

**Clinical Prediction Rules for the
Diagnosis of Venous
Thromboembolism : Systematic
review and Meta-analysis**

Leonardo Tamariz M.D., M.P.H

Johns Hopkins University

Background: Venous Thromboembolism (VTE)

- 269,000 cases diagnosed each year
- Independent contributions of the medical history and physical exam have limited predictive value in the diagnosis of VTE.

Background: Clinical Prediction Rules (CPRs)

- A clinical prediction rule is a clinical tool that quantifies the individual contributions that various components of the history, physical examination and basic laboratory results make toward the diagnosis, prognosis, or likely response to treatment in an individual patient.

McGinn TG, Guyatt GH, Wyer PC, et al. Users' guides to the medical literature. XXII: how to use articles about clinical decision rules. Evidence-Based Medicine Working Group. JAMA. 2000;284:79-84.

Background: Objectives

- To identify validated clinical prediction rules for the diagnosis of VTE
- To describe the key components of each prediction rule
- To report the predictive value of each rule

Methods: Project

- Conducted by the Johns Hopkins Evidence-based practice center through contract (No.290-97-0006) from the Agency for Healthcare Research and Quality.
- The Diagnosis and Management of Venous Thromboembolism

Methods: Search Strategy

- Electronic databases
 - MEDLINE using Pubmed
 - Cochrane Controlled Trials Register
 - Cochrane Database of Systematic Reviews
 - EMBASE
- Hand-searched relevant journals
- Hand-searched reference lists of key articles
- Queried experts

Methods: Search Strategy

- Search terms: “sensitivity” “specificity” AND “DVT” “PE” AND “clinical”
- Inclusion criteria:
 - English
 - original data
 - diagnosis of VTE confirmed by appropriate reference standards (ultrasonography, venography, ventilation perfusion scanning, arteriography, or autopsy)
 - clinical prediction rule included at least two out of the three: elements from the patient’s history, findings from physical exam, or laboratory test results
 - clinical prediction rule was prospectively validated against a reference standard

Methods: Qualitative Assessment

- Representativeness of study population
- Bias and confounding
- Description of test protocols
- Test interpretation
- Statistical quality and interpretation

Methods: Quantitative Assessment

- Geographical area
- Inclusion/exclusion criteria
- Baseline characteristics of the patients
- Clinical prediction rule
- Contingency table

Methods: Contingency Tables

	Yes DVT/PE	No DVT/PE
High PTP		
Moderate PTP		
Low PTP		

Sensitivity=
True Pos./All
with DVT

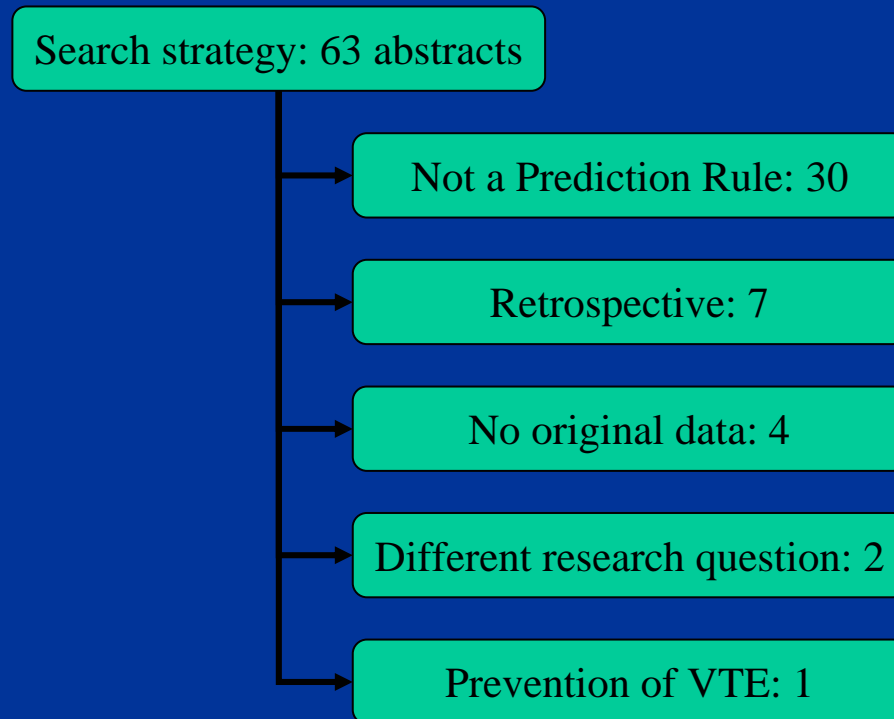
Specificity=
True neg./All
without DVT

Negative predictive
value = True Neg./
All with a neg. test

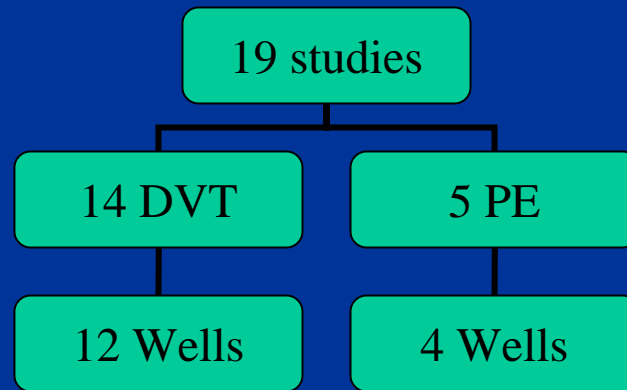
Methods: Statistical Analysis

- Measures of diagnostic accuracy
- Area under the curve of the receiver operating characteristic (AUC)
- Summary ROC curve using the Moses and Littenberg method

Results: Search results and exclusion



Results: Eligible studies



Wells DVT Prediction Model (1995)

**3 or more points – high probability, 1 or 2 points- moderate probability,
fewer than 1 point – low probability**

- | | | |
|----|--|---------------|
| 1. | active cancer (on-going treatment or diagnosed within 6 months or palliative care) | 1-point |
| 2. | paresis, paralysis or recent cast immobilization of lower extremity | 1-point |
| 3. | recently bedridden for > 3 days and/or major surgery within 4 weeks | 1-point |
| 4. | localized tenderness over distribution of deep veins | 1-point |
| 5. | entire leg swollen | 1-point |
| 6. | calf swelling more than 3 cm compared with asymptomatic side, measured 10 cm below tibial tubercle | 1-point |
| 7. | pitting edema (greater in symptomatic leg) | 1-point |
| 8. | collateral superficial veins (non-varicose) | 1-point |
| 9. | alternative diagnosis as likely or greater than that of DVT | Minus 2-point |

Wells PE Prediction Model (2000)

**> 6 points: high probability 2-6 moderate probability
<2 low probability**

1. Clinical signs and symptoms of deep venous thrombosis (objectively measured leg swelling and pain with palpation in the deep-vein region) 3-point
2. heart rate higher than 100 beats/min 1.5-point
3. immobilization (bedrest, except to access the bathroom, for 3 consecutive days) or surgery in the previous 4 weeks 1.5-point
4. previous objectively diagnosed deep venous thrombosis or pulmonary embolism 1.5-point
5. hemoptysis 1-point
6. malignancy (patients with cancer who were receiving treatment, those in whom treatment had been stopped within the past 6 months, or those who were receiving palliative care), 1.0 point 1-point
7. pulmonary embolism as likely as or more likely than an alternative diagnosis 3-point

Results: Qualitative Results

- No work up or verification bias
- No imperfect reference standard bias
- Spectrum bias

Results: Range of Quality Scores

	1	2	3	4	5	6
DVT	63-88	38-100	25-60	67-100	67-100	50-100
PE	51-90	38-100	20-50	67-100	67-100	50-100

1. Overall
2. Representativeness of study population
3. Bias and confounding
4. Description of test protocol
5. Test interpretation
6. Statistical test & quality interpretation

Results: Baseline characteristics DVT (N=14 studies; 5411 patients)

Variable	Reported	Range
Hospital	3	
ER	3	
Outpatient	2	
Hosp+ER+Outpatient	6	
Mean Age	14/14	25-62
% males	14/14	25-49
Temporary risk	6/14	10-91
Family history	1/14	6.5
Malignancy	7/14	5-49

Results: Baseline characteristics PE (N=5 studies; 3284 patients)

Variable	Reported	Range
ER	1	
Hosp+ER+Outpatient	4	
Mean Age	5/5	51-64
% males	5/5	37-42
Temporary risk	1/5	16
Family history	1/5	20
Malignancy	2/5	10-72

Results: Wells model for DVT (N=12 studies)

	Prevalence range (%)	NPV range (%)	AUC
High	17-81	80-100	0.74-0.90
Moderate	0-28	97-100	
Low	0-13		

Results: Wells models for PE (N=4 studies)

	Prevalence range (%)	NPV range (%)	AUC
High	46-78	64-89	0.52-0.88
Moderate	18-39	72-98	
Low	1-28		

Results: Wells model+d-dimer for DVT (N=6 studies)

	NPV range (%)	AUC
High	96-100	0.87-0.91
Moderate	97-100	
Low		

Results: Wells DVT vs other models

- 2 studies compared the Wells DVT model to 3 other models
- Wells AUC 0.74-0.90

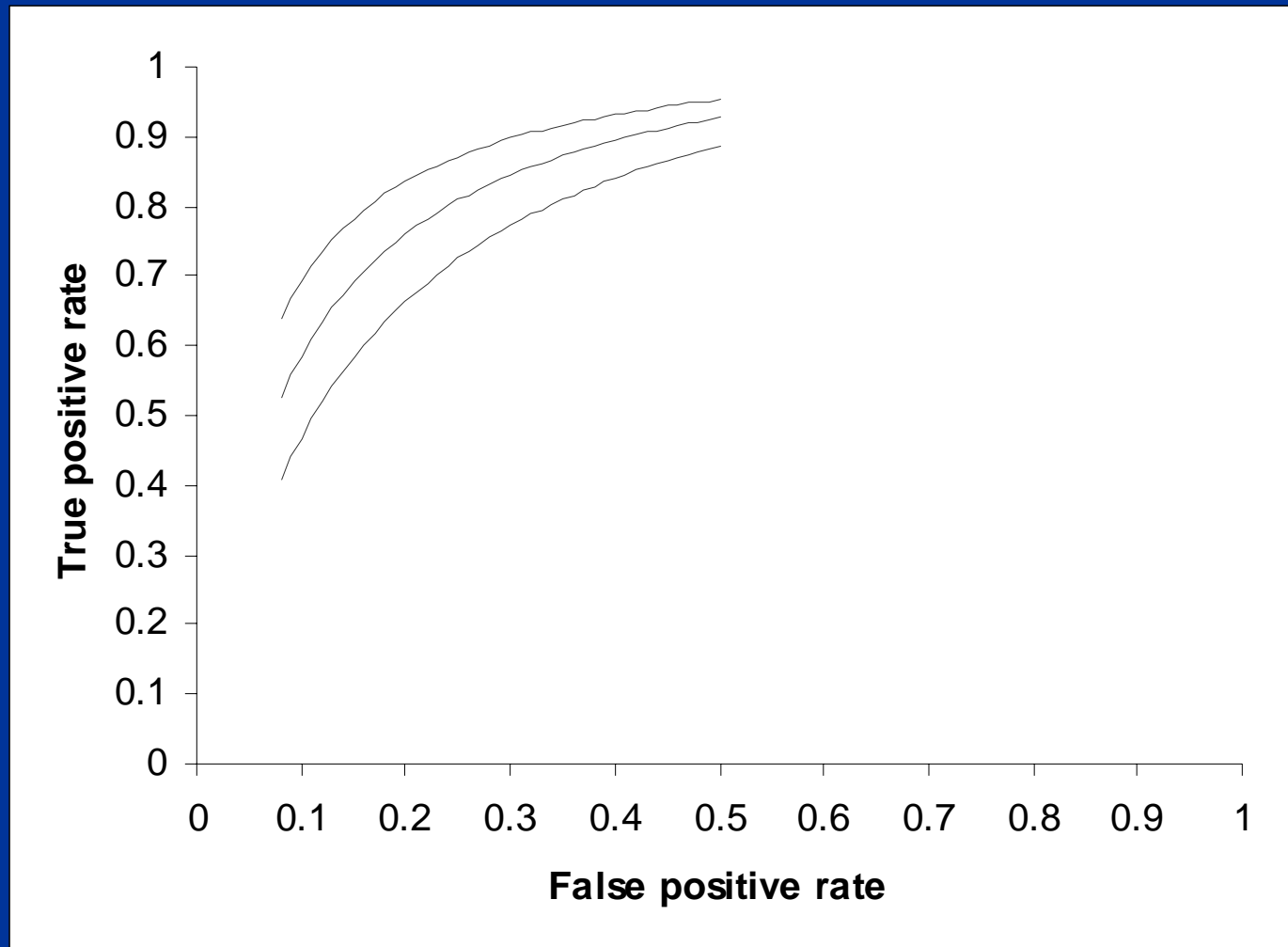
Model	AUC	NPV (%)
Kahn	0.59	75
St. Andre	0.77	79
RAS	0.87	90

Results: Wells model according to location of the DVT

- 3 studies evaluated the Wells DVT model according to the location of the DVT

Location	AUC
Proximal	0.81-0.92
Distal	0.65-0.79

Wells DVT: Summary ROC: 0.78 [95% CI 0.73 to 0.82]



Conclusions

- Wells DVT model is the most frequently evaluated model
- Wells DVT model had high negative predictive values and ROC curve acceptable for clinical practice
- Wells DVT model performed better for identification of proximal than distal DVT
- Addition of the d-dimer assay improved the performance of the Wells DVT model
- Wells PE model has not been extensively evaluated

Limitations

- No cost-effectiveness analysis
- Unknown whether clinical prediction rules are better than physicians informal assessment of risk
- Unclear whether the Wells model can be applied to patients with malignancy or family history of thrombosis
- Spectrum bias

Clinical implications

- Patients with low pretest probability for DVT estimated with the Wells model and a low d-dimer are very unlikely to have a DVT
- The Wells DVT and PE models can standardize physicians' estimates of pretest probability for future studies of testing strategies

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