PGY-4

**Critical Review Form**

 **Clinical Prediction or Decision Rule**

[van der Hulle T, Cheung WY, Kooij S, et al; YEARS study group. Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study. Lancet. 2017 Jul 15;390(10091):289-297.](http://pmid.us/28549662)

**Objectives: to prospectively evaluate this novel and simplified diagnostic algorithm [YEARS algorithm] for suspected acute pulmonary embolism [PE]." (p. 291)**

**Methods: This prospective, multicenter cohort study was conducted at 12 hospitals in the Netherlands between October 5, 2013 and July 9, 2015. Consecutive adult patients (outpatients and inpatients 18 years of age or older) with suspected PE were eligible for inclusion. Exclusion criteria were treatment with anticoagulants started 24 hours of more before enrollment, life expectancy < 3 months, geographic inaccessibility to follow-up, pregnancy, or allergy to IV contrast agent. The attending physician evaluated eligible patients with the** [**YEARS score followed by a pre-test probability-dependent D-dimer threshold**](https://www.mdcalc.com/years-algorithm-pulmonary-embolism-pe)**.**

**Per local practice, patients with no YEARS criteria and a D-dimer < 1000 ng/mL were considered ruled out for PE, as were those with one or more YEARS criteria and a D-dimer < 500 ng/mL. All other patients underwent CTPA. Patients ruled out for PE by the YEARS algorithm or CTPA underwent 3-month follow-up by a scheduled outpatient visit or a telephone interview. The primary outcome was the 3-month incidence of symptomatic venous thromboembolism (by objective diagnostic testing) in the overall population, in patients who did not undergo CTPA, and in patients who did undergo CTPA. Deaths were classified as caused by PE if confirmed by autopsy or found by objective testing prior to death. The secondary outcome was the proportion of CTPA exams performed according to the YEARS algorithm vs. the theoretical proportion of CTPA exams that would have been performed according to the** [**2-level Well's score**](https://www.mdcalc.com/wells-criteria-pulmonary-embolism) **and a fixed D-dimer threshold < 500 ng/mL.**

**Out of 3616 consecutive patients with a clinically suspected PE, 3465 met all inclusion criteria and were included in the analysis. Of these, 1743 met no YEARS criteria and 1722 met one or more YEARS criteria. PE was detected in 456 (13%) patients during the initial evaluation. An additional 18 patients were diagnosed with symptomatic venous thromboembolism at 3-month follow-up.**

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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). | No. This study involved prospective validation of the YEARS algorithm in 12 hospitals in the Netherlands. |
| **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 ay 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)? | In this particular study, prospective validation was performed in 12 different hospitals. These hospitals were all located in the Netherlands, and further validation in disparate locations will be necessary to generalize the results. |
| 3 | *How well did the validation study meet the following criteria?* |  |
| 3a | Did the patients represent a wide spectrum of severity of disease? | Purportedly yes. The authors make no specific mention of excluding patients felt to be at high-risk for PE (based on clinical gestalt or Geneva risk scores). As a result, this study appears to include a wide spectrum of potential disease severity and should be at low risk of [spectrum bias](http://www.cmaj.ca/content/173/4/385.full.pdf). Patient were divided evenly between those meeting 0 YEARS criteria and those meeting 1 or more YEARS criteria. Unfortunately, the authors do not break down this latter group by the number of patients meeting 1, 2, or 3 YEARS criteria. |
| 3b  | Was there a blinded assessment of the gold standard? | No. The authors do not mention whether radiologists or follow-up outcome assessors were blinded to risk stratification scores (included components of the YEARS score), D-dimer results, or level of clinician suspicion for PE. |
| 3c | Was there an explicit and accurate interpretation of the predictor variables & the actual rule without knowledge of the outcome? | Somewhat. While not specifically mentions, CTPA was presumably not ordered until the clinician had performed risk stratification using the YEARS criteria and the D-dimer result was back. "Physicians were not blinded for the D-dimer test result when they assigned the YEARS items." (p. 291) There is low risk of [incorporation bias](https://first10em.com/ebm/incorporation-bias/). |
| 3d | Did the results of the assessment of the variables or of the rule influence the decision to perform the gold standard? | Yes. CTPA was performed in 1814 patients, representing 52% of the overall cohort. All patients were followed up at 3 months by outpatient visit or telephone, but no further testing was required in cases managed without initial CTPA ([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)? | * In the intention-to-diagnose population, among 2946 patients ruled out for PE on the index visit, 18 were diagnosed with a symptomatic venous thromboembolism within 3 months (0.61%, 95% CI 0.36-0.96%).
	+ The incidence of fatal PE was 0.20% (95% CI 0.07-0.44%).
* By the per-protocol analysis, the failure rate of the diagnostic algorithm, including patients with an initial negative CTPA, was 0.51% (95% CI 0.31-0.84%).
	+ The failure rate among patients managed without CT was 0.43% (95% CI 0.17-0.88%).
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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)? | This was a prospective study with low risk of missing data. While clinicians were not blinded to D-dimer results, theoretically they would have risk-stratified patients using the YEARS criteria separate from lab results or CTPA results. Radiologists were not specifically blinded to YEARS criteria or D-dimer results. Not all patients underwent CTPA, leading to a risk of partial verification bias. |
| 2 | What was the impact on clinician behavior and patient-important outcomes? | * Use of the YEARS algorithm theoretically reduced CTPA use by 13% (95% CI 10-15%) compared to use of the Well's rule and a D-dimer threshold of < 500 ng/mL.
	+ Compared to the Well's rule and an age-adjusted D-dimer, the YEARS algorithm resulted in a theoretical 8.7% reduction in CTPA use (95% CI 6.4-11%).
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**Limitations:**

1. **The gold standard test (CTPA) was only performed in 52% of the cohort (**[**partial verification bias**](https://www.youtube.com/watch?v=qIFbU84IfmI)**).**
2. **There is no mention of blinding of radiologists to clinical criteria or D-dimer results, raising the possibility of** [**incorporation bias**](https://first10em.com/ebm/incorporation-bias/)**.**
3. **The authors do not mention who performed patient follow-up at 3 months, or whether such personnel were blinded to YEARS criteria or D-dimer results.**
4. **This study was conducted at hospitals in the Netherlands. Further validation of these findings in disparate settings with racial diversity will be needed to confirm these results (**[**external validity**](http://www.epmonthly.com/archives/features/understanding-external-validity/)**).**

**Bottom Line:**

**In this prospective multicenter study conducted in the Netherlands, a YEARS algorithm using a D-dimer theshold of < 1000 ng/mL in patients with 0 YEARS criteria and < 500 ng/mL in patients 1 or more YEARS criteria resulted in a miss rate of 0.51% (95% CI 0.31-0.84%). Notably, CTPA was performed in 11 of the 18 cases of thromboembolism found in patients with a negative initial work-up. This algorithm would theoretically have reduced CTPA performance by 13% compared to Well's criteria and a D-dimer < 500 ng/mL and by 8.7% compared to Well's criteria and an age-adjusted D-dimer.**