Venous thromboembolism risk and prophylaxis in hospitalised medically ill patients

The ENDORSE Global Survey

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Summary

Limited data are available regarding the risk for venous thromboembolism (VTE) and VTE prophylaxis use in hospitalised medically ill patients. We analysed data from the global ENDORSE survey to evaluate VTE risk and prophylaxis use in this population according to diagnosis, baseline characteristics, and country. Data on patient characteristics, VTE risk, and prophylaxis use were abstracted from hospital charts. VTE risk and prophylaxis use were evaluated according to the 2004 American College of Chest Physicians (ACCP) guidelines. Multivariable analysis was performed to identify factors associated with use of ACCP-recommended prophylaxis. Data were evaluated for 37,356 hospitalised medical patients across 32 countries. VTE risk varied according to medical diagnosis, from 31.2% of patients with gastrointestinal/hepatobiliary diseases to 100% of patients with acute heart failure, active non-infectious respiratory disease, or pulmonary infection (global rate, 41.5%). Among those at risk for VTE, ACCP-recommended prophylaxis was used in 24.4% haemorrhagic stroke patients and 40–45% of cardiopulmonary disease patients (global rate, 39.5%). Large differences in prophylaxis use were observed among countries. Markers of disease severity, including central venous catheters, mechanical ventilation, and admission to intensive care units, were strongly associated with use of ACCP-recommended prophylaxis. In conclusion, VTE risk varies according to medical diagnosis. Less than 40% of at-risk hospitalised medical patients receive ACCP-recommended prophylaxis. Prophylaxis use appears to be associated with disease severity rather than medical diagnosis. These data support the necessity to improve implementation of available guidelines for evaluating VTE risk and providing prophylaxis to hospitalised medical patients.

Keywords

ACCP guideline use, ENDORSE, hospitalised medical patients, prophylaxis, venous thromboembolism

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Introduction

Venous thromboembolism (VTE) is a common and potentially avoidable cause of morbidity and mortality in patients hospitalised for acute medical illnesses (1–3). Up to 75% of fatal pulmonary embolism cases occur in this patient population (4–6), and without prophylaxis, the frequency of confirmed hospital-acquired deep-vein thrombosis (DVT) is 10–20% (1).

Existing guidelines for VTE prevention recommend that certain groups of medically ill patients at high risk for VTE should receive thromboprophylaxis (1). These include patients with congestive heart failure or severe respiratory disease, those with an acute medical illness who are confined to bed and have one or more additional risk factors, such as active cancer or previous VTE, and those admitted to critical care units (CCU) (1).

However, despite the existence of these guidelines, the findings of the recent Epidemiologic International Day for the Evaluation of Patients at Risk for Venous Thromboembolism in the Acute Hospital Care Setting (ENDORSE) study indicated that up to 50% of all hospitalised patients at-risk for VTE are not receiving appropriate prophylaxis (7). Furthermore, medical patients at-risk for VTE were less likely than surgical patients to receive appropriate prophylaxis (7). ENDORSE encompasses the full spectrum of medical patients with varying VTE risk. It is, therefore, important to study how VTE risk and prophylaxis use vary according to key characteristics within the medical population.

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In this analysis of medical patients in 32 countries, we evaluate VTE risk, prophylaxis frequency, and factors associated with prophylaxis use in relation to medical diagnosis, baseline characteristics, hospital interventions, and country.

Materials and methods

The ENDORSE study was a cross-sectional, multinational survey designed to evaluate the VTE risk and prophylaxis practices in acute care hospitals across different countries and socioeconomic backgrounds (7). In this pre-specified analysis of ENDORSE data, we evaluated VTE risk and the use of American College of Chest Physicians (ACCP)-recommended prophylaxis in hospitalised medically ill patients.

The full methodology for the ENDORSE survey has been published (7). In brief, hospitals were considered eligible for participation if they had >50 acute care beds, regularly admitted patients for the treatment of acute medical illness, and routinely performed major surgical procedures (7). Eligible hospitals were randomly selected to participate, using country-specific hospital registers or equivalent lists obtained from the national hospital association or government health authority. Ethics committee approval to undertake the study was obtained for hospitals in each country according to national guidelines.

Selection of evaluable medical patients

Patients aged ≥40 years were eligible to be included in this study if they were admitted to an eligible medical ward for the treatment of an acute medical illness. Patients were excluded if they were not evaluable because of missing data, if their chart was unavailable, if they refused consent in countries where consent was necessary, if they were admitted to a surgical ward or ineligible medical ward, or were admitted solely for VTE treatment (▶Fig. 1).

Data collection

Data were collected from a review of hospital charts by trained data abstractors (7). Data abstraction from eligible charts in selected wards at each hospital was completed for an individual patient within 14 days of admission (the typical hospital was too large to allow data abstractors to complete all patient enrolments in one day only). Data collected included patient demographics, admission and post-admission diagnoses, VTE risk factors, and type of VTE prophylaxis (as defined in the ACCP guidelines [8]), bleeding risk factors, and duration of hospital stay.

Assessment of VTE risk and prophylaxis

Assessments of VTE risk and the use of ACCP-recommended prophylaxis in medically ill patients were performed in accordance with the 2004 ACCP guidelines (8). When assessing whether prophylaxis was compliant to the 2004 ACCP guidelines, only the type of prophylaxis received was considered, without looking at the dosing schedules or duration of treatment. ACCP-recommended VTE prophylaxis included anticoagulant prophylaxis (unfractionated heparin, low-molecular-weight heparin [LMWH], or vitamin K antagonists [VKA]), and mechanical prophylaxis (graduated compression stockings [GCS] or intermittent pneumatic compression) in medical patients with a contraindication to anticoagulant prophylaxis (8). VKA are not recommended for VTE prophylaxis in medical patients (8); however, medical patients enrolled in the survey may have received these anticoagulants for other associated or previous conditions.

VTE risk and prophylaxis use according to medical diagnosis were compared across participating countries in patients diagnosed with the following illnesses: acute heart failure; acute non-infectious respiratory disease; pulmonary infection; ischaemic stroke; active malignancy; and non-respiratory infection. Medical diagnoses were based on case report form data and patients could be classified as having more than one medical diagnosis. Various risk factors for VTE present before and after hospital admission were analysed including: previous VTE, obesity, varicose veins or venous insufficiency, thrombophilia, post-menopausal hormone therapy, chronic pulmonary disease, long-term immobility, immobility with bathroom privileges, complete immobilisation, pregnancy, use of contraceptives, chronic heart failure, admission to a CCU, central venous catheter, and mechanical ventilation. VTE risk and prophylaxis practices were also analysed according to patient age.

Patients who presented with or developed an intracranial haemorrhage, clinically relevant hepatic impairment, bleeding at hospital admission, active gastroduodenal ulcer, or a known bleeding disorder were considered to have a bleeding risk that was sufficient to be a contraindication to anticoagulation (9).

Statistical analyses

Quantitative data were summarised as medians (interquartile ranges). Categorical data were summarised as the number and percentage of the population. Summary data were reported globally, by country, and by type of medical illness. For the main outcomes, 95% confidence intervals (CI) were calculated.

Factors associated with the provision of ACCP-recommended VTE prophylaxis for all medical patients considered to be at risk were identified using backwards, stepwise, multivariable logistic regression analysis. Candidate variables included in the initial model were selected by the authors, based on clinical relevance, and included baseline patient characteristics, medical diagnoses, VTE risk factors, bleeding risk factors, and provision of antiplatelet

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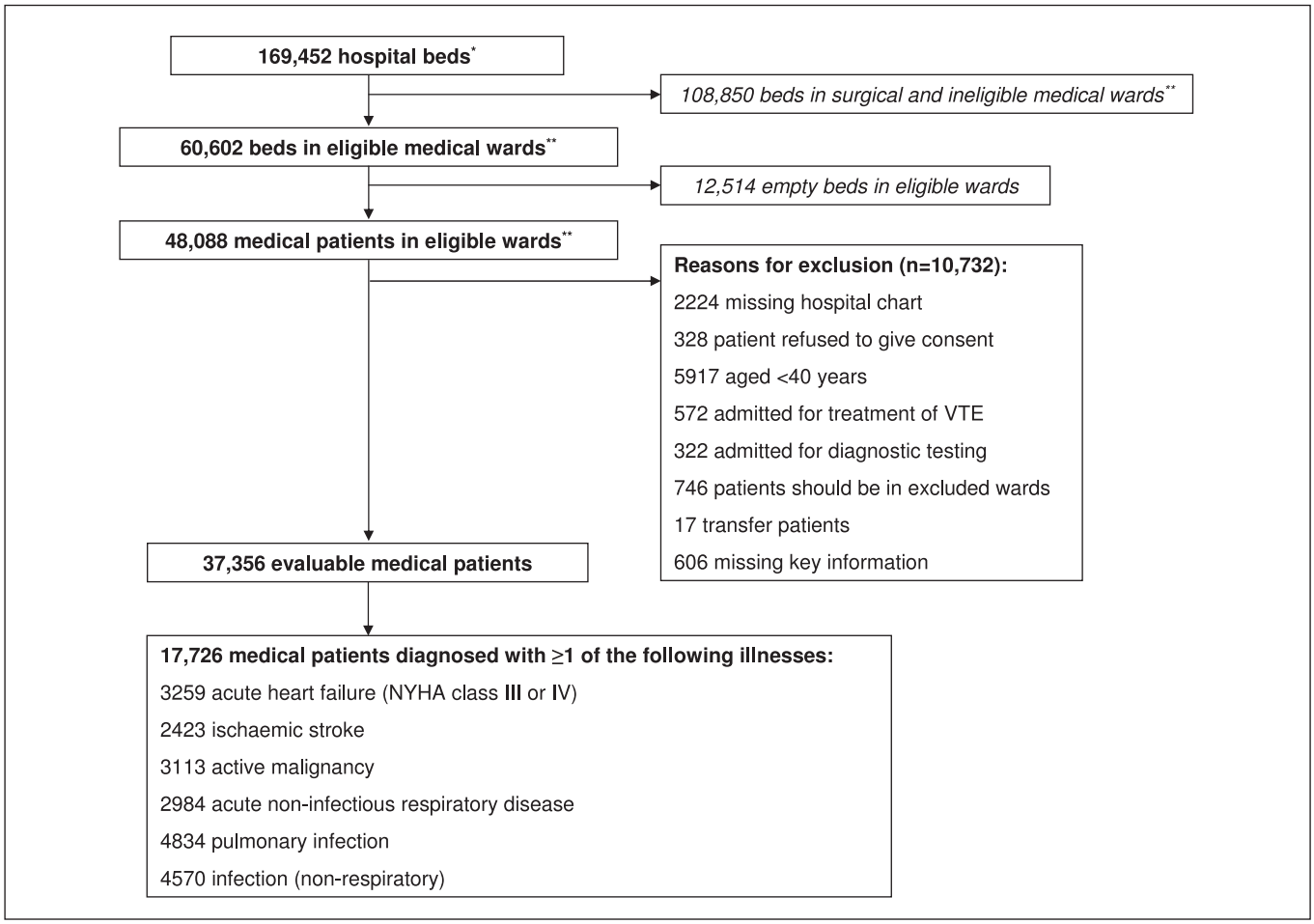


Figure 1: Selection of medical patient study population. *According to patient enrolment logs. **Eligible medical wards included general medical, cardiac and respiratory wards. Psychiatric, paediatric, eye, nose and throat, dermatology, alcohol/drug treatment, rehabilitation, accident and emergency, maternity, chronic, and palliative care wards were considered ineligible for inclusion. NYHA, New York Heart Association; VTE, venous thromboembolism.

agents as VTE prophylaxis. Criteria for entry and removal of candidate variables in the backwards, stepwise analysis were established at a significance level of $p<0.05$. Adjusted odds ratios (OR) and 95% CI were reported. SAS version 9.1 (Cary, NC, USA) was used for all statistical analyses.

Study data was held by the Center for Outcomes Research, University of Massachusetts Medical School (Worcester, MA, USA). All statistical analyses were performed by the Center for Outcomes Research.

Results

Study population

Eligible patients were enrolled between August 2006 and January 2007. Of the 68,183 inpatients enrolled, 37,356 were classified as evaluable medically ill patients (Fig. 1). Overall, 15,487 (41.5%; 95% CI 41.0–42.0%) evaluable hospitalised medically ill patients were considered to be at-risk for VTE and of these, 6,119 (39.5%; 95% CI 38.7–40.3%) received ACCP-recommended prophylaxis.

Baseline characteristics of the evaluable hospitalised medically ill patient population are provided in Supplementary Table (see online at www.thrombosis-online.com) (7). Globally, the five most common diagnoses were: various cardiovascular diseases without heart failure; endocrine/metabolic disorders; gastrointestinal/hepatobiliary disorders; pulmonary infection; and non-respiratory infection.

VTE risk in the hospitalised medically ill patient population

Among the different medical groups, all patients hospitalised for acute heart failure, acute non-infectious respiratory disease, or pulmonary infection were considered at risk for VTE. The propor-

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tion of patients with other medical illnesses who were deemed to be at risk for VTE ranged from 31.2% in patients admitted with gastrointestinal/hepatobiliary disease to 76.1% in those with haemorrhagic stroke (▶Table 1).

Provision of VTE prophylaxis in medical patients according to medical diagnosis

Of patients classified as at risk for VTE, the proportion at risk and receiving ACCP-recommended type of prophylaxis varied according to diagnosis, including 24.4% of patients with haemorrhagic stroke and 40–45% of patients with infectious (non-respiratory), pulmonary (infectious or non-infectious), or cardiovascular diseases (Table 1). The proportion of patients at-risk for VTE who received no prophylaxis ranged from 41.9% in patients with renal disease to 70.9% in those with haemorrhagic stroke.

Types of prophylaxis used

Anticoagulant prophylaxis was used more frequently than mechanical prophylaxis in all groups of medical patients (Table 1). The proportion of patients at risk for VTE who received prophylaxis with any anticoagulant ranged from 18.4% of those with haemorrhagic stroke to 50.0% of those with renal disease. The most commonly used anticoagulant was LMWH, prescribed to 70.9% (8,369 of 11,811) of patients who received this type of prophylaxis. The proportion of at-risk patients using the LMWH ranged from 12.2% of those with haemorrhagic stroke to 37.0% of those with acute non-infectious respiratory disease (Table 1).

Table 1: VTE risk and prophylaxis according to type of medical illness.

Reason for hospitalisation	Diagnosed patients, n*	At risk for VTE, n (%)	At risk receiving any prophylaxis, n (%)	At risk receiving ACCP prophylaxis, n (%)	At risk with contraindication to anticoagulation, n (%)†	Type of prophylaxis received by at-risk patients, n (%)			
						LMWH	UFH	Warfarin	Mechanical prophylaxis‡
Acute heart failure	3,259	3,259 (100)	1,716 (52.7)	1,329 (40.8)	207 (6.4)	1,037 (31.8)	318 (9.8)	266 (8.2)	194 (6.0)
Other cardiovascular disease	10,834	5,310 (49.0)	2,687 (50.6)	2,154 (40.6)	441 (8.3)	1,570 (29.6)	609 (11.5)	338 (6.4)	420 (7.9)
Acute non-infectious respiratory disease	2,984	2,984 (100)	1,582 (53.0)	1,335 (44.7)	231 (7.7)	1,103 (37.0)	244 (8.2)	170 (5.7)	221 (7.4)
Pulmonary infection	4,834	4,834 (100)	2,267 (46.9)	1,939 (40.1)	366 (7.6)	1,586 (32.8)	373 (7.7)	159 (3.3)	350 (7.2)
Infection (non-respiratory)	4,570	2,298 (50.3)	1,207 (52.5)	1,005 (43.7)	299 (13.0)	735 (32.0)	278 (12.1)	88 (3.8)	285 (12.4)
Ischaemic stroke	2,423	1,649 (68.1)	776 (47.1)	612 (37.1)	86 (5.2)	465 (28.2)	158 (9.6)	48 (2.9)	154 (9.3)
Haemorrhagic stroke	528	402 (76.1)	117 (29.1)	98 (24.4)	249 (61.9)	49 (12.2)	19 (4.7)	6 (1.5)	67 (16.7)
Malignancy (active)	3,113	1,072 (34.4)	475 (44.3)	397 (37.0)	153 (14.3)	305 (28.5)	75 (7.0)	27 (2.5)	113 (10.5)
Rheumatological/ inflammatory disease	1,588	714 (45.0)	336 (47.1)	265 (37.1)	85 (11.9)	214 (30.0)	47 (6.6)	46 (6.4)	70 (9.8)
Haematological diseases	2,025	796 (39.3)	390 (49.0)	312 (39.2)	165 (20.7)	194 (24.4)	107 (13.4)	31 (3.9)	111(13.9)
Neurological disease	3,942	1,460 (37.0)	805 (55.1)	653 (44.7)	192 (13.2)	490 (33.6)	157 (10.8)	63 (4.3)	209 (14.3)
Renal disease	3,635	1,768 (48.6)	1,027 (58.1)	837 (47.3)	225 (12.7)	579 (32.8)	254 (14.4)	106 (6.0)	254 (14.4)
Endocrine/metabolic disease	5,829	2,593 (44.5)	1,335 (51.5)	1,065 (41.1)	275 (10.6)	812 (31.3)	258 (10.0)	150 (5.8)	255 (9.8)
Gastrointestinal/ hepatobiliary disease	5,559	1,732 (31.2)	859 (49.6)	719 (41.5)	564 (32.6)	502 (29.0)	163 (9.4)	76 (4.4)	258 (14.9)
Other medical conditions	4,721	1,907 (40.4)	1,056 (55.4)	852 (44.7)	253 (13.3)	675 (35.4)	171 (9.0)	110 (5.8)	232 (12.2)
Total*	36,351	15,487 (42.6)	7,419 (47.9)	6,119 (39.5)	1,549 (10.0)	4,667 (30.1)	1,454 (9.4)	694 (4.5)	1,262 (8.2)

*Patients may have more than one diagnosis and may be counted more than once. †Intracranial haemorrhage, known bleeding disorder (congenital or acquired), clinically relevant hepatic impairment, bleeding at hospital admission, and/or active gastroduodenal ulcer defined in accordance with Baglin et al. 2006 (7). ‡Includes patients who receive mechanical prophylaxis, including graduated compression stockings or intermittent pneumatic compression, with and without anticoagulant prophylaxis. ACCP, American College of Chest Physicians; LMWH, low-molecular-weight heparin; UFH, unfractionated heparin; VTE, venous thromboembolism.

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The proportion of patients who received any mechanical prophylaxis ranged from 6.0% of those with acute heart failure to 16.7% of patients with haemorrhagic stroke (Table 1). With regards to mechanical prophylaxis, overall GCS were the most commonly used type of mechanical prophylaxis in patients at risk for VTE. The use of GCS ranged from 3.6% of patients with an acute non-infectious respiratory disease to 11.4% of patients with haemorrhagic stroke.

Contraindications to anticoagulant prophylaxis

For the majority of primary diagnoses reported in this study, <20% of patients at risk for VTE were considered to have contraindications to anticoagulant prophylaxis. However, the proportion of at-risk patients with contraindications was substantially greater in patients presenting with haemorrhagic stroke (61.9%) or gastrointestinal/hepatobiliary disorders (32.6%; Table 1).

Bleeding risk factors were identified in a similar proportion of patients at risk and those not at risk for VTE (10.0% and 11.2 %, respectively). The most common contraindications to anticoagulation in patients at-risk and not at risk for VTE were clinically relevant hepatic impairment and bleeding at hospital admission (7).

VTE risk and prophylaxis use in medical patients across different countries

The hospitalised medically ill patient population varied across the participating countries (▶Table 2). Although the proportion of patients at risk for VTE was similar among the different countries (global rate 42%; between-country range, 21.1–71.2%; ▶Fig. 2A), the use of prophylaxis was highly variable between the different participating countries (Fig. 2B). Use of ACCP-recommended types of prophylaxis varied from 3.1% to 70.4%. The difference between the rates of providing any type of VTE prophylaxis versus ACCP-recommended also differed across participating countries (between-country range, 0–19%; Fig. 2B).

Of the 36,351 hospitalised medically ill patients with case report forms permitting clear diagnoses to be made, 48.8% (17,726) were admitted with one or more of the following: acute heart failure (New York Heart Association class III or IV); ischaemic stroke; malignancy (active); acute non-infectious respiratory disease; pulmonary infection; infection (non-respiratory). Rates of ACCP-recommended VTE prophylaxis for these patients for each of the 32 participating countries are provided in Table 2.

Effects of age on VTE risk and prophylaxis practices

Globally, the proportion of patients at risk for VTE increased according to age, from 34.0% in patients aged 40–49 years, to 51.8% in those aged ≥90 years (▶Table 3). When patient data were analysed according to age, only 30.0% of patients aged 40–49 years received ACCP-recommended prophylaxis, compared to 50.6% of patients aged ≥90 years. The frequency of contraindications to anticoagulant use ranged from 8.7–12.2% across all age groups studied (Table 3).

Risk factors for VTE in hospitalised medically ill patients

The most common VTE risk factors present before hospital admission were chronic pulmonary disease, chronic heart failure, and obesity (see Supplementary Table online at www.thrombosis-online.com) (7). The most common VTE risk factors following hospitalisation were complete immobilisation, immobilisation with bathroom privileges, and being admitted to a CCU. There was an increase in the percentage of patients who received ACCP-recommended VTE prophylaxis as the number of risk factors for VTE increased: 30% of patients with one risk factor received ACCP-recommended VTE prophylaxis compared with 56% of patients with more than five risk factors.

A notable proportion of patients who were not classified as at-risk for VTE according to ACCP 2004 guidelines presented with VTE risk factors prior to hospitalisation or developed risk factors for VTE during hospitalisation (37.2% [7,586 of 20,414] and 12.6% [2,631 of 20,864] of patients, respectively; see Supplementary Table online at www.thrombosis-online.com) (7).

VTE risk factors associated with the use of ACCP-recommended prophylaxis

Multivariable analysis identified placement of a central venous catheter as the factor most strongly associated with the use of ACCP-recommended prophylaxis in patients at risk for VTE (▶Fig. 3). Only a diagnosis of acute non-infectious respiratory disease and 'other' medical conditions were in the top ten factors independently associated with an increased likelihood of at-risk patients receiving ACCP-recommended VTE prophylaxis. A primary medical diagnosis of haemorrhagic stroke, endocrine or metabolic disease, 'other' cardiovascular disease, and the use of cancer therapy were all associated with a reduced likelihood of at-risk patients receiving ACCP-recommended VTE prophylaxis (Fig. 3).

Discussion

Although VTE risk varied according to individual patient diagnosis, ACCP-recommended prophylaxis was consistently underused in the global ENDORSE medical patient population, and was provided to less than 40% of those at risk. We observed substantial

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Table 2: Country-specific VTE prophylaxis practices in patients with acute heart failure, non-infectious respiratory disease, pulmonary infection, ischaemic stroke, active malignancy, and infection (non-respiratory).

A)										
Country	Total evaluable medical patients, n	Acute heart failure (NYHA Class III/IV)			Active non-infectious respiratory disease			Pulmonary infection		
		Patient population, n (%)	At risk for VTE, n (%)	At risk receiving ACCP prophylaxis, n (%)	Patient population, n (%)	At risk for VTE, n (%)	At risk receiving ACCP prophylaxis, n (%)	Patient population, n (%)	At risk for VTE, n (%)	At risk receiving ACCP prophylaxis, n (%)
Algeria	425	41 (9.6)	41 (100)	9 (22.0)	27 (6.4)	27 (100)	9 (33.3)	50 (11.8)	50 (100)	11 (22.0)
Australia	805	39 (4.8)	39 (100)	19 (48.7)	69 (8.6)	69 (100)	26 (37.7)	154 (19.1)	154 (100)	77 (50.0)
Bangladesh	1,075	102 (9.5)	102 (100)	3 (2.9)	43 (4.0)	43 (100)	0	122 (11.3)	122 (100)	0
Brazil	649	52 (8.0)	52 (100)	27 (51.9)	37 (5.7)	37 (100)	21 (56.8)	102 (15.7)	102 (100)	67 (65.7)
Bulgaria	1,464	218 (14.9)	218 (100)	94 (43.1)	57 (3.9)	57 (100)	19 (33.3)	151 (10.3)	151 (100)	28 (18.5)
Colombia	532	20 (3.8)	20 (100)	17 (85.0)	64 (12.0)	64 (100)	48 (75.0)	51 (9.6)	51 (100)	30 (58.8)
Czech Republic	1,306	112 (8.6)	112 (100)	62 (55.4)	70 (5.4)	70 (100)	28 (40.0)	103 (7.9)	103 (100)	40 (38.8)
Egypt	521	30 (5.8)	30 (100)	9 (30.0)	24 (4.6)	24 (100)	3 (12.5)	74 (14.2)	74 (100)	20 (27.0)
France	1,857	142 (7.6)	142 (100)	61 (43.0)	255 (13.7)	255 (100)	136 (53.3)	220 (11.8)	220 (100)	125 (56.8)
Germany	1,127	101 (9.0)	101 (100)	64 (63.4)	75 (6.7)	75 (100)	52 (69.3)	165 (14.6)	165 (100)	124 (75.2)
Greece	880	73 (8.3)	73 (100)	27 (37.0)	56 (6.4)	56 (100)	17 (30.4)	129 (14.7)	129 (100)	39 (30.2)
Hungary	844	55 (6.5)	55 (100)	14 (25.5)	43 (5.1)	43 (100)	7 (16.3)	65 (7.7)	65 (100)	18 (27.7)
India	892	46 (5.2)	46 (100)	12 (26.1)	34 (3.8)	34 (100)	2 (5.9)	121 (13.6)	121 (100)	13 (10.7)
Ireland	243	14 (5.8)	14 (100)	6 (42.9)	20 (8.2)	20 (100)	14 (70.0)	50 (20.6)	50 (100)	18 (36.0)
Kuwait	324	37 (11.4)	37 (100)	10 (27.0)	32 (9.9)	32 (100)	14 (43.8)	88 (27.2)	88 (100)	39 (44.3)
Mexico	280	25 (8.9)	25 (100)	16 (64.0)	12 (4.3)	12 (100)	6 (50.0)	26 (9.3)	26 (100)	12 (46.2)
Pakistan	552	36 (6.5)	36 (100)	17 (47.2)	17 (3.1)	17 (100)	3 (17.6)	62 (11.2)	62 (100)	13 (21.0)
Poland	1,438	176 (12.2)	176 (100)	84 (47.7)	93 (6.5)	93 (100)	19 (20.4)	186 (12.9)	186 (100)	57 (30.6)
Portugal	853	51 (6.0)	51 (100)	30 (58.8)	53 (6.2)	53 (100)	32 (60.4)	153 (17.9)	153 (100)	92 (60.1)
Romania	3,167	388 (12.3)	388 (100)	89 (22.9)	131 (4.1)	131 (100)	24 (18.3)	259 (8.2)	259 (100)	30 (11.6)
Russia	1,918	173 (9.0)	173 (100)	29 (16.8)	130 (6.8)	130 (100)	6 (4.6)	114 (5.9)	114 (100)	7 (6.1)
Saudi Arabia	151	25 (16.6)	25 (100)	19 (76.0)	8 (5.3)	8 (100)	5 (62.5)	19 (12.6)	19 (100)	13 (68.4)
Slovakia	1,226	181 (14.8)	181 (100)	91 (50.3)	27 (2.2)	27 (100)	13 (48.1)	117 (9.5)	117 (100)	36 (30.8)
Spain	2,003	210 (10.5)	210 (100)	129 (61.4)	482 (24.1)	482 (100)	317 (65.8)	418 (20.9)	418 (100)	284 (67.9)
Switzerland	818	38 (4.6)	38 (100)	23 (60.5)	50 (6.1)	50 (100)	31 (62.0)	54 (6.6)	54 (100)	31 (57.4)
Thailand	809	53 (6.6)	53 (100)	13 (24.5)	45 (5.6)	45 (100)	1 (2.2)	131 (16.2)	131 (100)	1 (0.8)
Tunisia	647	45 (7.0)	45 (100)	10 (22.2)	71 (11.0)	71 (100)	20 (28.2)	113 (17.5)	113 (100)	44 (38.9)
Turkey	1,204	13 (1.1)	13 (100)	13 (100)	33 (2.7)	33 (100)	12 (36.4)	179 (14.9)	179 (100)	51 (28.5)
United Arab Emirates	170	37 (21.8)	37 (100)	10 (27.0)	6 (3.5)	6 (100)	1 (16.7)	40 (23.5)	40 (100)	18 (45.0)
United Kingdom	2,724	202 (7.4)	202 (100)	68 (33.7)	181 (6.6)	181 (100)	73 (40.3)	498 (18.3)	498 (100)	203 (40.8)
United States	5,127	481 (9.4)	481 (100)	227 (47.2)	725 (14.1)	725 (100)	371 (51.2)	753 (14.7)	753 (100)	376 (49.9)
Venezuela	320	43 (13.4)	43 (100)	27 (62.8)	14 (4.4)	14 (100)	5 (35.7)	67 (20.9)	67 (100)	22 (32.8)
Total	36,351	3,259 (9.0)	3,259 (100)	1,329 (40.8)	2,984 (8.2)	2,984 (100)	1,335 (44.7)	4,834 (13.3)	4,834 (100)	1,939 (40.1)

ACCP, American College of Chest Physicians; NA, not applicable; NYHA, New York Heart Association; VTE, venous thromboembolism.

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Table 2: Continued

B)										
Country	**Total evaluable medical patients, n**	**Ischaemic stroke**			**Active malignancy**			**Infection (non-respiratory)**		
		Patient population, n (%)	**At risk for VTE, n (%)**	**At risk receiving ACCP prophylaxis, n (%)**	**Patient population, n (%)**	**At risk for VTE, n (%)**	**At risk receiving ACCP prophylaxis, n (%)**	**Patient population, n (%)**	**At risk for VTE, n (%)**	**At risk receiving ACCP prophylaxis, n (%)**
Algeria	425	20 (4.7)	20 (100)	10 (50.0)	42 (9.9)	17 (40.5)	0	67 (15.8)	42 (62.7)	16 (38.1)
Australia	805	40 (5.0)	30 (75.0)	8 (26.7)	61 (7.6)	21 (34.4)	6 (28.6)	148 (18.4)	94 (63.5)	41 (43.6)
Bangladesh	1,075	140 (13.0)	105 (75.0)	1 (1.0)	56 (5.2)	19 (33.9)	1 (5.3)	137 (12.7)	40 (29.2)	0
Brazil	649	24 (3.7)	17 (70.8)	14 (82.4)	35 (5.4)	18 (51.4)	10 (55.6)	91 (14.0)	49 (53.8)	26 (53.1)
Bulgaria	1,464	128 (8.7)	103 (80.5)	43 (41.7)	49 (3.3)	14 (28.6)	3 (21.4)	183 (12.5)	69 (37.7)	15 (21.7)
Colombia	532	18 (3.4)	11 (61.1)	8 (72.7)	32 (6.0)	13 (40.6)	6 (46.2)	93 (17.5)	54 (58.1)	34 (63.0)
Czech Republic	1,306	76 (5.8)	47 (61.8)	22 (46.8)	107 (8.2)	38 (35.5)	13 (34.2)	146 (11.2)	73 (50.0)	28 (38.4)
Egypt	521	56 (10.7)	19 (33.9)	12 (63.2)	113 (21.7)	14 (12.4)	0	22 (4.2)	12 (54.5)	2 (16.7)
France	1,857	101 (5.4)	34 (33.7)	19 (55.9)	254 (13.7)	88 (34.6)	48 (54.5)	220 (11.8)	75 (34.1)	36 (48.0)
Germany	1,127	78 (6.9)	58 (74.4)	45 (77.6)	160 (14.2)	55 (34.4)	35 (63.6)	169 (15.0)	86 (50.9)	63 (73.3)
Greece	880	51 (5.8)	40 (78.4)	21 (52.5)	62 (7.0)	27 (43.5)	5 (18.5)	97 (11.0)	38 (39.2)	10 (26.3)
Hungary	844	44 (5.2)	23 (52.3)	11 (47.8)	131 (15.5)	31 (23.7)	9 (29.0)	31 (3.7)	15 (48.4)	8 (53.3)
India	892	66 (7.4)	50 (75.8)	7 (14.0)	48 (5.4)	5 (10.4)	0	141 (15.8)	58 (41.1)	11 (19.0)
Ireland	243	12 (4.9)	7 (58.3)	1 (14.3)	21 (8.6)	10 (47.6)	2 (20.0)	29 (11.9)	14 (48.3)	6 (42.9)
Kuwait	324	36 (11.1)	19 (52.8)	7 (36.8)	5 (1.5)	2 (40.0)	1 (50.0)	52 (16.0)	37 (71.2)	19 (51.4)
Mexico	280	10 (3.6)	9 (90.0)	6 (66.7)	8 (2.9)	4 (50.0)	0	42 (15.0)	34 (81.0)	19 (55.9)
Pakistan	552	37 (6.7)	32 (86.5)	7 (21.9)	13 (2.4)	4 (30.8)	2 (50.0)	67 (12.1)	32 (47.8)	12 (37.5)
Poland	1,438	56 (3.9)	31 (55.4)	13 (41.9)	132 (9.2)	26 (19.7)	5 (19.2)	72 (5.0)	22 (30.6)	10 (45.5)
Portugal	853	73 (8.6)	34 (46.6)	24 (70.6)	76 (8.9)	29 (38.2)	16 (55.2)	86 (10.1)	36 (41.9)	24 (66.7)
Romania	3,167	324 (10.2)	280 (86.4)	59 (21.1)	241 (7.6)	36 (14.9)	3 (8.3)	276 (8.7)	106 (38.4)	15 (14.2)
Russia	1,918	216 (11.3)	137 (63.4)	13 (9.5)	7 (0.4)	2 (28.6)	0	24 (1.3)	1 (4.2)	0
Saudi Arabia	151	24 (15.9)	18 (75.0)	13 (72.2)	3 (2.0)	0	NA	15 (9.9)	14 (93.3)	9 (64.3)
Slovakia	1,226	141 (11.5)	76 (53.9)	49 (64.5)	166 (13.5)	28 (16.9)	9 (32.1)	108 (8.8)	50 (46.3)	24 (48.0)
Spain	2,003	164 (8.2)	103 (62.8)	68 (66.0)	177 (8.8)	98 (55.4)	53 (54.1)	317 (15.8)	160 (50.5)	117 (73.1)
Switzerland	818	21 (2.6)	8 (38.1)	7 (87.5)	71 (8.7)	16 (22.5)	7 (43.8)	62 (7.6)	26 (41.9)	17 (65.4)
Thailand	809	37 (4.6)	35 (94.6)	2 (5.7)	178 (22.0)	48 (27.0)	0	203 (25.1)	119 (58.6)	2 (1.7)
Tunisia	647	2 (0.3)	1 (50.0)	0	66 (10.2)	27 (40.9)	8 (29.6)	75 (11.6)	32 (42.7)	13 (40.6)
Turkey	1,204	17 (1.4)	12 (70.6)	10 (83.3)	87 (7.2)	15 (17.2)	4 (26.7)	24 (2.0)	15 (62.5)	7 (46.7)
United Arab Emirates	170	21 (12.4)	19 (90.5)	9 (47.4)	11 (6.5)	6 (54.5)	3 (50.0)	17 (10.0)	9 (52.9)	2 (22.2)
United Kingdom	2,724	154 (5.7)	94 (61.0)	19 (20.2)	208 (7.6)	86 (41.3)	29 (33.7)	522 (19.2)	233 (44.6)	79 (33.9)
United States	5,127	190 (3.7)	135 (71.1)	69 (51.1)	478 (9.3)	264 (55.2)	115 (43.6)	964 (18.8)	608 (63.1)	325 (53.5)
Venezuela	320	46 (14.4)	42 (91.3)	15 (35.7)	15 (4.7)	11 (73.3)	4 (36.4)	70 (21.9)	45 (64.3)	15 (33.3)
Total	36,351	2,423 (6.7)	1,649 (68.1)	612 (37.1)	3,113 (8.6)	1,072 (34.4)	397 (37.0)	4,570 (12.6)	2,298 (50.3)	1,005 (43.7)

ACCP, American College of Chest Physicians; NA, not applicable; NYHA, New York Heart Association; VTE, venous thromboembolism.

variation in prophylaxis use according to medical diagnosis across participating countries. Furthermore, our study suggests that approximately 70% of hospitalised medical patients aged younger than 50 years and at risk for VTE do not receive ACCP-recommended prophylaxis. The presence of a central venous catheter, mechanical ventilation, or admission to intensive care unit (ICU)/CCU was most strongly associated with the use of ACCP-recommended prophylaxis in at-risk medical patients.

Although VTE prophylaxis use in at-risk medical patients varied according to diagnosis, even the highest rate of prophylaxis as-

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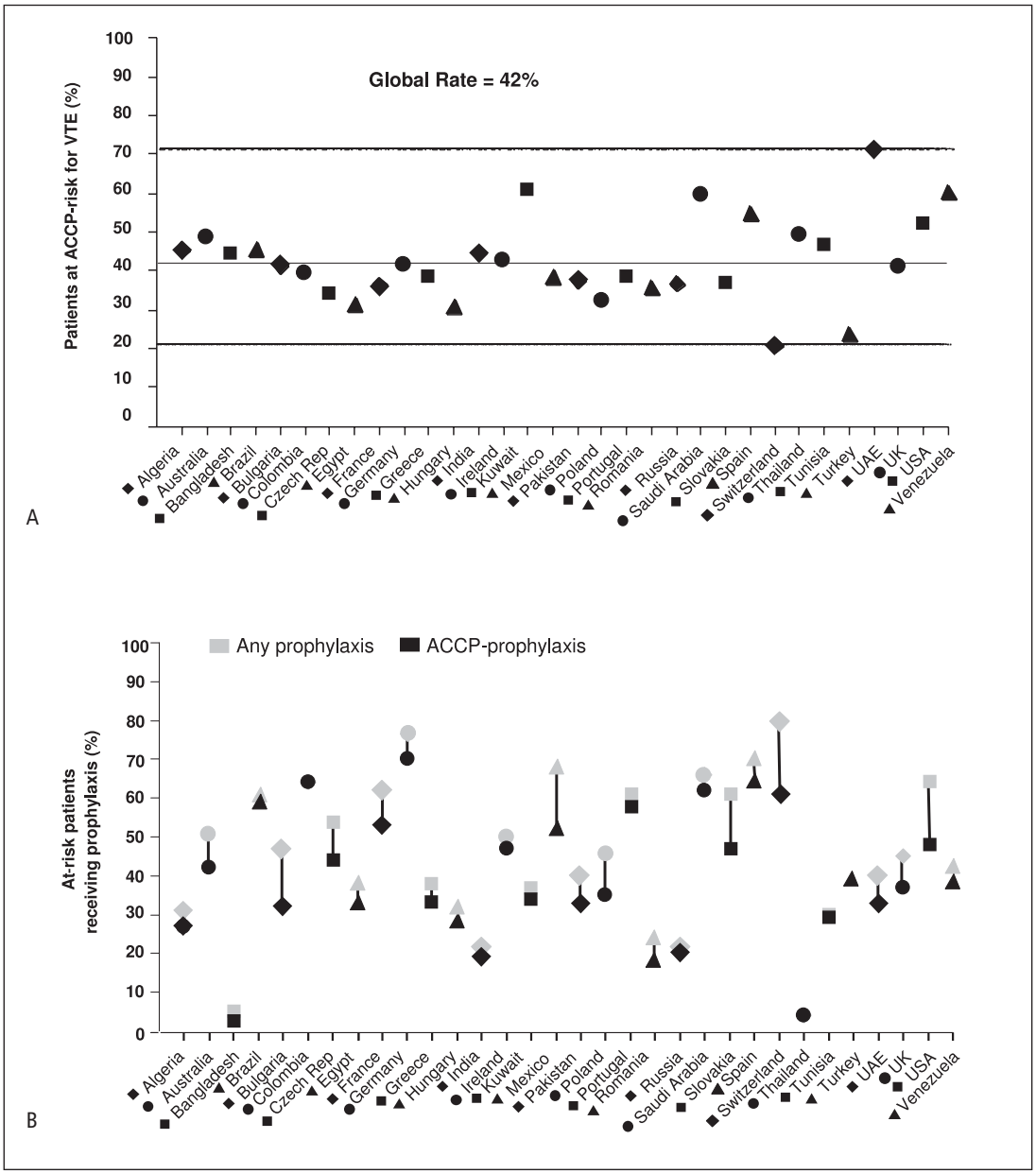


Figure 2: Proportion of medical patients. A) at ACCP-risk for VTE; B) at-risk patients receiving any form of prophylaxis and ACCP-recommended forms of prophylaxis in participating countries. ACCP, American College of Chest Physicians; VTE, venous thromboembolism.

Table 3: Effects of age on the incidence of risk for VTE, use of ACCP-recommended prophylaxis, and contraindications to anticoagulant use.

Patient age group, years	Total no. of patients, n	At risk for VTE, n (%)	At risk receiving ACCP-recommended prophylaxis, n (%)	At risk with contraindications to anticoagulant use, n (%)
40–49	4,726	1,606 (34.0)	481 (30.0)	196 (12.2)
50–59	7,248	2,656 (36.6)	902 (34.0)	311 (11.7)
60–69	7,918	3,309 (41.8)	1,241 (37.5)	337 (10.2)
70–79	9,080	4,154 (45.7)	1,702 (41.0)	362 (8.7)
80–89	6,162	3,131 (50.8)	1,474 (47.1)	281 (9.0)
≥90	1,217	631 (51.8)	319 (50.6)	62 (9.8)

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sociated with a given medical diagnosis remains lower than the rate of use in at-risk surgical patients (range, 50–88%) (7). This result is especially important, given that the prognosis for patients with DVT may be worse in medical than surgical patients (10).

Our data highlight the discrepancies between level of VTE risk and prophylaxis provision in patients with common diagnoses including acute infectious respiratory disease, heart failure, active malignancy, and ischaemic stroke. Our findings showed that a large proportion of haemorrhagic stroke patients was at risk for VTE; however, only approximately 25% received ACCP-recommended prophylaxis and more than half of patients had a contraindication to anticoagulant prophylaxis. These data emphasise

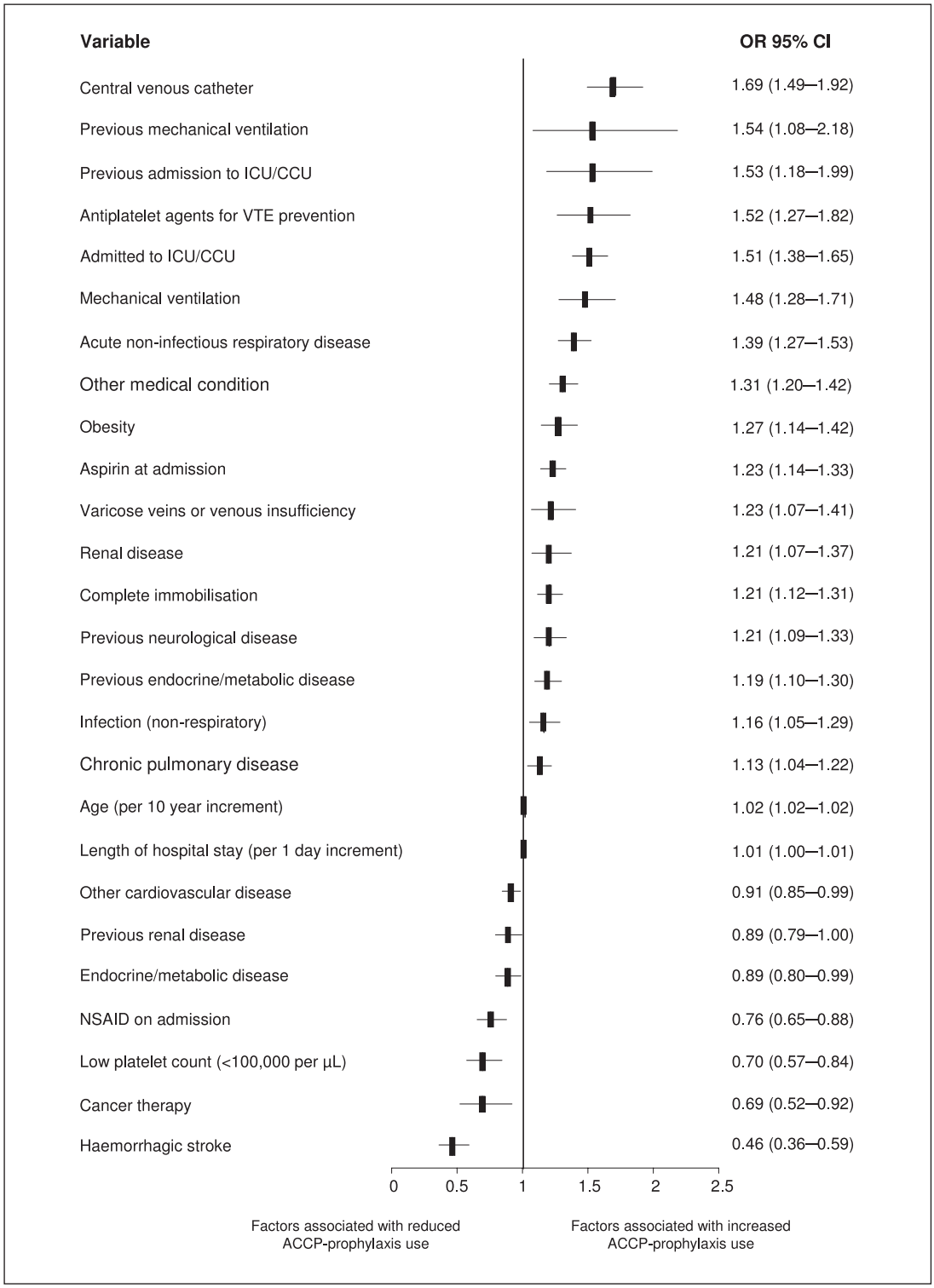


Figure 3: Multivariable analysis results to identify independent factors associated with the use of ACCP-recommended VTE prophylaxis in medical patients at-risk for VTE. ACCP, American College of Chest Physicians; CCU, critical care unit; CI, confidence interval; ICU, intensive care unit; NSAID, non-steroidal anti-inflammatory drug; OR, odds ratio; VTE, venous thromboembolism.

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What is known about this topic?

- The ENDORSE survey showed that up to 50% of all hospitalised patients at-risk for venous thromboembolism (VTE) are not receiving appropriate prophylaxis.
- Medical patients at VTE risk are less likely to receive prophylaxis than surgical patients.

What does this paper add?

- Use of prophylaxis varies according to medical diagnosis across different countries.
- Less than 45% of the patients at risk for VTE hospitalised for heart failure, pulmonary failure, severe sepsis or ischemic stroke received ACCP-recommended prophylaxis.
- About 70% of hospitalised medical patients with <50 years and at risk for VTE do not receive ACCP-recommended prophylaxis.
- Presence of a central venous catheter, mechanical ventilation, or admission to ICU/CCU is associated with use of ACCP-recommended prophylaxis in at-risk medical patients.
- There is a need to improve implementation of current guidelines for appropriate thromboprophylaxis in hospitalised medically ill patients at risk for VTE.

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ENDORSE is overseen by a medical advisory board of clinicians. The ENDORSE database is held by the Center for Outcomes Research at the University of Massachusetts Medical School. All statistical analyses were performed by the Center for Outcomes Research. Dr Anderson and W. Huang had full access to all the study data and take responsibility for the integrity of the data and the accuracy of the data analysis. A full list of the investigators who participated in ENDORSE and further information about the registry can be found at http://www.outcomes.org/endorse.

the difficulties in the management of these patients for whom both the risk for VTE and bleeding is high. Despite the well-recognised increase in VTE risk associated with malignancy (11, 12), our findings showed that less than 50% of cancer patients received ACCP-recommended prophylaxis, even though contraindications to anticoagulant prophylaxis were present in only 14% of these patients. Furthermore our multivariable analysis found that cancer therapy was associated with reduced use of prophylaxis. Concerns regarding bleeding risk do not legitimise this underuse of prophylaxis, as the ACCP recommends mechanical forms of prophylaxis in patients with contraindications to anticoagulant therapy. Similarly low rates of appropriate thromboprophylaxis use were observed in a recent study of 196,104 American inpatients (13) and in a cohort of 4,846 consecutive patients admitted to 27 internal medicine departments (14).

Treatment in a university-affiliated/teaching hospital, presence of VTE risk factors, and admission for a respiratory illness have previously been identified as being independent predictors of increased prophylaxis uptake (13, 15). In contrast, our study identified risk factors such as central venous catheterisation, previous mechanical ventilation, and previous admission to an ICU/CCU, as being most strongly associated with greater use of recommended prophylaxis. These findings suggest that the decision to provide prophylaxis is based on disease severity rather than medical diagnosis.

The lack of implementation of evidence-based guidelines for VTE prophylaxis in at-risk medical patients may be based on confusion regarding the assessment of VTE risk, a lack of awareness of VTE risk, or a strong fear of major bleeding. The classification of VTE risk in medical patients is perceived to be more challenging than in surgical patients. Risk must be assessed based upon medical diagnosis, combinations of illnesses, bleeding risk, and the presence of additional risk factors such as limited mobility (1, 16–19). Nevertheless there are some situations in medical patients, comparable to high-risk surgery cases, which by themselves should drive VTE prophylaxis, such as heart failure and chronic obstructive pulmonary disease. By comparison, most surgical patients will be admitted to undergo a specific surgery type and will have fewer co-morbidities and confounding factors to be considered when assessing the benefit-to-risk ratio of providing VTE prophylaxis. Many hospitals lack formal protocols for VTE prevention in at-risk medical patients, which may lead to reduced awareness of VTE risk, and compliance with available guidelines for VTE prophylaxis (20–22). The presence of a formal hospital protocol for VTE prevention is now an ACCP Grade IA recommendation (1).

There are potential limitations to our study. The duration of adherence to prophylactic treatment could not be assessed due to the cross-sectional study design. Due to the wide range in the number of patients enrolled at the individual country level, appropriate caution is warranted in the interpretation of country-specific rates, which have wider confidence intervals as the sample size decreases. Physicians may have altered their use of VTE prophylaxis as a result of becoming aware of the study and/or may have behaved differently towards specific groups of medical patients de-

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pending on where the patient was admitted. Furthermore, some differences in prophylaxis rates between countries are probably due to differences in drug access, public health priorities, and economic concerns. We focused on evaluating the use of VTE prophylaxis in patients defined by the ACCP as being at-risk for VTE. However, prophylaxis may also be appropriate in patients presenting with other VTE risk factors that are not assessed in the ACCP recommendations due to limited evidence on the risk for VTE in medical patients not covered by the guidelines. In addition, our estimates of appropriate prophylaxis received were affected by the definition used, which considered as appropriate prophylaxis the type of therapies recommended by the ACCP guidelines without looking at the dosing schedules or duration of treatment. Finally, our multivariable analysis may be limited as a result of the factors driving provision of VTE prophylaxis in at-risk patients, varying widely across the different participating countries.

The key strength of our study is its inclusion of a broad range of hospitalised medically ill patients from 32 countries across six continents with varying social and economic backgrounds. The observed large, between-country differences in level of prophylaxis and the types of prophylaxis prescribed (any versus ACCP-recommended types) also enable the tailoring of efforts to improve prophylaxis uptake and awareness within participating countries according to their individual needs.

The findings from this ENDORSE sub-analysis suggest that despite improving physician awareness of VTE risk in hospitalised medical patients, use of ACCP-recommended prophylaxis remains suboptimal in this patient population. There is an urgent need for effective and consistent implementation of existing guideline recommendations for appropriate thromboprophylaxis in hospitalised medically ill patients at risk for VTE.

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Underlined names correspond to the national coordinators for each country.

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