PGY-2

**Critical Review Form**

 **Clinical Prediction or Decision Rule**

[Kabrhel C, Van Hylckama Vlieg A, Muzikanski A, et al. Multicenter Evaluation of the YEARS Criteria in Emergency Department Patients Evaluated for Pulmonary Embolism. Acad Emerg Med. 2018 Sep;25(9):987-994.](http://pmid.us/29603819)

**Objectives: To test the hypothesis "that using a positivity threshold [for D-dimer] of 1,000 mg/dL in patients with no YEARS criteria would result in a reduction of unnecessary imaging with no increase in missed PE compared to the current standard of care." (p. 988)**

**Methods: This prospective, observational study was conducted in 15 EDs in the US between February 2014 and April 2015. Consecutive adult patients 18 years of age and older with suspected PE who were referred for objective testing (including d-dimer) were eligible for enrollment. Patients in whom PE was ruled out clinically (e.g. by negative** [**PERC criteria**](https://www.mdcalc.com/perc-rule-pulmonary-embolism)**) were excluded, as were patients who did not complete their diagnostic work-up and patients with a high pre-test probability for PE (**[**Wells' score**](https://www.mdcalc.com/wells-criteria-pulmonary-embolism) **> 6). Other exclusion criteria were unwillingness or inability to participate, pregnancy, previous enrollment in the study, or anticoagulant use for > 24 hours prior to blood sample collection.**

**The treating clinician answered the questions in the Wells' score/YEARS criteria prior to D-dimer or imaging results. All patients underwent d-dimer testing, with a threshold of 1000 mg/dL for patients with no YEARS criteria and 500 mg/dL for patients with any positive YEARS criteria. Patients with a positive D-dimer underwent advanced imaging and were considered to have a PE if a CTPA showed a filling defect in a pulmonary artery or a V/Q scan was read as high probability. Patients with a negative work-up (negative D-dimer or advanced imaging) received a telephone follow-up and review of medical records at 3 months. For cases in which diagnostic testing was equivocal, the diagnosis was adjudicated by a panel of 3 investigators blinded to D-dimer results.**

**A total of 1789 patients were enrolled. The mean age was 48 years and 63% were female. There were 1712 patients with a negative index visit for PE and 381 (22%) were lost to follow-up. There were 77 patients diagnosed with a PE on the index visit, representing 4% of the population.**

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| **Guide** | **Comments** |
| **I.** | ***Is this a newly derived instrument* (Level IV)?** |  |
| 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). | N/A |
| **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? | N/A |
| 1b | Were all important predictors present in significant proportion of the study population? | N/A |
| 1c | Does the rule make clinical sense? | Yes. The YEARS algorithm is a simplified clinical decision tool that uses 3 of the questions from the Wells' PE criteria. Using a [Bayesian statistical](https://www.analyticsvidhya.com/blog/2016/06/bayesian-statistics-beginners-simple-english/) approach, patients with no YEARS criteria present who hence have a low pre-test probability for PE were considered ruled out with a higher D-dimer threshold (1000 mg/dL), while patients with any YEARS criteria were felt to be higher risk and hence were ruled out with a lower D-dimer threshold (500 mg/dL). |
| 2 | 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)? | Yes. This was a prospective validation studies conducted at 15 EDs in the United States. The authors do not provide additional information on the study sites (size, location, academic affiliation). Enrollment at the sites varied from <2% to around 13% of total study subjects. Additional validation studies have been published as well. |
| 3 | *How well did the validation study meet the following criteria?* |  |
| 3a | Did the patients represent a wide spectrum of severity of disease? | No. The authors excluded high-risk patients whose Wells' scores were > 6, resulting in an overall low risk patient population ([spectrum bias](http://www.cmaj.ca/content/173/4/385.full.pdf)). |
| 3b  | Was there a blinded assessment of the gold standard? | No. The authors make no mention of blinding of radiologists reading CTPA and V/Q studies to Wells' criteria or D-dimer results, nor do they mention blinding of follow-up outcome assessors. "For rare cases where the results of diagnostic testing for PE were equivocal or unclear, the diagnosis or exclusion of PE was adjudicated by a panel of three study investigators, blinded to D- dimer result." (p. 989) |
| 3c | Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome? | Yes. "The treating clinician provided the answers to the questions required to complete the Wells PE score prior to D-dimer, or imaging tests being performed. The YEARS criteria were calculated based on the responses to the Wells PE score questions: “Does the patient have clinical signs or symptoms of DVT (yes/no)?” “Does the patient have hemoptysis (yes/no)?” “Are alternative diagnoses less likely than PE (yes/no)? Patients with a “yes” answer to any of the above questions were considered positive by YEARS criteria.” (p. 989) |
| 3d | Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard? | Yes. The gold standard (CTPA or V/Q) were only performed when it was felt to be indicated by the clinician. This was based primarily on the Wells' score and D-dimer results using the traditional threshold (500 mg/dL), although the authors do not specify how many patients with a D-dimer < 500 mg/dL underwent imaging. Forty-six percent of enrolled patients did not undergo imaging ([partial verification bias](https://www.youtube.com/watch?v=qIFbU84IfmI)). |
| 4 | How powerful is the rule (in terms of sensitivity & specificity; likelihood ratios; proportions with alternative outcomes; or relative risks or absolute outcome rates)? | * 940 (53%) patients were low to intermediate risk based on a Wells' PE score ≤ 6) and had a negative D-dimer; of these, two (0.2%) were diagnosed with a PE.
	+ Sensitivity 97.6%, 95% CI 91.7-99.7%
	+ Specificity 55.0%, 95% CI 52.6-57.4%
	+ Negative LR 0.04, 95% CI 0.01-0.17
* 982 (55%) patients had no YEARS criteria and a D-dimer < 1000, and 222 (12%) patients had a positive YEARS criteria and a D-dimer < 500; of these, 6 (0.5%) were diagnosed with PE (5 during the index visit and 1 on follow-up).
	+ Sensitivity 92.9%, 95% CI 85.1-97.3%
	+ Specificity 70.3%, 95% CI 68.0-72.4%
	+ Negative LR 0.10, 95% CI 0.05-0.22
* Using the single question "Are alternative diagnoses less likely than PE?" and a D-dimer < 1000 mg/dL when affirmative and D-dimer < 500 when negative, 1237 (67%) patients would have had a negative initial evaluation. Among these, 6 (0.4%) were diagnosed with a PE (5 during the index visit and 1 on follow-up):
	+ Sensitivity 92.9%, 95% CI 85.1-97.3%
	+ Specificity 72.2%, 95% CI 70.0-74.3%
	+ Negative LR 0.10, 95% CI 0.05-0.21
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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)? | Poorly. The authors ensured that adjudicators were blinded to D-dimer results in cases where imaging was equivocal, but radiologists and follow-up outcome assessors were not blinded to Wells' criteria or D-dimer results. Patients lost to follow-up, representing around 20% of the patient population, were deemed not to have a PE. |
| 2 | What was the impact on clinician behavior and patient-important outcomes? | An impact analysis was not specifically performed, but use of YEARS criteria and adjusted D-dimer would theoretically have spared 264 patients from imaging when compared to a Wells' score < 6 and a D-dimer threshold of 500 mg/dL. |

**Limitations:**

1. **This study was** [**industry-funded**](http://informahealthcare.com/doi/pdf/10.1185/03007995.2011.628651) **and hence at risk of outside influence.**
2. **No information was provided for the study sites (size, location, academic affiliation).**
3. **Because patients with a Wells' score > 6 were excluded, the sensitivity and specificity calculations do not represent the full spectrum of disease (**[**spectrum bias**](http://www.cmaj.ca/content/173/4/385.full.pdf)**).**
4. **Not all patients underwent the gold standard test (CTPA or V/Q) and hence there is a risk of** [**partial verification bias**](https://www.youtube.com/watch?v=qIFbU84IfmI)**.**
5. **Around 20% of patients were lost to follow-up and were considered not to have a PE or DVT (**[**attrition bias**](http://www.students4bestevidence.net/attrition-bias-randomized-controlled-trials/)**).**

**Bottom Line:**

**This prospective, observational, multicenter study of non-high risk adult patients being evaluated for a PE found that a YEARS algorithm with an adjusted D-dimer had a sensitivity of 92.9, secificity of 70.3, and a negative LR of 0.10 (95% CI 0.05-0.22) and would have theoretically spared 264 patients from advanced imaging. The negative LR of a traditional D-dimer threshold of 500 mg/DL was significantly lower at 0.04 (95% CI 0.01 to 0.17). This study was primarily limited by a 20% loss to follow-up.**