Triaging acute pulmonary embolism for home treatment by Hestia or simplified PESI criteria: the HOME-PE randomized trial

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Received 2 December 2020; revised 2 February 2021; editorial decision 28 May 2021; accepted 2 June 2021; online publish-ahead-of-print 7 August 2021

See page 3158 for the editorial comment on this article (doi:10.1093/eurheartj/ehab491)
Aims

The aim of this study is to compare the Hestia rule vs. the simplified Pulmonary Embolism Severity Index (sPESI) for triaging patients with acute pulmonary embolism (PE) for home treatment.

Methods and results

Normotensive patients with PE of 26 hospitals from France, Belgium, the Netherlands, and Switzerland were randomized 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 hospitalization was required. The main outcomes were the 30-day composite of recurrent venous thromboembolism, major bleeding or all-cause death (non-inferiority analysis with 2.5% absolute risk difference as margin), and the rate of patients discharged home within 24 h after randomization (NCT02811237). From January 2017 through July 2019, 1975 patients were included. In the per-protocol population, the primary outcome occurred in 3.82% (34/891) in the Hestia arm and 3.57% (32/896) in the sPESI arm (P = 0.004 for non-inferiority). In the intention-to-treat population, 38.4% of the Hestia patients (378/984) were treated at home vs. 36.6% (361/986) of the sPESI patients (P = 0.41 for superiority), with a 30-day composite outcome rate of 1.33% (5/375) and 1.11% (4/359), respectively. No recurrent or fatal PE occurred in either home treatment arm.

Conclusions

For triaging PE patients, the strategy based on the Hestia rule and the strategy based on sPESI had similar safety and effectiveness. With either tool complemented by the overruling of the physician-in-charge, more than a third of patients were treated at home with a low incidence of complications.

Graphical Abstract

The international randomized HOME-PE study demonstrates that, for triaging patients with acute pulmonary embolism for home treatment, the Hestia rule and the simplified Pulmonary Embolism Severity Index, complemented by the physician’s overruling, are equally safe and efficient.
Introduction

International guidelines suggest home treatment in patients with low-risk acute pulmonary embolism (PE), when home circumstances are adequate.1,2 However, current evidence is mainly based on cohort studies using different sets of eligibility criteria.3,4 Therefore, controversy persists about the optimal triaging strategy and eligibility criteria for home treatment.3

The approach proposed by the European Society of Cardiology firstly refers to a 30-day all-cause mortality risk assessment using the Pulmonary Embolism Severity Index (PESI) or the simplified PESI (sPESI)1,5,6 (Table 1). The Hestia rule, a checklist of medical and social criteria precluding home treatment, is proposed as an alternative.7–9 (Table 2). Although the Hestia rule was not primarily designed as a risk assessment model, the rate of complications in patients treated at home on the basis of a negative Hestia rule was low in prospective cohort studies, the 3-month mortality rate ranging from 0.5% to 1%.7–9 Moreover, the strategy based on the Hestia rule may lead to a higher proportion of PE patients treated at home than the strategy based on the sPESI.10 Indeed, around 50% of normotensive PE patients were discharged home within 24 h of diagnosis in studies applying the Hestia rule alone.7–9 Conversely, in studies using the PESI or the sPESI, medical or social exclusion criteria complemented the index, leading to a proportion of patients treated at home of <30%.11,12 However, the two strategies had never been prospectively compared head-to-head.

The aim of the present trial was to compare the safety and effectiveness of the Hestia rule vs. the sPESI for triaging PE patients for home treatment, in the way they are applied in routine practice, i.e. with the possibility of the physician to overrule the triaging tool result and to take into account the patient’s opinion in a shared decision-making. Our research hypothesis was that the 30-day rate of complications of a triaging strategy based on the Hestia rule would be non-inferior to a strategy based on the sPESI and that the Hestia strategy would lead to a higher rate of patients treated at home than the sPESI strategy.

Methods

Trial design

HOME-PE study was an international randomized open-label non-inferiority trial, to compare a triaging strategy based on the Hestia rule with a strategy based on the sPESI for home treatment of patients with acute PE. The detailed trial protocol is available in the Supplementary material online. The trial was conducted in 26 hospitals from France (n = 15), Belgium (n = 5), the Netherlands (n = 5), and Switzerland (n = 1). Among them, 18 (69%) were university hospitals and 8 (31%) general hospitals. Prior to study initiation, 9 (35%) centres had a very-low level, 8 (31%) a low level, 5 (19%) an intermediate level and 4 (15%) a high level of experience in home treatment of patients with PE according to local investigators. There was no difference between university hospitals and general hospitals, 12/18 (67%) and 5/8 (62%) having a low or very-low level of experience, respectively. The study was approved by the relevant regulatory authorities and by the ethics committee CPP—Ouest I (France) for all the hospitals in France and by the ethics committee of the participating hospitals for Belgium, Switzerland, and the Netherlands. An independent Data and Safety Monitoring Board provided a timely review of data quality and safety of the clinical trial.

Keywords

Pulmonary embolism • Emergency department • Home treatment • Randomized controlled trial • Clinical decision-making • Risk assessment
international guidelines, the choice of which was left to the discretion of the physician-in-charge. All patients were followed for 90 days. They were contacted within 3 days following randomization and at 14 ± 3, 30 ± 5, and 90 ± 15 days.

Outcomes
The primary outcome of the study was the composite rate of recurrent venous thrombo-embolism (VTE), major bleeding or all-cause death within 30 days after randomization. Recurrent VTE was defined as symptomatic, objectively confirmed DVT, non-fatal or fatal PE. Major bleeding was defined according to the criteria proposed by the International Society on Thrombosis and Hemostasis. All clinical events were adjudicated by an independent event adjudication committee, whose members were unaware of group assignments.

The first secondary outcome was home treatment, strictly defined as patients discharged home within 24 h following randomization. The exact times of discharge were extracted from the patients’ administrative report forms, independently of patient allocation and whether the patient qualified for home treatment. The second secondary outcome was qualification for home treatment according to the allocated rule, i.e., patients meeting no criteria of the Hestia rule, or patients with an sPESI of 0 points.

We further assessed and compared the rate of the 30-day composite outcome in patients treated at home. Lastly, we determined and compared the applicability of both triaging tools defined as the proportion of those who qualified for home treatment.

Statistical analysis
The analyses were performed in compliance with the CONSORT statement. The analyses for the primary outcome and the two main secondary outcomes followed a hierarchical approach in three steps. The 1st step was a non-inferiority analysis of the primary outcome for the Hestia vs. the sPESI strategy and was performed in the per-protocol population by logistic regression adjusted for hospital organization regarding PE. The 2nd and 3rd steps were two-sided difference superiority analyses, with an alpha level set at 5% and were performed in the randomized population with application of the intention-to-treat principle, using the same model as for the primary outcome.

Protocol deviations were defined as disregarding of an inclusion and/or exclusion criterion and/or of the recommended delay for home discharge (patients designated for home treatment but discharged home more than 24 h after the randomization or patients designated for hospitalization but discharged within 24 h following randomization).

The absolute risk difference of the primary outcome was calculated and the upper limit of the one-sided 95% confidence interval (CI), i.e., two-sided 90% CI, was compared with the pre-specified non-inferiority margin of 2.5%. This non-inferiority margin is consistent with the International Conference on Harmonization Guidelines and lower than those used in previous studies of home treatment in acute PE. Considering this non-inferiority margin, a 5% rate of the primary outcome in each study arm, and a dropout rate of 5%, 1975 patients were needed to achieve an 80% power using a one-sided alpha level at 5%.

For all outcomes based on categorical variables, results are presented as the adjusted absolute difference in rates between the two strategies and their 95% CI. Missing data were not imputed and no adjustment for competing risk of death was performed for the secondary outcomes, recurrent VTE, and major bleeding, when assessed as binary variables at 14, 30, or 90 days of follow-up.

All statistical analyses were performed with SAS software (SAS Institute, Cary, NC, USA) and R software (R Core Team, R Foundation for Statistical Computing, Vienna, Austria). Details including patients’ recruitment, definition of the populations, and other pre-specified subgroup analyses are provided in the protocol and the statistical analysis plan of the trial.

Role of the funding source
The trial was funded by a grant from the French Health Ministry (PHRC-N-15-0480) and by an unrestricted grant of the participating hospitals in the Netherlands. Angers University Hospital sponsored the participating hospitals in France, Belgium, and Switzerland, and the Leiden University
Medical Center was the sponsor for the participating hospitals in the Netherlands. The sponsors had no role in the study design, analysis of the data or in the preparation of the manuscript.

**Results**

**Patients**

Between 2 January 2017 and 7 July 2019, 1974 patients were randomized. Four patients withdrew their consent after randomization, leaving 984 patients in the Hestia arm and 986 in the sPESI arm (Figure 1). The baseline characteristics of the randomized patients are presented in Table 3. A total of 72.6% of patients in the Hestia arm and 74.1% in the sPESI arm were treated with a direct oral anticoagulant.

**Primary outcome and clinical events**

In the overall randomized population, a protocol deviation occurred in 162 patients, 9 patients opted out of the study and 12 patients were lost to follow-up at Day 30, leaving 891 patients in the Hestia arm and 896 in the sPESI arm for the per-protocol main analysis (Figure 1). The 30-day primary composite outcome occurred in...
3.82% (34/891) in the Hestia arm and in 3.57% (32/896) in the sPESI arm, for an adjusted absolute difference of 0.20% (upper limit of the one-sided 95% CI 1.43%; \( P = 0.004 \) for non-inferiority; Table 4).

Similar results were observed in the overall intention-to-treat population: 3.93% (38/966) in the Hestia arm and 3.37% (33/978) in the sPESI arm, for an adjusted absolute difference of 0.49% (upper limit of the one-sided 95% CI 1.68%; \( P = 0.0076 \) for non-inferiority) (Table 4). The rate of the primary composite outcome and each of its components, i.e. recurrent VTE, major bleeding, and all-cause death, was comparable between the study arms at Days 14, 30, and 90 (Table 4).

Likewise, the time-to-event curves were comparable (Supplementary material online, eFigures S1–4).

**First secondary outcome**

In the Hestia arm, 38.4% (378/984) of the patients were treated at home vs. 36.6% (361/986) in the sPESI arm, for an adjusted absolute difference of 1.78% (95% CI -2.40 to 5.96; \( P = 0.41 \) for superiority; Table 4).

**Second secondary outcome and selection for home treatment**

The Hestia rule was negative in 39.4% (388/984) of patients and the sPESI was 0 points in 48.4% of patients (477/986), for an adjusted absolute difference of -8.91% (95% CI: -13.3 to -4.56; Table 4 and Figure 2).

The negative Hestia rule was overruled in 3.4% of patients (13/388): 10 patients refused home treatment and 3 had a contraindication to a low molecular weight heparin and a direct oral anticoagulant. A positive Hestia rule was overruled in 0.5% of patients (3/596): all those patients refused to be hospitalized. The sPESI of 0

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**Table 3**  
Demographic and clinical characteristics of the randomized patients at baseline

| Characteristics | Hestia strategy (N = 984) | sPESI strategy (N = 986) |
|-----------------|--------------------------|--------------------------|
| Age, years, median ± IQ | 63.5 ± 17.7 | 62.3 ± 17.5 |
| >80 years, n (%) | 185 (18.8) | 161 (16.3) |
| Female sex, n (%) | 475 (48.3) | 473 (48.0) |
| ED presentation to randomization, h, median ± IQ | 15.7 ± 16.2 | 14.5 ± 16.2 |
| Medical history, n (%) | | |
| Previous venous thrombo-embolism | 253 (25.9) | 257 (26.3) |
| Current oestrogen therapy | 54 (5.5) | 55 (5.6) |
| Bed rest >72 h within past 3 months | 122 (12.5) | 110 (11.2) |
| Surgery within past 3 months | 94 (9.6) | 86 (8.8) |
| Current pregnancy | 4 (0.8) | 2 (0.4) |
| Active cancer or remission <1 year | 148 (15.1) | 101 (10.3) |
| History of cancer or active cancer | 217 (22.2) | 183 (18.7) |
| Chronic heart failure | 42 (4.3) | 38 (3.9) |
| Chronic lung disease | 101 (10.3) | 92 (9.4) |
| PE diagnosed during anticoagulation | 44 (4.5) | 40 (4.1) |
| Signs and symptoms, n (%) | | |
| Syncope | 59 (6.0) | 42 (4.3) |
| Systolic blood pressure <100 mmHg | 23 (2.4) | 10 (1.0) |
| Heart rate ≥110 b.p.m. | 178 (18.2) | 157 (16.0) |
| Oxygen saturation <90% | 57 (5.9) | 87 (8.9) |
| Right ventricular dilatation\(^a\) | 221 (22.4) | 225 (22.8) |
| High level of troponin \(^b\) | 294 (29.9) | 268 (27.2) |
| High level of BNP or NT-proBNP \(^c\) | 190 (19.3) | 187 (18.8) |
| Anticoagulant treatment\(^d\), n (%) | | |
| Direct oral anticoagulant | 714 (72.6) | 731 (74.1) |
| Vitamin K antagonist | 50 (5.1) | 52 (5.3) |
| Low molecular weight or unfractionated heparin | 180 (18.3) | 154 (15.6) |
| Miscellaneous | 40 (4.1) | 49 (5.0) |

\(^a\)Right ventricle/left ventricle >1 on computed tomography pulmonary angiography or on transthoracic echocardiography; assessed in 819 (83%) patients in the Hestia group and 845 (85%) patients in the sPESI group.

\(^b\)Troponin level >99th percentile according to local technique; assessed in 729 (74%) patients in the Hestia group and 719 (73%) patients in the sPESI group.

\(^c\)BNP (B-type natriuretic peptide) >100 ng/L or NT-proBNP (N-terminal proBNP) >600 ng/L; assessed in 562 (57%) patients in the Hestia group and 539 (55%) patients in the sPESI group.

\(^d\)Main anticoagulant treatment, i.e. drug prescribed ≥90% of the time, within 30 days following inclusion.

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points was overruled in 28.5% of patients (136/477): 96 patients had a concomitant illness necessitating hospitalization and 13 patients a social reason for hospitalization; 13 patients required specific PE treatment, including reperfusion therapy or vena cava filter insertion according to the physician-in-charge; 11 patients refused home treatment; and 3 patients had a contra-indication to low molecular weight heparin or direct oral anticoagulant. An sPESI of 1 point or more was overruled in 3.3% of patients (17/509): all 17 patients refused to be hospitalized. Therefore, 38.4% (378/984) of the patients in the Hestia arm and 36.3% (358/986) in the sPESI arm were designated by the physician-in-charge for home treatment (Figure 2).

### Applicability of the triaging tools

The applicability of the triaging tools, i.e. the proportion of patients with a negative Hestia rule or an sPESI of 0 points, who were discharged to home in the first 24 h after randomization, was 88.4% (343/388) for the Hestia rule and 64.8% (309/477) for the sPESI, for an adjusted absolute difference of +25.3% in favour of the Hestia rule (95% CI 19.5 to 31.1; Table 4).

### Patients treated at home

The baseline characteristics of the patients treated at home are presented in Table 5. The median in-hospital length of stay...
between emergency department presentation and discharge to home was 19.2 h in the Hestia arm and 16.7 h in sPESI arm (Supplementary material online, eTable S2). In the Hestia arm, the proportion of patients older than 80 years (absolute difference +4.72%, 95% CI 1.31 to 8.14), with active cancer (+4.77%, 95% CI 0.66 to 8.87), history of cancer (+8.55%, 95% CI 3.46 to 13.63), chronic lung disease (+3.55%, 95% CI 0.31 to 6.80), and heart rate ≥110 b.p.m. (+4.63%, 95% CI 0.38 to 8.89) was higher than in the sPESI arm (Supplementary material online, eTable S3).

Within 14 days following home discharge, 9 (2.4%) and 17 (4.7%) patients had an unscheduled hospitalization in the Hestia arm and in the sPESI arm, respectively (Supplementary material online, eTable S2).

Among patients treated at home, the 30-day primary composite outcome occurred in 1.33% (5/375) of patients assigned to the Hestia arm and in 1.11% (4/359) in patients assigned to the sPESI arm (adjusted absolute difference 0.19%, 95% CI -1.15 to 1.52; Table 6). No patient suffered from fatal PE, recurrent non-fatal PE, or haemodynamic collapse in either study arm. Four out of five non-fatal major bleedings were metro- or menorrhagia, all in women receiving direct oral anticoagulant treatment. Two patients had a symptomatic extension, objectively confirmed by compression ultrasonography, of a pre-existing DVT despite anticoagulation (Supplementary material online, eTable S4).

**Further subgroup analysis**

Characteristics and outcomes of patients (i) qualified for home treatment by Hestia and sPESI, (ii) designated for home treatment after physician-in-charge overruling, and (iii) treated in hospital are shown in Supplementary material online, eTables S5, S6, eTables S7, S8, and eTables S9, S10, respectively. The outcomes were similar between the two study arms in all of these subgroup analyses.
Discussion

Principal findings

In the HOME-PE study, the Hestia rule strategy was non-inferior to the sPESI strategy for triaging normotensive PE patients for home treatment, with respect to the 30-day composite complication rate. Compared with the sPESI, the Hestia rule qualified fewer patients as eligible for home treatment but its applicability was higher, because fewer home treatment qualifications were overruled by the physician-in-charge taking into account the patient’s preference. Despite differences in the characteristics of patients treated at home, the proportion of patients discharged home within the 24 h following inclusion, did not differ between the two strategies. More than a third of PE patients were treated at home using either the Hestia rule or the sPESI, with a low 30-day rate of complications (Graphical abstract).

Meaning of the study and comparison with other studies

Several studies have previously evaluated these two triaging tools, but most of them were single-arm cohort studies precluding direct comparison of their safety, applicability, and effectiveness.3,4 To our knowledge, only two studies previously compared the sPESI and the Hestia rule. The first one was retrospective,18 and the other a single-centre observational prospective study where the investigators did not use the triaging tools for decision-making of home treatment.19 The aim of the present trial was to compare the two triaging strategies as they would be applied in routine practice, to directly guide clinical decision-making. In light of the 30-day rates of the main primary composite outcome and its individual components, our data demonstrate that, while the patients managed at home differed between the two strategies in several aspects, their safety was comparable in both the per-protocol and intention-to-treat populations. Of note, the rates

Table 5  Demographic and clinical characteristics of patients treated at home

| Characteristics                                      | Hestia strategy (N = 378) | sPESI strategy (N = 361) |
|------------------------------------------------------|---------------------------|--------------------------|
| Age, years, mean ± SD                                | 57.9 ± 16.7               | 55.4 ± 15.5              |
| >80 years, n (%)                                     | 26 (6.9)                  | 9 (2.5)                  |
| Female sex, n (%)                                    | 177 (46.8)                | 164 (45.4)               |
| ED presentation to randomization, h, median ± IQ     | 13.1 ± 15.3               | 10.0 ± 15.1              |
| Medical history, n (%)                               |                           |                          |
| Previous venous thrombo-embolism                     | 83 (22.3)                 | 106 (29.9)               |
| Current oestrogen therapy                            | 32 (8.6)                  | 32 (9.0)                 |
| Bed rest >72 h within past 3 months                  | 31 (8.3)                  | 25 (7.0)                 |
| Surgery within past 3 months                         | 38 (10.2)                 | 29 (8.2)                 |
| Current pregnancy                                    | 2 (0.5)                   | 1 (0.6)                  |
| Active cancer or remission <1 year                   | 34 (9.1)                  | 17 (4.8)                 |
| History of cancer or active cancer                   | 59 (15.9)                 | 28 (7.9)                 |
| Chronic heart failure                                | 7 (1.9)                   | 1 (0.3)                  |
| Chronic lung disease                                 | 26 (7.0)                  | 12 (3.4)                 |
| PE diagnosed during anticoagulant treatment          | 7 (1.9)                   | 10 (2.8)                 |
| Signs and symptoms at baseline, n (%)                |                           |                          |
| Syncope                                              | 10 (2.7)                  | 8 (2.2)                  |
| Systolic blood pressure <100 mmHg                    | 2 (0.5)                   | 2 (0.6)                  |
| Heart rate ≥110 b.p.m                                | 42 (11.3)                 | 24 (6.7)                 |
| Oxygen saturation <90%                               | 1 (0.5)                   | 2 (0.6)                  |
| Right ventricular dilatation a                       | 46 (12.2)                 | 44 (12.2)                |
| High level of troponin b                             | 54 (14.3)                 | 37 (10.2)                |
| High level of BNP or NT-proBNP c                      | 19 (5.0)                  | 11 (3.0)                 |
| Anticoagulant treatment d                            |                           |                          |
| Direct oral anticoagulant treatment                  | 321 (84.9)                | 315 (87.3)               |
| Vitamin K antagonist                                 | 7 (1.9)                   | 12 (3.3)                 |
| Low molecular weight heparin                         | 37 (9.8)                  | 24 (6.6)                 |
| Miscellaneous                                        | 13 (3.4)                  | 10 (2.8)                 |

a Right ventricle/left ventricle >1 on computed tomography pulmonary angiography or on transthoracic echocardiography; assessed in 312 (82%) patients in the Hestia arm and 304 (84%) patients in the sPESI arm of outpatients.

b Troponin level >99th percentile according to local technique; assessed in 242 (64%) patients in the Hestia subgroup and 218 (60%) in the sPESI subgroup of outpatients.

c BNP (B-type natriuretic peptide) >100 ng/L or NT-proBNP (N-terminal proBNP) >600 ng/L; assessed in 185 (49%) patients in the Hestia subgroup and 145 (40%) patients in the sPESI subgroup of outpatients.

d Main anticoagulant treatment, i.e. drug prescribed ≥90% of the time, within 30 days following inclusion.
of recurrent VTE and all-cause death in the overall HOME-PE population were lower than reported in historical cohorts of normotensive PE patients. Improvements of hospital adherence to evidence-based guidelines, e.g., the introduction of risk stratification-based initial management and direct oral anticoagulants, may have contributed to a clear decrease in PE mortality over time.20

Contrary to our hypotheses, a lower proportion of patients was qualified for home treatment with the Hestia rule than with the sPESI and a similar proportion of patients was actually treated at home. The 39.4% rate of patients with a negative Hestia rule was lower in our study than in Dutch hospitals, which first described and used the Hestia study. However, despite these differences in patients’ characteristics, the rate of patients managed at home was not higher from home treatment. The proportion of these patients treated at home was therefore higher in the Hestia arm than in the sPESI arm. The same findings were observed in a retrospective assessment of home treatment. The addition of these implicit criteria to the sPESI criteria could have resulted in a lower proportion of patients sent home than when only the explicit Hestia criteria would have been used. For instance, according to sPESI, patients older than 80 years or with cancer or cardiorespiratory disease are precluded from home treatment. The proportion of these patients treated at home was therefore higher in the Hestia arm than in the sPESI arm. The same findings were observed in a retrospective assessment of the Hestia study. However, despite these differences in patients’ characteristics, the rate of patients managed at home was not higher with the Hestia strategy than with the sPESI strategy. This unexpected result emphasizes the relevance and importance of physicians’ and patients’ related factors in the real-world applicability and effectiveness of the two triaging tools.

Importantly, the rate of adverse events in patients treated at home in our study was low and similar between the two triaging strategies. It compares well to that in recent studies on this topic, supporting the external validity of our study. Notably, the most commonly occurring complication was major uterine bleeding in women treated with a direct oral anticoagulant.27

Nearly, a quarter of our patients had right ventricular dilatation as assessed by echocardiography or computed tomography pulmonary angiography. How the presence of right ventricular dilatation should influence the decision to treat normotensive PE patients at home is an ongoing debate.28 The HOME-PE study was not designed to solve this issue and assessment of right ventricular function was not compulsory. However, none of the 90 patients, who had right ventricular

| Table 6  | Outcomes in patients treated at home | Hestia strategy | sPESI strategy | Adjusted absolute difference (95% CI)* |
|----------|-------------------------------------|-----------------|---------------|------------------------------------------|
|          | n of patients with event/total n of patients (%) | ceiling patients | floor patients |                                   |
| Clinical events at Day 14 | Composite of recurrent VTE, major bleeding, and all-cause death | 3/376 (0.80) | 2/360 (0.56) | +0.20% (-0.76 to 1.16) |
|          | Recurrent VTE | 0/376 (-) | 2/360 (0.56) | -0.26% (-0.62 to 0.10) |
|          | Major bleeding | 3/376 (0.80) | 0/360 (-) | +0.81% (-0.34 to 1.96) |
|          | All-cause death | 1/376 (0.27) | 0/360 (-) | +0.13% (-0.12 to 0.37) |
| Clinical events at Day 30 | Composite of recurrent VTE, major bleeding, and all-cause death | 5/375 (1.33) | 4/359 (1.11) | +0.19% (-1.15 to 1.52) |
|          | Recurrent VTE | 0/375 (-) | 2/358 (0.56) | -0.26% (-0.63 to 0.10) |
|          | Major bleeding | 5/375 (1.33) | 1/358 (0.28) | +1.07% (-0.38 to 2.53) |
|          | All-cause death | 1/375 (0.27) | 1/359 (0.28) | -0.01% (-0.36 to 0.35) |
| Clinical events at Day 90 | Composite of recurrent VTE, major bleeding, and all-cause death | 11/371 (2.96) | 5/357 (1.40) | +1.07% (-0.43 to 2.57) |
|          | Recurrent VTE | 3/369 (0.81) | 3/356 (0.84) | -0.03% (-1.38 to 1.32) |
|          | Major bleeding | 9/370 (2.43) | 2/356 (0.56) | +1.45% (-0.07 to 2.97) |
|          | All-cause death | 2/371 (0.54) | 1/357 (0.28) | +0.12% (-0.31 to 0.56) |

The total number of patients (denominator) corresponds to the number of patients in the subgroup minus the number of patients who opted out of the trial or who were lost to follow-up.

VTE, venous thromboembolism.

* Differences are expressed as absolute rate differences adjusted for hospital organization regarding PE.

The divergent original purposes of the two triaging rules, i.e., to predict 30-day mortality for the sPESI and to identify conditions precluding home treatment for the Hestia rule,27 the sPESI cannot be applied as a standalone rule to decide on the feasibility of home treatment. It requires an implicit assessment of medical or social conditions precluding home treatment. The addition of these implicit criteria to the sPESI criteria could have resulted in a lower proportion of patients sent home than when only the explicit Hestia criteria would have been used. For instance, according to sPESI, patients older than 80 years or with cancer or cardiorespiratory disease are precluded from home treatment. The proportion of these patients treated at home was therefore higher in the Hestia arm than in the sPESI arm. The same findings were observed in a retrospective assessment of the Hestia study.18 However, despite these differences in patients’ characteristics, the rate of patients managed at home was not higher with the Hestia strategy than with the sPESI strategy. This unexpected result emphasizes the relevance and importance of physicians’ and patients’ related factors in the real-world applicability and effectiveness of the two triaging tools.

Table 6

| Clinical events at Day 14 | Hestia strategy | sPESI strategy | Adjusted absolute difference (95% CI)* |
|--------------------------|-----------------|---------------|------------------------------------------|
| Composite of recurrent VTE, major bleeding, and all-cause death | 3/376 (0.80) | 2/360 (0.56) | +0.20% (-0.76 to 1.16) |
| Recurrent VTE | 0/376 (-) | 2/360 (0.56) | -0.26% (-0.62 to 0.10) |
| Major bleeding | 3/376 (0.80) | 0/360 (-) | +0.81% (-0.34 to 1.96) |
| All-cause death | 1/376 (0.27) | 0/360 (-) | +0.13% (-0.12 to 0.37) |
| Clinical events at Day 30 | Composite of recurrent VTE, major bleeding, and all-cause death | 5/375 (1.33) | 4/359 (1.11) | +0.19% (-1.15 to 1.52) |
| Recurrent VTE | 0/375 (-) | 2/358 (0.56) | -0.26% (-0.63 to 0.10) |
| Major bleeding | 5/375 (1.33) | 1/358 (0.28) | +1.07% (-0.38 to 2.53) |
| All-cause death | 1/375 (0.27) | 1/359 (0.28) | -0.01% (-0.36 to 0.35) |
| Clinical events at Day 90 | Composite of recurrent VTE, major bleeding, and all-cause death | 11/371 (2.96) | 5/357 (1.40) | +1.07% (-0.43 to 2.57) |
| Recurrent VTE | 3/369 (0.81) | 3/356 (0.84) | -0.03% (-1.38 to 1.32) |
| Major bleeding | 9/370 (2.43) | 2/356 (0.56) | +1.45% (-0.07 to 2.97) |
| All-cause death | 2/371 (0.54) | 1/357 (0.28) | +0.12% (-0.31 to 0.56) |
dilatation at presentation and were treated at home, returned to the hospital because of haemodynamic deterioration or experienced a PE recurrence or PE-related death. Similar results have been reported in another study.29

**Strengths and limitations of this study**

HOME-PE is the largest trial of PE home treatment to date, providing robust results with a narrow 95% CI on the rate of adverse events. Several strengths reinforce the generalizability of its results. HOME-PE was performed in four European countries with different healthcare organization and in 26 hospitals with, for most of them, a very low or low level of experience in home treatment of PE patients prior to study initiation. Although we had a strict randomization process, the trial was designed and conducted in real-world clinical practice. Especially, the physician-in-charge had the possibility to overrule the qualification issued from the triaging tool in each study arm and could involve the patient’s preference in the decision-making, as would occur in daily practice.

Our study also has limitations. First, we chose a pragmatic trial design over an explanatory design, since the goal of HOME-PE was to provide clinicians with robust evidence to safely triage PE patients for home treatment directly transferable into their everyday clinical practice.24 Second, HOME-PE was not formally powered to compare the rate of adverse events in the subgroups of patients treated at home, but the very low rate of complications reinforces the validity of using either triage tool. Third, participating hospitals had to set up a specific patient pathway for home treatment that may be difficult to organize in lack of local expert availability, especially in community hospitals. Finally, as a double-blind study design was not feasible, physicians may have incorporated some criteria of one rule when assessing patients randomized to the other one. Nonetheless, the characteristics of patients treated at home were different between the two study arms, confirming that the physicians made different decisions in patients assigned to the Hestia triaging strategy or to the sPESI triaging strategy.

**Implications for policy and practice**

Our findings add evidence to current guidelines supporting home treatment with either the Hestia rule or the sPESI. The sPESI consists of fewer and exclusively objective criteria but requires an additional assessment of the suitability of home treatment. The Hestia rule includes medical and social conditions that preclude home treatment. Its applicability is better but certain criteria leave room for the physician’s judgement. In our study, both strategies safely led to home treatment in more than one-third of patients. Widespread implementation of either Hestia or sPESI triaging strategy could therefore result in considerable cost savings, as more than 90% of PE patients are currently hospitalized in several European countries and in the USA.30,31 One important feature is that all participating hospitals had set up a specific patient pathway based on local experts, to organize home treatment, with timely follow-up and clear instructions for discharged patients. This may have contributed to the low rate of complications. In our view, and in line with current guidelines1,2 and with the organization in place in the countries that have a wide experience in home treatment of PE patients,3,2,3 such an organization should optimally be in place before home treatment is implemented.

**Conclusions**

For triaging normotensive PE patients for home treatment, the strategy based on the Hestia rule and the strategy based on the sPESI had similar safety and effectiveness. With either triaging tool complemented by the overruling of the physician-in-charge, more than a third of patients were treated at home, with a low rate of complications.

**Supplementary material**

Supplementary material is available at European Heart Journal online.

**Acknowledgements**

The authors thank the patients for their participation in the trial, all the investigators of the HOME-PE study group, and all the members of the different study committees. They dedicate HOME-PE to our late friend and inspirator Guy Meyer, who greatly contributed to its design and chaired the steering committee of the study.

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Funding
This work was supported by a grant from the French Health Ministry (PHRC-N-15-0480) and by an unrestricted grant of the participating hospitals in the Netherlands. Angers University Hospital sponsored the participating hospitals in France, Belgium, and Switzerland, and the Leiden University Medical Center was the sponsor for the participating hospitals in the Netherlands. The sponsors had no role in the study design, analysis of the data or in the preparation of the manuscript.

Conflict of interest: All authors have completed the ICMJE uniform disclosure form at www.icmje.org/doi/declaration and declare no support from any organization for the submitted work; no financial relationships with any organizations that might have an interest in the submitted work in the previous 3 years; no other activities that could appear to have influenced the submitted work. The following authors report, outside the submitted work, to have served as an advisor, lecturer, consultant and/or to have received grant or personal fees or non-financial support: P.M.R. from Bayer HealthCare, Boehringer Ingelheim, Bristol Myers Squibb, Pfizer, Aspen, Daichi Sankyo, and Sanofi-Aventis; A.P. from Bayer HealthCare, Boehringer Ingelheim, Bristol Myers Squibb, Roche, Aspen, Daichi Sankyo, Sanofi-Aventis, and Stago; F.K. from Bayer, Bristol Myers Squibb, Boehringer Ingelheim, MSD, Daichi Sankyo, Actelion, the Dutch thrombosis association, the Dutch Heart foundation, and the Netherlands Organisation for Health Research and Development; A.A. from APHP; F.C. from Bayer HealthCare, Boehringer Ingelheim, Bristol Myers Squibb, Astra Zeneca, Leo Pharma, and Actelion; J.S. from Boehringer Ingelheim, Bristol Myers Squibb, Pfizer, and Leo Pharma; I.M. from Stago, Bayer HealthCare, Bristol Myers Squibb, and Leo Pharma; I.Q. from Bayer HealthCare, Bristol Myers Squibb, Pfizer, and Leo Pharma; Y.B. from Bayer HealthCare, Bristol Myers Squibb, Pfizer, and Leo Pharma; N.D. from Leo Pharma, Bayer HealthCare, and Molnlycke HealthCare; G.M. from Bayer HealthCare, Bristol Myers Squibb, Pfizer, and Leo Pharma; O.S. from Bayer HealthCare, Bristol Myers Squibb, Pfizer, Daichi Sankyo, Sanofi-Aventis, Boehringer Ingelheim, Boston Scientifics, Chiesi, and MSD; O.H., A.E., L.M.J., R.L., L.F., M.D.-E., B.P., J.B., D.V., H.J., F.S., M.B., R.C., T.M., N.F., K.M., D.D., C.S., S.H., T.A.S., G.P., F.X.L., A.G., and M.S. had nothing to declare.

Ethics
This study complies with the Declaration of Helsinki. It was approved by the ethics committee CPP—Ouest II (France) for all the hospitals in France and by the ethic committee of the participating hospitals for Belgium, Switzerland, and the Netherlands.

Copyright
This study has not previously been published and is not currently submitted elsewhere.

Transparency
The corresponding author (P.M.R.) has access to the data and affirms that the manuscript is an honest, accurate, and transparent account of the study being reported; that no important aspects of the study have been omitted; and that any discrepancies from the study as planned have been explained.

Data availability
All anonymized raw data on individual patients on which the analysis, results, and conclusions reported in the paper are based are available to a third-party auditor and to researchers on reasonable request to the corresponding author.

References
1. Konstantinides SV, Meyer G, Becattini C, Bueno H, Geering GJ, Harjola VP, Huismans MW, Humbert M, Jennings CS, Jimenez D, Kucher N, Lang IM, Lankteit M, Lorusso R, Mazzolai L, Meneveau N, Ni Aine F, Prandoni P, Pruszczyn P,
