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ORIGINAL RESEARCH

Societal Costs of Venous Thromboembolism and Subsequent Major Bleeding Events: A National Register-Based Study

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Abstract

Aims

Detailed evidence on the societal costs of venous thromboembolism (VTE), i.e. deep vein thrombosis (DVT) and pulmonary embolism (PE), and of subsequent major bleeding events, e.g. intracranial and gastrointestinal bleedings, is limited. The objective was to estimate the average three-year societal event costs attributable to VTE and subsequent major bleedings in Denmark.

Methods and results

Based on nationwide Danish registers, each incident patient diagnosed with VTE in the period from 2004 to 2016 was identified and matched with four non-VTE patients by nearest-neighbour propensity score matching. For bleeding patients, the reference cohort was VTE patients without bleedings. Event costs in terms of VTE, DVT, PE, and major bleedings in VTE patients were measured by the "difference-in-actual-cost" method within three years after the incidence. Societal costs included healthcare costs (primary care, hospital, prescription medicine), municipality home care services, and production loss.

The study population included 74,137 VTE incident patients (DVT: 43,099; PE: 31,038), and 4,887 VTE patients with a major bleeding within three years from VTE diagnosis. The three-year attributable societal VTE event costs were 40,024 EUR (DVT: 34,509 EUR; PE: 50,083 EUR) with 53% of these costs appearing in the first incident year. Similar results for major bleedings were 51,168 EUR with 46% of these costs appearing in the first incident year.

Conclusion

The societal costs of VTE and subsequent major bleedings are substantial and ought to be considered. Estimated costs of events may be informative in evaluating the impact of preventive interventions targeting VTE and subsequent major bleedings.

Keywords

Venous thromboembolism, Major bleedings, Total costs, Societal costs

Introduction

Venous thromboembolism (VTE) is the third most common cause of death due to cardiovascular disease, after ischemic heart disease and stroke (1). In the general population, the annual incidence of VTE is around one to two diseased persons per 1,000 persons (1). Pulmonary embolism (PE) and deep vein thrombosis (DVT) constitute the two major clinical manifestations of symptomatic venous thromboembolism, with approximately half of patients having DVT and half having PE (2). The incidence of first-time VTE rises exponentially with age, with a significant increase in incidence after the age of 60 (3). With cumulative risk estimates between 7.0% and 12.9% within the first year after VTE and around 30% within 10 years, the recurrence rate of VTE is of great significance and contributes substantially to the burden of the disease (4,5). Despite advances in prophylaxis and treatment the incidence of VTE has increased in the past decades, due mostly to an increase in PE (2, 6–8). Thus, there is still a need for improvement in prevention strategies, and event cost estimates will be informative for evaluations.

Most commonly, a VTE event is treated either with a parenteral anticoagulant followed by warfarin or with one of the oral anticoagulants for at least three months after the event (9–12). Patients are treated both in the acute phase of the disease and in the immediate period after VTE to prevent recurrence. Treatment with anticoagulants is, however, associated with an increased risk of bleeding. Bleedings may be minor or major. The cumulative risk of major bleedings due to anticoagulation treatment varies from 0.6% to 2.0% within the first six months from VTE diagnosis which contributes to the burden of VTE (9–12).

The costs of VTE are substantial, yet only limited evidence from patient populations in Europe is available. A study on the annual costs associated with incident VTE events in the United States conservatively sets the direct medical costs to 7-10 billion USD each year (2014 USD), with a cost per event estimate between 18,000 USD and 23,000 USD per individual incident (13). A US modelling study estimated the direct and indirect costs of VTE annually to range between 13.5 and 69.3 billion USD (2011 USD) (14). The same model was used in a similar European study estimating the direct and indirect costs of VTE in the European Union to be 1.5-13.2 billion EUR (2014 EUR) annually. Another study, covering seven European countries, investigated the burden of PE in terms of workforce participation after PE diagnosis (15). This study found 60% of PE patients being employed at the time of diagnosis returned to work within a month, while 28% still had not returned after one year from diagnosis.

A review of studies on VTE healthcare costs from 2015 identified 18 cost studies, including 13 from the United States, four European, and one Canadian (16). The review showed that the costs of VTE are considerable and are increasing faster than the general inflation for medical care services, with hospitalisation costs as the primary cost driver. To our knowledge, however, no detailed and up-to-date population-based register studies on the societal costs (including both direct and indirect costs) of VTE and the major bleeding events in the VTE population have been published.

With this in mind, the objective of the present study was to estimate the average attributable event costs of VTE, and DVT and PE respectively, as well as the average attributable event costs of major bleeding events in VTE patients in Denmark.

Methods

A population-based follow-up study was designed using nationwide Danish registries. The study population was defined as incident VTE patients in 2004-2016 with reference cohort individuals without VTE identified by nearest-neighbour propensity matching. Cost components included primary healthcare sector costs, hospital costs (including admission and outpatient costs), prescription medicine costs, costs of municipality-provided home care services, and production loss associated with the disease. The study period for the event costs of the VTE analysis covered the first three years after the patient's VTE diagnosis. The study period for the event costs of the major bleeding analysis also covered the first three years after the bleeding event among incident patients with VTE. The last year of follow-up for all analyses was 2016.

Data sources

In Denmark, there is a long tradition of having national registers that contain detailed and exhaustive information on all residents at the individual level within several areas, including healthcare services, home care services, and labour market attachment. All Danish residents have a unique civil registration number (CPR number) which allows for the identity-secure linkage of information among the national registers.

The Danish healthcare registers include the National Patient Register, the National Health Insurance Service Register, and the Register of Medicinal Product Statistics (17). The National Patient Register contains information on all hospital admissions and outpatient visits, including diagnosis codes corresponding to the International Classification of Diseases, 10th revision (ICD-10) (18,19). The National Health Insurance Service Register contains information on the activities of health professionals under contract with the tax-funded public healthcare system, including general

practitioners, private practising medical specialists, physiotherapists, dentists, psychologists, chiropractors, and chiropodists (20), who together constitute the primary healthcare sector in Denmark. The Register of Medicinal Product Statistics contains information on all prescription medicine sold at community pharmacies. The medicine is classified according to the international Anatomical Therapeutic Chemical (ATC) Classification System (21). The Danish Register of Sickness Absence, Compensation Benefits, and Social Transfer Payments (the DREAM database) contains information on all residents regarding weekly labour market public transfer payments, e.g. unemployment benefits or disability payments (22). Information on all residents regarding home care services provided by municipalities, including home nursing and other services, are available in the Database on Elderly Documentation (23).

Study population

For the analysis of VTE event costs, we included incident patients in 2004-2016 aged 18 or older at the time of diagnosis. VTE patients in 1994-2016 were identified in the National Patient Register as patients having at least one hospital admission or outpatient contact with a primary diagnosis of VTE with ICD-10 codes I801-I803 (DVT) or I26 (PE). For 2004-2016, we identified the incident patients by using 1994-2003 as a 10-year wash-out period to estimate the date of the first VTE diagnosis. To determine the diagnosis date, we applied the first registered DVT or PE diagnosis and date from the 2004-2016 period. Incident patients in 2004-2016 were excluded if they had a registered diagnosis of atrial fibrillation or atrial flutter (ICD-10 code: I48) in 1994-2016 because the anticoagulant treatment for atrial fibrillation, atrial flutter, and VTE is similar, including the associated risk of major bleedings, with the aim to design this study to analyse major bleedings following VTE.

The included incident VTE patients were each matched with four individuals from the general population without VTE, atrial fibrillation, or atrial flutter aged 18 years or more (reference cohort). This reference cohort was identified in the Danish Civil Registration System which contains information on all Danish residents. For the matching procedure, we applied nearest-neighbour propensity score matching with an 8 to 1 digit caliper and matched individuals with VTE to those without at the beginning of the quarter in which the diseased individual was diagnosed with VTE. The matching variables in the propensity score included age, gender, and several medical conditions with relevance to the occurrence of VTE. The four identified individuals in the reference cohort were for the analysis assigned the same index date as the time of the diagnosis of VTE in the individual they were to be compared with.

For the analysis of event costs of major bleedings following a VTE diagnosis, the group of diseased individuals included all VTE patients from the study population who had a major bleeding event within three years after their VTE diagnosis. The index date was defined as the date of the first registered major bleeding event within three years from diagnosis. Major bleeding events included intracranial bleedings (ICD-10 codes: I60-I62, I690-I692, S064-S066), gastrointestinal bleedings (ICD-10 codes: K250, K252, K254, K256, K260, K262, K264, K266, K270, K272, K274, K276, K280, K282, K284, K286, K290, K920-K922), and other major bleedings (ICD-10 codes: J942, N02, R04, R31). The group of potential individuals for the reference cohort in the bleeding analysis included all VTE patients from the study population who did not experience a major bleeding event within six years after their VTE diagnosis. Again, we applied nearest-neighbour propensity score matching by using the variables described above but defined according to the bleeding diagnosis. Additionally, we applied the person's VTE incidence year as a matching variable. We identified up to four individuals in the reference cohort per diseased individual with a major bleeding. Since the VTE reference cohort without a major bleeding event most likely did not have the exact same VTE diagnosis date as their matched individuals with VTE experiencing a major bleeding, the index date for the reference cohort was defined as the date that was the same number of days after VTE diagnosis as the diseased individual's bleeding event date.

It is well known that misclassification of VTE diagnoses may occur in routine administrative registries (24). Thus, in addition to the primary study populations described above, we identified secondary study populations both for VTE and bleeding analysis with higher positive predictive values and used these populations for sensitivity analyses. The secondary study populations were restricted to VTE patients from the primary study populations who had redeemed a prescription for anticoagulant drugs within 30 days after their VTE diagnosis. This is a verified method to identify VTE patients where the positive predictive value is estimated to be 90%, according to a Danish validation study (25). We included prescriptions of the following anticoagulants (mentioned in alphabetic order) to identify the secondary study populations (ATC codes in brackets): apixaban (B01AF02), dabigatran (B01AE07), dalteparin (B01AB04), edoxaban (B01AF03), enoxaparin (B01AB05), phenprocoumon (B01AA04), rivaroxaban (new: B01AF01; old: B01AX06), tinzaparin (B01AB10), and warfarin (B01AA03).

Cost measures

Based on a societal perspective, our study included both direct and indirect costs attributable to a VTE event as well as the direct and indirect costs attributable to a major bleeding event among incident VTE patients. Direct costs included costs related to healthcare (primary and secondary sectors), prescription medicine, and municipality-provided home care services. Indirect costs included

production loss attributable to the VTE and bleeding events. Primary sector healthcare costs were available in the National Health Insurance Service Register where each registration includes the gross fee the healthcare professional received in payment for that contact. Hospital admission and outpatient costs were available in the National Patient Register where each registration includes information on the cost estimate for the hospital contact by applying the Diagnosis-Related Grouping and the Danish Outpatient Grouping systems, including charges. Costs of prescription medicine were available in the Register of Medicinal Product Statistics; each redeemed prescription includes the pharmacy selling prices (including the Danish value-added tax of 25%) which cover both the public reimbursement and the patient co-payment.

Costs related to home care services were estimated by using the weekly and hourly fees for municipality-provided home care per individual, available in the Database on Elderly Documentation and multiplied by the hourly wages for social and healthcare workers in private homes available from Statistics Denmark (26). The Database on Elderly Documentation includes data from 2008 and onwards, which means the estimated home care costs are based on a smaller study population covering the period from 2008 to 2016. The indirect costs of production loss were estimated by calculating the annual production value per individual using the weekly employment data from the DREAM database. The DREAM database allowed for an estimate of the individual annual employment rate, which we multiplied with a gender-specific gross average yearly wage adjusted for the number of effective weekly working hours (27,28). The estimation of production loss included only individuals between the ages of 18 and 65 in a given year because this age range constitutes the general workforce in Denmark.

All costs were inflated to 2016 prices and converted to euros with the following exchange rate: EUR 1 = DKK 7.5. Fees in the primary and secondary healthcare sectors were inflated by using the relevant combined price and wage index for healthcare services estimated by the Danish Regions (29). Prescription medicine prices were not inflated, because the price index fluctuates inexplicably. Production values and home care costs were estimated by using wage indices at 2016 levels. In 2016, the estimated annual average labour productivity value was 72,411 EUR for men and 54,778 EUR for women.

Statistical analyses

This study included two main analyses: 1) the three-year VTE event costs and 2) the three-year event costs of a major bleeding following a VTE diagnosis. The methodology of the two analyses was the same, but the index date from which the event costs were estimated depended on the date of VTE

diagnosis and the date of the major bleeding event, respectively. All analyses were conducted for the total VTE population as well as stratified by the type of VTE (i.e. DVT and PE). Additionally, the event costs of major bleedings were stratified by the three bleeding categories: intracranial bleedings, gastrointestinal bleedings, and other major bleedings.

Average costs for each of the six cost components (primary sector costs, outpatient costs, admission costs, prescription medicine costs, home care costs, and lost production) were calculated on a yearly basis for the three-year period following the index date. The present value of the three-year event costs was calculated using a discount rate of 4% as currently recommended by the Danish Ministry of Finance (30). A Student's t-test was applied to determine cost differences between individuals with VTE and the reference cohort. Average attributable event costs were estimated for each of the cost components and for each year as the average costs of individuals with VTE or bleedings minus the average costs of the reference cohort without VTE or bleedings. The total attributable societal event costs per individual were calculated as the sum of the attributable costs of each of the cost components. The same method has also been applied by others, e.g. in a recent Danish register study by Sortsø et al. (2016) that examined the attributable costs of diabetes mellitus (31).

All analyses were conducted on Statistics Denmark's research computers via a remote access; however, prescription medicine costs were available only on group level in an isolated project environment and could not be merged on the individual level with the rest of the register data. Thus, it was not possible to test for differences in the grand total costs between individuals with VTE or bleedings and the reference cohorts.

Individuals with VTE or bleedings and the reference cohorts were censored (i.e. excluded) at death or by the end of the study period, and the individual was included and weighted with a weight factor corresponding to the fraction of the year data were available for him/her. If a diseased person died, both the diseased individual and his/her matched reference cohort individuals were censored. Similarly, if all individuals in the reference cohort within a matched group died before the diseased individual, then the diseased individual was censored at the time of the last person's death in the reference cohort. Thus, we accounted for differing lengths of follow-up. However, the maximum follow-up period of each individual was three years.

All statistical analyses were conducted in SAS version 9.4. Only anonymised data without contacts or the active participation of research subjects were used, and the present study complied with regulations of the Danish Data Protection Agency. Supplementary material is available online.

Results

A total of 91,411 unique incident VTE patients were identified in the period 2004-2016, including 51,024 DVT patients and 40,387 PE patients. Patients with an invalid CPR number or sporadic residence in Denmark (699 patients), patients below the age of 18 at the time of diagnosis (570 patients), and patients with an atrial fibrillation or atrial flutter diagnosis (16,004 patients) were excluded from the study. Additionally, one VTE patient was excluded because all four identified individuals in the reference cohort for this VTE patient died before the patient's incidence date; this was possible because the individuals with VTE were matched with their reference individuals at the beginning of the quarter of the person's VTE diagnosis. These exclusions resulted in a study population for the VTE event cost analysis of 74,137 patients, including 43,099 DVT patients and 31,038 PE patients; the matched reference cohort consisted of 296,548 individuals (

Figure 1).

The outcome of the propensity score matching procedure was very well balanced for all the selected matching variables (Table S 4). The study population had a slight preponderance of women (52.9%), and the mean age at the time of diagnosis was 63 years (60 years for DVT patients; 65 years for PE patients) (Table 1). There was significant excess mortality in the VTE group compared with the reference cohort in the immediate period after the VTE diagnosis. By the end of the first year after diagnosis, 12% of the individuals with DVT had died compared with only 2% of the matched individuals in the reference cohort. For individuals with PE, the numbers were 30% deaths versus 3% deaths for individuals in the reference cohort by the end of the first year after diagnosis.

Within the first three years after VTE diagnosis, 4,892 VTE patients experienced a major bleeding event, whereas 68,031 VTE patients did not experience a major bleeding within six years after their VTE diagnosis. This smaller group was therefore the reference cohort for analysis of the VTE patients experiencing major bleedings. Four VTE patients with a major bleeding event were excluded because we could not identify any reference patients, and one VTE patient with a major bleeding was excluded because the bleeding event was incorrectly registered after the person's date of death. This resulted in a study population for the event cost analysis of major bleedings of 4,887 VTE patients (2,496 DVT patients and 2,391 PE patients) with major bleedings and 19,413 matched VTE patients without major bleedings (

Figure 1). Again, the outcome of the propensity score matching procedure was very well balanced for all the selected matching variables for both the DVT and PE populations (Table S 5).

The average attributable societal VTE event costs summed to 22,128 EUR in the first year after diagnosis, 10,902 EUR in the second year after diagnosis, and 9,750 EUR in the third year after diagnosis (Table 2). This means that after three years these societal VTE event costs were 42,780 EUR (present value: 40,024 EUR). The societal PE event costs were 67% higher than those of DVT in the first year after diagnosis, with PE costs of 29,751 EUR and DVT costs of 17,796 EUR. PE costs were 30% higher than DVT costs in the second year after diagnosis and 17% higher in the third year. We found a significant difference in costs between the diseased individuals and the individuals without VTE in the reference cohort for all six cost types in all three years after diagnosis, except for hospital admission costs for the DVT population in the third year after diagnosis. Of the six cost types, production loss represented the largest percentage of the societal event costs in all three years after diagnosis, with an average production loss of 10,470 EUR (47%) per VTE event in the first year after diagnosis, followed by 73% of the total costs in the second year after diagnosis and 78% in the third year after diagnosis. The second-largest percentage of VTE event costs was attributed to hospital admission costs in the first year after diagnosis (6,896 EUR) and medicine costs in the second year (1,080 EUR) and third year (1,006 EUR) after diagnosis. Primary sector costs and home care costs constituted minor shares of the total societal VTE event costs.

The results of the three-year attributable VTE event costs for the secondary study population of VTE patients who had redeemed a prescription for anticoagulant drugs within 30 days after their VTE diagnosis were on the same level as the results of the primary study population (Table S 6).

The three-year attributable societal event costs of major bleedings were 51,168 EUR (present value calculated in the incidence year) on average for all major bleedings following a VTE diagnosis. Intracranial bleedings had the highest three-year attributable event costs of 92,023 EUR (DVT: 84,190 EUR; PE: 103,216 EUR) followed by gastrointestinal bleedings of 72,105 EUR (DVT: 75,409 EUR; PE: 67,655 EUR). The lowest societal costs were seen for other major bleedings: 32,327 EUR (DVT: 35,324 EUR; PE: 27,936 EUR) (Table 3). Production loss also constituted the largest share of societal costs for all types of bleedings, followed by hospital admission costs. Attributable outpatient event costs were negative for intracranial bleedings, implying that the reference cohort without bleedings had higher costs on average during the three years, compared with the group of VTE patients experiencing major bleeding events. However, this result was not significant (Table S 1-Table S 3). The attributable event costs of major bleedings were highest in the first year after the bleeding diagnosis, particularly for

intracranial bleedings. Except for production losses, none of the cost types showed significant differences, in all three years after bleeding diagnosis, between VTE patients with major bleedings and VTE patients without major bleedings (Table S 1-Table S 3).

The results of the three-year attributable event costs of major bleedings for the secondary study population of VTE patients who had redeemed a prescription for anticoagulant drugs within 30 days after their VTE diagnosis were somewhat lower than the results of the primary study population (Table S 7).

Discussion

This study provided estimates of the average three-year societal costs attributable to a VTE event and a subsequent major bleeding event among VTE patients. The three-year societal VTE event costs were substantial, with the costs being highest in the first year after diagnosis. Similar results were found upon stratifying the results into DVT and PE diagnoses. The three-year event costs of major bleedings were higher than the VTE costs, with the highest attributable costs related to intracranial bleeding, followed by gastrointestinal bleedings and then other bleedings. Furthermore, the event costs of major bleedings were highest in the first year after the bleeding event. Production loss was the dominant cost driver in all the event costs, meaning that VTE and subsequent major bleedings highly influence a patient's workforce participation.

Due to structural differences between countries in relation to healthcare costs, as well as differences in methodology, study design, population characteristics, time horizon, and the cost perspective of the analyses, it may be difficult to compare the results of the present study directly with cost estimates from other published studies. However, previous American studies estimated the attributable first-year VTE event costs at 12,000-15,000 USD (2014 USD) (13), including only direct medical costs. If we focus on our findings regarding direct medical costs, the first-year VTE event costs from our study equalled 11,296 EUR (approximately 12,750 USD), which puts our estimate on the lower end of the scale compared with the American studies.

Costs attributable to VTE and subsequent major bleedings are substantial, and together with the increasing incidence it justifies greater attention to the prevention, treatment, and management of patients. Although this study does not provide information about the health benefits behind the costs, *as this was not was not part of the study aim. However, the evidence regarding the event cost estimates provided with the study is important for the calculation of the total costs of a VTE-treatment from the broadest possible cost perspective, which has previously been carried out in*

atrial fibrillation (32). *Furthermore, the event cost estimates can be found useful in* future cost-effectiveness or cost-utility studies examining new preventive or therapeutic interventions targeting VTE and subsequent major bleeding. It is notable that production loss is the dominant cost driver in both VTE and subsequent major bleedings. Thus, prevention efforts aiming at promoting patient's work ability appear as a rewarding target for future economic evaluations.

Strengths and limitations

This study has several strengths. First, the use of national registers has helped prevent selection and information bias because all Danish residents are included. This also means that the generalisability of the results is high because the study covers all VTE incident patients (excluding VTE patients with comorbidities of atrial fibrillation or atrial flutter) above the age of 18 at the time of diagnosis in Denmark between 2004 and 2016. Second, the study population is large. Because of the large population, the cost estimates of this study are precise and the risk of random variation influencing the findings is consequently small. Another strength is the broad societal perspective, which includes home care and loss of production costs in addition to healthcare costs. Additionally, an important strength is the use of propensity score matching, which minimises the risk of confounding by gender, age, and several factors with prognostic relevance for VTE. Moreover, the data from the Danish registers are internationally considered to be some of the most comprehensive of their kind. Because of their unique content of detailed and exhaustive records at the individual level covering the entire population over a long period of time, these data are considered to be of very high quality (33–35).

We acknowledge that this study has some limitations. Not all relevant costs were included, e.g. the cost of short-term sick leave (less than 30 days), transportation time related to consultations, and non-prescription drugs. Moreover, possible costs of informal care provided by relatives or friends were not included in the estimation of costs attributable to VTE because these data are not available in the registers. Therefore, the presented societal cost estimates remain conservative. Additionally, it is important to be aware that cost data are rarely distributed normally. This applies to the costs related to home care and production loss, where several patients do not contribute with any costs: not everyone receives municipality-provided home care, and some patients are already retired before the diagnosis. Furthermore, the identification of VTE patients relies on the accuracy of the ICD-10 coding in the National Patient Register, and there might be a risk of misclassification. However, it is estimated that the secondary study populations for both VTE and bleeding analysis has been found with a high positive predictive value of 90% (25). Nevertheless, we conducted a sensitivity analysis where the study population was restricted to VTE patients in the primary study population who had redeemed a prescription for anticoagulant drugs within 30 days after their VTE diagnosis. This

secondary study population has a higher positive predictive value of their VTE diagnosis. The results of the attributable VTE event costs were very similar for the primary and secondary study populations, which supports the robustness of these results.

Conclusion

We found societal VTE event costs to be substantial in the first three years after diagnosis, with costs being highest in the first year after diagnosis. Societal PE event costs were higher than the societal DVT event costs in all three years after diagnosis. Of the six cost types included in the study, production loss represented the largest share of the societal event costs in all three years after diagnosis. The second-largest share of the VTE event costs comprised hospital admission costs in the first year after diagnosis and medicine costs in the second and third years after diagnosis. The estimated VTE event costs were statistically significant.

We also found the three-year societal event costs of a major bleeding after VTE to be substantial; the costs were highest in the first year after the bleeding event. Intracranial bleedings had the highest three-year attributable event costs, followed by gastrointestinal bleedings and other bleedings.

The societal event costs found in the present study — as a result of both VTE and major bleedings — are therefore substantial and ought to be considered. The event cost estimates presented in this study may be informative in evaluating the impact of interventions to prevent VTE or major bleedings following the treatment of VTE.

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Disclosure statement

Nina Gustafsson and Sandra Elkjær Stallknecht are employees of Incentive. Incentive was a paid vendor to Pfizer Denmark and Bristol-Myers Squibb Denmark in the present study. Søren Paaske Johnsen was a paid clinical consultant of Pfizer Denmark and Bristol-Myers Squibb Denmark in the

present study. Outside the present study Søren Paaske Johnsen received research grants from Pfizer Denmark, lecture and advisory board fees from Bristol-Myers Squibb and Pfizer, lecture fees from Boehringer Ingelheim and St Jude Medical, and lecture, consultant, and advisory board fees from Bayer. Peter Bo Poulsen and Lars Dybro are employees of Pfizer Denmark and both own shares in Pfizer Inc.

Conflict of interest

There are no other conflicts of interest in this work, besides those described in the Funding and Disclosure statement sections above.

Figure legends

Figure 1. Flow chart of the study populations

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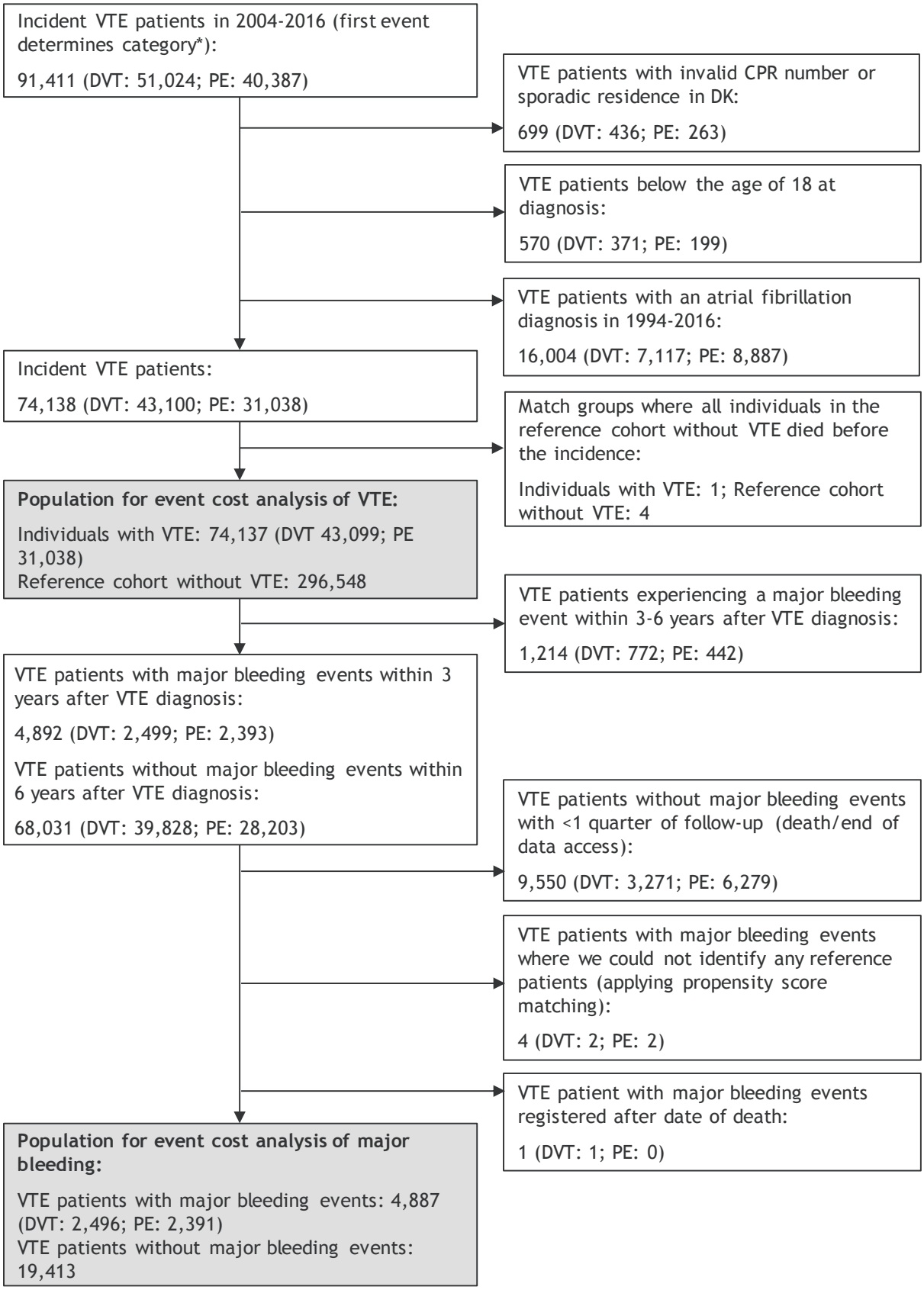
Figure 1. Flow chart of the study populations



*6,968 persons were diagnosed with both DVT and PE.

Table 1. Characteristics of the study population

	VTE	DVT	PE
Study population, N	74,137	43,099	31,038
Gender, N (%)			
Male	34,923 (47.1)	20,647 (47.9)	14,276 (46.0)
Female	39,214 (52.9)	22,452 (52.1)	16,762 (54.0)
Age at the time of diagnosis, mean (SD)	63 (17.1)	60 (17.4)	65 (16.3)
Age at the time of diagnosis, N (%)			
18-30 years	3,680 (5)	2,486 (5.8)	1,194 (3.8)
31-40 years	5,521 (7.4)	3,882 (9.0)	1,639 (5.3)
41-50 years	9,109 (12.3)	6,226 (14.4)	2,883 (9.3)
51-60 years	11,928 (16.1)	7,555 (17.5)	4,373 (14.1)
61-70 years	17,064 (23.0)	9,442 (21.9)	7,622 (24.6)
71-80 years	15,711 (21.2)	7,976 (18.5)	7,735 (24.9)
81-90 years	9,478 (12.8)	4,632 (10.7)	4,846 (15.6)
90+ years	1,646 (2.2)	900 (2.1)	746 (2.4)
All major bleedings[1], N (%)	4,887 (6.6)	2,496 (5.8)	2,391 (7.7)
Intracranial bleedings	1,609 (2.2)	790 (1.8)	819 (2.6)
Gastrointestinal bleedings	814 (1.1)	410 (1.0)	404 (1.3)
Other bleedings	2,464 (3.3)	1,296 (3.0)	1,168 (3.8)

[1]Includes the VTE patients with major bleedings in the analysis of bleeding event costs.

Table 2. Attributable VTE event costs in the first three years after diagnosis — EUR 2016 prices

	Primary sector costs	Outpatient costs	Hospital admission costs	Medicine costs	Home care costs	Production loss	Grand total, not discounted[1]	Grand total, discounted[1]	N
VTE									
Year 1	296*	2,503*	6,896*	1,601*	362*	10,470*	22,128	22,128	73,657
Year 2	154*	915*	583*	1,080*	248*	7,921*	10,902	10,483	53,750
Year 3	145*	599*	116*	1,006*	232*	7,653*	9,750	9,014	44,448
DVT									
Year 1	276*	1,920*	4,521*	1,330*	328*	9,421*	17,796	17,796	43,077
Year 2	142*	668*	384*	891*	242*	7,591*	9,918	9,537	34,270
Year 3	136*	507*	9	875*	218*	7,509*	9,255	8,556	29,103
PE									
Year 1	328*	3,464*	10,816*	2,049*	412*	12,682*	29,751	29,751	30,580
Year 2	176*	1,367*	948*	1,427*	257*	8,681*	12,858	12,363	19,480
Year 3	161*	778*	326*	1,261*	255*	8,004*	10,786	9,972	15,345

*Significant difference in costs between individuals with VTE and the reference cohort at the 5% significance level.

[1]It was not possible to test for significant differences in the grand total because the medicine costs came from a separate register that could not be merged on the patient level with the rest of the register data.

Table 3. Three-year attributable event costs of major bleedings[1] after VTE diagnosis (present value calculated in the incidence year) — EUR 2016 prices

	Primary sector costs	Outpatient costs	Hospital admission costs	Medicine costs	Home care costs	Production loss	Grand total	N
VTE								
Intracranial bleedings	1,325	-1,553	26,308	2,366	4,127	59,449	92,023	814
Gastrointestinal bleedings	311	676	13,104	2,580	1,784	53,649	72,105	1,609
Other bleedings	403	2,574	6,672	1,343	638	20,696	32,327	2,464
All major bleedings	508	1,425	11,326	1,846	1,443	34,620	51,168	4,887
DVT								
Intracranial bleedings	1,458	-580	26,940	2,138	4,095	50,139	84,190	410
Gastrointestinal bleedings	252	233	13,690	2,769	2,271	56,194	75,409	790
Other bleedings	428	2,835	7,759	1,560	538	22,203	35,324	1,296
All major bleedings	531	1,583	12,287	1,992	1,512	34,707	52,611	2,496
PE								
Intracranial bleedings	1,149	-2,887	25,188	2,612	4,079	73,075	103,216	404
Gastrointestinal bleedings	381	1,196	12,299	2,383	1,308	50,089	67,655	819
Other bleedings	372	2,208	5,220	1,018	739	18,380	27,936	1,168
All major bleedings	480	1,205	10,020	1,628	1,348	34,469	49,150	2,391

[1]Including major bleeding events occurring within the first three years after VTE diagnosis.

Supplementary material

Table S 1. Annual attributable costs of major bleeding events after VTE diagnosis, VTE population — EUR 2016 prices

	Primary sector costs	Outpatient costs	Hospital admission costs	Medicine costs	Home care costs	Production loss	Grand total, not discounted[1]	Grand total, discounted[1]	N
Intracranial bleedings									
Year 1	271*	-325	23,923*	727	1,809*	23,078*	49,483	47,580	771
Year 2	493*	-525	1,620	994	1,384*	19,813*	23,779	21,985	408
Year 3	686*	-850*	2,033	841	1,246*	21,305*	25,262	22,458	320
Gastrointestinal bleedings									
Year 1	149*	408	9,081*	868*	742*	19,568*	30,815	29,630	1,589
Year 2	95*	44	2,891*	988*	750*	18,853*	23,620	21,838	857
Year 3	90*	274	1,913*	936*	424	19,576*	23,214	20,637	632
Other bleedings									
Year 1	147*	1,937*	4,103*	702	159	8,365*	15,413	14,820	2,458
Year 2	157*	637*	1,402*	499	179	6,935*	9,808	9,068	1,660
Year 3	132*	138	1,609*	233	360	7,020*	9,492	8,438	1,256
All major bleedings									
Year 1	165*	1,163*	8,361*	755*	555*	13,425*	24,423	23,484	4,818
Year 2	186*	300	1,866*	712*	504*	11,769*	15,336	14,179	2,925
Year 3	200*	34	1,756*	520*	498*	12,182*	15,191	13,505	2,208

* Significant difference in costs between individuals with major bleedings and the reference cohort at the 5% significance level.

[1]It was not possible to test for significant differences in the grand total because the medicine costs came from a separate register that could not be merged on the patient level with the rest of the register data.

Table S 2. Annual attributable costs of major bleeding events after VTE diagnosis, DVT population — EUR 2016 prices

	Primary sector costs	Outpatient costs	Hospital admission costs	Medicine costs	Home care costs	Production loss	Grand total, not discounted[1]	Grand total, discounted[1]	N
Intracranial bleedings									
Year 1	342*	-113	22,606*	361	1,484*	20,024*	44,703	42,983	391
Year 2	526*	72	2,797*	903	1,404*	16,980*	22,683	20,971	230
Year 3	723*	-606	2,945	1,075	1,541*	17,084*	22,762	20,236	189
Gastrointestinal bleedings									
Year 1	145*	197	8,820*	1,100*	930*	20,910*	32,102	30,867	780
Year 2	52	-32	3,178*	921*	881	19,939*	24,939	23,057	447
Year 3	72	83	2,554*	968	632	19,858*	24,168	21,485	349
Other bleedings									
Year 1	148*	1,831*	4,202*	617	49	8,262*	15,109	14,528	1,295
Year 2	166*	775*	1,571*	463	192	7,565*	10,732	9,922	895
Year 3	148*	403	2,549*	606	353	8,172*	12,232	10,874	710
All major bleedings									
Year 1	176*	1,071*	8,239*	720*	493*	13,207*	23,906	22,987	2,466
Year 2	187*	440	2,212*	659*	551*	12,011*	16,060	14,848	1,572
Year 3	213*	164	2,609*	777*	593*	12,265*	16,621	14,776	1,248

*Significant difference in costs between individuals with major bleedings and the reference cohort at the 5% significance level.

[1]It was not possible to test for significant differences in the grand total because the medicine costs came from a separate register that could not be merged on the patient level with the rest of the register data.

Table S 3. Annual attributable costs of major bleeding events after VTE diagnosis, PE population — EUR 2016 prices

	Primary sector costs	Outpatient costs	Hospital admission costs	Medicine costs	Home care costs	Production loss	Grand total, not discounted[1]	Grand total, discounted[1]	N
Intracranial bleedings									
Year 1	183*	-589	25,563*	1,184	2,147*	27,150*	55,638	53,498	380
Year 2	446*	-1,344	5	1,118	1,359*	24,160*	25,744	23,802	178
Year 3	631*	-1,213	679	495	853	27,708*	29,152	25,916	131
Gastrointestinal bleedings									
Year 1	152*	629	9,353*	625*	586*	17,736*	29,080	27,961	809
Year 2	145*	132	2,556*	1,067*	625*	17,317*	21,842	20,194	410
Year 3	113	528	1,061	895*	187	19,151*	21,934	19,499	283
Other bleedings									
Year 1	146*	2,058*	3,992*	798	269	8,506*	15,768	15,161	1,163
Year 2	145*	468	1,196	543	165	6,030*	8,548	7,903	765
Year 3	109*	-229	311	-283	369	5,203*	5,480	4,871	546
All major bleedings									
Year 1	153*	1,265*	8,497*	795	614*	13,723*	25,046	24,083	2,352
Year 2	185*	128	1,444*	776*	454*	11,419*	14,406	13,319	1,353
Year 3	182*	-146	579	166	380	12,054*	13,215	11,748	960

*Significant difference in costs between individuals with major bleedings and the reference cohort at the 5% significance level.

[1]It was not possible to test for significant differences in the grand total because the medicine costs came from a separate register that could not be merged on the patient level with the rest of the register data.

Table S 4. Balance in matching criteria of study population for event costs of VTE analysis

Match variable	Register (Code)	Reference cohort without VTE N=296,552	Individuals with VTE N=74,138
Gender (female)	The Central Person Register	53%	53%
Age by the time of diagnosis (categorised)[1]	The Central Person Register	4.64 (between 51-60 and 61-70 years)	4.66 (between 51-60 and 61-70 years)
Surgery (within 90 days before diagnosis)	The National Patient Register (SKS code: KA-KQ, KX, KY)	17%	17%
Cancer (ever before diagnosis)	The National Patient Register (ICD-10 code: DC00-DC99, DD45, DD473)	22%	22%
Trauma or fracture (within 90 days before diagnosis)	The National Patient Register (ICD-10 code: DS00-DT14)	8%	8%
Pregnancy (within 90 days before diagnosis)	The National Patient Register (ICD-10 code: DO00-DO99)	1%	1%
Congenital or acquired thrombophilia (ever before diagnosis)	The National Patient Register (ICD-10 code: DD68)	1%	1%
Heart failure (ever before diagnosis)	The National Patient Register (ICD-10 code: DI50, DI110, DI130, DI132)	4%	4%
Autoimmune disorders (ever before diagnosis)	The National Patient Register (ICD-10 code: DD590, DD591, DD693, DE050, DE063, DE271, DG35, DG700, DD510, DK900, DK50, DM074, DK51, DM075, DK743, DL20, DL100, DL101, DL102, DL104, DL120, DL130, DL40, DM070-DM073, DL80, DM05, DM06, DG737D, DI328A, DI398E, DI418A, DI528A, DM08, DM45, DH221B, DM33, DM32, DG058A, DG737C, DI328B, DI398C, DL931, DL932, DN085A, DN164B, DM340-DM349, DM351, DM350, DG737A, DN164A, DD86, DG532, DH221A, DI418B, DK778B, DM633, DD690B, DI776, DL95, DM30-DM31, DM353, DM356, DM793, DN085B-DN085E, DJ841A, DJ841B, DJ841C, DH200, DH201)	11%	10%
Nephrotic syndrome (ever before diagnosis)	The National Patient Register (ICD-10 code: DN04)	<1%	<1%
Severe obesity (ever before diagnosis)	The National Patient Register (ICD-10 code: DE66)	7%	7%
Pulmonary hypertension (ever before diagnosis)	The National Patient Register (ICD-10 code: DI27)	1%	1%
Diabetes mellitus (ever before diagnosis)	The National Patient Register (ICD-10 code: DE10-DE14)	8%	8%
Ischemic stroke (ever before diagnosis)	The National Patient Register (ICD-10 code: DI63, DI64)	6%	6%
Myocardial infarction (ever before diagnosis)	The National Patient Register (ICD-10 code: DI21-DI23)	5%	5%
Bleeding history (ever before diagnosis)	The National Patient Register (ICD-10 code: DI60, DI61, DI62, DR040, DR042, DI850, DK250, DK252, DK254, DK256, DK260, DK262, DK264, DK266, DK270, DK272, DK274, DK276, DK280, DK282, DK284, DK286, DK290, DK625, DK920-DK922, DR319, DN02, DD62)	13%	13%

[1]Age is categorized in the following eight age groups: 1: 18-30 years, 2: 31-40 years, 3: 41-50 years, 4: 51-60 years, 5: 61-70 years, 6: 71-80 years, 7: 81-90 years, 8: 90+ years.

Table S 5. Balance in matching criteria of study population for event costs of major bleedings

Match variable	Register (Code)	DVT		PE	
		Without major bleeding N=9,933	With major bleeding N=2,497	Without major bleeding N=9,484	With major bleeding N=2,391
Gender (female)	The Central Person Register	42%	42%	44%	43%
Age at the time of diagnosis (categorised)[1]	The Central Person Register	5.41 (between 61-70 and 71-80 years)	5.35 (between 61-70 and 71-80 years)	5.59 (between 61-70 and 71-80 years)	5.55 (between 61-70 and 71-80 years)
Surgery (within 90 days before bleeding diagnosis)	The National Patient Register (SKS code: KA-KQ, KX, KY)	18%	19%	19%	20%
Cancer (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DC00-DC99, DD45, DD473)	28%	28%	30%	30%
Trauma or fracture (within 90 days before bleeding diagnosis)	The National Patient Register (ICD-10 code: DS00-DT14)	9%	9%	8%	8%
Pregnancy (within 90 days before bleeding diagnosis)	The National Patient Register (ICD-10 code: DO00-DO99)	0%	0%	0%	0%
Congenital or acquired thrombophilia (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DD68)	3%	3%	2%	2%
Heart failure (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DI50, DI110, DI130, DI132)	5%	5%	10%	11%
Autoimmune disorders (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DD590, DD591, DD693, DE050, DE063, DE271, DG35, DG700, DD510, DK900, DK50, DM074, DK51, DM075, DK743, DL20, DL100, DL101, DL102, DL104, DL120, DL130, DL40, DM070-DM073, DL80, DM05, DM06, DG737D, DI328A, DI398E, DI418A, DI528A, DM08, DM45, DH221B, DM33, DM32, DG058A, DG737C, DI328B, DI398C, DL931, DL932, DN085A, DN164B, DM340-DM349, DM351, DM350, DG737A, DN164A, DD86, DG532, DH221A, DI418B, DK778B, DM633, DD690B, DI776, DL95, DM30-DM31, DM353, DM356, DM793, DN085B-DN085E, DJ841A, DJ841B, DJ841C, DH200, DH201)	11%	12%	11%	11%
Nephrotic syndrome (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DN04)	0%	0%	0%	0%
Severe obesity (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DE66)	5%	5%	5%	6%
Pulmonary hypertension (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DI27)	0%	1%	2%	3%
Diabetes mellitus (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DE10-DE14)	12%	13%	11%	12%
Ischemic stroke (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DI63, DI64)	11%	11%	9%	10%
Myocardial infarction (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DI21-DI23)	4%	5%	8%	8%
Bleeding history (ever before bleeding diagnosis)	The National Patient Register (ICD-10 code: DI60, DI61, DI62, DR040, DR042, DI850, DK250, DK252, DK254, DK256, DK260, DK262, DK264, DK266, DK270, DK272, DK274, DK276, DK280, DK282, DK284, DK286, DK290, DK625, DK920-DK922, DR319, DN02, DD62)	32%	32%	29%	30%
VTE incidence year	The National Patient Register	2009.8	2009.7	2010.7	2010.7

[1]Age is categorized in the following eight age groups: 1: 18-30 years, 2: 31-40 years, 3: 41-50 years, 4: 51-60 years, 5: 61-70 years, 6: 71-80 years, 7: 81-90 years, 8: 90+ years.

Table S 6. Attributable VTE event costs in the first three years after diagnosis, secondary study population[1] — EUR 2016 prices

	Primary sector costs	Outpatient costs	Hospital admission costs	Medicine costs	Home care costs	Production loss	Grand total, not discounted[2]	Grand total, discounted[2]	N
VTE									
Year 1	359*	2,287*	6,259*	1,924*	273*	10,701*	21,803	20,965	42,509
Year 2	158*	748*	351*	1,095*	228*	7,573*	10,152	9,386	32,923
Year 3	147*	496*	-9	974*	243*	7,481*	9,334	8,298	27,242
DVT									
Year 1	339*	2,011*	4,242*	1,644*	237*	9,798*	18,271	17,568	23,942
Year 2	141*	582*	183*	878*	212*	7,379*	9,375	8,667	19,326
Year 3	135*	417*	-93	827*	221*	7,448*	8,956	7,962	16,457
PE									
Year 1	387*	2,660*	8,986*	2,303*	322*	12,285*	26,944	25,907	18,567
Year 2	182*	992*	598*	1,415*	251*	7,943*	11,382	10,523	13,597
Year 3	166*	622*	125	1,206*	278*	7,549*	9,946	8,842	10,785

*Significant difference in costs between individuals with VTE and the reference cohort at the 5% significance level.

[1]The secondary study population was restricted to VTE patients in the primary study population who had redeemed a prescription for anticoagulant drugs within 30 days after their VTE diagnosis.

[2]It was not possible to test for significant differences in the grand total because the medicine costs came from a separate register that could not be merged on the patient level with the rest of the register data.

Table S 7. Three-year attributable event costs of major bleedings[1] after VTE diagnosis for the secondary study population[2] — EUR 2016 prices

	Primary sector costs	Outpatient costs	Hospital admission costs	Medicine costs	Home care costs	Production loss	Grand total	N
VTE								
Intracranial bleedings	1,336	-984	18,847	2,743	4,129	45,876	71,947	321
Gastrointestinal bleedings	442	131	10,542	3,254	2,736	34,501	51,607	805
Other bleedings	381	1,112	4,901	1,799	696	25,478	34,367	1,498
All major bleedings	521	558	8,244	2,324	1,705	30,504	43,856	2,624
DVT								
Intracranial bleedings	1,521	-617	20,306	2,631	3,455	40,564	67,861	162
Gastrointestinal bleedings	427	210	11,436	4,043	2,694	40,521	59,331	401
Other bleedings	469	735	5,629	1,943	997	27,412	37,184	725
All major bleedings	596	399	9,245	2,634	1,804	32,933	47,610	1,288
PE								
Intracranial bleedings	1,121	-1,438	17,075	2,849	4,926	55,532	80,065	159
Gastrointestinal bleedings	459	109	9,616	2,402	2,810	25,417	40,813	404
Other bleedings	285	1,492	4,175	1,563	393	22,702	30,611	773
All major bleedings	437	730	7,222	1,943	1,617	26,963	38,912	1,336

[1]Including major bleeding events occurring within the first three years after VTE diagnosis.

[2]The secondary study population was restricted to VTE patients in the primary study population who had redeemed a prescription for anticoagulant drugs within 30 days after their VTE diagnosis.

Tables

Table 1. Characteristics of the study population

	VTE	DVT	PE
Study population, N	74,137	43,099	31,038
Gender, N (%)			
Male	34,923 (47.1)	20,647 (47.9)	14,276 (46.0)
Female	39,214 (52.9)	22,452 (52.1)	16,762 (54.0)
Age at the time of diagnosis, mean (SD)	63 (17.1)	60 (17.4)	65 (16.3)
Age at the time of diagnosis, N (%)			
18-30 years	3,680 (5)	2,486 (5.8)	1,194 (3.8)
31-40 years	5,521 (7.4)	3,882 (9.0)	1,639 (5.3)
41-50 years	9,109 (12.3)	6,226 (14.4)	2,883 (9.3)
51-60 years	11,928 (16.1)	7,555 (17.5)	4,373 (14.1)
61-70 years	17,064 (23.0)	9,442 (21.9)	7,622 (24.6)
71-80 years	15,711 (21.2)	7,976 (18.5)	7,735 (24.9)
81-90 years	9,478 (12.8)	4,632 (10.7)	4,846 (15.6)
90+ years	1,646 (2.2)	900 (2.1)	746 (2.4)
All major bleedings[1], N (%)	4,887 (6.6)	2,496 (5.8)	2,391 (7.7)
Intracranial bleedings	1,609 (2.2)	790 (1.8)	819 (2.6)
Gastrointestinal bleedings	814 (1.1)	410 (1.0)	404 (1.3)
Other bleedings	2,464 (3.3)	1,296 (3.0)	1,168 (3.8)

[1]Includes the VTE patients with major bleedings in the analysis of bleeding event costs.

Table 2. Attributable VTE event costs in the first three years after diagnosis — EUR 2016 prices

	Primary sector costs	Outpatient costs	Hospital admission costs	Medicine costs	Home care costs	Production loss	Grand total, not discounted[1]	Grand total, discounted[1]	N
VTE									
Year 1	296*	2,503*	6,896*	1,601*	362*	10,470*	22,128	22,128	73,657
Year 2	154*	915*	583*	1,080*	248*	7,921*	10,902	10,483	53,750
Year 3	145*	599*	116*	1,006*	232*	7,653*	9,750	9,014	44,448
DVT									
Year 1	276*	1,920*	4,521*	1,330*	328*	9,421*	17,796	17,796	43,077
Year 2	142*	668*	384*	891*	242*	7,591*	9,918	9,537	34,270
Year 3	136*	507*	9	875*	218*	7,509*	9,255	8,556	29,103
PE									
Year 1	328*	3,464*	10,816*	2,049*	412*	12,682*	29,751	29,751	30,580
Year 2	176*	1,367*	948*	1,427*	257*	8,681*	12,858	12,363	19,480
Year 3	161*	778*	326*	1,261*	255*	8,004*	10,786	9,972	15,345

*Significant difference in costs between individuals with VTE and the reference cohort at the 5% significance level.

[1]It was not possible to test for significant differences in the grand total because the medicine costs came from a separate register that could not be merged on the patient level with the rest of the register data.

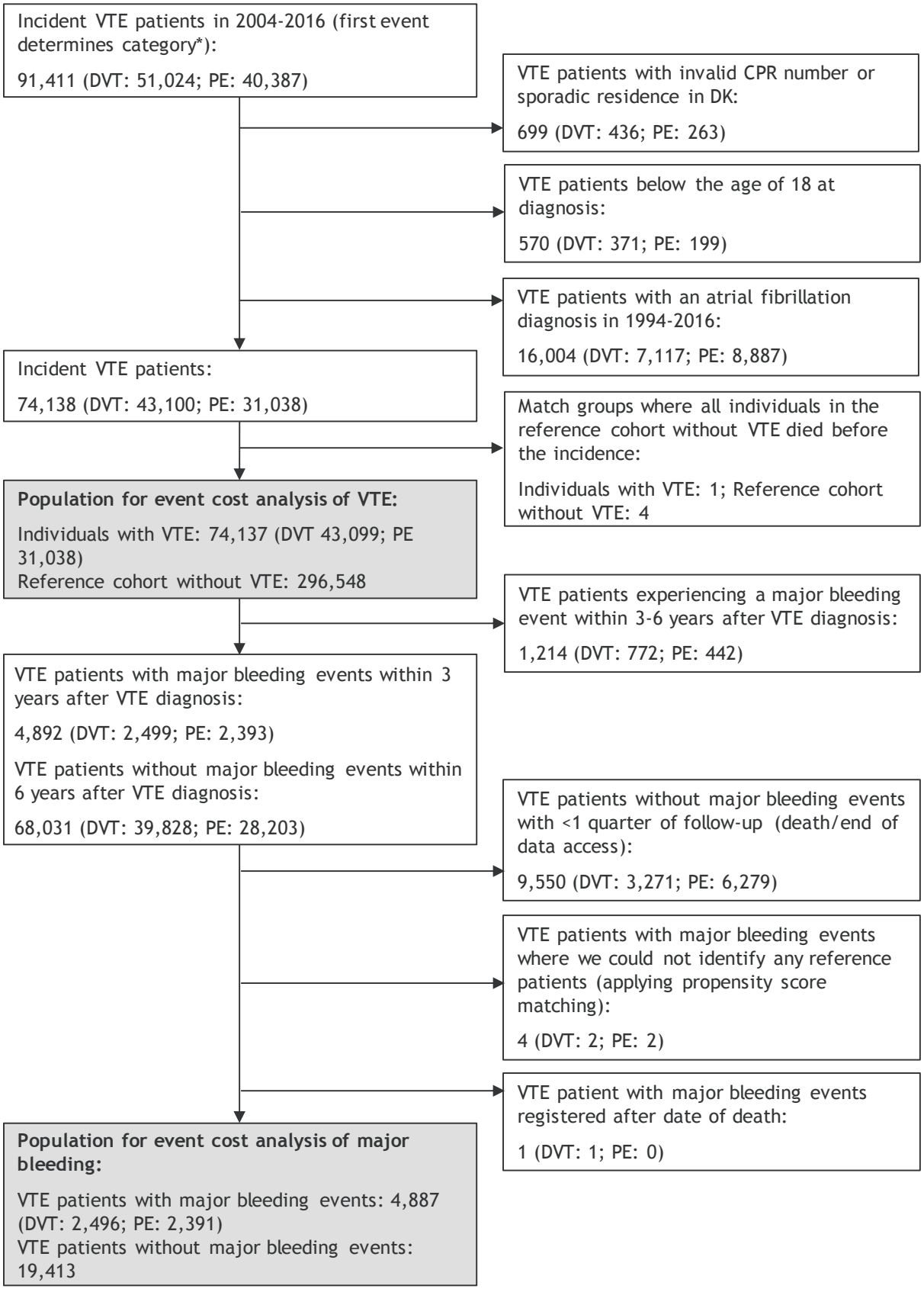
Table 3. Three-year attributable event costs of major bleedings[1] after VTE diagnosis (present value calculated in the incidence year) — EUR 2016 prices

	Primary sector costs	Outpatient costs	Hospital admission costs	Medicine costs	Home care costs	Production loss	Grand total	N
VTE								
Intracranial bleedings	1,325	-1,553	26,308	2,366	4,127	59,449	92,023	814
Gastrointestinal bleedings	311	676	13,104	2,580	1,784	53,649	72,105	1,609
Other bleedings	403	2,574	6,672	1,343	638	20,696	32,327	2,464
All major bleedings	508	1,425	11,326	1,846	1,443	34,620	51,168	4,887
DVT								
Intracranial bleedings	1,458	-580	26,940	2,138	4,095	50,139	84,190	410
Gastrointestinal bleedings	252	233	13,690	2,769	2,271	56,194	75,409	790
Other bleedings	428	2,835	7,759	1,560	538	22,203	35,324	1,296
All major bleedings	531	1,583	12,287	1,992	1,512	34,707	52,611	2,496
PE								
Intracranial bleedings	1,149	-2,887	25,188	2,612	4,079	73,075	103,216	404
Gastrointestinal bleedings	381	1,196	12,299	2,383	1,308	50,089	67,655	819
Other bleedings	372	2,208	5,220	1,018	739	18,380	27,936	1,168
All major bleedings	480	1,205	10,020	1,628	1,348	34,469	49,150	2,391

[1]Including major bleeding events occurring within the first three years after VTE diagnosis.

Figure

Figure 1. Flow chart of the study populations



*6,968 persons were diagnosed with both DVT and PE.