Chi² = 3.18, df = 2 (P = 0.20); I² = 37%				
Test for overall effect: Z = 3.11 (P = 0.002)				
1.1.2 Face-to-face education				
Bolam 1998	-0.0101	0.1691	14.6%	0.99 [0.71, 1.38]
Usman 2009	0.1655	0.0603	26.8%	1.18 [1.05, 1.33]
Usman 2011	0.4055	0.083	24.2%	1.50 [1.27, 1.77]
Subtotal (95% CI)			65.5%	1.24 [1.01, 1.53]
Heterogeneity: Tau² = 0.02; Chi² = 7.63, df = 2 (P = 0.02); I² = 74%				
Test for overall effect: Z = 2.04 (P = 0.04)				
Total (95% CI)			100.0%	1.36 [1.14, 1.62]
Heterogeneity: Tau² = 0.03; Chi² = 14.26, df = 5 (P = 0.01); I² = 65%				
Test for overall effect: Z = 3.41 (P = 0.0006)				
Test for subgroup differences: Chi² = 1.97, df = 1 (P = 0.16), I² = 49.3%				

Figure 4: Forest plot of the meta-analysis for information or education for improving vaccination coverage

Study or Subgroup	log[Risk Ratio]	SE	Weight	Risk Ratio IV, Random, 95% CI
1.2.1 Community-based information				
Owais 2011	0.3293	0.1355	19.2%	1.39 [1.07, 1.81]
Andersson 2009	0.7734	0.2124	12.3%	2.17 [1.43, 3.29]
Subtotal (95% CI)			31.5%	1.68 [1.09, 2.59]
Heterogeneity: Tau² = 0.07; Chi² = 3.11, df = 1 (P = 0.08); I² = 68%				
Test for overall effect: Z = 2.37 (P = 0.02)				
1.2.2 Face-to-face education				
Bolam 1998	-0.0101	0.1691	15.8%	0.99 [0.71, 1.38]
Usman 2009	0.1655	0.0603	27.6%	1.18 [1.05, 1.33]
Usman 2011	0.4055	0.083	25.1%	1.50 [1.27, 1.77]
Subtotal (95% CI)			68.5%	1.24 [1.01, 1.53]
Heterogeneity: Tau² = 0.02; Chi² = 7.63, df = 2 (P = 0.02); I² = 74%				
Test for overall effect: Z = 2.04 (P = 0.04)				
Total (95% CI)			100.0%	1.36 [1.12, 1.64]
Heterogeneity: Tau² = 0.03; Chi² = 14.18, df = 4 (P = 0.007); I² = 72%				
Test for overall effect: Z = 3.17 (P = 0.002)				
Test for subgroup differences: Chi² = 1.56, df = 1 (P = 0.21), I² = 35.8%				

Figure 5: Forest plot of the meta-analysis for information or education for improving DTP3 coverage

			Risk Ratio	Risk Ratio
Study or Subgroup	log[Risk Ratio]	SE	IV, Random, 95% CI	IV, Random, 95% CI
Andersson 2009	0.4889	0.2347	1.63 [1.03, 2.58]	

0.01   0.1   1   10   100

Favours standard care   Favours health education
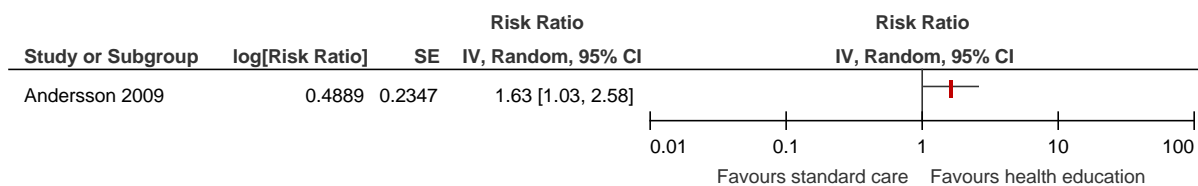
Figure 6: Forest plot of the meta-analysis for information or education for improving measles vaccine coverage

			Risk Ratio	Risk Ratio
Study or Subgroup	log[Risk Ratio]	SE	IV, Random, 95% CI	IV, Random, 95% CI
Pandey 2007	0.3577	0.3536	1.43 [0.72, 2.86]	

0.01   0.1   1   10   100

Favours standard care   Favours inform campaign
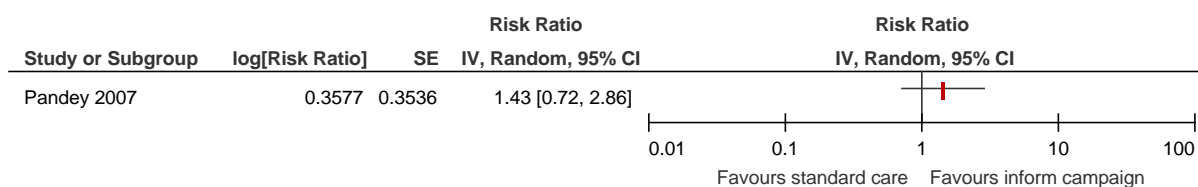
Figure 7: Forest plot of the meta-analysis for information or education for improving coverage with at least one vaccine

Discussion

In low and middle-income countries, educational interventions have been successful in raising awareness regarding vaccine. We observed that caregivers' education regarding importance of vaccines was significantly associated with higher vaccination coverage.

Summary of main results

Data were summarised as immunisation coverage (DPT3 or as reported by authors) or vaccination coverage with individual vaccine (DTP3, Measles vaccine, Received at least one vaccine)

1. Immunisation Vaccination coverage (DTP3 or as reported by authors)

- Six studies reported immunisation status after community-based information [5,22,24] and face-to-face education [23,25,26], Five reported coverage with DTP3[5,22,23,25,26]; and one reported coverage with at least one vaccine [24],

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Combining the data shows that information or education improves vaccination coverage (RR 1.36, 95% CI 1.14 to 1.62).

- Three studies used community-based information. Two reported DTP3 coverage [5,22]; and one reported coverage with at least one vaccine [24]. Combining data for the three studies show that community-based information improves vaccination coverage (RR 1.61, 95% CI 1.19 to 2.18).

- Three studies used face-to-face education and reported DTP3 coverage [23, 25, 26]. Combining data for the three studies show that face-to-face education improves vaccination coverage (RR 1.24, 95% CI 1.01 to 1.53).

- The differences between the subgroups were not significant.

2. Vaccination coverage with individual vaccine (DTP3, Measles vaccine, received at least one vaccine)

- Children's immunisation status was measured in the two studies [5, 22]. We considered the studies to be sufficiently clinically homogenous for pooling the data, Subtotal (95 % CI): Risk Ratio 1.68, 95% (1.09, 2.59).

- Three studies assessed face-to-face education versus control on DTP3 coverage [23, 25, 26] with the outcome measured three months after the delivery of the intervention. The interventions were assessed by [23] a study with low risk of bias and had shown no evidence of the effect, while studies[25, 26] with higher risk of bias and larger sample size have shown significant increases in DPT3 vaccine .The results from [23] showed no evidence of a significant effect(Risk Ratio 0.99, 95 % CI :0.71 to 1.38), while[25, 26] have shown statistically significant improvements in DPT3 vaccine for the intervention group when compared with control ((Risk Ratio 1.18; 95 % CI :1.05, 1.33) ; Risk Ratio 1.50, 95 % CI :1.27, 1.77))

- According to [22], the intervention show moderate evidence in measles vaccine coverage, compare to control group (Risk Ratio 1.63, 95% (1.03, 2.58).

- In [24] study, the trail suggested that the intervention may make no improvements in receiving at least one vaccine, compare to control group (Risk Ratio 1.43, 95% CI (0.72, 2.86).

Our review demonstrates that providing vaccine-related education to caregivers is an effective manner may improve childhood immunization rates in LMCS settings such as in our

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included studies. This review show a significant improvement in infant childhood vaccine immunization coverage that was observed in caregivers who received education or information on the importance of vaccines, compared to those who received standard health promotion messages only. The review included six studies; all the trials were conducted in LMICS as the setting may limit the applicability of the results to high-income settings.

Overall completeness and applicability of evidence

A comprehensive search strategy was used which was not restricted to any publication and by language .However we faced challenges because we could not find article by using the entire search term "the effects of interventions to inform or educate caregivers about childhood vaccination in low and middle-income countries". With these we used different approaches for indexing the information or education intervention in each databases. This may miss studies with intervention to educate or inform was use alongside other intervention. Usage of filters was also a factor that may limit relevant including studies for this review. The six included studies were RCTs with are high ranking in study design for a systematic review.

The majority of included trials were conducted in LMICs. This may limit the global applicability of the evidence, but for LMIC audiences where vaccination is a critical health issue, it may be beneficial to see evidence from a related setting [30].

Quality of the evidence

 We have summarised the quality of the evidence of primary outcome with relevancy to decision-making:

Children's vaccination status:

We used GRADE to assessed the quality of the evidence was low to very low for each outcome available. All studies had limitations in design. Due to the nature of the intervention, participants and personnel were unable to be blinded in all of the trials. Three studies had inadequate allocation concealment [25, 26] and four had inadequate blinding of outcome assessment [23, 25, 26] had a high rate of attrition and intention-to- treat analysis was not performed. We assessed the trial [22, 24] at low risk of bias.

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The reasons for these judgements are outlined in the Summary of findings for the main comparison.

Potential biases in the review process

To reduced potential biases in the review process we used rigorous search methods and that should be relatively low in bias. We adhere to the protocol (Lukusa A L 2015) and we have defined inclusion criteria (regarding participants, interventions, comparisons, and outcomes), and conducted exhaustive searches of both peer-reviewed and grey literature. We also assessed study eligibility, extracted data, and assessed the risk of bias in each included study in duplicate; disagreements between authors were resolved through consensus and arbitration. We included only studies conducted in low and middle-income countries, as defined by the World Bank., this may restricted us to identify more eligible studies.

Agreements and disagreements with other studies or reviews

The results of our review are different from those of the Cochrane review of face to face interventions for informing or educating parents about early childhood vaccination [30], which had incorporated three of our included studies [23, 25, 26]. This review concluded that " there is insufficient evidence to inform decisions about changing current practice related to face to face interventions to inform or educate parents about early childhood vaccination ". This review found low certainty evidence suggesting that face-to-face interventions to inform or educate parents about childhood vaccination may have little to no impact on immunisation status, or knowledge or understanding of vaccination [30]. Our results are also different from the Cochrane review of interventions for improving coverage of child immunization in low- and middle-income countries; which concluded that there is "insufficient evidence of effectiveness of any of the interventions in improving immunization coverage in LMIC". The reason is due to the paucity of rigorous studies and the low quality of available evidence [2].

Authors' conclusions

Implications for practice

This review provides evidence that assessed the effects on vaccination coverage of interventions to inform or educate caregivers about childhood vaccination in low and middle-income countries, compared to standard immunisation practices. Interventions directed to

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caregivers as face to face or community based may increase the coverage of vaccines. The results of six studies reported immunisation status after community-based information and face-to-face education combining the data, shows that information or education improves vaccination coverage. Evidence based discussion that aims at knowledge translation to the community members may prove to be effective than conventional health education strategies. However the setting and scale of targeted population may influence this findings. The findings of this review are limited to data from low and middle-income countries, a future study which combine multi-country studies involving both LMICs and high-income countries will give a better evidence.

Implications for research

The findings of the review will make a significant contribution to the knowledge base of interventions for improving childhood vaccination coverage in low and middle-income countries. The study gathered evidence on how vaccination information or education impacts childhood vaccine uptake. We anticipate that this information will be useful to national and international stake-holders interested in improving the performance of childhood immunisation programmes in low and middle-income countries.

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Contributions of authors

LAL led the development of the review, wrote the first draft, coordinated and integrated comments from supervisor, approved the final version and is the guarantor of the manuscript. CSW conceived the study, provided supervision and mentorship to LAL, critically revised successive drafts of the manuscript, provided important intellectual input and approved the final version of the review. LAL and CSW conducted the analyses. LAL wrote the discussion and conclusion section with input from CSW.

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Declarations of interest

LAL completed this systematic review for his research project of the MSc Clinical Epidemiology degree at Stellenbosch University (South Africa). He received a bursary from Novartis that covered his study fees. There has been no direct funding for this systematic review. CW salary is paid by the Centre for Evidence-based Health Care, South Africa.

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APPENDICES

Appendix 1: Search Strategies

PubMed

#7: (#5 OR #6)

#6: (#1 AND #2 AND #3) Filters: Randomized Controlled Trial

#5: (#1 AND #2 AND #3) Filters: Clinical Trial

#4: (#1 AND #2 AND #3)

#3: (Parent* or Caregiver* or guardian* or Mother*)

#2: (education* or teaching or learning or instruction * or training or skills)

#1: (Vaccination or immunization or immunisation or revaccination)

 CENTRAL (Cochrane Central Register of Controlled Trails)

 #1: (Vaccinat* or Immuniz* or Immunis* or revaccinat*): ti,ab,kw

 #2: (education* or teaching or learning or instruction * or training or skills)

 #3: (#1 AND #2)

 CINHAL

 (vaccinat* or Immuniz* or Immunis* or revaccinat*) AND (education* or teaching or learning or instruction * or training or skills) AND (Parent or Caregiver or guardian or Mother)

ISI Web of Science (Science Citation Index)

#6: (#4 AND #5)

#5: (randomis* or randomiz* or randomly   allocat* or random allocat*)

#4: (#3 AND #2 AND #1)

#3: (Parent or Caregiver or guardian or Mother)

#2: (education* or teaching or learning or instruction * or training or skills)

#1: (Vaccinat* or Immuniz* or Immunis* or revaccinat*)

PDQ EVIDENCE

(Vaccinat* OR Immuniz* OR Immunis* OR revaccinat*) AND (education* OR teaching OR learning OR instruction * OR training OR skills) AND (Parent OR Caregiver OR guardian OR Mother)

Appendix 2

Appendix 2. Assessment of risk of bias in included RCTs

Domain 1: sequence generation

Adequate: investigators described a random component in the sequence generation process such as the use of:

• A random number table;

• Coin tossing;

• Throwing dice;

• Shuffling cards or envelopes.

Inadequate: investigators described a non-random component in the sequence generation process such as the use of:

• Odd or even date of birth;

• The day or date of admission;

• The hospital or clinic record number;

• Preference of the participant;

• The results of a laboratory test or series of tests.

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Unclear: there is insufficient information to permit judgement of the way in which sequence generation was performed.

Domain 2: Allocation concealment

Adequate: neither participants nor investigators enrolling participants could foresee assignment due to:

• Central allocation (e.g. via the telephone or pharmacy-controlled);

• Sequentially numbered drug containers of a matching appearance;

• Sequentially numbered, opaque and sealed envelopes.

Inadequate: both participants and investigators enrolling participants could foresee upcoming assignment based on, for example:

• Using an open random allocation schedule;

• Assigned envelopes were unsealed, non-opaque or not numbered appropriately;

• Date of birth;

• Case record number.

Unclear: there is insufficient information to permit judgement to the sequence generation process.

Domain 3: Blinding

Adequate: when any one of the following are applicable:

• No blinding, but the review authors judge that the outcome would not be influenced by a lack of blinding;

• Blinding of both the key study personnel and participants are ensured, and it is unlikely that blinding could have been broken;

• Either participants or some key study personnel were not blinded, but the outcome measurement was blinded and the non-blinding of others are not likely to introduce bias.

Inadequate: when any one of the following is applicable:

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• No blinding or incomplete blinding;

• Blinding of key study personnel and participants were attempted, but it is likely that the blinding could have been broken;

• Either key study personnel or participants were not blinded, which is likely to introduce bias.

Unclear: there is insufficient information to permit judgement, or the study did not address this outcome at all.

Domain 4: incomplete outcome data

Adequate: when any one of the following is applicable:

• No missing outcome data;

• The reasons for missing outcome data are unlikely to be related to the true outcome;

• Missing outcome data are balanced in numbers across intervention groups;

• Missing data have been imputed using appropriate methods;

• For dichotomous data, the proportion of missing outcomes compared with the observed event risk is not enough to have a clinically relevant impact on the intervention effect estimate;

• For continuous data, the plausible effect size among missing outcomes is not enough to have a clinically relevant impact on the observed effect size.

Inadequate: when any one of the following is applicable:

• The reasons for missing outcome data are likely to be related to true outcome;

• The application of simple imputation is potentially inappropriate;

• 'As-treated' analysis done with substantial departure of the intervention received from that assigned at randomisation;

• For dichotomous data, the proportion of missing outcomes compared with the observed event risk is enough to introduce clinically relevant bias in the intervention effect estimate;

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• For dichotomous outcome data, the plausible effect size among missing outcomes is enough to induce clinically relevant bias in the observed effect size.

Unclear: there is insufficient reporting of exclusions to permit judgement, or the study did not address this outcome at all.

Domain 5: selective outcome reporting

Adequate: when any one of the following is applicable:

• The study protocol is available and all of the prespecified outcomes are addressed in the review in the prespecified way;

• The study protocol is not available, but it is clear that the published reports include all the prespecified and expected outcomes.

Inadequate: when any one of the following is applicable:

• Not all of the prespecified primary outcomes have been reported;

• One or more of the primary outcomes is reported using measurements of analysis methods that were not prespecified;

• One or more reported primary outcomes were not prespecified;

• One or more outcomes of interest in the review are reported incompletely so that they cannot be entered in a meta-analysis;

• The study report fails to include results for a key outcome that would be expected to have been reported for such a study.

Unclear: there is insufficient information to permit judgement of compliance.

Domain 6: other potential threats to validity

Adequate: when the study seems to be free of other sources of bias.

Inadequate: when there is the possibility of at least one important risk of bias such as:

• The quality of the specific study design is in question;

• The study is stopped early due to some data-dependent process;

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• The study has been claimed to have been fraudulent.

Unclear: when there may be a risk of bias, but there is either:

• Insufficient information to assess whether an important risk of bias exists;

• Insufficient rationale or evidence that an identified problem will introduce bias.