Anticoagulant use in patients with cancer associated venous thromboembolism: A retrospective cohort study

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A B S T R A C T

Introduction: Long term anticoagulant therapy is recommended for treatment and secondary prevention of venous thromboembolism in cancer patients. We assessed outpatient anticoagulants [warfarin, low molecular weight heparins (LMWHs), fondaparinux and unfractionated heparin (UFH)] use in adult, cancer patients, 20 years of age or older, who incurred a venous thromboembolism (primary or secondary in-hospital diagnosis) in Quebec, Canada between 2007 and 2009.

Materials and methods: Data were obtained from the Quebec Health Insurance Agency. Patients with an in-hospital cancer diagnosis between April 2007 and June 2009 and an in-hospital venous thromboembolism diagnosis either concurrently or consequently were eligible at the date of discharge (index date). Those patients registered with the provincial drug plan and discharged to the community were included in the study and followed for 6 months.

Results: Among 2,070 study patients, 72.4% received anticoagulant therapy at index date, 60% of whom were persistent with therapy and received it for ≥80% of follow-up days. Outpatient anticoagulant use was more likely in those with primary versus secondary diagnosis of venous thromboembolism and less likely in patients with cerebrovascular disease, peptic ulcer disease or previous anticoagulant use. The small number of patients who used either UFH (n=11) or fondaparinux (n=5) at index date were included in the LMWH group. Warfarin use was less likely than LMWH use in corticosteroid users, previous anticoagulant users, patients with metastatic cancer and those with catheter or chemotherapy in the previous three months. Warfarin use was more likely than LMWH use in: older patients, those residing in rural areas, those with lower income and those suffering from ischemic heart disease, atrial fibrillation or chronic kidney disease. Patients with ischemic heart disease were more likely to have used a non-dalteparin LMWH versus dalteparin (currently, the only LMWH approved by health Canada for chronic treatment of VTE), while those residing in rural areas and those with catheter/chemotherapy were less likely to have used them. A primary (versus secondary) discharge diagnosis of venous thromboembolism [Odds Ratio 1.42; 95% confidence interval (1.14, 1.76)], and metastatic cancer 1.27 (1.00, 1.60) were associated with persistence on anticoagulant treatment.

Conclusion: Guideline recommended outpatient use of anticoagulant in cancer patients hospitalized with venous thromboembolism was influenced by cancer status, old age and low income. Risk factors for bleeding prevented outpatient anticoagulant use in some patients.

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risk of VTE. In addition, this hypercoagulable state can be worsened by the pro-coagulant effects of cancer treatment (chemotherapy and radiotherapy), surgery, infection, immobilization [5,8–10], and central venous catheter placement [11,12]. The risk of VTE in cancer patients increases with age, comorbidity and tumour stage [13–17]. It is higher in women than in men, varies by tumour site and is higher in cancers associated with short life-expectancies, such as pancreatic cancer [3,5,10,18,19].

Anticoagulant treatment is required in these patients to prevent VTE recurrence and potentially mortality, although response to treatment varies between agents [20,21]. The American College of Chest Physicians (ACCP) and the American Society of Clinical Oncology (ASCO) guidelines recommend low molecular weight heparins (LMWHs) for 3 to 6 months for the treatment of VTE in cancer patients [22,23]. Among the LMWHs, dalteparin is the only one approved by Health Canada for chronic treatment of VTE [24,15,25]. LMWHs are superior to unfractionated heparin (UFH) in decreasing the risk of mortality in the initial phase of VTE treatment [11]. LMWHs have also been shown to be superior to the vitamin-K-antagonist, warfarin; it reduces the risk of VTE recurrence by half in the maintenance phase [6,13,26,27]. The use of warfarin is further disadvantaged in this patient population because of its slow onset of action (72–96 hours), lengthy clearance from the body (2–5 days) [1] and the requirement to closely monitor patients with frequent blood tests while they achieve the target therapeutic international normalized ratio (INR) [1]. In addition, INR target achievement is complicated by the interference of commonly used medications [e.g., aspirin, birth control pills, antibiotics and non steroidal anti-inflammatory drugs (NSAIDs)], and food high in vitamin K (e.g., broccoli, lettuce and spinach) [28]. However, in spite of these disadvantages, warfarin is oftentimes preferred to LMWHs because of the convenience of outpatient oral use and its lower cost. LMWHs are therefore frequently co-prescribed with warfarin during the initial phase until the therapeutic INR (between 2 and 3) is reached, at which point treatment with warfarin alone is maintained for at least 3 months [1,29].

Among Quebec cancer patients, 20 years of age or older, who experienced a VTE in-hospital and were discharged alive between April 1, 2007 and June 30, 2009, we aimed to describe the profile of those who received anticoagulant therapy for treatment and/or prevention of VTE recurrence in the following 6 months.

Materials and methods

Study design and data sources

We conducted a retrospective cohort study using demographic, physician billing, prescription drug and hospital discharge abstract records obtained from the Quebec public drug insurance program administered by the Régie de l’Assurance Maladie du Québec (RAMQ) for the period of April 2005–December 2009. In Quebec, all residents are covered by the RAMQ for outpatient and inpatient physician services. Available data from the RAMQ physician services database include details of the service provided, specialty of the physician, location of the service [e.g. hospital, emergency department (ED) or outpatient clinic], and diagnostic (International Classification of Disease (ICD)-9th revision) and procedure codes pertinent to the service. In addition, drug insurance coverage is mandatory in Quebec for all residents. Therefore, citizens eligible for coverage by the RAMQ drug plan include: those aged 65 years or older (1,091,618 individuals; 92% of that population), individuals younger than 65 years of age who receive social assistance (493,673 individuals; 100% of that population), and all residents younger than 65 years of age who do not have a collective private drug insurance [e.g., those self-employed (1,763,277 individuals; 32% of that population)] [30]. The RAMQ prescription claims database provides information on all dispensed prescriptions including drug name, dispensation date, dosage, drug form, duration and quantity of the drug dispensed. Drugs dispensed to patients in hospitals or nursing homes and over the counter medications are not included in this database. All other medication dispensations have been demonstrated to be accurately and reliably recorded in the RAMQ prescription claims database [31]. The Québec hospital discharge abstract database provides information on all hospital admissions for the entire province including primary and secondary discharge diagnoses (ICD-9 codes until April 2006 and ICD-10 codes thereafter), comorbid conditions, and admission/discharge dates and destination. Permissions from the Government of Quebec Ethics Committee, the Commission d’Accès à l’Information, were obtained to link the data and conduct this study.

Study patients

Adult patients who had a principal or secondary diagnosis (ICD-10 code for cancer between April 2007 and June 2009) were identified as cancer patients at the date of their first cancer diagnosis in that period. Cancer patients who had an in-hospital diagnosis (principal or secondary) for VTE concurrently or any time following their cancer diagnosis were identified at the time of VTE hospital discharge (index date). VTE codes included: I26 (PE), I80.1–I80.9, I82.8 and I82.9 (DVT). Among those patients with a VTE code, patients discharged alive and registered with the RAMQ drug plan from one year prior to 6 months after the index date were included. Women who were pregnant or became pregnant at anytime during the study period and patients discharged to an institution at index date were excluded. Study patients were followed for 6 months or until death, whichever occurred first.

Exposure to study drugs

The anticoagulants available in Quebec during the study period included warfarin, UFH, LMWHs and the selective factor Xa inhibitor, fondaparinux (rivaroxaban, an oral selective factor Xa inhibitor that was approved for reimbursement by RAMQ in June 2009 in patients with knee replacement, and dabigatran, an oral selective factor II A inhibitor that was approved for reimbursement by RAMQ in April 2011 for patients with atrial fibrillation were not included in our database during the study period) [32,33] patients were said to have used an anticoagulant at index date if they filled a prescription for that anticoagulant within the first two days following index date. Anticoagulant treatment was assessed during the 6-month follow-up in terms of agents received at index date and switch to another anticoagulant agent (any dispensed and total duration of anticoagulant use until the switch). A switch was deemed to occur when a patient was dispensed a different anticoagulant during the days supplied or within the 7 days following the last supplied day on another anticoagulant. Patients who were dispensed a LMWH and warfarin at index date and then stopped using the LMWH and continued warfarin did not constitute a switch as this is considered usual clinical practice. Medication possession ratio (MPR) was also calculated, and was defined as the ratio of the total number of supplied days of any anticoagulant until the first interruption (at least 7 days without anticoagulant supply) over the duration of follow-up. The 6 patients who used UFH and the 11 patients who used fondaparinux at index date were included in the LMWH group, as described below.

Patient baseline characteristics

Patient characteristics assessed at index date included: age, sex, type of insurance plan [based on patient eligibility for premium subsidies; low income patients receiving premium subsidies Guaranteed Income Supplement (GIS), those receiving partial premium subsidies (partial-GIS), and those not receiving premium subsidies (no-GIS), GIS and partial GIS were grouped in one category and labelled 'low income'], region of residence (urban or rural), specialty of the physician who prescribed
the anticoagulant, comorbidity (hypertension, diabetes, ischemic heart disease, heart failure, peptic ulcer disease, cerebrovascular disease, atrial fibrillation, and blood disease), medication used within one week of index date (antihypertensive agents, anti diabetic agents, corticosteroids, gastroprotective agents (proton pump inhibitors, misoprostol and histamine-2 receptor blocker), serotonin reuptake inhibitors (SSRI), NSAIDs, and hormone replacement therapy), and cancer stage (metastatic or not).

Statistical analyses

Patients who received an anticoagulant prescription at index date were identified. Descriptive analyses [mean and standard deviation (SD), median and interquartile range, or proportion] were used as appropriate to report patient characteristics by anticoagulant use. Four categories of anticoagulant use were defined: warfarin only, LMWH only, warfarin in combination with LMWH and no-use. Because dalteparin is currently the only anticoagulant approved by Health Canada for chronic treatment of VTE [15,24,25], differences in utilisation may exist between dalteparin and other LMWHs Therefore, we also conducted an analysis comparing dalteparin to other LMWH use. Patient characteristics were determined by category of anticoagulant use. A multivariable logistic regression model was used to identify factors associated with anticoagulant use versus no use and pytomous logistic regression models were used to identify factors associated with warfarin, either alone or in combination with a LMWH versus LMWH alone, and factors associated with warfarin and other LMWHs versus dalteparin, respectively. Independent variables that were thought to be clinically relevant were entered in the models, and the C-statistic was used to assess the model fit [34]. Anticoagulant use in the 6 months following index date (switch to another agent, total duration of anticoagulant use and proportion of patients with MPR ≥ 80%) was also reported in the descriptive statistics section. Logistic regression models were used to compare characteristics of patients with MPR ≥ 80% versus those with MPR < 80% among users of anticoagulants at index date. MPR ≥ 80% has been frequently used in the literature as a marker of patient persistence on medication [35].

Sensitivity analyses

The main analyses included patients who had their index VTE recorded as an in-hospital principal or secondary diagnosis code. Included in this group were those patients who had a VTE diagnosis code in an unspecified site (ICD-10 codes I80.3, I80.8, I80.9, I82.8, I82.9), patients who had hospitalizations that exceeded 30 days and patients who had used an anticoagulant in the prior year. Medication use, in the main analyses, was defined as a prescription dispensed within two days of discharge. To assess the impact of these decisions on the results, four sensitivity analyses were conducted. The first sensitivity analysis only included patients with a principal diagnosis of VTE, the second excluded patients who had VTE in an unspecified site and patients hospitalized for more than 30 days, the third excluded patients who used anticoagulants in the prior year and the fourth considered patients who used an anticoagulant anytime in the 3 and 7 days following index date as anticoagulant users. All statistical analyses were performed using SAS version 9.2 for UNIX (SAS Institute Inc., Cary, NC).

Results

Patient characteristics

In total, 2,070 patients were included in the study cohort (Fig. 1). There were 980 (47.3%) cases of PE and 1,090 (52.7%) cases of DVT (Table 1). About a quarter (27.6%) of patients did not fill an anticoagulant prescription within 2 days of the index date. Among the 1,499 anticoagulant users, 63.5% were 65 years or older and 46.2% were men; and among the 571 non-users, 68.0% were 65 years or older and 47.6% were men. The median length of hospital stay was similar among the different categories of anticoagulant use [median (first quartile, third quartile); warfarin users: 14 days (8 days, 25 days); LMWH users: 11 days (6 days, 22 days), and no use: 13 days (6 days, 26 days)], although the patients who used a combination of warfarin and a LMWH were hospitalized for a shorter period of time: 8 days (4 days, 16 days). Table 2 displays patient characteristics at index date by anticoagulant use. Table 2 also displays the results [crude and adjusted odds ratios (OR) and 95% confidence intervals (CI)] of the logistic regression models comparing patient characteristics at index date by anticoagulant use. Patients with cerebrovascular or peptic ulcer disease and those who used anticoagulants in the six months prior to index date were less likely to receive an anticoagulant at index date, while patients who had a primary diagnosis record for VTE, those with catheter/chemotherapy and those with metastatic cancer were more likely to receive anticoagulants at index date (Table 2).

![Fig. 1. Patients satisfying the inclusion criteria and included in the study cohort.](image)
Among patients who filled a prescription for an anticoagulant at index date, 29.5% used warfarin, 60.1% a LMWH and 10.4% used a combination of warfarin and any LMWH. Table 3 displays patient characteristics by type of anticoagulant used at index date. One patient used both dalteparin and another LMWH at index date and was excluded from this analysis. In polytomous logistic regression models (Table 4), factors associated with warfarin versus LMWH use were: older age (OR 1.02 for every one year increase; 95% CI 1.00–1.03), residing in a rural area (1.59; 1.18–2.14), lower income (1.83; 1.43–2.34), ischemic heart disease (1.46; 1.13–1.89) and atrial fibrillation (1.47; 1.05–2.04). Use of corticosteroid within one week of index date (0.67; 0.49–0.91), use of anticoagulants in the six months prior to index date (0.67; 0.49–0.91), having metastatic cancer (0.50; 0.37–0.67) and having a catheter/chemotherapy within the three month period prior to index date were less likely to be associated with warfarin use in this analysis (0.42; 0.30–0.58). Similar results were observed for the combination warfarin and dalteparin as those observed for the warfarin only group except for ischemic heart disease and atrial fibrillation that were not significant. Table 4 also displays the result of the polytomous regression model comparing use of other (non-dalteparin) LMWHs to dalteparin.

In this analysis, rural residence was significantly associated with a lower use of other LMWHs versus dalteparin, while ischemic heart disease was associated with a higher use.

### Duration of use

We investigated the duration of anticoagulant use for those who started anticoagulants at index date and identified those persistent on their medication during follow-up. Patients were considered to be persistent if they had a MPR ≥ 80%, where MPR was the number of days supplied for the anticoagulant until the first interruption in use (at least 7 days of no anticoagulant supply) divided by the total number of follow-up days (6 months or until death, if death occurred within 6 months of index date). Among users of anticoagulants, 897 (59.8%) were persistent (Table 5). More persistent patients had their VTE recorded as a primary diagnosis (41.7% versus 33.6%) and had a metastatic cancer (29.8% versus 25.1%) (Table 5). Other characteristics did not seem to differ between persistent and non-persistent patients. These observations were confirmed by the results of a multivariable logistic regression model [OR for VTE primary diagnosis 1.41 (95% CI: 1.14, 1.75); OR for metastatic cancer 1.23 (95% CI: 0.97, 1.56) (Table 5)]. Patients with chronic kidney disease were less persistent.

Around 22% of patients who used a single anticoagulant at index date switched medications in follow-up, while 9.6% of non-users at index date used anticoagulants later on during follow-up (Table 6). As expected, all patients using the combination warfarin and any other medication ‘switched’ medications (stopped the combination) during follow-up and continued on warfarin alone (Table 6).

### Table 1

| ICD-10 Code | N of patients |
|-------------|---------------|
| I26.0, I26.9 (Pulmonary embolism) | 980 |
| I80.1, I80.2 (Phlebitis and thrombophlebitis of femoral vein/ of other deep vessels of lower extremities) | 711 |
| Unspecified (I80.3, I80.8, I80.9, I82.8, I82.9) | 379 |

### Table 2

| Any anticoagulant | No use | Crude Odds Ratio* (95% CI) | Adjusted Odds Ratio* (95% CI) |
|-------------------|--------|---------------------------|-------------------------------|
| N patients        | 1,499  | 571                       | -                             |
| Age (mean±SD)     | 67.5±11.1 | 67.9±11.7 | 1.00 (0.99, 1.01) a          |
| ≥65 years (%)     | 63.5   | 68.0                      | -                             |
| Sex (male)        | 46.2   | 47.6                      | 0.94 (0.78, 1.14)             |
| Rural residence   | 20.8   | 17.7                      | 1.22 (0.95, 1.57)             |
| Lower income      | 45.5   | 41.5                      | 1.18 (0.97, 1.43)             |
| Primary diagnosis | 38.4   | 13.7                      | 3.94 (3.04, 5.12)             |
|                   |        |                           | 3.74 (2.88, 4.87)             |
| Specialty of prescriber |    |                      | -                             |
| Oncology          | 7.8    | -                         | -                             |
| Internal medicine | 11.3   | -                         | -                             |
| General practitioner | 62.6 | -                         | -                             |
| General surgery   | 2.5    | -                         | -                             |
| Other             | 15.7   | -                         | -                             |
| Comorbidity factors (2 years prior) |          |                     | -                             |
| Hypertension      | 52.9   | 55.7                      | 0.89 (0.74, 1.08)             |
| Diabetes          | 24.4   | 27.5                      | 0.85 (0.68, 1.06)             |
| Ischemic heart disease | 34.5 | 33.3                      | 1.06 (0.86, 1.29)             |
| Congestive heart failure | 20.3 | 20.7                      | 0.98 (0.77, 1.24)             |
| Cerebrovascular disease | 8.7 | 12.8                      | 0.65 (0.48, 0.89)             |
| Atrial fibrillation | 15.3 | 17.7                      | 0.84 (0.65, 1.09)             |
| Anemia/blood disease | 54.0 | 60.6                      | 0.76 (0.63, 0.93)             |
| Peptic ulcer disease | 2.1 | 4.9                       | 0.42 (0.25, 0.71)             |
| Chronic kidney disease | 16.3 | 16.6                      | 0.97 (0.75, 1.26)             |
| Medications 1 week within index date | |                     | -                             |
| Corticosteroids    | 24.8   | 22.2                      | 1.15 (0.92, 1.45)             |
| Serotonin reuptake inhibitors | 8.6 | 10.0                      | 0.85 (0.61, 1.18)             |
| Gastroprotective agents | 57.4 | 58.8                      | 0.94 (0.77, 1.14)             |
| NSAID/Celecoxib    | 11.7   | 10.0                      | 1.20 (0.87, 1.64)             |
| Hormone replacement therapy | 2.4 | 1.4                       | 1.73 (0.80, 3.75)             |
| Anticoagulants in the 6 months prior | 22.3 | 33.3                      | 0.57 (0.46, 0.71)             |
| Antiplatelet in the year prior | 38.9 | 39.1                      | 0.99 (0.82, 1.21)             |
| Aspirin in the year prior | 37.1 | 36.4                      | 1.03 (0.84, 1.26)             |
| Metastatic cancer | 27.9   | 23.6                      | 1.25 (1.00, 1.56)             |
| Catheter/Chemotherapy in the 3 months prior to index date | 25.8 | 20.8                      | 1.32 (1.04, 1.66)             |
| Patients died in the 6-month follow-up | 33.5 | 35.9                      | -                             |

* Logistic regression model.

a 1 year difference.
Table 3
Patient characteristics by anticoagulant agent used at index date.

|                     | Warfarin | LMWH+ | All | Dalteparin | Other | Warfarin + LMWH |
|---------------------|----------|-------|-----|------------|-------|----------------|
| N patients          | 442      | 901   | 447 | 454        | 156   |                |
| Age (mean ± SD)     | 70.5 ± 10.0 | 65.6 ± 11.4 | 65.6 ± 11.1 | 65.6 ± 11.6 | 69.5 ± 10.6 |
| Sex (male)          | 46.4     | 44.6  | 42.5 | 46.7       | 54.5  |                |
| Rural residence     | 25.1     | 17.3  | 21.9 | 12.8       | 28.9  |                |
| Lower income        | 58.1     | 38.2  | 38.3 | 38.1       | 51.9  |                |
| Primary diagnosis   | 45.5     | 34.0  | 37.4 | 30.6       | 44.2  |                |
| Specialty of prescriber |          |       |     |            |       |                |
| Oncology            | 3.6      | 10.8  | 14.8 | 6.8        | 2.6   |                |
| Internal medicine   | 9.1      | 11.2  | 11.6 | 10.8       | 18.6  |                |
| General practitioner| 68.8     | 61.3  | 55.0 | 67.4       | 53.2  |                |
| General surgery     | 2.9      | 1.7   | 2.0  | 1.3        | 6.4   |                |
| Other               | 15.6     | 15.1  | 16.6 | 13.7       | 19.2  |                |
| Comorbidity factors (2 years prior) |          |       |     |            |       |                |
| Hypertension        | 60.9     | 48.8  | 48.8 | 48.9       | 53.8  |                |
| Diabetes            | 26.5     | 23.9  | 24.2 | 23.6       | 21.8  |                |
| Ischemic heart disease | 45.0     | 29.2  | 25.1 | 33.3       | 35.3  |                |
| Congestive heart failure | 28.5     | 16.6  | 17.0 | 16.3       | 18.6  |                |
| Cerebrovascular disease | 9.3      | 8.4   | 7.8  | 9.0        | 9.0   |                |
| Atrial fibrillation | 24.0     | 13.3  | 12.1 | 14.5       | 9.6   |                |
| Anemia/blood disease | 53.6     | 55.0  | 54.4 | 55.7       | 49.4  |                |
| Peptic ulcer disease | 1.4      | 2.3   | 1.6  | 3.1        | 3.2   |                |
| Chronic kidney disease | 35.5     | 12.7  | 13.9 | 11.5       | 16.7  |                |
| Medications 1 week within index date |          |       |     |            |       |                |
| Corticosteroids     | 15.8     | 30.2  | 32.7 | 27.8       | 19.2  |                |
| Serotonin reuptake inhibitors | 6.6     | 9.9   | 9.4  | 10.4       | 7.1   |                |
| Gastroprotective agents | 55.9     | 59.6  | 61.7 | 57.5       | 48.7  |                |
| NSAID/Celecoxib     | 8.1      | 13.1  | 13.6 | 12.6       | 14.1  |                |
| Hormone replacement therapy | 2.0    | 2.7   | 2.0  | 3.3        | 1.9   |                |
| Anticoagulants in the 6 months prior | 19.0    | 25.1  | 24.6 | 25.6       | 15.4  |                |
| Antiplatletes in the year prior | 46.2   | 35.0  | 35.6 | 34.4       | 41.0  |                |
| Aspirin in the year prior | 43.4   | 33.7  | 33.6 | 33.9       | 38.5  |                |
| Metastatic cancer   | 17.0     | 34.4  | 36.0 | 32.8       | 21.2  |                |
| Catheter/Chemotherapy in the 3 months prior to index date | 13.1 | 35.0 | 39.8 | 30.2 | 8.3 |

Notes:
- LMWH: Low molecular weight heparin.
- LMWH+: Concurrent use of warfarin with a low molecular weight heparin.

Sensitivity analyses

In a first sensitivity analysis, only patients with VTE recorded as a principal diagnosis were analysed (654 patients). Among these, 78 (11.9%) did not use anticoagulants at index date. Among those who did, patients with diabetes (0.53; 0.32–0.89) and those with prior anticoagulant use (0.55; 0.31–0.95) were less likely to use anticoagulants. Similar results as those obtained in the main analysis were observed for warfarin versus LMWH use. Among those who used anticoagulants at index date, 39.6% were not persistent on treatment (35.8% were not persistent among those with primary diagnosis) and only primary diagnosis was associated with an increased likelihood of persistence.

The fourth sensitivity analysis considered patients who used an anticoagulant anytime in the 3 and 7 days following the index date as anticoagulant users. Adopting this definition of use at index date decreased the proportion of non-users to 27.6% and 23.0%, respectively and increased the proportions of non-persistent patients to 40.2% and 39.8%, respectively. However, the results of the multivariable analyses assessing predictors of non-use and non-persistence revealed similar results as those of the main analysis.

Discussion

Our study used a large administrative database to assess use of outpatient anticoagulant treatment among cancer patients admitted for VTE or who incurred a VTE in-hospital. Our study found that 28% of patients did not use any anticoagulant therapy at discharge. Excluding patients who used anticoagulants in the six-month period preceding the index date revealed a similar proportion of anticoagulant non-use at index date (24%), and extending the definition of use at index date to use within 3 and 7 days of index date lowered the proportion of non-users to 27.6% and 23.0%, respectively. Our study also found that patients with cerebrovascular disease, those with peptic ulcer disease and those who had used anticoagulants in the six months prior to index date were less likely to receive an anticoagulant at index date. These results are not surprising because individuals with cerebrovascular disease might be at high risk of intracranial haemorrhage, while those with peptic ulcer disease and those using anticoagulants prior to the event are at higher risk of gastrointestinal bleeding which may explain their lower likelihood of receiving an anticoagulant post hospital.
In our study, only 60% of the patients who used anticoagulants at index date were persistent on their medication. Patients who were discharged with a primary diagnostic code of VTE and those with metastatic cancer were more likely to be persistent, while those with chronic kidney disease were less persistent. A primary diagnosis code may be associated with more serious and life-threatening conditions in which case physicians and their patients may be more inclined to adhere to VTE treatment recommendations. Similarly, patients with metastatic cancer are at high risk of VTE recurrence which explains their better adherence to treatment recommendation for anticoagulant use; while LMWHs are contraindicated in chronic kidney disease which explains the low persistence in this group [25]. Concerns about an increased risk of bleeding with extended prophylaxis use may be the main reason for the lack of extended anticoagulant use [41]. In the Switzerland study, among those who received extended prophylaxis, only 27% received a prescription for at least 28 days [38]. And in a survey conducted in the UK, more than 25% of British oncologists reported that thromboprophylaxis was rarely used [42].

Almost four out of ten study patients who used anticoagulants at index date used warfarin or warfarin in combination with a LMWH.
ing in these databases; however, the in use in our study population. Information on genetic defects and gene
agulant use and it is doubtful that it explains the lack of anticoagulant risk of recurrent VTE is controversial and unlikely explains the large
sence of clinical data to con
find an association between high body mass index (BMI) and VTE oc-
tion on diet, lifestyle and clinical data. Epidemiological studies have
bias. Nonetheless, our study suffers from limitations that are common
care coverage to all citizens, thus limiting participation and observation
Limitation
The study was funded by Pfizer Canada Inc. The sponsor was in-
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Dr. Rahme declares that she had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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