Accepted Manuscript online: 2024-12-19 Article published online: 2025-01-09



# Socioeconomic Burden of Pulmonary Embolism in Europe: Shifting Priorities and Challenges for Novel Reperfusion Strategies

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## Abstract

In-hospital case fatality related to acute pulmonary embolism (PE) has been falling since the beginning of this century. However, annual incidence rates continue to climb, and an increasing number of PE survivors need long-term follow-up, chronic anticoagulation treatment, and readmission(s) to the hospital. In European countries, median reimbursed hospital costs for acute PE are still moderate compared with the United States but can increase several-fold in patients with comorbidities and those necessitating potentially life-saving reperfusion treatment. The use of catheter-directed treatment (CDT) has constantly increased in the United States since the past decade, and it has now entered a rapid growth phase in Europe as well, estimated to reach an annual penetration rate of up to 31% among patients with intermediate–high- or high-risk PE by 2030. Ongoing randomised controlled trials are currently investigating the clinical efficacy and safety of these devices. In addition, they will deliver data permitting calculation of their cost-effectiveness in different health care reimbursement systems, by revealing the extent to which they can reduce complications and consequently the need for intensive care and the overall length of hospital stay. After discharge, key cost drivers are related to chronic cardiopulmonary diseases (other than PE itself) leading to frequent readmissions, persistent symptoms, and functional limitations which result in poor quality of life, productivity loss, and substantial indirect costs. Implementation of structured outpatient programmes with a holistic approach to post-PE care, targeting overall cardiovascular health and the patient's well-being, bears the potential to cost-effectively reduce the overall socioeconomic burden of PE.

**Keywords**
- pulmonary embolism
- burden of disease
- catheter-directed treatment
- cost effectiveness

**received**
November 4, 2024
**accepted after revision**
December 18, 2024
**accepted manuscript online**
December 19, 2024

**DOI** https://doi.org/10.1055/a-2505-8711.
**ISSN** 0340-6245.



Georg Thieme Verlag KG, Oswald-Hesse-Straße 50, 70469 Stuttgart, Germany

## Pulmonary Embolism: Recent Trends in the Acute and Chronic Disease Burden

Acute pulmonary embolism (PE) is the most serious clinical manifestation of venous thromboembolism (VTE) and a frequent cardiovascular cause of death in the population.[1,2] Observational studies from several continents reported an annual VTE incidence ranging from 0.75 to 2.69 per 1,000 population, corresponding to 1 in 12 individuals over a lifetime; in approximately one-third of the cases, PE was the primary diagnosis.[2,3] The annual incidence of acute PE continues to climb as consistently confirmed by studies from both the United States and Europe.[4–7] This fact is closely related to a globally aging population facing a physiological rise in the incidence of chronic diseases and other conditions predisposing to thrombosis.

Annual PE-related mortality rates kept falling in the first years of this century,[8,9] paralleling a decline in early case fatality.[4,10] However, frailty in the elderly is translated into consistently high in-hospital death rates after the sixth decade of life.[10] Moreover, and importantly, trends in PE mortality in the U.S. population reached an inflection point between 2006 and 2009, after which they reversed in young and middle-aged adults aged 25 to 64 years, with persistent racial/ethnic and geographic disparities.[11,12]

After discharge, an ever-increasing number of survivors of acute PE need chronic follow-up and treatment, since extended anticoagulation beyond the first 3 to 6 months is often necessary,[13,14] and up to 50% of the patients are readmitted to the hospital at least once during the first year.[15] Finally, a broad spectrum of clinical and/or functional abnormalities may persist or appear after PE, exerting a substantial impact on the patient's morbidity and quality of life over the long term.[16–19]

## The Society's Perspective: Cost Drivers in Hospitals and over the Long-Term

Cardiovascular diseases, defined by the International Statistical Classification of Diseases and Related Health Problems (ICD)-10 categories I00 to I99 in the World Health Organization (WHO) classification, were responsible for more than 1.7 million deaths in the 27 countries of the European Union (EU) in 2021.[20] Recently, a study of European country-specific data collected at multiple levels of population health care provided an updated estimate of the annual costs associated with cardiovascular disease.[21] The estimated costs totalled 155 billion euros annually, which corresponds to 11% of the total direct health care costs in the EU. However, in contrast to coronary atherosclerosis and cerebrovascular disease, no data were provided regarding the socioeconomic burden of PE at a national or European level.[21] At a much smaller scale, a cost-of-illness analysis based on data from 1,349 patients diagnosed with PE and included in a prospective European registry provided a cost estimate of 2,328 to 3,533 euros for the hospitalisation related to the acute event.[22] Earlier models based on sources from European cohort studies had given higher estimates, between 3,891 and 4,197 euros.[23] Such approximations may have limitations given the relatively small size and heterogeneity of the populations as well as the adjustments and assumptions that need to be made to account for differences between health care systems across Europe.

More recently, we analysed actual documented and reimbursed hospital costs in the acute phase of PE in the entire population of a single country, Germany, with a population of approximately 84 million.[24] Our results in almost half a million patients hospitalised with acute PE between 2016 and 2020 revealed median costs of 3,572 (interquartile range [IQR] 2,804–5,869) euros per patient, being largely in line with the earlier European estimates mentioned above. By comparison, hospitalisation costs for acute myocardial infarction amounted to 4,714 (3,166–6,586) euros and those for ischemic stroke to 5,257 (3,725–7,258) euros. Not surprisingly, the cost of illness of acute PE in this European health care system remained, over the years studied, lower than the costs reported for PE-related hospitalisations in the United States which had already reached a median as high as 10,032 (IQR 4,467–20,330) U.S. dollars in the years 2016 to 2018.[25] Age, PE severity based on right ventricular (RV) dysfunction with or without hemodynamic instability, and comorbidity reflected by the Charlson Comorbidity Index were identified, in addition to in-hospital complications (particularly bleeding), as key cost drivers in the study population by multivariable logistic regression.[24] It should be mentioned that the use of advanced reperfusion treatment options for PE, notably catheter-directed therapy (CDT), was still rare in Europe during that period and thus had no impact on hospitalisation costs.

Data on the cost of illness of PE after the acute phase are also sparse. An analysis published in 2016 built decision trees for long-term VTE outcomes, populating them with data pooled from 25 studies of various designs conducted in different European countries in the first years of the 21st century.[23] Estimated direct costs concentrated on recurrent VTE events and bleeding complications along with heparin-induced thrombocytopenia, prothrombotic syndrome, and chronic thromboembolic pulmonary hypertension. High and low estimates of cost sources were adjusted for purchasing power parity within the EU-28 and for inflation to 2,014 euros. Besides the base case model, sensitivity analyses were performed, accounting for different ratios of incident versus prevalent VTE cases. These calculations led to a broad range of estimated total costs, ranging between 3,500 and 20,000 euros per patient (for a total EU-28 population of ~427 million in 2015). Less than 50% of the costs were reportedly generated after discharge, while indirect costs were highly variable (between 12 and 44%), depending on the value attributed to premature loss of life.[23] It is possible that a substantial proportion of costs can be attributed to complications occurring during transitions of care, notably patient transfer between health care practitioners or settings.[26] In a more recent VTE registry of 1,349 patients followed over a 12-month period,[22] annual per-patient costs ranged from 9,135 to 10,620 euros; in this study, more than 70% of the costs were generated after discharge, and the total socioeconomic burden included a substantial proportion (up to 50%) of indirect costs

 

related to loss of productivity.[22] In fact, it appears that the indirect disease burden remains substantial regardless of the severity of the acute PE event since the predefined analysis of a prospective management study focusing on early discharge and home treatment of patients with low-risk PE[27] revealed indirect per-patient costs as high as 4,010 euros, or 57% of total costs, over an only 3-month follow-up period.[28]

Based on prospectively collected data from a large, multicentre cohort study of unselected consecutive patients with acute PE in Germany,[16] we calculated the cost of illness during the first year after the index event.[29] A total of 1,017 patients were enrolled at 17 centres; of these, 958 (94%; primary analysis population) completed 3-month and 837 (82%; sensitivity analysis population) 12-month follow-up. There was an average of 34 (95% confidence interval [CI] 30–39) readmissions per 100 survivors of acute PE, and the estimated average total rehospitalisation costs amounted to 1,138 (896–1,420) euros per patient included in the main analysis. This seemingly "small" average amount accounts for the fact that, although rehospitalisations were by themselves costly, many patients (in this study, the majority) were never rehospitalised during the follow-up period and thus generated no costs in this category; this is also to be expected in the general population after PE.[15] An important finding was that recurrent VTE or bleeding was the primary diagnosis in only a minority (3.7% and 4.3%, respectively) of hospital readmissions, and thus had a minor impact on the annual costs after PE (►**Fig. 1**). Instead, we identified chronic heart, lung, and kidney diseases, diabetes, and cancer as key predictors of the number and the cost of rehospitalisations. Annual median costs related to chronic anticoagulant treatment were estimated at 972 (IQR 458–1,197) euros, and costs of guidelines-recommended[1,30] follow-up outpatient visits at 181 euros per patient. Based on these results and considering an annual incidence of 98,000 hospitalisations for acute PE along with a 13% in-hospital case fatality for the most recent years available,[24] total annual direct costs *after* acute PE might conservatively be expected to range between 2,369 and 2,542 euros per patient.[29] This estimate does not include costs related to loss of productivity, which may be substantial as highlighted above.

## Catheter-directed Treatment Options: A Rapidly Evolving Field

CDT, encompassing (i) catheter-delivered (local) low-dose thrombolysis with or without ultrasound assistance,[31,32] and (ii) large-bore mechanical thrombectomy[33–35] or vacuum aspiration,[36,37] has emerged as an effective and safe reperfusion option for patients with acute PE in need of advanced treatment. The candidates for CDT are patients with haemodynamic instability or those considered to be at risk of imminent decompensation, corresponding to the high-risk and intermediate–high-risk PE category, respectively, based on clinical, imaging and laboratory findings.[1,38,39] Several CDT systems have obtained approval by the U.S. Food and Drug Administration and the European Medicines Agency.[40,41] In the United States, the use of CDT has continuously increased since 2014,[42,43] whereas European guidelines[1,41] and most health care systems await the results of ongoing randomised controlled trials with clinical endpoints before endorsing (and reimbursing) these procedures. In current clinical practice, decisions met jointly by multidisciplinary PE response teams (PERTs), established to represent the local (in a given hospital) expertise in managing severe PE cases, are the best way to streamline therapeutic procedures and optimise the allocation of the institute's resources when choosing the most appropriate reperfusion option on a case-by-case basis.[39,44–46]

How might the use of CDT options evolve in the future? Are we to expect a rapid increase as that observed in the treatment of acute coronary syndromes or, more recently, valvular heart disease? Beginning to address this question, we modelled the recent time trends of CDT use in the United States and used them as the basis for predicting future (for the period 2025–2030) rates of CDT penetration and PE hospitalisation costs in

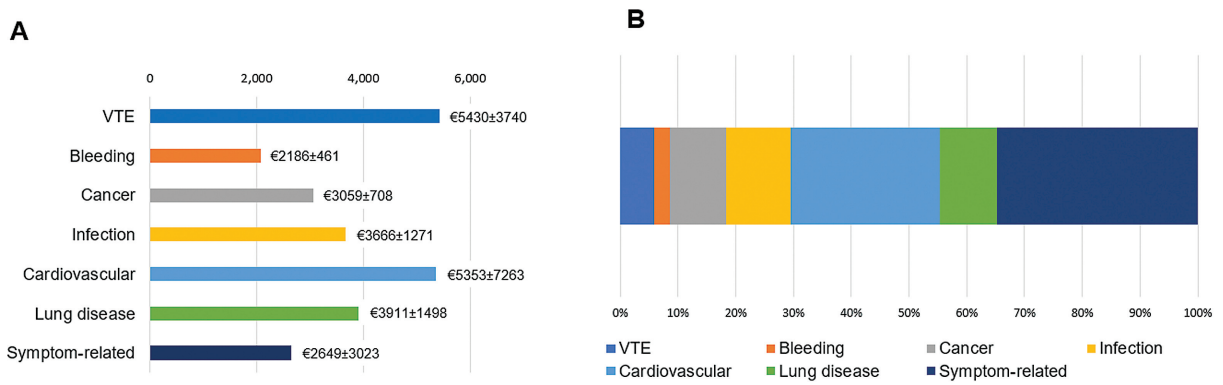


**Fig. 1** Estimated annual rehospitalisation costs in survivors of acute pulmonary embolism included in the Follow-up After Acute Pulmonary Embolism (FOCUS) study, stratified by main diagnosis on admission (based on data from ref.[29]). (**A**) Calculated hospital reimbursement (mean ± standard deviation) for each specific primary diagnosis based on the German Diagnosis-Related Groups (G-DRG) reimbursement system for the years 2023 to 2024. (**B**) Contribution of each diagnosis to total rehospitalisation costs, taking into account both the current DRG-based reimbursement and the frequency of the respective diagnosis among all rehospitalised patients in the FOCUS study. Symptom-related: admissions for which a specific symptom (such as dyspnoea or vomiting) was coded as the primary diagnosis because no other diagnosis could be established. VTE, venous thromboembolism.

 

the German health care system (►**Fig. 2**).[47] Specifically, we built two statistical models to generate an upper and a lower estimate of future monthly CDT use in patients with intermediate-risk and high-risk PE. The first model used data from the U.S. PERT™ Consortium's national quality assurance database registry, spanning the time period from 2018 to 2021. This registry includes a fairly large number of referral hospitals with expertise in CDT, thus considered appropriate to yield the upper estimate. The second model was based on data from the National Inpatient Sample (NIS) in the time period 2016 to 2020. This database represents an unselected sample of all U.S. hospital admissions, being suitable for yielding the lower, conservative estimate. Subsequently, we obtained the annual incidence of hospitalisations for PE from the German Federal Statistical Office for the most recent years available (2016–2020),[24] along with the Office's publicly available forecast for the entire German population size for the period 2025 to 2030, in a scenario of moderate birth rate, life expectancy and immigration.[48] By separately applying each United States-derived model to the predicted number of high-risk and intermediate–high-risk PE cases for this future period, we estimated an annual rate of CDT use between 11 and 31% among the candidates for advanced PE treatment[41] by the end of 2030. These rates correspond to 3.1 to 8.7% of the (approximately three times larger) entire patient population hospitalised with acute PE each year.[47]

## Determining the Cost Effectiveness of Innovative Advanced Therapies: What Parameters and Data Do We Need?

Our model based on recent U.S. trends estimates a 4.0 to 11.2% rise of Diagnosis-Related Groups-based hospital reimbursement costs in Germany by the end of the year 2030.[47] For a country with almost 100,000 hospitalisations with PE annually,[24] this might be translated into an overall increase by up to 50 million euros per year. Obviously, however, such models have limitations. First, the direct costs of catheter-directed systems and procedures for advanced PE therapy need to be determined separately for each country's hospital reimbursement system. Furthermore, and importantly, the (predicted) uptake of a new intervention and the future intervention mix as well as the current reimbursement amounts are only some of the parameters needed to determine the cost-effectiveness of a new treatment procedure in a given health care system.[49] Apart from the necessity to account for data heterogeneity and uncertainty as well as for time dependencies, including inflation adjustments and discounting,[49–51] a crucial component involves dependable data on the potential cost savings related to future growth in CDT use, both in hospital and in the long-term (►**Fig. 3**). In this context, preliminary data suggest that use of CDT may be associated with a low incidence of intracranial and other major bleeding complications as well as early decompensation mandating rescue treatment; consequently, CDT may contribute, among others, to a reduced length of treatment in an intensive care unit and an overall shorter hospital stay. However, it needs to be emphasised that the existing evidence remains weak to this date as it is mostly based on uncontrolled cohort studies with considerable heterogeneity and a high likelihood of bias in patient selection.[24,32,34,45,52,53]

Several randomised controlled trials, directly comparing various CDT procedures to the current standard of care in intermediate–high-risk or high-risk PE, are currently underway to deliver high-quality data on their efficacy and safety, and to provide the basis for calculating their cost

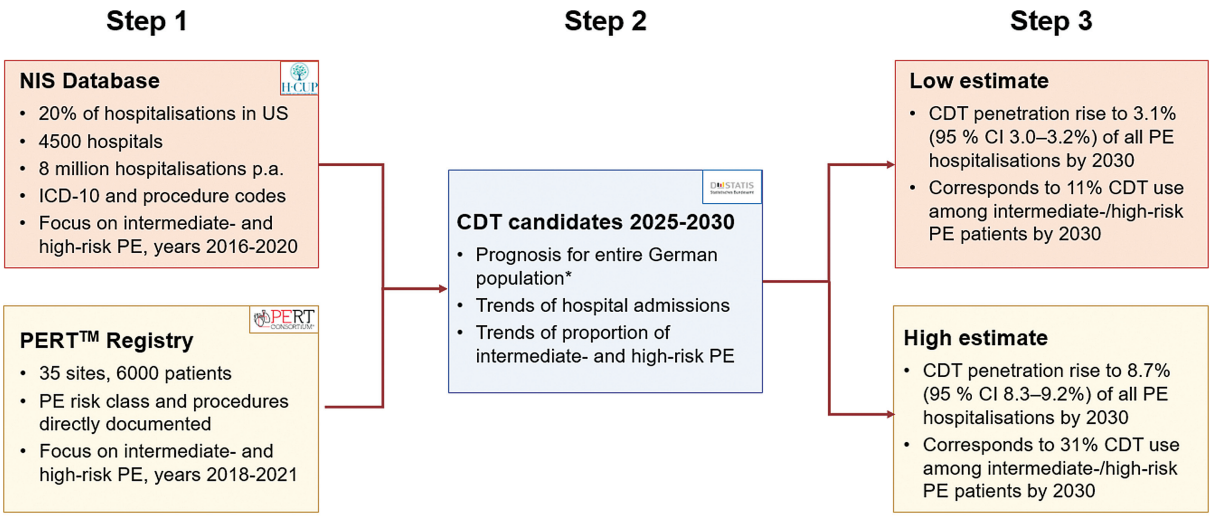


**Fig. 2** Modelling the trends of CDT use in a European country (Germany) based on the U.S. experience (adapted from ref.[47]). *Prognosis by the German Federal Bureau of statistics (DESTATIS), considering (i) a birth rate of 1.55 children per woman; (ii) a life expectancy of 84.6 years for newborn boys and 88.2 years for newborn girls; and (iii) migration rates declining from 1.3 million individuals in the year 2022 to 250,000 in 2033, thereafter remaining unchanged.[48] CDT, catheter-directed therapy; ICD-10, International Statistical Classification of Diseases and Related Health Problems; NIS, Nationwide Inpatient Sample (United States); p.a., per annum; PE, pulmonary embolism; PERT™, Pulmonary Embolism Response Teams Consortium and quality-assurance database (United States).

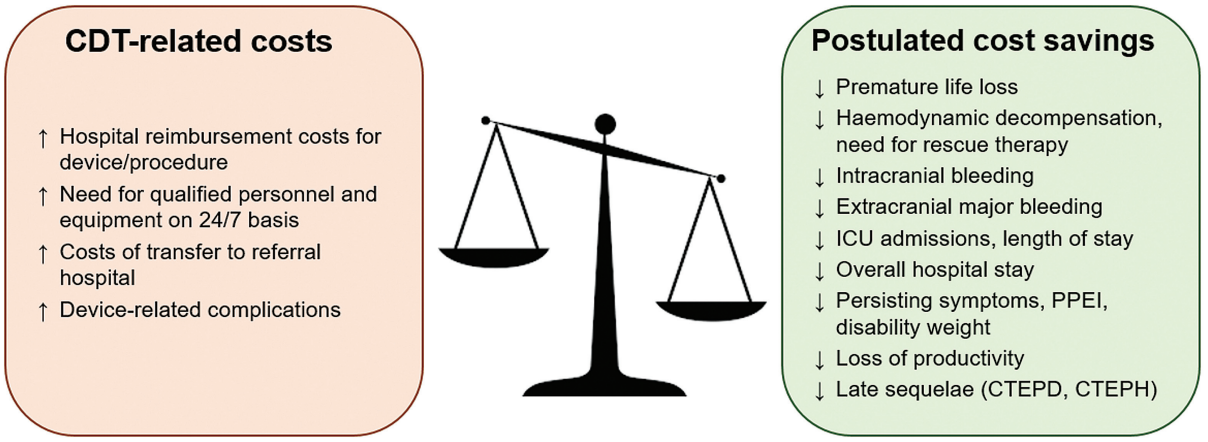


**Fig. 3** Parameters that will determine the cost-effectiveness of catheter-directed treatment based on the results of ongoing randomised controlled trials. CDT, catheter-directed treatment, with or without local thrombolysis; CTEPD, chronic thromboembolic pulmonary disease; CTEPH, chronic thromboembolic pulmonary hypertension; ICU, intensive care unit; PPEI, post-pulmonary embolism impairment (as defined in ref.[16]).

effectiveness; ►**Table 1** provides an overview of their design and endpoints. Another major trial, not included in this table, assesses the "evolution" of a pharmacological (non-catheter) approach to this PE risk category, namely reduced-dose intravenous thrombolysis.[54] Several of these trials have an adequately long follow-up period and will assess, besides the in-hospital clinical course, long-term functional outcomes, and quality of life indicators covering the entire spectrum of the so-called post-PE syndrome.[16,17] Since health economic models exist to calculate the impact of differences in quality-of-life years on both direct (reflecting the payer's perspective) and indirect (societal) costs related to loss of productivity,[55,56] the results of these trials are expected to inform not only future clinical practice guidelines but also the decisions of national policymakers regarding endorsement and reimbursement of the new procedures. Ultimately, comprehensive economic analyses will need to take into account not only the costs and potential savings of novel reperfusion strategies but also those of evolving diagnostic pathways and post-hospitalisation follow-up care.

## The Changing Landscape of Pulmonary Embolism Management: Focus on Overall Cardiovascular Health and Prevention

Progress in the management of acute PE and its long-term sequelae cannot be limited to new antithrombotic drugs or catheter interventions if it aspires to successfully reduce its overall socioeconomic burden. Preventive strategies targeting the broader spectrum of cardiovascular health deserve at least as much attention. In fact, our findings summarised above revealed that, in the era of effective and safe direct oral anticoagulants, VTE recurrence or bleeding complications no longer appear to be major determinants of the chronic disease burden imposed by PE.[29] In the future, comprehensive decentralised models, including telemedicine and integrating several specialities may lead to broader anticoagulant use and significantly reduced thromboembolic complications, especially among the elderly.[57] Furthermore, analysis of data from the German health care system showed that structured outpatient post-PE care, as recommended by current guidelines,[1,30] can be implemented without substantially increasing the costs after PE.[29] These findings add support to the establishment of outpatient follow-up programmes focusing on overall cardiovascular prevention[58] in addition to the detection and treatment of late PE complications.[55] In fact, the detrimental effects, for individuals and society, of unhealthy lifestyles on the risk of cardiovascular disease, including VTE, cannot be overemphasised.[59] Among 275,000 participants recruited from the UK Biobank, those with a high level of cardiovascular health had up to 41% lower risk of VTE over a median follow-up period of 12.6 years.[60] Obesity is a typical example in this context,[61] as is dyslipidaemia, with a recent network meta-analysis adding strong support to the notion that effective lipid-lowering may (also) reduce the disease burden of VTE.[62] However, drugs (or any other individually focused interventions) alone cannot modify behavioural patterns and lifestyle in the population,[63] and simply giving "good advice" and standard instructions to patients during ambulatory PE follow-up visits has very low chances of resulting in sustainable improvement of cardiovascular health. Moreover, these measures alone are insufficient to alleviate the frequent persisting complaints of patients having suffered acute PE, and the resulting costs related to excessive health care resource utilisation and productivity loss. By addressing this need, outpatient cardiopulmonary rehabilitation programmes may improve the patient's well-being and quality of life, also offering the potential for reduction of the chronic disease burden of PE over the long-term.[64] If successfully tested in randomised trials which are currently in the planning phase, these interventions may become the next focus of health economic analyses on the

**Table 1** Contemporary randomised controlled trials on catheter-directed treatment of pulmonary embolism*

| Study/current status | CDT system tested | Patient number/ FU duration | Main inclusion criterion | Treatment arms | Primary endpoint | Further endpoints |
|---|---|---|---|---|---|---|
| CATCH-PE (NCT05456789) Recruiting | Catheter-directed thrombectomy + local endovascular lysis | $n = 20$ FU: 12 months | Intermediate–high risk | Catheter-directed thrombectomy + local endovascular lysis *versus* SOC | • Change of RV/LV ratio (echo) | • Mortality<br>• Right heart failure<br>• Bleeding |
| HI-PEITHO (NCT04790370) Recruiting | Ultrasound-assisted catheter-directed lysis (EKOS™ endovascular system) | $n = 544$ FU: 24 months | Intermediate–high risk | Ultrasound-assisted catheter-directed lysis (CDL) versus anticoagulation | • PE-related death in hospital<br>• Hemodynamic decompensation/ collapse<br>• PE recurrence | • All individual components of the primary endpoint<br>• Change RV/LV ratio (TTE)<br>• GUSTO- und ISTH major bleeding<br>• Stroke<br>• Overall mortality<br>• Functional outcomes (6MWD, PVFS, WHO dyspnoea scale)<br>• CTEPH |
| PEERLESS (NCT05111613) Completed, main results published[65] | Catheter-directed thrombectomy (FlowTriever® system) | $n = 550$ FU: 30 days | Intermediate–high risk | Mechanical catheter-directed thrombectomy versus CDL (any system) | • Hierarchical testing: in-hospital mortality →ICB or *other major* bleeding → cardiorespiratory decompensation → ICU admission and length of stay | • All individual components of the primary endpoint<br>• Length of stay<br>• Overall and PE-related readmissions<br>• Change RV/LV ratio<br>• Functional endpoints (mMRC dyspnoea scale)<br>• QoL |
| PEERLESS II (NCT06055920) Recruiting | Catheter-directed thrombectomy (FlowTriever® system) | $n = 1200$ FU: 3 months | Intermediate–high risk | Mechanical CDT versus SOC | • Hierarchical testing: cardiorespiratory decompensation—rehospitalization for any cause—emergency therapy escalation—dyspnoea (mMRC scale) on day 2 | • All individual components of the primary endpoint<br>• BARC 3b, 3c, 5a, or 5b bleeding<br>• Overall and PE-related mortality<br>• Overall and PE-related rehospitalizations<br>• Change RV/LV ratio<br>• Functional outcomes (6MWD, mMRC scale)<br>• QoL<br>• PPEI |

 

**Table 1** (*Continued*)

| Study/current status | CDT system tested | Patient number/ FU duration | Main inclusion criterion | Treatment arms | Primary endpoint | Further endpoints |
|---|---|---|---|---|---|---|
| PERSEVERE (NCT06588634) Recruitment pending | Catheter-directed thrombectomy (FlowTriever® system) | $n = 200$ FU: 3 months | High risk | Mechanical CDT versus standard of care—reperfusion for patients with hemodynamic instability | • Hierarchical testing within 7 days of randomisation: All-cause mortality in hospital → cardiac arrest → emergency escalation of therapy → major bleeding → ECMO | • All individual components of the primary endpoint<br>• PE-related death<br>• Length of survival outside the hospital<br>• Overall and PE-related rehospitalisations<br>• Change RV/LV ratio<br>• QoL<br>• PPEI |
| PE-TRACT (NCT05591118) Recruiting | Pharmacomechanical or purely mechanical catheter-directed thrombectomy | $n = 500$ FU: 12 months | Intermediate risk with signs of RV dysfunction | CDL or mechanical CDT versus anticoagulation alone | • $PVO_2$<br>• NYHA class<br>• ISTH major bleeding | • Cardiorespiratory decompensation<br>• 6MWD<br>• SF-36 health score |
| PRAGUE-26 (NCT05493163) Recruiting | Catheter-directed thrombolysis | $n = 558$ FU: 24 months | Intermediate–high risk | CDL versus anticoagulation alone | • Overall mortality<br>• PE recurrence<br>• Cardiorespiratory decompensation/ collapse | • All individual components of the primary endpoint<br>• Primary treatment failure<br>• GUSTO- and ISTH major bleeding<br>• Stroke<br>• Hospital costs<br>• Functional outcomes (6MWD)<br>• Laboratory and imaging (echo) parameters at FU<br>• QoL<br>• CTEPH |
| STRATIFY (NCT04088292) Active, not recruiting | Ultrasound-assisted catheter-directed lysis (EKOS™ endovascular system) Low-dose IV alteplase | $n = 210$ FU: 3 months | Intermediate–high risk | 1:1:1 randomisation: CDL versus IV lysis versus anticoagulation alone | • Change in thrombus load (Miller score) on follow-up CTPA | • In-hospital mortality<br>• Bleeding<br>• Functional and imaging (echo) parameters at 3-month FU<br>• Disease-specific and generic QoL at 3-month FU |

(*Continued*)

**Table 1** (*Continued*)

| Study/current status | CDT system tested | Patient number/ FU duration | Main inclusion criterion | Treatment arms | Primary endpoint | Further endpoints |
|---|---|---|---|---|---|---|
| STRATIFY II (NCT06453876) Active, not recruiting | Catheter-directed thrombectomy (FlowTriever® system) Ultrasound-assisted catheter-directed lysis (EKOS™ endovascular system) | $n = 210$ FU: 3 months | Intermediate–high risk | 1:1:1 randomisation: Mechanical CDT versus CDL versus anticoagulation alone | • Change in thrombus load (Miller score) on follow-up CTPA | • In-hospital mortality<br>• Bleeding<br>• Length of hospital stay<br>• Functional and imaging (echo) parameters at 3-month FU<br>• Disease-specific and generic QoL at 3-month FU |
| STORM-PE (NCT05684796) Recruiting | Catheter-directed thrombectomy (Indigo® aspiration system) | $n = 100$ FU: 3 months | Intermediate-high risk | Mechanical catheter-directed aspiration versus anticoagulation alone | • Change of RV/LV ratio | • Overall mortality<br>• Length of stay<br>• TIMI major bleeding<br>• Dyspnoea (VAS)<br>• Laboratory and imaging (echo) parameters at FU |

*The Table includes active trials registered in Clinicaltrials.gov as of 30 October 2024.

Abbreviations: 6MWD, 6-minute walking distance; BARC, Bleeding Academic Research Consortium bleeding score; CDL, catheter-directed lysis; CDT, catheter-directed treatment (with or without local lysis); CTEPH, chronic thromboembolic pulmonary hypertension; CTPA, computer tomography pulmonary angiography; FU, follow-up; GUSTO, Global Use of Streptokinase and t-PA for Occluded Coronary Arteries; ICB, intracranial bleeding; ICU, intensive care unit; ISTH, International Society on Thrombosis and Haemostasis; IV, intravenous; mMRC, modified Medical Research Council dyspnoea scale; NYHA, New York Heart Association; PE, pulmonary embolism; PPEI, post-pulmonary embolism impairment; PVFS, post venous thromboembolism functional status; $PVO_2$, peak oxygen consumption; QoL, quality of life; RV/LV ratio, right to left ventricular end diastolic diameter ratio on echocardiography or CTPA; SF-36, Short-Form Health Survey-36; SOC, standard of care; TIMI, thrombolysis in myocardial ischemia; TTE, transthoracic echocardiography; VAS, visual analog scale (dyspnoea scale); WHO, World Health Organization.

way to validation of a holistic approach to PE prevention and management.

## What is known about this Topic?

- Annual incidence of PE continues to rise, and mortality rates are also rebounding in some countries.
- The burden of disease of PE extends to persisting symptoms, reduced quality of life, and late complications over the long term.
- Novel interventional reperfusion methods are rapidly entering the market, promising improved outcomes and cost savings.

## What is still needed to inform guideline recommendations and change clinical practice?

- Large ongoing randomised trials are investigating the clinical benefits of catheter-directed treatment options against the current standard of care.
- Their results will form the basis for comprehensive and robust budget impact and cost-effectiveness analyses to support endorsement and reimbursement decisions for health care systems in different countries.
- Cost-effective management of acute pulmonary embolism survivors over the long term should focus on overall cardiovascular health and prevention.

Conflict of Interest
K.M. and T.N. report no conflict of interest. S.B. reports institutional research support by the Board from Boston Scientific, Medtronic, Bayer, and Sanofi; and personal fees/honoraria from Boston Scientific, Penumbra and Viatris. S.K. reports institutional grants and personal lecture/advisory fees from Bayer AG, Daiichi Sankyo, Boston Scientific and Penumbra Inc.; and institutional grants from Inari Medical.

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