

Online Supplementary Material

Segal J, Eng J, Tamariz L, Bass E. Review of the evidence on diagnosis of deep venous thrombosis and pulmonary embolism. *Ann Fam Med.* 2007;5(1):63-73.

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Supplemental Appendix 1. Table 1. Design of Studies of Clinical Prediction Rules

Author, Year, Site	Study Aims	Dates	Study Test	Reference Standard	Inclusions	Exclusions	N
Nypaver et al, ¹ 1993, United States	Define clinical criteria that might predict the diagnostic value of VDS	NR	Clinical model	NR	Suspected DVT in inpatients	PE	68
Wells et al, ² 1995, Canada	Assess the ability of a clinical model to stratify symptomatic outpatients with suspected DVT into groups with high, moderate, and low probability of DVT, and evaluate this model in combination with ultrasound	1992 - 1993	Wells model	Venogram, central	Referral for suspected DVT in outpatients	Pregnancy/childbirth, contrast dye allergy, renal failure, suspected PE, amputation below the knee	605
Wells et al, ³ 1997, Canada	Test a simplified model used in combination with ultrasound to guide management of patients with suspected DVT	1994 - 1996	Wells model	Venogram, ultrasound	Referral for suspected DVT in outpatients	Age < 18 y, previous VTE, requires long-term anticoagulation, PE, imminent death	593
Wells et al, ⁴ 1998, Canada	Find a clinical model for safe management of patients with suspected PE	1993 - 1996	Wells PE model	Ventilation-perfusion scan	PE, suspected PE in inpatients and outpatients	Upper extremity VTE, pregnancy/childbirth, short life expectancy, contrast dye allergy, recent anticoagulant use	1,401
Anderson et al, ⁵ 1999, Canada	Determine the accuracy of a clinical model, and determine whether the model is safe and feasible	NR	Wells model	Ultrasound	Suspected DVT in emergency department	Age < 18 y, pregnancy/childbirth, previous VTE, short life expectancy, unlikely to be compliant, hereditary bleeding, contraindication to anticoagulation, thrombolytic therapy	344

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Author, Year, Site	Study Aims	Dates	Study Test	Reference Standard	Inclusions	Exclusions	N
Anderson et al, ⁵ 1999, Canada	Determine the accuracy of a clinical model, and determine whether the model is safe and feasible	NR	Wells model	Ultrasound	Suspected DVT in emergency department	Age < 18 y, pregnancy/childbirth, previous VTE, short life expectancy, unlikely to be compliant, hereditary bleeding, contraindication to anticoagulation, thrombolytic therapy	344
Aschwanden et al, ⁶ 1999, Europe	Not specified	1997 - 1997	Wells model Wells model + D-dimer	Ultrasound	Referral for suspected idiopathic DVT	Missing data	343
Lennox et al, ⁷ 1999, Europe	Determine the actual value of the D-dimer test and its combination with clinically derived risk stratification in the diagnostic work-up of patients with suspected DVT	NR	Risk assessment score for DVT Risk assessment score + D-dimer	Ultrasound	Suspected DVT in inpatients and outpatients	Previous VTE, chronic DVT on ultrasound, symptoms > 1 mo, anticoagulants > 48 h, PE	200
Wells et al, ⁸ 1999, Canada	Evaluate the accuracy of D-dimer in hospitalized patients	1994 - 1996	Wells model Wells model + D-dimer	Ultrasound, thigh/popliteal	Referral for suspected DVT in inpatients	Age < 18 y, previous VTE, short life expectancy, unlikely to be compliant, requires long-term anticoagulation, PE, screening	150
Anderson et al, ⁹ 2000, Canada	Determine the accuracy of D-dimer and to determine the potential of combining the D-dimer	NR	Wells model Wells model + D-dimer	Ultrasound	Suspected DVT in emergency department	Age < 18 y, hereditary bleeding, contraindication to anticoagulation, thrombolytic therapy, PE	214
Sanson et al, ¹⁰ 2000, Europe	Compare the accuracy and variability of both the clinical probability estimate between the PIOPED (Perrier et al) and the 2 clinical models by Wells	1997-1998	PIOPED study model Wells simplified model Wells extended model for PE pulmonary angiography	Ventilation-perfusion scan, single photon emission computer tomography, helical CT	Suspected PE in inpatients and outpatients	Age < 18 y, pregnancy/childbirth, undergone testing for PE, inability to complete protocol	517

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Supplemental Appendix 1. Table 1. Design of Studies of Clinical Prediction Rules

Author, Year, Site	Study Aims	Dates	Study Test	Reference Standard	Inclusions	Exclusions	N
Stollberger et al, ¹¹ 2000, Europe	Derive and validate a prediction rule based on clinical and easily obtained instrumental findings by which PE can be diagnosed		Clinical model	Ventilation-perfusion scan	High suspicion for PE	Contraindication for PE evaluation	168
Wells et al, ¹² 2000, Canada	Simplify the clinical model	NR	Wells PE model	Ventilation-perfusion scan	Suspected PE inpatients and outpatients	NR	295
Wells et al, ¹³ 2001, Canada	Demonstrate the safety of excluding PE in an emergency department using algorithm based on pretest probability and D-dimer	1998-1999	Wells PE model	Ventilation-perfusion scan	Acute dyspnea or chest pain for < 30 d	DVT of upper extremity, anti-coagulation > 24 h, contraindication to contrast, pregnancy, < 18 y	903
Constans et al, ¹⁴ 2001, Europe	Determine whether 1 or 2 of these scores maintained the same level of performance in various hands	1999 - 1999	Kahn Wells model Sant-Andre Hospital	Ultrasound, thigh/popliteal	Patients referred with suspicion of DVT	Previous VTE	273
Dryjski et al, ¹⁵ 2001, United States	Evaluate the efficacy and cost effectiveness of a DVT screening protocol consisting of global pretest probability, selective D-dimer, and selective venous Doppler imaging	2000 - 2001	Wells model Wells + D-dimer + PTP	Ultrasound, thigh/popliteal	Suspected DVT in emergency department	NR	66
Funfsinn et al, ¹⁶ 2001	Determine the reliability of several rapid D-Dimer tests in combination with a simple clinical model to predict the pretest probability	NR	Wells model	Venogram, central, thigh/popliteal, calf ultrasound, thigh/popliteal, calf	Referral for suspected DVT	Pregnancy/childbirth, hospitalized, anticoagulation for 24 h	106
Kearon et al, ¹⁷ 2001, Canada	Test whether ultrasound can be withheld from low probability	1995 - 1997	Wells model Wells model + D-dimer	Ultrasound	Referral for suspected DVT	NR	445
Cornuz et al, ¹⁸ 2002, Europe	Compare clinical assessment and the Wells score, in isolation and in combination with rapid quantitative D-dimer	NR	Wells model Wells model + D-dimer	Venogram, thigh/popliteal, ultrasound	Referral for suspicion of DVT	Pregnancy/childbirth, PE	278

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Author, Year, Site	Study Aims	Dates	Study Test	Reference Standard	Inclusions	Exclusions	N
Shields et al, ¹⁹ 2002, United States	Validate the predictive value of the Canadian (Wells) clinical probability model	"6-mo period"	Wells model Wells model + D-dimer	Ultrasound and any other needed diagnostic test	Signs or symptoms of VTE	PE, previous VTE or PE, pregnancy, oral anticoagulant	102
Schutgens et al, ²⁰ 2002, Europe	Investigate the safety of the combination of a non-high pretest clinical probability score and a normal D-dimer	NR	Wells model	Ultrasound and clinical follow-up	Symptoms of DVT, outpatients	Pregnancy, previous DVT, PE, anticoagulants	812
Chagnon et al, ²¹ 2002, Europe	Substudy of Perrier et al, 2004, aimed at comparing Wells model and Geneva score	2000-2001	Wells model and Geneva score for PE	Ultrasound, CT, or pulmonary angiography	Suspicion of PE	Anticoagulants, contraindication to CT, shock, pregnancy	277
Tick et al, ²² 2002, Europe	Study a combination of a clinical probability test, Ultrasound, and a D-dimer test	1997-2000	Wells model	Ultrasound and clinical follow-up	Suspicion of DVT	Treatment for more than 48 h, suspected PE, VTE in past 6 mo, < 18 y, allergy	811
Kraaijenhagen et al, ²³ 2002, Europe	Study whether a combination of normal results of compression ultrasonography and rapid whole blood bedside D-dimer assay at referral can safely exclude the presence of thrombosis	1995-1999	Wells model	Ultrasound	NR	< 18 y, previous VTE/PE, anti-coagulation > 48 h, geographic inaccessibility	1,726
Ilkhanipour et al, ²⁴ 2004, United States	Determine whether the combination of D-dimer and a low or intermediate clinical risk can eliminate need for ultrasound	2000-2002	Wells model	Ultrasound	> 18 y symptoms of DVT for < 1 mo	Symptoms > 1 mo	336
Perrier et al, ²⁵ 2004, Europe	Evaluate the efficacy and safety of a diagnostic strategy combining clinical probability, D-dimer, ultrasound, and CT	2000-2002	Wells model or Geneva rule, or implicit probability assessment	Ultrasound and helical CT	Suspicion of PE	Anticoagulants, contraindication to CT, shock, pregnancy	965
Righini et al, ²⁶ 2004, Europe	Includes same data as in Perrier et al, 2004, and Perrier et al, 1999	1996-1997, and 2000-2002	Implicit assessment in first study, Geneva rule in second	Ultrasound, ventilation-perfusion scan, or helical CT	Suspicion of DVT or PE, age > 16 y	Anticoagulants, admission more than 24 h after symptom onset, no follow-up data, contraindications, massive PE	1,409

NR = not reported; DVT = deep vein thrombosis; PE = pulmonary embolism; CT = computed axial tomography.

Supplemental Appendix 1, Table 2. Results of Studies of Clinical Prediction Rules for Diagnosis of Venous Thromboembolism

Author, Year	Study, Test	Cutoff	Proportion of Patients with VTE	Sensitivity	Specificity	PPV	NPV	ROC	
Nypaver et al, ¹ 1993	Clinical model	—	—	90.90	50.90	26.30	96.70	—	
Wells et al, ² 1995	Wells model	High	69/85	—	—	—	—	0.9	
		Moderate	34/143	0.91	0.70	0.45	0.97	—	
		Low	10/301	—	—	—	—	—	
Wells et al, ³ 1997	Wells model	High	53/71	0.53	0.96	0.75	0.91	0.87	
		Moderate	35/193	0.88	0.64	0.33	0.96	—	
		Low	12/329	—	—	—	—	—	
Wells et al, ⁴ 1998	Wells PE model	High	80/102	0.37	0.98	0.78	0.88	0.88	
		Moderate	112/403	0.88	0.69	0.38	0.97	—	
		Low	25/734	—	—	—	—	—	
Anderson et al, ⁵ 1999	Wells model	High	24/49	0.53	0.92	0.49	0.93	0.79	
		Moderate	15/105	0.87	0.62	0.25	0.97	—	
		Low	6/190	—	—	—	—	—	
Aschwanden et al, ⁶ 1999	Wells model	High	NR	0.84	0.53	0.26	0.95	—	
	Wells model + D-dimer	High	NR	0.96	0.46	0.32	0.98	—	
Lennox et al, ⁷ 1999	Risk assessment score for DVT (RAS)	High	30/45	0.65	0.90	0.67	0.90	0.87	
		Moderate	12/67	0.91	0.55	0.38	0.95	—	
		Low	4/88	—	—	—	—	—	
		RAS + D-dimer	—	—	—	—	—	—	0.91
Wells et al, ⁸ 1999	Wells model	High	22/29	0.54	0.94	0.76	0.84	0.81	
		Moderate	14/71	0.88	0.41	0.36	0.90	—	
		Low	5/50	—	—	—	—	—	
	Wells model + D-dimer	High	—	—	—	—	0.79	30.00	—
		Moderate	—	—	—	—	0.28	0.89	—
		Low	—	—	—	—	0.20	0.96	—
Anderson et al, ⁹ 2000	Wells model	High	15/30	0.54	0.92	0.50	0.93	0.83	
		Moderate	9/64	0.86	0.61	0.25	0.97	—	
		Low	4/118	—	—	—	—	—	
	Wells Model + D-Dimer	—	—	—	—	—	—	0.87	
Sanson et al, ¹⁰ 2000	Pioped study model	High	35/77	0.28	0.85	0.45	0.73	0.61	
		Moderate	80/278	0.91	0.16	0.32	0.81	—	
		Low	11/58	—	—	—	—	—	
	Wells simplified model	High	3/8	0.02	0.98	0.38	0.71	0.52	
		Moderate	78/259	0.66	0.36	0.30	0.72	—	
		Low	41/147	—	—	—	—	—	

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Supplemental Appendix 1, Table 2. Results of Studies of Clinical Prediction Rules for Diagnosis of Venous Thromboembolism

Author, Year	Study, Test	Cutoff	Proportion of Patients with VTE	Sensitivity	Specificity	PPV	NPV	ROC	
	Wells extended model for PE PA-gram	High	18/39	0.20	0.86	0.46	0.64	0.58	
		Moderate	54/138	0.81	0.29	0.41	0.72		
		Low	17/60	—	—	—	—	—	
Stollberger et al, ¹¹ 2000	Clinical model	> 0.65	—	0.55	1.00	—	—	—	
		> 0.35	—	0.98	0.82	—	—	—	
		>0.02	—	1.00	0.05	0.35	1.00	—	
Wells et al, ¹² 2000	Wells PE model	High	10/20	0.28	0.95	0.50	0.89	0.82	
		Moderate	24/128	0.94	0.46	0.23	0.98	—	
		Low	2/99	—	—	—	—	—	
Wells et al, ¹³ 2001	Wells PE model + D-dimer	—	—	—	—	—	—	0.85	
		Wells PE model	High	24/59	0.28	0.96	0.41	0.93	0.85
			Moderate	55/344	0.92	0.62	0.20	0.99	
Constans et al, ¹⁴ 2001	Wells model	Low	7/538	—	—	—	—	—	
		High	33/65	0.50	0.85	0.51	0.84	0.74	
		Moderate	26/135	0.89	0.32	0.30	0.90		
	Kahn	High	2/19	0.03	1.00	1.00	0.75	0.59	
		Moderate	47/165	0.74	0.38	0.29	0.81	—	
		Low	17/89	—	—	—	—	—	
	Sant-Andre hospital	High	13/17	0.20	0.98	0.76	0.79	0.77	
		Moderate	38/115	0.77	0.61	0.39	0.89		
		Low	15/141	—	—	—	—	—	
Dryjski et al, ¹⁵ 2001	Wells model	High	6/84	1.00	0.50	0.17	1.00	0.75	
		Moderate	0/23	1.00	0.12	0.10	1.00		
		Low	0/7	—	—	—	—	—	
	Wells model + D-dimer + PTP	—	—	—	—	—	—	—	
		Clinical model (Well's DVT)	High	30/42	0.75	0.77	0.71	0.80	0.77
			Moderate	10/50	1.00	0.27	0.51	1.00	
Low	0/14		—	—	—	—	—		
Funfsinn et al, ¹⁶ 2001, Europe	Clinical model + auto dimer test (D-dimer)	—	—	—	—	—	1.00	—	
		Wells model	High	35/51	0.55	0.96	0.69	0.93	0.87
			Moderate	24/188	0.92	0.53	0.25	0.98	
Low	5/206		—	—	—	—	—		

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Supplemental Appendix 1, Table 2. Results of Studies of Clinical Prediction Rules for Diagnosis of Venous Thromboembolism

Author, Year	Study, Test	Cutoff	Proportion of Patients with VTE	Sensitivity	Specificity	PPV	NPV	ROC
Cornuz et al, ¹⁸ 2002	Wells model + D-dimer	—	—	—	—	—	0.99	—
	Wells model	High	32/48	0.39	0.92	0.67	0.78	0.75
		Moderate	36/121	0.83	0.48	0.40	0.87	—
Low		14/109	—	—	—	—	—	
Shields et al, ¹⁹ 2002	Wells model + D-dimer	High	—	—	—	—	—	—
		Moderate	—	—	—	—	—	—
		Low	—	—	—	—	1.00	—
	Wells model	High	10/17	0.59	0.92	0.59	0.92	—
		Moderate	6/44	0.94	0.47	0.26	0.98	—
		Low	1/41	—	—	—	—	—
Tick et al, ²² 2002	Wells model + D-dimer	High	—	0.80	0.71	—	0.71	—
		Moderate	—	1.00	0.53	—	1.00	—
		Low	—	1.00	0.80	—	1.00	—
	Well's model	High/moderate	300/531	0.91	0.52	0.56	0.89	—
		Low	30/280	—	—	—	—	—
		Well's model with D-dimer	High/moderate	10/231	1.00	0.67	0.12	1.00
Kraaijenhagen et al, ²³ 2002	Wells model	High	228/345	0.54	0.90	0.66	0.85	0.87
		Moderate	135/500	0.85	0.60	0.43	0.92	—
		Low	62/775	—	—	—	—	—
Schutgens et al, ²⁰ 2003	Wells model	High	116/279	0.44	0.70	0.42	0.72	—
		Moderate	125/332	0.91	0.32	0.39	0.88	—
		Low	25/201	—	—	—	—	—
	Wells model + D-dimer	High	—	0.98	0.34	—	0.91	—
		Moderate	—	1.00	0.40	—	1.00	—
		Low	—	0.96	0.51	—	0.99	—
Ruiz-Gimenez et al, ²⁷ 2004	Derived from Wells model	High	55/112	0.52	0.81	0.49	0.83	—
		Moderate	33/144	0.84	0.43	0.34	0.88	—
		Low	17/145	—	—	—	—	—
	Derived from Wells model + D-dimer	High	—	0.99	0.36	0.60	0.95	—
		Moderate	—	1.00	0.51	0.38	1.00	—
		Low	—	0.94	0.59	0.23	0.99	—
Perrier et al, ²⁵ 2004	Clinical prediction	High	62/74	0.28	0.98	0.84	0.82	—
		Moderate	124/369	0.85	0.66	0.42	0.94	—
		Low	32/522	—	—	—	—	—
	Clinical prediction + D-dimer*	High	—	—	—	—	—	—
		Moderate	—	—	—	—	—	—
		—	—	—	—	—	—	—

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Supplemental Appendix 1, Table 2. Results of Studies of Clinical Prediction Rules for Diagnosis of Venous Thromboembolism

Author, Year	Study, Test	Cutoff	Proportion of Patients with VTE	Sensitivity	Specificity	PPV	NPV	ROC	
Righini et al, ²⁶ 2004	Clinical prediction	Low	—	—	—	—	—	—	
		High	93/121	0.29	0.97	0.77	0.82	—	
		Moderate	176/502	0.83	0.67	0.43	0.93	—	
	D-dimer applied first with results stratified by clinical probability	Low	57/786	—	—	—	—	—	
		High	—	1.00	0.46	—	—	—	
		Moderate	—	1.00	0.22	—	—	—	
Chagnon et al, ²¹ 2002	Wells model	High	—	0.14	1.00	0.91	0.77	0.73	
		Moderate	—	0.73	0.69	0.45	0.88	—	
		Low	—	—	—	—	—	—	
	Geneva score	High	—	—	0.11	0.98	0.67	0.76	0.69
		Moderate	—	—	0.72	0.64	0.41	0.87	—
		Low	—	—	—	—	—	—	—

VTE = venous thromboembolism; PPV = positive predictive value; NPV = negative predictive value; ROC = receiver operating curve.

* Insufficient data to calculate.

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