Supplement 1

Summary of Searches - SR:

Total No. Retrieved:		**1915**	
	Medline:	254	
	Embase:	367	
	Cochrane Library:	1294	
Duplicates:		163	
No. Total without duplicates**:**		**1752**	ENDNOTE FILE READY
Screening (Title and Abstract Review)			
No. Excluded:			
Included for Full Text review:			
Selection (Full Text Review)			
No. Excluded:			
Reasons for exclusions:			
1.			

Summary of Searches – Not SR :

Total No. Retrieved:		**17160**	
	Medline:	8558	
	Embase:	8592	
	Cochrane Library:	--	
Duplicates:			
No. Total without duplicates**:**			
Screening (Title and Abstract Review)			
No. Excluded:			
Included for Full Text review:			
Selection (Full Text Review)			
No. Excluded:			
Reasons for exclusions:			
1.			

Guideline Question: GENERAL SEARCH FOR ALL QUESTIONS (BUT Cancer Screening)
Medline
z – GL10 – SR - General_Medline

z – GL10 – General_ not SR_Medline

OVERVIEW	
Interface:	Ovid
Database:	Ovid MEDLINE(R) In-Process & Other Non-Indexed Citations and Ovid MEDLINE(R) 1946 to Present
Date of Search:	May 9th, 2016
Study Types:	Systematic reviews;
Limits:	Publication date: not limits

Search Strategy: search terms (number of results)

Any Dx intervention (CTPA, CUS, D-dimer, VQ)

1 ultrasonography/ or ultrasonography, doppler/ (77097)

2 (ultrasound$ or ultrason$ or sonograph$).mp. (365834)

3 or/1-2 (365834)

4 Fibrin Fibrinogen Degradation Products/ (7338)

5 (D-dimer or d dimer).mp. (7096)

6 (label$ adj2 (fibrogen or fibrinogen)).mp. (631)

7 4 or 5 or 6 (11390)

8 exp Cone-Beam Computed Tomography/ (5051)

9 Tomography, Spiral Computed/ (6878)

10 Tomography, X-Ray Computed/ (317079)

11 (compute* tomograph* or compute*-tomograph*).mp. (222821)

12 or/8-11 (431702)

13 exp Ventilation-Perfusion Ratio/ (5575)

14 (lung adj1 (ventilation or perfusion)).ti,ab,kw. (5817)

15 (lung adj ventilation adj scan).ti,ab,kw. (1)

16 (lung adj perfusion adj scan).ti,ab,kw. (146)

17 (lung adj1 scan).ti,ab,kw. (1081)

18 VQ scan.mp. (25)

19 13 or 14 or 15 or 16 or 17 or 18 (11400)

20 3 or 7 or 12 or 19 (773789)

VTE terms:

21 exp Thromboembolism/ or exp Venous Thromboembolism/ (47568)

22 exp Pulmonary Embolism/ (33893)

23 exp Venous Thrombosis/ (48320)

24 Thrombophlebitis/ (21375)

25 (DVT or VTE or PE).mp. (39840)

26 ((Pulmon$ or vein or venous or lung) adj (Emboli$ or thromb$)).mp. (92654)

27 (thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or embol*).mp. (326912)

28 (((deep or thromb* or stasis) adj2 (vein* or venous)) or (blood flow stasis or blood clot)).mp. (67667)

29 or/21-28 (368661)

Dx filter:

30 exp "Sensitivity and Specificity"/ (469183)

31 (sensitivity or specificity).tw. (809446)

32 (predictive adj3 value$).tw. (81055)

33 exp diagnostic errors/ (101771)

34 ((false adj positiv$) or (false adj negativ$)).tw. (62229)

35 (observer adj variation$).tw. (1026)

36 (roc adj curve$).tw. (18740)

37 (likelihood adj3 ratio$).tw. (11054)

38 likelihood functions/ (18752)

39 *Thromboembolism/di, ra, ri, us (798)

40 *Thrombophlebitis/di, ra, ri, us (3026)

41 *Venous Thrombosis/di, ra, ri, us (3030)

42 or/30-41 (1283612)

43 20 and 29 and 42 (8812) → Annotation: Any Dx and VTE AND DxFilter

SR filter:

44 meta-analysis/ (65208)

45 meta-analysis as topic/ (14831)

46 (meta analy* or metanaly* or metaanaly*).ti,ab. (90932)

47 (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. (30721)

48 ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. (105255)

49 (search strategy or search criteria or systematic search or study selection or data extraction).ab. (33398)

50 (search* adj4 literature).ab. (37180)

51 (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. (119376)

52 ((pool* or combined) adj2 (data or trials or studies or results)).ab. (38566)

53 cochrane.jw. (12302)

54 or/44-53 (287349)

55 animals/ not humans/ (4203767)

56 exp Animals, Laboratory/ (770845)

57 exp Animal Experimentation/ (7910)

58 exp Models, Animal/ (464566)

59 exp Rodentia/ (2869455)

60 (rat or rats or mouse or mice).ti. (1189636)

61 or/55-60 (4963714)

62 54 not 61 (274387)

63 43 and 62 (254) → Annotation: (Any Dxinterv + VTE + DxFilter Not animal) and SR Filter

64 43 not 63 (8558) → (Any Dxinterv + VTE + DxFilter Not animal) (not in previous SR)

Records Retrieved:

1- SR = 254

2- Others= 8558

Embase

z - GL10 - General _SR _Embase
z - GL10 - General _Not SR _Embase

OVERVIEW	
Interface:	Ovid
Database:	Embase 1974 to 2016 Week 07
Date of Search:	May 9th, 2016
Study Types:	Systematic reviews;
Limits:	Publication date: not limited

Search Strategy: search terms (number of results)

Any Dx intervention (CTPA, CUS, D-dimer, VQ)

1 ultrasonography/ or ultrasonography, doppler/ (195494)

2 (ultrasound$ or ultrason$ or sonograph$).mp. (479288)

3 1 or 2 (554916)

4 fibrin degradation product/ (3142)

5 D dimer/ (13156)

6 (D-dimer or d dimer).mp. (16014)

7 (label$ adj2 (fibrogen or fibrinogen)).mp. (557)

8 4 or 5 or 6 or 7 (18440)

9 exp cone beam computed tomography/ (8539)

10 spiral computer assisted tomography/ (10925)

11 computer assisted tomography/ (580883)

12 (compute* tomograph* or compute*-tomograph*).mp. (360312)

13 or/9-12 (744247)

14 exp lung scintiscanning/ (6764)

15 exp Ventilation-Perfusion Ratio/ (6101)

16 (lung adj1 (ventilation or perfusion)).ti,ab,kw. (7981)

17 (lung adj ventilation adj scan).ti,ab,kw. (3)

18 (lung adj perfusion adj scan).ti,ab,kw. (218)

19 (lung adj1 scan).ti,ab,kw. (1348)

20 VQ scan.mp. (105)

21 14 or 15 or 16 or 17 or 18 or 19 or 20 (18644)

22 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 or 16 or 17 or 18 or 19 or 20 or 21 (1239511)→Annotation: in - Any Dx intervention_Embase

VTE terms:

23 exp vein thrombosis/ (100825)

24 exp Venous Thromboembolism/ (111295)

25 exp 'lung embolism'/ (70029)

26 Thrombophlebitis/ (16025)

27 (PE or DVT or VTE).mp. (62340)

28 ((Pulmon$ or vein or venous or lung) adj (Emboli$ or thromb$)).mp. (166579)

29 (thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or embol*).mp. (527773)

30 (((deep or thromb* or stasis) adj2 (vein* or venous)) or (blood flow stasis or blood clot)).mp. (158324)

31 or/23-30 (597688)

32 exp "sensitivity and specificity"/ (245520)

33 (sensitivity or specificity).tw. (958912)

34 (predictive adj3 value$).tw. (114518)

35 ((false adj positiv$) or (false adj negativ$)).tw. (77829)

36 (observer adj variation$).tw. (1345)

37 (roc adj curve$).tw. (33158)

38 (likelihood adj3 ratio$).tw. (14400)

39 *Diagnostic Accuracy/ (6352)

40 *Thromboembolism/di (2018)

41 *Thrombophlebitis/di (1624)

42 *Venous Thrombosis/di (926)

43 32 or 33 or 34 or 35 or 36 or 37 or 38 or 39 or 40 or 41 or 42 (1192770)

44 22 and 31 and 43 (8959) → Annotation: (Any Dx intervention + VTE + DxFilter)

SR filter:

45 systematic review/ (105938)

46 meta-analysis/ (108354)

47 (meta analy* or metanaly* or metaanaly*).ti,ab. (119945)

48 (reference list* or bibliograph* or hand search* or manual search* or relevant journals).ab. (35710)

49 ((systematic* or evidence*) adj2 (review* or overview*)).ti,ab. (129874)

50 (search strategy or search criteria or systematic search or study selection or data extraction).ab. (38947)

51 (search* adj4 literature).ab. (46763)

52 (medline or pubmed or cochrane or embase or psychlit or psyclit or psychinfo or psycinfo or cinahl or science citation index or bids or cancerlit).ab. (147674)

53 ((pool* or combined) adj2 (data or trials or studies or results)).ab. (49701)

54 cochrane.jw. (13184)

55 or/45-54 (384419)

56 animals/ not humans/ (1150971)

57 nonhuman/ (4742930)

58 exp Animal Experiment/ (1824805)

59 exp Experimental Animal/ (508398)

60 animal model/ (868145)

61 exp Rodent/ (3009466)

62 (rat or rats or mouse or mice).ti. (1283287)

63 56 or 57 or 58 or 59 or 60 or 61 or 62 (6713559)

64 55 not 63 (347559)

65 44 and 64 (367) → Annotation: (Any Dx intervention + VTE + DxFilter) and SR filter not animal

66 44 not 65 (8592) → Annotation: (Any Dx intervention + VTE + DxFilter) not SR

Records Retrieved:
1. And SR filter=367
2. And RCT filter (not in previous 367)=8592

Cochrane Library z – GL10-General_

OVERVIEW

Interface:	Cochrane Library
Database:	Cochrane Database of Systematic Reviews
Date of Search:	Month X, 2016
Study Types:	Systematic reviews;
Limits:	Publication date:

Search Strategy: search terms (number of results)

Any Dx intervention (CTPA, CUS, D-dimer, VQ)

#1 MeSH descriptor: [Ultrasonography] this term only 940
#2 MeSH descriptor: [Ultrasonography, Doppler] this term only 542
#3 (ultrasound* or ultrason* or sonograph*) 24608
#4 #1 or #2 or #3 24608
#5 MeSH descriptor: [Ventilation-Perfusion Ratio] explode all trees 132
#6 (lung near/1 (ventilation or perfusion)):ti,ab,kw 1068
#7 (lung near ventilation near scan):ti,ab,kw 19
#8 (lung near perfusion near scan):ti,ab,kw 42
#9 (lung near/1 scan):ti,ab,kw 66
#10 (VQ scan) 11
#11 #5 or #6 or #7 or #8 or #9 or #10 1218
#12 MeSH descriptor: [Fibrin Fibrinogen Degradation Products] this term only 488
#13 (D-dimer or d dimer) 1190
#14 (label* near/2 (fibrogen or fibrinogen)) 63
#15 #12 or #13 or #14 1400
#16 MeSH descriptor: [Tomography, X-Ray Computed] this term only 4171
#17 MeSH descriptor: [Cone-Beam Computed Tomography] explode all trees 139
#18 MeSH descriptor: [Tomography, Spiral Computed] this term only 215
#19 (compute* tomograph* or compute*-tomograph*) 13501
#20 (CT or CAT or CAPT):ti,ab 10276
#21 #16 or #17 or #18 or #19 or #20 18898
#22 #4 or #11 or #15 or 21 130946

VTE terms:

#23 MeSH descriptor: [Venous Thrombosis] explode all trees 2448
#24 MeSH descriptor: [Thromboembolism] explode all trees 1892
#25 MeSH descriptor: [Venous Thromboembolism] explode all trees 513
#26 MeSH descriptor: [Pulmonary Embolism] explode all trees 982
#27 MeSH descriptor: [Thrombophlebitis] this term only 1095
#28 (DVT or VTE or PE) 9108
#29 ((Pulmon* or vein or venous or lung) near (Emboli* or thromb*)) 9413
#30 (Thrombus* or thrombotic* or thrombolic* or thromboemboli* or thrombos* or embol*) 22668
#31 (((deep or thromb* or stasis) near/2 (vein* or venous)) or (blood flow stasis or blood clot)) 8726
#32 #23 or #24 or #25 or #26 or #27 or #28 or #29 or #30 or #31 30977

#33 #22 and #32 7717 → Any Dx Intervention AND VTE

Dx filter:

#34 MeSH descriptor: [Sensitivity and Specificity] explode all trees 17846
#35 (sensitivity or specificity) 59020

#36 (predictive adj3 value$) 157
#37 MeSH descriptor: [Diagnostic Errors] explode all trees 2854
#38 (false adj positiv*) or (false adj negativ*) 202
#39 (observer adj variation*) 263
#40 (roc adj curve*) 43
#41 (likelihood adj3 ratio*) 638
#42 MeSH descriptor: [Likelihood Functions] explode all trees 393
#43 MeSH descriptor: [Thromboembolism] explode all trees and with qualifier(s): [Diagnosis - DI, Radiography - RA, Radionuclide imaging - RI, Ultrasonography - US] 229
#44 MeSH descriptor: [Thrombophlebitis] explode all trees and with qualifier(s): [Diagnosis - DI, Radiography - RA, Radionuclide imaging - RI, Ultrasonography - US] 260
#45 MeSH descriptor: [Venous Thrombosis] explode all trees and with qualifier(s): [Diagnosis - DI, Radiography - RA, Radionuclide imaging - RI, Ultrasonography - US] 537
#46 #34 or #35 or #36 or #37 or #38 or #39 or #40 or #41 or #42 or #43 or #44 or #45 67078

#47 #33 and #46 Publication Year from 2006 to 2016 1935→ Any Dx and VTE and Dxfilter → z – GL10-General_

All Results (1935)
Cochrane Reviews (1443)
All
Review (1206) endnote
Protocol
Other Reviews (87) endnote
Trials (342) endnote
Methods Studies (2)
Technology Assessments (1) endnote
Economic Evaluations (48)
Cochrane Groups (12)

Records Retrieved: 1294
Cochrane reviews: 1206
Other reviews: 87
Technology Assessments (1)

Supplement 2. Evidence profiles for intermediate-risk and high-risk patients with suspected lower extremity deep vein thrombosis

Intermediate risk (25% and 35%)

Table S1. Proximal Compression ultrasound test accuracy in intermediate-risk patients
Click link for interactive summary of findings (iSoF) table.
Patient or population: Patients with suspected lower extremity deep vein thrombosis
New test: Proximal CUS
Setting: Inpatient and outpatient
Pooled sensitivity: 0.90 (95% CI: 0.87 to 0.93) | **Pooled specificity:** 0.99 (95% CI: 0.98 to 0.99)

Test result	Number of results per 1,000 patients tested (95% CI)		Number of participants (studies)	Quality of the Evidence (GRADE)
	Prevalence **25%**[1,2] in intermediate-risk patients with suspected LE DVT	Prevalence **35%**[1,2] in intermediate-risk patients with suspected LE DVT		
True positives	**225** (218 to 233)	**315** (305 to 326)	2889 (12)	⊕⊕⊕⊕ **HIGH** [a,b,c]
False negatives	**25** (17 to 32)	**35** (24 to 45)		
True negatives	**742** (735 to 742)	**644** (637 to 644)	2889 (12)	⊕⊕⊕⊕ **HIGH** [a,b,c]
False positives	**8** (7 to 15)	**6** (6 to 13)		
Inconclusive test results	19		2908 (12)	-
Complications arising from the diagnostic test	Not reported			

CI: Confidence interval
[1]Fancher T et al. BMJ 2004; 329(7470):821. Clinical PTP and rapid D-dimer testing; mean prevalence of DVT in accuracy studies 11%; mean prevalence of DVT in management studies 25%
[2]Disease prevalence applies to the index test in each pathway. Prevalence applied to the accuracy of each subsequent test depends on the result of the previous test in the pathway.
Explanations
a. Certainty of evidence not downgraded for risk of bias, although few studies had a combination of reference standards that were judged to be acceptable by the panel.
b. Minor inconsistency for sensitivity noted but judged to be insufficient to downgrade the certainty of evidence. Minor inconsistency for specificity noted but judged to be insufficient to downgrade the certainty of evidence.
c. Certainty of evidence was downgraded for indirectness in instances where this test was not the index test in a diagnostic pathway. There was a lack of data on the accuracy of this test following a previous test in a pathway. Thus, sensitivity and specificity used for modeling in these instances were based on the test accuracy of the individual test rather than using the test in a pathway.

Table S2. Whole leg ultrasound test accuracy in intermediate-risk patients

Click link for interactive summary of findings (iSoF) table. **Patient or population:** Patients with suspected lower extremity deep vein thrombosis

New test: Whole Leg US

Setting: Inpatient and outpatient

Pooled sensitivity: 0.94 (95% CI: 0.91 to 0.96) | **Pooled specificity:** 0.97 (95% CI: 0.95 to 0.99)

Test result	Number of results per 1,000 patients tested (95% CI)		Number of participants (studies)	Quality of the Evidence (GRADE)
	Prevalence **25%**[1,2] in intermediate-risk patients with suspected LE DVT	Prevalence **35%**[1,2] in intermediate-risk patients with suspected LE DVT		
True positives	**235** (228 to 240)	**329** (320 to 336)	1725 (10)	⊕⊕⊕⊕ **HIGH** [a,b,c]
False negatives	**15** (10 to 22)	**21** (14 to 30)		
True negatives	**730** (711 to 740)	**632** (616 to 641)	1725 (10)	⊕⊕⊕⊕ **HIGH** [a,b,c]
False positives	**20** (10 to 39)	**18** (9 to 34)		
Inconclusive test results	8		1733 (10)	
Complications arising from the diagnostic test	Not reported			

CI: Confidence interval

[1]Fancher T et al. BMJ 2004; 329(7470):821. Clinical PTP and rapid D-dimer testing; mean prevalence of DVT in accuracy studies 11%; mean prevalence of DVT in management studies 25%

[2]Disease prevalence applies to the index test in each pathway. Prevalence applied to the accuracy of each subsequent test depends on the result of the previous test in the pathway.

Explanations

a. Certainty of evidence not downgraded for risk of bias, although few studies had a combination of reference standards that were judged to be acceptable by the panel.

b. Minor inconsistency for sensitivity noted but judged to be insufficient to downgrade the certainty of evidence. Minor inconsistency for specificity noted but judged to be insufficient to downgrade the certainty of evidence.

c. Certainty of evidence was downgraded for indirectness in instances where this test was not the index test in a diagnostic pathway. There was a lack of data on the accuracy of this test following a previous test in a pathway. Thus, sensitivity and specificity used for modeling in these instances were based on the test accuracy of the individual test rather than using the test in a pathway.

Table S3. Serial ultrasound test accuracy in intermediate-risk patients

Click link for interactive summary of findings (iSoF) table

Patient or population: Patients with suspected lower extremity deep vein thrombosis

New test: Serial US

Setting: Inpatient and outpatient

Pooled sensitivity: 0.98 (95% CI: 0.96 to 0.99) | **Pooled specificity:** 0.998 (95% CI: 0.993 to 0.999)

Test result	Number of results per 1,000 patients tested (95% CI)		Number of participants (studies)	Quality of the Evidence (GRADE)
	Prevalence **25%**[1,2] in intermediate-risk patients with suspected LE DVT	Prevalence **35%**[1,2] in intermediate-risk patients with suspected LE DVT		
True positives	**245** (240 to 248)	**343** (336 to 347)	2415 (6)	⨁⨁⨁⨁ **HIGH** [a,b,c]
False negatives	**5** (2 to 10)	**7** (3 to 14)		
True negatives	**749** (745 to 749)	**649** (645 to 649)	2415 (6)	⨁⨁⨁⨁ **HIGH** [a,b,c]
False positives	**1** (1 to 5)	**1** (1 to 5)		
Inconclusive test results	0		2415 (6)	
Complications arising from the diagnostic test	Not reported			

CI: Confidence interval

[1]Fancher T et al. BMJ 2004; 329(7470):821. Clinical PTP and rapid D-dimer testing; mean prevalence of DVT in accuracy studies 11%; mean prevalence of DVT in management studies 25%

[2]Disease prevalence applies to the index test in each pathway. Prevalence applied to the accuracy of each subsequent test depends on the result of the previous test in the pathway.

Explanations

a. Certainty of evidence not downgraded for risk of bias, although few studies had a combination of reference standards that were judged to be acceptable by the panel.

b. Minor inconsistency for sensitivity noted but judged to be insufficient to downgrade the certainty of evidence. Minor inconsistency for specificity noted but judged to be insufficient to downgrade the certainty of evidence.

c. Certainty of evidence was downgraded for indirectness in instances where this test was not the index test in a diagnostic pathway. There was a lack of data on the accuracy of this test following a previous test in a pathway. Thus, sensitivity and specificity used for modeling in these instances were based on the test accuracy of the individual test rather than using the test in a pathway.

Table S4. D-dimer test accuracy in intermediate-risk patients

Click link for interactive summary of findings (iSoF) table. **Patient or population:** Patients with suspected lower extremity deep vein thrombosis
New test: D-dimer
Setting: Inpatient and outpatient
Pooled sensitivity: 0.96 (95% CI: 0.93 to 0.98) | **Pooled specificity:** 0.36 (95% CI: 0.29 to 0.42)

Test result	Number of results per 1,000 patients tested (95% CI)		Number of participants (studies)	Quality of the Evidence (GRADE)
	Prevalence **25%**[1,2] in intermediate-risk patients with suspected LE DVT	Prevalence **35%**[1,2] in intermediate-risk patients with suspected LE DVT		
True positives	**240** (233 to 245)	**336** (326 to 343)	5253 (16)	⊕⊕⊕◯ **MODERATE** a,b,c
False negatives	**10** (5 to 17)	**14** (7 to 24)		
True negatives	**270** (217 to 315)	**234** (189 to 273)	5253 (16)	⊕⊕⊕◯ **MODERATE** a,b,c
False positives	**480** (435 to 533)	**416** (377 to 461)		
Inconclusive test results	Not applicable		5253 (16)	
Complications arising from the diagnostic test	Not reported			

CI: Confidence interval

[1]Fancher T et al. BMJ 2004; 329(7470):821. Clinical PTP and rapid D-dimer testing; mean prevalence of DVT in accuracy studies 11%; mean prevalence of DVT in management studies 25%

[2]Disease prevalence applies to the index test in each pathway. Prevalence applied to the accuracy of each subsequent test depends on the result of the previous test in the pathway.

Explanations

a. Certainty of evidence not downgraded for risk of bias, although few studies had a combination of reference standards that were judged to be acceptable by the panel.

b. Minor inconsistency for sensitivity noted but judged to be insufficient to downgrade the certainty of evidence. Certainty of evidence was downgraded for serious unexplained inconsistency in specificity, with a range from 5.2% to 59.6%.

c. Certainty of evidence was downgraded for indirectness in instances where this test was not the index test in a diagnostic pathway. There was a lack of data on the accuracy of this test following a previous test in a pathway. Thus, sensitivity and specificity used for modeling in these instances were based on the test accuracy of the individual test rather than using the test in a pathway.

High risk (50% and 75%)

Table S5. Proximal compression ultrasound test accuracy in high prevalence population
Click link for interactive summary of findings (iSoF) table.
Patient or population: Patients with suspected lower extremity deep vein thrombosis
New test: Proximal CUS
Setting: Inpatient and outpatient
Pooled sensitivity: 0.90 (95% CI: 0.87 to 0.93) | **Pooled specificity:** 0.99 (95% CI: 0.98 to 0.99)

Test result	Number of results per 1,000 patients tested (95% CI)		Number of participants (studies)	Quality of the Evidence (GRADE)
	Prevalence **50%**[1,2] in patients with suspected LE DVT	Prevalence **75%**[1,2] in patients with suspected LE DVT		
True positives	**450** (435 to 465)	**675** (653 to 698)	2889 (12)	⊕⊕⊕⊕ **HIGH** [a,b,c]
False negatives	**50** (35 to 65)	**75** (52 to 97)		
True negatives	**495** (490 to 495)	**248** (245 to 248)	2889 (12)	⊕⊕⊕⊕ **HIGH** [a,b,c]
False positives	**5** (5 to 10)	**2** (2 to 5)		
Inconclusive test results	19		2908 (12)	-
Complications arising from the diagnostic test	Not reported			

CI: Confidence interval
[1]Fancher T et al. BMJ 2004; 329(7470):821. Clinical PTP and rapid D-dimer testing; mean prevalence of DVT in accuracy studies 11%; mean prevalence of DVT in management studies 25%
[2]Disease prevalence applies to the index test in each pathway. Prevalence applied to the accuracy of each subsequent test depends on the result of the previous test in the pathway.
Explanations
a. Certainty of evidence not downgraded for risk of bias, although few studies had a combination of reference standards that were judged to be acceptable by the panel.
b. Minor inconsistency for sensitivity noted but judged to be insufficient to downgrade the certainty of evidence. Minor inconsistency for specificity noted but judged to be insufficient to downgrade the certainty of evidence.
c. Certainty of evidence was downgraded for indirectness in instances where this test was not the index test in a diagnostic pathway. There was a lack of data on the accuracy of this test following a previous test in a pathway. Thus, sensitivity and specificity used for modeling in these instances were based on the test accuracy of the individual test rather than using the test in a pathway.

Table S6. Whole leg ultrasound test accuracy in high prevalence population

Click link for interactive summary of findings (iSoF) table. **Patient or population:** Patients with suspected lower extremity deep vein thrombosis

New test: Whole Leg US

Setting: Inpatient and outpatient

Pooled sensitivity: 0.94 (95% CI: 0.91 to 0.96) | **Pooled specificity:** 0.97 (95% CI: 0.95 to 0.99)

Test result	Number of results per 1,000 patients tested (95% CI)		Number of participants (studies)	Quality of the Evidence (GRADE)
	Prevalence **50%**[1,2] in patients with suspected LE DVT	Prevalence **75%**[1,2] in patients with suspected LE DVT		
True positives	**470** (455 to 480)	**705** (683 to 720)	1725 (10)	⊕⊕⊕⊕ **HIGH** [a,b,c]
False negatives	**30** (20 to 45)	**45** (30 to 67)		
True negatives	**485** (475 to 495)	**243** (238 to 248)	1725 (10)	⊕⊕⊕⊕ **HIGH** [a,b,c]
False positives	**15** (5 to 25)	**7** (2 to 12)		
Inconclusive test results	8		1733 (10)	
Complications arising from the diagnostic test	Not reported			

CI: Confidence interval

[1]Fancher T et al. BMJ 2004; 329(7470):821. Clinical PTP and rapid D-dimer testing; mean prevalence of DVT in accuracy studies 11%; mean prevalence of DVT in management studies 25%

[2]Disease prevalence applies to the index test in each pathway. Prevalence applied to the accuracy of each subsequent test depends on the result of the previous test in the pathway.

Explanations

a. Certainty of evidence not downgraded for risk of bias, although few studies had a combination of reference standards that were judged to be acceptable by the panel.

b. Minor inconsistency for sensitivity noted but judged to be insufficient to downgrade the certainty of evidence. Minor inconsistency for specificity noted but judged to be insufficient to downgrade the certainty of evidence.

c. Certainty of evidence was downgraded for indirectness in instances where this test was not the index test in a diagnostic pathway. There was a lack of data on the accuracy of this test following a previous test in a pathway. Thus, sensitivity and specificity used for modeling in these instances were based on the test accuracy of the individual test rather than using the test in a pathway.

Table S7. Serial Ultrasound test accuracy in high prevalence population

Click link for interactive summary of findings (iSoF) table.

Patient or population: Patients with suspected lower extremity deep vein thrombosis

New test: Serial US

Setting: Inpatient and outpatient

Pooled sensitivity: 0.98 (95% CI: 0.96 to 0.99) | **Pooled specificity:** 0.998 (95% CI: 0.993 to 0.999)

Test result	Number of results per 1,000 patients tested (95% CI)		Number of participants (studies)	Quality of the Evidence (GRADE)
	Prevalence **50%**[1,2] in patients with suspected LE DVT	Prevalence **75%**[1,2] in patients with suspected LE DVT		
True positives	**490** (480 to 495)	**735** (720 to 742)	2415 (6)	⊕⊕⊕⊕ **HIGH** [a,b,c]
False negatives	**10** (5 to 20)	**15** (8 to 30)		
True negatives	**499** (497 to 500)	**250** (248 to 250)	2415 (6)	⊕⊕⊕⊕ **HIGH** [a,b,c]
False positives	**1** (0 to 3)	**0** (0 to 2)		
Inconclusive test results	0		2415 (6)	
Complications arising from the diagnostic test	Not reported			

CI: Confidence interval

[1]Fancher T et al. BMJ 2004; 329(7470):821. Clinical PTP and rapid D-dimer testing; mean prevalence of DVT in accuracy studies 11%; mean prevalence of DVT in management studies 25%

[2]Disease prevalence applies to the index test in each pathway. Prevalence applied to the accuracy of each subsequent test depends on the result of the previous test in the pathway.

Explanations

a. Certainty of evidence not downgraded for risk of bias, although few studies had a combination of reference standards that were judged to be acceptable by the panel.

b. Minor inconsistency for sensitivity noted but judged to be insufficient to downgrade the certainty of evidence. Minor inconsistency for specificity noted but judged to be insufficient to downgrade the certainty of evidence.

c. Certainty of evidence was downgraded for indirectness in instances where this test was not the index test in a diagnostic pathway. There was a lack of data on the accuracy of this test following a previous test in a pathway. Thus, sensitivity and specificity used for modeling in these instances were based on the test accuracy of the individual test rather than using the test in a pathway.

Table S8. D-dimer test accuracy in high prevalence population

Click link for interactive summary of findings (iSoF) table.

Patient or population: Patients with suspected lower extremity deep vein thrombosis
New test: D-dimer
Setting: Inpatient and outpatient
Pooled sensitivity: 0.96 (95% CI: 0.93 to 0.98) | **Pooled specificity:** 0.36 (95% CI: 0.29 to 0.42)

Test result	Number of results per 1,000 patients tested (95% CI)		Number of participants (studies)	Quality of the Evidence (GRADE)
	Prevalence **50%**[1,2] in patients with suspected LE DVT	Prevalence **75%**[1,2] in patients with suspected LE DVT		
True positives	**480** (465 to 490)	**720** (698 to 735)	5253 (16)	⊕⊕⊕◯ **MODERATE** [a,b,c]
False negatives	**20** (10 to 35)	**30** (15 to 52)		
True negatives	**180** (145 to 210)	**90** (73 to 105)	5253 (16)	⊕⊕⊕◯ **MODERATE** [a,b,c]
False positives	**320** (290 to 355)	**160** (145 to 177)		
Inconclusive test results	Not applicable		5253 (16)	
Complications arising from the diagnostic test	Not reported			

CI: Confidence interval

[1]Fancher T et al. BMJ 2004; 329(7470):821. Clinical PTP and rapid D-dimer testing; mean prevalence of DVT in accuracy studies 11%; mean prevalence of DVT in management studies 25%

[2]Disease prevalence applies to the index test in each pathway. Prevalence applied to the accuracy of each subsequent test depends on the result of the previous test in the pathway.

Explanations

a. Certainty of evidence not downgraded for risk of bias, although few studies had a combination of reference standards that were judged to be acceptable by the panel.

b. Minor inconsistency for sensitivity noted but judged to be insufficient to downgrade the certainty of evidence. Certainty of evidence was downgraded for serious unexplained inconsistency in specificity, with a range from 5.2% to 59.6%.

c. Certainty of evidence was downgraded for indirectness in instances where this test was not the index test in a diagnostic pathway. There was a lack of data on the accuracy of this test following a previous test in a pathway. Thus, sensitivity and specificity used for modeling in these instances were based on the test accuracy of the individual test rather than using the test in a pathway.

Supplement 3. List of excluded studies during full-text review (n=245)

Duplicate (n=1)

1. Fisher BWM, S. R.; McAlister, F. A. Clinical prediction of deep venous thrombosis using two risk assessment methods in combination with rapid quantitative D-dimer testing. *American Journal of Medicine*. 2002;112(3):198-203.

Incorrect study design/type (n=67)

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Incorrect population (n=17)

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Sample size <100 patients (n=23)

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Calf DVT only (n=4)

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Unable to obtain full-text (n=4)

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Supplement 4. Risk of bias assessment for individual studies.

Low: low risk of bias introduced by study methods
High: high risk of bias introduced by study methods
Unclear: unclear risk of bias due to insufficient data reported to permit a judgment

Whiting PF, Rutjes AWS, Westwood ME, Mallett S, Deeks JJ, Reitsma JB, Leeflang MMG, Sterne JAC, Bossuyt PMM: **QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies**. *Ann Intern Med* 2011, **155**(8):529-536.

Recurrent DVT

Study	Patient Selection	Index Test	Reference Standard	Flow and Timing
Aguilar 2007	Low	Low	Low	Low
Prandoni 2002	Low	High	Low	Low

Proximal compression ultrasound

Study	Patient Selection	Index Test	Reference Standard	Flow and Timing
Anderson 1999	Low	Low	Low	Low
Aronen 1994	Low	Low	Low	Low
Birdwell 2000	Low	Low	Low	Low
Cogo 1993	Low	Low	Low	Low
Friera 2002	Low	Low	Low	Low
Gudmundensen 1990	Low	Low	Low	Low
Lensing 1989	Low	Low	Low	Low
Pedersen 1991	Low	Low	Low	Low
Quintavallaa 1991	Low	Low	Low	Low
van Ramshorst 1991	Low	Low	Low	Low
Wells 1995a	Low	Unclear	Low	Low
Wells 1995b	Low	Low	Low	Low
Wells 2003	Low	Unclear	Unclear	Low

Serial ultrasound

Study	Patient Selection	Index Test	Reference Standard	Flow and Timing
Anderson 1999	Low	Low	Low	Low
Bernardi 1998	Low	High	Low	Low
Birdwell 1998	Low	Low	Low	Low
Friera 2002	Low	Low	Unclear	Low
Schutgens 2002	Low	Unclear	Low	Low

Williams 2005	Low	Unclear	Unclear	Low

Whole leg ultrasound

Study	Patient Selection	Index Test	Reference Standard	Flow and Timing
Bradley 1993	Low	Low	Low	Low
De Valois 1990	Low	Low	Low	Low
Habscheid 1990	Low	Low	Low	Low
Kalodiki 1993	Low	Low	Low	Low
Miller 1996	Low	Low	Low	Low
Montefusco-von Kleist 1993	Low	Low	Low	Low
Theodorou 2003	Low	Low	Low	Low
Bendayan 1991	Low	Low	Low	Low
Grosser 1990	Low	Low	Low	Low
Grosser 1991	Low	Low	Low	Low

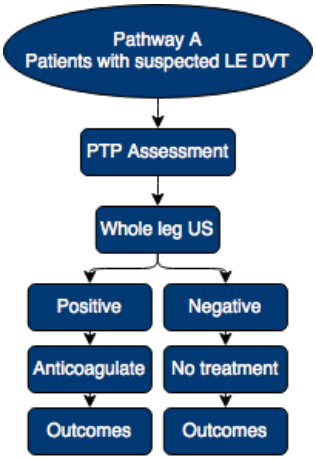
D-dimer

Study	Patient Selection	Index Test	Reference Standard	Flow and Timing
Canan 2012	Low	Low	Low	Low
Cornuz 2002	Low	Low	Low	Low
D'Angelo 1996	Low	Low	Low	Low
Diamond 2005	Low	Low	Low	Low
Haenssle 2013	Low	Low	Low	Low
Hansson 1984	Low	Low	Low	Low
Jennersjo 2005	Low	Low	Low	Low
Knecht 1997	Low	Low	Low	Low
LeBlanche 1999	Low	Low	Low	Low
Luxembourg 2012	Low	Low	Low	Low
Nata 2013	Low	Low	Low	Low
Oudega 2005	Low	Low	Low	Low
Schutgens 2005	Low	Unclear	Low	Low
Williams 2005	Low	Unclear	Low	Low
Ilkhanipour 2004	Low	Low	Low	Low
Mantoni 2008	Low	Unclear	Unclear	High

Supplement 5. Diagnostic Pathways Assessed for Lower Extremity DVT

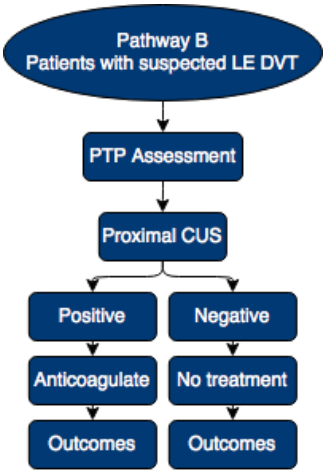
a. Whole leg US

- Positive whole leg US → anticoagulate
- Negative whole leg US → no treatment



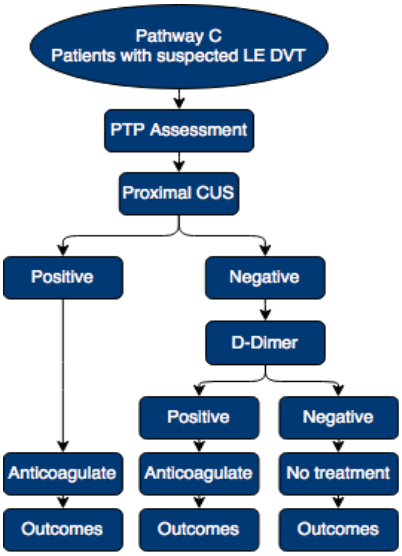
b. Proximal CUS

- Positive proximal CUS → anticoagulate
- Negative proximal CUS → no treatment



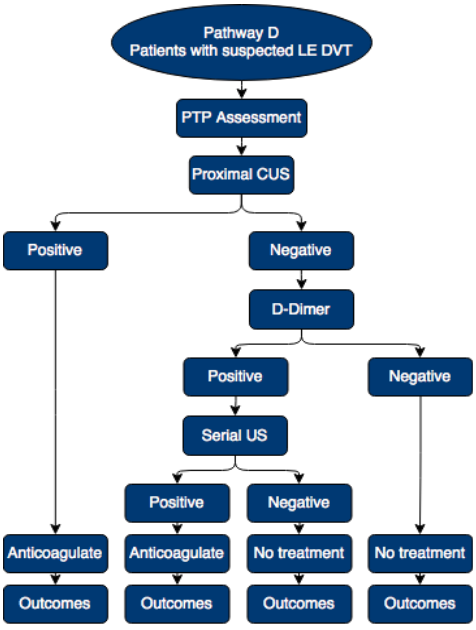
c. Proximal CUS

- Positive proximal CUS → anticoagulate
- Negative proximal CUS → D-Dimer
    - Positive D-Dimer → anticoagulate
    - Negative D-Dimer → no treatment



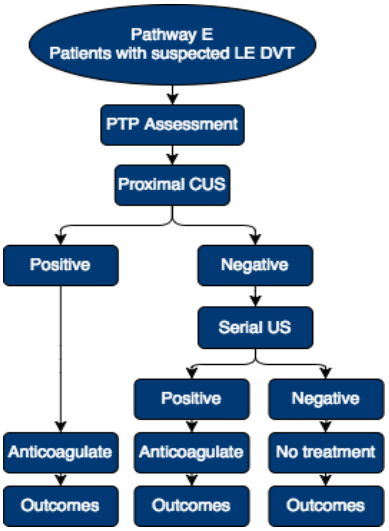
d. Proximal CUS

- Positive proximal CUS → anticoagulate
- Negative proximal CUS → D-dimer
    - Positive D-dimer → serial US
        - Positive serial US → anticoagulate
        - Negative serial US → no treatment
    - Negative D-dimer → no treatment



e. Proximal CUS

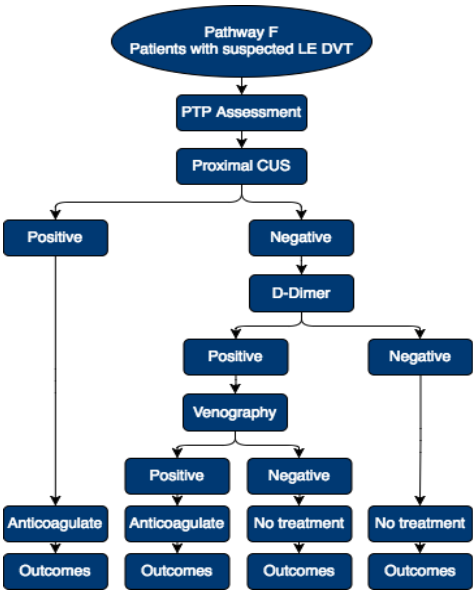
- Positive proximal CUS → anticoagulate
- Negative proximal CUS → Serial US
    - Positive Serial US → anticoagulate
    - Negative Serial US → no treatment



f. Proximal CUS

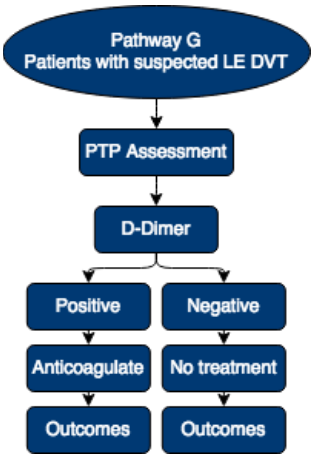
- Positive proximal CUS→ anticoagulate
- Negative proximal CUS → D-Dimer
    - Positive D-Dimer → venography
        - Positive venography → anticoagulate
        - Negative venography → No treatment
    - Negative D-Dimer →No treatment

*Venography was deemed not suitable as a follow-up test due to the use of ultrasound as the accepted reference standard for DVT diagnosis.



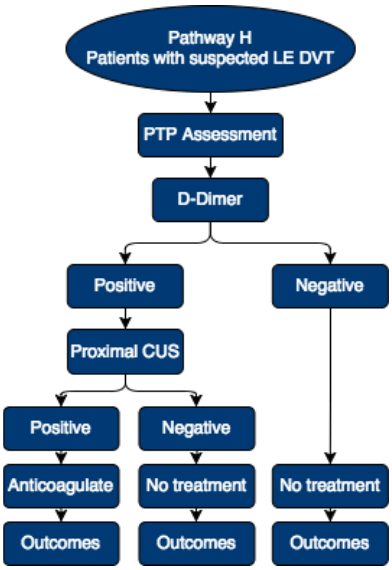
g. D-dimer

- Positive D-dimer → anticoagulate
- Negative D-dimer → no treatment



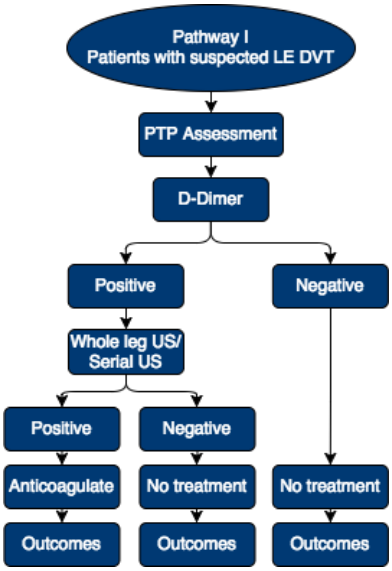
h. D-dimer

- Positive D-dimer → proximal CUS
  - Positive proximal CUS → anticoagulate
  - Negative proximal CUS → no treatment
- Negative D-dimer → no treatment



i. D-dimer

- Positive D-dimer → whole leg/serial US
  - Positive whole leg/serial US → anticoagulate
  - Negative whole leg/serial US → no treatment
- Negative D-dimer → no treatment



** Whole Leg US sensitivity and specificity estimates were used to model Pathway I.

Note: in the algorithms, watchful waiting will follow negative tests and low/normal probability unless stated otherwise.

Legend	
DVT	deep vein thrombosis
US	ultrasound
CUS	compression ultrasound

PRISMA-DTA Checklist

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
TITLE / ABSTRACT			
Title	1	Identify the report as a systematic review (+/- meta-analysis) of diagnostic test accuracy (DTA) studies.	1
Abstract	2	Abstract: See PRISMA-DTA for abstracts.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known.	3
Clinical role of index test	D1	State the scientific and clinical background, including the intended use and clinical role of the index test, and if applicable, the rationale for minimally acceptable test accuracy (or minimum difference in accuracy for comparative design).	3
Objectives	4	Provide an explicit statement of question(s) being addressed in terms of participants, index test(s), and target condition(s).	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.	3
Eligibility criteria	6	Specify study characteristics (participants, setting, index test(s), reference standard(s), target condition(s), and study design) 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.	3
Search	8	Present full search strategies for all electronic databases and other sources searched, including any limits used, such that they could be repeated.	Supplement 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
Definitions for data extraction	11	Provide definitions used in data extraction and classifications of target condition(s), index test(s), reference standard(s) and other characteristics (e.g. study design, clinical setting).	4-5
Risk of bias and applicability	12	Describe methods used for assessing risk of bias in individual studies and concerns regarding the applicability to the review question.	5, Supplement 4
Diagnostic accuracy measures	13	State the principal diagnostic accuracy measure(s) reported (e.g. sensitivity, specificity) and state the unit of assessment (e.g. per-patient, per-lesion).	5
Synthesis of results	14	Describe methods of handling data, combining results of studies and describing variability between studies. This could include, but is not limited to: a) handling of multiple definitions of target condition. b) handling of multiple thresholds of	5

PRISMA-DTA Checklist

		test positivity, c) handling multiple index test readers, d) handling of indeterminate test results, e) grouping and comparing tests, f) handling of different reference standards	

Section/topic	#	PRISMA-DTA Checklist Item	Reported on page #
Meta-analysis	D2	Report the statistical methods used for meta-analyses, if performed.	5
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	Provide numbers of studies screened, assessed for eligibility, included in the review (and included in meta-analysis, if applicable) with reasons for exclusions at each stage, ideally with a flow diagram.	5-6, Figure 1
Study characteristics	18	For each included study provide citations and present key characteristics including: a) participant characteristics (presentation, prior testing), b) clinical setting, c) study design, d) target condition definition, e) index test, f) reference standard, g) sample size, h) funding sources	5-6, Table 1
Risk of bias and applicability	19	Present evaluation of risk of bias and concerns regarding applicability for each study.	6
Results of individual studies	20	For each analysis in each study (e.g. unique combination of index test, reference standard, and positivity threshold) report 2x2 data (TP, FP, FN, TN) with estimates of diagnostic accuracy and confidence intervals, ideally with a forest or receiver operator characteristic (ROC) plot.	Figures 2-5
Synthesis of results	21	Describe test accuracy, including variability; if meta-analysis was done, include results and confidence intervals.	6-12
Additional analysis	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression; analysis of index test: failure rates, proportion of inconclusive results, adverse events).	N/A
DISCUSSION			
Summary of evidence	24	Summarize the main findings including the strength of evidence.	12-13
Limitations	25	Discuss limitations from included studies (e.g. risk of bias and concerns regarding applicability) and from the review process (e.g. incomplete retrieval of identified research).	13
Conclusions	26	Provide a general interpretation of the results in the context of other evidence. Discuss implications for future research and clinical practice (e.g. the intended use and clinical role of the index test).	13
FUNDING			
Funding	27	For the systematic review, describe the sources of funding and other support and the role of the funders.	14

Adapted From: McInnes MDF, Moher D, Thombs BD, McGrath TA, Bossuyt PM, The PRISMA-DTA Group (2018). Preferred Reporting Items for a Systematic Review and Meta-analysis of Diagnostic Test Accuracy Studies: The PRISMA-DTA Statement. JAMA. 2018 Jan 23;319(4):388-396. doi: 10.1001/jama.2017.19163.