Risk stratification of outpatient management in acute venous thromboembolism

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Home treatment compared to initial hospitalization in normotensive patients with acute pulmonary embolism in the Netherlands: a cost analysis

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ABSTRACT

Background: Venous thromboembolism constitutes substantial healthcare costs amounting to about 60 million euros per year in the Netherlands. Compared to initial hospitalization, home treatment of pulmonary embolism (PE) is associated with a cost reduction. An accurate estimation of cost savings per patient treated at home is currently lacking.

Aim: The aim of this study was to compare healthcare utilization and costs during the first 3 months after a PE diagnosis in patients who are treated at home versus those who are initially hospitalized.

Methods: Patient-level data of the YEARS cohort study, including 383 normotensive patients diagnosed with PE, was used to estimate the proportion of patients treated at home, mean hospitalization duration in those who were hospitalized and rates of PE-related readmissions and complications. To correct for baseline differences within the two groups, regression analyses was performed. The primary outcome was the average total healthcare costs during a 3-month follow-up period for patients initially treated at home or in hospital.

Results: Mean hospitalization duration for the initial treatment was 0.69 days for those treated initially at home (n=181) and 4.3 days for those initially treated in hospital (n=202). Total average costs per hospitalized patient were €3.209 and €1.512 per patient treated at home. The adjusted mean difference was €1,483 (95%CI €1,181 – 1,784).

Conclusions: Home treatment of hemodynamically stable patients with acute PE was associated with an estimated net cost reduction of €1,483 per patient. This difference underlines the advantage of triage-based home treatment of these patients.

INTRODUCTION

Venous thromboembolism (VTE), consisting of pulmonary embolism (PE) and deep vein thrombosis (DVT), constitutes a major global health issue. It represents the third leading cause of vascular disease with nearly 10 million annual cases worldwide.[1-3] Therefore, the yearly economic burden of VTE is substantial. In the Netherlands costs of VTE related medical care in 2015 amounted to nearly 60 million euros, not including the costs of VTE-associated intensive care admissions, which accounted for another 8 million euro.[4]

Home treatment of VTE is associated with improvement of quality of life and prevention of hospital overcrowding. Moreover, the potential reduction of healthcare costs is a frequently suggested argument in favor of home treatment compared to initial hospitalization.[5,6] For DVT, the strategy to treat patients at home has been widely accepted since the introduction of low molecular weight heparins.[7,8] For PE, there has been a change over the last decade, as the safety and feasibility of home treatment have been shown in several large trials.[9-16] With the recent introduction of direct oral anticoagulants (DOACs) that have a better safety profile than conventional anticoagulants[17], the threshold to treat a PE patient at home has been further lowered.[18] A reduced length-of stay and resultant decrease in total hospital costs in patients treated with a DOAC has already been demonstrated.[19-21] An accurate estimation of cost saving per patient when choosing for home treatment is currently however still lacking.

We therefore aimed to evaluate the healthcare utilization and medical costs of home treatment compared to initial hospitalization in the treatment of acute PE in the setting of Dutch clinical practice.

METHODS

Patient selection

This was a post-hoc analysis of the YEARS study, performed in 12 academic and non-academic centers across the Netherlands.[22] For the present analysis, data of all normotensive outpatients who were diagnosed with acute PE and in whom home treatment may have been considered were studied, reflecting daily practice circumstances. The YEARS study was a prospective, multicenter, diagnostic management study between October 2013 to July 2015 in the Netherlands that aimed to validated the safety and efficacy of the YEARS algorithm in the diagnostic management of suspected PE.[22] Patient level data from the YEARS study was used to estimate the mean hospitalization duration of patients with confirmed PE, as well as the rates of PE-related scheduled and unscheduled readmissions. Further, we extracted details of home treatment and discharge from the original patient charts. Lastly, demographic data of PE patients in the YEARS cohort was used to adjust the health economic model for baseline characteristics and to estimate pharmaceutical costs.

Study objectives and outcomes

The primary aim of this study was to compare healthcare utilization and costs of normotensive PE patients treated at home to those treated initially in hospital. The primary outcome of this analysis was the amount of average total healthcare costs during a 3-month follow-up period.

Definitions

Acute PE was defined as intraluminal filling defects of the subsegmental or more proximal pulmonary arteries confirmed by computed tomographic pulmonary angiography (CTPA).[23] Home treatment was defined as hospital discharge within 24 hours after diagnosis of VTE. A PE-related readmission was defined as any scheduled or unscheduled visit to the outpatient clinic, emergency room or readmission in hospital due to PE-related complications, such as thoracic pain, dyspnea, major bleeding, clinically relevant non-major bleeding or (suspected) recurrent VTE.

Medical costs are reported in Euros at price level 2018 (updated using the general consumer price index, if necessary) and include pharmaceutical, radiological, and hospital costs. These reference prices are designed to reflect realistic costs and to standardize health-economic evaluations in the Netherlands.

Pharmaceutical costs

For the calculation of medication costs in the 3-month period following the PE diagnosis, we included the costs of the medication itself (including VAT) and an additional €6 pharmacy delivery costs per regular delivery.[24] Deductibles were not included in this analysis as they have to be paid by the patients themselves and are the same for both the in-hospital and outpatient treated patients. Because no individual data on types of anticoagulant were available, data on anticoagulant use were obtained from IQVIA's Real-World Data Longitudinal Prescription database (LRx, Amsterdam, The Netherlands). From anonymous patient prescription records, data on basic patient characteristics, dispensing (e.g. pharmacy, prescription date and duration), medication (e.g. generic and brand name, dosage, dosing regimen) and prescriber information were collected. The database covers approximately 75% of all prescriptions dispensed in the Netherlands, represented by both retail pharmacies and dispensing general practitioners. The price per day of apixaban use was €4.49 for the first 7 days and €2.25 thereafter. For rivaroxaban the price per day was €4.71 for the first 21 days and €2.35 thereafter. The prices per day of dabigatran and edoxaban were €2.44, with a recommended prior 5 day use of low molecular weight heparin (LMWH). For the cost of vitamin k antagonists (VKA), we included €0.09 per day, plus a 7-day run-in period with LMWH. The price of LMWH was based on the price of nadroparin, the most used LMWH in the Netherlands.[25] We used the price per day of €10.34, for a 0.8mL 19,000IE/mL syringe, closest to the recommend 171 IE/ml per kilogram for an average weight of 86 kilograms, derived as mean weight from the YEARS study cohort.[22]

Additional costs when carrying out vitamin K antagonist controls were obtained from annual reports of the Dutch thrombosis service and included the average annual costs for diagnostics and treatment in a primary care setting. For the patients with venous thromboembolism the yearly average additional costs were €333, corresponding with a 3-month costs of €83. We conservatively assumed no cost difference for treatment options and monitoring of VKA when initial therapy was started in a clinical setting or at home.[26]

Radiological costs

The costs of radiological imaging were set at € 183 and € 43 per CTPA and chest X-ray respectively.[27,28] Every PE patient in the YEARS study was diagnosed with CTPA. X-ray testing had been performed in 86% of all patients diagnosed with PE in the initial diagnostic assessment.[29]

Laboratory costs

Laboratory costs were obtained by the price level 2018 (updated using the general consumer price index, if necessary) and were derived from laboratory analysis of the 12 academic and non-academic centers and included costs for: complete blood count, kidney function, liver function, electrolytes, inflammatory markers and d-dimer.

Hospital costs

Hospital days, outpatient visits and emergency visits were valued in accordance with the reference prices from the Dutch guidelines for economic evaluations in health care, at €495, €95 and €269 respectively. This includes costs for administration, specialist time and nursing care.[27,28] Estimated hospital costs did not include ICU care, since patients with high-risk PE were not included in the YEARS study and these patients cannot be treated at home. Total hospital costs were based on the average costs per hospital day multiplied by the length of stay, as diagnosis-related group based reimbursement systems in the Dutch healthcare setting have to the substantiated with interventions and days of admission to reach to the total amount of costs.

The proportion of patients who needed an unscheduled visit to the ER or outpatient clinical ward was obtained from a post-hoc analysis of the YEARS study.[30] If patients were readmitted, we assumed a mean readmission duration of 5.0 days, obtained from previous publications.[31] The price per day for a readmission was assumed equal to the initial hospitalization. To calculate the number of planned outpatient clinic visits, we used the hospitals protocol for VTE management for patients after home treatment or initial hospitalization. As detailed data was lacking, we could not take visits to the general practitioner into account.

Statistical analysis

Total medical costs were calculated for each patient in the YEARS study cohort. For the presentation of the baseline characteristics, categorical data are presented as percentages or

as proportion and continuous variables as means with standard deviation (SD). To compare average costs of home treatment to initial hospitalization, costs for the mean hospitalization duration were compared for both treatment modalities. In multivariate analysis we will provide the adjusted cost differences with a 95% confidence interval as well as adjusted p-values for significance. To correct for baseline differences within the two groups, regression analyses will be performed to estimate a proper estimation between those initially treated at home or after hospitalization. We also planned a sensitivity analysis restricted to those patients who were admitted but discharged after 2 and 3 days, respectively, as these are likely patients that are most comparable to those treated at home. SPSS version 25.0.0 (SPSS, IBM) was used to perform all analyses.

RESULTS

Study patients

Of all 383 normotensive patients diagnosed with PE, 181 (47%) were treated at home. Overall, the mean age was 59 years (standard deviation (SD) 17), 50% was female and 12% had active malignancy at time of diagnosis. Patients initially treated at home were younger with a mean age of 56 years versus 62 years in those initially hospitalized (mean difference 6.9 years (95%CI 3.6-10.2)), and the prevalence of cardiopulmonary comorbidity was higher among those with initial hospitalization. Other baseline patient characteristics between those treated at home and initially hospitalized were comparable. Of note, relevant inter-hospital differences were observed in the proportion of patients treated initially at home treatment with percentages ranging from 13% to 83%.

Healthcare utilisation

All patients diagnosed with acute PE visited the emergency room at initial diagnosis and were subjected to laboratory testing and CTPA. The mean hospitalization duration of those treated at home was 0.69 days, whereas patients with initial hospitalization had a mean hospitalization duration of 4.3 days. The 3-month rate of total PE-associated unscheduled readmissions in patients treated at home was 9.7% versus 8.6% for initially hospitalized patients. Proportions for each type of unscheduled visit are shown in **table 1**. As part of the hospitals' VTE management protocol, all patients who required in hospital care were followed at the outpatient clinic two times at week 6 and after 3 month. For those with initial home treatment, an additional visit in the first two weeks after the index event was scheduled. The most frequent prescribed anticoagulant was rivaroxaban (56%), followed by apixaban and VKA (both 17%). Dabigatran and edoxaban were each prescribed in 5% of patients .

Healthcare costs

Initial costs for an emergency room visit with subsequent laboratorial costs were €269 and €35, respectively, independent of initial treatment modality. Average total radiological costs for each patient amounted to €220. An overview of the pharmaceutical costs are provided in **table 2.** Average hospital admission costs per patient were € 342 for home treatment compared to average cost per patient treated initially in hospital of € 2,148. Readmission costs were calculated separately for hospital readmissions, emergency room visits or unscheduled visits to the outpatient clinic. An overview of these specific extra costs are summarized in **table 2.** No relevant differences were found in total readmission costs for home treatment compared to initial hospitalization, for a mean difference of €34 (95%CI €-79 to €146).

Primary outcome

Total average costs per hospitalized patient were €3,209 and €1,512 per patient treated at home. Thus, the crude average reduction per PE patient in a 3-month follow-up period was €1,697 when selecting for home treatment. The adjusted mean difference was €1,483 (95%CI €1,181 - €1,784).

We also performed sensitivity analyses for those with a mean admission duration of two or three days, and still found considerable mean differences compared to home treatment: the adjusted mean differences were €414 (95%CI €268 - €560) and €1,115 (95%CI €900 - €1,330) respectively.

DISCUSSION

In this analysis we estimated a €1,483 reduction per acute normotensive PE patient if they were treated at home, instead of initial hospitalization. The decrease in total costs was adjusted for relevant patient characteristics and mainly driven by the reduction in costs for hospital admission. No relevant differences were found in costs for pharmacological treatment and readmissions in patients with home treatment versus those with initial hospitalization.

Global growth in healthcare expenditure demands effective cost-containment policies to keep healthcare payable. Introducing home treatment of PE as standard of care is likely to result in considerable cost savings. For example, it is estimated that US health care costs could be reduced by $1 billion per year if home treatment would have been applied properly.[32] These numbers reflect an US perspective, with globally the highest healthcare costs and also with early hospital discharge initiated in the vast minority of all PE patients.[5] Our data support these US data by showing that significant healthcare cost reductions can be realized by treating PE patients at home. Current evidence suggests that as much as 30% to 55% of patients with acute PE could be selected for home treatment, which could lead to a considerable global cost reduction.[32,33]

Table 1: Baseline characteristics and outcome for patients with acute pulmonary embolism of the YEARS study

		Home treatment (n=181)	Initial hospitalization (n=202)
Demographics			
Age, mean (SD)		56 (16)	62 (16)
Male sex, no (%)		92 (51)	96 (49)
Weight in kg, mean (SD)		85 (17)	86 (18)
Body Mass Index, mean (SD)		28 (5.4)	28 (5.3)
VTE risk factors			
COPD (%)		6 (3.3)	13 (6.6)
Heart failure (%)		2 (1.1)	6 (3.1)
Previous VTE no. (%)		49 (27)	41 (21)
	DVT	19 (11)	13 (6.6)
	PE +/- DVT	26 (14)	28 (14)
Estrogen Use (%)		23 (13)	17 (8.7)
Active malignancy no. (%)		20 (11)	26 (13)
Treatment			
Admission days, no (%)			
	0	56 (31)	
	1	125 (69)	
	2		62 (32)
	3		51 (26)
	4		21 (11)
	5		23 (12)
	6-28		38 (19)
	>28		1 (0.5)
Readmissions, no (%)			
	outpatient visit	-	2 (1.0)
	ER visit	9 (5.0)	7 (3.6)
	Admission	9 (5.0)	9 (4.6)
Diagnostic imaging performed for suspected VTE recurrence, no (%)		3 (1.7)	3 (1.5)
Major bleeding , no (%)		4 (2.2)	4 (2.0)

Abbreviations: PE, pulmonary embolism; SD, standard deviation; VTE, venous thromboembolism; DVT, Deep vein thrombosis
Data of admission days was 7 missing for seven patients

This is the first analysis focusing on costs in a detailed patient level with an accurate estimation of costs per patient. The validity and robustness of our model depends on the impact of uncertainties in key input variables. First of all, not all PE patients are candidates for home treatment. Even despite the fact that high-risk PE patients were not taken into account, not all patients who were admitted were candidates for home treatment, which is among others

Table 2: Average healthcare utilization and costs during a 3-month follow-up period, for patients initially treated at home or in hospital

Type of healthcare		Unit price	Home treatment		Hospitalization		Cost difference	Adjusted cost difference*	95% CI	p-value adjusted
			Volume	Costs	Volume	Costs				
Initial ER visit		€ 269	1	269	1	€ 269	-	-	-	-
Laboratory testing		€ 35	1	€ 35	1	€ 35	-	-	-	-
Radiological imaging	X-ray	€ 43	0.88	€ 38	0.88	€ 37.4	€ 0.03	€ 2.5	-0.7 – 5.7	0.13
	CTPA	€ 186	1	€ 186	1	€ 186	-	-	-	-
Room and board		€ 495	0.69	€ 342	4.34	€ 2,148	€ -1,806	€ -1.612	-1,900 to -1,324	< 0.001
Pharmacy		€ 228	1	€ 228	1	€ 228	-	-	-	-
PE-related readmission	Admission	€ 2,475	0.05	€ 124	0.046	€ 113	€ 11	€ 55	-55 – 164	0.33
	ER	€ 269	0.05	€ 13	0.036	€ 9	€ 4	€ -2.6	-15 – 10	0.68
	Outpatient visit	€ 95	-	0	0.01	€ 1	€ 1	€ 0.8	-2.4 – 0.78	0.31
Outpatient clinic		€ 95	3	€ 285	2	€ 190	€ 95	-	-	-
All costs				**€1,512**		**€ 3,209**	**€ -1,697**	**€ -1,483**	**€-1,784 to -1,181**	**< 0.001**

Abbreviations: CI, confidence interval; ER, emergency room; PE, pulmonary embolism; CTPA, computed tomography pulmonary angiogram

* Adjusted for : age, gender, COPD, heart failure, kidney injury, malignancy, tachycardia, oxygen administration

Definitions:

Heart failure: A history of known heart failure requiring active treatment

Kidney injury: MDRD < 60ml/min

Malignancy: Active cancer was defined as a diagnosis of cancer that occurred within 6 months before the diagnosis of index VTE (excluding basal-cell or squamous-cell carcinoma of the skin), or any treatment for cancer within the previous 6 months, or recurrent or metastatic cancer

Tachycardia: Heart rate > 100 beats/min

shown by relevant differences in baseline characteristics. These differences reflect the selection of PE patients by the Hesta criteria, selecting lower-risk PE patients eligible for home treatment.[11] With regression analysis we performed a correction for relevant baseline characteristic differences, but we acknowledge that still some degree of residual confounding may be present. Comorbid conditions that may prolong the hospital stay, e.g. delirium, were not available in the original YEARS database, and could therefore have a potential effect on the cost difference between patients treated at home or in the hospital. Even so, we think that our present cost estimate is accurate. Moreover, the clear heterogenicity of initiated home treatment between hospitals (ranging from 13% to 83%) suggest the eligibility of home treatment in a considerable proportion of PE patients with current hospitalization, which is favorable to the validity our analysis. Due to the design of our study, it was not possible to distinguish hospitalized patients who may have been candidates for home treatment from those who were not. Therefore, we performed sensitivity analysis for PE patients with a short hospitalization duration, in which still considerable cost savings were calculated.

Secondly, readmission costs did not include costs for the treatment of adverse events, i.e. major bleeding or recurrent VTE, which could underestimate the total readmission costs. However, adverse events occurred similarly in both groups and costs for readmission will largely be determined by the length of hospital admission, which was taken into account. Considering the comparable readmission rates between each initial treatment strategy, we think that our present cost estimate is reasonably accurate.

Thirdly, we could not provide differences in pharmaceutical costs between patients treated initial in hospital or at home due to lack of detailed data on medication use. However, total pharmaceutical costs were relatively low compared to the other costs and potential excessive differences within this category between both initial treatment strategies are not expected. Therefore we do not think no major changes in outcome for this analysis are expected.

Lastly, this analysis reflects a the Dutch health care setting. Cost estimates of hospitalization for VTE vary by country; for example, a study estimating costs per hospitalization for PE estimated the cost to be over $8700 in the US (where healthcare costs are generally highest globally) and over €3400 in Italy and Belgium.[34] Therefore, the generalizability of this analysis remains to be proven. We have provided our cost analysis calculator in the supplementary materials to be adapted based on local circumstances elsewhere.

To our knowledge this is the first economic comparison for home treatment of PE patients in the current literature. Strengths of this analysis include the detailed estimation of costs per patient working towards total average costs. In contrast to most research on health care and health economics using ICD-10 codes to select for patient eligibility, our database does not contain flaws caused by imperfect coding practice. Further, with patient data of both academic and non-academic centres, including smaller and larger peripheral hospitals, we consider our results representative for a daily practice cohort in the Netherlands. Lastly, although these results must be interpreted within the framework and limitations of findings of the YEARS study,

a management study with possible underrepresentation of high-risk subgroups, the YEARS algorithm was implemented as standard diagnostic strategy in all participating hospitals. Therefore, we consider the YEARS study patients representative.

In conclusion, home treatment of hemodynamically stable patients with acute PE was estimated to result in a net cost reduction of €1,483. Although, this could be a slight overestimation of real cost difference, it certainly shows the potential for major cost savings on regional or national level, if patients eligible for home treatment for acute PE are not hospitalized. Of note, we only included direct medical costs in this analysis, indirect medical costs (e.g., loss of productivity in hospitalized patients) would probably further increase the cost difference between patient treated initially in-hospital or as outpatient. With the safety and feasibility of home treatment already been proven in carefully selected patients with PE, this difference underlines the advantage of triage-based home treatment of these patients.

REFERENCES

1. Raskob GE, Angchaisuksiri P, Blanco AN, et al. Thrombosis: a major contributor to global disease burden. Arteriosclerosis, thrombosis, and vascular biology 2014;34:2363-71.
2. Barco S, Mahmoudpour SH, Valerio L, et al. Trends in mortality related to pulmonary embolism in the European Region, 2000-15: analysis of vital registration data from the WHO Mortality Database. The Lancet Respiratory medicine 2019.
3. Barco S, Valerio L, Ageno W, et al. Age-sex specific pulmonary embolism-related mortality in the USA and Canada, 2000-18: an analysis of the WHO Mortality Database and of the CDC Multiple Cause of Death database. The Lancet Respiratory medicine 2020.
4. Zorginstituut N. Screeningsrapport Systematische analyse Bloed- en immuunziekten Zinnige Zorg.
5. Stein PD, Matta F, Hughes PG, et al. Home Treatment of Pulmonary Embolism in the Era of Novel Oral Anticoagulants. Am J Med 2016;129:974-7.
6. van der Wall SJ, Hendriks SV, Huisman MV, Klok FA. Home treatment of acute pulmonary embolism: state of the art in 2018. Curr Opin Pulm Med 2018;24:425-31.
7. Koopman MM, Prandoni P, Piovella F, et al. Treatment of venous thrombosis with intravenous unfractionated heparin administered in the hospital as compared with subcutaneous low-molecular-weight heparin administered at home. The Tasman Study Group. The New England journal of medicine 1996;334:682-7.
8. Levine M, Gent M, Hirsh J, et al. A comparison of low-molecular-weight heparin administered primarily at home with unfractionated heparin administered in the hospital for proximal deep-vein thrombosis. The New England journal of medicine 1996;334:677-81.
9. Agterof MJ, Schutgens RE, Snijder RJ, et al. Out of hospital treatment of acute pulmonary embolism in patients with a low NT-proBNP level. J Thromb Haemost 2010;8:1235-41.
10. Otero R, Uresandi F, Jimenez D, et al. Home treatment in pulmonary embolism. Thromb Res 2010;126:e1-5.
11. Zondag W, Mos IC, Creemers-Schild D, et al. Outpatient treatment in patients with acute pulmonary embolism: the Hestia Study. Journal of thrombosis and haemostasis : JTH 2011;9:1500-7.
12. den Exter PL, Zondag W, Klok FA, et al. Efficacy and Safety of Outpatient Treatment Based on the Hestia Clinical Decision Rule with or without N-Terminal Pro-Brain Natriuretic Peptide Testing in Patients with Acute Pulmonary Embolism. A Randomized Clinical Trial. Am J Respir Crit Care Med 2016;194:998-1006.
13. Aujesky D, Roy PM, Verschuren F, et al. Outpatient versus inpatient treatment for patients with acute pulmonary embolism: an international, open-label, randomised, non-inferiority trial. Lancet 2011;378:41-8.
14. SJ van der Wall SH. Home treatment of acute pulmonary embolism – state of the art in 2018 Current Opinion in Pulmonary Medicine 2018.
15. Huisman MV, Barco S, Cannegieter SC, et al. Pulmonary embolism. Nature reviews Disease primers 2018;4:18028.
16. Zondag W, Kooiman J, Klok FA, Dekkers OM, Huisman MV. Outpatient versus inpatient treatment in patients with pulmonary embolism: a meta-analysis. The European respiratory journal 2013;42:134-44.
17. van der Hulle T, Kooiman J, den Exter PL, Dekkers OM, Klok FA, Huisman MV. Effectiveness and safety of novel oral anticoagulants as compared with vitamin K antagonists in the treatment of acute symptomatic venous thromboembolism: a systematic review and meta-analysis. Journal of thrombosis and haemostasis : JTH 2014;12:320-8.

18. Klok FA, Huisman MV. When I treat a patient with acute pulmonary embolism at home. Hematology American Society of Hematology Education Program 2020;2020:190-4.
19. Weeda ER, Wells PS, Peacock WF, et al. Hospital length-of-stay and costs among pulmonary embolism patients treated with rivaroxaban versus parenteral bridging to warfarin. Internal and emergency medicine 2017;12:311-8.
20. Badreldin H. Hospital length of stay in patients initiated on direct oral anticoagulants versus warfarin for venous thromboembolism: a real-world single-center study. J Thromb Thrombolysis 2018;46:16-21.
21. Basto AN, Fewel NP, Vo K, Stock EM, Ta M. Initiation of direct oral anticoagulants versus warfarin for venous thromboembolism: impact on time to hospital discharge. J Thromb Thrombolysis 2018;45:51-5.
22. van der Hulle T, Cheung WY, Kooij S, et al. Simplified diagnostic management of suspected pulmonary embolism (the YEARS study): a prospective, multicentre, cohort study. Lancet 2017;390:289-97.
23. Huisman MV, Klok FA. How I diagnose acute pulmonary embolism. Blood 2013;121:4443-8.
24. Zorginstituut N. https://www.medicijnkosten.nl/. 2019.
25. (FNT) FDTS. Samenvatting Medische Jaarverslagen 2018. https://www.fnt.nl/algemeen/jaarverslagen. . [Accessed december 2019].
26. Zorginstituut N. Evaluatie van de ervaringen en kosten van antistollingszorg. 2020.
27. Costing manual: Methodology of costing research and reference prices for economic evaluations in healthcare [in Dutch: Kostenhandleiding: Methodologie van kostenonderzoek en referentieprijzen voor economische evaluaties in de gezondheidszorg]. 2015.
28. Kanters TA, Bouwmans CAM, van der Linden N, Tan SS, Hakkaart-van Roijen L. Update of the Dutch manual for costing studies in health care. PLoS One 2017;12:e0187477.
29. van der Pol LM, Dronkers CEA, van der Hulle T, et al. The YEARS algorithm for suspected pulmonary embolism: shorter visit time and reduced costs at the emergency department. Journal of thrombosis and haemostasis : JTH 2018;16:725-33.
30. Hendriks SV, Bavalia R, T. vB, al e. Current practice patterns of outpatient management of acute pulmonary embolism: a post-hoc analysis of the YEARS study Thrombosis Research 2020;in press.
31. Amin A, Deitelzweig S, Bucior I, et al. Frequency of hospital readmissions for venous thromboembolism and associated hospital costs and length of stay among acute medically ill patients in the US. J Med Econ 2019;22:1119-25.
32. Dalen JE, Dalen JE, Jr. Unnecessary Hospitalizations for Pulmonary Embolism: Impact on US Health Care Costs. Am J Med 2016;129:899-900.
33. Vanni S, Becattini C, Nazerian P, et al. Early discharge of patients with pulmonary embolism in daily clinical practice: A prospective observational study comparing clinical gestalt and clinical rules. Thromb Res 2018;167:37-43.
34. Fernandez MM, Hogue S, Preblick R, Kwong WJ. Review of the cost of venous thromboembolism. Clinicoecon Outcomes Res 2015;7:451-62.