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Risk Stratification and Outpatient Anticoagulant Management of Acute Pulmonary Embolism: A Narrative Review

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Abstract

Acute pulmonary embolism (PE) remains an important cause of cardiovascular morbidity and mortality. Historically, patients with acute PE were routinely hospitalized for parenteral anticoagulation and clinical monitoring. Advances in risk stratification and the availability of direct oral anticoagulants (DOACs) have supported a shift toward outpatient management for carefully selected patients at low risk of adverse outcomes. This narrative review examines three validated clinical tools, the Pulmonary Embolism Severity Index (PESI), simplified PESI (sPESI), and Hestia criteria, and their roles in identifying adults with acute PE who may be suitable for home-based treatment. The review focuses on clinically relevant outcomes, including short-term mortality, recurrent venous thromboembolism, and major bleeding. Available evidence suggests that outpatient treatment appears to be an appropriate option for carefully selected patients with low-risk PE when medication access and reliable follow-up are available, provided that validated assessment tools are combined with evaluation of hemodynamic stability, bleeding risk, comorbid conditions, social circumstances, and access to follow-up care. Contemporary guidelines support structured risk assessment while emphasizing that clinical judgment and shared decision-making remain essential. Appropriate patient selection and reliable outpatient follow-up are central to safely expanding home-based treatment for acute PE.

Categories: Cardiology, Pulmonology, Internal Medicine
Keywords: clinical decision rules, direct oral anticoagulants, hestia criteria, low-risk pulmonary embolism, outpatient management, pulmonary embolism, pulmonary embolism severity index, risk stratification, simplified pesi, venous thromboembolism

Introduction And Background

Acute pulmonary embolism (PE) is an important cause of cardiovascular morbidity and mortality, with prognosis varying substantially according to clinical severity and hemodynamic status [1,2]. Although hospitalization was historically routine for patients with acute PE, accumulating evidence supporting structured risk assessment has expanded the role of outpatient treatment for carefully selected patients at low risk of early adverse outcomes [1,2].

Pulmonary embolism typically occurs when a thrombus originating in the deep venous circulation travels to the pulmonary arteries, potentially increasing pulmonary vascular resistance and causing right ventricular (RV) dysfunction. Clinical severity is traditionally categorized as low, intermediate, or high risk based on hemodynamic stability and evidence of cardiac strain or injury. High-risk PE requires urgent hospital-based management, while intermediate-risk patients generally warrant closer evaluation and monitoring. In contrast, carefully selected low-risk patients may be managed as outpatients when bleeding risk, clinical stability, and appropriate follow-up arrangements permit [1,2].

Two developments have supported this transition. First, validated clinical decision tools, including the Pulmonary Embolism Severity Index (PESI), simplified Pulmonary Embolism Severity Index (sPESI), and Hestia criteria, provide structured approaches to estimating short-term risk and assessing suitability for outpatient care [1-3]. PESI estimates short-term mortality risk using clinical and demographic variables, whereas sPESI provides a simplified assessment using fewer variables. In contrast, the Hestia criteria focus on identifying medical and practical factors that may preclude safe outpatient treatment [1]. Second, direct oral anticoagulants (DOACs) have simplified anticoagulant treatment through fixed oral dosing and the absence of routine international normalized ratio monitoring, facilitating treatment outside the hospital in appropriately selected patients [1,2].

This narrative review examines the roles of PESI, sPESI, and the Hestia criteria in identifying adults with acute PE who may be suitable for outpatient management. The review focuses on clinically relevant outcomes, including 30-day mortality, recurrent venous thromboembolism (VTE), and major bleeding, while considering the complementary roles of anticoagulant selection, clinical judgment, social circumstances,

and reliable outpatient follow-up.

Review

Literature search strategy

This narrative review was informed by a targeted literature search. The search was not systematic, and literature was selected based on its relevance to the review topic. PubMed/MEDLINE, Google Scholar, and the Cochrane Library were searched using combinations of the following terms: pulmonary embolism, pulmonary thromboembolism, PE, venous thromboembolism, VTE, risk stratification, PESI, sPESI, Pulmonary Embolism Severity Index, Hestia criteria, prognostic score, outpatient, ambulatory, home treatment, early discharge, direct oral anticoagulants, and DOACs. The search included English-language publications from January 2010 through June 30, 2026. Foundational references published before 2010, including the original derivation study of the PESI, were identified by reviewing the reference lists of relevant publications. Regulatory prescribing information was also consulted for approved medication dosing.

Selection of relevant literature

Literature was selected based on its relevance to the risk stratification and outpatient management of adults aged 18 years or older with confirmed acute PE. The review focused on studies evaluating the PESI, sPESI, or Hestia criteria; outpatient or early-discharge management; and treatment with DOACs. Priority was given to randomized controlled trials, prospective and retrospective cohort studies, validation studies, systematic reviews, meta-analyses, and clinical practice guidelines reporting outcomes such as mortality, recurrent VTE, major bleeding, hospital readmission, or patient satisfaction. Literature focused exclusively on pediatric populations, hemodynamically unstable PE, or chronic thromboembolic pulmonary disease was not considered central to the scope of this review. Case reports, editorials, letters, conference abstracts, and non-English publications were generally not used.

As this was a narrative rather than a systematic review, study selection was guided by clinical relevance and applicability to outpatient PE management rather than a formal systematic screening protocol. Accordingly, a PRISMA flow diagram was not prepared, and no formal risk-of-bias assessment was performed.

Risk stratification tools

Pulmonary Embolism Severity Index

The PESI is an 11-variable clinical prediction rule developed by Aujesky and colleagues using 15,531 inpatient discharges with PE from 186 Pennsylvania hospitals [4]. The score incorporates age, male sex, history of cancer, heart failure, chronic lung disease, heart rate ⩾110 beats/min, systolic blood pressure <100 mmHg, respiratory rate ⩾30 breaths/min, temperature <36°C, altered mental status, and arterial oxygen saturation <90%. Based on the weighted total score, patients are stratified into five risk classes, ranging from class I to class V, with classes I and II categorized as low risk [3,5]. The 11 PESI variables, organized by domain, are summarized in Figure *1*, and the five risk classes with reported 30-day mortality ranges are presented in Figure *2*.

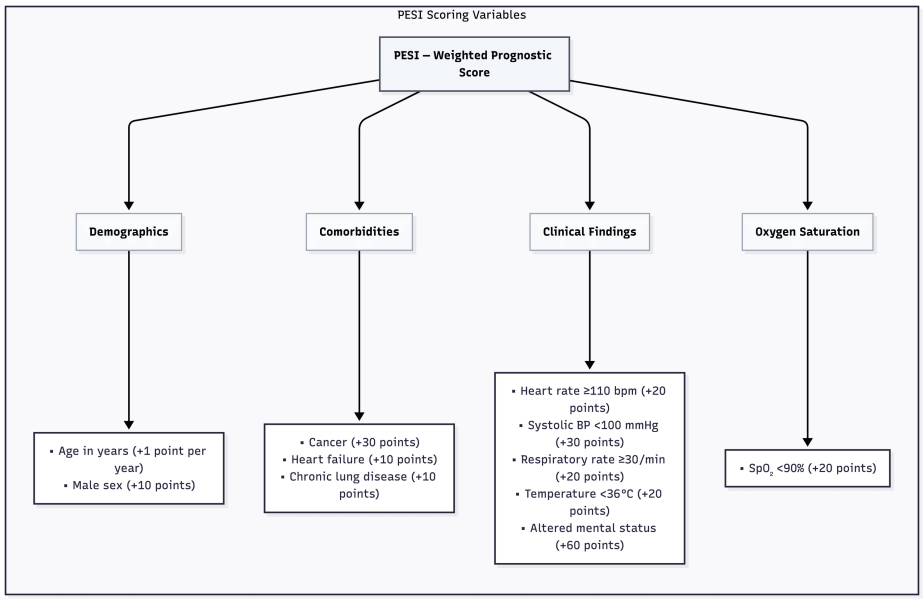


FIGURE 1: Pulmonary Embolism Severity Index Scoring Variables

The PESI is an 11-variable weighted prognostic score organized into four domains: demographics (age in years and male sex), comorbidities (cancer, heart failure, and chronic lung disease), clinical findings (heart rate ≥110 bpm, systolic blood pressure <100 mmHg, respiratory rate ≥30/min, temperature <36°C, and altered mental status), and oxygen saturation (SpO_2 <90%). The total score is calculated by adding the patient's age in years to the weighted points assigned for each applicable variable. Higher total scores correspond to greater short-term mortality risk [1,4,6,7].

PESI, Pulmonary Embolism Severity Index; bpm, beats per minute; BP, blood pressure; SpO_2, peripheral oxygen saturation.

Figure credits: Authors, using Mermaid.js (Mermaid Chart Inc., San Francisco, CA, USA).

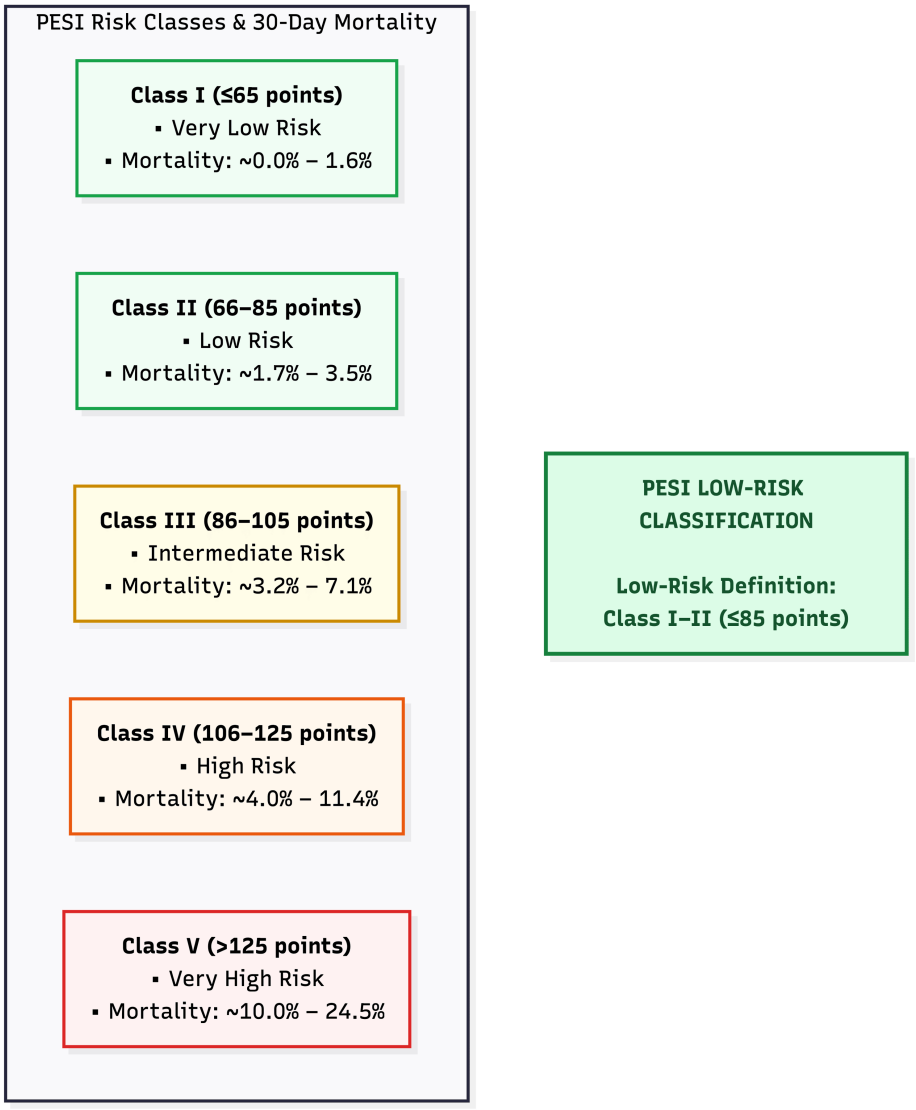


FIGURE 2: Pulmonary Embolism Severity Index Risk Classes and 30-Day Mortality

Patients are stratified into five PESI risk classes, ranging from class I to class V, according to cumulative point totals. Classes I (≤65 points) and II (66-85 points) are categorized as low risk and have reported 30-day all-cause mortality rates of approximately 0%-3.5% across derivation and validation cohorts [1,4,7]. Patients in these classes may be considered for outpatient management when no additional medical, bleeding, social, or follow-up concerns are present. Classes III through V are associated with progressively higher mortality and warrant further clinical evaluation rather than being considered suitable for outpatient treatment on the basis of PESI alone. Accordingly, PESI should be used as part of a broader assessment of clinical stability and outpatient treatment suitability [1].

PESI, Pulmonary Embolism Severity Index.

Figure credits: Authors, using Mermaid.js (Mermaid Chart Inc., San Francisco, CA, USA).

In a prospective European validation study of 357 patients with acute PE, 186 patients (52%) were classified as low risk according to PESI classes I and II. The 90-day mortality rate was 1.1% (95% CI, 0.1%-3.8%) among low-risk patients compared with 11.1% (95% CI, 6.8%-16.8%) among the 171 patients classified as higher risk in classes III through V. For predicting 90-day mortality, the PESI demonstrated a sensitivity of 91% (95% CI, 71%-97%), a negative predictive value of 99% (95% CI, 96%-100%), and an area under the receiver operating characteristic curve of 0.78 (95% CI, 0.70-0.86) [3]. A subsequent validation study involving 302 patients demonstrated a significant association between increasing PESI risk class and mortality ($P < 0.001$), with no deaths observed among patients in classes I through III. The study also demonstrated good interrater reliability, with a kappa value of 0.69 ($P < 0.0001$) [5].

The principal strengths of the PESI are its extensive validation across diverse patient populations and its high sensitivity and negative predictive value for identifying patients at low risk of short-term mortality. However, its 11-variable structure may be cumbersome for routine bedside use. In addition, the PESI was designed to estimate mortality risk rather than directly determine eligibility for outpatient treatment. It does not account for several factors relevant to discharge planning, including bleeding risk, treatment feasibility, social support, medication adherence, and access to timely follow-up. Therefore, PESI classification should be combined with clinical judgment and an assessment of the medical and practical suitability of outpatient care [1,8].

Simplified Pulmonary Embolism Severity Index

The simplified Pulmonary Embolism Severity Index (sPESI) was developed by Jiménez and colleagues to address the complexity of the original PESI. It consists of six binary variables: age >80 years, active cancer, chronic cardiopulmonary disease, heart rate ⩾110 bpm, systolic blood pressure <100 mmHg, and oxygen saturation <90% on room air. Each positive variable is assigned 1 point, and a score of 0 classifies the patient as low risk [2,9]. The six sPESI variables and the resulting risk classification are summarized in Figure *3*.

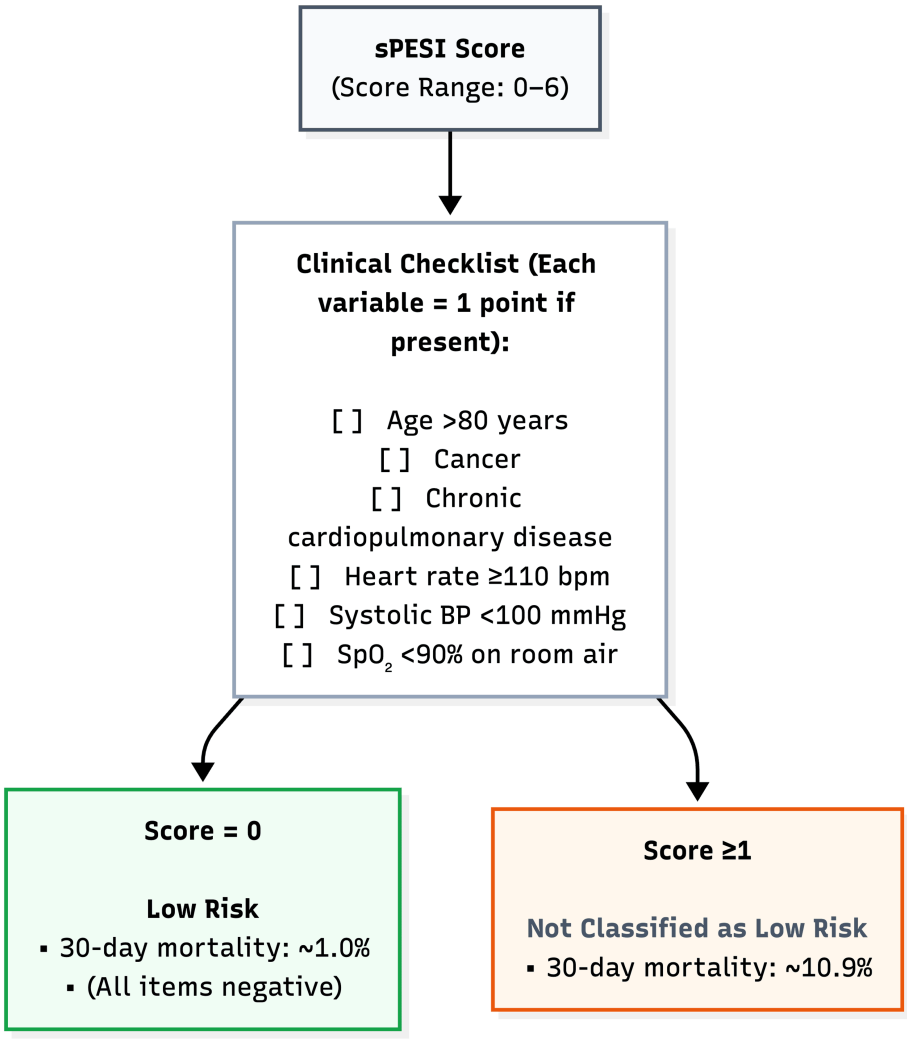


FIGURE 3: sPESI: Variables and Risk Classification

The sPESI is a six-variable binary simplification of the original PESI, assigning 1 point for each variable present: age >80 years, active cancer, chronic cardiopulmonary disease, heart rate ≥110 bpm, systolic blood pressure <100 mmHg, and SpO_2 <90% on room air. A score of 0 identifies low-risk patients with a reported 30-day all-cause mortality rate of approximately 1.0% (95% CI, 0.0%-2.1%) and a recurrent VTE rate of approximately 1.5%, whereas a score of ≥1 classifies patients as not low risk, with a reported 30-day mortality rate of approximately 10.9% (95% CI, 8.5%-13.2%) [2,9].

sPESI, simplified Pulmonary Embolism Severity Index; bpm, beats per minute; BP, blood pressure; SpO_2, peripheral oxygen saturation; VTE, venous thromboembolism.

Figure credits: Authors, using Mermaid.js (Mermaid Chart Inc., San Francisco, CA, USA).

In a study of 995 patients with acute PE treated with low-molecular-weight heparin followed by a vitamin K antagonist (VKA), patients with an sPESI score of 0 had a 30-day mortality rate of 1.0% (95% CI, 0.0%-2.1%) and a recurrent VTE rate of 1.5% [2,9]. The sPESI has been endorsed by the 2019 European Society of Cardiology (ESC)/European Respiratory Society (ERS) guidelines and the 2026 American Heart Association (AHA)/American College of Cardiology (ACC) guideline as a validated tool for identifying patients with low-risk PE [1,10,11].

A notable limitation of the sPESI is that it predicts the risk of death rather than nonfatal complications and does not account for practical factors such as the availability of home support, bleeding risk, or the need for supplemental oxygen. These factors remain important when determining whether outpatient treatment is appropriate [8].

Hestia Criteria

The Hestia criteria represent a fundamentally different approach to risk stratification. Rather than

generating a prognostic score, the Hestia rule uses a bedside checklist of 11 clinical and social conditions that may preclude outpatient treatment. These include hemodynamic instability, the need for thrombolysis, active bleeding or a high risk of bleeding, a requirement for more than 24 hours of supplemental oxygen, PE diagnosed during existing anticoagulation therapy, severe pain requiring intravenous analgesia for more than 24 hours, medical or social conditions requiring hospitalization, creatinine clearance <30 mL/min, severe liver impairment, pregnancy, and a history of heparin-induced thrombocytopenia. If none of these criteria are present, the patient may be considered eligible for outpatient management [1,12]. The 11 Hestia exclusion criteria are summarized in Figure *4*.

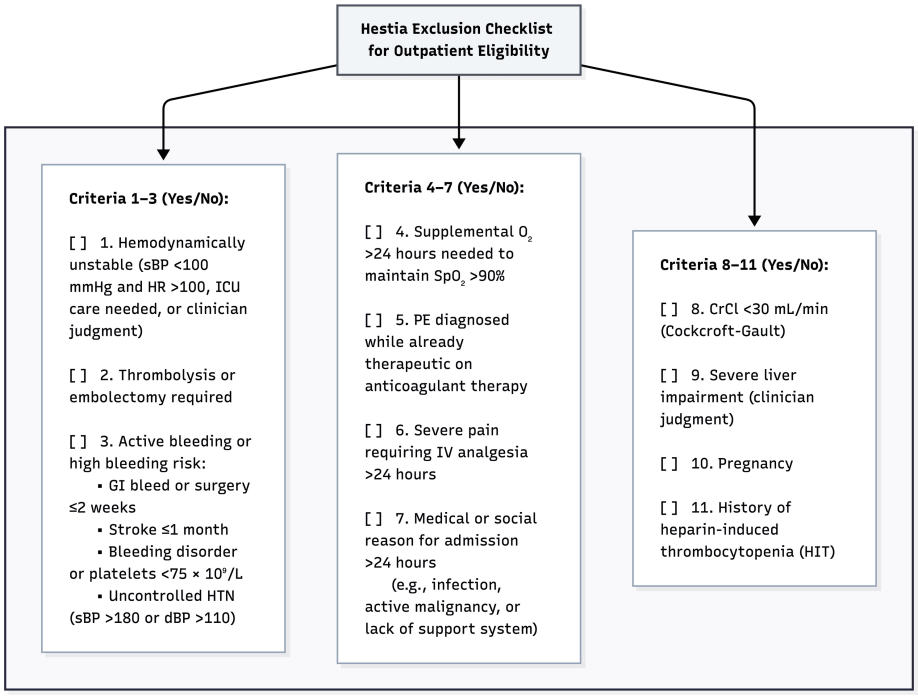


FIGURE 4: Hestia Exclusion Checklist for Outpatient Eligibility

The Hestia criteria comprise 11 binary (yes/no) exclusion items used to assess eligibility for outpatient treatment of acute pulmonary embolism. Criteria 1-3 address hemodynamic instability, the need for thrombolysis or embolectomy, and active bleeding or high bleeding risk, including gastrointestinal bleeding or surgery within two weeks, stroke within one month, bleeding disorder or platelets <75 × 10^9/L, and uncontrolled hypertension (sBP >180 mmHg or dBP >110 mmHg). Criteria 4-7 address the need for supplemental oxygen for more than 24 hours, PE diagnosed while already therapeutic on anticoagulant therapy, severe pain requiring intravenous analgesia for more than 24 hours, and medical or social reasons for admission. Criteria 8-11 address creatinine clearance <30 mL/min by Cockcroft-Gault, severe liver impairment, pregnancy, and a history of heparin-induced thrombocytopenia [7,12].

PE, pulmonary embolism; IV, intravenous; GI, gastrointestinal; sBP, systolic blood pressure; dBP, diastolic blood pressure; HR, heart rate; ICU, intensive care unit; CrCl, creatinine clearance; HIT, heparin-induced thrombocytopenia; SpO_2, peripheral oxygen saturation.

Figure credits: Authors, using Mermaid.js (Mermaid Chart Inc., San Francisco, CA, USA).

Five prospective studies comprising 1,504 patients used the absence of Hestia criteria to determine outpatient eligibility, with 90-day mortality, bleeding, and recurrent VTE rates each below 1.5% [1]. The HOME-PE trial also evaluated Hestia-guided outpatient selection, with its comparative findings discussed in the following section [1,13]. A key advantage of the Hestia criteria is their direct incorporation of practical discharge considerations, including social circumstances, bleeding risk, and comorbidity burden, which are not fully addressed by purely prognostic tools such as the PESI and sPESI [8]. The clinical interpretation of the Hestia criteria and the resulting disposition pathway are illustrated in Figure *5*.

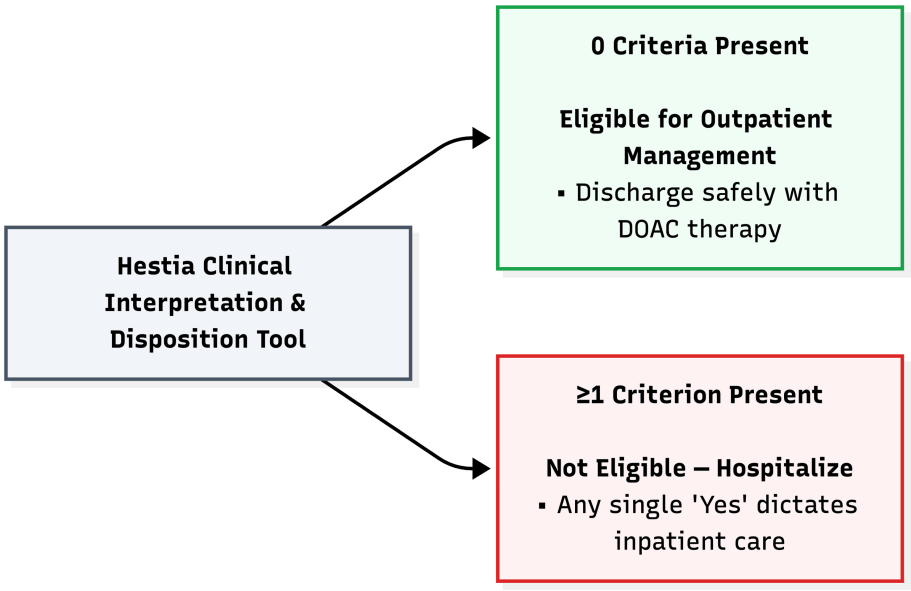


FIGURE 5: Hestia Clinical Interpretation and Disposition Tool

The Hestia criteria function as an exclusion checklist rather than a prognostic score and are used to assess suitability for outpatient management of acute PE. If no Hestia criteria are present, the patient may be considered eligible for outpatient anticoagulant treatment, provided that no additional medical or practical barriers to safe discharge exist. The original Hestia study evaluated outpatient treatment with low-molecular-weight heparin followed by a vitamin K antagonist; the use of a DOAC in the figure reflects a contemporary adaptation consistent with current outpatient management recommendations. If one or more Hestia criteria are present, the patient is not eligible for outpatient management and should be hospitalized [1,7,12].

PE, pulmonary embolism; DOAC, direct oral anticoagulant; LMWH, low-molecular-weight heparin; VKA, vitamin K antagonist.

Figure credits: Authors, using Mermaid.js (Mermaid Chart Inc., San Francisco, CA, USA).

Comparative Performance of Risk-Stratification Tools

The 2026 AHA/ACC/ACCP/ACEP/CHEST/SCAI/SHM/SIR/SVM/SVN guideline states that “Hestia, PESI, and sPESI all have good predictive ability in identifying low-risk patients suitable for outpatient management” and that “none of the PE-specific risk scores appear to have substantially superior performance” [1]. This conclusion is supported by the HOME-PE trial, the only randomized controlled trial to directly compare risk-stratification tools for outpatient treatment decision-making [13].

The HOME-PE trial was a multicenter, international, open-label randomized controlled trial that included 1,975 patients, of whom 1,974 were randomized. Following four withdrawals of consent, 984 patients remained in the Hestia group and 986 in the sPESI group [13]. The Hestia rule was negative, indicating eligibility for outpatient treatment, in 39.4% of patients (388/984), whereas the sPESI score was 0 in 48.4% of patients (477/986). This statistically significant difference indicated that the sPESI classified a greater proportion of patients as eligible for home treatment.

Despite this difference in eligibility classification, similar proportions of patients were ultimately treated at home. Outpatient treatment was provided to 38.4% of patients (378/984) in the Hestia group and 36.6% of patients (361/986) in the sPESI group, reflecting the influence of physician judgment and shared decision-making. The 30-day composite rate of recurrent VTE, major bleeding, or all-cause mortality was low and did not differ significantly between groups, occurring in 1.3% of patients (5/375) in the Hestia group and 1.1% of patients (4/359) in the sPESI group. The smaller denominators used for the outpatient composite outcomes (375 and 359 patients, respectively) reflect the patients with evaluable 30-day outcome data, rather than the entire randomized treatment-strategy groups [13]. Clinicians overruled the sPESI recommendation more frequently than the Hestia recommendation, suggesting that the Hestia criteria may align more closely with clinical decision-making because they incorporate practical considerations relevant to safe discharge [1,13].

An important caveat noted in the 2026 guideline is that prospective studies evaluating the PESI incorporated several exclusion criteria also included in the Hestia rule. Consequently, it is difficult to attribute the safety of outpatient management to PESI classification alone [1]. The principal characteristics,

performance measures, strengths, and limitations of PESI, sPESI, and the Hestia criteria are summarized in Table 1.

Feature	PESI	sPESI	Hestia Criteria
Tool type	Weighted prognostic score	Simplified binary prognostic score	Exclusion checklist (decision rule)
Number of variables	11 (differentially weighted)	6 (binary, equally weighted)	11 (binary, any-positive rule)
Primary outcome predicted	30-day all-cause mortality	30-day all-cause mortality	Suitability for outpatient management
Low-risk definition	Class I-II (≤85 points)	Score = 0	0 criteria present
Proportion classified low-risk	~25-46% of PE patients	~37-48% of PE patients	~39-50% of PE patients
30-day mortality in low-risk group	~0-3.5%	~1.0% (95% CI, 0.0-2.1%)	~0.3-1.0%
NPV for 30-day mortality	High (>97%)	High (~99%)	High (>98%)
Key strength	Most extensively validated; granular five-tier risk stratification	Simpler to calculate; comparable NPV to PESI	Directly assesses outpatient eligibility; incorporates practical/social factors
Key limitation	Complex (11 weighted variables); age-driven (elderly patients often classified higher risk regardless of PE severity)	May over-classify patients as "not low risk" (lower specificity); does not assess practical barriers	Not a prognostic score per se; does not quantify mortality risk; relies on clinician judgment for some items
Guideline-supported use	ESC/ERS 2019; AHA/ACC 2026; CHEST	ESC/ERS 2019; AHA/ACC 2026; CHEST	ESC/ERS 2019; AHA/ACC 2026; CHEST

TABLE 1: Side-by-Side Comparison of the PESI, sPESI, and Hestia Criteria for Risk Stratification in Acute PE

The three validated tools are presented in parallel to highlight their structural differences and complementary roles in identifying low-risk patients with acute pulmonary embolism who may be suitable for outpatient management. PESI is an 11-variable weighted prognostic score that stratifies patients into five risk classes, with classes I-II defining low risk [4,7,14]. The sPESI simplifies this approach to six equally weighted binary variables and classifies patients as low risk when the score is 0 [2,9]. The Hestia criteria represent an exclusion checklist that directly assesses outpatient treatment eligibility by identifying clinical, bleeding, and social factors that preclude home management; the absence of all criteria identifies patients eligible for outpatient care [1,12]. The table also summarizes the principal strengths, limitations, and key performance characteristics of each tool, including the proportion of patients classified as low risk and their negative predictive value for 30-day mortality. All three tools are endorsed by the 2019 ESC/ERS and 2026 AHA/ACC guidelines for identifying low-risk patients suitable for outpatient management [1,11].

Sources: Tool type, number of variables, and low-risk definitions[4,7,9,12,14,15]; intended outcomes and performance characteristics, including the proportion classified as low risk [1,2,13], 30-day mortality [1,14], and negative predictive value [2]; principal strengths [1,14,15] and limitations [1,2]; guideline-supported use [1,11,16].

PESI, Pulmonary Embolism Severity Index; sPESI, simplified Pulmonary Embolism Severity Index; PE, pulmonary embolism; NPV, negative predictive value; CI, confidence interval; DOAC, direct oral anticoagulant; ESC, European Society of Cardiology; ERS, European Respiratory Society; AHA, American Heart Association; ACC, American College of Cardiology.

The role of biomarkers and imaging in refining risk stratification

Although clinical risk scores form the foundation of PE risk stratification, cardiac biomarkers and RV imaging provide additional prognostic information, particularly for patients at intermediate risk.

Elevated troponin levels are associated with increased short-term all-cause mortality in patients with PE, with a pooled OR of 4.33 based on a meta-analysis of 46 studies comprising 10,842 patients [1,17]. Elevated brain natriuretic peptide (BNP) levels are similarly associated with increased short-term all-cause mortality,

with an OR of 6.57 [1]. Among normotensive patients, cardiac biomarkers may help distinguish intermediate-risk from low-risk PE [18].

Right ventricular dysfunction detected by echocardiography or computed tomography (CT) is associated with increased odds of all-cause mortality, even among patients classified as low risk by the PESI, sPESI, or Hestia criteria. In a systematic review of 22 studies comprising 3,295 patients, RV dysfunction was associated with an OR of 4.19 for all-cause mortality (95% CI, 1.39-12.58) [1,19]. An individual patient data meta-analysis of 5,010 patients with low-risk PE similarly demonstrated that RV dysfunction was associated with increased odds of PE-related death (OR, 22.9; 95% CI, 2.89-181) [1,20].

The 2026 AHA/ACC guideline recommends measurement of at least one cardiac biomarker, either troponin or BNP, in patients with an elevated clinical severity score who do not have hypotension (Class 1, Level of Evidence B-NR). The guideline also recommends RV imaging for risk stratification in patients with elevated clinical severity scores (Class 1, Level of Evidence A) [1]. These recommendations apply primarily to patients at intermediate risk (e.g., PESI class III-V or sPESI ⩾1) rather than to all patients with acute PE [1]. For patients already classified as low risk by PESI, sPESI, or Hestia criteria, routine biomarker testing and RV imaging are not required, although a normal troponin level has been incorporated as an additional safety criterion in some outpatient protocols [1,19,20]. In the randomized controlled trial by Peacock et al., patients with a negative Hestia assessment and a normal troponin level were safely randomized to outpatient treatment with rivaroxaban [21]. Hemodynamic stability alone does not establish suitability for outpatient treatment. Patients with RV dysfunction or elevated cardiac biomarkers may remain at increased risk of adverse outcomes despite the absence of hypotension. When these abnormalities are identified, further evaluation of overall clinical risk and the need for inpatient monitoring is warranted before considering early discharge [1,19,20].

Integrated risk stratification and outpatient disposition

The preceding clinical risk-stratification tools, biomarker findings, imaging considerations, and practical discharge factors can be integrated into a structured approach to disposition decision-making. Figure *6* illustrates this process in adults with confirmed acute PE.

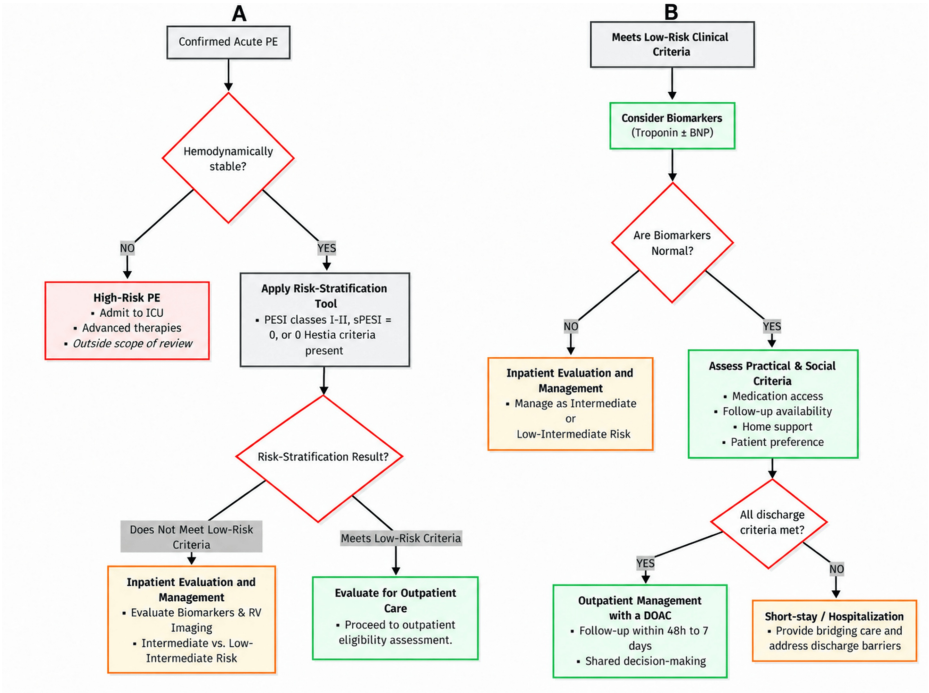


FIGURE 6: Integrated Risk Stratification and Outpatient Management Pathway for Adults With Confirmed Acute Pulmonary Embolism

(A) Initial hemodynamic assessment and clinical risk stratification following confirmation of acute PE. Hemodynamically unstable patients are classified as high-risk and require urgent inpatient management, including consideration of advanced therapies [1]. Hemodynamically stable patients undergo clinical risk stratification using validated tools, including the PESI, sPESI, or Hestia criteria [1]. (B) Patients meeting low-risk clinical criteria undergo further evaluation for outpatient management. Cardiac biomarkers and RV imaging may be considered when additional risk refinement is clinically indicated [1,10]. Practical considerations include access to anticoagulation, reliable follow-up, adequate home support, and patient preference [1,8]. Patients who satisfy appropriate clinical and practical discharge criteria may be considered for outpatient treatment with a DOAC, early follow-up, and shared decision-making [1]. Patients with higher-risk features or unresolved discharge barriers may require additional evaluation, short-stay observation, or hospitalization [1,8].

PE, pulmonary embolism; ICU, intensive care unit; PESI, Pulmonary Embolism Severity Index; sPESI, simplified Pulmonary Embolism Severity Index; RV, right ventricular; BNP, B-type natriuretic peptide; DOAC, direct oral anticoagulant.

Figure credits: Authors, using Mermaid.js (Mermaid Chart Inc., San Francisco, CA, USA).

Direct oral anticoagulants in the treatment of acute pulmonary embolism

The availability of DOACs has facilitated outpatient PE management through fixed oral dosing and the absence of routine international normalized ratio monitoring. Rivaroxaban and apixaban can also be initiated without preceding parenteral anticoagulation, reducing logistical barriers to outpatient treatment. In contrast, dabigatran and edoxaban require at least five days of initial parenteral anticoagulation before oral treatment can begin, potentially limiting their convenience for immediate outpatient management. Anticoagulant selection should also account for renal function, bleeding risk, contraindications, and medication accessibility [1].

Rivaroxaban

The EINSTEIN-PE trial was an open-label, noninferiority randomized controlled trial involving 4,832 patients with acute symptomatic PE who were assigned to rivaroxaban at a dose of 15 mg twice daily for three weeks followed by 20 mg once daily, or standard therapy with enoxaparin followed by a VKA, for three, six, or 12 months [22]. Rivaroxaban was noninferior to standard therapy for the primary efficacy outcome of recurrent symptomatic VTE, which occurred in 2.1% and 1.8% of patients, respectively (hazard ratio (HR), 1.12; 95% CI, 0.75-1.68; P = 0.003 for noninferiority). Major bleeding occurred significantly less frequently with rivaroxaban than with standard therapy (1.1% vs. 2.2%; HR, 0.49; 95% CI, 0.31-0.79; P = 0.003) [22,23].

Apixaban

The AMPLIFY trial was a double-blind, noninferiority randomized controlled trial involving 5,395 patients with acute VTE, including both deep vein thrombosis (DVT) and PE, who were assigned to apixaban at a dose of 10 mg twice daily for seven days followed by 5 mg twice daily, or conventional therapy with enoxaparin followed by warfarin, for six months [24,25]. Apixaban was noninferior to conventional therapy for recurrent VTE or VTE-related death (2.3% vs. 2.7%; relative risk [RR], 0.84; 95% CI, 0.60-1.18; P < 0.001 for noninferiority). Apixaban was also associated with a 69% reduction in major bleeding (0.6% vs. 1.8%; RR, 0.31; 95% CI, 0.17-0.55; P < 0.001) [24,25].

Comparative DOAC Data

A meta-analysis of 27,127 patients with VTE from six clinical trials demonstrated that DOACs were noninferior to conventional therapy for recurrent PE and were associated with a lower risk of major bleeding, with an absolute risk difference of -0.6% (95% CI, -1.0% to -0.3%) [2]. The 2026 AHA/ACC guideline recommends DOACs as preferred agents for the long-term management of acute PE because of their comparable efficacy, lower bleeding risk, particularly for intracranial hemorrhage, fixed dosing, and fewer drug and dietary interactions compared with VKAs [1].

The COBRRA trial, a recent head-to-head randomized controlled trial comparing apixaban and rivaroxaban during the first three months of treatment for acute VTE, including both DVT and PE, demonstrated a significantly lower rate of clinically relevant bleeding, defined as major bleeding or clinically relevant nonmajor bleeding, with apixaban. No apparent difference in recurrent VTE was observed between the treatment groups [26].

Notably, the EINSTEIN-PE, AMPLIFY, and COBRRA trials enrolled broad populations of patients with acute VTE and were not specifically designed to evaluate outpatient management of low-risk PE. Evidence supporting DOACs in the outpatient setting is discussed below.

DOAC selection requires individualized assessment. Rivaroxaban and apixaban are contraindicated or require dose adjustment in patients with severe renal impairment or hepatic disease, and neither agent is recommended during pregnancy or in patients with antiphospholipid syndrome [1,8,25]. Active bleeding or high bleeding risk, clinically significant drug interactions (particularly with strong dual CYP3A4 and P-glycoprotein inhibitors or inducers), medication affordability, and anticipated patient adherence are additional factors that influence anticoagulant selection and may affect suitability for outpatient management [1,8,25]. In special populations, anticoagulant selection requires additional consideration. Low-molecular-weight heparin is generally preferred during pregnancy, whereas VKAs are generally favored over DOACs in patients with thrombotic antiphospholipid syndrome. Patients with active malignancy require individualized assessment of bleeding risk, thrombocytopenia, potential drug interactions, and treatment feasibility; however, malignancy alone does not necessarily preclude outpatient management [1,8].

DOACs in the Outpatient Setting

A systematic review of 12 studies, including four randomized controlled trials and eight nonrandomized studies, enrolled a total of 3,191 patients with low-risk PE. Among 1,814 outpatients in high-quality studies, the pooled rates of 90-day major adverse outcomes were each below 1%: 0.7% for all-cause mortality (95% CI, 0.4%-1.2%), 0.06% for PE-related mortality (95% CI, 0.01%-0.3%), 0.8% for recurrent VTE (95% CI, 0.5%-1.4%), and 0.8% for major bleeding (95% CI, 0.5%-1.4%). Exploratory analysis demonstrated no association between anticoagulant treatment class, DOAC versus VKA, and the rates of major adverse outcomes [27].

The HoT-PE trial was a prospective, international, multicenter, single-arm management trial that directly evaluated early discharge and home treatment with rivaroxaban in patients with low-risk acute PE. Eligibility required the absence of hemodynamic instability, RV dysfunction, or intracardiac thrombi, and serious comorbidities. Patients were discharged within 48 hours of presentation [28]. The trial was stopped early for efficacy following a prespecified interim analysis of 525 patients. In this interim population, the primary composite outcome of symptomatic recurrent VTE or PE-related death within three months occurred in three patients (0.6%; one-sided upper 99.6% CI, 2.1%). Major bleeding occurred in six of 519 patients in the safety population (1.2%), and no PE-related deaths were reported [28]. A subsequent analysis of the complete trial population of 576 patients reported the same three primary outcome events (0.5%; one-sided upper 95% CI, 1.3%), along with improvements in disease-specific quality of life and treatment satisfaction over three months [29].

An individual patient-level meta-analysis cited in the 2026 guideline reported low 30-day event rates among patients with PE managed as outpatients. Mortality occurred in 0.30% of patients (95% CI, 0.09%-0.51%), recurrent VTE in 0.57% (95% CI, 0.28%-0.86%), and major bleeding in 0.45% (95% CI, 0.19%-1.71%) [1].

Outpatient versus inpatient management: Evidence from randomized controlled trials

Two randomized controlled trials directly compared outpatient and inpatient treatment among patients with low-risk acute PE.

The Aujesky et al. trial (2011) was a multicenter, open-label randomized controlled trial conducted across 19 centers in Switzerland, France, Belgium, and the United States. The study enrolled 344 patients with PESI class I or II PE who also met additional eligibility criteria and randomized them to outpatient or inpatient treatment with low-molecular-weight heparin plus warfarin. Patients were followed for 90 days, and no significant differences in clinical outcomes were observed between the two groups [1,30].

The Peacock et al. trial (2018) was conducted across 35 hospitals in the United States and enrolled 114 patients with a negative Hestia assessment, a normal serum troponin level, no contraindications to anticoagulation, and no barriers to treatment or follow-up. Patients randomized to outpatient treatment received rivaroxaban and were followed for 90 days. No significant differences in clinical outcomes were observed between the outpatient and inpatient groups [21].

A 2022 Cochrane systematic review incorporating these two randomized controlled trials concluded that outpatient treatment was not associated with an increased risk of adverse clinical outcomes compared with inpatient treatment among patients with low-risk acute PE [7].

Interpretation of the available evidence requires consideration of differences in study design and patient selection. HOME-PE directly compared Hestia- and sPESI-guided triage strategies in a randomized trial, whereas HoT-PE evaluated early discharge and rivaroxaban treatment in a prospective single-arm study that excluded patients with RV dysfunction. Furthermore, EINSTEIN-PE and AMPLIFY primarily evaluated anticoagulant efficacy and safety rather than directly comparing inpatient and outpatient disposition strategies. These methodological differences limit direct comparisons across studies and emphasize the importance of applying trial findings to appropriately selected patient populations [13,22,24,28].

Guideline recommendations

Multiple international guidelines now support outpatient management for appropriately selected patients with low-risk PE.

The 2026 AHA/ACC/ACCP/ACEP/CHEST/SCAI/SHM/SIR/SVM/SVN guideline provides the following recommendations [1]:

- It is reasonable to use a validated decision tool, including the Hestia criteria, PESI, or sPESI, to assess suitability for outpatient treatment in patients diagnosed with acute PE in a clinic or emergency department setting (Class 2a, Level of Evidence B-R).

- In selected patients with low-risk PE, corresponding to AHA/ACC PE Categories A and B, outpatient treatment is a reasonable alternative to hospitalization when the expected rate of 90-day adverse outcomes is low, and the treatment plan aligns with the patient's goals and preferences (Class 2a, Level of Evidence B-R).

- Patients considered suitable for discharge should have immediate access to anticoagulant therapy and rapid, reliable follow-up with an experienced clinician.

The 2019 ESC/ERS guidelines recommend considering early discharge and home treatment when three conditions are met: the risk of early PE-related death or serious complications is low, no serious comorbidity or aggravating condition requires hospitalization, and appropriate outpatient care and anticoagulant therapy can be provided [11]. The ESC/ERS guidelines recommend the use of PESI or sPESI, or alternatively the Hestia criteria, to support clinical risk assessment and triage [11].

The 2021 CHEST guideline update recommends outpatient treatment rather than hospitalization for patients with low-risk PE when access to anticoagulant medication, the ability to obtain outpatient care, and appropriate home circumstances are established [16].

A comparative analysis of international guidelines demonstrated broad agreement in supporting home-based treatment for appropriately selected patients with low-risk PE. Across guidelines, reliable follow-up, access to anticoagulant therapy, medication adherence, and suitable home circumstances remain essential components of safe outpatient management [10].

Outcomes summary

Table *2* summarizes the key clinical outcomes reported in major randomized and pooled studies of outpatient management for low-risk acute PE. Outcome timeframes vary across studies, with some reporting 30-day and others 90-day event rates; the specific follow-up period for each study is indicated in the table. It is important to distinguish mortality from composite outcomes when interpreting these findings. The

HOME-PE and HoT-PE trials reported composite endpoints incorporating multiple adverse events, whereas other studies reported mortality and individual clinical outcomes separately. These differences in outcome definitions should be considered when comparing results across studies [13,28].

Study/Source	Design	Outpatient Cohort, n	Risk-Stratification Tool	Follow-up	Mortality or Composite Outcome	Recurrent VTE	Major Bleeding
HOME-PE (Hestia arm)	RCT	375	Hestia	30 days	Composite 1.3%	Included in composite	Included in composite
HOME-PE (sPESI arm)	RCT	359	sPESI	30 days	Composite 1.1%	Included in composite	Included in composite
Aujesky et al., 2011 [30]	RCT	~170	PESI classes I-II	90 days	No significant difference vs. inpatient	No significant difference	No significant difference
Peacock et al., 2018 [21]	RCT	~51	Hestia + troponin	90 days	No significant difference vs. inpatient	No significant difference	No significant difference
Maughan et al., 2021 [27] (SR)	Systematic review	1,814	PESI/sPESI/Hestia	90 days	0.7%	0.8%	0.8%
Individual-patient MA (2026 guideline)	Meta-analysis	Pooled	Various	30 days	0.30%	0.57%	0.45%
HoT-PE (Barco et al. 2020 [28])	Prospective, multicenter, single-arm management trial	525	Clinical criteria (no RV dysfunction, no hemodynamic instability, no serious comorbidities)	90 days	Composite 0.6%; 0 PE-related deaths	0.6%	1.2%

TABLE 2: Summary of Key Clinical Outcomes in Studies of Outpatient Management of Low-Risk Acute Pulmonary Embolism

Sources: HOME-PE Hestia and sPESI arms [13], Aujesky et al. (2011) [30], and Peacock et al. (2018) [21]; Maughan et al. (2021) [27]; individual-patient meta-analysis cited in the 2026 guideline [1,2]; HoT-PE trial [28].

PE, pulmonary embolism; RCT, randomized controlled trial; SR, systematic review; MA, meta-analysis; PESI, Pulmonary Embolism Severity Index; sPESI, simplified Pulmonary Embolism Severity Index; VTE, venous thromboembolism; RV, right ventricular; HoT-PE, Home Treatment of Pulmonary Embolism.

Follow-up care and practical considerations

Structured follow-up is essential to the safety of outpatient PE management. The 2026 AHA/ACC guideline recommends initial follow-up communication within 48 hours to seven days after diagnosis. Follow-up may be facilitated by nurses, advanced practice providers, pharmacists, or physicians and may occur in person or through telehealth [1]. These early encounters should focus on patient education, medication adherence, and identification of barriers to care.

At approximately three months after acute PE, a dedicated follow-up visit should occur to discuss the duration of anticoagulation, evaluate ongoing symptoms, and determine whether additional testing is needed, including evaluation for chronic thromboembolic pulmonary disease (CTEPD) [1]. Between one-third and one-half of patients with symptomatic PE report persistent dyspnea or limitations in physical activity during follow-up, and CTEPD with pulmonary hypertension develops after approximately 2.3% to 4% of acute PE events [1]. In addition to assessing physical symptoms, follow-up should include evaluation of quality of life, depression, and anxiety [1].

Although approximately 50% of patients with PE may meet criteria for outpatient discharge, only approximately 7.5%-15% are discharged directly from the emergency department, highlighting a substantial gap between eligibility and implementation [2].

Limitations and knowledge gaps

Several limitations of the current evidence base warrant discussion. First, the available randomized controlled trials comparing outpatient and inpatient PE management enrolled relatively small samples [21,30], and larger trials would strengthen the evidence supporting outpatient treatment [1].

Second, existing risk-stratification tools were developed using clinical variables measured at the time of presentation or diagnosis. The role of longitudinally assessed dynamic variables, such as the National Early Warning Score 2 (NEWS2), in predicting subsequent clinical deterioration remains an area of active investigation [1].

Third, none of the currently available risk-stratification tools strongly predict clinical deterioration among patients with hemodynamically stable PE. These tools are more accurate in identifying patients at low risk than in identifying those who will experience adverse outcomes [1].

Fourth, data regarding hospital readmission rates and patient satisfaction with outpatient PE management remain limited, representing areas for future investigation. Finally, the generalizability and successful implementation of outpatient management protocols depend on healthcare system infrastructure, including access to rapid follow-up, anticoagulant availability, and adequate social support [11,16].

This review also has several methodological limitations. As a narrative review, the literature search was not systematic, and article selection was based on author judgment rather than predefined inclusion and exclusion criteria applied across a standardized search protocol. The search was limited to English-language publications, which may have excluded relevant studies published in other languages. No formal quality assessment or risk-of-bias evaluation was performed for the included studies. In addition, the two randomized controlled trials that directly compared outpatient and inpatient PE management were relatively small, enrolling 344 and 114 patients [21,30], which limits the statistical power to detect uncommon adverse events. These limitations should be considered when interpreting the conclusions of this review.

Conclusions

The PESI, sPESI, and Hestia criteria are validated tools that can identify adults with acute PE who are at low risk for short-term adverse outcomes, and no single tool has demonstrated substantially superior performance. However, no risk-stratification tool replaces clinical judgment; scores do not fully account for bleeding risk, comorbidity burden, treatment feasibility, or patient preferences, and shared decision-making remains essential when determining suitability for outpatient care. Outpatient management appears to be an appropriate option for carefully selected patients with low-risk PE when immediate access to anticoagulant therapy, adequate social support, and reliable follow-up within 48 hours to seven days are available.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

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