Association between hospitalised childhood pneumonia and follow-up chest radiographs in high-risk populations: a secondary analysis of a multicentre randomised controlled trial

Hing Cheong Kok ,[1,2,3] Stephanie T Yerkovich,[1,3] Gabrielle B McCallum,[1] Keith Grimwood ,[1,4,5] Ian Brent Masters,[3,6] Nicholas Fancourt,[1,7] Siew Moy Fong,[2] Anna M Nathan,[8] Catherine A Byrnes,[9,10] Robert S Ware ,[5] Nachal Nachiappan,[11] Noorazlina Saari,[11] Peter S Morris,[1,12] Tsin Wen Yeo,[1,13] Victor M Oguoma,[1,14] Jessie Anne de Bruyne,[8] Kah Peng Eg ,[8] Bilawara Lee,[1,15] Mong How Ooi,[16,17] John W Upham,[18] Paul J Torzillo,[19,20] Anne B Chang[1,3,6]

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For numbered affiliations see end of article.

Correspondence to
Dr Hing Cheong Kok; hingcheong.kok@menzies.edu.au

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ABSTRACT

Objective As children hospitalised with community-acquired pneumonia (CAP) are at risk of persistent chest radiograph (CXR) abnormalities and respiratory sequelae, we investigated factors associated with incomplete CXR resolution at 4 weeks and 12 months post-discharge in children from populations at high-risk of chronic lung disease.

Design Secondary analysis—multicentre, placebo-controlled, randomised controlled trial.

Settings and patients 324 children aged 3 months to ≤5 years hospitalised with radiographic-confirmed CAP were enrolled from seven hospitals in Australia, New Zealand and Malaysia. After 1–3 days of intravenous antibiotics, then 3 days of oral amoxicillin–clavulanate, they were randomised to extended (13–14 days) or standard (5–6 days) courses of antibiotics.

Intervention CXRs were performed at admission, 4 weeks, and 12 months post-discharge and reviewed in a blinded manner.

Main outcome measures Radiographic changes of pneumonia at 4 weeks and 12 months post-discharge compared with admission CXRs.

Results Among children with interpretable CXRs, incomplete resolution was seen in 42/253 (17%) at 4 weeks, and 29/212 (14%) at 12 months. Characteristics at admission associated with incomplete CXR resolution at 4 weeks were previous pneumonia hospitalisation (adjusted odds ratio [OR_{adj}])=6.46, 95% confidence interval [CI] 2.21 to 18.85) and increasing age (OR_{adj}=0.60 per-year, 95% CI 0.38 to 0.94). Continuing respiratory symptoms/signs at 4 weeks post-discharge was also associated with incomplete resolution (OR=5.63, 95% CI 2.38 to 13.32). At 12 months, previous pneumonia hospitalisation was associated with persistent incomplete CXR resolution (OR=4.03, 95 % CI 1.25 to 13.02).

Conclusion In high-risk settings, younger age, those with previous pneumonia hospitalisation, or ongoing respiratory symptoms/signs 4 weeks post-discharge from hospitalised CAP may be associated with incomplete CXR resolution. Consequently, follow-up imaging and monitoring may be warranted in these children.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ The necessity of performing a chest radiograph (CXR) post-hospitalisation for community-acquired pneumonia (CAP) in children, particularly those at high risk of chronic lung disease, remains unclear, while factors associated with persistent CXR changes are unknown.

WHAT THIS STUDY ADDS

⇒ CXR follow-up of children from high-risk settings hospitalised for radiographic-confirmed pneumonia found that prior pneumonia hospitalisation and younger age were associated with persistent CXR abnormalities at 4 weeks. Furthermore, prior pneumonia hospitalisation was also significantly associated with CXR abnormalities at 12 months.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ Our findings help inform targeted follow-up strategies for chronic lung disease in children hospitalised with CAP from high-risk settings. This primarily involves post-discharge CXR and closer monitoring of children with identified risk factors and the potential of long-term respiratory sequelae.

INTRODUCTION

Community-acquired pneumonia (CAP) is the leading cause of global mortality in children aged 1–59 months.[1] It is also associated with long-term respiratory sequelae,[2 3] including impaired lung function in children and adults,[4–6] premature adult respiratory-related death (hazard ratio [HR]=1.93, 95% confidence interval [CI] 1.10 to 3.37)[7] and bronchiectasis.[8 9] A case-control study found Australian Indigenous children hospitalised previously for pneumonia were significantly more likely to develop bronchiectasis than other Indigenous

children hospitalised for non-respiratory illnesses (odds ratio [OR=15.2, 95% CI 4.4 to 52.7).[8]

Children in low- and middle-income countries (LMICs),[10] and Indigenous children living in socially-disadvantaged communities in high-income countries (HICs), have the greatest burden of CAP[1 11] and its sequelae.[12 13] In a prospective study involving indigenous Australian children hospitalised with chest radiograph (CXR) evidence of airspace consolidation, those with 'minimal' (0–20%) resolution of consolidation on their pre-discharge CXR, compared with those with 'near-complete' (80–100%) resolution, had increased risk (relative risk [RR]=6.93, 95% CI 1.78 to 26.60) of chronic suppurative lung disease (CSLD) or bronchiectasis.[14]

Follow-up CXRs for children hospitalised with CAP are considered important for those at high risk of chronic lung disorders.[14] However, performing follow-up CXRs for uncomplicated pneumonia is controversial.[15] The British Thoracic Society guidelines state routine follow-up CXRs are not required in previously healthy children but should be considered in those with round pneumonia, atelectasis, or persisting symptoms.[16] Several studies have examined the necessity of follow-up CXRs after childhood pneumonia in both inpatient and outpatient settings.[17–21] However, these focused on short-term (3–7 weeks post-discharge) outcomes. Nevertheless, CXRs beyond these time periods are crucial, as children with incomplete CXR resolution at 6 and 12 months after acute lower respiratory infections (ALRIs) or pneumonia may have persistent lung abnormalities, suggesting underlying chronic respiratory disorders.[22 23]

Furthermore, previous studies[17–21] did not explore associations of specific characteristics of children hospitalised with CAP, such as age, illness severity, or clinical features and follow-up CXRs. Understanding these associations could help identify factors influencing persistent CXR abnormalities, allowing for more timely interventions. Finally, prior studies were conducted in HICs and were single-centre investigations (except one involved two centres within the same region of the United States),[17] potentially limiting generalisability. Data on long-term respiratory outcomes, the value of follow-up CXRs, and risk factors for persistent CXR abnormalities to inform future clinical practice for following children hospitalised with CAP are clearly needed.

We aimed to determine factors associated with incomplete CXR resolution at 4 weeks and 12 months post-discharge in children in high-risk settings who were hospitalised with uncomplicated CAP. We also assessed the association between incomplete CXR resolution at 4 weeks and the time to the next hospitalised ALRI episode. We used data from our multicentre, randomised controlled trial (RCT), conducted between 1 March 2016 and 30 June 2022, which compared an extended 13–14 day versus a standard 5–6 day antibiotic course for children hospitalised with CAP from communities at high risk of chronic lung diseases.[24 25] As the extended-course did not improve respiratory outcomes at 4 weeks or 24 months, data from both treatment arms were combined for this analysis.[24 25]

METHODS (DETAILED FURTHER IN ESM ONLINE SUPPLEMENTAL METHODS)

Study design

Children were enrolled at seven hospitals; one in Australia (Darwin), two in New Zealand (Auckland) and four in Malaysia (Kota Kinabalu, Kuching, Klang, Kuala Lumpur). Informed consent was obtained for all children (ESM online supplemental methods).

Participants and procedures

Children aged 3 months to ≤5 years were eligible for enrolment if they were Aboriginal/Torres Strait Islander (Australia), Māori/Pacific Islander (New Zealand) or any child (Malaysia) with clinical and radiographic signs of pneumonia. After receiving intravenous antibiotics for 1–3 days, eligible children were switched to oral amoxicillin–clavulanate for the next 3 days and randomised to then receive either extended-course (8 days oral amoxicillin–clavulanate) or standard-course (8 days oral placebo). Children were reviewed at 4 weeks, 12 and 24 months post-discharge. Children were considered 'clinically cured' if all respiratory symptoms/signs had resolved at the 4-week review.[24]

CXRs were obtained at admission and repeated during the 4-week and 12-month reviews (when feasible). The CXRs at 4 weeks and 12 months were compared with admission CXRs. An independent senior respiratory paediatrician (IBM), masked to patient information, interpreted the CXRs. The CXRs were assessed for quality, categorised as acceptable, suboptimal, or uninterpretable.[26] Acceptable and suboptimal CXRs were interpreted based on six lung zones: (1) right [upper, middle, lower] and (2) left [upper, middle, lower]. Each lung zone was scored according to the presence/absence of: (1) airspace changes; (2) interstitial changes; or (3) pleural effusion/thickening, cavities, or nodules/mass.

Each affected lung zone on follow-up CXRs was scored as: (1) complete resolution; (2) 75% to <100% resolution; (3) 50% to <75% resolution; (4) 25% to <50% resolution; or (5) <25% resolution. If more than one lung zone was affected, the most severe category was used as the overall score. For 4-week CXRs, near-complete/complete resolution was grouped as '≥75% resolution' (groups 1−2) and '<75% resolution' for incomplete resolution (groups 3−5). For 12-month CXRs, incomplete resolutions were assessed for those in groups 2−5. Incomplete resolution was defined as persistent abnormality in the same lung zone on follow-up CXR. Complete resolution was defined as the resolution of the abnormality in the same lung zone on follow-up CXR.

Statistical analysis

Descriptive statistics are presented as median (interquartile range [IQR) for continuous data and frequency (percentage) for categorical data. Continuous data were analysed using the Mann-Whitney U test and categorical data were analysed using Fisher's exact test. All tests were two-tailed and $p<0.05$ considered significant.

We undertook logistic regression analyses based on backward elimination with a p-value criterion of 0.157 and limited the number of variables in our analyses.[27] We selected variables based on risk factors identified by the World Health Organization (WHO),[28] systematic review evidence,[29] and findings from well-established literature.[8 30] In the regression analysis considering radiographic changes at 4 weeks, the five variables included in the initial model were tachypnoea and/or chest wall recession, poor feeding/unable to drink, age, hypoxaemia, and previous pneumonia hospitalisation. In the regression analysis considering radiographic changes at 12 months, the variables were tachypnoea and/or chest wall recession, age, hypoxaemia and previous pneumonia hospitalisation. A Kaplan-Meier plot was used to display time to the next hospitalised ALRI episode and Cox proportional hazard modelling to calculate HRs. All were censored at 730 days (24 months). Missing data were not imputed. We used Stata V.17 (StataCorp) to analyse data.

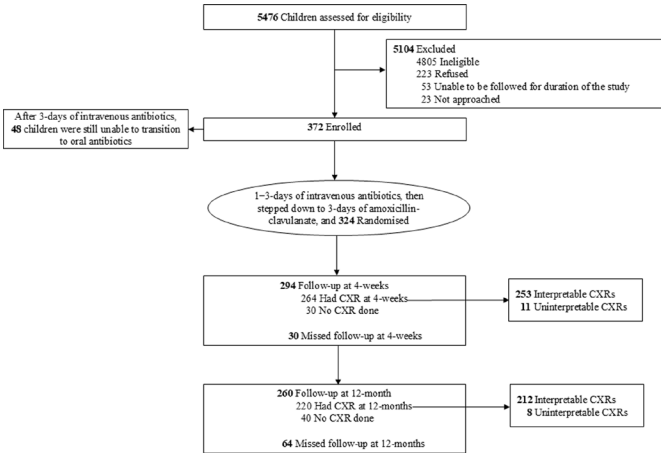

Figure 1 Participant flow diagram. CXR, chest radiograph.

RESULTS

Patient characteristics

We enrolled 372 children, whereby 324 (52% male) were randomised. The median age was 1.3 years (IQR=0.9–1.9). Overall, 264 (81%) and 220 (68%) CXRs were performed at 4 weeks and 12 months, respectively (figure 1). Of these, 253/264 (96%) were interpretable at 4 weeks, and 212/220 (96%) were interpretable at 12 months. Thirty (10%) and 64 (25%) children were lost to follow-up at 4 weeks and 12 months, respectively. Baseline characteristics of those without CXRs at 4 weeks and 12 months were broadly similar to those with follow-up CXRs (ESM online supplemental table 1). However, children without follow-up CXRs had higher preterm birth rates, exposure to maternal and household cigarette smoke and C-reactive protein (CRP) levels than those with at least one follow-up CXR, but these factors did not influence our outcomes presented below (ESM online supplemental table 2). Table 1 details the radiographic findings at 4 weeks and 12 months. Overall, 83% of children with CXRs at 4 weeks had complete (53%) or near-complete (30%) radiographic resolution, while 86% had complete radiographic resolution at 12 months.

Baseline characteristics of children with interpretable CXRs included in our study are displayed in table 2. In the multivariable regression model, the two most important factors associated with incomplete CXR resolution at 4 weeks were previous pneumonia hospitalisation (adjusted OR [OR_{adj}]=6.46, 95% CI 2.21 to 18.85) and age (OR_{adj}=0.60 per-year, 95% CI 0.38 to 0.94). The only significant factor associated with incomplete CXR resolution at 12 months was previous pneumonia hospitalisation (OR=4.03, 95% CI 1.25 to 13.02) (table 3).

Table 1 Radiographic findings at 4 weeks and 12 months

	CXR at 4 weeks	CXR at 12 months
	n=253*	n=212*
Complete resolution	135 (53)	183 (86)†
75% to <100% resolution	76 (30)	19 (9)
50% to <75% resolution	7 (3)	3 (1)
25% to <50% resolution	9 (4)	3 (1)
<25% resolution	26 (10)	4 (2)

*Data are expressed as number (%).
†Percentages do not add up to 100 due to rounding.
CXR, chest radiograph.

Among children with interpretable 4-week CXRs, 34/253 (13%) had ≥1 subsequent hospitalised ALRI between 4 weeks and 24 months post-discharge (figure 2). There was no difference in the 4-week CXR outcomes and the time to the next hospitalised ALRI.

An outcome of our RCT was clinical cure (all respiratory symptoms/signs resolved at 4 weeks).[24] Children without clinical cure at 4 weeks were more likely to have incomplete CXR resolution at 4 weeks than those with clinical cure (OR=5.63, 95% CI 2.38 to 13.32).

At medical chart review, 5/324 (2%) children had chest computed-tomography (cCT) scans ordered by their paediatrician revealing bronchiectasis within 2 years of their hospitalisation. Of these, two had incomplete CXR resolution at both 4 weeks and 12 months, one had complete resolution at 4 weeks and 12 months, another had no follow-up CXRs, and one had uninterpretable CXRs. At the 12 months review, 29/212 (14%) children had persistent CXR abnormalities. Of these, 14/29 (48%) did not have chronic cough or observed wet/productive cough in the clinic.

DISCUSSION

In children aged ≤5 years hospitalised for CAP in settings with a high risk of chronic lung disease among community members, we found at 4 weeks post-discharge, previous pneumonia hospitalisation and age were associated with incomplete CXR resolution. Children without a clinical cure at 4 weeks also had increased odds of incomplete CXR resolution at this time point. Furthermore, previous pneumonia hospitalisation was also positively associated with persistent CXR abnormalities at 12 months. However, the time to the next respiratory-related hospitalisation was not significantly different between those with incomplete versus those with near-complete/complete CXR resolution at 4 weeks.

Our findings are novel for several reasons. First, they suggest that recurrent pneumonia hospitalisation may be associated with abnormal follow-up CXRs, possibly indicating an underlying chronic pulmonary disorder. These findings align with a previous study of Australian Indigenous children where recurrent (>1) hospitalised pneumonia and severe pneumonia episodes increased the risk of developing bronchiectasis (P_{trend} <0.01 for both).[8] A South African birth cohort study also revealed infants with >1 ALRI episode had impaired lung function with a lower tidal volume (−1.7 mL, 95% CI −3.27 to −0.21) and a higher lung clearance index (LCI) indicating less efficient lung function (0.13 turnovers, 95% CI 0.00 to 0.26) at 1 year of age, compared with infants without ALRI.[31] The impact on LCI was greatest in infants hospitalised for ALRI (0.36 turnovers, 95% CI 0.09 to 0.63).

Second, as postnatal lung development is a continuous process that is most critical in early childhood,[32] an infectious insult to the developing alveoli and growing airways may result in long-term consequences.[3 5 6] Similarly, we observed a possible association between younger age and incomplete CXR resolution at 4 weeks. Furthermore, a national Great Britain birth cohort study demonstrated ALRI before age 1 year was associated with an increased risk of premature adult respiratory mortality (HR=2.12, 95% CI 1.16 to 3.88), especially if recurrent (≥3 episodes, HR=2.87, 95% CI 1.18 to 7.02) or needing hospitalisation (HR=4.35, 95% CI 1.31 to 14.5) compared with those without ALRI.[7]

Third, children with persistent respiratory symptoms/signs at 4 weeks post-discharge were more likely to have

Table 2 Baseline characteristics

Characteristics*	CXR at 4 weeks: Near-complete/complete resolution† n=211	CXR at 4 weeks: Incomplete resolution† n=42	P value	CXR at 12 months: Complete resolution‡ n=183	CXR at 12 months: Incomplete resolution‡ n=29	P value
Sociodemographic						
Age (years)	1.36 (0.95–2.00)	1.10 (0.82–1.81)	0.05	1.28 (0.92–1.90)	1.24 (0.89–1.81)	0.49
Male	108/211 (52)	19/42 (45)	0.50	21/183 (50)	15/29 (52)	1.00
Household demographic						
Exposure to household tobacco smoke	124/208 (60)	21/42 (50)	0.30	101/181 (56)	17/29 (59)	0.84
Overcrowding	99/211 (47)	19/42 (45)	0.87	83/183 (45)	12/29 (42)	0.84
Medical history						
Preterm birth (<37 weeks)	14/211 (7)	3/42 (7)	1.00	12/183 (7)	1/29 (3)	1.00
Breastfed for at least 6 months	144/209 (69)	24/42 (57)	0.15	122/182 (67)	18/29 (62)	0.67
Mother smoked tobacco during pregnancy	12/205 (6)	1/41 (2)	0.70	8/176 (5)	0/29 (0)	0.60
Previous pneumonia hospitalisation	8/211 (4)	8/42 (19)	0.001	9/183 (5)	5/29 (17)	0.03
Fever	205/211 (97)	42/42 (100)	0.60	178/183 (97)	29/29 (100)	1.00
Cough	208/211 (99)	41/42 (98)	0.52	179/183 (98)	28/29 (98)	0.52
Poor feeding/unable to drink	88/193 (46)	22/39 (56)	0.23	79/169 (47)	15/27 (56)	0.42
Persistent vomiting	44/189 (23)	11/39 (28)	0.54	40/163 (25)	7/27 (26)	1.00
Lethargy	87/185 (47)	19/37 (51)	0.72	77/162 (48)	14/27 (52)	0.68
Clinical features on admission						
Fever (temperature ≥38.0°C)	104/211 (49)	19/42 (45)	0.74	91/183 (50)	14/29 (48)	1.00
Tachypnoea§	121/210 (58)	26/40 (65)	0.48	101/182 (55)	16/28 (57)	1.00
Chest wall recession	63/98 (64)	18/22 (82)	0.14	54/85 (64)	9/14 (64)	1.00
Crackles on auscultation	188/211 (89)	40/42 (95)	0.39	166/183 (91)	26/29 (90)	0.74
Hypoxaemia (oxygen saturation ≤92%)	19/211 (9)	4/42 (10)	1.00	17/183 (9)	2/29 (7)	1.00
Blood indices						
White blood cell count (x10^9/L)	13.5 (8.9–20.1)	14.0 (9.8–18.8)	0.93	14.4 (10.2–21.0)	11.4 (9.0–15.8)	0.10
Neutrophil count (x10^9/L)	8.6 (5.2–17.8)	7.7 (4.6–11.7)	0.24	8.9 (5.4–17.9)	6.7 (3.7–9.1)	0.02
C-reactive protein (mg/L)	13.8 (1.6–58.7)	16.5 (4.0–32.0)	0.84	12.3 (0.6–52.6)	19.6 (6.0–31.1)	0.50
Management						
Oxygen supplementation	146/211 (69)	23/42 (55)	0.07	125/183 (68)	16/29 (55)	0.20
Intravenous or nasogastric tube fluid supplementation	76/202 (38)	14/39 (36)	1.00	59/172 (34)	10/29 (35)	1.00
Length of stay (days)	3 (2–4)	3 (2–3)	0.84	3 (2–4)	3 (2–4)	0.27
Extended course (13–14-days) antibiotics	109/211 (52)	19/42 (45)	0.50	93/183 (51)	14/29 (48)	0.84
4-week clinic review						
Chronic cough (>4 weeks)	NA	NA	NA	7/183 (4)	1/28 (4)	1.00
Crackles on auscultation	NA	NA	NA	13/183 (7)	5/29 (17)	0.08
Wheeze on auscultation	NA	NA	NA	9/183 (5)	5/29 (17)	0.03
Medical chart review (from 4 weeks to 12 months post-discharge)						
≥1 subsequent hospitalised ALRI episode(s)	NA	NA	NA	23/188 (12)	6/24 (25)	0.11

*Data are expressed as number (%) or median (IQR).
†At the 4-week CXR review, near-complete/complete resolution = 75–100% resolution and incomplete resolution = <75% resolution.
‡At the 12-month CXR review, complete resolution = 100% resolution and incomplete resolution = <100% resolution.
§World Health Organization criteria: children aged 2–11 months: respiratory rate ≥50 breaths/minute; children aged 1–5 years: respiratory rate ≥40 breaths/minute.
ALRI, acute lower respiratory infection; CXR, chest radiograph; NA, not applicable.

continuing CXR abnormalities, which may herald an underlying chronic pulmonary disorder. While under such circumstances major international guidelines advocate clinical review and follow-up CXRs,[16 33] we provide supporting evidence for this recommendation.

Fourth, nearly half the children with persistent CXR abnormalities at 12 months have no chronic respiratory symptoms/signs, although these may be under-reported or not apparent clinically. Nevertheless, some may be asymptomatic during a stable phase of the disease despite ongoing pathology. Without follow-up imaging, these children risk delayed diagnosis, highlighting the importance of post-hospitalisation CXR in detecting long-term respiratory complications.

Our findings suggest that omitting routine follow-up CXRs in children hospitalised with uncomplicated CAP may warrant re-evaluation.[17–21] In a prospective Finnish study, of the 196 children hospitalised with pneumonia with follow-up CXRs performed 3–7 weeks post-discharge, 30% showed abnormalities.[20] Medical records and parental questionnaires were collected 8–10 years later. Twenty-six patients had recurrent pneumonia, and 6 had underlying diseases. The study concluded that no new illnesses during the 8–10 years were linked to the previous

Table 3 Multivariable logistic regression analyses

Baseline characteristics	Incomplete CXR resolution at 4 weeks*	
	Multivariable analysis	
	OR_{adj} (95% CI)	P value
Age (years)	0.60 (0.38 to 0.94)	0.03
Previous pneumonia hospitalisation	6.46 (2.21 to 18.85)	0.001
Baseline characteristics	**Incomplete CXR resolution at 12 months†**	
	Multivariable analysis	
	OR_{adj} (95% CI)	P value
Previous pneumonia hospitalisation	4.03 (1.25 to 13.02)	0.02

*At the 4-week CXR review, incomplete resolution = <75% resolution.
†At the 12-month CXR review, incomplete resolution = <100% resolution.
CI, confidence interval; CXR, chest radiograph; OR_{adj}, adjusted odds ratio.

pneumonia.[20] However, the findings may be influenced by recall bias affecting the accuracy of the reported outcomes, given the very long delay of 8–10 years. Moreover, including children with comorbidities in that study[20] could have confounded the results, which might not be generalisable to the broader population.

A Norwegian retrospective study found that of 245 children hospitalised for CAP, 133 had follow-up CXRs, with 27 (20%) showing abnormalities.[21] Among those with follow-up CXRs, 1 had chronic lung disease, and another had recurrent pneumonia, whereas of 112 children without follow-up CXRs, 3 were later suspected of chronic lung disease. The authors concluded a follow-up CXR could benefit just 5/245 (2%) cases.

Our study differs from previous studies in two key aspects. First, it was conducted in populations with high rates of chronic lung disease in children, including CSLD and bronchiectasis,[34–36] where early detection of these conditions is crucial for managing and halting disease progression.[37] Second, we prospectively performed follow-up CXRs at 4 weeks and 12 months, correlating clinical with radiographic findings. This contrasts with other studies,[17 18 20] where all but one[23] conducted

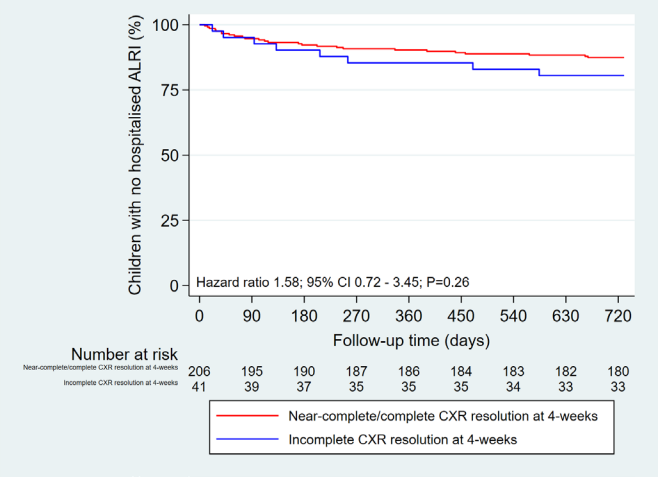

Figure 2 Kaplan-Meier curves showing the proportion of children without hospitalised ALRI during the 24-month follow-up period. *The total number of children with an interpretable CXR at 4 weeks was 247 (instead of n=253), as 6 had another hospitalised ALRI episode before 4 weeks post-discharge and were excluded from the analysis. ALRI, acute lower respiratory infection; CXR, chest radiograph.

follow-up CXRs 3–7 weeks post-index pneumonia. Therefore, our study contributes valuable data on the long-term outcomes of follow-up imaging in children hospitalised with CAP.

Our results corroborate findings of a retrospective case-control study that evaluated 95 Alaska Native children aged <3 years hospitalised with respiratory syncytial viral infection.[22] The researchers found the risk of bronchiectasis was increased in children aged <2 years with CXRs showing lung parenchymal densities (RR=3.92, p=0.013), densities persisting >6 months (RR=3.0, p=0.024) and densities occurring in >1 episode (P_{trend}=0.003). Pneumonia in children aged <2 years was also significantly associated with developing bronchiectasis (RR=9.83, p=0.007).

The main strength of our study is that enrolment was based on a pre-established set of strict inclusion and exclusion criteria for CAP. The international and multicentre design increased the generalisability of our findings to LMICs and disadvantaged Indigenous communities in HICs. Moreover, the 24-month follow-up of children ensured all hospitalised ALRI episodes were captured in our study, and CXRs were assessed by a single, masked expert.

The foundation study cited in this report used the following categories: 80–100% as 'near-complete' resolution, 20–80% as 'moderate' resolution and 0–20% as 'minimal' resolution.[14] However, we adopted a different threshold system to allow a more even distribution of percentage categories. Dividing the broad 20–80% range into smaller intervals increased the granularity of the CXR data, providing a more detailed assessment of resolution.

Nevertheless, important limitations exist. First, 19% and 32% of participants had no follow-up CXRs performed at 4 weeks and 12 months, respectively. This occurred mainly in children from remote communities facing travel difficulties when transport or accompanying parents/guardians were unavailable to take the child for a CXR. Furthermore, travel limitations were aggravated by the 'wet season' and enforced isolation during the coronavirus disease 2019 pandemic. Although differences were observed between children with or without follow-up CXRs (ie, household tobacco smoke exposure, maternal smoking during pregnancy, preterm birth and CRP levels), these factors were unlikely to have significantly affected the overall findings, as shown in the ESM online supplemental file 1. It is also possible that children lost to follow-up had better clinical outcomes, including complete CXR resolution, than those who returned for follow-up CXRs. While this may have overestimated the prevalence of persistent radiographic abnormalities, it is unlikely as children without follow-up CXRs were more likely to be preterm-born and have tobacco-smoke exposure, both risk factors for chronic lung disease. Nevertheless, given the limited number of outcome events and the exploratory nature of this secondary analysis, we did not impute missing data, as it could introduce additional uncertainty.

Second, routine cCT scans to exclude bronchiectasis were not included in our RCT.[30 37] Consequently, there are no cCT data for children with incomplete CXR resolution at 12 months. However, given their young age (median age=2.3 years), cCT scans would have required general anaesthesia, making this impractical for study participants.

Third, although previous pneumonia hospitalisation was independently associated with incomplete CXR resolution at 4 weeks and 12 months, the number of pneumonia episodes was not collected. These dose-response data would help assess the risk of complications, such as CSLD or bronchiectasis, which are more likely in children with recurrent pneumonia.[8 22]

Fourth, we acknowledge the gold standard for CXR interpretation is a paediatric radiologist. However, in our study setting, most CXRs are typically interpreted by clinicians, as dedicated paediatric radiology expertise is not routinely available. This reflects real-world practice in similar healthcare settings. To reduce variability, all CXRs were reviewed by a single respiratory paediatrician in a blinded manner. Despite these limitations, our study provides valuable insights, as it represents the largest cohort, specifically evaluating radiographic follow-up of pneumonia in children.[17–21]

Fifth, our sample size may limit our ability to identify all prognostic variables. When determining prognostic factors, we did not use a univariable prefiltering method as this can lead to unstable results, since it relies on p values that may vary randomly due to chance. Important predictors may also be excluded simply because they do not show statistical significance in univariable analysis, despite being relevant in a multivariable context due to confounding or interaction effects. Consequently, we used backward elimination and limited the number of variables chosen for the initial full multivariable model, and used a selection criterion of 0.157 as recommended.[27] This arguably provides a more robust approach. Our chosen variables were selected carefully based on prior clinical plausibility. In the WHO case management guidelines, tachypnoea and chest wall recession are key clinical signs of pneumonia, while inability to drink is a danger sign of severe pneumonia.[28] Younger age and hypoxaemia are strong predictors of severe pneumonia and mortality,[29 38] while recurrent pneumonia is a known risk factor for bronchiectasis.[8 30] Nevertheless, the limited overall number of events may mean some important factors were not identified due to issues with statistical power. Consequently, it is important that future work confirms the relevance of the factors we identified, including conducting sensitivity analyses to assess the robustness of our findings in similar patient populations and in other settings.

In conclusion, in children aged ≤5 years from populations at high risk of chronic lung disease, we identified factors that may be associated with incomplete CXR resolution 4 weeks and 12 months post-hospitalisation for severe CAP. In this setting, children with previous pneumonia hospitalisation, younger age and persistent respiratory symptoms/signs 4 weeks post-discharge may benefit from follow-up CXRs. Children with persistently abnormal CXRs should be monitored closely for long-term respiratory complications, including CSLD and bronchiectasis. These considerations are important as early diagnosis of childhood bronchiectasis, along with optimal treatment, may lead to its reversal.[30 39 40]

Author affiliations
[1]Child and Maternal Health Division, Menzies School of Health Research, Charles Darwin University, Darwin, Northern Territory, Australia
[2]Department of Paediatrics, Sabah Women and Children's Hospital, Kota Kinabalu, Sabah, Malaysia
[3]Australian Centre for Health Services Innovation and School of Medicine, Queensland University of Technology, Brisbane, Queensland, Australia
[4]Departments of Infectious Diseases and Paediatrics, Gold Coast Health, Gold Coast, Queensland, Australia
[5]School of Medicine and Dentistry, Griffith University, Gold Coast, Queensland, Australia
[6]Department of Respiratory and Sleep Medicine, Queensland Children's Hospital, Brisbane, Queensland, Australia
[7]Sydney Children's Hospital at Westmead, Sydney, New South Wales, Australia
[8]Department of Paediatrics, Universiti of Malaya, Kuala Lumpur, Malaysia
[9]Respiratory Department, Starship Children's Hospital, Auckland, New Zealand
[10]Department of Paediatrics, University of Auckland, Auckland, New Zealand
[11]Department of Paediatrics, Tengku Ampuan Rahimah Hospital, Klang, Selangor, Malaysia
[12]Department of Paediatrics, Royal Darwin Hospital, Darwin, Northern Territory, Australia
[13]Lee Kong Chian School of Medicine, Nanyang Technological University, Singapore
[14]Poche Centre for Indigenous Health, The University of Queensland, Brisbane, Queensland, Australia
[15]First Nations Leadership & Engagement, Charles Darwin University, Darwin, Northern Territory, Australia
[16]Department of Paediatrics, Sarawak General Hospital, Kuching, Sarawak, Malaysia
[17]Institute of Health and Community Medicine, Universiti Malaysia Sarawak, Sarawak, Malaysia
[18]Frazer Institute, The University of Queensland and Translational Research Institute, Brisbane, Queensland, Australia
[19]Central Clinical School, University of Sydney, Sydney, New South Wales, Australia
[20]Department of Respiratory Medicine, Royal Prince Alfred Hospital, Sydney, New South Wales, Australia

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Competing interests ABC, KG, STY, RSW, GBM, NF, PSM, JWU and PJT report grants from the Australian National Health and Medical Research Council (NHMRC) and NHMRC-managed grants (Medical Research Futures Fund), during the conduct of the study. AC is also an independent data management committee member for clinical trials for Moderna (COVID-19 and EBV vaccines) and of an unlicensed vaccine (GlaxoSmithKline) and monoclonal antibody (AstraZeneca), received fees to the institution for consulting on the study designs for Zambon and Boehringer Ingelheim, airfares for travel from the European Respiratory Society and Boehringer Ingelheim and personal fees for being an author of two UpToDate chapters that are outside the submitted work. HCK, SMF, AMN, CAB, NN, NS, TWY, VMO, IBM, JAdB, KPE, BL and MHO have no conflicts of interest to disclose.

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ORCID iDs
Hing Cheong Kok http://orcid.org/0000-0002-9781-5905
Keith Grimwood http://orcid.org/0000-0003-3174-9834
Robert S Ware http://orcid.org/0000-0002-6129-6736
Kah Peng Eg http://orcid.org/0000-0002-6814-7418

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