Higher childhood pneumonia admission threshold remains in Lao PDR: an observational study

Ruth Lim ,[1] Molina Chaummanivong,[2] Chansathit Taikeophithoun,[2] Amy Gray,[3,4] Adam W J Jenney,[5] Vanphanom Sychareun,[2] Cattram Nguyen,[1,3] Fiona Russell [1,3]

► Additional supplemental material is published online only. To view, please visit the journal online (http://dx.doi.org/10.1136/archdischild-2021-323626).

[1]Asia-Pacific Health Research Group, Murdoch Children's Research Institute, Parkville, Victoria, Australia
[2]Faculty of Public Health, University of Health Sciences, Vientiane, Vientiane Capital, Lao People's Democratic Republic
[3]Department of Paediatrics, The University of Melbourne, Melbourne, Victoria, Australia
[4]Department of General Medicine, The Royal Children's Hospital Melbourne, Parkville, Victoria, Australia
[5]Department of Infectious Diseases, Monash University, Clayton, Victoria, Australia

Correspondence to
Dr Ruth Lim;
ruthie.lim@gmail.com

Received 1 December 2021
Accepted 22 April 2022
Published Online First
18 May 2022

ABSTRACT

Objectives WHO Integrated Management of Childhood Illness (IMCI) guidelines changed pneumonia hospitalisation criteria in 2014, which was implemented in Lao People's Democratic Republic (Lao PDR) in 2015. We determined adherence to: current (2014) IMCI guidelines for children presenting to hospitals with pneumonia, current outpatient management guidelines and identified hospitalisation predictors.

Design Prospective observational study (January 2017 to December 2018).

Setting Outpatient and emergency departments of four hospitals in Vientiane, Lao PDR.

Patients 594 children aged 2–59 months diagnosed with pneumonia.

Main outcome measures Number of children diagnosed, hospitalised, managed, administered preventive measures and followed-up accordant with current guidelines.

Results Non-severe and severe pneumonia were correctly diagnosed in 97% and 43% of children, respectively. Non-severe pneumonia with lower chest wall indrawing (LCI) was diagnosed as severe in 15%. Hospitalisation rates were: 80% for severe pneumonia, 86% and 3% for non-severe pneumonia with and without LCI, respectively. Outpatient oral antibiotic prescribing was high (99%), but only 30% were prescribed both the recommended antibiotic and duration. Appropriate planned follow-up was 89%. Hospitalisation predictors included age 2–5 months (compared with 24–59 months; OR 3.95, 95% CI 1.90 to 8.24), public transport to hospital (compared with private vehicle; OR 2.60, 95% CI 1.09 to 6.24) and households without piped drinking water (OR 4.67, 95% CI 2.75 to 7.95).

Conclusions Hospitalisation practice for childhood pneumonia in Lao PDR remains more closely aligned with the 2005 WHO IMCI guidelines than the currently implemented 2014 iteration. Compliance with current outpatient antibiotic prescribing guidelines was low.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Recent WHO severe pneumonia definition changes will result in apparent decreases in hospitalisation rates for severe pneumonia in the absence of any intervention.
⇒ The impact of these changes in high childhood mortality settings such as Lao People's Democratic Republic (Lao PDR) has not been studied widely.
⇒ There are few studies evaluating hospitalisation predictors for childhood pneumonia in low-income and middle-income countries (LMICs).

WHAT THIS STUDY ADDS

⇒ Correct classification of pneumonia with lower chest wall indrawing but without general danger signs (previously severe pneumonia) as non-severe pneumonia is high in Lao PDR.
⇒ Admission practice for childhood pneumonia remains more closely aligned with previous, rather than current, Integrated Management of Childhood Illness (IMCI) guidelines.
⇒ Adherence to outpatient antibiotic prescribing guidelines for childhood pneumonia is low but adherence to illness prevention measures is high.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Understanding the use of and adherence to IMCI definitions and management recommendations is crucial to measuring the impact of childhood pneumonia interventions.
⇒ Factors affecting pneumonia admission practice outside of guideline change in high-childhood mortality LMICs requires further research.
⇒ Factors affecting antibiotic prescribing practice in high-childhood mortality LMICs requires further research.

To cite: Lim R, Chaummanivong M, Taikeophithoun C, *et al*. *Arch Dis Child* 2022;**107**:872–877.

BACKGROUND

Pneumonia is the leading cause of postneonatal mortality in children under 5 years, the majority occurring in low-income and middle-income countries (LMICs).[1 2] Diagnosis remains clinical, with microbiological and radiological tests providing minimal improvement in diagnostic sensitivity and specificity.[1]

To standardise diagnosis, the WHO developed clinical definitions of pneumonia and severe pneumonia, outlined in the 2005 Integrated Management of Childhood Illness (IMCI) guidelines.[3] Aimed at integrating prevention, diagnosis and treatment of common childhood illnesses, these guidelines defined pneumonia as cough with tachypnoea (>50 breaths per minute and >40 breaths per minute for 2–11 months and 12–59 months). Children with pneumonia and lower chest wall indrawing (LCI), stridor or any general danger signs (eg, inability to drink) were classified as having severe pneumonia or very severe disease, requiring hospitalisation and parenteral antibiotics. Many LMICs have since adopted these guidelines.

Given the challenges of hospitalisation in LMICs—unreliable medicine supply, costs to families, nosocomial infection, healthcare access[4 5]—several non-inferiority studies conducted in LMICs compared outpatient oral antibiotics and inpatient parenteral antibiotics for pneumonia with LCI, and found no difference in treatment failure.[6 7] A systematic review subsequently concluded the evidence was low quality, with further research required,[4] however the WHO proceeded to modify pneumonia definitions and management recommendations in 2014.[8] LCI ceased to be a criterion for hospitalisation and parenteral antibiotics.

These modifications are likely to result in pneumonia hospitalisation rate changes in LMICs with widespread IMCI guideline use. A recent observational study of six LMICs, including Lao People's Democratic Republic (Lao PDR), reported an apparent decrease for infants aged 2–23 months in: (1) Severe pneumonia hospitalisations by up to 50%, and (2) Annual incidence of severe pneumonia by up to 3423 per 100 000 infants when comparing 2005 and 2014 IMCI definitions.[9]

The impact of case definition changes on childhood pneumonia hospitalisation practice has not been widely studied in high-mortality settings. This study in Lao PDR aims to determine the adherence to current (2014) IMCI diagnosis and hospitalisation guidelines with reference to LCI, and current outpatient management guidelines; and to describe predictors of hospitalisation.

METHODS

Study site

Largely rural, Lao PDR ranks among the poorest South-East Asian countries.[10] The estimated population of 7.27 million has 797 000 children under 5 years and an under-5 years mortality rate of 46 deaths per 1000 live births—the highest in the region.[11 12] The capital Vientiane comprises 13% of the population, 78 000 being under 5 years. Public health services operate under a user-pays system, with only 12.5% of the total population medically insured.[13] Vientiane has five hospitals with paediatric wards, where pulse oximetry is routinely available.

The IMCI guidelines were first implemented in Lao PDR in 1999.[14] The Lao language version of the WHO Pocketbook of Hospital Care for children, incorporating the 2005 IMCI pneumonia definition, was introduced in 2010,[15] updated with the new (2014) definition in 2015, and distributed across paediatric services in 2016.

Study design

This multicentre prospective observational study was conducted in the outpatient and emergency departments of four Vientiane hospitals with paediatric wards—Mahosot Hospital, National Child Hospital, Settathirath Hospital and Vientiane Provincial Hospital—between January 2017 and December 2018.

Study procedures

All children aged 2–59 months presenting to hospital and diagnosed with pneumonia of any severity by the treating clinician were eligible.

Following written informed consent by parent or guardian, data collection forms (DCFs) were completed by the treating clinician at first presentation. A complete list of variables collected is available in online supplemental appendix 1. In order to determine adherence to diagnosis, management and prevention guidelines, variables relating to clinical features, diagnosed pneumonia severity, management and preventive measures were recorded. To determine hospitalisation predictors, variables related to patient demographics, household environment, parental education, exclusive breast feeding and comorbidities were recorded.

For those managed as outpatients, a second DCF was completed by the treating clinician at follow-up, and clinical features and management variables were recorded. Two weeks following initial presentation, participants were contacted by the study team via telephone to determine remaining symptoms and outcome. All available phone numbers for participants' households were recorded at initial presentation. Where initial telephone contact was unsuccessful, three further attempts to make contact over the subsequent month using all provided phone numbers were made, after which they were deemed lost to follow-up.

Definitions

Current (2014) and previous (2005) IMCI case definitions for pneumonia and severe pneumonia were used.[3 8]

Current case definitions: non-severe pneumonia was defined as cough and/or difficulty breathing, and tachypnoea (age-specific) and/or LCI; severe pneumonia was defined as having criteria for pneumonia with at least one general danger sign including inability to drink, persistent vomiting, convulsions, lethargy, unconsciousness, stridor in calm child, severe malnutrition, central cyanosis or oxygen saturations less than 90% in room air.[8]

Previous case definitions: non-severe pneumonia was defined as cough and/or difficulty breathing, and tachypnoea (age-specific); severe pneumonia was defined as having criteria for pneumonia and LCI; very severe disease was defined as having criteria for pneumonia with at least one general danger sign (as above, except oxygen saturations less than 90% in room air).[3]

The following criteria were used to define adherence to current IMCI management guidelines: prescription of oral amoxicillin for 3 days if non-severe pneumonia without LCI and 5 days with LCI, and planned outpatient follow-up in 3 days; for severe pneumonia, hospitalisation and commencement of intravenous antibiotics.

The following criteria were used to define whether children had received appropriate preventive measures according to current IMCI illness prevention guidelines: vitamin A in the preceding 6 months for those older than 6 months; deworming treatment in the preceding 6 months for those older than 12 months; age-appropriate vaccinations according to the Lao PDR national schedule (BCG and hepatitis B vaccines at birth; diphtheria, tetanus, pertussis, hepatitis B, *Haemophilus influenzae* type B, pneumococcal and polio vaccines at 2 months, 4 months and 6 months; measles vaccine at 12 months). Correlation with hand-held immunisation records was performed where available.

Case fatality was defined as death occurring within 14 days of discharge home.

Data management and statistical analysis

Data were double entered onto EpiData (V.3.1); statistical analysis was performed using Stata (V.14, Stata Corporation, College Station, Texas, USA). Categorical variables were summarised using frequency distributions; continuous variables using means and SD, or medians and IQRs as appropriate. Where there were missing values, analyses were performed using available data, and missing data rates are reported.

A complete list of variables evaluated as hospitalisation predictors is available in online supplemental appendix 2. To identify

predictors of hospitalisation, univariable logistic regression was performed, and unadjusted ORs and 95% CIs reported. Adjusted ORs and 95% CIs were calculated using multivariable logistic regression which included variables selected *a priori* based on the literature (two or more people less than 5 years old in household, household biofuel exposure, household cigarette smoke exposure),[16–18] and any variables with p<0.2 by univariable analysis. The final regression model used data from those with complete data on all model variables and collinearity was checked using the variance inflation factor.

Sample size

To address the primary objective of determining adherence to current diagnosis and hospitalisation guidelines, a precision-based sample size calculation was performed. The calculation assumed that pneumonia admission practice would still concur with previous guidelines, with the majority of children with pneumonia and LCI hospitalised. Assuming hospitalisation of 90% of children with pneumonia and LCI, we calculated a sample size of 140 cases with pneumonia and LCI and/or general danger signs was required to estimate the percentage adherence to current hospitalisation guidelines with 95% CIs of width±5%.

We estimated that 600 children diagnosed with pneumonia of any severity would be required to meet the sample size requirement of 140 children with pneumonia and LCI and/or general danger signs. Data from children with pneumonia of any severity were included in the hospitalisation predictors analysis.

RESULTS

There were 594 eligible children enrolled between January 2017 and December 2018. Table 1 reports participant characteristics. The median age of participants was 19 months (IQR 10–30 months); the the most common age category was 24–59 months (40.1%). The majority resided in Vientiane (70.5%) and travelled to hospital in under 1 hour (78.1%), and almost 90% of participants had previous exposure to exclusive breast feeding by carer report.

Table 2 reports classification, management and outcomes of participants. According to current pneumonia case definitions, 13.5% of participants had severe pneumonia. Those with pneumonia and LCI but without general danger signs (previously classified 'severe pneumonia') comprised 14.6% of participants. Of these, the majority (85.1%) were diagnosed correctly as non-severe pneumonia, but most (86.2%) were hospitalised. Case fatality in those with severe pneumonia was 2.5% (two hospitalised participants). A fifth of participants were unable to be contacted for follow-up.

Adherence to outpatient pneumonia antibiotic guidelines was low (30.8%), although over 50% were prescribed amoxicillin of any duration and almost all were prescribed an antibiotic (table 3). Antibiotic prescribing outside guideline recommendations mainly comprised broad-spectrum antibiotics (table 3). Median duration of any oral antibiotic prescription was 3 days (IQR 3–3) and oral amoxicillin prescription outside of recommended guidelines was 2 days (IQR 2–2). Adherence to illness prevention guidelines was high for deworming (82%), vitamin A (70%) and age-appropriate immunisations (93%).

Table 4 reports univariable and multivariable logistic regression results for hospitalisation predictors. Complete data were available for 537 participants (90.4%) included in the final multivariable logistic regression model. Being aged 2–5 months was strongly positively associated with hospitalisation when compared with 24–59 months (OR 3.95, 95% CI 1.90 to 8.24).

Table 1 Characteristics of children aged 2–59 months presenting to central hospitals in Vientiane, Lao PDR with pneumonia (n=594)

Characteristics	Summary statistic
Demographics	
Age in months, median (IQR)	19 (10–30)
Age category, n/N (%)	
2–5 months	70/594 (11.8)
6–11 months	97/594 (16.3)
12–23 months	189/594 (31.8)
24–59 months	238/594 (40.1)
Female, n/N (%)	280/594 (47.1)
From Vientiane Capital province, n/N (%)	399/566 (70.5)
Time taken to get to hospital <1 hour, n/N (%)	461/590 (78.1)
Lao Loum ethnicity, n/N (%)	496/592 (83.8)
Household characteristics	
Travelled to hospital in private vehicle, n/N (%)	520/583 (89.2)
Less than two household members aged <5 years, n/N (%)	341/590 (57.8)
Cigarette smokers in household, n/N (%)	206/588 (35.0)
Biofuel used as household cooking fuel*, n/N (%)	478/592 (80.7)
Household drinking water piped into residence†, n/N (%)	336/591 (56.9)
Household income per month below the poverty line‡, n/N (%)	19/588 (3.2)
Mother completed primary school or above, n/N (%)	503/585 (86.0)
Health preventive measures	
Ever exclusively breast fed, n/N(%)	520/581 (89.5]
Previous presentation for current illness, n/N (%)	216/577 (37.4)
All age-appropriate immunisations received, n/N (%)	549/592 (92.7)
Received deworming treatment in last 6 months§, n/N (%)	329/400¶ (82.3)
Received vitamin A in last 6 months**, n/N (%)	329/471†† (69.9)

*Biofuel defined as wood and charcoal; non-biofuel defined as electricity, kerosene, gas.
†Other types of drinking water included public or protected well, unprotected well, river or canal.
‡Poverty line less than 250 000 Kip.[34]
§If over 12 months of age.
¶Denominator is those 12 months and over only (n=427) with available data.
**If over 6 months of age.
††Denominator includes those 6 months and over only (n=524) with available data.
Lao PDR, Lao People's Democratic Republic.

Participants who travelled to hospital using public transport compared with private vehicle, and lived in households without piped drinking water also had higher odds of hospitalisation (OR 2.60, 95% CI 1.09 to 6.24; OR 4.67, 95% CI 2.75 to 7.95 respectively).

DISCUSSION

To our knowledge, this is the first study to evaluate adherence to current IMCI guidelines for diagnosis, hospitalisation, management and prevention of childhood pneumonia, as well as hospitalisation predictors for children with pneumonia in South-East Asia. We have demonstrated that with the most recent changes to WHO pneumonia definitions, correct pneumonia severity classification is reasonably high, but adherence to current hospitalisation recommendations is low, suggesting that admission practice has not yet changed from previous guidelines. Moreover, although antibiotics were prescribed, adherence to outpatient oral antibiotic prescribing guidelines was low. Adherence to recommended illness prevention measures was high.

Changes to WHO pneumonia definitions in 2014 aimed to relieve the burden of hospitalisation to families, communities and governments for children with non-severe pneumonia with

Table 2 Classification, management and outcomes of children aged 2–59 months presenting to central hospitals in Vientiane, Lao PDR with pneumonia (n=594)

	Pneumonia without LCI* or general danger signs†, n(%)	Pneumonia with LCI* but without general danger signs‡, n(%)	Pneumonia with general danger signs§, n(%)
Pneumonia category, n (%)	427 (71.9)	87 (14.6)	80 (13.5)
Classification¶, n (col %)			
Classified as non-severe pneumonia	427 (100.0)**	74 (85.1)††	46 (57.5)‡‡
Classified as severe pneumonia	0 (0.0)‡‡	13 (14.9)§§	34 (42.5)**
Management, n (col %)			
Admitted to hospital	13 (3.0)‡‡	75 (86.2)§§	64 (80.0)**
Treated as outpatient	414 (97.0)**	12 (13.8)††	16 (20.0)‡‡
Outcome at follow-up phone call¶¶, n (col %)			
Better	326 (76.3%)	64 (73.6%)	51 (63.8%)
Still unwell***	27 (6.3%)	5 (5.7%)	6 (7.5%)
Died	0 (0.0%)	0 (0.0%)	2 (2.5%)
Unable to contact	74 (17.3%)	18 (20.7%)	21 (26.2%)

Pneumonia (2005) defined as: cough or dyspnoea, and tachypnoea (>50 breaths per minute (bpm) if 2–11 months old; or >40 bpm if 12–59 months old). Pneumonia (2014) defined as: cough or dyspnoea, and one of either tachypnoea or chest indrawing. Severe pneumonia (2005 and 2014) defined as: criteria for pneumonia, plus either central cyanosis, or oxygen saturation <90% in room air, severe respiratory distress, inability to drink, lethargy, unconsciousness or convulsions.
*Lower chest indrawing.
†Non-severe pneumonia as per 2005 and 2014 WHO pneumonia definitions.
‡Non-severe pneumonia as per 2014 WHO pneumonia definition (as above). Severe pneumonia as per 2005 definition.
§Severe pneumonia as per 2005 and 2014 WHO pneumonia definitions.
¶As per treating doctor.
**Consistent with 2005 and 2014 WHO pneumonia definitions.
††Consistent with 2014 WHO pneumonia definition.
‡‡Inconsistent with 2005 and 2014 WHO pneumonia definitions.
§§Consistent with 2005 WHO pneumonia definition.
¶¶Follow-up phone call planned for 2 weeks following initial presentation. Median time for follow-up phone call 21 days (IQR 16–29).
***One or more of the following symptoms: dry cough, productive cough, difficulty breathing, lethargy, inability to drink, vomiting or convulsions.
Lao PDR, Lao People's Democratic Republic; LCI, lower chest wall indrawing.

Table 3 Adherence to 2014 WHO guidelines for outpatient management of pneumonia (n=442‡‡) and child health preventive measures (n=594) in children aged 2–59 months in central hospitals in Vientiane, Lao PDR

Outpatient management	N/N (%)
Received oral antibiotics	438/442 (99.1)
Received amoxicillin*	234/442 (52.9)
Received amoxicillin for 3 days if non-severe pneumonia with no LCI and treated as outpatient (n=414)	130/414 (31.4)
Received amoxicillin for 5 days if non-severe pneumonia with LCI and treated as outpatient (n=12)	1/12 (8.3)
Planned follow-up in 3 days or less	392/442 (88.7)
Follow-up completed in those with planned follow-up	46/392 (11.7%)
Preventive measures†	
Deworming in last 6 months if >12 months old‡	329/400§ (82.3)
Vitamin A in last 6 months if >6 months old¶	329/471** (69.9)
Received all age-appropriate immunisations††	549/592 (92.7)

*Non-amoxicillin antibiotic prescribing included: third-generation cephalosporins (cefixime, 75/442, 17.0%), macrolides (azithromycin, clarithromycin and erythromycin, 84/442, 19%) and amoxicillin/clavulanic acid (25/442, 5.7%).
†As per parent report or recorded in parent-held record.
‡WHO recommendation for children >12 months of age.
§Denominator is those 12 months and over only (n=427) with available data.
¶WHO recommendation for children >6 months of age.
**Denominator includes those 6 months and over only (n=524) with available data.
††Received BCG and hepatitis B immunisations at birth; completed one, two or three doses of diphtheria, tetanus, pertussis, hepatitis B, haemophilus influenzae B (Hib), oral polio vaccine or inactivated polio vaccine and pneumococcal immunisations at 6 weeks, 10 weeks and 14 weeks; received measles and rubella immunisation at 9 months.
‡‡All patients discharged with diagnosis of pneumonia, regardless of severity. Does not include those hospitalised at first presentation.
Lao PDR, Lao People's Democratic Republic; LCI, lower chest wall indrawing.

LCI. Our study suggests, however, that while pneumonia severity classifications may have changed, admission practice remains unchanged. In neighbouring Vietnam, a recent study found high incidence of hospitalisation for non-severe respiratory illness, perhaps related to perceived community expectations and historical use of aggressive therapy (eg, intravenous antibiotics) in such cases.[19] In Lao PDR, the under-5 years mortality rate is the highest in South-East Asia, but has reduced by 70% since 1990.[11] Reluctance to raise the clinical admission threshold in high-childhood mortality settings may reflect perceived clinician need to lower the treatment failure risk through hospitalisation, in order to continue reducing mortality. It is conceivable that other high-childhood mortality LMICs face similar pressure, and factors affecting admission practice outside of guideline changes require further research.

Understanding adherence to guidelines is also important for pneumonia impact evaluations. Measuring the impact of vaccines, or other interventions, is challenging, not least because of the lack of highly sensitive and specific pneumonia definitions.[20] Countries such as Lao PDR are often heavily reliant on administrative hospitalisation data to document disease burden. If pneumonia admission practice changes, the incidence of pneumonia hospitalisations appears to decline regardless of intervention.[9] Moreover, LCI has been independently associated with mortality in high-mortality settings where bacterial pneumonia rates are high.[21 22] In high-childhood mortality LMICs, little is known about the impact these changes will have on mortality, and understanding the use of IMCI definitions and management recommendations becomes crucial to measuring impact.

Prescription of an antibiotic occurred in most outpatient-managed pneumonia cases, however the correct antibiotic and duration was low in our study. This finding is consistent with reports of variable, inconsistent antibiotic prescribing in LMICs.[23] Recent clinical trials have demonstrated lower treatment failure risk with amoxicillin compared with placebo for non-severe pneumonia with tachypnoea,[24 25] as well as non-inferiority of 5 days versus 3 days of amoxicillin for non-severe pneumonia with LCI.[26] This further highlights the importance of research into factors affecting prescribing practice, as well as ongoing training in IMCI guideline implementation to improve clinical care and outcomes.[15 27]

To our knowledge, there are no other studies to date examining potential childhood pneumonia hospitalisation predictors in South-East Asia. Consistent with our findings, several studies conducted in LMICs in other regions also demonstrated young age to be strongly predictive of hospitalisation.[28–32] Two studies examining demographic and environmental factors found low socioeconomic status, household smoke exposure and low parental education levels to be significant.[31 32] We found these factors to be significant in univariable analysis, but not in our multivariable model. Travel to hospital via public transport, and use of non-piped household water were significant predictive factors in our study, but not in other comparable studies. Household income was not found to be predictive in our final multivariable regression model. However, with few households in our cohort living in poverty, it is possible that use of public

Table 4 Univariable and multivariable logistic regression (n=537) for predictors of hospitalisation for pneumonia in children aged 2–59 months in Vientiane, Lao PDR

Predictor	Admission n/N (%)	Unadjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Age					
24–59 mo	47/238 (19.7)	ref			
12–23 mo	27/189 (14.3)	0.68 (0.41 to 1.14)	<0.001	1.22 (0.63 to 2.35)	**<0.001**
6–11 mo	28/97 (28.9)	1.73 (1.01 to 2.97)		0.59 (0.32 to 1.07)	
2–5 mo	42/70 (60.0)	6.10 (3.43 to 10.83)		**3.95 (1.90 to 8.24)**	
Sex					
Female	66/279	ref			
Male	78/312	1.08 (0.74 to 1.57)	0.704		
Ethnicity					
Lao Loum	88/496	ref			
Other	56/96	6.57 (4.11 to 10.49)	<0.001	1.87 (0.96 to 3.67)	0.067
Time taken to get to hospital					
<1 hour	85/461	ref			
≥1 hour	59/129	1.37 (1.06 to 1.78)	0.017	1.06 (0.58 to 1.94)	0.847
Mode of transport to hospital					
Private vehicle	97/520	ref			
Public transport	44/63	9.97 (5.58 to 17.83)	<0.001	**2.60 (1.09 to 6.24)**	**0.032**
No of household members aged <5 years					
<2	72/341	ref			
≥2	72/249	1.49 (1.02 to 2.18)	0.037	1.14 (0.71 to 1.84)	0.597
Cigarette smokers in household					
No	80/382	ref			
Yes	62/206	1.66 (1.13 to 2.45)	0.010	1.07 (0.63 to 1.80)	0.807
Household fuel					
Non-biofuel	13/114	ref			
Biofuel	131/478	1.59 (1.01 to 2.52)	0.047	1.55 (0.77 to 3.11)	0.223
Household drinking water					
Piped	34/336	ref			
Other	110/255	6.80 (4.41 to 10.48)	<0.001	**4.67 (2.75 to 7.95)**	**<0.001**
Household income					
Above poverty line*	131/569	ref			
Below poverty line*	10/19	1.45 (1.03 to 2.04)	0.031	0.75 (0.18 to 3.18)	0.693
Mother completed primary school					
Yes	109/503	ref			
No	35/82	2.77 (1.71 to 4.50)	<0.001	0.75 (0.36 to 1.59)	0.460
Ever exclusively breast fed					
Yes	134/520	ref			
No	8/61	0.43 (0.20 to 0.93)	0.032	0.67 (0.28 to 1.57)	0.351
Previous presentation for current illness					
No	74/361	ref			
Yes	69/216	0.55 (0.38 to 0.81)	0.002	0.63 (0.39 to 1.02)	0.062
All age-appropriate immunisations received					
Yes	116/549	ref			
No	28/43	6.91 (3.57 to 13.36)	<0.001	1.47 (0.56 to 3.84)	0.433

*Poverty line less than 250 000 Kip[34]
Lao PDR, Lao People's Democratic Republic.

transport and non-piped household water represented a more nuanced proxy for household income and socioeconomic status.

Study limitations included reliance on parental recall. Variables related to prior preventive measures may have been subject to recall bias—in particular, our reported rates of having ever exclusively breast fed and receiving age-appropriate immunisations are higher than reported elsewhere.[33] Our cohort of participants also had access to hospitals, possibly underrepresenting those with lower healthcare access as evidenced by the few participants living in poverty, and the higher reported immunisation rates than the national average (56%).[33]

Further limitations of our study included loss to follow-up at 2 weeks postinitial presentation due to incorrect phone numbers. There were no fatalities in children with non-severe pneumonia and LCI, however the high loss to follow-up rate in this group raises the possibility of unrecorded fatalities, as well as underestimation of other outcomes, including those who were better and still unwell.

Despite these limitations, this study provides the first report of current adherence to IMCI guidelines for diagnosis, management and prevention of pneumonia, and hospitalisation predictors for childhood pneumonia. Specifically, it highlights that

admission practice for childhood pneumonia in Lao PDR, a high childhood mortality setting, has not changed despite recent WHO pneumonia definition changes. Our results should be taken into account when reviewing trends in the burden of childhood pneumonia and impacts of various interventions in high childhood mortality LMIC settings.

Acknowledgements The authors thank the Ministry of Health, Lao PDR and University of Health Sciences, Vientiane, Lao PDR. The authors also thank the study staff and participating clinicians and families at Mahosot Hospital, National Child Hospital, Settathirath Hospital and Vientiane Provincial Hospital.

Contributors RL and FR conceptualised and designed the study. AG and AWJJ contributed to study design and protocol preparation. VS supervised data collection. MC and CT collected the data. CN contributed to statistical analysis. RL drafted the manuscript and undertook the analysis. All authors critically reviewed and approved the final manuscript. RL is the guarantor for the overall content.

Funding This study was funded by Gavi, the Vaccine Alliance, grant number PP344/1213A1. FR has an Australian National Health and Medical Research Council Investigator grant. This project was supported by the Victorian Government's Operational Infrastructure Support Programme.

Competing interests None declared.

Patient consent for publication Not applicable.

Ethics approval This study involves human participants and was approved by Royal Children's Hospital Human Research Ethics Committee, Melbourne, Australia (33177C) and University of Health Sciences Ethics Committee, Vientiane, Lao PDR (6680). Participants gave informed consent to participate in the study before taking part.

Provenance and peer review Not commissioned; externally peer reviewed.

Data availability statement Data are available upon reasonable request.

ORCID iDs
Ruth Lim http://orcid.org/0000-0003-3960-3661
Fiona Russell http://orcid.org/0000-0002-3077-9639

REFERENCES

1 Izadnegahdar R, Cohen AL, Klugman KP, *et al*. Childhood pneumonia in developing countries. *Lancet Respir Med* 2013;1:574–84.
2 Perin J, Mulick A, Yeung D, *et al*. Global, regional, and national causes of under-5 mortality in 2000-19: an updated systematic analysis with implications for the sustainable development goals. *Lancet Child Adolesc Health* 2022;6:106-115.
3 World Health Organization. *Handbook IMCI: integrated management of childhood illness*. Geneva: World Health Organization, Dept. of Child and Adolescent Health and Development, 2005.
4 Das RR, Singh M. Treatment of severe community-acquired pneumonia with oral amoxicillin in under-five children in developing country: a systematic review. *PLoS One* 2013;8:e66232.
5 Rojas MX, Granados C. Oral antibiotics versus parenteral antibiotics for severe pneumonia in children. *Cochrane Database Syst Rev* 2006;2:CD004979.
6 Addo-Yobo E, Anh DD, El-Sayed HF, *et al*. Outpatient treatment of children with severe pneumonia with oral amoxicillin in four countries: the mass study. *Trop Med Int Health* 2011;16:995–1006.
7 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.
8 World Health Organization. *Revised WHO classification and treatment of childhood pneumonia at health facilities: evidence summaries*. Geneva: World Health Organization, 2014.
9 Russell FM, Reyburn R, Chan J, *et al*. Impact of the change in WHO's severe pneumonia case definition on hospitalized pneumonia epidemiology: case studies from six countries. *Bull World Health Organ* 2019;97:386–93.
10 World population review. Poorest Asian countries 2021, 2021. Available: https://worldpopulationreview.com/country-rankings/poorest-asian-countries [Accessed 1 Mar 2021].
11 The United nations Inter-Agency group for child mortality estimation. levels and trends in child mortality report 2020. New York: UNICEF 2020. Available: https://www.unicef.org/reports/levels-and-trends-child-mortality-report-2020 [Accessed 1 Mar 2022].
12 United Nations, Department of Economic and Social Affairs, Population Division. World population prospects 2019. United nations, 2019. Available: https://population.un.org/wpp/Download/Standard/Population/ [Accessed 1 Mar 2022].
13 World Health Organisation Western Pacific Regional Office. WHO country cooperation strategy for the Lao People's Democratic Republic, 2012-2015. Manila: WHO, 2011. Available: https://iris.wpro.who.int/handle/10665.1/7873 [Accessed 1 Mar 2022].
14 United Nations Children's Fund. Assessment of the integrated management of newborn and childhood illnesses Lao PDR, 2017. Available: https://www.unicef.org/laos/reports/assessment-integrated-management-newborn-and-childhood-illnesses-lao-pdr [Accessed 1 Mar 2022].
15 Gray AZ, Soukaloun D, Soumphonphakdy B, *et al*. Implementing who Hospital guidelines improves quality of paediatric care in central hospitals in Lao PDR. *Trop Med Int Health* 2015;20:484–92.
16 Principi N, Marchisio P, Schito GC, *et al*. Risk factors for carriage of respiratory pathogens in the nasopharynx of healthy children. Ascanius project Collaborative group. *Pediatr Infect Dis J* 1999;18:517–23.
17 Dherani M, Pope D, Mascarenhas M, *et al*. Indoor air pollution from unprocessed solid fuel use and pneumonia risk in children aged under five years: a systematic review and meta-analysis. *Bull World Health Organ* 2008;86:390–8.
18 Greenberg D, Givon-Lavi N, Broides A, *et al*. The contribution of smoking and exposure to tobacco smoke to Streptococcus pneumoniae and Haemophilus influenzae carriage in children and their mothers. *Clin Infect Dis* 2006;42:897–903.
19 Nguyen TKP, Nguyen DV, Truong TNH, *et al*. Disease spectrum and management of children admitted with acute respiratory infection in Viet Nam. *Trop Med Int Health* 2017;22:688–95.
20 Goodman D, Crocker ME, Pervaiz F, *et al*. Challenges in the diagnosis of paediatric pneumonia in intervention field trials: recommendations from a pneumonia field trial Working group. *Lancet Respir Med* 2019;7:1068–83.
21 Reed C, Madhi SA, Klugman KP, *et al*. Development of the respiratory index of severity in children (RISC) score among young children with respiratory infections in South Africa. *PLoS One* 2012;7:e27793.
22 Agweyu A, Lilford RJ, English M, *et al*. Appropriateness of clinical severity classification of new who childhood pneumonia guidance: a multi-hospital, retrospective, cohort study. *Lancet Glob Health* 2018;6:e74–83.
23 World Health Organization. Promoting rational use of medicines. Geneva: who, 2021. Available: https://www.who.int/activities/promoting-rational-use-of-medicines [Accessed 1 Mar 2022].
24 Ginsburg AS, Mvalo T, Nkwopara E, *et al*. Placebo vs amoxicillin for nonsevere Fast-Breathing pneumonia in Malawian children aged 2 to 59 months. *JAMA Pediatr* 2019;173:21–8.
25 Jehan F, Nisar I, Kerai S, *et al*. Randomized trial of amoxicillin for pneumonia in Pakistan. *N Engl J Med* 2020;383:24–34.
26 Ginsburg A-S, Mvalo T, Nkwopara E, *et al*. Amoxicillin for 3 or 5 days for Chest-Indrawing pneumonia in Malawian children. *N Engl J Med* 2020;383:13–23.
27 Gray A, Chhor L, Sanyalack S, *et al*. Some sustained improvements in pneumonia case management four and five years following implementation of paediatric Hospital guidelines in Lao PDR. *Sci Rep* 2017;7:10679.
28 Nascimento-Carvalho CMC, Rocha H, Santos-Jesus R, *et al*. Childhood pneumonia: clinical aspects associated with hospitalization or death. *Braz J Infect Dis* 2002;6:22–8.
29 le Roux DM, Myer L, Nicol MP, *et al*. Incidence and severity of childhood pneumonia in the first year of life in a South African birth cohort: the Drakenstein child health study. *Lancet Glob Health* 2015;3:e95–103.
30 Shah N, Ramankutty V, Premila PG, *et al*. Risk factors for severe pneumonia in children in South Kerala: a hospital-based case-control study. *J Trop Pediatr* 1994;40:201–6.
31 Hassan MK, Al-Sadoon I. Risk factors for severe pneumonia in children in Basrah. *Trop Doct* 2001;31:139–41.
32 Murtagh P, Cerqueiro C, Halac A, *et al*. Acute lower respiratory infection in Argentinian children: a 40 month clinical and epidemiological study. *Pediatr Pulmonol* 1993;16:1–8.
33 World Health Organization and United Nations Children's Fund. Lao People's Democratic Republic: WHO and UNICEF estimates of immunization coverage: 2019 revision, 2020. Available: https://www.who.int/immunization/monitoring_surveillance/data/lao.pdf [Accessed 1 Mar 2022].
34 Lao Statistics Bureau and World Bank. Poverty profile in Lao PDR: poverty report for the Lao expenditure and consumption survey 2018-2019. Vientiane: the world bank, 2020. Available: https://thedocs.worldbank.org/en/doc/923031603135932002-0070022020/original/LaoPDRPovertyProfileReportENG.pdf [Accessed 1 Mar 2022].

APPENDIX 1. Complete list of variables collected on data collection forms

At first presentation to hospital, in order to determine adherence to diagnosis, management and prevention guidelines, variables recorded included:

a) clinical features (cough, dyspnoea, LCI, tachypnoea, tachycardia, fever, hypoxia, inability to drink, lethargy, decreased consciousness, stridor when calm, wheeze, cyanosis, convulsions)
b) diagnosed pneumonia severity
c) management (hospitalisation or outpatient management, type, route and duration of antibiotics)
d) preventive measures (vitamin A, deworming, immunisations) were recorded.

To determine hospitalisation predictors, variables recorded included:

a) patient demographics (age, sex, residence, ethnicity)
b) time and transport to hospital
c) household (number of persons, smokers, type of water consumed, toilet facilities, cooking fuel used, income)
d) parental education level
e) history of exclusive breastfeeding
f) comorbidities

For those managed as outpatients, a second data collection form was completed by the treating clinician at follow-up, and recorded clinical features and management variables (as above). Two weeks following initial presentation, participants were contacted by the study

team via telephone to determine remaining symptoms (cough, dyspnoea, lethargy, inability to drink, seizures) and outcome (better, still unwell, died, taken to another health facility).

APPENDIX 2. List of variables evaluated by univariable as predictors of hospitalisation

The following variables were evaluated as hospitalisation predictors:

a) age [two to five months, six to 11 months, 12-23 months or 24-59 months]
b) sex
c) ethnicity [Lao Loum or other (Hmong, Khmu, Prai, Ma Kong, Alak, Ngae, Talieng, Dak Kang)]
d) transport mode [private vehicle or public transport]
e) hospital travel time [under one hour or longer]
f) two or more people less than five years old in household
g) household cigarette smoke exposure
h) primary household cooking fuel [biofuel (wood, charcoal) or non-biofuel (electricity, gas, kerosene)]
i) household income below the poverty line [less than 250,000 kip per month]
j) maternal completion of primary school
k) any history of exclusive breastfeeding
l) previous presentation to a health facility for current illness
m) being age-appropriately immunised.