Effect of pneumonia case management on mortality in neonates, infants, and preschool children: a meta-analysis of community-based trials
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CRD summary
This review of the community-based case management approach proposed by the World Health Organization for developing countries concluded that intervention reduces mortality in neonates, infants and preschool children and should be part of primary health care. Significant heterogeneity was present for some outcomes, suggesting that the results may not be generalisable.

Authors' objectives
To estimate the effects of the pneumonia case-management approach advised by the World Health Organization (WHO) on mortality in pre-school children.

Searching
MEDLINE, SciMate, Current Contents and references from identified papers were searched; the search strategy was stated. Potential funding agencies for such research were contacted, e.g. the WHO Programme for the Control of Acute Respiratory Infections, the U.S. Agency for International Development and UNICEF. The authors of identified trials were also contacted for details of additional published and unpublished trials. Investigators in the identified trials were invited to join the Pneumonia Case Management Trials Group that reviewed the data and the analysis.

Study selection
Study designs of evaluations included in the review
Controlled trials were eligible for inclusion. The primary analysis included trials with a concurrent control group. Studies of a before-and-after design were analysed separately. One published trial in low birth weight infants was excluded since it was in a very selective group.

Specific interventions included in the review
Studies of the community-based case-management of pneumonia in developing countries, as proposed by the WHO (see Other Publications of Related Interest), were eligible for inclusion. The studies used education about the recognition of pneumonia and the need to seek attention at home or at a clinic, but this was not intensive in most studies. In some studies visits to the home were used to identify cases of pneumonia. Cointerventions included antibiotics (co-trimoxazole, injectable procaine penicillin and oral ampicillin), immunisation and treatment for diarrhoea.

Participants included in the review
Studies in pre-school children were eligible for inclusion. Studies in adults or in very selected groups of pre-school children were excluded. The included studies were of children in areas with a baseline infant mortality between 49 and 184 deaths per 1,000 live births, and with different levels of health service provision. Where reported, all of the studies were in areas where malnutrition was common.

Outcomes assessed in the review
The outcomes of interest were total mortality and mortality from pneumonia. The review classified any death with pneumonia (or acute lower respiratory infection) as a cause of pneumonia mortality, and not necessarily only deaths with pneumonia as the primary cause. The included studies used trained health workers to report deaths, with the cause of death usually being ascertained by a physician or panel of experts. Some studies also had episodic community assessments of deaths and of participants in the studies.

How were decisions on the relevance of primary studies made?
The authors did not state how the papers were selected for the review, or how many reviewers performed the selection.
Assessment of study quality
The validity of the individual studies was assessed and scored based on items assessing aspects of project design, data collection methods, training for and supervision of mortality data collection, and comparability of the treatment groups. The maximum possible validity score was 154 points. Intervention scores were based on intervention intensity, training, worker-to-population ratio, antibiotic availability and treatment compliance data. The maximum possible intervention score was 65 points. Cointervention scores were based on differential delivery between the treatment groups. The maximum possible co-intervention score was 45 points. The sum of the scores for validity, intervention and cointervention was used to assess methodological variability among the studies. Two reviewers who had not participated in the trials assessed and scored study design, intervention and cointerventions, based on data provided by the original trialists. The original trialists commented on the scoring of all studies and any disagreements were resolved by discussion.

Data extraction
The trial investigators completed standardised data extraction forms that were sent to the meta-analysis coordinating centre. The trial investigators provided information the study design, implementation of the intervention, cointerventions, person-time denominators for mortality data, and mortality for each year of the intervention. Information was also extracted on infant mortality, immunisation coverage, literacy, malnutrition, the availability of antibiotics, the availability of health services, treatment of diarrhea and antenatal care. All the investigators reviewed the data and the initial analysis, then additional data were obtained and the analysis was repeated. The results were circulated to the Pneumonia Case Management Trials Group for comments and correction.

Two reviewers who had not participated in the trials extracted summary data from the forms. Outcome data (total mortality and pneumonia mortality, together with denominators) were extracted for three age groups for each year of each study: neonatal, infants younger than 1 year, and children between 0 and 4 years. Where studies presented data for before-and-after and concurrent trials, both sets of data were extracted separately. Summary estimates were calculated for the total duration of each study using a random-effects model.

Methods of synthesis
How were the studies combined?
The characteristics of the included studies were summarised in the text of the review. Only data from studies with a concurrent control group were included in the meta-analysis. The pooled risk ratio (RR) and 95% confidence intervals (CIs) were calculated for total mortality and pneumonia mortality for each age group and for each study year, using a random-effects model. Risk reductions (RDs) and 95% CIs were also calculated. A funnel plot was used to assess publication bias.

How were differences between studies investigated?
Statistical heterogeneity was tested using the Mantel-Haenszel method. The influence of each individual study and each year of the intervention was assessed. A random-effects meta-regression was used to explore the influence of study quality and characteristics for both outcomes and for the three age groups separately. Two different models were used: the covariates for the first year of the intervention were methodological, intervention and cointervention scores; the covariates for the second year were infant mortality rate, health service score and type of antibiotic. The results from trials with a concurrent intervention group were compared with those from before-and-after studies.

Results of the review
Data from 7 studies with a concurrent control group were included in the meta-analysis. There were 5 studies of neonates (n=31,041), 6 studies of infants (n=19,191) and 7 studies of pre-school children (n=89,242). Two studies were of a before-and-after design, while an additional 4 concurrent studies introduced the intervention into control areas and reported before-and-after data. Data from one additional unpublished trial could not be obtained.

The validity scores ranged from 70 to 109, the intervention characteristic scores ranged from 32 to 49, and the cointervention scores ranged from 11 to 45. The reviewers felt that although all the studies had methodological flaws,
none were so great as to invalidate the results.

Neonates.

The intervention significantly reduced total neonatal mortality. The RR was 0.73 (95% CI: 0.65, 0.82) and the RD was 27% (95% CI: 18, 35). No significant heterogeneity was detected (P=0.895). The meta-regression showed no significant association with any of the covariates.

The intervention significantly reduced pneumonia mortality. The RR was 0.58 (95% CI: 0.43, 0.78) and the RD was 42% (95% CI: 22, 57). No significant heterogeneity was detected (P=0.711). The meta-regression showed no significant association with any of the covariates.

Infants.

Significant heterogeneity was detected in the meta-analysis of total mortality (P=0.053). After excluding one study conducted in the Philippines, no significant heterogeneity was detected (P=0.17).

The intervention significantly reduced total infant mortality. The RR for homogeneous studies was 0.80 (95% CI: 0.72, 0.89) and the RD was 20% (95% CI: 11, 28). The meta-regression showed no significant association with any of the covariates. Studies with a higher methods score showed a lower effect, while studies with a higher intensity of intervention showed a greater effect.

The intervention significantly reduced pneumonia mortality. The RR was 0.64 (95% CI: 0.52, 0.80) and the RD was 36% (95% CI: 20, 48). Homogeneity was borderline (P=0.088). The effect size was greater in the first year of the intervention (P=0.07). In the second year, the effect size was greater with advancing years (P=0.02) and greater with an increased health service score (P=0.04).

Children aged 0 to 4 years.

Significant heterogeneity was detected in the meta-analysis of total mortality (P<0.001). The intervention significantly reduced total infant mortality. The RR was 0.76 (95% CI: 0.67, 0.86) and the RD was 24% (95% CI: 14, 33). Only the year was significantly associated with the effect size (P=0.04).

Significant heterogeneity was detected in the meta-analysis of pneumonia mortality (P=0.005). The intervention significantly reduced pneumonia mortality. The RR was 0.64 (95% CI: 0.51, 0.80) and the RD was 36% (95% CI: 20, 49). Only the year of the intervention was significantly associated with the effect size (P=0.05).

Funnel plots for each of the six outcomes showed no evidence of publication bias.

The results were similar after excluding each study year in turn. The results from trials with a concurrent intervention group were similar to those from before-and-after studies.

Authors' conclusions

Community-based interventions that identify and treat pneumonia reduce neonatal, infant and pre-school mortality, and should be part of primary health care.

CRD commentary

The review addressed a clear question in terms of the participants, intervention, outcomes and study design. The strategy undertaken to identify trials was extensive and a collaborative group of trial investigators was established to review the results from the analysis. The authors stated the number of identified trials with unavailable data. Adequate data on the included studies were presented. The methods used to assess the relevance of the primary studies were not reported; hence, the potential for bias and errors cannot be assessed. However, funnel plots showed no evidence of publication bias. The validity assessment and data extraction were performed by two reviewers and checked by the original trialists.
The data were analysed using appropriate methods and heterogeneity was assessed. Where heterogeneity was detected, this was discussed in the text, although in some cases heterogeneity appears to have remained unexplained. The influence of each study and each year of the intervention was assessed. The reviewers also used meta-regression to assess the influence on the results of various other factors, such as study quality. Limitations of the evidence were discussed in the text. The finding of significant heterogeneity for some outcomes suggests that the results may not be generalisable.

**Implications of the review for practice and research**

**Practice:** The authors stated that community-based interventions that identify and treat pneumonia should be part of primary health care.

**Research:** The authors stated that drug resistance rates and treatment failure rates should be monitored as part of pneumonia case-management.

**Bibliographic details**


**PubMedID**

12954560

**Other publications of related interest**


**Indexing Status**

Subject indexing assigned by NLM

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This is a critical abstract of a systematic review that meets the criteria for inclusion on DARE. Each critical abstract contains a brief summary of the review methods, results and conclusions followed by a detailed critical assessment on the reliability of the review and the conclusions drawn.