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Accuracy of Lung Ultrasonography in the Hands of Non-imaging Specialists to Diagnose and Assess the Severity of Community-Acquired Pneumonia in Adults: A Systematic Review

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Abbreviations

CAP: Community-acquired pneumonia
CT: Computed tomography scan
CXR: Chest X-ray
LUS: Lung ultrasonography
QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies 2

Abstract

Objectives: We aimed to systematically review the published literature regarding adults with clinical suspicion of pneumonia that compares the accuracy of lung ultrasonography (LUS) performed by non-imaging specialists to other reference standards in diagnosing and evaluating the severity of community acquired pneumonia (CAP). Moreover, we aimed to describe LUS training and the specialty of the physician performing LUS, time spent on the LUS procedure, and potential harms to patients.

Material and Methods: We searched MEDLINE, EMBASE, CINAHL, Web of Science, and Cochrane Central Register of Controlled Trials up until May 2019. We included studies that used LUS to diagnose pneumonia, but also confirmed pneumonia by other means. Publications were excluded if LUS was performed by a sonographer or radiologist (imaging specialists) or performed on other indications than suspicion of pneumonia. Two review authors screened and selected articles, extracted data and assessed quality using QUADAS-2.

Results: We included 17 studies. The sensitivity of LUS to diagnose pneumonia ranged from 0.68 to 1.00; however, in 14 studies sensitivity was ≥ 0.91. Specificities varied from 0.57 to 1.00. We found no obvious differences between studies with low and high diagnostic accuracy. The non-imaging specialists were emergency physicians, internal medicine physicians, intensivists, or "specialty not described". Five studies described LUS training, which varied from a one-hour course to fully credentialed ultrasound education.

Conclusions: LUS in the hands of non-imaging specialists physicians working clinically has high accuracy in diagnosing pneumonia in adults.

Trial registration: Prospectively registered in PROSPERO (CRD42017057804).

Strengths and limitations of this study

- This is the first systematic review to focus specifically on LUS to diagnose CAP in adults in the hands of non-imaging specialists physicians working clinically.
- We rigorously followed the Cochrane recommendations for conducting systematic literature reviews and searched five major databases using a broadly defined search string.
- We distinguished between imaging specialists defined as sonographers or radiologists and non-imaging specialist defined as physician working clinically, eventhough some physicians working clinically may have an experience with ultrasonography similar to that of an imaging specialist.

Keywords

Ultrasonography; Echography; Pneumonia, General Medicine, Primary Health Care.

Introduction

Community-acquired pneumonia (CAP) is a frequent and serious health concern, leading to increased morbidity and mortality if not detected and treated properly [1, 2]. CAP accounts for 2.5% of all patient contacts in Danish general practice [3] and globally it causes countless hospital admissions, laboratory tests, and imaging procedures [4].

Today, the typical imaging procedures for diagnosing pneumonia are computed tomography (CT) scan of the chest and chest X-ray (CXR), with CT considered the gold standard (5). However, far from all patients have these imaging procedures performed due to high radiation dose, high costs, and low availability [6].

An alternative mode of imaging is lung ultrasonography (LUS). The advantages of LUS are absence of radiation, high availability, and low cost [7]. Moreover, LUS can be performed as a bedside point-of-care test to supplement the physician's clinical examination. Numerous reviews and meta-analyses indicate that LUS has excellent accuracy for the diagnosis of pneumonia in adults [8-13]. None of the existing literature, however, differentiates between LUS operators despite the fact that LUS is a highly user-dependent examination [14]. To our knowledge, no previous review has focused solely on the accuracy of LUS in the hands of physicians working clinically.

The aim of this study was to systematically review the published literature regarding adults with clinical suspicion of pneumonia that compares the accuracy of LUS performed by physicians working clinically (non-imaging specialists) to other reference standards in diagnosing and evaluating the severity of CAP. Moreover, to describe LUS training and the specialty of the physician performing LUS, time spent on the LUS procedure, and potential harms to patients.

Methods

Data sources and search strategy

This review was prospectively registered in PROSPERO (CRD42017057804). We followed the Cochrane guideline [15] for conducting a systematic literature review, and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline for reporting the results. The literature search was conducted by a medical librarian and JJS in February 2017 and updated in May 2019. We searched the following databases: MEDLINE and EMBASE via Ovid, CINAHL via Ebsco, Web of Science, and Cochrane Central Register of Controlled Trials.

The search terms "ultrasonography" and "pneumonia" were used in combination and with thesaurus terms (e-Appendix 1). Reference lists of included articles and identified reviews were evaluated manually for further eligible studies. Patients or the public were not involved in our research. All data relevant to the study are included in the article or uploaded as supplementary information.

Eligibility and selection of studies

Studies were eligible if a full-text paper with original data was available, the paper described the use of LUS for diagnosing CAP in adults (≥ 18 years), and the diagnosis of CAP was confirmed by other means, e.g. other imaging. Hence, we included all diagnostic accuracy studies that used any reference standard other than LUS. Studies were excluded if not published in English, Danish, Norwegian, or Swedish, if LUS was performed on other indications than suspicion of pneumonia, if LUS was performed by an imaging specialist, or if the pneumonia was considered to be ventilator-associated or nosocomial. We defined an imaging specialist as a sonographer or radiologist and a non-imaging specialist as a physician working clinically.

Two review authors (JJS and PSH or MPH) independently screened the titles and abstracts of all studies identified. Any disagreements were resolved by consensus or by consulting other review authors (CAA and MBJ).

Two review authors (JJS and PSH or MPH) independently extracted data using an adapted version of the Cochrane data exaction template (e-Appendix 2). We contacted study authors when information about the physician performing the LUS was incomplete or missing, or if important data could not be derived directly from the published study.

Methodological assessment

Methodological quality of the selected studies was evaluated according to the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) [16]. Two reviewers (JJS and PSH or MPH) independently performed the assessment of methodological quality. Any disagreements were resolved by consensus or by consulting a third review author (CAA).

Results

The database search identified 7285 individual, non-duplicate articles and one potential article was identified through the reference lists (Figure 1). Twelve studies had little or no information about the physician performing LUS [17-28] and we contacted the corresponding authors of these studies. Based on additional information provided by the study authors, two studies were included [18, 27] and two studies were excluded [21, 25]. No elaboration was available for the remaining eight studies. They were thoroughly assessed and four were included, as they clearly described the scanning physicians as a non-imaging specialist physician working clinically [17, 19, 20, 22]. The remaining four studies were excluded [23, 24, 26, 28].

One study included both patients with CAP and nosocomial pneumonia [29]. However, data on the CAP subgroup was obtained by correspondence with the study authors.

In total, 17 studies describing LUS in the hands of the non-imaging specialist to diagnose CAP in adults were included [17-20, 22, 27, 29-39] (Figure 1).

Study characteristics

The studies were published between 1996 and 2019; 16 were prospective diagnostic accuracy cohort studies, and one was a retrospective study [27] (e-Table 1).

The majority of studies included patients admitted to hospital, although one multi-center study enrolled both hospitalized patients and outpatients [20] (Table 1). The studies included between 11 and 356 adult patients with a mean age from 34.0 to 84.8 years of whom between 47% and 93% were men. Two studies included only patients aged ≥ 65 years [27, 36].

The signs and symptoms of pneumonia described in the American Thoracic Society guidelines (ATS) (cough, pleuritic pain, sputum production, fever, dyspnea) were used as inclusion criteria in nine studies [19, 20, 22, 29, 31, 33-36] and six studies based inclusion on comparable, but not identical, criteria [17, 27, 30, 37-39]. The remaining two studies only included patients with respiratory complaints like cough, dyspnea, chest pain, or hemoptysis leading to a chest CT being ordered [18, 32].

The reference standard varied from CT, qualitative assessment of the final diagnosis based on clinical, laboratory, and microbiological data including CXR or chest CT results, and CXR combined with CT when LUS and CXR were discordant (Table 1).

Overall, the methodological quality of the included studies, according to QUADAS-2, was good (e-Table 2). Some studies, however, had a high risk of bias regarding flow and timing due to heterogeneity in the reference standard between patients, and high risk of bias in patient selection due to the exclusion of patients with pulmonal or cardiac comorbidities. The study populations, severity of condition (intensive care unit vs. non-intensive care unit), and the reference standard were heterogeneous across studies. As a result, the specific requirements for including results in a meta-analysis (e.g. comparable populations, LUS performer, and reference standard), were not met by the included studies, nor by a subgroup of included studies.

Diagnostic accuracy of LUS

Diagnostic accuracy is presented in Table 1. The sensitivity of LUS to diagnose CAP ranged from 0.68 to 1.00; in 14 of the 17 studies it was ≥ 0.91. The specificity could be calculated in 13 of the studies. It varied from 0.57 to 1.00, but in seven studies it was ≥ 0.94. We found no systematic differences between studies with low and high diagnostic accuracy in terms of study setting, participant training or experience, or choice of reference standard. Inter-observer agreement was reported in two studies with κ-values of 0.83 and 0.90 [32, 36].

None of the studies compared sonographic findings to clinical outcomes. Three studies assessed the severity of pneumonia in patients with either CURB-65 score [18, 22] or Pneumonia Outcome Research Team (PORT) [34], but these were not compared to LUS findings.

Bourcier et al. [30] stratified their results according to onset of symptoms of pneumonia (< 24h versus > 24h). They found that LUS (sensitivity of 0.97) was significantly more effective than CXR (sensitivity of 0.30) in diagnosing pneumonia when time from clinical onset was < 24 hours.

Specialty and training of non-imaging specialists

Information about specialty, experience, and training of physicians performing LUS is presented in Table 2. LUS was performed by emergency physicians, internal medicine physicians, and by intensivists, while four studies did not declare the specific specialty of the non-imaging specialists [17, 19, 20, 22]. Nine studies reported that physicians had previous experience with LUS or ultrasonography in general [17, 18, 20, 27, 31-34, 38]. Prior experience of performing LUS varied from one week in the emergency department to more than ten years' clinical experience.

Five studies described a LUS training program for the participating physicians [30, 31, 36-38]. Two studies provided a reference for an established educational program [31, 36], whereas the remaining studies described training specifically designed for their study [30, 37, 38]. All training programs included both theoretical and practical sessions. A large variation in the extent of the training programs was noted, ranging from a few hours at a course facility [37] to completion of a European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) [40] Level 1 qualification [36]. Four studies reported the time spent performing LUS, which was overall < 10 min.

Potential harms to patients

Twelve studies reported false positive results from LUS, and fourteen studies described false negative results (Table 3). Corradi et al. reported a high number of false negative results as they found 14 (22%) false negative hemithorax LUS examinations [18]. However, five of these were reported in patients with bilateral pneumonia, in whom LUS examination only detected pneumonia in one hemithorax. Moreover, Corradi et al. described that LUS-positive pneumonia were larger in diameter

(81 ± 55 mm) and close to the pleural line (1 ± 3 mm) [18]. Likewise, more studies described false-negative results that were mainly seen in patients with small consolidations where pneumonia did not reach the pleura [20, 22, 30, 32].

Parlamento et al. reported two incidental findings of subpleural consolidations in patients without pneumonia [34]. In both cases, LUS findings were verified by chest CT scan and confirmed to be, respectively, an atelectasis caused by a large pleural effusion, and a case of pulmonary embolism.

Discussion

To our knowledge, this is the first systematic review to focus specifically on LUS to diagnose CAP in adults in the hands of non-imaging specialists physicians working clinically. These non-imaging specialists were emergency physicians, internal medicine physicians, intensivists or unclassified physicians and obtained LUS sensitivities and specificities that were typically above 0.90. We found no overall difference in diagnostic accuracy when compared to study setting or the physicians' specialty, experience, or training. Importantly, the variation in sensivitity and specificity was found across reference standards. No study compared sonographic findings to the severity of pneumonia. Only a few studies described LUS training of the non-imaging specialists and these training programs varied from short lectures to fully accredited ultrasound education.

The diagnostic accuracy of LUS for diagnosing pneumonia described in this review is consistent with results from previous reviews that made no distinction between imaging specialists and physicians working clinically [8-13]. Recently, Orso et al. obtained a pooled sensitivity of 0.92 and a specificity of 0.93 in a review based on studies performed in emergency departments [41]. Of course, the majority of LUS operators were emergency physicians, corresponding to the non-specialists in the present review. Consequently, Orso et al. and this study have included many of the same studies. However, Orso et al. also included studies with imaging specialists and patients with "acute respiratory failure". Our review included LUS performed by non-imaging specialists from different specialties and in different settings. One study was even partly conducted in outpatient settings with non-hospitalized patients [20]. Importantly, the results of this particular study did not differ from the remaining studies. Hence, LUS might also be applied on non-hospitalized patients with suspected CAP, which supports the vision that LUS could be a useful tool for any clinician in the future [42].

Non-imaging specialists working in primary care are first in line to see patients with CAP and general practitioners have already begun using point-of-care ultrasound [43, 44]. The results by Bourcier et al. suggest that LUS is a better diagnostic tool for achieving an early diagnosis (≤ 24 hours from clinical onset) compared to CXR. The ability of LUS to accurately diagnose pneumonia early in the course of the disease may improve outcomes for patients attending primary care[44]. Furthermore, improved diagnostic performance in patients with suspected CAP may reduce the need for antibiotics. The size of pulmonary lesions might be smaller in the early stages of disease, however, and the results indicate that the usability of LUS to diagnose CAP is compromised by its inability to visualize pulmonary lesions that are not in contact with the pleura. Further evaluation of LUS in the hands of general practitioners in the diagnosis of CAP requires studies designed for this purpose.

LUS is a user-dependent examination and several guidelines [40, 45, 46] stress that diagnostic performance requires sufficient training to gain the necessary competencies. A meta-analysis by Tsou et al. found a significant difference in diagnostic accuracy between LUS performed by "advanced" versus "novice" sonographers in the diagnosis of pneumonia in children [47]. However, they defined "novice sonographers" as physicians with little or no prior LUS experience or training (≤ 7 days); most of the non-imaging specialists in the present review would be classified as "advanced sonographers" according to this definition. Today, there are no guidelines or recommendations specifying the amount of training or level of competence needed to perform LUS [48, 49]. As this review has shown, however, these competencies can be reached by the non-imaging specialist physician even after a short, tailored training program. To ensure that physicians maintain and develop skills over time and learn to incorporate LUS findings into clinical decision-making, longitudinal training elements must be incorporated into the training programs [49].

This study describes the different specialties of the non-imaging specialists and demonstrates great heterogeneity in their prior experience and training in LUS. However, sensitivities and specificities are comparable, thereby implying that LUS can be performed by physicians in various specialties, and by less experienced physicians, with comparable results to those of physicians with considerable experience in LUS.

Limitations

The aim of this study was to describe the diagnostic accuracy of LUS for diagnosing CAP when performed by physicians with considerably less ultrasound experience than imaging specialists. In four of the included studies, the speciality of the physician was not reported [17, 19, 20, 22]. These studies were included as we assessed from the clinical setting that the physicians were not radiologists or sonographers. The results from these four studies did not differ from the remaining studies. Furthermore, while some of the physicians had extensive experience with LUS [17, 18, 34], and their ultrasonography competencies may be compared to those of an imaging specialist, we did not find in general that sensitivity and specificity increased with experience. Comparison of studies was difficult due to sparse information on the non-imaging specialists' training, their experience with LUS, and the heterogeneity in the reference standards used.

Conclusions

LUS in the hands of the non-imaging specialists demonstrated high sensitivities and specificities in diagnosing pneumonia. Physicians from different specialties and less experienced physicians performed LUS with accuracies comparable to those with specialist training and high levels of LUS experience.

Author contribution

JJS is the guarantor of the study. JJS, PSH, MPH, MBJ, OG and CAA contributed to the concept, design and drafting of the study. JJS, PSH and MPH conducted the systematic search strategy and the review. All authors revised critically and approved the final manuscript.

References

1. Polverino E, Torres Marti A. Community-acquired pneumonia. Minerva Anestesiol. 2011;77(2):196-211.
2. Meehan TPT. Quality of care, process, and outcomes in elderly patients with pneumonia. JAMA : the journal of the American Medical Association. 1997;278(23):2080-4.
3. Bjerrum L. Pneumoni. Luftvejsinfektioner - diagnose og behandling. 2014;1(1):30-5.
4. Prina E. Community-acquired pneumonia. The Lancet (British edition). 2015;386(9998):1097-108.
5. Syrjälä HH. High-resolution computed tomography for the diagnosis of community-acquired pneumonia. Clinical infectious diseases. 1998;27(2):358-63.
6. Brenner DJDJ. Computed tomography--an increasing source of radiation exposure. The New England journal of medicine. 2007;357(22):2277-84.
7. Sartori S, Tombesi P. Emerging roles for transthoracic ultrasonography in pulmonary diseases. World journal of radiology. 2010;2(6):203-14.
8. Llamas-Alvarez AM, Tenza-Lozano EM, Latour-Perez J. Accuracy of Lung Ultrasonography in the Diagnosis of Pneumonia in Adults: Systematic Review and Meta-Analysis. Chest. 2017;151(2):374-82.
9. Long LL. Lung ultrasound for the diagnosis of pneumonia in adults: A meta-analysis. Medicine (Baltimore). 2017;96(3):e5713.
10. Xia Y, Ying YH, Wang SB, Li W, Shen HH. Effectiveness of lung ultrasonography for diagnosis of pneumonia in adults: a systematic review and meta-analysis. Journal of Thoracic Disease. 2016;8(10):2822-31.
11. Chavez MA, Shams N, Ellington LE, Naithani N, Gilman RH, Steinhoff MC, et al. Lung ultrasound for the diagnosis of pneumonia in adults: a systematic review and meta-analysis. Respiratory research. 2014;15:50.
12. Ye X, Xiao H, Chen B, Zhang SY. Accuracy of Lung Ultrasonography versus Chest Radiography for the Diagnosis of Adult Community-Acquired Pneumonia: Review of the Literature and Meta-Analysis. Plos One. 2015;10(6).
13. Alzahrani SA, Al-Salamah MA, Al-Madani WH, Elbarbary MA. Systematic review and meta-analysis for the use of ultrasound versus radiology in diagnosing of pneumonia. Critical ultrasound journal. 2017;9(1):6.
14. Brandli L. Benefits of protocol-driven ultrasound exams. Radiology management. 2007;29(4):56-9.
15. Deeks JJ BP, Gatsonis C (editors). Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy Version 1.0.0. The Cochrane Collaboration. 2009;Available from: http://srdta.cochrane.org/.
16. Whiting PFPF. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Annals of internal medicine. 2011;155(8):529-36.
17. Benci A, Caremani M, Menchetti D, Magnolfi A. Sonographic diagnosis of pneumonia and bronchopneumonia. European Journal of Ultrasound [Internet]. 1996; 4(3):[169-76 pp.]. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/916/CN-00168916/frame.html.
18. Corradi F, Brusasco C, Garlaschi A, Paparo F, Ball L, Santori G, et al. Quantitative analysis of lung ultrasonography for the detection of community-acquired pneumonia: A pilot study. BioMed Research International. 2015;2015:no pagination.
19. Cortellaro F, Colombo S, Coen D, Duca PG. Lung ultrasound is an accurate diagnostic tool for the diagnosis of pneumonia in the emergency department. Emergency medicine journal : EMJ. 2012;29(1):19-23.
20. Reissig A, Copetti R, Mathis G, Mempel C, Schuler A, Zechner P, et al. Lung ultrasound in the diagnosis and follow-up of community-acquired pneumonia: a prospective, multicenter, diagnostic accuracy study. Chest. 2012;142(4):965-72.

21. Nafae R, Eman SR, Mohamad NA, El-Ghamry R, Ragheb AS. Adjuvant role of lung ultrasound in the diagnosis of pneumonia in intensive care unit-patients. Egyptian Journal of Chest Diseases and Tuberculosis. 2013;62(2):281-5.
22. Fares Auf MDAA-N, M.D.; Moustafa Zedan, M.D.; Mohammad Al-Sokromi, M.Sc. Role of transthoracic ultrasound in detection of pneumonia in ICU patients. Med J Cairo Univ. 2015;83(No 1, Juni):307-14.
23. Targhetta R, Chavagneux R, Bourgeois JM, Dauzat M, Balmes P, Pourcelot L. Sonographic approach to diagnosing pulmonary consolidation. Journal of Ultrasound in Medicine. 1992;11(12):667-72.
24. Elkholy MM, Mohammad HA, Osman NM, Ibraheem B, Emam R. Accuracy of gray scale and color Doppler sonographic mapping in diagnosis of pneumonia in adult. Egyptian Journal of Chest Diseases and Tuberculosis. 2016;65(2):491-8.
25. Sperandeo M, Carnevale V, Muscarella S, Sperandeo G, Varriale A, Filabozzi P, et al. Clinical application of transthoracic ultrasonography in inpatients with pneumonia. European Journal of Clinical Investigation. 2011;41(1):1-7.
26. Alawaji OM, Yones DK, Almalki MA, Babiker RA, Awadallah MF. Value of Lung Ultrasonography for the Diagnosis of Acute Pneumonia in Emergency Department, Multicenter Study in Medina, Saudi Arabia. Indo Am J Pharm Sci. 2019;6(1):1441-50.
27. Cipollini F, Mirauta CM. Bedside lung ultrasound in the diagnosis of pneumonia in very old patients. Italian Journal of Medicine. 2018;12(2):126-30.
28. D'Amato M, Rea G, Carnevale V, Grimaldi MA, Saponara AR, Rosenthal E, et al. Assessment of thoracic ultrasound in complementary diagnosis and in follow up of community-acquired pneumonia (cap). BMC Med Imag. 2017;17(1):52.
29. Bitar ZI, Maadarani OS, El-Shably AM, Al-Ajmi MJ. Diagnostic accuracy of chest ultrasound in patients with pneumonia in the intensive care unit: A single-hospital study. Health science reports. 2019;2(1):e102.
30. Bourcier JE, Paquet J, Seinger M, Gallard E, Redonnet JP, Cheddadi F, et al. Performance comparison of lung ultrasound and chest x-ray for the diagnosis of pneumonia in the ED. American Journal of Emergency Medicine. 2014;32(2):115-8.
31. Liu XL, Lian R, Tao YK, Gu CD, Zhang GQ. Lung ultrasonography: An effective way to diagnose community-acquired pneumonia. Emergency Medicine Journal. 2015;32(6):433-8.
32. Nazerian P, Volpicelli G, Vanni S, Gigli C, Betti L, Bartolucci M, et al. Accuracy of lung ultrasound for the diagnosis of consolidations when compared to chest computed tomography. American Journal of Emergency Medicine. 2015;33(5):620-5.
33. Pagano A, Numis FG, Visone G, Pirozzi C, Masarone M, Olibet M, et al. Lung ultrasound for diagnosis of pneumonia in emergency department. Internal and emergency medicine. 2015;10(7):851-4.
34. Parlamento S, Copetti R, Di Bartolomeo S. Evaluation of lung ultrasound for the diagnosis of pneumonia in the ED. The American journal of emergency medicine. 2009;27(4):379-84.
35. Taghizadieh A, Ala A, Rahmani F, Nadi A. Diagnostic accuracy of chest x-ray and ultrasonography in detection of community acquired pneumonia; a brief report. Emergency. 2015;3(3):114-6.
36. Ticinesi A, Lauretani F, Nouvenne A, Mori G, Chiussi G, Maggio M, et al. Lung ultrasound and chest x-ray for detecting pneumonia in an acute geriatric ward. Medicine. 2016;95(27):e4153.
37. Unluer EE, Karagoz A, Senturk GO, Karaman M, Olow KH, Bayata S. Bedside lung ultrasonography for diagnosis of pneumonia. Hong Kong Journal of Emergency Medicine. 2013;20(2):98-104.
38. Amatya Y, Rupp J, Russell FM, Saunders J, Bales B, House DR. Diagnostic use of lung ultrasound compared to chest radiograph for suspected pneumonia in a resource-limited setting. International journal of emergency medicine. 2018;11(1):8.
39. Karimi E. Comparing Sensitivity of Ultrasonography and Plain Chest Radiography in Detection of Pneumonia; a Diagnostic Value Study. Archives of academic emergency medicine. 2019;7(1):e8.

40. Minimum training requirements for the practice of Medical Ultrasound in Europe. Ultraschall in der Medizin. 2010;31(4):426-7.
41. Orso D, Guglielmo N, Copetti R. Lung ultrasound in diagnosing pneumonia in the emergency department: a systematic review and meta-analysis. European journal of emergency medicine. 2018;25(5):312-21.
42. Volpicelli GG. International evidence-based recommendations for point-of-care lung ultrasound. Intensive care medicine. 2012;38(4):577-91.
43. Andersen CA, Holden S, Vela J, Rathleff MS, Jensen MB. Point-of-Care Ultrasound in General Practice: A Systematic Review. Ann Fam Med. 2019;17(1):61-9.
44. Sorensen BA-Ohoo, Hunskaar S. Point-of-care ultrasound in primary care: a systematic review of generalist performed point-of-care ultrasound in unselected populations. (2524-8987 (Electronic)).
45. Ultrasound TSoPoC. Guidelines for Point of Care Ultrasound Utilization in Clinical Practice 2017 [Available from: https://spocus.org/Practice-Guidelines.
46. Medicine IFfE. Point of Care Ultrasound Curriculum Guidelines 2014 [Available from: https://www.ifem.cc/wp-content/uploads/2016/03/IFEM-Point-of-Care-Ultrasound-Curriculum-Guidelines-2014.pdf.
47. Tsou P-Y, Chen KP, Wang Y-H, Fishe J, Gillon J, Lee C-C, et al. Diagnostic accuracy of lung ultrasound performed by novice versus advanced sonographers for pneumonia in children: A systematic review and meta-analysis. Academic emergency medicine. 2019.
48. Pietersen PI, Madsen KR, Graumann O, Konge L, Nielsen BU, Laursen CB. Lung ultrasound training: a systematic review of published literature in clinical lung ultrasound training. The Ultrasound Journal. 2018;10(1):23-.
49. Olgers TJ, Azizi N, Blans MJ, Bosch FH, Gans ROB, Ter Maaten JC. Point-of-care Ultrasound (PoCUS) for the internist in Acute Medicine: a uniform curriculum. Netherlands journal of medicine. 2019;77(5):168-76.

Tables

Table 1. Diagnostic accuracy of lung ultrasonography.

Study	Setting	Reference standard	Hours or days of LUS training	Experience in LUS or US in general	Sensitivity	Specificity
Amatya 2018 **(38)**	ED	CT	1 hour	1 week	0.91	0.61
Corradi 2015 **(18)**	ED	CT	-	> 10 yrs.[a]	0.68	0.95
Fares 2015 **(22)**	ICU	CT	-	-	0.93	0.75
Karimi 2019 **(39)**	ED	CT	-	-	0.94 (0.90-0.96)	Not calculable
Liu 2015 **(31)**	ED	CT	28 hours	> 50 scans	0.95	0.99
Nazerian 2015 **(32)**	ED	CT	-	> 1 yr.	0.83 (0.73-0.90)	0.96 (0.92-0.98)
Taghizadieh 2015 **(35)**	ED	CT	-	-	1.00 (0.95-1.00)	Not calculable
Parlamento 2009 **(34)**	ED	CXR/CT	-	> 10 yrs.	0.97	No conclusive data
Reissig 2012 **(20)**	Multicentre[b]	CXR/CT	-	> 100 scans	0.93 (0.89-0.96)	0.98 (0.89-0.96)
Unluer 2013 **(37)**	ED	CXR/CT	6 hours	-	0.96 (0.82-1.00)	(0.70-0.93)
Benci 1996 **(17)**	Department of infectious diseases	QA	-	-	1.00	1.00
Bitar 2018 **(29)**	ICU	QA	-	-	0.99[a]	0.80[a]
Bourcier 2014 **(30)**	ED	QA	2 days	-	0.95	0.57
Cipollini 2018 **(27)**	Medicine/geriatric ward	QA	-	> 1 yr.	0.82	Not calculable
Cortellaro 2012 **(19)**	ED	QA	-	-	0.99 (0.93-1.00)	0.95 (0.83-0.99)
Pagano	ED	QA	-	> 2 yrs.	0.99 (0.94-1.00)	0.65 (0.56-0.67)

2015 **(33)**						
Ticinesi 2016 **(36)**	Geriatric ward	QA	-	> 1 yr.	0.92 (0.86-0.97)	0.94

Abbreviations: LUS: Lung ultrasonography; US: Ultrasonography; ED: Emergency department; ICU: Intensive care unit; QA: Qualitative assessment; CT: Computed tomography; CXR: Chest X-ray; Yr./Yrs.: Year/Years; -: Not described.

a) Data collected by correspondence with author

b) 2 University hospitals, 7 hospitals of internal medicine, 1 hospital of pulmonary medicine, 2 practices, 2 EDs

Table 2. Specialty of non-specialists, experience and training in lung ultrasonography

Study	Number of and specialty of physicians performing LUS	Prior experience in LUS or ultrasonography in general	Description of training in LUS	Time consumption on LUS
Amatya 2018 **(38)**	Four emergency resident physicians	One week of performing LUS in the ED.	One hour lecture on LUS. Five pre-enrollment LUS scans and interpretation reviewed by expert sonographer.	7 min. 9 s. (SD 1 min 57 s.)
Corradi 2015 **(18)**	One intensivist with PhD in US[a]	More than 10 years of experience in LUS[a]	-	-
Fares 2015 **(22)**	A single physician.	-	-	-
Karimi 2019 **(39)**	Trained emergency residents under supervision of the attending emergency specialist in charge.	-	-	-
Liu 2015 **(31)**	Three emergency physicians.	At least 50 cases of LUS examination.	Twenty-eight hours course based on US emergency medicine guidelines issued by the American College of Emergency Physicians in 2001	-
Nazerian 2015 **(32)**	Four internal medicine and emergency medicine attending physicians. Four resident physicians (two internal medicine and two	Attending physicians; at least five years of experience in POC-US. Resident physicians; at least one year of training	-	-

	emergency medicine).	in emergency US.		
Taghizadieh 2015 **(35)**	One emergency specialist.	-	-	-
Parlamento 2009 **(34)**	One emergency physician.	Thirty years of experience in general and cardiac US and 10 years of training in LUS.	-	< 5 min.
Reissig 2012 **(20)**	Experienced physicians (number and specialty not described).	At least 100 chest US procedures done prior to study.	-	-
Unluer 2013 **(37)**	Three attending emergency physicians.	-	Three hours of didactic and three hours of hands-on thoracic US taught by an experienced radiology specialist to learn the diagnostic criteria of alveolar consolidation.	< 10 min.
Benci 1996 **(17)**	Physicians (number and specialty not described).	Considerable experience in US techniques.	-	-
Bitar 2018 **(29)**	Intensivist (number not described).	-	-	-
Bourcier 2014 **(30)**	Five emergency physicians.	-	Two days of theoretical formation alternating with practical ultrasounds sessions in groups of three people	-
Cipollini 2018 **(27)**	Internal medicine specialist[a]	More than one year of bedside US experience[a]	-	-
Cortellaro 2012 **(19)**	One expert operator.	-	-	< 5 min.
Pagano 2015 **(33)**	Five trained emergency physicians.	More than two years of experience in LUS.	-	-
Ticinesi 2016 **(36)**	Three internal and emergency medicine physicians.	More than one year of bedside US experience.	Level one of training completed according to the guidelines by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)	-

Abbreviations: LUS: Lung ultrasonography; US: Ultrasonography; Min.: Minutes; S: Seconds; SD: Standard deviation; POC-US: Point-of-care ultrasonography; -: Not described

a) Data collected by correspondence with author

Table 3. Potential harms to patients.

Study	True positive LUS results, n (%)	False positive LUS results, n (%)	False negative LUS results, n (%)	True negative LUS results, n (%)	Nature of false positive LUS results
Amatya 2018 **(38)**	40 (64.5)	7 (11.3)	4 (6.5)	11 (17.7)	3 bronchiectasis, 2 interstitial lung diseases, 1 tuberculosis, 1 normal lung.
Corradi 2015 **(18)**	30[a] (46.8)	1[a] (1.6)	14[a] (22.0)	19[a] (29.6)	-
Fares 2015 **(22)**	28 (73.7)	2 (5.3)	2 (5.3)	6 (15.7)	-
Karimi 2019 **(39)**	263 (93.9)	0 (0.0)	17 (6.1)	0	-
Liu 2015 **(31)**	106 (59.2)	1 (0.6)	6 (3.4)	66 (36.8)	-
Nazerian 2015 **(32)**	72 (25.3)	9 (3.1)	15 (5.3)	189 (66.3)	3 cancers, 3 parenchymal impaired ventilation not due to infection 3 pulmonary fibrosis
Taghizadieh 2015 **(35)**	29 (96.7)	1 (3.3)	0	0	-
Parlamento	31 (63.3)	0 (0.0)	1 (2.0)	17 ((34.7)	-

2009 **(34)**					
Reissig 2012 **(20)**	211 (59.3)	3 (0.8)	15 (4.2)	127 (35.7)	-
Unluer 2013 **(37)**	27 (37.5)	7 (9.7)	1 (1.4)	37 (51.4)	4 pulmonary embolisms, 3 exacerbations of COPD.
Benci 1996 **(17)**	37 (46.3)	0 (0.0)	0 (0.0)	43 (53.7)	-
Bitar 2018 **(29)**	-	-	-	-	-
Bourcier 2014 **(30)**	117 (81.2)	9 (6.3)	6 (4.2)	12 (8.3)	4 sepsis of other origin, 2 pulmonary embolisms, 1 ARDS, 1 pulmonary fibrosis, 1 acute anemia.
Cipollini 2018 **(27)**	105 (82.0)	-	23 (18.0)	-	-
Cortellaro 2012 **(19)**	80 (66.7)	2 (1.7)	1 (0.8)	37 (30.8)	1 congestive heart failure 1 subphrenic abscess with lung atelectasia.
Pagano 2015 **(33)**	67 (63.8)	13 (12.4)	1 (1.0)	24 (22.8)	7 exacerbations of COPD 2 congestive heart failure, 3 cancers, 1 pulmonary infarction.
Ticinesi 2016 **(36)**	89 (52.3)	3 (1.8)	8 (4.7)	70 (41.2)	2 pulmonary embolisms, 1 cancer

Abbreviations: LUS: Lung ultrasonography; ND: Not described; ARDS: Acute respiratory distress syndrome; COPD: Chronic obstructive pulmonary disease; n: number

a) Hemithoraxes

Figure legends

Figure 1. PRISMA flow diagram.

Abbreviations: PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; LUS: Lung ultrasonography; Yr.: Years; VAP: Ventilator-associated pneumonia; HAP: Hospital-acquired pneumonia.

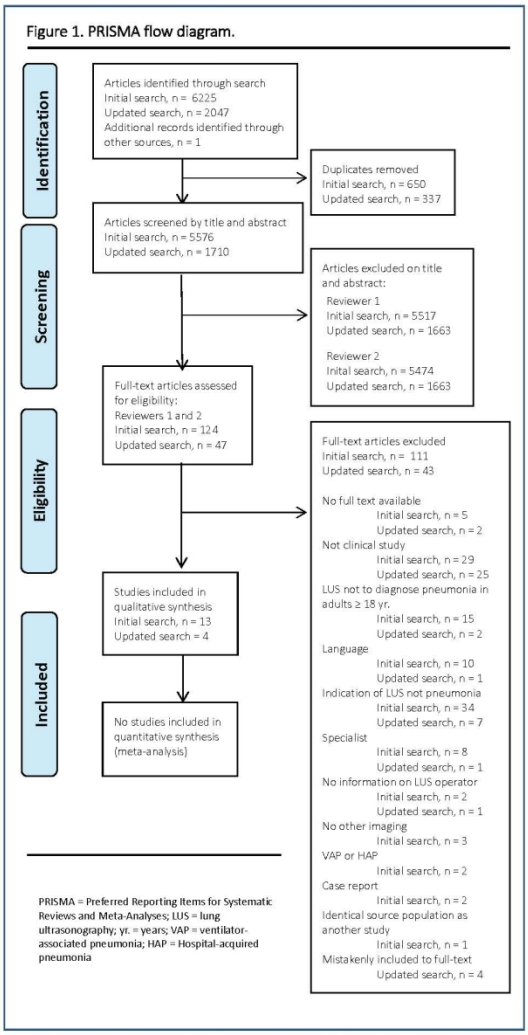

Figure 1. PRISMA flow diagram.
Abbreviations: PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; LUS: Lung ultrasonography; Yr.: Years; VAP: Ventilator-associated pneumonia; HAP: Hospital-acquired pneumonia.

215x279mm (200 x 200 DPI)

Supplemental materials for:

Strøm JJ, Haugen PS, Hansen MP, Graumann O, Jensen MB, Andersen CA.

Accuracy of Lung Ultrasonography in the Hands of Non-Specialists to Diagnose and Assess the Severity of Community-Acquired Pneumonia in Adults: A Systematic Review

e-Appendix 1. Search string.

This appendix includes a full description of the literature search conducted in MEDLINE via OVID, EMBASE via OVID, CINAHL via Ebsco, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) on August 10th 2017 and updated on May 16th 2019. The search was conducted by the principal investigator (Julie Jepsen Strøm) and a medical librarian at the medical library at Aalborg University Hospital, Aalborg, Denmark. All databases were searched from inception date until May 16 th 2019.

Database	Interface	Number of hits 08.10.2017	Number of hits 05.16.2019
EMBASE	OVID	4255	1407
MEDLINE	OVID	958	242
Cinahl	Ebsco	99	67
Web of Science		884	320
Cochrane		29	11

Embase 08.10.2017 (updated 05.16.2019)

Interface: OVID

Search: Embase via OVID

Date: 10.08.17

Database: Embase <1974 to 2017 Week 32>

Search Strategy:

---

1 exp pneumonia/ (251394)

2 ((lung or pulmon*) adj3 inflammation*).mp. (18840)

3 inflammatory lung disease*.mp. (1603)

4 lobitis.mp. (19)

5 peripneumonia*.mp. (18)

6 pleuropneumonia*.mp. (2829)

7 (pneumonic adj3 (lung or pleuri*)).mp. (170)

8 pneumonitis.mp. (21629)

9 acute chest syndrome.mp. (2070)

10 acute respiratory syndrome.mp. (9328)

11 bronchopneumonia*.mp. (8482)

12 lung infiltrate*.mp. (11288)

13 legionnaire disease*.mp. (5515)

14 pulmonary candidiasis.mp. (259)

15 or/1-14 (271290)

16 exp animal/ (23458059)

17 exp human/ (18773067)

18 16 not 17 (4684992)

19 ((doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or ultrasonograph* or ultrasound*) adj (chest or lung or thoracic)).mp. (415)

20 (chest or lung or thoracic).mp. (1664235)

21 exp echography/ (640345)

22 20 and 21 (85682)

23 19 or 22 (85829)

24 15 and 23 (4463)

25 24 not 18 (4386)

26 remove duplicates from 25 (4255)

MEDLINE 08.10.2017 (updated 05.16.2019)

Interface: OVID

Search: Medline via OVID

Date: 10.08.17

Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid MEDLINE(R) <1946 to Present>

Search Strategy:

---

1 exp pneumonia/ (85977)

2 pneumonia*.mp. (187473)

3 ((lung or pulmon*) adj3 inflammation*).mp. (12982)

4 inflammatory lung disease*.mp. (1145)

5 lobitis.mp. (20)

6 peripneumonia*.mp. (28)

7 pleuropneumonia*.mp. (3244)

8 (pneumonic adj3 (lung or pleuri*)).mp. (187)

9 pneumoniti*.mp. (12993)

10 acute chest syndrome.mp. (925)

11 acute respiratory syndrome.mp. (6465)

12 bronchopneumonia*.mp. (6283)

13 lung infiltrat*.mp. (1007)

14 legionnaire* disease*.mp. (5277)

15 pulmonary candidiasis.mp. (111)

16 or/1-15 (224155)

17 exp animal/ (21731287)

18 human/ (17207961)

19 17 not 18 (4523326)

20 (doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or ultrasonograph* or ultrasound*).mp. (447143)

21 (chest or lung or thoracic).mp. (1021945)

22 exp Ultrasonography/ (400320)

23 20 or 22 (568053)

24 21 and 23 (35801)

25 16 and 24 (1134)

26 25 not 19 (1019)

27 remove duplicates from 26 (958)

Cinahl 08.10.2017 (updated 05.16.2019)

Interface: Ebsco

Search: Cinahl

Date: 10.08.17

Interface - EBSCOhost Research Databases

Search Screen - Advanced Search

Database - CINAHL with Full Text

#	Query	Limiters/Expanders	Results
S21	S15 AND S20	Search modes - Boolean/Phrase	99

S20	S17 AND S19	Search modes - Boolean/Phrase	4,172
S19	S16 OR S18	Search modes - Boolean/Phrase	61,797
S18	(MH "Ultrasonography+")	Search modes - Boolean/Phrase	38,167
S17	(chest or lung or thoracic)	Search modes - Boolean/Phrase	79,460
S16	(doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or ultrasonograph* or ultrasound*)	Search modes - Boolean/Phrase	50,815
S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14	Search modes - Boolean/Phrase	15,379
S14	pulmonary candidiasis	Search modes - Boolean/Phrase	2
S13	legionnaire* disease*	Search modes - Boolean/Phrase	576
S12	lung infiltrat*	Search modes - Boolean/Phrase	61
S11	bronchopneumonia*	Search modes - Boolean/Phrase	98

S10	acute respiratory syndrome	Search modes - Boolean/Phrase	1,771
S9	acute chest syndrome	Search modes - Boolean/Phrase	123
S8	pneumoniti*	Search modes - Boolean/Phrase	831
S7	(pneumonic n3 (lung or pleuri*))	Search modes - Boolean/Phrase	1
S6	pleuropneumonia*	Search modes - Boolean/Phrase	3
S5	peripneumonia*.	Search modes - Boolean/Phrase	0
S4	lobitis	Search modes - Boolean/Phrase	0
S3	inflammatory lung disease*	Search modes - Boolean/Phrase	62
S2	((lung or pulmon*) n3 inflammation*)	Search modes - Boolean/Phrase	965
S1	(MH "Pneumonia+")	Search modes - Boolean/Phrase	11,441

Web of Science 08.10.2017 (updated 05.16.2019)

Interface: Ebsco

Search: Web of Science

Date: 10.08.17

Set	Results	Save History / Create Alert	Open Saved History	Edit Sets	Combine Sets AND OR	Delete Sets
# 3	884	#2 AND #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*		Edit		
# 2	340,710	TOPIC: (echograph*) *OR* TOPIC: (ultrasonograph*) *OR* TOPIC: (ultrasound*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*		Edit		
# 1	118,598	TOPIC: (pneumonia) *OR* TOPIC: (pneumonitis) *OR* TOPIC: ("acute respiratory syndrome") *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI Timespan=All years*		Edit		

Cochrane 08.10.2017 (updated 05.16.2019)

Interface: Ebsco

Search: Cochrane

Date: 10.08.17

Date Run: 10/08/17 11:42:13.790

Description:

ID	Search	Hits
#1	MeSH descriptor: [Pneumonia] explode all trees	2935
#2	"lung inflammation*":ti,ab,kw (Word variations have been searched)	123
#3	"pulmon* inflammation*":ti,ab,kw (Word variations have been searched)	135
#4	"inflammatory lung disease*":ti,ab,kw (Word variations have been searched)	27
#5	lobitis:ti,ab,kw (Word variations have been searched)	0
#6	peripneumonia*:ti,ab,kw (Word variations have been searched)	0
#7	"pneumonic lung":ti,ab,kw (Word variations have been searched)	2
#8	"pneumonic pleuri*":ti,ab,kw (Word variations have been searched)	0
#9	pneumonitis:ti,ab,kw (Word variations have been searched)	715
#10	"acute chest syndrome":ti,ab,kw (Word variations have been searched)	120
#11	"acute respiratory syndrome":ti,ab,kw (Word variations have been searched)	68
#12	"bronchopneumonia*":ti,ab,kw (Word variations have been searched)	254
#13	"lung infiltrate*":ti,ab,kw (Word variations have been searched)	109
#14	"legionnaire disease*":ti,ab,kw (Word variations have been searched)	39
#15	"pulmonary candidiasis":ti,ab,kw (Word variations have been searched)	1
#16	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15	4300
#17	doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or ultrasonograph* or ultrasound*:ti,ab,kw (Word variations have been searched)	24916
#18	MeSH descriptor: [Ultrasonography] explode all trees	12570
#19	#17 or #18	29065
#20	chest or lung or thoracic:ti,ab,kw (Word variations have been searched)	56834
#21	#19 and #20	1597
#22	#21 and #16	29

e-Appendix 2. Data extraction template.

This appendix lists the data extraction template used in this review. The template is an adapted version of the Cochrane data extraction form (1).

General information

Date extraction completed
Name of person extracting data
Report title
Year of publication
Report ID (Author name and number)
Published in
Publication type
Study funding source
Possible conflict of interest

Eligibility

Review inclusion criteria:
Published full-text paper?
Contains original data from a clinical study?
LUS to diagnose pneumonia?
LUS performed by non-specialist?
Adults (>18 yr.)?
Verification of pneumonia by other means than LUS?
Eligibility criteria met?

Type of study

Methods

Aim of study
Design
Start date
End date
Duration of participation
Ethical approval needed/obtained for study?

Participants (patients):

Clinical suspicion of CAP?
Patients > 18 yr.?
Total no. Participants (patients)
Withdrawals and exclusions
Age
Sex
Inclusion criteria (patients)
Exclusion criteria (patients)
Methods of recruitment of participants (patients)
Severity of illness
Co-morbidities
Other relevant sociodemographics
Subgroups?
Subgroups characterisation

Intervention

LUS performed to support the diagnosis of CAP
LUS scanning procedure described?
Type of ultrasonography scanner
Verification of pneumonia by what means?
Subgroup, difference in intervention

Participants (Non-specialists)

Number of physicians performing LUS
Specialty of physician performing LUS
Training in LUS
Which type of training did the non-specialist recieve?
How many hours of training did the non-specialist receive?
Which elements did the traning consist of?
Was the training assesed?
Who assesed the training?
Was there an examination/certification at the end of training?
Experience
Age
Sex
Exclusion (physicians)
Other relevant information

Setting

Country
Location: City/rural
Location: Hospital/private clinic

Outcomes

Accuracy of LUS to diagnose CAP

Diagnostic Accuracy

Accuracy compared to what?

LUS Sensitivity

Specificity

Other imaging sensitivity

LUS to asses/predict severity

Time consumption on performing LUS

Harms to patients

Overdiagnosis and overtreatment

False positives

False negatives

Incidental findings

Applicability

Have important populations been excluded from the study?

Does the study directly address the review question?

Other information

Key conclusions by author

e-Table 1. Characteristics of studies and patients.

e-Table 1. Characteristics of studies and patients.

Study	Country	Location [a]	Study design	Number of patients	Age[b]	Men/Women	Inclusion criteria[d]

Amatya 2018 (2)	Nepal	City	Prospective cohort	62	Pneumonia: 58.5 ± 13.8. No pneumonia: 61.2 ± 16.3.	29/33	SP with at least 3 of: Temp. > 38°C, history of fever, cough, dyspnea, tachypnea (RR>20), sat. < 92%.
Benci 1996 (3)	Italy	City	Prospective cohort	80	38.5	50/30	SP on the basis of fever and respiratory signs.
Bitar 2018 (4)	Kuwait	City	Prospective cohort	11	34.0	5/6	ATS + physical examination with; Temp > 38°C or < 36°C, RR > 22/min, HR > 90 bpm., audible crackles, decreased or bronchial breath sounds, dullness to percussion, or tactile fremitus.
Bourcier 2014 (5)	France	City	Prospective cohort	144	77.6 ± 15.2	72/72	SP with at least 3 of: Temp. ≥ 38°C, cough, dyspnea, HR ≥ 100 bpm., Sat. ≤ 92%
Cipollini 2018 (6)	Italy	City	Retrospective cohort	128	84.8 (78-94)	61/67	Age ≥65 years and fever and/or respiratory symptoms. Discharged with final diagnosis of pneumonia, where CXR and LUS were performed on admission.
Corradi 2015 (7)	Italy	City	Prospective cohort	32	62 ± 19	17/15	SP on basis of: Temp. ≥ 38°C or ≤ 35°C, cough, dyspnea, heart rate > 90 bpm., tachypnea (RR>20), rales or crackles on auscultation, abnormal oxygen sat.
Cortellaro 2012 (8)	Italy	City	Prospective cohort	120	69 ± 18	77/43	ATS
Fares 2015 (9)	Egypt	City	Prospective cohort	38	61 ± 11.2	20/10[c]	ATS. ICU admission on basis of CURB65 score ≥ 3. General and local physical signs suggestive of pneumonia.
Karimi 2019 (10)	Iran	City	Prospective cohort	280	56.5 ± 19.8	160/120	Clinical symptoms of pneumonia such as cough, phlegm, shortness of breath, hemoptysis, temp. ≥ 38°C.
Liu 2015 (11)	China	City	Prospective cohort	179	71.5 (36-88)	100/79	ATS
Nazerian 2015 (12)	Italy	City	Prospective cohort	285	71 ± 14	133/152	At least 1 unexplained respiratory complaint among: cough, chest pain, hemoptysis, dyspnea for which a chest CT was ordered.

Pagano 2015 (13)	Italy	ND	Prospective cohort	105	59.0	59/46	ATS or crackles or localized absence of breath sounds on lung auscultation.
Parlamento 2009 (14)	Italy	City	Prospective cohort	49	60.9 ± 21.8	31/18	ATS.
Reissig 2012 (15)	Europe	ND	Prospective cohort	356	63.8 (19-95)	228/134	ATS or typical lung auscultation findings and able to undergo CXR in two planes.
Taghizadieh 2015 (16)	East Azerbaijan, Iran	City	Prospective cohort	30	63.8 ± 18.3	28/2	ATS.
Ticinesi 2016 (17)	Italy	City	Prospective cohort	169	83.0 ± 9.2	80/89	ATS and age ≥65 years and ≥2 chronic diseases.
Unluer 2013 (18)	China	ND	Prospective cohort	72	Men: 64.2 ± 12.4 Women: 68.4 ± 11.0	35/37	SP on basis of dyspnea, including acute onset dyspnea or worsening of chronic dyspnea.

a) ND: Not described.

b) Age is expressed according to data from each study as median years ± SD OR median years (range).

c) Only stated for patients positive for pneumonia.

d) SP: Suspected pneumonia; Temp: Temperature; RR: Respiratory rate; Sat: Oxygen saturation; ATS = Signs and symptoms suggestive of pneumonia according to American Thoracic Society guidelines (cough, pleuritic pain, sputum production, fever, dyspnea); HR: Heart rate; Bpm: Beats per minute; CXR: Chest X-ray; LUS: Lung ultrasonography;

e-Table 2. QUADAS-2 quality assessment.

This e-table lists the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2). Each domain is represented in a bar with the proportion of studies considered high risk red), low risk (green), or unclear (yellow). The same applies to applicability concerns.

e-Table 2. QUADAS-2 quality assessment.							
Study	**Risk of bias**				**Concerns about applicability**		
	Patient selection	**Index test**	**Reference standard**	**Flow and timing**	**Patient selection**	**Index test**	**Reference standard**

Amatya 2018 (2)	+	+	+	+	+	+	+
Benci 1996 (3)	?	?	?	-	+	?	+
Bitar 2018 (4)	+	+	?	-	?	+	+
Bourcier 2014 (5)	+	+	?	-	+	+	+
Cipollini 2018 (6)	?	?	?	-	+	+	+
Corradi 2015 (7)	-	?	+	+	-	+	+
Cortellaro 2012 (8)	+	+	+	+	+	?	+
Fares 2015 (9)	+	?	?	-	+	?	+
Karimi 2019 (10)	-	+	+	+	+	+	+
Liu 2015 (11)	+	+	+	+	+	+	+
Nazerian 2015 (12)	-	+	+	+	-	+	+
Pagano 2015 (13)	+	+	+	?	+	+	+
Parlamento 2009	+	+	+	-	+	+	+
Reissig 2012 (15)	+	+	+	-	+	?	+
Taghizadieh 2015	-	-	+	+	+	?	+
Ticinesi 2016 (17)	-	+	+	-	+	+	+
Unluer 2013 (18)	-	+	+	-	+	+	+

References

1. Sambunjak D CM, Watts C. Module 4: Selecting studies and collecting data. *Cochrane Interactive Learning: Conducting an Intervention Review*. Oxford: Cochrane; 2017 [Available from: https://training.cochrane.org/interactivelearning/module-4-selecting-studies-and-collecting-data.
2. Amatya Y, Rupp J, Russell FM, Saunders J, Bales B, House DR. Diagnostic use of lung ultrasound compared to chest radiograph for suspected pneumonia in a resource-limited setting. *Int J Emerg Med*. 2018;11(1):8.
3. Benci A, Caremani M, Menchetti D, Magnolfi A. Sonographic diagnosis of pneumonia and bronchopneumonia. *European Journal of Ultrasound* [Internet]. 1996; 4(3):[169-76 pp.]. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/916/CN-00168916/frame.html.
4. Bitar ZI, Maadarani OS, El-Shably AM, Al-Ajmi MJ. Diagnostic accuracy of chest ultrasound in patients with pneumonia in the intensive care unit: a single-hospital study. *Health Science Reports*. 2019;2(1):e102.
5. Bourcier JE, Paquet J, Seinger M, Gallard E, Redonnet JP, Cheddadi F, et al. Performance comparison of lung ultrasound and chest x-ray for the diagnosis of pneumonia in the ED. *Am J Emerg Med*. 2014;32(2):115-8.
6. Cipollini F, Mirauta CM. Bedside lung ultrasound in the diagnosis of pneumonia in very old patients. *Italian Journal of Medicine*. 2018;12(2):126-30.

7. Corradi F, Brusasco C, Garlaschi A, Paparo F, Ball L, Santori G, et al. Quantitative analysis of lung ultrasonography for the detection of community-acquired pneumonia: a pilot study. *BioMed Research International*. 2015;2015:no pagination.
8. Cortellaro F, Colombo S, Coen D, Duca PG. Lung ultrasound is an accurate diagnostic tool for the diagnosis of pneumonia in the emergency department. *Emergency Medicine Journal*. 2012;29(1):19-23.
9. Fares Auf MDAA-N, M.D.; Moustafa Zedan, M.D.; Mohammad Al-Sokromi, M.Sc. Role of transthoracic ultrasound in detection of pneumonia in ICU patients. *Medical Journal of Cairo University*. 2015;83(No 1, Juni):307-14.
10. Karimi E. Comparing sensitivity of ultrasonography and plain chest radiography in detection of pneumonia; a diagnostic value study. *Archives of Academic Emergency Medicine*. 2019;7(1):e8.
11. Liu X-l, Lian R, Tao Y-k, Gu C-d, Zhang G-q. Lung ultrasonography: an effective way to diagnose community-acquired pneumonia. *Emergency Medicine Journal*. 2015;32(6):433-8.
12. Nazerian P, Volpicelli G, Vanni S, Gigli C, Betti L, Bartolucci M, et al. Accuracy of lung ultrasound for the diagnosis of consolidations when compared to chest computed tomography. *Am J Emerg Med*. 2015;33(5):620-5.
13. Pagano A, Numis FG, Visone G, Pirozzi C, Masarone M, Olibet M, et al. Lung ultrasound for diagnosis of pneumonia in emergency department. *Internal and Emergency Medicine*. 2015;10(7):851-4.
14. Parlamento S, Copetti R, Di Bartolomeo S. Evaluation of lung ultrasound for the diagnosis of pneumonia in the ED. *Am J Emerg Med*. 2009;27(4):379-84.
15. Reissig A, Copetti R, Mathis G, Mempel C, Schuler A, Zechner P, et al. Lung ultrasound in the diagnosis and follow-up of community-acquired pneumonia: a prospective, multicenter, diagnostic accuracy study. *Chest*. 2012;142(4):965-72.
16. Taghizadieh A, Ala A, Rahmani F, Nadi A. Diagnostic accuracy of chest x-ray and ultrasonography in detection of community acquired pneumonia; a brief report. *Emergency*. 2015;3(3):114-6.
17. Ticinesi A, Lauretani F, Nouvenne A, Mori G, Chiussi G, Maggio M, et al. Lung ultrasound and chest x-ray for detecting pneumonia in an acute geriatric ward. *Medicine*. 2016;95(27):e4153.
18. Unluer EE, Karagoz A, Senturk GO, Karaman M, Olow KH, Bayata S. Bedside lung ultrasonography for diagnosis of pneumonia. *Hong Kong Journal of Emergency Medicine*. 2013;20(2):98-104.

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Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	e-appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A

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Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	5
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	5-6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	7
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	8
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	8
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

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Accuracy of Lung Ultrasonography in the Hands of Non-imaging Specialists to Diagnose and Assess the Severity of Community-Acquired Pneumonia in Adults: A Systematic Review

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Accuracy of Lung Ultrasonography in the Hands of Non-imaging Specialists to Diagnose and Assess the Severity of Community-Acquired Pneumonia in Adults: A Systematic Review

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Abbreviations

CAP: Community-acquired pneumonia
CT: Computed tomography scan
CXR: Chest X-ray
LUS: Lung ultrasonography
QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies 2

Abstract

Objectives: We aimed to systematically review the published literature regarding adults with clinical suspicion of pneumonia that compares the accuracy of lung ultrasonography (LUS) performed by non-imaging specialists to other reference standards in diagnosing and evaluating the severity of community acquired pneumonia (CAP). Moreover, we aimed to describe LUS training and the specialty of the physician performing LUS, time spent on the LUS procedure, and potential harms to patients.

Material and Methods: We searched MEDLINE, EMBASE, CINAHL, Web of Science, and Cochrane Central Register of Controlled Trials up until May 2019. We included studies that used LUS to diagnose pneumonia, but also confirmed pneumonia by other means. Publications were excluded if LUS was performed by a sonographer or radiologist (imaging specialists) or performed on other indications than suspicion of pneumonia. Two review authors screened and selected articles, extracted data and assessed quality using QUADAS-2.

Results: We included 17 studies. The sensitivity of LUS to diagnose pneumonia ranged from 0.68 to 1.00; however, in 14 studies sensitivity was ≥ 0.91. Specificities varied from 0.57 to 1.00. We found no obvious differences between studies with low and high diagnostic accuracy. The non-imaging specialists were emergency physicians, internal medicine physicians, intensivists, or "specialty not described". Five studies described LUS training, which varied from a one-hour course to fully credentialed ultrasound education. In general, the methodological quality of studies was good, though, some studies had a high risk of bias.

Conclusions: We found significant heterogeneity across studies. In the majority of studies, LUS in the hands of the non-imaging specialists demonstrated high sensitivities and specificities in diagnosing pneumonia. However, due to problems with methodology and heterogeneity there is a need for larger studies with uniform and clearly established criteria for diagnosis and blinding.

Trial registration: Prospectively registered in PROSPERO (CRD42017057804).

Strengths and limitations of this study

- This is the first systematic review to focus specifically on LUS to diagnose CAP in adults in the hands of non-imaging specialists physicians working clinically.
- We rigorously followed the Cochrane recommendations for conducting systematic literature reviews and searched five major databases using a broadly defined search string.
- We distinguished between imaging specialists defined as sonographers or radiologists and non-imaging specialist defined as physician working clinically, eventhough some physicians working clinically may have an experience with ultrasonography similar to that of an imaging specialist.

Keywords

Ultrasonography; Echography; Pneumonia, General Medicine, Primary Health Care.

Introduction

Community-acquired pneumonia (CAP) is a frequent and serious health concern, leading to increased morbidity and mortality if not detected and treated properly [1, 2]. CAP accounts for 2.5% of all patient contacts in Danish general practice [3] and globally it causes countless hospital admissions, laboratory tests, and imaging procedures [4].

Today, the typical imaging procedures for diagnosing pneumonia are computed tomography (CT) scan of the chest and chest X-ray (CXR), with CT considered the gold standard [5]. However, far from all patients have these imaging procedures performed due to high radiation dose, high costs, and low availability [6].

An alternative mode of imaging is lung ultrasonography (LUS). The advantages of LUS are absence of radiation, high availability, and low cost [7]. Moreover, LUS can be performed as a bedside point-of-care test to supplement the physician's clinical examination. Numerous reviews and meta-analyses indicate that LUS has excellent accuracy for the diagnosis of pneumonia in adults [8-13]. None of the existing literature, however, differentiates between LUS operators despite the fact that ultrasound generally is considered a highly user-dependent imaging modality[14]. To our knowledge, no previous review has focused solely on the accuracy of LUS in the hands of physicians working clinically.

The aim of this study was to systematically review the published literature regarding adults with clinical suspicion of pneumonia that compares the accuracy of LUS performed by physicians working clinically (non-imaging specialists) to other reference standards in diagnosing and evaluating the severity of CAP. Moreover, to describe LUS training and the specialty of the physician performing LUS, time spent on the LUS procedure, and potential harms to patients.

Methods

Data sources and search strategy

This review was prospectively registered in PROSPERO (CRD42017057804). We followed the Cochrane guideline [15] for conducting a systematic literature review, and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline for reporting the results. The literature search was conducted by a medical librarian and JJS in February 2017 and updated in May 2019. We searched the following databases: MEDLINE and EMBASE via Ovid, CINAHL via Ebsco, Web of Science, and Cochrane Central Register of Controlled Trials.

The search terms "ultrasonography" and "pneumonia" were used in combination and with thesaurus terms (e-Appendix 1). Reference lists of included articles and identified reviews were evaluated manually for further eligible studies. Patients or the public were not involved in our research. All data relevant to the study are included in the article or uploaded as supplementary information.

Eligibility and selection of studies

Studies were eligible if a full-text paper with original data was available, the paper described the use of LUS for diagnosing CAP in adults (≥ 18 years), and the diagnosis of CAP was confirmed by other means, e.g. other imaging. Hence, we included all diagnostic accuracy studies that used any reference standard other than LUS. Studies were excluded if not published in English, Danish, Norwegian, or Swedish, if LUS was performed on other indications than suspicion of pneumonia, if LUS was performed by an imaging specialist, or if the pneumonia was considered to be ventilator-associated or nosocomial. We defined an imaging specialist as a sonographer or radiologist and a non-imaging specialist as a physician working clinically.

Two review authors (JJS and PSH or MPH) independently screened the titles and abstracts of all studies identified. Any disagreements were resolved by consensus or by consulting other review authors (CAA and MBJ).

Two review authors (JJS and PSH or MPH) independently extracted data using an adapted version of the Cochrane data exaction template (e-Appendix 2). We contacted study authors when information about the physician performing the LUS was incomplete or missing, or if important data could not be derived directly from the published study.

Methodological assessment

Methodological quality of the selected studies was evaluated according to the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) [16]. Two reviewers (JJS and PSH or MPH) independently performed the assessment of methodological quality. Any disagreements were resolved by consensus or by consulting a third review author (CAA).

Patient and Public Involvement

No patient involved.

Results

The database search identified 7285 individual, non-duplicate articles and one potential article was identified through the reference lists (Figure 1). Twelve studies had little or no information about the physician performing LUS [17-28] and we contacted the corresponding authors of these studies. Based on additional information provided by the study authors, two studies were included [18, 27] and two studies were excluded [21, 25]. No elaboration was available for the remaining eight studies. They were thoroughly assessed and four were included, as they clearly described the scanning physicians as a non-imaging specialist physician working clinically [17, 19, 20, 22]. The remaining four studies were excluded [23, 24, 26, 28].

One study included both patients with CAP and nosocomial pneumonia [29]. However, data on the CAP subgroup was obtained by correspondence with the study authors.

In total, 17 studies describing LUS in the hands of the non-imaging specialist to diagnose CAP in adults were included [17-20, 22, 27, 29-39] (Figure 1).

Study characteristics

The studies were published between 1996 and 2019; 16 were prospective diagnostic accuracy cohort studies, and one was a retrospective study [27] (e-Table 1).

The majority of studies included patients admitted to hospital, although one multi-center study enrolled both hospitalized patients and outpatients [20] (Table 1). The studies included between 11 and 356 adult patients with a mean age from 34.0 to 84.8 years of whom between 47% and 93% were men. Two studies included only patients aged ≥ 65 years [27, 36].

The signs and symptoms of pneumonia described in the American Thoracic Society guidelines (ATS) (cough, pleuritic pain, sputum production, fever, dyspnea) were used as inclusion criteria in nine studies [19, 20, 22, 29, 31, 33-36] and six studies based inclusion on comparable, but not identical, criteria [17, 27, 30, 37-39]. The remaining two studies only included patients with respiratory complaints like cough, dyspnea, chest pain, or hemoptysis leading to a chest CT being ordered [18, 32].

Definition of pneumonia based on LUS varied across studies. Still, presence of subpleural or alveolar consolidation or a tissue-like lesion was part of the definition in all studies except one, in which no definition was described[35]. The physicians performing and interpreting LUS were generally blinded to the reference standard; however, in four studies this matter was unclear [17, 22, 27, 35]. The definitions of pneumonia, blinding, scanning procedure and characteristics of LUS are listed in e-Table 2. The reference standard varied from CT, qualitative assessment of the final diagnosis based on clinical, laboratory, and microbiological data including CXR or chest CT results, and CXR combined with CT when LUS and CXR were discordant (Table 1).

Overall, the methodological quality of the included studies, according to QUADAS-2, was good (e-Table 3). Some studies, however, had a high risk of bias regarding flow and timing due to heterogeneity in the reference standard between patients, and high risk of bias in patient selection due to the exclusion of patients with pulmonal or cardiac comorbidities. The study populations, severity of condition (intensive care unit vs. non-intensive care unit), and the reference standard were heterogeneous across studies. As a result, the specific requirements for including results in a meta-

analysis (e.g. comparable populations, LUS performer, and reference standard), were not met by the included studies, nor by a subgroup of included studies.

Diagnostic accuracy of LUS

Diagnostic accuracy is presented in Table 1. The sensitivity of LUS to diagnose CAP ranged from 0.68 (95% CI, 0.52-0.81) to 1.00 (95% CI, 0.95-1.00); in 14 of the 17 studies it was ≥ 0.91. The specificity could be calculated in 13 of the studies. It varied from 0.57 (95% CI, 0.34-0.78) to 1.00 (95% CI, 0.92-1.00), but in seven studies it was ≥ 0.94. We found no systematic differences between studies with low and high diagnostic accuracy in terms of study setting, participant training or experience, or choice of reference standard. Inter-observer agreement was reported in two studies with κ-values of 0.83 and 0.90 [32, 36].

The studies by Liu et al. and Amatya et al. were the two studies of highest methodological quality (e-Table 3). Both studies compared LUS to CT (Table 1) and LUS was performed by emergency physicians whose prior experience and training was described (Table 2). However, they differed with regards to procedure and characteristics of LUS in terms of areas examined and definition of pneumonia on LUS (e-Table 2). They found sensitivities of respectively 0.95 (95% CI, 0.89-0.98) and 0.91 (95% CI, 0.78-0.98) and specificities of 0.99 (95% CI, 0.92-1.00) and 0.61 (95% CI, 0.36-0.83).

None of the studies compared sonographic findings to clinical outcomes. Three studies assessed the severity of pneumonia in patients with either CURB-65 score [18, 22] or Pneumonia Outcome Research Team (PORT) [34], but these were not compared to LUS findings.

Bourcier et al. [30] stratified their results according to onset of symptoms of pneumonia (< 24h versus > 24h). They found that LUS (sensitivity of 0.97) was significantly more effective than CXR (sensitivity of 0.30) in diagnosing pneumonia when time from clinical onset was < 24 hours.

Specialty and training of non-imaging specialists

Information about specialty, experience, and training of physicians performing LUS is presented in Table 2. LUS was performed by emergency physicians, internal medicine physicians, and by intensivists, while four studies did not declare the specific specialty of the non-imaging specialists [17, 19, 20, 22]. Nine studies reported that physicians had previous experience with LUS or ultrasonography in general [17, 18, 20, 27, 31-34, 38]. Prior experience of performing LUS varied from one week in the emergency department to more than ten years' clinical experience.

Five studies described a LUS training program for the participating physicians [30, 31, 36-38]. Two studies provided a reference for an established educational program [31, 36], whereas the remaining studies described training specifically designed for their study [30, 37, 38]. All training programs included both theoretical and practical sessions. A large variation in the extent of the training programs was noted, ranging from a few hours at a course facility [37] to completion of a European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) [14] Level 1 qualification [36]. Four studies reported the time spent performing LUS, which was overall < 10 min.

Potential harms to patients

Twelve studies reported false positive results from LUS, and fourteen studies described false negative results (Table 3). Corradi et al. reported a high number of false negative results as they found 14 (22%) false negative hemithorax LUS examinations [18]. However, five of these were reported in patients with bilateral pneumonia, in whom LUS examination only detected pneumonia in one hemithorax. Moreover, Corradi et al. described that LUS-positive pneumonia were larger in diameter (81 ± 55 mm) and close to the pleural line (1 ± 3 mm) [18]. Likewise, more studies described false-negative results that were mainly seen in patients with small consolidations where pneumonia did not reach the pleura [20, 22, 30, 32].

Parlamento et al. reported two incidental findings of subpleural consolidations in patients without pneumonia [34]. In both cases, LUS findings were verified by chest CT scan and confirmed to be, respectively, an atelectasis caused by a large pleural effusion, and a case of pulmonary embolism.

Discussion

To our knowledge, this is the first systematic review to focus specifically on LUS to diagnose CAP in adults in the hands of non-imaging specialists physicians working clinically. These non-imaging specialists were emergency physicians, internal medicine physicians, intensivists or unclassified physicians and obtained LUS sensitivities and specificities that were typically above 0.90. We found no overall difference in diagnostic accuracy when compared to study setting or the physicians' specialty, experience, or training. Importantly, the variation in sensivitity and specificity was found across reference standards. No study compared sonographic findings to the severity of pneumonia. Only a few studies described LUS training of the non-imaging specialists and these training programs varied from short lectures to fully accredited ultrasound education.

We highlighted the results of Liu et al. and Amatya et al. due to the quality of the studies, still, the studies were not completely comparable in other parameters. Both studies found high and comparable sensitivities of 0.95 (95% CI, 0.89-0.98) and 0.91 (95% CI, 0.78-0.98) respectively. However, in Amatya et al., LUS specificity was 0.61 (95% CI, 0.36-0.83) and significantly lower than the specificity in Liu et al. of 0.99 (95% CI, 0.92-1.00). According to Amatya et al., this was due to a higher prevalence of pulmonal co-morbidities which resulted in false positive LUS results. Low specificity may lead to over-diagnosis of pneumonia and inappropriate use of antibiotics.

The diagnostic accuracy of LUS for diagnosing pneumonia described in this review is consistent with results from previous reviews that made no distinction between imaging specialists and physicians working clinically [8-13]. Recently, Orso et al. obtained a pooled sensitivity of 0.92 and a specificity of 0.93 in a review based on studies performed in emergency departments [40]. Of course, the majority of LUS operators were emergency physicians, corresponding to the non-specialists in the present review. Consequently, Orso et al. and this study have included many of the same studies. However, Orso et al. also included studies with imaging specialists and patients with "acute respiratory failure". Our review included LUS performed by non-imaging specialists from different

specialties and in different settings. One study was even partly conducted in outpatient settings with non-hospitalized patients [20]. Importantly, the results of this particular study did not differ from the remaining studies. Hence, LUS might also be applied on non-hospitalized patients with suspected CAP, which supports the vision that LUS could be a useful tool for any clinician in the future [41].
Non-imaging specialists working in primary care are first in line to see patients with CAP and general practitioners have already begun using point-of-care ultrasound [42, 43]. The results by Bourcier et al. suggest that LUS is a better diagnostic tool for achieving an early diagnosis (≤ 24 hours from clinical onset) compared to CXR. The ability of LUS to accurately diagnose pneumonia early in the course of the disease may improve outcomes for patients attending primary care [43]. Furthermore, improved diagnostic performance in patients with suspected CAP may reduce the need for antibiotics. Though, the size of pulmonary lesions might be smaller in the early stages of disease and the results indicate that the usability of LUS to diagnose CAP is compromised by its inability to visualize pulmonary lesions that are not in contact with the pleura. However, according to Lichtenstein et al. who looked for lung consolidation in intensive care patients, this occurred in only 1.5% cases of lung consolidation[44]. Due to a lower prevalence and less severe disease in a general practice population, further evaluation of LUS for the diagnosis of CAP in general practice is required.
LUS is a user-dependent examination and several guidelines [14, 45, 46] stress that diagnostic performance requires sufficient training to gain the necessary competencies. A meta-analysis by Tsou et al. found a significant difference in diagnostic accuracy between LUS performed by "advanced" versus "novice" sonographers in the diagnosis of pneumonia in children [47]. However, they defined "novice sonographers" as physicians with little or no prior LUS experience or training (≤ 7 days); most of the non-imaging specialists in the present review would be classified as "advanced sonographers" according to this definition. Though, the learning curve appears steep from pediatric data and in a randomized controlled trial by Jones et al. [48] they found that substitution of CXR with LUS when evaluating children suspected of having pneumonia was feasible and safe, also in the hands of novice sonographers (≤ 25 examinations). Today, there are no guidelines or recommendations specifying the amount of training or level of competence needed to perform LUS [49, 50]. As this review has shown, however, these competencies can be reached by the non-imaging specialist physician even after a short, tailored training program. To ensure that physicians maintain and develop skills over time and learn to incorporate LUS findings into clinical decision-making, longitudinal training elements must be incorporated into the training programs [50].
This study describes the different specialties of the non-imaging specialists and demonstrates great heterogeneity in their prior experience and training in LUS. However, sensitivities and specificities are comparable, thereby implying that LUS can be performed by physicians in various specialties, and by less experienced physicians, with comparable results to those of physicians with considerable experience in LUS.

Limitations

The aim of this study was to describe the diagnostic accuracy of LUS for diagnosing CAP when performed by physicians with considerably less ultrasound experience than imaging specialists. In four of the included studies, the speciality of the physician was not reported [17, 19, 20, 22]. These studies

were included as we assessed from the clinical setting that the physicians were not radiologists or sonographers. The results from these four studies did not differ from the remaining studies. Furthermore, while some of the physicians had extensive experience with LUS [17, 18, 34], and their ultrasonography competencies may be compared to those of an imaging specialist, we did not find in general that sensitivity and specificity increased with experience. Comparison of studies was difficult due to sparse information on the non-imaging specialists' training, their experience with LUS, and the heterogeneity in the reference standards used. Due to the significant heterogeneity across studies, it was not possible to pool data and perform a meta-analyses.

Conclusions

We found significant heterogeneity across studies. In the majority of studies, LUS in the hands of the non-imaging specialists demonstrated high sensitivities and specificities in diagnosing pneumonia. However, due to problems with methodology and heterogeneity there is a need for larger studies with uniform and clearly established criteria for diagnosis and blinding.

Author contribution

JJS is the guarantor of the study. JJS, PSH, MPH, MBJ, OG and CAA contributed to the concept, design and drafting of the study. JJS, PSH and MPH conducted the systematic search strategy and the review. All authors revised critically and approved the final manuscript.

Data availability statement

Data extraction is available upon reasonable request.

References

1. Polverino E, Torres Marti A. Community-acquired pneumonia. Minerva Anestesiol. 2011;77(2):196-211.
2. Meehan TPT. Quality of care, process, and outcomes in elderly patients with pneumonia. JAMA : the journal of the American Medical Association. 1997;278(23):2080-4.
3. Bjerrum L. Pneumoni. Luftvejsinfektioner - diagnose og behandling. 2014;1(1):30-5.
4. Prina E. Community-acquired pneumonia. The Lancet (British edition). 2015;386(9998):1097-108.
5. Syrjälä HH. High-resolution computed tomography for the diagnosis of community-acquired pneumonia. Clinical infectious diseases. 1998;27(2):358-63.
6. Brenner DJDJ. Computed tomography--an increasing source of radiation exposure. The New England journal of medicine. 2007;357(22):2277-84.
7. Sartori S, Tombesi P. Emerging roles for transthoracic ultrasonography in pulmonary diseases. World journal of radiology. 2010;2(6):203-14.
8. Llamas-Alvarez AM, Tenza-Lozano EM, Latour-Perez J. Accuracy of Lung Ultrasonography in the Diagnosis of Pneumonia in Adults: Systematic Review and Meta-Analysis. Chest. 2017;151(2):374-82.
9. Long LL. Lung ultrasound for the diagnosis of pneumonia in adults: A meta-analysis. Medicine (Baltimore). 2017;96(3):e5713.
10. Xia Y, Ying YH, Wang SB, Li W, Shen HH. Effectiveness of lung ultrasonography for diagnosis of pneumonia in adults: a systematic review and meta-analysis. Journal of Thoracic Disease. 2016;8(10):2822-31.
11. Chavez MA, Shams N, Ellington LE, Naithani N, Gilman RH, Steinhoff MC, et al. Lung ultrasound for the diagnosis of pneumonia in adults: a systematic review and meta-analysis. Respiratory research. 2014;15:50.
12. Ye X, Xiao H, Chen B, Zhang SY. Accuracy of Lung Ultrasonography versus Chest Radiography for the Diagnosis of Adult Community-Acquired Pneumonia: Review of the Literature and Meta-Analysis. Plos One. 2015;10(6).
13. Alzahrani SA, Al-Salamah MA, Al-Madani WH, Elbarbary MA. Systematic review and meta-analysis for the use of ultrasound versus radiology in diagnosing of pneumonia. Critical ultrasound journal. 2017;9(1):6.
14. Minimum training requirements for the practice of Medical Ultrasound in Europe. Ultraschall in der Medizin. 2010;31(4):426-7.
15. Deeks JJ BP, Gatsonis C (editors). Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy Version 1.0.0. The Cochrane Collaboration. 2009;Available from: http://srdta.cochrane.org/.
16. Whiting PFPF. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Annals of internal medicine. 2011;155(8):529-36.
17. Benci A, Caremani M, Menchetti D, Magnolfi A. Sonographic diagnosis of pneumonia and bronchopneumonia. European Journal of Ultrasound [Internet]. 1996; 4(3):[169-76 pp.]. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/916/CN-00168916/frame.html.
18. Corradi F, Brusasco C, Garlaschi A, Paparo F, Ball L, Santori G, et al. Quantitative analysis of lung ultrasonography for the detection of community-acquired pneumonia: A pilot study. BioMed Research International. 2015;2015:no pagination.
19. Cortellaro F, Colombo S, Coen D, Duca PG. Lung ultrasound is an accurate diagnostic tool for the diagnosis of pneumonia in the emergency department. Emergency medicine journal : EMJ. 2012;29(1):19-23.
20. Reissig A, Copetti R, Mathis G, Mempel C, Schuler A, Zechner P, et al. Lung ultrasound in the diagnosis and follow-up of community-acquired pneumonia: a prospective, multicenter, diagnostic accuracy study. Chest. 2012;142(4):965-72.

21. Nafae R, Eman SR, Mohamad NA, El-Ghamry R, Ragheb AS. Adjuvant role of lung ultrasound in the diagnosis of pneumonia in intensive care unit-patients. Egyptian Journal of Chest Diseases and Tuberculosis. 2013;62(2):281-5.
22. Fares Auf MDAA-N, M.D.; Moustafa Zedan, M.D.; Mohammad Al-Sokromi, M.Sc. Role of transthoracic ultrasound in detection of pneumonia in ICU patients. Med J Cairo Univ. 2015;83(No 1, Juni):307-14.
23. Targhetta R, Chavagneux R, Bourgeois JM, Dauzat M, Balmes P, Pourcelot L. Sonographic approach to diagnosing pulmonary consolidation. Journal of Ultrasound in Medicine. 1992;11(12):667-72.
24. Elkholy MM, Mohammad HA, Osman NM, Ibraheem B, Emam R. Accuracy of gray scale and color Doppler sonographic mapping in diagnosis of pneumonia in adult. Egyptian Journal of Chest Diseases and Tuberculosis. 2016;65(2):491-8.
25. Sperandeo M, Carnevale V, Muscarella S, Sperandeo G, Varriale A, Filabozzi P, et al. Clinical application of transthoracic ultrasonography in inpatients with pneumonia. European Journal of Clinical Investigation. 2011;41(1):1-7.
26. Alawaji OM, Yones DK, Almalki MA, Babiker RA, Awadallah MF. Value of Lung Ultrasonography for the Diagnosis of Acute Pneumonia in Emergency Department, Multicenter Study in Medina, Saudi Arabia. Indo Am J Pharm Sci. 2019;6(1):1441-50.
27. Cipollini F, Mirauta CM. Bedside lung ultrasound in the diagnosis of pneumonia in very old patients. Italian Journal of Medicine. 2018;12(2):126-30.
28. D'Amato M, Rea G, Carnevale V, Grimaldi MA, Saponara AR, Rosenthal E, et al. Assessment of thoracic ultrasound in complementary diagnosis and in follow up of community-acquired pneumonia (cap). BMC Med Imag. 2017;17(1):52.
29. Bitar ZI, Maadarani OS, El-Shably AM, Al-Ajmi MJ. Diagnostic accuracy of chest ultrasound in patients with pneumonia in the intensive care unit: A single-hospital study. Health science reports. 2019;2(1):e102.
30. Bourcier JE, Paquet J, Seinger M, Gallard E, Redonnet JP, Cheddadi F, et al. Performance comparison of lung ultrasound and chest x-ray for the diagnosis of pneumonia in the ED. American Journal of Emergency Medicine. 2014;32(2):115-8.
31. Liu XL, Lian R, Tao YK, Gu CD, Zhang GQ. Lung ultrasonography: An effective way to diagnose community-acquired pneumonia. Emergency Medicine Journal. 2015;32(6):433-8.
32. Nazerian P, Volpicelli G, Vanni S, Gigli C, Betti L, Bartolucci M, et al. Accuracy of lung ultrasound for the diagnosis of consolidations when compared to chest computed tomography. American Journal of Emergency Medicine. 2015;33(5):620-5.
33. Pagano A, Numis FG, Visone G, Pirozzi C, Masarone M, Olibet M, et al. Lung ultrasound for diagnosis of pneumonia in emergency department. Internal and emergency medicine. 2015;10(7):851-4.
34. Parlamento S, Copetti R, Di Bartolomeo S. Evaluation of lung ultrasound for the diagnosis of pneumonia in the ED. The American journal of emergency medicine. 2009;27(4):379-84.
35. Taghizadieh A, Ala A, Rahmani F, Nadi A. Diagnostic accuracy of chest x-ray and ultrasonography in detection of community acquired pneumonia; a brief report. Emergency. 2015;3(3):114-6.
36. Ticinesi A, Lauretani F, Nouvenne A, Mori G, Chiussi G, Maggio M, et al. Lung ultrasound and chest x-ray for detecting pneumonia in an acute geriatric ward. Medicine. 2016;95(27):e4153.
37. Unluer EE, Karagoz A, Senturk GO, Karaman M, Olow KH, Bayata S. Bedside lung ultrasonography for diagnosis of pneumonia. Hong Kong Journal of Emergency Medicine. 2013;20(2):98-104.
38. Amatya Y, Rupp J, Russell FM, Saunders J, Bales B, House DR. Diagnostic use of lung ultrasound compared to chest radiograph for suspected pneumonia in a resource-limited setting. International journal of emergency medicine. 2018;11(1):8.
39. Karimi E. Comparing Sensitivity of Ultrasonography and Plain Chest Radiography in Detection of Pneumonia; a Diagnostic Value Study. Archives of academic emergency medicine. 2019;7(1):e8.

40. Orso D, Guglielmo N, Copetti R. Lung ultrasound in diagnosing pneumonia in the emergency department: a systematic review and meta-analysis. European journal of emergency medicine. 2018;25(5):312-21.
41. Volpicelli GG. International evidence-based recommendations for point-of-care lung ultrasound. Intensive care medicine. 2012;38(4):577-91.
42. Andersen CA, Holden S, Vela J, Rathleff MS, Jensen MB. Point-of-Care Ultrasound in General Practice: A Systematic Review. Ann Fam Med. 2019;17(1):61-9.
43. Sorensen BA-Ohoo, Hunskaar S. Point-of-care ultrasound in primary care: a systematic review of generalist performed point-of-care ultrasound in unselected populations. (2524-8987 (Electronic)).
44. Lichtenstein DA, Lascols N, Meziere G, Gepner A. Ultrasound diagnosis of alveolar consolidation in the critically ill. Intensive Care Medicine. 2004;30(2):276-81.
45. Ultrasound TSoPoC. Guidelines for Point of Care Ultrasound Utilization in Clinical Practice 2017 [Available from: https://spocus.org/Practice-Guidelines.
46. Medicine IFfE. Point of Care Ultrasound Curriculum Guidelines 2014 [Available from: https://www.ifem.cc/wp-content/uploads/2016/03/IFEM-Point-of-Care-Ultrasound-Curriculum-Guidelines-2014.pdf.
47. Tsou P-Y, Chen KP, Wang Y-H, Fishe J, Gillon J, Lee C-C, et al. Diagnostic accuracy of lung ultrasound performed by novice versus advanced sonographers for pneumonia in children: A systematic review and meta-analysis. Academic emergency medicine. 2019.
48. Jones BP, Tay ET, Elikashvili I, Sanders JE, Paul AZ, Nelson BP, et al. Feasibility and Safety of Substituting Lung Ultrasonography for Chest Radiography When Diagnosing Pneumonia in Children: A Randomized Controlled Trial. Chest. 2016;150(1):131-8.
49. Pietersen PI, Madsen KR, Graumann O, Konge L, Nielsen BU, Laursen CB. Lung ultrasound training: a systematic review of published literature in clinical lung ultrasound training. The Ultrasound Journal. 2018;10(1):23-.
50. Olgers TJ, Azizi N, Blans MJ, Bosch FH, Gans ROB, Ter Maaten JC. Point-of-care Ultrasound (PoCUS) for the internist in Acute Medicine: a uniform curriculum. Netherlands journal of medicine. 2019;77(5):168-76.

Tables

Table 1. Diagnostic accuracy of lung ultrasonography.

Study	Setting	Reference standard	Hours or days of LUS training	Experience in LUS or US in general	Pneumonia positive (n) / Total number of patients examined for pneumonia (N)	Sensitivity (95% CI)	Specificity (95% CI)
Amatya 2018 **(38)**	ED	CT	1 hour	1 week	44/62	0.91 (0.78-0.98)[d]	0.61 (0.36-0.83)[d]
Corradi 2015 **(18)**	ED	CT	-	> 10 yrs.[a]	44[b]/62[b]	0.68 (0.52-0.81)[d]	0.95 (0.75-1.00)[d]
Fares 2015 **(22)**	ICU	CT	-	-	30/38	0.93 (0.78-0.99)[d]	0.75 (0.35-0.97)[d]
Karimi 2019 **(39)**	ED	CT	-	-	280/280	0.94 (0.90-0.96)	Not calculable
Liu 2015 **(31)**	ED	CT	28 hours	> 50 scans	112/179	0.95 (0.89-0.98)[d]	0.99 (0.92-1.00)[d]
Nazerian 2015 **(32)**	ED	CT	-	> 1 yr.	87/285	0.83 (0.73-0.90)	0.96 (0.92-0.98)
Taghizadieh 2015 **(35)**	ED	CT	-	-	29/30	1.00 (0.95-1.00)	Not calculable
Parlamento 2009 **(34)**	ED	CXR/CT	-	> 10 yrs.	32/49	0.97 (0.84-1.00)[d]	No conclusive data
Reissig 2012 **(20)**	Multicentre[c]	CXR/CT	-	> 100 scans	226/356	0.93 (0.89-0.96)	0.98 (0.89-0.96)
Unluer 2013 **(37)**	ED	CXR/CT	6 hours	-	28/72	0.96 (0.82-1.00)	0.84 (0.70-0.93)
Benci 1996 **(17)**	Department of infectious diseases	QA	-	-	37/80	1.00 (0.91-1.00)[d]	1.00 (0.92-1.00)[d]
Bitar 2018 **(29)**	ICU	QA	-	-	11/11	0.99[a]	0.80[a]
Bourcier 2014 **(30)**	ED	QA	2 days	-	123/144	0.95 (0.90-0.98)[d]	0.57 (0.34-0.78)[d]
Cipollini 2018 **(27)**	Medicine/geriatric ward	QA	-	> 1 yr.	128/128	0.82 (0.74-0.88)[d]	Not calculable
Cortellaro	ED	QA	-	-	81/120	0.99 (0.93-	0.95 (0.83-0.99)

2012 **(19)**						1.00)	
Pagano 2015 **(33)**	ED	QA	-	> 2 yrs.	68/105	0.99 (0.94-1.00)	0.65 (0.56-0.67)
Ticinesi 2016 **(36)**	Geriatric ward	QA	-	> 1 yr.	97/169	0.92 (0.86-0.97)	0.94 (0.89-0.99)

Abbreviations: LUS: Lung ultrasonography; US: Ultrasonography; ED: Emergency department; ICU: Intensive care unit; QA: Qualitative assessment; CT: Computed tomography; CXR: Chest X-ray; Yr./Yrs.: Year/Years; -: Not described.

a) Data collected by correspondence with author

b) Hemithoraxes

c) 2 University hospitals, 7 hospitals of internal medicine, 1 hospital of pulmonary medicine, 2 practices, 2 EDs

d) 95% CI calculated from true positives, false negatives, true negatives and false negatives. (Clopper-Pearson method)

Table 2. Specialty of non-specialists, experience and training in lung ultrasonography

Study	**Number of and specialty of physicians performing LUS**	**Prior experience in LUS or ultrasonography in general**	**Description of training in LUS**	**Time consumption on LUS**
Amatya 2018 **(38)**	Four emergency resident physicians	One week of performing LUS in the ED.	One hour lecture on LUS. Five pre-enrollment LUS scans and interpretation reviewed by expert sonographer.	7 min. 9 s. (SD 1 min 57 s.)
Corradi 2015 **(18)**	One intensivist with PhD in US[a]	More than 10 years of experience in LUS[a]	-	-
Fares 2015 **(22)**	A single physician.	-	-	-
Karimi 2019 **(39)**	Trained emergency residents under supervision of the attending emergency specialist in charge.	-	-	-
Liu 2015 **(31)**	Three emergency physicians.	At least 50 cases of LUS examination.	Twenty-eight hours course based on US emergency medicine guidelines issued by the American College of Emergency Physicians in 2001	-

Nazerian 2015 **(32)**	Four internal medicine and emergency medicine attending physicians. Four resident physicians (two internal medicine and two emergency medicine).	Attending physicians; at least five years of experience in POC-US. Resident physicians; at least one year of training in emergency US.	-	-
Taghizadieh 2015 **(35)**	One emergency specialist.	-	-	-
Parlamento 2009 **(34)**	One emergency physician.	Thirty years of experience in general and cardiac US and 10 years of training in LUS.	-	< 5 min.
Reissig 2012 **(20)**	Experienced physicians (number and specialty not described).	At least 100 chest US procedures done prior to study.	-	-
Unluer 2013 **(37)**	Three attending emergency physicians.	-	Three hours of didactic and three hours of hands-on thoracic US taught by an experienced radiology specialist to learn the diagnostic criteria of alveolar consolidation.	< 10 min.
Benci 1996 **(17)**	Physicians (number and specialty not described).	Considerable experience in US techniques.	-	-
Bitar 2018 **(29)**	Intensivist (number not described).	-	-	-
Bourcier 2014 **(30)**	Five emergency physicians.	-	Two days of theoretical formation alternating with practical ultrasounds sessions in groups of three people	-
Cipollini 2018 **(27)**	Internal medicine specialist[a]	More than one year of bedside US experience[a]	-	-
Cortellaro 2012 **(19)**	One expert operator.	-	-	< 5 min.
Pagano 2015 **(33)**	Five trained emergency physicians.	More than two years of experience in LUS.	-	-
Ticinesi 2016 **(36)**	Three internal and emergency medicine physicians.	More than one year of bedside US experience.	Level one of training completed according to the guidelines by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)	-

Abbreviations: LUS: Lung ultrasonography; US: Ultrasonography; Min.: Minutes; S: Seconds; SD: Standard deviation; POC-US: Point-of-care ultrasonography; -: Not described

a) Data collected by correspondence with author

Table 3. Potential harms to patients.

Study	True positive LUS results, n (%)	False positive LUS results, n (%)	False negative LUS results, n (%)	True negative LUS results, n (%)	Nature of false positive LUS results
Amatya 2018 **(38)**	40 (64.5)	7 (11.3)	4 (6.5)	11 (17.7)	3 bronchiectasis, 2 interstitial lung diseases, 1 tuberculosis, 1 normal lung.
Corradi 2015 **(18)**	30[a] (46.8)	1[a] (1.6)	14[a] (22.0)	19[a] (29.6)	-
Fares 2015 **(22)**	28 (73.7)	2 (5.3)	2 (5.3)	6 (15.7)	-
Karimi 2019 **(39)**	263 (93.9)	0 (0.0)	17 (6.1)	0	-
Liu 2015 **(31)**	106 (59.2)	1 (0.6)	6 (3.4)	66 (36.8)	-
Nazerian 2015 **(32)**	72 (25.3)	9 (3.1)	15 (5.3)	189 (66.3)	3 cancers, 3 parenchymal impaired ventilation not due to infection 3 pulmonary fibrosis
Taghizadieh 2015 **(35)**	29 (96.7)	1 (3.3)	0	0	-
Parlamento	31 (63.3)	0 (0.0)	1 (2.0)	17 ((34.7)	-

2009 **(34)**					
Reissig 2012 **(20)**	211 (59.3)	3 (0.8)	15 (4.2)	127 (35.7)	-
Unluer 2013 **(37)**	27 (37.5)	7 (9.7)	1 (1.4)	37 (51.4)	4 pulmonary embolisms, 3 exacerbations of COPD.
Benci 1996 **(17)**	37 (46.3)	0 (0.0)	0 (0.0)	43 (53.7)	-
Bitar 2018 **(29)**	-	-	-	-	-
Bourcier 2014 **(30)**	117 (81.2)	9 (6.3)	6 (4.2)	12 (8.3)	4 sepsis of other origin, 2 pulmonary embolisms, 1 ARDS, 1 pulmonary fibrosis, 1 acute anemia.
Cipollini 2018 **(27)**	105 (82.0)	-	23 (18.0)	-	-
Cortellaro 2012 **(19)**	80 (66.7)	2 (1.7)	1 (0.8)	37 (30.8)	1 congestive heart failure 1 subphrenic abscess with lung atelectasia.
Pagano 2015 **(33)**	67 (63.8)	13 (12.4)	1 (1.0)	24 (22.8)	7 exacerbations of COPD 2 congestive heart failure, 3 cancers, 1 pulmonary infarction.
Ticinesi 2016 **(36)**	88 (52.1)	3 (1.8)	8 (4.7)	70 (41.2)	2 pulmonary embolisms, 1 cancer

Abbreviations: LUS: Lung ultrasonography; ND: Not described; ARDS: Acute respiratory distress syndrome; COPD: Chronic obstructive pulmonary disease; n: number

a) Hemithoraxes

Figure legends

Figure 1. PRISMA flow diagram.

Abbreviations: PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; LUS: Lung ultrasonography; Yr.: Years; VAP: Ventilator-associated pneumonia; HAP: Hospital-acquired pneumonia.

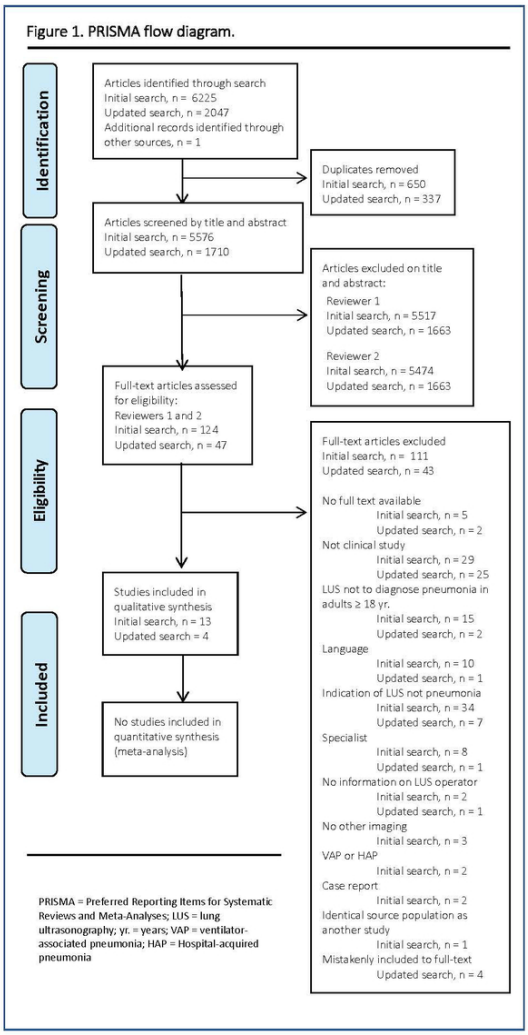

Figure 1. PRISMA flow diagram.Abbreviations: PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; LUS: Lung ultrasonography; Yr.: Years; VAP: Ventilator-associated pneumonia; HAP: Hospital-acquired pneumonia.

86x111mm (300 x 300 DPI)

Supplemental materials for:

Strøm JJ, Haugen PS, Hansen MP, Graumann O, Jensen MB, Andersen CA.

Accuracy of Lung Ultrasonography in the Hands of Non-Specialists to Diagnose and Assess the Severity of Community-Acquired Pneumonia in Adults: A Systematic Review

e-Appendix 1. Search string.

This appendix includes a full description of the literature search conducted in MEDLINE via OVID, EMBASE via OVID, CINAHL via Ebsco, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) on August 10th 2017 and updated on May 16th 2019. The search was conducted by the principal investigator (Julie Jepsen Strøm) and a medical librarian at the medical library at Aalborg University Hospital, Aalborg, Denmark. All databases were searched from inception date until May 16 th 2019.

Database	Interface	Number of hits 08.10.2017	Number of hits 05.16.2019
EMBASE	OVID	4255	1407
MEDLINE	OVID	958	242
Cinahl	Ebsco	99	67
Web of Science		884	320
Cochrane		29	11

Embase 08.10.2017 (updated 05.16.2019)

Interface: OVID

Search: Embase via OVID
Date: 10.08.17
Database: Embase <1974 to 2017 Week 32>
Search Strategy:
---

1 exp pneumonia/ (251394)
2 ((lung or pulmon*) adj3 inflammation*).mp. (18840)
3 inflammatory lung disease*.mp. (1603)
4 lobitis.mp. (19)
5 peripneumonia*.mp. (18)
6 pleuropneumonia*.mp. (2829)
7 (pneumonic adj3 (lung or pleuri*)).mp. (170)
8 pneumonitis.mp. (21629)
9 acute chest syndrome.mp. (2070)
10 acute respiratory syndrome.mp. (9328)

11 bronchopneumonia*.mp. (8482)
12 lung infiltrate*.mp. (11288)
13 legionnaire disease*.mp. (5515)
14 pulmonary candidiasis.mp. (259)
15 or/1-14 (271290)
16 exp animal/ (23458059)
17 exp human/ (18773067)
18 16 not 17 (4684992)
19 ((doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or
ultrasonograph* or ultrasound*) adj (chest or lung or thoracic)).mp. (415)
20 (chest or lung or thoracic).mp. (1664235)
21 exp echography/ (640345)
22 20 and 21 (85682)
23 19 or 22 (85829)
24 15 and 23 (4463)
25 24 not 18 (4386)
26 remove duplicates from 25 (4255)

MEDLINE 08.10.2017 (updated 05.16.2019)

Interface: OVID

Search: Medline via OVID
Date: 10.08.17
Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid
MEDLINE(R) <1946 to Present>
Search Strategy:
---

1 exp pneumonia/ (85977)
2 pneumonia*.mp. (187473)
3 ((lung or pulmon*) adj3 inflammation*).mp. (12982)
4 inflammatory lung disease*.mp. (1145)
5 lobitis.mp. (20)
6 peripneumonia*.mp. (28)
7 pleuropneumonia*.mp. (3244)
8 (pneumonic adj3 (lung or pleuri*)).mp. (187)
9 pneumoniti*.mp. (12993)
10 acute chest syndrome.mp. (925)
11 acute respiratory syndrome.mp. (6465)
12 bronchopneumonia*.mp. (6283)
13 lung infiltrat*.mp. (1007)

14 legionnaire* disease*.mp. (5277)
15 pulmonary candidiasis.mp. (111)
16 or/1-15 (224155)
17 exp animal/ (21731287)
18 human/ (17207961)
19 17 not 18 (4523326)
20 (doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or ultrasonograph* or ultrasound*).mp. (447143)
21 (chest or lung or thoracic).mp. (1021945)
22 exp Ultrasonography/ (400320)
23 20 or 22 (568053)
24 21 and 23 (35801)
25 16 and 24 (1134)
26 25 not 19 (1019)
27 remove duplicates from 26 (958)

Cinahl 08.10.2017 (updated 05.16.2019)

Interface: Ebsco

Search: Cinahl
Date: 10.08.17
Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL with Full Text

#	Query	Limiters/Expanders	Results
S21	S15 AND S20	Search modes - Boolean/Phrase	99
S20	S17 AND S19	Search modes - Boolean/Phrase	4,172
S19	S16 OR S18	Search modes - Boolean/Phrase	61,797
S18	(MH "Ultrasonography+")	Search modes - Boolean/Phrase	38,167
S17	(chest or lung or thoracic)	Search modes - Boolean/Phrase	79,460
S16	(doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or ultrasonograph* or ultrasound*)	Search modes - Boolean/Phrase	50,815

S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14	Search modes - Boolean/Phrase	15,379
S14	pulmonary candidiasis	Search modes - Boolean/Phrase	2
S13	legionnaire* disease*	Search modes - Boolean/Phrase	576
S12	lung infiltrat*	Search modes - Boolean/Phrase	61
S11	bronchopneumonia*	Search modes - Boolean/Phrase	98
S10	acute respiratory syndrome	Search modes - Boolean/Phrase	1,771
S9	acute chest syndrome	Search modes - Boolean/Phrase	123
S8	pneumoniti*	Search modes - Boolean/Phrase	831
S7	(pneumonic n3 (lung or pleuri*))	Search modes - Boolean/Phrase	1
S6	pleuropneumonia*	Search modes - Boolean/Phrase	3
S5	peripneumonia*.	Search modes - Boolean/Phrase	0
S4	lobitis	Search modes - Boolean/Phrase	0
S3	inflammatory lung disease*	Search modes - Boolean/Phrase	62
S2	((lung or pulmon*) n3 inflammation*)	Search modes - Boolean/Phrase	965
S1	(MH "Pneumonia+")	Search modes - Boolean/Phrase	11,441

Web of Science 08.10.2017 (updated 05.16.2019)

Interface: Ebsco

Search: Web of Science
Date: 10.08.17

Set Results	Save History / Create Alert	Open Saved History	Edit Sets	Combine Sets AND OR	Delete Sets

# 3	884	#2 AND #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=All years*	Edit
# 2	340,710	**TOPIC:** (echograph*) *OR* **TOPIC:** (ultrasonograph*) *OR* **TOPIC:** (ultrasound*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=All years*	Edit
# 1	118,598	**TOPIC:** (pneumonia) *OR* **TOPIC:** (pneumonitis) *OR* **TOPIC:** ("acute respiratory syndrome") *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=All years*	Edit

Cochrane 08.10.2017 (updated 05.16.2019)

Interface: Ebsco

Search: Cochrane
Date: 10.08.17
Date Run: 10/08/17 11:42:13.790
Description:

ID	Search	Hits
#1	MeSH descriptor: [Pneumonia] explode all trees	2935
#2	"lung inflammation*":ti,ab,kw (Word variations have been searched)	123
#3	"pulmon* inflammation*":ti,ab,kw (Word variations have been searched)	135
#4	"inflammatory lung disease*":ti,ab,kw (Word variations have been searched)	27
#5	lobitis:ti,ab,kw (Word variations have been searched)	0
#6	peripneumonia*:ti,ab,kw (Word variations have been searched)	0
#7	"pneumonic lung":ti,ab,kw (Word variations have been searched)	2
#8	"pneumonic pleuri*":ti,ab,kw (Word variations have been searched)	0
#9	pneumonitis:ti,ab,kw (Word variations have been searched)	715
#10	"acute chest syndrome":ti,ab,kw (Word variations have been searched)	120
#11	"acute respiratory syndrome":ti,ab,kw (Word variations have been searched)	68
#12	"bronchopneumonia*":ti,ab,kw (Word variations have been searched)	254
#13	"lung infiltrate*":ti,ab,kw (Word variations have been searched)	109
#14	"legionnaire disease*":ti,ab,kw (Word variations have been searched)	39
#15	"pulmonary candidiasis":ti,ab,kw (Word variations have been searched)	1
#16	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15	4300

#17 doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or ultrasonograph* or ultrasound*:ti,ab,kw (Word variations have been searched) 24916
#18 MeSH descriptor: [Ultrasonography] explode all trees 12570
#19 #17 or #18 29065
#20 chest or lung or thoracic:ti,ab,kw (Word variations have been searched) 56834
#21 #19 and #20 1597
#22 #21 and #16 29

e-Appendix 2. Data extraction template.

This appendix lists the data extraction template used in this review. The template is an adapted version of the Cochrane data extraction form (1).

General information
Date extraction completed
Name of person extracting data
Report title
Year of publication
Report ID (Author name and number)
Published in
Publication type
Study funding source
Possible conflict of interest

Eligibility
Review inclusion criteria:
Published full-text paper?
Contains original data from a clinical study?
LUS to diagnose pneumonia?
LUS performed by non-specialist?
Adults (>18 yr.)?
Verification of pneumonia by other means than LUS?
Eligibility criteria met?

Type of study

Methods

Aim of study
Design
Start date
End date
Duration of participation
Ethical approval needed/obtained for study?

Participants (patients):

Clinical suspicion of CAP?
Patients > 18 yr.?
Total no. Participants (patients)
Withdrawals and exclusions
Age
Sex
Inclusion criteria (patients)
Exclusion criteria (patients)
Methods of recruitment of participants (patients)
Severity of illness
Co-morbidities
Other relevant sociodemographics
Subgroups?
Subgroups characterisation

Intervention

LUS performed to support the diagnosis of CAP
LUS scanning procedure described?
Type of ultrasonography scanner
Verification of pneumonia by what means?
Subgroup, difference in intervention

Participants (Non-specialists)

Number of physicians performing LUS
Specialty of physician performing LUS
Training in LUS
Which type of training did the non-specialist recieve?
How many hours of training did the non-specialist receive?
Which elements did the traning consist of?
Was the training assesed?
Who assesed the training?
Was there an examination/certification at the end of training?
Experience

Age
Sex
Exclusion (physicians)
Other relevant information

Setting

Country
Location: City/rural
Location: Hospital/private clinic

Outcomes

Accuracy of LUS to diagnose CAP

Diagnostic Accuracy
Accuracy compared to what?
LUS Sensitivity
Specificity
Other imaging sensitivity

LUS to asses/predict severity

Time consumption on performing LUS

Harms to patients

Overdiagnosis and overtreatment
False positives
False negatives
Incidental findings

Applicability

Have important populations been excluded from the study?
Does the study directly address the review question?

Other information

Key conclusions by author

e-Table 1. Characteristics of studies and patients.

e-Table 1. Characteristics of studies and patients.

Study	Country	Location[a]	Study design	Number of patients	Age[b]	Men/Women	Inclusion criteria[d]
Amatya 2018 (2)	Nepal	City	Prospective cohort	62	Pneumonia: 58.5 ± 13.8. No pneumonia: 61.2 ± 16.3.	29/33	SP with at least 3 of: Temp. > 38°C, history of fever, cough, dyspnea, tachypnea (RR>20), sat. < 92%.
Benci 1996 (3)	Italy	City	Prospective cohort	80	38.5	50/30	SP on the basis of fever and respiratory signs.
Bitar 2018 (4)	Kuwait	City	Prospective cohort	11	34.0	5/6	ATS + physical examination with; Temp > 38°C or < 36°C, RR > 22/min, HR > 90 bpm., audible crackles, decreased or bronchial breath sounds, dullness to percussion, or tactile fremitus.
Bourcier 2014 (5)	France	City	Prospective cohort	144	77.6 ± 15.2	72/72	SP with at least 3 of: Temp. ≥ 38°C, cough, dyspnea, HR ≥ 100 bpm., Sat. ≤ 92%
Cipollini 2018 (6)	Italy	City	Retrospective cohort	128	84.8 (78-94)	61/67	Age ≥65 years and fever and/or respiratory symptoms. Discharged with final diagnosis of pneumonia, where CXR and LUS were performed on admission.
Corradi 2015 (7)	Italy	City	Prospective cohort	32	62 ± 19	17/15	SP on basis of: Temp. ≥ 38°C or ≤ 35°C, cough, dyspnea, heart rate > 90 bpm., tachypnea (RR>20), rales or crackles on auscultation, abnormal oxygen sat.
Cortellaro 2012 (8)	Italy	City	Prospective cohort	120	69 ± 18	77/43	ATS
Fares 2015 (9)	Egypt	City	Prospective cohort	38	61 ± 11.2	20/10[c]	ATS. ICU admission on basis of CURB65 score ≥ 3. General and local physical signs suggestive of pneumonia.
Karimi 2019 (10)	Iran	City	Prospective cohort	280	56.5 ± 19.8	160/120	Clinical symptoms of pneumonia such as cough, phlegm, shortness of breath, hemoptysis, temp. ≥ 38°C.
Liu 2015 (11)	China	City	Prospective cohort	179	71.5 (36-88)	100/79	ATS
Nazerian 2015 (12)	Italy	City	Prospective cohort	285	71 ± 14	133/152	At least 1 unexplained respiratory complaint among: cough, chest pain, hemoptysis, dyspnea for which a chest CT was ordered.
Pagano 2015 (13)	Italy	ND	Prospective cohort	105	59.0	59/46	ATS or crackles or localized absence of breath sounds on lung auscultation.
Parlamento 2009 (14)	Italy	City	Prospective cohort	49	60.9 ± 21.8	31/18	ATS.
Reissig 2012 (15)	Europe	ND	Prospective cohort	356	63.8 (19-95)	228/134	ATS or typical lung auscultation findings and able to undergo CXR in two planes.
Taghizadieh 2015 (16)	East Azerbaijan, Iran	City	Prospective cohort	30	63.8 ± 18.3	28/2	ATS.
Ticinesi 2016 (17)	Italy	City	Prospective cohort	169	83.0 ± 9.2	80/89	ATS and age ≥65 years and ≥2 chronic diseases.
Unluer 2013 (18)	China	ND	Prospective cohort	72	Men: 64.2 ± 12.4	35/37	SP on basis of dyspnea, including acute onset dyspnea or worsening of chronic dyspnea.

					Women: 68.4 ± 11.0		

a) ND: Not described.
b) Age is expressed according to data from each study as median years ± SD OR median years (range).
c) Only stated for patients positive for pneumonia.
d) SP: Suspected pneumonia; Temp: Temperature; RR: Respiratory rate; Sat: Oxygen saturation; ATS = Signs and symptoms suggestive of pneumonia according to American Thoracic Society guidelines (cough, pleuritic pain, sputum production, fever, dyspnea); HR: Heart rate; Bpm: Beats per minute; CXR: Chest X-ray; LUS: Lung ultrasonography;

e-Table 2. Procedure and characteristics of LUS.

e-Table 2. Procedure and characteristics of LUS

Study	Ultrasonography device	Areas examined	Definition of pneumonia on LUS	LUS operator blinded to reference standard
Amatya 2018 (2)	A Sonosite M Turbo (Fujifilm Sonosite, Inc.) with a curvilinear probe.	Each hemithorax divided into five areas: Two anterior, two lateral and one posterior. A total of 10 areas bilaterally.	Presence of unilateral B lines or subpleural lung consolidation.	Yes
Benci 1996 (3)	Ansaldo AU-560 with convex probe of 3.5 MHz.	Medio-lateral anterior and posterior intercostal imaging.	Presence of paranchymatous-like hypoechoic lesions indicative of alveolar pneumonia.	Unclear
Bitar 2018 (4)	GE Vivid S6N with a phased-array 5-MHz probe	Each hemithorax divided into five areas: Two anterior, two lateral and one posterior. A total of 10 areas bilaterally.	Presence of lung consolidation attaching to the pleural (subpleural) presenting tissue-like pattern or focal interstitial syndrome (focal distribution of B lines).	Yes
Bourcier 2014 (5)	Portable US device SONOSITE M TURBO with convex 3.5 MHz probe.	Examination of 8 areas of the chest wall in accordance with international guidelines (reference not reported in study)	Presence of a unilateral or bilateral alveolar-interstitial syndrome defined as disappearance of the pleural line associated with aeric or water bronchograms within an image of tissue echogenicity.	Yes
Cipollini 2018 (6)	Mindray M7 portable device using a 3.5 MHz convex probe.	A systematic examination of intercostal spaces was performed anteriorly	Presence of a hypoechoic solid area with shred margins indicative for consolidation.	Unclear
Corradi 2015 (7)	Logiq-e unit (GE Healthcare) with broadband convex-array probe at 4 MHz and high frequency linear-array probe at 10 MHz.	Each hemithorax was scanned over every intercostal space along the conventional parasternal, midclavicular, axillary, and paravertebral lines.	Presence, distribution and extent of artifacts suggestive of interstitial involvement, pleural line abnormalities and alveolar consolidation.	Yes
Cortellaro 2012 (8)	Esaote Medical Systems, 3.5-5 MHz convex probe.	Each hemithorax divided into five areas: Two anterior, two lateral and one posterior. A total of 10 areas bilaterally.	Presence of subpleural lung consolidation, presenting a tissular pattern.	Yes
Fares 2015 (9)	Sonoescape B5 with 3- to 6 MHz convex probe.	Longitudinal and oblique scans of the anterior, lateral and posterior chest wall. The probe was set perpendicular, oblique, and parallel to the ribs. A total of 12 areas bilaterally.	Presence of subpleural lung consolidation presenting as a tissular pattern, air bronchograms with or without pleural effusion.	Unclear
Karimi 2019 (10)	Samsung HM70A device with a curved 3.5 – 5 MHz probe	Each hemithorax divided into anterior (from the parasternal line to the anterior auxiliary line), lateral (between the posterior and middle auxiliary lines), and posterior (from the posterior auxiliary line to the paravertebral line).	Presence of air bronchogram, fluid bronchogram, pleural effusion, b lines (comet tail sign), or subpleural consolidation.	Yes
Liu 2015 (11)	Sonosite M-Turbo with 3.5- 5 MHz convex array probe.	Each intercostal space in the mid-clavicular line, anterior axillary line, midaxillary line, and paravertebral line, from lung apex to the diaphragm.	Presence of; 1) Consolidation, 2) Focal interstitial pattern, 3) ≥ 2 Subpleural lesions or 4) ≥ 5 Intercostal spaces with pleural-line abnormalities.	Yes
Nazerian 2015 (12)	MyLab30 Gold (Esaote) and HD7 (Philips).	Each hemithorax divided into anterior-lateral areas (extending from parasternal to posterior axillary line) and posterior areas (from the posterior axillary to paravertebral line). A total of 4 areas bilaterally.	Presence of at least one subpleural lung consolidations with tissue- like or anechoic pattern and blurred, irregular margins.	Yes
Pagano 2015 (13)	C60 Sonosite Micro Maxx with 2-5 MHz convex probe.	Each hemithorax divided into 4 areas; 1) upper anterior, 2) lower anterior, 3) upper posterior, 4) lower posterior. A total of 8 areas bilaterally.	Presence of 1) Alveolar syndrome: Image of tissue echogenicity associated with aerial bronchogram or 2) Focal interstitial syndrome: Presence of 3 or more B- lines in a single lung area.	Yes
Parlamento 2009 (14)	Megas CVX, Esaote Medical Systems, with convex 3.5-5 MHz probe.	Each hemithorax divided into 5 areas: 1) Two anterior, 2) Two lateral, 3) One posterior. A total of 10 areas bilaterally.	Presence of subpleural lung consolidation with evidence of static or dynamic air bronchograms.	Yes

Reissig 2012 (15)	Machines not reported; 5- or 3.5 MHz convex probe, occasionally 7.5 MHz linear probe.	Systematically all intercostal spaces.	Unclear definition. Number, shape and size of pneumonic lesions were reported and incidence of necrotic areas, positive air bronchogram, fluid bronchogram, and local and basal pleural effusion was reported.	Yes
Taghizadieh 2015 (16)	LOGIQ 200 (GE Healthcare) with convex 3.5 MHz probe.	Not described	Not described	Unclear
Ticinesi 2016 (17)	Acuson X300 5.0 (Siemens) with convex 2-5 MHz probe.	Each hemithorax divided into anterior-lateral areas (extending from parasternal to posterior axillary line) and posterior areas (from the posterior axillary to paravertebral line). Each area divided into upper and lower half. A total of 8 areas bilaterally.	Presence of tissue-like echogenicity associated with dynamic air bronchograms, defined as punctiform or linear hyperechoic artifacts with centrifugal inspiratory dynamicity.	Yes
Unluer 2013 (18)	M7 model ultrasound machine with 3.6 MHz microconvex probe.	Each hemithorax divided into four areas (upper, anterior, lower, lateral and posterior) and four points (two in the anterior zone, one lateral and one posterior). A total of 8 areas bilaterally.	Presence of alveolar consolidation defined as: 1) A tissue-like pattern with regular trabeculations reminiscent of the liver, 2) Demonstration of the shred sign in longitudinal view with an uneven surface of the lung line, 3) Detection of unilateral localized B lines based on the BLUE protocol.	Yes

e-Table 3. QUADAS-2 quality assessment.

This e-table lists the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2). Each domain is represented in a bar with the proportion of studies considered high risk (red), low risk (green), or unclear (yellow). The same applies to applicability concerns.

e-Table 3. QUADAS-2 quality assessment.							
Study	Risk of bias				Concerns about applicability		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Amatya 2018 (2)	+	+	+	+	+	+	+
Benci 1996 (3)	?	?	?	-	+	?	+
Bitar 2018 (4)	+	+	?	-	?	+	+
Bourcier 2014 (5)	+	+	?	-	+	+	+
Cipollini 2018 (6)	?	?	?	-	+	+	+
Corradi 2015 (7)	-	+	+	+	-	+	+
Cortellaro 2012 (8)	+	+	+	+	+	?	+
Fares 2015 (9)	+	?	?	-	+	?	+
Karimi 2019 (10)	-	+	+	+	+	+	+
Liu 2015 (11)	+	+	+	+	+	+	+
Nazerian 2015 (12)	-	+	+	+	-	+	+
Pagano 2015 (13)	+	+	+	?	+	+	+
Parlamento 2009 (14)	+	+	+	-	+	+	+
Reissig 2012 (15)	+	+	+	-	+	?	+
Taghizadieh 2015 (16)	-	-	+	+	+	?	+
Ticinesi 2016 (17)	-	+	+	-	+	+	+
Unluer 2013 (18)	-	+	+	-	+	+	+

References

1. Sambunjak D CM, Watts C. Module 4: Selecting studies and collecting data. *Cochrane Interactive Learning: Conducting an Intervention Review*. Oxford: Cochrane; 2017 [Available from: https://training.cochrane.org/interactivelearning/module-4-selecting-studies-and-collecting-data.

2. Amatya Y, Rupp J, Russell FM, Saunders J, Bales B, House DR. Diagnostic use of lung ultrasound compared to chest radiograph for suspected pneumonia in a resource-limited setting. *Int J Emerg Med*. 2018;11(1):8.

3. Benci A, Caremani M, Menchetti D, Magnolfi A. Sonographic diagnosis of pneumonia and bronchopneumonia. *European Journal of Ultrasound* [Internet]. 1996; 4(3):[169-76 pp.]. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/916/CN-00168916/frame.html.

4. Bitar ZI, Maadarani OS, El-Shably AM, Al-Ajmi MJ. Diagnostic accuracy of chest ultrasound in patients with pneumonia in the intensive care unit: a single-hospital study. *Health Science Reports*. 2019;2(1):e102.
5. Bourcier JE, Paquet J, Seinger M, Gallard E, Redonnet JP, Cheddadi F, et al. Performance comparison of lung ultrasound and chest x-ray for the diagnosis of pneumonia in the ED. *Am J Emerg Med*. 2014;32(2):115-8.
6. Cipollini F, Mirauta CM. Bedside lung ultrasound in the diagnosis of pneumonia in very old patients. *Italian Journal of Medicine*. 2018;12(2):126-30.
7. Corradi F, Brusasco C, Garlaschi A, Paparo F, Ball L, Santori G, et al. Quantitative analysis of lung ultrasonography for the detection of community-acquired pneumonia: a pilot study. *BioMed Research International*. 2015;2015:no pagination.
8. Cortellaro F, Colombo S, Coen D, Duca PG. Lung ultrasound is an accurate diagnostic tool for the diagnosis of pneumonia in the emergency department. *Emergency Medicine Journal*. 2012;29(1):19-23.
9. Fares Auf MDAA-N, M.D.; Moustafa Zedan, M.D.; Mohammad Al-Sokromi, M.Sc. Role of transthoracic ultrasound in detection of pneumonia in ICU patients. *Medical Journal of Cairo University*. 2015;83(No 1, Juni):307-14.
10. Karimi E. Comparing sensitivity of ultrasonography and plain chest radiography in detection of pneumonia; a diagnostic value study. *Archives of Academic Emergency Medicine*. 2019;7(1):e8.
11. Liu X-l, Lian R, Tao Y-k, Gu C-d, Zhang G-q. Lung ultrasonography: an effective way to diagnose community-acquired pneumonia. *Emergency Medicine Journal*. 2015;32(6):433-8.
12. Nazerian P, Volpicelli G, Vanni S, Gigli C, Betti L, Bartolucci M, et al. Accuracy of lung ultrasound for the diagnosis of consolidations when compared to chest computed tomography. *Am J Emerg Med*. 2015;33(5):620-5.
13. Pagano A, Numis FG, Visone G, Pirozzi C, Masarone M, Olibet M, et al. Lung ultrasound for diagnosis of pneumonia in emergency department. *Internal and Emergency Medicine*. 2015;10(7):851-4.
14. Parlamento S, Copetti R, Di Bartolomeo S. Evaluation of lung ultrasound for the diagnosis of pneumonia in the ED. *Am J Emerg Med*. 2009;27(4):379-84.
15. Reissig A, Copetti R, Mathis G, Mempel C, Schuler A, Zechner P, et al. Lung ultrasound in the diagnosis and follow-up of community-acquired pneumonia: a prospective, multicenter, diagnostic accuracy study. *Chest*. 2012;142(4):965-72.
16. Taghizadieh A, Ala A, Rahmani F, Nadi A. Diagnostic accuracy of chest x-ray and ultrasonography in detection of community acquired pneumonia; a brief report. *Emergency*. 2015;3(3):114-6.
17. Ticinesi A, Lauretani F, Nouvenne A, Mori G, Chiussi G, Maggio M, et al. Lung ultrasound and chest x-ray for detecting pneumonia in an acute geriatric ward. *Medicine*. 2016;95(27):e4153.
18. Unluer EE, Karagoz A, Senturk GO, Karaman M, Olow KH, Bayata S. Bedside lung ultrasonography for diagnosis of pneumonia. *Hong Kong Journal of Emergency Medicine*. 2013;20(2):98-104.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	e-appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A

PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	5
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	5-6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	7
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	8
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	8
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

PRISMA 2009 Checklist

The PRISMA for Abstracts Checklist

TITLE	CHECKLIST ITEM	REPORTED ON PAGE #
1. Title:	Identify the report as a systematic review, meta-analysis, or both.	1
BACKGROUND		
2. Objectives:	The research question including components such as participants, interventions, comparators, and outcomes.	2
METHODS		
3. Eligibility criteria:	Study and report characteristics used as criteria for inclusion.	2
4. Information sources:	Key databases searched and search dates.	2
5. Risk of bias:	Methods of assessing risk of bias.	2
RESULTS		
6. Included studies:	Number and type of included studies and participants and relevant characteristics of studies.	2
7. Synthesis of results:	Results for main outcomes (benefits and harms), preferably indicating the number of studies and participants for each. If meta-analysis was done, include summary measures and confidence intervals.	2
8. Description of the effect:	Direction of the effect (i.e. which group is favoured) and size of the effect in terms meaningful to clinicians and patients.	2
DISCUSSION		
9. Strengths and Limitations of evidence:	Brief summary of strengths and limitations of evidence (e.g. inconsistency, imprecision, indirectness, or risk of bias, other supporting or conflicting evidence)	2
10. Interpretation:	General interpretation of the results and important implications	2
OTHER		
11. Funding:	Primary source of funding for the review.	1
12. Registration:	Registration number and registry name.	2

BMJ Open

Accuracy of Lung Ultrasonography in the Hands of Non-imaging Specialists to Diagnose and Assess the Severity of Community-Acquired Pneumonia in Adults: A Systematic Review

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Secondary Subject Heading:	Radiology and imaging, Infectious diseases, General practice / Family practice
Keywords:	ULTRASONOGRAPHY, Respiratory infections < THORACIC MEDICINE, GENERAL MEDICINE (see Internal Medicine), PRIMARY CARE

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Accuracy of Lung Ultrasonography in the Hands of Non-imaging Specialists to Diagnose and Assess the Severity of Community-Acquired Pneumonia in Adults: A Systematic Review

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Abbreviations

CAP: Community-acquired pneumonia
CT: Computed tomography scan
CXR: Chest X-ray
LUS: Lung ultrasonography
QUADAS-2: Quality Assessment of Diagnostic Accuracy Studies 2

Abstract

Objectives: We aimed to systematically review the published literature regarding adults with clinical suspicion of pneumonia that compares the accuracy of lung ultrasonography (LUS) performed by non-imaging specialists to other reference standards in diagnosing and evaluating the severity of community acquired pneumonia (CAP). Moreover, we aimed to describe LUS training and the specialty of the physician performing LUS, time spent on the LUS procedure, and potential harms to patients.

Material and Methods: We searched MEDLINE, EMBASE, CINAHL, Web of Science, and Cochrane Central Register of Controlled Trials up until May 2019. We included studies that used LUS to diagnose pneumonia, but also confirmed pneumonia by other means. Publications were excluded if LUS was performed by a sonographer or radiologist (imaging specialists) or performed on other indications than suspicion of pneumonia. Two review authors screened and selected articles, extracted data and assessed quality using QUADAS-2.

Results: We included 17 studies. The sensitivity of LUS to diagnose pneumonia ranged from 0.68 to 1.00; however, in 14 studies sensitivity was ≥ 0.91. Specificities varied from 0.57 to 1.00. We found no obvious differences between studies with low and high diagnostic accuracy. The non-imaging specialists were emergency physicians, internal medicine physicians, intensivists, or "specialty not described". Five studies described LUS training, which varied from a one-hour course to fully credentialed ultrasound education. In general, the methodological quality of studies was good, though, some studies had a high risk of bias.

Conclusions: We found significant heterogeneity across studies. In the majority of studies, LUS in the hands of the non-imaging specialists demonstrated high sensitivities and specificities in diagnosing pneumonia. However, due to problems with methodology and heterogeneity there is a need for larger studies with uniform and clearly established criteria for diagnosis and blinding.

Trial registration: Prospectively registered in PROSPERO (CRD42017057804).

Strengths and limitations of this study

- This is the first systematic review to focus specifically on LUS to diagnose CAP in adults in the hands of non-imaging specialists physicians working clinically.
- We rigorously followed the Cochrane recommendations for conducting systematic literature reviews and searched five major databases using a broadly defined search string.
- We distinguished between imaging specialists defined as sonographers or radiologists and non-imaging specialist defined as physician working clinically, eventhough some physicians working clinically may have an experience with ultrasonography similar to that of an imaging specialist.

Keywords

Ultrasonography; Echography; Pneumonia, General Medicine, Primary Health Care.

Introduction

Community-acquired pneumonia (CAP) is a frequent and serious health concern, leading to increased morbidity and mortality if not detected and treated properly [1, 2]. CAP accounts for 2.5% of all patient contacts in Danish general practice [3] and globally it causes countless hospital admissions, laboratory tests, and imaging procedures [4].

Today, the typical imaging procedures for diagnosing pneumonia are computed tomography (CT) scan of the chest and chest X-ray (CXR), with CT considered the gold standard [5]. However, far from all patients have these imaging procedures performed due to high radiation dose, high costs, and low availability [6].

An alternative mode of imaging is lung ultrasonography (LUS). The advantages of LUS are absence of radiation, high availability, and low cost [7]. Moreover, LUS can be performed as a bedside point-of-care test to supplement the physician's clinical examination. Numerous reviews and meta-analyses indicate that LUS has excellent accuracy for the diagnosis of pneumonia in adults [8-13]. None of the existing literature, however, differentiates between LUS operators despite the fact that ultrasound generally is considered a highly user-dependent imaging modality[14]. To our knowledge, no previous review has focused solely on the accuracy of LUS in the hands of physicians working clinically.

The aim of this study was to systematically review the published literature regarding adults with clinical suspicion of pneumonia that compares the accuracy of LUS performed by physicians working clinically (non-imaging specialists) to other reference standards in diagnosing and evaluating the severity of CAP. Moreover, to describe LUS training and the specialty of the physician performing LUS, time spent on the LUS procedure, and potential harms to patients.

Methods

Data sources and search strategy

This review was prospectively registered in PROSPERO (CRD42017057804). We followed the Cochrane guideline [15] for conducting a systematic literature review, and the Preferred Reporting Items for Systematic Reviews and Meta-analyses (PRISMA) guideline for reporting the results. The literature search was conducted by a medical librarian and JJS in February 2017 and updated in May 2019. We searched the following databases: MEDLINE and EMBASE via Ovid, CINAHL via Ebsco, Web of Science, and Cochrane Central Register of Controlled Trials.

The search terms "ultrasonography" and "pneumonia" were used in combination and with thesaurus terms (e-Appendix 1). Reference lists of included articles and identified reviews were evaluated manually for further eligible studies. Patients or the public were not involved in our research. All data relevant to the study are included in the article or uploaded as supplementary information.

Eligibility and selection of studies

Studies were eligible if a full-text paper with original data was available, the paper described the use of LUS for diagnosing CAP in adults (≥ 18 years), and the diagnosis of CAP was confirmed by other means, e.g. other imaging. Hence, we included all diagnostic accuracy studies that used any reference standard other than LUS. Studies were excluded if not published in English, Danish, Norwegian, or Swedish, if LUS was performed on other indications than suspicion of pneumonia, if LUS was performed by an imaging specialist, or if the pneumonia was considered to be ventilator-associated or nosocomial. We defined an imaging specialist as a sonographer or radiologist and a non-imaging specialist as a physician working clinically.

Two review authors (JJS and PSH or MPH) independently screened the titles and abstracts of all studies identified. Any disagreements were resolved by consensus or by consulting other review authors (CAA and MBJ).

Two review authors (JJS and PSH or MPH) independently extracted data using an adapted version of the Cochrane data exaction template (e-Appendix 2). We contacted study authors when information about the physician performing the LUS was incomplete or missing, or if important data could not be derived directly from the published study.

Methodological assessment

Methodological quality of the selected studies was evaluated according to the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2) [16]. Two reviewers (JJS and PSH or MPH) independently performed the assessment of methodological quality. Any disagreements were resolved by consensus or by consulting a third review author (CAA).

Patient and Public Involvement

No patient involved.

Results

The database search identified 7285 individual, non-duplicate articles and one potential article was identified through the reference lists (Figure 1). Twelve studies had little or no information about the physician performing LUS [17-28] and we contacted the corresponding authors of these studies. Based on additional information provided by the study authors, two studies were included [18, 27] and two studies were excluded [21, 25]. No elaboration was available for the remaining eight studies. They were thoroughly assessed and four were included, as they clearly described the scanning physicians as a non-imaging specialist physician working clinically [17, 19, 20, 22]. The remaining four studies were excluded [23, 24, 26, 28].

One study included both patients with CAP and nosocomial pneumonia [29]. However, data on the CAP subgroup was obtained by correspondence with the study authors.

In total, 17 studies describing LUS in the hands of the non-imaging specialist to diagnose CAP in adults were included [17-20, 22, 27, 29-39] (Figure 1).

Study characteristics

The studies were published between 1996 and 2019; 16 were prospective diagnostic accuracy cohort studies, and one was a retrospective study [27] (e-Table 1).

The majority of studies included patients admitted to hospital, although one multi-center study enrolled both hospitalized patients and outpatients [20] (Table 1). The studies included between 11 and 356 adult patients with a mean age from 34.0 to 84.8 years of whom between 47% and 93% were men. Two studies included only patients aged ≥ 65 years [27, 36].

The signs and symptoms of pneumonia described in the American Thoracic Society guidelines (ATS) (cough, pleuritic pain, sputum production, fever, dyspnea) were used as inclusion criteria in nine studies [19, 20, 22, 29, 31, 33-36] and six studies based inclusion on comparable, but not identical, criteria [17, 27, 30, 37-39]. The remaining two studies only included patients with respiratory complaints like cough, dyspnea, chest pain, or hemoptysis leading to a chest CT being ordered [18, 32].

Definition of pneumonia based on LUS varied across studies. Still, presence of subpleural or alveolar consolidation or a tissue-like lesion was part of the definition in all studies except one, in which no definition was described[35]. The physicians performing and interpreting LUS were generally blinded to the reference standard; however, in four studies this matter was unclear [17, 22, 27, 35]. The definitions of pneumonia, blinding, scanning procedure and characteristics of LUS are listed in e-Table 2. The reference standard varied from CT, qualitative assessment of the final diagnosis based on clinical, laboratory, and microbiological data including CXR or chest CT results, and CXR combined with CT when LUS and CXR were discordant (Table 1).

Overall, the methodological quality of the included studies, according to QUADAS-2, was good (e-Table 3). Some studies, however, had a high risk of bias regarding flow and timing due to heterogeneity in the reference standard between patients, and high risk of bias in patient selection due to the exclusion of patients with pulmonal or cardiac comorbidities. The study populations, severity of condition (intensive care unit vs. non-intensive care unit), and the reference standard were heterogeneous across studies. As a result, the specific requirements for including results in a meta-

analysis (e.g. comparable populations, LUS performer, and reference standard), were not met by the included studies, nor by a subgroup of included studies.

Diagnostic accuracy of LUS

Diagnostic accuracy is presented in Table 1. The sensitivity of LUS to diagnose CAP ranged from 0.68 (95% CI, 0.52-0.81) to 1.00 (95% CI, 0.95-1.00); in 14 of the 17 studies it was ≥ 0.91. The specificity could be calculated in 13 of the studies. It varied from 0.57 (95% CI, 0.34-0.78) to 1.00 (95% CI, 0.92-1.00), but in seven studies it was ≥ 0.94. We found no systematic differences between studies with low and high diagnostic accuracy in terms of study setting, participant training or experience, or choice of reference standard. Inter-observer agreement was reported in two studies with κ-values of 0.83 and 0.90 [32, 36].

The studies by Liu et al. and Amatya et al. were the two studies of highest methodological quality (e-Table 3). Both studies compared LUS to CT (Table 1) and LUS was performed by emergency physicians whose prior experience and training was described (Table 2). However, they differed with regards to procedure and characteristics of LUS in terms of areas examined and definition of pneumonia on LUS (e-Table 2). They found sensitivities of respectively 0.95 (95% CI, 0.89-0.98) and 0.91 (95% CI, 0.78-0.98) and specificities of 0.99 (95% CI, 0.92-1.00) and 0.61 (95% CI, 0.36-0.83).

None of the studies compared sonographic findings to clinical outcomes. Three studies assessed the severity of pneumonia in patients with either CURB-65 score [18, 22] or Pneumonia Outcome Research Team (PORT) [34], but these were not compared to LUS findings.

Bourcier et al. [30] stratified their results according to onset of symptoms of pneumonia (< 24h versus > 24h). They found that LUS (sensitivity of 0.97) was significantly more effective than CXR (sensitivity of 0.30) in diagnosing pneumonia when time from clinical onset was < 24 hours.

Specialty and training of non-imaging specialists

Information about specialty, experience, and training of physicians performing LUS is presented in Table 2. LUS was performed by emergency physicians, internal medicine physicians, and by intensivists, while four studies did not declare the specific specialty of the non-imaging specialists [17, 19, 20, 22]. Nine studies reported that physicians had previous experience with LUS or ultrasonography in general [17, 18, 20, 27, 31-34, 38]. Prior experience of performing LUS varied from one week in the emergency department to more than ten years' clinical experience.

Five studies described a LUS training program for the participating physicians [30, 31, 36-38]. Two studies provided a reference for an established educational program [31, 36], whereas the remaining studies described training specifically designed for their study [30, 37, 38]. All training programs included both theoretical and practical sessions. A large variation in the extent of the training programs was noted, ranging from a few hours at a course facility [37] to completion of a European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB) [14] Level 1 qualification [36]. Four studies reported the time spent performing LUS, which was overall < 10 min.

Potential harms to patients

Twelve studies reported false positive results from LUS, and fourteen studies described false negative results (Table 3). Corradi et al. reported a high number of false negative results as they found 14 (22%) false negative hemithorax LUS examinations [18]. However, five of these were reported in patients with bilateral pneumonia, in whom LUS examination only detected pneumonia in one hemithorax. Moreover, Corradi et al. described that LUS-positive pneumonia were larger in diameter (81 ± 55 mm) and close to the pleural line (1 ± 3 mm) [18]. Likewise, more studies described false-negative results that were mainly seen in patients with small consolidations where pneumonia did not reach the pleura [20, 22, 30, 32].

Parlamento et al. reported two incidental findings of subpleural consolidations in patients without pneumonia [34]. In both cases, LUS findings were verified by chest CT scan and confirmed to be, respectively, an atelectasis caused by a large pleural effusion, and a case of pulmonary embolism.

Discussion

To our knowledge, this is the first systematic review to focus specifically on LUS to diagnose CAP in adults in the hands of non-imaging specialists physicians working clinically. These non-imaging specialists were emergency physicians, internal medicine physicians, intensivists or unclassified physicians and obtained LUS sensitivities and specificities that were typically above 0.90. We found no overall difference in diagnostic accuracy when compared to study setting or the physicians' specialty, experience, or training. Importantly, the variation in sensivitity and specificity was found across reference standards. No study compared sonographic findings to the severity of pneumonia. Only a few studies described LUS training of the non-imaging specialists and these training programs varied from short lectures to fully accredited ultrasound education.

We highlighted the results of Liu et al. and Amatya et al. due to the quality of the studies, still, the studies were not completely comparable in other parameters. Both studies found high and comparable sensitivities of 0.95 (95% CI, 0.89-0.98) and 0.91 (95% CI, 0.78-0.98) respectively. However, in Amatya et al., LUS specificity was 0.61 (95% CI, 0.36-0.83) and significantly lower than the specificity in Liu et al. of 0.99 (95% CI, 0.92-1.00). According to Amatya et al., this was due to a higher prevalence of pulmonal co-morbidities which resulted in false positive LUS results. Low specificity may lead to over-diagnosis of pneumonia and inappropriate use of antibiotics.

The diagnostic accuracy of LUS for diagnosing pneumonia described in this review is consistent with results from previous reviews that made no distinction between imaging specialists and physicians working clinically [8-13]. Recently, Orso et al. obtained a pooled sensitivity of 0.92 and a specificity of 0.93 in a review based on studies performed in emergency departments [40]. Of course, the majority of LUS operators were emergency physicians, corresponding to the non-specialists in the present review. Consequently, Orso et al. and this study have included many of the same studies. However, Orso et al. also included studies with imaging specialists and patients with "acute respiratory failure". Our review included LUS performed by non-imaging specialists from different

specialties and in different settings. One study was even partly conducted in outpatient settings with non-hospitalized patients [20]. Importantly, the results of this particular study did not differ from the remaining studies. Hence, LUS might also be applied on non-hospitalized patients with suspected CAP, which supports the vision that LUS could be a useful tool for any clinician in the future [41].
Non-imaging specialists working in primary care are first in line to see patients with CAP and general practitioners have already begun using point-of-care ultrasound [42, 43]. The results by Bourcier et al. suggest that LUS is a better diagnostic tool for achieving an early diagnosis (≤ 24 hours from clinical onset) compared to CXR. The ability of LUS to accurately diagnose pneumonia early in the course of the disease may improve outcomes for patients attending primary care [43]. Furthermore, improved diagnostic performance in patients with suspected CAP may reduce the need for antibiotics. Though, the size of pulmonary lesions might be smaller in the early stages of disease and the results indicate that the usability of LUS to diagnose CAP is compromised by its inability to visualize pulmonary lesions that are not in contact with the pleura. However, according to Lichtenstein et al. who looked for lung consolidation in intensive care patients, this occurred in only 1.5% cases of lung consolidation[44]. Due to a lower prevalence and less severe disease in a general practice population, further evaluation of LUS for the diagnosis of CAP in general practice is required.
LUS is a user-dependent examination and several guidelines [14, 45, 46] stress that diagnostic performance requires sufficient training to gain the necessary competencies. A meta-analysis by Tsou et al. found a significant difference in diagnostic accuracy between LUS performed by "advanced" versus "novice" sonographers in the diagnosis of pneumonia in children [47]. However, they defined "novice sonographers" as physicians with little or no prior LUS experience or training (≤ 7 days); most of the non-imaging specialists in the present review would be classified as "advanced sonographers" according to this definition. Though, the learning curve appears steep from pediatric data and in a randomized controlled trial by Jones et al. [48] they found that substitution of CXR with LUS when evaluating children suspected of having pneumonia was feasible and safe, also in the hands of novice sonographers (≤ 25 examinations). Today, there are no guidelines or recommendations specifying the amount of training or level of competence needed to perform LUS [49, 50]. As this review has shown, however, these competencies can be reached by the non-imaging specialist physician even after a short, tailored training program. To ensure that physicians maintain and develop skills over time and learn to incorporate LUS findings into clinical decision-making, longitudinal training elements must be incorporated into the training programs [50].
This study describes the different specialties of the non-imaging specialists and demonstrates great heterogeneity in their prior experience and training in LUS. However, sensitivities and specificities are comparable, thereby implying that LUS can be performed by physicians in various specialties, and by less experienced physicians, with comparable results to those of physicians with considerable experience in LUS.

Limitations

The aim of this study was to describe the diagnostic accuracy of LUS for diagnosing CAP when performed by physicians with considerably less ultrasound experience than imaging specialists. In four of the included studies, the speciality of the physician was not reported [17, 19, 20, 22]. These studies

were included as we assessed from the clinical setting that the physicians were not radiologists or sonographers. The results from these four studies did not differ from the remaining studies. Furthermore, while some of the physicians had extensive experience with LUS [17, 18, 34], and their ultrasonography competencies may be compared to those of an imaging specialist, we did not find in general that sensitivity and specificity increased with experience. Comparison of studies was difficult due to sparse information on the non-imaging specialists' training, their experience with LUS, and the heterogeneity in the reference standards used. Due to the significant heterogeneity across studies, it was not appropriate to pool data and perform a meta-analyses.

Conclusions

We found significant heterogeneity across studies. In the majority of studies, LUS in the hands of the non-imaging specialists demonstrated high sensitivities and specificities in diagnosing pneumonia. However, due to problems with methodology and heterogeneity there is a need for larger studies with uniform and clearly established criteria for diagnosis and blinding.

Author contribution

JJS is the guarantor of the study. JJS, PSH, MPH, MBJ, OG and CAA contributed to the concept, design and drafting of the study. JJS, PSH and MPH conducted the systematic search strategy and the review. All authors revised critically and approved the final manuscript.

Data availability statement

Data extraction is available upon reasonable request.

References

1. Polverino E, Torres Marti A. Community-acquired pneumonia. Minerva Anestesiol. 2011;77(2):196-211.
2. Meehan TPT. Quality of care, process, and outcomes in elderly patients with pneumonia. JAMA : the journal of the American Medical Association. 1997;278(23):2080-4.
3. Bjerrum L. Pneumoni. Luftvejsinfektioner - diagnose og behandling. 2014;1(1):30-5.
4. Prina E. Community-acquired pneumonia. The Lancet (British edition). 2015;386(9998):1097-108.
5. Syrjälä HH. High-resolution computed tomography for the diagnosis of community-acquired pneumonia. Clinical infectious diseases. 1998;27(2):358-63.
6. Brenner DJDJ. Computed tomography--an increasing source of radiation exposure. The New England journal of medicine. 2007;357(22):2277-84.
7. Sartori S, Tombesi P. Emerging roles for transthoracic ultrasonography in pulmonary diseases. World journal of radiology. 2010;2(6):203-14.
8. Llamas-Alvarez AM, Tenza-Lozano EM, Latour-Perez J. Accuracy of Lung Ultrasonography in the Diagnosis of Pneumonia in Adults: Systematic Review and Meta-Analysis. Chest. 2017;151(2):374-82.
9. Long LL. Lung ultrasound for the diagnosis of pneumonia in adults: A meta-analysis. Medicine (Baltimore). 2017;96(3):e5713.
10. Xia Y, Ying YH, Wang SB, Li W, Shen HH. Effectiveness of lung ultrasonography for diagnosis of pneumonia in adults: a systematic review and meta-analysis. Journal of Thoracic Disease. 2016;8(10):2822-31.
11. Chavez MA, Shams N, Ellington LE, Naithani N, Gilman RH, Steinhoff MC, et al. Lung ultrasound for the diagnosis of pneumonia in adults: a systematic review and meta-analysis. Respiratory research. 2014;15:50.
12. Ye X, Xiao H, Chen B, Zhang SY. Accuracy of Lung Ultrasonography versus Chest Radiography for the Diagnosis of Adult Community-Acquired Pneumonia: Review of the Literature and Meta-Analysis. Plos One. 2015;10(6).
13. Alzahrani SA, Al-Salamah MA, Al-Madani WH, Elbarbary MA. Systematic review and meta-analysis for the use of ultrasound versus radiology in diagnosing of pneumonia. Critical ultrasound journal. 2017;9(1):6.
14. Minimum training requirements for the practice of Medical Ultrasound in Europe. Ultraschall in der Medizin. 2010;31(4):426-7.
15. Deeks JJ BP, Gatsonis C (editors). Cochrane Handbook for Systematic Reviews of Diagnostic Test Accuracy Version 1.0.0. The Cochrane Collaboration. 2009;Available from: http://srdta.cochrane.org/.
16. Whiting PFPF. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Annals of internal medicine. 2011;155(8):529-36.
17. Benci A, Caremani M, Menchetti D, Magnolfi A. Sonographic diagnosis of pneumonia and bronchopneumonia. European Journal of Ultrasound [Internet]. 1996; 4(3):[169-76 pp.]. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/916/CN-00168916/frame.html.
18. Corradi F, Brusasco C, Garlaschi A, Paparo F, Ball L, Santori G, et al. Quantitative analysis of lung ultrasonography for the detection of community-acquired pneumonia: A pilot study. BioMed Research International. 2015;2015:no pagination.
19. Cortellaro F, Colombo S, Coen D, Duca PG. Lung ultrasound is an accurate diagnostic tool for the diagnosis of pneumonia in the emergency department. Emergency medicine journal : EMJ. 2012;29(1):19-23.
20. Reissig A, Copetti R, Mathis G, Mempel C, Schuler A, Zechner P, et al. Lung ultrasound in the diagnosis and follow-up of community-acquired pneumonia: a prospective, multicenter, diagnostic accuracy study. Chest. 2012;142(4):965-72.

21. Nafae R, Eman SR, Mohamad NA, El-Ghamry R, Ragheb AS. Adjuvant role of lung ultrasound in the diagnosis of pneumonia in intensive care unit-patients. Egyptian Journal of Chest Diseases and Tuberculosis. 2013;62(2):281-5.
22. Fares Auf MDAA-N, M.D.; Moustafa Zedan, M.D.; Mohammad Al-Sokromi, M.Sc. Role of transthoracic ultrasound in detection of pneumonia in ICU patients. Med J Cairo Univ. 2015;83(No 1, Juni):307-14.
23. Targhetta R, Chavagneux R, Bourgeois JM, Dauzat M, Balmes P, Pourcelot L. Sonographic approach to diagnosing pulmonary consolidation. Journal of Ultrasound in Medicine. 1992;11(12):667-72.
24. Elkholy MM, Mohammad HA, Osman NM, Ibraheem B, Emam R. Accuracy of gray scale and color Doppler sonographic mapping in diagnosis of pneumonia in adult. Egyptian Journal of Chest Diseases and Tuberculosis. 2016;65(2):491-8.
25. Sperandeo M, Carnevale V, Muscarella S, Sperandeo G, Varriale A, Filabozzi P, et al. Clinical application of transthoracic ultrasonography in inpatients with pneumonia. European Journal of Clinical Investigation. 2011;41(1):1-7.
26. Alawaji OM, Yones DK, Almalki MA, Babiker RA, Awadallah MF. Value of Lung Ultrasonography for the Diagnosis of Acute Pneumonia in Emergency Department, Multicenter Study in Medina, Saudi Arabia. Indo Am J Pharm Sci. 2019;6(1):1441-50.
27. Cipollini F, Mirauta CM. Bedside lung ultrasound in the diagnosis of pneumonia in very old patients. Italian Journal of Medicine. 2018;12(2):126-30.
28. D'Amato M, Rea G, Carnevale V, Grimaldi MA, Saponara AR, Rosenthal E, et al. Assessment of thoracic ultrasound in complementary diagnosis and in follow up of community-acquired pneumonia (cap). BMC Med Imag. 2017;17(1):52.
29. Bitar ZI, Maadarani OS, El-Shably AM, Al-Ajmi MJ. Diagnostic accuracy of chest ultrasound in patients with pneumonia in the intensive care unit: A single-hospital study. Health science reports. 2019;2(1):e102.
30. Bourcier JE, Paquet J, Seinger M, Gallard E, Redonnet JP, Cheddadi F, et al. Performance comparison of lung ultrasound and chest x-ray for the diagnosis of pneumonia in the ED. American Journal of Emergency Medicine. 2014;32(2):115-8.
31. Liu XL, Lian R, Tao YK, Gu CD, Zhang GQ. Lung ultrasonography: An effective way to diagnose community-acquired pneumonia. Emergency Medicine Journal. 2015;32(6):433-8.
32. Nazerian P, Volpicelli G, Vanni S, Gigli C, Betti L, Bartolucci M, et al. Accuracy of lung ultrasound for the diagnosis of consolidations when compared to chest computed tomography. American Journal of Emergency Medicine. 2015;33(5):620-5.
33. Pagano A, Numis FG, Visone G, Pirozzi C, Masarone M, Olibet M, et al. Lung ultrasound for diagnosis of pneumonia in emergency department. Internal and emergency medicine. 2015;10(7):851-4.
34. Parlamento S, Copetti R, Di Bartolomeo S. Evaluation of lung ultrasound for the diagnosis of pneumonia in the ED. The American journal of emergency medicine. 2009;27(4):379-84.
35. Taghizadieh A, Ala A, Rahmani F, Nadi A. Diagnostic accuracy of chest x-ray and ultrasonography in detection of community acquired pneumonia; a brief report. Emergency. 2015;3(3):114-6.
36. Ticinesi A, Lauretani F, Nouvenne A, Mori G, Chiussi G, Maggio M, et al. Lung ultrasound and chest x-ray for detecting pneumonia in an acute geriatric ward. Medicine. 2016;95(27):e4153.
37. Unluer EE, Karagoz A, Senturk GO, Karaman M, Olow KH, Bayata S. Bedside lung ultrasonography for diagnosis of pneumonia. Hong Kong Journal of Emergency Medicine. 2013;20(2):98-104.
38. Amatya Y, Rupp J, Russell FM, Saunders J, Bales B, House DR. Diagnostic use of lung ultrasound compared to chest radiograph for suspected pneumonia in a resource-limited setting. International journal of emergency medicine. 2018;11(1):8.
39. Karimi E. Comparing Sensitivity of Ultrasonography and Plain Chest Radiography in Detection of Pneumonia; a Diagnostic Value Study. Archives of academic emergency medicine. 2019;7(1):e8.

40. Orso D, Guglielmo N, Copetti R. Lung ultrasound in diagnosing pneumonia in the emergency department: a systematic review and meta-analysis. European journal of emergency medicine. 2018;25(5):312-21.
41. Volpicelli GG. International evidence-based recommendations for point-of-care lung ultrasound. Intensive care medicine. 2012;38(4):577-91.
42. Andersen CA, Holden S, Vela J, Rathleff MS, Jensen MB. Point-of-Care Ultrasound in General Practice: A Systematic Review. Ann Fam Med. 2019;17(1):61-9.
43. Sorensen BA-Ohoo, Hunskaar S. Point-of-care ultrasound in primary care: a systematic review of generalist performed point-of-care ultrasound in unselected populations. (2524-8987 (Electronic)).
44. Lichtenstein DA, Lascols N, Meziere G, Gepner A. Ultrasound diagnosis of alveolar consolidation in the critically ill. Intensive Care Medicine. 2004;30(2):276-81.
45. Ultrasound TSoPoC. Guidelines for Point of Care Ultrasound Utilization in Clinical Practice 2017 [Available from: https://spocus.org/Practice-Guidelines.
46. Medicine IFfE. Point of Care Ultrasound Curriculum Guidelines 2014 [Available from: https://www.ifem.cc/wp-content/uploads/2016/03/IFEM-Point-of-Care-Ultrasound-Curriculum-Guidelines-2014.pdf.
47. Tsou P-Y, Chen KP, Wang Y-H, Fishe J, Gillon J, Lee C-C, et al. Diagnostic accuracy of lung ultrasound performed by novice versus advanced sonographers for pneumonia in children: A systematic review and meta-analysis. Academic emergency medicine. 2019.
48. Jones BP, Tay ET, Elikashvili I, Sanders JE, Paul AZ, Nelson BP, et al. Feasibility and Safety of Substituting Lung Ultrasonography for Chest Radiography When Diagnosing Pneumonia in Children: A Randomized Controlled Trial. Chest. 2016;150(1):131-8.
49. Pietersen PI, Madsen KR, Graumann O, Konge L, Nielsen BU, Laursen CB. Lung ultrasound training: a systematic review of published literature in clinical lung ultrasound training. The Ultrasound Journal. 2018;10(1):23-.
50. Olgers TJ, Azizi N, Blans MJ, Bosch FH, Gans ROB, Ter Maaten JC. Point-of-care Ultrasound (PoCUS) for the internist in Acute Medicine: a uniform curriculum. Netherlands journal of medicine. 2019;77(5):168-76.

Tables

Table 1. Diagnostic accuracy of lung ultrasonography.

Study	Setting	Reference standard	Hours or days of LUS training	Experience in LUS or US in general	Pneumonia positive (n) / Total number of patients examined for pneumonia (N)	Sensitivity (95% CI)	Specificity (95% CI)
Amatya 2018 **(38)**	ED	CT	1 hour	1 week	44/62	0.91 (0.78-0.98)[d]	0.61 (0.36-0.83)[d]
Corradi 2015 **(18)**	ED	CT	-	> 10 yrs.[a]	44[b]/62[b]	0.68 (0.52-0.81)[d]	0.95 (0.75-1.00)[d]
Fares 2015 **(22)**	ICU	CT	-	-	30/38	0.93 (0.78-0.99)[d]	0.75 (0.35-0.97)[d]
Karimi 2019 **(39)**	ED	CT	-	-	280/280	0.94 (0.90-0.96)	Not calculable
Liu 2015 **(31)**	ED	CT	28 hours	> 50 scans	112/179	0.95 (0.89-0.98)[d]	0.99 (0.92-1.00)[d]
Nazerian 2015 **(32)**	ED	CT	-	> 1 yr.	87/285	0.83 (0.73-0.90)	0.96 (0.92-0.98)
Taghizadieh 2015 **(35)**	ED	CT	-	-	29/30	1.00 (0.95-1.00)	Not calculable
Parlamento 2009 **(34)**	ED	CXR/CT	-	> 10 yrs.	32/49	0.97 (0.84-1.00)[d]	No conclusive data
Reissig 2012 **(20)**	Multicentre[c]	CXR/CT	-	> 100 scans	226/356	0.93 (0.89-0.96)	0.98 (0.89-0.96)
Unluer 2013 **(37)**	ED	CXR/CT	6 hours	-	28/72	0.96 (0.82-1.00)	0.84 (0.70-0.93)
Benci 1996 **(17)**	Department of infectious diseases	QA	-	-	37/80	1.00 (0.91-1.00)[d]	1.00 (0.92-1.00)[d]
Bitar 2018 **(29)**	ICU	QA	-	-	11/11	0.99[a]	0.80[a]
Bourcier 2014 **(30)**	ED	QA	2 days	-	123/144	0.95 (0.90-0.98)[d]	0.57 (0.34-0.78)[d]
Cipollini 2018 **(27)**	Medicine/geriatric ward	QA	-	> 1 yr.	128/128	0.82 (0.74-0.88)[d]	Not calculable
Cortellaro	ED	QA	-	-	81/120	0.99 (0.93-	0.95 (0.83-0.99)

2012 **(19)**						1.00)	
Pagano 2015 **(33)**	ED	QA	-	> 2 yrs.	68/105	0.99 (0.94-1.00)	0.65 (0.56-0.67)
Ticinesi 2016 **(36)**	Geriatric ward	QA	-	> 1 yr.	97/169	0.92 (0.86-0.97)	0.94 (0.89-0.99)

Abbreviations: LUS: Lung ultrasonography; US: Ultrasonography; ED: Emergency department; ICU: Intensive care unit; QA: Qualitative assessment; CT: Computed tomography; CXR: Chest X-ray; Yr./Yrs.: Year/Years; -: Not described.

a) Data collected by correspondence with author

b) Hemithoraxes

c) 2 University hospitals, 7 hospitals of internal medicine, 1 hospital of pulmonary medicine, 2 practices, 2 EDs

d) 95% CI calculated from true positives, false negatives, true negatives and false negatives. (Clopper-Pearson method)

Table 2. Specialty of non-specialists, experience and training in lung ultrasonography

Study	**Number of and specialty of physicians performing LUS**	**Prior experience in LUS or ultrasonography in general**	**Description of training in LUS**	**Time consumption on LUS**
Amatya 2018 **(38)**	Four emergency resident physicians	One week of performing LUS in the ED.	One hour lecture on LUS. Five pre-enrollment LUS scans and interpretation reviewed by expert sonographer.	7 min. 9 s. (SD 1 min 57 s.)
Corradi 2015 **(18)**	One intensivist with PhD in US[a]	More than 10 years of experience in LUS[a]	-	-
Fares 2015 **(22)**	A single physician.	-	-	-
Karimi 2019 **(39)**	Trained emergency residents under supervision of the attending emergency specialist in charge.	-	-	-
Liu 2015 **(31)**	Three emergency physicians.	At least 50 cases of LUS examination.	Twenty-eight hours course based on US emergency medicine guidelines issued by the American College of Emergency Physicians in 2001	-

Nazerian 2015 **(32)**	Four internal medicine and emergency medicine attending physicians. Four resident physicians (two internal medicine and two emergency medicine).	Attending physicians; at least five years of experience in POC-US. Resident physicians; at least one year of training in emergency US.	-	-
Taghizadieh 2015 **(35)**	One emergency specialist.	-	-	-
Parlamento 2009 **(34)**	One emergency physician.	Thirty years of experience in general and cardiac US and 10 years of training in LUS.	-	< 5 min.
Reissig 2012 **(20)**	Experienced physicians (number and specialty not described).	At least 100 chest US procedures done prior to study.	-	-
Unluer 2013 **(37)**	Three attending emergency physicians.	-	Three hours of didactic and three hours of hands-on thoracic US taught by an experienced radiology specialist to learn the diagnostic criteria of alveolar consolidation.	< 10 min.
Benci 1996 **(17)**	Physicians (number and specialty not described).	Considerable experience in US techniques.	-	-
Bitar 2018 **(29)**	Intensivist (number not described).	-	-	-
Bourcier 2014 **(30)**	Five emergency physicians.	-	Two days of theoretical formation alternating with practical ultrasounds sessions in groups of three people	-
Cipollini 2018 **(27)**	Internal medicine specialist[a]	More than one year of bedside US experience[a]	-	-
Cortellaro 2012 **(19)**	One expert operator.	-	-	< 5 min.
Pagano 2015 **(33)**	Five trained emergency physicians.	More than two years of experience in LUS.	-	-
Ticinesi 2016 **(36)**	Three internal and emergency medicine physicians.	More than one year of bedside US experience.	Level one of training completed according to the guidelines by the European Federation of Societies for Ultrasound in Medicine and Biology (EFSUMB)	-

Abbreviations: LUS: Lung ultrasonography; US: Ultrasonography; Min.: Minutes; S: Seconds; SD: Standard deviation; POC-US: Point-of-care ultrasonography; -: Not described

a) Data collected by correspondence with author

Table 3. Potential harms to patients.

Study	True positive LUS results, n (%)	False positive LUS results, n (%)	False negative LUS results, n (%)	True negative LUS results, n (%)	Nature of false positive LUS results
Amatya 2018 **(38)**	40 (64.5)	7 (11.3)	4 (6.5)	11 (17.7)	3 bronchiectasis, 2 interstitial lung diseases, 1 tuberculosis, 1 normal lung.
Corradi 2015 **(18)**	30[a] (46.8)	1[a] (1.6)	14[a] (22.0)	19[a] (29.6)	-
Fares 2015 **(22)**	28 (73.7)	2 (5.3)	2 (5.3)	6 (15.7)	-
Karimi 2019 **(39)**	263 (93.9)	0 (0.0)	17 (6.1)	0	-
Liu 2015 **(31)**	106 (59.2)	1 (0.6)	6 (3.4)	66 (36.8)	-
Nazerian 2015 **(32)**	72 (25.3)	9 (3.1)	15 (5.3)	189 (66.3)	3 cancers, 3 parenchymal impaired ventilation not due to infection 3 pulmonary fibrosis
Taghizadieh 2015 **(35)**	29 (96.7)	1 (3.3)	0	0	-
Parlamento	31 (63.3)	0 (0.0)	1 (2.0)	17 ((34.7)	-

2009 **(34)**					
Reissig 2012 **(20)**	211 (59.3)	3 (0.8)	15 (4.2)	127 (35.7)	-
Unluer 2013 **(37)**	27 (37.5)	7 (9.7)	1 (1.4)	37 (51.4)	4 pulmonary embolisms, 3 exacerbations of COPD.
Benci 1996 **(17)**	37 (46.3)	0 (0.0)	0 (0.0)	43 (53.7)	-
Bitar 2018 **(29)**	-	-	-	-	-
Bourcier 2014 **(30)**	117 (81.2)	9 (6.3)	6 (4.2)	12 (8.3)	4 sepsis of other origin, 2 pulmonary embolisms, 1 ARDS, 1 pulmonary fibrosis, 1 acute anemia.
Cipollini 2018 **(27)**	105 (82.0)	-	23 (18.0)	-	-
Cortellaro 2012 **(19)**	80 (66.7)	2 (1.7)	1 (0.8)	37 (30.8)	1 congestive heart failure 1 subphrenic abscess with lung atelectasia.
Pagano 2015 **(33)**	67 (63.8)	13 (12.4)	1 (1.0)	24 (22.8)	7 exacerbations of COPD 2 congestive heart failure, 3 cancers, 1 pulmonary infarction.
Ticinesi 2016 **(36)**	88 (52.1)	3 (1.8)	8 (4.7)	70 (41.2)	2 pulmonary embolisms, 1 cancer

Abbreviations: LUS: Lung ultrasonography; ND: Not described; ARDS: Acute respiratory distress syndrome; COPD: Chronic obstructive pulmonary disease; n: number

a) Hemithoraxes

Figure legends

Figure 1. PRISMA flow diagram.

Abbreviations: PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; LUS: Lung ultrasonography; Yr.: Years; VAP: Ventilator-associated pneumonia; HAP: Hospital-acquired pneumonia.

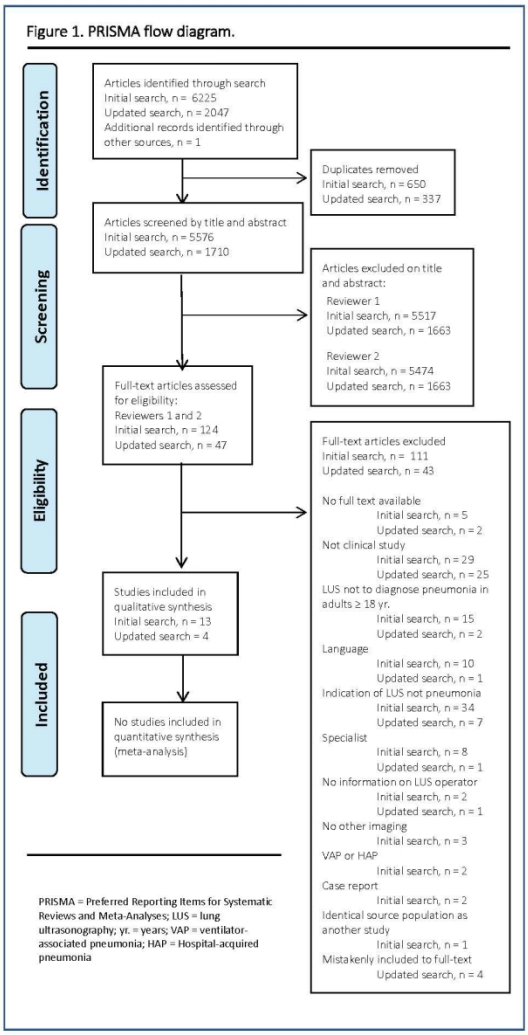

Figure 1. PRISMA flow diagram.Abbreviations: PRISMA: Preferred Reporting Items for Systematic Reviews and Meta-Analyses; LUS: Lung ultrasonography; Yr.: Years; VAP: Ventilator-associated pneumonia; HAP: Hospital-acquired pneumonia.

86x111mm (500 x 500 DPI)

Supplemental materials for:

Strøm JJ, Haugen PS, Hansen MP, Graumann O, Jensen MB, Andersen CA.

Accuracy of Lung Ultrasonography in the Hands of Non-Specialists to Diagnose and Assess the Severity of Community-Acquired Pneumonia in Adults: A Systematic Review

e-Appendix 1. Search string.

This appendix includes a full description of the literature search conducted in MEDLINE via OVID, EMBASE via OVID, CINAHL via Ebsco, Web of Science, and Cochrane Central Register of Controlled Trials (CENTRAL) on August 10th 2017 and updated on May 16th 2019. The search was conducted by the principal investigator (Julie Jepsen Strøm) and a medical librarian at the medical library at Aalborg University Hospital, Aalborg, Denmark. All databases were searched from inception date until May 16 th 2019.

Database	Interface	Number of hits 08.10.2017	Number of hits 05.16.2019
EMBASE	OVID	4255	1407
MEDLINE	OVID	958	242
Cinahl	Ebsco	99	67
Web of Science		884	320
Cochrane		29	11

Embase 08.10.2017 (updated 05.16.2019)

Interface: OVID

Search: Embase via OVID
Date: 10.08.17
Database: Embase <1974 to 2017 Week 32>
Search Strategy:
---

1 exp pneumonia/ (251394)
2 ((lung or pulmon*) adj3 inflammation*).mp. (18840)
3 inflammatory lung disease*.mp. (1603)
4 lobitis.mp. (19)
5 peripneumonia*.mp. (18)
6 pleuropneumonia*.mp. (2829)
7 (pneumonic adj3 (lung or pleuri*)).mp. (170)
8 pneumonitis.mp. (21629)
9 acute chest syndrome.mp. (2070)
10 acute respiratory syndrome.mp. (9328)

11 bronchopneumonia*.mp. (8482)
12 lung infiltrate*.mp. (11288)
13 legionnaire disease*.mp. (5515)
14 pulmonary candidiasis.mp. (259)
15 or/1-14 (271290)
16 exp animal/ (23458059)
17 exp human/ (18773067)
18 16 not 17 (4684992)
19 ((doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or
ultrasonograph* or ultrasound*) adj (chest or lung or thoracic)).mp. (415)
20 (chest or lung or thoracic).mp. (1664235)
21 exp echography/ (640345)
22 20 and 21 (85682)
23 19 or 22 (85829)
24 15 and 23 (4463)
25 24 not 18 (4386)
26 remove duplicates from 25 (4255)

MEDLINE 08.10.2017 (updated 05.16.2019)

Interface: OVID

Search: Medline via OVID
Date: 10.08.17
Database: Ovid MEDLINE(R) Epub Ahead of Print, In-Process & Other Non-Indexed Citations, Ovid MEDLINE(R) Daily and Ovid
MEDLINE(R) <1946 to Present>
Search Strategy:
---

1 exp pneumonia/ (85977)
2 pneumonia*.mp. (187473)
3 ((lung or pulmon*) adj3 inflammation*).mp. (12982)
4 inflammatory lung disease*.mp. (1145)
5 lobitis.mp. (20)
6 peripneumonia*.mp. (28)
7 pleuropneumonia*.mp. (3244)
8 (pneumonic adj3 (lung or pleuri*)).mp. (187)
9 pneumoniti*.mp. (12993)
10 acute chest syndrome.mp. (925)
11 acute respiratory syndrome.mp. (6465)
12 bronchopneumonia*.mp. (6283)
13 lung infiltrat*.mp. (1007)

14 legionnaire* disease*.mp. (5277)
15 pulmonary candidiasis.mp. (111)
16 or/1-15 (224155)
17 exp animal/ (21731287)
18 human/ (17207961)
19 17 not 18 (4523326)
20 (doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or ultrasonograph* or ultrasound*).mp. (447143)
21 (chest or lung or thoracic).mp. (1021945)
22 exp Ultrasonography/ (400320)
23 20 or 22 (568053)
24 21 and 23 (35801)
25 16 and 24 (1134)
26 25 not 19 (1019)
27 remove duplicates from 26 (958)

Cinahl 08.10.2017 (updated 05.16.2019)

Interface: Ebsco

Search: Cinahl
Date: 10.08.17
Interface - EBSCOhost Research Databases
Search Screen - Advanced Search
Database - CINAHL with Full Text

#	Query	Limiters/Expanders	Results
S21	S15 AND S20	Search modes - Boolean/Phrase	99
S20	S17 AND S19	Search modes - Boolean/Phrase	4,172
S19	S16 OR S18	Search modes - Boolean/Phrase	61,797
S18	(MH "Ultrasonography+")	Search modes - Boolean/Phrase	38,167
S17	(chest or lung or thoracic)	Search modes - Boolean/Phrase	79,460
S16	(doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or ultrasonograph* or ultrasound*)	Search modes - Boolean/Phrase	50,815

S15	S1 OR S2 OR S3 OR S4 OR S5 OR S6 OR S7 OR S8 OR S9 OR S10 OR S11 OR S12 OR S13 OR S14	Search modes - Boolean/Phrase	15,379
S14	pulmonary candidiasis	Search modes - Boolean/Phrase	2
S13	legionnaire* disease*	Search modes - Boolean/Phrase	576
S12	lung infiltrat*	Search modes - Boolean/Phrase	61
S11	bronchopneumonia*	Search modes - Boolean/Phrase	98
S10	acute respiratory syndrome	Search modes - Boolean/Phrase	1,771
S9	acute chest syndrome	Search modes - Boolean/Phrase	123
S8	pneumoniti*	Search modes - Boolean/Phrase	831
S7	(pneumonic n3 (lung or pleuri*))	Search modes - Boolean/Phrase	1
S6	pleuropneumonia*	Search modes - Boolean/Phrase	3
S5	peripneumonia*.	Search modes - Boolean/Phrase	0
S4	lobitis	Search modes - Boolean/Phrase	0
S3	inflammatory lung disease*	Search modes - Boolean/Phrase	62
S2	((lung or pulmon*) n3 inflammation*)	Search modes - Boolean/Phrase	965
S1	(MH "Pneumonia+")	Search modes - Boolean/Phrase	11,441

Web of Science 08.10.2017 (updated 05.16.2019)

Interface: Ebsco

Search: Web of Science
Date: 10.08.17

Set Results	Save History / Create Alert	Open Saved History	Edit Sets	Combine Sets AND OR	Delete Sets

# 3	884	#2 AND #1 *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=All years*	Edit
# 2	340,710	**TOPIC:** (echograph*) *OR* **TOPIC:** (ultrasonograph*) *OR* **TOPIC:** (ultrasound*) *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=All years*	Edit
# 1	118,598	**TOPIC:** (pneumonia) *OR* **TOPIC:** (pneumonitis) *OR* **TOPIC:** ("acute respiratory syndrome") *Indexes=SCI-EXPANDED, SSCI, A&HCI, CPCI-S, CPCI-SSH, ESCI* *Timespan=All years*	Edit

Cochrane 08.10.2017 (updated 05.16.2019)

Interface: Ebsco

Search: Cochrane
Date: 10.08.17
Date Run: 10/08/17 11:42:13.790
Description:

ID	Search	Hits
#1	MeSH descriptor: [Pneumonia] explode all trees	2935
#2	"lung inflammation*":ti,ab,kw (Word variations have been searched)	123
#3	"pulmon* inflammation*":ti,ab,kw (Word variations have been searched)	135
#4	"inflammatory lung disease*":ti,ab,kw (Word variations have been searched)	27
#5	lobitis:ti,ab,kw (Word variations have been searched)	0
#6	peripneumonia*:ti,ab,kw (Word variations have been searched)	0
#7	"pneumonic lung":ti,ab,kw (Word variations have been searched)	2
#8	"pneumonic pleuri*":ti,ab,kw (Word variations have been searched)	0
#9	pneumonitis:ti,ab,kw (Word variations have been searched)	715
#10	"acute chest syndrome":ti,ab,kw (Word variations have been searched)	120
#11	"acute respiratory syndrome":ti,ab,kw (Word variations have been searched)	68
#12	"bronchopneumonia*":ti,ab,kw (Word variations have been searched)	254
#13	"lung infiltrate*":ti,ab,kw (Word variations have been searched)	109
#14	"legionnaire disease*":ti,ab,kw (Word variations have been searched)	39
#15	"pulmonary candidiasis":ti,ab,kw (Word variations have been searched)	1
#16	#1 or #2 or #3 or #4 or #5 or #6 or #7 or #8 or #9 or #10 or #11 or #12 or #13 or #14 or #15	4300

#17 doptone* or echograph* or echogram* or echoscop* or echosound* or sonogram* or sonograph* or ultrasonic or ultrasonograph* or ultrasound*:ti,ab,kw (Word variations have been searched) 24916
#18 MeSH descriptor: [Ultrasonography] explode all trees 12570
#19 #17 or #18 29065
#20 chest or lung or thoracic:ti,ab,kw (Word variations have been searched) 56834
#21 #19 and #20 1597
#22 #21 and #16 29

e-Appendix 2. Data extraction template.

This appendix lists the data extraction template used in this review. The template is an adapted version of the Cochrane data extraction form (1).

General information
Date extraction completed
Name of person extracting data
Report title
Year of publication
Report ID (Author name and number)
Published in
Publication type
Study funding source
Possible conflict of interest

Eligibility
Review inclusion criteria:
Published full-text paper?
Contains original data from a clinical study?
LUS to diagnose pneumonia?
LUS performed by non-specialist?
Adults (>18 yr.)?
Verification of pneumonia by other means than LUS?
Eligibility criteria met?

Type of study

Methods

Aim of study
Design
Start date
End date
Duration of participation
Ethical approval needed/obtained for study?

Participants (patients):

Clinical suspicion of CAP?
Patients > 18 yr.?
Total no. Participants (patients)
Withdrawals and exclusions
Age
Sex
Inclusion criteria (patients)
Exclusion criteria (patients)
Methods of recruitment of participants (patients)
Severity of illness
Co-morbidities
Other relevant sociodemographics
Subgroups?
Subgroups characterisation

Intervention

LUS performed to support the diagnosis of CAP
LUS scanning procedure described?
Type of ultrasonography scanner
Verification of pneumonia by what means?
Subgroup, difference in intervention

Participants (Non-specialists)

Number of physicians performing LUS
Specialty of physician performing LUS
Training in LUS
Which type of training did the non-specialist recieve?
How many hours of training did the non-specialist receive?
Which elements did the traning consist of?
Was the training assesed?
Who assesed the training?
Was there an examination/certification at the end of training?
Experience

Age
Sex
Exclusion (physicians)
Other relevant information

Setting

Country
Location: City/rural
Location: Hospital/private clinic

Outcomes

Accuracy of LUS to diagnose CAP

Diagnostic Accuracy
Accuracy compared to what?
LUS Sensitivity
Specificity
Other imaging sensitivity

LUS to asses/predict severity

Time consumption on performing LUS

Harms to patients

Overdiagnosis and overtreatment
False positives
False negatives
Incidental findings

Applicability

Have important populations been excluded from the study?
Does the study directly address the review question?

Other information

Key conclusions by author

e-Table 1. Characteristics of studies and patients.

e-Table 1. Characteristics of studies and patients.

Study	Country	Location[a]	Study design	Number of patients	Age[b]	Men/Women	Inclusion criteria[d]
Amatya 2018 (2)	Nepal	City	Prospective cohort	62	Pneumonia: 58.5 ± 13.8. No pneumonia: 61.2 ± 16.3.	29/33	SP with at least 3 of: Temp. > 38°C, history of fever, cough, dyspnea, tachypnea (RR>20), sat. < 92%.
Benci 1996 (3)	Italy	City	Prospective cohort	80	38.5	50/30	SP on the basis of fever and respiratory signs.
Bitar 2018 (4)	Kuwait	City	Prospective cohort	11	34.0	5/6	ATS + physical examination with; Temp > 38°C or < 36°C, RR > 22/min, HR > 90 bpm., audible crackles, decreased or bronchial breath sounds, dullness to percussion, or tactile fremitus.
Bourcier 2014 (5)	France	City	Prospective cohort	144	77.6 ± 15.2	72/72	SP with at least 3 of: Temp. ≥ 38°C, cough, dyspnea, HR ≥ 100 bpm., Sat. ≤ 92%
Cipollini 2018 (6)	Italy	City	Retrospective cohort	128	84.8 (78-94)	61/67	Age ≥65 years and fever and/or respiratory symptoms. Discharged with final diagnosis of pneumonia, where CXR and LUS were performed on admission.
Corradi 2015 (7)	Italy	City	Prospective cohort	32	62 ± 19	17/15	SP on basis of: Temp. ≥ 38°C or ≤ 35°C, cough, dyspnea, heart rate > 90 bpm., tachypnea (RR>20), rales or crackles on auscultation, abnormal oxygen sat.
Cortellaro 2012 (8)	Italy	City	Prospective cohort	120	69 ± 18	77/43	ATS
Fares 2015 (9)	Egypt	City	Prospective cohort	38	61 ± 11.2	20/10[c]	ATS. ICU admission on basis of CURB65 score ≥ 3. General and local physical signs suggestive of pneumonia.
Karimi 2019 (10)	Iran	City	Prospective cohort	280	56.5 ± 19.8	160/120	Clinical symptoms of pneumonia such as cough, phlegm, shortness of breath, hemoptysis, temp. ≥ 38°C.
Liu 2015 (11)	China	City	Prospective cohort	179	71.5 (36-88)	100/79	ATS
Nazerian 2015 (12)	Italy	City	Prospective cohort	285	71 ± 14	133/152	At least 1 unexplained respiratory complaint among: cough, chest pain, hemoptysis, dyspnea for which a chest CT was ordered.
Pagano 2015 (13)	Italy	ND	Prospective cohort	105	59.0	59/46	ATS or crackles or localized absence of breath sounds on lung auscultation.
Parlamento 2009 (14)	Italy	City	Prospective cohort	49	60.9 ± 21.8	31/18	ATS.
Reissig 2012 (15)	Europe	ND	Prospective cohort	356	63.8 (19-95)	228/134	ATS or typical lung auscultation findings and able to undergo CXR in two planes.
Taghizadieh 2015 (16)	East Azerbaijan, Iran	City	Prospective cohort	30	63.8 ± 18.3	28/2	ATS.
Ticinesi 2016 (17)	Italy	City	Prospective cohort	169	83.0 ± 9.2	80/89	ATS and age ≥65 years and ≥2 chronic diseases.
Unluer 2013 (18)	China	ND	Prospective cohort	72	Men: 64.2 ± 12.4	35/37	SP on basis of dyspnea, including acute onset dyspnea or worsening of chronic dyspnea.

					Women: 68.4 ± 11.0		

a) ND: Not described.
b) Age is expressed according to data from each study as median years ± SD OR median years (range).
c) Only stated for patients positive for pneumonia.
d) SP: Suspected pneumonia; Temp: Temperature; RR: Respiratory rate; Sat: Oxygen saturation; ATS = Signs and symptoms suggestive of pneumonia according to American Thoracic Society guidelines (cough, pleuritic pain, sputum production, fever, dyspnea); HR: Heart rate; Bpm: Beats per minute; CXR: Chest X-ray; LUS: Lung ultrasonography;

e-Table 2. Procedure and characteristics of LUS.

e-Table 2. Procedure and characteristics of LUS

Study	Ultrasonography device	Areas examined	Definition of pneumonia on LUS	LUS operator blinded to reference standard
Amatya 2018 (2)	A Sonosite M Turbo (Fujifilm Sonosite, Inc.) with a curvilinear probe.	Each hemithorax divided into five areas: Two anterior, two lateral and one posterior. A total of 10 areas bilaterally.	Presence of unilateral B lines or subpleural lung consolidation.	Yes
Benci 1996 (3)	Ansaldo AU-560 with convex probe of 3.5 MHz.	Medio-lateral anterior and posterior intercostal imaging.	Presence of paranchymatous-like hypoechoic lesions indicative of alveolar pneumonia.	Unclear
Bitar 2018 (4)	GE Vivid S6N with a phased-array 5-MHz probe	Each hemithorax divided into five areas: Two anterior, two lateral and one posterior. A total of 10 areas bilaterally.	Presence of lung consolidation attaching to the pleural (subpleural) presenting tissue-like pattern or focal interstitial syndrome (focal distribution of B lines).	Yes
Bourcier 2014 (5)	Portable US device SONOSITE M TURBO with convex 3.5 MHz probe.	Examination of 8 areas of the chest wall in accordance with international guidelines (reference not reported in study)	Presence of a unilateral or bilateral alveolar-interstitial syndrome defined as disappearance of the pleural line associated with aeric or water bronchograms within an image of tissue echogenicity.	Yes
Cipollini 2018 (6)	Mindray M7 portable device using a 3.5 MHz convex probe.	A systematic examination of intercostal spaces was performed anteriorly	Presence of a hypoechoic solid area with shred margins indicative for consolidation.	Unclear
Corradi 2015 (7)	Logiq-e unit (GE Healthcare) with broadband convex-array probe at 4 MHz and high frequency linear-array probe at 10 MHz.	Each hemithorax was scanned over every intercostal space along the conventional parasternal, midclavicular, axillary, and paravertebral lines.	Presence, distribution and extent of artifacts suggestive of interstitial involvement, pleural line abnormalities and alveolar consolidation.	Yes
Cortellaro 2012 (8)	Esaote Medical Systems, 3.5-5 MHz convex probe.	Each hemithorax divided into five areas: Two anterior, two lateral and one posterior. A total of 10 areas bilaterally.	Presence of subpleural lung consolidation, presenting a tissular pattern.	Yes
Fares 2015 (9)	Sonoescape B5 with 3- to 6 MHz convex probe.	Longitudinal and oblique scans of the anterior, lateral and posterior chest wall. The probe was set perpendicular, oblique, and parallel to the ribs. A total of 12 areas bilaterally.	Presence of subpleural lung consolidation presenting as a tissular pattern, air bronchograms with or without pleural effusion.	Unclear
Karimi 2019 (10)	Samsung HM70A device with a curved 3.5 – 5 MHz probe	Each hemithorax divided into anterior (from the parasternal line to the anterior auxiliary line), lateral (between the posterior and middle auxiliary lines), and posterior (from the posterior auxiliary line to the paravertebral line).	Presence of air bronchogram, fluid bronchogram, pleural effusion, b lines (comet tail sign), or subpleural consolidation.	Yes
Liu 2015 (11)	Sonosite M-Turbo with 3.5- 5 MHz convex array probe.	Each intercostal space in the mid-clavicular line, anterior axillary line, midaxillary line, and paravertebral line, from lung apex to the diaphragm.	Presence of; 1) Consolidation, 2) Focal interstitial pattern, 3) ≥ 2 Subpleural lesions or 4) ≥ 5 Intercostal spaces with pleural-line abnormalities.	Yes
Nazerian 2015 (12)	MyLab30 Gold (Esaote) and HD7 (Philips).	Each hemithorax divided into anterior-lateral areas (extending from parasternal to posterior axillary line) and posterior areas (from the posterior axillary to paravertebral line). A total of 4 areas bilaterally.	Presence of at least one subpleural lung consolidations with tissue- like or anechoic pattern and blurred, irregular margins.	Yes
Pagano 2015 (13)	C60 Sonosite Micro Maxx with 2-5 MHz convex probe.	Each hemithorax divided into 4 areas; 1) upper anterior, 2) lower anterior, 3) upper posterior, 4) lower posterior. A total of 8 areas bilaterally.	Presence of 1) Alveolar syndrome: Image of tissue echogenicity associated with aerial bronchogram or 2) Focal interstitial syndrome: Presence of 3 or more B- lines in a single lung area.	Yes
Parlamento 2009 (14)	Megas CVX, Esaote Medical Systems, with convex 3.5-5 MHz probe.	Each hemithorax divided into 5 areas: 1) Two anterior, 2) Two lateral, 3) One posterior. A total of 10 areas bilaterally.	Presence of subpleural lung consolidation with evidence of static or dynamic air bronchograms.	Yes

Reissig 2012 (15)	Machines not reported; 5- or 3.5 MHz convex probe, occasionally 7.5 MHz linear probe.	Systematically all intercostal spaces.	Unclear definition. Number, shape and size of pneumonic lesions were reported and incidence of necrotic areas, positive air bronchogram, fluid bronchogram, and local and basal pleural effusion was reported.	Yes
Taghizadieh 2015 (16)	LOGIQ 200 (GE Healthcare) with convex 3.5 MHz probe.	Not described	Not described	Unclear
Ticinesi 2016 (17)	Acuson X300 5.0 (Siemens) with convex 2-5 MHz probe.	Each hemithorax divided into anterior-lateral areas (extending from parasternal to posterior axillary line) and posterior areas (from the posterior axillary to paravertebral line). Each area divided into upper and lower half. A total of 8 areas bilaterally.	Presence of tissue-like echogenicity associated with dynamic air bronchograms, defined as punctiform or linear hyperechoic artifacts with centrifugal inspiratory dynamicity.	Yes
Unluer 2013 (18)	M7 model ultrasound machine with 3.6 MHz microconvex probe.	Each hemithorax divided into four areas (upper, anterior, lower, lateral and posterior) and four points (two in the anterior zone, one lateral and one posterior). A total of 8 areas bilaterally.	Presence of alveolar consolidation defined as: 1) A tissue-like pattern with regular trabeculations reminiscent of the liver, 2) Demonstration of the shred sign in longitudinal view with an uneven surface of the lung line, 3) Detection of unilateral localized B lines based on the BLUE protocol.	Yes

e-Table 3. QUADAS-2 quality assessment.

This e-table lists the Quality Assessment of Diagnostic Accuracy Studies 2 (QUADAS-2). Each domain is represented in a bar with the proportion of studies considered high risk (red), low risk (green), or unclear (yellow). The same applies to applicability concerns.

e-Table 3. QUADAS-2 quality assessment.							
Study	Risk of bias				Concerns about applicability		
	Patient selection	Index test	Reference standard	Flow and timing	Patient selection	Index test	Reference standard
Amatya 2018 (2)	+	+	+	+	+	+	+
Benci 1996 (3)	?	?	?	-	+	?	+
Bitar 2018 (4)	+	+	?	-	?	+	+
Bourcier 2014 (5)	+	+	?	-	+	+	+
Cipollini 2018 (6)	?	?	?	-	+	+	+
Corradi 2015 (7)	-	+	+	+	-	+	+
Cortellaro 2012 (8)	+	+	+	+	+	?	+
Fares 2015 (9)	+	?	?	-	+	?	+
Karimi 2019 (10)	-	+	+	+	+	+	+
Liu 2015 (11)	+	+	+	+	+	+	+
Nazerian 2015 (12)	-	+	+	+	-	+	+
Pagano 2015 (13)	+	+	+	?	+	+	+
Parlamento 2009 (14)	+	+	+	-	+	+	+
Reissig 2012 (15)	+	+	+	-	+	?	+
Taghizadieh 2015 (16)	-	-	+	+	+	?	+
Ticinesi 2016 (17)	-	+	+	-	+	+	+
Unluer 2013 (18)	-	+	+	-	+	+	+

References

1. Sambunjak D CM, Watts C. Module 4: Selecting studies and collecting data. *Cochrane Interactive Learning: Conducting an Intervention Review*. Oxford: Cochrane; 2017 [Available from: https://training.cochrane.org/interactivelearning/module-4-selecting-studies-and-collecting-data.

2. Amatya Y, Rupp J, Russell FM, Saunders J, Bales B, House DR. Diagnostic use of lung ultrasound compared to chest radiograph for suspected pneumonia in a resource-limited setting. *Int J Emerg Med*. 2018;11(1):8.

3. Benci A, Caremani M, Menchetti D, Magnolfi A. Sonographic diagnosis of pneumonia and bronchopneumonia. *European Journal of Ultrasound* [Internet]. 1996; 4(3):[169-76 pp.]. Available from: http://onlinelibrary.wiley.com/o/cochrane/clcentral/articles/916/CN-00168916/frame.html.

4. Bitar ZI, Maadarani OS, El-Shably AM, Al-Ajmi MJ. Diagnostic accuracy of chest ultrasound in patients with pneumonia in the intensive care unit: a single-hospital study. *Health Science Reports*. 2019;2(1):e102.
5. Bourcier JE, Paquet J, Seinger M, Gallard E, Redonnet JP, Cheddadi F, et al. Performance comparison of lung ultrasound and chest x-ray for the diagnosis of pneumonia in the ED. *Am J Emerg Med*. 2014;32(2):115-8.
6. Cipollini F, Mirauta CM. Bedside lung ultrasound in the diagnosis of pneumonia in very old patients. *Italian Journal of Medicine*. 2018;12(2):126-30.
7. Corradi F, Brusasco C, Garlaschi A, Paparo F, Ball L, Santori G, et al. Quantitative analysis of lung ultrasonography for the detection of community-acquired pneumonia: a pilot study. *BioMed Research International*. 2015;2015:no pagination.
8. Cortellaro F, Colombo S, Coen D, Duca PG. Lung ultrasound is an accurate diagnostic tool for the diagnosis of pneumonia in the emergency department. *Emergency Medicine Journal*. 2012;29(1):19-23.
9. Fares Auf MDAA-N, M.D.; Moustafa Zedan, M.D.; Mohammad Al-Sokromi, M.Sc. Role of transthoracic ultrasound in detection of pneumonia in ICU patients. *Medical Journal of Cairo University*. 2015;83(No 1, Juni):307-14.
10. Karimi E. Comparing sensitivity of ultrasonography and plain chest radiography in detection of pneumonia; a diagnostic value study. *Archives of Academic Emergency Medicine*. 2019;7(1):e8.
11. Liu X-l, Lian R, Tao Y-k, Gu C-d, Zhang G-q. Lung ultrasonography: an effective way to diagnose community-acquired pneumonia. *Emergency Medicine Journal*. 2015;32(6):433-8.
12. Nazerian P, Volpicelli G, Vanni S, Gigli C, Betti L, Bartolucci M, et al. Accuracy of lung ultrasound for the diagnosis of consolidations when compared to chest computed tomography. *Am J Emerg Med*. 2015;33(5):620-5.
13. Pagano A, Numis FG, Visone G, Pirozzi C, Masarone M, Olibet M, et al. Lung ultrasound for diagnosis of pneumonia in emergency department. *Internal and Emergency Medicine*. 2015;10(7):851-4.
14. Parlamento S, Copetti R, Di Bartolomeo S. Evaluation of lung ultrasound for the diagnosis of pneumonia in the ED. *Am J Emerg Med*. 2009;27(4):379-84.
15. Reissig A, Copetti R, Mathis G, Mempel C, Schuler A, Zechner P, et al. Lung ultrasound in the diagnosis and follow-up of community-acquired pneumonia: a prospective, multicenter, diagnostic accuracy study. *Chest*. 2012;142(4):965-72.
16. Taghizadieh A, Ala A, Rahmani F, Nadi A. Diagnostic accuracy of chest x-ray and ultrasonography in detection of community acquired pneumonia; a brief report. *Emergency*. 2015;3(3):114-6.
17. Ticinesi A, Lauretani F, Nouvenne A, Mori G, Chiussi G, Maggio M, et al. Lung ultrasound and chest x-ray for detecting pneumonia in an acute geriatric ward. *Medicine*. 2016;95(27):e4153.
18. Unluer EE, Karagoz A, Senturk GO, Karaman M, Olow KH, Bayata S. Bedside lung ultrasonography for diagnosis of pneumonia. *Hong Kong Journal of Emergency Medicine*. 2013;20(2):98-104.

PRISMA 2009 Checklist

Section/topic	#	Checklist item	Reported on page #
TITLE			
Title	1	Identify the report as a systematic review, meta-analysis, or both.	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Objectives	4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	3
METHODS			
Protocol and registration	5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address), and, if available, provide registration information including registration number.	4
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale.	4
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	4
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	e-appendix 1
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	4
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	4
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	4
Risk of bias in individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	4
Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means).	N/A

PRISMA 2009 Checklist

Synthesis of results	14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I^2) for each meta-analysis.	N/A

Section/topic	#	Checklist item	Reported on page #
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	4
Additional analyses	16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	N/A
RESULTS			
Study selection	17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	5
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment (see item 12).	5
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: (a) simple summary data for each intervention group (b) effect estimates and confidence intervals, ideally with a forest plot.	5-6
Synthesis of results	21	Present results of each meta-analysis done, including confidence intervals and measures of consistency.	N/A
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies (see Item 15).	5
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy makers).	7
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review-level (e.g., incomplete retrieval of identified research, reporting bias).	8
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	8
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review.	1

From: Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group (2009). Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement. PLoS Med 6(7): e1000097. doi:10.1371/journal.pmed1000097

PRISMA 2009 Checklist

The PRISMA for Abstracts Checklist

TITLE	CHECKLIST ITEM	REPORTED ON PAGE #
1. Title:	Identify the report as a systematic review, meta-analysis, or both.	1
BACKGROUND		
2. Objectives:	The research question including components such as participants, interventions, comparators, and outcomes.	2
METHODS		
3. Eligibility criteria:	Study and report characteristics used as criteria for inclusion.	2
4. Information sources:	Key databases searched and search dates.	2
5. Risk of bias:	Methods of assessing risk of bias.	2
RESULTS		
6. Included studies:	Number and type of included studies and participants and relevant characteristics of studies.	2
7. Synthesis of results:	Results for main outcomes (benefits and harms), preferably indicating the number of studies and participants for each. If meta-analysis was done, include summary measures and confidence intervals.	2
8. Description of the effect:	Direction of the effect (i.e. which group is favoured) and size of the effect in terms meaningful to clinicians and patients.	2
DISCUSSION		
9. Strengths and Limitations of evidence:	Brief summary of strengths and limitations of evidence (e.g. inconsistency, imprecision, indirectness, or risk of bias, other supporting or conflicting evidence)	2
10. Interpretation:	General interpretation of the results and important implications	2
OTHER		
11. Funding:	Primary source of funding for the review.	1
12. Registration:	Registration number and registry name.	2