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Invited Review

Chest ultrasound for the diagnosis of paediatric pulmonary diseases: a systematic review and meta-analysis of diagnostic test accuracy

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Abstract

Background: Chest ultrasound is an emerging imaging modality, for several paediatric pulmonary diseases.

Sources of data: MEDLINE and EMBASE (1946–47 to 10 March 2017) were searched to collect evidence on the diagnostic accuracy of chest ultrasound, compared to other imaging modalities, for the diagnosis of paediatric pulmonary diseases.

Areas of agreement: Eighteen pneumonia studies, comprising 2031 children, were included for meta-analysis; the summary estimate sensitivity was 95.0% (95%CI: 90.7–97.3%) and specificity was 96.1% (95%CI: 89.1–98.7%).

Areas of controversy: Other pulmonary diseases also yielded high sensitivity and specificity, but a meta-analysis could not be conducted due to a limited number of studies includable, and their heterogeneity.

Growing points: Chest ultrasound should be considered as a first-line imaging modality for children with suspected pneumonia.

Areas timely for developing research: Further research should focus on the diagnostic accuracy of chest ultrasound for the diagnosis of paediatric pulmonary diseases, other than pneumonia, comparing against a valid gold standard.

Key words: chest ultrasound, paediatric pulmonary diseases, pneumonia

Background

Lower respiratory tract infection is a leading infectious cause of morbidity and mortality in the world, particularly in children younger than 5 years (1 billion episodes per year and 703 918 deaths [104.8 deaths per 100 000 children under 5 years]),[1] while other pulmonary diseases are amongst the most common health problems for which acute care is sought for children.[2,3] Accurate diagnosis is important to implement effective treatment. Conventional imaging for the diagnosis of pulmonary disease in children relies largely on chest X-ray (CXR), which exposes children to harmful ionizing radiation.[4] Chest computed tomography (CT) and chest magnetic resonance imaging (MRI) have the potential to delineate more detailed abnormalities but require radiologic infrastructure and expertise and are therefore more expensive; also CT is associated with higher exposure to ionizing radiation, and MRI requires sedation of young children.

Chest ultrasound is an attractive alternative as it is devoid of ionizing radiation, is quick to perform and easily repeatable and can be performed and interpreted by non-radiologists. Improved technology has made ultrasound machines smaller and portable, making bedside ultrasound and point-of-care testing feasible. In addition, ultrasound is cheaper and more readily at hand than CT and MRI, especially in resource-limited settings.

Chest ultrasound was first used in 1986 to diagnose pneumonia in children, by demonstrating air bronchograms within areas of consolidation.[5] In the past decade, there have been increasing numbers of studies of chest ultrasound for the diagnosis of paediatric pulmonary diseases.

Recent systematic reviews found high diagnostic accuracy of chest ultrasound for the diagnosis of pneumonia,[6,7] concluding that it is a useful imaging alternative to CXR for the diagnosis of childhood pneumonia.[7] Could chest ultrasound also be used for other paediatric pulmonary diseases, like pleural effusion, respiratory distress syndrome (RDS), pneumothorax, atelectasis and bronchitis for example? Chest ultrasound is not the standard imaging technique for those diseases. The aim of this systematic review and meta-analysis was to evaluate the diagnostic accuracy of chest ultrasound for the diagnosis of paediatric pulmonary diseases, including pneumonia.

Methods

This systematic review and meta-analysis were conducted following the PRISMA-DTA guidelines (M. Leeflang (personal communication), October 10, 2017, http://www.prisma-statement.org/Extensions/DTA.aspx). The protocol was registered in the international prospective register for systematic reviews, PROSPERO (*CRD42016033321*).

Eligibility criteria

Studies evaluating the diagnostic accuracy of chest ultrasound for the diagnosis of pulmonary diseases (for example but not exclusively pneumonia, pleural effusion, pneumothorax, bronchiolitis or pulmonary tuberculosis) in children up to the age of 18 years were included in this systematic review and meta-analysis. Studies using other imaging modalities like CXR, CT or MRI or clinical diagnosis as a reference standard were included. Studies that used clinical diagnosis as a reference standard had to compare chest ultrasound with another imaging modality to be considered for inclusion. Echocardiography, prenatal ultrasound, intra-operative chest ultrasound and chest ultrasound conducted for underlying diseases other than pulmonary diseases were excluded.

Randomized controlled trials, clinical controlled trials, case-control studies and observational cohort studies were included, systematic reviews were used for reference searching, case reports were excluded from this review.

Search strategy and selection criteria

An experienced information specialist (R.S.) developed and conducted the search strategy with input from the clinical reviewers (C.H., S.B.). We searched MEDLINE (Ovid, 1946 to present) and EMBASE (Ovid, 1947 to present) on March 10, 2017 (see Supplementary Material 1 for details of the sources searched and the search strategies used). We checked reference lists of relevant systematic reviews and included studies for additional relevant citations. No date or language restrictions were applied. In summary, the search terms covered the population (children under the age of 18 years), the intervention (chest ultrasound) and pulmonary diseases (including pneumonia, bronchitis, pulmonary effusion, pneumothorax, pulmonary tuberculosis). Only studies reporting the sensitivity and specificity as an outcome or studies providing enough information to calculate the sensitivity and specificity were included. Authors of abstracts which had not been published as full-text articles were contacted to verify if the full text will be published and if accepted by a journal we asked for access to their preliminary full-text articles to included them in the study.

Study selection and data management

Deduplicated citations were uploaded in a database (Rayyan),[8] two reviewers (C.H. and S.B.) screened titles and abstracts to exclude citations beyond the scope of this review. The first 5% of the identified citations were used for pilot testing and refining of the inclusion and exclusion criteria. The full text of potentially relevant citations was retrieved to assess eligibility. Double screening for inclusion was conducted by C.H. and S.B.; disagreement was resolved by discussion. Agreement after title and abstract screening was 98.6% with a good inter-rater reliability (Cohen's kappa, $\kappa = 0.93$).

Data collection

Per included citations title, author, journal, year of publication, research question, population size, mean age, gender proportion, study setting, details of index test (chest ultrasound) and reference test (CXR, CT or MRI), sonographer, study methodology, recruitment methods, outcomes, true positives, false positives, true negatives, false negatives, sensitivity, specificity, study conclusion, bias assessment by study authors, bias assessment by review authors, source of funding and conflict of interest were extracted. For two of the included citations, the data extraction forms were pilot-tested by two reviewers (C.H. and S.B.). For the remaining citations, data extraction was conducted by one reviewer (C.H.) and checked by a second reviewer (S.B.); disagreement was resolved by discussion. Study authors were contacted by email for any missing or confusing data.[9–15] Complete data extraction forms can be found in Supplementary Material 2.

Quality assessment

The risk of bias and methodological quality was assessed by two reviewers (C.H. and S.B.) independently by using the QUADAS-2 (Quality Assessment of Diagnostic Accuracy Studies-2) assessment tool.[16] This tool was pilot-tested on two of the included citations; for the remaining citations, the risk of bias/quality assessments was performed by one reviewer (C.H.) and checked by a second reviewer (S.B.). Disagreement was resolved by discussion.

Data analysis

The studies were categorized per diseases, the summary estimate of sensitivity and specificity with corresponding 95% confidence intervals (95%CI) and the positive and negative likelihood ratios (LR) were calculated for every disease. The bivariate model and the hierarchical summary receiver operating characteristic (HSROC) model were used. Forest plots as well as HSROC curves were created. We performed a subgroup analysis to explore the influence of operator experience and age of the children on the accuracy of chest ultrasound. Data analysis was conducted using STATA 14.2 (StataCorp; 2015, TX, USA) and R 3.4.1 (the R Foundation for Statistical Computing; 2016, Vienna, Austria).

Results

We screened 3042 unique citations, of which 2893 citations were excluded after title and abstract screening, as they did not fulfil the inclusion criteria (see Supplementary Material 3 for protocol including inclusion criteria). Of the remaining 149 citations, 74 citations were excluded after full-text assessment as they did not meet the inclusion criteria. Full text was irretrievable for 18 citations, 18 citations were conference abstracts and 8 citations were reviews. We included 31 studies[9–15,17–40] in this systematic review (Fig. 1).

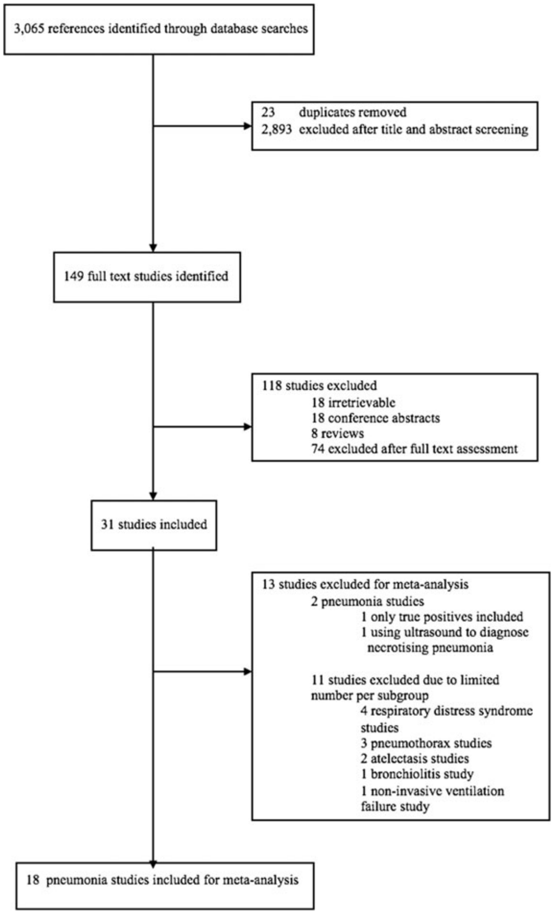

Figure 1 Flow chart literature search.

Of the 31 included studies, 20 reported on pneumonia,[9–12,17–32] 4 RDS[13,33–35] of which 1 study also reported on transient tachypnoea of the newborn,[34] 3 on pneumothorax,[36–38] 2 on atelectasis,[14,39] 1 on bronchiolitis[40] and 1 on non-invasive ventilation failure.[15] The study characteristics of each study are presented in Table 1. Nine studies were conducted in neonates.[13,15,28,33–37,39] The remaining studies were conducted in the general paediatric population.[9–12,14,17–27,29–32,38,40] Ten studies were conducted in an intensive care unit (ICU),[13,15,25,28,33–37,39] of which nine were in a neonatal ICU (NICU)[13,15,28,33–37,39] and one in a paediatric ICU (PICU),[25] eight studies in a paediatric ward,[11,22–24,26,27,31,40] eight studies in a (paediatric) emergency department[9,10,12,19–21,29,32] and five studies in a radiology department.[14,17,18,30,38] The majority of the studies were conducted in high-income countries (23 studies),[9–12,15,17,20–27,29–32,34,36–38,40] 8 studies in middle-income countries,[13,14,18,19,28,33,35,39] none of the included studies were conducted in low-income countries. Across all studies, there were 2796 children included; of which 2073 were in the pneumonia studies, 369 in the RDS studies, 154 in the pneumothorax studies, 95 in the atelectasis studies, 54 in the non-invasive ventilation failure study and 51 in the bronchiolitis study. The majority of the included children were male (54.5%), with a mean age of 3.0 years (range 0–17 years).

A linear probe, varying from 5 to 12 MHz, was used to perform chest ultrasound in all studies but two,[23,31] which only used a convex probe. Eleven studies used a linear and convex (2–9 MHz) probe to scan their patients.[9–12,17,18,20,25,30,32,33,38] In 11 studies, a radiologist performed the chest ultrasound,[9,10,12–15,17,18,28,33,35] in one study experienced ultrasound technologists scanned the chest,[30] and in 18 studies clinicians performed the chest ultrasound,[11,17,19–27,29,31,34,36,37,39,40] of which 5 studies reported that the clinician had minimal ultrasound experience (1 h to 3 days of ultrasound training).[20–22,25,29] In all studies, but three,[15,23,30] the same doctor performed and analysed the chest ultrasound. In the study using ultrasound technicians as the sonographer, the chest ultrasound was evaluated by a paediatric radiologist or a radiology resident.[30] In one retrospective study, it was unclear who analysed the chest ultrasound,[23] and in one study it was unclear who performed the chest ultrasound but the images were analysed by an experienced radiologist.[15]

In the majority of the studies (*n* = 23), patients were scanned in a sitting or supine position, obtaining images of the anterior, posterior and mid-axillary chest from the apex down to the diaphragm, using an intercostal approach in transverse and longitudinal planes,[9–13,17,19–32,38–40] similar to the method earlier described by Copetti and Cattarossi.[32] Four studies scanned only the anterior and lateral chest, with the patient in a supine or lateral decubitus position.[15,18,34,38] Three studies used the transabdominal approach in addition to the transthoracic approach (Table 2).[15,33,35]

Fourteen studies used CXR as a reference standard,[11–13,15,17,20–22,25,29,31,33,35,37–39] in 12 studies the CXR was interpreted by a radiologist, in 2 studies the person reviewing the CXR images was not reported.[13,31] In two studies, chest CT was used to confirm the CXR diagnosis in some patients;[38,39] two further studies used chest CT as a reference standard[18,30] and one study used MRI as a reference standard,[14] in all these studies the reference standard was analysed by a radiologist. Eleven studies used the clinical diagnosis as the reference standard, of which seven studies included CXR to arrive at a diagnosis;[9,19,24,26,27,32,34] the four remaining studies compared the accuracy of chest ultrasound with the accuracy of CXR to the clinical diagnosis.[10,23,28,40] The clinical diagnosis was made by a clinician,[19] paediatrician,[9,23,24,26,27,32,40] neonatologist[28,34] or pulmonologist,[26]; one study did not record who made the clinical diagnosis.[10] One study used the detection of a pneumothorax by aspiration as a reference standard.[36]

In all studies but three,[28,35,39] the sonographer was blinded to the findings of the other imaging modality/reference standard (Table 2).

The quality of most of the included studies was high but the risk of bias for patient selection was high in 10 studies,[10,13,15,23–25,28,29,31,39] unclear in 11 studies,[18,19,27,30,32–36,38,40] and only 10 studies[9,11,12,14,17,20–22,26,37] had a low risk of bias for patient selection (Supplementary Material 4).

The true positive, false positive, false negative and true negative rate, as well as sensitivity and specificity of each individual study are presented in Table 1.

Two pneumonia studies were excluded for meta-analysis, one study reported on the sensitivity for the detection of necrotizing pneumonia[31] and for one study it was difficult to calculate the diagnostic accuracy as only patients with a positive reference test were included.[30] Eighteen pneumonia studies were included for meta-analysis;[9–12,17–29,32] comprising 2031 children with a mean age of 4.0 years (range 0–16 years). The summary estimate of sensitivity was 95.0% (95%CI: 90.7–97.3%), and the summary specificity was 96.1% (95%CI: 89.1–98.7%) for chest ultrasound. The positive LR was 24.41 (95% CI 8.39–71.02) and the negative LR was 0.05 (95%CI 0.03–0.10) (see Fig. 2a for a forest plot of the pneumonia studies and Fig. 2b for the HSROC curve).

Due to the limited number of studies for other pulmonary diseases, a meta-analysis was not considered useful for RDS (four studies), pneumothorax (three studies), atelectasis (two studies); and not possible for bronchiolitis (one study) and non-invasive ventilation failure (one study).

The four prospective RDS studies were conducted on NICU's in Egypt (2x),[13,32] Italy[34] and Serbia.[35] The studies included a total of 369 neonates (sample size range 59–120). The sonographer was an experienced radiologist in three studies[13,33,35] and a trained neonatologist in one study.[34] A linear probe

Table 1 Characteristics and diagnostic accuracy per included study

Disease	First author (Year)	Country	Study design	Setting	Sample size	% Male	Mean age (years [gestational age])	TP	FP	FN	TN	Sensitivity	Specificity
Pneumonia	Claes[15]	Belgium	Prospective	Radiology department	143	54	3.4	44	8	1	90	97.8	91.8
	Saraya[16]	Egypt	Prospective	Radiology department	56	48	2.3	26	1	10	19	72.2	95.0
	Yilmaz[17]	Turkey	Prospective	Emergency department	160	55	3.3	142	0	7	0	95.3	.
	Boursiani[7]	Greece	Prospective	Emergency department	69	39	4.5	62	0	4	3	93.9	100
	Guerra[18]	Italy	Prospective	Emergency department	222	49	4.8	190	17	7	6	96.4	26.1
	Ianniello[8]	Italy	Retrospective	Emergency department	84	52	6	60	0	1	23	98.4	100
	Samson[19]	Spain	Prospective	Emergency department	200	58	2.5	74	6	11	109	87.1	94.8
	Zhan[20]	Denmark	Prospective	Paediatric ward	82	57	1.5	33	7	49	75	40.2	91.5
	Ho[21]	Taiwan	Retrospective	Paediatric ward	163	56	7.8	159	0	4	0	97.5	.
	Iorio[22]	Italy	Retrospective	Paediatric ward	52	52	3.5	28	1	1	22	96.5	95.6
	Urbankowska[9]	Poland	Prospective	Paediatric ward	106	63	4.6	71	0	5	30	93.4	100
	Esposito[23]	Italy	Prospective	PICU	103	54	5.6	47	3	1	52	97.9	94.5
	Reali[24]	Italy	Prospective	Paediatric ward	107	56	4	76	1	5	25	93.8	96.2
	Caiulo[25]	Italy	Prospective	Paediatric ward	102	52	5	88	0	1	13	98.9	100
	Seif El Dien[26]	Egypt	Prospective	NICU	75	48	0 [37.0]	68	0	5	2	93.2	100
	Shah[27]	USA	Prospective	Emergency department	200	61	2.9	31	18	5	146	86.1	89.0
	Iuri[10]	Italy	Prospective	Emergency department	28	61	4.5	22	0	2	8	91.7	100
	Kurian[28]	USA	Retrospective	Radiology department	19	47	5.4	18	0	0	0	100	.
	Chiu[29]	Taiwan	Retrospective	Paediatric ward	23	NR	3.5	8	0	15	14	35.0	100
	Copetti[30]	Italy	Prospective	Emergency department	79	47	5.1	60	0	0	19	100	100
RDS	El-Malah[31]	Egypt	Prospective	NICU	100	66	0 [37.9]	88	8	2	2	98.0	25.0
	Sawires[11]	Egypt	Prospective	NICU	90	40	0 [29.9]	90	19	0	21	100	52.5
	Vergine[32]	Italy	Prospective	NICU	59	61	0 [33.0]	22	2	1	34	95.6	94.4
	Lovrenski[33]	Serbia	Prospective	NICU	120	NR	0 [31.0]	43	0	2	2	95.6	100
Pneumothorax	Cattarossi[34]	Italy	Prospective	NICU	49	67	0 [36.0]	23	0	0	26	100	100
	Raimondi[35]	Italy, Spain, France	Prospective	NICU	42	NR	0 [31.0]	26	0	0	16	100	100
	Kosiak[36]	Poland	Prospective	Radiology department	63	60	7.8	4	0	0	59	100	100
Atelectasis	Liu[37]	China	Prospective	NICU and neonatology ward	80	53	0 [NR]	60	0	20	0	75.0	0
	Acosta[12]	Argentina	Prospective	Radiology department	15	60	4.5	39	15	4	122	90.7	89.1
Bronchiolitis	Caiulo[38]	Italy	Prospective	Paediatric ward	52	54	0.2	47	0	5	52	90.4	100
NVF	Raimondi[13]	Italy	Prospective	NICU	54	NR	0 [NR]	18	0	0	36	100	100

CT, computed tomography; CXR, chest X-ray; FN, false negative; FP, false positive; MRI, magnetic resonance imaging; NICU, neonatal intensive care unit; NR, not reported; NVF, non-invasive ventilation failure; PICU, paediatric intensive care unit; RDS, respiratory distress syndrome; TN, true negative; TP, true positive.

Table 2 Chest ultrasound technique, sonographer, reference test, blinding and funding per included study

Disease	First author (Year)	Probe	Technique	Operator experience	Reference test	Reference test reader	Blinding	Funding source
Pneumonia	Claes[15]	Linear (5–12 MHz) ± convex (4–9 MHz) probe	Anterior, posterior and lateral parts of chest were scanned in the longitudinal and the transverse plane, with the patient in supine and/or prone or sitting position.	Three paediatric radiologists + one final-year radiology intern	CXR	Paediatric radiologist	Yes	NR
	Saraya[16]	Linear (6–12 MHz) and convex (2–5 MHz) probe	Anterior and lateral parts of chest were scanned in longitudinal and oblique planes with the patient in supine and lateral decubitus position.	Radiologist	CT chest	Radiologist	Yes	NR
	Yilmaz[17]	Linear probe (6–13 MHz)	Anterior, lateral and posterior parts of chest were scanned obtaining oblique and parallel views, with the patient in the supine and lateral decubitus position.	Experienced paediatric emergency physician	Clinical diagnosis including CXR	Clinician	Yes	None
	Boursiani[7]	Linear (5–12 MHz), convex (3–5 MHz) and micro-convex (5–8 MHz) probe	Along the parasternal, mid-clavicular, axillary, paravertebral and axial lines, longitudinal and intercostal scans were obtained with the patient in the sitting and/or supine position.	Experienced paediatric radiologist	Clinical diagnosis including CXR	Paediatrician	Yes	NR
	Guerra[18]	Linear (7.5–10-MHz) and convex (3.5–5-MHz) probe	Anterior, posterior and lateral parts of chest were scanned in the longitudinal and the transverse plane, with the patient in supine and/or prone or sitting position. The costophrenic angles and the areas adjacent to lung consolidation were checked for effusion.	Three paediatricians with minimal ultrasound experience	CXR	Radiologist	Yes	None
	Ianniello[8]	Linear (7.5–10 MHz) and convex (4 MHz) probe	Anterior, posterior and lateral parts of chest were scanned in the longitudinal and the transverse plane, with the patient in supine position.	Radiologist	Clinical diagnosis	NR	Blinded to CXR, aware of clinical data	NR
	Samson[19]	Linear probe (6–15 MHz)	Anterior, posterior and lateral parts of chest were scanned in the longitudinal and the transverse plane, with the patient in supine and/or sitting position.	Seven paediatricians and five paediatric residents with varying ultrasound experience	CXR	Radiologist	Yes	NR

Continued

Table 2 *Continued*

Disease	First author (Year)	Probe	Technique	Operator experience	Reference test	Reference test reader	Blinding	Funding source
	Zhan[20]	Two linear probes (5–10 MHz and 5–13 MHz)	Anterior, posterior and lateral parts of chest were scanned in the longitudinal and the transverse plane, with the patient in supine and/or sitting position.	A paediatric resident with minimal ultrasound experience	CXR	Paediatric radiologist	Yes	Ultrasound by GE Healthcare
	Ho[21]	Convex probe (5 MHz)	The anterior, lateral and posterior parts of chest were scanned; oblique and parallel views were obtained with the patient in supine or lateral decubitus position.	Experienced paediatric pulmonologists	Clinical diagnosis	Paediatrician	Unclear	Kaohsiung Medical University Hospital
	Iorio[22]	Linear probe (5–10 MHz)	Anterior, lateral and posterior parts of chest were scanned with the patient in the supine and sitting position.	A paediatrician with ultrasound experience	Clinical diagnosis including CXR	Paediatrician	Yes	None
	Urbankowska[9]	Linear (5–9 MHz) and convex (3–7 MHz) probe	Anterior, posterior and lateral parts of chest were scanned in the longitudinal and the transverse plane, with the patient in supine position.	Paediatric sonographer	CXR	Radiologist	Blinded to CXR, aware of clinical data	NR
	Esposito[23]	Linear (7.5–12 MHz) and convex (2.5–6.6 MHz) probe	The anterior, lateral and posterior parts of chest were scanned with the patient in a supine or sitting and/or lateral decubitus position.	Paediatric resident with limited ultrasound experience	CXR	Radiologist	Yes	NR
	Reali[24]	Linear probe (7.5–10 MHz)	The chest was scanned down the parasternal, mid-clavicular, anterior, mid-axillary, paravertebral, scapular and posterior axillary lines, longitudinal and transverses views were obtained with the patient in the supine or sitting position.	Pulmonologist and two residents	Clinical diagnosis and CXR	Pulmonologist and paediatrician	Blinded to CXR, aware of clinical data	NR
	Caiulo[25]	Linear probe (6–12 MHz)	The chest was scanned down the parasternal, mid-clavicular, anterior axillary, mid-axillary, paravertebral, scapular and posterior axillary lines, longitudinal and transverse planes.	A paediatrician with ultrasound experience	Clinical diagnosis including CXR	Paediatrician	Blinded to CXR, aware of clinical data	NR
	Seif El Dien[26]	Linear probe (7 MHz)	Anterior, posterior and lateral parts of chest were scanned in the longitudinal and the transverse plane, with the patient in supine and lateral decubitus position.	Radiologist	Clinical diagnosis	Neonatologist	No	NR
	Shah[27]	Linear probe (7.5–10 MHz)	Anterior, posterior and lateral parts of chest were scanned in the longitudinal and the transverse plane, with the patient in lateral decubitus and sitting position.	Fifteen paediatric emergency physicians with varying ultrasound experience	CXR	Paediatric radiologist	Yes	NR

	Iuri[10]	Linear (5–12 MHz) and convex (2–5 MHz) probe	The anterior and posterior parts of chest were scanned along the clavicular, parasternal and axillary lines with the patient in sitting position. Longitudinal and axial (intercostal) scans were acquired.	Radiologist	CXR	Radiologist	Yes	NR
	Kurian[28]	Linear (5–12 MHz), convex (2–5, 4–9, or 5–8 MHz), and vector (5–8 MHz) probe	Anterior, posterior, and mid-axillary parts of chest were scanned in transverse and longitudinal planes with the patient in a supine or decubitus position.	Two experienced ultrasound technologists performed US, radiologist reviewed US	CT chest	Paediatric radiologist	Yes	NR
	Chiu[29]	Convex probe (5.0 MHz)	Patients were scanned in a supine or sitting position by means of an intercostal approach.	Pulmonologist	CXR	NR	Unclear	NR
	Copetti[30]	Linear (7.5–10 MHz) and convex (3.5–5 MHz) probe	Anterior, posterior and lateral parts of chest were scanned in the longitudinal and the transverse plane, with the patient in lateral decubitus and sitting position.	Emergency physician	Clinical findings and CXR, CT, ultrasound	Paediatrician	Yes	NR
RDS	El-Malah[31]	Linear (7.5 MHz) and convex (5 MHz) probe	The anterior, lateral and posterior parts of chest were scanned with the patient in supine and lateral decubitus position. Longitudinal, transverse and oblique views. The transabdominal approach (transhepatic and transsplenic) in supine position was used to examine the lung bases.	Radiologists	CXR	Radiologist	Yes	NR
	Sawires[11]	Linear probe (7 MHz)	Anterior, lateral and posterior parts of chest were scanned in longitudinal and transverse sections.	Radiologist	CXR	NR	Yes	NR
	Vergine[32]	Linear probe (10–12 MHz)	The anterior and lateral parts of chest were scanned between the parasternal and anterior axillary lines and between the anterior and posterior axillary lines, in the longitudinal plane.	Trained neonatologist	Clinical diagnosis including CXR	Neonatologist	Yes	None
	Lovrenski[33]	Linear probe (7.5 MHz)	The anterior, lateral and posterior parts of chest were scanned with the patient in supine and lateral decubitus position. Longitudinal, transverse and oblique scans were included. The transabdominal approach (transhepatic and transsplenic) in supine position was used to examine the lung bases.	Experienced paediatric radiologist	CXR	Radiologist	Chest US reported first by same radiologist	NR

Continued

Table 2 *Continued*

Disease	First author (Year)	Probe	Technique	Operator experience	Reference test	Reference test reader	Blinding	Funding source
Pneumothorax	Cattarossi[34]	A high-frequency linear probe (13 MHz)	Not described	Five neonatologists trained in chest ultrasound	Pneumothorax confirmed by aspiration	NA	Blinded to CXR, aware of clinical data	None
	Raimondi[35]	High-frequency linear probe (10 MHz)	Not described	A neonatologist skilled in chest ultrasound	CXR	Radiologist	Yes	NR
	Kosiak[36]	Linear (8.0–12.0 MHz) and convex (3.5–5.0 MHz) probes	The anterior and lateral parts of chest were scanned with the patient in the supine position, longitudinal and transverse views were obtained.	Paediatrician with ultrasound experience	CXR or CT	Radiologist	Unclear	None
Atelectasis	Liu[37]	High-frequency linear (9–12 MHz) probe	The anterior, lateral and posterior parts of chest were scanned with the infants in supine, lateral, or prone position. The probe was positioned perpendicular and parallel to the ribs.	Neonatal expert sonographer	CXR and CT	Radiologist	CXR was performed after chest US if US was positive	None
	Acosta[12]	Linear probe (6–12 MHz)	The anterior, lateral and posterior parts of chest were scanned with the probe perpendicular to the ribs. Intercostal postero-basal (IPB) view for assessment of posterior para-diaphragmatic atelectasis. The probe transvers in intercostal space above hemi-diaphragm and below posterior axillary line.	Two radiologists	MRI	Radiologist	Yes	NR
Bronchiolitis	Caiulo[38]	High-resolution linear probe (6–12 MHz)	Anterior, lateral and posterior parts of chest were scanned, longitudinal and transverse sections were obtained.	A paediatrician with ultrasound experience	Clinical diagnosis	Paediatrician	Blinded to CXR, aware of clinical data	NR
NVF	Raimondi[13]	Linear probe (5–12 MHz)	Anterior and lateral parts of chest were scanned with the infant in supine position.	Analysed by experienced paediatric radiologist	CXR	Radiologist	Yes	None

CT, computed tomography; CXR, chest X-ray; MHz, megahertz; MRI, magnetic resonance imaging; NVF, non-invasive ventilation failure; RDS, respiratory distress syndrome; US, ultrasound.

(7–12 MHz) was used in all four studies and one study[33] used a convex probe (5 MHz) as well, the anterior and lateral approaches were used to scan the chest in all four studies, three studies[13,33,35] scanned used the posterior approach and two studies[33,35] included the transabdominal approach as well. CXR was used the reference standard in three studies[13,33,35] one study[34] used the clinical diagnosis, including CXR, as the reference standard. The sonographer was blinded for the CXR findings in all four studies but in one study[35] the sonographer, a radiologist, reported the CXR after performing the chest ultrasound. The sensitivity ranged from 95.6% to 100% and the specificity from 25.0% to 100% (see Table 1, and Fig. 2c for a forest plot).

The three prospective pneumothorax studies were conducted at the NICU[36,37] and radiology department[38] in Italy,[36,37] Spain,[37] France[37] and Poland.[38] The threes studies combined included 154 children (sample size range: 42–63), aged 0–17 years. The scans were performed by trained neonatologists[36,37] and a paediatrician with ultrasound experience.[38] A linear probe (8–13 MHz) was used in all three studies, one study[38] used a convex probe as well (3.5–5 MHz). Only one study[38] described the scanning technique, the anterior and lateral parts of the chest were scanned. The three studies used a different reference standard, confirmation by aspiration,[36] CXR,[37] CXR or CT chest.[38] Two studies[36,37] reported that the sonographer was blinded to CXR readings, one study[38] did not report on blinding. The sensitivity and specificity for chest ultrasound to detect a pneumothorax was 100% in all three studies (see Table 1, and Fig. 2d for a forest plot).

The two prospective studies reporting on atelectasis were conducted on the NICU,[39] neonatology ward[39] and the radiology department[14] in China[39] and Argentina.[14] One study included 80 neonates and one study included 15 children with a mean age of 4.5 years. The Chinese study used an expert neonatal sonographer and the Argentine study used a radiologist to scan the chest. Both studies used a linear probe (6–12 MHz) and the anterior, lateral and posterior approaches were used. The Chinese study used CXR and CT as a reference standard, but only used it if the chest ultrasound was positive, the Argentine study used MRI. The sensitivity were 75[39] and 90.7%,[14] only the specificity of the Argentine study could be calculated and was 89.1% (see Table 1, and Fig. 2e for a forest plot).

We included one Italian, prospective, bronchiolitis study,[40] they included 52 children, median age of 2.1 months, from the paediatric ward. A paediatrician with ultrasound experience used a linear probe (6–12 MHz) to scan the anterior, lateral and posterior parts of the chest. The reference standard was clinical diagnosis. The sensitivity was 90.4% and the specificity was 100% (Table 1).

We included one study that reported on the diagnostic accuracy of chest ultrasound to diagnose non-invasive ventilation failure.[15] This prospective study was conducted in Italy on the NICU, 54 neonates were included. An experience paediatric radiologist used a linear probe (5–12 MHz) to scan the anterior and lateral parts of the chest. CXR was used the reference standard, the radiologist was blinded to the CXR findings. A sensitivity and specificity of 100% were found (Table 1).

Three studies[17,28,29] reported their findings on small consolidations detected on chest ultrasound but not visible on CXR. Claes *et al.* found that in the eight patients with a consolidation only seen on chest ultrasound, the mean size of the consolidation was significantly smaller (9.4 mm) than in children with a consolidation seen on both imaging modalities (mean size 26 mm).[17] Shah *et al.* compared chest ultrasound with CXR and found 18 consolidations on chest ultrasound that were not detected on CXR; 13 of these were smaller than 1 cm.[29] Seif El Dien and Abd Ellatif found that chest ultrasound detected a small apical or basal consolidation in 18 patients (39.1%) this was not seen on CXR, in seven patients (15.0%) more extensive consolidations were seen on chest ultrasound than on CXR.[28]

Only three pneumonia studies, with a total of 79 patients, compared chest ultrasound against the gold standard, chest CT.[18,30,32] Kurian *et al.* showed that chest CT did not provide any additional information to chest ultrasound for the detection of effusion, lung necrosis or abscess as a complication of pneumonia,[30]

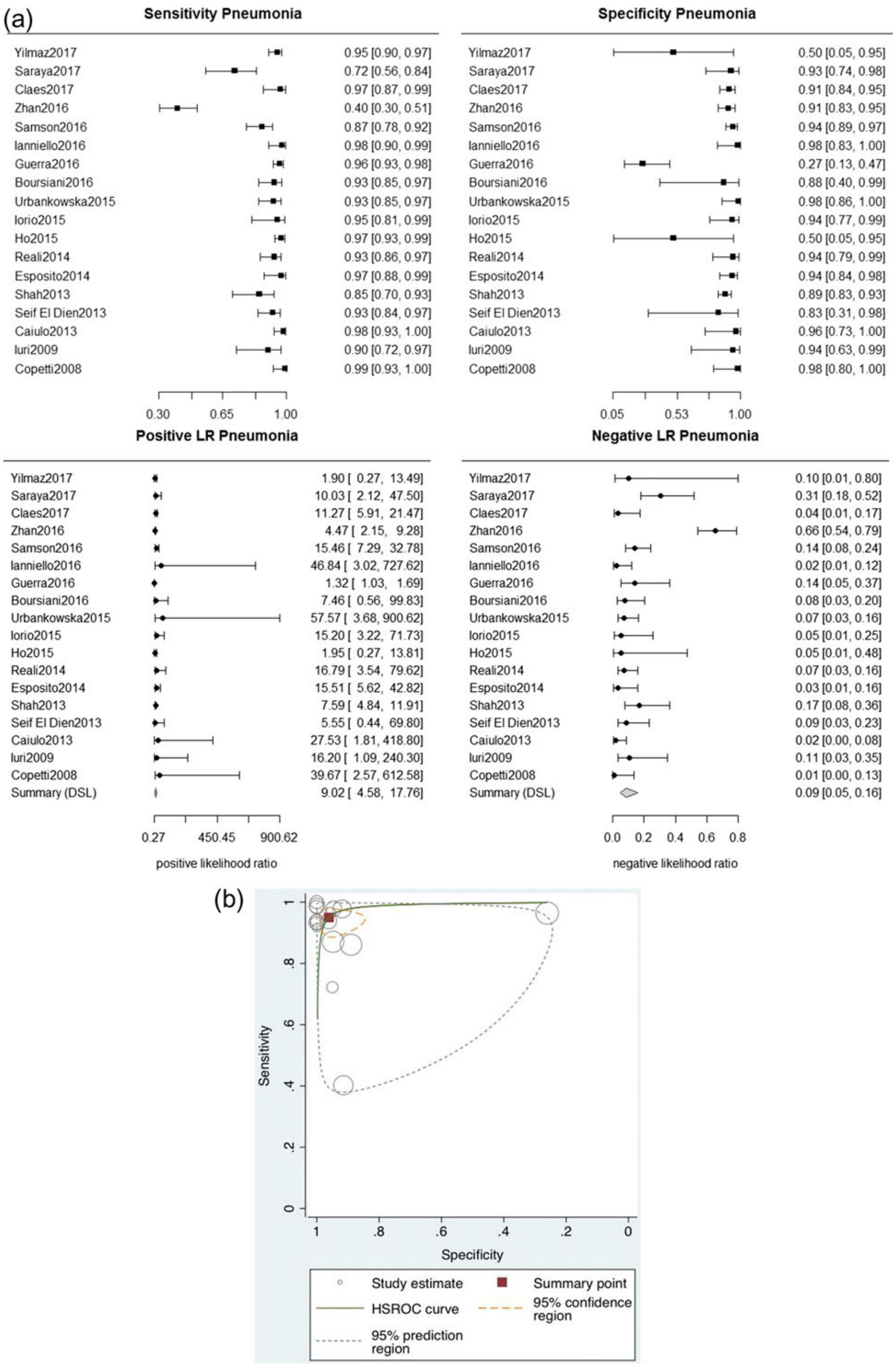

Figure 2 (a) Forest plot of sensitivity, specificity, positive LR and negative LR for chest ultrasound in children with pneumonia. (b) HSROC curve chest ultrasound for the diagnosis of childhood pneumonia. (c) Forest plot of sensitivity, specificity, positive likelihood ratio (LR) and negative LR for chest ultrasound in children with RDS. (d) Forest plot of sensitivity, specificity, positive LR and negative LR for chest ultrasound in children with pneumothorax. (e) Forest plot of sensitivity, specificity, positive LR and negative LR for chest ultrasound in children with atelectasis.

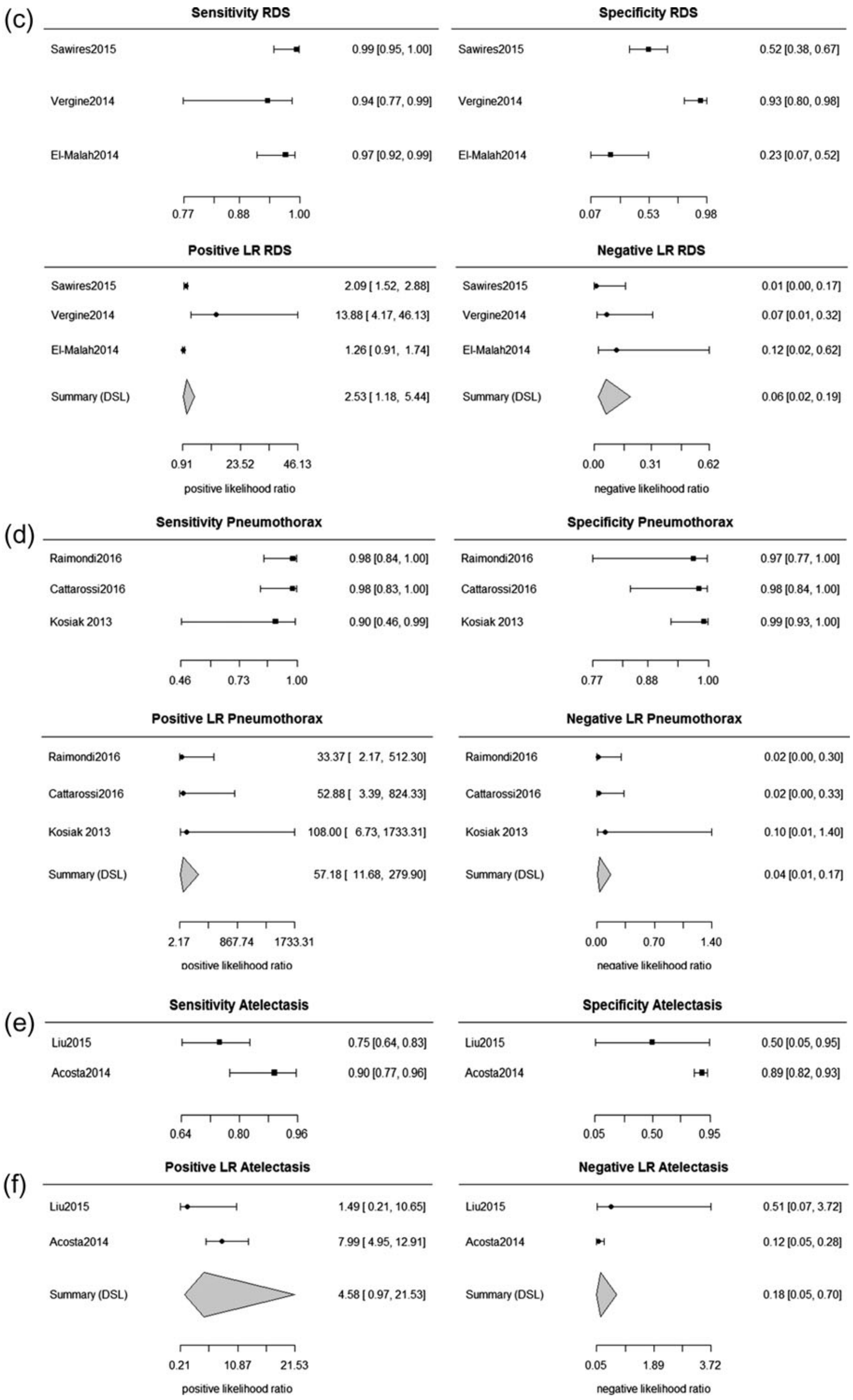

Figure 2 *Continued*

suggesting that chest ultrasound could replace chest CT to evaluate complications of pneumonia. Saraya *et al.* found a high specificity (95.0%) for the diagnosis of pneumonia when comparing chest ultrasound with chest CT, and a lower sensitivity (72.2%),[18] but the false negative cases were coded as pneumonitis and bronchiolitis on CT, which are diseases other than pneumonia, rendering those cases true negatives, so the sensitivity may be higher. Copetti and Cattarossi used chest CT in <10% ($n = 4$) of their included patients; they found that chest ultrasound correctly identified a consolidation not diagnosed by CXR in all of the four cases.[32]

Five studies (three pneumonia[10,23,28], one pneumothorax[36] and one bronchiolitis[40] study) did not use an imaging modality as the reference standard but used clinical diagnosis or confirmation by aspiration. In all five studies, the sensitivity of chest ultrasound was higher than the sensitivity of CXR (pneumonia chest ultrasound: 93.2–98.4%, CXR: 78.3–92.6%; pneumothorax chest ultrasound: 100%, CXR 96.0%; bronchiolitis chest ultrasound: 90.4%, CXR: 73.1%), the specificity was similar for both imaging modalities. Unfortunately, we could not perform a meta-analysis due to limited studies comparing the two imaging modalities.

The diagnostic accuracy of chest ultrasound performed by a radiologist (6 studies, 455 children)[9,10,12,17,18,28] or a clinician (12 studies, 1 576 children)[11,19–27,29,32] yielded similar results (sensitivity: radiologist 94.3% [95% CI 88.4–97.3%], clinician 95.3% [95%CI 88.4–98.2%]; specificity: radiologist 97.1% [95%CI 82.8–99.6%], clinician 94.0% [95%CI 81.6–98.2%]). The diagnostic accuracy was better when the operator was more experienced (13 studies, 1221 children[9,10,12,17–19,23–28,32] vs 5 studies, 810 children, on unexperienced operator[11,20–22,29]); sensitivity: experienced operator 96.4% [95%CI 93.4–98.0%], unexperienced operator 86.7% [95%CI 66.9–95.4%]; specificity: experienced operator 95.2% [95%CI 89.7–97.8%], unexperienced operator 89.3% [95% CI 61.8–97.7%]). The diagnostic accuracy was better in studies with children of a mean age over 5 years (five studies,[10,23,25,27,32] 531 children, sensitivity 98.0% [95%CI 96.0–99.0%], specificity 97.0% [95%CI 82.0– 100%]) than in studies with children with a mean age under 5 years (13 studies,[9,11,12,17–22,24,26,28,29] 1500 children, sensitivity 91.0% [95%CI 85.0–95.0%], specificity 93.0% [95%CI 84.0–98.0%]).

Nine studies reported the duration of completing chest ultrasound;[9,15,17,22,26,29,33,35,38] the mean time to complete chest ultrasound was 7.4 min (range 2–20 min). Chest ultrasound was performed quicker in neonates; mean time 3.1 min (range 2–4 min)[15,33,35] than in non-neonate children; mean time 9.6 min (range 2–20 min).[9,17,22,26,29,38]

Raimondi *et al.* compared the time between clinical decompensation and completing chest ultrasound vs CXR in neonates with a pneumothorax. Chest ultrasound was completed quicker, mean time 5.3 ± 5.6 min, then CXR, mean time 19.0 ± 11.7 min ($P < 0.001$).[37]

Discussion

This systematic review collates the evidence on the diagnostic accuracy of chest ultrasound for the diagnosis of pulmonary diseases in children; the meta-analysis was only performed for children with pneumonia due to insufficient studies on other pulmonary diseases. We found that chest ultrasound had an overall high sensitivity (95.0%) and specificity (96.1%) for the diagnosis of pneumonia in children, in line with a previous meta-analysis.[41] There is however an issue of expertise in interpreting the chest ultrasound and CXR, the chest ultrasounds are predominantly interpreted by clinicians, while the CXRs were predominantly interpreted by radiologists.

Chest ultrasound detected small consolidations not visible on CXR,[17,25,28,29] suggesting that chest ultrasound is better in detecting small consolidations than CXR. However, it remains unclear whether detection of small consolidations changes patient management. Small consolidations may be a correlate of bacterial pneumonia but these findings could also be correlated to other pulmonary diseases, like bronchiolitis or asthma.

Even though the learning curve for chest ultrasound has been reported to be steep,[42] chest ultrasound performed by an experienced operator had a better diagnostic accuracy than chest ultrasound performed by an unexperienced operator. Therefore, chest ultrasound training followed by supervised ultrasound scans should be done to ensure more reliable diagnostic outcomes. Further studies should evaluate the duration and optimal contents of training and the level of nature of ultrasound scanning supervision post-training needed, also exploring the capacity for remote supervision in the context of telemedicine applications.

The few studies[18,30,32] comparing chest ultrasound with chest CT, suggest that chest ultrasound is a valid diagnostic tool for the diagnosis of pneumonia and the complications of pneumonia. However, the number of patients included in studies published to date is low, and CT technology exposes the child to ionizing radiation therefore further studies should carefully consider the need of comparing chest ultrasound with chest CT.

The average time to perform chest ultrasound was 7.4 min, allowing for early diagnosis and treatment. Furthermore, chest ultrasound may be cost-effective especially in resource-limited settings but cost-effectiveness studies are lacking. Chest ultrasound could be performed at primary or secondary care facilities, minimizing the need for referral to tertiary care.

A limitation of this review is that the majority of the included studies focused on children with pneumonia. Only a few studies were available on RDS, pneumothorax, atelectasis, bronchiolitis or non-invasive ventilation failure; therefore, a meta-analysis on these subgroups could not be performed. Further research should focus on other pulmonary diseases than pneumonia, to evaluate if chest ultrasound is a good diagnostic tool for other pulmonary diseases in children.

Another limitation is that not all studies used the same reference standard. Most studies compared chest ultrasound directly to CXR, which is not the perfect gold standard for most pulmonary diseases. Using clinical reference as the reference standard increases the risk of bias. As said before, further studies should carefully consider comparing chest ultrasound with chest CT, to evaluate the diagnostic accuracy of chest ultrasound against a valid gold standard and to minimize overdiagnosis and overtreatment with antibiotics as a result of that.

The variability in expertise of the sonographer used in the different studies is another limitation, this could affect the comparability of the studies as well as the wide variability in healthcare professionals who interpreted the images. To address this issue, we performed a subgroup analysis on operator experience.

One pneumonia study[18] used a different ultrasound scanning protocol, did not scan the posterior chest, the rest of the pneumonia studies used the protocol earlier described by Copetti and Cattarossi.[32] This study[18] showed a lower sensitivity but this could also have been caused by the more sensitive reference test, chest CT.

The risk of bias for patient selection was high in 10 studies and unclear in 11 studies, this raises the question about the generalizability of the data. The risk of bias of the index test and reference test was low in most studies.

Most studies were conducted in high-income countries. It is peculiar that chest ultrasound studies for the diagnosis of pulmonary diseases in children in low-income countries are lacking as chest ultrasound is an easy to perform, mobile and a cheap imaging modality.

Conclusion

CXR has been the traditional imaging modality for the diagnosis of pulmonary diseases in children for years, but this systematic review shows that chest ultrasound should be considered to replace CXR as the first-line imaging modality especially in children with suspected pneumonia. Chest ultrasound has an excellent diagnostic accuracy for the diagnosis of pneumonia; and likely for pneumothorax, RDS, atelectasis, bronchiolitis and non-invasive ventilation failure. The many other advantages of ultrasound over X-ray, like no exposure to ionizing radiation, performed at the bedside by non-radiological trained clinicians, reproducibility and low-costs make chest ultrasound an even more attractive alternative for CXR. However, there is a limited number of studies evaluating chest ultrasound in pulmonary diseases other than pneumonia. Further research should focus on the diagnostic accuracy of chest ultrasound for the diagnosis of pulmonary diseases in children, especially other than pneumonia, comparing against a valid gold standard, like final diagnosis or CT or MRI chest if ethically justified. Furthermore, the optimal training of chest ultrasound, duration and content should be evaluated, cost-effectiveness studies should be conducted and the usefulness and diagnostic accuracy of chest ultrasound in low-income countries should be evaluated.

Contributors

C.H. and S.B. created the potocol, the inclusion and exclusion criteria. R.S. performed the literature search. C.H. and S.B. performed the title and abstract screening, data extraction, quality assessment and analysed the data. C.H. drafted the first version of the manuscript and created the tables. M.F. performed the data analysis and created the figures. M.G. and H.Z. coordinated the whole project. All authors worked on the final version of the manuscript.

Supplementary material

Supplementary material is available at *British Medical Bulletin* online.

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Conflict of interest statement

We declare no competing interests.

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