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IN FOCUS

Thromboprophylaxis rates in US medical centers: success or failure?

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Summary. *Background:* As hospitalized medical patients may be at risk of venous thromboembolism (VTE), evidence-based guidelines are available to help physicians assess patients' risk for VTE, and to recommend prophylaxis options. The rate of appropriate thromboprophylaxis use in at-risk medical inpatients was assessed in accordance with the 6th American College of Chest Physicians (ACCP) guidelines. *Methods:* Hospital discharge information from the Premier Perspective™ inpatient data base from January 2002 to September 2005 was used. Included patients were 40 years old or more, with a length of hospital stay of 6 days or more, and had no contraindications for anticoagulation. The appropriateness of VTE thromboprophylaxis was determined in seven groups with acute medical conditions by comparing the daily thromboprophylaxis usage, including type of thromboprophylaxis, dosage of anticoagulant and duration of thromboprophylaxis, with the ACCP recommendations. *Results:* A total of 196 104 discharges from 227 hospitals met the inclusion criteria. The overall VTE thromboprophylaxis rate was 61.8%, although the appropriate thromboprophylaxis rate was only 33.9%. Of the 66.1% discharged patients who did not receive appropriate thromboprophylaxis, 38.4% received no prophylaxis, 4.7% received mechanical prophylaxis only, 6.3% received an inappropriate dosage, and 16.7% received an inappropriate prophylaxis duration based on ACCP recommendations. *Conclusions:* This study highlights the low rates of appropriate thromboprophylaxis in US acute-care hospitals, with two-thirds of discharged patients not receiving prophylaxis in accordance with the 6th ACCP guidelines. More effort is required to improve the use of appropriate thromboprophylaxis in accordance with the ACCP recommendations.

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Introduction

Venous thromboembolism (VTE), including deep-vein thrombosis (DVT) and pulmonary embolism (PE), is the third most prevalent cardiovascular disease in the USA after myocardial infarction (MI) and stroke [1]. Recent national estimates suggest that there are more than 600 000 symptomatic VTE events each year in the USA, many of which are hospital-acquired. The annual death toll for VTE is estimated at 300 000 persons per year [2]. Therefore VTE is a major US health problem, and remains a problem in hospitalized medical patients [2,3].

The mandate to practice according to evidence-based guidelines was established in 1986 with the publication of the 1st American College of Chest Physicians (ACCP) guidelines on antithrombotic therapy [4]. These guidelines have been updated regularly and provide clear and explicit recommendations for the use of appropriate VTE prophylaxis in particular groups of patients who are at risk of hospital-acquired VTE. They highlight that hospitalized medical patients with immobility and additional risk factors are at significant risk of VTE, and remain so even when receiving suboptimal prophylaxis [4]. Randomized clinical trials provide evidence that thromboprophylaxis reduces the incidence of VTE [4]. In general medical patients, VTE occurred in 2.8–5.6% of patients receiving thromboprophylaxis compared with 5.0–14.9% of patients receiving placebo [5–7].

The guidelines outline the type and dose of medication, time of initiation of therapy, and duration of prophylaxis that has been deemed appropriate for thromboprophylaxis [8,9]. Thus physicians are guided as to what constitutes the most appropriate prophylactic practises and regimens across a range of patient populations. Appropriate prophylaxis is achieved only by providing the patient with the appropriate drug (or device) at the appropriate dose and for the appropriate duration [8].

Despite this long-standing guidance on appropriate VTE prophylaxis, a number of international and national registry studies have identified suboptimal adoption of and adherence to guidelines on appropriate VTE prophylaxis in most at-risk populations [3,10–14]. Although two-thirds of medical inpatients with risk factors for VTE received some form of thromboprophylaxis, less than a quarter of these at-risk patients had thromboprophylaxis maintained until hospital discharge as recommended in the ACCP guidelines [11]. In a retrospective study examining VTE prophylaxis practises in patients with confirmed DVT, only 29% of patients had received any form of thromboprophylaxis prior to the VTE event [13]. It seems that the problem is not simply one of physicians failing to prescribe thromboprophylaxis, but also that appropriate VTE prophylaxis is not used, either in terms of the therapy chosen or the regimen adopted [14].

Few studies to date have evaluated whether the thromboprophylaxis was appropriate in all of the recommended aspects, namely thromboprophylaxis type, dose and duration [3]. The present study specifically investigates the rate of appropriate thromboprophylaxis as defined by the 6th ACCP guidelines, using a large, national, administrative hospital data base. The use of a large, geographically diverse sample has allowed longitudinal evaluation of appropriate prophylaxis practises for 3.5 years following the introduction of the guidelines.

Patients and methods

We used patient discharge information from the Premier Perspective™ data base, which contains information from approximately 5.5 million patient discharges per year from not-for-profit, non-governmental, community and teaching hospitals, and health systems.

Information collection

Hospital and patient demographics, discharge information, principal and secondary diagnoses and procedures, and detailed resource consumption information for each discharge by day of hospitalization were extracted from the Premier Perspective™ data base. All patient records used in this study were de-identified in compliance with the Health Insurance Portability and Accountability Act of 1996 [15]. Records relating to the same hospital discharge were linked using a non-personal identifier assigned by the provider that prevented patient identification and the linking of identifiers to patients. This study did not involve 'human subjects' and was exempt from Institutional Review Board overview under the Common Rule [45 CFR §46.101(b)(4)] [16].

Patient discharge selection criteria

The study population comprised records from patients discharged from January 2002 to September 2005 from 227 hospitals across the USA. These hospitals submitted detailed patient hospitalization information by day of stay in monthly extracts to the Premier Perspective™ data base.

Patient discharge records were included, if the patient fulfilled the following criteria:

1. Was aged 40 years or older.
2. Had a minimum hospital length of stay of 6 days, and was not transferred from, or discharged to, another acute care facility (based on the MEDical patients with ENOXaparin trial) [5].
3. Was deemed at 'high risk' of VTE because of the presence of one or more of the VTE risk factors identified by the 6th ACCP guidelines [8]. This version of the guidelines was used so that the hospitals included in this study had sufficient time to educate their physicians and implement the recommendations in advance of the study period (January 2002 to September 2005).
4. Had a principal medical diagnosis [based on the International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9 CM) coding system] that fell into the acute medical illness category. Diagnosis groups within the acute medical illness category were acute MI (AMI), heart failure, ischemic stroke, severe lung disease, cancer, acute spinal cord injury (without surgery), and trauma (without surgery) (see Appendix SA in Supplementary material for details of the ICD-9 CM Diagnosis and Procedure Code Definitions used in this study). A principal diagnosis was assigned to each patient by the hospital.
5. Did not have a potential contraindication to or a disease condition that required modification of the ACCP-recommended anticoagulant therapy. Patient discharges were excluded if ICD-9 codes suggested the presence of active peptic ulcer disease, malignant hypertension, blood disease (iron deficiency and other anemias, hereditary hemolytic anemias, hereditary elliptocytosis, anemias because of disorders of glutathione metabolism, thalassemias, sickle-cell trait and disease, other hemoglobinopathies, acquired hemolytic anemias, aplastic and other unspecified anemias, coagulation defects, purpura and other hemorrhagic conditions), HIV infection, pregnancy, VTE present on admission, intubations of the gastrointestinal and respiratory tracts, liver disease, thrombocytopenia, or insufficient renal function (modified from McGarry *et al.* [17], see Appendix SB for the list of the exclusion criteria used in this study, with the ICD-9 CM Diagnosis and Procedure Code).

Rates of any VTE prophylaxis

The use of any guideline-recommended pharmacological (unfractionated heparin (UFH), enoxaparin, dalteparin, tinzaparin, or warfarin) or mechanical [intermittent pneumatic compression (IPC), or elasticated stockings (ES)] prophylaxis

was measured for each patient discharge that met the inclusion criteria. We report the rates of 'any VTE prophylaxis' as any patient discharged who had received at least one dose of an anticoagulant at any dose, or mechanical compression, or both during their hospital stay.

Rates of appropriate VTE prophylaxis

In order to determine whether the use of pharmacological and mechanical prophylaxis in at-risk patients was appropriate in accordance with the 6th ACCP guidelines, a detailed examination of hospital administrative records by day of hospital stay was undertaken for each patient discharge. The use of specific anticoagulant medication and compression devices was assessed, as well as the use of the appropriate VTE prophylaxis type, regimen, daily dosage, and duration of therapy across hospital service days, as defined by the 6th ACCP guidelines [8]. The specific criteria used in this study defining appropriate prophylaxis are shown in Appendix SC.

Drug choice

Appropriate drug choice was defined as UFH alone for AMI discharges; UFH, enoxaparin, dalteparin or tinzaparin for ischemic stroke, heart failure, severe lung disease, cancer and acute spinal cord injury; and enoxaparin, dalteparin or tinzaparin for trauma discharges.

Duration

The requirements for duration of therapy were based on the patient's length of stay. We set the duration of therapy required for UFH, enoxaparin, dalteparin and tinzaparin as the patient's length of stay minus 2 days, to accommodate the possibility of partial days of stay occurring at admission and discharge, or the possibility of an invasive procedure occurring during hospitalization for which anticoagulation is not recommended on the day of the procedure.

Dosage

The appropriate drug dosages (per hospital service day) were at least: 10 000 U for UFH; 40 mg for enoxaparin; 2500 U for dalteparin; and 3500 U for tinzaparin.

Mechanical prophylaxis

For appropriate prophylaxis, patients discharged with acute spinal cord injury were required to have received IPC or ES, in addition to pharmacological prophylaxis, for the duration of their hospital stay minus 2 days.

Appropriate prophylaxis rates for each quarter and for the study period were determined for each medical diagnosis group and weighted by discharge volume within each study period.

We also examined the breakdown of the ways in which thromboprophylaxis was not appropriate. For example, we assessed whether they had received no prophylaxis, had received an inappropriate prophylaxis regimen, or inappropriate duration or dosage of pharmacological thromboprophylaxis. Patient discharges that indicated anticoagulation therapy for a sufficient number of days, but at daily doses below the minimum appropriate daily dose for the medications administered, were deemed to be inappropriate by not meeting the dosing criteria. Patient discharges that indicated anticoagulation therapy for fewer than the minimum appropriate number of days were designated inappropriate by not meeting the duration criterion. Patient discharges that did not indicate pharmacological thromboprophylaxis were further divided into patients who received no prophylactic medication and no mechanical compression, and patients who received only mechanical prophylaxis. Furthermore, we also assessed the impact of hospital and patient characteristics, including urban or rural service areas, census region, hospital size, patient admission source, and attending physician specialty, on the rate of appropriate prophylaxis.

Results

From an initial 9 895 049 patients in the data base who were discharged within the study period, a total of 196 104 (2.0%) met the inclusion criteria for medical patients at high risk of VTE (Fig. 1). The characteristics of the hospitals included in this analysis are shown in Table 1.

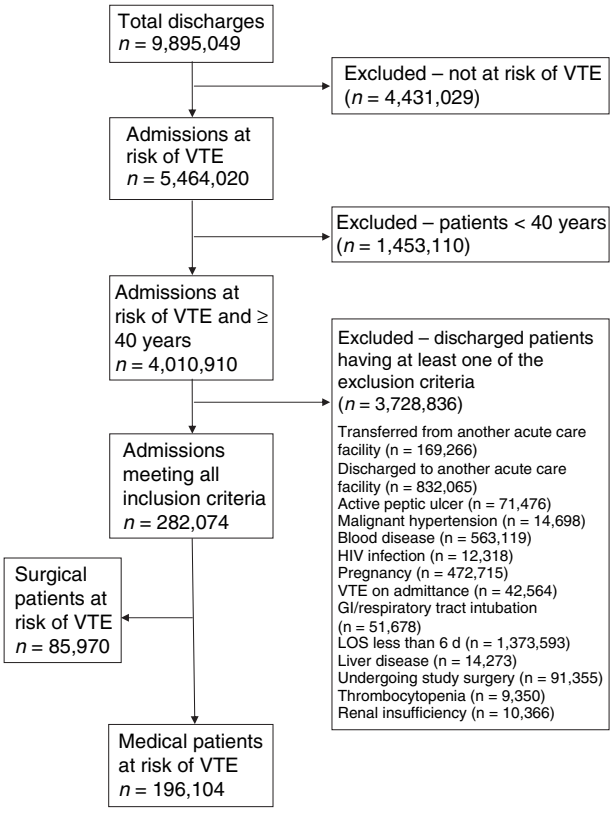

Fig. 1. Study population.

Table 1 Hospital characteristics

	No. of patients	%
Total discharges	196 104	100.0
Geographic region		
East North Central	16 681	8.5
East South Central	15 628	8.0
Middle Atlantic	16 515	8.4
Mountain	4 895	2.5
New England	2 659	1.4
Pacific	21 171	10.8
South Atlantic	81 613	41.6
West North Central	10 293	5.2
West South Central	26 649	13.6
Teaching status		
Non-teaching	124 926	63.7
Teaching	71 178	36.3
Population served		
Rural	26 042	13.3
Urban	170 062	86.7
Bed numbers		
6–99	7434	3.8
100–199	19 295	9.8
200–299	28 675	14.6
300–499	69 732	35.6
500+	70 968	36.2

Table 2 Study population and thromboprophylaxis rates

Discharge group	No. of patients	Any prophylaxis (%)	Appropriate prophylaxis (%)
Total medical patients	196 104	61.8	33.9
Acute myocardial infarction	22 563	95.4	43.0
Heart failure	36 861	72.0	40.1
Ischemic stroke	8962	70.8	49.2
Trauma (without surgery)	9999	64.2	20.3
Cancer	30 708	56.4	27.6
Severe lung disease	86 891	49.8	31.0
Acute spinal cord injury (without surgery)	120	40.8	20.8

The most common medical diagnosis was severe lung disease, followed by heart failure, cancer and AMI (Table 2). The any thromboprophylaxis rate for all at-risk medical discharges was 61.8%, and ranged from 40.8% for discharges with acute spinal cord injury to 95.4% for those discharges with AMI (Table 2).

However, the appropriate prophylaxis rate among all of the at-risk medical patient discharges was much lower, at 33.9%. The rate ranged from 20.3% in trauma discharges not requiring surgery to 49.2% in discharges with ischemic stroke (Table 2). Appropriate prophylaxis was observed in 43.0% of AMI, 27.6% of cancer, 40.1% of heart failure, and 31.0% of severe lung disease discharges. Appropriate VTE prophylaxis appeared to be low for discharges with spinal cord injury, at 20.8%.

Comparison of the rates of appropriate prophylaxis for each calendar quarter suggests a slight trend (since the issue of the 6th guidelines in 2001) towards increasing use of appropriate prophylaxis in at-risk medical discharges (Fig. 2). While the use of prophylaxis appears to have been quite constant in discharges with cardiovascular diseases (stroke, heart failure, and AMI), the use of appropriate VTE prophylaxis in cancer and severe lung disease discharges appears to have increased modestly.

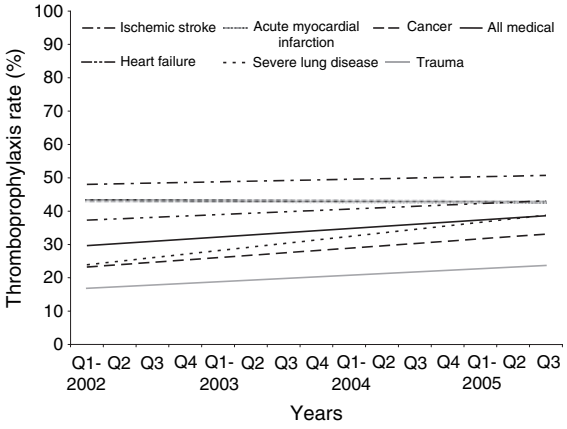

Fig. 2. Adherence to thromboprophylaxis guidelines in at-risk medical patients by calendar quarter.

Reasons for lack of appropriate prophylaxis

The reasons for lack of appropriate thromboprophylaxis in each medical group are shown in Table 3. Overall, the primary reason for lack of appropriate thromboprophylaxis was the absence of any thromboprophylaxis, accounting for 58.1% of all inappropriate prophylaxis. Insufficient duration of thromboprophylaxis was the second most frequent reason (25.3% of inappropriate prophylaxis). Variation was also observed between individual groups, with AMI discharges more often receiving inappropriate prophylaxis duration, whereas the other groups most often received no prophylaxis.

Factors affecting the rates of appropriate prophylaxis

The impact of both hospital and physician characteristics on the rates of appropriate VTE prophylaxis are shown in Table 4.

Geographical variations in the appropriate prophylaxis rates were noted. For example, while appropriate VTE prophylaxis was adopted for almost 40% of discharges managed in the Middle Atlantic region, values in West North Central and New England were below 30%. Appropriate VTE prophylaxis across all inpatient groups was found to be 4.3% higher in teaching hospitals than in non-teaching hospitals, and 5.2% higher in urban compared with rural hospitals. A trend towards more frequent use of appropriate prophylaxis in larger hospitals was also evident, with those offering beds for more than 300 inpatients achieving compliance rates of more than 33.7% compared with appropriate prophylaxis rates of less than 30% in smaller hospitals.

Table 3 Reasons for lack of appropriate thromboprophylaxis

	Patients received no prophylaxis (%)*	Patients received mechanical prophylaxis only (%)*	Patients received insufficient duration of prophylaxis (%)*	Patients did not receive appropriate dose of prophylaxis (%)*	Total rate for lack of appropriate prophylaxis (%)*
All medical patients	38.4	4.7	16.7	6.3	66.1
Acute myocardial infarction	4.6	0.4	44.2	7.8	57.0
Heart failure	28.0	1.7	23.9	6.3	59.9
Ischemic stroke	29.2	3.9	12.6	5.0	50.7
Trauma (w/o surgery)	35.8	20.6	16.8	6.6	79.8
Cancer	46.0	10.6	5.9	9.5	72.0
Severe lung disease	50.2	3.2	10.7	4.8	68.9
Acute spinal cord injury (w/o surgery)	59.2	0.0	20.0†	0.0	79.2

*Percentage of the whole population 'at-risk' of venous thromboembolism.
†Of these discharges, 9.2% received pharmacological and mechanical prophylaxis for an inappropriate duration, and 10.8% received pharmacological but not mechanical prophylaxis for the correct duration.

Observed thromboprophylaxis rates also varied with the specialty of the attending physician. The highest rates were observed for cardiologists (41.6%), followed by surgeons (37.1%), emergency physicians (25.9%), internal medicine specialists (33.8%) and pulmonologists (34.4%); the lowest rates were noted among urologists (17.3%) and anesthetists (12.5%). Other factors assessed included the patient's insurance status. Thromboprophylaxis rates ranged from 32.5% for patients who had a government-supported scheme (other than Medicare/Medicaid or Veterans Affairs) up to 38.2% for those with Managed Care, 34.9% for Medicaid and 32.6% for Medicare patients.

Discussion

This study demonstrates that appropriate prophylaxis, as defined by recommendations for the drug, dose and duration of thromboprophylaxis in evidence-based guidelines, was used in less than 40% of acute medical inpatients in subgroups of patients considered to be at high risk of VTE.

This large-scale evaluation confirms the preliminary findings of previous smaller, less rigorous studies, indicating that rates of appropriate VTE prophylaxis in US medical inpatient populations are low [11,12,18]. A retrospective registry study of 1595 acutely ill medical patients found that only 54% of patients who met the criteria for VTE prophylaxis received any form of prophylaxis while in hospital [12]. This latter study, however, did not take into account dose or duration when considering whether thromboprophylaxis was appropriate. This may explain the higher rates of appropriate thromboprophylaxis compared with the results of the present study.

This study extends the findings of previously published reports on non-adherence to VTE prevention guidelines, demonstrating that a high percentage of at-risk patients do not receive appropriate VTE prophylaxis during their acute hospital stay. For example, our study shows that the rate of appropriate prophylaxis in the cancer medical diagnosis group remains low. Therefore there is an opportunity to improve the rate of thromboprophylaxis in cancer patients, particularly considering that malignancy alone has been shown to be associated with a 4-fold increased risk for VTE and malignancy with chemotherapy has been shown to be associated with a 6.5-fold increased risk for VTE [19]. In patients with AMI, the use of pharmacological prophylaxis was much higher, but where prophylaxis was not considered appropriate, the problem was most frequently insufficient duration. In patients with AMI, this is likely to be explained by the fact that these patients would have received anticoagulants as therapy for AMI itself.

Our study highlights shortcomings in the levels of appropriate prophylaxis offered to at-risk patients in the hospital setting. Unless patients are receiving recommended therapies at the correct time, for an adequate duration and at doses that are within a suitable therapeutic range to match known risk levels, the use of prophylactic intervention may be suboptimal and may constitute a wasteful and costly intervention in terms of healthcare resources and clinical outcomes. Although VTE rates during hospitalization were not evaluated in this study, it is likely that patients not receiving appropriate prophylaxis are at increased risk of VTE. Further studies are required to test this hypothesis.

The reasons for lack of appropriate prophylaxis varied, but the majority of discharged patients who received inappropriate prophylaxis were found to have received no pharmacological prophylaxis at all. One of the possible reasons for the lack of prophylaxis may include the delay in adopting clinical practise guidelines by physicians, who often view guidelines as difficult to apply, fail to appreciate the applicability of guidelines to their field of practise, or show inertia when required to change [20]. Increased education of physicians may help to raise awareness and lead to better implementation of existing guidelines. Many physicians may still fail to appreciate the natural history of VTE and the interventions or series of risk factors that lead to symptomatic VTE [21]. For some at-risk groups (e.g. elderly patients) anticoagulant therapy may be associated with an increased bleeding risk, and physicians may be cautious over their use despite good evidence that choosing anticoagulant therapy can confer greater benefits than risks [22]. Furthermore, practical and administrative barriers can

Table 4 Factors affecting the rates of appropriate thromboprophylaxis

Hospital/physician characteristics	Patient discharges (*n*)	Appropriate prophylaxis rate (%)
Rural or urban		
Urban	170 062	34.6
Rural	26 042	29.4
Admission source		
Emergency department	133 523	35.3
Physician referral	57 482	31.2
Other	5099	26.2
Bed numbers		
0–99	7434	28.1
100–199	19 295	28.5
200–299	28 675	29.7
300–499	69 732	33.7
500+	70 968	37.8
Payment		
Medicare	126 989	32.6
Managed care	30 700	38.2
Commercial	11 622	35.5
Medicaid	13 454	34.9
Other payer	11 669	33.2
Other government*	1670	32.5
Region		
South Atlantic	81 613	35.2
West South Central	26 649	35.4
Pacific	21 171	30.3
East North Central	16 681	33.4
Middle Atlantic	16 515	36.6
East South Central	15 628	31.0
West North Central	10 293	28.9
Mountain	4895	34.2
New England	2659	28.0
Attending physician specialty		
Internal medicine	74 356	33.8
Surgery specialty	19 151	37.1
Other	45 034	31.4
Cardiology	23 855	41.6
Pulmonology	18 275	34.4
Hematology/oncology	6287	24.4
Medical oncology	3894	25.0
Nephrology	2217	28.5
Gastroenterology	1132	23.2
Urology	503	17.3
Emergency	893	25.9
Geriatrics	491	28.7
Anesthesia	16	12.5
Hospital teaching status		
Non-teaching	124 926	32.3
Teaching	71 178	36.6

*Insurance coverage through state/federal government-funded welfare program (e.g. Indian Health Service).

also contribute to poor adoption of recommended practises. For example, the lack of a consistent process (e.g. in medical education, IT systems, hospital order forms) may act as a barrier to guideline adherence, and may explain some of the low rates of thromboprophylaxis identified in our study. The availability of tools such as electronic alerts has led to an increase in thromboprophylaxis rates and may therefore be beneficial to hospitals [23].

For each of the medical diagnosis groups described in this study, there is a strong evidence base for use of specific prophylactic therapies. However, we found little evidence of a trend towards an increase in thromboprophylaxis over the study period, despite the publication of the 6th ACCP guidelines on VTE prevention in 2001 [8]. The need to improve VTE prevention and treatment in the USA has been recognized. Both The Joint Commission (VTE Technical Advisory Panel, National Consensus Standard for Prevention and Care of Venous Thromboembolism) and the National Quality Forum are working to establish national consensus standards and develop performance measures that promote the wider use of evidence-based thromboprophylaxis [24]. It is therefore the responsibility of individual hospitals to identify areas in which they can improve their VTE prophylaxis.

As our study is based on retrospective discharge records, we cannot fully evaluate the circumstances that may have led to a physician choosing not to adopt thromboprophylactic practises in accordance with current guidelines. The study is also limited by its need to evaluate practise based only on a principal diagnosis. While the thromboprophylaxis rates are based on the primary reason for the patient being in hospital, there is the potential that inappropriate thromboprophylaxis may have resulted from other factors or diagnoses that precluded optimal VTE prophylaxis for the principal diagnosis. The application of inclusion and exclusion criteria regarding concomitant clinical conditions and length of stay may have contributed to underestimates of the appropriateness of VTE prophylaxis regimens and interventions used in this disparate group of patients. Patients may not have been at high risk of VTE, and therefore would not require prophylaxis. Only patients at higher risk of VTE have been included in the study.

This study highlights the current under-use of appropriate VTE prophylaxis in a wide range of medical inpatients at risk of VTE. The findings indicate that while VTE prophylaxis may be considered and then used in acute care inpatients with known risk factors for VTE, often thromboprophylaxis is not used at all or the use of therapies does not match with evidence-based medicine guidelines in terms of choice of therapeutic modality, and dose and duration of treatment. Improvement in appropriate thromboprophylaxis is urgently required to reduce the burden of VTE on the US healthcare system.

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Disclosure of Conflict of Interests

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ski and G. Yang work for Premier Inc., who received funding to carry out this work from sanofi-aventis US Inc. J. Lin is an employee of sanofi-aventis US Inc. A. Amin and S. Stemkowski both had full access to the raw data set and take responsibility for the integrity of the data and the accuracy of the data analysis.

Supplementary material

The following supplementary material is available for this article:

Appendix SA. International Classification of Diseases, 9th Revision, Clinical Modification (ICD-9 CM) diagnosis and procedure codes for medical conditions.
Appendix SB. Patient discharge exclusion criteria.
Appendix SC. Definitions of appropriate prophylaxis regimens by study group.

This material is available as part of the online article from: http:/www.blackwell-synergy.com/doi/abs/10.1111/j.1538-7836.2007.02650.x
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