

Johns Hopkins University School of Medicine
Appropriate Use Criteria
Priority Clinical Area: Known or Suspected Pulmonary Embolism
Clinical Presentation: Suspected Pulmonary Embolism
Setting: Ambulatory and Emergency Department

INTRODUCTION

The Centers for Medicare and Medicaid Services (CMS) Appropriate Use Criteria (AUC) program took effect January 2020, and it requires ambulatory and emergency medicine providers to consult AUC using a CMS-approved clinical decision support mechanism when ordering advanced imaging (CT, MRI or nuclear medicine) in eight priority clinical areas (PCAs). Known or suspected pulmonary embolism (PE) is included in the PCAs. , As a CMS approved Qualified Provider Led Entity, evaluate the highest-grade evidence in the literature pertaining to appropriate use of pulmonary CTA and ventilation-perfusion (VQ) scanning for outpatients and emergency department patients with suspected pulmonary embolism.

LITERATURE REVIEW

The Johns Hopkins University School of Medicine (JHUSOM) partnered with the [Harvard Medical School \(HMS\) Library of Evidence \(LOE\)](#), which performed the necessary literature reviews and evidence grading as required by CMS for the eight PCAs and more. The HMS created a master database that all qualified provider-led entities (QPLEs) can use. JHUSOM creates, modifies and/or endorses our own AUC by reviewing the HMS LOE literature review and evidence grade assigned for each logic point, and by making an assessment regarding whether the review and grading are acceptable when developing or modifying our AUC, as required under CMS AUC program regulations. JHUSOM will disclose use of the HMS LOE resources and outputs on our website, and all faculty members involved in the HMS LOE provide conflict of interest disclosures on their website.

To design our original AUC for pulmonary embolism advanced imaging, we searched the HMS LOE for Oxford Grade 1 or 2 evidence, as detailed in the evidence table below. The HMS LOE details its literature review and grading process on [its website](#).

[To update the evidence, we conducted our own](#) pulmonary embolism literature search designed by Welch informationist Katie Lobner on May 19, 20:

("pulmonary embolism"[mh] OR "pulmonary embolism" OR "pulmonary thromboembolism" OR "lung embolism" OR "Lung thromboembolism") AND ("diagnostic imaging"[mh] OR "diagnostic imaging" OR "computerized tomography" OR "CT"[tiab] OR "magnetic resonance imaging"[mh] OR "magnetic resonance" OR "MRI" OR "nuclear medicine") AND ("clinical study"[Pt] OR "clinical trial"[Pt] OR "clinical trial protocol"[Pt] OR "comparative study"[Pt] OR "controlled clinical trial"[Pt] OR "evaluation study"[Pt] OR "meta-analysis"[Pt] OR "multicenter study"[Pt] OR "observational study"[Pt] OR "practice guideline"[Pt] OR "randomized controlled trial"[Pt] OR

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""systematic review""[Pt] OR ""validation study""[Pt] OR ""review""[ti] OR ""meta-analysis""[ti] OR ""randomized""[tiab] OR ""randomisedrandomized""[tiab] OR ""clinical study""[ti] OR ""clinical trial""[ti] OR ""observational study""[ti] OR ""guideline""[ti] OR ""guidelines""[ti]), NOT (""case reports""[pt]) AND 2019:3000[dp] AND eng[la].

PRISMA

137 references imported for screening as 137 studies

- 0 duplicates removed

137 studies screened against title and abstract

- 121 studies excluded

16 studies assessed for full-text eligibility

- 9 studies excluded

7 studies included

APPROPRIATE USE CRITERIA

HMS LOE identified 13 publications that were graded Level 1 or 2 by the Oxford scoring system, as detailed in the evidence table below.

Additionally, the HLOE Clinical Practice Guidelines rules for suspected pulmonary embolism were referenced to confirm consistency. Repeat literature search in May 2020 provided six publications graded Level 1 or 2 by the Oxford scoring system: two publications supported our clinical rules and three publications indicated that syncope can be caused by pulmonary embolism. Accordingly, unexplained syncope was added to clinical scenarios that have an increased risk of pulmonary embolism.

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Summary Statement: computerized tomography angiography (CTA) or ventilation perfusion imaging (VQ scan) is appropriate in patients with moderate suspicion (as defined by Wells score > 4 OR Wells ≤ 4 and positive D-dimer OR clinical risk factors) and should be avoided in those with low suspicion (as defined by PERC = 0 OR Wells ≤ 4 and negative D-dimer).

Clinical scenario	Clinical scenario 1: High likelihood of pulmonary embolism	Clinical scenario 2: Moderate likelihood of pulmonary embolism	Clinical scenario 3: Low likelihood of pulmonary embolism
Definition	Patient at high risk (e.g., recent surgery, clotting disorder) with classic signs and symptoms (e.g., hemoptysis, chest pain, dyspnea, hypoxia +/- hypotension). This is a life-threatening condition.	Any of the following: <ul style="list-style-type: none"> • Wells ≤ 4 and positive D-dimer • Wells > 4 • Cardiopulmonary signs and symptoms in patients with elevated risk of pulmonary embolism (e.g. history of VTE, clotting disorder, cancer, sickle cell disease, unexplained syncope). 	Any of the following: <ul style="list-style-type: none"> • PERC 0 • Wells ≤ 4 and negative D-Dimer
AUC rules			
Consistent with AUC	Pulmonary CTA (consensus)	Pulmonary CTA (evidentiary)	No cross-sectional imaging is consistent with AUC for this clinical scenario
Allowable by AUC	VQ scan (consensus)	VQ scan (evidentiary)	No cross-sectional imaging is allowable by AUC for this clinical scenario

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Does not meet AUC	Pulmonary MRI (consensus)	Pulmonary MRI (consensus)	<ul style="list-style-type: none"> • Pulmonary CTA • VQ scan • Pulmonary MRI (all evidentiary)
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EVIDENCE TABLES

Original evidence from HLOE:

ARTICLE/GUIDELINE TITLE	PRIORITY CLINICAL AREA	IMAGING MODALITY	DX/SYMPTOM(S)	PIECE OF LOGIC	SIMPLIFIED RULE		OXFORD GRADE (2011)	
					CTA NOT INDICATED			
PERC pulmonary embolism rule. 2004 ncbi.nlm.nih.gov/pubmed/15304025	Suspected pulmonary embolism	CT	Suspected pulmonary embolism	IF NOT ([age >= 50] OR [heart rate >=100] OR [O2 saturation on room air <95%] OR [prior venous thromboembolism] OR [trauma in the past four weeks] OR [surgery in the past four weeks] OR [hemoptysis] OR [exogenous estrogen] OR [unilateral leg swelling] OR [oral hormone use]), THEN NOT [D-dimer]	PERC = 0		Level 1	(Diagnosis)

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The pulmonary embolism rule-out criteria rule in a community hospital ED: a retrospective study of its potential utility. 2011 ncbi.nlm.nih.gov/pubmed/20708891	Suspected pulmonary embolism	CT	Suspected pulmonary embolism	IF [suspected pulmonary embolism] AND NOT ([age >=50] AND [pulse rate >99 bpm] AND [pulse oximetry <95% on room air] AND [history of hemoptysis] AND [taking exogenous estrogen] AND [prior diagnosis of venous thromboembolism] AND [surgery in last four weeks] AND [trauma in last four weeks] AND [unilateral leg swelling]), THEN NOT [CT chest]	PERC = 0	Level 2	(Diagnosis)
Outcomes and radiation exposure of emergency department patients with chest pain, shortness of breath and ultralow pretest probability: a multicenter study. 2014 ncbi.nlm.nih.gov/pubmed/24120629	Suspected pulmonary embolism	CT	Chest pain, shortness of breath, worsened shortness of breath	IF [age >17] AND [chest pain] AND [new shortness of breath] OR [worsened shortness of breath] AND [ultralow pretest probability (<2.5 of PE)] OR [ultralow pretest probability (<2.5 of ACS)], THEN NOT [CT chest]	Ultralow pretest probability	Level 2	(Diagnosis)
Further validation and simplification of the Wells clinical decision rule in pulmonary embolism. 2008 ncbi.nlm.nih.gov/pubmed/18217159	Suspected pulmonary embolism	CT	Suspected pulmonary embolism	IF [suspected pulmonary embolism] AND NOT [low molecular weight heparin for >24 hours] OR [age <18] OR [pregnant] OR [renal failure] AND [simplified Wells score <=1] AND [normal D-dimer], THEN NOT [CT chest]	Simplified Wells ≤ 1 and negative D-Dimer	Level 2	(Diagnosis)

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Further validation and simplification of the Wells clinical decision rule in pulmonary embolism. 2008 ncbi.nlm.nih.gov/pubmed/18217159	Suspected pulmonary embolism	CT	Suspected pulmonary embolism	IF [suspected pulmonary embolism] AND NOT [low molecular weight heparin for >24 hours] OR [age <18] OR [pregnant] OR [renal failure] AND [modified Wells score <=2] AND [normal D-dimer], THEN NOT [CT chest]	Modified Wells ≤ 2 and negative D-dimer	Level 2	(Diagnosis)
Effectiveness of a diagnostic algorithm combining clinical probability, D-dimer testing and computerized tomography in patients with suspected pulmonary embolism in an emergency department. 2012 ncbi.nlm.nih.gov/pubmed/?term=23330286	Suspected pulmonary embolism	CT	Wells score, suspected pulmonary embolism	IF [suspected pulmonary embolism] AND [Wells score <=4] AND [D-dimer <500 ng/mL] AND NOT [pregnant] OR [allergy to intravenous contrast] OR [renal insufficiency] OR [treatment with therapeutic doses of unfractionated or low molecular weight heparin for more than 24 hours], THEN NOT [CT]	Wells ≤ 4 and negative D-dimer	Level 2	(Diagnosis)
Further validation and simplification of the Wells clinical decision rule in pulmonary embolism. 2008 ncbi.nlm.nih.gov/pubmed/18217159	Suspected pulmonary embolism	CT	Suspected pulmonary embolism	IF [suspected pulmonary embolism] AND NOT [low molecular weight heparin for >24 hours] OR [age <18] OR [pregnant] OR [renal failure] AND [Wells score <=4] AND [normal D-dimer], THEN NOT [CT chest]	Wells ≤ 4 and negative D-dimer	Level 2	(Diagnosis)

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Accuracy of the Wells clinical prediction rule for pulmonary embolism in older ambulatory adults. 2014 ncbi.nlm.nih.gov/pubmed/25366538	Suspected pulmonary embolism	CT	Pulmonary embolism	IF [age >=60] AND [suspected pulmonary embolism] AND NOT [anticoagulant treatment], THEN NOT [Wells score and qualitative point of care D-dimer]	Wells score and point of care D-Dimer are less accurate in patients age ≥ 60	Level 2	(Diagnosis)
					CT INDICATED		
The pulmonary embolism rule-out criteria rule in a community hospital ED: a retrospective study of its potential utility. 2011 ncbi.nlm.nih.gov/pubmed/20708891	Suspected pulmonary embolism	CT	Suspected pulmonary embolism	IF [suspected pulmonary embolism] AND [age >=50] OR [pulse rate >99 bpm] OR [pulse oximetry <95% on room air] OR [history of hemoptysis] OR [taking exogenous estrogen] OR [prior diagnosis of venous thromboembolism] OR [surgery in last four weeks] OR [trauma in last four weeks] OR [unilateral leg swelling], THEN [CT chest]	PERC > 0	Level 2	(Diagnosis)
Effectiveness of a diagnostic algorithm combining clinical probability, D-dimer testing and computerized tomography in patients with suspected pulmonary embolism in an	Suspected pulmonary embolism	CT	Wells score, suspected pulmonary embolism	IF [suspected pulmonary embolism] AND [Wells score <=4] AND [D-dimer >500ng/mL] AND NOT [pregnant] OR [allergy to intravenous contrast] OR [renal insufficiency] OR [treatment with therapeutic doses of unfractionated OR low-molecular weight heparin for more than 24 hours], THEN [CT]	Wells ≤ 4 and D-dimer positive	Level 2	(Diagnosis)

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emergency department. 2012 ncbi.nlm.nih.gov/pubmed/23330286							
The value of 64-detector row computerized tomography for the exclusion of pulmonary embolism. 2011 https://pubmed.ncbi.nlm.nih.gov/21301781/	Suspected pulmonary embolism	CT	Wells score, suspected pulmonary embolism	IF [suspected PE] AND [simplified Wells score <=4] AND [positive D-dimer] AND NOT [previous episodes of pulmonary embolism] OR [concomitant deep-vein thrombosis of the upper or lower extremities] OR [indication for preventive or therapeutic doses of anticoagulant drugs for reasons other than venous thromboembolism] OR [contraindications to the contrast medium] OR [life expectancy <3 months] OR [pregnant] OR [age <18], THEN [64-detector row CT]	Simplified Wells ≤ 4 and D-dimer positive	Level 2	(Diagnosis)
Effectiveness of a diagnostic algorithm combining clinical probability, D-dimer testing and computerized tomography in patients with suspected pulmonary embolism in an	Suspected pulmonary embolism	CT	Suspected pulmonary embolism	IF [suspected pulmonary embolism] AND [Wells score >4] AND NOT [pregnant] OR [allergy to intravenous contrast] OR [renal insufficiency] OR [treatment with therapeutic doses of unfractionated or low-molecular weight heparin for more than 24 hours], THEN [CT]	Wells >4	Level 2	(Diagnosis)

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<p>emergency department. 2012 ncbi.nlm.nih.gov/pubmed/23330286</p>							
<p>The value of 64-detector row computerized tomography for the exclusion of pulmonary embolism. 2011 pubmed.ncbi.nlm.nih.gov/21301781/</p>	<p>Suspected pulmonary embolism</p>	<p>CT</p>	<p>Simplified Wells score, suspected pulmonary embolism</p>	<p>IF [suspected pulmonary embolism] AND [simplified Wells score >4] AND NOT [previous episodes of pulmonary embolism] OR [concomitant deep-vein thrombosis of the upper or lower extremities] OR [indication for preventive or therapeutic doses of anticoagulant drugs for reasons other than venous thromboembolism] OR [contraindications to the contrast medium] OR [life expectancy <3 months] OR [pregnant] OR [age <18], THEN [64-detector row CT]</p>	<p>Simplified Wells score >4 without deep vein thrombus (DVT), contraindications to anticoagulation or limited life expectancy</p>	<p>Level 2</p>	<p>(Diagnosis)</p>

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Evidence from May 2020 literature review

Publication	Oxford Grade	Rule	Condensed Rule
<p>Pop, C.; Ianos, R.; Matei, C.; Mercea, D.; Todea, B.; Dicu, D.; Tarus, M.; Filip, D.; Kozma, G.; Cotoraci, C.; Petris, A.; Tint, D. Prospective Study of Pulmonary Embolism Presenting as Syncope. <i>Am J Ther</i> 2019;26(3):e301–e307</p>	<p>1b (Prospective observational study with 392 subjects. Validating)</p>	<p>“Among the PE patients presenting with syncope, the most frequent location of the embolus was proximal bilateral in 24 patients (53.33%), in a main pulmonary artery in 10 patients (22.22%), in a lobar artery in 10 patients (22.22%) and in a segmental artery in 1 patient (2.22%).” “PE was confirmed in approximately 1 of every 9 patients (11.47%) admitted to the hospital for syncope and in 1 of every 40 patients who visited the ED for syncope (2.52%).”</p>	<p>Patients with syncope need systematic assessment for pulmonary embolism, given the relatively high incidence and severity of PE in those diagnosed.</p>
<p>Thiruganasambandamoorthy, V.; Sivilotti, M. L. A.; Rowe, B. H.; McRae, A. D.; Mukarram, M.; Malveau, S.; Yagapen, A. N.; Sun, B. C. Prevalence of Pulmonary Embolism Among Emergency Department Patients with Syncope: A Multicenter Prospective Cohort Study. <i>Ann Emerg Med</i> 2019;73(5):500–510</p>	<p>1b (Prospective multicenter cohort study in 17 large EDs across Canada (Risk Stratification of Emergency Department Syncope Study) and the United States (Improving Syncope Risk Stratification in Older Adults Study) to enroll patients presenting with syncope. 9,091 patients total with 547* (6.0%) evaluated for pulmonary embolism.)</p>	<p>“Of the 547 patients evaluated for pulmonary embolism, 56 (10.2%; 95% CI 8.0% to 13.1%) had an underlying pulmonary embolism identified” “In this large prospective multicenter study of patients presenting to EDs across Canada and the United States who had syncope, only 1 in approximately 160 patients had an underlying pulmonary embolism identified.”</p>	<p>In the right clinical context, patients with syncope need systematic assessment for pulmonary embolism. Incidence is low among all patients who present with syncope.</p>

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<p>Raynal, P. A.; Cachanado, M.; Truchot, J.; Damas-Perrichet, C.; Feral-Pierssens, A. L.; Goulet, H.; Deltour, S.; Boussouar, S.; Donciu, V.; Simon, T.; Freund, Y.; Philippon, A. L. Prevalence of pulmonary embolism in emergency department patients with isolated syncope: a prospective cohort study. <i>Eur J Emerg Med</i> 2019;26(6):458-461</p>	<p>1b (Prospective cohort of 411 patients in 7 EDS in France, Validating diagnostic test)</p>	<p>"In this multicenter prospective cohort study, the prevalence of pulmonary embolism was 2.2% in patients that presented to the ED with syncope and no other sign of pulmonary embolism, with a 95% CI from 1.1 to 4.3%. This prevalence, although from an underpowered study, may be seen in favor of the need for systematic assessment for pulmonary embolism in patients with isolated syncope, as it is the case for patients with chest pain or dyspnea....even in the absence of chest pain or dyspnea. "</p>	<p>Patients with isolated syncope need systematic assessment for pulmonary embolism. Start with D-Dimer.</p>
<p>Buntine, P.; Thien, F.; Stewart, J.; Woo, Y. P.; Koolstra, M.; Bridgford, L.; Datta, M.; Gwini, S. M. Effect of a clinical flowchart incorporating Wells score, PERC rule and age-adjusted D-dimer on pulmonary embolism diagnosis, scan rates and diagnostic yield. <i>Emerg Med Australas</i> 2019;31(2):216–224</p>	<p>2b (Observational ITS with 1815 pre and 1116 post intervention. Tested CDR rules after derivation)</p>	<p>"The introduction of a clinical flowchart incorporating Wells score, PERC rule and age-adjusted D-dimer was associated with an increase in ED combined CTPA/VQ imaging yield rate from 9.9% to 16.5% across the three enrolment hospitals when investigating possible PE. This corresponded to a 40% relative reduction in PE imaging."</p>	<p>A diagnostic algorithm combining PERC, Wells, D-Dimer can reduce overutilization of pulmonary CTA.</p>

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<p>Qdaisat, A.; Yeung, S. J.; Variyam, D. E.; Badugu, P.; Ghaly, F.; Rice, T. W.; Halm, J. K.; Carter, B. W.; Sun, J.; Gonzalez, C. E.; Viets-Upchurch, J.; Steele, J. R.; Wu, C. C. Evaluation of Cancer Patients With Suspected Pulmonary Embolism: Performance of the American College of Physicians Guideline. <i>J Am Coll Radiol</i> 2020;17(1 Pt A):22–30</p>	<p>2b (Retrospective evaluation of 380 patients; tested CDR rules after derivation)</p>	<p>"Our logistic regression model revealed that the PE rate was significantly higher for patients with high age-adjusted D-dimer levels than for patients with low D-dimer levels (odds ratio [OR] ¼ 10.9 [95% CI ¼ 2.3–196.4], P ¼ .019); for patients with high PE risk than for patients with low PE risk (OR ¼ 5.5 [95% CI ¼ 2.0–16.7], P ¼ .001); and for patients who met more PERC (OR ¼ 1.8 [95% CI ¼ 1.3–2.6], P ¼ .001)."</p>	<p>D-Dimer and PERC are reliable assessment tools to predict likelihood of pulmonary embolism in cancer patients.</p>
<p>Bates, D. D. B.; Liu, Z.; Gibbons, J.; LeBedis, C. A.; Holalkere, N. S. Sick cell disease and venous thromboembolism: A retrospective comparison of the rate of positive CT pulmonary angiography in the emergency department. <i>Eur J Radiol</i> 2019;110():256–259</p>	<p>2b (Retrospective comparison of 75 SCD patients and 78 controls, exploratory cohort)</p>	<p>"Our study demonstrates no significant difference in the rate of acute PE for patients with SCD when compared with matched controls undergoing CTPA in the ED. These results are of interest because of the previous reports of increased rates of acute PE in patients with SCD [12–14]...with one study reporting a 55 to 100-fold increase in incidence of acute PE in SCD patients [13]. "</p>	<p>One retrospective study not consistent with multiple prior investigations. Insufficient evidence to guide practice.</p>

MULTIDISCIPLINARY TEAM

JHUSOM requires that all practicing physicians participating in the development of AUC disclose any conflicts of interest using the International Community of Medical Journal Editors (ICJME) form. This information is publicly available in a timely fashion upon request, for not less than five years after the most recent published update of the relevant appropriate use criteria.

Practicing physician members of the pulmonary embolism AUC development team are listed here:

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Paul O'Rourke	General Internal Medicine, Johns Hopkins Bayview Medical Center
Panagis Galiatsatos	Pulmonary Medicine, Johns Hopkins Bayview Medical Center
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Pamela Johnson	Radiology, The Johns Hopkins Hospital
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Disclosure: The Johns Hopkins University School of Medicine may receive future royalties from licensure of AUCs to CMS-approved CDSMs.