CHEST Online Data Supplement

Diagnosis of DVT

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

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Table S1—*Modeled Diagnostic Strategies*

Number	Strategy	Source
0	No testing or treatment	
1	Venography for all patients	
2	Proximal US, repeat if negative	
3	Whole-leg US, repeat if isolated calf vein DVT diagnosed	
4	Whole-leg US, treat if calf vein DVT diagnosed	Gibson et al,[1] Bernardi et al,[2] Johnson et al,[3] Elias et al,[4] Schellong et al,[5] Sevestre et al,[6] Sevestre et al,[7] Stevens et al,[8] Subramaniam et al[9]
5	Proximal US, no repeat	
6	Wells score and proximal US. If PTP low, discharge if US negative; venogram if positive. If PTP moderate, repeat US if negative, treat if positive. If high PTP, venogram if US negative, treat if US positive.	Anderson et al,[10] Wells et al,[11] Wells et al[12]
7	SimpliRED DD and proximal US. If US positive, then treat. If both are negative, then discharge. If DD positive and US negative, repeat US.	Kraaijenhagen et al[13]
8	Wells score and proximal US. If PTP high or moderate, perform proximal US. If positive treat, venogram if negative. If PTP low, perform proximal US. If positive treat, discharge if negative.	Walsh et al[14]
9	Wells score and full-leg US. If PTP high or moderate, perform full-leg US; treat if positive, venogram if negative. If PTP low, full-leg US; treat if positive, discharge if negative.	Walsh et al[14]
10	Quantitative latex DD. If positive, perform proximal US and repeat. If DD negative, perform Wells score. If high, perform proximal US and repeat if negative. If PTP moderate or low, discharge.	Bates et al[15]
11	Quantitative latex DD: if positive, perform above-knee US and repeat. If DD negative, perform Wells score. If PTP high, perform proximal US. PTP low or moderate, discharge.	Schutgens et al[16]
12	Wells score. If PTP high, perform proximal US, treat if positive, perform SimpliRED DD if negative. If DD positive, perform venogram, if negative repeat US. If PTP moderate, perform US; treat if positive, SimpliRED DD if negative. If DD positive, repeat proximal US. If DD negative, discharge. If PTP low, perform SimpliRED DD. If DD positive, perform proximal US. Discharge if DD negative.	Anderson et al[17]
13	Wells score and SimpliRED DD. If PTP high or moderate, or DD positive, perform full-leg US. If PTP low and DD negative, then discharge.	Janes and Ashford[18]
14	ELISA DD. If negative, discharge. If DD positive, perform proximal US. Treat if US positive. If US negative, perform Wells score. If PTP high, perform venogram. If PTP moderate or low, discharge.	Perrier et al[19]
15	Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD positive, discharge if DD negative. If PTP low, perform US. Discharge if negative, treat if positive.	Tick et al[20]
16	Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD positive and discharge if DD negative. If PTP low, perform SimpliRED DD; discharge if negative, perform proximal US if positive.	Wells et al,[21] intervention group (high and moderate combined)
17	Wells score. If PTP high, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD positive, discharge if DD negative. If PTP moderate or low, perform SimpliRED DD. Discharge if negative, perform proximal US if positive.	Wells et al,[21] intervention group (moderate and low combined)
18	Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative repeat US. If PTP low, perform proximal US; treat if positive, discharge if negative.	Wells et al,[21] control group (high and moderate combined)
19	Wells score. If PTP high, perform proximal US. If positive treat, if negative repeat US. If PTP moderate or low, perform proximal US; treat if positive, discharge if negative.	Wells et al,[21] control group (moderate and low combined)
20	Wells score. If PTP high or moderate, perform proximal US. Treat if positive, if negative discharge. If PTP low, discharge.	UK survey
21	Perform SimpliRED DD. Discharge if negative, perform above-knee US if positive. Treat if US positive, repeat US if initial US is negative.	UK survey

In all algorithms, repeat US means that a proximal US is performed 1 week later. DD = D-dimer; ELISA = enzyme-linked immunosorbent assay; PTP = pretest probability; US = ultrasound.

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Table S2—*Methodology Table for Diagnostic Studies Assessing Venography in Patients With Suspected Lower Extremity DVT: Individual Management Studies With Cohorts*

Study Details								
Patient Population	Diagnostic Test	Outcome	Methods (Single-Arm Cohort vs Cohort From RCT)	Consecutive Patients	Follow-up	Received Alternative Tests	Comments	Source
Suspected DVT	Technically adequate, normal venogram	Probability of VTE during follow-up	Single-arm cohort	Yes	3 mo	No	N = 160 outpatients with normal venography; 2 patients returned for investigation of new symptoms in the same leg during follow-up (day 2, day 8). New DVT was diagnosed by abnormal IPG in one (venography unsuccessful) and by repeat venography in another (calf vein DVT)	Hull et al[22]

Cohorts from single-arm studies or cohorts representing one of the arms of an RCT. IPG = impedance plethysmography; RCT = randomized controlled trial.

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Table S3—*Descriptive Table for Cross-sectional Accuracy and Prospective Cohort Studies Assessing Venography for Evaluation of Suspected Lower Extremity DVT*

Question From Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
Suspected lower extremity DVT (Section 2.0)	What are the consequences of using venography to diagnose lower extremity DVT?	N/A	N/A	Patients with suspected DVT	N/A	N/A	Implied reference standard	N/A
	What are the consequences of using venography to rule out lower extremity DVT?	Primary study	3-mo follow-up	Patients with suspected DVT	3 mo follow-up	DVT diagnosed during follow-up in 2 of 160 patients (NPV, 98.8%; 95% CI, 95.6%-99.8%)	N = 160 outpatients with normal venography; 2 patients returned for investigation of new symptoms in the same leg during follow-up (day 2, day 8). New DVT was diagnosed by abnormal IPG in one (venography unsuccessful) and by repeat venography in another (calf vein DVT)	Hull et al[22]

N/A = not applicable; NPV = negative predictive value; TP = test probability. See Table S1 and S2 legends for expansion of other abbreviations.

[a]eg, Post-TP during 3 mo follow-up; sensitivity or specificity, and so forth.

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Table S4—*Evidence Profile Table for Diagnostic Studies Assessing Venography in Patients With Suspected DVT: Should a Normal Venogram Be Used to Rule Out DVT?*

Quality Assessment							Summary of Findings		
							Accuracy Indices % (95% CI)		
No of Studies (Patients)	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Normal Venogram	Quality	Importance
Negative predictive value of a normal venogram for DVT compared with confirmed recurrent VTE during 3-mo follow-up									
1 (160)	Single-arm prospective cohort study	Serious[a]	Single study	N/A	95% CI, 95.6%-99.8%	3-mo follow-up as reference standard	98.8%	Moderate	Critical

Bibliography: Hull R, Hirsh J, Sackett DL, et al. Clinical validity of a negative venogram in patients with clinically suspected venous thrombosis. *Circulation*. 1981;64(3):622-625. Settings: outpatients.

[a] Prevalence of DVT in original population not specified.

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Table S5—*[Sections 3.1-3.5] Methodology of Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Meta-analysis of Accuracy Studies*

	Study Eligibility				
Study/Year	Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Exploration of Heterogeneity	Comments
Goodacre et al[23]/2005	Clinically suspected DVT	US	Venography	Tested for influence of consecutive patients, blind reading of tests, underlying prevalence	Accuracy
Geersing et al[24]/2009	Suspected DVT, point of care, 23 studies, 13,959 patients	Point of care DD	US, venography, or 3 mo clinical follow-up or combined	Tested for a number of factors (ie, recurrent DVT, % with malignancy or surgery, DVT vs PE)	VTE (PE or DVT examined). Both accuracy and management studies (no imaging for some groups) included
Goodacre et al[25]/2005	Suspected DVT	DD	US, venography and/or plethysmography	Tested for patient-mix, ED only, outpatients only, and so forth	
DiNisio et al[26]/2007	Suspected DVT	DD	US, venography, and/or plethysmography	17 patient and design characteristics examined	VTE (DVT and PE) included
Stein et al[27]/2004	Suspected DVT	DD	US, venography, and/or plethysmography	Tested for DD used	

All studies are cross-sectional unless otherwise indicated under Comments. PE = pulmonary embolism. See Table S1 legend for expansion of other abbreviation.

Table S6—*[Sections 3.1-3.5] Methodology of Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Individual Accuracy Studies*

	Study Details				
Study/Year	Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Consecutive Patients	Independent Test Assessment
Subramaniam et al[28] 2006	ED patients	Wells score (likely or unlikely), moderately sensitive DD	Whole-leg US plus 3-mo follow-up in those with a negative US result at presentation	Yes	Yes

See Table S1 legend for expansion of abbreviations.

Table S7—*[Sections 3.1-3.5] Methodology of Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Meta-analysis of Management Cohort Studies*

	Study Eligibility				
Study/Year	Patient Population	Diagnostic Test	Outcome	Methods (Single-Arm Cohort vs Cohort From RCT)	Exploration of Heterogeneity
Fancher et al[29]/2004	Clinically suspected DVT, primary vs referred not specified; 12 studies, 5,431 patients	DD combined with different PTP	3-mo probability of symptomatic VTE	Cohorts from both single-arm prospective studies and RCT	Presence of previous VTE, type of DD used
Wells et al[30]/2006	Mixed; 14 studies, 8,329 patients	PTP and DD	3-mo probability of VTE	Single-arm cohorts	
Righini et al[31]/2008	Clinically suspected DVT; 6 studies, 5,876 patients	Serial proximal CUS (one did CUS once)	3-mo probability of symptomatic VTE	Single-arm cohorts	No formal analysis

Cohorts from single arm studies or cohorts representing one of the arms of an RCT. CUS = compression ultrasound. See Table S1 and S2 legends for expansion of other abbreviations.

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Table S8—*[Sections 3.1-3.5] Methodology of Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Individual Management Studies With Cohorts*

	Study Details							
Study/Year	Patient Population	Diagnostic Test	Outcome	Methods (Single-Arm Cohort vs Cohort From RCT)	Consecutive Patients	Loss to Follow-up	Received Alternative Tests	Comments
Büller et al[32]/2009	Outpatients in primary care, overall prevalence 13%	Clinical decision rule including moderately sensitive DD	3 mo symptomatic VTE	Single-arm cohort	Invited	3 of 1,002	No	Negative assessment meant negative DD and ≤ 3 points on 8-point scale (likely low-moderate PTP)
Kraijenhagen et al[13]/2002	Patients referred to thrombosis center, prevalence 22%	Moderately sensitive DD and proximal US	3 mo symptomatic VTE	Single-arm cohort	Yes	17 of 1,756 excluded from analysis because DD not performed with knowledge of US result	No	PTP assessed but only used in scenario analysis.
Bernardi et al[33]/1998	University center, likely referred, overall prevalence 27.5%	If normal US → highly sensitive DD	3 mo symptomatic VTE	Single-arm cohort	Yes	2 of 686	No	
Wells et al[12]/1997	Outpatients, referral, overall prevalence 16%	Wells score, DD alone for low PTP, or with US (for moderate and high PTP)	3 mo symptomatic VTE	Single-arm cohort	Yes	?	No	Low PTP and positive CUS was followed by venography. Negative CUS and high PTP led to venography
Anderson et al[17]/2003	ED patients, overall prevalence 18.1%	Combination of Wells score, US, mixed highly sensitive and moderately sensitive DD	3 mo symptomatic VTE	Single-arm cohorts	Yes	?	No	
Tick et al[20]/2002	Outpatients referred to center by family doctor, overall prevalence 42.5%	Low PTP underwent CUS. Moderate to high PTP underwent US and if positive DD. If DD positive, US was repeated at day 8	3 mo symptomatic VTE	Single-arm cohort	Yes	Not reported	2 patients were asymptomatic DVT diagnosed on CT scan performed for other reason	

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Table S8—*Continued*

Study/Year	Study Details: Patient Population	Diagnostic Test	Outcome	Methods (Single-Arm Cohort vs Cohort From RCT)	Consecutive Patients	Loss to Follow-up	Received Alternative Tests	Comments
Cogo et al[34]/1998	Outpatients referred	2-Point US, with repeat	6 mo symptomatic VTE	Single-arm cohort	Yes	0	No	
Aguilar et al[35]/2002	ED patients with moderate pretest probability	If negative highly sensitive DD, no further testing	3 mo	Single-arm cohort	Yes	?	No	
Bates et al[15]/2003	Patients referred to thrombosis service	Highly sensitive DD, if negative and low or moderate PTP, no further investigation	3 mo symptomatic VTE	Single-arm cohort	Yes	1 of 90	No	
Schutgens et al[16]/2003	Referred to thrombosis service	Highly sensitive DD, if negative and low or moderate PTP, no further investigation	3 mo symptomatic VTE	Cohorts	Yes	1 of 812	No	
Anderson et al[10]/1999	ED patients	Wells score and proximal US. If pretest low and US negative, no further testing. Patients with a moderate pretest and negative US and a repeat US in 1 wk. High PTP patients with a negative US underwent venography	3 mo symptomatic VTE	Single-arm cohort	Yes	3 of 344	Venogram if low pretest and positive US or if high pretest and negative US	
Ruiz-Gimenes et al[36]/2004	ED patients		3 mo symptomatic VTE	Single-arm cohort	Yes	?		
Oudega et al[37]/2005	Primary care, overall prevalence 22%, 1,295 patients	Modified Wells score plus highly sensitive DD	Serial US	Single-arm cohort	Yes	N/A	No	

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Table S8—*Continued*

Study/Year	Study Details: Patient Population	Study Details: Diagnostic Test	Study Details: Outcome	Study Details: Methods (Single-Arm Cohort vs Cohort From RCT)	Consecutive Patients	Loss to Follow-up	Received Alternative Tests	Comments
Kearon et al[38]/2001	Low pretest probability and negative moderate sensitivity DD. Referred to thrombosis service, pretest prevalence 14%, for low PTP 2%	Low pretest and negative moderately sensitive DD	3 mo symptomatic VTE	Single-arm cohort	Yes	0 of 177	No	

Cohorts from single-arm studies or cohorts representing one of the arms of an RCT. See Table S1, S3, and S5 legends for expansion of abbreviations.

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Table S9—*[Sections 3.1-3.5] Methodology of Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Individual RCT With Direct Comparison of Diagnostic Strategies*

	Study Details								
Study/Year	Patient Population	Test 1/Strategy 1	Test 2/Strategy 2	Outcome	Concealment of Randomization	Blinding	Follow-up	Intention to Treat	Comments
Wells et al[21]/2003	Outpatients (thrombosis units, ED), Wells score applied (unlikely or likely)	Pretest unlikely: DD with clinical follow-up if negative and US if positive Pretest likely: US, if negative, DD and repeat US if DD positive	Unlikely: US with clinical follow-up if negative. Likely: Serial US in all	3 mo symptomatic VTE	Yes	N/A	Strategy 1: 7 of 601 lost Strategy 2: 7 of 495 lost	N/A	Mixed DD: SimpliRED (moderately sensitive) and IL DD (sensitive)
Kearon et al[39]/2005	Referral centers of 4 university hospitals, prevalence 7.5%, randomized after first negative US	Moderately sensitive DD with no testing if negative and venogram if positive	Repeat US	3 mo symptomatic VTE	Yes	N/A	9 of 810 lost	N/A	

See Table 1 legend for expansion of abbreviation.

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Table S10—*[Sections 3.1-3.5] Description and Results of Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Results of Cross-sectional Accuracy and Cohort Management Studies*

Question From Structured Clinical Question Table	Study/Year	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort[s] is From an RCT)	Patient Population	Outcome Measure[a]	Result	Comments
What are the consequences of using US to diagnose proximal DVT?	Goodacre et al[23]/2005	Suspected DVT	Meta-analysis	Accuracy	Mixed	Sensitivity/ specificity	Estimates of sensitivity and specificity differ only slightly among different US techniques. Sensitivity for detection of proximal DVT from 93.8% for CUS (95% CI, 92%-95.3%) to 96.5% for duplex US (95% CI, 95.1%-97.6%). Specificity of CUS was 97.8% (95% CI, 97%-98.4%), numerically slightly higher than for duplex (94%; 95% CI, 92.8%-95.1%) or triplex US (94.3%; 95% CI, 92.5–95.8).	
	Wells et al[12]/1997	Low pretest and positive US	Primary	Cohort	3% prevalence	Post-TP (reference standard: venography)	9 of 11, 82% (48-98)	
	Anderson et al[10]/1999	Low pretest and positive US	Primary	Cohort	3.2% prevalence	Post-TP (reference standard: venography)	5 of 5 (100%, proximal)	
	Model Goodacre et al[23]/2005; Jaeschke et al[40]/2009		Meta-analysis of accuracy studies		Assuming sensitivity of 94% and specificity of 98% for US:			
					5% PTP negative post-TP positive 71% (lower 95% CI, 63), negative 0.3 (0.4%)			
					10% PTP negative post-TP positive 84% (77%); negative 0.7% (0.9%)			
					13% PTP negative post-TP positive 88% (lower 95% CI, 82), negative 0.9 (1.2%)			
					20% PTP negative post-TP positive 92% (87%); negative 1.5% (1.3%-2%)			
					38% PTP negative post-TP positive 97% (lower 95% CI, 95), negative 4.8 (lower 3%)			
					50% PTP negative post-TP positive 98% (98%); negative 8% (lower 5%)			
What are the consequences of using PTP with a single negative proximal US to exclude DVT?	Tick et al[20]/2002	Low pretest and negative US	Primary	Management	Outpatients (prevalence in low pretest = 11%)	3 mo follow-up	5 of 250, 2%	Prevalence in low pretest = 11%
	Wells et al[12]/1997	Low pretest and negative US	Primary	Management	3% prevalence	3 mo follow-up	1 of 320, (0.3%)	
	Kraaijenhagen et al[13]/2002	Low pretest and negative US	Primary	Management according to US and DD; results according to PTP via scenario analysis	6.9% prevalence	3 mo follow-up	13 of 834, 1.6%	Scenario analysis

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Table S10—*Continued*

Question From Structured Clinical Question Table	Study/Year	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort[s] is From an RCT)	Patient Population	Outcome Measure[a]	Result	Comments
	Anderson et al[10]/1999	Low pretest and negative US	Primary	Management	3.2% prevalence	3 mo follow-up	1 of 185 (calf DVT)	
	Wells et al[21]/2003	Unlikely Wells score and negative US	Primary	Management, RCT	4.4% prevalence	3 mo follow-up	4 of 272, 1.4% (0.4-3.8%)	
	Anderson et al[10]/1999	Moderate pretest and negative US	Primary	Management	13 of 105 initial US	3 mo follow-up	2 of 92 (1 at 1 wk US, 1 calf during follow-up) 2.2%	
	Wells et al[12]/1997	Moderate pretest and negative US	Primary	Management	16.6% prevalence	3 mo follow-up	5 of 166 (3 at 1 wk and 2 during follow-up) 3.0%	
	Tick et al[20]/2002	Moderate-high pretest and negative US	Primary	Cohort	56.5% on initial US	3 mo follow-up	Would miss 13 of 231 5.6%	Second US performed due to positive SimpliRED DD detected 13 of 15, 2 still missed
	Wells et al[21]/2003	Likely Wells score and negative US	Primary	Cohort from RCT	27.4% prevalence	3 mo follow-up	1 of 182 on 1 wk repeat, 2 during follow-up; total = 3 of 182 1.6%	
	Wells et al[12]/1997	High pretest and negative US	Primary	Single cohort	75% prevalence	3 mo follow-up	4 of 22, 18.2%	
	Anderson et al[10]/1999	High pretest and negative US	Primary	Single cohort	20 of 49 on original CUS	Venography	4 of 29 (2 proximal, 2 calf) = 13.2%	
	Ruiz-Gimenez et al[36]/2004	High pretest and negative US	Primary	Cohort	49% prevalence	Repeat US	5 of 62 8.1%	4 detected on repeat US
What are the consequences of using serial proximal US to exclude DVT (regardless of pretest)?	Righini et al[31]/2008	Prevalence of 16%-28% in different studies	Meta-analysis	6 studies, 1 looked at single US	Mixed	3 mo follow-up	0.6% (0.4-0.9%)	

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Question From Structured Clinical Question Table	Study/Year	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort[s] is From an RCT)	Patient Population	Outcome Measure[a]	Result	Comments
	Wells et al[12]/1997	Moderate pretest, negative serial (2) proximal US	Primary	Management	Outpatients, 16% prevalence	3 mo follow-up	2 of 163 (1.2%)	Included in Righini et al[31] meta-analysis
	Anderson et al[10]/1999	Moderate pretest, negative serial (2) proximal US	Primary	Management	Outpatients, ED, 14.3% prevalence	3 mo follow-up	1 of 91 (3.2%)	
	Kearon et al[39]/2005	7.5% Prevalence	Primary	Management, cohort from RCT	3 of 350 detected on repeat US	6 mo follow-up	2 of 347 (0.6%)	
	Wells et al[21]/2003	Likely Wells score plus serial (2) negative proximal US	Primary	Management, RCT cohort	27.4% prevalence	3 mo follow-up	2 of 181 (1.1%)	
	Cogo et al[34]/1998	24% Pretest, 2 negative proximal US	Primary	Management	24% prevalence	3 mo follow-up	8 of 1301 (0.6%)	Included in Righini et al[31] meta-analysis
	Ruiz-Gimenes et al[36]/2004	Overall prevalence 22.6%	Primary	Management	44.6% among high pretest	3 mo follow-up	0 of 41	
What are the consequences of using a highly sensitive DD as a stand-alone test to exclude DVT?	Geersing et al[24]/2009	Suspected DVT, point of care testing	Meta-analysis	Accuracy and management studies included	ED or office or home (point of care)	Sensitivity/specificity	Highest sensitivity of 96% and 93%, within the range of previous meta-analysis	Results for moderately sensitive tests: 85%; 95% CI, 62%-74% (within range of Goodacre et al[25] 2005 meta-analysis); for 50% pretest, 18% posttest; for 5% pretest, 1.1% posttest
	Goodacre et al[25]/2005	Suspected DVT	Meta-analysis	Accuracy studies	Mixed	Sensitivity/specificity	Highest sensitivity 94%	For moderately sensitive assays, sensitivity 85%-87%
	Stein et al[27]/2004	Suspected DVT	Meta-analysis	Prospective accuracy		Sensitivity/specificity	Highest sensitivity for ELISA 96% (95% CI, 91%-100%)	Authors claim as good as US (but serial US needed if PTP high)

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Table S10—*Continued*

Question From Structured Clinical Question Table	Study/Year	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort[s] is From an RCT)	Patient Population	Outcome Measure[a]	Result	Comments
	Di Nisio et al[26]/2007	Suspected DVT	Meta-analysis	Prospective accuracy	Mixed	Sensitivity/specificity	Range consistent with other meta-analyses; highest sensitivity of 97%	Assuming 50% prevalence (high pretest) and 50% specificity, the test would miss 15 of 500 cases, and posttest negative is 15 of 265 or 0.6%
	Fancher et al[29]/2004	Suspected DVT	Meta-analysis	Accuracy and management studies	Mixed	Sensitivity/specificity	Overall sensitivity 98% (95% CI, 96%-99%), specificity 46% (95% CI, 28%-67%) If pretest 5% → posttest 0.3% If pretest 10% → posttest 0.6% If pretest 20% → posttest 1.2% If pretest 30% → posttest 2.1%	
What are the consequences of using PTP and DD to exclude DVT?	Fancher et al[29]/2004	Low pretest and negative moderately sensitive DD	Meta-analysis	Cohorts from management and accuracy studies	Frequency of DVT at presentation, 10.1%-43.2%	3 mo follow-up	0.5% (95% CI, 0.1%-1.1%)	Likely includes people with previous DVT
	Kearon et al[38]/2001	Low pretest and negative moderately sensitive DD	Primary	Management	Referred to thrombosis service, pretest prevalence 14%, for low pretest 2%	3 mo follow-up	1 of 171 (0.6%; 95% CI, 0-2.9%)	Included in Fancher et al[29] meta-analysis
	Wells et al[30]/2006	Low pretest and negative moderately sensitive DD	Meta-analysis	Cohorts from management and accuracy studies	5% prevalence	3 mo follow-up	0.9% LR negative, 0.20 (0.12-0.31)	

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Table S10—*Continued*

Question From Structured Clinical Question Table	Study/Year	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort[s] is From an RCT)	Patient Population	Outcome Measure[a]	Result	Comments
	Geersing et al[24]/2009	Low PTP and negative moderately sensitive DD	Meta-analysis	Cohorts from management and accuracy studies		Posttest calculated	SimpliRED: 1.1% (95% CI, 0.8%-1.5%); Clearview Simplify: 1.1% (0.9%-1.5%)	Calculated assuming 5% pretest
	Anderson et al[17]/2003	Low pretest and negative DD	Primary	Management	ED patients, overall prevalence 3.7%	3 mo follow-up	3 of 316 (0.95%)	Mixed DD; SimpliRED and IL DD; included in Fancher et al[29] meta-analysis
	Subraminian et al[28]/2006	Low Hamilton score and negative moderately sensitive DD	Primary	Accuracy with 3-mo follow-up	ED	3 mo follow-up	1 of 103 (1.0%) by low Hamilton, 1 of 81 (1.2%) by low Wells	Calf thrombosis
	Büller et al[32]/2009	Primary care, lower score on unique prediction rule, and negative moderately sensitive DD,	Primary	Management	Outpatients, primary practice, prevalence 13%	3 mo follow-up	7 of 500, 1.4% (95% CI, 0.6%-2.9%)	Two-level CDR incorporating negative SimpliRED DD and unique prediction rule
	Wells et al[21]/2003	Unlikely Wells score and negative moderately sensitive DD	Primary	Cohort from RCT	Outpatients, primary practice, prevalence 4.4%	3 mo follow-up	2 of 218, 0.9% (95% CI, 0.1%-3.3%)	
	Fancher et al[29]/2004	Moderate pretest and negative moderately sensitive DD	Meta-analysis	Cohorts from management and accuracy studies	Frequency of DVT at presentation, 10.1%-43.2%	3 mo follow-up	3.5% (95% CI, 1.4%-6.9%)	
	Wells et al[30]/2006	Moderate pretest and negative moderately sensitive DD	Meta-analysis	Cohorts from management and accuracy studies	Frequency of DVT at presentation, 17%	3 mo follow-up	4.4% LR negative 0.23 (0.13-0.39)	

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Table S10—*Continued*

Question From Structured Clinical Question Table	Study/Year	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort[s] is From an RCT)	Patient Population	Outcome Measure[a]	Result	Comments
	Geersing et al[24]/2009	Moderate pretest and negative moderately sensitive DD, point of care	Meta-analysis	Cohorts from management and accuracy studies		Posttest calculated	SimpliRED: 4.9% (95% CI, 3.6%-6.8%) or Clearview Simplify 5.2% (4.1%-6.5%)	Calculated assuming 20% pretest
	Büller et al[32]/2009	Higher score on unique prediction rule and negative moderately sensitive DD	Primary	Cohort	Approximately 26% prevalence	Positive or negative US	12 of 63, 19%	
	Fancher et al[29]/2004	High pretest and negative moderately sensitive DD	Meta-analysis	Cohorts from management and accuracy studies	Frequency of DVT at presentation,n 10.1%-43.2%	3 mo follow-up	21.4% (95% CI, 8.5%-37.9%)	
	Wells et al[30]/2006	High pretest and negative moderately sensitive DD	Meta-analysis	Cohorts from management and accuracy studies	Frequency of DVT at presentation, 53%	3 mo follow-up	19% LR negative 0.20 (0.10-0.38)	
	Geersing et al[24]/2009	High pretest and negative moderately sensitive DD	Meta-analysis	Cohorts from management and accuracy studies		Posttest calculated	> 10 for lower end of CI	Calculated assuming 50% pretest
	Wells et al[30]/2006	Low pretest and negative highly sensitive DD	Meta-analysis	Cohorts from management and accuracy studies	Frequency of DVT at presentation, 10.1%-43.2%	3 mo follow-up	NPV, 99 (97-100); LR negative, 0.1 (0.03-0.37); estimated posttest 0.5%	Low only
	Geersing et al[24]/2009	Low pretest and negative highly sensitive DD, point of care	Meta-analysis	Cohorts from management and accuracy studies		Post-TP calculated	Cardiac: 0.4% (95% CI, 0.2%-0.8%) or Triage: 0.9 (95% CI, 0.4%-2.2%)	Calculated assuming 5% pretest

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Table S10—*Continued*

Question From Structured Clinical Question Table	Study/Year	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort[s] is From an RCT)	Patient Population	Outcome Measure[a]	Result	Comments
	Oudega et al[37]/2005	Lowest pretest and negative highly sensitive DD	Single cohort (repeat US as reference standard)	Accuracy	12% Prevalence	Posttest on repeat CUS	5 of 222, 2.3%	
	Fancher et al[29]/2004	Low and moderate pretest; highly sensitive DD	Meta-analysis	Cohorts from management and accuracy studies	Frequency of DVT at presentation 10.1%-43.2%	3 mo follow-up	0.4% (95% CI, 0.04%-1.1%)	
	Wells et al[30]/2006	Moderate pretest and negative highly sensitive DD	Meta-analysis	Cohorts from management and accuracy	17% Prevalence	3 mo follow-up	NPV, 99% (95% CI, 96%-100%); LR negative, 0.05 (0.01-0.21); estimated posttest 1%	
	Aguilar et al[35]/2002	Moderate pretest and negative highly sensitive DD	Primary	Cohort of moderate pretest, accuracy	19.4% Prevalence	3 mo follow-up also performed	0 of 35	
	Bates et al[15]/2003	Moderate pretest and negative highly sensitive DD	Primary	Cohort	9.0% Prevalence	3 mo follow-up	1 of 90, 1.1%	
	Schutgens et al[16]/2003	Moderate pretest and negative sensitive DD	Primary	Cohort	37.7% Prevalence	3 mo follow-up	0 of 89	
	Geersing et al[24]/2009	Moderate pretest and negative highly sensitive DD, point of care	Meta-analysis	Cohorts from management and accuracy studies		Posttest calculated	Cardiac: 1.7% (95% CI, 1.0%-3.8%) or Triage: 4.3% (95% CI, 2.0%-9.7%)	Calculated assuming 20% pretest
	Fancher et al[29]/2004	High pretest and negative highly sensitive DD	Meta-analysis	Cohorts from management and accuracy studies	Frequency of DVT at presentation 10.1%-43.2%	3 mo follow-up	6.4% (95% CI, 1.7%-14.5%)	

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Table S10—*Continued*

Question From Structured Clinical Question Table	Study/Year	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort[s] is From an RCT)	Patient Population	Outcome Measure[a]	Result	Comments
	Wells et al[30]/2006	High pretest and negative highly sensitive DD	Meta-analysis	Cohorts from management and accuracy studies	Frequency of DVT at presentation 53%	3 mo follow-up	NPV, 92% (95% CI, 81%-97%); LR negative, 0.07 (95% CI, 0.03-0.18); estimated posttest 8.6%	
	Geersing et al[24]/2009	High PTP and negative highly sensitive DD, point of care	Meta-analysis	Cohorts from management and accuracy studies		Posttest calculated	Cardiac: 6.5% (95% CI, 3.8%-13.7%) or Triage: 15.3% (95% CI, 7.4%-30.1%)	Calculated assuming 50% pretest
What are the consequences of using single proximal US to rule out DVT among those with low pretest and positive moderately sensitive DD	Anderson et al[17]/2003	ED, low pretest, positive DD, negative US	Primary	ED cohort	ED, 18.1% overall, low pretest, prevalence 3.8% to start	Posttest	0 of 113, 0%	Mixed DD: SimpliRED and IL DD; both events confined to calf veins
	Wells et al[21]/2003	Unlikely Wells score and positive DD and negative US	Primary	Cohort (from RCT)	Outpatients, prevalence 4.4%,	Posttest	0 of 85	Mixed DD: SimpliRED and IL DD
What are the consequences of using US to rule out DVT among those with moderate pretest and positive moderately sensitive DD?	Tick et al[20]/2002	Negative US and positive moderately sensitive DD and combination of moderate-high pretest	Primary	Cohort management	11% Prevalence	Posttest	15 of 83, 18.1% (95% CI, 10.5%-28.1%)	18.1% in mixed moderate to high. Unable to determine results for moderate alone

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Table S10—*Continued*

Question From Structured Clinical Question Table	Study/Year	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort[s] is From an RCT)	Patient Population	Outcome Measure[a]	Result	Comments
What are the consequences of using US to rule out DVT among those with moderate pretest and a positive highly sensitive DD?	Aguilar et al[35]/2002	Moderate PTP and positive sensitive DD, followed by negative proximal US	Primary	Cohort management	Referral to ED, 19.4%	3 mo follow-up	0 of 73, 0%	Highly sensitive DD
What are the consequences of using serial proximal US to exclude DVT in patients with a positive DD?	Tick et al[20]/2002	Moderate to high pretest, positive moderately sensitive DD, first US negative	Primary	Management	Referral practice, 56.5% prevalence	3 mo follow-up	2 of 64 missed on second US (3.1%)	Overall 15 of 83 with abnormal SimpliRED DD had VTE (18%), 13 detected on second US, 2 of 64 missed, 3.1%
	Bernardi et al[33]/1998	PTP not specified; positive highly sensitive DD and first US negative	Primary	Management	University practice, 27.5% prevalence	3 mo follow-up	2 of 83 missed on second US (2.4%)	Overall 7 of 88 (8%) had VTE, 5 detected on repeat US at 1 wk
	Schutgens et al[16]/2003	Irrespective of pretest, positive highly sensitive DD, first US negative	Primary	Management	Referral practice, 39% prevalence	3 mo follow-up	6 of 291 missed on second US (2.1%)	
What are the consequences of using a negative DD to obviate the need for serial testing in patients with a negative proximal US and moderate or high pretest at presentation?	Tick et al[20]/2002	Moderate to high pretest, negative US, negative moderately sensitive DD	Primary	Management	56.5% prevalence	3 mo follow-up	0 of 148	

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Table S10—*Continued*

Question From Structured Clinical Question Table	Study/Year	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort[s] is From an RCT)	Patient Population	Outcome Measure[a]	Result	Comments
	Kraaijenagen et al[13]/2002	22% Original prevalence	Primary	Accuracy plus follow-up	22% prevalence	3 mo follow-up	6 of 828, 0.7%; (95% CI, 0.3%-1.6%)	
	Kearon et al[39]/2005	No pretest established, but 7.5% prevalence, likely low to moderate and negative US and negative moderately sensitive DD	Primary	Management	7.5%	Posttest, 6 mo follow-up	3 of 309, 1%	
	Anderson et al[17]/2003	Moderate pretest, negative US, negative DD (mixed)	Primary	Management	18.1% prevalence	33 mo follow-up	0 of 244	Mixed DD: SimpliRED and IL DD
	Wells et al[21]/2003	Likely Wells score, negative US, negative DD	Primary	Management cohort from RCT	27.3% prevalence	3 mo follow-up	0 of 81	Mixed DD: SimpliRED and IL DD
	Schutgens et al[16]/2003	Consecutive referred, high pretest plus negative highly sensitive DD and negative US	Primary	Management	At least 39%	Posttest	1 of 37, 2.7%	
	Bates et al[15]/2003	Consecutive outpatients, high pretest, negative highly sensitive DD and negative US	Primary	Management	29.6%	Posttest	0 of 20	

CDR = clinical decision rule; LR = likelihood ratio. See Tables S1-S3 legends for expansion of abbreviations.

[a]eg, Post-TP during 3-mo follow-up sensitivity or specificity, and so forth.

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Table S11—*[Sections 3.1-3.5] Evidence Profiles for Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Among Patients With Low PTP, What Is the 3-mo Post-TP of VTE Following Exclusion of DVT With a Given Diagnostic Strategy?*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Strategy Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
Low PTP and negative moderately sensitive DD											
3 meta-analyses	Management and accuracy studies	…	…	Some (−1) (calculated in one meta-analysis; accuracy studies included)	…	…	…	Assumed 0	N/A	0.5 (0.07-1.1), 0.9 (LR, 0.2; 95% CI, 0.12-0.31), 1.1 (0.8-1.5)	Moderate
Low PTP and negative highly sensitive DD											
5	Management	…	…	…	…	…	1,270/824	Assumed 0	N/A	1.0 (0.5-1.7)	High
3 meta-analyses	Management and accuracy studies	…	…	Some (−1), includes accuracy studies	Upper limit of CI in one meta-analysis > 2%	…	…	Assumed 0	N/A	0.4 (0.04-1.1), 0.4 (0.2-0.8); 0.9 (0.4-2.2)	Moderate

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Table S11—*Continued*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Strategy Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
Low PTP and single negative proximal US											
4	Management cohorts	…	…	Some were calf vein thrombosis	…	…	944/885	Assumed 0	N/A	0.9 (0.5-1.6)	High
Low PTP and positive DD (moderately or highly sensitive) followed by negative proximal US											
2	Management cohorts	…	…	…	…	Mixed DD tests; number of patients tested with each assay not clear	765/198	Assumed 0	N/A	0 (0-1.5)	High

Bibliography: Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. *N Engl J Med*. 2003;349(13):1227-1235. Geersing GJ, Janssen KJ, Oudega R, et al. Excluding venous thromboembolism using point of care D-dimer tests in outpatients: a diagnostic meta-analysis. *BMJ*. 2009:339:2990. Fancher TL, White RH, Kravitz RL. Combined use of rapid D-dimer testing and estimation of clinical probability in the diagnosis of deep vein thrombosis: a systematic review. *BMJ*. 2004;329(7470):821. Anderson DR, Kovacs MJ, Kovacs G, et al. Combined use of clinical assessment and d-dimer to improve the management of patients presenting to the emergency department with suspected deep vein thrombosis (the EDITED Study). *J Thromb Haemost*. 2003;1(4):645-651. Bates SM, Kearon C, Crowther M, et al. A diagnostic strategy involving a quantitative latex d-dimer assay reliably excludes deep venous thrombosis. *Ann Intern Med*. 2003;138(10): 787-794. Schutgens REG, Ackermark P, Haas FJLM, et al. Combination of a normal D-dimer concentration and a non-high pretest clinical probability score is a safe strategy to exclude deep venous thrombosis. *Circulation*. 2003;107(4):593-659. Elf JL, Strandberg K, Nilsson C, et al. Clinical probability assessment and D-dimer determination in patients with suspected deep vein thrombosis, a prospective multicenter management study. *Thromb Res*. 2009;123:612-616. Dewar C, Selby C, Jamieson K, et al. Emergency department nurse-based outpatient diagnosis of DVT using an evidence-based protocol. *Emerg Med J*. 2008;25:411-416. Anderson DR, Wells PS, Stiell I, et al. Thrombosis in the emergency department: use of a clinical diagnosis model to safely avoid the need for urgent radiological investigation. *Arch Intern Med*. 1999;159(5):477-482. Tick LW, Ton E, ven Voorthuizen R, et al. Practical diagnostic management of paitents with clinically suspected deep vein thrombosis by clinical probability test, compression ultrasonography and D-dimer test. *Am J Med*. 2002;113(8):630-635. Wells PS, Anderson DR, Bormanis J, et al. Value of assessment of pre-test probability of deep vein thrombosis in clinical management. *Lancet*. 1997;350(9094):1795-1798. Ruiz-Gimenez N, Friera A, Artieda P, et al. Rapid D-dimer test combined a clinical model for deep vein thrombosis. Validation with ultrasonography and clinical follow-up in 383 patients. *Thromb Haemost*. 2004;91(6):1237-1246. Wells PS, Owen C, Doucette S, Fergusson D, Tran H. Does this patient have deep vein thrombosis? *JAMA*. 2006;295(2):199-207. ceR *Am J Roetgenol*. 2007;189(5):1071-1076. Consequences of presenting with VTE when specified strategies are used to rule out suspected first lower extremity DVT in patient with a low PTP. Settings: outpatients. See Table S1, S3, and S10 legends for expansion of abbreviations.

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Table S12—*[Sections 3.1-3.5] Evidence Profiles for Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Among Patients With Low to Moderate PTP, What Is the 3-mo Post-TP of VTE Following Exclusion of Proximal DVT with a Given Diagnostic Strategy?*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
Low to moderate PTP and negative moderately sensitive DD											
1	Management cohort	…	…	…	Some (−1), upper limit of CI >2%	…	852/500	Assumed 0	N/A	1.4 (0.7-2.6)	Moderate
Low to moderate PTP and negative moderately or highly sensitive DD											
1	Management cohort	…	…	…	Some (−1), upper limit of CI >2%	Number of patients tested with each assay not clear	317/218	Assumed 0	N/A	0.9 (0.2-2.9)	Moderate
Low to moderate PTP and negative highly sensitive DD											
1	Management cohort	…	…	…	…	…	1,169/718	Assumed 0	N/A	0.4 (0.1-1.5)	Moderate
1	Meta-analysis of management and accuracy studies	…	…	Some (−1) accuracy studies included	…	…	…	Assumed 0	N/A	0.4 (0.1-1.1)	Moderate
Low to moderate PTP and single negative proximal US											
1	Management cohort	…	…	…	Some (−1), upper limit of CI >2%	…	284/272	Assumed 0	N/A	1.5 (0.5-3.5)	Moderate
Low to moderate PTP and positive DD (highly or moderately sensitive) followed by negative proximal US											
1	Management cohort	…	…	…	Some (−1), upper limit of CI >2%	Mixed DD tests used in the study; number of patients tested with each assay not clear	317/85	Assumed 0	N/A	0 (0-3.5)	Moderate

Bibliography: Buller HR, Ten Cate-Hoek AJ, Hoes AW, et al. AMUSE (Amsterdam Maastricht Utrecht Study on thromboEmbolism in primary care. *Ann Intern Med*. 2009;150(4):229-235. Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. *N Engl J Med*. 2003;349(13):1227-1235. Gibson NS, Schellong WM, Kheir DY, et al. Safety and sensitivity of two ultrasound strategies in patients with clinically suspected deep venous thrombosis: a prospective management study. *J Thromb Haemost*. 2009;7(12):2035-2041. Fancher TL, White RH, Kravitz RL. Combined use of rapid D-dimer testing and estimation of clinical probability in the diagnosis of deep vein thrombosis: systematic review. *BMJ*. 2004;239(7590):821.
Consequences of presenting with VTE when specified strategies are used to rule suspected first lower extremity DVT in patients with a low to moderate PTP. Settings: outpatients. See Table S1 and S3 legends for expansion of abbreviation.

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Table S13—*[Sections 3.1-3.5] Evidence Profiles for Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Among Patients With Moderate PTP, What Is the 3-mo Post-TP of VTE Following Exclusion of DVT With a Given Diagnostic Strategy?*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
Moderate PTP and negative moderately sensitive DD											
3	Meta-analyses of management and cohort studies	…	…	Some (−1), accuracy studies included	…	…	…	Assumed 0	N/A	4.4; 3.5 (1.4-6.9), 4.9, or 5.2 (depending on DD, SimpliRED or Simplify), lower limit of CI > 3%	Moderate
Moderate PTP and negative highly sensitive DD											
3	Management cohort	…	…	…	Some (−1), upper limit of CI > 2%	…	655/214	Assumed 0	N/A	0.6 (0.1-2.2)	Moderate
2	Management and accuracy	…	…	Some (−1), accuracy studies included	Some (−1), upper limit of CI > 2%		…	Assumed 0	N/A	NPV, 99 (96-100); estimated post-TP 1% Point-of-care meta-analysis: 1.7 (1.0-3.8) or 4.3 (2.0-9.7) for Cardiac and Triage test	Low
Moderate PTP and single negative proximal US											
1	Management cohort	…	…	…	Some (−1), upper limit of CI > 2%	-	144/114	Assumed 0	N/A	0.9 (0.1-4.1)	Moderate
Moderate PTP with negative US and negative DD (either moderately or highly sensitive)											
2	Management cohort	…	…	…	…	Number of patients tested with each assay not clear	675/325	Assumed 0	N/A	0 (0-0.9)	High
Moderate PTP and negative serial proximal US											
3	Management cohort	…	…	…	Some (−1), upper limit of CI > 2%		?/365	Assumed 0	N/A	1.1 (0.4-2.5)	Moderate

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Table S13—*Continued*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
1	Meta-analysis	…	…	Some (−1), includes accuracy and management studies	…	…	…	Assumed 0	N/A	0.6 (0.4-0.9)	Moderate
Moderate PTP and positive highly sensitive DD followed by single negative US											
1	Management cohort	…	…	…	Some (−1), upper limit of CI > 2%	…	134/73	Assumed 0	N/A	0 (0-4.0)	Moderate
Moderate PTP with negative initial US and positive DD (either moderately or highly sensitive) followed by negative US											
1	Management cohort	…	…	…	Some (−1), upper limit of CI > 2%	Number of patients tested with each assay not clear	426/94	Assumed 0	N/A	0 (0-0.3.1)	Moderate

Bibliography: Wells PS, Owen C, Doucette S, Fergusson D, Tran H. Does this patient have deep vein thrombosis? *JAMA*. 2006;295(2):1997-2207. Geersing GJ, Janssen KJ, Oudega R, et al. Excluding venous thromboembolism using point of care D-dimer tests in outpatients: a diagnostic meta-analysis. *BMJ*. 2009;339:2990. Fancher TL, White RH, Kravitz RL. Combined use of rapid D-dimer testing and estimation of clinical probability in the diagnosis of deep vein thrombosis: a systematic review. *BMJ*. 2004;329(7470):821. Bates SM, Kearon C, Crowther M, et al. A diagnostic strategy involving a quantitative latex d-dimer assay reliably excludes deep venous thrombosis. *Ann Intern Med*. 2003;138(10):787-794. Schutgens REG, Ackermark P, Haas FJLM, et al. Combination of a normal D-dimer concentration and a non-high pretest clinical probability score is a safe strategy to exclude deep venous thrombosis. *Circulation*. 2003;107(4):593-597. Aguilar C, Martinez A, Artinez A, Del rio C, Vasquez M, Rodriguez FJ. Diagnostic value of D-dimer in patients with a moderate pre-test probability of deep venous thormbosis. *Br J Haematol*. 2002;118(1):275-277. Ruiz-Gimenez N, Friera A, Artieda P, et al. Rapid D-dimer test combined a clinical model for deep vein thrombosis. Validation with ultrasonography and clinical follow-up in 383 patients. *Thromb Haemost*. 2004;91(6):1237-1246. Anderson DR, Kovacs MJ, Kovacs G, et al. Combined use of clinical assessment and d-dimer to improve the management of patients presenting to the emergency department with suspected deep vein thrombosis (the EDITED Study). *J Thromb Haemost*. 2003;1(4):645-651. Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-dimer in the diagnosis of suspected deep-vein thrombosis. *N Engl J Med*. 2003;349(13):1227-1235. Anderson DR, Wells PS, Stiell I, et al. Thrombosis in the emergency department: use of a clinical diagnosis model to safely avoid the need for urgent radiological investigation. *Arch Intern Med*. 1999;159(5):477-482. Wells PS, Anderson DR, Bormanis J, et al. Value of assessment of pre-test probability of deep vein thrombosis in clinical management. *Lancet*. 1997;350(9094):1795-1798. Kearon C, Ginsberg JS, Douketix J, et al. A randomized trial of diagnostic strategies after normal proximal vein ultrasonography for suspected deep venous thrombosis: D-dimer testing compared with repeated ultrasonography. *Ann Intern Med*. 2005;142(7):490-496. Righini M, Perrier A, De Moerloose P, et al. D-dimer for venous thromboembolism diagnosis: 20 years later. *J Thromb Haemost*. 2008;6:1059-1071. Consequences of presenting with VTE when specified strategies are used to rule out suspected first lower extremity DVT in patients with a moderate PTP. Settings: outpatients. See Table S1 and S3 legends for expansion of abbreviations.

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Table S14—*[Sections 3.1-3.5] Evidence Profiles for Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Among Patients With Moderate to High PTP, What Is the 3-mo Post-TP of VTE Following Exclusion of Proximal DVT With a Given Diagnostic Strategy?*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
Moderate to high PTP and negative single proximal US and moderately sensitive DD											
1	Management cohort	…	…	…	Some (−1) with upper limit of CI reaching 2%	…	531/148	Assumed 0	N/A	0 (0-2.0)	Moderate
Moderate to high PTP and negative single proximal US and DD (moderately or highly sensitive)											
1	Management cohort	…	…	…	Some (−1), upper limit of CI > 2%	Number of patients tested with each assay not clear	249/81	Assumed 0	N/A	0 (0-3.6)	Moderate
Pooling of above two studies	Management cohort	…	…	…	…	Number of patients tested with each assay not clear	780/229	Assumed 0	N/A	0 (0-1.3)	High
Moderate to high PTP and negative serial proximal US											
1	Management cohort	…	…	…	Some (−1), upper limit of CU > 2%	…	246/181	Assumed 0	N/A	1.1 (0.2-3.4)	Moderate
Moderate to high PTP with negative proximal US and positive moderately sensitive DD followed by negative proximal US											
1	Management cohort	…	…	…	Some (lower limit of CI < 2%), major if we want to use it to exclude (upper CI > 5)	…	531/83	Assumed 0	N/A	3.6 (1-9.1)	Moderate not to use, low to use

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Table S14—*Continued*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
Moderate to high PTP with negative proximal US and positive DD (either moderately or highly sensitive) followed by negative proximal US											
1	Management cohort	…	…	…	Some (−1), upper limit of CI >2%	Not sure how many patients had which DD	249/97	Assumed 0	N/A	0 (0-3.0)	Moderate
Moderate to high PTP with negative proximal US and positive DD (either moderately or highly sensitive) followed by negative proximal US; above two studies pooled											
2	Management cohort	…	…	…	Some (−1), upper limit of CI >2%	Not sure how many patients had which DD	780/180	Assumed 0	N/A	1.7 (0.5-4.2)	Moderate

Bibliography: Tick LW, Ton E, van Voorthuizen T, et al. Practical diagnostic management of patients with clinically suspected deep vein thrombosis by clinical probability test, compression ultrasonography and D-dimer test. *Am J Med*. 2002;113(8):630-635. Wells PS, Anderson DR, Rodger M, et al. Evaluation of D-dimer in the diagnosis of suspected deep vein thrombosis. *N Engl J Med*. 2003;349(13): 1227-1235. Consequences of presenting with VTE when specified strategies are used to rule out suspected first lower extremity DVT in patients with moderate to high PTP. Settings: outpatients. See Table S1 legend for expansion of abbreviation.

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Table S15—*[Sections 3.1-3.5] Evidence Profiles for Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Among Patients With High PTP, What Is the 3-mo Post-TP of VTE Following Exclusion of DVT With a Given Diagnostic Strategy?*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
High PTP and negative moderately sensitive DD											
2	Meta-analysis of management and cohort studies	…	…	Some (−1), accuracy studies	…	…	…	Assumed 0	N/A	In each case point estimate > 10%	Moderate
High PTP and negative highly sensitive DD											
3	Meta-analysis of management and cohort studies	…	…	Some (−1), accuracy studies	Minimal, in one case lower limit of CI < 2%	…	…	Assumed 0	N/A	In each case point estimate > 5%	Moderate
High PTP and negative single proximal US and highly sensitive DD											
2	Management cohort	…	…	…	Large, upper limit of CI 7.8%	…	350/59	Assumed 0	N/A	1.7 (0.1-7.8)	Low
High PTP and negative serial (×2) proximal US											
4	Management cohort	…	…	…	Some (−1), upper limit of CI > 2%	…	291/221	Assumed 0	N/A	0.9 (0.2-2.8)	Moderate

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Table S15—*Continued*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
High PTP and negative proximal US and positive highly sensitive DD followed by negative proximal US											
1	Management cohort	…	…	…	Major (−2), CI from 0.1% to 12.5%	Scant data	279/36	Assumed 0	N/A	2.8 (0.1-12.5)	Low
High PTP and negative proximal US followed by negative venography											
3	Management cohort	…	…	…	Major (−2), upper limit of CI over 5	Scant data	168/43	Assumed 0	N/A	0 (0-6.7)	Low

Bibliography: Wells PS, Owen C, Doucette S, Fergusson D, Tran H. Does this patient have deep vein thrombosis? *JAMA*. 2006;295(2):1997-2207. Fancher TL, White RH, Kravitz RL. Combined use of rapid D-dimer testing and estimation of clinical probability in the diagnosis of deep vein thrombosis: a systematic review. *BMJ*. 2004;329(7470):821. Geersing GJ, Janssen KJ, Oudega R, et al. Excluding venous thromboembolism using point of care D-dimer tests in outpatients: a diagnostic meta-analysis. *BMJ*. 2009;339:2990. Bates SM, Kearon C, Crowther M, et al. A diagnostic strategy involving a quantitative latex d-dimer assay reliably excludes deep venous thrombosis. *Ann Intern Med*. 2003;138(10):787-794. Schutgens REG, Ackermark P, Haas FJLM, et al. Combination of a normal D-dimer concentration and a non-high pretest clinical probability score is a safe strategy to exclude deep venous thrombosis. *Circulation*. 2003;107(4):593-597. Dewar C, Selby C, Jamieson K, et al. Emergency department nurse-based outpatient diagnosis of DVT using an evidence-based protocol. *Emergency Med*. 2008;25:411-416. Ruiz-Gimenez N, Friera A, Artieda P, et al. Rapid D-dimer test combined a clinical model for deep vein thrombosis. Validation with ultrasonography and clinical follow-up in 383 patients. *Thromb Haemost*. 2004;91(6):1237-1246. Kearon C, Ginsberg JS, Douketis J, et al. A randomized trial of diagnostic strategies after normal proximal vein ultrasonography for suspected deep venous thrombosis: D-dimer testing compared with repeated ultrasonography. *Ann Intern Med*. 2005;142(7):490-496. Anderson DR, Wells PS, Stiell I, et al. Thrombosis in the emergency department: use of a clinical diagnosis model to safely avoid the need for urgent radiological investigation. *Arch Intern Med*. 1999;59(5):477-482. Perrier A, Desmarais S, Miron MJ, et al. Non-invasive diagnosis of venous thromboembolism in outpatients. *Lancet*. 1999;353(9148):190-195. Wells PS, Anderson DR, Bormanis J, et al. Value of assessment of pre-test probability of deep vein thrombosis in clinical management. *Lancet*. 1997;350(9094):1795-1798. Consequences of presenting with VTE when specified strategies are used to rule out suspected first lower extremity DVT in patients with a high PTP. Settings: outpatients. See Table S1 legend for expansion of abbreviation.

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Table S16—*[Sections 3.1-3.5] Evidence Profiles for Diagnostic Studies Assessing DD, PTP, and Proximal US for the Diagnosis of Suspected First Lower Extremity DVT: Among Patients With an Unspecified PTP, What Is the 3-mo Post-TP of VTE Following Exclusion of Proximal DVT With a Given Diagnostic Strategy?*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
Unspecified PTP and negative highly sensitive DD											
5 meta-analyses	Meta-analysis of accuracy studies	…	Some inconsistency (−1)	Some (−1), accuracy studies	Some (−1)	…	…	…	…	Sensitivity from 93%-96% (point of care) to 97.7%, in modeling assuming best sensitivity (97.7%), post-TP > 2% for PTP of 30%	Moderate
Unspecified PTP and negative single proximal US and moderately sensitive DD											
2	Management and cohort studies	…	…	…	…	Prevalence 22.1%	2,209/1,137	Assumed 0	N/A	0.8 (0.4-1.4)	High
Unspecified PTP and negative single proximal US followed by negative moderately sensitive DD or positive moderately sensitive DD and then negative second proximal US											
1	Management cohort	…	…	…	…	Prevalence 23.3%	1,045/828	Assumed 0	N/A	1.1 (0.6-1.9)	High
Unspecified PTP and negative single proximal US followed by negative highly sensitive DD											
1	Management cohort	…	…	…	…	Prevalence 39.1%	686/598	Assumed 0	N/A	0.2 (0.2-0.8)	High
Unspecified PTP and negative serial proximal US											
3	Management cohort	…	…	…	…	Prevalence 20.9%	2,662/2071	Assumed 0	N/A	1.0 (0.7-1.5)	High
1	Meta-analysis	…	…	Some (−1), both accuracy and management studies	…	…	…	Assumed 0	N/A	0.6 (0.4-0.9)	Moderate
Unspecified PTP and negative proximal US plus positive moderately sensitive DD followed by negative proximal US											
1	Management cohort	…	…	…	Some (−1), lower limit of CI < 2%	Prevalence 24.4%	1,739/520	Assumed 0	N/A	2.1 (1.2-3.5)	Moderate

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Table S16—*Continued*

Quality Assessment							Summary of Findings				
							No. of Patients		Effect		
No. of Studies	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Starting Strategy/ For Follow-up After Negative for DVT	Control Risk	Relative	Absolute, % (95% CI)	Quality
Unspecified PTP with negative proximal US and positive highly sensitive DD (done in all or in those with a negative US) followed by a negative proximal US											
3	Management cohort	…	…	…	Some (−1), lower limit of CI < 2%	Prevalence 31.6%	2,011/577	Assumed 0	N/A	2.2 (1.3-3.5)	Moderate
Unspecified PTP with negative proximal US and positive moderately sensitive DD followed by venography											
1[8]	Management cohort	…	…	…	Major (−2), only 2 events with wide CI	Prevalence 13.2%	470/58	Assumed 0	N/A	3.5 (0.6-10.5)	Low
Unspecified PTP with negative proximal US followed by venography among those with a high PTP											
1[2]	Management cohort	…	…	…	Some (−1), lower limit of CI < 2%	Prevalence 25.3%	474/343	Assumed 0	N/A	2.6 (1.4-4.5)	Moderate

Bibliography: Di Nisio M, Squizzato A, Rutjes AWS, et al. Diagnostic accuracy of D-dimer test for exclusion of venous thromboembolism: a systematic review. *J Thromb Haemost*. 2007;5:296-304. Geersing GJ, Janssen KJ, Oudega R, et al. Excluding venous thromboembolism using point of care D-dimer tests in outpatients: a diagnostic meta-analysis. *BMJ*. 2009;339:b2990. Goodacre S, Sampson FC, Sutton AJ, et al. Variation in the diagnostic performance of D-dimer for suspected deep vein thrombosis. *QJM*. 2005;98(7):513-527. Stein PD, Hull RD, Patel KC, et al. D-dimer for the exclusion of acute venous thrombosis and pulmonary embolism: a systematic review. *Ann Intern Med*. 2004;140:589-602. Fancher TL, White RH, Kravitz RL. Combined use of rapid D-dimer testing and estimation of clinical probability in the diagnosis of deep vein thrombosis: a systematic review. *BMJ*. 2004;329(7470):821. Kraaijenhagen RA, Piovella F, Bernardi E, et al. Simplification of the diagnostic management of suspected deep vein thrombosis. *Arch Intern Med*. 2002;162(8):907-911. Kearon C, Ginsberg JS, Douketis J, et al. A randomized trial of diagnostic strategies after normal proximal vein ultrasonography for suspected deep venous thrombosis: D-dimer testing compared with repeated ultrasonography. *Ann Intern Med*. 2005;142(7):490-496. Bernardi E, Camporese G, Buller HR, et al. Serial 2-point ultrasonography plus D-dimer vs whole-leg color-coded Doppler ultrasonography for diagnosing suspected symptomatic deep vein thrombosis: a randomized controlled trial. *JAMA*. 2008;300:1653-1659. Bernardi E, Prandoni P, Lensing AW, et al. D-dimer testing as an adjunct to ultrasonography in patients with clinically suspected deep vein thrombosis: prospective cohort study. The Multicentre Italian D-dimer Ultrasound Study Investigators Group. *BMJ*. 1998;317(7165):1037-1040. Heijboer H, Buller HR, Lensing AW, et al. A comparison of real-time compression ultrasonography with impedance plethysmography for the diagnosis of deep-vein thrombosis in symptomatic outpatients. *N Engl J Med*. 1993;329:1365-1369. Cogo A, Lensing AW, Koopman MM, et al. Compression ultrasonography for diagnostic management of patients with clinically suspected deep vein thrombosis: prospective cohort study. *BMJ*. 1998;316(7124):17-20. Righini M, Perrier A, De Moerloose P, et al. D-Dimer for venous thromboembolism diagnosis: 20 years later. *J Thromb Haemost*. 2008;6:1059-1071. Bates SM, Kearon C, Crowther M, et al. A diagnostic strategy involving a quantitative latex d-dimer assay reliably excludes deep venous thrombosis. *Ann Intern Med*. 2003;138(10):787-794. Schutgens REG, Ackermark P, Haas FJLM, et al. Combination of a normal D-dimer concentration and a non-high pretest clinical probability score is a safe strategy to exclude deep venous thrombosis. *Circulation*. 2003;107(4):593-559. Perrier A, Desmarais S, Miron MJ, et al. Non-invasive diagnosis of venous thromboembolism in outpatients. *Lancet*. 1999;353(9148):190-195. Consequences of presenting with VTE when specified strategies are used to rule suspected first lower extremity DVT in patients with an unspecified PTP. Settings: outpatients.
See Table S1 legend for expansion of abbreviation.

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Table S17—*[Sections 3.2-3.5] Methodology of Diagnostic Studies Evaluating Whole-Leg US in First Suspected Lower Extremity DVT: Meta-analysis of Accuracy Studies*

	Study Eligibility				
Study/Year	Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Exploration of Heterogeneity	Comments
Goodacre et al[41]/2006	Broad population, analyzed subgroup with symptoms of DVT	Tested 31 possible diagnostic algorithms using meta-analysis and modeling; whole-leg US, repeat if distal DVT imaged	All strategies compared against venography for all patients and no diagnostic testing at all	Varied with strategy	The modeling provided reporting for specificity of US for all DVT
Kearon et al[42]/1998	Symptomatic inpatients and outpatients	Whole-leg US	Venography	χ^2 comparison derived from fixed-effects model	Included 11 studies, 9 reporting specificity for distal DVT, which met methodologic criteria

All studies are cross-sectional unless otherwise indicated under Comments. IPD = individual patient data. See Table S1 legend for expansion of other abbreviation.

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Table S18—*[Sections 3.2-3.5] Methodology of Diagnostic Studies Evaluating Whole-Leg US in First Suspected Lower Extremity DVT: Individual Accuracy Studies*

	Study Details					
Study/Year	Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Consecutive Patients	Independent Test Assessment	Comments
Atri et al[43]/1996	Symptomatic for DVT	US of calf veins	Venography	Yes	No	
Baxter et al[44]/1990	Symptomatic for DVT	US of calf veins	Venography	No	Yes	
Baxter et al[45]/1992	Symptomatic for DVT	US of calf veins	Venography	No	Yes	
Belcaro et al[46]/1992	Symptomatic for DVT	US of calf veins	Venography	Yes	No	
Bendick et al[47]/1983	Symptomatic for DVT	US of calf veins	Venography	No	No	
Biondetti et al[48]/1990	Symptomatic for DVT	US of calf veins	Venography	Yes	No	
Bradley et al[49]/1993	Symptomatic for DVT	US of calf veins	Venography	Yes	No	
Burke et al[50]/1994	Symptomatic for DVT	US of calf veins	Venography	Yes	Yes	
Cogo et al[51]/1993	Symptomatic for DVT	US of calf veins	Venography	Yes	No	
De Laveaucoup et al[52]/1989	Symptomatic for DVT	US of calf veins	Venography	No	Yes	
Elias[53]/1987	Symptomatic for DVT	US of calf veins	Venography	Yes	Yes	
Forbes et al[54]/1998	Symptomatic for DVT	US of calf veins	Venography	Yes	No	
Grobety et al[55]/1996	Symptomatic for DVT	US of calf veins	Venography	Yes	No	
Guazzaloca et al[56]/1997	Symptomatic for DVT	US of calf veins	Venography	Yes	Yes	
Habscheid et al[57]/1990	Symptomatic for DVT	US of calf veins	Venography	No	Yes	
Kalodiki et al[58]/1993	Symptomatic for DVT	US of calf veins	Venography	No	No	
Labropoulos et al[59]/1995	Symptomatic for DVT	US of calf veins	Venography	No	Yes	
Lensing et al[60]/1989	Symptomatic for DVT	US of calf veins	Venography	Yes	Yes	
Leven and Hassan[61]/1990	Symptomatic for DVT	US of calf veins	Venography	No	No	
Lindqvist[62]/1977	Symptomatic for DVT	US of calf veins	Venography	No	No	
Mattos et al[63]/1992	Symptomatic for DVT	US of calf veins	Venography	Yes	Yes	
McCandless et al[64]/1985	Symptomatic for DVT	US of calf veins	Venography	Yes	No	
Miller et al[65]/1996	Symptomatic for DVT	US of calf veins	Venography	Yes	Yes	
Mitchell et al[66]/1991	Symptomatic for DVT	US of calf veins	Venography	Yes	Yes	
Monreal et al[67]/1989	Symptomatic for DVT	US of calf veins	Venography	Yes	Yes	
Puls et al[68]/1999	Symptomatic for DVT	US of calf veins	Venography	No	No	
Quintavalla et al[69]/1992	Symptomatic for DVT	US of calf veins	Venography	Yes	No	
Robertson et al[70]/1995	Symptomatic for DVT	US of calf veins	Venography	No	Yes	
Robertson et al[71]/1994	Symptomatic for DVT	US of calf veins	Venography	No	Yes	
Rose et al[72]/1990	Symptomatic for DVT	US of calf veins	Venography	Yes	Yes	
Rosier et al[73]/1992	Symptomatic for DVT	US of calf veins	Venography	No	No	

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Table S18—*Continued*

Study/Year	Study Details: Patient Population	Study Details: Diagnostic Test	Study Details: Outcome (Criterion Standard)	Consecutive Patients	Independent Test Assessment	Comments
Savy-Stortz et al[74]/1995	Symptomatic for DVT	US of calf veins	Venography	No	No	
Simons et al[75]/1995	Symptomatic for DVT	US of calf veins	Venography	No	No	
Size et al[76]/1993	Symptomatic for DVT	US of calf veins	Venography	No	Yes	
Yucel et al[77]/1991	Symptomatic for DVT	US of calf veins	Venography	No	No	
Zhou et al[78]/1990	Symptomatic for DVT	US of calf veins	Venography	No	No	
Palareti et al[79]/2010	Suspected DVT, ambulatory patients. No proximal DVT seen on proximal CUS, "DVT likely" PTP or positive highly sensitive DD	Single whole-leg US	Results of serial proximal US and 3-mo follow-up	?	Yes, patients received alternate tests as management driven by proximal US results; whole-leg US results blinded and not used for management. Patients with isolated calf DVT on whole-leg US not anticoagulated but followed with serial proximal US and if negative followed for outcome	Single-arm cohort study

In addition to meta-analysis, all studies are cross-sectional unless otherwise indicated under Comments. See Table S1 legend for expansion of abbreviation.

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Table S19—*[Sections 3.2-3.5] Methodology of Diagnostic Studies Evaluating Whole-Leg US in First Suspected Lower Extremity DVT: Meta-analysis of Management Cohort Studies*

	Study Eligibility					
Study/Year	Patient Population	Diagnostic Test	Outcome	Methods (Single-Arm Cohort vs Cohort From RCT)	Exploration of Heterogeneity	Comments
Johnson et al[3]/2010	Clinically suspected DVT	Single whole-leg US	≥ 90 d probability of VTE	Single-arm cohort (6 trials) one arm of RCT (1 trial)	Random effects model	Included IPD met-analysis from 2 included studies to assess PTP groups

Cohorts from single-arm studies or cohorts representing one of the arms of an RCT. See Table S1 and S2 legends for expansion of abbreviations.

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Table S20—*[Sections 3.2-3.5] Methodology of Diagnostic Studies Evaluating Whole-Leg US in First Suspected Lower Extremity DVT: Individual Management Studies With Cohorts*

	Study Details							
Study/Year	Patient Population	Diagnostic Test	Outcome	Methods (Single-Arm Cohort vs Cohort From RCT)	Consecutive Patients	Follow-up	Received Alternative Tests	Comments
Bernardi et al[3]/2008	Clinically suspected, first episode DVT (ambulatory patients)	Single whole-leg US	3-mo probability of VTE	Arm of RCT	Yes (1,053)	Telephone or in person	No	DVT diagnosed by noncompressibility and lack of augmentation in muscular calf veins
Gibson et al[1]/2009	Clinically suspected, first episode DVT, likely Wells score or positive highly sensitive DD (Tina-quant)	Single whole-leg US	3-mo probability of VTE	Arm of RCT	Yes (1,002)	Telephone or in person	No	DVT diagnosed by noncompressibility
Elias et al[4]/2003	Clinically suspected, first episode DVT (ambulatory patients)	Single whole-leg US	3-mo probability of VTE	Single-arm cohort	Yes (623)	Telephone or in person	No	Excluded patients with high pretest by the original Wells criteria DVT diagnosed by noncompressibility and intraluminal thrombus
Schellong et al[5]/2003	Clinically suspected DVT (ambulatory and inpatients)	Single whole-leg US	90-d probability of VTE	Single-arm cohort	Yes (1,646)	Telephone, mail, in person	No	DVT diagnosed by noncompressibility
Sevestre et al[6]/2009	Clinically suspected DVT (ambulatory patients)	Single whole-leg US	3-mo probability of VTE	Single-arm cohort	No	Telephone interview and record review, vital status	No	A priori random selection of population to complete follow-up DVT diagnosed by noncompressibility and lack of augmentation in muscular calf veins
Sevestre et al[7]/2010	Clinically suspected DVT (inpatients)	Single whole-leg US	3-mo probability of VTE	Single-arm cohort	No	Telephone interview and record review, vital status	No	A priori random selection of population to complete follow-up

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Table S20—*Continued*

Study/Year	Study Details: Patient Population	Study Details: Diagnostic Test	Study Details: Outcome	Study Details: Methods (Single-Arm Cohort vs Cohort From RCT)	Consecutive Patients	Follow-up	Received Alternative Tests	Comments
								DVT diagnosed by noncompressibility and lack of augmentation in muscular calf veins
Stevens et al[8]/2004	Clinically suspected, first episode DVT (ambulatory and inpatients)	Single whole-leg US	3-mo probability of VTE	Single-arm cohort	Yes (445)	Telephone or in person, record review	No	DVT diagnosed by noncompressibility
Subramaniam et al[9]/2005	Clinically suspected DVT (ambulatory patients)	Single whole-leg US	3-mo probability of VTE	Single-arm cohort	Yes (526)	Telephone or in person, record review	No	DVT diagnosed by noncompressibility

Cohorts from single-arm studies or cohorts representing one of the arms of an RCT. See Table S1 and S2 legends for expansion of abbreviations.

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Table S21—*[Sections 3.2-3.5] Methodology of Diagnostic Studies Evaluating Whole-Leg US in First Suspected Lower Extremity DVT: Individual RCTs With Direct Comparison Of Diagnostic Strategies*

Study/Year	Study Details				Concealment of Randomization	Blinding	Follow-up	Intention to Treat
	Patient Population	Test 1/ Strategy 1	Test 2/ Strategy 2	Outcome				
Bernardi et al[2]/2008	Clinically suspected DVT	Single whole-leg US	Serial proximal US; single proximal US if DD	VTE during 3-mo follow-up	Not concealed	Not blinded	Telephone or in person	N/A (no crossover occurred)
Gibson et al[1]/2009	Clinically suspected DVT; likely Wells score and/or positive highly sensitive DD (Tina-quant)	Single whole-leg US	Serial proximal US	VTE during 3-mo follow-up	Not concealed	Not blinded	Telephone or in person	N/A (no crossover occurred)

See Table S1 and S2 legends for expansion of abbreviations.

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Table S22—*[3.2-3.5] Description and Results of Diagnostic Studies Evaluating Whole-Leg US in First Suspected Lower Extremity DVT: Cross-sectional Accuracy and Cohort Management Studies*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort Is From an RCT)	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
What are the consequences of using whole-leg CUS to diagnose distal DVT?	All patients	Primary	Accuracy	Symptomatic	Specificity (vs venography)	96 (86.3-99.5)		Atri et al[43]/1996
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (86.8-100)		Baxter et al[44]/1990
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (83.2-100)		Baxter et al[45]/1992
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (79.4-100)		Belcaro et al[46]/1992
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	96.6 (90.4-99.3)		Bendick et al[47]/1983
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (96.9-100)		Biondetti et al[48]/1990
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (92.9-100)		Bradley et al[49]/1993
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (95.4-100)		Burke et al[50]/1994
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (63.1-100)		Cogo et al[51]/1993
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	97.9 (92.5-99.7)		De Laveaucoup et al[52]/1989
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	96.4 (94.4-97.9)		Elias et al[53]/1987
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	79.3 (60.3-92.0)		Forbes et al[54]/1998
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	95.5 (84.5-99.4)		Grobety et al[55]/1996
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (96.0-100)		Habscheid et al[57]/1990
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	94.3 (84.3-98.8)		Kalodiki et al[58]/1993
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	98.1 (90.1-100)		Labropoulos et al[59]/1995

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Table S22—*Continued*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort Is From an RCT)	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	99.3 (96.2-100)		Lensing et al[60]/1989
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (59.0-100)		Leven et al[61]/1990
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (85.2-100)		Lindqvist et al[62]/1977
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	75.0 (58.8-87.3)		Mattos et al[63]/1992
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (90.3-100)		McCandless et al[64]/1985
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	99.2 (95.9-100)		Miller et al[65]/1996
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	89.3 (71.8-97.7)		Mitchell et al[66]/1991
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (81.5-100)		Monreal et al[67]/1989
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	72.7 (39.0-94.0)		Puls et al[68]/1999
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	42.1 (20.3-66.5)		Robertson et al[70]/1995
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	60.6 (42.1-77.1)		Robertson et al[71]/1994
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	73.3 (54.1-87.7)		Rose et al[72]/1990
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	89.5 (80.3-95.3)		Rosier et al[73]/1992
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	76.2 (52.8-91.8)		Savy-Stortz et al[74]/1995
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (59.0-100)		Simons et al[75]1995
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	84.6 (54.6-98.1)		Size et al[76]/1993
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	88.2 (63.6-98.5)		Yucel et al[77]/1991
		Primary	Accuracy	Symptomatic	Specificity (vs venography)	100 (47.8-100)		Zhou et al[78]/1990

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Table S22—*Continued*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort Is From an RCT)	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
	Patients without proximal DVT by proximal CUS, "DVT-likely" pretest, or positive highly sensitive DD	Primary	Accuracy	Symptomatic	Result of serial proximal US and ≥ 90-d follow-up	All: 1.2 (0.4-2.7) No calf DVT: 0.8 (0-2) Calf DVT: 7.8 (3-17)		Palareti et al[79]/2010
	If low pretest	N/A	N/A	N/A	N/A	N/A		
	If moderate pretest	N/A	N/A	N/A	N/A	N/A		
	If high pretest	N/A	N/A	N/A	N/A	N/A		
	If positive highly sensitive DD	N/A	N/A	N/A	N/A	N/A		
	If positive moderately sensitive DD	N/A	N/A	N/A	N/A	N/A		
	If negative highly sensitive DD	N/A	N/A	N/A	N/A	N/A		
	If negative moderately sensitive DD	N/A	N/A	N/A	N/A	N/A		
What are the consequences of using a single whole-leg CUS to exclude DVT?	Negative single whole-leg US on day of presentation – all patients	Meta-analysis	Management cohort (6 trials) arm of RCT (1 trial)	Clinically suspected DVT (Analyzed studies included inpatients, ambulatory patients, or both. Some restricted to first-episode DVT)	≥ 90-d probability of VTE	0.57 (0.25-0.89) pooled event rate		Johnson et al[3]/2010
		Primary	Management	Symptomatic first episode	≥ 90-d probability of VTE	0.5 (0.1-1.8)	Excluded patients with high pretest by the original Wells criteria DVT diagnosed by noncompressibility plus intraluminal thrombus	Elias et al[4]/2003

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Table S22—*Continued*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort Is From an RCT)	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
		Primary	Management	Symptomatic	≥ 90-d probability of VTE	0.3 (0.1-0.8)	DVT diagnosed by noncompressibility	Schellong et al[5]/2003
		Primary	Management	Symptomatic outpatients	≥ 90-d probability of VTE	0.4 (0.1-0.9)	DVT diagnosed by noncompressibility plus lack of augmentation in muscular calf veins	Sevestre et al[6]/2009
		Primary	Management	Symptomatic inpatients	≥ 90-d probability of VTE	1.9 (0.9-3.5)	DVT diagnosed by noncompressibility plus lack of augmentation in muscular calf veins	Sevestre et al[7]/2010
		Primary	Management	Symptomatic inpatients	≥ 90-d probability of VTE	0.80 (0.16-2.33)	DVT diagnosed by noncompressibility	Stevens et al[8]/2004
		Primary	Management	Symptomatic inpatients	≥ 90-d probability of VTE	0.24 (0.01-1.3)	DVT diagnosed by noncompressibility	Subramaniam et al[9]/2005
	Negative single whole-leg US on day of presentation – if low pretest	Meta-analysis	IPD meta-analysis from 2 management cohort studies	Clinically suspected DVT. (Analyzed studies included inpatients, ambulatory patients, or both. Some restricted to first-episode DVT)	3-mo probability of VTE	0.29 pooled event rate		Johnson et al[3]/2010
	Negative single whole-leg US on day of presentation – if moderate pretest	Meta-analysis	IPD meta-analysis from 2 management cohort studies	Clinically suspected DVT. (Analyzed studies included inpatients, ambulatory patients, or both. Some restricted to first-episode DVT)	3-mo probability of VTE	0.82 pooled event rate		Johnson et al[3]/2010

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Table S22—*Continued*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort Is From an RCT)	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
	Negative single whole-leg US on day of presentation – if high pretest	Meta-analysis	IPD meta-analysis from 2 management cohort studies	Clinically suspected DVT. (Analyzed studies included inpatients, ambulatory patients, or both. Some restricted to first-episode DVT)	3-mo probability of VTE	2.49 pooled event rate		Johnson et al[3]/2010

See Table S1-S3, S7, and S19 legends for expansion of abbreviations.

[a]eg, Post-TP during 3 mo follow-up, sensitivity or specificity, and so forth.

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Table S23—*[Sections 3.2-3.5] Description and Results of Diagnostic Studies Evaluating Whole-Leg US in First Suspected Lower Extremity DVT: RCTs*

Question from Structured Clinical Question Table	Study/Year	Patients	Intervention 1	Intervention 2	Outcomes	Results	Comments
Comparison of 2-point US based strategy vs whole-leg US	Bernardi et al et al[2]/2008	Symptomatic outpatients	2-point proximal US followed by moderately sensitive DD (and repeat US if positive DD)	Whole-leg US, no further tests if negative	VTE in 3-mo follow-up	0.9% vs 1.2%; absolute difference, − 0.3% (95% CI, − 1.4 to 0.8)	DVT diagnosed by noncompressibility and lack of augmentation (lack of increase in venous flow by Doppler with manual squeeze) in muscular calf veins
	Gibson et al et al[1]/2009	Symptomatic patients with likely Wells score and/or positive highly sensitive DD (Tina-quant)	Serial 2-point proximal US	Whole-leg US, no further tests if negative	VTE in 3-mo follow-up	2.0% vs 1.2%; absolute difference, − 0.8% (95% CI, − 1.8 to 3.4)	DVT diagnosed by noncompressibility

See Table S1 and S2 legends for expansion of abbreviations.

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Table S24—*[Sections 3.1-3.5] Outcome Events for Various Diagnostic Strategies According to Decision Analytic Modeling*

Intervention (All Patients/1,000 Cohort)	Average No. of Outcome Events Per 1,000 Patients (95% Credible Interval)							
	No. Treated	Fatal PE	Nonfatal PE	Nonfatal Intracranial Bleeding Event	Fatal Bleeding Event	Nonfatal Nonintracranial Bleeding Event	No Bleeding	Venographic Mortality
No testing or treatment	0	3.77 (1.27-8.17)	19.44 (11.90-28.39)	0	0	0	1,000	0
Venography for all patients	209	0.65 (0.41-0.96)	3.12 (2.42-4.15)	0.25 (0.13-0.42)	0.71 (0.48-0.99)	4.38 (3.54-5.38)	994.65 (993.53-995.60)	0.03 (0.01-0.14)
Proximal US; repeat if negative	245	0.76 (0.49-1.09)	3.68 (2.91-4.70)	0.30 (0.15-0.49)	0.84 (0.58-1.15)	5.14 (4.26-6.24)	993.72 (992.49-994.76)	0
Whole-leg US; repeat if distal DVT found	240	0.83 (0.51-1.31)	4.06 (3.07-5.72)	0.29 (0.15-0.48)	0.82 (0.57-1.12)	5.03 (4.19-5.99)	993.86 (992.71-994.82)	0
Whole-leg US; treat if distal DVT found	265	0.82 (0.51-1.28)	401 (3.04-5.59)	0.32 (0.16-0.54)	0.91 (0.62-1.27)	5.50 (4.48-6.94)	993.18 (991.57-994.43)	0
Proximal US. No repeat.	229	1.00 (0.56-1.85)	4.94 (3.26-8.43)	0.28 (0.15-0.46)	0.78 (0.54-1.06)	4.81 (4.01-5.61)	994.13 (993.18-995.00)	0
Wells score and proximal US. If PTP low, discharge if US negative, venogram if positive. If PTP moderate, repeat US if negative, treat if positive. If high PTP, venogram if US negative, treat if US positive.	228	0.71 (0.45-1.06)	3.43 (2.64-4.68)	0.28 (0.14-0.46)	0.78 (0.54-1.08)	4.79 (3.92-5.77)	994.15 (993.00-995.12)	0.004 (0.00-0.02)
SimpliRED DD and proximal US. If US positive then treat. If both are negative then discharge. If DD positive and US negative repeat US.	239	0.85 (0.51-1.35)	4.14 (3.08-6.05)	0.29 (0.15-0.48)	0.82 (0.56-1.12)	5.02 (4.18-5.98)	993.88 (992.76-994.83)	0
Wells score and proximal US. If PTP high or moderate, perform proximal US. If positive treat, venogram if negative. If TP low, perform US. If positive treat, discharge if negative.	249	0.68 (0.43-1.00)	3.26 (2.50-4.47)	0.30 (0.16-0.49)	0.85 (0.59-1.17)	5.22 (4.36-6.26)	993.62 (992.41-994.63)	0.01 (0.00-0.06)
Wells score and full-leg US. If PTP high or moderate, perform full-leg US, treat if positive, venogram if negative. If PTP low, full-leg US, treat if positive, discharge if negative.	251	0.65 (0.42-0.94)	3.11 (2.44-4.08)	0.30 (0.15-0.50)	0.86 (0.60-1.18)	5.27 (4.37-6.36)	993.57 (992.34-994.62)	0.01 (0.00-0.06)

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Table S24—*Continued*

Intervention (All Patients/1,000 Cohort)	Average No. of Outcome Events Per 1,000 Patients (95% Credible Interval)							
	No. Treated	Fatal PE	Nonfatal PE	Nonfatal Intracranial Bleeding Event	Fatal Bleeding Event	Nonfatal Nonintracranial Bleeding Event	No Bleeding	Venographic Mortality
Quantitative latex DD; if positive, perform proximal US and repeat. If DD negative, perform Wells score. If high, perform proximal US and repeat if negative. If PTP moderate or low, discharge.	214	0.85 (0.53-1.26)	4.13 (3.17-5.45)	0.26 (0.13-0.43)	0.73 (0.51-1.01)	4.50 (3.66-5.50)	994.50 (993.37-995.45)	0
Quantitative latex DD; if positive, perform above-knee US and repeat. If DD negative perform Wells score. If PTP high perform proximal US. If PTP low or moderate, discharge.	213	0.86 (0.53-1.32)	4.22 (3.20-5.70)	0.26 (0.13-0.43)	0.73 (0.51-1.01)	4.49 (3.66-5.46)	994.53 (993.40-995.47	0
Wells score. If PTP high, proximal US, treat if positive, SimpliRED DD if negative. If DD positive, venogram; if negative, repeat US. If PTP moderate, US; treat if positive, SimpliRED DD if negative. If DD positive, repeat US. If DD negative, discharge. If PTP low, SimpliRED. If DD positive, proximal US. Discharge if DD negative.	225	0.80 (0.49-1.27)	3.90 (2.88-5.65)	0.27 (0.14-0.44)	0.77 (0.53-1.05)	4.72 (3.90-5.65)	994.24 (993.17-995.20)	0.0017 (0.00-0.01)
Wells score and SimpliRED DD. If PTP high or moderate, or DD positive, perform full-leg US. If PTP low and DD negative, then discharge.	220	0.88 (0.53-1.40)	4.29 (3.18-6.08)	0.27 (0.14-0.44)	0.75 (0.52-1.04)	4.61 (3.80-5.55)	994.36 (993.33-995.29)	0
ELISA DD. If negative, discharge. If DD positive, perform proximal US. Treat if US positive. If US negative, perform Wells score. If PTP high, perform venogram. If PTP moderate or low, discharge.	214	0.90 (0.53-1.57)	4.44 (3.07-7.18)	0.26 (0.13-0.42)	0.73 (0.51-0.99)	4.47 (3.71-5.31)	994.53 (993.57-995.40)	0.002 (0.00-0.01)

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Table S24—*Continued*

Intervention (All Patients/1,000 Cohort)	Average No. of Outcome Events Per 1,000 Patients (95% Credible Interval)							
	No. Treated	Fatal PE	Nonfatal PE	Nonfatal Intracranial Bleeding Event	Fatal Bleeding Event	Nonfatal Nonintracranial Bleeding Event	No Bleeding	Venographic Mortality
Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD positive, discharge if DD negative. If PTP low, perform US. Discharge if negative, treat if positive.	240	0.82 (0.51-1.30)	4.04 (3.04-5.67)	0.29 (0.15-0.48)	0.82 (0.57-1.13)	5.08 (4.21-5.99)	993.85 (992.71-994.82)	0
Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD positive and discharge if DD negative. If PTP low perform SimpliRED DD, discharge if negative, perform proximal US if positive.	218	0.91 (0.54-1.49)	4.65 (3.20-6.63)	0.26 (0.14-0.43)	0.73 (0.52-1.02)	4.57 (3.79-5.47)	994.42 (993.39-995.32)	0
Wells score. If PTP high, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD positive, discharge if negative. If PTP low or moderate, perform SimpliRED DD. Discharge if negative, perform proximal US if positive.	195	1.06 (0.60-1.87)	5.26 (3.67-8.08)	0.24 (0.12-0.38)	0.67 (0.46-0.91)	4.09 (3.34-4.88)	995.12 (994.10-995.84)	0
Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative repeat US. If PTP low, perform proximal US, treat if positive, discharge if negative.	242	0.80 (0.50-1.18)	3.90 (2.99-5.27)	0.29 (0.15-0.48)	0.83 (0.57-1.14)	5.08 (4.23-6.09)	993.80 (992.62-994.81)	0

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Table S24—*Continued*

Intervention (All Patients/1,000 Cohort)	Average No. of Outcome Events Per 1,000 Patients (95% Credible Interval)							
	No. Treated	Fatal PE	Nonfatal PE	Nonfatal Intracranial Bleeding Event	Fatal Bleeding Event	Nonfatal Nonintracranial Bleeding Event	No Bleeding	Venographic Mortality
Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative repeat US. If PTP low, perform proximal US; treat if positive, discharge if negative.	234	0.92 (0.54-1.57)	4.50 (3.17-7.02)	0.28 (0.15-0.47)	0.80 (0.56-1.09)	4.92 (4.09-5.79)	993.99 (992.99-994.89)	0
Wells score. If PTP high or moderate, perform proximal US. Treat if positive; if negative discharge. If PTP low, discharge.	194	1.19 (0.63-2.21)	5.94 (3.89-9.49)	0.24 (0.12-0.38)	0.66 (0.46-0.90)	4.08 (3.34-4.84)	995.02 (994-12-995.78)	0
Perform SimpliRED DD. Discharge if negative, perform proximal US if positive. Treat if US positive, repeat US if initial US is negative	176	1.30 (0.69-2.25)	6.49 (4.58-9.13)	0.21 (0.11-0.35)	0.60 (0.41-0.83)	3.70 (2.99-4.84)	995.48 (994.55-996.27)	0

The model applies each strategy to a population with 19% prevalence of proximal DVT and 5% prevalence of distal DVT, using sensitivities and specificities derived from meta-analyses, to determine what proportion of patients with proximal, distal, and no DVT are treated with anticoagulant therapy. Untreated distal DVT are assumed to have a 21.4% probability of subsequent propagation to form proximal DVT, but do not directly cause PE. Patients with treated proximal DVT have a 0.3% probability of fatal PE and a 1.4% probability of nonfatal PE over the following 3 mo. The respective probabilities for untreated proximal DVT are 1.9% and 9.3%. Bleeding outcomes are assumed to be entirely due to anticoagulant therapy. Patients receiving treatment have a 0.3% probability of fatal bleeding, a 0.1% probability of nonfatal intracranial bleeding, and a 2.1% probability of major nonfatal non-intracranial bleeding. All parameters are modeled with a probability distribution to generate a credible range for the outcomes. See Table S1, S5, and S19 legends for expansion of abbreviations.

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Table S25—*[Sections 3.1-3.5] Additional Outcome Events for Various Diagnostic Strategies Compared With Serial CUSs According to Decision Analytic Modeling*

Intervention (All Patients/1,000 Cohort)	Additional Number of Outcome Events Per 1,000 Patients Compared With Serial CUS					
	Fatal PE	Nonfatal PE	Nonfatal Intracranial Bleeding Event	Fatal Bleeding Event	Nonfatal Nonintracranial Bleeding Event	No Bleeding
No testing or treatment	3.02	15.76	−0.30	−0.84	−5.14	6.27
Venography for all patients	−0.11	−0.55	−0.04	−0.12	−0.75	−0.92
Proximal US; repeat if negative	0	0	0	0	0	0
Whole-leg US; repeat if distal DVT found	0.07	0.39	−0.01	−0.02	−0.10	0.12
Whole-leg US; treat if distal DVT found	0.06	0.34	0.03	0.07	0.45	−0.55
Proximal US. No repeat.	0.24	1.26	−0.02	−0.05	−0.33	0.40
Wells score and proximal US. If PTP low, discharge if US negative; venogram if positive. If PTP moderate, repeat US if negative, treat if positive. If high PTP, venogram if US negative, treat if US positive.	−0.05	−0.24	−0.02	−0.06	−0.34	0.42
SimpliRED DD and proximal US. If US positive then treat. If both are negative then discharge. If DD positive and US negative, repeat US.	0.09	0.46	−0.01	−0.02	−0.12	0.15
Wells score and proximal US. If PTP high or moderate, perform proximal US. If positive treat, venogram if negative. If PTP low, perform proximal US. If positive treat, discharge if negative.	−0.08	−0.41	0.01	0.01	0.09	−0.11
Wells score and full leg US. If PTP high or moderate perform proximal US. If positive treat, venogram if negative. If PTP, low, full-leg US, treat if positive, discharge if negative.	−0.11	−0.57	0.01	0.02	0.13	−0.16
Quantitative latex DD. If positive perform proximal US and repeat. If DD negative, perform Wells score. If high, perform proximal US and repeat if negative. If PTP moderate or low, discharge.	0.09	0.46	−0.04	−0.10	−0.63	0.78
Quantitative latex DD: if positive perform above-knee US and repeat. If DD negative, perform Wells score. If high perform proximal US. If PTP low or moderate, then discharge.	0.10	0.55	−0.04	−0.11	−0.65	0.80
Wells score. If PTP high, proximal US; treat if positive, SimpliRED DD if negative. If DD positive, venogram, if negative, repeat US. If PTP moderate, US; treat if positive, SimpliRED if negative. If DD positive, repeat US; if DD negative, discharge. If PTP low, SimpliRED DD. If DD positive, proximal US.	0.04	0.21	−0.02	−0.07	−0.42	0.51

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Table S25—*Continued*

Intervention (All Patients/1,000 Cohort)	Additional Number of Outcome Events Per 1,000 Patients Compared With Serial CUS					
	Fatal PE	Nonfatal PE	Nonfatal Intracranial Bleeding Event	Fatal Bleeding Event	Nonfatal Nonintracranial Bleeding Event	No Bleeding
Wells score and SimpliRED DD. If PTP high or moderate, or DD positive, perform full-leg US. If PTP low and DD negative, then discharge.	0.12	0.61	−0.03	−0.08	−0.52	0.63
ELISA DD. If negative, discharge. If DD positive, perform proximal US. Treat if US positive. If US negative, perform Wells score. If PTP high, perform venogram. If PTP moderate or low, discharge.	0.15	0.77	−0.04	−0.11	−0.65	0.79
Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD positive, discharge if negative. If PTP low, perform US. Discharge if negative, treat if positive.	0.07	0.37	−0.005	−0.02	−0.10	0.12
Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD positive, and discharge if DD negative. If PTP low, perform SimpliRED DD, discharge if negative and perform US if positive.	0.15	0.77	−0.03	−0.09	−0.56	0.69
Wells score. If PTP high, perform proximal US. If positive treat, if negative, perform SimpliRED DD. Repeat US if DD positive, discharge if DD negative. If PTP moderate or low, perform SimpliRED DD. Discharge if negative, perform proximal US if positive.	0.30	1.59	−0.06	−0.17	−1.05	1.28
Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative repeat US. If PTP low, perform proximal US, treat if positive, discharge if negative.	0.04	0.23	−0.003	−0.01	−0.06	0.07
Wells score. If PTP high, perform proximal US. If positive treat, if negative repeat US. If PTP moderate or low perform proximal US, if positive treat, if negative then discharge.	0.16	0.83	−0.012	3.67	−0.21	0.26
Wells score. If PTP high or moderate, perform proximal US. Treat if positive, if negative discharge. If PTP low, discharge.	0.43	2.27	−0.06	−0.17	−1.05	1.28
Perform SimpliRED DD. Discharge if negative, perform proximal US if positive. Treat if US positive, repeat US if initial US is negative	0.54	2.81	−0.08	−0.23	−1.43	1.74

The model applies each strategy to a population with 19% prevalence of proximal DVT and 5% prevalence of distal DVT, using sensitivities and specificities derived from meta-analyses, to determine what proportion of patients with proximal, distal, and no DVT are treated with anticoagulant therapy. Untreated distal DVT are assumed to have a 21.4% probability of subsequent propagation to form proximal DVT, but do not directly cause PE. Patients with treated proximal DVT have a 0.3% probability of fatal PE and a 1.4% probability of nonfatal PE over the following 3 mo. The respective probabilities for untreated proximal DVT are 1.9% and 9.3%. Bleeding outcomes are assumed to be entirely due to anticoagulant therapy. Patients receiving treatment have a 0.3% probability of fatal bleeding, a 0.1% probability of nonfatal intracranial bleeding, and a 2.1% probability of major nonfatal non-intracranial bleeding. All parameters are modeled with a probability distribution to generate a credible range for the outcomes. See Table S1, S5, S7, and S19 legends for expansion of abbreviations.

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Table S26—*[Sections 3.1-3.5] Additional Testing Maneuvers Compared With a Strategy Involving Serial CUSs According to Decision Analytic Modeling*

Intervention (All Patients/1,000 Cohort)	Number of Testing Maneuvers Per 1,000 Patients					Additional Tests Per 1,000 Patients		
	Wells Score	Proximal CUS	Whole-Leg US	DD Tests	Venogram	Proximal CUS	Wells Score	DD Tests
No testing or treatment	0	0	0	0	0	−1,771	0	0
Venography for all patients	0	0	0	0	1,000	−1,771	0	0
Proximal US. Repeat if negative.	0	1,771	0	0	0	0	0	0
Whole-leg US. Repeat if distal found.	0	39	1,000	0	0	−1,732	0	0
Whole-leg US. Treat if distal DVT found.	0	0	1,000	0	0	−1,771	0	0
Proximal US. No repeat.	0	1,000	0	0	0	−771	0	0
Wells score and proximal US. If PTP low, discharge if US negative; venogram if positive. If PTP moderate, repeat US if negative. If high PTP, venogram if negative, treat if positive.	1,000	1,347	0	0	138	−424	1,000	0
SimpliRED DD and proximal US. If US positive, then treat. If both are negative, then discharge. If DD positive and US negative, repeat US.	0	1,244	0	1,000	0	−527	0	1,000
Wells score and proximal US. If PTP high or moderate, perform proximal US. If positive treat, venogram if negative. If PTP low, perform proximal US, if positive treat, if negative discharge.	1,000	1,081	0	0	422	−690	1,000	0
Wells score and full-leg US. If PTP high or moderate, perform full-leg US; treat if positive, venogram if negative. If PTP low, full-leg US; treat if positive, discharge if negative.	1,000	91	1,000	0	390	−680	1,000	0
Quantitative latex DD. If positive, perform proximal US and repeat. If DD negative, perform Wells score. If high, perform proximal US and repeat if negative. If PTP moderate or low, then discharge.	458	975	0	1,000	0	−796	458	1,000
Quantitative latex DD. If positive perform above-knee US and repeat. If DD negative, perform Wells score. If PTP high, perform proximal US. If PTP low or moderate, then discharge.	458	938	0	1,000	0	−833	458	1,000
Wells score. If PTP high, proximal US; treat if positive, SimpliRED DD if negative. If DD positive, venogram if negative, repeat US; if DD negative, discharge. If PTP low, SimpliRED. If PTP moderate, US treat if positive, SimpliRED DD if negative. If DD positive, repeat US; if negative, then discharge. If PTP low, SimpliRED DD.	1,000	890	0	806	55	−881	1,000	806
Wells score and SimpliRED DD. If PTP high or moderate, or DD positive, perform full-leg US. If PTP low and DD negative, then discharge.	1,000	36	709	1,000	0	−1,026	1,000	1,000
ELISA DD. If negative, discharge. If positive, perform proximal US. Treat if US positive; if US negative, perform Wells score. If PTP high, perform venogram. If PTP low or moderate, then discharge.	429	654	0	1,000	74	−1,117	429	1,000

(Continued)

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Table S26—*Continued*

Intervention (All Patients/1,000 Cohort)	Number of Testing Maneuvers Per 1,000 Patients					Additional Tests Per 1,000 Patients		
	Wells Score	Proximal CUS	Whole-Leg US	DD Tests	Venogram	Proximal CUS	Wells Score	DD Tests
Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD negative, discharge if negative. If PTP low, perform US; discharge if negative, treat if positive.	1,000	1,258	0	422	0	−513	1,000	422
Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD negative, discharge if DD negative. If PTP low, perform SimpliRED DD, discharge if negative, perform proximal US if positive.	1,000	876	0	806	0	−895	1,000	806
Wells score. If PTP high, perform proximal US. If positive treat, if negative perform SimpliRED DD. Repeat US if DD positive, discharge if negative, perform proximal US if negative.	1,000	537	0	871	0	−1,234	1,000	871
Wells score. If PTP high or moderate, perform proximal US. If positive treat, if negative, repeat US. If PTP low, perform proximal US; treat if positive, discharge if negative.	1,000	1,422	0	0	0	−349	1,000	0
Wells score. If PTP high, perform proximal US. If positive treat, if negative repeat US. If PTP low, perform proximal US; treat if positive, discharge if negative	1,000	1,103	0	0	0	−668	1,000	0
Wells score. If PTP high or moderate, perform proximal US. Treat if positive, if negative, discharge. If PTP low discharge.	1,000	616	0	0	0	−1,155	1,000	0
Perform SimpliRED DD. Discharge if negative, perform proximal US if positive. Treat if US positive, repeat US if initial US is negative	0	656	0	1,000	0	−1,115	0	1,000

See Table S1 and S7 legends for expansion of abbreviations.

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Table S27—*[Sections 3.2-3.6] Methodology of Diagnostic Studies Evaluating CT Scan Venography in Patients With Suspected First Lower Extremity DVT: Meta-analysis of Accuracy Studies of CT Scan Venography*

Study Eligibility					
Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Exploration of Heterogeneity	Comments	Source
Suspected DVT or suspected PE	CT scan venography	US or contrast venography	χ^2 test for heterogeneity. No formal analysis for sources of heterogeneity	Most of the primary studies were of patients with suspected PE and used US as a reference standard. Summary estimates were calculated despite significant unexplained heterogeneity	Thomas et al et al[80]/2008

See Table S1 and S5 legends for expansion of abbreviations.

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Table S28—*[Sections 3.2-3.6] Methodology of Diagnostic Studies Evaluating CT Scan Venography in Patients With Suspected First Lower Extremity DVT: Individual Accuracy Studies of CT Scan Venography*

	Study Details					
Study/Year	Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Consecutive Patients	Independent Test Assessment	Comments
Byun et al[81]/2008	Asymptomatic, Post-arthroplasty	CT scan venography	US	No	Yes	
Rhee et al[82]/2007	Suspected PE	CT scan venography	US	No	Yes	
Goodman et al[83]/2007	Suspected PE	CT scan venography	US	Yes	Yes	
Garcia-Bolado et al[84]/2007	Suspected PE	CT scan venography	US	Yes	Yes	
Kim et al[85]/2004	Suspected PE and DVT	CT scan venography	US	Unclear	Yes	Included in Thomas et al[80]
Lim et al[86]/2004	Suspected PE	CT scan venography	US	Yes	Yes	Included in Thomas et al[80]
Lim et al[86]/2004	Suspected PE	CT scan venography	US	Yes	Yes	Included in Thomas et al[80]
Begeman et al[88]/2003	Suspected PE	CT scan venography	US	No	Yes	
Loud et al[89]/2001	Suspected PE	CT scan venography	US	Yes	Yes	Included in Thomas et al[80]
Peterson et al[90]/2001	Suspected PE	CT scan venography	US	No	Yes	Included in Thomas et al[80]
Yoshida et al[91]/2001	Suspected DVT	CT scan venography	US	Yes	Yes	Included in Thomas et al[80]
Ghaye et al[92]/2000	Suspected PE	CT scan venography	US	No	Yes	Included in Thomas et al[80]
Cham et al[93]/2000	Suspected PE	CT scan venography	US	Yes	Unclear	Included in Thomas et al[80]
Garg et al[94]/2000	Suspected PE	CT scan venography	US	Yes	Yes	Included in Thomas et al[80]
Coche et al[95]/2000	Suspected PE	CT scan venography	US	Yes	Yes	Included in Thomas et al[80]
Duwe et al[96]/2000	Suspected PE	CT scan venography	US	Unclear	Unclear	Included in Thomas et al[80]
Shah et al[97]/1999	Suspected PE and DVT	CT scan venography	US	Unclear	Unclear	Included in Thomas et al[80]
Baldt et al[98]/1996	Suspected DVT	CT scan venography	Contrast venography	Yes	Yes	Included in Thomas et al[80]

See Table S1 and S5 legends for expansion of abbreviations.

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Table S29—*[Sections 3.2-3.6] Description and Results of Diagnostic Studies Evaluating CT Scan Venography in Patients With Suspected First Lower Extremity DVT: Meta-Analyses and Cross-sectional Accuracy Studies of CT Scan Venography*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort	Patient Population	Outcome Measure	Result, % (95% CI)	Comments	Reference
What are the consequences of using CT scan venography to diagnose DVT?	Suspected DVT	Meta-analysis	Accuracy	Mixed, but mostly suspected PE	Specificity	Summary estimate: 95.2 (93.6-96.5) Range, 93-100		Thomas et al[80]/2008
	Suspected DVT	Primary study	Accuracy	Asymptomatic	Specificity	96.9 (84.3-99.4)		Byun et al[81]/2008
	Suspected DVT			Suspected PE	Specificity	95.0 (90.8-97.5)		Garcia-Bolado et al[84]/2007
	Suspected DVT	Primary study	Accuracy	Suspected PE	Specificity	97.2 (95.6-98.3)	Results were reported as agreement between CT scan and US, rather than US as reference	Goodman et al[83]/2007
	Suspected DVT	Primary study	Accuracy	Suspected PE	Specificity	92.6 (85.6-96.4)	Results were reported as agreement between CT scan and US, rather than US as reference	Rhee et al[82]/2007
	Suspected DVT	Primary study	Accuracy	Suspected PE	Specificity	96.7 (83.3-99.4)		Begeman et al[88]/2003
What are the consequences of using CT scan venography to exclude DVT?	Suspected DVT	Meta-analysis	Accuracy	Mixed, but mostly suspected PE	Sensitivity	Summary estimate: 95.9 (93.0-97.8) Range: 71-100		Thomas et al[80]/2008
	Suspected DVT	Primary study	Accuracy	Asymptomatic	Sensitivity	90.0 (74.4-96.5)		Byun et al[81]/2008
	Suspected DVT	Primary study	Accuracy	Suspected PE	Sensitivity	58.8 (40.8-74.9)		Garcia-Bolado et al[84]/2007
	Suspected DVT	Primary study	Accuracy	Suspected PE	Sensitivity	84.4 (75.8-90.3)	Results were reported as agreement between CT scan and US, rather than US as reference	Goodman et al[83]/2007
	Suspected DVT	Primary study	Accuracy	Suspected PE	Sensitivity	72.3 (43.4-90.3)	Results were reported as agreement between CT scan and US, rather than US as reference	Rhee et al[82]/2007
	Suspected DVT	Primary study	Accuracy	Suspected PE	Sensitivity	100 (74.1-100)		Begeman et al[88]/2003

See Table S1 and S5 legends for expansion of abbreviations.

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Table S30—*[Sections 3.2-3.6] Evidence Profile: Should CT Scan Venography Be Used for the Diagnosis of First Suspected DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	Meta-analysis of 13, plus 5 additional primary studies[125-129,133]	Accuracy cohort	Serious	Moderate	Serious	Moderate	Low	Prev 53%: 508 Prev 17%: 163 Prev 5%: 48
True negative (patients without DVT)								Prev 53%: 447 Prev 17%: 790 Prev 5%: 904
False negative (patients incorrectly classified DVT negative)								Prev 53%: 22 Prev 17%: 7 Prev 5%: 2
False positive (patients incorrectly classified DVT positive)								Prev 53%: 23 Prev 17%: 40 Prev 5%: 46

Bibliography: Thomas SM, Goodacre SW, Sampson FC, et al. Diagnostic value of CT for deep vein thrombosis: results of a systematic review and meta-analysis. *Clin Radiol*. 2008;63(3):299-304. Byun SS, Kim JH, Kim YJ, et al. Evaluation of deep vein thrombosis with multidetector row CT after orthopedic arthroplasty: a prospective study for comparison with Doppler sonography. *Korean J Radiol*. 2008;9(1):59-66. Rhee KH, Iyer RS, Cha S, et al. Benefit of CT venography for the diagnosis of thromboembolic disease. *Clin Imaging*. 2007;31(4):253-258. Goodman LR, Stein PD, Matta F, et al. CT venography and compression sonography are diagnostically equivalent: data from PIOPED II. *AJR Am J Roentgenol*. 2007;189(5):1071-1076. Garcia-Bolado A, Del Cura JL. CT venography vs ultrasound in the diagnosis of thromboembolic disease in patients with clinical suspicion of pulmonary embolism. *Emerg Radiol*. 2007;14(6):403-409. Begemann PG, Bonacker M, Kemper J, et al. Evaluation of the deep venous system in patients with suspected pulmonary embolism with multi-detector CT: a prospective study in comparison to Doppler sonography. *J Comput Assist Tomogr*. 2003;27(3):399-409. Setting: predominantly suspected PE. Reference test: predominantly single US. See Table S1 and S5 legends for expansion of abbreviations.

[a] Most used a single US as a reference standard.

[b] Significant heterogeneity between studies.

[c] Few studies in suspected DVT; most in suspected PE. No management studies.

[d] Reported specificities range from 93%-100%; reported sensitivities range from 59%-100%.

[e] Based on a combined summary specificity of 95.2% (95% CI, 93.6%-96.5%) and sensitivity of 95.9% (95% CI, 93.0%-97.8%). Prevalences for high (53%), moderate (17%), and low (5%) taken from Wells et al.[30]

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Table S31—*[Sections 3.2-3.6] Methodology of Diagnostic Studies Evaluating MR Venography in Patients With Suspected First DVT: Meta-analysis of Accuracy Studies of MR Venography or Direct Thrombus Imaging*

Study Eligibility					
Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Exploration of Heterogeneity	Comments	Source
Suspected DVT, suspected PE, or high-risk asymptomatic patients	MR venography and direct MRI	US or contrast venography	χ^2 test for heterogeneity. No formal analysis for sources of heterogeneity.	Summary estimates were calculated despite significant unexplained heterogeneity. Prevalence of DVT was high in primary studies.	Sampson et al[99]/2007

See Table S1 and S5 legends for expansion of abbreviations.

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Table S32—*[Sections 3.2-3.6] Methodology of Diagnostic Studies Evaluating MR Venography in Patients With Suspected First DVT: Individual Accuracy Studies of MR Venography*

	Study Details					
Study/Year	Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Consecutive Patients	Independent Test Assessment	Comments
Cantwell et al[100]/2006	Suspected DVT	MR venography	Contrast venography	No	Yes	
Fraser et al[101]/2003	Suspected DVT	MR venography	Contrast venography	No	Yes	Included in Sampson et al[99]
Sica et al[102]/2001	Suspected DVT, with negative above-knee US	MR venography	Contrast venography	No	Yes	Included in Sampson et al[99]
Jensen et al[103]/2001	Asymptomatic, lower limb injuries	MR venography	Contrast venography	Yes	Yes	Included in Sampson et al[99]
Catalano et al[104]/1997	Suspected DVT	MR venography	Contrast venography	Unclear	Yes	Included in Sampson et al[99]
Laissy et al[105]/1996	Suspected DVT/PE	MR venography	Contrast venography	Unclear	Yes	Included in Sampson et al[99]
Larcom et al[106]/1996	Asymptomatic, post-arthroplasty	MR venography	Contrast venography	Yes	Yes	Included in Sampson et al[99]
Evans et al[107]/1996	Suspected DVT	MR venography	US	No	Yes	Included in Sampson et al[99]
Evans et al[108]/1993	Suspected DVT	MR venography	Contrast venography	Unclear	Yes	Included in Sampson et al[99]
Carpenter et al[109]/1993	Suspected DVT	MR venography	Contrast venography	Unclear	Yes	Included in Sampson et al[99]
Spritzer et al[110]/1993	Suspected DVT	MR venography	Contrast venography	Yes	Yes	Included in Sampson et al[99]
Pope et al[111]/1991	Suspected DVT	MR venography	Contrast venography	Unclear	Yes	Included in Sampson et al[99]
Vukov et al[112]/1991	Suspected DVT	MR venography	Contrast venography	Yes	Yes	Included in Sampson et al[99]
Erdman et al[113]/1990	Suspected DVT	MR venography	Contrast venography	Yes	Yes	Included in Sampson et al[99]

See Table S1 and S5 legends for expansion of abbreviations.

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Table S33—*[Sections 3.2-3.6] Description and Summary of Results of Diagnostic Studies Evaluating MR Venography in Patients With Suspected First DVT: Results: Meta-analyses and Cross-Sectional Accuracy Studies of MR Venography*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort	Patient Population	Outcome Measure	Result, %	Comments	Reference
What are the consequences of using contrast MR venography to diagnose DVT?	Suspected DVT	Meta-analysis	Accuracy	Mixed, but mostly suspected DVT	Specificity	Summary estimate: 94.8 (95% CI, 92.6-96.5) Range: 43-100	Technique not always clear in primary studies. Included one study of direct MRI	Sampson et al[99]/2007
	Suspected DVT	Primary study	Accuracy	Suspected DVT	Specificity	77.8 (95% CI, 54.8-91.0)	Results were reported as agreement between MR venography and contrast venography, rather than contrast venography as reference	Cantwell et al[100]/2006
What are the consequences of using contrast MR venography to exclude DVT?	Suspected DVT	Meta-analysis	Accuracy	Mixed, but mostly suspected DVT	Sensitivity	Summary estimate: 91.5 (95% CI, 87.5-94.5) Range: 0 to 100	Technique not always clear in primary studies. Included one study of direct MRI. Sensitivity was lower in two studies of asymptomatic patients. When these were excluded, summary sensitivity was 95.7%. Pooled sensitivities for proximal and distal DVT were 93.9% (95% CI: 88.8%-97.2%) and 62.1% (95% CI: 42.3%-79.3%)	Sampson et al[99]/2007
	Suspected DVT	Primary study	Accuracy	Suspected DVT	Sensitivity	100% (95% CI, 61.0-100)	Results were reported as agreement between MR venography and contrast venography, rather than contrast venography as reference	Cantwell et al[100]/2006

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Table S34—*[Sections 3.2-3.6] Evidence Profile: Should MR Venography Be Used for the Diagnosis of First Suspected DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	Meta-analysis of 13 plus 1 additional primary study[144,145]	Accuracy cohort	…	Moderate	Moderate	Serious	Low	Prev 53%: 486 Prev 17%: 158 Prev 5%: 46
True negative (patients without DVT)								Prev 53%: 446 Prev 17%: 787 Prev 5%: 901
False negative (patients incorrectly classified DVT negative)								Prev 53%: 45 Prev 17%: 14 Prev 5%: 4
False positive (patients incorrectly classified DVT positive)								Prev 53%: 24 Prev 17%: 43 Prev 5%: 49

Bibliography: Sampson FC, Goodacre SW, Thomas SM, et al. The accuracy of MRI in diagnosis of suspected deep vein thrombosis: systematic review and meta-analysis. *Eur Radiol*. 2007;17(1):175-181. Cantwell CP, Cradock A, Bruzzi J, et al. MR venography with true fast imaging with steady-state precession for suspected lower-limb deep vein thrombosis. *J Vasc Interv Radiol*. 2006;17(11 pt 1):1763-1769.
Setting: predominantly suspected DVT. Reference test: predominantly contrast venography.

[a] No major limitations.

[b] Significant heterogeneity between studies.

[c] No management studies.

[d] Reported specificities range from 43%-100%; reported sensitivities range from 0-100%.

[e] Based on a combined summary specificity of 94.8% (95% CI, 92.6%-96.5%) and sensitivity of 91.5% (95% CI, 87.5%-94.5%). Prevalences for high (53%), moderate (17%), and low (5%) taken from Wells et al.[10]

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Table S35—*[Sections 3.2-3.6] Methodology of Diagnostic Studies Evaluating MR Direct Thrombus Imaging in Patients with Suspected First DVT: Individual Accuracy Studies of MR Direct Thrombus Imaging*

	Study Details					
Study/Year	Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Consecutive Patients	Independent Test Assessment	Comments
Fraser et al[114]/2002	Suspected DVT	Direct MRI	Contrast venography	No	Yes	Included in Sampson et al[99]/2007

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Table S36—*[Sections 3.2-3.6] Description and Results of Diagnostic Studies Evaluating MR Direct Thrombus Imaging in Patients With Suspected First DVT: Cross-Sectional Accuracy Studies of MR Direct Thrombus Imaging*

Question From Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Accuracy vs Management Cohort (Indicate if Cohort is From an RCT)	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
What are the consequences of using MR direct thrombus imaging to diagnose DVT?	Suspected DVT	Primary study	Accuracy	Suspected DVT	Specificity	92 (80-98)	Included in Sampson et al[99] meta-analysis	Fraser et al[114]/2002
What are the consequences of using MR direct thrombus imaging to exclude DVT?	Suspected DVT	Primary study	Accuracy	Suspected DVT	Sensitivity	94 (84-97)	Included in Sampson et al[99] meta-analysis	Fraser et al[99]/2002

See Table S2 legend for expansion of abbreviation.

[a]eg, Post-TP during 3 mo follow-up; sensitivity or specificity, and so forth.

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Table S37—*[Sections 3.2-3.6] Evidence Profile: Should Direct MRI Be Used for the Diagnosis of First Suspected DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	1 Primary study[159]	Accuracy cohort	…	Not applicable	Moderate	Moderate	Low	Prev 53%: 498 Prev 17%: 160 Prev 5%: 47
True negative (patients without DVT)								Prev 53%: 432 Prev 17%: 764 Prev 5%: 874
False negative (patients incorrectly classified DVT negative)								Prev 53%: 32 Prev 17%: 10 Prev 5%: 3
False positive (patients incorrectly classified DVT positive)								Prev 53%: 38 Prev 17%: 66 Prev 5%: 76

Bibliography: Fraser DG, Moody AR, Morgan PS, Martel AL, Davidson I. Diagnosis of lower-limb deep venous thrombosis: a prospective blinded study of magnetic resonance direct thrombus imaging. *Ann Intern Med*. 2002;136(2)89-98. Setting: suspected DVT. Reference test: venography.

[a] No significant limitations

[b] Only one study

[c] No management studies.

[d] Reported specificities range from 93%-100%; reported sensitivities range from 59%-100%.

[e] Based on a specificity of 92% (95% CI, 80%-98%) and sensitivity of 94.9% (95% CI, 84%-97%). Prevalences for high (53%), moderate (17%), and low (5%) taken from Wells et al.[30]

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Table S38—*[Sections 4.1-4.3] Methodology of Diagnostic Studies in Patients With Suspected Recurrent Lower Extremity DVT: Individual Accuracy Studies*

Study Details						
Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Consecutive Patients	Independent Test Assessment	Comments	Source
Suspected recurrent DVT	CUS with measurement of residual venous diameter in abnormal venous segments	Venography	Yes	Yes	N = 29 patients with suspected recurrent DVT; 12 with confirmed recurrence (1 with isolated distal DVT)	Prandoni P, Cogo A, Bernardi E, et al. A simple ultrasound approach for detection of recurrent proximal-vein thrombosis. *Circulation*. 1993;88:1730-1735
		Venography	Yes	Not stated	N = 86 patients with suspected recurrent DVT; 16 patients with confirmed recurrence	Villalta S, Rossi L, Bernardi E, Bagatella P, Marchiori A, Scudellar A. Serial compression ultrasonography in the diagnostic approach of patients with clinically suspected recurrent deep vein thrombosis. Interim report of an ongoing study [abstract]. *Thromb Haemost*. 1997;78(Suppl):588.
		Venography	Not stated	Not stated	N = 16 patients with suspected recurrent DVT; 7 with confirmed recurrence	Koopman MM, Jongbloets L, Lensing AW, Buller H, ten Cate JW. Clinical utility of a quantitative B-mode ultrasonography method in patients with suspected recurrent deep vein thrombosis (DVT) [abstract]. *Thromb Haemost*. 1993;69:623.
		Venography	Yes	Yes	N = 205 patients with suspected recurrent DVT; 10 of 52 patients with initially abnormal CUS either could not undergo venography or had inadequate venography	Prandoni P, Lensing AWA, Bernardi E, Villalta S, Bagatella P, Girolami A for the DERECUS Investigators Group. The diagnostic value of compression ultrasonography in patients with suspected recurrent deep vein thrombosis. *Thromb Haemost*. 2002;88:402-406.

All studies are cross-sectional unless otherwise indicated under Comments. See Table S7 legend for expansion of abbreviation.

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Table S39—*[Sections 4.1-4.3] Methodology of Diagnostic Studies in Patients With Suspected Recurrent Lower Extremity DVT: Individual Management Studies with Cohorts*

Study Details								
Patient Population	Diagnostic Test	Outcome	Methods (Single-Arm Cohort vs Cohort From RCT)	Consecutive Patients	Follow-up	Received Alternative Tests	Comments	Source
Suspected recurrent DVT	Normal serial CUS (day of presentation, day 2 [± 1], and day 7 [± 1])	Probability of VTE during follow-up	Single-arm cohort	Yes	6 mo	No	N = 150 patients with normal serial CUS; recurrence confirmed by venography	Prandoni P, Lensing AWA, Bernardi E, Villalta S, Bagatella P, Girolami A for the DERECUS Investigators Group. The diagnostic value of compression ultrasonography in patients with suspected recurrent deep vein thrombosis. *Thromb Haemost*. 2002;88:402-406.
	Normal serial CUS (day of presentation, day 1-3, and day 6-10)	Probability of VTE during follow-up	Single-arm cohort	Yes	3 mo	No	N = 488 patients with suspected recurrence; 129 patients with normal serial CUS	Bates SM, Kearon C, Kahn SR, et al. A negative DD excludes recurrent deep vein thrombosis: results of a multicentre management trial. *Blood*. 2007;110:214a (abstract #698).
	Negative (normal or unchanged/decreased residual venous diameter) on serial CUS (day of presentation, day 2 [± 1], and day 7 [± 1])	Probability of VTE during follow-up	Single-arm cohort	Yes	6 mo	No	N = 65 patients with negative serial CUS; recurrence confirmed by venography	Villalta S, Rossi L, Bernardi E, Bagatella P, Marchiori A, Scudellar A. Serial compression ultrasonography in the diagnostic approach of patients with clinically suspected recurrent deep vein thrombosis. Interim report of an ongoing study [abstract]. *Thromb Haemost*. 1997;78(suppl):588.
	Unchanged residual venous diameter (< 4-mm increase in residual venous diameter) on serial CUS (day of presentation and day 7)	Probability of VTE during follow-up	Single-arm cohort	Yes	3 mo	No	N = 42 patients with unchanged residual venous diameter on serial CUS	Le Gal G, Kovacs MJ, Carrier M, et al. Validation of a diagnostic approach to exclude recurrent venous thromboembolism. *J Thromb Haemost*. 2009;7:752-759.

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Table S39—Continued

Study Details								
Patient Population	Diagnostic Test	Outcome	Methods (Single-Arm Cohort vs Cohort From RCT)	Consecutive Patients	Follow-up	Received Alternative Tests	Comments	Source
	Unchanged residual venous diameter (< 4-mm increase) at presentation and negative sensitive DD (Biopool Autodimer, threshold level not specified)	Probability of VTE during follow-up	Single-arm cohort	Yes	3 mo	No	N = 146 patients with suspected recurrence, all of whom underwent CUS; 38 patients diagnosed at presentation with recurrence (new noncompressible segment or increased residual venous diameter of > 4 mm); 75 of 108 remaining patients had a negative DD and were followed for recurrence	Prandoni P, Tormene D, Dalla Valle F, Concolator A, Pesavento R. D-Dimer as an adjunct to compression ultrasonography in patients with suspected recurrent deep vein thrombosis. *J Thromb Haemost*. 2007;5:1076-1077.
	Unlikely PTP according to Wells model and negative sensitive (STA Liatest, < 0.4 μg/mL) DD	Probability of VTE during follow-up	Single-arm cohort	Yes	3 mo	No	N = 105 patients with suspected recurrent DVT; 61 had an "unlikely" PTP for DVT using the Wells model; 16 had a negative DD and were followed for recurrence	Aguilar C, del Villar V. Combined D-dimer and clinical probability are useful for exclusion of recurrent deep venous thrombosis. *Am J Hematol*. 2007;82:41-44.
	Negative sensitive (STA Liatest, 0.4 μg/mL) DD	Probability of VTE during follow-up	Single-arm cohort	Yes	3 mo	No	N = 300 patients with suspected recurrent DVT; 134 had a negative DD – recurrence confirmed in 1 patient; however, recurrence could not be excluded in an additional 6 patients	Rathbun SW, Whitsett TL, Raskob GE. Negative D-dimer result to exclude recurrent deep vein thrombosis: a management trial. *Ann Intern Med*. 2004;141:839-845.
	Negative sensitive (MDA, < 0.5 μg/mL) DD	Probability of VTE during follow-up	Single-arm cohort	Yes	3 mo	No	N = 488 patients with suspected recurrent DVT; 229 had a negative DD – recurrence confirmed in 4 patients	Bates SM, Kearon C, Kahn SR, et al. A negative D-dimer excludes recurrent deep vein thrombosis: results of a multicentre management trial. *Blood*. 2007;110:214a (abstract # 698).

Cohorts from single-arm studies or cohorts representing one of the arms of an RCT. See Table S1, S2, and S7 legends for expansion of abbreviations.

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Table S40—*[Sections 4.1-4.3] Description and Results for Diagnostic Studies in Patients With Suspected Recurrent Lower Extremity DVT*

Question From Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
Suspected recurrent lower extremity DVT (Section 4.0)	What are the consequences of using venography to diagnose recurrent lower extremity DVT?	N/A	N/A	Patients with suspected recurrent DVT	N/A	N/A	Implied reference standard	N/A
	What are the consequences of using venography to rule out recurrent lower extremity DVT?	N/A	N/A	Patients with suspected recurrent DVT	N/A	N/A	Implied reference standard	N/A
	What are the consequences of using CUS (new noncompressible segment or increased residual venous diameter compared with previous CUS) to diagnose recurrent DVT?	Primary study	Venography	Patients with suspected recurrent DVT	Specificity: new noncompressible segment or increased residual venous diameter ≥ 2 mm compared with previous CUS	100 (81-100)	N = 29 patients with suspected recurrent DVT; 12 with confirmed recurrence (1 with isolated distal DVT)	Prandoni P, Cogo A, Bernardi E, et al. A simple ultrasound approach for detection of recurrent proximal-vein thrombosis. *Circulation*. 1993;88:1730-1735.
		Primary study	Venography	Patients with suspected recurrent DVT	Specificity: new noncompressible segment or increased residual venous diameter ≥ 2 mm compared with previous CUS	97 (90-99)	N = 86 patients with suspected recurrence; 16 patients with confirmed recurrence	Villalta S, Rossi L, Bernardi E, Bagatella P, Marchiori A, Scudellar A. Serial compression ultrasonography in the diagnostic approach of patients with clinically suspected recurrent deep vein thrombosis. Interim report of an ongoing study [abstract]. *Thromb Haemost*. 1997;78(Suppl):588.

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Table S40—*Continued*

Question From Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
		Primary study	Venography	Patients with suspected recurrent DVT	Specificity (a) New noncompressible segment or increased residual venous diameter 1-2 mm compared with previous CUS	(a) 78 (45-94)	N = 16 patients with suspected recurrence; 7 with confirmed recurrence	Koopman MM, Jongbloets L, Lensing AW, Buller H, ten Cate JW. Clinical utility of a quantitative B-mode ultrasonography method in patients with suspected recurrent deep vein thrombosis (DVT) [abstract]. *Thromb Haemost*. 1993;69:623.
					Specificity (b) New noncompressible segment or increased residual venous diameter ≥ 4 mm compared with previous CUS	(b) 100 (70-100)		
		Primary study	Venography	Patients with suspected recurrent DVT	Positive predictive value (a) New noncompressible segment	(a) 100 (72-100)	N = 205 patients with suspected recurrent DVT; 10 of 52 patients with initially abnormal CUS either could not undergo venography or had inadequate venography; results of 42 patients used to calculate positive predictive value	Prandoni P, Lensing AWA, Bernardi E, Villalta S, Bagatella P, Girolami A for the DERECUS Investigators Group. The diagnostic value of compression ultrasonography in patients with suspected recurrent deep vein thrombosis. *Thromb Haemost*. 2002;88:402-406.
					Positive predictive value (b) New noncompressible segment and/or increased residual venous diameter ≥ 2 mm compared with previous compression US	(b) 86 (69-94)		
					Positive predictive value (c) New noncompressible segment and/or increased residual venous diameter ≥ 2 but < 4 mm compared with previous CUS	(c) 50 (22-79)		
					Positive predictive value (d) Increased residual venous diameter > 4 mm compared with previous CUS	(d) 100 (84-100)		

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Table S40—*Continued*

Question From Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
	What are the consequences of using a single CUS (full compressibility, unchanged or improved residual venous diameter) to exclude recurrent DVT?	Primary study	Venography	Patients with suspected recurrent DVT	Sensitivity: Full compressibility, unchanged (< 2 mm) or improved residual venous diameter compared with previous CUS	Overall: 91 (59-100) Proximal only: 100 (69-100)	N = 29 patients with suspected recurrent DVT; 12 with confirmed recurrence (1 with isolated distal DVT)	Prandoni P, Cogo A, Bernardi E, et al. A simple ultrasound approach for detection of recurrent proximal-vein thrombosis. *Circulation*. 1993;88:1730-1735.
		Primary study	Venography	Patients with suspected recurrent DVT	Sensitivity: Full compressibility, unchanged (< 2 mm) or improved residual venous diameter compared with previous CUS	100 (81-100)	N = 86 patients with suspected recurrence; 16 patients with confirmed recurrence	Villalta S, Rossi L, Bernardi E, Bagatella P, Marchiori A, Scudellar A. Serial compression ultrasonography in the diagnostic approach of patients with clinically suspected recurrent deep vein thrombosis. Interim report of an ongoing study [abstract]. *Thromb Haemost*. 1997;78(suppl):588.
		Primary study	Venography	Patients with suspected recurrent DVT	Sensitivity (a) New noncompressible segment or increased residual venous diameter 1-2 mm compared with previous CUS	(a) 29 (8-64)	N = 16 patients with suspected recurrence; 7 with confirmed recurrence	Koopman MM, Jongbloets L, Lensing AW, Buller H, ten Cate JW. Clinical utility of a quantitative B-mode ultrasonography method in patients with suspected recurrent deep vein thrombosis (DVT) [abstract]. *Thromb Haemost*. 1993;69:623.
					Sensitivity (b) New noncompressible segment or increased residual venous diameter ≥ 4 mm compared with previous CUS	(b) 71 (36-92)		

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Table S40—*Continued*

Question From Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
	What are the consequences of using serial CUS to exclude recurrent DVT?	Primary	Confirmed VTE during 6 mo of follow-up	Patients with suspected recurrent DVT and normal serial CUS (day of presentation, day 2 [± 1] and day 7 [± 1])	NPV	99 (95-100)	N = 150 patients with normal serial CUS; 1 patient died of confirmed myocardial infarction during follow-up and analysis based on 149 remaining patients; recurrence confirmed by venography	Prandoni P, Lensing AWA, Bernardi E, Villalta S, Bagatella P, Girolami A for the DERECUS Investigators Group. The diagnostic value of compression ultrasonography in patients with suspected recurrent deep vein thrombosis. *Thromb Haemost*. 2002;88:402-406.
		Primary	Confirmed VTE during 3 mo of follow-up	Patients with suspected recurrent DVT and normal serial CUS (day of presentation, day 1-3, and day 6-10)	NPV	98 (92-99)	N = 488 patients with suspected recurrence; 129 with normal serial CUS	Bates SM, Kearon C, Kahn SR, et al. A negative DD excludes recurrent deep vein thrombosis: results of a multicentre management trial. *Blood*. 2007;110:214a (abstract #698).
		Primary	Confirmed VTE during 6 mo of follow-up	Patients with suspected recurrent DVT and negative (normal or unchanged/ improved residual venous diameter) serial CUS (day of presentation, day 2 [± 1] and day 7 [± 1])	NPV	97 (90-99)	N = 65 patients with negative serial CUS; recurrence confirmed by venography	Villalta S, Rossi L, Bernardi E, Bagatella P, Marchiori A, Scudellar A. Serial compression ultrasonography in the diagnostic approach of patients with clinically suspected recurrent deep vein thrombosis. Interim report of an ongoing study [abstract]. *Thromb Haemost*. 1997;78(*Suppl*):588.
		Primary	Confirmed thromboembolism during 3 mo of follow-up	Patients with unchanged residual venous diameter (< 4-mm increase in residual venous diameter) on serial CUS (day of presentation and day 7)	NPV	95 (84-99)	N = 42 patients with unchanged residual venous diameter on serial CUS	Le Gal G, Kovacs MJ, Carrier M, et al. Validation of a diagnostic approach to exclude recurrent venous thromboembolism. *J Thromb Haemost*. 2009;7:752-759.

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Table S40—*Continued*

Question From Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
	What are the consequences of using an unchanged CUS at presentation and negative sensitive DD to exclude recurrent DVT?	Primary	Confirmed thromboembolism during 3 mo of follow-up	Patients with unchanged residual venous diameter (< 4-mm increase) at presentation and negative sensitive DD (Biopool Autodimer)	NPV	100 (95-100)	N = 146 patients with suspected recurrence, all of whom underwent CUS; 38 patients diagnosed at presentation with recurrence (new noncompressible segment or increased residual venous diameter of > 4 mm; 75 of 108 remaining patients had a negative DD and were followed for recurrence	Prandoni P, Tormene D, Dalla Valle F, Concolator A, Pesavento R. D-Dimer as an adjunct to compression ultrasonography in patients with suspected recurrent deep vein thrombosis. *J Thromb Haemost*. 2007;5:1076-1077.
	What are the consequences of using an unchanged CUS at presentation and a negative SimpliRED DD to exclude recurrent DVT?	N/A	N/A	N/A	N/A	N/A	There are no accuracy or management studies of the SimpliRED DD in combination with CUS in this patient population	N/A
	What are the consequences of using an unlikely PTP with the Wells model in combination with a negative sensitive DD to exclude recurrent DVT?	Primary study	Confirmed thromboembolism during 3 mo of follow-up	Patients with unlikely PTP and negative sensitive DD (STA Liatest, < 0.4 ug/mL)	NPV	100 (81-100)	N = 105 patients with suspected recurrent DVT; 61 had an "unlikely" PTP for DVT using the Wells model; 16 had a negative DD and were followed for recurrence	Aguilar C, del Villar V. Combined D-dimer and clinical probability are useful for exclusion of recurrent deep venous thrombosis. *Am J Hematol*. 2007;82:41-44.

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Table S40—*Continued*

Question From Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
	What are the consequences of using a low PTP with the Wells model with a negative sensitive DD to exclude recurrent DVT?	N/A	N/A	N/A	N/A	N/A	There are no accuracy or management studies of the combination of sensitive DD and PTP in this patient population	N/A
	What are the consequences of using a low or moderate PTP with the Wells model with a negative sensitive DD to exclude recurrent DVT?	N/A	N/A	N/A	N/A	N/A	There are no accuracy or management studies of the combination of sensitive DD and PTP in this patient population	N/A
	What are the consequences of using a sensitive DD as a stand-alone test to exclude recurrent DVT?	Primary	Confirmed recurrence during 3 mo of follow-up	Patients with suspected recurrent DVT	NPV of the STA Liatest DD	Confirmed recurrence: 99 (96-100) Confirmed or possible recurrence: 95 (90-97)	N = 300 patients with suspected recurrent DVT; 134 had a negative DD, recurrence confirmed in 1 patient; however, recurrence could not be excluded in an additional 6 patients	Rathbun SW, Whitsett TL, Raskob GE. Negative D-dimer result to exclude recurrent deep vein thrombosis: a management trial. *Ann Intern Med*. 2004;141:839-845.
		Primary	Confirmed recurrence during 3 mo of follow-up	Patients with suspected recurrent DVT	NPV of the MDA DD	98 (96-100)	N = 488 patients with suspected recurrent DVT; 229 had a negative DD, recurrence confirmed in 4 patients	Bates SM, Kearon C, Kahn SR, et al. A negative D-dimer excludes recurrent deep vein thrombosis: results of a multicentre management trial. *Blood*. 2007;110:214a (abstract #698).

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Table S40—*Continued*

Question From Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result, % (95% CI)	Comments	Reference
	What are the consequences of using a SimpliRED DD as a stand-alone test to recurrent DVT?	N/A	N/A	N/A	N/A	N/A	There are no accuracy or management studies of the SimpliRED DD alone in this patient population	N/A
	What are the consequences of using CT scan venography to diagnose recurrent DVT?	N/A	N/A	Patients with suspected recurrent DVT	N/A	N/A	There are no accuracy or management studies of CT scan venography in this population	N/A
	What are the consequences of using CT scan venography to exclude recurrent DVT?	N/A	N/A	Patients with suspected recurrent DVT	N/A	N/A	There are no accuracy or management studies of CT scan venography in this population	N/A
	What are the consequences of using MRI to diagnose recurrent DVT?	N/A	N/A	Patients with suspected recurrent DVT	N/A	N/A	There are no accuracy or management studies of MR venography or direct MR imaging in this population	N/A
	What are the consequences of using MRI to exclude recurrent DVT?	N/A	N/A	Patients with suspected recurrent DVT	N/A	N/A	There are no accuracy or management studies of MR venography or direct MR imaging in this population	N/A

[a]eg, Post-TP during 3 month follow-up; sensitivity or specificity, and so forth. See Table S1, S3, and S7 legends for expansion of abbreviations.

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Table S41—*[Sections 4.1-4.3] Evidence Profile: Should Serial Normal Proximal CUS Be Used to Rule Out Recurrent DVT?*

Quality Assessment							Summary of Findings	
							Accuracy Indices, %	Quality
No. of Studies (Patients)	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Normal Serial CUS	
Negative predictive value of serial normal CUS (day of presentation, day 2 [± 1], day 7 [± 1]) for recurrent DVT during 6-mo follow-up								
2 Studies Study 1 = 150 Study 2 = 129	Single-arm prospective management cohort studies	Moderate[a]	None	N/A	Study 1: 95% CI, 95%-100% Study 2: 95% CI, 92%-99%	3- (Study 2) or 6-(Study 1) mo follow-up as reference standard. Confined to patients with a positive DD in Study 2	Study 1: 99 Study 2: 98	Moderate

Bibliography: Prandoni P, Lensing AWA, Bernardi E, Villalta S, Bagatella P, Girolami A for the DERECUS Investigators Group. The diagnostic value of compression ultrasonography in patients with suspected deep vein thrombosis. *Thromb Haemost*. 2002;88(3):402-406. Bates SM, Kearon C, Kahn SR, et al. A negative DD excludes recurrent deep vein thrombosis: results of a multicentre management trial. *Blood*. 2007;110:214a (abstract #698). Settings: predominantly outpatients. See Table S7 legend for expansion of abbreviation.

[a]Study by Bates et al only in abstract form.

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Table S42—*[Sections 4.1-4.3] Evidence Profile: Should the Criterion of New Noncompressible Segment or Increased Residual Venous Diameter of 1-2 mm on CUS Be Used to Rule Out or Diagnose Recurrent DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	1 (16 participants)	Accuracy cohort	Serious	N/A	Serious	Very serious	Low	Prev 53%: 154 Prev 17%: 49 Prev 5%: 14
True negative (patients without DVT)								Prev 53%: 367 Prev 17%: 647 Prev 5%: 741
False negative (patients incorrectly classified DVT negative)								Prev 53%: 376 Prev 17%: 121 Prev 5%: 36
False positive (patients incorrectly classified DVT positive)								Prev 53%: 103 Prev 17%: 183 Prev 5%: 209

Bibliography: Koopman MM, Jongbloets L, Lensing AWA, Buller H, ten Cate JW. Clinical utility of a quantitative B-mode ultrasonography method in patients with suspected recurrent deep vein thrombosis (DVT) [abstract]. *Thromb Haemost*. 1993;69:623. Settings: not stated. Reference standard: venography. See Table S7 legend for expansion of abbreviation.

[a] Setting not stated, published only in abstract form, unclear if consecutive or selected patients used; technique requires local expertise and previous CUS for comparison.

[b] Single study.

[c] Accuracy study.

[d] Wide 95% CIs.

[e] Based on a specificity of 78% (95% CI, 45%-94%) and sensitivity of 29% (95% CI, 8%-64%). Prevalences taken from Wells et al.[30]

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Table S43—*[Sections 4.1-4.3] Evidence Profile: Should the Criterion of New Noncompressible Segment or Increased Residual Venous Diameter of ≥ 2 mm on Proximal CUS Be Used to Rule Out or Diagnose Recurrent DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	2 (115 Participants)	Accuracy cohorts	Serious	No	Serious	Serious	Low	Prev 53%: 482 Prev 17%: 456 Prev 5%: 49
True negative (patients without DVT)								Prev 53%: 155 Prev 17%: 805 Prev 5%: 921
False negative (patients incorrectly classified DVT negative)								Prev 53%: 49 Prev 17%: 15 Prev 5%: 5
False positive (patients incorrectly classified DVT positive)								Prev 53%: 14 Prev 17%: 25 Prev 5%: 29

Bibliography: Prandoni P, Cogo A, Bernardi E, et al. A simple ultrasound approach for detection of recurrent proximal-vein thrombosis. *Circulation.* 1993;88:1730-1735. Villalta S, Rossi L, Bernardi E, Bagatella P, Marchiori A, Sculdellar A. Serial compression ultrasonography in the diagnostic approach of patients with clinically suspected recurrent deep vein thrombosis. Interim report of an ongoing study [abstract]. *Thromb Haemost.* 1997;78 (suppl):588. Setting: suspected recurrent DVT. Reference test: venography. See Table S7 legend for expansion of abbreviation.

[a] Villalta et al published only in abstract form, unclear if consecutive or selected patients used; technique requires local expertise and previous CUS for comparison.

[b] Two studies only.

[c] Accuracy study.

[d] Wide 95% CIs.

[e] Based on a specificity of 97% and sensitivity of 91%. Prevalences taken from Wells et al.[30]

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Table S44—*[Sections 4.1-4.3] Evidence Profile: Should the Criterion of New Noncompressible Segment or Increased Residual Venous Diameter of > 4 mm on Proximal CUS Be Used to Rule Out or Diagnose Recurrent DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	2, but estimates of both sensitivity and specificity only in 1 (16 participants; Koopman et al)	Accuracy cohort	Serious	N/A	Serious	Very serious	Moderate	Prev 53%: 376 Prev 17%: 121 Prev 5%: 36
True negative (patients without DVT)								Prev 53%: 470 Prev 17%: 830 Prev 5%: 950
False negative (patients incorrectly classified DVT negative)								Prev 53%: 154 Prev 17%: 50 Prev 5%: 14
False positive (patients incorrectly classified DVT positive)								Prev 53%: 0 Prev 17%: 0 Prev 5%: 0

Bibliography: Koopman MM, Jongbloets L, Lensing AWA, Buller H, ten Cate JW. Clinical utility of a quantitative B-mode ultrasonography method in patients with suspected recurrent deep vein thrombosis (DVT) [abstract]. *Thromb Haemost*. 1993;69:623. Prandoni P, Lensing AWA, Bernardi E, Villalta S, Bagatella P, Girolami A for the DERECUS Investigators Group. The diagnostic value of compression ultrasonography in patients with suspected deep vein thrombosis. *Thromb Haemost*. 2002;88:402-406. Setting: suspected recurrent DVT. Reference test: venography. See Table S3 and S7 legends for expansion of abbreviations.

[a] Setting not stated, published only in abstract form, unclear if consecutive or selected patients used; technique requires local expertise and previous CUS for comparison (Koopman et al); positive predictive value only of 100% (95% CI, 84%-100%) (Prandoni et al).

[b] Single study only for sensitivity and specificity.

[c] Accuracy studies.

[d] Wide 95% CIs.

[e] Based on a specificity of 100% (95% CI, 70%-100%) and sensitivity of 71% (95% CI, 36%-92%) (Koopman et al); positive predictive value of 100% (95% CI, 84%-100%); sensitivity and specificity not provided (Prandoni et al). Prevalences taken from Wells et al.[30]

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Table S45—*[Sections 4.1-4.3] Evidence Profile: Should the Combination of an Unchanged CUS (Change in Residual Venous Diameter of < 4 mm) and a Negative Highly Sensitive DD (Biopool Autodimer) Be Used to Exclude Recurrent DVT?*

Quality Assessment							Summary of Findings	
							NPV	
No. of Studies (Patients)	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Sensitive DD and Unchanged (4-mm Increase) Residual Venous Diameter	Quality
NPV of an unchanged proximal CUS (change in residual venous diameter of < 4 mm) and a sensitive DD during 3-mo follow-up								
1 (145; 75 patients had an unchanged CUS and negative Biopool Autodimer)	Prospective single-arm cohort study	Serious[a]	Single study	N/A	95% CI, 95%-100%	…	100%	Moderate

Bibliography: Prandoni P, Tormeni D, Dalla Valle, A Concolato, Pesaventao R. DD as an adjunct to compression ultrasonography in patients with suspected recurrent deep vein thrombosis. *J Thromb Haemost*. 2007;5:1076-1077. Settings: not stated. See Table S1, S3, and S7 legends for expansion of abbreviations.

[a] Single-center study; setting not specified; unclear if patients receiving long-term warfarin included; technique requires local expertise and previous CUS for comparison

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Table S46—*[Sections 4.1-4.3] Evidence Profile: Should the Combination of an Unlikely PTP and Negative Highly Sensitive DD (STA Liatest) Be Used to Exclude Recurrent DVT?*

Quality Assessment							Summary of Findings	
							NPV	
No. of Studies (Patients)	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	Sensitive DD and Unlikely PTP	Quality
NPV compared with confirmed recurrent VTE during 3-mo follow-up								
1 (105; 16 with unlikely PTP and negative STA Liatest DD (<0.4 μg/mL)	Prospective single-arm cohort study	Very serious[a]	Single study	N/A	Very serious; 95% CI, 81%-100%	Study excluded patients receiving long-term warfarin therapy	100%	Low

Bibliography: Aguilar C, del Villar V. Combined D-dimer and clinical probability are useful for exclusion of recurrent deep venous thrombosis. *Am J Hematol*. 2007;82:41-44. Settings: ED. See Table S1, S3, and S7 legends for expansion of abbreviations.

[a]Only outpatients presenting to the ED were enrolled; patients receiving long-term warfarin were excluded; only 15% of patients could be managed with this approach.

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Table S47—*[Sections 4.1-4.3] Evidence Profile: Should a Highly Sensitive DD Be Used to Exclude Recurrent DVT?*

Quality Assessment							Summary of Findings	
							NPV, % (95% CI)	
No. of Studies (Patients)	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Sensitive DD	Quality
NPV of a sensitive DD for recurrent VTE during 3-mo follow-up								
2 Studies	Prospective single-arm cohort studies	Serious[a]	None	N/A	Serious; in both studies 95% CI, 96%-100%	Both studies included patients receiving long-term warfarin		Moderate
Study 1 (300; 134 with negative DD)							Study 1: STA Liatest DD: 99, 96-100	
Study 2 (488; 229 with negative DD, 82 with confirmed VTE)							Study 2: MDA DD: 98 (96-100)	

Bibliography: Rathbun SW, Whitsett TL, Raskob GE. Negative D-dimer result to exclude recurrent deep vein thrombosis: a management trial. *Ann Intern Med.* 2004;141:839-845. Bates SM, Kearon C, Kahn SR, et al. A negative D-dimer excludes recurrent deep vein thrombosis: results of a multicentre management trial. *Blood.* 2007;110:214a (abstract 698). Settings: Predominantly outpatient; includes patients receiving long-term warfarin. See Table S1 and S3 legends for expansion of abbreviation.

[a]Study by Bates et al only in abstract form; Rathbun et al enrolled only outpatients and 97% of patients in study by Bates et al were outpatients; studies used different sensitive DD assays; in Rathbun et al, NPV could have been as low as 95% (95% CI, 90%-97%) if possible recurrences included; no data provided on proportion of patients with various PTPs; unable to determine exact overall prevalence of recurrent DVT in Rathbun et al study.

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Table S48—*[Sections 5.1-5.3] Methodology of Diagnostic Studies in Patients with Suspected Pregnancy-Related DVT: Individual Accuracy Studies*

Study Details						
Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Consecutive Patients	Independent Test Assessment	Comments	Source
Pregnant and postpartum women with suspected DVT	Single complete US extending from the inferior vena cava to the soleal veins	VTE during 3 mo of follow-up	No	No	Retrospective cohort study of 162 women; 82 women were postpartum. Twenty-five women were diagnosed with DVT at presentation; the proportion of patients with calf vein thrombosis only not specified. Nineteen women received anticoagulant therapy despite US that demonstrated no DVT (muscular or superficial thrombosis present only); 3 additional women received who extended ($\geq$6 wk) postpartum prophylaxis were excluded from analysis; 11 women discharged without anticoagulant therapy (9%) were lost to follow-up	Le Gal, Prins A-M, Righini M, et al. Diagnostic value of a negative single complete compression ultrasound of the lower limbs to exclude the diagnosis of deep venous thrombosis in pregnant or postpartum women: a retrospective hospital based study. *Thromb Res*. 2006;118:691-697
Suspected pregnancy-related DVT	Clinical model	CUS at presentation; some patients had follow-up testing on day 3 and 7; all patients were followed for 3 mo	Not stated; "unselected patients"	Clinical assessment performed prior to performance of diagnostic testing; however, diagnostic test results not blinded	Failure to use accepted reference standard (venography); small number of events (n = 17; prevalence 8.8%); internal validation only	Chan WS, Lee A, Spencer FA, et al. Predicting deep venous thrombosis in pregnancy: out in "LEFt" field? *Ann Intern Med*. 2009;151:85-92
	VIDAS DD (bioMerieux) Asserachrome DD (Stago) IL Test DD (Instrumentation Laboratories) Sta-Lia Test (Stago) Innovance DD (Siemens)	CUS at presentation (including examination of the iliac vein in patients with suspicious symptoms), an unspecified proportion underwent serial US on day 3 and 7; all patients with negative testing were followed for 3 mo	Not stated; "unselected patients"	Yes	Frozen samples, failure to use accepted reference standard (venography); small number of events (n-15; prevalence 6.6%)	Chan WS, Lee A, Spencer FA, et al. D-Dimer testing in pregnant patients: toward determining the next "level" in the diagnosis of deep vein thrombosis. *J Thromb Haemost*. 2010;8:1004-1011

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Table S48—*Continued*

Study Details						
Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Consecutive Patients	Independent Test Assessment	Comments	Source
	SimpliRED DD	CUS at presentation (including examination of the iliac vein in patients with suspicious symptoms), an unspecified proportion underwent serial US on day 3 and 7; all patients with negative testing were followed for 3 mo	Yes	Yes	Frozen samples, failure to use accepted reference standard (venography); small number of events (n = 13; prevalence 8.7%);	Chan WS, Chunilal SD, Lee AYY, Crowther M, Rodger M, Ginsberg JS. A red blood cell agglutination D-dimer test to exclude deep venous thrombosis in pregnancy. *Ann Intern Med.* 2007;147:165-170

In addition to meta-analysis, all studies are cross-sectional unless otherwise indicated under Comments. See Table S1 and S7 legends for expansion of abbreviations.

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Table S49—*[Sections 5.1-5.3] Methodology of Diagnostic Studies in Patients With Suspected Pregnancy-Related DVT: Individual Management Studies With Cohorts*

Study Details								
Patient Population	Diagnostic Test	Outcome	Methods (Single-Arm Cohort vs Cohort From RCT)	Consecutive Patients	Follow-up	Received Alternative Tests	Comments	Source
Suspected pregnancy-related DVT	CUS of the proximal veins and calf trifurcation at presentation (including examination of the iliac vein in patients with suspicious symptoms); an unspecified proportion underwent serial US on day 3 and 7	Confirmed VTE at 3-mo follow-up	Single-arm cohort	Yes	3 mo	No	The proportion of patients who underwent single vs serial CUS not specified. Prevalence of DVT 8.7% (12 patients at presentation and 1 during follow-up)	Chan WS, Chunilal SD, Lee AYY, Crowther M, Rodger M, Ginsberg JS. A red blood cell agglutination D-dimer test to exclude deep venous thrombosis in pregnancy. *Ann Intern Med.* 2007;147:165-170
	Single complete US extending from the inferior vena cava to the soleal veins	VTE during 3 mo of follow-up	Single-arm cohort	Yes	3 mo	No	Patient population included an unspecified number of postpartum women. Prevalence of DVT was 9.3%; proportion of calf thrombosis not specified. Three patients received full-dose anticoagulants despite negative US results.	Le Gal G, Righini M, Kercret L, et al. Diagnosis of deep vein thrombosis by compression ultrasonography during pregnancy and the postpartum period: a management study [abstract]. *J Thromb Haemost.* 2009; 7 (2):abstract PP-TH-508

Cohorts from single-arm studies or cohorts representing one of the arms of an RCT. See Table S1, S2, and S7 legends for expansion of abbreviations.

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Table S50—*[Sections 5.1-5.3] Description and Results of Diagnostic Studies in Patients with Suspected Pregnancy-Related DVT*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
Suspected Pregnancy-Related DVT (Section 5.0)	What are the consequences of using venography to diagnose pregnancy-related DVT?	N/A	N/A	Pregnant patients with suspected DVT	N/A	N/A	Implied reference standard	N/A
	What are the consequences of using venography to rule out pregnancy-related DVT?	N/A	N/A	Pregnant patients with suspected DVT	N/A	N/A	Implied reference standard	N/A
	What are the consequences of using CUS to diagnose pregnancy-related DVT?	N/A	N/A	Pregnant patients with suspected DVT	N/A	N/A	N/A	N/A
	What are the consequences of using CUS of the proximal veins and calf trifurcation (with imaging of the iliac veins in symptomatic women) to exclude pregnancy-related DVT	Primary, cohort management	3-mo follow-up	Pregnant patients with suspected DVT	NPV	NPV, 99.3% (95% CI, 96.0%-99.9%)	N = 149 (prevalence 8.7%); CUS of the proximal veins and calf trifurcation at presentation (including examination of the iliac vein in patients with suspicious symptoms), an unspecified proportion underwent serial US on day 3 and 7; proportion of inpatients and outpatients not specified	Chan WS, Chunilal SD, Lee AYY, Crowther M, Rodger M, Ginsberg JS. A red blood cell agglutination D-dimer test to exclude deep venous thrombosis in pregnancy. *Ann Intern Med*. 2007;147:165-170

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Table S50—*Continued*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using a single complete US to exclude pregnancy-related DVT?	Primary, cohort management	3-mo follow-up	Pregnant and postpartum patients with suspected DVT	NPV	NPV, 100% (95% CI, 96.4%-100%)	N = 162; retrospective cohort study. Eighty-two women were postpartum; 25 women were diagnosed with DVT at presentation; 19 women received anticoagulant therapy despite US that demonstrated no DVT (muscular or superficial thrombosis); 3 additional women received extended (≥6 wk) postpartum prophylaxis were excluded from analysis; 11 women discharged without anticoagulant therapy (9%) were lost to follow-up	Le Gal, Prins A-M, Righini M, et al. Diagnostic value of a negative single complete compression ultrasound of the lower limbs to exclude the diagnosis of deep venous thrombosis in pregnant or postpartum women: a retrospective hospital based study. *Thromb Res*. 2006;118:691-697
		Primary, cohort management	3-mo follow-up	Pregnant and postpartum patients with suspected DVT	NPV	NPV, 98.2 (95% CI, 94.9%-99.4%)	N = 194; prospective cohort study. Patient population included an unspecified number of postpartum women. Prevalence of DVT was 9.3%; proportion of calf thrombosis not specified. Three patients received full-dose anticoagulants despite negative US results.	Le Gal G, Righini M, Kercret L, et al. Diagnosis of deep vein thrombosis by compression ultrasonography during pregnancy and the postpartum period: a management study [abstract]. *J Thromb Haemost*. 2009; 7 (2): abstract PP-TH-508

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Table S50—*Continued*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using a clinical score to diagnose pregnancy-related DVT?	Primary, cohort accuracy	CUS and 3-mo follow-up	Pregnant patients with suspected DVT	Specificity	Specificity (for one or more variables) 50% (43%-58%)	N = 194 (prevalence 8.8%)	Chan WS, Lee A, Spencer FA, et al. Predicting deep venous thrombosis in pregnancy: out in "LEFt" field? *Ann Intern Med.* 2009;151:85-92
					Positive LR	LR positive, 2.0 (1.7-2.3)	Clinical score based on presence of left leg symptoms, difference in calf circumference of ≥ 2 cm, and first trimester presentation. Proportion of inpatients and outpatients not specified.	
	What are the consequences of using a clinical score to exclude pregnancy- DVT?	Primary, cohort accuracy	CUS and 3-mo follow-up	Pregnant patients with suspected DVT	Sensitivity	Sensitivity 100% (81%-100%)	N = 194 (prevalence 8.8%)	Chan WS, Lee A, Spencer FA, et al. Predicting deep venous thrombosis in pregnancy: out in "LEFt" field? *Ann Intern Med.* 2009;151:85-92
					Negative LR	LR negative, 0 (0-0)	Clinical score based on presence of left leg symptoms, difference in calf circumference of ≥ 2 cm, and first trimester presentation. Proportion of inpatients and outpatients not specified.	
	What are the consequences of using a highly sensitive DD to diagnose pregnancy-related DVT?	Primary, cohort accuracy	CUS and 3-mo follow-up	Pregnant patients with suspected DVT	Specificity	VIDAS DD, μg FEU/mL Traditional (0.5) 10.3 (6.6-15.5) Pregnancy (1.89) 78.8 (72.7-84.1)	N = 228 (prevalence 6.6%, n = 15). Five highly sensitive DD assays evaluated. Frozen samples. Cut-point based on ROC analysis. Proportion of inpatients and outpatients not specified.	Chan WS, Lee A, Spencer FA, et al. D-Dimer testing in pregnant patients: toward determining the next "level" in the diagnosis of deep vein thrombosis. *J Thromb Haemost.* 2010;8:1004-1011

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Table S50—*Continued*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
						Asserachrome, μg FEU/mL		
						Traditional (0.5) 12.3 (8.3-17.8)		
						Pregnancy (1.51) 73.9 (67.5-79.7)		
						IL Test, μg DD/mL		
						Traditional (0.23) 17.8 (13.0-24.0)		
						Pregnancy (0.57) 74.8 (68.3-80.5)		
						STA-Lia, μg FEU/mL		
						Traditional (0.5) 22.9 (17.5-29.4)		
						Pregnancy (1.38) 75.6 (69.3-81.2)		
						Innovance, μg FEU/mL		
						Traditional (0.5) 6.2 (3.5-10.6)		
						Pregnancy (1.5) 61.2 (54.3-67.8)		

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Table S50—*Continued*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using a highly sensitive DD to exclude pregnancy-related DVT?	Primary, cohort accuracy	CUS and 3-mo follow-up	Pregnant patients with suspected DVT	Sensitivity	VIDAS DD, μg FEU/mL Traditional (0.5) 100 (74.7-100) Pregnancy (1.89) 93.3 (68.1-99.8) Asserachrome, μg FEU/mL Traditional (0.5) 100 (74.7-100) Pregnancy (1.51) 100 (78.2-100) IL Test, μg DD/mL Traditional (0.23) 100 (74.7-100) Pregnancy (0.57) 80.0 (51.9-95.7) STA-Lia, μg FEU/mL Traditional (0.5) 100 (74.7-100) Pregnancy (1.38) 93.3 (68.1-99.8) Innovance, μg FEU/mL Traditional (0.5) 100 (74.7-100) Pregnancy (1.5) 100 (74.7-100)	N = 228 (prevalence 6.6%, n = 15). Five highly sensitive DD assays evaluated. Frozen samples. Cut-point based on ROC analysis. Proportion of inpatients and outpatients not specified.	Chan WS, Lee A, Spencer FA, et al. D-Dimer testing in pregnant patients: toward determining the next "level" in the diagnosis of deep vein thrombosis. *J Thromb Haemost*. 2010;8:1004-1011

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Table S50—*Continued*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
					Negative LR	VIDAS DD, μg FEU/mL		
						Traditional (0.5) 0.09 (0.01-0.56)		
						Asserachrome, μg FEU/mL		
						Traditional (0.5) 0 (Not calculable)		
						IL Test, μg DD/mL		
						Traditional (0.23) 0.27 (0.1-0.74)		
						STA-Lia, μg FEU/mL		
						Traditional (0.5) 0.09 (0.01-0.59)		
						Pregnancy (1.38) 75.6 (69.3-81.2)		
						Innovance, μg FEU/mL		
						Traditional (0.5) 0 (Not calculable)		
	What are the consequences of using a moderately sensitive DD to diagnose pregnancy-related DVT?	Primary, cohort accuracy	CUS and 3-mo follow-up	Pregnant patients with suspected DVT	Specificity	Specificity 60% (52%-68%)	N = 149 (prevalence 8.7%, n = 13) SimpliRED DD used. Frozen samples. Proportion of inpatients and outpatients not specified.	Chan WS, Chunilal SD, Lee AYY, Crowther M, Rodger M, Ginsberg JS. A red blood cell agglutination D-dimer test to exclude deep venous thrombosis in pregnancy. *Ann Intern Med*. 2007;147:165-170
					Positive LR	LR positive, 2.5 (2.0-3.1)		

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Table S50—*Continued*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using a moderately sensitive DD to exclude pregnancy-related DVT?	Primary, cohort accuracy	CUS and 3-mo follow-up	Pregnant patients with suspected DVT	Sensitivity	Sensitivity 100% (77%-100%)	N = 149 (prevalence 8.7%, n = 13) SimpliRED DD used. Frozen samples. Proportion of inpatients and outpatients not specified.	Chan WS, Chunilal SD, Lee AYY, Crowther M, Rodger M, Ginsberg JS. A red blood cell agglutination D-dimer test to exclude deep venous thrombosis in pregnancy. *Ann Intern Med.* 2007;147:165-170
					Negative LR	LR negative, 0 (0-0.9)		
	What are the consequences of using CT scan venography to diagnose DVT during pregnancy?	N/A	N/A	Pregnant patients with suspected DVT	N/A	N/A	N/A	N/A
	What are the consequences of using CT scan venography to exclude DVT during pregnancy?	N/A	N/A	Pregnant patients with suspected DVT	N/A	N/A	N/A	N/A
	What are the consequences of using contrast MR venography to diagnose DVT during pregnancy?	N/A	N/A	Pregnant patients with suspected DVT	N/A	N/A	N/A	N/A
	What are the consequences of using MR venography to exclude DVT during pregnancy?	N/A	N/A	Pregnant patients with suspected DVT	N/A	N/A	N/A	N/A

ROC = receiver operator curve. See Table S1-S3, S7, and S10 legends for expansion of other abbreviations.

[a]eg, Post-TP during 3 mo follow-up; sensitivity or specificity, and so forth.

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Table S51—*[Sections 5.1-5.3] Evidence Profile: Should Serial Negative CUSs of the Proximal Veins and Calf Trifurcation (With Imaging of the Iliac Veins in Symptomatic Women) Be Used to Exclude DVT During Pregnancy?*

Quality Assessment							Summary of Findings	
							Accuracy Indices, % (95% CI)	
No. of Studies (Patients)	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other Considerations	CUS of Proximal Veins and Calf Trifurcation (± Iliac Veins)	Quality
NPV for pregnancy-related DVT compared with 3 mo of clinical follow-up								
1 (149)	Single-arm prospective cohort	Serious[a]	Single study	N/A	Serious	Prevalence of DVT, 8.7%	99.3 (96.0-99.9)	Moderate

Bibliography: Chan WS, Chunilal SD, Lee AYY, Crowther M, Rodger M, Ginsberg JS. A red blood cell agglutination D-dimer test to exclude deep venous thrombosis in pregnancy. *Ann Intern Med*. 2007;147:165-170. Settings: not stated. See Table S3 and S7 legends for expansion of abbreviations.

[a]The proportion of patients who underwent single CUS vs those who underwent serial testing on days 3 and 7 not specified.

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Table S52—*[Sections 5.1-5.3] Evidence Profile: Should a Negative Complete US Be Used to Exclude DVT During Pregnancy?*

Quality Assessment							Summary of Findings	
							Accuracy Indices, % (95% CI)	
No. of Studies (Patients)	Design	Limitations	Inconsistency	Indirectness	Imprecision	Other considerations	Complete US	Quality
NPV for DVT during pregnancy as compared with 3 mo of clinical follow-up								
2 Studies		Very serious[a]	None	Serious[b]	Serious	Prevalence of DVT in retrospective study 15.4%; in prospective study 9.3%.		Low
Study 1 (162)	Study 1: retrospective cohort						Study 1: NPV, 100 (96.4-100)	
Study 2 (194)	Study 2: prospective cohort						Study 2: NPV, 98.2 (94.9-99.4)	

Bibliography: Le Gal, Prins A-M, Righini M, et al. Diagnostic value of a negative single complete compression ultrasound of the lower limbs to exclude the diagnosis of deep venous thrombosis in pregnant or postpartum women: a retrospective hospital based study. *Thromb Res*. 2006;118:691-697. Le Gal G, Righini M, Kercret L, et al. Diagnosis of deep vein thrombosis by compression ultrasonography during pregnancy and the postpartum period: a management study [abstract]. *J Thromb Haemost*. 2009;7 (2):abstract PP-TH-508. Settings: not stated. See Table S1 and S3 legends for expansion of abbreviations.

[a]In retrospective study, 51% of women were postpartum. Of 137 women without DVT at presentation, 19 women received anticoagulant therapy on the basis of USs that demonstrated muscular or superficial thrombosis; three additional women who received extended (≥ 6 wk) postpartum prophylaxis were excluded from analysis; 11 women discharged without anticoagulant therapy (9%) were lost to follow-up. Prospective study published only in abstract. An unspecified number of women in this study were postpartum. Of 176 women without DVT at presentation, three patients received full-dose anticoagulants despite negative US results. Follow-up only available on 167 women.

[b]A substantial proportion of the study population was postpartum.

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Table S53—*[Sections 5.1-5.3] Evidence Profile: Should a Clinical Model Be Used to Evaluate Pregnant Patients With Suspected DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	1 (195 patients)	Accuracy cohort	Very serious	N/A	Serious	Very serious	Low	Prev 24.6%: 246 Prev 8.7%: 87 Prev 1.5%: 15
True negative (patients without DVT)								Prev 24.6%: 377 Prev 8.7%: 457 Prev 1.5%: 493
False negative (patients incorrectly classified DVT negative)								Prev 24.6%: 0 Prev 8.7%: 0 Prev 1.5%: 0
False positive (patients incorrectly classified DVT positive)								Prev 24.6%: 377 Prev 8.7%: 456 Prev 1.5%: 492

Bibliography: Chan WS, Lee A, Spencer FA, et al. Predicting deep venous thrombosis in pregnancy: out in "LEFt" field? *Ann Intern Med*. 2009;151:85-92. Setting: Suspected pregnancy-related DVT. Reference test: proximal CUS and 3 mo follow-up. See Table S3 and S7 legends for expansion of abbreviations.

[a] Setting not stated, not clearly a sample of consecutive patients, accepted reference standard not used, reference standard results no blinded, internal validation only, small number of events (17).

[b] Single study.

[c] Accuracy study.

[d] Wide 95% CIs.

[e] Based on a specificity of 50% (95% CI, 43%-58%) for absence of left leg symptoms, difference in calf circumference of at least 2 cm, and first trimester presentation and sensitivity of 100% (95% CI, 71%-100%) for at least one of these characteristics. Prevalences taken from Chan et al.

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Table S54—*[Sections 5.1-5.3] Evidence Profile: Should a High Sensitivity DD (Standard Threshold) Be Used to Evaluate Pregnant Patients With Suspected DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	1 (249 patients)	Accuracy cohort	Very serious	N/A	Serious	Very serious	Low	Prev 24.6%: 246 Prev 8.7%: 87 Prev 1.5%: 15
True negative (patients without DVT)								Prev 24.6%: 78 Prev 8.7%: 94 Prev 1.5%: 101
False negative (patients incorrectly classified DVT negative)								Prev 24.6%: 0 Prev 8.7%: 0 Prev 1.5%: 0
False positive (patients incorrectly classified DVT positive)								Prev 24.6%: 676 Prev 8.7%: 819 Prev 1.5%: 884

Bibliography: Chan WS, Lee A, Spencer FA, et al. D-Dimer testing in pregnant patients: toward determining the next "level" in the diagnosis of deep vein thrombosis. *J Thromb Haemost*. 2010;8:1004-1011.
Setting: suspected pregnancy-related DVT. Reference test: proximal CUS and 3 mo follow-up. See Table S1, S3, and S7 legends for expansion of abbreviations.
[a] Setting not stated, not clearly a sample of consecutive patients, accepted reference standard not used, frozen samples, small number of events (15).
[b] Single study.
[c] Accuracy study.
[d] Wide 95% CIs.
[e] Based on a specificity of 10.3% (95% CI, 6.6%-15.5%) and sensitivity of 100% (95% CI, 74.7%-100%) for the VIDAS DD using the standard cut-point of 0.5 μg FEU/mL. Prevalences taken from Chan et al.

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Table S55—*[Sections 5.1-5.3] Evidence Profile: Should a Moderately Sensitive DD Be Used to Evaluate Pregnant Patients With Suspected DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	1 (149 patients)	Accuracy cohort	Serious	N/A	Serious	Very serious	Low	Prev 24.6%: 247 Prev 8.7%: 87 Prev 1.5%: 15
True negative (patients without DVT)								Prev 24.6%: 452 Prev 8.7%: 548 Prev 1.5%: 591
False negative (patients incorrectly classified DVT negative)								Prev 24.6%: 0 Prev 8.7%: 0 Prev 1.5%: 0
False positive (patients incorrectly classified DVT positive)								Prev 24.6%: 302 Prev 8.7%: 306 Prev 1.5%: 394

Bibliography: Chan WS, Chunilal SD, Lee AYY, Crowther M, Rodger M, Ginsberg JS. A red blood cell agglutination D-dimer test to exclude deep venous thrombosis in pregnancy. *Ann Intern Med*. 2007;147:165-170. Setting: Suspected pregnancy-related DVT. Reference test: proximal CUS and 3-mo follow-up. See Table S1, S3, and S7 legends for expansion of abbreviations.

[a] Accepted reference standard not used, frozen samples, small number of events (13).

[b] Single study.

[c] Accuracy study.

[d] Wide 95% CIs.

[e] Based on a specificity of 60% (95% CI, 52%-68%) and sensitivity of 100% (95% CI, 77%-100%) for the SimpliRED DD. Prevalences taken from Chan et al.

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Table S56—*[Section 6.2] Methodology of Diagnostic Studies in Patients With Suspected Upper Extremity DVT: Meta-analysis of Accuracy Studies*

Study Eligibility				
Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Exploration of Heterogeneity	Source
Suspected upper extremity DVT	CUS	Venography	Could not test for influence of study design characteristics given limited number of studies available for each specific test	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8: 684-692
	Doppler US	Venography		
	Doppler US and CUS	Venography		

All studies are cross-sectional. See Table S1 and S7 for expansion of abbreviations.

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Table S57—*[Section 6.2] Methodology of Diagnostic Studies in Patients With Suspected Upper Extremity DVT: Individual Accuracy Studies*

Study Details						
Patient Population	Diagnostic Test	Outcome (Criterion Standard)	Consecutive Patients	Independent Test Assessment	Comments	Source
Suspected upper extremity DVT	Clinical model	Duplex US	Not stated	Reference standard results not blinded	Failure to use accepted reference standard (venography)	Constans J, Salmi L-R, Sevestre-Pietri M-A, et al. A clinical prediction score for upper extremity deep venous thrombosis. *Thromb Haemost*. 2008;99:202-207
Suspected upper extremity DVT	VIDAS DD	CT scan; Duplex US	Yes	Blinding of criterion and diagnostic test unclear	Failure to use accepted reference standard (venography)	Merminod T, Pellicciotta S, Bounameaux H. Limited usefulness of D-dimer in suspected deep vein thrombosis of the upper extremities. *Blood Coagul Fibrinolysis*. 2006;17:225-227
Suspected upper extremity DVT	MRI	Venography	Yes	Yes	10 of 31 Patients unable to undergo diagnostic tests	Baarslag H-J, van Beek EJR, Reekers JA. Magnetic resonance venography in consecutive patients with suspected deep vein thrombosis of the upper extremity: initial experience. *Acta Radiol*. 2004;45:38-43

In addition to meta-analysis, all studies are cross-sectional unless otherwise indicated under Comments.

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Table S58—*[Sections 6.1, 6.2] Description and Results of Diagnostic Studies in Patients with Suspected Upper Extremity DVT*

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
Suspected upper extremity DVT (Section 6.0)	What are the consequences of using venography to diagnose upper extremity DVT?	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	Implied reference standard	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost.* 2010;8:684-692
	What are the consequences of using venography to rule out upper extremity DVT?	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	Implied reference standard	
	What are the consequences of using CUS to diagnose upper extremity DVT?	Meta-analysis	Venography	Patients with suspected upper extremity DVT	Specificity	Specificity 96% (87%-100%)	2 studies; N = 65 patients	Prandoni P, Polistena P, Bernardi E, et al. Upper extremity deep vein thrombosis. Risk factors, diagnosis, and complications. *Arch Intern Med*. 1997; 157:57-62. Sullivan ED, Peter DJ, Cranley JJ. Real-time B-mode venous ultrasound. *J Vasc Surg*. 1984;1:365-571.
	What are the consequences of using a single CUS to exclude upper extremity DVT?	Meta-analysis	Venography	Patients with suspected upper extremity DVT	Sensitivity	Sensitivity 97% (90%-100%)	2 studies; N = 65 patients	Prandoni P, Polistena P, Bernardi E, et al. Upper extremity deep vein thrombosis. Risk factors, diagnosis, and complications. *Arch Intern Med*. 1997;157: 57-62. Sullivan ED, Peter DJ, Cranley JJ. Real-time B-mode venous ultrasound. *J Vasc Surg*. 1984;1:365-571.
	What are the consequences of using serial CUS to exclude upper extremity DVT?	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies with serial USs	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.

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Table S58—Continued

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using Doppler US to diagnose upper extremity DVT?	Meta-analysis	Venography	Patients with suspected upper extremity DVT	Specificity	Specificity 94% (86%-100%)	3 studies; N = 101 patients	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using a single Doppler US to exclude upper extremity DVT?	Meta-analysis	Venography	Patients with suspected upper extremity DVT	Sensitivity	Sensitivity 84% (72%-97%)	3 studies; N = 101 patients	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using serial Doppler US to exclude upper extremity DVT?	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies with serial Doppler US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using CUS plus Doppler to diagnose upper extremity DVT?	Meta-analysis	Venography	Patients with suspected upper extremity DVT	Specificity	Specificity 93% (80%-100%)	6 studies; N = 320 patients	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using a single CUS plus Doppler to exclude upper extremity DVT?	Meta-analysis	Venography	Patients with suspected upper extremity DVT	Sensitivity	Sensitivity 91% (85%-97%)	6 studies; N = 320 patients	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.

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Table S58—Continued

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using a serial CUS plus Doppler to exclude upper extremity DVT?	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies with serial duplex US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using a negative CUS and negative DD to exclude upper extremity DVT	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of US and DD	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using a negative Doppler US and negative DD to exclude upper extremity DVT?	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of US and DD	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using a negative CUS plus Doppler and negative DD to exclude upper extremity DVT?	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of US and DD	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using low PTP with a negative CUS to exclude upper extremity DVT?	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of PTP and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.

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Table S58—Continued

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using low PTP with a negative Doppler US to exclude upper extremity DVT?	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of PTP and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using low pretest with a negative CUS plus Doppler to exclude upper extremity DVT	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of PTP and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using serial CUS to exclude DVT in patients with a low, moderate, or high PTP of upper extremity DVT?	N/A	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of PTP and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using serial Doppler US to exclude DVT in patients with a low, moderate, or high PTP of upper extremity DVT?	Meta-analysis	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of PTP and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using serial CUS plus Doppler to exclude DVT in patients with a low, moderate, or high PTP of upper extremity DVT?	Meta-analysis	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of PTP and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.

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Table S58—Continued

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using serial CUS to exclude upper extremity DVT in patients with a positive DD and either a low, moderate, or high PTP?	Meta-analysis	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of DD, PTP and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using serial Doppler US to exclude upper extremity DVT in patients with a positive DD and either a low, moderate, or high PTP?	Meta-analysis	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of DD, PTP, and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using serial CUS plus Doppler to exclude upper extremity DVT in patients with a positive DD and either a low, moderate, or high PTP?	Meta-analysis	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of DD, PTP, and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.

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Table S58—Continued

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using a negative DD to obviate the need for serial testing in patients with suspected upper extremity DVT and a negative CUS and either a low, moderate, or high PTP?	Meta-analysis	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of DD, PTP, and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using a negative DD to obviate the need for serial testing in patients with suspected upper extremity DVT and a negative Doppler US and either a low, moderate, or high PTP?	Meta-analysis	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of DD, PTP, and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using a negative DD to obviate the need for serial testing in patients with suspected upper extremity DVT and a negative CUS plus Doppler and either a low, moderate, or high PTP?	Meta-analysis	NA	Patients with suspected upper extremity DVT	N/A	N/A	No studies using a combination of DD, PTP, and US	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.

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Table S58—Continued

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using a sensitive DD as a stand-alone test to exclude upper extremity DVT?	Primary	Venography	Patients with suspected upper extremity DVT	Sensitivity	Sensitivity 100% (78%-100%) Specificity, 14% (4%-29%)	N = 52 patients; 23 had cancer; Vidas DD. Mixed inpatient and outpatient population	Merminod T, Pellicciotta S, Bounameaux H. Limited usefulness of D-dimer in suspected deep vein thrombosis of the upper extremities. *Blood Coagul Fibrinolysis*. 2006;17:225-227.
	What are the consequences of using a SimpliRED DD as a stand-alone test to exclude upper extremity DVT?	Meta-analysis	N/A	Patients with suspected upper extremity DVT	N/A	N/A	No studies using the SimpliRED DD alone	Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692.
	What are the consequences of using MRI to diagnose upper extremity DVT?	Primary	Venography	Patients with suspected upper extremity DVT	Specificity	Time of flight MRI; specificity, 89% (52%-100%) Gadolinium-enhanced; specificity, 80% (44%-97%)	N = 31; 10 patients unable to undergo MRI. Mixed inpatient and outpatient population	Baarslag H-J, van Beek EJR, Reekers JA. Magnetic resonance venography in consecutive patients with suspected deep vein thrombosis of the upper extremity: initial experience. *Acta Radiol*. 2004;45:38-43.

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Table S58—Continued

Question from Structured Clinical Question Table	Clinical Situation/ Question	Meta-analysis vs Primary Study	Reference Standard	Patient Population	Outcome Measure[a]	Result	Comments	Reference
	What are the consequences of using MRI to exclude upper extremity DVT?	Primary	Venography	Patients with suspected upper extremity DVT	Sensitivity	Time of flight MRI; sensitivity, 71% (26%-96%) Gadolinium-enhanced; sensitivity, 50% (12%-88%)	N = 31; 10 patients unable to undergo MRI. Mixed inpatient and outpatient population	Baarslag H-J, van Beek EJR, Reekers JA. Magnetic resonance venography in consecutive patients with suspected deep vein thrombosis of the upper extremity: initial experience. *Acta Radiol*. 2004;45:38-43.
	What are the consequences of using a clinical score to diagnose upper extremity DVT?	Primary	Duplex US	Patients with suspected upper extremity DVT	Specificity	Specificity, 64% (57%-72%)	N = 214; clinical score based on presence of localized pain, unilateral pitting edema, presence of central line or pacemaker, and presence of an alternative diagnosis. Mixed inpatient and outpatient population. Duplex US used as reference standard	Constans J, Salmi L-R, Sevestre-Pietri M-A, et al. A clinical prediction score for upper extremity deep venous thrombosis. *Thromb Haemost*. 2008;99:202-207.
	What are the consequences of using a clinical score to exclude upper extremity DVT?	Primary	Duplex US	Patients with suspected upper extremity DVT	Sensitivity	Sensitivity, 78% (68%-88%)	N = 214; Clinical score based on presence of localized pain, unilateral pitting edema, presence of central line or pacemaker, and presence of an alternative diagnosis. Mixed inpatient and outpatient population. Duplex US used as reference standard	Constans J, Salmi L-R, Sevestre-Pietri M-A, et al. A clinical prediction score for upper extremity deep venous thrombosis. *Thromb Haemost*. 2008;99:202-207.

See Table S1, S3, and S7 legends for expansion of abbreviations.

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Table S59—*[Sections 6.1, 6.2] Evidence Profile: Should a Clinical Model Be Used to Evaluate Patients With Suspected Upper Extremity DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	1 (214 Patients)	Accuracy cohort	Very serious	N/A	Serious	Serious	Low	Prev 53%: 413 Prev 17%: 133 Prev 5%: 39
True negative (patients without DVT)								Prev 53%: 301 Prev 17%: 531 Prev 5%: 608
False negative (patients incorrectly classified DVT negative)								Prev 53%: 117 Prev 17%: 37 Prev 5%: 11
False positive (patients incorrectly classified DVT positive)								Prev 53%: 169 Prev 17%: 299 Prev 5%: 342

Bibliography: Constans J, Salmi L-R, Sevestre-Pietri M-A, et al. A clinical prediction score for upper extremity deep venous thrombosis. *Thromb Haemost.* 2008;99:202-207. Setting: Suspected upper extremity DVT. Reference test: single US.

[a] Not clearly a representative sample, accepted reference standard not used, reference standard results not blinded, no data on withdrawals

[b] Single study.

[c] Accuracy study.

[d] Wide 95% CIs.

[e] Based on a specificity of 64% (95% CI, 57%-72%) and a sensitivity of 78% (95% CI, 68%-88%). Prevalences taken from Wells et al.[30]

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Table S60—*[Sections 6.1, 6.2] Evidence Profile: Should a Highly Sensitive DD Be Used to Evaluate Suspected Upper Extremity DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	1 (52 patients)	Accuracy cohort	Very serious	N/A	Serious	Very serious	Low	Prev 53%: 530 Prev 17%: 170 Prev 5%: 50
True negative (patients without DVT)								Prev 53%: 66 Prev 17%: 116 Prev 5%: 133
False negative (patients incorrectly classified DVT negative)								Prev 53%: 0 Prev 17%: 0 Prev 5%: 0
False positive (patients incorrectly classified DVT positive)								Prev 53%: 404 Prev 17%: 714 Prev 5%: 817

Bibliography: Merminod T, Pellicciotta S, Bounameaux H. Limited usefulness of D-dimer in suspected deep vein thrombosis of the upper extremities. *Blood Coagul Fibrinolysis*. 2006;17:225-227. Setting: Suspected upper extremity DVT. Reference test: single US. See Table 1 legend for expansion of abbreviation.

[a] Differential verification, accepted reference standard not used, no data on withdrawals

[b] Single study

[c] Accuracy study

[d] Wide 95% CIs.

[e] Based on a specificity of 14% (95% CI, 4%-29%) and a sensitivity of 100% (95% CI, 78%-100%). Prevalences taken from Wells et al.[30]

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Table S61—*[Sections 6.1, 6.2] Evidence Profile: Should CUS Be Used to Evaluate Patients With Suspected Upper Extremity DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	2 (65 Patients)	Accuracy cohort	Very serious	None	Serious	Serious	Low	Prev 53%: 514 Prev 17%: 165 Prev 5%: 49
True negative (patients without DVT)								Prev 53%: 442 Prev 17%: 780 Prev 5%: 893
False negative (patients incorrectly classified DVT negative)								Prev 53%:16 Prev 17%: 5 Prev 5%: 1
False positive (patients incorrectly classified DVT positive)								Prev 53%: 28 Prev 17%: 50 Prev 5%: 57

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[a] In one study, CUS results unverified against reference standard in 26 of 33 patients; unclear if representative sample; unclear if reference standard results blinded, withdrawals not reported.

[b] Two studies

[c] No management studies.

[d] Wide 95% CIs.

Based on a specificity of 94% (95% CI, 80%-99%) and a sensitivity of 97% (95% CI, 90%-100%). Prevalences taken from Wells et al.[30]

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Table S62—*[Sections 6.1, 6.2] Evidence Profile: Should Doppler US Be Used to Evaluate Patients With Suspected Upper Extremity DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	3 (101 Patients)	Accuracy cohort	Very serious	None	Serious	Serious for specificity, very serious for sensitivity	Low	Prev 53%: 445 Prev 17%: 143 Prev 5%: 42
True negative (patients without DVT)								Prev 53%: 451 Prev 17%: 797 Prev 5%: 912
False negative (patients incorrectly classified DVT negative)								Prev 53%: 85 Prev 17%: 27 Prev 5%: 8
False positive (patients incorrectly classified DVT positive)								Prev 53%: 19 Prev 17%: 33 Prev 5%: 38

Bibliography: Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692. Setting: suspected upper extremity DVT. Reference test: venography.

[a] In one study, three of 21 Doppler US results unverified against reference standard and four of 18 patients verified against CT scan, rather than venography; in another study, CUS also performed with potential for bias.

[b] Three studies.

[c] No management studies.

[d] Wide 95% CIs.

[e] Based on a specificity of 96% (95% CI, 86%-100%) and a sensitivity of 84% (95% CI, 72%-87%). Prevalences taken from Wells et al.[10]

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Table S63—*[Sections 6.1, 6.2] Evidence Profile Should Doppler US Plus CUS Be Used to Evaluate Patients With Suspected Upper Extremity DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	6 (320 Patients)	Accuracy cohort	Very serious	None	Serious	Serious	Low	Prev 53%: 482 Prev 17%: 155 Prev 5%: 45
True negative (patients without DVT)								Prev 53%: 437 Prev 17%: 772 Prev 5%: 883
False negative (patients incorrectly classified DVT negative)								Prev 53%: 48 Prev 17%: 15 Prev 5%: 5
False positive (patients incorrectly classified DVT positive)								Prev 53%: 33 Prev 17%: 58 Prev 5%: 67

Bibliography: Di Nisio M, van Sluis GL, Bossuyt PM, Buller HR, Porreca E, Rutjes AW. Accuracy of diagnostic tests for clinically suspected upper extremity deep vein thrombosis: a systematic review. *J Thromb Haemost*. 2010;8:684-692. Setting: suspected upper extremity DVT. Reference test: venography. See Table S1 and S7 legends for expansion of abbreviations.

[a] In one study, 19 of 42 duplex US results unverified against reference standard; in another nine of 130 results unverified against reference standard and 22 of 121 duplex results verified against venography with remainder against CT scan, MRI, and clinical follow-up; four of six studies unclear if representative patient spectrum; two of six studies unclear if blinding of reference standard and index test results.

[b] Six studies

[c] No management studies.

[d] Wide 95% CIs.

[e] Based on a specificity of 93% (95% CI, 80%-100%) and a sensitivity of 91% (95% CI, 85%-97%). Prevalences taken from Wells et al.[30]

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Table S64—*[Sections 6.1 and 6.2] Evidence Profile: Should MRI (Time of Flight) Be Used to Evaluate Patients With Suspected Upper Extremity DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000[e]
True positive (patients with DVT)	1 (31 Patients)	Accuracy cohort	Very serious	N/A	Serious	Very serious	Low	Prev 53%: 376 Prev 17%: 121 Prev 5%: 35
True negative (patients without DVT)								Prev 53%: 418 Prev 17%: 739 Prev 5%: 845
False negative (patients incorrectly classified DVT negative)								Prev 53%: 154 Prev 17%: 49 Prev 5%: 15
False positive (patients incorrectly classified DVT positive)								Prev 53%: 52 Prev 17%: 91 Prev 5%: 105

Bibliography: Baarslag HJ, van Beek EJR, Reekers JA. Magnetic resonance venography in consecutive patients with suspected deep vein thrombosis of the upper extremity: initial experience. *Acta Radiol*. 2004;45:38-43. Setting: suspected upper extremity DVT. Reference test: venography.

[a] Twenty-three of initial 44 patients were lost and not available for follow-up.

[b] Single study.

[c] No management studies.

[d] Wide 95% CIs.

[e] Based on a specificity of 89% (95% CI, 52%-100%) and a sensitivity of 71% (95% CI, 26%-96%). Prevalences taken from Wells et al.[10]

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Table S65—*[Sections 6.1 and 6.2] Evidence Profile: Should MRI (Gadolinium) Be Used to Evaluate Patients With Suspected Upper Extremity DVT?*

Outcome	No. of Studies	Study Design	Limitations[a]	Inconsistency[b]	Indirectness[c]	Imprecision[d]	Final Quality	Effect/1,000 [e]
True positive (patients with DVT)	1 (31 Patients)	Accuracy cohort	Very serious	N/A	Serious	Very serious	Low	Prev 53%: 265 Prev 17%: 85 Prev 5%: 25
True negative (patients without DVT)								Prev 53%: 376 Prev 17%: 664 Prev 5%: 760
False negative (patients incorrectly classified DVT negative)								Prev 53%: 265 Prev 17%: 85 Prev 5%: 25
False positive (patients incorrectly classified DVT positive)								Prev 53%: 94 Prev 17%: 166 Prev 5%: 190

Bibliography: Baarslag HJ, van Beek EJR, Reekers JA. Magnetic resonance venography in consecutive patients with suspected deep vein thrombosis of the upper extremity: initial experience. *Acta Radiol*. 2004;45:38-43. Setting: suspected upper extremity DVT. Reference test: venography.

[a] Twenty-three of initial 44 patients were lost and not available for follow-up.

[b] Single study.

[c] No management studies.

[d] Wide 95% CIs.

[e] Based on a specificity of 80% (95% CI, 44%-97%) and a sensitivity of 50% (95% CI, 12%-88%). Prevalences taken from Wells et al.[30]

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