Electronic supplementary material:
The online version of this article contains supplementary material.

journal of global health

Cite as: Kevat PM, Morpeth M, Graham H, Gray AZ. A systematic review of the clinical features of pneumonia in children aged 5-9 years: Implications for guidelines and research. J Glob Health 2022;12:10002

A systematic review of the clinical features of pneumonia in children aged 5-9 years: Implications for guidelines and research

Priya M Kevat[1,2,3], Melinda Morpeth[2,3], Hamish Graham[1,2,3], Amy Z Gray[1,2,3]

[1]Murdoch Children's Research Institute, Melbourne, Victoria, Australia
[2]University of Melbourne, Melbourne, Victoria, Australia
[3]Royal Children's Hospital Melbourne, Melbourne, Victoria, Australia

Background Childhood pneumonia presents a large global burden, though most data and guidelines focus on children less than 5 years old. Less information is available about the clinical presentation of pneumonia in children 5-9 years of age. Appropriate diagnostic and treatment algorithms may differ from those applied to younger children. This systematic literature review aimed to identify clinical features of pneumonia in children aged 5-9 years, with a focus on delineation from other age groups and comparison with existing WHO guidance for pneumonia in children less than 5 years old.

Methods We searched MEDLINE, EMBASE and PubMed databases for publications that described clinical features of pneumonia in children 5-9 years old, from any country with no date restriction in English. The quality of included studies was evaluated using a modified Effective Public Health Project Practice (EPHPP) tool. Data relating to research context, study type, clinical features of pneumonia and comparisons with children less than 5 years old were extracted. For each clinical feature of pneumonia, we described mean percentage (95% confidence interval) of participants with this finding in terms of aetiology (all cause vs *Mycoplasma pneumoniae*), and method of diagnosis (radiological vs clinical).

Results We included 15 publications, eight addressing all-cause pneumonia and seven addressing *Mycoplasma pneumoniae*. Cough and fever were common in children aged 5-9 years with pneumonia. Tachypnoea was documented in around half of patients. Dyspnoea/difficulty breathing and chest indrawing were present in approximately half of all-cause pneumonia cases, with no data on in-drawing in the outpatient setting. Chest and abdominal pain were documented in around one third of cases of all-cause pneumonia, based on limited numbers. In addition to markers of pneumonia severity used in children <5 years, pallor has been identified as being associated with poorer outcomes alongside comor-bidities and nutritional status.

Conclusions Quality research exploring clinical features of pneumonia, treatment and outcomes in children aged 5-9 years using consistent inclusion criteria, definitions of features and age ranges are urgently needed to better inform prac-tice and guidelines. Based on limited data fever and cough are common in this age group, but tachypnoea cannot be relied on for diagnosis. While waiting for better evidence, broader attention to features such as chest and abdominal pain, the role of chest radiographs for diagnosis in the absence of symptoms such as tachypnoea, and risk factors which may influence patient disposition (chest in-drawing, pallor, nutritional status) warrant consideration by clinicians.

Protocol registration PROSPERO: CRD42020213837.

Correspondence to:
Amy Gray
Level 2, West Building
University of Melbourne, Department of Paediatrics
The Royal Children's Hospital Melbourne
52 Flemington Road
Parkville 3052
Melbourne

Childhood pneumonia is responsible for a large mortality burden globally however most guidelines for low resource settings are focused on pneumonia in children less than 5 years old [1,2]. Focus on young children has been justified by the fact that more than 90% of childhood pneumonia deaths occur in young children less than 5 years of age [3]. Yet pneumonia is also important for older children. Global Burden of Disease estimates suggest that pneumonia accounts for around 7% of deaths in children aged 5-9 years [3].

While children aged 5-9 years are generally regarded as at lower risk for pneumonia and pneumonia death, the risk may still be substantial in certain contexts or patient cohorts (for example, children with chronic health conditions or disability). Appropriate diagnostic and treatment algorithms may differ from those applied to younger children and this group has not been addressed in previous guidelines.

The aim of this review was to describe the available evidence for clinical features of pneumonia in children aged 5-9 years in community, primary care, or hospital settings, with a focus on delineation from other age groups and comparison with existing WHO guidance for pneumonia in young children.

METHODS

The protocol for this study was registered on PROSPERO, the international prospective register of systematic reviews (registration number CRD42020213837). We searched MEDLINE via Ovid, EMBASE via Ovid and PubMed in August 2020 using key search terms including synonyms for pneumonia, ages 5-9 years, and clinical findings or diagnosis (example in Appendix S1 in the **Online Supplementary Document**). No date restriction was applied. We did not restrict by location of study but for practical reasons we restricted the search to studies available in English language.

We included studies that contained original data on the clinical features of pneumonia among children aged 5-9 years, published in English language. We excluded case reports, small case series (<10 participants), conference abstracts, or those in which data relating to children aged 5-9 years was not meaningfully disaggregated.

PK completed initial title and abstract screening. Full-text screening was completed by three reviewers (PK, MM, AG), with each article screened by two of these reviewers (PK, MM, AG) and any conflicts resolved by the majority opinion from the third remaining reviewer (PK, MM, AG). Reference lists of included articles were searched to identify additional relevant studies missed from the search.

We extracted data from included studies with a standardised data extraction tool. Information extracted included: year of publication, study details, inclusion and exclusion criteria, pneumonia diagnostic/case definition criteria, aetiological agent(s), participant characteristics (including socioeconomic status), presence of comorbid conditions, respiratory and extra-pulmonary clinical features, chest radiograph findings, treatment received, and outcomes, with comparison to the under 5 years age group wherever possible. Data extraction was completed by two reviewers (PK, MM), with data from each article extracted by one of these reviewers (PK, MM) and the extracted information checked by the second reviewer (PK, MM). Any conflicts were resolved by the majority opinion from a third reviewer (AG).

We separated data from studies describing pneumonia of any aetiology (all-cause pneumonia) and studies describing pneumonia attributed to *Mycoplasma pneumoniae*, given that several studies addressed *Mycoplasma pneumoniae* specifically. For each clinical feature, we described the number and percentage of patients who were documented to have the feature in each study. Using aggregated data of all studies which included each clinical feature we calculated the mean percentage and 95% confidence interval according to the cause of pneumonia (all-cause and attributable to *Mycoplasma pneumoniae*) and the method of diagnosis (radiological or clinical). If studies stipulated their inclusion criteria as a clinical diagnosis with or without radiological diagnosis, they were included in the studies based on clinical diagnosis for analysis (as we were unable to identify which participants had a radiograph performed). Due to the relatively weak quality of the studies identified and the variable nature of the data from the studies we did not perform any additional statistical analysis, to avoid over-interpretation of the data available.

We used the EPHPP tool to evaluate the risk of bias in included studies [4]. This tool was modified to assess the study designs included (Table S1 in the **Online Supplementary Document**). Application of the EPHPP tool required separate evaluation and consensus between two reviewers (PK, MM).

The Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) 2020 statement was followed, with a checklist completed (Table S2 in the **Online Supplementary Document**) [5].

RESULTS

A total of 2641 references were retrieved, and an additional four relevant publications were identified through reference list screening (**Figure 1**). After duplicates were removed, 1776 references were screened, and 301 proceeded to full-text review. Two articles were excluded as the full text was unavailable, after authors were contacted twice to request them. Fifteen studies were included in qualitative synthesis after inclusion and exclusion criteria were applied.

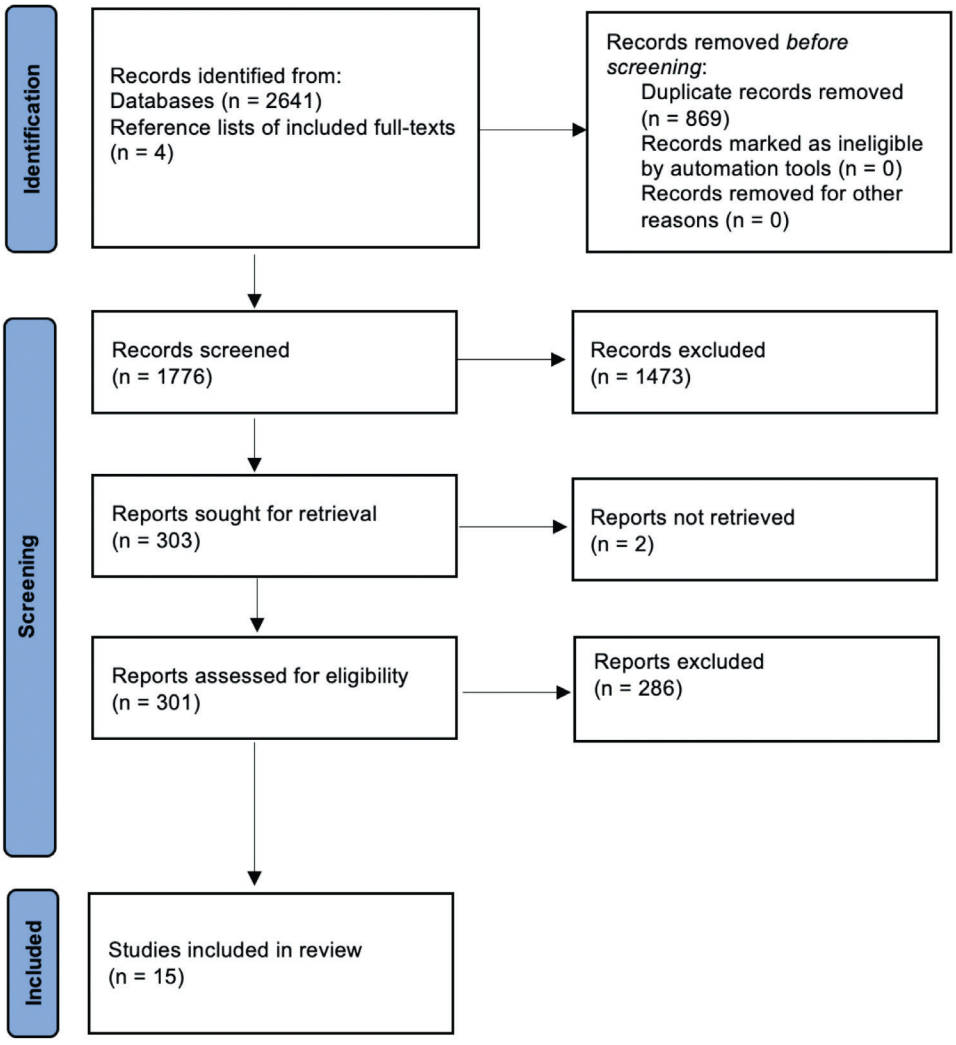

Figure 1. Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) flow diagram.

Study descriptions

Studies had variable methods to identify patients with pneumonia. Seven of the 15 studies included children with radiologically confirmed pneumonia (two of these requiring clinical features in addition) and eight of the 15 studies were based on clinical diagnosis with or without a radiograph. The heterogeny in diagnostic methods was significant. For example, one study based on radiological diagnosis only included patients with obvious chest indrawing. Furthermore, of those based on clinical diagnosis, three studies included children with or without a radiograph being performed, three required clinician diagnosis alone, and two studies were of *Mycoplasma pneumoniae* positive patients that described clinical features and/or chest radiograph changes consistent with pneumonia. Eight studies addressed all-cause pneumonia (**Table 1**) whilst seven discussed pneumonia attributable to *Mycoplasma pneumoniae*, based on a variety of diagnostic assays (**Table 2**). Three out of the 15 studies, Macpherson et al [12], Salih et al [13] and Forgie et al [11], were from low or lower-middle income settings. Twelve studies described inpatients only, one study by Harris et al [9] was of outpatients, and two studies by Korppi et al [8] and Othman et al [19] included a combination of inpatients and outpatients.

Table 1. Clinical features described in children aged 5-9 y diagnosed with pneumonia of any aetiology (all-cause pneumonia)

Authors, year	Study location, design & population	Patient numbers	Respiratory symptoms/ signs	Extra-pulmonary symptoms/ signs	Chest x-ray findings	Comparison with <5 y age group	EPHPP global rating score
Studies based on radiological pneumonia diagnosis:							
Crocker et al, 2012 [6]	South Wales, UK	79 total	Most relevant data not disaggregated by age	Most relevant data not disaggregated by age	For 3-16 y:	Less common in <3 y compared with 3-16 y:	Weak
	Questionnaire + interview with prospectively recruited carers of inpatients with radiographic CAP or empyema (excluding chronic conditions)	43 (54%) 3-16 y		For 3-16 y: Symptoms reported when asked about presence or absence by the interviewer: 36/43 (84%) pain in torso (usually chest or abdomen) including all 12 with pleural effusion or empyema 23/43 (54%) headache 12/43 (28%) general aching 15/43 (35%) back pain 10/43 (23%) side pain 6/43 (14%) shoulder pain 14/43 (33%) pain at other sites (legs/ neck/arm)	12/43 (28%) with pleural effusion or empyema	Pain in torso (symptom volunteered as unusual or concerning): 2/36 (5.6%) vs 15/43 (34.9%) ($P<0.01$) NB: The number of children 3-16 y with pain in the torso was 36/43 (84%) when the interviewer asked about the presence or absence of the symptom as a closed question.	
Juvén et al, 2003 [7]	Turku, Finland	254 total	For children ≥5 y:	For children ≥5 y:	Not specified	More common in <2 y compared with 2-4 y and children ≥5 y:*	Weak
	Prospective study of inpatients with radiologically confirmed CAP (information regarding comorbid conditions not specified)	62 (24%) children ≥5 y	50/62 (81%) cough 24/62 (39%) rhinorrhoea 12/62 (19%) dyspnoea 13/62 (21%) rhonchi 9/62 (15%) wheezing ~12/62 (20%) rales/crackles 22/62 (36%) normal breath sounds 13/62 (21%) decreased breath sounds 12/41 (29%) breath rate ≥40/min (tachypnoea) 7/41 (17%) breath rate ≥50/ min (tachypnoea)	60/62 (97%) fever >37.5°C ~12/62 (20%) poor appetite 20/62 (32%) malaise/lethargy 19/62 (31%) vomiting 4/62 (7%) diarrhoea 18/62 (29%) abdominal pain 23/62 (37%) headache 20/62 (32%) thoracic pain		Rhinorrhoea: 58% vs 41% and 39% respectively Dyspnoea: 53% vs 29% and 19% respectively Rhonchi: 49% vs 22% and 21% respectively Wheezing: 28% vs 15% and 15% respectively Breath rate ≥40/min: 61/86 (71%) vs 28/61 (48%) and 5/41 (12%) respectively Breath rate ≥50/min (tachypnoea): 40/86 (47%) vs 14/66 (21%) and 3/41 (7%) respectively Less common in <2 y compared with 2-4 y and children ≥5 y*: Abdominal pain: 5% vs 21% and 29% respectively Headache: 3% vs 16% and 37% respectively Thoracic pain: 0% vs 6% and 32% respectively Normal breath sounds: 19% vs 33% and 36% respectively Decreased breath sounds: 7% vs 20% and 21% respectively	

Table 1. Continued

Authors, year	Study location, design & population	Patient numbers	Respiratory symptoms/ signs	Extra-pulmonary symptoms/ signs	Chest x-ray findings	Comparison with <5 y age group	EPHPP global rating score
Korppi et al, 2008 [8]	Udine, Italy Prospective enrolment of inpatients and outpatients with radiologically confirmed CAP with retrospective chart review of data (previously healthy children)	101 total 38 (38%) children ≥5 y old	For children ≥5 y: 34/38 (90%) cough 6/38 (16%) rhinitis 4/38 (11%) dyspnoea 9/38 (24%†) tachypnoea‡ 16/38 (42%†) crackles 3/38 (8%†) dullness 26/38 (68%) decreased breath sounds	For children ≥5 y: 35/38 (92%) fever >37.5°C 4/38 (11%) fever >39.5°C 11/38 (29%) chest pain 15/38 (40%) vomiting 8/38 (21%) refusal to eat 5/38 (13%) headache 11/38 (29%) abdominal pain 9/38 (24%) looking ill 1/38 (3%) chills	For children ≥5 y: 26/38 (68%) alveolar infiltration 3/38 (8%) pleural fluid	More common in <2 y and 2-4 y compared with children ≥5 y: Looking ill 9/19 (47.4%) and 22/44 (50.0%) vs 9/38 (23.7%) respectively ($P=0.0381$) Less common in <2 y and 2-4 y compared with children ≥5 y: Chest pain: 0/19 (0.0%) and 4/44 (9.1%) vs 11/38 (28.9%) respectively ($P=0.0049$) Vomiting: 1/19 (5.3%) and 14/44 (31.8%) vs 15/38 (39.5%) respectively ($P=0.0184$)	Weak
Harris et al, 1998 [9]	Multiple centres in USA Double-blind RCT to evaluate effectiveness of oral azithromycin vs "conventional" therapy§ for CAP. Outpatients with radiologic pneumonia finding + tachypnoea + fever/ history of fever within 24 h/cough/ WCC≥12000/mm^3 /positive clinical chest findings (excluding chronic issues)	420 total 225 (54%)>5-16 y including 156 (69%) in the azithromycin arm and 69 (31%) receiving conventional therapy	For >5-16 y: 212/225 (94%) abnormal respiratory rate‖ 221/225 (98%) cough 155/225 (69%) rales 59/225 (26%) wheezes	For >5-16 y: 104/225 (46%) fever¶	Not specified	More common in ≤5 y compared with >5-16 y**: Fever: 140/195 (72%) vs 104/225 (46%) ($P<.005$) Wheezes: 74/195 (38%) vs 59/225 (26%) ($P<0.001$) Less common in ≤5 y compared with >5-16 y**: Rales: 109/195 (56%) vs 155/225 (69%) ($P<0.007$)	Moderate
Studies based on clinical pneumonia diagnosis with or without chest radiograph:							
Udomittipong et al, 2011 [10]	Bangkok, Thailand Retrospective study of inpatients with a clinical diagnosis of pneumonia to compare non-H1N1 with H1N1 cases + prospectively follow-up PFTs (including chronic conditions)	88 total 88 (100%) 5-15 y	78/88 (89%) cough 30/88 (34%) dyspnoea 59/88 (67%) rhinorrhoea 37/88 (42%) sore throat 48/88 (55%) injected pharynx 3/88 (34%) injected tympanic membrane 27/88 (31%) chest retraction	74/88 (84%) fever ≥37.8°C 29/88 (33%) muscle pain 28/88 (32%) headache 25/88 (28%) nausea-vomiting 8/88 (9%) diarrhoea 4/88 (4.5%) joint pain	Not specified	Not specified	Weak
Forgie et al, 1991 [11]	Fajara, The Gambia Prospective study of inpatients with clinical diagnosis of ALRI and obvious chest indrawing (information regarding comorbid conditions not specified)	74 total 10 (14%) 5-9 y	For 5-9 y: 10/10 (100%) indrawing (study selected for this clinical feature) 5/10 (50%) flaring 5/10 (50%) bronchial breathing 1/10 (10%) crepitations 6/10 (60%) diminished air entry 1/10 (10%) wheeze 0/10 (0%) normal breath sounds 0/10 (0%) cyanosis	For 5-9 y: 0/10 (0%) inability to drink	For 5-9 y: 9/10 (90%) abnormal CXR 7/10 (70%) lobar consolidation	More common in 1-4 y compared with 5-9 y††: Flaring: 50/64 (78%) vs 5/10 (50%) Inability to drink: 14/64 (22%) vs 0/10 (0%) Crepitations: 31/64 (48%) vs 1/10 (10%) Normal breath sounds: 10/64 (16%) vs 0/10 (0%) Less common in 1-4 y compared with 5-9 y††: Diminished air entry: 24/64 (38%) vs 6/10 (60%)	Weak

Table 1. Continued

Authors, year	Study location, design & population	Patient numbers	Respiratory symptoms/ signs	Extra-pulmonary symptoms/ signs	Chest x-ray findings	Comparison with <5 y age group	EPHPP global rating score
Macpherson et al, 2019 [12]	Multicentre study in Kenya Retrospective study of inpatients with a clinician diagnosis of pneumonia at discharge or death (including comorbid conditions)	1832 total 1467 (80%) 5-9 y	For 5-9 y: 937/1216 (77%) respiratory rate >30/min (tachypnoea) 24/1418 (2%) central cyanosis 232/1394 (17%) grunting 58/1382 (4%) acidotic breathing 46/1356 (3%) stridor 743/1416 (52%) difficulty breathing 189/1396 (14%) wheeze 504/1387 (36%) crackles 609/1400 (44%) chest wall indrawing 151/661 (23%) oxygen saturation <90%	For 5-9 y: 559/1321 (42%) temperature ≥38°C (fever) 108/1400 (8%) reduced consciousness 235/1347 (17%) cannot eat or drink 89/1411 (6%) severe pallor 158/1411 (11%) mild/moderate pallor 1164/1411 (82%) no pallor ie, 247/1411 (18%) any pallor present 212/1406 (15%) convulsions	Not specified	Not specified	Moderate
Salih et al, 1994 [13]	Khartoum, Sudan Prospective study of inpatients with ALRI based on clinical or radiological findings (excluding cases with measles but including other comorbid conditions, 11/24 (46%) of children aged 5-14 y were underweight‡‡)	213 total 24 (11%) 5-14 y	For 5-14 y: 22/24 (92%) cough 2/24 (8%) cyanosis 11/24 (46%) nasal flaring 18/24 (75%) chest recession 1/24 (4%) inspiratory stridor 11/24 (46%) wheezes 19/24 (79%) crackles (rales or crepitations)	For 5-14 y: 21/24 (88%†) fever 2/24 (8%) feeding difficulties	For 5-14 y: 18/23 (78%) abnormal CXR 4/23 (17%) lobal consolidation	More common in 12-59 mo compared with 5-14 y††: Crackles (rales or crepitations): 88/92 (96%) vs 19/24 (79%) Less common in 12-59 mo compared with 5-14 y††: Wheezes: 25/92 (27%) vs 11/24 (46%) Abnormal CXR: 57/89 (64%) vs 18/23 (78%) Lobal consolidation on CXR: 3/89 (3%) vs 4/23 (17%)	Weak

CAP – community acquired pneumonia, RCT – randomised controlled trial, WCC – white cell count, PFTs – pulmonary function tests, ALRI – acute lower respiratory infection, CXR – chest x-ray, y – year

*Values significant with $P<0.05$ when the <2 years group was compared to the ≥2 years group (combined data for 2-4 years and ≥5 years).

†Corrected percentage value due to error in calculated percentage within study.

‡Tachypnoea was defined by age-specific WHO criteria: respiratory rate >50 breaths/min in infants <12 months old, >40 breaths/min in children aged 1-5 years and >30 breaths/min in children aged ≥6 years.

§Conventional therapy = amoxicillin/clavulanate if ≤5 years of age and erythromycin if >5 y of age.

‖Abnormal respiratory rate was defined as >24 breaths/min for patients ≤2 year of age and >20 breaths/min for patients >2 year of age.

¶Fever was defined as ≥100.5°F oral or ≥101°F rectal, or history in the last 24 h.

**Absolute numbers and percentages are extrapolated data.

††*P* values not calculated in this study.

‡‡Weight <80% of median value using National Center for Health Statistics reference values (United States Department of Health, Education and Welfare, 1976).

Table 2. Clinical features described in children aged 5-9 y diagnosed with pneumonia attributable to *Mycoplasma pneumoniae*

Authors, year	Study location, design & population	Patient numbers	Respiratory symptoms/ signs	Extra-pulmonary symptoms/signs	Chest x-ray findings	Comparison with <5 y age group	EPHPP global rating score
Studies based on radiological pneumonia diagnosis							
Gao et al, 2015 [14]	Weifang, China	1933 patients with Mycoplasma pneumonia. 1249 patients with non-segmental/lobar Mycoplasma pneumoniae +684 patients with segmental/lobar Mycoplasma pneumoniae	For 4-6 y with segmental/lobar Mycoplasma pneumoniae:	For 4-6 y with segmental/lobar Mycoplasma pneumoniae:	Study selected those with segmental/lobar pattern on CXR:	More common in ≤3 y compared with 4-6 y and ≥7-14 y with segmental/lobar Mycoplasma pneumoniae:	Weak
	Retrospective study of inpatients with pneumonia defined by ICD-10 specifications, positive CXR findings* and positive Mycoplasma serology + PCR (excluding chronic conditions)		Cough	301/336 (90%) fever	For 4-6 y with segmental/ lobar Mycoplasma pneumoniae:		
			Mean 9.34±5.03 d	Mean 3.68±4.64 d		Extra-pulmonary manifestations: 54/169 (32%) vs 88/336 (26%) and 37/179 (21%) respectively (P=0.017)	
			90/336 (27%) gasping	88/336 (26%) extra-pulmonary manifestations	12/336 (4%) pleural effusion		
		336/684 (49%) 4-6 y	118/336 (35%) pulmonary crackles at onset	For ≥7-14 y with segmental/lobar Mycoplasma pneumoniae:	For ≥7-14 y with segmental/lobar Mycoplasma pneumoniae:	Less common in ≤3 y compared with 4-6 y and ≥7-14 y with segmental/lobar Mycoplasma pneumoniae:	
		179/684 (26%)≥7-14 y	For ≥7-14 y with segmental/ lobar Mycoplasma pneumoniae:	168/179 (94%) fever	9/179 (5%) pleural effusion	Fever: 148/169 (88%) vs 301/336 (90%) and 168/179 (94%) respectively (P=0.048)	
			Cough	Mean 5.25±4.77 d			
			Mean 9.78±7.23 d	37/179 (21%) extra-pulmonary manifestations			
			40/179 (22%) gasping				
			73/179 (41%) pulmonary crackles at onset				
Ma et al, 2015 [15]	Multicentre study in Taiwan	127 total	For >5-<18 y:	For >5-<18 y:	For >5-<18 y:	More common in <5 y compared with >5-<18 y:	Weak
	Prospective study of inpatients with radiographic evidence of CAP and positive Mycoplasma serology or PCR (including chronic conditions)	66 (52%)>5-<18 y	64/66 (97%) cough	66/66 (100%) fever	~33/66 (50%)† lobar consolidation	Tachypnoea: 21/61 (34.4%) vs 8/66 (12.1%) (P=0.003)	
			8/66 (12%) tachypnoea	Mean duration 7.94±3.81 d	9/66 (14%) pleural effusion	Vomiting: 17/61 (27.9%) vs 9/66 (13.6%) (P=0.005)	
				9/66 (14%) vomiting	0/66 (0%) pneumatocele	ICU Admission: 20/61 (32.8%) vs 8/66 (12.1%) (P=0.006)	
				11/66 (17%) abdominal pain		O_2 requirement: 29/61 (47.5%) vs 19/66 (28.8%) (P=0.016)	
				8/66 (12%) diarrhoea		VATS: 9/61 (14.8%) vs 0/66 (0%) (P=0.001)	
Youn et al, 2010 [16]	Daejeon, South Korea	191 total	For 6-14 y:	For ≥6-14 y:	For ≥6-14 y:	More common in ≤2 y and 3-5 y compared with ≥6-14 y:	Weak
	Retrospective study of inpatients with radiologically confirmed pneumonia and acute Mycoplasma infection reflected on serology testing at admission and discharge (information regarding comorbid conditions not specified)	81 (42%)≥6-14 y	81/81 (100%) cough	81/81 (100%) fever >38°C per axilla	25/81 (31%) bronchopneumonia	Bronchopneumonia: 23/29 (79%) and 48/81 (59%) vs 25/81 (31%) respectively (P<0.001)	
			Data for other respiratory signs/ symptoms not disaggregated by age	40/81 (49%) fever ≥7 d	56/81 (69%) segmental/ lobar pneumonia	Less common in ≤2 y and 3-5 y compared with ≥6-14 y:	
				Duration of fever before admission 4.2±2.3 d	33/81 (41%) mild segmental/lobar	Fever ≥7 d: 9/29 (31%) and 29/81 (36%) vs 40/81 (49%) respectively (P=0.04)	
				Total duration of fever 6.1±2.9 d	23/81 (28%) severe segmental/lobar	Segmental/lobar pneumonia: 6/29 (21%) and 33/81 (41%) vs 56/81 (69%) respectively (P<0.001)	
				Duration of fever for severe segmental/lobar pneumonia (7.1±2.6 d) longer than bronchopneumonia group (5.4±2.8 d) (P<0.05)			
				Data for other extra-pulmonary signs/ symptoms not disaggregated by age			

Table 2. Continued

Authors, year	Study location, design & population	Patient numbers	Respiratory symptoms/ signs	Extra-pulmonary symptoms/signs	Chest x-ray findings	Comparison with <5 y age group	EPHPP global rating score
Gordon et al, 2019 [17]	Jerusalem, Israel	353 total	For 6-18 y with CXR confirmed pneumonia:	For 6-18 y with CXR confirmed pneumonia:	For 6-18 y with CXR confirmed pneumonia:	Less common in <6 y compared with 6-18 y with CXR confirmed pneumonia:	Weak
	Retrospective study of inpatients with oropharyngeal swab positive for Mycoplasma on PCR testing (including chronic conditions)	172/353 (49%) 6-18 y	90/104 (87%) cough				
			17/104 (16%) sputum production	52/104 (50%) gastrointestinal symptoms	84/104 (81%) consolidation	Pharyngitis: 5/90 (6%) vs 18/104 (17%) ($P=0.018$)	
			18/104 (17%) pharyngitis	18/104 (17%) headache	10/104 (10%) bilateral consolidation	Headache: 4/90 (4%) vs 18/104 (17%) ($P=0.014$)	
			50/104 (48%) tachypnoea	91/104 (88%) fever >38°C	20/104 (19%) interstitial pattern		
			28/104 (27%) oxygen saturation <90%				
			77/104 (74%) any finding on lung auscultation				
Studies based on clinical pneumonia diagnosis with or without chest radiograph:							
Defilippi et al, 2008 [18]	Genoa, Italy	102 total	For 5 –<10 y:	For 5 –<10 y:	For 5 –<10 y:	More common in <5 y compared with 5 –<10 y‡,§:	Weak
	Prospective study of inpatients with clinical and/or radiological evidence of LRTI and Mycoplasma positive PCR (excluding chronic conditions)	42 (41%) 5–<10 y	12/42 (29%) wheezing	34/42 (81%) fever ≥38.0°C	34/38 (89%) consolidation		
			31/42 (74%) cough	2/42 (5%) diarrhoea	24/34 (71% unilateral consolidation	Dyspnoea: 18/39 (46.15%) vs 6/42 (14.28%) ($P=0.004$)	
			6/42 (14%) dyspnoea	5/42 (12%) vomiting		Interstitial changes on CXR: 11/26 (42.31%) vs 2/38 (5.26%) ($P<0.0001$)	
			5/42 (12%) coryza		10/34 (29%) bilateral consolidation	Less common in <5 y compared with 5 –<10 y§:	
			20/42 (48%) crackles		2/38 (5%) interstitial changes	Consolidation on CXR: 14/26 (53.85%) vs 34/38 (89.47%) ($P=0.004$)	
Othman et al, 2005 [19]	Sydney, Australia	76 total	For 5-15 y:	For 5-15 y:	Data not disaggregated by age	More common in <5 y compared with 5-15 y:	Weak
	Retrospective study of hospital presentations/ admissions with clinical and/or radiological features compatible with pneumonia and positive Mycoplasma serology (including comorbid conditions)	46 (61%) 5-15 y	11/46 (24%) coryza	20/46 (44%) lethargy		Coryza: 15/30 (50.0%) vs 11/46 (23.9%) ($P=0.019$)	
			14/46 (30%) wheeze	15/46 (33%) vomiting		Vomiting: 17/30 (56.7%) vs 15/46 (32.6%) ($P=0.038$)	
			15/46 (33%) breathlessness	1/46 (2%) diarrhoea		Diarrhoea: 11/30 (36.7%) vs 1/46 (2.2%) ($P=0.0001$)	
			20/46 (44%) tachypnoea			Tachypnoea: 22/30 (73.3%) vs 20/46 (43.5%) ($P=0.023$)	
			14/46 (30%) recession			Recession: 18/30 (60%) vs 14/46 (30.4%) ($P=0.016$)	
			30/46 (65%) crackles				

Table 2. Continued

AUTHORS, YEAR	STUDY LOCATION, DESIGN & POPULATION	PATIENT NUMBERS	RESPIRATORY SYMPTOMS/ SIGNS	EXTRA-PULMONARY SYMPTOMS/SIGNS	CHEST X-RAY FINDINGS	COMPARISON WITH <5 Y AGE GROUP	EPHPP GLOBAL RATING SCORE
Sondergaard et al, 2018 [20]	Hillerød, Denmark Retrospective study of inpatients with clinical and/or radiological features compatible with pneumonia and positive Mycoplasma serology or PCR (including chronic conditions)	134 total 88 (66%) 7-15 y	For 7-15 y: 87/88 (99%) cough 14/88 (16%) wheezing 10/88 (11%) rhinorrhoea 23/88 (26%) sore throat 4/88 (5%) croup symptoms 50/88 (57%) tachypnoeal 20/88 (23%) auscultation – wheezing 50/88 (57%) auscultation – crackles/decreased breath sounds	For 7-15 y: 79/88 (90%) fever ≥38°C 21/88 (24%) skin manifestation (all)¶ 11/88 (13%) urticarial rash 2/88 (2%) Stevens-Johnson Syndrome 26/88 (30%) nausea and/or vomiting	For 7-15 y**: 5% hilar adenopathy (exclusively) 82% lobar infiltration 19% atelectasis 9% pleural effusion 1/88 (1%) empyema	Objective wheezing and cough (asthma-like symptoms): more common†† in <3 y compared to older children ($P=0.01$) Children <2 y were admitted to the hospital earlier after the onset of symptoms than older children ($P=0.01$)	Weak

ICD-10 - International Classification of Diseases 10th edition, CXR – chest x-ray, PCR – polymerase chain reaction, CAP – community acquired pneumonia, LRTI – lower respiratory tract infection, ICU – intensive care unit, VATS – video-assisted thoracopic surgery, y – years, d – days

*Pneumonia pattern characterised by WHO Standardization of Interpretation of Chest Radiographs for the diagnosis of community acquired pneumonia in children.

†Study text states that "one-half of the children had lobar pneumonia in both groups", however study Figure 3 suggests a higher number (between 40 and 60 patients with lobar pneumonia for each of the ≤5 years and >5 years groups).

‡Data for a symptom/sign was included if able to be disaggregated from combined data.

§P values relate to comparison of <5 years group with 5 to <10 years and 10-14 years groups.

‖Tachypnoea was defined as a respiratory rate >99th percentile for age.

¶Includes any type of rash, urticaria and Stevens-Johnson Syndrome.

**112/134 total patients had CXRs, fraction of children aged 7-15 years who had CXRs not specified.

††Absolute numbers and percentages not described.

Three of the eight studies that explored all-cause pneumonia included patients with comorbid conditions, three specifically excluded those with comorbidities, and two did not specify information about comorbidities. A significant proportion of participants aged 5-9 years in study by Macpherson et al had comorbid disease including malaria (28.77%), asthma (10.91%), neurological disorders (10.77%), severe malnutrition (9.48%) or HIV (8.32%) [12]. Meanwhile, 46% of children aged 5-14 years in study by Salih et al were underweight [13], and a variety of underlying chronic comorbid conditions were described by Udomittipong et al but not disaggregated by age [10]. Within the group of studies addressing *Mycoplasma pneumoniae*, four included those with chronic conditions or comorbidities, two excluded children with these and one did not specify information about comorbidities. Chronic pulmonary disease and asthma were most frequently described as pre-existing underlying disease [17,19,20].

Most studies were of weak quality when assessed with the EPHPP tool (**Table 1** and **Table 2**). The exceptions were Macpherson et al [12] and Harris et al [9], which were assessed as moderate quality. There were seven retrospective observational studies, six studies with prospective recruitment of participants, one randomized controlled trial (RCT) and one descriptive study based on interview and questionnaire data. Describing clinical features of pneumonia was a primary objective in thirteen of the studies; two were not conducted with this as a primary aim but included clinical features of pneumonia in a description of participants. Many studies (8/15) did not specify or utilise a standardised data collection method. Although all studies included participants aged 5-9 years, study populations also included older and younger children. Three studies provided data disaggregated for the 5-9 age range exactly; the remaining twelve studies overlapped with the target population with a sufficiently close age range to be representative. In some studies, there was a paucity of disaggregated data relating to clinical features in children 5-9 years old. There were also differing definitions and terms for some clinical features between studies. Most importantly, the definition of fast breathing varied from >20 breaths per minute [9], to >40 breaths per minute [8], to a respiratory rate >99th percentile for age [20].

Study outcomes

Aggregated data regarding the proportion of older children with specific respiratory symptoms and extra-pulmonary clinical features is summarised in **Table 3**.

Cough was the most common clinical feature, documented in around 90% of patients in both all-cause and *Mycoplasma* cohorts, whether diagnosed clinically or radiologically. Fever was also common in both cohorts but more common in *Mycoplasma* (91.7%, 95% confidence interval (CI) = 91.2-92.3) compared to all-cause pneumonia (74.8%, 95% CI = 73.6-76.0).

Table 3. Overall data regarding proportion of children with specific clinical features in included studies

	All-cause pneumonia				Mycoplasma pneumoniae			
	Overall, mean (95% CI), range, (%)	Radiological diagnosis, mean (95% CI), (%)	Clinical diagnosis, mean (95% CI), (%)	Number of studies, number of total patients in whom feature was sought (n, n)	Overall, mean (95% CI), range, (%)	Radiological diagnosis, mean (95% CI), (%)	Clinical diagnosis, mean (95% CI), (%)	Number of studies, number of total patients in whom feature was sought (n, n)
Respiratory symptoms/signs:								
Cough	89.7 (89.2-90.3) [R: 81-98]	89.4 (88.4-89.1)	90 (89.6-90.4)	Overall (5, 437), Radiological (3, 112), Clinical (2, 325)	91.4 (90.3-92.5) [R: 74-100]	94.5 (93.5-95.3)	86.3 (83.3-89.3)	Overall (5, 381), Radiological (3, 251), Clinical (2, 381)
Dyspnoea/difficulty breathing*	29.1 (28.2-30.8) [R: 11-52]	14.9 (13.7-16.1)	43 (42.3-43.7)	Overall (4, 1604), Radiological (2, 100), Clinical (2, 1504)	23.1 (22.4-23.8) [R: 14-33]	24.6 (NA)	23.4 (20.7-26.1)	Overall (3, 603), Radiological (1, 515), Clinical (2, 88)
Nasal flaring†	50 (46.7-53.3) [R: 46-50]	–	50 (46.7-53.3)	Overall (2, 34), Clinical (2, 34)	–	–	–	0
Grunting	17 (NA) [R: 17]	–	17 (NA)	Overall (1, 1394), Clinical (1, 1394)	–	–	–	0
Chest wall indrawing‡	50.0 (48.8-51.2) [R: 31-75]	–	50.0 (48.8-51.2)	Overall (3, 1512), Clinical (3, 1512)	30.0 (NA) [R: 30]	30.0 (NA)	–	Overall (1, 46), Radiological (1, 46)
Tachypnoea§	55.4 (53.6-57.2) [R: 24-94]	48 (42.9-53.1)	77 (NA)	Overall (4, 1520), Radiological (3, 304), Clinical (1, 1216)	40.1 (37.9-42.3) [R: 12-57]	8.5 (7.7-9.2)	50.1 (48.5-51.7)	Overall (4, 304), Radiological (2, 170), Clinical (2, 134)
Hypoxia (oxygen saturation <90%)	23 [R: 23]	–	23 (NA)	Overall (1, 661), Clinical (1, 661)	27 (NA) [R: 27]	27.0 (NA)		Overall (1, 104), Radiological (1, 104)
Central cyanosis/cyanosis	3.3 (3.1-3.5) [R: 0-8]	–	3.3 (3.1-3.5)	Overall (3, 1452), Clinical (3, 1452)	–	–	–	0
Cracklesǁ	42.9 (41.6-44.2) [R: 10-79]	44.0 (42.4-45.6)	42 (41.2-43.8)	Overall (6, 1746), Radiological (3, 325), Clinical (3, 1421)	51.2 (50.2-52.2) [R: 37-65]	40.8 (NA)	56.4 (53.8-59.0)	Overall (3, 603), Radiological (1,515), Clinical (2, 113)
Wheeze	22.0 (21.3-22.7) [R: 0-46]	20.4 (19.4-21.4)	23.2 (22.2-24.2)	Overall (5, 1717), Radiological (2, 287), Clinical (3, 1430)	25.0 (23.8-26.2) [R: 23-30]	–	25.0 (23.8-26.2)	Overall (3, 176) Clinical (3, 176)
Extra-pulmonary symptoms/signs:								
Fever**	74.8 (73.6-76.0) [R: 42-97]	51.2 (46.5-56.9)	71.3 (70.0-72.6)	Overall (6, 1758), Radiological (3, 325), Clinical (3, 1433)	91.7 (91.2-92.3) [R: 81-100]	94.2 (93.8-94.8)	85.4 (84.4-86.5)	Overall (6, 896) Radiological (4, 766) Clinical (2, 130)
Headache	33.9 (31.8-36.0) [R: 13-54]	45.3 (43.4-47.2)	31.8 (NA)	Overall (4, 231), Radiological (3, 143), Clinical (1, 88)	17.0 (NA) [R: 17]	17.0	–	Overall (1, 104) Radiological (1, 104)
Reduced consciousness	8.0 (NA) [R: 8]	–	8.0 (NA)	Overall (1, 1400), Clinical (1, 1400)	–	–	–	0
Convulsions	15 (NA) [R: 15]	–	15 (NA)	Overall (1, 1406), Clinical (1, 1406)	–	–	–	0

Table 3. Continued

	All-cause pneumonia				Mycoplasma pneumoniae			
	Overall, mean (95% CI), range, (%)	Radiological diagnosis, mean (95% CI), (%)	Clinical diagnosis, mean (95% CI), (%)	Number of studies, number of total patients in whom feature was sought (n, n)	Overall, mean (95% CI), range, (%)	Radiological diagnosis, mean (95% CI), (%)	Clinical diagnosis, mean (95% CI), (%)	Number of studies, number of total patients in whom feature was sought (n, n)
Pallor††	18 (NA) [R: 18]	–	18 (NA)	Overall (1, 1411), Clinical (1, 1411)	–	–	–	0
Feeding difficulties‡‡	13.2 (12.7-13.7) [R: 0-21]	20.2 (20.0-20.4)	8.6 (8.1-9.1)	Overall (5, 1481), Radiological (3, 100), Clinical (2, 1381)	–	–	–	0
Nausea/vomiting§§	32.8 (30.0-33.6) [R: 28-40]	35.1 (33.9-36.3)	28.4 (NA)	Overall (3, 188), Radiological (2, 100), Clinical (1, 88)	21.9 (20.6-23.1) [R: 12-33]	13.6 (NA)	24.7 (23.0-26.4)	Overall (4, 242), Radiological (1, 66), Clinical (3, 176)
Abdominal pain‖‖	29.0 (28.99-29.01) [R: 29]	29.0 (28.99-29.01)	–	Overall (2, 100), Radiological (2, 100)	17.0 (NA) [R: 17]	17.0 (NA)	–	Overall (1, 66), Radiological (1, 66)
Chest pain‖‖,¶¶	30.6 (30.1-31.1) [R: 29-32]	30.6 (30.1-31.1)	–	Overall (2, 100), Radiological (2, 100)	–	–	–	0
Skin manifestation***	–	–	–	0	24.0 (NA) [R: 24]	24.0 (NA)	–	Overall (1, 88), Radiological (1, 88)

*Includes dyspnoea/difficulty breathing/gasping/breathlessness, combined data from 4-6 and ≥7-14 age groups from Gao et al included [14].
†Includes flaring/nasal flaring.
‡Includes indrawing/recession/chest wall indrawing/chest recession/chest retraction, Forgie et al excluded from analysis as study selected for patients with indrawing [11].
§Includes all utilised definitions of tachypnoea and abnormal respiratory rate, data pertaining to respiratory rate of ≥40 breaths per minute rather than ≥50 breaths per minute included from Juvén et al [7].
‖Includes crepitations/rales/crackles/pulmonary crackles at onset, data included if able to be disaggregated from other abnormal breath sounds, combined data from 4-6 and ≥7-14 age groups from Gao et al included [14].
¶Includes wheeze/wheezes/wheezing/auscultation – wheezing, data included if able to be disaggregated from other abnormal breath sounds, fraction and percentage of children with auscultation finding rather than reported symptom included from Sondergaard et al [20].
**Includes all utilised definitions of fever, data pertaining to fever >37.5°C rather than fever >39.5°C included from Korppi et al [8].
††includes any pallor present
‡‡Includes inability to drink/poor appetite/refusal to eat/cannot eat or drink/feeding difficulties.
§§Data included if able to be disaggregated from other gastrointestinal symptoms.
‖‖Data included if able to be disaggregated from pain at other sites.
¶¶Includes chest pain/thoracic pain.
***Includes any type of rash, urticaria and Stevens-Johnson Syndrome.

Tachypnoea was identified in around half of patients overall but less frequently in the *Mycoplasma* cohort (all-cause pneumonia 55.4%, 95% CI = 53.6-57.2 and *Mycoplasma pneumoniae* 40.1%, 95% CI = 37.9-42.3). The study of outpatients by Harris et al had the highest prevalence of tachypnoea but the lowest threshold for defining tachypnoea (>20 breaths per minute for children older than 2 years) [9]. The percentage of patients with tachypnoea was lower for patients with a radiological diagnosis (all-cause pneumonia 48.0%, 95% CI = 42.9-53.1 and *Mycoplasma pneumoniae* 8.5%, 95% CI = 7.7-9.2) compared to a clinical diagnosis (all-cause pneumonia 77.0% comprising 1 study with 937/1216 patients and *Mycoplasma pneumoniae* 50.1%, 95% CI = 48.5-51.7). Of note, less than 10% of patients with a radiological diagnosis of *Mycoplasma pneumoniae* had documented tachypnoea.

Dyspnoea/difficulty breathing was documented in 29.1% (95% CI = 28.2-30.8) of all-cause pneumonia patients and 23.1% (95% CI = 22.4-23.8) of *Mycoplasma pneumoniae* patients. In the all-cause pneumonia cohort, the proportion of patients with dyspnoea was higher in the clinical diagnosis group (43.0%, 95% CI = 42.3-43.7) compared to the radiological (14.9%, 95% CI = 13.7-16.1). Chest indrawing was observed in approximately half of all-cause pneumonia cases, all of which were based on clinical diagnosis. There was only one small study of *Mycoplasma pneumoniae* patients which documented chest-indrawing in 30.0% (14/46) of patients [19]. Crackles or crepitations were variably described between studies but documented in around one half of patients overall. Wheeze or rhonchi were described in around one quarter of patients.

Chest and abdominal pain were each included in two studies of all-cause pneumonia (radiological diagnosis) and both were documented in around one third of patients. Abdominal pain was included in one small study of *Mycoplasma pneumoniae* patients (radiological diagnosis) and was found in 17% (11/66) of patients [15]. Headache, nausea and vomiting also occurred in around one third of patients in the all-cause pneumonia cohort, though these are non-specific symptoms that may occur in a range of illnesses. Skin manifestations were described in one study addressing *Mycoplasma pneumoniae* with data disaggregated by age and, in this study, were found in 25% (21/88) children [20].

With respect to chest radiograph findings in all studies, one study by *Gao et al* selected for patients with segmental/lobar *Mycoplasma pneumoniae* and additionally reported on the presence of pleural effusions (4%-5%) [14]. Aside from this, only a small number of study participants overall in the 5-9 year age range had disaggregated chest radiograph findings reported (**Table 4**). Lobar changes were documented in around half of patients who had chest radiographs but any further conclusions are limited by the variable inclusion and diagnostic criteria and limited data.

Table 4. Chest radiograph findings document in studies in children 5-9 y with pneumonia

Chest radiograph findings*	All-cause pneumonia, mean (95% CI), range, (%)	Number of studies, number of patients, (n, n)	*Mycoplasma pneumoniae*, mean (95% CI), range, (%)	Number of studies, number of patients, (n, n)
Lobar/segmental pneumonia†	43.7 (31.0-57.4)	2, 33	59.6 (57.4 -61.8)	2, 147
	[R: 17-70]		[R: ~50-69]	
Interstitial changes‡	–	0	12.2 (10.6-13.8)	2, 142
			[R: 5-19]	
Pleural effusion/empyema§	17.9 (14.8-21.0)	2, 81	7.4 (7.0-7.8)	2, 581
	[R: 8-28]		[R: 4-14]	

*Data included if able to be disaggregated from other chest x-ray findings and both numerator and denominator clearly stated.

†Includes lobar consolidation/lobal consolidation/lobar infiltration and segmental/lobar pneumonia, Gao et al excluded from analysis as selected for patients with segmental/lobar pneumonia [14].

‡Includes interstitial changes/interstitial pattern.

§Includes pleural effusion/empyema, combined data from 4-6 y and ≥7-14 y groups from Gao et al included [14], data for pleural effusion rather than single case of empyema included from Sondergaard et al [20].

Outcome data for children aged 5-9 years with pneumonia were available from a single study of inpatients in Kenya, which was also the largest study in the review [12]. Macpherson et al described risk factors associated with mortality in children aged 5-14 years admitted to hospital with pneumonia [12]. Outcome information was available for 1825/1832 (99.5%) patients, of whom 145 (7.9%) died. Inpatient case fatality was higher in children aged 10-14 years compared to the 5-9 year age group (14.05% vs 6.43%, $P<0.001$). For children aged 5-10 years, risk factors for death demonstrated in multi-variate analysis included the presence of severe pallor (OR = 9.89, 95% CI = 4.68 to 20.93, $P<0.001$), mild/moderate pallor (OR = 2.85, 95% CI = 1.35-6, $P<0.006$), reduced consciousness (OR = 6.27, 95% CI = 2.8-14.08, $P<0.001$), central cyanosis (OR = 6.35, 95% CI = 1.33-30.25, $P<0.02$), a weight for age Z-score of≤-3 SD (OR = 2.99, 95% CI = 1.61-5.55, $P<0.001$) and comorbid HIV (OR = 2.49, 95% CI = 1.18-5.28, $P<0.017$). A respiratory rate >30 breaths per minute and inability to

drink were associated with poor outcome, though did not reach statistical significance. Sex, presence of grunting, crackles, chest wall indrawing and comorbid malaria were not associated with mortality and wheeze was found to be relatively protective (not statistically significant). Additional analysis demonstrated that the combination of clinical characteristics used by WHO to define severe pneumonia in children less than 5 years old was poor in discriminating those at risk of death (sensitivity: 0.56, specificity: 0.68 and AUC: 0.62) in this study.

Regarding pneumonia severity and the need for inpatient treatment in children aged 5-9 years, there is little additional data to draw upon beyond the study by Macpherson et al [12]. Studies involving outpatients either did not describe chest indrawing or did not disaggregate data by age in combination with admission status [8,9,19]. Whilst lethargy was documented frequently, reduced consciousness as a specific sign was only described in the study by Macpherson et al [12].

Comparison with clinical features of pneumonia in younger children was made in six out of eight all-cause pneumonia studies and all seven *Mycoplasma pneumoniae* studies (**Table 1** and **Table 2**). In all studies which included chest and abdominal pain and compared frequency between older and younger children, they were found to be more common in older children [6-8]. Crocker et al found that abdominal pain was a reported symptom in all 12 cases in which pleural effusion or empyema were detected in children aged 3-16 years [6]. Comparison of chest auscultation findings between age groups demonstrated no clear trends, with some studies finding crackles and wheeze to be more common in younger children but other studies reporting greater frequency in older children [7,9,13]. Similarly, one study found that normal breath sounds were more common in children older than 5 years and another found that it was less common [7,11]. Inconsistent use of terms for auscultation findings between studies limited comparison. In a study of 127 children with *Mycoplasma pneumoniae*, Ma et al found that children less than 5 years of age were more likely to have a severe illness course, including intensive care unit admission, supplemental oxygen requirement and need for video-assisted thoracoscopic surgery (VATS) [15]. Vomiting also occurred more often in younger children with *Mycoplasma pneumoniae* [15,19]. Segmental or lobar consolidation on chest radiograph was a more common finding in older children for both all-cause pneumonia and *Mycoplasma pneumoniae* groups [13,16,18].

Comparative analysis of clinical features between those with and without comorbidities was not possible as data was not disaggregated for subgroups of participants with comorbidities in the 5-9 year age range in studies that included such participants.

DISCUSSION

There is a paucity of quality evidence describing clinical features of pneumonia in children aged 5-9 years. This review explored findings from 15 studies, eight addressing pneumonia of all causes and seven addressing pneumonia attributable to *Mycoplasma pneumoniae*. The lack of evidence highlights the urgent need for research to understand clinical features, treatment approaches and outcomes for children 5-9 years of age with pneumonia, which remains one of the highest causes of death in this age group globally [3]. However, the evidence that does exist indicates that applying existing WHO definitions of pneumonia for children under 5 years of age, to this older age group, is likely to lower the diagnostic yield.

Current WHO guidelines for children under 5 years old distinguish simple cough from pneumonia based on the presence or absence of tachypnoea. Among studies in this review, tachypnoea lacked standard definitions and this complicates interpretation of findings. However approximately only half of patients in the all-cause pneumonia cohort were documented to have tachypnoea, and this was lower for *Mycoplasma pneumoniae* patients, notably those diagnosed radiologically. Higher proportions of children with pneumonia in clinically diagnosed groups may represent later diagnosis. Alternatively, it may reflect greater emphasis on accurate measurement and recording of respiratory rate in clinicians using clinical diagnosis. The data on clinical diagnosis regarding tachypnoea in the all-cause pneumonia cohort is based on the Kenyan study, which is a cohort of sick children in a high burden setting. Yet, even amongst these patients around 1 in 4 did not have tachypnoea (respiratory rate >30 breaths per minute) documented on admission [12]. The measurement of respiratory rate is a skill which is often not performed well or documented correctly; the evidence indicates that it cannot be relied upon to identify pneumonia among older children with cough [21].

If tachypnoea cannot be relied on to diagnose pneumonia in older children, then addition of other symptoms to aid diagnostic approaches should be considered. Although the study numbers are small, chest pain and abdominal pain were relatively common in children aged 5-9 years with all-cause pneumonia, whether due to their ability to report symptoms, or to the likelihood that researchers sought to identify these symptoms in older children. Chest radiographs may also have a greater role in diagnosing children with pneumonia in this

age group, particularly in the setting of persistent cough and fever without other signs to confirm pneumonia (or alternative diagnoses). It should be noted, the data on chest radiograph findings in pneumonia in this age group is limited and there is insufficient data supporting the use of radiographs to distinguish pneumonia aetiology (eg, *Mycoplasma* from all-cause).

Symptoms used to define severe pneumonia in children <5 years of age, such as reduced conscious state, central cyanosis and/or hypoxia (oxygen saturation <90%) and inability to eat or drink [1,2], still have relevance in older children in low and lower-middle income settings in terms of their risk of mortality and therefore the severity of pneumonia. Similarly, nutritional status and underlying chronic conditions (including HIV) are associated with mortality in older children and should be part of any risk stratification approach used by clinicians to determine the need for admission and treatment [1,2]. Pallor, whether mild, moderate or severe, was identified as being associated with a higher risk of mortality in children 5-9 years old and should also be part of a clinician's consideration of risk and patient disposition [12]. This is consistent with recent evidence suggesting that pallor is an important marker of serious disease in younger age groups [22-24]. The sign of chest indrawing has been an important and evolving marker of pneumonia severity and therefore need for admission in guidelines for children under 5 years old [25]. This review identified no data on the management of chest indrawing in children aged 5-9 years in the outpatient setting. Given chest compliance reduces with age [25], it is reasonable to suspect that chest indrawing may indicate greater severity in older children, as its presence may suggest generation of greater intrathoracic pressures to maintain ventilation. The Kenyan study in this review examined risk of death in older children with pneumonia and found no association between chest indrawing and mortality [12]. This finding, among others described above, is based on a single study in one context and should be interpreted with caution. Of note no radiological studies of all-cause pneumonia documented the presence or absence of chest indrawing in patients, despite its potential importance in guiding treatment.

Our review identified several studies relating to *Mycoplasma pneumoniae* in children 5-9 years of age mostly from high income countries, from which data has been reported separately to not unduly influence data on all-cause pneumonia, and to consider differences in clinical features. While *Mycoplasma pneumoniae* is important in pneumonia in older children, the emphasis on this organism in this review may represent bias on the part of researchers in considering it above other aetiologies. There is a clear need for more data on other potential aetiologies (eg, influenza), but particularly those relevant in the global context, such as HIV and tuberculosis.

Based on the available evidence for *Mycoplasma pneumoniae*, there are no respiratory clinical features that can distinguish it from pneumonia of other aetiologies in children aged 5-9 years. This is consistent with other studies that demonstrated no clinical or radiological features to identify *Mycoplasma pneumoniae* and guide therapeutic decisions [26,27]. Considering *Mycoplasma pneumoniae* as an aetiology and treating this possibility is therefore important, including in HIV positive children among whom it has also been shown to be common [28]. Skin symptoms may be useful in distinguishing *Mycoplasma pneumoniae* as a potential aetiological agent in pneumonia in older children, however there may be bias in seeking and reporting on these symptoms in studies focused on *Mycoplasma pneumoniae* and disaggregated supportive evidence was available from only one study in this review [20]. Separately, a review by Schalock and Dinulos [29] specifically addressing *Mycoplasma pneumoniae*-induced cutaneous disease in paediatric and adult populations and a study by Sauteur et al [30] in paediatric patients aged 3-18 years described skin manifestations as a feature of *Mycoplasma pneumoniae*, such as exanthematous skin eruptions, urticaria, erythema nodosum, *Mycoplasma pneumoniae*-induced rash and mucositis (MIRM) and Stevens-Johnson Syndrome. A key limitation in determining aetiology is that available diagnostic tests for *Mycoplasma pneumoniae* may not distinguish infection from carriage [31].

Implications for WHO pneumonia guidelines

The relatively weak quality of studies and limited evidence in this review should be kept in mind when interpreting the findings. Evidence related to risk factors for death, for example, is derived from a single study of moderate quality. Different definitions (eg, for tachypnoea), different nomenclatures (eg, crepitations) and absence of documentation of key signs (eg, chest indrawing) should be noted. Nonetheless, there are some implications to be considered for WHO guidelines while further research is conducted and evidence is generated.

Cough and fever are common clinical features in pneumonia in children aged 5-9 years. However, tachypnoea, used to define pneumonia according to WHO criteria in children <5 years of age, may not be present in older children with pneumonia. Inclusion of chest pain and abdominal pain in diagnostic approaches for older

children might expand recognition of pneumonia in this age group, especially if other signs are absent. Furthermore, chest radiographs may have greater importance for diagnosis. Clear definitions of tachypnoea are required for both clinical application and to standardise future research.

Symptoms reflecting severity of pneumonia in children <5 years of age (eg, reduced conscious state, hypoxia and inability to drink) have relevance in older children in low resource settings with respect to risk of mortality, and therefore severity of pneumonia. Separate to these markers of severe disease, other patient factors such as poor nutritional status, comorbid chronic conditions and pallor are associated with poor outcomes. As a result, they should be part of the clinician's consideration of risk of a poor outcome for children aged 5-9 years with pneumonia, and inform decision making on patient disposition.

There is minimal data on chest indrawing in children aged 5-9 years, particularly its management in outpatient settings, to guide management recommendations. Without further evidence, it may be safest to recommend admission if chest indrawing is present.

Although there are differences in the proportions of patients with clinical features between the all-cause pneumonia and *Mycoplasma* cohorts, these cannot be used to distinguish pneumonia of different aetiologies in children aged 5-9 years on an individual level. Guidelines should account for causative agents other than pneumococcus and antibiotic recommendations should be altered accordingly. The addition of an antibiotic to cover for *Mycoplasma pneumoniae* (eg, macrolide) when treating pneumonia in this age group should be strongly considered, particularly in severe cases, in children with malnutrition and/or other co-morbidities, and when deterioration occurs on alternate therapy. Skin symptoms may be useful in distinguishing *Mycoplasma pneumoniae* as a potential aetiological agent in pneumonia in children aged 5-9 years, though there is limited evidence available and large potential for bias.

Limitations

This review was conducted with a rigorous systematic approach, broad search strategy to capture relevant publications and methods to minimise risk of bias. It was limited by the databases that were searched, restriction of publications to the English language and unavailability of two full-text articles. Overall, the key limitation is the breadth and depth of existing research pertaining to pneumonia in children aged 5-9 years that is available to inform decision making.

Further studies exploring clinical features of pneumonia in children aged 5-9 years are warranted to strengthen evidence and understanding of the presentation of pneumonia in this age group. Studies using consistent definitions of clinical features and age ranges would enable aggregation of data and comparison between studies and settings. A wider range of studies in outpatient and inpatient settings, which identify clinical features associated with pneumonia severity and help to define critical values of concern for key signs, eg, tachypnoea, would better identify children at risk of poor outcomes. Conversely, understanding the prevalence of features such as chest indrawing in outpatient settings would aid in guiding safe management of children in the community.

Studies describing pneumonia aetiology and associated clinical features in children aged 5-9 years are needed to better inform antimicrobial choices, or clinical scenarios in which particular antimicrobial choices should be prioritised.

Studies should also explore the presentation of pneumonia in children aged 5-9 years with comorbid chronic conditions, given that this group is likely to be at higher risk of recurrent and more severe pneumonia.

CONCLUSIONS

There is a lack of evidence describing clinical features of pneumonia in children aged 5-9 years highlighting an urgent need for further research to guide best practice. Despite the quality and quantity of data, there are some findings which should be considered in relation to whether existing WHO definitions of pneumonia in children less than 5 years of age can be applied to older children. Based on limited data fever and cough are common in this age group, but tachypnoea cannot be relied on for diagnosis. While waiting for better evidence, broader attention to features such as chest and abdominal pain, the role of chest radiographs for diagnosis in the absence of symptoms such as tachypnoea, and risk factors which may influence patient disposition (chest indrawing, pallor, nutritional status) warrants consideration by clinicians.

Full list of ARI Review group: Trevor Duke, Hamish Graham, Steve Graham, Amy Gray, Amanda Gwee, Claire von Mollendorf, Kim Mulholland, Fiona Russell (leadership group, MCRI/University of Melbourne); Maeve Hume-Nixon, Saniya Kazi, Priya Kevat, Eleanor Neal, Cattram Nguyen, Alicia Quach, Rita Reyburn, Kathleen Ryan, Patrick Walker, Chris Wilkes (lead researchers, MCRI); Poh Chua (research librarian, RCH); Yasir Bin Nisar, Jonathon Simon, Wilson Were (WHO).

Acknowledgements: We would like to acknowledge librarian, Poh Chua, at the Royal Children's Hospital Melbourne, who assisted with formulating and conducting our literature search.

Disclaimer: The authors alone are responsible for the views expressed in this publication and they do not necessarily represent the views, decisions or policies of the World Health Organization.

Funding: Funding was provided by the World Health Organization (WHO).

Authorship contributions: HG, AG and members of the ARI Review group conceived the study and initiated the study design. PK and AG led the conduct of searches. Data extraction was led by MM and PK with input from AG. Data analysis was conducted by PK, AG, and MM. The manuscript was drafted by PK, with input from AG, MM and HG. All authors contributed to revisions and approved the final manuscript.

Competing interests: The authors completed the ICMJE Unified Competing Interest Form (available upon request from the corresponding author), and declare no conflicts of interest.

Additional material
Online Supplementary Document

REFERENCES

1 World Health Organization. Pocket Book of Hospital Care for Children: Guidelines for the Management of Common Childhood Illnesses. Geneva: World Health Organization; 2013. Available: https://apps.who.int/iris/bitstream/handle/10665/81170/9789241548373_eng.pdf?sequence=1. Accessed: 27 October 2021.

2 World Health Organization. Integrated Management of Childhood Illness: Chart Booklet. Geneva: World Health Organization; 2014.

3 Institute for Health Metrics and Evaluation. Global Burden of Disease Study 2019. Available: http://ghdx.healthdata.org/gbd-2019. Accessed: 27 October 2021.

4 Ciliska D, Miccuci S, Dobbins M, Thomas BH. Effective Public Health Practice Project Quality Assessment Tool for Quantitative Studies. Available: http://www.ephpp.ca/quality-assessment-tool-for-quantitative-studies/. Accessed: 22 September 2021.

5 Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, et al. The PRISMA 2020 statement: an updated guideline for reporting systematic reviews. BMJ. 2021;372:n71. Medline:33782057

6 Crocker JC, Evans MR, Butler CC, Hood K, Powell CV. Carers' perspectives on the presentation of community-acquired pneumonia and empyema in children: a case series. BMJ Open. 2012;2:e001500. Medline:22952163 doi:10.1136/bmjopen-2012-001500

7 Juvén T, Ruuskanen O, Mertsola J. Symptoms and signs of community-acquired pneumonia in children. Scand J Prim Health Care. 2003;21:52-6. Medline:12718462 doi:10.1080/02813430310000573

8 Korppi M, Don M, Valent F, Canciani M. The value of clinical features in differentiating between viral, pneumococcal and atypical bacterial pneumonia in children. Acta Paediatr. 2008;97:943-7. Medline:18422803 doi:10.1111/j.1651-2227.2008.00789.x

9 Harris JAS, Kolokathis A, Campbell M, Cassell GH, Hammerschlag MR. Safety and efficacy of azithromycin in the treatment of community- acquired pneumonia in children. Pediatr Infect Dis J. 1998;17:865-71. Medline:9802626 doi:10.1097/00006454-199810000-00004

10 Udomittipong K, Chokephaibulkit K, Susiva C, Nithipunyathumrong S, Mahoran K. Clinical presentation and lung function of children hospitalized with 2009 pandemic influenza A (H1N1) pneumonia. Southeast Asian J Trop Med Public Health. 2011;42:824-30. Medline:22299464

11 Forgie IM, O'Neill KP, Lloyd-Evans N, Leinonen M, Campbell H, Whittle HC, et al. Etiology of acute lower respiratory tract infections in Gambian children: II. Acute lower respiratory tract infection in children ages one to nine years presenting at the hospital. Pediatr Infect Dis J. 1991;10:42-7. Medline:2003054 doi:10.1097/00006454-199101000-00009

12 Macpherson L, Ogero M, Akech S, Aluvaala J, Gathara D, Irimu G, et al. Risk factors for death among children aged 5-14 years hospitalised with pneumonia: a retrospective cohort study in Kenya. BMJ Glob Health. 2019;4:e001715. Medline:31544003 doi:10.1136/bmjgh-2019-001715

13 Salih MA, Herrmann B, Grandien M, El Hag MM, Yousif BE, Abdelbagi M, et al. Viral pathogens and clinical manifestations associated with acute lower respiratory tract infections in children of the Sudan. Clin Diagn Virol. 1994;2:201-9. Medline:15566766 doi:10.1016/0928-0197(94)90023-X

14 Gao J, Yue B, Li H, Chen R, Wu C, Xiao M. Epidemiology and clinical features of segmental/lobar pattern Mycoplasma pneumoniae pneumonia: A ten-year retrospective clinical study. Exp Ther Med. 2015;10:2337-44. Medline:26668638 doi:10.3892/etm.2015.2818

15 Ma YJ, Wang SM, Cho YH, Shen CF, Liu CC, Chi H, et al. Clinical and epidemiological characteristics in children with community-acquired mycoplasma pneumonia in Taiwan: A nationwide surveillance. J Microbiol Immunol Infect. 2015;48:632-8. Medline:25311405 doi:10.1016/j.jmii.2014.08.003

REFERENCES

16 Youn YS, Lee KY, Hwang JY, Rhim JW, Kang JH, Lee JS, et al. Difference of clinical features in childhood Mycoplasma pneumoniae pneumonia. BMC Pediatr. 2010;10:48. Medline:20604923 doi:10.1186/1471-2431-10-48

17 Gordon O, Oster Y, Michael-Gayego A, Marans RS, Averbuch D, Engelhard D, et al. The Clinical Presentation of Pediatric Mycoplasma pneumoniae Infections-A Single Center Cohort. Pediatr Infect Dis J. 2019;38:698-705. Medline:30985519 doi:10.1097/INF.0000000000002291

18 Defilippi A, Silvestri M, Tacchella A, Giacchino R, Melioli G, Di Marco E, et al. Epidemiology and clinical features of Mycoplasma pneumoniae infection in children. Respir Med. 2008;102:1762-8. Medline:18703327 doi:10.1016/j.rmed.2008.06.022

19 Othman N, Isaacs D, Kesson A. Mycoplasma pneumoniae infections in Australian children. J Paediatr Child Health. 2005;41:671-6. Medline:16398873 doi:10.1111/j.1440-1754.2005.00757.x

20 Søndergaard MJ, Friis MB, Hansen DS, Jorgensen IM. Clinical manifestations in infants and children with Mycoplasma pneumoniae infection. PLoS One. 2018;13:e0195288. Medline:29698412 doi:10.1371/journal.pone.0195288

21 Ginsburg AS, Lenahan JL, Izadnegahdar R, Ansermino JM. A systematic review of tools to measure respiratory rate in order to identify childhood pneumonia. Am J Respir Crit Care Med. 2018;197:1116-27. Medline:29474107 doi:10.1164/rccm.201711-2233CI

22 Blacklock C, Mayon-White R, Coad N, Thompson M. Which symptoms and clinical features correctly identify serious respiratory infection in children attending a paediatric assessment unit? Arch Dis Child. 2011;96:708-14. Medline:21586436 doi:10.1136/adc.2010.206243

23 Agweyu A, Lilford RJ, English M. Appropriateness of clinical severity classification of new WHO childhood pneumonia guidance: a multi-hospital, retrospective, cohort study. Lancet Glob Health. 2018;6:e74-83. Medline:29241618 doi:10.1016/S2214-109X(17)30448-5

24 Jroundi I, Mahraoui C, Benmessaoud R, Moraleda C, Tligui H, Seffar M, et al. Risk factors for a poor outcome among children admitted with clinically severe pneumonia to a university hospital in Rabat, Morocco. Int J Infect Dis. 2014;28:164-70. Medline:25305555 doi:10.1016/j.ijid.2014.07.027

25 McCollum ED, Ginsburg AS. Outpatient management of children with world health organization chest indrawing pneumonia: implementation risks and proposed solutions. Clin Infect Dis. 2017;65:1560-4. Medline:29020216 doi:10.1093/cid/cix543

26 Principi N, Esposito S, Blasi F, Allegra L. Role of Mycoplasma pneumoniae and Chlamydia pneumoniae in children with community-acquired lower respiratory tract infections. Clin Infect Dis. 2001;32:1281-9. Medline:11303262 doi:10.1086/319981

27 Kumar S, Garg IB, Sethi GR. Serological and molecular detection of Mycoplasma pneumoniae in children with community-acquired lower respiratory tract infections. Diagn Microbiol Infect Dis. 2019;95:5-9. Medline:31097260 doi:10.1016/j.diagmicrobio.2019.03.010

28 Kumar S. Mycoplasma pneumoniae: A significant but underrated pathogen in paediatric community-acquired lower respiratory tract infections. Indian J Med Res. 2018;147:23-31. Medline:29749357 doi:10.4103/ijmr.IJMR_1582_16

29 Schalock PC, Dinulos JG. Mycoplasma pneumoniae-induced cutaneous disease. Int J Dermatol. 2009;48:673-80, quiz 80-1. Medline:19570071 doi:10.1111/j.1365-4632.2009.04154.x

30 Meyer Sauteur PM, Theiler M, Buettcher M, Seiler M, Weibel L, Berger C. Frequency and clinical presentation of mucocutaneous disease due to Mycoplasma pneumoniae Infection in children with community-acquired pneumonia. JAMA Dermatol. 2020;156:144-50. Medline:31851288 doi:10.1001/jamadermatol.2019.3602

31 Meyer Sauteur PM, Unger WW, Nadal D, Berger C, Vink C, van Rossum AM. Infection with and Carriage of Mycoplasma pneumoniae in Children. Front Microbiol. 2016;7:329. Medline:27047456 doi:10.3389/fmicb.2016.00329