Adv Ther (2015) 32:138–147
DOI 10.1007/s12325-015-0187-3

ORIGINAL RESEARCH

The Cost of Thromboembolic Events in Hospitalized Patients with Breast or Prostate Cancer in France

Florian Scotte · Nicolas Martelli · Alexandre Vainchtock · Isabelle Borget

To view enhanced content go to www.advancesintherapy.com
Received: January 12, 2015 / Published online: February 26, 2015

ABSTRACT

Aims: The aim of the present study was to determine the number of admissions and the cost of hospital management of venous thromboembolism (VTE) events occurring in patients with breast cancer (BC) or prostate cancer (PC).

Methods: The French national hospital database (PMSI) was analyzed to identify patients diagnosed with BC or PC in 2010 and followed for 2 years. The number of admissions for VTE (or with VTE occurring during hospitalization) and the corresponding number of patients hospitalized were determined using disease-specific International Classification of Diseases, 10th revision (ICD-10) codes. Associated hospital costs were estimated from the healthcare payer perspective, using the French official tariffs.

Results: 62,365 and 45,551 patients diagnosed with BC and PC, respectively, in 2010 were identified from PMSI data; 1,271 (2.0%) and 997 (2.2%) were hospitalized for or had VTE during hospitalization. During the 2 years of follow-up, 346 patients (15%) presented a recurrence of thrombosis requiring hospitalization. A total of 1,604 and 1,210 inpatient VTE-related admissions (stays) in the BC and PC cohorts, respectively, were analyzed. Pulmonary embolism (PE) was the most frequent diagnosis leading to hospital admission in those cancer patients, followed by deep venous thrombosis. Mean cost per admission was €3,302 and €2,916 for first event and

Electronic supplementary material The online version of this article (doi:10.1007/s12325-015-0187-3) contains supplementary material, which is available to authorized users.

F. Scotte
Medical Oncology and Oncology Supportive Care Unit, Georges Pompidou European Hospital, Paris, France

N. Martelli
Pharmacy, Georges Pompidou European Hospital, Paris, France

A. Vainchtock
HEVA, Lyon, France

I. Borget (✉)
Research and Study in Health Economics, Biostatistics and Epidemiology Department, Gustave Roussy Institute, 94805 Villejuif, France
e-mail: isabelle.borget@igr.fr

I. Borget
Pharmaceutical Law and Economics Chair, Paris-Sud University, 5 Rue Jean-Baptiste Clément, 92190 Chatenay-Malabry, France

recurrence, respectively, in BC patients (total cost €1.98 million over 2 years) and €3,611 and €3,363 for first event and recurrence in PC patients (total cost €1.43 million over 2 years). In patients who had at least one recurrence, mean hospitalization cost was €5,545 and €5,692 in BC and PC, respectively.

Conclusion: The burden of VTE in cancer patients is important; costs should be reduced by decreasing the occurrence of thrombotic recurrences. In this respect, better prevention and follow-up measures may reduce recurrence and VTE costs.

Keywords: Breast cancer; Hospital admission; Hospital costs; Prostate cancer; Recommendations; Supportive care; Thromboembolic events

INTRODUCTION

In France, total healthcare expenditure is about 12% of gross domestic product [1] and cancer-related costs are increasing. All available options to reduce or at least stabilize the costs without decreasing the quality of patient care must be considered. Patients with cancer have a 4- to 6-fold increased risk of venous thromboembolism (VTE), including deep vein thrombosis (DVT) and pulmonary embolism (PE) [2–4], associated with hospitalizations that dramatically increase the economic burden. Most data on this topic have been published in the US. They show that the mean cost of VTE management ranges from $7,700 to 16,000 [5–8], with at least one half of the expenditure being attributable to hospitalization [5, 8]. In cancer patients, VTE-associated costs can reach $20,000 [9]. The average annual cost per patient is significantly higher in patients with VTE than in those without VTE, whether it affects all-cause costs ($33,531 vs. $17,590) or disease-related costs ($3,141 vs. $228) [8]. Preventable VTE costs are estimated between $14 and $39 billion per year in the United States which means that one-third of expenses could be avoided [10]. According to a large observational study of cancer patients treated with chemotherapy, the overall incidence of VTE was 7.3% and 13.5% at 3.5 and 12 months, respectively [11]. Healthcare costs were significantly higher in patients with VTE ($110,719 vs. $76,804, respectively, $p < 0.0001$). In addition, complications and recurrences are frequent, resulting in additional costs: the risk of recurrence has been estimated at 20.6% in cancer patients, compared to 6.8% in patients without cancer [12]. The cost of a recurrent thrombosis can be as high as $15,000 in the US [5]. Apart from recurrences, the risk of bleeding is high after VTE and increased in cancer patients [13], leading to other additional costs. Taken together, these studies demonstrate that VTEs have significant costs, mainly due to hospitalizations, but also because of recurrences. However, data are not easily applicable to other countries, due to differences in patients and treatment pathways and in costs of hospital admissions and treatments. The objectives of the present study were to determine the number of hospital admissions related to VTE in patients with breast cancer (BC) or prostate cancer (PC) in France and to calculate the associated hospital costs. Even in cancer patients, VTE cases are now also treated as outpatients. The analysis presented here did not consider those cases.

METHODS

Data Sources

Data from the French national hospital database [Programme de Médicalisation des Systèmes d'Information (PMSI)] was used, which covers all French public and private hospitals involved in medicine, surgery and obstetrics. Since 2004, when French hospitals adopted a prospective payment system (called "Tarification à l'Activité"), the PMSI database has become the basis of hospital funding, following a national tariff for each diagnosis related group (DRG). Each hospital stay resulted in the production of a standard discharge summary ["Résumé Standard de Sortie" (RSS)]. This RSS contains information such as patient characteristics (gender, age, residence code), main diagnosis that led to hospital admission, examinations carried out, comorbidities and possible complications. Diagnoses are coded using the International Classification of Diseases, 10th revision (ICD-10) either as primary diagnosis (PD), related diagnosis (RD), or significant associated-diagnosis (SAD). This RSS is then related to a DRG, used for the classification of hospital stays. All hospital stays are collected in the national PMSI database, used as the basis of hospital public funding by the third-party payer but also to produce indicators by disease (number of patients hospitalized annually, number of stays per patient and per year, hospital cost per disease, etc.) with a completeness close to 98% [14].

Data Collection of VTE-Related Stays

Cases were extracted from the PMSI database using the ICD-10 codes. Patients with BC (code C50) or PC (code C61) hospitalized in 2010 (prevalent cases) were identified. As a 5-year relapse-free period is considered as the remission delay for cancer, patients with BC or PC that were hospitalized between 2006 and 2010 were excluded, in order to select only newly diagnosed cancer patients (incident cancer cases). Among these new BC or PC patients, those hospitalized with DVT (code I80) or PE (code I26) as PD, RD or SAD were searched for. Incident patients with DVT or PE were followed for 2 years (2011 and 2012) using PMSI database, in order to identify the number of thromboembolic recurrences, if any.

Number of Patients

Since patients can be hospitalized several times during the same year, the number of patients hospitalized at least once in each of the considered years (2010, 2011 and 2012) was obtained by linking all hospital admissions and sessions, based on unique patient identification numbers. Indeed, all patients who are hospitalized receive a personal number, built on the patient's social security number, date of birth and gender. This number allows linking all hospital admissions that occur in public and private sectors. It is then possible to estimate the total number of patients hospitalized at least once for VTE in a given year.

Economic Evaluation

Among all hospitalizations related to VTE, stays with VTE classified as SAD were excluded, since specific cost related to VTE management cannot be isolated among the global cost of such hospitalizations. Costs were therefore estimated among admissions for VTE classified as PD/RD only, from the French healthcare payer's perspective, including hospitalization costs related to public and private sectors. Costs of chemotherapy, ambulatory and

indirect costs were not included. For public hospitals, costs were calculated using the official 2010, 2011 and 2012 public hospitals DRG tariffs, which include nursing care, treatments, drugs, accommodation and investment costs as well as medical and technical acts. For private hospitals, costs were estimated using the official 2010, 2011 and 2012 private hospitals DRG tariffs, to which physicians' fees were added, as they are not included in private DRG tariffs and are reimbursed on a fee-for-service basis. Costs are presented as mean cost per stay, mean cost per patient (based on patients for whom data were linked) and global cost.

This article does not contain any new studies with human or animal subjects performed by any of the authors.

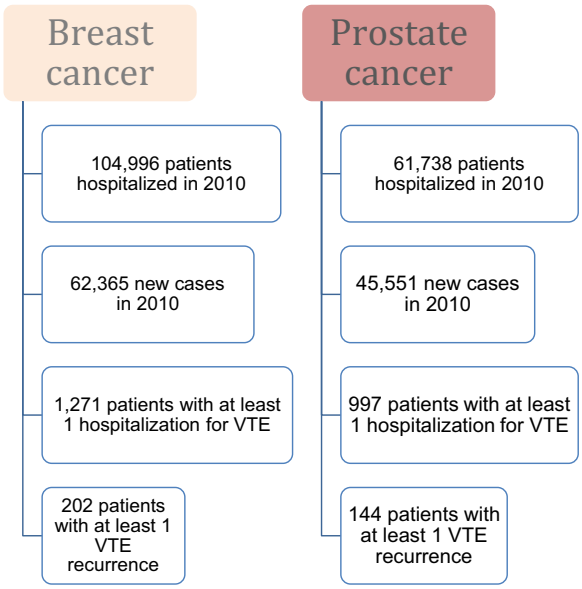

Fig. 1 Flow-chart of patients. *VTE* venous thromboembolic event

RESULTS

In 2010, 104,996 patients with BC and 61,738 patients with PC were hospitalized in French hospitals. Among them, 62,365 new BC cases and 45,551 new PC cases, i.e., patients without hospitalization related to BC or PC within the previous 5 years (2006–2010) were identified. Among these new patients, 1,271 in the BC cohort (2.0%) and 997 in the PC cohort (2.2%) were hospitalized at least once with VTE during the 2 years of follow-up (Fig. 1), for a total of 1,604 and 1,210 admissions, respectively. Moreover, 333 and 213 additional hospital admissions for recurrent thrombosis were reported, respectively, for 202 BC patients and 144 PC patients (Table 1). Thus, within a 2-year follow-up, 15.9% of BC patients and 14.4% of PC patients who were hospitalized for VTE experienced a VTE recurrence that required hospitalization. Recurrences represented 20.8% and 17.6% of the VTE-associated stays in BC and PC, respectively.

During the follow-up period (2 years), the mean number of admissions for VTE was then 1.26 and 1.21 per patient on average, for BC and PC, respectively. VTE was classified as the PD or RD of admissions in 606 (37.8%) and in 398 (32.9%) cases for BC and PC, respectively. Patients were hospitalized more frequently in public than in private hospitals (78.2% vs. 21.8% and 64.4% vs. 35.6% for BC and PC, respectively).

Mean costs per VTE-related admission ranged from €2,916 to €3,611, depending on the event (first or recurrence) and the type of cancer (Fig. 2). In BC patients, the mean cost per stay amounted to €3,302 and €2,916 for first event and recurrence, respectively, and in PC patients, €3,611 and €3,363 for first event and recurrence, respectively. In patients without recurrence, the mean cost was €3,302 and €3,611 for BC and PC, respectively. Coherently, the mean cost for one patient without recurrence represents the mean cost of one admission for a first VTE event. Yet, the cost

per patient was dramatically increased for patients with recurrent VTE: the cost rose by 67.9% in a BC patient with recurrent event (up to €5,545), and 57.6% in PC patients (up to €5,692), compared to patients without recurrence (Fig. 2).

Table 1 Number of hospital admissions and number of patients hospitalized for VTE from 2010 to 2012 (breast and prostate cancer)

	Overall VTE admissions (VTE as PD/RD)	Patients
Breast cancer patients		
First event	1,271 (542)	1,271
Recurrence	333 (64)	202
Total	1,604 (606)	1,271
Prostate cancer patients		
First event	997 (354)	997
Recurrence	213 (44)	144
Total	1,210 (398)	997

VTE venous thromboembolic event, *PD* primary diagnosis, *RD* related diagnosis

Over the 2-year period, the total cost of thrombosis-related admissions was €1.98 million in BC patients and €1.42 million (including €0.148 million for recurrences) in PC patients.

The distribution of admissions for BC patients with VTE according to the DRG classification showed that PE and DVT accounted for 62.4% and 22.3% of the total number of admissions. For PC patients with VTE, the distribution of admissions showed that PE and DVT accounted for 62.3% and 28.4% of the total number of admissions.

DISCUSSION

This is the first study that provides an objective estimation of the number of admissions, the number of patients and the cost of VTE-related hospitalizations in BC and PC patients in the French context.

These 2 cancers were chosen for several reasons: they are among the most frequent,

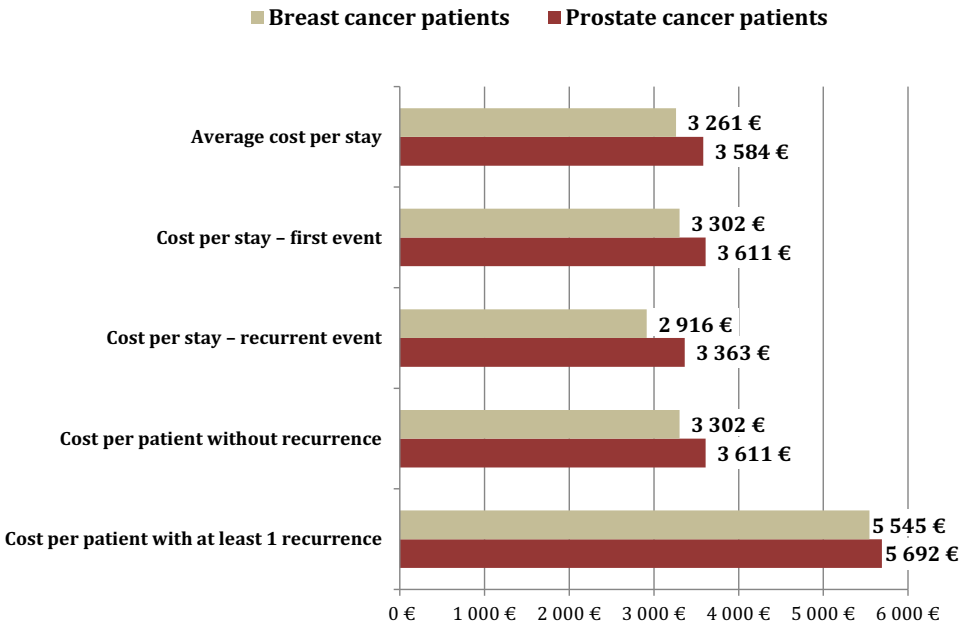

Fig. 2 Mean costs per hospital admission and per patient, first venous thromboembolic event and recurrences

they are usually associated with long overall survival, which allows long-term follow-up and makes prevention of complications still more relevant. The risk of VTE varies according to the stage of the disease [15]. The data presented here are consistent with the literature [16–18]: in women treated with chemotherapy for BC, 1.2% were hospitalized or visited the emergency room for DVT or PE during the year following diagnosis in a US study [16]. In contrast, PC is associated with a higher risk of thrombosis, and considered to be among malignant tumors most frequently associated with VTE [17], particularly after radical prostatectomy [18].

The study confirmed that the burden of VTE is important, with about 2,800 hospital admissions. The cost appeared to be very elevated, close to €3.4 million over 2 years.

It was found that the cost per admission was between €3,300 and €3,600 for the first event and between €2,900 and €3,400 for recurrences for BC and PC, respectively. These costs are below those calculated by US studies, where the lowest estimation for hospitalization was $7,700 for a DVT (approximately €5,600) [5], which can probably be explained by major differences in healthcare management systems and costs between France and the US. In a French study on healthcare-associated adverse events, the estimated additional cost of VTE after surgery was €4,900, thus also higher than in this study [19]. However, the objectives of the study were different (evaluation of avoidable iatrogenic events) and this study dealt with operated patients with all-cause hospitalizations. Nevertheless, the total cost is important: €3.4 million dedicated over 2 years to the management of a single complication in quite a small population (107,000 patients). Considering that the mean yearly expenditure for a patient with cancer is €10,000 [20], it can be considered that VTE increased the cost of management by nearly €1,500 per patient with cancer.

The present study showed that 15.9% of BC and 14.4% of PC patients, who had a first VTE, presented a recurrence requiring hospitalization during the first 2 years after diagnosis, a recurrence rate in line with previous studies [5, 6, 9, 12]. For these patients, the cost of management is still higher.

Yet, thrombosis could be avoided in many cases [10]. Primary VTE prophylaxis is effective in reducing the occurrence of thrombosis in various settings (surgical or medical treatment) [3, 4] and recommendations have been issued in the US and in Europe [21–26]. Although guidelines are roughly consistent and easy to implement, they are poorly followed. In the prophylactic setting, the ENDORSE study (Epidemiologic International Day for the Evaluation of Patients at Risk for Venous Thromboembolism in the Acute Hospital Care Setting) conducted in 32 countries enrolled more than 68,000 hospitalized patients, among which 51.8% were at risk for VTE [27]. Only 58.5% and 39.5% of surgical and medical patients, respectively, received appropriate VTE prophylaxis. In the French cohort, comprising 2,844 patients, only 53.5% of medical at-risk patients were administered prophylaxis (55% in cancer patients) [28]. In cancer outpatients receiving or not receiving chemotherapy, the interest of thromboprophylaxis remains unclear and not yet supported by strong clinical evidence.

Recommendations for curative treatment of cancer patients who experienced VTE state that low molecular weight heparin (LMWH) should be preferred and pursued for at least 3 months [29]. However, these guidelines are also insufficiently respected. For example, in France, the CARMEN cross-sectional observational study (Compliance with

Recommendations of Clinical Practice in the Management of Venous Thromboembolism in Cancer) performed in 2010 included 500 cancer patients with VTE (mean age 64 ± 14 years, 63.6% metastatic malignancies, DVT 63.2%, PE 29.9%) [30]. Only 57.8% were treated in accordance with recommendations, i.e., LMWH for 10 days followed by LMWH for at least 3 months [21]. These findings are consistent with those observed in the Swiss SWIVTER II study (SWIss Venous ThromboEmbolism Registry), in which long-term anticoagulation was planned in only 47% of cancer patients with VTE [31]. Similarly, another Swiss study [OTIS-DVT, (Outpatient Treatment of Deep Vein Thrombosis in Switzerland)] showed that ambulatory cancer patients with DVT received a 3-month LMWH therapy in only one-third of cases [32]. In the RIETE registry (Registro Informatizado de Enfermedad TromboEmbólica) that included patients with active cancer and VTE, 53% received LMWH for at least 3 months after the thrombotic event, while 38% received Vitamin K antagonists [33]. A retrospective study of 1,089 cancer patients who experienced VTE between January 2000 and December 2007 showed that, overall, 25.0% had LMWH monotherapy as primary treatment [34]. Although this percentage increased over time, from 18% in 2000 to 31% in 2007, the follow-up of recommendations remains clearly insufficient. In Canada, the multicenter, prospective observational study enrolled 868 outpatients with acute symptomatic VTE [35]. Among those with cancer-related VTE, 59.5% were prescribed LMWH monotherapy and 43.2% received this treatment for at least 3 months. Another Canadian study analyzed data from the Quebec Health Insurance Agency [36]. Cancer patients with an in-hospital diagnosis of VTE had anticoagulant therapy at the time of discharge in 72.4% of cases, among which 60% received the treatment for at least 80% of the 6-month follow-up period. Despite this improvable rate of patients treated accordingly to guidelines, some reasons remain not to prescribe long-term LMWH therapy, as low platelet counts following chemotherapy, allergies, previous heparin-induced thrombocytopenia, as well as injection site bruising, for example.

Costs can also be reduced by choosing ambulatory management, whenever possible. In a French study, 210 patients with DVT, who received LMWH followed by vitamin K antagonists, were randomly assigned to initial inpatient treatment (10 days) or full outpatient management [37]: the rate of recurrent thrombosis or severe bleeding (primary endpoint of the study) was similar in both groups (3.0% vs. 3.9%, respectively), but costs were reduced by 56% in patients treated at home, due to the high basic cost of hospital stay, which far exceeds the costs of physicians' and nurses' home visits. A prospective observational Spanish study showed similar findings with a yet higher cost reduction for outpatient management (85%), without increase in mortality or severe bleeding [38]. Further studies are needed in France to measure accurately the cost of various types of VTE management and estimate the potential cost reduction.

The utilization of the PMSI tool ensured the comprehensiveness of data in a large sample size and a high quality since these data are the basis of reimbursement to hospitals. However, the costs may have been underestimated in the present study. Firstly, patients with VTE events treated in an ambulatory basis were not considered, since the only aim was to identify those who were hospitalized. The number of uncomplicated DVT or PE cases in cancer patients managed without hospitalization

remains yet important and increasing. Secondly, estimation was limited to hospital costs, excluding transport, indirect costs and post-hospitalization ambulatory costs. Thirdly, there is a risk of coding omission when patients are hospitalized for another reason (VTE is then a SAD) and/or the VTE event is not serious. Fourthly, as incident 2010 cases were selected by excluding patients hospitalized between 2006 and 2010, some cancer patients diagnosed before 2006 may have been missed. Finally, only 2 types of cancer were targeted and the total cost of VTE in all cancer patients cannot be extrapolated.

CONCLUSION

The cost of VTE-related hospital admissions reached €3.4 million in BC and PC patients in France. The burden of the disease is increased by frequent and costly recurrences: 15.9% of BC and 14.4% of PC patients had at least another VTE. Thus, every effort should be made to prevent thromboembolic events by an appropriate prophylaxis and to avoid recurrences using an adequate and prolonged curative treatment and a good follow-up of recommendations.

ACKNOWLEDGMENTS

Sponsorship and article processing charges for this study were funded by LEO Pharma, Voisins-Le-Bretonneux, France. Medical writing assistance for this study was provided by Dr. Anne Visbecq and funded by LEO Pharma, Voisins-Le-Bretonneux, France. All named authors meet the International Committee of Medical Journal Editors (ICMJE) criteria for authors for this manuscript, take responsibility for the integrity of the work as a whole, and have given final approval for the version to be published.

Conflict of interest. Florian Scotté, Nicolas Martelli, Alexandre Vainchtock and Isabelle Borget declare no conflicts of interest.

Compliance with ethics guidelines. This article does not contain any new studies with human or animal subjects performed by any of the authors.

REFERENCES

1. OCDE. Panorama de la santé 2011: les indicateurs de l'OCDE. 2011. http://www.oecd.org/fr/els/systemes-sante/49105873.pdf. Accessed Jan 12, 2015.
2. Chew HK, Wun T, Harvey D, Zhou H, White RH. Incidence of venous thromboembolism and its effect on survival among patients with common cancers. Arch Intern Med. 2006;166(4):458–64.
3. Robert F. The potential benefits of low-molecular-weight heparins in cancer patients. J Hematol Oncol. 2010;3:3.
4. MacLellan DG, Richardson A, Stoodley MA. Venous thromboembolism and cancer. ANZ J Surg. 2012;82(5):294–8.
5. Bullano MF, Willey V, Hauch O, Wygant G, Spyropoulos AC, Hoffman L. Longitudinal evaluation of health plan cost per venous thromboembolism or bleed event in patients with a prior venous thromboembolism event during hospitalization. J Manag Care Pharm. 2005;11(8):663–73.
6. Spyropoulos AC, Lin J. Direct medical costs of venous thromboembolism and subsequent hospital readmission rates: an administrative claims analysis from 30 managed care organizations. J Manag Care Pharm. 2007;13(6):475–86.
7. MacDougall DA, Felice AL, Boccuzzi SJ, Lin J. Economic burden of deep-vein thrombosis, pulmonary embolism, and post-thrombotic syndrome. Am J Health Syst Pharm. 2006;63(20 Suppl 6):S5–15.
8. Lefebvre P, Laliberte F, Nutescu EA, Duh MS, LaMori J, Bookhart BK, et al. All-cause and

potentially disease-related health care costs associated with venous thromboembolism in commercial, Medicare, and Medicaid beneficiaries. J Manag Care Pharm. 2012;18(5):363–74.

9. Elting LS, Escalante CP, Cooksley C, Avritscher EB, Kurtin D, Hamblin L, et al. Outcomes and cost of deep venous thrombosis among patients with cancer. Arch Intern Med. 2004;164(15):1653–61.

10. Mahan CE, Borrego ME, Woersching AL, Federici R, Downey R, Tiongson J, et al. Venous thromboembolism: annualised United States models for total, hospital-acquired and preventable costs utilising long-term attack rates. Thromb Haemost. 2012;108(2):291–302.

11. Lyman GH, Eckert L, Wang Y, Wang H, Cohen A. Venous thromboembolism risk in patients with cancer receiving chemotherapy: a real-world analysis. Oncologist. 2013;18(12):1321–9.

12. Prandoni P, Lensing AW, Piccioli A, Bernardi E, Simioni P, Girolami B, et al. Recurrent venous thromboembolism and bleeding complications during anticoagulant treatment in patients with cancer and venous thrombosis. Blood. 2002;100(10):3484–8.

13. Liu X, Xie L, Phatak H, Mardekian J, Tan W, Baser O, Ramacciotti E. Bleeding incidence among patients with venous thromboembolism: a large US insurance database analysis. Blood. 2013;122(21):2916.

14. Direction de la recherche de l'évaluation et des statistiques (DREES), Redressements du Programme de Médicalisation des Systèmes d'Informations (PMSI). 2005. http://www.drees.sante.gouv.fr/redressements-du-programme-de-medicalisation-des-systemes-d-informations-pmsi,5334.html. Accessed Jan 12, 2015.

15. Medioni J, Guastalla JP, Drouet L. Thrombosis and breast cancer: incidence, risk factors, physiopathology and treatment. Bull Cancer. 2012;99(2):199–210.

16. Hassett MJ, O'Malley AJ, Pakes JR, Newhouse JP, Earle CC. Frequency and cost of chemotherapy-related serious adverse effects in a population sample of women with breast cancer. J Natl Cancer Inst. 2006;98(16):1108–17.

17. Yu YB, Gau JP, Liu CY, Yang MH, Chiang SC, Hsu HC, et al. A nation-wide analysis of venous thromboembolism in 497,180 cancer patients with the development and validation of a risk-stratification scoring system. Thromb Haemost. 2012;108(2):225–35.

18. Beyer J, Wessela S, Hakenberg OW, Kuhlisch E, Halbritter K, Froehner M, et al. Incidence, risk profile and morphological pattern of venous thromboembolism after prostate cancer surgery. J Thromb Haemost. 2009;7(4):597–604.

19. Nestrigue C, Or Z. Surcoût des évènements indésirables associés aux soins à l'hôpital. Questions d'économie de la santé—IRDES 2011;171. http://www.irdes.fr/Publications/2011/Qes171.pdf. Accessed Jan 12, 2015.

20. French Ministry of Health. Améliorer la qualité du système de santé et maitriser les dépenses : proposition de l'Assurance Maladie pour 2014. 2013. http://www.ameli.fr/fileadmin/user_upload/documents/cnamts_rapport_charges_produits_2014.pdf. Accessed Jan 12, 2015.

21. Debourdeau P, Farge-Bancel D, Bosquet L, Kassab-Chahmi D, Cajfinger F, Desmurs-Clavel H, et al. 2008 Standards, options: recommendations for venous thromboembolic events (VTE) treatment and central venous catheter thrombosis (CVCT) management in cancer patients. Bull Cancer. 2008;95(7):750–61.

22. Lyman GH, Khorana AA, Kuderer NM, Lee AY, Arcelus JI, Balaban EP, et al. Venous thromboembolism prophylaxis and treatment in patients with cancer: American Society of Clinical Oncology clinical practice guideline update. J Clin Oncol. 2013;31(17):2189–204.

23. Lyman GH, Khorana AA, Falanga A, Clarke-Pearson D, Flowers C, Jahanzeb M, et al. American Society of Clinical Oncology guideline: recommendations for venous thromboembolism prophylaxis and treatment in patients with cancer. J Clin Oncol. 2007;25(34):5490–505.

24. National Comprehensive Cancer Network. NCCN clinical practice guidelines in oncology (NCCN Guidelines®). Venous Thromboembolic disease. Version 2.2013. 2013. http://www.nccn.org/professionals/physician_gls/f_guidelines.asp. Accessed Jan 12, 2015.

25. Mandala M, Falanga A, Roila F. Venous thromboembolism in cancer patients: ESMO Clinical Practice Guidelines for the management. Ann Onco. 2010;21(Suppl 5):v274–6. http://annonc.oxfordjournals.org/content/22/suppl_6/vi85.full.pdf+html. Accessed Jan 12, 2015.

26. AFSSAPS. Recommandations de bonne pratique—prévention et traitement de la maladie thromboembolique veineuse en médecine. 2009. http://ansm.sante.fr/var/ansm_site/storage/original/application/5e0d9dde31597a32d4f5c315a7690521.pdf. Accessed Jan 12 2015.

27. Cohen AT, Tapson VF, Bergmann JF, Goldhaber SZ, Kakkar AK, Deslandes B, et al. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): a multinational cross-sectional study. Lancet. 2008;371(9610):387–94.

28. Bergmann JL-L, Rami C, Cohen A, et al. Venous thromboembolism risk and prophylaxis in the acute hospital care setting (ENDORSE study): results obtained in France. Presse Medicale. 2011;40(12):528–37.

29. Mahe I, Chidiac J. Cancer-associated venous thromboembolic recurrence: disregard of treatment recommendations. Bull Cancer. 2014;101(3):295–301.

30. Sevestre M-A, Belizna C, Durant C, Bosson J-L, Vedrine C, Cajfinger F, Debourdeau P, Farge D; Carmen Investigators for the Groupe Francophone Thrombose et Cancer (GFTC). Compliance of recommendations with French clinical practice in the management of thromboembolism in patients with cancer: the CARMEN study. J Mal Vasc. 2014;39(3):161–8.

31. Spirk D, Ugi J, Korte W, Husmann M, Hayoz D, Baldi T, et al. Long-term anticoagulation treatment for acute venous thromboembolism in patients with and without cancer. The SWIss Venous ThromboEmbolism Registry (SWIVTER) II. Thromb Haemost. 2011;105(6):962–7.

32. Spirk D, Banyai M, Jacomella V, Frank U, Baldi T, Baumgartner I, et al. Outpatient management of acute deep vein thrombosis: results from the OTIS-DVT registry. Thromb Res. 2011;127(5):406–10.

33. Trujillo-Santos J, Nieto JA, Ruiz-Gamietea A, Lopez-Jimenez L, Garcia-Bragado F, Quintavalla R, et al. Bleeding complications associated with anticoagulant therapy in patients with cancer. Thromb Res. 2010;125(Suppl 2):S58–61.

34. Delate T, Witt DM, Ritzwoller D, Weeks JC, Kushi L, Hornbrook MC, et al. Outpatient use of low molecular weight heparin monotherapy for first-line treatment of venous thromboembolism in advanced cancer. Oncologist. 2012;17(3):419–27.

35. Kahn SR, Springmann V, Schulman S, Martineau J, Stewart JA, Komari N, et al. Management and adherence to VTE treatment guidelines in a national prospective cohort study in the Canadian outpatient setting. The Recovery Study. Thromb Haemost. 2012;108(3):493–8.

36. Rahme E, Feugere G, Sirois C, Weicker S, Ramos E. Anticoagulant use in patients with cancer associated venous thromboembolism: a retrospective cohort study. Thromb Res. 2013;131(3):210–7.

37. Boccalon H, Elias A, Chale JJ, Cadene A, Gabriel S. Clinical outcome and cost of hospital vs home treatment of proximal deep vein thrombosis with a low-molecular-weight heparin: the Vascular Midi-Pyrenees study. Arch Intern Med. 2000; 160(12):1769–73.

38. Jara Palomares L, Caballero Eraso C, Elias Hernandez T, Ferrer Galvan M, Marquez Pelaez S, Cayuela A, et al. Outpatient management of patients with deep vein thrombosis and cancer: a study of safety, cost and budget impact. Med Clin 2012;138(8):327–31.