# An electronic tool for venous thromboembolism prevention in medical and surgical patients

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Background and Objectives. Venous thromboembolism (VTE) is a complex disorder influenced by numerous risk factors, and occurs frequently in at-risk hospitalized patients. Because appropriate prevention with thromboprophylaxis is underused, we wanted to create an electronic tool to provide a simple risk assessment and suggest appropriate prophylaxis.

Design and Methods. To develop the risk matrix, iterative rating of odds ratios was performed for 60 predisposing VTE risk factors, using analytical methods that account for multiple risk factors in a single patient and their non-independence. For exposing risk factors, a single score was assigned to each set of factors, both medical (25 items) and surgical conditions (144 items). A CART regression model was used to integrate the risk scales into a 4-level measure of overall risk. The validity of the level of risk and the appropriateness of 11 different prophylactic approaches was assessed using the RAND/UCLA appropriateness method and validated by expert opinion ratings (n=1998) on sample case scenarios (n=108).

Results. Correlation between the level of risk calculated by the risk matrix and that offered by expert opinion for individual surgical and medical clinical cases was high (65% and 70%, respectively). The matrix over-estimated the level of risk, compared with that offered by expert opinion, in 28% and 20% of surgical and medical cases, respectively, but the appropriate prophylaxis suggested was no different. Between-expert agreement on the appropriateness of the prophylaxis recommendations was high (90-94% of indications).

Interpretation and Conclusions. This computer-based electronic tool for individualized assessment of venous thromboembolic risk successfully identified both the perceived risk of thrombosis and the appropriate prophylactic approach for medical and surgical patients.

Key words: venous thromboembolism, risk matrix, prophylaxis, RAND/UCLA appropriateness method.

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The appropriate provision of prophylaxis for venous thromboembolism (VTE) (deep-vein thrombosis (DVT) and pulmonary embolism (PE)), relies on risk assessment as part of the daily clinical decision-making and is dependent on the clinicians personal knowledge of thrombosis risk. Although several evidence-based guidelines, which generally stratify patients into three (low/moderate/high) or four (low/moderate/high/very high) risk groups,[1-3] are available to assist, they do not provide individualized risk assessment. Risk assessment models have been reported for both medical[4-8] and surgical patients,[6,9-12] but assigning patient groups to risk categories is not always straightforward. Given the low level of thromboprophylaxis provision that has been reported,[13] particularly in acutely ill medical patients, there is a clear need for simpler models that are based on more formal risk analysis and that provide individual risk assessment coupled with appropriate suggestions for prophylactic therapies. Adequate use of thromboprophylaxis remains elusive for a number of reasons, including uncertainty concerning both risk stratification of individual patients and appropriate prophylaxis for particular levels of VTE risk.[13-17] Recently, the value of using a computer-based alert to highlight at-risk patients, through calculation of a simple risk score based on eight principal risk factors, was validated and shown to improve patients' outcome.[18] In a complementary approach, we reasoned that an electronic risk matrix, based on a complex assessment of a large number of predisposing and exposing risks, but providing a simple recommendation on the need for thromboprophylaxis, and validated using case scenarios interpreted by an expert, multidisciplinary panel would be of value and potentially improve clinical decisions on appropriate thromboprophylaxis and, ultimately, clinical outcome in medical and surgical patients.

## Design and Methods

The methodological approach adopted for development of the Risk Matrix was based on the *RAND/UCLA appropriateness method*, widely accepted as a tool to assess *non-measurable* practice beyond evidence based guidelines.[19,20] This method utilizes a comprehensive review of the medical literature to assess efficacy and effectiveness in combination with structured, quantitative techniques for incorporating the judgment of expert clinicians to produce appropriateness assessments for clinical conditions. Briefly, an expert multidisciplinary panel of clinicians rates a comprehensive series of clinical relevant cases on a harms–benefit scale. Between ratings, panelists meet to receive feedback on each others' responses and discuss their judgments. After a second rating, each panelist has equal weight in determining an explicit appropriateness rating for clinical scenarios. An appropriate treatment is one in which the expected health benefit exceeds the expected negative consequences by a sufficiently wide margin that the treatment is worth giving, exclusive of cost.[19,20]

The methodological approach we used is summarized in Figure 1. First, a taskforce group from various countries was established in 2002 and, as previously described,[21] the group conducted a comprehensive literature review of risk factors for venous thromboembolism to assess the level of evidence for each risk factor at that time and to provide some quantification of individual risk. The risk factors were then categorized as predisposing or exposing risks, listed in Tables 1-4. This analysis was completed in 2002.

Two types of predisposing risk groups, termed general and inherent, were considered separately (Tables 1 and 2). General risk factors included risks related to patients' general characteristics (e.g. age), recent clinical conditions (e.g. stroke), and/or any chronic clinical conditions (e.g. cancer). Inherent major risk factors included any personal and/or family history of thromboembolism, a coagulation factor abnormality, or a certain genetic marker. In general, inherent risk factors do not change while general risk factors may evolve with time. Exposing risks were separately enumerated for medical conditions and surgical interventions, the latter involving general surgery, gynecological surgery and urological surgery, corresponding to surgical situations for which definitive studies are inconclusive or lacking (Tables 3 and 4). Pregnancy was not included.

Two international panels of medical (n=9) and surgical (n=12) experts provided both quantitative and qualitative expressions of opinion on the risk factors and appropriateness of different prophylactic therapies. Predisposing risks were evaluated using an odds-ratio (OR) measure. Panel members were asked to assign an OR representing the risk of a particular patient characteristic or clinical situation, compared with a *standard healthy patient*. Exposing risk was defined as the added risk resulting from a surgical intervention or medical condition and was evaluated using a 5-point Likert-type scale anchored by standard conditions from 1 (insignificant risk) to 5 (high risk) (*Online Appendix Table 1*). The panelists reviewed a series of clinical scenarios and were asked to rate the appropriateness of prophylactic therapies for each scenario. For each scenario, the panel assessed the relative degree of benefit-to-harm for individual patients on a scale from 1 to 9 (*See Online Appendix for full description*).

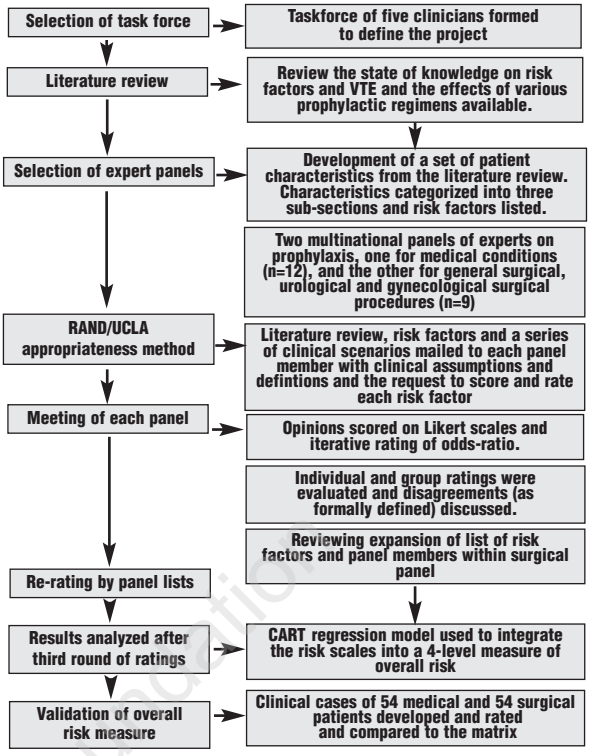


**Figure 1.** Steps involved in the development of the risk assessment model. CART: classification and regression tree, VTE: venous thromboembolism.

Following an initial round of ratings, each panel attended a meeting, led by a moderator experienced in the RAND/UCLA appropriateness method (JPK), in which areas of confusion and disagreement were discussed. During the meeting, the medical and surgical items were revised, and expanded into a final list of items, documented in Table 3 (medical items, n=25) and Table 4 (surgical items, n=14 in three groups). Following the meeting an increased number of surgeons rated the clinical cases, due to the complexity of the panelists' rating conditions, outside their own subspeciality. Overall, the surgical groups rated 144 items for general surgery (42 items), gynecological surgery (50 items) and urological surgery (52 items) (Table 4). Each panel then rated the appropriateness of 11 prophylactic therapies (Table 5) using the RAND/UCLA appropriateness method.[20,22] Each prophylaxis was assessed to determine whether or not the panel members disagreed about its appropriateness (*See Online Appendix*).

In order to construct the overall risk matrix, predisposing and exposing risks were combined[23] (*Online Appendix Table 2*) to produce a four-level measure of risk – low, medium, high, and very high. Since multi-

**Table 1.** Aggregate odds ratios for general predisposing risk factors.*

| Parameter | All Panelists Mean† | SD |
|---|---|---|
| **Patient's general characteristics** | | |
| Normal female younger than 40 | 1.00 | |
| Gender - Male (versus female) | 1.11 | 1.18 |
| Age | | |
| 40-59 yr (compared to <40 yr) | 1.67 | 1.28 |
| 60-74 yr (compared to <40 yr) | 2.91 | 1.47 |
| over 75 yr (compared to <40 yr) | 4.11 | 1.48 |
| Blood group / Non-O group | 1.63 | 1.43 |
| Obesity / Body mass index > 30 kg/m$^2$ | 2.17 | 1.38 |
| Smoking / >15 cigarettes per day | 1.57 | 1.59 |
| Oral contraceptive pill combined estrogen/progesterone treatment | 2.95 | 1.29 |
| Hormone replacement therapy combined estrogen/progesterone treatment | 2.96 | 1.26 |
| Specific drug use - with protective effects such as statins, aspirin | 0.70 | 1.52 |
| **Recent clinical conditions (less than 3 months)** | | |
| Recent major surgery (<=3 months) | | |
| With complications | 5.10 | 1.63 |
| Without complications | 2.95 | 1.72 |
| Recent myocardial infarction - within last 3 months | 3.71 | 1.54 |
| Recent Ischemic stroke within last 3 months, disregarding paralysis | 3.69 | 1.66 |
| Prolonged travel-more than 6 hours | 1.60 | 1.47 |
| Dehydration-severe dehydration as defined by 10% weight loss | 2.05 | 1.42 |
| Increased hematocrit - >45% for women; >50% for men | 2.03 | 1.39 |
| Hyperviscosity ‡ - Increased blood viscosity | 2.39 | 1.33 |
| **Chronic clinical conditions** | | |
| Malignancy | | |
| Local stage (compared to no malignancy) | 2.61 | 1.61 |
| Locally advanced stage (compared to no malignancy) | 3.69 | 1.65 |
| Metastatic cancer (compared to no malignancy) | 5.48 | 1.48 |
| Additional risk if specific type is pancreatic, gastrointestinal, ovarian, prostatic, pulmonary, malignant glioma (compared to no malignancy) | 6.03 | 1.74 |
| Additional risk with radiotherapy (compared to no malignancy) | 5.05 | 1.85 |
| Additional risk if treated with chemotherapy but not hormonal therapy (compared to no malignancy) | 5.60 | 1.61 |
| Additional risk if treated with hormonal therapy (compared to no malignancy) | 5.88 | 1.65 |
| Heart failure/Cardiac disease | | |
| NYHA I or II | 1.86 | 1.53 |
| NYHA III or IV | 5.08 | 1.73 |
| Chronic respiratory disease - chronic obstructive pulmonary disease or emphysema | 1.74 | 1.53 |
| Nephrotic syndrome - syndrome of proteinuria, hypoalbuminemia of <20g/L | 1.86 | 1.52 |
| Acute severe illness | | |
| With hospitalization | 4.85 | 1.58 |
| Systemic sepsis (septicemia) | 6.69 | 1.59 |
| Immobilization | | |
| Confinement to bed or (wheel) chair > 3 days (without bathroom privileges) | 3.89 | 1.75 |
| Confinement to bed or (wheel) chair > 3 days (with bathroom privileges) | 3.29 | 1.77 |
| Lower limb paralysis (hemiplegia/paraplegia/neurological disease) | 5.70 | 1.63 |
| Inflammatory bowel disease - Crohn's disease and ulcerative colitis | 2.87 | 1.43 |
| Venous insufficiency | | |
| Varicose veins, prominence of superficial veins on standing | 2.20 | 1.42 |
| Lower limb swelling, discomfort | 2.24 | 1.46 |
| Ulceration | 3.01 | 1.35 |
| Lower limb arterial disease – Intermittent claudication | 1.41 | 1.37 |
| Diabetes – Including both type I and II, of any etiology | 1.32 | 1.31 |

*Aggregate results for the surgical (n = 12) and medical (n= 9) panels. Predisposing risks are those conditions, independent of the surgical procedure or medical condition for which a patient is admitted to hospital. † Mean = geometric mean of the odds ratios which is the average product (that is the n* root of the product of the n items), is the more mathematically correct measure of central tendency for odds-ratios because combining multiple odds-ratios is done by multiplication rather than addition. ‡ Normal relative serum viscosity ranges from 1.4-1.8 units; symptoms usually are not seen at viscosities of less than 4 units, and the hyperviscosity syndrome typically requires a viscosity greater than 4 units:; ASA: acetyl salicylic acid, BMI: body mass index, NYHA: New York Heart Association.*

ple predisposing risks may exist within an individual, analytical methods were used to compensate for the non-independence of predisposing risk factors and their positive correlation (*see Online Appendix*).[20,23] The

**Table 2.** Aggregate odds ratios for inherent major predisposing risk factors.*

| Parameter | All panelists Mean† | SD |
|---|---|---|
| Antiphospholipid syndrome | | |
| Primary, without another autoimmune disease e.g. SLE | 7.17 | 1.50 |
| Secondary with SLE with LA (with aCL) | 4.95 | 1.61 |
| Secondary with SLE without LA (with aCL) | 3.09 | 1.78 |
| Secondary, with other autoimmune disease or due to drugs | 3.11 | 1.76 |
| Myeloproliferative disorders-including polycythemia vera, essential thrombocytosis | 3.10 | 1.33 |
| Hyperhomocysteinemia–fasting homocysteine plasma levels above 40 μmol/L in women; 18 μmol/L in men | 2.36 | 1.42 |
| Antithrombin deficiency–Heterozygotic | 7.89 | 2.08 |
| Protein C deficiency–Heterozygotic | 4.65 | 1.67 |
| Protein S deficiency–Heterozygotic | 3.98 | 1.59 |
| Factor V Leiden mutation–Heterozygotic | 4.08 | 1.67 |
| Factor II mutation–Heterozygotic | 2.97 | 1.47 |
| Factor V or II mutation–Homozygotic | 8.82 | 2.78 |
| More than one factor (of the previous 6) | 11.18 | 2.17 |
| Previous history of venous thromboembolism | | |
| Proximal saphenous/superficial vein thrombosis | 3.33 | 1.33 |
| Proximal with or without distal deep-vein thrombosis | 6.22 | 1.45 |
| Distal deep vein thrombosis only | 4.07 | 1.47 |
| Pulmonary embolism | 8.65 | 1.45 |
| Additional risk caused by clinical idiopathic VTE event‡ | 6.86 | 1.87 |
| Family history of venous thromboembolism-in first degree relatives, parents or siblings | 3.85 | 1.45 |

*Aggregate results for the surgical (n = 12) and medical (n= 9) panels; †mean = geometric mean of the odds ratios; ‡compared with a specific precipitating cause for VTE event; aCL: anticardiolipin antibodies, LA: lupus anticoagulant; SD: standard deviation, SLE: systemic lupus erythematosus.*

Risk Matrix was then encapsulated into a single executable computer application. To further test the validity of the risk matrix, a series of medical and surgical cases were developed which systematically varied the degree of general predisposing, inherent major predisposing and exposing risk, so that representative samples of all four levels of overall risk would be present. A total of 54 medical cases (864 ratings) and 54 general surgery cases (1134 ratings) were validated.

## Results

### *Predisposing and exposing risk factors*

The aggregate ratings for general and inherent predisposing risks are shown in Tables 1 and 2. The highest rated predisposing risk factors by the panels with their corresponding OR (compared with the basecase) were: more than one thrombophilia factor (11.2), previous history of pulmonary embolism (8.6), history of proximal deep vein thrombosis (6.2), lower limb paralysis (5.7), metastatic malignancy (5.5), and recent major surgery with complications (5.1). For certain conditions, such as malignancy, a range of ratings was seen depending on the disease and the treatment given. For example, the OR for malignancies treated with hormonal therapy (5.9) was twice that

**Table 3.** Aggregate ratings for exposing risk factors in medical patients.*

| *Medical Condition* | *Mean†* | *SD* |
|---|---|---|
| Acute ischemic stroke with paralysis (standard) | 5.00 | – |
| Acute spinal cord injury | 4.78 | 0.44 |
| Other general medical patient in ICU with mechanical ventilation | 4.33 | 0.71 |
| Active malignant disease requiring treatment | 4.22 | 0.83 |
| Septicemia | 3.89 | 0.78 |
| Acute myocardial infarction | 3.33 | 0.50 |
| Other general medical patient in ICU without mechanical ventilation | 3.33 | 0.50 |
| Pulmonary edema | 3.33 | 0.80 |
| Acute severe infections | 3.22 | 1.09 |
| Acute exacerbation of chronic obstructive pulmonary disease | 3.01 | 1.15 |
| Heart failure, NYHA III or IV (standard) | 3.00 | – |
| Acute inflammatory bowel disease | 2.89 | 0.33 |
| Ischemic stroke without paralysis | 2.89 | 1.05 |
| Patient with shock | 2.78 | 0.67 |
| Acute exacerbation of chronic renal failure | 2.67 | 0.75 |
| Acute exacerbation of lung disease other than chronic obstructive pulmonary disease | 2.63 | 1.17 |
| Other general medical patient with acute severe disease | 2.56 | 0.73 |
| Bone marrow transplantation | 2.44 | 0.53 |
| Acute renal failure without hemodialysis | 2.42 | 0.72 |
| Acute exacerbation of rheumatological disorders | 2.22 | 0.67 |
| Infective endocarditis | 2.22 | 0.83 |
| Pneumonia | 2.19 | 1.28 |
| Decompensated liver cirrhosis | 1.67 | 0.71 |
| Psychiatric disorder | 1.67 | 0.71 |
| Acute asthma (standard) | 1.00 | – |

**Results for the medical (n= 9) panel. Exposing risks comprise those occurring while a patient is hospitalized for a certain medical condition or surgical procedure. †mean: arithmetic mean of the 5-point Likert-type scale; ICU: intensive care unit, NYHA: New York Heart Association; SD: standard deviation.*

**Table 4.** Aggregate ratings for highest exposing risk factors in surgical patients.

| *Surgical Procedure* | *Mean** | *SD* |
|---|---|---|
| General surgery† | | |
| Pancreatic surgery for cancerous disease | 4.25 | 0.68 |
| Hepatectomy for cancerous disease | 4.19 | 0.83 |
| Colorectal surgery for cancerous disease | 4.13 | 0.62 |
| Hepatic resection for metastases | 4.00 | 0.85 |
| Gastric surgery for cancerous disease | 3.88 | 0.72 |
| Esophageal surgery for cancerous disease | 3.81 | 0.91 |
| Small intestine surgery for cancerous disease | 3.56 | 0.73 |
| Open cholecystectomy | 2.19 | 0.75 |
| Urological surgery‡ | | |
| Radical prostatectomy for cancer | 4.31 | 0.63 |
| Nephrectomy enlarged for cancer | 4.15 | 0.69 |
| Gynecological surgery§ | | |
| Oophorectomy for cancerous disease, abdominal | 4.00 | 0.45 |
| Hysterectomy without oophorectomy for cancerous disease, vaginal | 3.82 | 0.60 |
| Hysterectomy with oophorectomy for cancerous disease, vaginal | 3.55 | 0.82 |
| Mastectomy with axillary node dissection for cancerous disease and reconstitution | 3.45 | 0.93 |

**mean: arithmetic mean of the 5-point Likert-type scale. Exposing risks are those conditions occurring while a patient is hospitalized for a certain medical condition or surgical procedure. †Aggregate results for the general surgeons (n=16). Only the nine highest ratings out of 42 items are shown here. ‡Aggregate results for the urological surgeons (n = 13). Only the two highest ratings out of 50 items are shown here. § Aggregate results for the gynecological surgeons (=11). Only the five highest ratings out of 52 items are shown here. SD: standard deviation.*

for locally treated malignancies (2.6). Different ratings were given depending on whether the tumor was metastatic (5.5), treated with radiotherapy (5.0) or chemotherapy (5.6). Similarly, the OR for different medical conditions varied according to the severity of disease. The risk for congestive heart failure of stage III or IV according to the New York Heart Association classification (5.1) was twice that for stage I or II (1.9). Aggregate ratings for the exposing risks are shown in Tables 4 and 5. Medical conditions associated with the highest exposing risk (out of 5) were: acute spinal cord injury (4.8), ventilated patients in intensive care (4.3), active malignancy (4.2), and septicemia (3.9). For surgical exposing risks, the highest ratings were generally assigned to those procedures that were extensive in nature and involved patients suffering from malignant disease. For example, pancreatic surgery for cancerous disease had the highest rating (4.25 out of 5) for general surgery, while radical prostatectomy for cancer (4.3) and abdominal oophorectomy for cancerous disease (4.0) were the two highest rated conditions in the other surgical groups.

### Validation of the matrix with patient cases

For the medical cases, overall agreement was achieved in 70% of the cases. The risk was under estimated in few cases (4%); in 14 cases (26%) the risk was over-estimated compared with the expert ratings. Case validation for the general surgical cases showed overall agreement with the matrix risk estimate in nearly 65% of cases. Similar levels of under- and over-estimation (7% vs. 28%, respectively) were seen. For both patient groups, the majority of the risk over-estimation was in those assigned to the very high risk category, compared to the expert's rating of high risk.

### Appropriateness of prophylactic therapies

Disagreement was seen in 10% (21 of 209) of indications rated by the medical panel and in 6% (22 of 396) rated by the surgical panel. These levels of disagreement are within the range typical for RAND studies and represent good clinical consensus.[24,25] The appropriateness results for both panels are shown in Table 5. Neither panel considered aspirin to be appropriate for any indication. In the medical panel, treatment options for patients having a moderate overall risk were largely influenced by whether the patient had a previous history of venous thromboembolism. With no history, lower doses of low-molecular-weight heparin (LMWH) were considered most appropriate. For those with a previous history

**Table 5.** Medical and surgical panels' ratings of appropriateness of prophylactic therapy.

| | *Overall risk in medical patients* | | | | | *Overall risk in surgical patient* | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | *Low* | *Moderate* | | *High* | *Very High* | *Low* | | *Moderate* | | | *High* | *Very High* |
| *History of VTE* | *Either* | *No* | *Yes* | *Either* | *Either* | – | – | *Either* | *No/Susp** | *Yes* | *Either* | *Either* |
| *Anesthesia* | – | – | – | – | – | *Local* | *Gen/Reg* | *Local* | *Gen/Reg*† | *Gen/Reg* | *Either* | *Either* |
| *Prophylactic options* | | | | | | | | | | | | |
| No prophylaxis | A | I | I | I | I | I | I | I | I | I | I | I |
| Aspirin | I | I | I | I | I | I | I | I | I | I | I | I |
| GCS alone | I | U | U | U | U | A | A | U | I | I | I | I |
| Vitamin K Antagonists | I | I | U | U | U | I | I | I | I | I | I | I |
| Unfractionated heparin | I | U | U | A | A | I | U | U | U | A | A | A |
| Low-molecular-weight heparin | | | | | | | | | | | | |
| Low dose Enoxaparin/Dalteparin‡ | I | U | I | I | I | U | U | U | A | A | U | I |
| Low dose Nadroparin§ | I | U | U | I | I | U | U | U | A | A | U | I |
| High dose Enoxaparin/Dalteparin¶ | I | A | A | A | A | I | I | I | U | A | A | A |
| High dose Nadroparin** | I | A | A | A | A | I | I | I | I | U | A | A |
| Heparin (UFH or LMWH) + GCS†† | I | U | A | A | A | I | U | U | U | A | A | A |
| Prolonged prophylaxis†† | I | U | U | U | A | I | I | I | I | I | U | A |

** No/Susp: VTE is either not known or is suspected but has not been diagnosed; †Gen/Reg: general or regional anesthesia; ‡low dose refers to enoxaparin 20 mg, dalteparin 2500IU; §low dose refers to nadroparin 0.3 mL; ¶high dose refers to enoxaparin 40 mg, dalteparin 5000IU; **high dose refers to body weight adjusted nadroparin; ††heparin (UFH/LMWH) + GCS = UFH or LMWH associated with graduated compression stockings; ‡‡prophylaxis given for a maximum of 6 weeks; GCS: graduated compression stockings, I: inappropriate, A: appropriate, U: uncertain, LMWH: low-molecular-weight heparin, UFH: unfractionated heparin; VTE: venous thromboembolism.*

of thrombosis, there was uncertainty regarding the use of the LMWH nadroparin, at a dose of 0.3 mL, because anti-Xa levels for this dose are higher than those for two other LMWH, enoxaparin (20 mg) and dalteparin (2,500 IU); these low doses of enoxaparin and dalteparin were considered inappropriate.

The role of vitamin K antagonists for moderate, high and very high risk medical patients was largely uncertain reflecting the lack of evidence in these situations. For both high risk groups, unfractionated heparin was considered appropriate, although high doses of LMWH were considered more appropriate. The combined use of heparin and compression stockings was also considered to be an appropriate strategy. Uncertainty existed concerning the use of prolonged prophylaxis for high-risk medical patients; however, for those with a very high risk, prophylaxis for up to 6 weeks was considered an appropriate therapy.

In the surgical panel, among low risk patients receiving local anesthesia the use of stockings alone was considered appropriate, with uncertainty concerning the use of low dose LMWH for patients undergoing surgery using general or regional anesthesia. For moderate and higher risk patients, LMWH was considered the most appropriate treatment, although the dosage varied according to the overall risk, history of thrombosis, and type of anesthesia performed. For moderate risk patients undergoing regional or general anesthesia and who had a confirmed history of thrombosis, stockings, unfractionated heparin and LMWH were all considered appropriate. For high and very high risk patients, high dose LMWH was the most appropriate therapy, with or without the use of stockings. The usefulness of prolonged prophylaxis was considered uncertain for high risk patients but appropriate for very high risk individuals.

## Discussion

The electronic Risk Matrix that we developed, using experts' quantitative and qualitative opinions on VTE risk factors, successfully identified the perceived thrombosis risk in multiple case scenarios. Although the matrix over-estimated risk in approximately one quarter of clinical cases, the deviant findings were mainly found in the distinction between high and very high risk cases, which made little difference to the appropriate prophylactic therapies suggested. Overall, the RAND/UCLA appropriateness method appeared to validate the methodological approach adopted in creating the matrix, with quite high levels of agreement between the model results and the expert opinion offered for the clinical cases. Although validation of this risk matrix in a real clinical environment is lacking, we suggest that this computer-based application is likely to improve the awareness and provision of thromboprophylaxis in at-risk medical and surgical patients. Recent evidence suggests that uniform use of electronic alerts or local thromboprophylaxis guidelines are associated with improvements in both prophylactic provision and patients' outcomes,[18,26] and such practice-based care recommendations should be the target for future validation of the clinical use of the risk matrix.

The strengths of the study include the formulation

of the aggregate ratings for predisposing and exposing risk factors, which provide some level of quantification concerning levels of risk for the individual medical and surgical conditions included. Furthermore, a greater understanding of the interrelationship of risk factors and their evolving nature during the course of a medical illness or surgical procedure was included. Other strengths of the study include the approach taken to formulate the treatment recommendations, which were assessed using a harms-benefit evaluation, thereby reflecting both efficacy and safety aspects of the therapies assessed. The appropriateness of thromboprophylaxis therapy suggested for different conditions goes beyond licensed indications and, although the recommendations are generally in line with other guidelines,[1,2] the treatment recommendations would be enhanced by prospective evaluation in well organized centers.

Our study has several limitations. Although the risk matrix is available for use as a simple, computer desk-top application, which could be made available across a hospital network for widespread usage, individual hospitals would be required to prospectively assess and validate the efficacy and safety of the approaches recommended before widespread adoption of the tool. Several surgical and medical conditions, including trauma, orthopedic surgery, vascular surgery and pregnancy, were not included in the study because of the logistics of recruiting experts in these disciplines to take part. We hope that these specialized groups of patients can be evaluated in the future. Second, only three different LMWH were included in the prophylactic options, because these agents (enoxaparin, nadroparin and dalteparin) are most widely prescribed worldwide. However, it is likely that the results are appropriate for similar doses of other LMWH. Furthermore, we did not evaluate new antithrombotic agents (e.g. fondaparinux) now available for many of the medical and surgical conditions. Third, the design of the study, with the identification of risk factors and recommendations for prophylactic treatment made by a panel specifically formed for the purposes of this study, is open to the inherent biases of the panel. Although the RAND/UCLA appropriateness method is generally reliable,[27] a replication of the study with different experts would have been beneficial to extend the confirmation of the matrix as a valid tool. Finally, prospective validation of the risk assessment tool in a clinical setting would have been very valuable given the largely opinion-driven nature of this matrix.

Other risk assessment models have been developed, predominantly based on risk scores provided by expert groups. Russell *et al.*[28] used a multiple logistic regression analysis to identify independent risk factors for venous thromboembolism with risk scores then arbitrarily assigned to calculate the annual risk of thrombosis. Motykie and colleagues proposed a similar model for both medical and surgical patients[6] using evidence-based guidelines.[29] Clinical settings and individual patient characteristics were combined into an overall score, although without patient case validation.[30] Lindqvist and colleagues[31] created a web-based user interface for individual assessment during pregnancy. Lutz and colleagues developed a tool for medical patients that evaluated patients' baseline (or predisposing) risk in conjunction with their acute (or exposing) risk to create an overall score.[8] To our knowledge, although these risk appropriateness models are predominantly based on expert group recommendations and various statistical models, none provides guidelines for individual clinical conditions or has undergone a validation process.

In summary, we have developed an electronic Risk Matrix that we hope will serve as both a practical and educational tool for healthcare providers to improve the prescribing of appropriate prophylactic therapies to medical and surgical patients at risk of venous thromboembolism.

*Participation in Clinical Taskforce Panel: MMS, OED, PM, DJQ, NR; conception and implementation of RAND/UCLA Appropriateness Method: MC, HDV, IVB, JPK; analysis and interpretation of the data: MC, HDV, IVB, JPK; drafting of the article: MMS, OED, DJQ,JPK; Critical revision of the article for important intellectual content: MMS, OED, PM, DJQ, NR, MC, HDV, IVB, JPK; final approval of the article: MMS, OED, PM, DJQ, NR, MC, HDV, IVB, JPK; statistical expertise: MC, HDV, IVB, JPK.*

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