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Integrated management of childhood illness (IMCI) strategy for children under five (Review)

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TABLE OF CONTENTS

[Intervention Review]

Integrated management of childhood illness (IMCI) strategy for children under five

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ABSTRACT

Background

More than 7.5 million children younger than age five living in low- and middle-income countries die every year. The World Health Organization (WHO) developed the integrated management of childhood illness (IMCI) strategy to reduce mortality and morbidity and to improve quality of care by improving the delivery of a variety of curative and preventive medical and behavioral interventions at health facilities, at home, and in the community.

Objectives

To evaluate the effects of programs that implement the IMCI strategy in terms of death, nutritional status, quality of care, coverage with IMCI deliverables, and satisfaction of beneficiaries.

Search methods

We searched the Cochrane Central Register of Controlled Trials (CENTRAL; 2015, Issue 3), including the Cochrane Effective Practice and Organisation of Care (EPOC) Group Specialised Register; MEDLINE; EMBASE, Ovid; the Cumulative Index to Nursing and Allied Health Literature (CINAHL), EbscoHost; the Latin American Caribbean Health Sciences Literature (LILACS), Virtual Health Library (VHL); the WHO Library & Information Networks for Knowledge Database (WHOLIS); the Science Citation Index and Social Sciences Citation Index, Institute for Scientific Information (ISI) Web of Science; Population Information Online (POPLINE); the WHO International Clinical Trials Registry Platform (WHO ICTRP); and the Global Health, Ovid and Health Management, ProQuest database. We performed searches until 30 June 2015 and supplemented these by searching revised bibliographies and by contacting experts to identify ongoing and unpublished studies.

Selection criteria

We sought to include randomised controlled trials (RCTs) and controlled before-after (CBA) studies with at least two intervention and two control sites evaluating the generic IMCI strategy or its adaptation in children younger than age five, and including at minimum efforts to improve health care worker skills for case management. We excluded studies in which IMCI was accompanied by other interventions including conditional cash transfers, food supplementation, and employment. The comparison group received usual health services without provision of IMCI.

Data collection and analysis

Two review authors independently screened searches, selected trials, and extracted, analysed and tabulated data. We used inverse variance for cluster trials and an intracluster co-efficient of 0.01 when adjustment had not been made in the primary study. We used the GRADE (Grades of Recommendation, Assessment, Development and Evaluation Working Group) approach to assess the certainty of evidence.

Main results

Two cluster-randomised trials (India and Bangladesh) and two controlled before-after studies (Tanzania and India) met our inclusion criteria. Strategies included training of health care staff, management strengthening of health care systems (all four studies), and home visiting (two studies). The two studies from India included care packages targeting the neonatal period.

One trial in Bangladesh estimated that child mortality may be 13% lower with IMCI, but the confidence interval (CI) included no effect (risk ratio (RR) 0.87, 95% CI 0.68 to 1.10; 5090 participants; low-certainty evidence). One CBA study in Tanzania gave almost identical estimates (RR 0.87, 95% CI 0.72 to 1.05; 1932 participants).

One trial in India examined infant and neonatal mortality by implementing the integrated management of neonatal and childhood illness (IMNCI) strategy including post-natal home visits. Neonatal and infant mortality may be lower in the IMNCI group compared with the control group (infant mortality hazard ratio (HR) 0.85, 95% CI 0.77 to 0.94; neonatal mortality HR 0.91, 95% CI 0.80 to 1.03; one trial, 60,480 participants; low-certainty evidence).

We estimated the effect of IMCI on any mortality measured by combining infant and child mortality in the one IMCI and the one IMNCI trial. Mortality may be reduced by IMCI (RR 0.85, 95% CI 0.78 to 0.93; two trials, 65,570 participants; low-certainty evidence).

Two trials (India, Bangladesh) evaluated nutritional status and noted that there may be little or no effect on stunting (RR 0.94, 95% CI 0.84 to 1.06; 5242 participants, two trials; low-certainty evidence) and there is probably little or no effect on wasting (RR 1.04, 95% CI 0.87 to 1.25; two trials, 4288 participants; moderate-certainty evidence).The Tanzania CBA study showed similar results.

Investigators measured quality of care by observing prescribing for common illnesses at health facilities (727 observations, two studies; very low-certainty evidence) and by observing prescribing by lay health care workers (1051 observations, three studies; very low-certainty evidence). We could not confirm a consistent effect on prescribing at health facilities or by lay health care workers, as certainty of the evidence was very low.

For coverage of IMCI deliverables, we examined vaccine and vitamin A coverage, appropriate care seeking, and exclusive breast feeding. Two trials (India, Bangladesh) estimated vaccine coverage for measles and reported that there is probably little or no effect on measles vaccine coverage (RR 0.92, 95% CI 0.80 to 1.05; two trials, 4895 participants; moderate-certainty evidence), with similar effects seen in the Tanzania CBA study. Two studies measured the third dose of diphtheria, pertussis, and tetanus vaccine; and two measured vitamin A coverage, all providing little or no evidence of increased coverage with IMCI.

Four studies (2 from India, and 1 each from Tanzania and Bangladesh) reported appropriate care seeking and derived information from careful questioning of mothers about recent illness. Some studies on effects of IMCI may report better care seeking behavior, but others do not report this.

All four studies recorded maternal responses on exclusive breast feeding. They provided mixed results and very low-certainty evidence. Therefore, we do not know whether IMCI impacts exclusive breast feeding.

No studies reported on the satisfaction of mothers and service users.

Authors' conclusions

The mix of interventions examined in research studies evaluating the IMCI strategy varies, and some studies include specific inputs to improve neonatal health. Most studies were conducted in South Asia. Implementing the integrated management of childhood illness

strategy may reduce child mortality, and packages that include interventions for the neonatal period may reduce infant mortality. IMCI may have little or no effect on nutritional status and probably has little or no effect on vaccine coverage. Maternal care seeking behavior may be more appropriate with IMCI, but study results have been mixed, providing evidence of very low certainty about whether IMCI has effects on adherence to exclusive breast feeding.

PLAIN LANGUAGE SUMMARY

Integrated management of childhood illness (IMCI) strategy for children younger than five years of age

What is the aim of this review?

The aim of this Cochrane review is to assess the effects of programs that use the World Health Organization integrated management of childhood illness (IMCI) strategy. Cochrane researchers searched for all potentially relevant studies and found four studies that met review criteria.

Key messages

This review shows that use of the World Health Organization IMCI strategy may led to fewer deaths among children from birth to five years of age. Effects of IMCI on other issues, such as illness or quality of care, were mixed, and some evidence of this was of very low certainty. In the future, researchers should explore how the IMCI strategy can best be delivered.

What was studied in the review?

More than 7.5 million children globally die each year before reaching the age of five. Most are from poor communities and live in the poorest countries. These children are more likely than others to suffer from malnutrition and from infections such as neonatal sepsis, measles, diarrhoea, malaria, and pneumonia.

Effective strategies to prevent and treat sick children are available but do not reach them. One reason for this is that health care services are often too far away or too expensive. Health facilities in these settings often lack supplies and well-trained health care workers. In addition, ill children may have several health problems at the same time, and this can make diagnosis and treatment difficult for health care workers.

In the 1990s, the World Health Organization (WHO) developed a strategy called integrated management of childhood illness (IMCI) to address these problems. This strategy aims to prevent death and disease while improving the quality of care for ill children up to the age of five. It consists of three parts.

• Improving the skills of health care workers by providing training and guidelines.

• Improving how health care systems are organized and managed, including access to supplies.

• Visiting homes and communities to promote good child rearing practices and good nutrition, while encouraging parents to bring their children to a clinic when the children are ill.

The WHO encourages countries to adapt the IMCI strategy to their own national settings. Types of childhood illnesses prioritised and ways in which services are delivered may vary from country to country.

What are the main results of the review?

This Cochrane review included four studies assessing the effectiveness of the IMCI strategy. These studies were conducted in Tanzania, Bangladesh, and India. The IMCI strategy was used very differently across studies. For instance, the study from Tanzania implemented health care worker training and improved drug supply but did not include home visits or community activities; the study from Bangladesh added new health care workers while training existing health care workers; and the two Indian studies specifically targeted newborns as well as older children.

This review showed that use of IMCI:

• may lead to fewer deaths among children from birth to five years of age (low-certainty evidence);

• may have little or no effect on the number of children suffering from stunting (low-certainty evidence);

• probably has little or no effect on the number of children suffering from wasting (moderate-certainty evidence);

• probably has little or no effect on the number of children who receive measles vaccines; and

• may lead to mixed results on the number of parents seeking care for their child when he or she is ill.

We do not know whether IMCI has any effect on the way health care workers treat common illnesses because certainty of the evidence was assessed as very low.

We do not know whether IMCI has any effect on the number of mothers who exclusively breast feed their child, because certainty of the evidence was assessed as very low.

None of the included studies assessed the satisfaction of mothers and service users by using an IMCI strategy.

How up-to-date is this review?

Review authors searched for studies that had been published up to 30 June 2015.

SUMMARY OF FINDINGS FOR THE MAIN COMPARISON [Explanation]

Patient or population: children < 5 years of age
Settings: middle- and low-income countries
Intervention: integrated management of childhood illness
Comparison: usual health services

Outcomes	Illustrative comparative risks* (95% CI)		Relative effect (95% CI)	Number of participants (studies)	Certainty of the evidence (GRADE)	Comments
	Assumed risk	**Corresponding risk**				
	Control	IMCI				
Mortality	Child mortality		Risk ratio 0.87[a] (0.68 to 1.10)	5090 children (1 trial)[1]	⊕⊕◯◯ **Low**[b,c] due to indirectness and imprecision	Child mortality may be decreased, but confidence intervals include no effect
	31 per 1000 live births	27 per 1000 live births (21 to 34)				
	Infant mortality		HR 0.85 (0.77 to 0.94)	60,480[e] (1 trial)[2]	⊕⊕◯◯ **Low**[f,g,h] due to indirectness and imprecision	Infant mortality may decrease
	69 per 1000 live births	59 per 1000 live births (54 to 65)[d]				
Nutritional status	Stunting		Risk ratio 0.94[i] (0.84 to 1.06)	5242 (2 trials)[1,2]	⊕⊕◯◯ **Low**[b,f,j] due to indirectness and imprecision	Little or no effect on stunting possible
	57 per 100	53 per 100 (48 to 60)				
	Wasting		Risk ratio 1.04[i] (0.87 to 1.25)	4288 (2 trials)[1,2]	⊕⊕⊕◯ **Moderate**[b,j] due to indirectness	Probably little or no effect on wasting
	13 per 100	14 per 100 (11 to 16)				

Quality of care	**Prescribing at health facilities**	Mixed effects[k]	727 (2 studies)[1,3]	⊕◯◯◯ **Very low**[l,m] due to imprecision, inconsistency, and indirectness	Not known whether consistent effect on prescribing quality at health facilities
	Prescribing by lay health care workers	No consistent effects	1051 observations (3 studies)[1,3,4]	⊕◯◯◯ **Very low**[l,m] due to imprecision, inconsistency, and indirectness	Not known whether consistent effect on prescribing quality of lay health care workers
Coverage of IMCI deliverables	**Vaccine coverage (measles)**	**RR 0.92** (0.80 to 1.05)	4895 (2 trials)[1,2]	⊕⊕⊕◯ **Moderate**[n,j] due to indirectness	Probably little or no effect on measles vaccine coverage[n]
	57/100	54/100 (46 to 60)			
	Supplement coverage (vit A)	**RR 0.93** (0.88 to 0.98)	831 (1 trial)[1]	⊕⊕⊕◯ **moderate**[n,j] due to indirectness	Probably little or no effect on vitamin A coverage
	83 per 100	77 per 100 (73 to 81)			
	Appropriate care seeking	Mixed effects[o]	4182 (3 studies)[1,2,3]	⊕⊕◯◯ **Low**[p] due to inconsistency	Appropriate care seeking possibly improved in some studies, but not in others
	Exclusive breast feeding	Mixed effects[q]	7975 (4 studies)[1,2,3,4]	⊕◯◯◯ **Very low**[p,r,s,t,u] due to indirectness and inconsistency	Not known whether effect on exclusive breast feeding
Satisfaction of beneficiaries	Not measured				Not known whether users prefer IMCI or usual clinics

The basis for **assumed risk** is median control group risk across studies. The **corresponding risk** (and its 95% confidence interval) is based on assumed risk in the comparison group and **relative effect** of the intervention (and its 95% CI)

CI: confidence interval; **ICC:** intracluster correlation co-efficient; **RR:** risk ratio

GRADE Working Group grades of evidence

High certainty: We are very confident that the true effect lies close to the estimate of effect

Moderate certainty: We are moderately confident in the effect estimate: The true effect is likely to be close to the estimate of effect but may be substantially different

Low certainty: Our confidence in the effect estimate is limited: The true effect may be substantially different from the estimate of effect

Very low certainty: We have very little confidence in the effect estimate: The true effect is likely to be substantially different from the estimate of effect

[a]In the Bangladesh trial, mortality declined over the 5 years from 43 per 1000 live births to 27 per 1000 live births in the intervention area (reduced by 37%), and from 44.8 per 1000 live births to 31.2 per 1000 live births in control areas (reduced by 30%). A small difference in the reduction in child mortality was noted in the 2 groups (8.6% in the intervention group vs 7.8% in control groups).

The Tanzanzia CBA study had mortality estimates that were very similar to the Bangladesh trial (RR 0.87, 95% CI 0.72 to 1.05).

[b]Downgraded by 1 for serious indirectness: The Bangladesh trial modified the intervention after early analysis for care seeking and referral completion, suggesting that coverage was not increasing as expected. This included modification of treatment and referral guidelines and introduction of a new cadre of village health care workers trained and equipped to provide community case management for pneumonia and diarrhoea in 2005. These adjustments, including the new staff cadre, were in response to an intermediate process evaluation in the trial, and are unlikely to be mirrored in routine implementation programmes.

[c]Downgraded by 1 for imprecision: 95% CI is wide and includes a clinically important reduction in mortality and no effect. In addition, dominant change was secular (see note 1)

[d]Absolute rates were calculated from hazard ratio by using the formula $RR = (1 - exp(HR \times ln(1 - assumed\ risk)))/assumed\ risk$

[e]IMCI in this trial included perinatal and neonatal components

[f]Downgraded for serious imprecision. Confidence intervals include no important effect to an important effect

[g]Downgraded by 1 for serious indirectness: This single study was conducted in a mixed rural/urban population in northern India with a substantive neonatal component with home visiting. Findings may not be easily generalized to other settings in Asia or elsewhere

[h]Subgroup analysis showed lower mortality in the intervention group among babies delivered at home, with no effect apparent in the subgroup delivering at hospital. This subgroup effect was evident for both neonatal and infant mortality

[i]Confidence intervals for Arifeen adjusted assuming ICC of 0.01

[j] The Tanzania CBA study has very similar estimates compatible with this estimate

[k]Large improvements in 6 parameters in Arifeen; no clear effect in 2 parameters in Schellenberg

[l]Downgraded by 1 for both imprecision and inconsistency. Small numbers of participants observed; effect varies between trials and parameters measured

[m]Downgraded by 1 for indirectness. All measurements through direct observation of health care worker; may not represent behavior unobserved

[n]Downgraded by 1 for indirectness. Approximately 80% of the estimate taken from 1 study, so generalisability to other settings is uncertain

[o]Point estimate for vaccine coverage suggests higher coverage in control group, and 95% confidence intervals exclude beneficial effect of IMCI on coverage.

[p]This outcome was measured in various ways by different studies on samples of patients. Large improvements noted in some studies but not in others. As the outcome was so varied, we did not prepare a meta-analysis

[q]Downgraded by 2 for inconsistency. Some large effects in some studies, and modest/no effects in others

[r]Mixed effects between the 4 studies preclude meta-analysis

[s]Downgraded by 2 for inconsistency. Large amounts of qualitative heterogeneity

[t]Downgraded by 1 for indirectness. See (b) above and the large effects seen in Bhandari associated with several home visits, which would not be feasible in other settings

[u]Downgraded by 1 for risk of bias. Breast feeding was reported through questionnaire from health care workers to mothers

Studies

[1] Arifeen 2009;[2] Bhandari 2012; [3] Schellenberg 2004 ; [4] Mohan 2011

BACKGROUND

Description of the condition

More than 7.5 million children globally die each year before reaching the age of five. Most of these deaths occur in low- and middle-income countries (LMICs) (Black 2003; Liu 2012), where interaction of common infections (including neonatal sepsis, measles, diarrhoea, malaria, and pneumonia) with poor nutritional status, combined with inadequate health infrastructure and poverty, results in poor health outcomes (Liu 2012; Tulloch 1999). Statistical projections over the past decade suggest that these common childhood illnesses will continue to be major contributors to the child morbidity and mortality burden until 2020 (Murray 1996). These projections have been uncannily accurate, as shown by recent mortality data (WHO 2012), providing a strong case for introducing new strategies to tackle problems contributing to poor outcomes.

In addition to overall high child mortality globally, there are large differences in mortality between countries, with earlier studies indicating that 95% of global mortality happens in 42 less-developed countries (Victora 2003); there are also differences in mortality between socio-economic groups within countries. Children who belong to the more underprivileged sections of society are more likely to suffer from malnutrition and to experience greater severity of illness and higher mortality (Black 2003; Victora 2003). These inequalities are reflected in the quality of health care received. Studies have shown that at first-level health facilities in LMICs, assessment by health care workers is poor, treatment facilities are inadequate, and parents receive improper advice (Barros 2012; World Health Organization 1998).

Providing quality care to sick children in LMICs is important. Effective and affordable interventions have been known to reduce childhood morbidity and mortality for some time, but their availability, accessibility, and acceptability to the ultimate beneficiaries have been unacceptably low (Bryce 2003; Jones 2003).

Description of the intervention

Individual health interventions shown to be effective in reducing child mortality include exclusive breast feeding, improved vaccination coverage, oral rehydration therapy, pneumonia therapy, and early treatment for malaria in endemic areas (Bhutta 2008; Markowitz 1991; Mathew 2011; Thwing 2011). However, children presenting to first-level health facilities seldom present with a single ailment. The presence of multiple and overlapping morbidities makes diagnosis and treatment difficult for the health care worker. Although each of these interventions has been individually shown to be effective, it has gradually become clear to health care planners that a more integrated approach is needed to achieve better outcomes. This has resulted in a policy push toward a multi-pronged strategy aimed at integrating improved health care services with better case management skills and healthier community practices to reduce child mortality and morbidity (WHO 1996). Health care packages that aim to integrate these components of health care strategy have been designed and implemented at community, national, and international levels. In the mid-1990s, the World Health Organization (WHO), in collaboration with the United Nations Children's Emergency Fund (UNICEF) and other agencies, developed a strategy known as integrated management of childhood illness (IMCI) in response to these challenges.

The IMCI strategy includes both curative and preventive interventions targeted at improving health practices at health care facilities, at home, and in the community. This strategy includes three main components (Tulloch 1999): (1) improvement in the case management skills of health care staff through provision of locally adapted guidelines on IMCI and activities to promote their use; (2) improvement in the overall health care system required for effective management of childhood illnesses; and (3) improvement in family and community health care practices.

In 1995, WHO technical programs and partners, supported by sound research, introduced case management guidelines for IMCI (WHO 1997), with a core intervention targeting five of the most important causes of child mortality: acute respiratory infection (ARI), diarrhoea, measles, malaria, and malnutrition. The following year, a training program was targeted at first-level health care workers. These case management guidelines were adapted to local epidemiology and clinical practice, and training of the first health care workers started in 1995. This was followed by a short period of exploratory implementation and documentation in a small number of countries (Lambrechts 1999). After an initial pilot phase, IMCI was introduced in Tanzania and Uganda in 1996 (Bryce 2005). Results from these two countries were encouraging, with improvements noted in quality of care and health care worker practices (Lambrechts 1999). In the early phase of its implementation, IMCI was focused on training health care workers, with less attention paid to the other two components, namely, strengthening health care systems and improving community practices. Initial guidelines and training materials were considered appropriate for countries with an infant mortality rate greater than 40/1000 live births, and with documented transmission of *Plasmodium falciparum* malaria. The guidelines and training materials represented an attempt to outline what needed to be done at a first-level health facility by any health worker - doctor, nurse, or paramedical worker - seeking to treat sick children while reducing mortality.

Upon receipt of an encouraging response from partner organizations, various countries, and the World Bank, the WHO provided a detailed blueprint of a three-phase rollout for countries wishing to adopt IMCI (WHO 1999). The process consisted of the introduction phase, the early implementation phase, and the expansion phase. The purpose of the introduction phase is to ensure that policymakers understand IMCI. This involves initiating contact to provide information, holding orientation meetings, and

building national capacity in IMCI. In the early implementation phase, health care staff conduct and monitor IMCI activities in a limited number of districts to study impact. Other issues studied during this phase include the relationship of IMCI to other health care sector activities, drug availability, and policy and supervision. The expansion phase involves increasing access to interventions introduced in the first two stages. The WHO and collaborating agencies provide technical assistance in preparation for early implementation of IMCI.

Anecdotal data, qualitative reviews, and systematic reviews from various countries suggest that IMCI has been effective in improving health service quality and increasing health care cost savings (Ahmad 2010; Amaral 2008). Since its introduction, IMCI has been taken up by numerous countries, initially as a pilot project, and later as a national program. The three components of IMCI have been implemented in various ways in different countries. Key features of IMCI include its evidence-based approach to diagnosis and treatment and its flexibility in terms of adapting guidelines to local epidemiological situations. The adaptation process involves detailed comparisons of existing guidelines in a country with IMCI and application of the most effective components of both. Consensus is needed on the conditions that should be covered. Malaria can be removed from guidelines in which falciparum malaria is not a problem. Other countries have included dengue fever as an important problem. IMCI has already been adapted to include the neonatal period, and some countries, like India, have incorporated neonatal care in implementation of the program. Selection of antibiotics for ARI and diarrhoea is based on local sensitivity patterns and availability. Some countries have shortened the duration of training to reduce costs. In many countries, especially in sub-Saharan Africa, HIV/AIDS contributes significantly to child morbidity and mortality, resulting in the need to include specific assessment and management of symptomatic HIV infection in IMCI guidelines. A draft HIV component of the IMCI guidelines, which included management of symptomatic HIV cases with referral for counselling and testing, was evaluated in South Africa. A revised version was then validated in Ethiopia and Uganda, where prevalence of HIV, malnutrition, and malaria is different from South Africa. IMCI materials were then adapted to include an HIV component (Qazi 2006). The WHO has formulated an Adaptation Guide to describe the process of adaptation by a country and facilitate continuous evolution of the program (WHO 1999a).

Large-scale rollout and continuation of IMCI require money. In several countries, external donors have largely funded IMCI implementation. Within 10 years, donor support began to wane, leaving health departments of poor countries with inadequate funds (Duke 2009). Indeed the places where IMCI is needed most, and in which it provides the greatest impact, are those in which the health care system is weakest and implementation of the strategy often fades. Therefore, it is important to ensure adequate development along with the introduction of newer innovations. A global

study conducted across 27 countries cited high cost as a major challenge to scaling up of the program (Goga 2011). Apart from modifications such as shortening of training duration, new technology such as the IMCI computerized adaptation and training tool (ICATT) is being introduced. Trials are currently under way to assess the effectiveness of these tools.

How the intervention might work

The IMCI clinical guidelines target children up to five years of age - the age group that bears the greatest burden of death from common childhood diseases. These guidelines are derived from an evidence-based, syndromic approach to case management and emphasize rational, effective, and affordable use of drugs and diagnostic tools (Gove 1997; Hill 2004). With well-formulated guidelines and proper training of health care workers, it would be possible to systematically assess common symptoms and clinical signs, ultimately leading to rational and effective actions. Such an approach can help in diagnosing the clinical condition, assessing the severity of the condition, and implementing actions that can be taken to care for the child (e.g. refer the child immediately, manage within available resources, manage at home).

Initially, IMCI referred to case management of children. It later became a vehicle for WHO and UNICEF child survival strategies at household, community, health facility, and referral levels. Thus it incorporated health service strengthening on the one hand and, on the other hand, face-to-face nutrition and health advice provided through home visits and active involvement of family members and the community in the health care process (Gove 1997; Hill 2004). Thus, over the years, implementation of IMCI, called the IMCI strategy, has come to include three components.

• Training component: training of health care workers in clinical care with the use of IMCI guidelines.

• Systems component: investment in health care systems organization and management, including supplies, related specifically to delivery of IMCI.

• Community health component: Auxiliary health care staff and community health care workers attached to clinics conduct home visits and community health promotion to promote good child rearing practices, good nutrition, and access to services when the child is ill (Hill 2004).

Why it is important to do this review

Currently, more than 75 countries are implementing the IMCI strategy on a large scale. For years, individual aspects of child health, often contained within trials evaluating the efficacy of one intervention, have been carried out, for example, in vitamin A supplementation. Individual components of IMCI have often been tested and have proved effective in rigorously conducted randomised controlled trials and systematic reviews. However, it is

unclear whether delivery of this package impacts hard outcomes such as mortality. As provision of IMCI is expensive, solid evidence of an impact on child health contributes to continued provision of political and financial support of this comprehensive child health strategy.

Global evaluation of IMCI, called "the multi-country evaluation of IMCI," was started in the early 1990s to generate information on effectiveness, cost, and impact, alongside other initiatives, such as the IMCI evaluation by the Centers for Disease Control and Prevention (CDC) (Schellenberg 2004); investigators reported across five study sites (WHO 2002). Other reviews have described health care worker performance as the primary outcome indicator (Amaral 2008) or have assessed the impact of the duration of training for IMCI (Rowe 2008), thereby not analysing the impact of the intervention on beneficiaries. A comprehensive systematic review is therefore required to evaluate the effectiveness of IMCI in improving child health (as measured by mortality or nutritional status), its impact on the quality of care delivered, and whether basic healthy practices delivered by caregivers improve.

O B J E C T I V E S

To evaluate the effects of programs that implement the integrated management of childhood illnesses (IMCI) strategy in terms of death, nutritional status, quality of care, coverage with IMCI deliverables, and satisfaction of beneficiaries.

M E T H O D S

Criteria for considering studies for this review

Types of studies

Randomised controlled trials, including cluster-randomised trials. Non-randomised trials with a concurrent comparison group (no IMCI intervention) and adjustment for baseline characteristics and confounders.

Controlled before-after (CBA) studies in which allocation to different comparison groups was not made by study investigators, and outcomes were measured in both intervention and control groups at baseline and after the IMCI program had been introduced.

All studies required at least two intervention sites and at least two control sites.

Types of participants

The unit of study was primary health care services in low- and middle-income countries (as categorized by The World Bank using gross national income per capita in US dollars and the Atlas conversion factor (World Bank 2012)). This could be provided by the public, private, or non-government agency sector.

Participants were children younger than five years of age and health care providers in low- and middle-income countries (as categorized by The World Bank using gross national income per capita in US dollars and the Atlas conversion factor (World Bank 2012)).

Types of interventions

Children younger than five years of age allocated to receive the generic WHO/UNICEF IMCI intervention or its adaptation. To be included, the IMCI intervention needed to include improving health care worker skills for case management as one component. We included studies of (1) IMCI training alone; (2) IMCI training plus systems interventions to improve care delivery; (3) IMCI training with additional activities to improve community health practices; and (4) all three interventions.

We excluded studies that included IMCI only as a part of a wider intervention package that could include conditional cash transfers, food supplementation, employment, and vertical disease-specific measures.

Studies providing specific additional interventions in both intervention and control areas were eligible for inclusion as long as these additional interventions were similar across intervention and control areas.

Comparison

We included studies in which the comparison group received usual health services without the integrated health care package (IMCI).

Types of outcome measures

- Measures of mortality (neonatal, infant, and under-five mortality) rates.
- Measures of nutritional status, including stunting and wasting.
- Quality of care assessed by adherence to standard practice guidelines.
- Coverage of key IMCI deliverables, including (1) vaccine coverage; (2) appropriate care seeking for common illnesses; and (3) exclusive breast feeding.
- Satisfaction of beneficiaries.

As one study also reported on other newborn care practices, which we did not anticipate, we describe these results under "coverage." In addition, in the protocol, we stated that we would assess morbidity episodes as secondary outcomes. As it is unlikely that IMCI would influence the incidence of disease, and studies did not report on this, we have not commented further on this outcome.

Search methods for identification of studies

Electronic searches

We attempted to identify all relevant trials irrespective of language or publication status. We used the search term "IMCI" OR "IM-NCI" OR "integrated management of childhood illness" across various databases. A more complex search strategy was not needed, as "IMCI" does not have a corresponding medical subject heading (MeSH) term, and all papers that consider IMCI use this term in the title, abstract, or text.

We (TG and DS) searched the following databases using the strategy described above.

- Cochrane Central Register of Controlled Trials (CENTRAL) (www.cochranelibrary.com), including the Cochrane Effective Practice and Organisation of Care (EPOC) Group Specialised Register (searched 30 June 2015).
  - MEDLINE (1946 to date), Ovid (searched 30 June 2015).
  - EMBASE (1980 to date), Ovid (searched 30 June 2015).
  - Cumulative Index to Nursing and Allied Health Literature (CINAHL) Plus (2000 to date), EbscoHost (searched 30 June 2015).
  - Latin American Caribbean Health Sciences Literature (LILACS), Virtual Health Library (VHL) (searched 30 June 2015).
  - World Health Organization (WHO) Library & Information Networks for Knowledge Database (WHOLIS) (searched 30 June 2015).
  - Science Citation Index and Social Sciences Citation Index, Institute for Scientific Information (ISI) Web of Science (1950 to present) (searched 30 June 2015).
  - Population Information Online (POPLINE) (searched 30 June 2015).
  - World Health Organization (WHO) International Clinical Trials Registry Platform (WHO ICTRP) (searched 30 June 2015).
  - Global Health (1973 to 2016 Week 17), OvidSP (searched 08 May 2016).
  - Health Management (1986 to present), ProQuest (searched to 17 December 2012. We did not have access to this database after this date).

We have listed in Appendix 1 search strategies used for the various databases and the number of trials identified.

Searching other resources

We scanned the reference lists of all included papers and relevant reviews to identify citations that could have been missed in the primary search. We contacted authors of other relevant reviews in the field regarding relevant studies of which they were aware.

Data collection and analysis

Selection of studies

Two review authors (TG and DS) removed duplicate records, then independently scanned the titles and abstracts of studies identified in the computerized search to exclude literature that clearly did not meet the inclusion criteria. We examined full-text articles against eligibility criteria while using a structured form. We resolved uncertainties about inclusion by discussion and consensus between all review authors. Controlled before-after studies were required to include at least two control groups and at least two intervention groups, as otherwise differences detected are totally confounded by study site.

Data extraction and management

Two review authors (TG and DS) used a structured form to independently extract relevant data, including details of methods, participants, setting, context, interventions, outcomes and results, publications, and investigators. We resolved discrepancies by mutual discussion. When discrepancies could not be resolved, we sought assistance from a third review authors (HSS).

We described the IMCI strategy by using a matrix to detail inputs and activities. This matrix includes (1) training inputs; (2) tools and manuals, including guidelines; (3) additional equipment and drugs provided; (4) managerial supervision and monitoring, including additional health information collected; and (5) engagement, training, and support of community volunteers, as well as health care providers involved in the program. We intended to stratify the analysis to reflect inputs (separating simple training; training and systems support; training and community engagement; and training, systems support, and community engagement) but found that data were insufficient.

Assessment of risk of bias in included studies

Two review authors (TG and DS) independently assessed the risk of bias for each controlled trial and controlled before-after study using criteria outlined in the *Cochrane Handbook for Systematic Reviews of Interventions* and those recommended by EPOC (EPOC 2015; Higgins 2011). For randomised controlled trials, non-randomised controlled trials, and CBA studies, these criteria include the following.

- Sequence generation (selection bias).
- Allocation sequence concealment (selection bias).
- Blinding of participants and personnel (performance bias).
- Blinding of outcome assessment (detection bias).
- Incomplete outcome data (attrition bias).
- Selective outcome reporting (reporting bias).
- Comparability of baseline outcome and characteristics.
- Protection from contamination.
- Other potential sources of bias.

For cluster-randomised trials, particular biases to consider include the following.

- Recruitment bias.
- Baseline imbalance.
- Loss of clusters.
- Incorrect analysis.

We omitted "comparability with individually randomised trials", as this intervention could be tested only in the context of a cluster trial (Higgins 2011).

The judgment for each entry involves assessing risk of bias as "low," "high," or "unclear," with the last category indicating lack of information or uncertainty over the potential for bias. We resolved disagreements by discussion between review authors.

Measures of treatment effect

We expressed results as risk ratios (RRs) with 95% confidence intervals (CIs) for binary outcomes. We analysed continuous outcomes using mean differences (MDs).

Unit of analysis issues

When a cluster-randomised trial was adjusted for clustering, we extracted cluster-adjusted results and used them in analyses.

When a cluster-randomised trial did not adjust for clustering, we extracted unadjusted results. As we were not able to obtain an estimate of intracluster correlation co-efficients (ICCs) from the trials themselves, we used sensitivity analyses and an estimated ICC of 0.01 to investigate the impact of clustering on estimates of effectiveness.

Dealing with missing data

We anticipated that we would need to impute values to estimate cluster effects, but this was not required.

Assessment of heterogeneity

We described the context in which the intervention was implemented. We described in the table of included studies variability among participants, interventions, and outcomes studied. Statistical heterogeneity was to be identified and measured as recommended by the *Cochrane Handbook for Systematic Reviews of Interventions* (Section 9.5.2) (Higgins 2011). As we found so few

studies, we were careful about conducting meta-analysis and carried this out only when it made sense to do so. If heterogeneity based on Chi^2 was assessed as greater than 50%, we used a random-effects model and interpreted results carefully.

Assessment of reporting biases

We anticipated using funnel plots to examine for publication bias but found insufficient trials to do this.

Data synthesis

Overall, the review provides a structured synthesis. When meta-analysis made sense, we used Review Manager software (RevMan 5.3), expressing results as risk ratios with 95% confidence intervals, or mean differences, as applicable. We used CBA results alongside the trials results, but did not combine them statistically. We assessed the certainty of the evidence by using the GRADE approach and summarized key findings in Summary of findings for the main comparison.

Subgroup analysis and investigation of heterogeneity

Our planned subgroup analyses were not possible, as data were insufficient.

R E S U L T S

Description of studies

Results of the search

Searches of various databases yielded 1499 records to be screened, after duplicates were deleted. Of these, we found 1433 irrelevant to the review on screening. We obtained full texts of the remaining 50 studies, reported in 66 publications. Of these, four studies (two cluster RCTs and two CBA studies) described in 12 articles met our inclusion criteria (Figure 1). We reported reasons for excluding studies in the Characteristics of excluded studies table. We identified one trial through other sources in May 2016 (Boone 2016). We included this study amongst Studies awaiting classification and will consider it in an update in due course.

Figure 1. Study flow diagram.
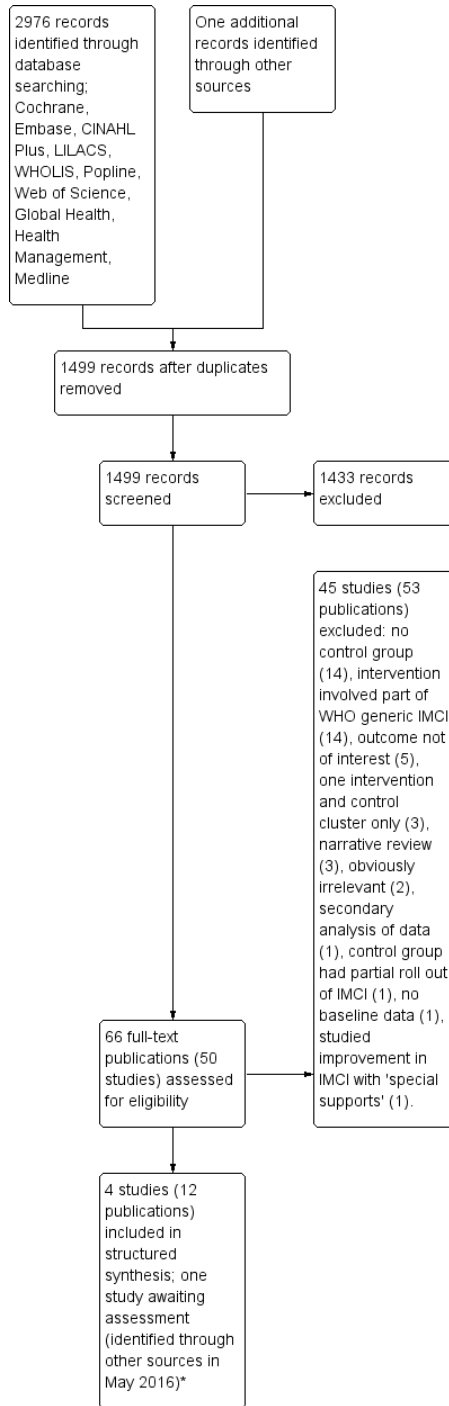
Included studies

Locations and populations

Studies were conducted in Tanzania (data collection from 1997 to 2002), Bangladesh (1999 to 2007), and India (2006 to 2010). One analysis was obtained from India's national program (2005 to 2009).

Schellenberg 2004 was carried out in four rural districts of Tanzania, with two intervention clusters and two control clusters that were geographically contiguous and matched for mortality rates. Arifeen 2009 was conducted in Bangladesh, in areas of a subdistrict where the sampling frame consisted of first-level outpatient facilities. Bhandari 2012 was carried out in primary care health centres within a single district of a state in Haryana, India. In a second study from India, Mohan 2011 collected data from 12 districts of India that had initiated IMCI and compared them with data from matched control districts.

Strategies

Interventions are summarized as an input matrix (Table 1) related to human resource policies, health systems strengthening, and strategies for community engagement. Trials varied substantially in range of inputs provided. The earliest trial comprised two IMCI components: training for basic health care workers, and drug supply combined with tools and manuals (Schellenberg 2004).

Arifeen 2009 included training of basic health care workers but provided more substantive supervision, health service strengthening, and strategies for community engagement. Investigators added a new cadre of health worker halfway into the study for treatment of community pneumonia and diarrhoea.

Bhandari 2012 included training of all cadres of health care workers consisting of human resource management strategies, drug supply, and community engagement, including support to village doctors, women's groups, and women's leaders.

Mohan 2011 reported fewer inputs than Bhandari 2012 but included home visits and drug supply.

The two trials in India (Bhandari 2012; Mohan 2011) modified the IMCI package to include a series of interventions specifically targeted at the neonate. These interventions were defined in the IMNCI guidelines by the Government of India (WHO 1998; WHO 2003).

Details of the interventions are included in Table 2. Routine health care was used for comparison in all trials.

Study design

Two studies were cluster-randomised trials (Arifeen 2009; Bhandari 2012); two were controlled before-after studies (Mohan 2011; Schellenberg 2004). Both cluster RCTs used appropriate methods to take clustering into account when reporting measures of treatment effect.

Outcomes

Arifeen 2009 reported mortality in children younger than five years of age, while excluding death in the first week of life. Schellenberg 2004 reported under-five mortality rates at baseline and at two years after implementation of IMCI. Bhandari 2012 reported neonatal mortality, neonatal mortality beyond the first 24 hours of birth, and infant mortality.

In Arifeen 2009, in the abstract of the article but not in the main text, study authors reported on the percentage difference in mortality rates in the last two years of the study (27.0/1000 in the IMCI group, 31.2/1000 in the control group). This is not corrected for baseline (which is lower in the IMCI group), thus this estimate is inflated. We calculated absolute differences in death between the two groups in Summary of findings for the main comparison, as these data are more informative.

For nutritional status, three studies reported wasting and stunting (Arifeen 2009; Bhandari 2012; Schellenberg 2004).

For quality of care, Arifeen 2009 reported on health facility readiness and quality of assessment and treatment of sick children.

For coverage of key IMCI deliverables, studies included the following.

- All studies reported on measles immunization coverage.
- Studies reporting appropriate care seeking used different approaches
- All studies reported on exclusive breast feeding but at different time points: four weeks (Bhandari 2012); four months (Schellenberg 2004); and six months (Arifeen 2009; Mohan 2011). Other outcomes are listed in the Characteristics of included studies table.

No study reported satisfaction of mothers and service users.

Funding

Arifeen 2009 and Schellenberg 2004 were included in the Multi-Country Evaluation of IMCI Effectiveness, Cost, and Impact (MCE), which was co-ordinated by the Department of Child and Adolescent Health and Development of WHO. The World Health Organization funded Bhandari 2012. No source of funding was given for Mohan 2011, but three study authors were (at the time of publication) affiliated with WHO or UNICEF.

Excluded studies

The Characteristics of excluded studies table summarizes the reasons why studies were excluded. Of the 45 studies (53 reported papers):

- we excluded three, as they had just one intervention and control cluster (Atakuoma Dzayisse 2006; Esaghi 2012; Rowe 2011);
- we excluded five, as the outcome was not of interest (Adam 2009; Gilroy 2004; Kelley 2001; Mahalli 2011; Prado 2006);
- we excluded 14, as a component of the IMCI was implemented but not the complete generic WHO IMCI (Ali 2005, Ebuehi 2009; Ebuehi 2010; Ertem 2006; Gebresellasie 2011; Ghimire 2010; Hamad 2011; Harkins 2008; Igarashi 2010; Jin 2007; Pelto 2004; Santos 2001; Talsania 2011; Zaman 2008);
- we excluded 16, as they did not include a control group (Camara 2008; Chopra 2005; Chowdhury 2008; Core Group 2009; Edward 2007; Huicho 2005; Huicho 2008; Kumar 2009; Mohan 2004; Pariyo 2005; Rakha 2013; Senn 2011; Thompson 2009; Uzochukwu 2008; Wammanda 2003; Zhang 2007). In

addition, the control group had partial rollout of the IMCI program in one trial (Moti 2008); and

- we excluded one of the remaining studies as it was a cross-sectional survey with no baseline data and therefore did not qualify as a CBA trial (Naimoli 2006). Three publications were narrative reviews pertaining to IMCI that presented no data (Almagambetova 2000; Lulseged 2002; Oluwole 2000), and one was a secondary analysis of data (Gouws 2004). One trial assessed improvements to IMCI with addition of special "supports" (Osterholt 2009). Two trials did not pertain to IMCI and were obviously irrelevant (Bradley 2005; Zurovac 2006).

Risk of bias in included studies

See Figure 2 and Figure 3 for summaries of risk of bias, and the Characteristics of included studies table for details of risk of bias and methods used in each trial. Arifeen changed the intervention when care seeking and referral completion did not turn out as expected. This impacted the indirectness and generalisability of the trial.

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

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

Effects of interventions

See: **Summary of findings for the main comparison** Integrated management of childhood illness strategy compared with routine care

Mortality

Three studies summarized in Table 3 reported effects of IMCI on mortality.

Child mortality

One trial and one CBA evaluated this. The Bangladesh trial estimated that child mortality may be 13% lower in the IMCI group, but the confidence intervals include no effect (RR 0.87, 95% CI 0.68 to 1.10, 5090 participants, *low-certainty evidence*). The Tanzania CBA study produced very similar estimates (RR 0.87, 95% CI 0.72 to 1.05). (Analysis 1.1).

In the Bangladesh trial, it is important to note that mortality in both intervention and control groups fell markedly over the six-year period. When the first two years were compared with the last two years, the rate fell from 70.0 to 49.3/1000 live births in the IMCI group, and from 65.6 to 50.5/1000 live births in the control group, but investigators detected no differences between intervention and control groups. Study authors reported that IMCI group mortality was slightly lower by 3.3% (95% CI -3.4 to 10.0, adjusted for baseline imbalance), but the estimate includes a null effect (Arifeen 2009).

Infant and neonatal mortality

Bhandari 2012, who included a neonatal component to IMCI, reported data on these outcomes, adjusted for potential confounders (Table 3). The infant mortality hazard ratio (HR) suggests that infant mortality may be lower in the IMNCI group than in the control group (cluster-adjusted HR 0.85, 95% CI 0.77 to 0.94; low certainty of evidence; Analysis 1.1), although neonatal effects were marginal and confidence intervals included no effect (cluster-adjusted HR 0.91, 95% CI 0.80 to 1.03; Analysis 1.1). In a subgroup analysis, the neonatal mortality rate was lower in IMCI clusters in the subgroup delivered at home (cluster-adjusted HR 0.80,95% CI 0.68 to 0.93) but not in those delivered at a health facility (cluster-adjusted HR 1.06, 95% CI 0.91 to 1.23). This subgroup effect was preserved for infant mortality (home deliveries, cluster-adjusted HR 0.77, 95% CI 0.69 to 0.87; facility-based deliveries, cluster-adjusted HR 0.98, 95% CI 0.87 to 1.10). Study authors attributed the difference in mortality to more effective change in newborn care practices (including early breast feeding, exclusive breast feeding, delayed bathing, appropriate cord care) among home born babies compared with those delivered at the facility. The intervention may have improved timely seeking of health care for sick newborns, thereby affecting neonatal and infant mortality.

In a subsidiary analysis, we examined mortality among participants younger than five years of age, conducting a meta-analysis that combined child mortality with infant mortality. This post hoc analysis was justified on the basis that infant mortality accounts for 70% of under-five mortality (Analysis 1.2). Overall, under-five mortality may be reduced by IMCI (RR 0.85, 95% CI 0.78 to 0.93; two trials; 65,570 participants).

Nutritional status

Three studies assessed nutritional status; we have summarized their findings in Table 4 (Arifeen 2009; Bhandari 2012; Schellenberg 2004). Published data from Arifeen 2009 were not cluster-adjusted, so we used an ICC of 0.01 in the meta-analysis (see Methods).

For stunting, all confidence intervals overlap, and we considered it not unreasonable to pool study results for the trials. Overall, we noted that there may be little or no effect on stunting (RR 0.94, 95% CI 0.84 to 1.06; two trials; *low-certainty evidence*; Analysis 1.3).

For wasting, we used the same estimate for the ICC. Analysis shows there is probably little or no effect of IMCI on wasting (RR 1.04, 95% CI 0.87 to 1.25; two trials; *moderate-certainty evidence*; Analysis 1.4).

The Tanzania CBA study gave similar estimates for both parameters.

Quality of care

Arifeen 2009 conducted extensive assessments of quality of care in facilities, but Schellenberg 2004 measured fewer parameters (Table 5). Again, these data were collected by direct observation. Prescribing at health facilities was measured in two studies. Performance in IMCI groups appeared considerably improved in the Bangladesh trial, and a small improvement in pneumonia correctly treated was found in Schellenberg 2004, although the base performance level was low. Schellenberg 2004 also measured administration of antimalarials for fever and found little or no difference following IMCI implementation (Table 5). As certainty of the evidence was very low, we do not know whether IMCI has a consistent effect on prescribing at health facilities.

Three studies measured prescribing by lay health care workers (Table 6). Investigators examined appropriate treatment under direct observation for three common illnesses: diarrhoea (and oral rehydration salts (ORS) use), pneumonia (antibiotic use), and fever (malaria treatment). As certainty of the evidence was very low, we do not know whether IMCI had a consistent effect on prescribing by lay health care workers.

Arifeen 2009 examined the appropriateness of referrals (percentage of children coming to a facility who required referral and were actually referred) and found little or no difference between IMCI and non-IMCI clusters (Table 5).

Overall we found no consistent effect of the intervention on quality of care provided to beneficiaries.

Coverage of IMCI deliverables

Vaccine coverage

All four studies evaluated immunization coverage among children in the study populations (Arifeen 2009; Bhandari 2012; Mohan 2011; Schellenberg 2004). Among these, three studied coverage of the measles vaccine and found probably little or no effect on measles vaccine coverage (RR 0.92, 95% CI 0.80 to 1.05; two trials; Tanzania CBA showed a similar result; Analysis 1.5).

Two studies evaluated coverage of the third dose of diphtheria, pertussis, and tetanus vaccine - one with very low coverage at follow-up (15.6% in the control group, 21.2% in the IMCI group; Bhandari 2012) and one with much higher coverage at follow-up (81.9% IMCI; 93% control; Schellenberg 2004; Analysis 1.6). The pattern was the same as for measles vaccine, with little or no evidence of improved coverage with IMCI.

Vitamin A coverage

Two studies reported vitamin A supplementation coverage. In the Bangladesh trial (Arifeen 2009), coverage was high in both intervention and control areas at baseline and at follow-up. In the Tanzania study, vitamin A coverage was low at baseline in both groups

and was high at follow-up in both groups (Table 7). Analysis of end values shows that there was probably slightly better coverage in the control group of the Bangladesh trial (Analysis 1.7). Overall, there is probably little or no effect of IMCI on vitamin A coverage.

Appropriate care seeking

Care seeking was studied through various parameters in all four included studies with mixed results: Arifeen 2009 suggested improvement in the IMCI group, as did Bhandari 2012 (Table 8; Analysis 1.9). Schellenberg 2004 did not demonstrate improvement. Mohan 2011 reported on this and suggested better care seeking for ARI.

Mohan 2011 also reported end values for "change in percentage of institutional deliveries," with 9.2% for IMCI and 5.0% for control and no differences in change detected (RR 4.2%, 95% CI -3.8 to 12.2).

Exclusive breast feeding

Exclusive breast feeding was reported in four studies (Table 9), which showed mixed results of very low certainty (Analysis 1.8): One study (Bhandari 2012), which included home visits to encourage breast feeding, found a large effect. Other measures related to breast feeding in this study followed this pattern; in the intervention group, fewer pre-lacteal feeds were given and breast feeding was commenced within an hour of birth more commonly, although these measures were self reported. We noted little difference in relation to complementary feeding. The other three studies demonstrated no differences in breast feeding-related parameters.

Newborn care practices

Bhandari 2012 examined several newborn care practices following implementation of IMCI. These practices included delayed bathing, cord care, and appropriate temperature maintenance. Investigators found improvement in all practices, except use of appropriate clothing to maintain newborn temperature while preventing hypothermia.

D I S C U S S I O N

Summary of main results

See Summary of findings for the main comparison.
The integrated management of childhood illness (IMCI) strategies evaluated in these four studies included training of health care staff and management strengthening of health systems (all four studies), as well as home visiting (two studies). Two studies from India included care packages targeting the neonatal period.

Two studies (Tanzania and Bangladesh) showed that child mortality may be lower with IMCI, possibly as much as 28-32% lower, but the confidence interval also included no effect.

One study in India, which implemented the integrated management of neonatal and childhood illness (IMNCI) strategy, including post-natal home visits, examined infant and neonatal mortality, suggesting that neonatal and infant mortality may be lower in the IMNCI group than in the control group.

Three studies (Tanzania, India, Bangladesh) evaluated nutritional status and noted little or no effect on both stunting and wasting. Investigators measured quality of care by observing prescribing for common illnesses in two studies (Tanzania and Bangladesh). Effects were mixed and ranged from no effect to quite large effects, so we do not know whether the effect on prescribing quality was consistent.

For coverage of IMCI deliverables, we examined vaccine coverage, appropriate care seeking, and exclusive breast feeding. Three studies (Tanzania, India, Bangladesh) estimated vaccine coverage for measles, reporting probably little or no effect on measles vaccine coverage; two of these studies measured the third dose of diphtheria, pertussis, and tetanus vaccine; and two measured vitamin A coverage, all providing little or no evidence of increased coverage with IMCI.

Four studies (two from India and one each from Tanzania and Bangladesh) reported appropriate care seeking, using information derived from careful questioning of mothers about recent illness. IMCI areas may show better reported care seeking behavior in some studies, but not in others.

All four studies recorded maternal responses on exclusive breast feeding. Results were mixed and were of very low certainty, with some studies indicating that exclusive breast feeding was higher in IMCI areas but was not very different in others.

No study reported satisfaction of mothers and service users.

Overall completeness and applicability of evidence

All included studies involved study populations from low- to middle-income countries (LMICs) with high infant and child mortality rates; these settings are expected to benefit from IMCI interventions. Three of the four studies evaluated the impact of all three components of IMCI, and the fourth did not include the community component. Thus all four studies did include the two important components, namely, training of workers and strengthening of health care systems, but most also included the community component. The nature of interventions under each heading varied among trials (see Table 1).

All included studies were substantive in scope and in length of follow-up. Control groups in all trials were comparable with intervention groups at baseline and continued to receive routine health care services as per ongoing programs. Thus any observed effects in the intervention groups are more likely to be attributable to

the IMCI strategy than to spontaneous improvements noted over time. Evidence from these trials is largely applicable to real-life situations among populations in LMICs.

Three (out of four) studies were conducted in South Asia - two of these in India; thus the evidence base from African settings is particularly sparse.

Control groups in all studies received health care, so these studies evaluated the added value of IMCI or IMNCI. Such added value is likely to show a modest effect.

Quality of the evidence

Integrated management of childhood illness is a complex intervention, and conducting field trials to assess its impact is undoubtedly a challenging task. Therefore, generated evidence is valuable even if it is graded by the GRADE (Grades of Recommendation, Assessment, Development and Evaluation Working Group) approach as having low to moderate certainty (Summary of findings for the main comparison). Of the four studies included in this review, two were carefully conducted cluster-randomised controlled trials (Arifeen 2009; Bhandari 2012) with low risk of selection and recruitment bias, no attrition (loss of clusters), and good baseline comparability. The two controlled before-after studies (Mohan 2011; Schellenberg 2004) were cluster studies with purposive selection of control and intervention clusters.

All studies included in this systematic review had been funded or supported by the World Health Organization (WHO) or had serving employees of WHO as co-authors. As the World Health Organization is the primary institution responsible for facilitating global advocacy and implementation of IMCI, we were concerned about competing interests resulting in over-optimistic interpretation of study results. However, included studies were generally well conducted and reported.

Potential biases in the review process

Two of the studies were conducted in India, and the lead and senior authors are familiar with these research studies in their own country. However, the authorship team was aware of this potential bias and ensured that application of inclusion criteria, data extraction, and interpretation were neutral. During the process of peer review, we became aware of another trial (Boone 2016) that might be eligible for inclusion in the review and will be included when we update this review. It is unlikely that we missed any trials because such trials are likely to be large, to require extensive funding, and to be of interest to the World Health Organization, which promotes this strategy. Therefore they are likely to have been picked up by our exhaustive search strategy, which included contacting all relevant stakeholders to identify eligible trials.

Agreements and disagreements with other studies or reviews

To our knowledge, no published systematic review has assessed the impact of IMCI implementation in population settings (in children younger than five) on mortality and other outcomes.

A recently published systematic review (Willey 2013) assessed the effectiveness of interventions to strengthen national health service delivery; the findings are consistent with our review.

Another systematic review (Nguyen 2013) assessed the impact of IMCI on the skills of health care workers. This review included cluster-randomised controlled trials (RCTs), pre/post studies, and cross-sectional studies and found that IMCI-trained workers performed better in classifying illnesses, prescribing medications, vaccinating children, counselling families, and administering oral therapies. We did not consider these outcomes in our review.

We identified two trials (Amorim 2008; Rowe 2011) that were excluded because they were non-randomised controlled trials with single comparison units. Notes of these findings are appended in the Characteristics of excluded studies table).

A U T H O R S '   C O N C L U S I O N S

Implications for practice

Providing accessible comprehensive primary health care services to children in low- and middle-income countries seems a good approach to providing health care. This review indicates that IMCI may have a modest effect on mortality and may well be worth implementing, but policymakers need to be careful about justifying the considerable investment on the basis that it will result in large improvements in mortality.

One study measured neonatal and infant mortality and showed that these may be lower in the IMNCI group than in the control group. In this study, the strategy included neonatal care, emphasizing that these services have the potential to create impact during this period when mortality is high. IMCI programmes should consider including services directed at the neonate ("IMCNI") as an integral component of the strategy.

In addition, this strategy, variously implemented in these studies, did not show consistent effects on quality of care, and the certainty of evidence was very low because of concerns regarding precision, consistency, and directness. Therefore we do not know whether IMCI improves quality of care.

There is a continuing need to assure the components of the IMCI package are delivered appropriately, that coverage is maintained and that managerial and support approaches are taken to assure that appropriate, good quality care is in place.

Implications for research

Demonstrating an effect on mortality of effective implementation of routine primary neonatal and child health care services is a large and expensive undertaking. Many influences on child mortality occur over time, and studies must be large. Efforts by researchers to evaluate effects of IMCI help to demonstrate this. In the meantime, services and health may be improving over time, as was clear in Arifeen 2009, which reported dramatic falls in child mortality over the five years of the study in both intervention and control arms.

Important further research will involve evaluating strategies that improve access to, and the quality of, various components of delivery of a comprehensive package of primary child health care, with the IMCI package serving as a base for countries to draw on and modify as appropriate.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Arifeen 2009

Methods	**Design:** cluster-randomised controlled trial **Unit of randomisation:** first-level government health facilities
Participants	Children in the health facility catchment area Bangladesh in one subdistrict not covered by ICCDR,B health care services Inclusion criteria: 20 of 24 first-level outpatient facilities in the study area, along with their catchment areas. We excluded four units because substantial portions of their catchment populations received child health care services from ICDDR,B, not from government facilities Mean numbers of children < 5 years of age in final census 2006-2007: 2045 (intervention) ; 3045 (control)
Interventions	**IMCI training** **Systems interventions:** community health interventions
Outcomes	**Mortality** • Mortality in those younger than 5 years of age (7th day to 5 years) **Healthy practices by care giver** • Exclusive breast feeding until 6 months of age • Complementary feeding • Care seeking **Quality of care** • Quality of care • Coverage of IMCI deliverables **Nutritional status** • Wasting • Stunting Mortality estimates obtained from population surveys
Notes	**Objective:** to assess effects (and cost-effectiveness) of IMCI on mortality and nutritional status in children < 5 years of age **Location:** Bangladesh, in Matlab upazilla (subdistrict), not covered by child and reproductive health services provided by the ICDDR,B: Centre for Health and Population Research Total study population was about 350,000

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	Random allocation of 20 facility/catchment area units between pairs matched for facility type, geographical distribution, baseline mortality levels, and catchment

Arifeen 2009 (*Continued*)

		population size Allocated by blindly drawing a card with unit names from each pair and assigning it to IMCI, then assigning the other to comparison
Allocation concealment (selection bias)	Low risk	"concealed until groups assigned"
Recruitment bias	Low risk	Units in each pair were randomly selected (see above)
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Not mentioned
Blinding of outcome assessment (detection bias) All outcomes	Unclear risk	Not mentioned
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss of clusters
Selective reporting (reporting bias)	Low risk	No evidence of selective reporting
Other bias	High risk	Study teams monitored coverage throughout the study. Early findings for care seeking and referral completion suggest that coverage was not increasing as rapidly as expected, leading to changes in the intervention
Baseline imbalance	Low risk	IMCI and comparison areas were similar at baseline
Were baseline outcome measurements similar	Low risk	Yes
Loss of clusters	Low risk	No loss of clusters reported
Incorrect analysis	Low risk	Done correctly. Adjusted at catchment/facility level for clustering, using STATA
Study adequately protected against contamination	Low risk	The same children were monitored for health-related outcomes as at the first visit for data collection

Bhandari 2012

Methods	**Design:** cluster-randomised controlled trial **Unit of randomisation:** health centre
Participants	Children in the catchment area of health centres included Inclusion criteria: 18 clusters selected in the state of Haryana for the purpose of this study Exclusion criteria: none stated
Interventions	• Training health care workers to implement integrated management of neonatal and childhood illness • Providing systems intervention to improve care delivery • Improving community health practices
Outcomes	**Mortality** • Infant mortality • Neonatal mortality • Post-neonatal mortality **Standard health practices** • Newborn care practices • Care seeking behavior • Immunization coverage • Wasting and stunting • Complementary feeding
Notes	**Objective:** to assess India's adapted IMCI policy (which included home visits for early newborn care) on newborn and infant mortality, and on newborn care practices **Location:** communities with 1.1 million population served by 18 primary health centres in the district of Faridabad, Haryana, India. The population of each primary health centre ranged from 10,694 to 72,059. About half the mothers had never been to school, and two-thirds of births took place at home. Previous studies in the same area showed that 35% of newborns were of low birth weight and 60% of sick children were taken for care to medically unqualified private practitioners

Risk of bias

Bias	Authors' judgement	Support for judgement
Random sequence generation (selection bias)	Low risk	"...divided the clusters into three strata containing six clusters each based on neonatal mortality rate. An independent epidemiologist generated 10 stratified randomisation schemes to allocate the clusters to intervention or control groups. The authors examined all 10 potential randomisation schemes, and excluded three because of chance large differences between the groups. The authors then randomly selected one of the remaining seven allocation schemes by a computer generated ran-

Bhandari 2012 *(Continued)*

		dom number"
Allocation concealment (selection bias)	High risk	Not mentioned, study author clarification sought
Recruitment bias	Low risk	No obvious recruitment bias (see above)
Blinding of participants and personnel (performance bias) All outcomes	Low risk	Blinding of community not clear. Surveillance team was not told the intervention status of the community they were visiting
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not done
Incomplete outcome data (attrition bias) All outcomes	Low risk	Low attrition for neonatal mortality - the primary outcome. During outcome assessment period (January 2008 to March 2010), study authors registered a total of 77,587 pregnancies, for which outcomes were not known in 10,239 (13.2%). Of these, 9954 women were still pregnant when recruitment of live births in the trial was stopped; few pregnant women (285) had left the area or died. Study authors recorded 5147 (6.6%) miscarriages/abortions, 1499 (1.9%) stillbirths, and 60,702 (78.2%) live births in the study area. According to plan, follow-up ended 6 weeks after recruitment was completed. Consequently, although almost all recruited live born infants were followed for the newborn period (97.8%), only 75.4% were followed for 6 months and 52.6% until the end of infancy
Selective reporting (reporting bias)	Low risk	All primary outcomes reported. Perinatal mortality (stillbirths and deaths between birth and day 7 of life) 16 and post-neonatal mortality were added to reported outcomes for completeness
Other bias	Low risk	None detected
Baseline imbalance	Low risk	Not apparent
Were baseline outcome measurements similar	Low risk	Yes, all similar (except on average, IMCI centres slightly farther from main road)

Bhandari 2012 *(Continued)*

Loss of clusters	Low risk	No loss of clusters reported
Incorrect analysis	Low risk	Correct for cluster design, using shared frailty option to account for cluster randomisation (except for neonatal deaths beyond first 24 hours of birth and post-neonatal deaths, for which investigators adjusted for cluster design with robust standard errors, as the shared frailty option failed)
Study adequately protected against contamination	Low risk	Although contiguous, the 18 clusters are large, and the way health care and worker responsibilities are organized within a primary health centre area makes risk of contamination low

Mohan 2011

Methods	**Design:** controlled before-after study. Design was retrospective based on implementation **Unit of study:** district
Participants	Children in districts evaluated **Inclusion criteria:** The 12 districts (of India) that had initiated IMNCI in 2005 were selected (subsequently referred to as "early" IMNCI districts). For each "early" IMNCI district, a control district from the same state, matched on IMR and proportion of scheduled caste or scheduled tribe, was identified **Exclusion criteria:** none stated
Interventions	• Training health care workers to implement IMNCI • Providing systems intervention to improve care delivery • Improving community health practices
Outcomes	**Home practices** • Early initiation of breast feeding • Exclusive breast feeding until 6 months • ORS-use rates **Service use and coverage** • Percentage of deliveries conducted at a health facility (institutional delivery) • Full immunization • Percentage of children with ARI who sought care
Notes	

Risk of bias

Bias	Authors' judgement	Support for judgement

Mohan 2011 *(Continued)*

Random sequence generation (selection bias)	High risk	Non-randomised trial
Allocation concealment (selection bias)	High risk	Retrospective data analyses with no mention in text of allocation concealment
Recruitment bias	High risk	No mention has been made of criteria for selection of intervention clusters
Blinding of participants and personnel (performance bias) All outcomes	Unclear risk	Observational study using district-level household survey: blinding not relevant
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not mentioned but unlikely to have been done based on study design
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss of clusters, as this is a retrospective analysis
Selective reporting (reporting bias)	Low risk	All coverage indicators mentioned in methods section (Table 1) have been reported
Other bias	High risk	Data from independent surveys incidentally conducted before and after intervention used for coverage indicators. May not be exactly before-after data
Baseline imbalance	Low risk	For each "early" IMNCI district, a control district from the same state, matched on IMR and proportion of scheduled caste or scheduled tribe, was identified
Were baseline outcome measurements similar	Unclear risk	Baseline outcome measurements not mentioned in published text
Loss of clusters	Low risk	No loss of clusters mentioned in results/analysis, as the study analysed data on a retrospective basis
Incorrect analysis	Low risk	Weighted averages of percentage change in coverage levels were calculated for intervention and control districts. Net difference in changes in coverage was then compared between intervention and control districts using linear regression with adjustment for clustering and for sampling weights

Mohan 2011 *(Continued)*

Study adequately protected against contamination	Unclear risk	Not mentioned

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Schellenberg 2004

Methods	**Design:** controlled before-after comparison (also called a "non-randomised controlled clinical trial"), with monitoring of process measures to improve internal validity and to determine whether changes are the result of intervention or other factors **Unit of allocation:** district

Participants	Children in study districts
	Inclusion criteria
	  • The 2 IMCI districts - Morogoro Rural and Rufiji - started to implement IMCI in 1997-1998, and the 2 comparison districts - Kilombero and Ulanga - started implementation in 2002
	  • The 2 comparison districts were chosen for several reasons: They were geographically contiguous although separated from intervention districts by an uninhabited game reserve, so population movement between intervention and comparison areas was negligible; investigators reported continuing demographic surveillance; had similar or lower mortality rates; and had no immediate plans to implement IMCI
	1932 children < 5 years of age in final survey

Interventions	• IMCI training given • Systems intervention provided
Outcomes	**Mortality** • Child mortality* **Standard health practices** • Exclusive breast feeding* • Care seeking for children with danger signs* **Quality of care** • ORS prescription for diarrhoea* • Antimalarials for fever* • Vaccine coverage* **Nutritional** • Wasting • Stunting • Underweight *Specified primary outcomes
Notes	**Objective:** to measure effects of IMCI on child health and survival **Location:** southern area of Tanzania, poor, rural area with a network of public health facilities

Risk of bias

Bias	Authors' judgement	Support for judgement

Schellenberg 2004   (*Continued*)

Random sequence generation (selection bias)	High risk	Not random
Allocation concealment (selection bias)	High risk	No allocation
Recruitment bias	High risk	Intervention sites chose to implement IMCI; control sites had "no immediate plans"
Blinding of participants and personnel (performance bias) All outcomes	High risk	Not blinded
Blinding of outcome assessment (detection bias) All outcomes	High risk	Not blinded
Incomplete outcome data (attrition bias) All outcomes	Low risk	No loss of clusters/population
Selective reporting (reporting bias)	Low risk	Quality outcomes appear comprehensive
Other bias	Low risk	No other apparent source of bias
Baseline imbalance	Unclear risk	Baseline data available from 1999, when IMCI had been partially rolled out in intervention areas
Were baseline outcome measurements similar	Unclear risk	Baseline data available from 1999, when IMCI had been partially rolled out in intervention areas. Study authors also mention: "We could not do a before-IMCI health facility survey because implementation of IMCI had already started before this study began in 1999"
Loss of clusters	Low risk	No loss of clusters
Incorrect analysis	Low risk	Adjustments for age (< 1 year and 1 to 4 years) and rainfall (estimated from remote sensing data) were made with Poisson regression models, and between-district differences were compared by *t*-test-based methods of adjusted residuals, as appropriate for clustered data, with a small number of clusters in only 4 districts. P values from this approach are likely to be conservative

Schellenberg 2004   (*Continued*)

Study adequately protected against contamination	Low risk	The 2 comparison districts were chosen for several reasons: They were geographically contiguous although separated from intervention districts by an uninhabited game reserve, so population movement between intervention and comparison areas was negligible

ARI: acute respiratory infection
ICDDR,B: International Center for Diarrheal Disease Research, Bangladesh
IMCI: integrated management of childhood illness
IMNCI: integrated management of neonatal and childhood illness
ORS: oral rehydration salts

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

Study	Reason for exclusion
Adam 2009	Involves secondary analysis from an included trial; outcome not of interest
Ali 2005	CBA study with 1 intervention and 1 control cluster (district) Intervention comprised a non-specific community-based public health intervention derived from community component of IMCI
Almagambetova 2000	Short report summarizing conclusions from a strategy implementation conference on IMCI, not primary research
Amorim 2008	• Retrospective analysis in which allocation was done by level of performance of clusters in implementation of IMCI, which is likely to confound results as well • Baseline data (before implementation of IMCI) not available • ITT analysis not done [The analysis, mentioned in the Discussion, showed 72% of 175 children were correctly managed in IMCI areas; 56% of 183 were correctly managed in non-IMCI facilities (P value = 0.02). IMCI was associated with 30% higher quality of case management]
Atakuoma Dzayisse 2006	Non-randomised controlled cross-sectional trial with 1 intervention and 1 control cluster
Bradley 2005	Intervention did not involve IMCI
Camara 2008	No control group
Chopra 2005	No control group

Chowdhury 2008	Observational study, no control group (subset of Arifeen study that studies the outcome of treatment guidelines for pneumonia in IMCI area)
Core Group 2009	Study has no control group Studies the impact of community IMCI component only
Ebuehi 2009	Studies the impact of community IMCI component only (3 components vs 2 components of IMCI). Only 2 study clusters: 1 in the intervention arm and the other in the control arm
Ebuehi 2010	CBA study with only 1 intervention and 1 control cluster; intervention involved assessed only the C-IMNCI component of IMCI. Intervention zone had all 3 components vs first 2 components of IMCI in control area
Edward 2007	Pre- and post-intervention study with **no control group**
Ertem 2006	Intervention involved care for development, which is a component of IMCI, and not generic IMCI; outcome studied was mental development, which was not of interest
Esaghi 2012	Non-randomised controlled trial with 1 study group and 1 control cluster. Excluded because fewer than 2 clusters in study and control groups
Gebresellasie 2011	Intervention consisted of health education component only for IMCI. Essential component of health worker training was missing. Only 1 control and 1 intervention component in a non-randomised controlled trial
Ghimire 2010	Intervention involved health education component only for IMCI. Essential component of health worker training was missing
Gilroy 2004	Outcome not of interest; pertains to counselling tasks by IMCI provider
Gouws 2004	Study is a secondary analysis of data collected from WHO MCE studies
Hamad 2011	Intervention consisted only of health education component of IMCI. Essential component of health worker training was missing
Harkins 2008	Assesses effects of community IMCI only; no control group
Huicho 2005	No control group
Huicho 2008	Observational study, no control group Outcomes not of interest
Igarashi 2010	Intervention consisted of assessment of GMP+, which is a community-based program based on PHC and IMCI. IMCI services provided in both control and intervention areas
Jin 2007	Intervention involved care for development module, which is part of IMCI, and not the WHO generic IMCI Outcome studied was mental development, which was not of interest

Kelley 2001	Intervention consisted of performance feedback on compliance with IMCI protocol by health care workers
Kumar 2009	Study compared 5 days vs 8 days of training of health care workers on the basis of performance; no control group included
Lulseged 2002	Narrative review of Ethiopia's experience with IMCI; no data presented
Mahalli 2011	Retrospective cohort study with 1 study group and 1 control cluster Excluded because fewer than 2 clusters were included in study and control groups, and outcome was drug prescribing practices, which was not of interest
Mohan 2004	Doctors in both intervention and control clusters received training of different duration; no control group
Moti 2008	• Comparison of 1 implementation cluster vs 1 control cluster • Control cluster also had partial rollout of IMCI program
Naimoli 2006	Study is a cross-sectional survey conducted in 2 control and 2 intervention clusters 6 to 12 months after implementation of IMCI, with no baseline data; does not qualify as a CBA trial
Oluwole 2000	Editorial reviewing the impact of IMCI, not an original research study
Osterholt 2009	Study compared provision of IMCI with "usual" supports vs IMCI training with special supports (job aids, non-financial incentives, and supervision of workers and Supervisors). Thus health care workers received IMCI training in both groups with no control group included
Pariyo 2005	No study and intervention population. Analysis compares the performance of health care workers by IMCI training No data on performance of health care workers before they were trained for IMCI
Pelto 2004	Intervention involved an IMCI derived nutrition counselling protocol, not the entire generic IMCI training
Prado 2006	Intervention involved Family Health Program, in whose context IMCI is being implemented, but involved 1 control and intervention cluster only. Outcome of maternal knowledge, which was not of interest
Rakha 2013	No control group (retrospective analysis of mortality data before and after implementation of IMCI)
Rowe 2011	Non-randomised controlled trial with 1 intervention and 1 control cluster. Excluded because fewer than 2 clusters were found in study and control groups [the analysis is mentioned in the Discussion. In intervention area, mortality decreased (risk ratio (RR) 0.870, 95% CI 0.841 to 0.900); in comparison area, mortality unchanged (RR 1.013, 95% CI 0.979 to 1.049). Intervention-area trend was 14.1% lower than comparison-area trend (95% CI 9.8% to 18.2%)]
Santos 2001	Intervention consisted of IMCI-derived nutrition counselling protocol, not the entire generic IMCI training

Senn 2011	No control group
Talsania 2011	Intervention consisted of health education component only for IMCI. Essential component of health care worker training was missing
Thompson 2009	Study has no control group. Studies the impact of community IMCI component only
Uzochukwu 2008	Assesses effects of short-term training of IMCI on health care worker performance with **no control group**
Wammanda 2003	No control group; intervention does not involve IMCI training; outcome (cost of drugs prescribed) not of interest
Zaman 2008	Study had just 1 module of IMCI, namely, nutrition counselling, not generic IMCI as the intervention
Zhang 2007	Pre- and post-intervention field survey with **no control group**
Zurovac 2006	Qualitative review of studies on treatment of febrile illness in sub-Saharan Africa - obviously irrelevant

CBA: controlled before-after study
CI: confidence interval
C-IMNCI: community integrated management of neonatal and childhood illness
IMCI: integrated management of childhood illness
ITT: intention-to-treat
MCE: Multi-Country Evaluation of IMCI Effectiveness, Cost and Impact
PHC: primary health care
RR: risk ratio
WHO: World Health Organization

Characteristics of studies awaiting assessment *[ordered by study ID]*

Boone 2016

Methods	**Design:** cluster RCT **Unit of allocation:** villages or groups of villages
Participants	Women between 15 and 49 years of age; those who were primary care givers of children younger than 5 years of age Children younger than 5 years of age
Interventions	• Providing IMCI training of community health care workers • Improving community health practices
Outcomes	• Under 5 mortality • Neonatal and infant mortality • Child morbidity • Maternal mortality

Boone 2016   *(Continued)*

	• Treatment practices for sick children
Notes	

· Characteristics of studies, Characteristics of studies awaiting classification: Insert these footnotes at end of section:

IMCI: integrated management of childhood illness

RCT: randomised controlled trial

DATA AND ANALYSES

Comparison 1. IMCI versus standard services

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Mortality	3		Rate Ratio (Fixed, 95% CI)	Totals not selected
1.1 Neonatal mortality (RCT)	1		Rate Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]
1.2 Infant mortality (RCT)	1		Rate Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]
1.3 Child mortality (RCT)	1		Rate Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]
1.4 Child mortality (CBA)	1		Rate Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]
2 Mortality (infant and child combined)	2		Rate Ratio (Fixed, 95% CI)	0.85 [0.78, 0.93]
2.1 Child mortality	1		Rate Ratio (Fixed, 95% CI)	0.87 [0.68, 1.10]
2.2 Infant mortality	1		Rate Ratio (Fixed, 95% CI)	0.85 [0.77, 0.94]
3 Stunting	3		Risk Ratio (Random, 95% CI)	Subtotals only
3.1 Cluster RCTs	2		Risk Ratio (Random, 95% CI)	0.94 [0.84, 1.06]
3.2 CBA studies	1		Risk Ratio (Random, 95% CI)	1.06 [0.92, 1.23]
4 Wasting	3		Risk Ratio (Fixed, 95% CI)	Subtotals only
4.1 Cluster RCTs	2		Risk Ratio (Fixed, 95% CI)	1.04 [0.87, 1.25]
4.2 CBA studies	1		Risk Ratio (Fixed, 95% CI)	1.20 [0.54, 2.68]
5 Measles vaccine coverage	3		Risk Ratio (Fixed, 95% CI)	Subtotals only
5.1 Cluster RCTs	2		Risk Ratio (Fixed, 95% CI)	0.92 [0.80, 1.05]
5.2 CBA studies	1		Risk Ratio (Fixed, 95% CI)	0.95 [0.89, 1.01]
6 DPT vaccine coverage	2		Risk Ratio (Fixed, 95% CI)	Subtotals only
6.1 Cluster RCTs	1		Risk Ratio (Fixed, 95% CI)	0.95 [0.68, 1.33]
6.2 CBA studies	1		Risk Ratio (Fixed, 95% CI)	0.86 [0.80, 0.92]
7 Vitamin A vaccine coverage	2		Risk Ratio (Fixed, 95% CI)	Subtotals only
7.1 Cluster RCTs	1		Risk Ratio (Fixed, 95% CI)	0.93 [0.88, 0.98]
7.2 CBA studies	1		Risk Ratio (Fixed, 95% CI)	1.00 [0.90, 1.12]
8 IMCI deliverable - exclusive breast feeding	3		Risk Ratio (Fixed, 95% CI)	Totals not selected
8.1 Cluster RCTs	2		Risk Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]
8.2 CBA studies	1		Risk Ratio (Fixed, 95% CI)	0.0 [0.0, 0.0]
9 Appropriate care seeking	3		Risk Ratio (Fixed, 95% CI)	Totals not selected

Analysis 1.1. Comparison 1 IMCI versus standard services, Outcome 1 Mortality.

Review: Integrated management of childhood illness (IMCI) strategy for children under five

Comparison: 1 IMCI versus standard services

Outcome: 1 Mortality

Study or subgroup	log [Rate Ratio] (SE)	Rate Ratio IV,Fixed,95% CI	Rate Ratio IV,Fixed,95% CI
1 Neonatal mortality (RCT)			
Bhandari 2012	-0.0943 (0.0632)		0.91 [0.80, 1.03]
2 Infant mortality (RCT)			
Bhandari 2012	-0.1625 (0.0504)		0.85 [0.77, 0.94]
3 Child mortality (RCT)			
Arifeen 2009	-0.1438704 (0.1229592)		0.87 [0.68, 1.10]
4 Child mortality (CBA)			
Schellenberg 2004	-0.1392621 (0.0943878)		0.87 [0.72, 1.05]

                                    0.01   0.1   1   10   100
                                    Favours IMCI   Favours control
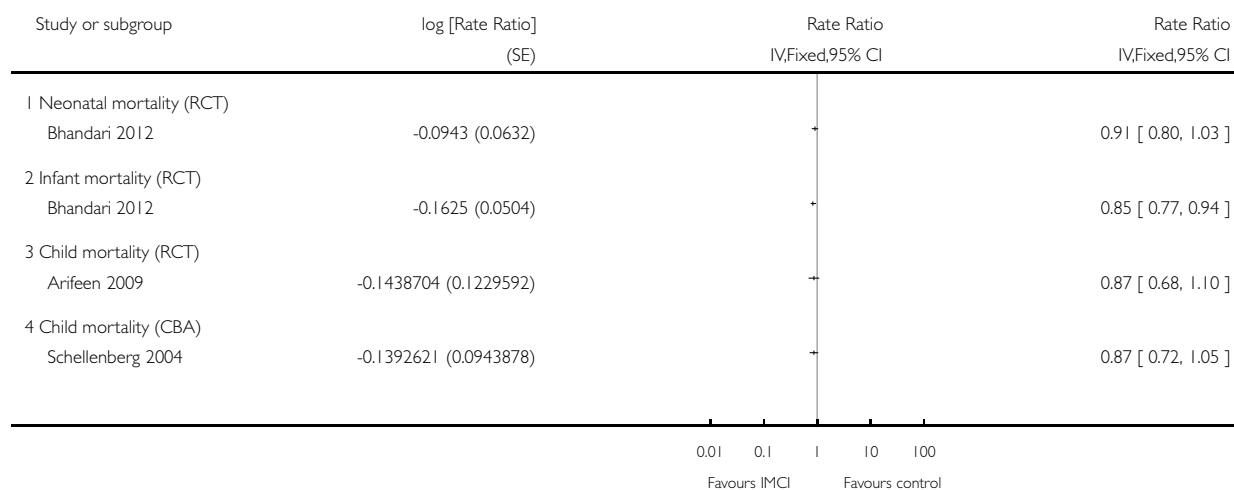
Analysis 1.2.   Comparison 1 IMCI versus standard services, Outcome 2 Mortality (infant and child combined).

Review: Integrated management of childhood illness (IMCI) strategy for children under five

Comparison: 1 IMCI versus standard services

Outcome: 2 Mortality (infant and child combined)

Study or subgroup	log [Rate Ratio] (SE)	Rate Ratio IV,Fixed,95% CI	Weight	Rate Ratio IV,Fixed,95% CI
1 Child mortality				
Arifeen 2009	-0.1438704 (0.1229592)		14.4 %	0.87 [0.68, 1.10]
Subtotal (95% CI)			**14.4 %**	**0.87 [0.68, 1.10]**
Heterogeneity: not applicable				
Test for overall effect: Z = 1.17 (P = 0.24)				
2 Infant mortality				
Bhandari 2012	-0.1625 (0.0504)		85.6 %	0.85 [0.77, 0.94]
Subtotal (95% CI)			**85.6 %**	**0.85 [0.77, 0.94]**
Heterogeneity: not applicable				
Test for overall effect: Z = 3.22 (P = 0.0013)				
Total (95% CI)			**100.0 %**	**0.85 [0.78, 0.93]**
Heterogeneity: Chi² = 0.02, df = 1 (P = 0.89); I² =0.0%				
Test for overall effect: Z = 3.43 (P = 0.00061)				
Test for subgroup differences: Chi² = 0.02, df = 1 (P = 0.89), I² =0.0%				

```
            0.01   0.1    1    10    100
            Favours IMCI      Favours control
```

Analysis 1.3. Comparison 1 IMCI versus standard services, Outcome 3 Stunting.

Review: Integrated management of childhood illness (IMCI) strategy for children under five

Comparison: 1 IMCI versus standard services

Outcome: 3 Stunting

Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Random,95% CI	Weight	Risk Ratio IV,Random,95% CI
1 Cluster RCTs				
Arifeen 2009 (1)	-0.1272 (0.0565)		40.9 %	0.88 [0.79, 0.98]
Bhandari 2012	-0.0101 (0.0264)		59.1 %	0.99 [0.94, 1.04]
Subtotal (95% CI)			**100.0 %**	**0.94 [0.84, 1.06]**
Heterogeneity: Tau² = 0.00; Chi² = 3.53, df = 1 (P = 0.06); I² =72%				
Test for overall effect: Z = 1.01 (P = 0.31)				
2 CBA studies				
Schellenberg 2004	0.0611 (0.0738)		100.0 %	1.06 [0.92, 1.23]
Subtotal (95% CI)			**100.0 %**	**1.06 [0.92, 1.23]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.83 (P = 0.41)				
Test for subgroup differences: Chi² = 1.62, df = 1 (P = 0.20), I² =38%				

```
       0.5   0.7    1    1.5    2
         Favours IMCI    Favours control
```

(1) Arifeen adjusted for clustering using an ICC of 0.01. Bhandari is adjusted

Analysis 1.4. Comparison 1 IMCI versus standard services, Outcome 4 Wasting.

Review: Integrated management of childhood illness (IMCI) strategy for children under five

Comparison: 1 IMCI versus standard services

Outcome: 4 Wasting

Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Cluster RCTs				
Arifeen 2009 (1)	-0.1215 (0.1772)		25.9 %	0.89 [0.63, 1.25]
Bhandari 2012	0.0998 (0.1047)		74.1 %	1.10 [0.90, 1.36]
Subtotal (95% CI)			**100.0 %**	**1.04 [0.87, 1.25]**
Heterogeneity: Chi² = 1.16, df = 1 (P = 0.28); I² =14%				
Test for overall effect: Z = 0.47 (P = 0.64)				
2 CBA studies				
Schellenberg 2004	0.1862 (0.4075)		100.0 %	1.20 [0.54, 2.68]
Subtotal (95% CI)			**100.0 %**	**1.20 [0.54, 2.68]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.46 (P = 0.65)				
Test for subgroup differences: Chi² = 0.12, df = 1 (P = 0.73), I² =0.0%				

```
        0.5   0.7   1   1.5   2
      Favours IMCI    Favours Control
```

(1) Arifeen adjusted for clustering using ICC 0.01. Bhandari is adjusted

Review: Integrated management of childhood illness (IMCI) strategy for children under five

Comparison: 1 IMCI versus standard services

Outcome: 5 Measles vaccine coverage

Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Cluster RCTs				
Arifeen 2009 (1)	-0.086 (0.0744)		85.0 %	0.92 [0.79, 1.06]
Bhandari 2012	-0.0834 (0.1772)		15.0 %	0.92 [0.65, 1.30]
Subtotal (95% CI)			**100.0 %**	**0.92 [0.80, 1.05]**
Heterogeneity: Chi² = 0.00, df = 1 (P = 0.99); I² =0.0%				
Test for overall effect: Z = 1.25 (P = 0.21)				
2 CBA studies				
Schellenberg 2004	-0.0523 (0.0326)		100.0 %	0.95 [0.89, 1.01]
Subtotal (95% CI)			**100.0 %**	**0.95 [0.89, 1.01]**
Heterogeneity: not applicable				
Test for overall effect: Z = 1.60 (P = 0.11)				
Test for subgroup differences: Chi² = 0.19, df = 1 (P = 0.66), I² =0.0%				

```
        0.5   0.7   1   1.5   2
     Favours control    Favours IMCI
```

(1) Adjusted for clustering using an estimated ICC of 0.01

Analysis 1.6.   Comparison 1 IMCI versus standard services, Outcome 6 DPT vaccine coverage.

Review: Integrated management of childhood illness (IMCI) strategy for children under five

Comparison: 1 IMCI versus standard services

Outcome: 6 DPT vaccine coverage

Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Cluster RCTs				
Bhandari 2012	-0.0513 (0.1706)		100.0 %	0.95 [0.68, 1.33]
Subtotal (95% CI)			**100.0 %**	**0.95 [0.68, 1.33]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.30 (P = 0.76)				
2 CBA studies				
Schellenberg 2004	-0.1503 (0.0369)		100.0 %	0.86 [0.80, 0.92]
Subtotal (95% CI)			**100.0 %**	**0.86 [0.80, 0.92]**
Heterogeneity: not applicable				
Test for overall effect: Z = 4.07 (P = 0.000046)				
Test for subgroup differences: Chi² = 0.32, df = 1 (P = 0.57), I² =0.0%				

```
        0.5    0.7    1    1.5    2
      Favours control    Favours IMCI
```

Analysis 1.7. Comparison 1 IMCI versus standard services, Outcome 7 Vitamin A vaccine coverage.

Review: Integrated management of childhood illness (IMCI) strategy for children under five

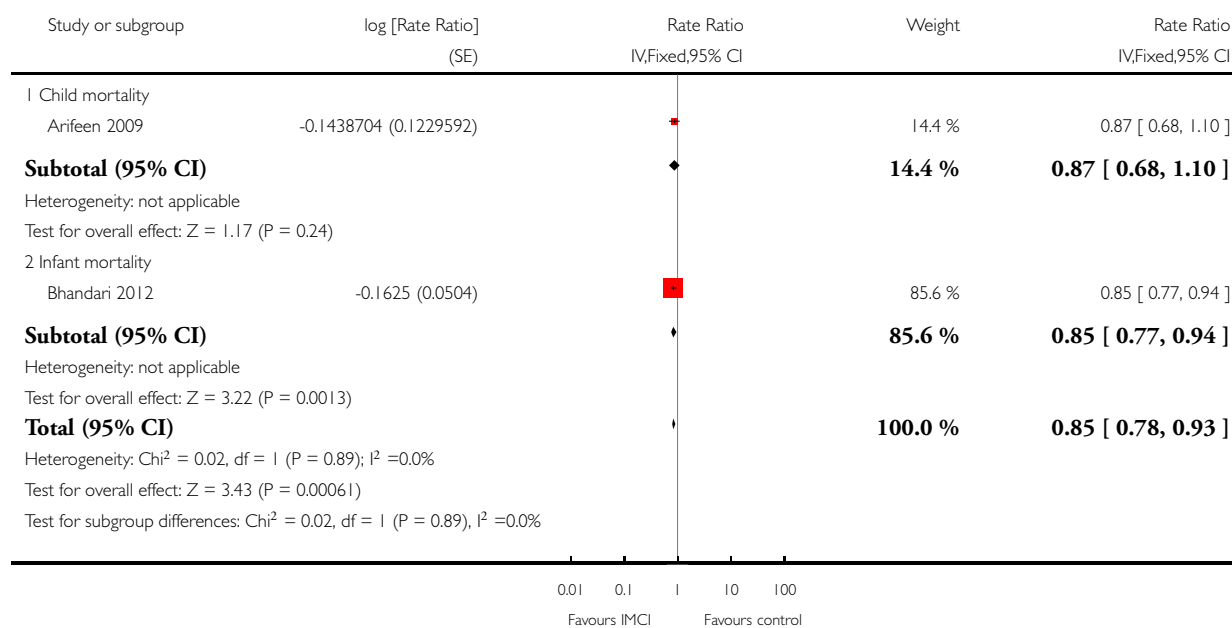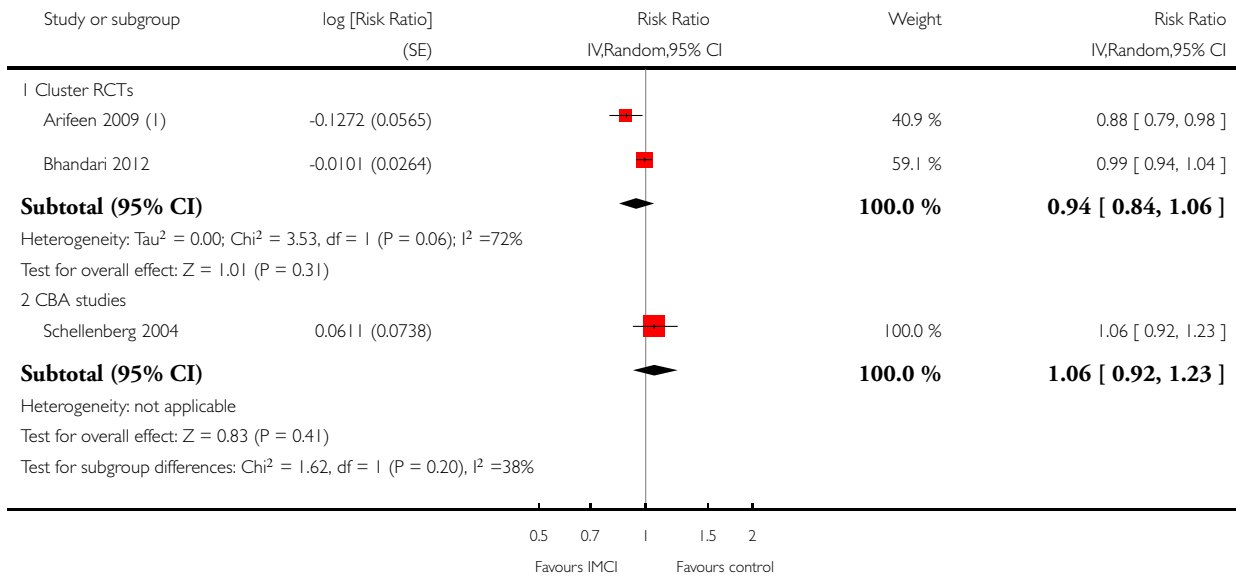Comparison: 1 IMCI versus standard services

Outcome: 7 Vitamin A vaccine coverage

Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Fixed,95% CI	Weight	Risk Ratio IV,Fixed,95% CI
1 Cluster RCTs				
Arifeen 2009 (1)	-0.0738 (0.0292)		100.0 %	0.93 [0.88, 0.98]
Subtotal (95% CI)			**100.0 %**	**0.93 [0.88, 0.98]**
Heterogeneity: not applicable				
Test for overall effect: Z = 2.53 (P = 0.011)				
2 CBA studies				
Schellenberg 2004	0.0032 (0.0559)		100.0 %	1.00 [0.90, 1.12]
Subtotal (95% CI)			**100.0 %**	**1.00 [0.90, 1.12]**
Heterogeneity: not applicable				
Test for overall effect: Z = 0.06 (P = 0.95)				
Test for subgroup differences: Chi² = 1.49, df = 1 (P = 0.22), I² =33%				

```
                    0.5   0.7    1    1.5    2
                  Favours control   Favours IMCI
```

(1) We adjusted for clustering using ICC 0.01

Analysis 1.8. Comparison 1 IMCI versus standard services, Outcome 8 IMCI deliverable - exclusive breast feeding.

Review: Integrated management of childhood illness (IMCI) strategy for children under five

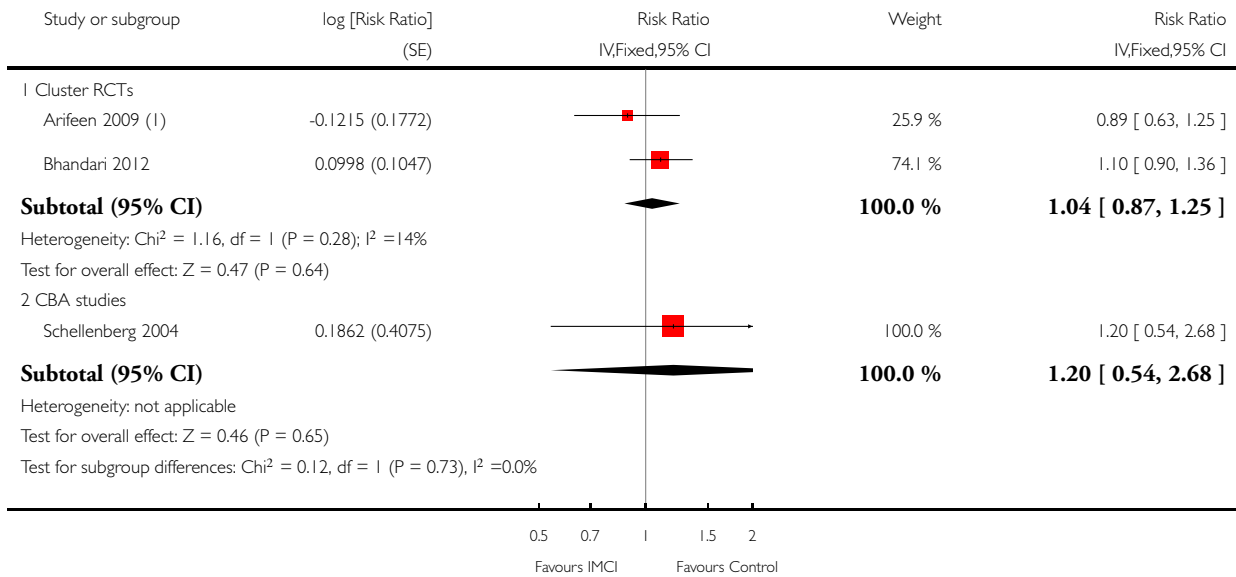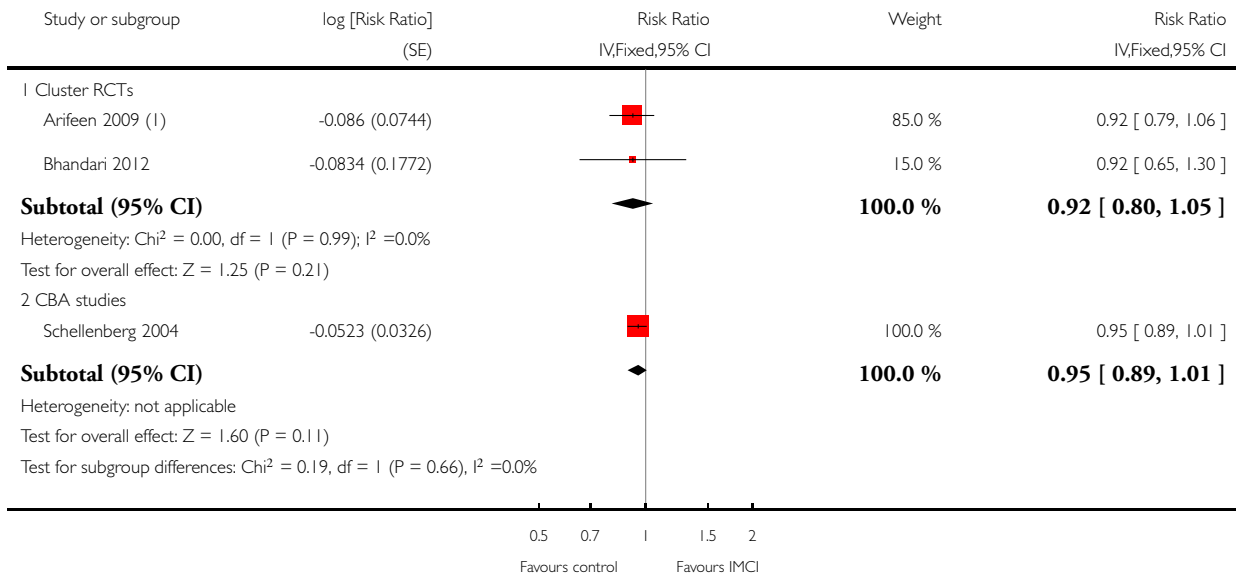Comparison: 1 IMCI versus standard services

Outcome: 8 IMCI deliverable - exclusive breast feeding

Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Fixed,95% CI	Risk Ratio IV,Fixed,95% CI
1 Cluster RCTs			
Arifeen 2009 (1)	0.4759 (0.2386)		1.61 [1.01, 2.57]
Bhandari 2012	1.8437 (0.0908)		6.32 [5.29, 7.55]
2 CBA studies			
Schellenberg 2004	-0.4735 (0.4158)		0.62 [0.28, 1.41]

```
            0.05   0.2    1    5    20
         Favours control    Favours IMCI
```
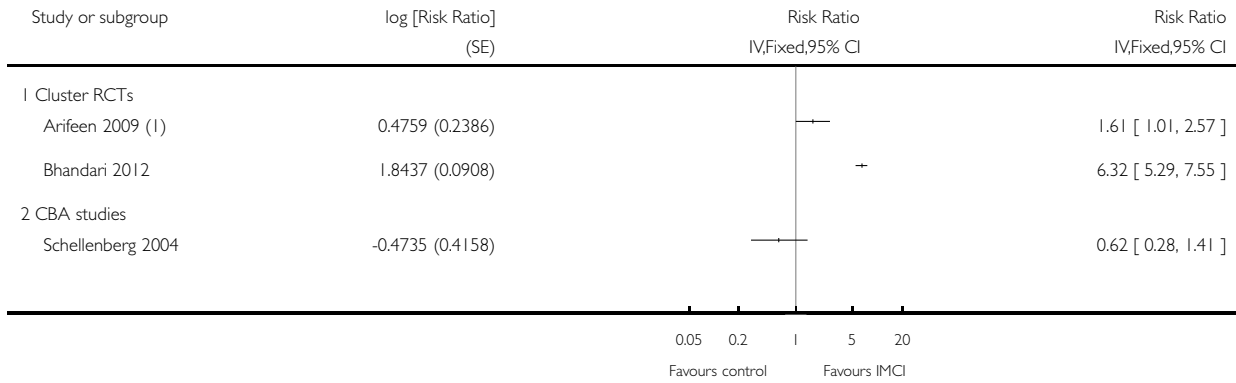
(1) Arifeen adjusted for clustering using ICC 0.01. Bhandari already adjusted

Analysis 1.9.   Comparison 1 IMCI versus standard services, Outcome 9 Appropriate care seeking.

Review: Integrated management of childhood illness (IMCI) strategy for children under five

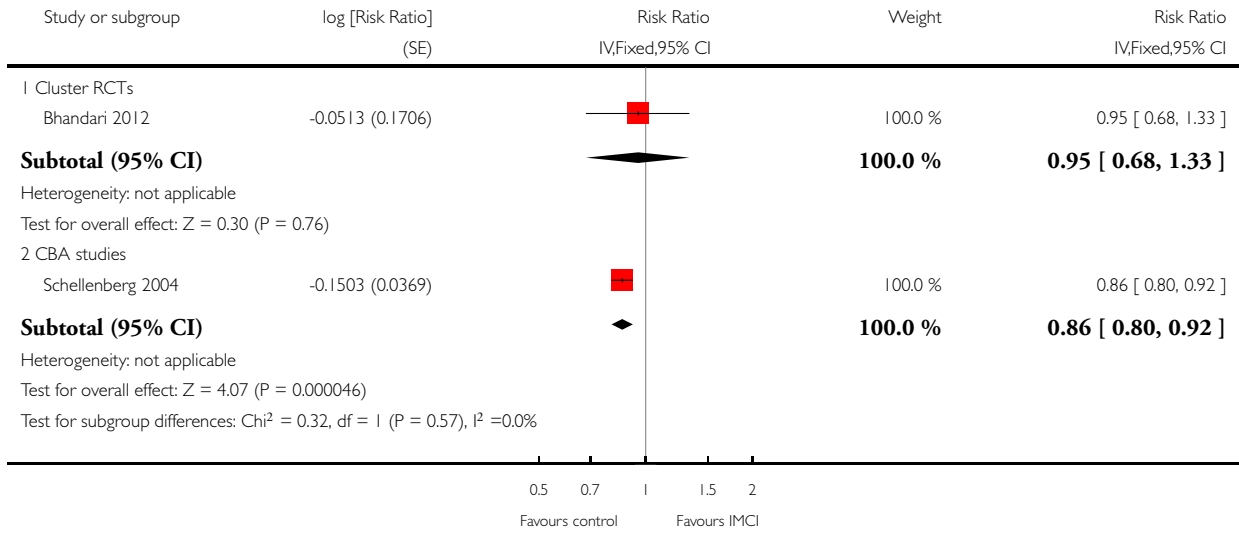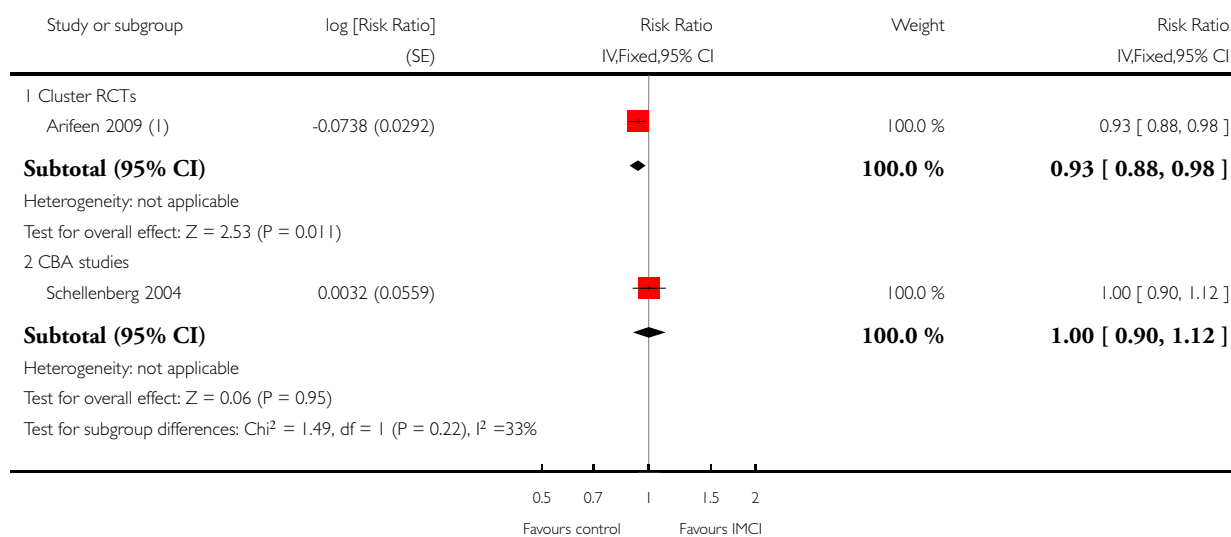Comparison: 1 IMCI versus standard services

Outcome: 9 Appropriate care seeking

Study or subgroup	log [Risk Ratio] (SE)	Risk Ratio IV,Fixed,95% CI	Risk Ratio IV,Fixed,95% CI
Arifeen 2009	1.6015 (0.2636)		4.96 [2.96, 8.32]
Bhandari 2012	0.5653 (0.1241)		1.76 [1.38, 2.24]
Schellenberg 2004	0.168 (0.0891)		1.18 [0.99, 1.41]

```
            0.01   0.1    1    10    100
         Favours control    Favours IMCI
```
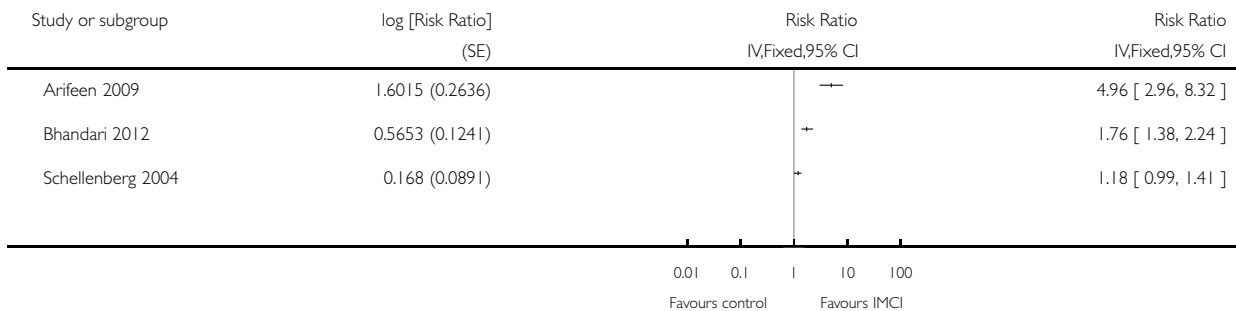
ADDITIONAL TABLES

Table 1. IMCI components

			Schellenberg 2004	Arifeen 2009	Mohan 2011	Bhandari 2012
Human resources policies for health care professionals	IMCI training	Basic health care worker	Y	Y	Y	Y
		Senior/other			Y	Y
		Doctors				Y
		TBA				Y
		Refresher				
		Private sector				Y
	Staff recruitment	Filling vacancies				Y
		New cadre of community health care worker (CHW)		Y		
	Conditions of service	Cash incentives				Y
	Management	Home visits		Y	Y	Y
		Supervision and monitoring		Y	Y	Y
Health system strengthening	Tools and manuals including guidelines	Supply education materials	Y	Y		
	Additional equipment and drugs	Drug supply	Y[a]	Y	Y	Y
		Supply minor equipment		Y		
Strategies for community engagement	Training	Unqualified village doctors		Y		Y
	Social development	Establishing mother/women group meetings		Y		Y

Table 1. IMCI components *(Continued)*

		Support of com-munity leaders/volunteers		Y	
		Community the-atre		Y	

IMCI: integrated management of childhood illness; **TBA:** traditional birth attendant

[a]Assumed, as the study is an assessment of first 2 components of World Health Organization (WHO) generic integrated management of childhood illness (IMCI)

Table 2. Details of inputs described narratively

Study	Input
Schellenberg 2004	Incorporated 2 components of integrated management of childhood illness (IMCI), namely, training of health care workers and health system strengthening. All health care workers at the primary level received 11 days of training. IMCI nutrition education and counselling cards for educating mothers were prepared after operational research and subsequently translated into Swahili language to improve community practices. Health systems were strengthened using IMCI processes and by providing financial resources of approximately $0.92 per capita to implementing districts
Arifeen 2009	Incorporated all 3 components of IMCI. Health care workers were trained using the 11-day course, followed by a 3-day course on breast feeding counselling. Health systems strengthening consisted of making additional drugs available in the intervention area, and setting up a facility-level drug tracking and reporting system. Job aids such as weighing scales, timer to count respiratory rate, thermometers, chart booklets, and locally adapted cards as aids for counselling mothers were provided to all intervention clusters. To improve community practices, special emphasis was given to messages related to pneumonia and malnutrition and to 3 practice areas, namely, care seeking for sick children, home management of illness, and responsive feeding
Mohan 2011	Retrospectively collected data about IMCI implementation from 12 districts that started implementation in 2005. Details of the intervention have not been described specifically for these 12 districts but are available for the entire country as part of a standard guideline. Training consisted of the 8-day course for community-based workers and auxiliary nurse midwives and an additional 2 days for supervisors. Workers are supposed to receive basic drugs and supplies as per guidelines of the Reproductive and Child Health II and Integrated Child Development Scheme (ICDS) programs. Community health practices include home visits to all newborns during which health care workers ensure exclusive breast feeding, provide counsel on temperature maintenance, explain danger signs, assess newborns (and other sick children) and refer them to an appropriate health facility, if required
Bhandari 2012	Health care workers were trained with the 8-day IMNCI Basic Health Worker Course, and specialists received the 11-day IMNCI Course for Physicians. Health systems interventions included (1) strengthened supervision of community health care workers and nurses and filling of vacant supervisor positions; (2) task-based incentives to include IMNCI activities; and (3) establishment of drug depots in villages to ensure regular supply of drugs. Community health care workers made scheduled post-natal home visits, promoted breast feeding, delayed bathing, provided cord care, and responded to care seeking for illness. They also ran women's health group meetings to increase awareness of healthy newborn care practices

Table 3. Results: mortality

Outcome	Trial ID	Study design	Pre-intervention mortality rate		Post-intervention mortality rate		Cluster-adjusted relative effect (95% CI)	Coverage indicators analysis summary
			IMCI	Control	IMCI	Control		
Neonatal mortality	Bhandari 2012[a]	Cluster RCT	32.6/1000 live births (n NA)	32.4/1000 live births (n NA)	41.9/1000 live births (1244/29, 667)	43/1000 live births (1326/30, 813)	**Hazard ratio 0.91**[b,c] (0.80 to 1.03)	Adjusted for confounders
Infant mortality	Bhandari 2012	Cluster RCT	44.9/1000 live births (n NA)	43.9/1000 live births (n NA)	65 per 1000 live births (1925/29, 667)	69 per 1000 live births (2136/30, 813)	**Hazard ratio 0.85**[b] (0.77 to 0.94)	Adjusted for confounders
Child mortality	Arifeen 2009[d]	Cluster RCT	43.0 per 1000 live births (144/3348)	44.8 per 1000 live births (179/3996)	27.0 per 1000 live births (157/5815)	31.2 per 1000 live births (221/7083)	**Risk ratio 0.87** (0.66 to 1.14)	No effect after exclusion of injuries[e]
	Schellenberg 2004[f]	CBA	27.2 per 1000 child-years (639/23, 515)	27.0 per 1000 child-years (242/8977)	24.4 per 1000 child-years (1220/49, 964)	28.2 per 1000 years (619/21, 965)	**Risk ratio 0.87** (0.72 to 1.05)	No effect after adjustment

CBA: controlled before-after study; **IMCI**: integrated management of childhood illness; **RCT**: randomised controlled trial

[a] Bhandari 2012: Fieldworkers not involved with IMNCI implementation visited households monthly to identify new pregnancies. Infants were visited at 1, 3, 6, 9, and 12 months to determine survival

[b] Bhandari 2012: Hazard ratio was calculated after adjustment for cluster design and potential confounders between groups (markers of poverty, literacy, access to services)

[c] Bhandari 2012: Although the overall effect was not statistically significant, a subgroup analysis found that a statistically significant reduction in neonatal mortality was significantly lower in the subgroup born at home (adjusted HR 0.80, 95% CI 0.68 to 0.93)

[d] Arifeen conducted a household census in 2000 and 2007 where the complete birth history of all ever married women between the age of 15 and 49 years was used to estimate yearly and 2 year mortality rates. The data pertains to mortality between day 7 and 5 years of life.

[e] After exclusion of deaths due to malformation and injury (causes not related to IMCI), no effect of IMCI was noted on mortality (data not available)

[f] This is the value adjusted for baseline differences in mortality. Unadjusted value is 4.2/1000 fewer deaths (95% CI -4.1 to 12.4). Mortality was slightly higher in the control group at baseline. Schellenberg study (Schellenberg 2004)

Also estimated mortality difference after "ignoring the between district variation" as 13% lower mortality (95% CI 5% to 21% lower) (P value = 0.004); risk ratio 0.87 (95% CI 0.79 to 0.95)

Table 4. Results: nutritional parameters

Parameter	Study	Study design	Pre-intervention		Post-intervention	
			IMCI % (n/N)	Control % (n/N)	IMCI % (n/N)	Control % (n/N)
Wasting	Arifeen 2009[a]	Cluster RCT	21.5% (74/346)	21.6% (95/439)	12.6% (89/706)	14.3% (101/709)
	Schellenberg 2004[b]	CBA	12.57% (21/167)	10.5% (21/200)	6.8% (13/191)	5.6% (10/177)
	Bhandari 2012	Cluster RCT			16.6% (243/1461)	14.3% (202/1412)
Stunting	Arifeen 2009[c]	Cluster RCT	63.1% (334/530)	62.5% (432/692)	50.4% (599/1189)	57.1% (674/1180)
	Schellenberg 2004[c,d]	CBA	59.7% (297/497)	51.1% (247/483)	42.6% (249/585)	40.0% (191/477)
	Bhandari 2012	Cluster RCT			49.6% (725/1461)	48.2% (680/1412)
Low weight for age	Schellenberg 2004[e]	CBA	30.6% (290/947)	26.3% (238/905)	23.4% (234/1001)	19.5% (161/825)
HAZ score Mean (SD)	Arifeen 2009	Cluster RCT	-2.35 (0.20)	-2.39 (0.33)	-2.01 (0.14)	-2.17 (0.20)
WHZ score Mean (SD)	Arifeen 2009	Cluster RCT	-1.18 (0.20)	-1.23 (0.19)	-0.77 (0.25)	-0.84 (0.14)

CBA: controlled before-after; **HAZ:** height for age z-score; **IMCI:** integrated management of childhood illness; **RCT:** randomised controlled trial; **WHZ:** weight for age z-score

[a] WHZ $\leq$ 2 in children 0 to 23 months of age. Data from baseline and end surveys

[b] WHZ $\leq$ 2 in children 12 to 23 months of age. Data from baseline and end surveys

[c] HAZ $\leq$ 2 in children 24 to 59 months of age. Data from baseline and end surveys

[d] When expressed as mean haz scores, differential change between IMCI and comparison districts reached statistical significance (data not available/depicted)

[e] WAZ $\leq$ 2. Data from baseline and end surveys

Table 5. Results: quality (facility level)

Outcome	Study	Pre-intervention		Post-intervention	
		IMCI % (n/N)	Control % (n/N)	IMCI % (n/N)	Control % (n/N)
Index of integrated assessment (0 to 100)	Arifeen 2009[a]	-	-	85.0% (150/176)	11.0% (15/132)
Correct management of all illness	Arifeen 2009[a]	-	-	64.6% (111/172)	10.2% (13/131)
Children with dehydration correctly treated	Arifeen 2009[a]	-	-	28.7% (1/4)	0.0% (0/2)
	Schellenberg 2004[b]	-	-	20.0% (1/5)	0.0% (0/3)
Child with pneumonia correctly treated	Arifeen 2009[a]	-	-	80.8% (46/ 57)	3.4% (1/ 31)
	Schellenberg 2004[b]	-	-	19.5% (45/231)	10.1% (19/188)
Child with anaemia correctly treated	Arifeen 2009[a]	-	-	0.0% (3)	0.0% (5)
Child needing referral was referred	Arifeen 2009[a]	-	-	35.7% (2/6)	25.0 % (1/4)
Children with fever treated with antimalarials	Schellenberg 2004[b]	39.4% (147/373)	44.5% (153/344)	27.4% (108/394)	34.2% (80/234)

IMCI: integrated management of childhood illness

[a] Data from health facility surveys done in 2003 and 2005 and estimates weighted by total number of sick children seen in facilities on survey days.

Baseline data collected in 2003, 1 year after initiation of facility-based IMCI. Indicators based on IMCI health facility survey guidelines

[b] Data from household surveys conducted in 1999 and 2002

Table 6. Results: quality (prescribing by lay health care workers)

Outcome	Study	Study design	Pre-Intervention		Post-intervention	
			IMCI % (n/N)	Control % (n/N)	IMCI % (n/N)	Control % (n/N)
Children with diarrhoea treated with ORS	Arifeen 2009	Cluster RCT	-	-	48% (60/125)	30% (32/108)
	Schellenberg 2004[a]	CBA	24.7% (21/85)	10.4% (10/96)	25.3% (23/91)	19.0% (15/79)
Change in % of children with diarrhoea treated with ORS	Mohan 2011[b]	CBA	-	-	1.6%	0.7%
Children with suspected pneumonia treated with antibiotics	Arifeen 2009	Cluster RCT	-	-	52% (156/300)	48% (167/348)

CBA: controlled before-after study; **IMCI:** integrated management of childhood illness; **ORS:** oral rehydration salts; **RCT:** randomised controlled trial

[a] Proportion of children ill in the last 2 weeks of the survey at baseline and at end of study period who were taken to an appropriate health care provider

[b] Data collected from 2 rounds of district-level health surveys in districts that implemented IMCI in 2005 and in control districts matched for IMR and proportion of scheduled castes and scheduled tribes. Weighted average of percentage change in coverage levels calculated for the 2 groups

Table 7. Results: coverage (vaccines)

Parameter	Study	Study design	Pre-intervention		Post-intervention	
			IMCI % (n/N)	Control % (n/N)	IMCI % (n/N)	Control % (n/N)
Measles vaccine coverage	Arifeen 2009[a,b]	Cluster RCT	36.9% (124/335)	32.2% (131/406)	52.7% (219/416)	57.4% (239/417)
	Bhandari 2012	Cluster RCT			11.1% (226/2045)	16.8% (339/2017)
	Schellenberg 2004[c]	CBA	88.3% (159/180)	89.4% (194/217)	88.2% (180/204)	93.0% (172/185)

Table 7. Results: coverage (vaccines) *(Continued)*

Change in coverage of all vaccines	Mohan 2011[d,e]	CBA	-	-	3.8%	11.1%
DPT3 vaccine coverage	Bhandari 2012	Cluster RCT			15.6% (318/2045)	21.2% (427/2017)
	Schellenberg 2004[c]	CBA	87.2% (157/180)	85.3% (185/217)	81.9% (167/204)	95.1% (176/185)
Vitamin A supplementation coverage	Arifeen 2009[a]	Cluster RCT	82.1% (272/331)	74.4% (301/405)	85.3% (355/416)	91.7% (381/415)
	Schellenberg 2004[c]	CBA	12.9% (25/194)	13.5% (28/208)	77% (154/200)	76.8% (142/185)

CBA: controlled before-after study; **DPT:** Diphtheria-Pertussis-Tetanus; **IMCI:** integrated management of childhood illness; **RCT:** randomised controlled trial

[a] Data available from 6 monthly household surveys at baseline and at end

[b] Data collected from vaccination cards

[c] Data collected through information or registration during household surveys

[d] Data collected from 2 rounds of district-level health surveys in districts that implemented IMCI in 2005 and in control districts matched for IMR and proportion of scheduled castes and scheduled tribes. Weighted average of percentage change in coverage levels calculated for the 2 groups

[e] Change in proportion of children fully immunized

Table 8. Results: coverage (care seeking behavior)

Outcome	Study	Study design	Pre-intervention		Post-intervention	
			IMCI % (n/N)	Control % (n/N)	IMCI % (n/N)	Control % (n/N)
Change (%) children with ARI seeking care	Mohan 2011[a]	CBA	NA	NA	+6.7%	-11.1%
Appropriate care seeking	Bhandari 2012[b]	Cluster RCT	NA	NA	46.9% (474/1010)	29.5% (374/1269)
	Arifeen 2009[c]	Cluster RCT	6% (18/302)	4% 14/360)	24% (111/462)	5% (24/483)
	Schellenberg 2004[d]	CBA	41.2% 211/512	42.2% (212/502)	38.2% (203/531)	32.3% (138/427)

Table 8. Results: coverage (care seeking behavior) *(Continued)*

Care seeking for children with danger signs	Schellenberg 2004[d]	CBA	53.1% (86/162)	68% (100/147)	54.9% (78/142)	43.4% (49/113)

ARI: acute respiratory infection; CBA: controlled before-after study; IMCI: integrated management of childhood illness; IMR: infant mortality rate; RCT: randomised controlled trial

[a] Data collected from 2 rounds of district-level health surveys in districts that implemented IMCI in 2005 and in control districts matched for IMR and proportion of scheduled castes and scheduled tribes. Weighted average of percentage change in coverage levels calculated for the 2 groups

[b] Proportion of neonates with danger signs who were taken to an appropriate health care provider (physician in government or private health facility or community health care worker)

[c] Proportion of children ill in the last 2 weeks of the survey at baseline and at end of study period who were taken to an appropriate health care provider

[d] Data from household surveys conducted in 1999 and 2002

Table 9. Results: coverage (breast feeding and other child rearing practices)

Practice	Study	Study design	Pre-intervention		Post-intervention	
			IMCI % (n/N)	Control % (n/N)	IMCI % (n/N)	Control % (n/N)
Exclusive breast feeding	Bhandari 2012 [a,b]	Cluster RCT	-	-	77.6% (4811/6204)	37.3% (2300/6163)
	Arifeen 2009[c]	Cluster RCT	56.3% (825/1466)	56.2% (1021/1817)	75.5% (1024/1356)	65.3% (1149/1759)
	Schellenberg 2004[d]	CBA	20.7% (23/111)	26.1% (18/69)	22.7% (15/66)	32.1% (17/53)
	Mohan 2011[e]	CBA	-	-	30.0%	24.3%
Complementary feeding	Arifeen 2009[f]	Cluster RCT	60.4% (734/1216)	52.8% (873/1653)	67.6% (792/1172)	57.2% (783/1369)
	Schellenberg 2004[f]	CBA	89.9% (71/79)	95.9% (70/73)	98.8% (80/81)	98.7% (74/75)
	Bhandari 2012[g]	Cluster RCT			33.6% (687/2045)	37.6% (759/2017)
Pre-lacteal feeds not given	Bhandari 2012[a]	Cluster RCT	-	-	80.2% (4977/6204)	32.6% (2006/6163)
Breast feeding initiated within 1 hour of	Bhandari 2012[a]	Cluster RCT	-	-	40.7% (2527/6204)	11.2% (689/6163)

Table 9. Results: coverage (breast feeding and other child rearing practices) *(Continued)*

birth						
	Mohan 2011[e]	CBA	-	-	18.1%	13.6%
Newborn care practices Delayed bathing	Bhandari 2012[a]	Cluster RCT	-	-	84.5% (5243/6204)	46.2% (2848/6163)
Cord care	Bhandari 2012 [a,h]	Cluster RCT			84.1% (5219/6204)	39.5% (2436/6163)
Appropriate clothing Skin-to-skin contact on day of birth	Bhandari 2012[a]	Cluster RCT			97.5% (6048/6204) 1.7% (108/6204)	97.9% (6036/6163) 0.0% (2/6163)

CBA: controlled before-after study; IMCI: integrated management of childhood illness; RCT: randomised controlled trial

[a] A separate team of research assistants interviewed a randomly selected subset of mothers at 29 days to ascertain newborn care practices

[b] Exclusive breast feeding at 4 weeks of life

[c] Children < 6 months exclusively breast feeding. Data from baseline and end population surveys

[d] Children younger than 4 months exclusively breast fed

[e] Data collected from 2 rounds of district-level health surveys in districts that implemented IMCI in 2005 and in control districts matched for IMR and proportion of scheduled castes and scheduled tribes. Weighted average of percentage change in coverage levels calculated for the 2 groups

[f] Children aged 6 to 9 months receiving both breast feeding and complementary food. Data from baseline and end population surveys

[g] Infants who received solid, semi solid, or soft foods in previous 24 hours and started complementary feeding between 6 and 8 months of age

[h] Nothing or Gentian Violet applied to the cord

APPENDICES

Appendix 1. Search log and Search strategy for Identification of trials from various databases

Database	Date Searched	Strategy	Hits
The Cochrane Central Register of Controlled Trials (CENTRAL)	30 June 2015	("IMCI") OR ("IMNCI") OR ("integrated management of childhood illness") OR ("integrated management of childhood illnesses") in All	28

(Continued)

		fields	
EMBASE, Ovid	30 June 2015	("IMCI") OR ("IMNCI") OR ("integrated management of childhood illness") OR ("integrated management of childhood illnesses") in All fields	468
CINAHL Plus, EbscoHost	30 June 2015	("IMCI") OR ("IMNCI") OR ("integrated management of childhood illness") OR ("integrated management of childhood illnesses") in All fields	375
LILACS, VHL	30 June 2015	("IMCI") OR ("IMNCI") OR ("integrated management of childhood illness") OR ("integrated management of childhood illnesseses") in All fields	198
WHOLIS, WHO	30 June 2015	("IMCI") OR ("IMNCI") OR ("integrated management of childhood illness") OR ("integrated management of childhood illnesseses") in All fields	58
POPLINE	30 June 2015	("IMCI") OR ("IMNCI") in All fields	427
Science Citation Index and Social Sciences Citation Index, ISI Web of Science	30 June 2015	("IMCI") OR ("IMNCI") OR ("integrated management of childhood illness") OR ("integrated management of childhood illnesses") in All fields	544
Global Health, OvidSP	08 May 2015	(IMCI or IMNCI or integrated management of childhood illness*).af	359
Health Management, ProQuest	17 December 2012	("IMCI") OR ("IMNCI") OR ("integrated management of childhood illness") OR ("integrated management of childhood illnesseses") in All fields	155
MEDLINE, Ovid	30 June 2015	("IMCI") OR ("IMNCI") OR ("integrated management of childhood illness") OR ("integrated management of childhood illnesseses") in All fields	381

CONTRIBUTIONS OF AUTHORS

TG drafted the protocol and developed and ran the search strategy, obtained copies of studies and selected studies for inclusion, extracted data, entered data into RevMan, performed the analysis, interpreted results, and drafted and updated the final review. DS ran the search strategy, obtained copies of studies and selected studies for inclusion, extracted data, carried out duplicate data entry, and provided critical inputs in the final review. HSS co-drafted the protocol and obtained copies of studies, resolved conflicts in selecting studies for inclusion, performed the analysis and interpreted results, and co-drafted the final review and provided guidance at all steps of the process. PG helped in drafting the protocol, assisted in interpreting the analysis, drafted the summary of findings table and rewrote the final review. MR provided statistical input, including the sensitivity analysis, interpreted cluster trials, entered data into Revman and helped draft the review. All authors agreed the final version of the review.

DECLARATIONS OF INTEREST

Prof. Harshpal S. Sachdev has served as a consultant to the Child and Adolescent Health Division of the World Health Organization, Geneva, to collate and interpret evidence related to the mortality benefit of the integrated management of childhood illness strategy.

SOURCES OF SUPPORT

Internal sources

- Sitaram Bhartia Institute of Science and Research, India.

Time Support for Prof. Harshpal S. Sachdev

External sources

- Department for International Development, UK.

This review is supported by the Effective Health Care Research Consortium funded by UKaid from the Department for International Development

DIFFERENCES BETWEEN PROTOCOL AND REVIEW

"If there are sufficient studies, we also summarised trials with a concurrent comparison group (no IMCI intervention) and adjustment for baseline characteristics and confounders" - as we found insufficient studies, we did not carry out this analysis. Two outcomes specified in the protocol were dropped from the review: illness episodes of diarrhoea and pneumonia, as it would be unusual for curative services to reduce the incidence of disease. One study also reported on other newborn care practices, which we did not anticipate, and we describe these results under "coverage."

We specified measures of mortality (neonatal, infant, and under-five mortality) rates and reported on these. We added a measure called "any mortality" and carried out meta-analysis on the study that reported infant mortality with the study that reported child mortality.