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Review

Home treatment for patients with cancer-associated venous thromboembolism

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ABSTRACT

Patients hospitalised with acute venous thromboembolism (VTE), and notably patients with pulmonary embolism, often remain in hospital for extended periods due to the perceived risk of complications. However, several studies have shown that home treatment of selected patients is feasible and safe, with a low incidence of adverse events. This may offer clear benefits for patients' quality of life, hospital planning and cost to the health service. Nonetheless, there is a need for a VTE risk-stratification tool specifically addressing prognosis in patients with cancer. This may aid in the selection of low-risk patients with cancer and VTE who are suitable for outpatient treatment. Although several prognostic scores have been proposed, we suggest using a pragmatic clinical decision-making tool such as the Hestia criteria for selecting patients for home care in everyday clinical practice. Once patients have been discharged, it is mandatory to monitor patients regularly (we suggest after 3 days, 10 days, 1 month and 3 months, or more frequently if needed) with the involvement of a multidisciplinary team, so that appropriate and timely remedial action can be taken in case of warning signs of complications. If patients are selected carefully and monitored effectively, many patients who experience acute VTE can be cared for safely at home.

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Abbreviations

AE	adverse event
AUC	area under the curve
BCC	basal cell carcinoma
CAT	cancer-associated thrombosis
CTPA	computed tomography pulmonary angiography

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[1] A full list of the INNOVTE CAT Working Group can be found at the end of the article, in Appendix B. INNOVTE CAT Reviewers are listed in Appendix C.

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DOAC	direct acting oral anticoagulants
DVT	deep vein thrombosis
ECOG	Eastern Cooperative Oncology Group
GP	general practitioner
GPS	Geneva Prognostic/Prediction Score
IQR	interquartile range
LMWH	low-molecular weight heparin
NS	not significant
OR	odds ratio
PE	pulmonary embolism
PESI	Pulmonary Embolism Severity Index
RIETE	Registro Informatizado de Enfermedad TromboEmbólica
SBP	systolic blood pressure
SCC	squamous cell carcinoma
SD	standard deviation
TTE	trans-thoracic echocardiography
VKA	vitamin K antagonist
VTE	venous thromboembolism

Introduction

Venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE), is a common complication in patients with cancer [1]. These patients are at higher risk for PE related death [2], VTE recurrence and bleeding than patients without cancer [3]. For these reasons, only a small minority of patients with cancer-associated VTE were included in studies assessing the feasibility and safety of home management [4–13]. One of the reasons could be that certain decision-making tools such as the PESI or sPESI categorise all patients with VTE and cancer as being at risk for complications, which precludes proposing them home treatment.

Whereas outpatient treatment for patients with DVT has been the standard of care for many years, evidence supporting outpatient management of patients with PE is more recent. Several studies have shown that home treatment of selected patients with PE is feasible and safe, with a low incidence of adverse events [4–13]. In these studies, patients with low-risk PE eligible for home treatment were selected either according to validated clinical prognostic scores suggestive of a low risk of death (PESI score $\leq$ 85 (class I/II) or simplified PESI score = 0) [14,15], or according to pragmatic criteria which consider all patients who do not require in-hospital care due to PE or another condition as candidates for home treatment. These criteria have been grouped together in the Hestia rule (Table 1) [13]. It should be noted that, in studies using a prognostic score, for example the OTPE study which used the PESI, pragmatic clinical criteria were also added, including several items used in the Hestia criteria, for the selection of low-risk patients [4]. Based on these results, European guidelines propose using the PESI score (or the sPESI score), or alternatively the Hestia criteria, combined with the absence of right ventricular dysfunction on imaging (computed tomography pulmonary angiography [CTPA] or transthoracic echocardiography [TTE]) for qualifying low-risk patients with PE for home treatment, whereas the ACCP propose selecting patients only on the basis of pragmatic criteria even if it is stated that the presence of right ventricular dysfunction or increased cardiac biomarker should discourage outpatient treatment [16,17]. Recently, the HOME-PE study compared the Hestia criteria to the sPESI for triaging patients with acute PE for home treatment [10]. In this study, 1975 patients were randomised to either triaging with Hestia or sPESI. They were designated for home treatment if the triaging tool was negative and if the physician-in-charge, taking into account the patient's opinion, did not consider that hospitalisation was required. The results showed that the Hestia criteria were at least as safe as the sPESI score with respect to the 30-day composite of recurrent VTE, major bleeding or all-cause death, for triaging patients for home treatment [10]. With both strategies, around 35% of patients could be managed at home with a low 30-day composite outcome rate (1.33% in the Hestia group and 1.11% in the sPESI group) [10].

The aim of this review is to provide guidance on home treatment for patients with cancer-associated thromboembolism (CAT) with a focus on patients with cancer-associated PE who represent the principal population of patients included in published studies.

Prognostic models for the selection of low-risk patients with cancer associated thromboembolism

The clinical course (in terms of mortality, recurrent VTE and bleeding complications) of patients with cancer-associated PE differs from that of patients without cancer [3]. In addition, comorbid malignancy contributes to a substantial proportion of the risk in general risk assessment scores for VTE. For these reasons, there is a need for a VTE risk-stratification tool specifically addressing prognosis in patients with cancer. This may aid in the selection of low-risk patients with cancer and PE who are suitable for outpatient treatment. Several prognostic models have been proposed and these are summarised in Table 1. Some of them, the Ottawa score, the RIETE score, the POMPE-C score, the clinical decision rule developed by Carmona Bayonas, the criteria proposed by Font, the EPIPHANY index and the Hull 5 risk score, were developed and dedicated specifically to risk stratification of patients with cancer-associated PE [18–23]. The prognostic performance of risk stratification tools used in the general population of patients with acute PE (with and without cancer), such as the PESI, sPESI, Geneva Prognostic Score and Hestia criteria, have also been evaluated in patients with cancer-associated PE [24–26]. In both the modified PESI and the modified sPESI, investigators replaced the 'cancer' variable with a more specific requirement for 'metastatic' disease (Table 2).

Data from studies assessing risk-stratification tools derived from, or validated in, patients with cancer-associated PE have been pooled in a systematic review and bivariate meta-analysis published by Nguyen et al in 2017 [24]. Since its publication, four additional studies have been published [26–29]. The available studies were published between 2012 and 2021 and enrolled patients between 2001 and 2015 with various anticoagulant treatments including VKAs, but principally LMWH. The age of the enrolled patients ranged from 59 to 74 years (mean or median). All studies required an objective confirmation of PE whereas the definition of active cancer varied. The proportion of incidental PE varied from 0 to 100%. The majority of included patients were receiving chemotherapy or radiotherapy (33–75% of patients) and had a metastatic disease (40–74% of patients). All studies reported 30-day all-cause mortality. The results of these studies are summarised in Table 3.

Taken together, these results are difficult to interpret and the use of these "cancer-specific" prognostic models are not recommended in everyday clinical practice to identify patients with low-risk cancer-associated PE because they were derived from retrospective databases and have certain limitations. For example, some of them require information to calculate the score, which may be difficult to collect in the emergency department ("tumor response" for EPIPHANY index, "TNM stage" for modified Ottawa score, "Do not resuscitate status" for POMPE-C) [19,22,23]. These prognostic models were mostly designed to predict early mortality risk and only a few of them also predicted other PE-related complications, such as bleeding events or VTE recurrence [24]. Their prognostic performance does not appear to be superior to pragmatic clinical criteria such as those used in the Hestia checklist [24,25]. Lastly, none of them have been used in prospective dedicated studies of impact

Table 1
Other Clinical prediction rules.

Hestia criteria[13]
- Items
  - Haemodynamically unstable
  - Thrombolysis or embolectomy needed
  - Active bleeding or high risk of bleeding, defined as any of the following
    - Gastrointestinal bleeding in the preceding 14 days
    - Recent stroke (< 4 weeks ago)
    - Recent operation (< 2 weeks ago)
    - Bleeding disorder or thrombocytopenia (platelet count < 75 × 109/L)
    - Uncontrolled hypertension (systolic blood pressure > 180 mmHg or diastolic blood pressure > 110 mmHg)
  - > 24 hours of oxygen supply needed to maintain oxygen saturation > 90%
  - Pulmonary embolism diagnosed during anticoagulant treatment
  - Severe pain needing intravenous pain medication for > 24 hours
  - Medical or social reason for treatment in hospital for > 24 hours (infection, malignancy, no support system)
  - Creatinine clearance of < 30 mL/minute; calculated according to the Cockroft-Gault formula
  - Severe liver impairment (left to physician discretion)
  - Pregnant
  - Documented history of heparin-induced thrombocytopenia
- Decision rule
  - Patients considered low-risk if none of the above criteria are present

Geneva Prognostic Score (GPS) [36]
- Items
  - Cancer (2 points)
  - Heart failure (1 point)
  - Previous deep vein thrombosis (1 point)
  - Systolic blood pressure < 100 mmHg (2 points)
  - Partial pressure of arterial oxygen while breathing room air < 8 kPa (1 point)
  - Deep vein thrombosis shown by ultrasound (1 point)
- Decision rule
  - Patients considered low-risk if sum of points is ≤ 2

Pulmonary Embolism Severity Index (PESI) [14]
- Items
  - Male sex (10 points)
  - Cancer (30 points)
  - Heart failure (10 points)
  - Chronic lung disease (10 points)
  - Pulse ≥ 110/minutes (20 points)
  - Systolic blood pressure < 100 mmHg (30 points)
  - Respiratory rate ≥ 30/minute (20 points)
  - Temperature < 36 °Celsius (20 points)
  - Altered mental status; defined as disorientation, lethargy, stupor or coma (60 points)
  - Arterial oxygen saturation < 90%; with and without the administration of supplemental oxygen (20 points)
- Decision rule
  - Patients considered low-risk if sum of points is ≤ 85

Modified Pulmonary Embolism Severity Index (Modified PESI)[37]
- Male sex (10 points)
- Metastatic cancer (30 points)
- Heart failure (10 points)
- Chronic lung disease (10 points)
- Pulse ≥ 110/minutes (20 points)
- Systolic blood pressure < 100 mmHg (30 points)
- Respiratory rate ≥ 30/minute (20 points)
- Temperature < 36 °Celsius (20 points)
- Altered mental status; defined as disorientation, lethargy, stupor or coma (60 points)
- Arterial oxygen saturation < 90%; with and without the administration of supplemental oxygen (20 points)
- Decision rule
  - Patients considered low-risk if sum of points is ≤ 85

Modified Simplified Pulmonary Embolism Severity Index (Modified sPESI)[15,37,38]
- Age > 80 years
- Metastatic cancer
- History of chronic cardiopulmonary disease
- Pulse ≥ 110 beats/minute
- Systolic blood pressure < 100 mmHg
- Arterial oxyhaemoglobin saturation level < 90%
- Decision rule
  - Patients considered low-risk if none of the above criteria are present

for the selection of low-risk patients eligible for home treatment. Of note, the anatomical location of the thrombus in the pulmonary arteries (i.e., proximal versus distal PE) was not taken into account in the decision to treat at home a patient.

Given these limitations, pragmatic clinical criteria as well as other patient-specific clinical factors should continue to be used for identifying patients with low-risk cancer-associated PE suitable for home treatment, rather than using the above prognostic

Table 2
Clinical prediction rules in patients with cancer-associated venous thromboembolism: derivation and definition.

POMPE-C (Kline et al., 2012) [23]

Source data	*Enrolment dates*	*Key inclusion criteria*	*Cancer definition*	*Comparator clinical prediction rule*
EMPEROR registry Prospective/retrospective inclusion Multicentre study in USA	2005–2008	Objectively confirmed PE AND Active cancer	Metastatic disease OR Cancer under the care of an oncologist	PESI
		Patients $n = 408$ Age range: 62–63 yrs	*Incidental PE* Not reported	*Outcome evaluated* 30-day all-cause mortality: $n = 51$ (12.5%)
Items Body weight Respiratory rate (RR) SaO_2% Heart rate > 100 beats/min (HR) Altered mental status (AMS) Respiratory distress (Resp Dis) Do not resuscitate status (DNR) Unilateral limb swelling (ULS)		*Score calculation* Probability of death (P) = 100 × (1–1/(1 + Exp(3.718 + DNR × 1.551 + RespDist × 0.800 + ULS × 0.734 + AMS × 1.473 + HR + (RR × 0.044) + (SaO_2 × −0.063) + (bodyweight × −0.012)	*Decision rule* Patients considered low-risk if *P* is < 5%	

Modified Ottawa score(Louzada et al., 2012) [22]

Source data	*Enrolment dates*	*Key inclusion criteria*	*Cancer definition*	*Comparator clinical prediction rule*
Retrospective single centre study in Canada	2002–2004 (derivation) 2007–2008 (validation)	*At least one of the following* Objectively confirmed PE Proximal DVT Proximal DVT of the upper extremities Unusual site thrombosis	Cancer, other than BCC or SCC, within 6 months before or after VTE diagnosis OR Any treatment for cancer within the previous 6 months, or OR Recurrent or metastatic cancer regardless of treatment	None
		Patients Derivation set: $n = 543$ Validation set: $n = 819$	*Incidental PE* None	*Outcome evaluated* VTE recurrence within the first 6 months of anticoagulation Derivation set: 10.1% Validation set: 10.5%
Items Female sex (+1) Lung cancer (+1) Breast cancer (−1) TNM stage I (−2) Prior VTE (+1)		*Score calculation* Sum of item points	*Decision rule* Score < 0: low risk of VTE recurrence (< 4.5%) Score > 1: high risk of VTE recurrence (> 19%)	

RIETE score(Den Exter et al., 2013) [20]

Source data	*Enrolment dates*	*Key inclusion criteria*	*Cancer definition*	*Comparator clinical prediction rule*
RIETE VTE patient registry Prospective/retrospective inclusion Multicentre, international	Not reported	Objectively confirmed PE Active cancer	Cancer diagnosed within the 6 months before the index PE AND Metastatic cancer OR Any malignancy requiring antineoplastic or palliative treatment within the previous 6 months	None
		Patients Derivation set: $n = 1048$ Median age [IQR]: 71 [61–78] years Internal validation set: $n = 508$ Median age [IQR]: 70 [60–78] years	*Incidental PE* None	*Outcome evaluated* 30-day all-cause mortality: Derivation set: 21% Validation set: 24%
Items Metastatic disease (+4) Immobilisation (+2) Age > 80 years (+1) History of VTE disease (+1) Heart rate > 110 beats/min (+1) Systolic blood pressure < 100 mm Hg (+1) Body weight < 60 kg (+1)		*Score calculation* Sum of item points	*Decision rule* Score ≤ 2: low risk Score 2–4: intermediate risk Score 5–7: high risk Score > 7: very high risk	

Table 2
(*Continued*)

RIETE-2 score (Fuentes et al., 2019) [35]

Source data	*Enrolment dates*	*Key inclusion criteria*	*Cancer definition*	*Comparator clinical prediction rule*
RIETE VTE patient registry Prospective/retrospective inclusion Multicentre study worldwide	2001–2017	Objectively confirmed PE (47%) Limb DVT (52%) Splanchnic vein thrombosis (1%) AND Active cancer	Diagnosis of cancer within last 3 months AND Metastatic disease OR chemotherapy at the time of diagnosis of VTE NOT Skin malignancies	None
		Patients Derivation set: $n = 6675$ Internal validation set: $n = 3350$	*Incidental PE* None	*Outcome evaluated* 30-day all-cause mortality: $n = 1256$ (12.5%)
Items White blood cell count $\geq 11.5 \times 10^9$/L (+4) Metastatic disease (+3) Immobilisation (+3) BMI < 18.5 (+3) Any pulmonary embolism (+2) Platelet count $\leq 160 \times 10^9$/L (+2)		*Score calculation* Sum of item points	*Decision rule* Score 0–3: low risk Score 4–6: moderate risk Score ≥ 7: high risk	

Font criteria(Font et al., 2014) [21]

Source data	*Enrolment dates*	*Key inclusion criteria*	*Cancer definition*	*Comparator clinical prediction rule*
Prospective cohort Single centre study in Spain	2006–2009	Objectively confirmed PE AND Active cancer	Adjuvant chemotherapy	GPS PESI POMPE-C RIETE
		Patients $n = 138$ Age (mean ± SD): 63 ± 11 years	*Incidental PE* 47%	*Outcome evaluated* 30-day all-cause mortality: $n = 16$ (11.6%)
Items SBP < 100 mm Hg PaO_2 < 60 mmHg or SpO_2 < 90% Active bleeding Platelet count < 50×10^9/L Renal insufficiency Social reason Poor treatment compliance Presence of other admission criteria according to treating physicians		*Score calculation* Number of items present	*Decision rule* Patients considered low risk if none of the criteria are present	

Carmona-Bayonas criteria (Carmona-Bayonas et al., 2016) [21]

Source data	*Enrolment dates*	*Key inclusion criteria*	*Cancer definition*	*Comparator clinical prediction rule*
EPIPHANY patient registry Prospective/retrospective inclusion Multicentre study in Spain	2004–2015	Objectively confirmed PE Active cancer	Cancer diagnosed within 1 month before the index PE OR Completion of adjuvant chemotherapy within 1 month before the index PE	GPS Modified PESI Modified sPESI RIETE POMPE-C
		Patients $n = 585$ Mean age ± SD: 65 ± 12 years	*Incidental PE* None	*Outcome evaluated* 30-day all-cause mortality: 125 (21.3% [95%CI: 18.2–24.8%])
Items Heart rate > 110 beats/min (+1) Systolic blood pressure < 100 mm Hg SpO_2 < 90% Clinically relevant bleeding High risk of bleeding Platelet count < 50×10^9/L Respiratory rate ≥ 30 breaths/min Sudden or progressive dyspnoea		*Score calculation* Number of items present	*Decision rule* Patients considered low risk if none of the criteria are present	

EPIPHANY index (Carmona-Bayonas et al., 2017) [19,21]

Source data	*Enrolment dates*	*Key inclusion criteria*	*Cancer definition*	*Comparator clinical prediction rule*
EPIPHANY patient registry Prospective/retrospective inclusion Multicentre study in Spain	2004–2015	Objectively confirmed PE Active cancer	Cancer diagnosed within 1 month before the index PE OR Completion of adjuvant chemotherapy within 1 month before the index PE	None

Table 2
(*Continued*)

		Patients *n* = 1075 Mean age ± SD: 64 ± 12 years	*Incidental PE* 54%	*Outcome evaluated* 15-day serious complications[a] 208 (19.3% [95%CI: 17.1–21.8%)] 30-day all-cause mortality 153 (14.2% [95%CI: 12.2–16.5%])
Items Heart rate > 110 beats/min (+1) Systolic blood pressure < 100 mm Hg SpO_2 < 90% Respiratory rate ≥ 30 breaths/min Sudden or progressive dyspnoea Clinically relevant bleeding High risk of bleeding Platelet count < 50×10^9/L		*Score calculation* Number of items present	*Decision rule* Patients considered low risk if none of the criteria are present AND Tumour response assessment at the time of PE is considered one of the following Complete or partial response Stable disease No evidence of disease Progressive disease/unknown/not evaluated with surgery of the primary tumour 2.0% of low-risk patients present 15-day serious complications[a] and 1.3% 30-day all-cause mortality	
HULL 5 risk score(Bozas et al., 2018) [18,21]				
Source data Prospective cohort Single centre study in England	*Enrolment dates* Not reported	*Key inclusion criteria* Objectively confirmed PE Active cancer *Patients* *n* = 234 Median age [range]: 67 [27–91]	*Cancer definition* Not reported *Incidental PE* 100%	*Comparator clinical prediction rule* Modified PESI *Outcome evaluated* 30-day all-cause mortality 8 (3.4%)
Items ECOG performance status 0 (0) ECOG performance status 1–2 (+2) ECOG performance status 3–4 (+3) Presence of new or worsening symptoms (+1)		*Score calculation* Sum of item scores	*Decision rule* Low risk: 0 Intermediate risk: 1–2 High risk: 3–4	

BCC: basal cell carcinoma of the skin; DVT: deep vein thrombosis; ECOG: Eastern Cooperative Oncology Group; GPS: Geneva Prognostic Score; IQR: interquartile range; PE: pulmonary embolism; PESI: Pulmonary Embolism Severity Index; RIETE: Registro Informatizado de Enfermedad TromboEmbólica; SBP: systolic blood pressure; SCC: squamous cell carcinoma of the skin; VTE: venous thromboembolism.

[a] Events that lead to serious clinical deterioration or death; systolic blood pressure < 90 mmHg, acute respiratory failure, right-side heart failure, acute kidney failure, major bleeding, or any other event the investigator deems serious.

models. This was also the conclusion of the systematic review and meta-analysis of Nguyen at al [24]. The use of the Hestia checklist appears appropriate because, unlike the PESI or sPESI, assessment of the feasibility of home treatment and the bleeding risk are already integrated into the Hestia criteria. As demonstrated in the HOME-PE trial, application of the Hestia criteria (the proportion of patients with a negative Hestia rule) performed better than an sPESI score of 0 points (88.4% vs. 64.8% discharged to home, with an adjusted absolute difference of +25.3% in favour of the Hestia criteria) [10]. In addition, the Hestia criteria have been widely validated for triaging patients with low-risk PE for home treatment [17].

For patients with cancer-associated DVT, Fuentes et al. derived and internally validated a prognostic score to predict 30-day all-cause mortality in 10,025 patients included in the RIETE registry with active cancer and symptomatic VTE (DVT 52%, PE 31%, DVT + PE 16%, and splanchnic vein thrombosis 0.6%) [35] (Table 2). This score has never been used to select low-risk patients with cancer and proximal DVT for home treatment. Thus, the use of clinical pragmatic criteria, such as the absence of severe obstructive syndrome, other severe comorbidity than cancer itself or social reason, remains the most appropriate tool for selecting patients with cancer associated DVT eligible for home treatment.

Studies assessing home treatment in patients with cancer associated PE and DVT

As stated above, only a minority (between 1% to 13%) of patients with cancer have been included in studies assessing the feasibility and safety of home treatment for PE, and these studies did not provide a separate analysis of patients with and without cancer [4–6,10,11,13,30]. To date, four studies which results are summarised in Table 4 have been published. All but one study included both symptomatic and incidental PE; Siragusa et al. included only symptomatic patients [31]. Two of the studies included patients with both PE and proximal DVT [31,32]. Of note, all these studies used pragmatic clinical criteria or Hestia criteria to select low-risk patients with PE for home treatment. Using these criteria, 45 to 66% of the patients were treated at home with various rates of early all-cause mortality and complications (Table 4).

Recently, we performed a *post hoc* analysis of the HOME-PE trial to assess the effectiveness and safety of outpatient management of low-risk cancer-associated PE [33]. In the HOME-PE trial, low-risk patients with symptomatic PE were randomised to either triaging with Hestia or sPESI [10]. Three groups were analysed: 47 patients with active cancer treated at home (group 1, median age: 65 years), 691 patients without active cancer treated at home

Table 3
Performance of prognostic models in cancer-associated PE for 30-day all-cause mortality.

Study	Prognostic model	Patients (*n*)	Age, years (mean ± SD)	Incidence of PE (%)	30-day all-cause mortality (%)	Low risk patients (%)	30-day all-cause mortality in low-risk patients (%)	AUC	Sensitivity, % [95% CI]	Specificity, % [95%CI]
Nguyen et al., 2018 [24]	Hestia	124	66 ± 13	7		18.5	0	0.87	98.1 [75.6–99.9]	23.5 [16.2–32.8]
	EPIPHANY Index	1075	64 ± 12	54		28.4	1.3	0.88	97.4 [93.2–99.0]	32.6 [29.7–35.7]
	Carmona Bayonas	709	65 ± 12	1		13.8	6.6	0.27	96.6 [62.2–99.8]	15.8 [9.5–252]
	POMPE-C	1029	64 ± 13	7		19.3	3.2	0.83	95.6 [89.3–98.2]	22.0 [11.6–37.8]
	PESI	900	62 ± 13	8		6.6	6.9	0.78	95.3 [87.0–98.5]	6.0 [1.8–18.3]
	Modified PESI	709	65 ± 13	1		19.2	8.9	0.88	93.8 [86.2–97.4]	21.3 [6.0–53.6]
	Modified sPESI	709	65 ± 13	1		17.6	6.7	0.69	95.0 [84.8–98.5]	20.4 [10.3–36.5]
	RIETE	2664	67 ± 13	3		29.3	3.8	0.62	93.2 [80.2–97.9]	34.2 [23.3–47.1]
	Font	262	64 ± 13	29		43.2	5.1	0.51	87.8 [73.9–94.8]	48.9 42.3–55.4]
	GPS	847	65 ± 11	9		51.6	14.3	0.59	59.9 [49.2–69.7]	53.6 [43.4–63.4]
Li et al., 2021 [27]	Hestia	460			18.0	65.4		0.74		
	PESI							0.74		
	RIETE					30.9		0.74		
	POMPE-C					30.9		0.78		
	Modified Ottawa							0.64		
Yamashita et al., 2020 [26]	sPESI	368	67 ± 12	0	10.1	44[a]	6.3	–	–	–
Pfaundler et al., 2020 [28]	RIETE	178	74 (median) (IQR, 69–80)	0	8.4	35.4	0	0.75	100 [79.6–100]	38.7 [31.5–46.3]
	Modified Ottawa					31.5	0	0.84	100 [79.6–100]	34.4 [27.5–41.9]

AUC: area under the curve; GPS: Geneva prediction score; PE: pulmonary embolism; PESI: Pulmonary Embolism Severity Index; RIETE: Registro Informatizado de Enfermedad TromboEmbólica; SD: standard deviation.
[a] Defined as sPESI = 1.

Table 4
Summary of available studies assessing home treatment for patients with cancer-associated pulmonary embolism.

Muñoz Martín et al., 2020 [39]						
Design	*Population*	*Incidental PE*	*Active cancer definition*	*Eligibility for home treatment*	*Anticoagulant treatment*	*n treated at home/n patients with VTE*
Prospective cohort Single centre study in Spain	25 incidental PE	100%	Cancer diagnosis OR antineoplasic treatment within previous 6 months	Haemodynamically stable PE Low bleeding risk	LMWH	25/25 (100%)
	Outcome					
	VTE recurrence	0				
	Major bleeding events	1 (4%)				
	All-cause mortality at D90	0				
Hendricks et al., 2019 [32]						
Design	*Population*	*Incidental PE*	*Active cancer definition*	*Eligibility for home treatment*	*Anticoagulant treatment*	*n treated at home/n patients with VTE*
Retrospective cohort Single centre study in the Netherlands	183 incidental or symptomatic VTE 69 DVT 114 PE ± DVT	26%	Cancer diagnosis OR antineoplasic treatment within previous 6 months OR Recurrent or metastatic cancer	Hestia criteria for PE Clinical judgment for DVT	LMWH (70%) LMWH + VKA (13%) DOACs (16%)	All VTE: 120/183 (66%) PE: 63/114 (55%) DVT: 57/69 (83%)
	Outcome (VTE) 3 months incidence of at least one of the following VTE-related AEs Major bleeding events Recurrent VTE Suspected VTE-related mortality at D90		In patients with VTE Home treatment: 13% Hospital: 19% Hazard ratio: 0.48 [0.22–1.1]	In patients with PE Home treatment: 9.5% Hospital: 15.6% Hazard ratio: 0.38 [0.12–1.1]		
Font et al., 2014 [21]						
Design	*Population*	*Incidental PE*	*Active cancer definition*	*Eligibility for home treatment*	*Anticoagulant treatment*	*n treated at home/n patients with VTE*
Prospective cohort Single centre study in Spain	138 incidental or symptomatic PE	38%	Adjuvant chemotherapy	No Font criteria fulfilled SBP < 100 mm Hg PaO_2 < 60 mmHg or SpO_2 < 90% Active bleeding Platelet count < 50 × 109/L Renal insufficiency Social reason Poor treatment compliance Presence of other admission criteria according to treating physicians	LMWH	62/138 (45%) Most patients treated at home had an incidentally detected PE (89%)

Table 4
(*Continued*)

	Primary outcome All-cause death at D30 All-cause death at D90 *Secondary outcome* VTE recurrence at D30 VTE recurrence at D90 Major bleeding at D30 Major bleeding at D90	Home treatment vs. hospital 3.2% versus 18.4% ($P = 0.06$) 9.7% versus 34.2% ($P = 0.001$) 0% versus 2.6% 1.6% versus 5.3% 4.8% versus 5.3% 4.8% versus 9.2%				
Siragusa et al., 2005 [31]						
Design Prospective cohort Single centre study in Italy	*Population* 207 symptomatic VTE 139 DVT 68 PE	*Incidental PE* None	*Active cancer definition* Ongoing antineoplasic or palliative treatment	*Eligibility for home treatment* None of the following Poor clinical conditions related to concomitant medical disorders Illness that independently required hospitalisation Poor compliance High risk of bleeding or active bleeding Renal insufficiency Acute anaemia Pain requiring parenteral narcotics	*Anticoagulant treatment* LMWH (49%) LMWH + VKA (51%)	*n treated at home/n patients with VTE* All VTE: 127/207 (61%) DVT: 91/138 (66%) PE: 36/68 (53%)
	Outcome (VTE) Recurrent VTE at 6 months Major bleeding events at 6 months All cause death at 6 months		Home treatment vs. hospital 5.5% versus 9.3% (NS) 2.7% versus 0 (NS) 30.5% versus 37% (NS)			

AE: adverse events; DOAC: direct acting oral anticoagulants; DVT: deep vein thrombosis; LMWH: low-molecular weight heparins; NS: not significant; PE: pulmonary embolism; SBP: systolic blood pressure; VKA: vitamin K antagonists; VTE: venous thromboembolism.

(group 2, median age: 59 years), and 33 patients with active cancer hospitalised only because of their cancer (group 3, median age: 70 years). The main outcome was the composite of recurrent VTE, major bleeding, and all-cause death within 30 days after randomisation. Of the patients treated at home, the composite endpoint was met by 4.3% (95%CI, 0.5–14.5%) (2/47) in group 1, 1.0% (7/691) in group 2 and 3.0% (0.1–15.3%) (1/33) in group 3. The difference was not statistically different between patients treated at home with and without active cancer (OR 4.98, 95% CI [1.15–21.49], $P = 0.062$) or among patients with an active cancer treated at home or hospitalised (OR 1.19, 95%CI [0.15–9.47], $P = 0.87$) but this *post hoc* analysis was underpowered to answer whether home treatment is safe in patients with cancer associated PE. However, in multivariate analysis, for patients treated at home, active cancer was a risk factor for complications whereas, conversely, home treatment was not a risk factor of adverse outcome for patients with active cancer. Recently, Guman et al presented the results of a Dutch multicentre retrospective cohort study including 602 patients with an active cancer and a symptomatic or incidental PE of whom 285 (47%) were discharged from the emergency department [34]. Of the 382 patients with symptomatic PE, 105 were treated at home, compared to 180 of 220 (82%) patients with incidental PE. In symptomatic patients who were discharged, the cumulative 14-day mortality rate was 0% and PE related readmission rate was 2.9%. In patients with incidental PE, these rates were 1.1% and 0% respectively.

Taken together, these data suggest that home treatment of low-risk PE (and DVT) patients with active cancer selected on the basis of pragmatic criteria (for patients with DVT or PE) or Hestia criteria (for patients with PE only) seems feasible and does not have an unfavourable impact on prognosis. However, the level of evidence provided by these data remains limited and further validation in dedicated prospective studies is required. In the elderly population, an oncogeriatric evaluation should be proposed to these patients [40].

Follow-up for home treatment

In most studies assessing the efficacy and safety of home treatment in patients with PE, a specific follow-up for patients managed at home was implemented [9]. A dedicated team performed a first consultation or phone contact within the first week, often within the first three days after discharge from the emergency department. Patients were monitored at least at 1 month and 3 months, but often more frequently. Importantly, they were provided with a contact phone number in case of emergency [9].

The risk of inappropriate treatment and complications may be much higher without the provision of such care in patients with cancer-associated PE or DVT. Therefore, it would be strongly suggested to propose to such patients a close follow-up tailored to their individual needs and to integrate their management in the global care pathway for patients with CAT [41].

Proposals of the Expert Group (Central illustration)

- We suggest evaluating the possibility of home treatment in all normotensive patients with symptomatic or incidental cancer-associated PE or DVT. Expert panel ranking: 3.79 out of 4.00.
- We suggest not taking into account the anatomical location of the thrombus in pulmonary arteries (except for an intra cardiac thrombus) in the decision to treat patients with PE at home. Expert panel ranking: 3.33 out of 4.00.
- We recommend assessing the severity of PE according to ESC guidelines and not to propose home treatment for patients with high-risk PE (shock) or intermediate high-risk PE (RV dilatation and elevated troponin). Expert panel ranking: 3.86 out of 4.00.
- We suggest using the Hestia criteria for assessing the eligibility of patients with cancer-associated PE for home treatment. Expert panel ranking: 3.67 out of 4.00.
- We propose using pragmatic clinical criteria such as those proposed for non-cancer patients for assessing the eligibility of patients with cancer-associated DVT for home treatment. Expert panel ranking: 3.71 out of 4.00.
- We suggest treating patients with cancer-associated PE not meeting any Hestia criteria at home:

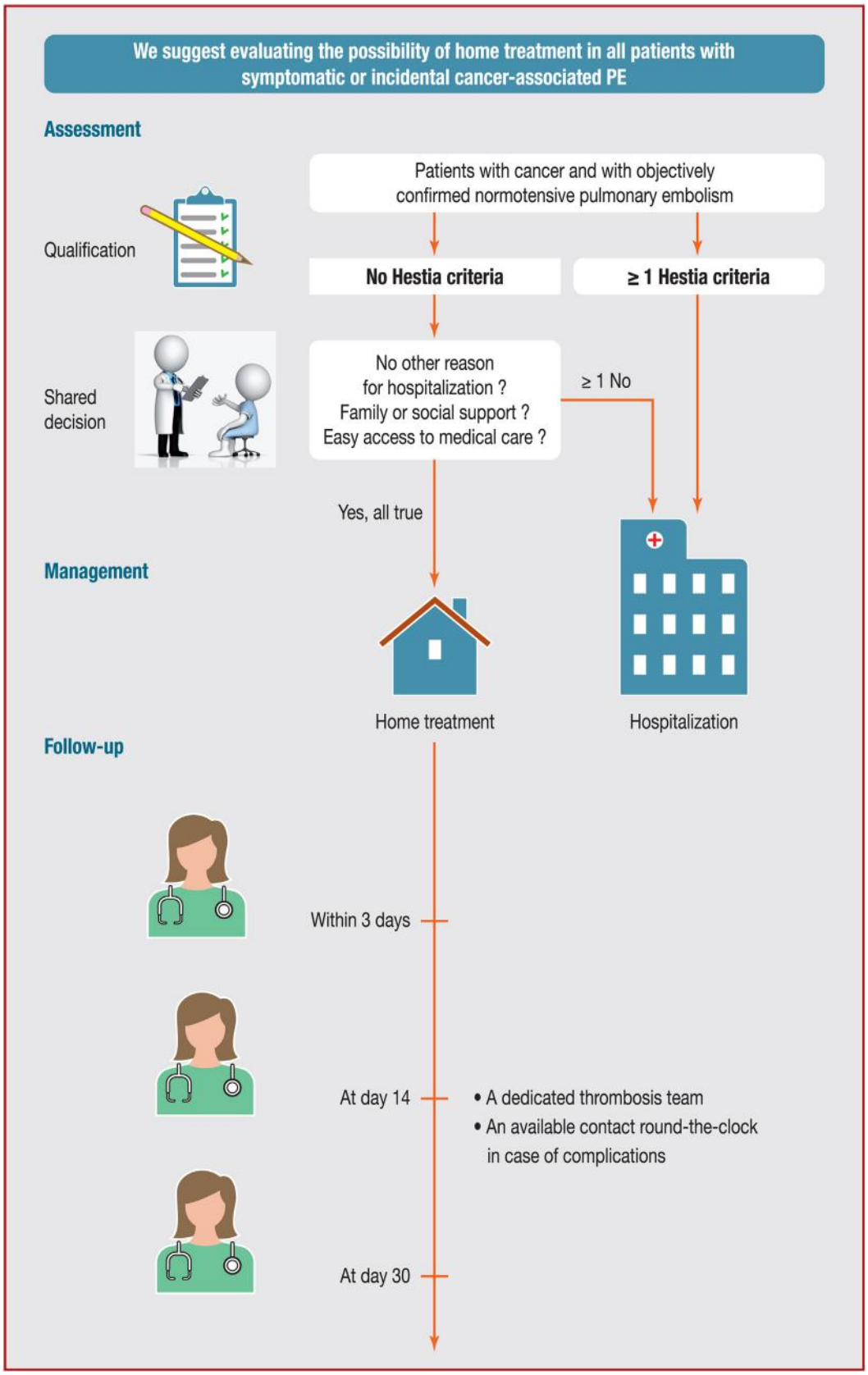
  - if appropriate outpatient care and anticoagulant treatment can be provided,
  - taking into account the patient's preference and expected compliance,
  - if the coordinating centre can organise close community follow-up with a "dedicated thrombosis team" and a contact available around-the-clock in case of complications.
  - Expert panel ranking: 3.82 out of 4.00.

- We suggest the following close follow-up in relation with the referring clinicians (GP, oncologist. . .) for all cancer patients with VTE treated at home:

  - within three days of diagnosis or discharge from the emergency department, a medical or advanced practice nurse consultation should be organised with the following goals:

    – to confirm the PE or DVT diagnosis and severity objectively,
    – to validate the nature of the anticoagulant treatment regimen (molecule, dose. . .),
    – to provide advice on VTE and its treatment,
    – to summarise the main information in a medical report for distribution to other key healthcare professionals in relation with the patient.

  - At day 14: a medical or advanced practice nurse consultation or a telephone contact to be organised.
  - At day 30: a medical or advanced practice nurse consultation to be organised.
  - Expert panel ranking: 3.61 out of 4.00.



Central Illustration. Proposals for home management of patients with cancer and pulmonary embolism.

Box 1: Search strategy for the literature review.

Key words	Pulmonary embolism OR Deep vein thrombosis OR Venous thromboembolism AND Home treatment OR Outpatient treatment OR Early discharge AND Cancer
Additional filters	Full text AND (Meta-analysis OR Randomised controlled trial OR Review OR Systematic review)
Time frame	Last 10 years

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Appendix A. Literature Search

The search was performed in the National Library of Medicine (PubMed, https://pubmed.ncbi.nlm.nih.gov/) database, accessed on 31st January 2023, using the following terms presented in the Box 1 below. The search was restricted to English and French articles. Articles were then selected according to their relevance and reliability after discussion between the study group. Additional references were selected manually on a case-by-case basis through searches in the references of relevant articles.

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Appendix D. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.acvd.2023.11.012.

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Dr. Sevestre, Dr. Gaboreau, Dr. Benmaziane and Dr. Espitia declare that they have no competing interest.

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