**Critical Review Form**
**Prognosis**

PGY-2

Costantino G, Ruwald MH, Quinn J, et al. Prevalence of Pulmonary Embolism in Patients With Syncope. JAMA Intern Med. 2018 Jan 29.

**Objectives:** **"to determine the prevalence of PE in patients with syncope using several international administrative databases." (p. E2)**

**Methods:** **This retrospective, observation study was conducted using data collected between January 1, 2000 and September 30, 2016 in five longitudinal administrative databases from Canada, Denmark, Italy, and the United States. Adult patients aged 18 years and older presenting to the ED for syncope (as identified using ICD-9 and ICD-10 discharge codes) were eligible for enrollment. For patients with multiple visits, only the first visit was eligible for inclusion. The outcome of interest the incidence of PE, which was also based on ICD-9 and ICD-10 codes at ED and hospital discharge. Two sensitivity analyses were also performed making the following assumptions:**

1. **Any PE identified within 90 days of follow-up was considered as being present at the initial ED evaluation.**

2. **Any venous thromboembolism identified was considered to represent a PE.**

**The combination of all five databases resulted in 1,671,944 adult patients presenting to the ED with syncope. The median age of patients presenting to the ED for syncope ranged from 53 to 74 among the five databases, while the median age of patients hospitalized for syncope ranged from 66 to 79.**

| Guide | | Comments |
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| **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?* | Uncertain. The authors attempted to identify all patients presenting to the ED for syncope, but as this was a retrospective analysis of previously collected data, some visits may have been missed. The authors report that the use of ICD-9 and ICD-10 codes to identify patients with PE is above 90% (Burles 2017), but the previously reported sensitivity for syncope is only around 63% (Ruwald 2013). Patients with syncope often receive as their final diagnosis the perceived cause of their syncope, and hence may not be captured when searching for prespecified ICD-9 or ICD-10 codes. This could potentially include patients with syncope whose final diagnosis was PE. It is unclear if this method of identifying patients would be more likely to under- or over-estimate the |

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| | | prevalence of PE in this patient population.<br><br>The only additional filter used was the analysis of a subset of patients who were hospitalized for syncope, whose risk of PE would be expected to be somewhat higher than all patients seen in the ED. |
| B. | **Were the patients sufficiently homogeneous with respect to prognostic risk?**<br>*In other words, did all patients share a similar risk from during the study period or was one group expected to begin with a higher morbidity or mortality risk?* | Uncertain. No clinical information is provided for the included patients, aside from age and gender. Clearly certain patients are at higher risk of PE based on risk factors and clinical signs and symptoms, but this study does not allow us to assess for this. |
| C. | **Was follow-up sufficiently complete?**<br>*In other words, were the investigators able to follow-up on subjects as planned or were a significant number lost to follow-up?* | Yes. Given that the only method of follow-up employed was identification of specific ICD-9 and ICD-10 codes, and that purportedly all patients enrolled in these databases had such information entered, there should be no "loss to follow-up." In the sensitivity analysis looking at diagnosis of PE up to 90 days, it is possible that some patients followed up in a manner that was not captured by the databases, but given the nature of the databases this seems unlikely. |
| D. | **Were objective and unbiased outcome criteria used?**<br>Investigators should clearly specify and define their target outcomes before the study and whenever possible they should base their criteria on objective measures. | Yes. The outcome (PE) was based on ICD-9 and ICD-10 diagnostic codes rather than imaging reports. How these diagnoses were made is not known, but presumably the majority of cases were based on CT or V/Q scans. |
| **II.** | **What are the results?** | |
| A. | **How likely are the outcomes over time?**<br>*For the defined follow-up period, how likely were subjects to have the outcome of interest.* | • The rate of PE diagnosis among all ED patients ranged from 0.06% (95% CI 0.05-0.06%) to 0.55% (95% CI 0.50-0.61%).<br>• The rate of PE among hospitalized patients ranged from 0.15% (95% CI 0.14-0.16%) to 2.10% (95% CI 1.84-2.39%).<br><br>For the two sensitivity analyses:<br>• The rate of diagnosis of PE within 90 days ranged from 0.14% (95% CI 0.13-0.14%) to 0.83% (0.80-0.86%) for all ED patients, and ranged from 0.35% (95% CI 0.34-0.37%) to 2.63% (95% CI 2.34-2.95%) for hospitalized patients.<br>• Rates of identification of any venous thromboembolism within 90 days ranged from 0.30% (95% CI 0.29-0.31%) to 1.37% (95% CI |

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| | | 1.33-1.41%) for all ED patients and ranged from 0.75% (95% CI 0.73-0.78%) to 3.86% (95% CI 3.51-4.24%) among hospitalized patients. |
| B. | **How precise are the estimates of likelihood?** *In other words, what are the confidence intervals for the given outcome likelihoods?* | See above. Given the large number of patients enrolled in the various databases, the 95% CIs are quite narrow for all of the outcomes and sensitivity analyses. |
| **III.** | **How can I apply the results to patient care?** | |
| A. | **Were the study patients and their management similar to those in my practice?** | Likely yes. This study was conducted using five different databases, two of which were US-based and included patients from all 50 states. While a large number of these patients are likely cared for in community and rural hospitals, where the rate of PE may be lower than we would see in our institute, it is doubtful that the prevalence among syncope patients would be vastly different. While the prevalence of PE among all ED patients did not vary significantly between the different databases, the prevalence in hospitalized patients did show significant variability (from 0.15% up to 2.10%). This high rate of variability is concerning, and suggests that the rate in our single institution may be quite different from those reported in this study. |
| B. | **Was the follow-up sufficiently long?** | Yes. The authors looked not only at diagnosis of PE at the index hospitalization, but also looked at outcomes out to 90 days. Beyond 90 days, it is doubtful that any additional venous thromboemboli would be related to the index syncope event. |
| C. | **Can I use the results in the management of patients in my practice?** | Likely yes. The prevalence of PE among all ED patients presenting with syncope was quite low in all five databases, and was well below the test threshold for PE of 1.8%. The prevalence of PE among hospitalized patients varied more between databases, with rates as high as 2.10%, which would be above the test threshold, but is quite low. If patients with obvious clinical signs and symptoms of PE were excluded, it is likely that this number would be below the test threshold. |

## Limitations:

1. **This was a retrospective look at data from several databases and represents an inferior level of evidence compared to prospective studies. Retrospective studies are subject to multiple sources of bias.**

2. **The use of ICD-9 and ICD-10 codes to identify patients with PE is close to 90% (Burles 2017), and the previously reported sensitivity for syncope is only around 63% (Ruwald 2013).**

3. **Very little patient information was provided; no medical history was reported and it is not possible to evaluate whether some patients were at higher risk of PE than others.**

4. **The range of rates of PE among hospitalized patients among the databases is quite wide (0.15% to 2.10%) despite similar methodology. This may be due to differences in admission threshold between countries, differences in the threshold to test for PE, or differences in the patient populations. Regardless of the cause, this broad range makes it difficult to generalize the results (external validity).**

5. **Not all patients in these databases were specifically evaluated for PE, and it is quite possible that some cases were missed, resulting in an underestimation of the true prevalence of PE.**

**Bottom Line:**

**This large, retrospective study using five databases from four different countries demonstrated a low prevalence of PE among all ED patients evaluated for syncope (0.06% to 0.55%). The prevalence of PE among hospitalized patients was lower than previously reported, but ranged broadly between the databases (0.15% to 2.10%), with the highest prevalence falling above the previously reported test threshold of 1.8%. The retrospective nature of the study and use of ICD-9 and ICD-10 codes to identify patients severely limits the internal validity of the study.**