Critical Review Form
Meta-analysis

Does This Patient Have Pulmonary Embolism?
JAMA 2003; 290:21; 2849-2858

Objectives: **"To determine whether, based on their clinical impression after collecting routine data (the clinical gestalt), experienced clinicians can accurately group patients into strata distinguished by an increasing probability of pulmonary embolism" and "to determine whether clinical prediction rules are useful in determining the pretest probability for pulmonary embolism". (p 2851)**

Methods: **Three authors conducted MEDLINE search of English language articles published between 1966 and March 2003 using several relevant PE Medical Subject Headings. To be eligible, studies had to include an estimate of the pretest probability of PE by clinical gestalt or use of a clinical decision rule (CDR) prior to the results of a validated Gold standard test for PE were available (see Box, p 2851). CDR studies had to have at least 50 confirmed cases of PE for inclusion. *A priori* the authors decided not to include CDR validation studies in this review.**

Guide	Question	Comments
I	***Are the results valid?***	
1.	Did the review explicitly address a sensible question?	Yes: can clinical gestalt or CDR's guide assessment of PE risk in individual patients when the diagnosis or PE is being considered?
2.	Was the search for relevant studies details and exhaustive?	No, the authors did not review EMBASE, LILACS, CINAHL, or Cochrane. They also neglected to contact industry experts, nor did they review meeting abstracts.
3.	Were the primary studies of high methodological quality?	Unknown, since the authors made no attempt to grade evidence quality
4.	Were the assessments of the included studies reproducible?	Unknown, since no Kappa was reported for article selection or evidence quality assessment.

II.	*What are the results?*	

1.	What are the overall results of the study?	• Search strategy identified 1709 articles with 16 ultimately selected for inclusion in this review studying a total of 8306 patients. • The prevalence of PE when clinically considered was 17-44% • Clinical gestalt was evaluated in 5 studies with low pretest probability associated with guesstimate 0-19% compared with actual PE prevalence 9-19%. Moderate pretest probability guesstimate 20-80% with actual PE prevalence 26-47%. High pretest probability guesstimate 80-100% and actual PE prevalence 46-91%. • Evidence available to physicians for clinical gestalt included history, physical exam, chest x-ray, ECG, and ABG. • Clinical Prediction Rules were studied in 5 papers and included Well's scoring (Geneva), Kline's decision tree, and the PISA-PED group decision model (Table 7, p 2855). o **(a) Well's Extended Model** Pre-test Prob. / Post-test Prob. / LR (95% CI) Low / 28 / 0.66 (0.4-1.1) Mod / 39 / 1.1 (0.86-1.3) High / 46 / 1.4 (0.35-5.9) o **(b) Well's Simplified Rule** Pre-test Prob. / Post-test Prob. / LR (95% CI) Low / 1.3-12 / 0.13-0.39 (0.06-0.58) Mod / 16.2-40 / 1.9 (1.5-2.6) High / 41-91 / 5.9-29 (3.7-223) o **(c) Geneva** Pre-test Prob. / Post-test Prob. / LR (95% CI) Low / 13 / 0.44 (0.30-0.65) Mod / 38 / 1.8 (1.4-2.3) High / 67 / 5.8 (1.8-19) o **(d) Kline** Pre-test Prob. / Post-test Prob. / LR Non-high / 13 / N/A High / 42 / N/A

		• Kappa (reproducibility) was 0.86 for extended Wells, 0.83 for Kline. No Kappa results availability for other CDR. • Kappa between Geneva and Well's simplified model was 0.43. D-Dimer LR+ LR- Organon (latex immunoassay) 1.7 (1.5-1.9) 0.09 (0.04-0.11) Vidas rapid ELISA assay 1.6 (1.4-1.8) 0.22 (0.11-0.44) SimpliRED D-dimer assay 2.7 (2.4-3.0) 0.22 (0.16-0.3)

2.	How precise are the results?	Not very, as many Likelihood Ratio CI above cross one (clinically useless diagnostic test).
3.	Were the results similar from study to study?	No. Sanson's results differ markedly by their methods (one physician looking retrospectively at charts rather than patient to score CDR).
III.	***Will the results help me in caring for my patients?***	
1.	How can I best interpret the results to apply them to the care of my patients?	On our patient vignette, simplified Well's score = 3 (moderate, pre-test probability 16-40%) and one is unable to use Geneva (no ABG or CXR). If you were to obtain a negative SimpliRED D-dimer you would reduce your probability to 4-13% and then you'd have to decide in conjunction with your patient whether to perform further testing (VQ or PE protocol CT or pulmonary angiogram).
2.	Were all patient important outcomes considered?	No patient outcomes were considered -- only diagnostic test performance of various methods of assessing for PE.
3.	Are the benefits worth the costs and potential risks?	No risk-benefit or cost-analysis was performed, but every clinician ought to be aware of the limitations of their diagnostic armamentarium.

Limitations

1. **Incomplete search strategy**
2. **Exclusion of non-English literature**
3. **No assessment of article quality**
4. **No inclusion of individual elements of history and physical exam**
   To better understand the limitations of these elements read one of these articles:
   a. **Stein PD, et al. History and physical examination in acute pulmonary embolism in patients without pre-existing cardiac or pulmonary disease, *Am J Cardiology* 1981; 47: 218-223.**
   b. **Hoellerich VL, et al. Diagnosing pulmonary embolism using clinical findings, *Arch Internal Medicine* 1986; 146: 1699-1704.**

Bottom Line: **Experienced clinicians' clinical gestalt estimate of PE pre-test probability correlates well with increasing PE prevalence. Less experienced clinicians (and experienced clinicians!) can replicate this successful pre-test estimate with CDR's all of which appear equally useful, although data on head-to-head CDR comparability, cost-effectiveness and reproducibility are lacking. Be aware of the test characteristics of your institution's D-dimer assay before using it. A reasonable pre-test probability for PE in the ED is 25-30%.**

The **Simplified Wells** Scoring System	
Findings	Score†
Clinical signs/symptoms of deep venous thrombosis (minimum of leg swelling and pain with palpation of the deep veins of the leg)	3.0
No alternate diagnosis likely or more likely than pulmonary emboli	3.0
Heart rate > 100/min	1.5
Immobilization or surgery in last 4 weeks.	1.5
Previous history of deep venous thrombosis or pulmonary emboli	1.5
Hemoptysis	1.0
Cancer actively treated within last 6 months	1.0

†Category scores are as follows: low, <2; moderate, 2-6; and high, >6. Patient's clinical score is calculated by the summing of the scores (weight) of the predictor variables that are present.

The **Geneva** Clinical Prediction Rule	
Variable	Point Score†
Age, y	
60-79	1
≥80	2
Previous pulmonary emboli or deep venous thrombosis	2
Recent surgery	3
Pulse rate >100/min	1
$PaCO_2$, kPa	
<4.8	2
4.8-5.9	1
$PaCO_2$, kPa	
<6.5	4
6.5-7.99	3
8-9.49	2
9.5-10.99	1
Chest radiograph appearance	
Platelike atelectasis	1
Elevated hemidiaphragm	1

† The pretest probability categories (clinical probability score range, prevalence of disease [95% confidence interval], and percentage of patients in the pretest probability category) are as follows: low (0.4, 10% [8%-13%], 49%); intermediate (5-8, 38% [34%-43%], 38%); and high (9-16, 81% [69%-90%], 6%), respectively.

Structured Clinical Model Derived by the **PISA-PED** Group

Factor	Regression Coefficient
Male sex	0.81
Age, y	
63-72	0.59
≥73	0.92
Preexisting disease	
Cardiovascular	-0.56
Respiratory	-0.97
Thrombophlebitis (ever)	0.69
Symptoms	
Dyspnea (sudden onset)	1.29
Chest pain	0.64
Hemoptysis	0.89
Temperature >38°C	-1.17
Electrocardiogram signs of acute right ventricular overload	1.53
Chest radiograph findings	
Oligemia	3.86
Amputation of hilar artery	3.92
Consolidation (infarction)	3.55
Consolidation (no infarction)	-1.23
Pulmonary edema	-2.83

Abbreviation: PISA-PED, Prospective Investigative Study of Acute Pulmonary Embolism Diagnosis

Charlotte Rule