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Contemporary adequacy of thromboprophylaxis in acutely ill medical patients in Switzerland: a bi-centric prospective cohort

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Summary

BACKGROUND: Venous thromboembolism is a dreaded complication of hospitalised patients, with associated morbidity, mortality and increased healthcare costs. Previous studies have shown that pharmacological thromboprophylaxis, though effective, is inadequately administered in a large proportion of medical inpatients.

STUDY AIMS: Our primary aim was to evaluate the contemporary adequacy of thromboprophylaxis in medical inpatients admitted to two Swiss hospitals (a university hospital and a regional hospital). The secondary aim was to estimate the 90-day incidence of relevant thrombotic and bleeding events.

METHODS: In this prospective cohort, patients were recruited at the University Hospital of Geneva and the Regional Hospital of Lugano between September 2020 and February 2021 and followed for 90 days for venous thromboembolism and bleeding events. The adequacy of thromboprophylaxis (pharmacological and/or mechanical) at 24h after hospital admission was evaluated according to the simplified Geneva risk score for hospital-associated venous thromboembolism.

RESULTS: Among 200 participants (100 at each site, mean age of 65 years), 57.5% were deemed at high risk of venous thromboembolism at admission. Thromboprophylaxis was adequate in 59.5% (95% CI 52.3–66.4%). Among high-risk and low-risk inpatients, thromboprophylaxis was adequate in 71.3% and 43.5%, respectively, with differences between sites. At 90 days, risks of adjudicated venous thromboembolism, major bleeding and mortality were 1.5%, 1.5% and 6.0%, respectively.

CONCLUSION: Despite the extensive literature on thromboprophylaxis, the adequacy of thromboprophylaxis has not improved and remains insufficient among medical inpatients. Implementation and evaluation of clinical decision support systems are critically needed in this field.

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Introduction

Venous thromboembolism, comprising deep vein thrombosis and pulmonary embolism, can complicate both medical and surgical hospital stays. Up to 800,000 to 1 million venous thromboembolism events are estimated to occur annually in Europe, 50% of which are related to current or recent hospitalisation [1]. Without thromboprophylaxis, approximately 1 in 20 patients after major orthopaedic surgery and 1 in 40 medical patients would develop pulmonary embolism or proximal deep vein thrombosis [2]. Furthermore, pulmonary embolism is considered a leading cause of preventable death in hospitals [3] and hospital-associated venous thromboembolism is associated with longer hospital stays and higher costs[4].

Pharmacological thromboprophylaxis (with unfractionated heparin, low-molecular-weight heparin [LMWH] or fondaparinux) reduces hospital-associated venous thromboembolism by 50–70% in high-risk medical and surgical patients and is cost-effective [5]. However, indiscriminate use of thromboprophylaxis in all inpatients is unreasonable, given its associated bleeding complications and financial costs. For medical inpatients, the current scheme is to use risk assessment models (Geneva, Padua, Improve scores) to stratify their risk and prescribe thromboprophylaxis only to high-risk patients.

Despite the extent of hospital-associated venous thromboembolism, the quality of thromboprophylaxis (i.e. prescribing thromboprophylaxis to high-risk patients and not prescribing it to low-risk patients) has consistently been shown to be insufficient. In an international study of 70,000 patients in >300 hospitals in 2006–2007, the use

of thromboprophylaxis was appropriate in only 58.5% of surgical and 39.5% of medical inpatients at risk of venous thromboembolism [6]. More recent estimates suggest an adequacy of thromboprophylaxis of 60–70% [7, 8]. In Switzerland, its adequacy is also low, at 38–47% according to a multicentre prospective cohort (2010–2011) [9–11].

Our main aim was to report the contemporary adequacy of thromboprophylaxis in a university and a regional hospital in Switzerland, along with 90-day complications. A secondary aim was to assess the economic burden of inadequate thromboprophylaxis.

Methods

This analysis is embedded in the TPX-ENHANCE clinical trial, a bicentric comparative quality-improvement effort to improve the adequacy of in-hospital medical thromboprophylaxis. This ongoing non-randomised clinical trial compares the effectiveness of two interventions (educational session + pocket card *versus* educational session + comprehensive electronic tool embedded in the electronic medical chart) to improve the adequacy of medical in-hospital thromboprophylaxis. We report here the baseline phase, with the primary aim of evaluating the adequacy of thromboprophylaxis prior to the interventions. The study was approved by the local ethics committee of Geneva and Ticino (CCER 2019-01976). Written informed consent was obtained from all patients. The study complies with the principles of the Declaration of Helsinki. Clinicaltrials.gov number: NCT05306821.

Participants

For the baseline (pre-intervention) phase, we enrolled 200 (100 per site) acutely ill adult medical inpatients from the university hospital of Geneva and the regional hospital of Lugano, between September 2020 and February 2021. An acutely ill medical inpatient was defined as a patient hospitalised in a medical ward for an acute condition. Exclusion criteria were ongoing therapeutic anticoagulation, a palliative care setting, pregnancy, a hospital stay ≤2 days or in the oncohaematology ward and an acute COVID-19 infection. Patients who had been transferred from a surgical ward or intensive care unit were also excluded. To minimise any influence of the study on thromboprophylaxis practice, the enrolment procedure was performed 24–48 hours prior to hospital discharge.

Study procedures

At the time of inclusion, demographic, clinical and laboratory data, as well as chronic antithrombotic and inpatient thromboprophylaxis prescription were collected using direct participant interviews and medical record extraction. At hospital discharge, relevant thrombotic and bleeding outcomes were assessed using the electronic medical record. Three months after hospital discharge, we collected serious adverse events and clinical outcomes during a telephone follow-up.

The choice of thromboprophylaxis use and its modalities was at the discretion of the physicians in charge. There was no recent educational session to guide its practice, and no formal risk stratification scheme was used in the electronic or paper medical records. In both hospitals, drugs available for pharmacological thromboprophylaxis were enoxaparin, fondaparinux and unfractionated heparin (UFH), while compression stockings and intermittent pneumatic compression boots were available for mechanical thromboprophylaxis.

Risk score and data definitions

The simplified Geneva risk assessment model (sGRS) is an externally validated clinical score with good discriminative and predictive performances for hospital-associated venous thromboembolism (table 1) [12]. We calculated this score with data corresponding to the time of hospital admission, found in the electronic medical chart and from the direct interview with the participant. A personal history of venous thromboembolism was defined as a prior pulmonary embolism or proximal or distal deep vein thrombosis of the lower or upper extremity. Acute cardiac or respiratory failure were defined by a selection of medical diagnoses with hypoxaemia and/or treatment (diuretics, oxygen). Acute infections were defined by a medical diagnosis of an acute infection, prescription of an antibiotic or antiviral drug, radiological evidence of infection, and/or laboratory demonstration of an infectious agent. An active diagnosis of cancer was defined by any solid or haematological cancer, excluding non-melanoma skin tumours, diagnosed or treated within 2 years or with objectively documented lesions. Mobility at the time of admission was evaluated by either interviewing the patient at study inclusion or measuring the mobility by means of the Braden scale (for pressure ulcer), as reported by nurses within 24 h of admission. A patient was considered immobile if bedbound or chairbound within 24 h of admission, with a severely limited ability to walk (Braden scale Activity 1–2).

The risk of bleeding was high in case of recent/ongoing major bleeding, severe thrombocytopenia (<25 x 10^9/l), severe coagulopathy or by assessment of an investigator (experienced physicians). Severe coagulopathy was defined by a previous diagnosis of a known coagulation disorder, such as haemophilia, or by severely prolonged clotting times on admission, suggestive of severe coagulopathy.

Outcomes

The primary outcome was the proportion of adequate thromboprophylaxis at 24 hours after hospital admission. Thromboprophylaxis was deemed adequate when thromboprophylaxis (adequate pharmacological thromboprophylaxis; mechanical thromboprophylaxis in case of a high risk of bleeding) was administered to patients considered at high risk according to the simplified Geneva risk score (sGRS ≥3) and when no thromboprophylaxis was administered to patients considered at low risk (<3) according to the same score.

Secondary outcomes were in-hospital and 90-day incidence of venous thromboembolism, major bleeding, death and heparin-induced thrombocytopenia. Venous thromboembolism was defined as symptomatic or asymptomatic objectively diagnosed pulmonary embolism or proximal deep vein thrombosis and symptomatic distal deep vein thrombosis. There was no screening for asymptomatic deep vein thrombosis. Major bleeding was defined according to the International Society of Thrombosis and

Haemostasis by a fatal bleeding, bleeding in a critical organ such as intracranial, spinal, intraocular, retroperitoneal, intra-articular, pericardial, intramuscular, a haemoglobin decrease >20 g/l or the need for >2 transfusions of whole blood or red cells [13]. Heparin-induced thrombocytopenia was defined as thrombocytopenia secondary to heparin-induced antibody response to complexes of platelet factor 4 (PF4) and heparin, according to American Society of Hematology (ASH) guidelines [14]. Deaths were categorised as pulmonary embolism-related death, undetermined cause of death or cause of death other than pulmonary embolism, following guidance from the International Society on Thrombosis and Haemostasis (ISTH) [15], of which only pulmonary embolism-related deaths were counted as venous thromboembolism events. Venous thromboembolism, causes of death and heparin-induced thrombocytopenia (HIT) were adjudicated by an experienced physician.

Economic impact

We estimated direct drug costs due to thromboprophylaxis misprescription, and compared drug costs of inadequate administration to low-risk patients with missing drug costs of inadequate non-administration to high-risk patients. Direct costs linked to nurse activity or indirect costs secondary to thromboprophylaxis inadequacy-related complications, such as venous thromboembolism and bleeding events, were not included in this analysis.

We calculated the costs of enoxaparin 40 mg once daily over the mean standard duration of hospital stay (6 days in Geneva, 9 days in Lugano) for the proportion of patients with a low sGRS with inadequately administered thromboprophylaxis. We extrapolated these costs to the annual volume of inpatient stays in the Department of Medicine of both hospitals (7000 in Geneva, 3400 in Lugano), minus 19% of inpatients with therapeutic anticoagulation [16]. The price for enoxaparin 40 mg was estimated at 3.78 CHF (lowest price for generic enoxaparin; source: Compendium.ch accessed on 13 June 2023). We assumed similar lengths of hospital stay in low-risk and high-risk inpatients.

Statistical analysis

Characteristics of participants were reported as proportions, mean ± standard deviation (SD) or median with the 25th and 75th percentiles according to variable distribution. The primary outcome was reported as a proportion with exact binomial 95% confidence intervals, with Chi-squared tests for between-site comparisons. The 90-day risk of clinical outcomes was evaluated by the Kaplan-Meier method, with the admission day as time 0 and censoring at the time of study end (90 days), or non-venous thromboembolism death (for venous thromboembolism) / non-bleeding death (for major bleeding) or at the last follow-up in case of loss to follow-up. Comparisons were done by log-rank tests. For the 90-day risk of venous thromboembolism and major bleeding, we also used a cumulative incidence function taking into account the competing risk of non-venous thromboembolism and non-bleeding deaths, respectively, as a sensitivity analysis.

In a post-hoc exploratory analysis, we evaluated associations of thrombotic risk factors (from the Geneva risk score) with the use of pharmacological and/or mechanical thromboprophylaxis within 24 h of admission, first in a univariable fashion and second in a multivariable logistic regression analysis. We included all 9 variables in the multivariable analysis, regardless of the statistical univariable association.

All tests were performed two-sided and a pvalue <0.05 was considered statistically significant.

There were no missing data for the calculation of the score and no imputation was done. Statistical analysis was performed using Stata Version 15 (StataCorp LP, College Station, TX, USA).

Results

Among the 200 medical inpatients, 49% were women and the mean age was 65.3 years (SD 17.6), ranging from 18 to 92 years (table 2). The mean BMI was 25.6 kg/m^2, with a prevalence of obesity of 19%. In the Lugano cohort, patients were older (mean age 69.7 years) than in the Geneva cohort (mean age 61.0 years). The majority of patients were admitted for infections (33%) in Lugano and for cardiorespiratory failure (20%) in Geneva. Most were hospitalised via the emergency room (88%).

The mean simplified Geneva score at the two sites was comparable (2.8 ± 1.9 in Geneva vs 2.8 ± 1.8 in Lugano). In Geneva, 53% were deemed at high risk of venous thromboembolism by the sGRS at the time of admission vs 62% in Lugano. The median length of stay was longer in Lugano than in Geneva (11d, IQR 7–17 vs 8d, IQR

Table 1:
The Geneva simplified risk assessment model.

Items	Points
Personal history of venous thromboembolism	3
Known thrombophilia	2
Active cancer or myeloproliferative disorder	2
Cardiac and/or respiratory failure	2
Acute infection and/or rheumatological disorder	2
Reduced mobility	2
Age >60 years	1
BMI >30 kg/m^2	1
Recent stroke or myocardial infarction (<1 month)	1

High venous thromboembolism risk: ≥3 points.

Low venous thromboembolism risk: <3 points.

6–13.5). We had no loss of follow-up until 90 days or death.

Adequacy of thromboprophylaxis

Overall, thromboprophylaxis was adequate in 59.5% (119/200, 95% CI 52.3–66.4%), and was similar in Geneva and Lugano (table 3).

At any time during the hospital stay, pharmacological thromboprophylaxis was used in 72% patients in Geneva and in 76% in Lugano. The modal drug was enoxaparin and the median duration of thromboprophylaxis was 6 days (IQR 4–10.5) in Geneva and 9 days (IQR 5–14) in Lugano. Use of mechanical thromboprophylaxis was rare (2 participants in Geneva, 0 in Lugano).

Among the 115 high-risk participants, adequate use of thromboprophylaxis (pharmacological or mechanical) was found in 62.3% and 79% in Geneva and Lugano, respectively (p = 0.048). The main reason for inadequate thromboprophylaxis was non-use of pharmacological or mechanical thromboprophylaxis within 24 h. When considering thromboprophylaxis at any time during the hospital stay, 45/53 (84.9%) and 49/62 (79%) of the high-

Table 2:
Baseline characteristics of the participants.

	Geneva cohort 1 (n = 100)	Lugano cohort 1 (n = 100)
Men	59 (59%)	44 (44%)
Caucasian	93 (93%)	98 (98%)
Age, years	61.0 (17.3)	69.7 (16.9)
Age >60 years	57 (57%)	74 (74%)
Weight, kg	71.6 (16.9)	71.2 (25.7)
BMI, kg/m^2	25.3 (5)	25.9 (7.1)
Obesity	21 (21%)	17 (17%)
History of venous thromboembolism	2 (2%)	9 (9%)
Thrombophilia	1 (1%)	0 (0%)
Active malignancy	8 (8%)	23 (23%)
Diabetes	31 (31%)	33 (33%)
Previous cardiovascular disease	28 (28%)	53 (53%)
Recent myocardial infarction or stroke	13 (13%)	0 (0%)
Cirrhosis	7 (7%)	5 (5%)
Haemoglobin, g/l	132.5 (23.5)	123.5 (24.9)
Cardiorespiratory failure	21 (21%)	6 (6%)
Acute infection / inflammatory disease	26 (26%)	44 (44%)
Immobility	34 (34%)	10 (10%)
Platelets, 10^9/l	241.2 (111.4)	261.3 (104.7)
Cockroft-estimated clearance, ml/min	73.7 (38.9)	63.0 (45.1)
Simplified Geneva risk score (mean ± SD)	2.8 (1.9)	2.8 (1.8)
Simplified Geneva risk score ≥3	53 (53%)	62 (62%)
Reason for admission		
Cardiovascular disease	19 (19%)	8 (8%)
Cardiorespiratory failure	20 (20%)	5 (5%)
Infection / sepsis	17 (17%)	33 (33%)
Other (delirium, fall, pain, post-transplant, etc)	12 (12%)	17 (17%)
Renal disease	9 (9%)	11 (11%)
Diabeto-endocrinology	7 (7%)	5 (5%)
Hepatobiliary / gastroenterological disease	7 (7%)	4 (4%)
Syncope	5 (5%)	4 (4%)
Rheumatological disease	0 (0%)	6 (6%)
Cancer	4 (4%)	7 (7%)

Categorical variables in n (%) and continuous variables in mean ± SD.

Table 3:
Adequacy of thromboprophylaxis.

	Geneva cohort 1 (n = 100)	Lugano cohort 1 (n = 100)	p value
Adequate use of pharmacological or mechanical thromboprophylaxis at 24 h after admission	58/100 (58%)	61/100 (61%)	0.67
High-risk	n = 53	n = 62	
Adequate use of pharmacological or mechanical thromboprophylaxis at 24 h after admission (n and %)	33/53 (62.3%)	49/62 (79.0%)	0.048
Inadequate non-use of pharmacological or mechanical thromboprophylaxis at 24 h after admission (n and %)	20/53 (37.7%)	13/62 (21.0%)	
Low-risk	n = 47	n = 38	
Adequate non-use of pharmacological or mechanical thromboprophylaxis at 24 h after admission (n and %)	25/47 (53.2%)	12/38 (31.6%)	0.046
Inadequate use of pharmacological or mechanical thromboprophylaxis at 24 h after admission (n and %)	22/47 (46.8%)	26/38 (68.4%)	

risk patients in Geneva and Lugano, respectively, received at least 1 dose.

Among the 85 low-risk participants, adequate non-use of thromboprophylaxis was found in 53.3% and 31.6% in Geneva and Lugano, respectively (p = 0.046). All low-risk participants with inadequate thromboprophylaxis received pharmacological thromboprophylaxis within 24 hours after admission.

An inadequate thromboprophylaxis was found among all strata of the sGRS, without graphical evidence of more adequate thromboprophylaxis in those with very low scores (0–1) or very high scores (6–8) (figure 1).

90-day clinical outcomes

The 90-day cumulative probability of all-cause mortality was 6% (95% CI 3.5–10.3%) and similar at both study sites (table 4). All deaths occurred after hospital discharge and were adjudicated as not pulmonary embolism-related deaths. Among the 12 deaths, 5 were deemed of undetermined cause and 7 as a cause of death other than pulmonary embolism.

Risks of 90-day adjudicated venous thromboembolism were similar with the Kaplan-Meier estimate (table 4) and with the competing risk cumulative incidence function (CIF; overall 1.4%, Geneva 1.8%, Lugano 0.9%). Two symptomatic distal deep vein thromboses and one pulmonary embolism were diagnosed in 3 participants in Geneva and Lugano during the hospital stay. All 3 were categorised as high-risk according to the sGRS at admission, but 2 had an inadequate non-use of thromboprophylaxis. There were no venous thromboembolism events after hospital discharge.

Major bleeding occurred in 3 participants (CIF of 1.4% at 90 days for both sites, 2.0% in Geneva, 0.9% in Lugano). All were gastrointestinal bleeding, occurring at the time of hospital admission (n = 1) and after hospital discharge (n = 2). None was related to the administration of thromboprophylaxis.

Economic impact of inadequate thromboprophylaxis

Among low-risk patients, we estimated that 7484 and 6444 days of thromboprophylaxis would be inadequately administered among medical inpatients of the hospitals of Geneva and Lugano, respectively. Conversely, we estimated that 6804 and 3222 days of thromboprophylaxis would be inadequately not administered in Geneva and Lugano, respectively. Therefore, considering only drug costs, the net outcome would be a cost saving (2572 CHF and 12180 CHF in Geneva and Lugano, respectively) if the current inadequateness of thromboprophylaxis were resolved.

Figure 1: Adequacy of thromboprophylaxis (TPX) according to the simplified Geneva risk score at hospital admission. An adequate thromboprophylaxis is defined as non-use of thromboprophylaxis with a risk score between 0–2 and administered thromboprophylaxis with a risk score ≥3.

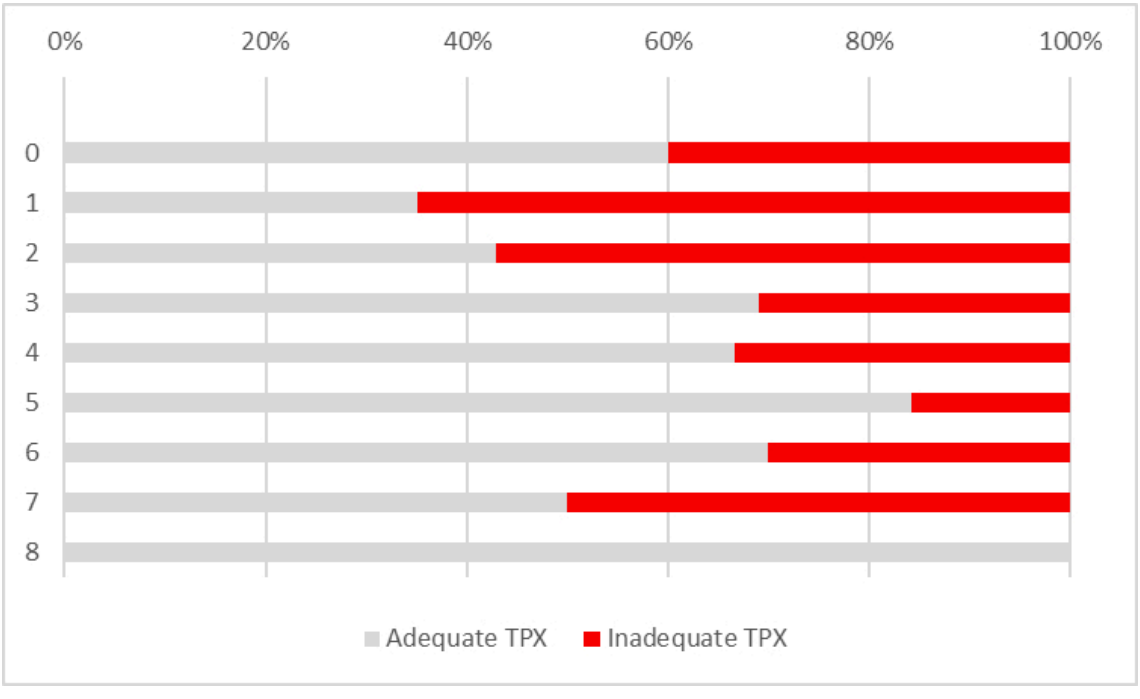

Table 4:
Observed 90-day risks of clinical outcomes and 95% confidence intervals.

	Overall (n = 200)	Geneva site (n = 100)	Lugano site (n = 100)	P value (log-rank)
All-cause mortality	6.0% (95% CI 3.5–10.3)	6.0% (95% CI 2.7–12.9)	6.0% (95% CI 2.7–12.9)	>0.99
Venous thromboembolism	1.5% (95% CI 0.5–4.6)	2.0% (95% CI 0.5–7.8)	1.0% (95% CI 0.1–6.9)	0.56
Major bleeding	1.5% (95% CI 0.5–4.7)	2.0% (95% CI 0.5–7.8)	1.1% (95% CI 0.1–7.2)	0.56
Heparin-induced thrombocytopenia	0%	0%	0%	NA

Associations with use of thromboprophylaxis

Among thrombotic risk factors of the Geneva risk score, only age above 60 years was statistically associated with the use of thromboprophylaxis within 24 h, regardless of its adequateness or inadequateness (adjusted odds ratio [OR] 1.9, 95% CI 1.0–3.6, p = 0.046, table 5). Most other risk factors had non-statistically significant positive associations with use of thromboprophylaxis, except cardiac/respiratory failure (OR 1.1) and reduced mobility (OR 0.9) which were not differentially distributed between patients with and without thromboprophylaxis.

Discussion

In our bi-centric prospective cohort study, 200 acutely ill adult medical inpatients were included in Geneva and Lugano. The overall adequacy of thromboprophylaxis was similarly low in both hospitals, at 58% and 61%, respectively. Thromboprophylaxis was more commonly used in the regional hospital of Lugano than the university hospital of Geneva, resulting in a higher adequacy among high-risk inpatients but a lower adequacy among low-risk patients. The risks of venous thromboembolism and bleeding at 3 months was low, <2%.

This disappointing portrait of the contemporary use of in-hospital medical thromboprophylaxis remains comparable to those previously reported. Twenty years ago, Cohen et al. observed an adequate thromboprophylaxis rate as low as 39.5% in medical inpatients [6] and subsequently several authors described an adequacy of 50–60% at most [7–10].In Switzerland, Chmelik et al. in 2002 found an inadequate thromboprophylaxis in 42% of high-risk patients and in almost 50% of low-risk patients [17]. Chopard et al. in 2005 presented the results of a longitudinal survey in 1372 patients at eight Swiss hospitals (both teaching and nonteaching), with inadequate prophylaxis in 44.9% and 41.3% of high- and low-risk patients, respectively, with no difference in adequacy between teaching and nonteaching hospitals [18]. Finally, in the ESTIMATE prospective study, thromboprophylaxis was inadequate in 38% of high-risk patients [16]. These results were comparable to those reported internationally [8]. Overall, our findings suggest that our hospitals have not improved the processes of prevention of venous thromboembolism despite various attempts using decision support systems [19] and highlight the critical need for improvement and evaluation of such support systems in this field. According to our rough economic assessment, improving the adequacy of thromboprophylaxis would save costs, even without considering the reduction in nursing time (injections) or indirect costs of venous thromboembolism and bleeding events linked to inadequate thromboprophylaxis.

When considering the administration of thromboprophylaxis at any time during the hospital stay, the proportion of high-risk patients with appropriate thromboprophylaxis was greater, between 79–85%. However, even though this analysis suggests that the assessment occurs later during the hospital stay, another explanation could be in-hospital complications or change in the clinical status leading to a greater perceived risk of venous thromboembolism during the stay. Furthermore, delaying the administration of thromboprophylaxis does not protect the initial hospital phase, when patients are most sick, and may perhaps result in venous thromboembolism events. Indeed, several authors and scientific societies recommend starting thromboprophylaxis as soon as possible after hospitalisation to minimise the risk of thromboembolic events [20–21], and special attention has been paid to the timing of the prescription following the SARS-CoV-2 pandemic [22–23].

The differences in adequacy of thromboprophylaxis between the two hospitals were probably due to the differences in the demographics of the patients. Likely, the older patients in Lugano are representative of a regional hospital, with both acutely ill medical and geriatric patients, with longer hospital stays. Our similar findings in both hospitals show that the subpar thromboprophylaxis administration is not restricted to specific hospital sizes or populations.

Rates of venous thromboembolism and bleeding were low, similar to other contemporary or less-recent cohorts [10,24–25] without systematic screening for venous thromboembolism. The cause of death remained undetermined after adjudication in almost half of deaths, and pulmonary embolism, while unlikely, remains possible in these events.

The strengths of this analysis include the prospective bi-centric design with a 90-day follow-up, the inclusion of patients towards the end of the hospital stay (so as not to influence thromboprophylaxis practices at the time of admission), the use of a validated risk assessment model (RAM) and the adjudication of clinical outcomes including deaths. For limitations, we acknowledge a possible selec-

Table 5:
Association of risk factors with use of thromboprophylaxis within 24 hours of admission.

	Thromboprophylaxis use if risk factor is present	Thromboprophylaxis use if risk factor is absent	Univariable odds ratio (95% CI)	Multivariable odds ratio (95% CI)
Personal history of venous thromboembolism	8/11 (72.7%)	122/189 (64.6%)	1.5 (0.4–5.7)	1.5 (0.4–6.1)
Known thrombophilia	1/1 (100%)	130/199 (65.3%)	–	–
Active cancer or myeloproliferative disorder	25/31 (80.7%)	105/169 (62.1%)	2.5 (1.0–6.5)	2.5 (0.9–6.6)
Cardiac and/or respiratory failure	18/27 (66.7%)	112/173 (64.7%)	1.1 (0.5–2.6)	1.1 (0.4–2.7)
Acute infection and/or rheumatological disorder	49/70 (70%)	81/130 (62.3%)	1.4 (0.8–2.6)	1.5 (0.8–3.0)
Reduced mobility	28/44 (63.6%)	102/156 (65.4%)	0.9 (0.5–1.9)	0.9 (0.4–2.0)
Age >60 years	93/131 (71.0%)	37/69 (53.6%)	2.1 (1.2–3.9)	1.9 (1.0–3.6)
Obesity	28/38 (73.7%)	102/162 (63.0%)	1.6 (0.7–3.6)	1.9 (0.9–4.4)
Recent stroke or myocardial infarction (<1m)	9/13 (69.2%)	121/187 (64.7%)	1.2 (0.4–4.1)	1.8 (0.5–6.7)

tion bias towards healthier patients, who for instance did not die in-hospital. Furthermore, in the economic analysis we made a strong assumption that the proportion of inadequacy of thromboprophylaxis, assessed at 24 h after admission, remained stable throughout the inpatient stay while also in our cohort we saw an improvement in inadequacy throughout the inpatient stay. Finally, we included an unweighted convenience sample, which may not be directly generalisable to Switzerland but provides estimates for both regional and tertiary hospitals, and we acknowledge that seasonal variations may influence the characteristics of patients and hospitalisations.

In conclusion, the adequacy of thromboprophylaxis among medical inpatients has not improved in recent years, despite better awareness and the availability of multiple RAMs [10,12,26–28]. This area is still in need of research and implementation efforts, in order to optimise the use of resources and minimise clinically important adverse events in medical inpatients.

Data sharing statement

Study data are available upon reasonable request to the steering committee at least 12 months after future publication of the clinical trial results.

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Author contributions: MB, PG, MR and MM designed the study. MB, PG and MM contributed to the acquisition of the data. MB analyzed the data. All authors interpreted the data, provided a critical assessment of the data and approved the final manuscript.

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Potential competing interests

All authors have completed and submitted the International Committee of Medical Journal Editors form for disclosure of potential conflicts of interest. No potential conflict of interest related to the content of this manuscript was disclosed.

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