Critical Review Form
Clinical Prediction or Decision Rule

Anderson DR, et al. Combined Use of Clinical Assessment & D-dimer to Improve the Management of Patients Presenting to the ED with Suspected DVT (EDITED Study), J Thrombosis & Haemostasis 2003; 1: 645-651.

Objective: **"To determine the safety of a management strategy for patients with suspected DVT in the emergency department setting using algorithms combining consideration of pretest probability and D-dimer testing."** (p. 646)

Methods: **Consecutive ED patients with non-joint related leg pain or swelling at four Canadian tertiary hospitals were screened for eligibility if the emergency physician could not clinically exclude the presence of acute DVT. Potential subjects were excluded if PE or upper extremity DVT were suspected, life-expectancy was under three months, contrast dye contraindications existed, bleeding diathesis, pregnant, < 18 years old, geographic inaccessibility, symptom resolution in under 72 hours, or if the patient was on heparin for over 24 hours. All subjects had the Well's DVT score and a D-dimer (either whole blood agglutination SimplyRED® or an immunoturbimetric latex agglutination assay). Subsequent management was based upon the patient's clinical pretest probability (Well's score) and D-dimer test results (Figure 1, p. 647). All patients had telephone follow-up at 3-months to ascertain the primary outcome: the development of symptomatic proximal DVT or PE after the index evaluation.**

Guide		Comments
I.	***Is this a newly derived instrument*** **(Level IV)?**	No
A.	Was validation restricted to the retrospective use of statistical techniques on the original database? (If so, this is a Level IV rule & is not ready for clinical application).	Level II clinical decision rule (CDR) – well validated in multiple centers as detailed by Tamariz (Am J Med 2004; 117: 676)
II.	**Has the instrument been validated? (Level II or III). If so, consider the following:**	
1a	Were all important predictors included in the derivation process?	Yes. See derivation studies (Arch IM 1999; 159: 477-482)
1b	Were all important predictors present in significant proportion of the study population?	Presumably so, in derivation set. Table 2 (p. 649) outlines prevalence of predictors in the current cohort. Note that there is no mention of prior DVT or hypercoaguable disorder. One might prefer to see the breakdown of clinical characteristics present, particularly what alternative diagnoses were considered.
1c	Does the rule make clinical sense?	Yes, the CDR, summarized on Table 1 (p. 646) makes intuitive sense

<table>
<tr><td>2</td><td>Did validation include prospective studies on several different populations from that used to derive it (II) or was it restricted to a single population (III)?</td><td>Well's criteria have been previously validated (Level II evidence), but the current study has incorporated latex agglutination D-dimer in conjunction with Well's CDR utilizing 4 tertiary care Canadian hospitals.</td></tr>
<tr><td>3</td><td>How well did the validation study meet the following criteria?</td><td></td></tr>
<tr><td>3a</td><td>Did the patients represent a wide spectrum of severity of disease?</td><td>Presumably so as consecutive ED patients enrolled, but presenting illness, admission rates, and other direct/indirect illness severity markers not provided.</td></tr>
<tr><td>3b</td><td>Was there a blinded assessment of the gold standard?</td><td>Assessment of Gold standard not stated to have been blinded.</td></tr>
<tr><td>3c</td><td>Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome?</td><td>Well's CDR is easy-to-use, validated, and reliable, so one would presume unbiased and reproducible interpretation of the rule in the current study, but the details to answer this question not provided in this paper.</td></tr>
<tr><td>3d</td><td>Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard?</td><td>Yes, see the description of Methods above.</td></tr>
<tr><td>4</td><td>How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)?</td><td>One can calculate the positive (LR^+) and negative (LR^-) from the data provided in Table 6. Using sample pre-test probabilities of 5, 10, & 20% below & Fagan's nomogram which you can access online at http://www.cebm.net/nomogram.asp you can then calculate the following numbers assuming for a negative D-dimer result:
<table>
<tr><th></th><th>Pre-Test Prob</th><th>LR^-</th><th>Post-Test Prob</th></tr>
<tr><td>Low</td><td>5%</td><td>0.20</td><td>1%</td></tr>
<tr><td>Mod</td><td>10%</td><td>0.27</td><td>3%</td></tr>
<tr><td>High</td><td>20%</td><td>0.30</td><td>7%</td></tr>
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III.	**Has an impact analysis demonstrated change in clinical behavior or patient outcomes as a result of using the instrument? (Level I). If so, consider the following:**	
1	How well did the study guard against bias in terms of differences at the start (concealed randomization, adjustment in analysis) or as the study proceeded (blinding, co-intervention, loss to follow-up)?	No blinding was stated. To avoid diagnostic suspicion bias, the assessment of patients during three-month follow-up was standardized based upon initial visit Well's CDR probability and D-dimer findings (see Methods).
2	What was the impact on clinician behavior and patient-important outcomes?	No impact analysis was performed.

Limitations

1. Use of non-ELISA D-dimer by design. Most institutions utilize the ELISA assays with higher sensitivity.
2. Surrogate endpoint of 3-month telephone follow-up (rather than criterion standard of serial Dopplers or venogram). Some (Egermayer P, Chest 1997; 111: 1410-1413) would argue against such a surrogate endpoint as unreliable, although others would argue for the 3-month follow-up without recurrence or subsequent venous thromboembolism as an equivalent criterion standard (Kruip MJ, Ann IM 2003; 138: 941-951).
3. Thirty patients (2.7% of cohort) lost to follow-up.
4. Limited to ED population. Actually this is a strength for our purposes, but you need to keep it in mind if applying the results to non-ED patient populations (office patients, ward patients, etc.).

Bottom Line

Utilization of Well's DVT clinical decision rule in conjunction with non-ELISA D-dimer assay (SimplyRED®) and non-invasive diagnostic testing can safely exclude DVT in ED patients with clinical suspicion of lower extremity DVT. The negative Likelihood Ratio of SimplyRED® can reduce the post-test probability of low pre-test probability patients to 1% and for high pre-test probability patients to 7%. Future research should assess the study's reproducibility using ELISA D-dimers and in urban settings were non-compliant, uninsured patients without reliable follow-up might impede recreating this study's structured, standardized evaluation protocol for those with moderate or high pre-test probability and/or "positive" D-dimers.