Critical Review Form
Meta-analysis

PGY-4

Oqab Z, Ganshorn H, Sheldon R. Prevalence of pulmonary embolism in patients presenting with syncope. A systematic review and meta-analysis. Am J Emerg Med. 2017 Sep 14. pii: S0735-6757(17)30740-4.

Objectives: **"to conduct a systematic review and meta-analysis to determine the prevalence of pulmonary embolism in patients presenting with syncope to the emergency department and in hospitalized patients." (p. 1)**

Methods: **The authors conducted a systematic search of Medline, CINAHL, EMBASE, LILACS, and Web of Science databases. They also hand searched reference lists of included studies to identify additional relevant studies. Studies that included patients who either presented to the ED or were admitted to the hospital for syncope, and for whom etiologies of syncope (including pulmonary embolism) were reported were potentially eligible for inclusion. Two authors independently reviewed the abstracts of potential articles and obtained full text articles when there was uncertainty.**

Two authors independently assessed study quality using an existing scale, modified for this particular scenario. Criteria included in this assessment were: 1) cohort case and site definition, 2) representativeness of the cases, 3) time between presentation and diagnosis of PE, and 4) clarity of reporting of diagnostic and important results.

From an initial search yield of 1902 articles, and after exclusion of the study by Prandoni et al, 12 studies meeting criteria were included in the review. There were 9 studies involving 6608 ED patients and 3 studies involving 975 admitted patients. Sample sizes of included studies ranged from 117 to 2871 patients with a mean sample size of 660. The weighted mean age of ED patients was 61.5 and 49% were male; the weighted mean age of hospitalized patients was 67.1 and 48.5% were male.

Guide	Question	Comments
I	***Are the results valid?***	
1.	Did the review explicitly address a sensible question?	Yes. Given the recent study by Prandoni et al documenting a prevalence of PE of around 17% in patients admitted for syncope, it seems reasonable to see if additional evidence supports or refutes this high prevalence. Given concerns regarding the potential risks of overtesting and overdiagnosis, working up every admitted syncope patient for PE may do more harm than good, particularly if the prevalence is below the

		previously documented test threshold of 1.8%.
2.	Was the search for relevant studies detailed and exhaustive?	No. While the authors searched most of the major databases, including Medline, CINAHL, EMBASE, LILACS, and Web of Science databases, they did not search conference abstracts for unpublished studies, which increases the risk of publication bias.
3.	Were the primary studies of high methodological quality?	Somewhat. The studies varied in their methodologic quality, primarily with regards to criteria for PE testing. All patients were tested in only 6 of the studies, and in none of the studies was a specific PE work-up conducted in all patients. This is in contrast to the Prandoni study, in which all patients underwent PE testing using an algorithm. Only 4 of the studies reported the method by which PE was diagnosed.
4.	Were the assessments of the included studies reproducible?	Somewhat. While no specific quality assessment tool exists for prognostic studies, the authors did use a previously described tool to assess study quality, looking at several key elements. This tool appears to be fairly reproducible, though it does not include an evaluation of whether the diagnosis of interest (PE in this case) was specifically evaluated in all patients included in the various studies.
II.	***What are the results?***	
1.	What are the overall results of the study?	• Among patients seen in the ED for syncope, the pooled prevalence of PE was 0.8% (95% CI 0.5-1.3%, I^2 = 0%). • Among patients hospitalized for syncope, the pooled prevalence of PE was 1.0% (95% CI 0.5-1.9%, I^2 = 0%). • The overall pooled prevalence of PE in all syncope patients was 0.9% (95% CI 0.6-1.3%, I^2 = 0%).
2.	How precise are the results?	See above. Given the large number of patients in all of the studies, the confidence interval was quite narrow.
3.	Were the results similar from study to study?	Yes. Both by inspection of the Forest plot and by quantitative analysis (I^2 values of 0% for all pooled results) the results varied little from study to study.
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?	Based on the results of this study, the overall prevalence of PE in all ED patients presenting with syncope and among patients hospitalized for syncope is quite low, and well below the test threshold for PE as previously calculated using the Pauker-Kassirer formula. If we are to believe these results, routine testing for PE in either of these patient populations is likely to do more harm than good. While it is reasonable to keep PE in the differential

		for all patients presenting to the ED with syncope, clinical acumen will likely direct further testing more appropriately than routinely checking D-dimers or performing advanced imaging (CT or V/Q scans). The prevalence of PE was only slightly higher among hospitalized patients, suggesting that admission does not confer significant additional risk and that the threshold to pursue further testing on these patients should still be based on clinical concern.
2.	Were all patient important outcomes considered?	No. While this meta-analysis was specifically designed to look at the prevalence of PE diagnosed among patients with syncope, patient-centered outcomes could have been evaluated as well. It would be interesting to know the clinical significance of those PEs that were diagnosed, including the necessary treatment (anticoagulation, IVC filter placement) and location (i.e. subsegmental). The risk of missed PE in this patient population would be of clinical importance as well.
3.	Are the benefits worth the costs and potential risks?	No. The prevalence of PE appears to be quite low among both ED and hospitalized patients with syncope, and is well below the test threshold. Routine testing for PE does not seem warranted based on this data, and clinical findings and risk factors should be used to determine who needs to undergo specific testing for PE.

Limitations:

1. **The authors did not adhere to the MOOSE (Meta-analysis of observational studies in epidemiology) guidelines. Specifically:**
    a. **They do not specify the date on which their search was conducted.**
    b. **There is no description of the qualifications of the searchers (e.g. medical librarians, physicians).**
    c. **There is no justification provided for the use of a random effects model.**
2. **Conference abstracts and the gray literature were not searched, increasing the risk of publication bias.**
3. **The evaluation of quality assessment did not include whether the studies were prospective vs. retrospective or whether all patients underwent standardized testing to rule-out PE.**

4. **The authors specifically excluded the study by Prandoni et al, which they were essentially trying to refute. While this study may appear to be an outlier, it is possible that this is due to the more rigorous methodology used in this study. Additionally, while they may feel the prevalence seen in this study was inflated, it fits all of the inclusion criteria for this meta-analysis and should have been included in the results. Sensitivity analyses excluding this study could have been incorporated into the results.**

Bottom Line:

This systematic review and meta-analysis suggests that the rate of PE among patients with syncope presenting to the ED or hospitalized is low (0.8% and 1.0%, respectively). This data is somewhat limited by the included studies, none of which appear to have routinely performed testing to diagnose PE. As a result, it is likely that at least some cases of PE were missed in these studies, though the clinical implications of this are unknown. While this data refutes the findings of Prandoni et al, the latter was a prospective study with rigorous methodology and a standardized approach to diagnosing PE among included patients, and its results are likely more robust than the results of the studies included in this review.