

# Appropriate Thromboprophylaxis In Hospitalized Cancer Patients

Alpesh Amin, MD, MBA, Stephen Stemkowski, MHA, PhD,  
Jay Lin, PhD, MBA, and Guiping Yang, MS

Dr. Amin is Professor of Medicine at the University of California, Irvine, California. Dr. Lin is Director, Health Outcomes, CV at Sanofi-Aventis in Bridgewater, New Jersey. Dr. Stemkowski is Director of Research and Analytics and Dr. Yang is Senior Statistical Programmer at Premier Inc. in Charlotte, North Carolina.

Alpesh N. Amin, MD, MBA  
University of California, Irvine  
101 The City Drive South, Building 58,  
Room 110, ZC-4076H,  
Orange, CA 92868  
Tel: 714-456-3785  
Fax: 714-456-3875  
E-mail: anamin@uci.edu

**Abstract: Background:** Cancer is associated with an increased risk of venous thromboembolism (VTE) in hospitalized patients. Despite availability of evidence-based guidelines recommending thromboprophylaxis in cancer patients, many cancer patients do not receive appropriate thromboprophylaxis. This study provides a large, real-world analysis of the rates of thromboprophylaxis use in hospitalized cancer patient discharges. **Methods:** Hospital discharge information from the Premier Perspective inpatient database from January 2002–September 2005 was used. Included discharges had a principal diagnosis of cancer, were aged 40 years or older, had a length of hospital stay of 6 days or more, and had no contraindications for anticoagulation. The rate of appropriate VTE prophylaxis was determined according to the 7th American College of Chest Physicians guidelines, taking into account mechanical compression and chemoprophylaxis, dosage of anticoagulant, and duration of therapy. **Results:** A total of 72,337 cancer discharges with an indication for thromboprophylaxis were identified (30,124 surgical, 42,213 nonsurgical). The overall rate of any level of VTE prophylaxis was 53.6%; however, the rate of appropriate thromboprophylaxis (according to the 7th ACCP guidelines) was 27.0% (27.0% surgical, 27.1% nonsurgical). The most common reason for inappropriate prophylaxis (46.0% of all discharges) was no prophylaxis received, despite having no contraindication to anticoagulation. **Conclusions:** This study highlights that despite the presence of evidence-based guidelines, appropriate thromboprophylaxis is severely underused in all types of at-risk cancer patients. Greater efforts are needed to improve the implementation of guidelines, and to ensure that more cancer patients receive appropriate thromboprophylaxis.

Venous thromboembolism (VTE), in the form of deep-vein thrombosis (DVT) and pulmonary embolism (PE), is the most frequent complication of cancer.<sup>1</sup> Indeed, VTE is the second most common cause of death in hospitalized cancer patients after cancer itself.<sup>1,2</sup> Annually, nearly 1 million people experience symptomatic VTE in the United States, and in approximately one-third of cases, the consequences are fatal.<sup>3</sup> Among cancer patients,

## Keywords

Venous thromboembolism, cancer, guidelines, audit

the annual incidence of VTE has been estimated to be 5 times higher than that for the general population.<sup>1</sup> Cancer alone is associated with a 4.1-fold increase in the risk of thrombosis, with the use of chemotherapy conferring additional risk.<sup>1</sup> Despite this increased risk, a recent study of prophylaxis practices using electronic alerts found that cancer patients were less likely to receive prophylaxis compared with patients without cancer.<sup>4</sup>

There is strong evidence from randomized controlled trials that prophylaxis with anticoagulant therapy can significantly reduce the incidence of thrombotic complications in acutely ill medical patients, including those with malignant disease. Compared with no thromboprophylaxis, the use of low-molecular-weight heparin (LMWH) anticoagulant therapy has been shown to significantly reduce the relative risk for VTE by 45–63% in acutely ill patients.<sup>5,6</sup> In cancer patients undergoing surgery, both unfractionated heparin (UFH) and LMWH have shown to be equally effective in preventing VTE.<sup>7,8</sup>

Today, there are many evidence-based guidelines with recommendations for the prevention and treatment of VTE.<sup>9–12</sup> Current guidelines highlight the importance of thromboprophylaxis in cancer patients to prevent avoidable VTE-related and potentially life-threatening complications of cancer and its management in both medical and surgical patients.<sup>9,11</sup>

However, real-world clinical practice may not be in line with current recommendations for the prevention of VTE. The Fundamental Research in Oncology and Thrombosis (FRONTLINE) global survey of oncologists' perceptions and practices regarding the management of VTE suggests that VTE risk is still underestimated and thromboprophylaxis is underused in cancer patients. Although more than 50% of surgeons reported using routine thromboprophylaxis when performing cancer surgery, less than 5% of medical oncologists reported using thromboprophylaxis.<sup>13</sup> Similarly, a recent multicenter hospital audit found that medical inpatients admitted for cancer were significantly less likely to receive any form of VTE prophylaxis when compared with other medical patients.<sup>14</sup> Another recent retrospective study of more than 12 million medically ill patient discharges from 330 US hospitals confirms the low-risk rating assigned to patients with cancer, with more than 75% unlikely to receive thromboprophylaxis.<sup>15</sup> The risk of VTE in cancer patients does not desist after the initial VTE event, as this population is also at high risk for recurrent VTE. In a study of patients with cancer and VTE, 17% of patients receiving long-term oral anticoagulation and 9% of patients receiving LMWH experienced recurrent VTE.<sup>16</sup>

Such studies highlight that the VTE risk faced by cancer patients is underappreciated and poorly managed. To our knowledge, no studies to date have reported on the rates of and factors affecting appropriate thrombo-

prophylaxis in cancer patients (as defined by evidence-based guidelines) according to whether or not they require surgery. Moreover, no studies have provided prophylaxis rates for subcategories of cancers, despite it being known that some cancers and treatments carry higher VTE risks than others.<sup>1,17</sup>

The objective of this study was to estimate the rate of appropriate prophylaxis in hospitalized nonsurgical and surgical cancer patients, and to assess the reasons for inappropriate thromboprophylaxis when observed. The study used discharge records from a large real-world US population to provide new, detailed and robust data on the prevention of VTE in cancer patients. The reported study population was used to compare rates of appropriate thromboprophylaxis according to definitions provided in the 7th edition of the American College of Chest Physicians (ACCP) guidelines on VTE prevention.<sup>9</sup>

## Methods

### *Information Source*

Patient discharge information was obtained from the Premier Perspective database,<sup>18</sup> which contains information on approximately 5.5 million patient discharges per year from not-for-profit, nongovernmental, community and teaching hospitals and health systems in the United States. The study population comprised records from both surgical and nonsurgical cancer patients discharged from 227 hospitals between January 2002 and September 2005. The participating hospitals submitted detailed patient hospitalization information by day of stay in the form of monthly data extracts to the Premier Perspective database.

### *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 database. All patient records used in this study were made anonymous in compliance with the Health Insurance Portability and Accountability Act of 1996.<sup>19</sup> Records relating to same-hospital discharge were linked using a nonpersonal identifier assigned by the provider, which prevented subject identification and the linking of identifiers to subjects. Therefore, this study did not involve "human subjects" and was exempt from Institutional Review Board oversight under the Common Rule [45 CFR §46.101(b)(4)].<sup>20</sup>

### *Patient Discharge Selection Criteria*

Patient discharge records were included in the study if they met the following criteria: 1) a principal cancer diagnosis (based on the International Classification of

Diseases, 9th Revision, Clinical Modification [ICD-9 CM] coding system). Subgroups of particular cancer types were formed based on the principal diagnosis assigned by the hospital. The types of cancer included were: oral cavity, stomach, colorectal, pancreatic, lung, melanoma, breast, uterine, ovarian, prostate, bladder, kidney, non-Hodgkin lymphoma, and "other cancers"; 2) age over 40 years; 3) minimum length of hospital stay of 6 days (a criterion based on the MEDENOX trial),<sup>5</sup> and not transferred from another acute-care facility; 4) no potential contraindications to, or other disease condition that required modification of ACCP-recommended anticoagulant therapies.<sup>9</sup>

Patient discharge records were excluded if secondary ICD-9 CM diagnosis codes suggested any of the following: the presence of active peptic ulcer disease; malignant hypertension; blood disease (iron deficiency and other anemias, hereditary hemolytic anemias, hereditary elliptocytosis, anemias due to 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 (exclusion criteria modified from McGarry and Thompson).<sup>21</sup>

The selected cancer discharges were further divided into discharges that did not undergo surgery (referred to as "nonsurgical" cancer discharges) and discharges that did undergo surgery whether cancer related or not (referred to as "surgical" cancer discharges).

### ***VTE Prophylaxis Use***

**Any VTE Prophylaxis** The rates of "any VTE prophylaxis" are the percentage of discharges where at least one dose of any guideline-recommended pharmacologic prophylaxis (UFH, enoxaparin, dalteparin, tinzaparin, or warfarin) was received, or where at least one order for mechanical prophylaxis (intermittent pneumatic compression [IPC] or elastic stockings [ES]) was made at any point during the hospital stay.

**Appropriate VTE Prophylaxis** In order to determine whether the use of pharmacologic and mechanical prophylaxis in at-risk cancer patients was appropriate in accordance with the 7th ACCP guidelines,<sup>9</sup> a detailed examination of hospital administrative records by day of hospital stay was undertaken for each discharge. As a large proportion of discharges in this analysis were taken from before the 7th ACCP guidelines were released, we compared the rates from before and after the release of the

guidelines (September 2004) to assess the likely impact of current guidelines on appropriate prophylaxis rates. "Appropriate" prophylaxis was defined as the use of an ACCP-guideline-recommended prophylactic regimen (or combination of regimens), at the appropriate daily dosage and duration, across hospital service days. Appropriate prophylaxis rates per quarter, and for the entire study period, were then determined for both the nonsurgical and surgical cancer groups, and weighted by discharge volume within each study period.

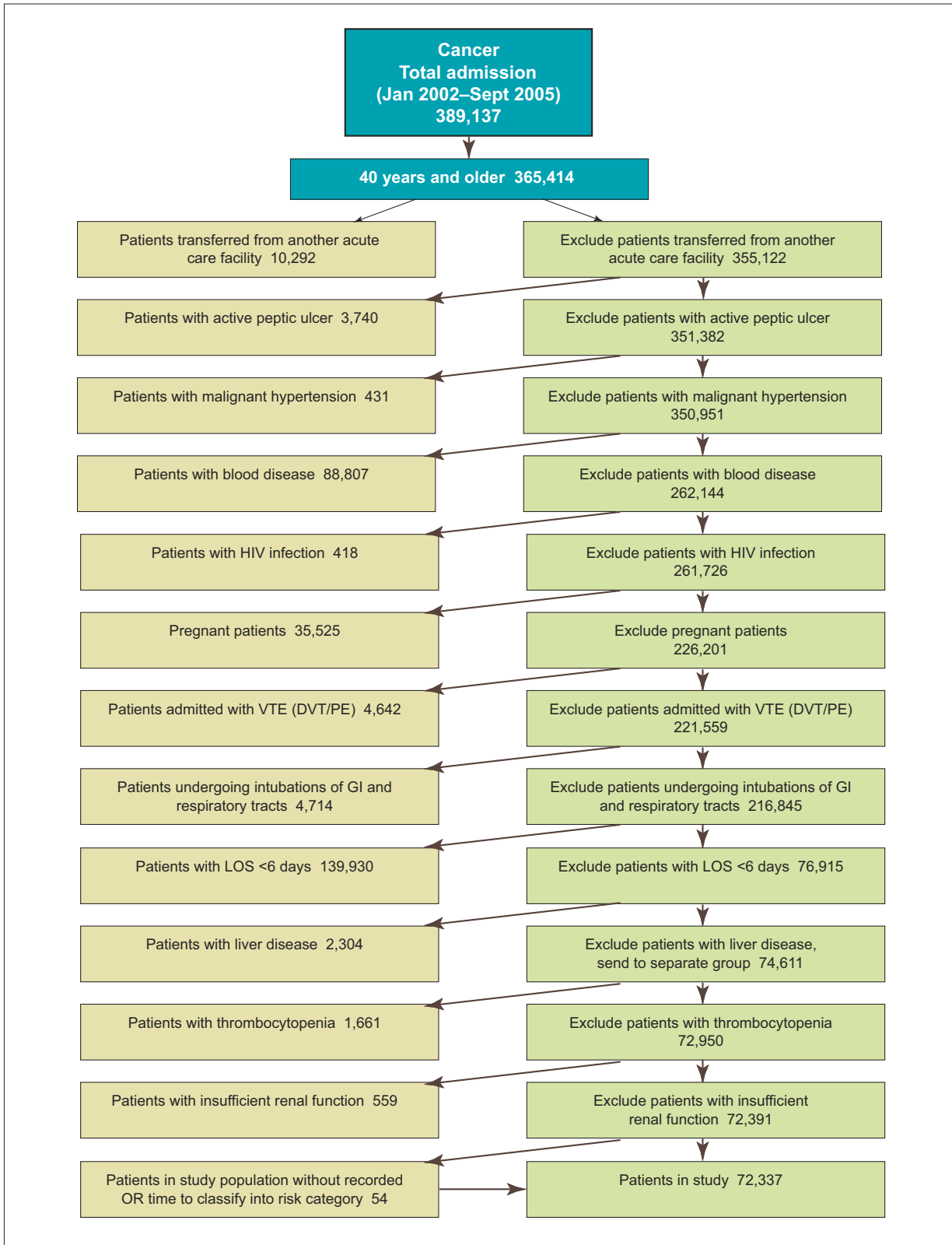
For nonsurgical cancer discharges, appropriate drug choice was defined as UFH or LMWH (eg, enoxaparin, dalteparin, or tinzaparin). For surgical cancer discharges, prophylaxis recommendations were based on the appropriate regimen for the type of surgery the patient had undergone: UFH or LMWH for general, urologic, neurologic, laparoscopic, elective spinal, vascular, and gynecologic surgery discharges; UFH, LMWH, fondaparinux, or warfarin for elective hip arthroplasty, elective knee arthroplasty, and hip fracture surgery discharges; and LMWH for knee arthroplasty discharges.

The study requirements for sufficient duration of therapy were based on the patient's length of stay. We set the duration of therapy required for UFH, enoxaparin, dalteparin, fondaparinux, and tinzaparin at 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.

For appropriate prophylaxis recommended by the 7th ACCP guidelines, patients discharged with moderate- to high-risk elective spinal surgery, moderate-risk gynecologic surgery, or high-risk laparoscopic surgery could have received IPC or ES alone. Discharges undergoing high-risk general surgery, high-risk neurosurgery, or high-risk urologic surgery were required to have received IPC or ES, in addition to the recommended pharmacologic prophylaxis.

### ***Reasons for Not Receiving Appropriate VTE Prophylaxis***

The study examined a breakdown of the types of insufficient preventative therapy observed in the study population. Discharge data were assessed according to whether there was no prophylaxis; an inappropriate prophylaxis regimen; an inappropriate duration or dosage of pharmacologic thromboprophylaxis; or whether an insufficient duration of mechanical compression therapy was employed. Patient discharges that did not indicate pharmacologic prophylaxis were further subdivided into patients who received neither prophylactic medication nor mechanical prophylaxis, and patients who received only mechanical prophylaxis.



**Figure 1.** Study population extracted from Premier Perspective database.

DVT=deep-vein thrombosis; GI=gastrointestinal; LOS=length of stay; OR=odds ratio; PE=pulmonary embolism; VTE=venous thromboembolism.

**Table 1.** Hospital Demographics of Centers That Contributed to Premier Perspective Database

	N (%)
Total discharges	72,337 (100)
Geographic region	
East North Central	6,570 (9.1)
East South Central	5,406 (7.5)
Middle Atlantic	5,494 (7.6)
Mountain	2,680 (3.7)
New England	1,122 (1.6)
Pacific	8,642 (12.0)
South Atlantic	27,990 (38.7)
West North Central	4,570 (6.3)
West South Central	9,863 (13.6)
Teaching status	
Non-teaching	43,748 (60.5)
Teaching	28,589 (39.5)
Population served	
Rural	8,355 (11.6)
Urban	63,982 (88.4)
No. of beds	
6–99	1,688 (2.3)
100–199	4,985 (6.9)
200–299	10,518 (14.5)
300–499	25,509 (35.3)
500+	29,636 (41.0)

In addition, the impact of hospital and patient demographics such as urban or rural service areas, census region, size, patient admission source, and attending physician specialty were assessed.

## Results

Of the 9,895,049 discharges in the Premier Perspective database over the study period, 72,337 cancer discharges (30,124 surgical and 42,213 nonsurgical) met the inclusion criteria (Figure 1). The hospital characteristics of centers contributing to the database are provided in Table 1.

The most common cancer subtypes, each accounting for 21% of the study population, were lung cancer with

14,983 discharges (472 surgical and 14,511 nonsurgical) and colorectal cancer with 14,896 discharges (13,437 surgical and 1,459 nonsurgical; Table 2).

In the study population, the overall rate of any (appropriate or inappropriate) thromboprophylaxis was 53.6%, with a rate of 42.2% in the nonsurgical group and 69.6% in the surgical group. The highest rate of any thromboprophylaxis was 86.3% in surgical bladder cancer discharges, and the lowest rate was 26.1% in nonsurgical prostate cancer discharges (Table 2).

The rate of appropriate thromboprophylaxis in accordance with the 7th ACCP guideline recommendations was lower than the rate of any prophylaxis at 27.0% overall (27.0% surgical and 27.1% nonsurgical). The lowest rate of appropriate thromboprophylaxis was for surgical prostate cancer discharges (14.3%), and the highest rate of 33.5% was noted in surgical colorectal cancer discharges (Table 2).

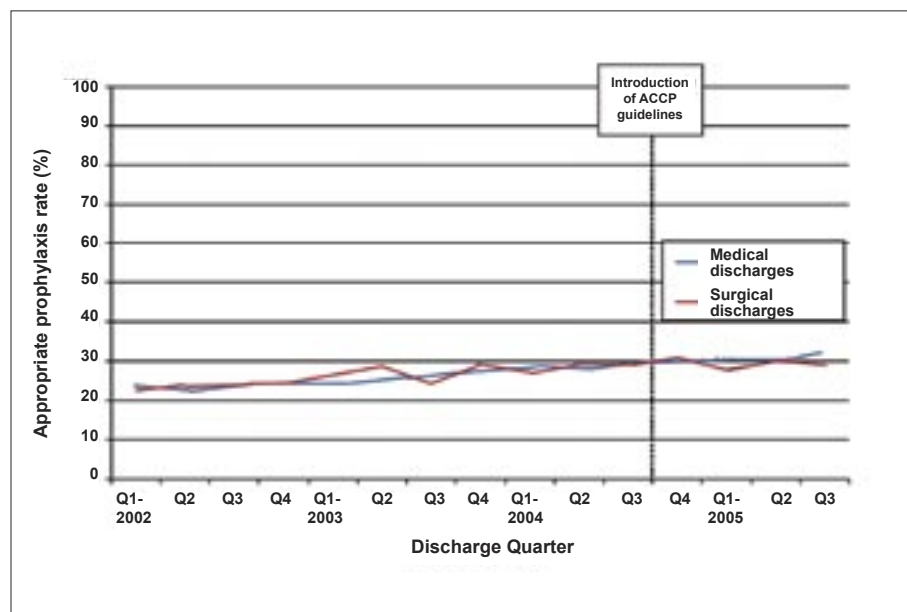
A total of 73.0% of all discharges did not receive appropriate thromboprophylaxis. Among nonsurgical discharges, 46.0% did not receive any prophylaxis despite an indication, 11.8% received only mechanical prophylaxis (despite having an indication for pharmacologic prophylaxis), 11.5% received an inappropriate prophylaxis dosage, and 3.5% received prophylaxis for an inappropriate duration (Table 3). Within the surgical discharge group, 18.1% did not receive any prophylaxis despite an indication, 33.2% received only mechanical prophylaxis, 12.8% received an inappropriate prophylaxis dosage, and 9.0% received prophylaxis for an inappropriate duration (Table 3).

It is important in this analysis to assess the temporal trends of the appropriate prophylaxis rates, especially for the period following the release of the 7th ACCP guidelines. Comparison of all discharges with those from October 2004 until September 2005 showed slight increases in the rates of appropriate prophylaxis for both nonsurgical (3.7% increase) and surgical (2.4%) discharges (Table 2). However, these increases appear to be consistent with the continuing trend of increase over the years, rather than a result of a leap forward following the publication of the guidelines (Figure 2). Assessment of discharges by cancer type and need for surgery revealed that there was substantial variation in the relative increases and decreases of appropriate prophylaxis with time in the individual groups (Table 4).

The effect of hospital characteristics on the rate of appropriate prophylaxis was also assessed (Table 5). Appropriate prophylaxis remained low irrespective of hospital characteristics, although a trend towards increased use of appropriate prophylaxis was observed as hospital size increased.

**Table 2.** Thromboprophylaxis Rates by Cancer Subgroups According to the 7th ACCP Guidelines

Cancer subgroup	N	Nonsurgical Discharges				Surgical Discharges			
		All discharges		Q4 2004–Q3 2005		All discharges		Q4 2004–Q3 2005	
		Any (%)	Appropriate (%)	Any (%)	Appropriate (%)	Any (%)	Appropriate (%)	Any (%)	Appropriate (%)
Bladder	1,908	27.2	17.7	31.9	18.4	86.3	21.9	89.8	25.3
Breast	936	38.8	25.6	40.3	27.1	77.0	18.4	77.9	23.4
Colorectal	14,896	42.4	28.0	45.6	32.7	62.8	33.5	65.7	37.8
Kidney	2,221	30.0	22.0	27.3	22.1	83.4	17.3	82.4	18.3
Lung	14,983	49.7	32.3	55.1	36.0	60.4	33.1	63.0	33.9
Lymphoma	3,322	40.5	23.4	42.6	23.5	67.9	23.5	75.4	26.7
Oral Cavity	1,038	37.2	22.2	39.1	22.7	67.4	14.9	67.0	12.3
Ovary	531	41.1	27.9	39.0	29.0	75.5	19.7	91.4	22.9
Pancreas	2,767	37.7	23.5	45.0	29.4	75.4	25.8	77.1	31.0
Prostate	1,129	26.1	17.4	29.5	22.9	79.8	14.3	75.0	14.2
Skin	352	38.7	29.3	48.1	40.4	73.1	16.9	71.4	16.7
Stomach	1,791	46.1	27.4	48.6	28.5	84.7	25.6	81.1	29.2
Uterus	159	34.0	20.4	37.9	20.7	55.4	17.9	50.0	20.0
Other	26,304	38.2	24.5	43.1	28.8	71.7	22.1	73.4	21.6
Total	72,337	42.2	27.1	47.0	30.8	69.6	27.0	71.6	29.4



**Figure 2.** Temporal trend of the rates of appropriate thromboprophylaxis according to the 7th ACCP guidelines.

**Table 3.** Reasons for Lack of Appropriate Thromboprophylaxis According to the 7th ACCP Guidelines by Cancer Subgroup

Cancer subgroup	Nonsurgical						Surgical					
	Receiving drug (%)			Not receiving drug (%)			Receiving drug (%)			Not receiving drug (%)		
	All	Dosage failure*	LOT failure	All	Mechanical only <sup>†</sup>	Not mechanical <sup>‡</sup>	All	Dosage failure*	LOT failure	All	Mechanical only <sup>†</sup>	Not mechanical <sup>‡</sup>
Bladder	9.5	5.8	3.7	72.8	14.3	58.5	25.3	17.4	8.0	52.8	39.6	13.2
Breast	13.2	10.5	2.7	61.2	11.3	49.9	28.1	12.8	15.3	53.5	30.5	23.0
Colorectal	14.4	10.0	4.4	57.6	16.0	41.5	18.2	10.9	7.2	48.4	35.5	12.8
Kidney	7.9	6.5	1.4	70.0	6.9	63.2	18.7	10.8	7.9	64.0	47.5	16.5
Lung	17.4	13.0	4.3	50.3	12.8	37.5	24.2	15.0	9.1	42.8	7.8	35.0
Lymphoma	17.1	13.0	4.1	59.5	6.0	53.5	26.4	13.9	12.6	50.1	22.2	27.8
Oral cavity	15.0	9.0	6.0	62.8	17.9	44.9	26.9	14.7	12.3	58.2	25.8	32.4
Ovary	13.3	10.7	2.6	58.9	8.3	50.5	30.6	15.6	15.0	49.7	28.6	21.1
Pancreas	14.2	11.2	3.0	62.3	7.9	54.4	29.0	16.8	12.2	45.2	21.3	23.9
Prostate	8.7	7.0	1.7	73.9	10.8	63.1	17.5	10.7	6.8	68.2	47.9	20.2
Skin	9.5	7.7	1.8	61.3	13.5	47.7	32.3	12.3	20.0	50.8	24.6	26.2
Stomach	18.7	14.8	3.9	53.9	13.2	40.7	27.0	13.0	14.0	47.5	32.3	15.1
Uterus	13.6	11.7	1.9	66.0	7.8	58.3	28.6	19.6	8.9	53.6	23.2	30.4
Other	13.6	10.7	2.9	61.8	11.7	50.2	24.9	14.7	10.3	53.0	28.9	24.1
Total	15.1	11.5	3.5	57.8	11.8	46.0	21.8	12.8	9.0	51.2	33.2	18.1

\*Patients received pharmacologic prophylaxis at an incorrect dose.

<sup>†</sup>Only including patients where mechanical prophylaxis alone was not deemed appropriate. Patients discharged with moderate- to high-risk elective spinal surgery, moderate-risk gynecologic surgery, or high-risk laparoscopic surgery could have received mechanical prophylaxis alone.

<sup>‡</sup>Patients received neither mechanical nor pharmacologic prophylaxis.

LOT=length of therapy

## Discussion

This study of patient discharge data from a large real-world US population demonstrates that nearly three quarters of hospitalized cancer patients with known risk of VTE do not receive appropriate thromboprophylaxis in accordance with evidence-based recommendations for thromboprophylaxis regimen, dose, and duration of therapy. At the time when the 7th ACCP guidelines identified cancer patients at high risk for VTE and recommended appropriate forms of prophylaxis, our study found that 15.0% of cancer discharges received pharmacologic thromboprophylaxis at an inappropriate dose or duration (11.8% of discharges received only mechanical prophylaxis and 46.0% received no prophylaxis). While the overall temporal trend for all cancer discharges

showed a slight improvement in rates of prophylaxis use from 2002 to 2005, the majority of patients in whom thromboprophylaxis was indicated did not receive appropriate prophylaxis.

These findings are in agreement with the prior literature. A previous US prospective registry (DVT FREE) of over 5,000 patients with confirmed DVT noted that only 42% had received prophylaxis in the month before VTE diagnosis.<sup>22</sup> More recently, a review of US hospital practices complying with the 6th ACCP guidelines reported that only 15.3% of patients with at-risk medical conditions received appropriate prophylaxis.<sup>23</sup>

A 4-year retrospective study assessing prophylaxis use in over 12 million medical discharges from US hospitals over the period of 2001–2004 found that the overall use of thromboprophylaxis was low, ranging from

**Table 4.** Appropriate Thromboprophylaxis Rates by Year and by Cancer Subgroups According to the 7th ACCP Guidelines

Cancer subgroup	Nonsurgical (%)				Surgical (%)			
	2002	2003	2004	2005	2002	2003	2004	2005
Bladder	15.6	17.3	19.9	18.9	21.1	18.7	23.9	25.0
Breast	25.2	20.0	30.5	28.7	15.6	18.2	17.8	26.2
Colorectal	21.3	28.0	30.9	35.2	29.0	33.4	36.3	37.0
Kidney	8.86	25.3	38.5	17.2	14.3	18.4	19.0	18.4
Lung	29.7	31.1	34.2	35.3	32.6	33.6	32.5	33.7
Lymphoma	21.4	23.4	25.2	23.7	18.4	24.3	27.8	25.0
Oral cavity	19	18.0	29.5	24.2	17.4	17.1	11.1	11.7
Ovary	22.1	29.0	27.5	34.3	16.3	17.4	28.1	19.2
Pancreas	20	19.4	27.8	28.6	23.8	21.5	27.1	32.5
Prostate	14.4	14.1	22.0	22.7	15.0	14.8	11.1	17.0
Skin	21.1	27.7	29.7	44.4	12.5	16.7	24.1	15.2
Stomach	24.6	28.7	27.8	28.7	19.4	28.3	27.5	29.3
Uterus	14.3	36.4	19.2	15.0	0.0	18.8	23.1	23.5
Other	20.7	23.3	26.3	29.5	20.3	23.3	23.9	20.6

26–33%. Among 5 distinct disease groups, the use of any thromboprophylaxis was lowest in cancer patients, ranging from just 18–25% over the study period.<sup>15</sup> The low rate of adoption and use of any thromboprophylaxis among cancer patients appears to be an international phenomenon. The International Medical Prevention Registry on Venous Thromboembolism (IMPROVE), a prospective cohort study, found that thromboprophylaxis is underused in acutely-ill, hospitalized, medical patients with only 39% receiving in-hospital prophylaxis.<sup>24</sup> In the recently published @RISTOS Project, which provides registry data from 31 Italian surgery departments with high rates of cancer operations, in-hospital prophylaxis was reportedly given to 81.6% of patients. However, this study did not report on the appropriateness of prophylaxis in terms of dosage and duration of therapy according to current evidence on VTE prevention and guideline recommendations.<sup>25</sup>

The FRONTLINE survey of opinions and prescribing practices among oncologists noted particularly poor rates of thromboprophylaxis among medical oncology patients, with 95% not given VTE prophylaxis.<sup>13</sup> Although 50% of cancer patients requiring surgery were offered thromboprophylaxis in this survey, it still falls short of appropriate practice for these at-risk patients. The multicenter audit study, CURVE, acknowledged that although as many as 90% of medical patients were

candidates for thromboprophylaxis, only 16% received appropriate therapy, and among patients with cancer, the odds of receiving appropriate thromboprophylactic therapy were significantly reduced.<sup>14</sup>

Our study found that there was a slight temporal trend in favor of greater use of thromboprophylaxis between 2002 and 2005. This slight increase in the use of thromboprophylaxis was also observed in the 2001–2004 assessment of 12 million medical discharges from US hospitals, which found an increase from 18% to 25% in the use of thromboprophylaxis.<sup>15</sup> However, our finding that the majority of cancer discharges were still not receiving appropriate thromboprophylaxis in 2005 highlights that an unacceptably low percentage of patients are protected against the real risks of VTE. Our study is the first to confirm, in a real-world setting and a large US population, that nearly three quarters of hospitalized cancer patients do not receive adequate thromboprophylaxis. Moreover, this inadequacy applies to both surgical and nonsurgical cancer patient discharges across all cancer types. The discharges in our study related to very high-risk cancer patients, as evidenced by a length of hospital stay in excess of 6 days, and the application of stringent exclusion criteria, which meant this population were at particular VTE risk.

Due to a large proportion of the data in this analysis being taken from before the release of the latest guide-

**Table 5.** Appropriate Thromboprophylaxis Rates by Hospital Characteristics

Hospital characteristics	Medical		Surgical	
	Patient discharges (N)	Appropriate prophylaxis rate (%)	Patient discharges (N)	Appropriate prophylaxis rate (%)
Geographic region	4,072	26.58	2,475	24.29
East North Central	5,208	30.67	3,937	31.11
East South Central	156	17.16	229	29.4
Middle Atlantic	1,059	26.82	633	24.15
Mountain	801	25.05	566	25.63
New England	1,023	30.7	958	44.31
Pacific	388	26.83	267	21.64
South Atlantic	151	25.21	74	14.15
West North Central	1,037	21.92	860	21.99
West South Central	4,769	28.42	3,030	27.03
Hospital teaching status				
Non-teaching	6,520	25.3	4,604	25.62
Teaching	4,923	29.95	3,520	28.97
Population served				
Urban	1,312	26.64	1,020	29.74
Rural	10,131	27.17	7,104	26.61
No. of beds				
0–99	156	17.16	229	29.4
100–199	590	20.43	451	21.51
200–299	1,417	23.17	1,032	23.44
300–499	4,072	26.58	2,475	24.29
500+	5,208	30.67	3,937	31.11
Admission source				
Emergency department	4,409	26.05	1,434	25.89
Physician referral	240	24.37	168	18.32

lines, the purpose of this study was not to judge the hospitals on the rates of appropriate prophylaxis, but to provide a historical perspective. However, the lack of a significant improvement in appropriate prophylaxis following the release of the guidelines suggests that the issue is not in the specifics of the recommendations, but in a general lack of guideline adoption. There are a number of recognized barriers to full adoption of thromboprophylaxis across the medical community. These include concerns that prophylactic therapies may increase bleeding risk, particularly in patients requiring surgery<sup>8,13,25</sup>; a continuing belief that VTE risk is low in cancer patients<sup>13</sup>; perceptions that VTE treatments are

less effective in cancer patients; and concerns over the cost of prophylaxis. It is also known that clinical guidelines, despite best intentions and supporting research, are not always successfully or widely implemented. Reasons for the failure of guideline recommendations in penetrating into everyday practice can include lack of awareness of guidelines, lack of familiarity with the issues, disagreement with guidance, and inertia.<sup>26,27</sup> In a survey of physician knowledge of the management of VTE, conducted at academic medical centers, very few physicians demonstrated a sound knowledge of lower extremity venous anatomy, and 70% of those surveyed stated that they would not treat symptomatic DVT.<sup>28</sup>

These issues with guideline compliance persist despite the publication of VTE guidelines not only by the ACCP, but also by cancer-specific networks, such as the National Comprehensive Cancer Network (NCCN).<sup>11</sup> In fact, the NCCN provides even stronger recommendations than the ACCP for cancer patients, stating that “all adult, hospitalized patients with cancer receive anticoagulation therapy in the absence of contraindications.”<sup>11</sup>

A number of proposals have been put forward to improve the uptake and use of thromboprophylaxis. These include initiatives that have improved VTE risk stratification among patients,<sup>29</sup> educational initiatives based on audit and feedback that doubled rates of appropriate prophylaxis over an 18-month period among medically ill patients,<sup>30</sup> and educational programs that have increased optimal VTE prophylaxis for medical patients 4-fold.<sup>31</sup> An electronic alert program designed to help assign patients to intervention groups according to VTE risk has been shown to reduce rates of DVT and PE.<sup>4</sup> Also, guidelines that have been actively applied to help physicians assess risk and direct patient management, have been shown to cut rates of VTE in at-risk patient groups.<sup>32</sup> National quality measures and initiatives, such as those proposed by the Agency for Healthcare Research and Quality (AHRQ), the Surgical Care Improvement Project (SCIP), the Joint Commission, and the National Quality Forum (NQF) performance measures for prevention and care of VTE, each highlight the high level of national awareness needed to tackle the risks posed by VTE.

### Strengths and Limitations

This study is one of the largest database reviews to date on US hospital care practices in cancer patients at risk for VTE. The study’s strengths lie in providing contemporary insights into real-world practices and assessing data drawn from a large and representative population that includes both surgical and nonsurgical cancer patients. Conversely, the study is limited because analyses are based on retrospective discharge data and, as such, this study cannot fully evaluate the special circumstances that may have led to a physician’s decision not to adopt prophylactic practices in accordance with current guidelines. The study is also limited by the fact that some cancer subtypes might have been under-represented, and that application of the strict inclusion and exclusion criteria ensured that only patients at high risk for VTE were included. This would have likely resulted in an overestimation of the rate of appropriate thromboprophylaxis. However, even in this most conservative population with the highest risk for VTE, we still found significant opportunity to improve the levels of VTE prevention in cancer patients according to the ACCP guidelines.

### Conclusions

This study provides a large, real-world, contemporary analysis of the rates of appropriate thromboprophylaxis among hospitalized cancer patients at high risk of VTE, assessing surgical and nonsurgical patients and specific cancer subtypes. Based on actual hospital discharges from US acute-care hospitals, this study has identified that thromboprophylaxis is severely underused in cancer patients. Despite cancer patients being at significantly higher risk of VTE than the general population, nearly three quarters of patients in whom prophylaxis is indicated did not receive appropriate thromboprophylaxis to prevent VTE. This trend of major underuse of thromboprophylaxis was evident regardless of the type of cancer, and of the known risks associated with surgery in cancer patients. Moreover, when thromboprophylaxis is provided to cancer patients, it often fails to meet the recommendations for adequate prevention of VTE outlined in current, evidence-based guidelines. In light of such evidence and the known risks of VTE, organizations such as the Joint Commission are highlighting the need for increased effort throughout hospital departments to actively improve the implementation of VTE thromboprophylaxis guidelines as part of its hospital core measures program.

*Financial and editorial support for this publication was provided by sanofi-aventis US, Inc. The authors, however, are fully responsible for content and editorial decisions for this manuscript. Alpesh Amin is a research consultant and is on the speakers bureau for sanofi-aventis US, Inc. Stephen Stemkowski and Guiping Yang work for Premier Inc, which received funding to carry out this work from sanofi-aventis US, Inc. Jay Lin is an employee of sanofi-aventis US.*

### References

1. Lee AY, Levine MN. Venous thromboembolism and cancer: risks and outcomes. *Circulation*. 2003;107:117-121.
2. Donati MB. Cancer and thrombosis. *Haemostasis*. 1994;24:128-131.
3. Heit JA, Cohen AT, Anderson FA Jr. Estimated annual number of incident and recurrent, non-fatal and fatal venous thromboembolism (VTE) events in the US. *Blood*. 2005;106:910.
4. Kucher N, Koo S, Quiroz R, et al. Electronic alerts to prevent venous thromboembolism among hospitalized patients. *N Engl J Med*. 2005;352:969-977.
5. Samama MM, Cohen AT, Darmon JY, et al, and Prophylaxis in Medical Patients with Enoxaparin Study Group. A comparison of enoxaparin with placebo for the prevention of venous thromboembolism in acutely ill medical patients. *N Engl J Med*. 1999;341:793-800.
6. Leizorovicz A, Cohen AT, Turpie AG, et al, and PREVENT Medical Thromboprophylaxis Study Group. Randomized, placebo-controlled trial of dalteparin for the prevention of venous thromboembolism in acutely ill medical patients. *Circulation*. 2004;110:874-879.
7. ENOXACAN Study Group. Efficacy and safety of enoxaparin versus unfractionated heparin for prevention of deep vein thrombosis in elective cancer surgery: a double-blind randomized multicentre trial with venographic assessment. *Br J Surg*. 1997;84:1099-1103.
8. Bergqvist D, Agnelli G, Cohen AT, et al, and ENOXACAN II Investigators. Duration of prophylaxis against venous thromboembolism with enoxaparin after surgery for cancer. *N Engl J Med*. 2002;346:975-980.

9. Geerts WH, Pineo GF, Heit JA, et al. Prevention of venous thromboembolism: the Seventh ACCP Conference on Antithrombotic and Thrombolytic Therapy. *Chest*. 2004;126:338S-400S.
10. Cardiovascular Disease Educational and Research Trust; Cyprus Cardiovascular Disease Educational and Research Trust; European Venous Forum; International Surgical Thrombosis Forum; International Union of Angiology; Union Internationale de Phlebologie. Prevention and treatment of venous thromboembolism. International Consensus Statement (guidelines according to scientific evidence). *Int Angiol*. 2006;25:101-161.
11. National Comprehensive Cancer Network. NCCN Clinical Practice Guidelines in Oncology. Venous Thromboembolic Disease, version 2.2006. Available at <http://www.nccn.org/>. Accessed October 16, 2006.
12. Snow V, Qaseem A, Barry P, et al, and the Joint American College of Physicians/American Academy of Family Physicians Panel on Deep Venous Thrombosis/Pulmonary Embolism. Management of venous thromboembolism: a clinical practice guideline from the American College of Physicians and the American Academy of Family Physicians. *Ann Intern Med*. 2007;146:204-210.
13. Kakkar AK, Levine M, Pinedo HM, et al. Venous thrombosis in cancer patients: insights from the FRONTLINE survey. *Oncologist*. 2003;8:381-388.
14. Kahn SR, Panju A, Geerts W, et al, and CURVE study investigators. Multi-center evaluation of the use of venous thromboembolism prophylaxis in acutely ill medical patients in Canada. *Thromb Res*. 2007;119:145-155.
15. Burleigh E, Wang C, Foster D, et al. Thromboprophylaxis in medically ill patients at risk for venous thromboembolism. *Am J Health Syst Pharm*. 2006;63(Suppl 6):S23-S29.
16. Lee AY, Levine MN, Baker RI, et al, and Randomized Comparison of Low-Molecular-Weight Heparin versus Oral Anticoagulant Therapy for the Prevention of Recurrent Venous Thromboembolism in Patients with Cancer (CLOT) Investigators. Low-molecular-weight heparin versus a coumarin for the prevention of recurrent venous thromboembolism in patients with cancer. *N Engl J Med*. 2003;349:146-153.
17. Chew HK, Wun T, Harvey D, et al. Incidence of venous thromboembolism and its effects on survival among patients with common cancers. *Arch Intern Med*. 2006;166:458-464.
18. Premier Perspective Data Warehouse – Premier Research Services. Available at <http://www.premierinc.com/quality-safety/tools-services/prs/data/perspective.jsp>; 9-9-2008.
19. US Department of Health and Human Services, Office for Civil Rights. HIPAA Medical Privacy—National Standards to Protect the Privacy of Personal Health Information. Available at <http://www.hhs.gov/ocr/hipaa/bkgrnd.html>. Accessed on December 22, 2003 and August 21, 2005.
20. Department of Health and Human Services Policy for Protection of Human Research Subjects. Available at <http://www.hhs.gov/ohrp/humansubjects/guidance/45cfr46.htm#46.101>. Accessed on November 17, 2005 and January 12, 2006.
21. McGarry LJ, Thompson D. Retrospective database analysis of the prevention of venous thromboembolism with low-molecular-weight heparin in acutely ill medical inpatients in community practice. *Clin Ther*. 2004;26:419-430.
22. Goldhaber SZ, Tapson VF. A prospective registry of 5,451 patients with ultrasound-confirmed deep vein thrombosis. *Am J Cardiol*. 2004;93:259-262.
23. Yu HT, Dylan ML, Lin J, Dubois RW. Hospitals' compliance with prophylaxis guidelines for venous thromboembolism. *Am J Health Syst Pharm*. 2007;64:69-76.
24. Tapson VF, Decousus H, Piovella F, et al. A multinational observational cohort study in acutely ill medical patients of practices in prevention of venous thromboembolism: findings of the International Medical Prevention Registry on Venous Thromboembolism (IMPROVE). *Blood*. 2003;11:321a.
25. Agnelli G, Bolis G, Capussotti L, et al. A clinical outcome-based prospective study on venous thromboembolism after cancer surgery: the @RISTOS project. *Ann Surg*. 2006;243:89-95.
26. Cabana MD, Rand CS, Powe NR, et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. *JAMA*. 1999;282:1458-1465.
27. Shojania KG, Grimshaw JM. Evidence-based quality improvement: the state of the science. *Health Aff (Millwood)*. 2005;24:138-150.
28. Zierler BK, Meissner MH, Cain K, Strandness DE Jr. A survey of physicians' knowledge and management of venous thromboembolism. *Vasc Endovascular Surg*. 2002;36:367-375.
29. Stinnett JM, Pendleton R, Skordos L, et al. Venous thromboembolism prophylaxis in medically ill patients and the development of strategies to improve prophylaxis rates. *Am J Hematol*. 2005;78:167-172.
30. Cohn SL, Adekile A, Mahabir V. Improved use of thromboprophylaxis for deep vein thrombosis following an educational intervention. *J Hosp Med*. 2006;1:331-338.
31. Dobesh PP, Stacy ZA. Effect of a clinical pharmacy education program on improvement in the quantity and quality of venous thromboembolism prophylaxis for medically ill patients. *J Manag Care Pharm*. 2005;11:755-762.
32. Sellier E, Labarere J, Bosson JL, et al, and Association pour la Promotion de l'Angiologie Hospitaliere. Effectiveness of a guideline for venous thromboembolism prophylaxis in elderly post-acute care patients: a multicenter study with systematic ultrasonographic examination. *Arch Intern Med*. 2006;166:2065-2071.