



Venous Thromboembolism Prevention: How to make this work

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Objectives

- Describe the benefits and limitations of pharmacologic and mechanical thromboprophylaxis (TP)
- Highlight implementation challenges
- Describe risk assessment models
- Describe how specific anti-thrombotic and mechanical TP are used in preventing VTE
- Highlight methods to break through barriers



Venous Thromboembolism (VTE)

- Annually, VTE is the cause of death of approximately 300,000 and 543,454 patients in the US ¹ and EU ², respectively.
- Approximately 200,000 of these US deaths are hospital-related with ~ 50%, or 100,000, being “preventable” ^{1,3,4}
- Several downstream morbidities occur from the incident VTE including post-thrombotic syndrome (PTS), chronic thrombembolic pulmonary hypertension (CTPH), recurrent VTE, death from recurrent VTE, major and minor bleeding, and heparin induced thrombocytopenia (HIT) from treatment dose heparin/low molecular weight heparins. ^{3,4}
- New annual estimates show that VTE costs the US \$13.5 to \$69.3 Billion with \$4.5 to \$39.3 Billion of this being “preventable” with improved intervention systems. ³

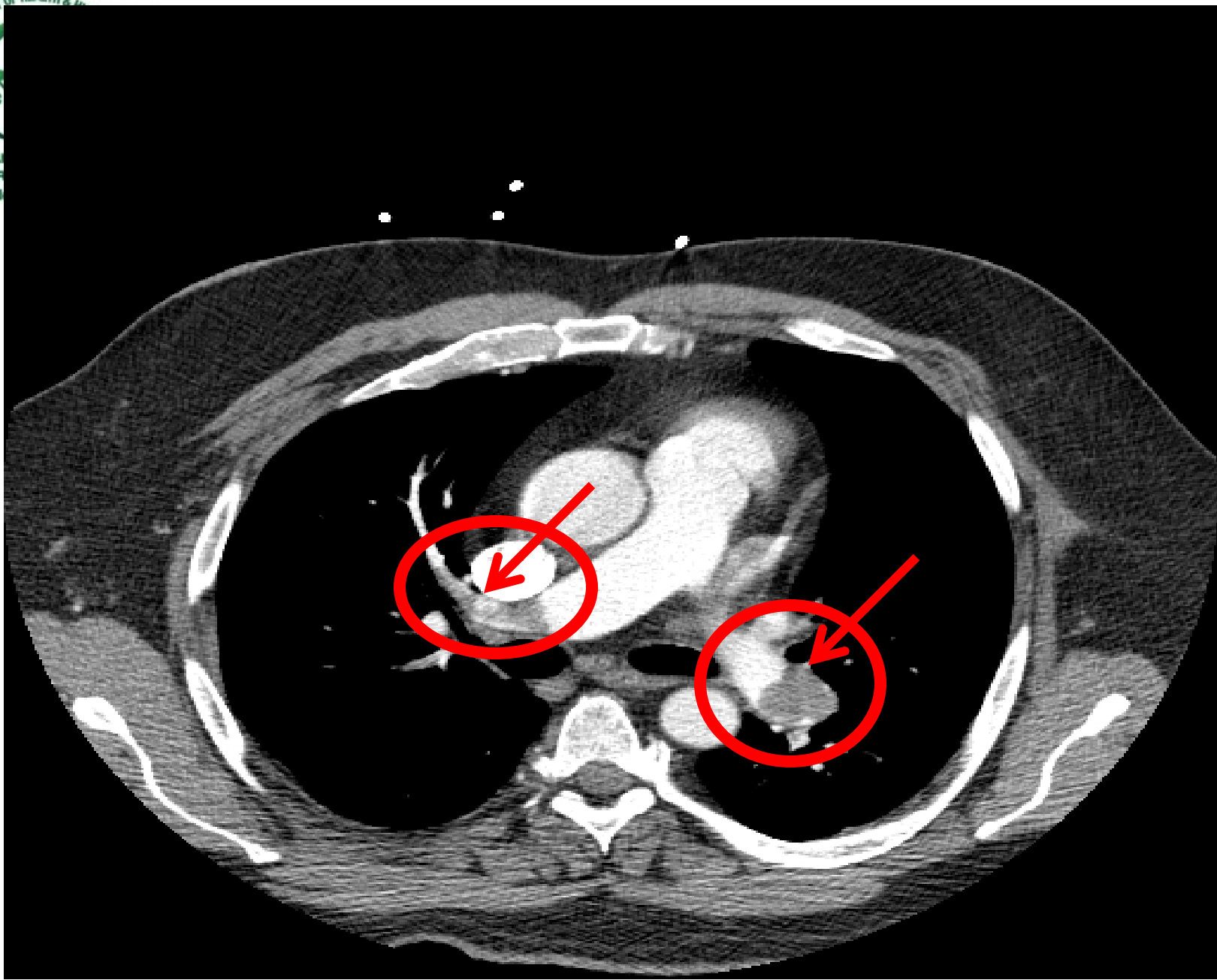
1. Heit JL, et al. *Blood*. 2005;106: Abstract #910
2. Cohen AT, et al. VTE Impact Assessment Group in Europe (VITAE). *Thromb Haemost* 2007; 98: 756–764
3. Mahan CE et al. *Thrombosis Hemostasis*. 2012 Jun 28;108(2). Epub ahead of print
4. Surgeon General’s Call to Action to Prevent DVT and PE 2008 DHHS



Emerging Changes with VTE

- Overall in recent years, definitions have shifted to include ***omission*** of a device or drug (i.e. mechanical or pharmacologic prophylaxis) as an adverse event (AE) or adverse drug event (ADE), respectively, if a VTE occurs in an at-risk patient due to an omission. ¹⁻⁴
- “Preventable” VTE and “appropriate” type, dose ***and duration*** of prophylaxis have emerged in the medical literature ⁵
 - “Preventable” VTE is defined as a hospital-acquired VTE event that occurs in the absence of “appropriate” prophylaxis between hospital admission and the day before the VTE diagnostic order date. ⁵
- Shift towards risk assessment for bleeding and VTE

1. WHO Draft Guidelines for adverse event reporting and learning systems. Available at http://www.who.int/patientsafety/events/05/Reporting_Guidelines.pdf
2. The Institute for Safe Medication Practices. Adverse drug event and potential adverse drug event. Available at <http://www.ismp.org/Tools/FrederickReporting.asp>
3. The Joint Commission. Sentinel Event Glossary of Terms. Available at http://www.jointcommission.org/SentinelEvents/se_glossary.htm.
4. Institute of Medicine “Preventing Medical Errors” Textbook
5. The Joint Commission (TJC). Specifications Manual for National Hospital Inpatient Quality Measures. Available at: http://www.jointcommission.org/specifications_manual_for_national_hospital_inpatient_quality_measures/. Accessed February 18, 2011.





Benefits and Limitations of Pharmacologic Prophylaxis

- Pharmacologic Prophylaxis
 - Benefit – Highly effective in at-risk patients in preventing VTE with an approximate 50-70% relative risk reduction versus placebo or no-prophylaxis. ¹
 - Benefit – If we prevent the incident VTE, the downstream complications are also prevented ²
 - Benefit – Compliance is fairly good in hospitals. Room for improvement.³
 - Limitations – Both major (~ 1 %) and minor bleeding, rare HIT, side effects
- Mechanical Prophylaxis
 - Benefit – Effective in preventing DVT if compliance (i.e. keeping on the patient) is good
 - Benefit – Does not cause an increased risk of bleeding ¹
 - Limitation – Difficult to keep on the patient. Compliance is measured at 20-70%.
 - Limitation – Uncomfortable. They can also cause skin breakdown over long periods of time.

1. Guyatt GH et al. CHEST 2012; 141(2) (Suppl): e185S-e194S

2. Mahan CE et al. *Thrombosis Hemostasis*. 2012; 2012 Jun 28;108(2). Epub ahead of print

3. Fanikos J et al. Am J Med 2010 Jun;123(6):536-41.



Barriers to VTE Prophylaxis

- Knowledge
 - Lack of awareness about the evidence
 - Lack of familiarity with the evidence
 - Comment - Is there ***too much evidence*** now? Hard to keep up?
- Attitudes
 - Lack of agreement with the evidence
 - Lack of motivation
- Behavior
 - Contradictory, or poorly-constructed, guidelines
 - Patient Factors, Values and Preferences
 - Lack of time, resources and/or organizational constraints

There may be multiple levels of these in any hospital. Studies on improving physician adherence may not be generalizable since barriers may vary by setting. Find out what works in your hospital

1. Cabana MD et al. Why don't physicians follow clinical practice guidelines? A framework for improvement. JAMA 1999; 282 (15): 1458-65



Barriers to VTE Prophylaxis

- Definition of Mobilization ?? – Important but clearly needs to be standardized
- Multi-disciplinary care as this may lead to unclear accountability by role confusion
- ***Suggested Solutions:***
 - Coordinated, comprehensive, systems approach that is aimed at patients, providers and administrators
 - May include frequently evaluated order sets, methods to screen and risk-stratify **ALL** patients, and audit and feedback
 - Standardize mobilization definition at your hospital and assessed and document daily in the medical record



Barriers to VTE Prophylaxis

- Lack of clear indications and contraindications for prophylaxis and concerns about bleeding risks
- Physicians and pharmacists recognized the underuse of VTE prophylaxis in medical patients, while nurses and physiotherapists tended to perceive prophylaxis strategies as appropriate.
- Therefore, the healthcare providers best able to conduct (proximity and contact time) a daily assessment of patients' need for prophylaxis under-recognize the problem that prophylaxis is underutilized in this population
- ***Suggested Solutions:***
 - Preprinted orders outlining VTE risk factors
 - Educating front-line care providers prior to implementation of a top-down approach.



Get with the Guidelines – But Which One ??



Get with the Guidelines – But which one?

- American College of CHEST Physicians ¹⁻³
- International Union of Angiology ⁴
- American Academy of Orthopaedic Surgeons ⁵
- American College of Physicians (i.e. Medical Patients) ⁶
- NCCN/ASCO – referred to later

The Surgical Care Improvement Project (SCIP) VTE measures and VTE Core Measures [Joint Commission (TJC) and Center for Medicaid Medicare Services (CMS)] are not **guideline** specific, they are **patient specific**.

Discordant Guidelines that are only updated every 2-6 years ??

1. Kahn et al. *CHEST* 2012; 141:(2 Suppl): e195S-226S
2. Falck-Ytter et al. *CHEST* 2012; 141:(2 Suppl): e278S-325S
3. Gould et al. *CHEST* 2012; 141:(2 Suppl): e227S-277S
4. Nicolaidis AN *Int Angiol* 2006;25:101-161
5. http://www.aaos.org/research/guidelines/VTE/VTE_guideline.asp
6. Qaseem A et al. *Ann Intern Med* 2011 Nov 1; 155 (9); 625-32



Get with the Guidelines – But which one?

- **Solution:** Use a mixture of the guidelines, current evidence-based medicine, and what works best at your hospital, but utilize a defined process with defined risk factors
- Try to keep it simple -- but do not overlook important risk factors
- The goal is to prevent “potentially preventable VTE”
- This means you need to:
 - Utilize some form of thromboprophylaxis (TP) in at-risk patients **OR**
 - Document the patient is ***NOT at-risk of VTE*** in the medical record **OR**
 - Document that pharmacologic and mechanical TP are contraindicated in the medical record in a patient at-risk of VTE (Note: VERY rare in clinical practice)
- **While no guideline is perfect, ACCP likely has the most rigorous methodological development and has recently been updated. Great resource or starting point for the development of your hospital guideline/practice/policy**



ACCP 9th Edition

- Separated the VTE prevention chapters into three primary groups:
 - Non-surgical (i.e. Medical) groups ¹
 - Orthopedic surgical ²
 - Non-orthopedic surgical ³, and
- For the Non-surgical and Non-orthopedic surgical chapters, a primary shift is towards an individualized approach of risk assessing the patients' bleeding risk factors as well as their VTE risk factors for the appropriate TP strategy



1. Kahn et al. *CHEST* 2012; 141:(2 Suppl): e195S-226S
2. Falck-Ytter et al. *CHEST* 2012; 141:(2 Suppl): e278S-325S
3. Gould et al. *CHEST* 2012; 141:(2 Suppl): e227S-277S



Background to Risk Assessment Models (RAMs) or Clinical Decision Rules



Background to Validation of Clinical Decision Rules

- Clinical Decision Rules, or RAMs, should be derived appropriately based off of evidence and validated after derivation. ¹⁻³
- RAMs may be validated at different levels with level 1 being the highest and level 4 being the lowest ³
- Validation provides evidence the model can be used with reproducible accuracy in other settings ³
- None of the RAMs in *medical patients* have been externally validated at this point.
 - Kucher/Padua /Maynard – somewhat internally validated

1. Altman DG, Statist. Med. 2000; 19:453-473

2. Harrell FE, Statist. Med 1996; 15: 361-387

3. McGinn TG JAMA. 2000; 284:79-84



Background to Validation of Clinical Decision Rules (cont)

- Level 1: Rules that can be used in a wide variety of settings with confidence that they can change clinician behavior and improve patient outcomes ¹
 - At least 1 prospective validation in a different population and 1 impact analysis, demonstrating change in clinician behavior with beneficial consequences
- Level 2: Rules that can be used in various settings with confidence in their accuracy ¹
 - Demonstrated accuracy in either 1 large prospective study including a broad spectrum of patients and clinicians or validated in several smaller settings that differ from one another



An Ideal RAM

- Enable clinicians to accurately identify patients who meet a threshold risk of developing a VTE in the absence of TP
- Predict the correct risk level (disease-specific and predisposing risk factors) allowing more tailored TP strategies
- Reliably exclude patients without a beneficial risk:benefit ratio
- Evidence-based derivation and validated
- Methodologically transparent
- Simple to use in clinical practice



Risk Assessment Models (RAMs) for VTE and Bleeding— **Medical Patients**



IMPROVE (IMPACT-ILL) Risk Assessment Model for VTE

VTE Risk Factor	Points For the Risk Score
Previous VTE	3
Thrombophilia	2
Lower limb paralysis	2
Current cancer	2
ICU/CCU stay	1
Immobilization ≥ 7 days	1
Age > 60 years	1

0-1 Points = Low Risk, 2-3 Points = Moderate Risk, ≥ 4 points = High Risk



IMPROVE VTE rates by VTE risk score (n=15,125)

Score	Patients, % (n)	3-Month Predicted VTE Risk*, %	Observed VTE Rate [†] , % (n)	Observed PE Rate [†] , % (n)
0	27 (4029)	0.4	0.3 (14)	0.3 (11)
1	42 (6350)	0.6	0.5 (33)	0.3 (19)
2	16 (2420)	1.0	1.3 (31)	0.5 (13)
3	9 (1335)	1.7	1.3 (18)	0.7 (9)
4	5 (729)	2.9	4.1 (30)	2.3 (17)
5-10	2 (262)	7.2	6.5 (17)	2.7 (7)

- ◆ 32% of patients with score ≥ 2
- ◆ Patients with a score ≥ 4 (7% of the study population) developed a 3-month VTE symptomatic event rate of 4.7% (47/991) and symptomatic PE event rate of 2.4% (24/991)



Padua Prediction Score - VTE

BASELINE FEATURES	SCORE
Active cancer	3
Previous VTE	3
Reduced mobility	3
Already known thrombophilic condition	3
Recent (< 1 month) trauma and/or surgery	2
Old age (≥ 70 years)	1
Heart and/or respiratory failure	1
Acute infection and/or rheumatologic disorder	1
AMI and/or ischemic stroke	1
Obesity (BMI ≥ 30)	1
Ongoing hormonal treatment	1

Scores ≥ 4 were high risk of VTE. Scores < 4 were low risk of VTE. Expert based derivation.

[Barbar et al. Journal of Thrombosis and Haemostasis, 8: 2450–2457](#)



IMPROVE BLEEDING RAM – High Bleeding Risk if score ≥ 7

Bleeding Risk Factor in Medical Patients	Points
Moderate renal failure - Glomerular Filtration Rate(GFR) 30 to 59 versus ≥ 60 mL/min/m ²	1
Male versus Female	1
Age 40 to 84 versus < 40 years	1.5
Current cancer	2
Rheumatic disease	2
Central venous catheter	2
Intensive care unit / coronary care unit	2.5
Severe renal failure -- GFR < 30 versus ≥ 60 mL/min/m ²	2.5
Hepatic failure (international normalized ratio > 1.5)	2.5
Age ≥ 85 versus < 40 years	3.5
Platelet count < 50×10^9 cells/L	4
Bleeding in 3 months before admission	4
Active gastroduodenal ulcer	4.5



Example RAM in the Medical Patient



VTE RISK Factor in Medical Patients	POINTS
Previous VTE	3
Thrombophilia	2
Lower Limb Paralysis	2
Current Cancer	2
Immobilization \geq 7 Days	1
ICU / CCU Stay	1
Age > 60 Years	1

BLEEDING RISK Factor in Medical Patients	Points
Moderate renal failure - Glom. Filtr. Rate 30-59 versus \geq 60 mL/min/m ²	1
Male versus Female	1
Age 40 to 84 versus < 40 years	1.5
Current cancer	2
Rheumatic disease	2
Central venous catheter	2
Intensive care unit / coronary care unit	2.5
Severe renal failure – GFR < 30 versus \geq 60 mL/min/m ²	2.5
Hepatic failure (international normalized ratio > 1.5)	2.5
Age \geq 85 versus < 40 years	3.5
Platelet count < 50×10^9 cells/L	4
Bleeding in 3 months before admission	4
Active gastroduodenal ulcer	4.5

Total VTE Risk Score: _____ Total BLEED Risk Score: _____

VTE and BLEED Risk	Intervention
LOW BLEED RISK (Bleeding Score < 7) LOW VTE RISK (VTE Score \leq 1)	No Prophylaxis -- Reassess Patient in 24 hours or with any clinically pertinent change
HIGH BLEED RISK (Bleeding score \geq 7) MODERATE or HIGH VTE RISK (VTE Score \geq 2)	Mechanical Prophylaxis -- Intermittent Pneumatic Compressions or Graduated Compression Stockings. Reassess Patient in 24 hours or with any clinically pertinent change to evaluate if bleeding risk subsides. Consider Pharmacologic TP if bleeding risk subsides.
LOW BLEED RISK (Bleeding score < 7) MODERATE or HIGH VTE RISK (VTE Score \geq 2)	Pharmacologic Prophylaxis -- UFH 5000 Units TID or LMWH per institution. Consider GCS/IPC adjunctive therapy in high risk VTE patients.



Antithrombotic Recommendations Medical

At-risk for VTE, Low Bleed Risk ¹

- Low molecular weight heparin (LMWH) (1B)
- Low dose unfractionated heparin (LDUH) BID or TID * (1B)
- Fondaparinux ** (1B)

At-risk for VTE, High Bleed Risk or actively bleeding ¹

- Optimal use of graduated compression stockings (GCS) or intermittent pneumatic compression (IPC) (2C)
- When bleeding risk subsides and if VTE risk persists, pharmacologic TP as above. (2B)

* Prefer TID UFH over BID. LMWH may be preferred by patient due to less frequent injections. Missed UFH doses in the hospital are not infrequent. ²⁻³

** No approved indication in the US in this patient group

1. Kahn et al. *CHEST* 2012; 141:(2 Suppl): e195S-226S
2. Intern Emerg Med. 2010 Aug;5(4):299-306. Epub 2010 Feb 23. Review.
3. Fanikos J et al. Am J Med 2010 Jun;123(6):536-41.



Risk Assessment Models (RAM) for VTE and Bleeding— Non-ORTHO *Surgical Patients*



Caprini Surgical RAM

Retrospective validation study of individualized risk assessment in 8216 surgical patients:

<u>Risk Level</u>	<u>Points</u>	<u>Percent</u>
Low	0-1	0.9
Moderate	2	10.4
High	3-4	36.5
Highest	≥ 5	52.1

Bahl V et al Ann Surg 2010; 251:34-35

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 The Feinberg School of Medicine:
 Professor of Biomedical Engineering,
 Northwestern University;
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 Website: venousdisease.com

Venous Thromboembolism Risk Factor Assessment

Patient's Name: _____ Age: ____ Sex: ____ Wgt: ____ lbs Joseph A. Caprini, MD, MS, FACS, RVT

Choose All That Apply

Each Risk Factor Represents 1 Point

- Age 41-60 years
- Minor surgery planned
- History of prior major surgery
- Varicose veins
- History of inflammatory bowel disease
- Swollen legs (current)
- Obesity (BMI >30)
- Acute myocardial infarction (< 1 month)
- Congestive heart failure (< 1 month)
- Sepsis (< 1 month)
- Serious lung disease incl. pneumonia (< 1 month)
- Abnormal pulmonary function (COPD)
- Medical patient currently at bed rest
- Leg plaster cast or brace
- Other risk factors _____

Each Risk Factor Represents 3 Points

- Age over 75 years
- Major surgery lasting 2-3 hours
- BMI > 50 (venous stasis syndrome)
- History of SVT, DVT/PE
- Family history of DVT/PE**
- Present cancer or chemotherapy
- Positive Factor V Leiden
- Positive Prothrombin 20210A
- Elevated serum homocysteine
- Positive Lupus anticoagulant
- Elevated anticardiolipin antibodies
- Heparin-induced thrombocytopenia (HIT)
- Other thrombophilia
Type _____

Each Risk Factor Represents 2 Points

- Age 60-74 years
- Major surgery (> 60 minutes)
- Arthroscopic surgery (> 60 minutes)
- Laparoscopic surgery (> 60 minutes)
- Previous malignancy
- Central venous access
- Morbid obesity (BMI >40)

Each Risk Factor Represents 5 Points

- Elective major lower extremity arthroplasty
- Hip, pelvis or leg fracture (< 1 month)
- Stroke (< 1 month)
- Multiple trauma (< 1 month)
- Acute spinal cord injury (paralysis)(< 1 month)
- Major surgery lasting over 3 hours

For Women Only (Each Represents 1 Point)

- Oral contraceptives or hormone replacement therapy
- Pregnancy or postpartum (<1 month)
- History of unexplained stillborn infant, recurrent spontaneous abortion (≥ 3), premature birth with toxemia or growth-restricted infant

Total Risk Factor Score



Incidence Rate of VTE by Risk Level – Retrospective Validation

