EVMS Critical Review Form
Prognosis

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Citation: de Wit K et al., Comparison of YEARS and Adjust-Unlikely D-dimer Testing for Pulmonary Embolism in the Emergency Department. Ann Emerg Med. 2022 Nov 10

Methodology: Prospective Diagnostic Accuracy Study comparing the previously validated YEARS criteria to a modified Adjust-Unlikely rule that includes CT imaging (without age-adjusting) in patients over the age of 50 who have PE as the "most likely diagnosis." Subjects were followed for 30 days but the application of the diagnostic tools was done after their initial visit was completed during review of their visit. Data was collected using patients who were evaluated using the PE order-set utilized in their emergency departments.

Goal: to reduce unnecessary harms associated with CT scanning. Wells/Geneva considered burdensome and therefore clinical compliance is not great**.**

YEARS criteria widely verified allows simplified Wells (signs DVT, hemoptysis, PE most likely). If the answer was **no to all 3**, you can use a D-dimer of < 1000 ng/mL to exclude PE.
If yes to any, use the standard < 500 ng/mL cutoff.

Adjust-Unlikely- Primary Outcome- Sensitivity for PE diagnosis. If PE is the most likely diagnosis, a D-dimer < 500 ng/mL can be used to exclude PE. If PE is **not** the most likely diagnosis, [age x 10] in patients > age 50. For patients ≤ age 50, use 500 ng/mL.

Guide		Comments
I.	**Are the results valid?**	
A.	**Was the sample of patients representative?** *In other words, how were subjects selected and did they pass through some sort of "filtering" system which could bias your results based on a non-representative sample. Also, were objective criteria used to diagnose the patients with the disorder?*	Subjects were likely representative of patients who visit ED's in Canada and demographic data such as comorbidities, race, BMI's was insufficient to apply directly to our patient population. Canadian healthcare and follow-up can make this different from the US population. It is likely somewhat generalizable.
B.	**Were the patients sufficiently homogeneous with respect to prognostic risk?**	Yes. All patients met criteria to undergo PE w/u and were evaluated post-hoc using both clinical tools, YEARS and Adjust-Unlikely.

C.	**Was follow-up sufficiently complete?** *In other words, were the investigators able to follow-up on subjects as planned or were a significant number lost to follow-up?*	Yes. Authors felt that 30-day blinded f/u determined by thrombosis specialists was sufficient and likely represented missed index visits PE whereas 90-day f/u would be representative of new event. All f/u was based on database review of visits to three hospitals in the Hamilton, Ontario and did not check patient database outside this geographic region.
D.	**Were objective and unbiased outcome criteria used?** Investigators should clearly specify and define their target outcomes before the study and whenever possible they should base their criteria on objective measures.	Yes: 61.1 % of all patients underwent the "gold standard" CTA. Surrogate for CTA was 30-day f/u.

II.	**What are the results?**	
A.	**How likely are the outcomes over time?** *For the defined follow-up period, how likely were subjects to have the outcome of interest.*	Overall PE prevalence 8% which is consistent with most previously published PE studies. **YEARS Score (**missed 10 cases) Sensitivity 92.6% (95% CI 87-96) Specificity 45.0% (95% CI 42.5-47.5) NPV 98.6% (95% CI 97.4-99.2) PPV 12.8% (10.7-14.9) *The **YEARS rule** increased the proportion of the total cohort who had PE **excluded** by D-dimer by **20.7%** (18.7, 22.7%) whereas the "**Adjust-Unlikely**" rule increased the proportion who could have PE **excluded** by D-dimer **by 8.5%** (7.1, 9.9%).* **Adjust-Unlikely Score** (missed 0 cases) Sensitivity 100.0% (95% CI 97.2, 100.0%), Specificity 32.4% (95% 30.1, 34.8%), NPV 100.0% (95% CI 99.2, 100.0%), PPV 11.4% (95%CI 9.7, 13.3%). **Posttest probabilities of PE:** **YEARS** 2.8% (96% CI1.6, 5.1%) and 0.0% **Adjust-Unlikely** 0% (95% CI 0.0, 2.6%)
B.	**How precise are the estimates of likelihood?***What are the confidence intervals for the given outcomes?*	**As above.**
III.	**How can I apply the results to patient**	

	care?	
A.	**Were the study patients and their management similar to those in my practice?**	Probably. Even split between male and female, tertiary care setting might not apply to all of our practice settings. Not sure whether our "PE is the most likely diagnosis" is as low as theirs at 23.1% . Race, BMI and comorbidities were not described.
B.	**Was the follow-up sufficiently long?**	According to their Thrombosis Specialists, yes; but a final phone call or follow-up would've been better. Did not include death records for 30-D follow up which would have been reasonable.
C.	**Can I use the results in the management of patients in my practice?**	Yes, the adjust-unlikely rule had a sensitivity of 100% however, at the cost of a small increase CT utilization in those whom PE is the most likely diagnosis and D-dimer was >500

Strengths:
Sample size met their 99% sensitivity requirement utilizing an 8% prevalence of PE reported in most studies.
The post-hoc data collectors were functionally blinded to the study intent/primary outcome
Data collected during the Pandemic, study published in 2022; so it's relevant now or arguably is it skewed because of the pandemic?
Majority of patients got the "gold standard" CTA

Limitations:
Done in Canada, in 1 city, 3 hospitals and limited f/u may limit generalizability.
Canada's healthcare system is different and can mean that ED utilization may be different with better access to primary care. Were some of these patients screened by primary care prior to referral?
What makes PE the most likely diagnosis? In this population only 23% met "most likely" criteria
"Most likely" was based on physician "implicit estimation."
Adjust-unlikely only changes the algorithm if you are over 50 years old.

Clinical Bottom Line:
Compared to using a stand-alone D-dimer threshold of 500 ng/ml:

The YEARS rule would've excluded PE for 20.7% (18.7, 22.7%) more patients than the standard cutoff for imaging. Though it would've missed 2.8% of patients who had a PE.

The "Adjust-Unlikely" could have excluded PE in 8.5% (7.1, 9.9%) more patients, without any misses.

According to this study, the Adjust-Unlikely rule can be considered a safe way to risk stratify patients using a combination of clinical judgement and an age-adjusted D-dimer. Though YEARS had a greater theoretical decrease in imaging utilization, it would've also missed several patient's with a PE who had a D-dimer between 500-1000.

Both of these rules still hinge on the **implicit judgement** of the provider for whether or not PE is the most likely diagnosis.