The effect of case management on childhood pneumonia mortality in developing countries

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Background With the aim of populating the Lives Saved Tool (LiST) with parameters of effectiveness of existing interventions, we conducted a systematic review of the literature assessing the effect of pneumonia case management on mortality from childhood pneumonia.

Methods This review covered the following interventions: community case management with antibiotic treatment, and hospital treatment with antibiotics, oxygen, zinc and vitamin A. Pneumonia mortality outcomes were sought where available but data were also recorded on secondary outcomes. We summarized results from randomized controlled trials (RCTs), cluster RCTs, quasi-experimental studies and observational studies across outcome measures using standard meta-analysis methods and used a set of standardized rules developed for the purpose of populating the LiST with required parameters, which dealt with the issues of comparability of the studies in a uniform way across a spectrum of childhood conditions.

Results We estimate that community case management of pneumonia could result in a 70% reduction in mortality from pneumonia in 0–5-year-old children. In contrast treatment of pneumonia episodes with zinc and vitamin A is ineffective in reducing pneumonia mortality. There is insufficient evidence to make a quantitative estimate of the effect of hospital case management on pneumonia mortality based on the published data.

Conclusion The available evidence reinforces the effectiveness of community and hospital case management with World Health Organization-recommended antibiotics and the lack of effect of zinc and vitamin A supportive treatment for children with pneumonia. Evidence from one trial demonstrates the effectiveness of oxygen therapy but further research is required to give higher quality evidence so that an effect estimate can be incorporated into the LiST model. We identified no trials that separately evaluated the effectiveness of...
Background

According to a UNICEF–World Health Organization (WHO) report from 2006, over 2 million children die from pneumonia each year, accounting for almost one in five under-5 deaths worldwide. Globally, the estimated incidence of clinical pneumonia in children aged <5 years in developing countries is 0.28 episodes per child-year, whereas in developed countries it is 0.05 episodes per child-year. Thus, ~155 million episodes of clinical pneumonia occur in children <5 years of age annually.

As part of the primary care approach, children with pneumonia require access to good-quality basic first-level care (community case management). Based on current WHO guidelines it has been estimated that ~10% of children presenting with pneumonia, i.e. those with severe or very severe pneumonia, may require referral to a first referral or district hospital for hospital treatment. Since pneumonia is the leading cause of death in children <5 years of age, interventions to promote the prevention and treatment of pneumonia are an essential part of child survival efforts to achieve Millennium Development Goal 4.

Previous reviews by Sazawal and Black have studied the effect of community case management on pneumonia mortality and overall child mortality. This article reviews a wider range of case management interventions and was conducted in a standard manner (adopted for a review of all child health interventions) following guidelines set by the Child Health Epidemiology reference Group (CHERG). The overall aim is to provide parameters needed for the Lives Saved Tool (LiST) software to model the preventable deaths childhood pneumonia and to document all steps of this process in a transparent manner, thus assisting the wider acceptance of the LiST tool.

Methods

Identification and selection of studies

We attempted to identify all randomized controlled trials (RCTs), cluster RCTs (cRCTs), quasi-experimental studies and observational studies investigating the effect of community and hospital case management on pneumonia mortality and other pneumonia-related outcomes in children <5 years old. Studies were identified from the following databases: Medline (1970 to August 2008), EMBASE (1970 to August 2008) and the Web of Knowledge (1970 to August 2008; only for the community case management review). Details of the exact search strategies used to identify relevant studies for (i) the community case management and (ii) hospital case management [including (a) antibiotic treatment for (very) severe pneumonia, (b) oxygen treatment, (c) treatment with zinc supplements and (d) treatment with vitamin A supplements are presented in Supplementary Tables S1 and S2]. In addition, relevant studies were identified by searching the references of the selected studies. Eligible studies were selected according to the pre-determined inclusion criteria. In particular: (i) included studies (a) were RCTs, cRCTs, quasi-RCTs or observational studies and (b) had a control arm of placebo or no treatment; (ii) children of included studies were (a) <5 years old, (b) were followed up until ≥2 years of age (in experimental studies; not applicable for the case–control studies) and (c) had a clear case definition consistent with pneumonia.

Due to the nature of the hospital-based interventions under review, no RCTs were identified as it would not be ethical to conduct such studies. Therefore observational studies were sought according to the following inclusion criteria: developing country setting; clear case definition of pneumonia (severe or very severe as defined by WHO); children <5 years of age; sample size of 100 or more; intervention is well defined (in terms of dose, administration, frequency of delivery). The following exclusion criteria were applied: ambulatory treatment for non-severe pneumonia; no data on deaths available; selective groups of preschool children [e.g. malnourished, human immunodeficiency virus (HIV) positive, specific pneumonia pathogens isolated] studied (Supplementary Table S3).

The main types of outcome measures for community case management were: pneumonia-specific mortality, all-cause mortality and incidence of moderate or severe episodes of acute lower respiratory infection (ALRI). The main outcomes for the hospital case management studies were (i) for antibiotic treatment studies: intervention case fatality ratios and treatment failure rates; (ii) for oxygen treatment study: all-cause mortality of children with pneumonia; (iii) for studies of zinc supplement treatment: length of hospitalization, time to resolution of severe illness, lethargy, inability to eat, low oxygen saturation, chest indrawing and tachypnoea; and (iv) for studies of vitamin A supplement treatment: all-cause mortality of children with pneumonia, length of hospitalization and time to resolution of low oxygen saturation and tachypnoea. There were no language or publication restrictions.

Keywords
care, pneumonia, case management, community, hospital, developing countries
One original and one parallel review were conducted by independent investigators and results from the two searches and study selections were compared and merged.

**Abstraction, quality assessment and meta-analyses**

Data from all studies that met final inclusion and exclusion criteria were abstracted into a standardized form for each outcome of interest. We abstracted key variables with regard to the study identifiers and context, study design and limitations, intervention specifics and outcome effects. The quality of each study was assessed and graded according to the CHERG adaptation of the GRADE technique (‘GRADE Profiler version 3.2’ scoring system) (Supplementary Table a).

We summarized the evidence by outcome including qualitative assessment of the quality of each specific outcome (Supplementary Table b). In addition, for any outcome with more than one study, a meta-analysis was conducted and pooled relative risk and corresponding 95% confidence interval (CI) reported using the fixed-effect model (Mantel–Haenszel method). In the case of heterogeneity ($P < 0.1$), the random effect model (DerSimonian–Laird method) was applied (although it is recognized that due to the variation in precise interventions, study methods and outcome definitions, the meta-estimates should be interpreted cautiously). All analyses were conducted using STATA 10.0 statistical software.

For the outcome of interest, namely the effect of community case management with antibiotics, oxygen treatment, zinc treatment and vitamin A treatment on pneumonia mortality, we applied the CHERG Rules for Evidence Review to the collective pneumonia morbidity and mortality outcomes to generate a final estimate for the reduction in pneumonia mortality (Supplementary Table c).

**Results**

**Community case management**

We identified 154 titles from the search conducted in Medline, 87 from Embase and 62 from Web of Knowledge. After elimination of duplicates, studies with alternative outcome parameters, review articles and studies that did not fit the inclusion criteria, a total of 12 studies were extracted from the bibliographic databases and two studies were identified from a published meta-analysis (Supplementary Figure S1). The characteristics of the studies that were identified to estimate the effect of community case management on pneumonia mortality are presented in Supplementary Table S4. A summary of the identified outcomes as well as their exact definitions are presented in Supplementary Table S5. Two of the identified studies did not report enough data, and therefore they were not included in the meta-analyses. In addition, although four studies reported data on the effect of community case management with antibiotics on incidence of moderate/severe episodes of ALRI, a morbidity analysis was not performed because the signs they used to identify ALRI were either reported by the child’s mother or were not based on the WHO classification (mild, moderate, severe), or were not specified.

In Table 1, we report the quality assessment of studies by outcome, as well as results from corresponding meta-analyses for the effect of community case management with antibiotic treatment on pneumonia-related outcomes. The summary effect of community case management with antibiotic treatment on ALRI mortality for children (i) 0–1-month-old after summarizing four concurrent studies was 42% (95% CI 23–54%); (ii) 0–1-year-old after summarizing eight concurrent studies was 49% (95% CI 33–55%); (iii) 1–4 years old after summarizing two before/after studies was 49% (95% CI 33–55%); (iv) 0–5 years old after summarizing seven concurrent studies was 35% (95% CI 18–48%) (Figure 1a). In addition, the summary effect of community case management with antibiotic treatment on all-cause morality for children: (i) 0–1 month old after summarizing five concurrent studies was 27% (95% CI 18–35%); (ii) 0–1 years old after summarizing eight concurrent studies was 27% (95% CI 18–35%); (iii) 1–4 years old after summarizing two before/after studies was 21% (95% CI 14–28%); (iv) 0–5 years old after summarizing eight concurrent studies was 51% (95% CI 30–66%); and (v) 0–5 years old after summarizing two before/after studies was 21% (95% CI 12–30%) (Table 1). According to the CHERG Rules 2 for Evidence Review in order to estimate the effect on pneumonia mortality, we used the effect of community case management with antibiotic treatment on ALRI mortality of children 0–5 years old (Figure 1b).

**Hospital case management**

**Antibiotic treatment for (very) severe pneumonia**

We identified 476 titles from the search conducted in Medline and 1241 from Embase. After elimination of duplicates, studies with alternative outcome parameters, review articles and studies that did not fit the inclusion criteria, a total of ten studies were extracted from the bibliographic databases (Supplementary Figure S2a). These studies included two before/after studies and observational data (large case series conducted in a structured manner often as one arm of a clinical trial) and reported mortality outcomes. The characteristics of these studies are presented in Supplementary Table S6. A summary of the identified outcomes as well as their exact definitions are presented in Supplementary Table S7. We have not reported observational studies that reported
Table 1  Quality assessment of studies of community case management with antibiotic treatment on pneumonia related outcomes

| Quality assessment | Directness | No. of events | Intervent | Control | RR (95% CI) |
|--------------------|------------|---------------|-----------|---------|-------------|
| ALRI-specific mortality 0–1 months: moderate outcome specific quality of evidence | Concurrent | No major | 3 of 4 studies show benefit | Africa and Asia | 384 636 | 0.58 (0.44–0.77) |
| ALRI specific mortality 0–1 year: moderate outcome specific quality of evidence | Concurrent | Mainly no major limitations; in 1 study differences between study populations | Heterogeneity from meta-analysis ($P = 0.03$); All studies show benefit | Africa and Asia | 916 1510 | 0.59 (0.46–0.75) |
| ALRI-specific mortality 1–4 years: low outcome specific quality of evidence | Before/after | High ALRI incidence and differences between study populations | Heterogeneity from meta-analysis ($P = 0.06$). Both studies show benefit | Only Asia | 917 1522 | 0.57 (0.44–0.75) |
| ALRI-specific mortality 0-4 years: moderate outcome specific quality of evidence | Concurrent | Mainly no major limitations; in one study differences between study populations | Heterogeneity from meta-analysis ($P = 0.004$); 5 of 6 studies show benefit | Africa and Asia | 1632 2546 | 0.64 (0.49–0.85) |
| ALRI-specific mortality 0–1 year: moderate outcome specific quality of evidence | Before/after | Mainly no major limitations; in one study | All studies show benefit | Africa and Asia | 190 253 | 0.68 (0.56–0.82) |

(continued)
| No. of studies (ref.) | Design | Limitations | Consistency | Directness | Generalizability to population of interest | Generalizability to intervention of interest | No. of events | RR (95% CI) |
|-----------------------|--------|-------------|-------------|------------|------------------------------------------|--------------------------------------------|--------------|------------|
|                        |        |             |             |            | Health workers or traditional birth attendants; 3 studies other ARI case management |                                             |              |            |
| 8^9,11,13,14,16–18, 22^f | Concurrent; before/after | See above | Heterogeneity from meta-analysis \((P = 0.003)\); 7 of 8 studies show benefit | Africa and Asia | See above | 1670 | 2584 | 0.64 (0.49–0.83) |
| 9^9,16,17,11,14,18,19,13,22 | Concurrent; before/after | See above | Heterogeneity from meta-analysis \((P = 0.006)\); 8 of 9 studies show benefit | Africa and Asia | See above | 1690 | 2630 | 0.65 (0.52–0.82) |

**All cause mortality**

All cause mortality 0–1 months: moderate outcome specific quality of evidence

5^11,13,14,16,18^ Concurrent | Mainly no major limitations; in 1 study differences between study populations | All studies show benefit | Africa and Asia | 4 of 5 studies WHO case management by local health workers or traditional birth attendants; 1 study other ARI case management | 925 | 957 | 0.73 (0.65–0.82) |

All-cause mortality 0–1 year: moderate outcome specific quality of evidence

6^11,13,14,16,18,22^&b Concurrent | Mainly no major limitations; in 1 study differences between study populations | All studies show benefit | Africa and Asia | 4 of 6 studies WHO case management by local health workers or traditional birth attendants; 2 studies other ARI case management | 2095 | 2487 | 0.78 (0.71–0.85) |

2^17,19^ & Before/after | High ALRI incidence and differences between study populations | Both studies show benefit | Only Asia | 1 of 2 studies WHO case management by local health workers; 1 study other ARI case management | 41 | 100 | 0.60 (0.42–0.85) |

7^11,13,14,16–18, 22^&a,b Concurrent; before/after | See above | All studies show benefit | Africa and Asia | See above | 2114 | 2524 | 0.77 (0.70–0.85) |

8^11–14,16–19,22^ Concurrent; before/after | See above | All studies show benefit | Africa and Asia | See above | 2230 | 2703 | 0.79 (0.72–0.86) |

All-cause mortality 1–4 years: low outcome specific quality of evidence

2^17,19^ Before/after | High ALRI incidence and intervention and control area different baseline mortality rates | Both studies show benefit | Only Asia | 1 of 2 studies WHO case management by local health workers; 1 study other ARI case management | 43 | 82 | 0.49 (0.34–0.70) |

(continued)
### Table 1 Continued

| No. of studies (ref.) | Design | Limitations | Consistency | Directness | No. of events | RR (95% CI) |
|-----------------------|--------|-------------|-------------|------------|---------------|---------------|
|                       |        |             |             |            | Intervention | Control       |
| All-cause mortality 0–4 years: moderate outcome specific quality of evidence | Concurrent | Mainly no major limitations; in 1 study differences between study populations | Heterogeneity from meta-analysis ($P=0.01$); All studies show benefit | Africa and Asia | 4 of 7 studies WHO case management by local health workers; 3 studies other ARI case management | 4558 | 5563 | 0.76 (0.67–0.86) |
| $^{7,21,16,11,18,13,22}$ | Before/after | Mainly no major limitations; in one study differences between study populations and in one study high ALRI incidence | All studies show benefit | Africa and Asia | 2 of 5 studies WHO case management by local health workers or traditional birth attendants; 3 studies other ARI case management | 984 | 919 | 0.75 (0.69–0.82) |
| $^{9,10,13,14,16–18}$ | Concurrent; before/after | See above | Heterogeneity from meta-analysis ($P=0.004$); 8 of 9 studies show benefit | Partly (Africa, Asia) | See above | 4833 | 5760 | 0.77 (0.72–0.82) |
| $^{9,11,13,14,16–18,21,22}$ | Concurrent; before/after | See above | Heterogeneity from meta-analysis ($P=0.001$); 9 of 10 studies show benefit | Africa and Asia | See above | 4934 | 5932 | 0.79 (0.70–0.88) |

*aDatta et al.*$^{12}$ excluded due to restriction in children of low birth weight.

*bReddaiah*$^{19}$ excluded because intervention and control area different baseline mortality rates.
other treatment outcomes such as failure to improve, need for change in antibiotic treatment or time to reduction in respiratory rate since these were applied in a non-standard manner that varied widely and had not a clear relationship to risk of mortality.

The reduction of the case fatality rate after the implementation of the WHO’s standard acute respiratory infection (ARI) case management guidelines was 23% (–100%, 70%) based on the results of two before/after studies.26,32 The summary case fatality rate of antibiotics on severe pneumonia after summarizing four studies (3945 episodes) 28–31 was 0.6% (95% CI 0.4–0.9%) (Table 2 and Figure 2). These studies were conducted in developing countries including Columbia, Ghana, India, Mexico, Pakistan, South Africa, Vietnam, Uruguay and Zambia (between 1991 and 2006). The reported case fatality rates ranged from 0 to 1% and the antimicrobial agents used to manage these children included oral amoxicillin, oral co-trimoxazole, parenteral ampicillin, parenteral penicillin and macrolides (Supplementary Table S6). Some studies did not contain information on co-interventions; however, where specified, these included oxygen therapy, bronchodilators and antipyretics when indicated (Supplementary Table S6).

The summary case fatality rates of antibiotics on very severe pneumonia after summarizing four studies (5376 episodes) 23–27 were 6.5% (95% CI 4.3–9.6%) (Table 2 and Figure 2). These studies were conducted in developing countries including Bangladesh, Ecuador, India, Pakistan, Papua New Guinea, Mexico, South Africa, Yemen and Zambia (between 1979 and 2004). The reported case fatality rates ranged from 2 to 19% and it is evident that case fatality rates were higher in children <12 months old than in older children (Supplementary Table S6).

Oxygen treatment
We identified 213 titles from the search conducted in Medline and 172 from Embase. After elimination of
Table 2 Quality assessment of studies of hospital case management on pneumonia related outcomes: (i) Antibiotic treatment for (very) severe pneumonia, (ii) oxygen systems for treatment of pneumonia, (iii) zinc supplementation for treatment of pneumonia and (iv) vitamin A supplementation for treatment of pneumonia

| Quality assessment | Directness | No. of events | CFR (%) |
|--------------------|------------|---------------|---------|
| No. of studies (ref.) | Design | Limitations | Consistency | Generalizability to population of interest | Generalizability to intervention of interest | After application of WHO ARI standard case management | Before application of WHO ARI standard case management |
| (i) Antibiotic treatment for (very) severe pneumonia | | | | | | | |
| Deaths among ARI admissions: very low outcome specific quality | | | | | | | |
| 2<sup>(26,32)</sup> | Before/after | No major | Heterogeneity from meta-analysis <sup>(P < 0.0005)</sup> | Asia | Benzyl penicillin or ampicillin (severe pneumonia), chloramphenicol (very severe pneumonia) | 126 | 123 | 0.77 (0.30–2.00) |

| Quality assessment | Directness | No. of events | CFR (%) |
|--------------------|------------|---------------|---------|
| No. of studies (ref.) | Design | Limitations | Consistency | Generalizability to population of interest | Generalizability to intervention of interest | Episodes | Control | CFR (%) (95% CI) |
| Case fatality ratio of severe pneumonia: very low outcome specific quality | | | | | | | | |
| 5<sup>(26,29,30,31)</sup> | Mainly no major; in 1 study many cases treated as bacterial; in 1 study potential for outcome misclassification | Africa, Asia, S.America, C.America | Amoxicillin, ampicillin/ macrolides, penicillin, | 19 | n/a | 0.6% (0.4–0.9%) |

| Case fatality ratio of very severe pneumonia: very low outcome specific quality | | | | | | | | |
| 10<sup>(23b,25,26a,27a)</sup> | In 1 study 28% were lost to follow up; In 1 study management protocol changed during course of study; in 1 study potential for misclassification of bacterial pneumonia | Africa, Asia, S.America, C.America | Chloramphenicol sodium succinate, benzylpenicillin, ampicillin, gentamicin, chloramphenicol | 420 | n/a | 6.5% (4.3–9.6%) |

(Continued)
Table 2 Continued

| No. of studies (ref.) | Design | Limitations | Consistency | Directness | No. of events | Median hours (95% CI) | Intervention | Control | Relative Risk (95% CI) |
|-----------------------|--------|-------------|-------------|------------|---------------|------------------------|--------------|---------|------------------------|
| (ii) Oxygen systems for treatment of pneumonia | | | | | | | | | |
| Risk of mortality of children with pneumonia: very low outcome specific quality | | | | | | | | | |
| 1(33) Before/after Possibility of secular n/a trends in mortality rate over time; ascertainment bias and altered thresholds for hospital admission | Only 1 study | Oxygen concentrators and pulse oximeters | 133 | 356 | 0.65 (0.52–0.78) |
| (iii) Zinc supplementation for treatment of pneumonia | | | | | | | | | |
| Duration of hospitalization (hours): low outcome specific quality | RCT | No major | Heterogeneity from meta-analysis ($P = 0.03$) | Only Asia; both studies 2–23 months | Zinc sulphate and acetate | 23089.3 (57.2, 139.4) | 23096.0 (54.8, 168.0) | 0.87 (0.55–1.37) |
| Duration of severe illness (hours to resolution; inability to feed, O2 saturation <93%, and respiratory rate >50 breaths/min): low outcome specific quality | RCT | No major | Heterogeneity from meta-analysis ($P = 0.02$) | Only Asia; both studies 2–23 months | Zinc sulphate and acetate | 23085.5 (77.1, 94.8) | 23082.9 (66.7, 103.1) | 0.83 (0.48–1.44) |
| Duration of hypoxia (hours to resolution): low outcome specific quality | RCT | No major | Heterogeneity from meta-analysis ($P = 0.08$) | Only Asia; both studies 2–23 months | Zinc sulphate and acetate | 230 78.2 (63.2, 96.9) | 230 82.6 (62.6, 109.0) | 0.91 (0.64–1.29) |
| Duration of tachypnoea (hours to resolution; >50 breaths/min): low outcome specific quality | RCT | No major; 1 study more loss to follow-up in placebo | Heterogeneity from meta-analysis ($P = 0.002$) | Only Asia; 3 of 4 studies 2–23 months; 1 study 9 months to 15 years | Zinc sulphate and acetate | 309 68.9 (59.5, 79.7) | 306 64.9 (51.4, 81.9) | 0.98 (0.70–1.37) |

(Continued)
| No of studies (ref.) | Design | Limitations | Consistency | Generalizability to population of interest | Generalizability to intervention of interest | No of events | Intervention | Control | RR (95% CI) |
|----------------------|--------|-------------|-------------|----------------------------------------|----------------------------------------|-------------|-------------|---------|-------------|
| (iv) Vitamin A supplementation for treatment of pneumonia |
| Mortality: very low outcome specific quality | 6(40-45) | RCT | Mainly no major; in 1 study initial vitamin A status of children was unknown | 3 of 6 studies show benefit, 2 show no effect and 1 show risk | Asia, Africa, S. America | 2 of 6 studies vitamin E in the vitamin A supplement | 22 | 21 | 1.09 (0.59–2.04) |
| Duration of hospitalization (days): low outcome specific quality | 3(40,45,46) | RCT | Mainly no major; in 1 study initial vitamin A status of children was unknown | All studies show no effect | Asia, Africa, S. America; 1 study 3–119 months | 6725.70 (5.37–6.05) | 6955.67 (5.35–6.01) | 0.04 (−0.40 to 0.48) |
| Duration of hypoxia (days to resolution): low outcome specific quality | 4(40,42–44) | RCT | No major | All studies show no effect | Africa, S. America | 1 of 4 studies vitamin E in the vitamin A supplement | 7131.75 (0.70–4.38) | 7091.81 (0.77–4.27) | −0.02 (−0.16 to 0.12) |
| Duration of tachypnoea (hours to resolution; >50 breaths/min): low outcome specific quality | 5(40,42–45) | RCT | Mainly no major; in 1 study initial vitamin A status of children was unknown | All studies show no effect | Asia, Africa, S. America | 1 of 5 studies vitamin E in the vitamin A supplement | 10264.28 (4.08–4.49) | 10374.15 (3.96–4.34) | 0.05 (−0.21 to 0.31) |

*aInclude both severe and very severe cases.
*bThe Zambia site of this multi-centre study was withdrawn from the study after 23 enrolments (2.4% of total) due to high mortality.
*cResults after excluding the Mahalanabis et al. study (due to the age range: 9 months to 15 years).
duplicates, studies with alternative outcome parameters, review articles and studies that did not fit the inclusion criteria, one study was extracted from the bibliographic databases (Supplementary Figure S2b). The characteristics of this study \(^3\) that were identified to estimate the effect of oxygen therapy on pneumonia mortality is presented in Supplementary Table S6. The exact definition of the outcome is presented in Supplementary Table S7. In Table 2, we report the quality assessment of the study as well as the effect of oxygen treatment on mortality for children with pneumonia (35%, 95% CI 22–48%).

**Treatment with zinc supplements**

We identified 55 titles from the search conducted in Medline and 153 from Embase. After elimination of duplicates, studies with alternative outcome parameters, review articles and studies that did not fit the inclusion criteria, a total of five studies were extracted.
from the bibliographic databases \(^{34–38}\) (Supplementary Figure S2c). The characteristics of the studies that were identified to estimate the effect of zinc supplementation on pneumonia-related outcomes are presented in Supplementary Table S6. A summary of the identified outcomes as well as their exact definitions are presented in Supplementary Table S7.

In Table 2, we report the quality assessment of studies by outcome, as well as results from corresponding meta-analyses for the effect of zinc supplementation treatment on pneumonia-related outcomes. Of the four outcomes related to the duration of pneumonia symptoms, the effect size ranged from 17% for hours to severe disease resolution (based on two RCTs \(^{34,35}\)) to 2% for hours to tachypnoea resolution (based on four RCTs \(^{34,35,37,38}\)). Since there were no mortality data in order to estimate the effect on pneumonia mortality, we used the hours of hospitalization effect based on the summary analysis of two RCTs \(^{34,35}\) [13% (−37, 45%)] (according to the CHERG Rules for Evidence Review. Since there is not clear evidence of the effect on pneumonia mortality this intervention against pneumonia will not be included in the LiST model) (Figure 3).

**Treatment with vitamin A supplements**

We identified 614 titles from the search conducted in Medline and 1099 from Embase. After elimination of duplicates, studies with alternative outcome parameters, review articles and studies that did not fit the inclusion criteria, a total of nine studies were extracted from the bibliographic databases \(^{39–47}\) (Supplementary Figure S2d). The characteristics of the studies that were identified to estimate the effect of oxygen therapy on pneumonia mortality are presented in Supplementary Table S6. A summary of the identified outcomes as well as their exact definitions are presented in Supplementary Table S7.

In Table 2, we report the quality assessment of studies by outcome, as well as results from corresponding meta-analyses for the effect of vitamin A supplementation treatment on pneumonia-related outcomes. Although there was an estimate of mortality based on six studies \(^{39,41–45}\) [−9% (95% CI = 104 to 41%)], the specific outcome quality was very low (since there were <50 total events) (Table 2). Therefore, according to the CHERG Rules 0 and 5 for Evidence Review in order to estimate the effect on pneumonia mortality, we used the summary effect of vitamin A on days of hospitalization, which was based on three studies \(^{39,45,46}\) (weighted mean difference 0.04 (95% CI = 0.40 to 0.48)). Since there is not clear evidence of the effect on pneumonia mortality, this intervention against pneumonia will not be included in the LiST model) (Figure 4). Regarding the other pneumonia-related outcomes, vitamin A supplementation had no effect on either duration of hypoxia resolution (weighted mean difference based on four studies \(^{39,42–44}\) −0.02 (95% CI = 0.16 to 0.12)) or duration of tachypnoea resolution [weighted mean difference based on five studies \(^{39,42–45}\) 0.05 (95% CI = 0.21 to 0.31)] (Table 2).

**Other supportive care**

We were unable to identify controlled trials or quasi-experimental studies or observational studies that met our study criteria, which are reported on the separate effect of supportive care interventions.
such as fluid therapy, temperature control or clinical monitoring on pneumonia mortality.

DISCUSSION

The estimates presented in this article represent a systematic and structured review of the published evidence of effectiveness of case management interventions for childhood pneumonia in developing countries. The aim of this review was to inform the LiST model and to make explicit the available evidence.

The effect of case management in areas where HIV is a major problem may substantially differ from the estimates in regions where HIV is not such a problem. The evidence presented in this review was generally reported from areas in which HIV Acquired Immuno Deficiency Syndrome (AIDS) was not a major public health problem so this should be borne in mind when interpreting the results. Further research is required to provide data to model the effect in HIV-affected regions, since there are data showing that HIV has an impact on case fatality ratios (CFRs) in hospital management and that pneumocystis pneumonia (mainly found in HIV/AIDS patients) accounts for a large proportion of these deaths.

Another important issue is the rapidly changing coverage with the new protein-polysaccharide conjugate vaccines against Hib and pneumococcal disease. The direct and indirect (herd immunity) effects of these vaccines at moderate to high coverage are likely to have a substantial impact on the major bacterial pathogens causing pneumonia mortality and this will necessitate a change in antibiotic treatment policies and will have an impact on the effect of case management strategies on pneumonia mortality impact. The studies reviewed in this report were conducted in settings where these vaccines were not used at all or not at a significant level of coverage.

Community case management with antibiotic treatment

The effect of community case management on pneumonia mortality has been established by previous reviews. However, there has been no previous attempt to estimate the effect of the major child health interventions using a common approach or to consider a wider range of case management interventions against pneumonia.

This systematic review clearly highlights again the effectiveness of community case management with antibiotic treatment in reducing mortality from childhood pneumonia and reinforces the findings of previous reviews. A majority of these studies have been carried out in Asia. This approach was effective even in rural areas with very limited access to health services and severely limited resources. However, it is notable that despite the clear evidence in favour of the effectiveness of this strategy first reviewed by Sazawal et al., community case management is still not readily accessible in many populations with high levels of child mortality.

Community case management models differ. On the one hand, it might mean a proper assessment using the Integrated Management of Childhood Illness guidelines and antibiotics given by a nurse with 2–3 years of training in a well-setup primary government or mission-run health clinic. On the other hand, it might mean antibiotics given by a volunteer health worker with as little as 2–6 weeks of training in a village setting, with limited connection with the formal health system. Recent programs considered are considering antibiotic treatment given at home by a health worker for children with severe pneumonia.

Several studies emphasized the importance of active case finding in reducing mortality levels although once community awareness has been generated and as maternal education develops within the community, the use of active case finding may become gradually less essential. It is suggested by these studies that maternal education is an important factor in the long-term success of the case management approach. It is clear that good levels of health worker supervision are needed for community case management. Most of the trials evaluated community case management in conjunction with other interventions suggesting that integration of case management into existing health systems will be essential to achieve the greatest impact on childhood pneumonia mortality. Ideally there should be a health system continuum from community to primary care to hospitals.

There are certain patient groups in which community case management for pneumonia is more
complex and may not be appropriate. These groups include children with very severe pneumonia, hypoxaemia, neonates, malnourished children and children with HIV. This systematic review is limited in that it does not report studies that addressed these contextual issues or high-risk groups.

One issue for the effectiveness of the community case management intervention is the coverage of the antibiotic treatment, since not all children with pneumonia in these trials were identified and given antibiotic treatment. In the recent meta-analysis in 2003 by Sazawal et al., the authors in cooperation with the principal investigators (PIs) of the trials conducted a structured assessment of a number of aspects related to the intervention intensity (intervention score), including antibiotic availability, percentage of detected cases, case treatment rates and treatment compliance. They then conducted a meta-regression that examined the correlation between intervention effectiveness and intervention score and they reported that community case management was more effective against pneumonia in higher intervention intensity studies. Although, the data used to construct the intervention score represent qualitative rather than quantitative views of the study PIs, they are consistent with ~50% of children with pneumonia receiving the intervention as planned. It is therefore probable that the impact on pneumonia mortality could have been higher than that reported in the current and previously published meta-analyses had a higher proportion of children with pneumonia received the intervention. Since the LISt tool is designed to provide the effectiveness of an intervention on an individual level, the meta-analysis estimate effect of community case management will be adjusted to take into consideration the 50% coverage of antibiotic treatment (adjusted effectiveness 70%).

Other issues such as the emergence of antibiotic resistance to simple oral antibiotics that can be prescribed by community health workers, increasing prevalence of HIV in a country or region and a change in the main causes of pneumonia deaths following high coverage with Hib and pneumococcal conjugate vaccines (discussed below) may necessitate a re-appraisal of the effectiveness of the specific antibiotics recommended or, more widely, of how this strategy is implemented.

**Hospital antibiotic treatment**

The current WHO guidelines for the acute management of very severe pneumonia in resource-limited settings recommend ampicillin and gentamicin for up to 10 days, or alternatively, chloramphenicol until improvement is seen. For pneumonia classified as severe, amoxicillin or benzylpenicillin is recommended for ≥5 days. This review was unable to identify any controlled trials, quasi-experimental studies or observational studies from which treatment effectiveness in reducing pneumonia mortality could be estimated. The main reason for this is that WHO (and other national paediatric and Ministry of Health) treatment recommendations are widely accepted and such studies would not be considered ethical. One before/after study was identified that reported a 52% reduction in case fatality rate in children admitted with ARI after the implementation of WHO’s standard ARI case management guidelines. In contrast, there were no significant differences in CFR in another study before and after implementation of ARI case management guidelines. Reports of very low CFRs for severe pneumonia and relatively low CFR for very severe pneumonia are consistent with a high level of effectiveness of hospital treatment. However, it is not possible from published data to quantify the precise effectiveness of hospital treatment with antibiotics since there is no control data available.

There is good general evidence that hospital care is often deficient in many countries, including a study of 21 hospitals across seven countries in Asia and Africa. Similar observations were made in a study in Kenya, Tanzania, Solomon Islands, Kazakhstan, Brazil, Angola and elsewhere. Attention to improving quality of hospital care is therefore required to ensure the appropriate, effective and timely treatment is given.

**Oxygen therapy**

Hypoxaemia is a major complication and cause of deterioration in pneumonia and is associated with a significantly increased mortality risk. It is estimated that ≥13% of children with severe pneumonia requiring admission to health facilities have hypoxaemia, and the prevalence rates are as high as 50% in some hospitals. There are 11–20 million children each year presenting to hospitals with pneumonia. This corresponds to 1.5–2.7 million annual cases of hypoxaemic pneumonia (13% prevalence).

WHO-recommended treatment of severe pneumonia includes oxygen therapy where oxygen saturation is ≥90% (where pulse oximetry is available). This review shows that there is now evidence that ensuring ample supplies of oxygen and promoting a routine and systematic approach of screening for hypoxaemia using pulse oximetry is associated with reduced mortality, and suggests that the technology required to do so is sustainable and affordable in district hospitals in developing countries. These findings are in accordance with the results of a pilot study that was conducted in one hospital (Goroka) and reported a 35–40% reduction in mortality with oxygen therapy. Regarding the oxygen delivery methods, a recent Cochrane review that summarized studies comparing oxygen delivery methods (nasal prongs, nasopharyngeal
catheters, nasal catheter, face mask, head box) found no difference in treatment failure. However, more research is required on the impact, cost and correct implementation of effective technology in different contexts, and on how to overcome barriers to access, particularly in remote regions where power supplies are unreliable. Further quasi-experimental studies, e.g. with a stepped wedge introduction design would provide more precise estimates of pneumonia mortality reduction in different settings.

**Supportive care**

This review was unable to identify any controlled trials, quasi-experimental studies or observational studies that reported separately the effectiveness of discrete supportive care interventions (a review of the effectiveness of breastfeeding will be published separately). Many supportive care interventions are recommended by WHO, national paediatric associations and Ministries of Health in paediatric treatment guidelines and are widely accepted but further research is required to better define effective supportive care.

**General issues related to case management interventions**

Any consideration of case management interventions for pneumonia should recognize that weak infrastructure, shortage of essential supplies and, most of all, the human resource crisis amongst health staff, especially in sub-Saharan Africa, are major factors limiting the achievement of the mortality reduction effects reported in these studies. In addition, risk factors that are likely to affect pneumonia mortality such as prevalence of bacterial aetiology, hypoxia, zinc deficiency and measles prevalence, will differ between different regions of the globe and therefore this will affect the effectiveness of the interventions aiming to the mentioned risk factors. Finally, community health workers that are likely to deliver the community case management interventions are most of the times not linked to the formal health system of the country and they are expected to work as volunteers. Addressing issues such as drug supplies, equipment issues and other supportive technology (such as oxygen systems), human resources, health financing, physical facilities and infrastructure are essential elements underlying the successful delivery of the interventions reviewed here.

**Conclusions**

Following the CHERG guidelines we estimate that community case management of pneumonia could result in a 70% reduction in mortality from pneumonia. In contrast, it is difficult to quantify the effectiveness of hospital case management of severe and very severe pneumonia with antibiotics due to the lack of studies with a comparison group and therefore any estimate will require a review of the available observational data coupled to expert opinion gathered through a Delphi or a similar process. A single trial of oxygen therapy suggests that this is effective in reducing pneumonia mortality but further research is required to give higher quality evidence so that an effect estimate can be incorporated into the LiST model. Finally, treatment of pneumonia episodes with zinc and vitamin A were found to be ineffective in reducing pneumonia mortality.

**Supplementary Data**

Supplementary data are available at *IJE* online.

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**KEY MESSAGES**

- Results of the current review reinforce the evidence of the effectiveness of community and hospital case management.
- Zinc and vitamin A supportive treatment does not affect pneumonia related outcomes in children.
- There is some evidence of an effect of oxygen therapy on pneumonia related outcomes but further research is required.
References

1. UNICEF, World Health Organisation. Pneumonia: the Forgotten Killer of Children. http://www.unicef.org/publications/files/Pneumonia_The_Forgotten_Killer_of_Children.pdf (26 October 2009, last accessed).

2. Rudan I, Boschi-Pinto C, Biloglav Z, Mulholland K, Campbell H. Epidemiology and etiology of childhood pneumonia. Bull World Health Organ 2008;86:108–16.

3. Rudan I, Tomaskovic L, Boschi-Pinto C, Campbell H. Global estimate of the incidence of clinical pneumonia among children under five years of age. Bull World Health Organ 2004;82:895–903.

4. Rudan I, El AS, Black RE, Campbell H. Childhood pneumonia and diarrhoea: setting our priorities right. Lancet Infect Dis 2007;7:56–61.

5. Sazawal S, Black RE. Meta-analysis of intervention trials on case-management of pneumonia in community settings. Lancet 1992;340:528–33.

6. Sazawal S, Black RE. Effect of pneumonia case management on mortality in neonates, infants, and preschool children: a meta-analysis of community-based trials. Lancet Infect Dis 2003;3:547–56.

7. Rudan I, Lawn J, Coursens S et al. Gaps in policy-relevant information on burden of disease in children: a systematic review. Lancet 2005;365:2031–40.

8. Egger M, Smith GD, Phillips AN. Meta-analysis: principles and procedures. BMJ 1997;315:1533–37.

9. Agarwal DK, Bhatia BD, Agarwal KN. Simple approach to control project in Bagamoyo District, Tanzania. Indian J Pediatr 1989;56:77–82.

10. Ali M, Emch M, Tofail F, Baqui AH. Implications of health care provision on acute lower respiratory infection mortality in Bangladeshi children. Soc Sci Med 2001;52:267–77.

11. Bang AT, Bang RA, Tale O et al. Reduction in pneumonia mortality and total childhood mortality by means of community-based intervention trial in Gadhichori, India. Lancet 1990;336:201–6.

12. Datta N, Kumar V, Kumar L, Singh S. Application of case management to the control of acute respiratory infections in low-birth-weight infants: a feasibility study. Bull World Health Organ 1987;65:77–82.

13. Fauveau V, Stewart MK, Chakraborty J, Khan SA. Impact on mortality of a community-based programme to control acute lower respiratory tract infections. Bull World Health Organ 1992;70:109–16.

14. Khan AJ, Khan JA, Akbar M, Addiss DG. Acute respiratory infections in children: a case management intervention in Abbottabad District, Pakistan. Bull World Health Organ 1990;68:577–85.

15. Lye MS, Nair RC, Choo KE, Kaur H, Lai KP. Acute respiratory tract infection: a community-based intervention study in Malaysia. J Trop Pediatr 1996;42:138–43.

16. Manguages FD, Neuvians D. Acute respiratory infections in children under five years. Control project in Bagamoyo District, Tanzania. Trans R Soc Trop Med Hyg 1986;80:851–58.

17. Pandey MR, Sharma PR, Gubhaju BB et al. Impact of a pilot acute respiratory infection (ARI) control programme in a rural community of the hill region of Nepal. Ann Trop Paediatr 1989;9:212–20.

18. Pandey MR, Daulaire NM, Starbuck ES, Houston RM, McPherson K. Reduction in total under-five mortality in western Nepal through community-based antimicrobial treatment of pneumonia. Lancet 1991;338:993–97.

19. Reddiah VP, Kapoor SK. Effectiveness of ARI control strategy on underfive mortality. Indian J Pediatr 1991;58:123–30.

20. Shimouchi A, Yaohua D, Zhonghan Z, Rabukawaqa VB. Effectiveness of control programs for pneumonia among children in China and Fiji. Clin Infect Dis 1995;21:5213–17.

21. Kiellmann AA, Taylor CE, DeSweemer C et al. The Narangwal experiment on interactions of nutrition and infections: II. Morbidity and mortality effects. Indian J Med Res 1978;68(Suppl):21–41.

22. World Health Organisation. WHO/ARI/88.2. Case Management of Acute Respiratory Infections in Children: Intervention Studies WHO/ARI/882. Geneva: WHO, 1998.

23. Asghar R, Banajeh S, Egas J et al. Chloramphenicol versus ampicillin plus gentamicin for community acquired very severe pneumonia among children aged 2–59 months in low resource settings: multicentre randomised controlled trial (SPEAR study). BMJ 2008;336:80–84.

24. McNally LM, Jeena PM, Gajee K et al. Effect of age, poly-microbial disease, and maternal HIV status on treatment response and cause of severe pneumonia in South African children: a prospective descriptive study. Lancet 2007;369:1440–51.

25. Duke T, Poka H, Dale F, Michael A, Mgone J, Wal T. Chloramphenicol versus benzylpenicillin and gentamicin for the treatment of severe pneumonia in children in Papua New Guinea: a randomised trial. Lancet 2002;359:474–80.

26. Banajeh SM. Outcome for children under 5 years hospitalised with severe acute lower respiratory tract infections in Yemen: a 5 year experience. J Trop Pediatr 1998;44:343–46.

27. Shann F, Barker J, Poore P. Chloramphenicol alone versus chloramphenicol plus penicillin for severe pneumonia in children. Lancet 1985;2:684–86.

28. Hazir T, Fox LM, Nisar YB et al. Ambulatory short-course high-dose oral amoxicillin for treatment of severe pneumonia in children: a randomised equivalency trial. Lancet 2008;371:49–56.

29. Addo-Yobo E, Chisaka N, Hassan M et al. Oral amoxicillin versus injectable penicillin for severe pneumonia in children aged 3 to 59 months: a randomised multicentre equivalency study. Lancet 2004;364:1141–48.

30. Pirozzi MC, Martinez O, Ferrari AM et al. Standard case management of pneumonia in hospitalized children in Uruguay, 1997 to 1998. Pediatr Infect Dis J 2001;20:283–89.

31. Strauss WL, Qazi SA, Kundzi Z, Nomani NK, Schwartz B. Antimicrobial resistance and clinical effectiveness of co-trimoxazole versus amoxicillin for pneumonia among children in Pakistan: randomised controlled trial. Pakistan Co-trimoxazole Study Group. Lancet 1998;352:270–74.

32. Qazi SA, Rehman GN, Khan MA. Standard management of acute respiratory infections in a children’s hospital in Pakistan: impact on antibiotic use and case fatality. Bull World Health Organ 1996;74:501–7.

33. Duke T, Wand F, Jonathan M et al. Improved oxygen systems for childhood pneumonia: a multihospital
effectiveness study in Papua New Guinea. *Lancet* 2008; 372:1328–33.
34 Bose A, Coles CL, Gunavathi *et al.* Efficacy of zinc in the treatment of severe pneumonia in hospitalized children <2 years old. *Am J Clin Nutr* 2006; 83:1089–96.
35 Brooks WA, Yunus M, Santosham M *et al.* Zinc for severe pneumonia in very young children: double-blind placebo-controlled trial. *Lancet* 2004; 363:1683–88.
36 Coles CL, Bose A, Moses PD *et al.* Infectious etiology modifies the treatment effect of zinc in severe pneumonia. *Am J Clin Nutr* 2007; 86:397–403.
37 Mahalanabis D, Chowdhury A, Jana S *et al.* Zinc supplementation as adjunct therapy in children with measles accompanied by pneumonia: a double-blind, randomized controlled trial. *Am J Clin Nutr* 2002; 76:604–7.
38 Mahalanabis D, Lahiri M, Paul D *et al.* Randomized, double-blind, placebo-controlled clinical trial of the efficacy of treatment with zinc or vitamin A in infants and young children with severe acute lower respiratory infection. *Am J Clin Nutr* 2004; 79:430–46.
39 Favzi WW, Mbise RL, Fataki MR *et al.* Vitamin A supplementation and severity of pneumonia in children admitted to the hospital in Dar es Salaam, Tanzania. *Am J Clin Nutr* 1998; 68:187–92.
40 Favzi WW, Mbise R, Spiegelman D, Fataki M, Hertzmark E, Ndossi G. Vitamin A supplements and diarrheal and respiratory tract infections among children in Dar es Salaam, Tanzania. *J Pediatr* 2000; 137:660–67.
41 Julien MR, Gomes A, Varandas L *et al.* A randomized, double-blind, placebo-controlled clinical trial of vitamin A in Mozambican children hospitalized with nonmeasles acute lower respiratory tract infections. *Trop Med Int Health* 1999; 4:794–800.
42 Kjolhede CL, Chew FJ, Gadomski AM, Marroquin DP. Clinical trial of vitamin A as adjuvant treatment for lower respiratory tract infections. *J Pediatr* 1995; 126(5 Pt 1):807–12.
43 Nacul LC, Kirkwood BR, Arthur P, Morris SS, Magalhaes M, Fink MC. Randomised, double blind, placebo controlled clinical trial of efficacy of vitamin A treatment in non-measles childhood pneumonia. *BMJ* 1997; 315:505–10.
44 Rodriguez A, Hamer DH, Rivera J *et al.* Effects of moderate doses of vitamin A as an adjunct to the treatment of pneumonia in underweight and normal-weight children: a randomized, double-blind, placebo-controlled trial. *Am J Clin Nutr* 2005; 82:1090–96.
45 Si NV, Grytter C, Vy NN, Hue NB, Pedersen FK. High dose vitamin A supplementation in the course of pneumonia in Vietnamese children. *Acta Paediatr* 1997; 86:1052–55.
46 Stephensen CB, Franchi LM, Hernandez H, Campos M, Gilman RH, Alvarez JO. Adverse effects of high-dose vitamin A supplements in children hospitalised with pneumonia. *Pediatrics* 1998; 101:E3.
47 Chang AB, Torzillo PJ, Boyce NC *et al.* Zinc and vitamin A supplementation in Indigenous Australian children hospitalised with lower respiratory tract infection: a randomised controlled trial. *Med. J. Aust.* 2009; 184:107–12.
48 Graham SM, English M, Hafiz T, Enarson P, Duke T. Challenges to improving case management of childhood pneumonia at health facilities in resource-limited settings. *Bull World Health Organ* 2008; 86:349–55.
49 Rudan I, Campbell H. Childhood pneumonia deaths: a new role for health workers? *Lancet* 2008; 372:781–82.
50 Nolan T, Angos P, Cunha AJ *et al.* Quality of hospital care for seriously ill children in less-developed countries. *Lancet* 2001; 357:106–10.
51 English M, Esamai F, Wasunna A *et al.* Assessment of inpatient paediatric care in first referral level hospitals in 13 districts in Kenya. *Lancet* 2004; 363:1948–53.
52 Reyburn H, Mwakasungula E, Chonya S *et al.* Clinical assessment and treatment in paediatric wards in the north-east of the United Republic of Tanzania. *Bull World Health Organ* 2008; 86:132–39.
53 Duke T, Keshishiyan E, Kuttumuratova A *et al.* Quality of hospital care for children in Kazakhstan, Republic of Moldova, and Russia: systematic observational assessment. *Lancet* 2006; 367:919–25.
54 Auto J, Nasi T, Ogaoga D, Kelly J, Duke T. Hospital services for children in the Solomon Islands: rebuilding after the civil conflict. *J Paediatr Child Health* 2006; 42:680–87.
55 Subhi R, Adamson M, Campbell H, Weber M, Smith K, Duke T. The prevalence of hypoxaemia among ill children in developing countries: a systematic review. *Lancet Infect Dis* 2009; 9:219–27.
56 *Cough or Difficult Breathing. Pocketbook of Hospital Care for Children: Guidelines for the Management of Common Illnesses with Limited Resources.* Geneva: World Health Organization, 2005, pp. 69–108.
57 Duke T, Mgome J, Frank D. Hypoxaemia in children with severe pneumonia in Papua New Guinea. *Int J Tuberc Lung Dis* 2001; 5:511–19.
58 Rojas MX, Granados RC, Charry-Anzola LP. Oxygen therapy for lower respiratory tract infections in children between 3 months and 15 years of age. *Cochrane Database Syst Rev* 2009; 1:CD005975.
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