Implementing guidelines for venous thromboembolism prophylaxis in a large Italian teaching hospital: lights and shadows

Luca Scaglione
Marina Piobbici
Eva Pagano
Luciana Ballini
Giacomo Tamponi
Giovannino Ciccone

Venous thromboembolism (VTE) remains a serious complication in hospitalized patients, in spite of several published guidelines (GL) on its prevention. The objective of this study (part of the TRiPSS-2 project) was to evaluate the impact of a locally adapted GL, supported by a multifaceted implementation strategy, in improving VTE prophylaxis in a large teaching hospital. A before and after controlled study was used to evaluate the impact of the recommendations on the appropriateness of prophylaxis. We evaluated the medical charts of two random samples, each of 250 patients, discharged in the first semester of the years 2000 and 2002. The hospital incidence of VTE (1996-2004) was also monitored, through the discharge summaries. Among high risk patients, appropriateness of prophylaxis increased both in medical (from 25% to 41.7%, p=0.0075) and in surgical patients (from 63.7% to 97.1%, p=0.0004). A parallel sharp increase (by 6-8 times) of consumption of elastic stockings was documented. In both medical and surgical patients the incidence of VTE decreased markedly and sustainedly in 2002-2004, with an adjusted odds ratio of 0.68 (95% confidence interval: 0.62-0.75). However, the use of lower than recommended doses of heparins and the increased use of prophylaxis in low risk patients represent unsolved problems. Implementing locally adapted GL may be highly effective in improving appropriateness of prophylaxis and in reducing the incidence of VTE; however a careful evaluation of changes is recommended in order to identify unsolved problems or undesired effects.

Key words: implementation, clinical practice guideline, venous thromboembolism prophylaxis

Haematologica 2005; 90:678-684

From the Emergency Department, S. Giovanni Battista Hospital, Torino, Italy (LS); Unit of Cancer Epidemiology, S. Giovanni Battista Hospital, CPO Piemonte and University of Turin, Italy (LS, MP, EP, GC); Centro per la Valutazione della Efficacia della Assistenza Sanitaria (CeVEAS), Modena, Italy (LB); Unit of Hematology, University of Turin, Italy (GT).

Correspondence:
Dr. Giovannino Ciccone,
Unit of Cancer Epidemiology,
S. Giovanni Battista Hospital,
via Santena 7, 10126, Torino, Italy.
E-mail: gianni.ciccone@cpo.it

In the last decade, a large number of evidence-based guidelines have been produced in order to improve the appropriateness of care in different settings. However, growing evidence over the limited impact of guidelines in promoting changes in many situations has stimulated new research to identify possible barriers that limit their effectiveness and to evaluate different strategies in implementing changes.[1,2]

Within this context, the Italian Ministry of Health in 1999 funded a multicenter project (TRiPSS-2), with the aim of evaluating the impact of evidence based guidelines, supported by tailored implementation strategies, in improving the quality of care for relevant clinical problems. The S. Giovanni Battista Hospital, a large (1500 beds) teaching hospital in Turin (Italy), identified the prophylaxis of venous thromboembolism (VTE) in hospitalized patients as one of the clinical problems to be addressed within the TRiPSS project.

Venous thromboembolism (in this study taken to include both deep vein thrombosis and pulmonary embolism) is a major cause of morbidity and mortality in hospitalized patients.[3,4] Prevention is the most effective strategy to reduce the burden of this disease, through a reduction in both fatal and non-fatal complications.[5] Moreover, appropriate prophylaxis has been clearly shown to be cost-effective, reducing treatment requirements and time spent in hospital stay.[6]

Several guidelines have been published on this topic;[7-10] nevertheless their application has not been uniform among different countries and medical specialties, and a general underuse of effective prophylaxis has been documented.[11-15] In this paper we report the results of a multifaceted strategy for the implementation of a clinical practice guidelines on VTE prophylaxis in our hospital, using both process and outcome measures.

Study design

The aim of this study was to evaluate the impact of a program to implement locally adapted guidelines through a

before and after controlled study on appropriateness of prophylaxis and on the occurrence of VTE complications.

Development of the guideline recommendations

A large multidisciplinary group was convened in September 2000, composed of medical members from the departments of emergency, surgery, internal medicine and from anesthesiology services of the S. Giovanni Battista Hospital in Turin (Italy). A specialist in coagulation disorders, a clinical epidemiologist and a pharmacist completed the working group. As several clinical practice guidelines were available, the working group decided to adapt an already published guideline; the documents retrieved were evaluated and assessed by two components of the group (GC and LS) using the AGREE instrument.[16] The document by the American College of Chest Physicians (ACCP)[7] was selected as the main source of the recommendations to be implemented. A review of the current published evidence was undertaken to cover further areas of interest selected by the working group: the use of low molecular weight heparin in the context of regional anesthesia, arthroscopic surgery, elective spinal surgery, and minor trauma. We used the following methods to incorporate the new evidence: (i) electronic databases (Medline and Cochrane Library) were searched and relevant papers were evaluated using standardized forms; (ii) the evidence was summarized and discussed; (iii) additional recommendations were formulated and graded according to the methods used in the ACCP document. The document was revised when the 2001 version of the ACCP guidelines was published[8] and submitted to three external experts and heads of department for further revision. Suggestions were discussed by the working group and the document revised; then the guidelines were adopted and disseminated (the guidelines are available at *www.cpo.it/lineeguida/LgProfilassiTVP.pdf*).

Implementation strategies

A combination of intervention strategies was selected to implement the recommendations of the guidelines. The guidelines were presented to all hospital physicians during a meeting held by a clinical opinion leader with recognized expertise in VTE prophylaxis (GT). A pocket version of the guideline containing easy to use tables for VTE prophylaxis for surgical and medical patients was distributed to all clinicians. A large multidisciplinary working group, with professionals from all specialties involved in the care of inpatients, was set up and deemed to be crucial to attain a significant change in practice. One of the main task of the working group was to identify possible barriers to the adoption of the guidelines by clinicians. A major issue that consistently emerged was the fear of bleeding caused by the use of low molecular weight heparin, in particular in the setting of regional anesthesia. This issue was addressed by providing physicians with clear recommendations on the timing of the prophylaxis to reduce the risk of bleeding and by the acquisition by the hospital pharmacy of alternative methods of prophylaxis (elastic stockings). Finally, a reminder specific for medical and surgical wards, indicating individual and procedure-related risk factors, with corresponding appropriate prophylaxis, was sent to all departments with the request to insert it into every clinical chart.

Adoption of the guideline

The clinical practice guidelines were officially adopted in September 2001, and after that were considered as the suggested clinical policy for VTE prophylaxis for clinicians caring for inpatients at the S. Giovanni Battista Hospital.

Evaluation of the impact of the guidelines

An increase in appropriate venous prophylaxis prescriptions was taken as the main outcome for the evaluation of the implementation strategy's impact.

A before/after design was used to estimate the increase in appropriateness of prophylaxis. The overall period was divided into two time intervals: one semester (baseline, from January to June 2000) before the beginning of the implementation and another semester representing the adoption phase (from January to June 2002). For each period, 250 patients were randomly sampled from the hospital discharge file; patients using antithrombotic drugs at entry or admitted for venous thromboembolic disease were excluded. The clinical records (both medical and nursing charts) were summarized by a trained nurse (M.P.), using a standardized form. The main information summarized included: (i) demographic data (age, sex, area of residence); (ii) speciality of the department; (iii) risk factors for VTE; (iv) medical diseases; (v) contraindications to the use of heparin or compression stockings; (vi) type of surgery and anesthesia; (vii) type of prophylaxis; (viii) objectively documented thrombotic (DVT/PE) and major bleeding events. Uncertain data were discussed by a panel including a clinical physician (LS) and an epidemiologist (GC). No evaluation of appropriateness of prophylaxis was made at this stage.

The evaluation of appropriateness of prophylaxis was made at the time of statistical analysis of data. Since elastic stockings were largely underreported in clinical and nursing records, the appropriateness of prophylaxis was based on heparin administration only. Each prescription was classified as appropriate, not appropriate or uncertain according to the recommendations (Table 1), after considering the patient's

Table 1. Risk levels and recommended VTE prophylaxis according to type of patient, clinical situation and VTE risk factors (*)

Type of patient and risk level	*Description*	*Recommended prophylaxis*
	Surgical Patients	
High/Very high	•Major surgery, age > 60 yrs old with/without VTE risk factors •Major surgery, age > 40 yrs old with VTE risk factors •Neurosurgery	LMWH (≥3400 U) or UH (5000 U/8 h) with/without ES
Moderate	•Minor surgery, age > 40 yrs old or with VTE risk factors •Major surgery, age < 60 yrs old, no VTE risk factors	LMWH (<3400 U) or UH (5000 U/12 h) or ES
Low	•Minor surgery, age < 40 yrs old, no VTE risk factors	Early deambulation
	Trauma patients	
Very high	•Hip fracture surgery	LMWH (≥3400 U)
Very high	•Major trauma	LMWH (≥3400 U) with/without ES
Moderate	•Minor trauma treated with cast/splint with VTE risk factors	LMWH (<3400 U) or UH (5000 U/12 h)
	Elective orthopedic surgey	
Very high	•Elective hip and knee replacement	LMWH (≥3400 U) with/without ES
Moderate	•Arthroscopic knee surgery and elective spinal surgery with VTE risk factors	LMWH (<3400 U) or UH (5000 U/12 h) or ES
	Medical patients	
High	•Acute diseases with/without VTE risk factors	LMWH or UH or ES
Low or Moderate	•Absence of VTE risk factors and/or acute disease	Early deambulation

(*)VTE risk factors: obesity, varicose veins, bedridden, pregnancy and puerperium, estrogens, inflammatory bowel disorders, nephrotic syndrome, active cancer, myeloproliferative disorders, previous VTE, paralysis, hypercoagulability, antiphospholipid syndrome, lupus anticoagulants.

risk of VTE and the presence of a contraindication (minor or major) to heparins. Two of the authors (GC, LS) evaluated the appropriateness of prophylaxis and uncertain data were discussed with a specialist in thromboembolic diseases (GT). Since the prophylactic heparin dose in medical patients was not standardized as clearly as in surgical patients, the drug dose was considered a criterion to judge the appropriate use of VTE prophylaxis only in surgical patients. Contraindications to heparins were classified as either minor (history of peptic ulcer, renal impairment, liver disease, etc.) or major (severe thrombocytopenia, coagulation disorders, active bleeding, etc.). The presence of massive leg edema, lower limb ischemia and skin diseases (ulcer, dermatitis, etc.) were considered contraindications to the use of elastic stockings.

Secondary outcomes were based on current administrative data: i) the consumption of elastic stockings and heparins in the two periods (January-June 2000 vs January-June 2002), taken from the pharmacy reports (limited to surgical departments); ii) the trend of incidence of VTE, including codes (in any position) for DVT (International Classification of Disease, Ninth Revision, Clinical Modifications – ICD-9-CM - diagnosis codes = 45111 - 4512, 45181, 4532) and PE (ICD9-CM = 41510 – 41519), between 1996 and 2004, taken from discharge summaries. These secondary outcomes were considered more informative for surgical patients as heparin consumption in medical patients may reflect indications other than prophylaxis; moreover, discharge data do not allow to medical patients admitted for VTE to be clearly distinguished from those with VTE complications.

Statistical analysis

Two samples of 250 patients were estimated to be necessary in order to detect with sufficient precision (α, two tails=0.05 and β=0.20) differences of at least 20% in prophylaxis prevalence between the two periods once analyses where stratified by type of patients (medical, surgical) and level of risk. The absolute difference in the proportion of patients receiving heparins between the two periods (2002-2000), and the 95% confidence interval of this difference, were calculated in each stratum.

The risk of VTE complications (considering both principal and secondary diagnoses) was estimated from the hospital discharge files between 1996 and 2004, adjusting the odds ratios (OR) with logistic regression models, stratified by type of DRG (medical, surgical), including age (in years), sex and the DRG's relative weights (log transformed).

Results

Five hundred clinical charts were evaluated, 22 were excluded (13 in the first and 9 in the second period), on the basis of the predefined criteria. The baseline clinical characteristics of included patients (Table 2) were slightly different, with the sample from the second period including more males, less patients from surgical wards, and a higher prevalence

Table 2. Characteristics of patients included in the samples in the two periods.

Characteristics	*January-June 2000 (N=237)*		*January-June 2002 (N=241)*		*p*
Age: mean (SD)	61.9	(18.8)	62.9	(17.3)	0.578
Gender (male): n (%)	107	(45.2)	130	(53.9)	0.055
Emergency admission: n (%)	114	(48.1)	124	(51.5)	0.464
Department of discharge: n (%)					
General medicine	71	(30.0)	98	(40.7)	0.106
Medical specialties	28	(11.8)	22	(9.1)	
General surgery	95	(40.1)	83	(34.4)	
Surgical specialties	43	(18.1)	38	(15.8)	
Patients undergoing surgery: n (%)	119	(50.2)	113	(46.9)	0.467
Length of stay: mean (median)	12.9	(10)	12.0	(9)	0.079
Mode of discharge: n (%)					
Alive (at home)	202	(85.2)	212	(88.0)	0.107
Transferred	17	(7.2)	21	(8.7)	
Died	18	(7.6)	8	(3.3)	
Risk of VTE: n (%)					
Low	39	(16.5)	47	(19.5)	0.664
Medium	122	(52.5)	122	(50.6)	
High-very high	76	(32.0)	72	(29.9)	
Contraindications to heparins: n (%)					
None	197	(83.1)	184	(76.4)	0.133
Minor	17	(7.2)	29	(12.0)	
Major	23	(9.7)	28	(11.6)	

of contraindications to heparins. After implementation of the guidelines, the use of unfractionated heparin (UH) dropped significantly from 9% of all heparin prescriptions to 1%. The variations in prophylaxis, according to the levels of VTE risk and contraindications to heparins, are shown in Table 3.

The use of VTE prophylaxis in medical patients increased significantly (+41.7%) from baseline to the post-implementation period for patients in the high risk category (from 25.0 to 66.7%); a smaller increase (+6.3%) was also observed in patients at low and medium risk.

Similarly, the use of VTE prophylaxis in surgical patients increased significantly both for medium (from 50.8% to 72.7%) and high/very high risk categories (from 63.9% to 97.1%). However, a large increase in prophylaxis was observed in low risk patients too (from 22.2% to 62.5%). In the high/very high risk category, surgeons' use of the recommended dose of heparin (> 3400 U for low molecular weight heparin or 5000 U every 8 hours for unfractioned heparin) rose from 8.3% in the control period to 20.0% in the intervention period (absolute difference= 11.7%; 95% C.I.= -5.1; 28.5). An increase of heparin use was also documented in patients with minor contraindications (from 29.4% to 55.2%): since most of these patients were at a medium or high risk of VTE, the appropriateness of prophylaxis was considered uncertain. The proportion of patients receiving heparin when major contraindications were present did not increase after implementation of the guidelines (30.4% vs 28.6%).

Our data show no differences between the two

Table 3. Differences in prevalence (%) of prophylaxis with heparins (H), according to patients' characteristics, between the two periods: before (January-June 2000) and after (January-June 2002) guideline implementation.

Characteristics of patients and risk level	*January-June 2000*			*January-June 2002*			*Difference (2002-2000)*		*Appropriateness of prophylaxis*
	N	*Tot*	*%*	*N*	*Tot*	*%*	*%*	*95% CI*	
Without contraindications to heparins									
Medical patients									
Low-medium risk	10	73	13.7	13	65	20.0	6.3	-6.2; 19.1	No/uncertain
High risk	5	20	25.0	14	21	66.7	41.7	11.1; 62.9	Yes
Surgical patients									
Low risk	2	9	22.2	5	8	62.5	40.3	-5.3; 68.9	No
Medium risk	30	59	50.8	40	55	72.7	21.9	4.0; 37.8	Yes
High/very high risk	23	36	63.9	34	35	97.1	33.3	15.3; 49.7	Yes
With contraindications to heparins									
Minor	5	17	29.4	16	29	55.2	25.8	-3.8; 48.8	Uncertain
Major	7	23	30.4	8	28	28.6	-1.9	-26.3; 21.8	No

Table 4. Trends of VTE incidence in medical and surgical patients, according to discharge summaries, at S. Giovanni Battista Hospital (Turin), from 1996 to 2004.

Type of patient and period	VTE cases	Discharged patients	OR (*)	95% CI
Medical patients				
1996-1997	662	53790	0.86	0.77-0.95
1998-1999	787	50527	1	-
2000-2001	618	42722	0.84	0.76-0.94
2002-2004	730	53595	0.67	0.61-0.74
Surgical patients				
1996-1997	159	44198	0.87	0.70-1.07
1998-1999	191	42753	1	-
2000-2001	178	38938	0.93	0.76-1.15
2002-2004	170	47387	0.63	0.51-0.78

**Odds ratios (OR) and 95% confidence intervals (95% CI) adjusted for age, gender and the DRG's relative weight (reference period: 1998-99).*

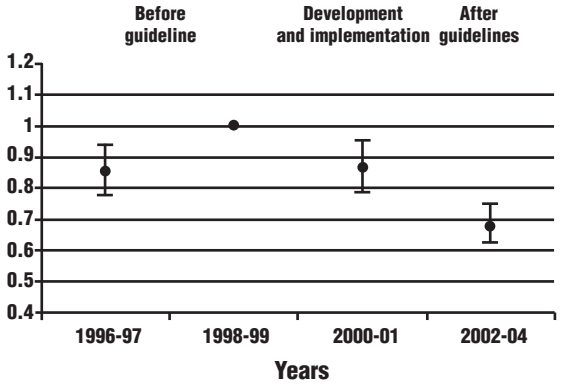

Figure 1. Adjusted (●) odds ratios (OR) and 95% confidence intervals (95% CI) for VTE complications in both surgical and medical patients (n=3495 out of 373893 discharge summaries) from S. Giovanni Battista Hospital (Turin), from 1996 to 2004. Logistic regression estimates, adjusted for age, sex, type of DRG (medical, surgical) and the DRG's relative weight (reference period=1998-99).

periods (2000 vs 2002) in the occurrence of VTE events (5/237 vs 5/241) and bleeding complications (7/237 vs 7/241). In the intervention period, at least 1 episode of PE (surgical patient, high risk, wrong heparin dose), and 2 bleeding episodes (surgical patients, 1 used heparin in the presence of contraindication, the other used heparin and acetyl-salicylic acid) were potentially preventable.

The use of elastic stockings in surgical wards, evaluated by the pharmacy consumer reports and adjusted for the number of hospitalized patients, showed a strong increase (+ 756%) in the post-implementation period. The consumption of low molecular weight heparins in surgical wards, extracted from the pharmacy reports and adjusted for the number of surgical patients times the length of hospital stay, significantly increased in the post-implementation period; the consumption of high doses of LMWH accounted for a relative increase of 93.2%.

Using the discharge data of the S. Giovanni Battista Hospital, we estimated the risk of VTE occurrence among 199481 medical patients and 174429 surgical patients, discharged from 1996 to 2004 (Table 4). In surgical patients VTE complications (n=700 cases in the whole period) increased between 1996 and 1999; from this time the incidence showed a reverse and sustained trend, with a minimum in the post implementation period (OR=0.63; 95% CI=0.51-0.78). In medical patients, the trend of VTE diagnoses and the reduction in the post-implementation period, were very similar. Overall, the burden of VTE complications among inpatients reduced 30-35% after guideline implementation (OR=0.68, 95% CI=0.62-0.75) (Figure 1).

Discussion

Despite the publication of several clinical guidelines in both North America and Europe,[7-10] recommending routine prophylaxis according to the patient's thrombotic risk, VTE prophylaxis was still largely underused in our hospital. In the first six months of 2000, 36% of high/very high risk surgical patients did not receive VTE prophylaxis, and most of those who received the prophylaxis were treated with lower than recommended doses of heparins.

There are a number of studies documenting a general underuse of effective prophylaxis, in surgical and medical inpatients.[11-15] Arnold *et al.*[11] found that in 44 cases of potentially preventable cases of VTE, occurring in hospitalized patients, the main reason for inadequacy of prophylaxis was omission of prophylaxis in almost 50% of cases. In another study, prophylactic measures were implemented for only 38% of patients undergoing abdominothoracic surgery, and these measures were adequate in only 66% of patients.[12] A study carried out in Italy reports prescription of VTE prophylaxis in 46% of medical inpatients at risk of thromboembolism and without contraindications to treatment.[14] In spite of these findings, few research programs aimed at improving VTE prophylaxis have been carried out.[17-19] Anderson *et al.*[17] found that the use of a formal CME program significantly increased the use of VTE prophylaxis. In another study a computerized reminder turned out to be a highly effective method for increasing the rate of VTE prophylaxis in surgical patients.[18] Durieux *et al.* showed that the implementation of a clinical guideline for VTE prophylaxis through a computer-based clinical decision support, integrated into the hospital information sys-

tem, changed physician behavior and improved compliance with the guidelines.[19] Another recent study[20] found that the use of computerized reminder systems, in surgical patients with a high baseline rate of prophylaxis, increased the rate of VTE prophylaxis without decreasing the rate of symptomatic DVT and PE.

In our study we observed a substantial improvement in VTE prophylaxis in medical and surgical wards, following the implementation of locally adapted clinical guidelines. In surgical wards, almost all patients at high/very high thrombotic risk and more than 70% of those at moderate thrombotic risk received VTE prophylaxis in the post-implementation period. In the moderate risk group the percentage of patients undergoing prophylaxis is probably higher than shown, due to underreporting of elastic stocking use in medical and nursing charts. The 7 to 8-fold increase in the consumption of elastic stockings, registered by the pharmacy records, suggests that they were given to patients, alone or in conjunction with heparins, but not recorded in clinical charts.

Finally, we observed a progressive decrease in the incidence of VTE episodes in both medical and surgical patients, as indicated by discharge data, starting from the second semester of 2000. These data should be interpreted with caution, as we cannot exclude that the observed reduction of VTE is due to a time trend variation in coding of complications or to the general hospital policy of earlier patient discharge. However, there are elements that support the evidence for a true reduction of VTE complications, particularly in surgical patients: (i) the quality of coding for comorbidity or complications reported in the discharge summaries has increased during the whole period: in surgical patients the mean number of codes per patient rose from 1.67 in 1996 to 2.77 in 2004; (ii) the incidence of other complications in surgical patients, such as cardiac arrest or acute myocardial infarction, showed an increasing trend during the same period, from 4.5 (*1000 patients) in 1996 to 11.7 in 2004; (iii) the possibility of an increasing proportion of early discharges of surgical patients is not supported by the data, since the shortening of the mean length of hospital stay - from 12.0 (1996) to 11.0 (2004) - is entirely due to a reduction in the pre-operative days (from 4.9 to 3.7, respectively); (iv) surgical patients with complications after discharge are usually readmitted to the same hospital responsible for the operative procedure and this policy did not change during the study period; we did not observe an increase of medical cases admitted for VTE; (v) finally, the size of the reduction of VTE estimated from discharge summaries (around 30-35%) is lower, though quite reasonable, when compared to a 50-60% reduction reported in randomized, controlled trials in which optimal prophylaxis with heparins was compared to placebo in experimental conditions.

Even if VTE prophylaxis is now used more widely in our hospital, 80% of high/very high risk surgical patients still receive a lower than correct dose of heparin. The fear of post-operative bleeding is probably the cause of this persistent underuse and specific interventions to overcome this obstacle have been planned. Another problem emerging in the post-implementation period is the use of pharmacological prophylaxis in patients at low thrombotic risk who do not need prophylaxis at all or in patients with contraindications and an uncertain risk/benefit ratio. Although the overuse of heparin is estimated on a small number of patients (and it is not statistically significant), we still think it should be considered as a potential side effect of the guidelines, requiring further intervention, including result feedback to the hospital's physicians.

In conclusion, we believe this project represents a positive example of quality improvement, obtained through a tailored implementation strategy of locally adapted, evidence-based guidelines, with valuable achievements in both process and outcome results. However, some of the shortcomings identified underline that quality improvement projects are not risk-free initiatives. Implementing the best evidence should be strictly monitored to steer the desired changes in practice.[21]

LS and GC have a responsibility for the whole work, including conception, design, conduction of the study, analysis and interpretation of data and drafting and revising the manuscript. LS, LB obtained funding; all authors have contributed to study concept and design; MP, LS, GC were involved in acquisition of the data; LS, GC, EP were responsible of data analysis; LS, GC, LB, GT interpreted the results and drafted the manuscript; all authors were involved in the discussion and revision of the manuscript and gave their permission for the final version submitted for publication.The authors declare that they have no potential conflict of interest.

We acknowledge the other components of the guideline working group: Annoscia S, Antro C, Arione R, Baù G, Berardino M, Bo S, Bonino L, Bronda M, Campra D, Capello T, Clara ME, Ferfoglia G, Gallo G, Gianferrari P, Perani R, Stecca S, Valpreda S. Special thanks to Alessandro Liberati and Angelo Penna, National and Regional TRiPSS coordinators, respectively.

The national project was funded by the National Ministry of Health; the local project was partly funded by a Regional Health Service grant. The work of EP was supported by the Compagnia San Paolo.

Manuscript received November 13, 2004. Accepted April 5, 2005.

References

1. Bero LA, Grilli R, Grimshaw JM, Harvey E, Oxman AD, Thomson MA. Closing the gap between research and practice: an overview of systematic reviews and interventions to promote the implementation of research findings. The Cochrane Effective Practice and Organization of Care Review Group. Br Med J 1998;317:465-8
2. Grimshaw JM, Thomas RE, MacLennan G, Fraser C, Ramsay CR, Vale L, et al. Effectiveness and efficiency of guideline dissemination and implementation strategies. Health Technol Assess 2004;8:1-72
3. Dismuke SE, Wagner EH. Pulmonary embolism as a cause of death. The changing mortality in hospitalized patients. JAMA 1986;255:2039-42.
4. Goldhaber SZ, Visani L, Rosa M. Acute pulmonary embolism: clinical outcomes in the International Cooperative Pulmonary Embolism Registry (ICOPER). Lancet 1999; 353: 1386-9.
5. Collins R, Scrimgeour A, Yusuf S, Peto R. Reduction in fatal pulmonary embolism and venous thrombosis by perioperative administration of subcutaneous heparin. Overview of results of randomized trials in general, orthopedic, and urologic surgery. N Engl J Med 1988;318:1162-73.
6. Oster G, Truden RL, Colditz GA. Cost-effective analysis of prophylaxis against deep-vein thrombosis in major orthopedic surgery. JAMA 1987; 257: 203-5.
7. Clagett GP, Anderson FA, Geerts W, Heit JA, Knudson M, Lieberman JR, et al. Prevention of VTE. Chest 1998; 114 Suppl 5:531S-60S.
8. Geerts WH, Heit JA, Clagett GP, Pineo GF, Colwell CW, Anderson FA Jr, et al. Prevention of venous thromboembolism. Chest 2001;119 Suppl 1:132S-75S.
9. Nicolaides AN, Arcelus J, Belcaro G, Bergqvist D, Borris LC, Buller HR, et al. Prevention of venous thromboembolism: European Consensus statement. Int Angiol 1992;11:151-9.
10. Thromboembolic Risk Factors (THRIFT) Consensus Group. Risk of and prophylaxis for venous thromboembolism in hospital patients. Br Med J 1992;305:567-74.
11. Arnold DM, Kahn SR, Shrier I. Missed opportunities for prevention of venous thromboembolism. An evaluation of the use of thromboprophylaxis guidelines. Chest 2001;120:1964-71.
12. Bratzler DW, Raskob GE, Murray CK, Bumpus LJ, Piatt DS. Underuse of venous thromboembolism prophylaxis for general surgery patients: physician practices in the community hospital setting. Arch Intern Med 1998; 158: 1909-12.
13. Lepaux DJ, Charpentier C, Pertek JP, Pinelli C, Delagoutte JP, Delorme N, et al. Assessment of deep vein thrombosis prophylaxis in surgical patients: a study conducted at Nancy University Hospital, France. Eur J Clin Pharmacol 1998;54:671-6.
14. Ageno W, Squizzato A, Ambrosini F, Dentali F, Marchesi C, Mera V, et al. Thrombosis prophylaxis in medical patients: a retrospective review of clinical practice patterns. Haematologica 2002;87:746-50.
15. Ahmad HA, Geissler A, MacLellan DG. Deep vein thrombosis prophylaxis: are guidelines being followed? ANZ J Surg 2002;72:331-4.
16. The AGREE Collaboration. Development and validation of an international appraisal instrument for assessing the quality of clinical practice guidelines: the AGREE project. Qual Saf Health Care 2003;12:18–23.
17. Anderson FA Jr, Wheeler HB, Goldberg RJ, Hosmer DW, Forcier A, Patwardhan NA. Changing clinical practice. Prospective study of the impact of continuing medical education and quality assurance programs on use of prophylaxis for venous thromboembolism. Arch Intern Med 1994;154: 669-77.
18. Patterson R. A computerized reminder for prophylaxis of deep vein thrombosis in surgical patients. Proc AMIA Symp 1998;573-5.
19. Durieux P, Nizard R, Ravaud P, Mounier N, Lepage E. A clinical decision support system for prevention of venous thromboembolism: effect on physician behavior. JAMA 2000; 283: 2816-21.
20. Mosen D, Elliott CG, Egger MJ, Mundorff M, Hopkins J, Patterson R, et al. The effect of a computerized reminder system on the prevention of postoperative venous thromboembolism. Chest 2004;125:1635-41.
21. Lo B, Groman M. Oversight of quality improvement: focusing on benefits and risks. Arch Intern Med 2003; 163:1481-6.