

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 16th 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		Edi	Combine	Delet
Results	Save History / Create Alert	Open Saved History	t	Sets
			Set	e Sets
			AND	O
			s	R

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

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 receive?
How many hours of training did the non-specialist receive?
Which elements did the training consist of?
Was the training assessed?
Who assessed 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 assess/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 axillary line), lateral (between the posterior and middle axillary lines), and posterior (from the posterior axillary 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

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