Evidence-based Practice in the Hospital setting

Reducing the risk of VTE in the Hospitalized Patient

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Disclosure of financial relationships

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Disclosures:
Research: Pfizer-BMS, Eisai, U. Mass, NIH
Honorarium: Sanofi-Aventis, Eisai, GSK
Advisory Board: Sanofi-Aventis, Eisai, GSK and BMS

Resolution of Potential Conflicts of Interest:
-All presented material is independent of industry produced content.
-Only material supported by published data and Evidence-based guidelines will be presented.

Other recent "real-life tragedies" . . .

- 51 year old with lung cancer (small cell) on chemotherapy recently admitted and treated for community acquired pneumonia - returned 11 days later with massive PE
- 63 year old with DM, Obesity and CKDz s/p recent total hip replacement returned 12 days post-op (6 days after discharge) with SFV DVT
- 46 year old without PMHx presented with new dx of Pancreatic cancer and ascites. Died of PEA arrest on HD#6 with massive PE at autopsy.
- 49 year old with dilated CM and COPD admitted for "CHF exacerbation" after recent ER visit for COPD exacerbation 1 week prior. Decompensated on HD#3 with hypotension and hypoxia . . .PE (survived)

Learning Objectives

1. Recognize the importance of VTE in hospitalized patients (medical) and why it is a healthcare priority
2. Identify the main factors contributing to the risk of VTE and methods for risk stratification
3. Critically review and assess the underlying evidence for prophylactic management strategies as it relates to both safety and efficacy.
4. Review the latest guidelines from the ACCP (2008), particularly with regard to the development of a formal prevention strategy at all hospitals

The Impact of VTE

VTE - Venous Thromboembolism

Pulmonary Embolism and Deep Vein Thrombosis

VTE Incidence

Incidence:[1]

- 900,000 PEs and DVTs in the USA in 2002
- Estimated 296,000 PE deaths
  - 7% treated unsuccessfully, 34% sudden and fatal, and 59% undetected
- Up to 10% of symptomatic DVT with severe Post-Thrombotic syndrome

Annual number at risk for VTE: US hospitals:[2]

- 7.7 million medical service inpatients
- 4.3 million surgical service inpatients
- 2/3 of VTE cases and deaths are hospital-acquired[1]

1. Heit J, et al. *Blood.* 2005;106:Abstract 910.
2. Anderson FA Jr, et al. *Am J Hematol.* 2007;82:777-782

Epidemiology

- Absolute risk of symptomatic events (Administrative DB):
  - Medical Pts - 1.7% within 90 days of hospitalization
  - Orthopedic surgery Pts- 2-3%
- Placebo arm of RCTs[1]:
  - All DVT - 15%
  - Proximal DVT - 5%
  - Pulmonary embolism - 0.5%
- DVT was detected by ultrasound in 33% of medical patients in the ICU during an 8-month screening study[2]
- Overall hospitalization confers a 6 - 11 fold increased risk for developing VTE.

1. Dentali F, et al. *Ann Intern Med.* 2007;146:278-288.
2. Hirsch DR, et al. *JAMA.* 1995;274:335-337.

VTE in Hospitalized Patients

- PE is responsible for 5-10% of hospital-associated deaths.
- 50%-70% of symptomatic VTEs occur in nonsurgical patients[1]
- *70%-80% of fatal PEs occur in nonsurgical patients*[1]
- 25 - 37% of all symptomatic VTE cases occur in patients recently hospitalized w/in 90 days[2]
- PE: most preventable cause of hospital death and the number one strategy to improve patient safety in hospitals[1]

1. Geerts WH, et al. *Chest.* 2008;133:381S-453S.
2. Heit JA, et al. *Arch Intern Med.* 2002;162:1245-1248

Real Numbers in the Insured Population

- Discharges from a PharMetrics database from Jan 2001 - Dec 2005 aged > 40 years hospitalized for cancer, CHF, severe infection, or lung disease.
- Outcome: VTE rate and type; time to event
- Results: Average VTE rate 5.6% (1.5%); highest for Cancer patients at 7.6%.
  - VTE occurred most frequently after discharge
  - Post discharge prophylaxis was provided to 13.1% of CHF patients and < 5% of the others.
  - Previous VTE and Cancer were independent predictors of post-discharge VTE

Spyropoulos AC et al. Thrombosis and Haemostasis 2009;102:951-7.

Important Lessons . . .

1. Most events occur in the "average hospitalized patient"
2. Most new symptomatic VTE events occur after hospital discharge
3. Most new events occur without warning with little opportunity to intervene
4. In 2010 this is still a very common and preventable disease. . .

Hospital-Acquired DVT/PE Increases Both Cost of Care and Length of Stay

- Data from discharge summaries and itemized bills at 220 US hospitals
  - Total of 67,293 patients who underwent total hip or total knee replacement
- Of these, 403 (0.6%) suffered hospital-acquired DVT, and 190 (0.3%) suffered PE

	Mean total costs of inpatient care	Mean LOS in the hospital
No VTE	$9541	4.7 days
DVT only	$13,300	8.3 days
PE	$17,965	11 days

- **Patients with DVT and PE had significantly higher costs and length of stay than those without (*P*<0.0001)**

DVT/PE=deep vein thrombosis/pulmonary embolism; LOS=length of stay; VTE=venous thromboembolism=DVT and/or PE.

Ollendorf et al. *Am J Health-Syst Pharm.* 2002;59(18):1750-1754.

VTE and its Complications Can be Prevented!

- Probability model to estimate the number of VTE events in the 2003 United States Healthcare Cost and Utilization Project.
- Inpatient sample of 8,077,919:
  - DVT - 122,235
  - PE - 32,654
  - Recurrent DVT's - 28,052; Recurrent PE's - 6,680
  - PTS - 140,156
- Total VTE events reduced by 60%

Fanikos et al. 2009 Thrombosis and Haemostasis

"Never events don't just live in Neverland . . ."

Hospital Acquired Conditions (HAC) - Preventable complications that will not be compensated by payors (ie. CMS)

Why do gaps persists?

- Systems and Institutions have too much on their "Plate of Priorities"
- Poor understanding of the natural history of VTE risk - particularly in medical patients as they represent a vary heterogenous population
- Perpetuation of "risk over benefit" - ie. bleeding and cost
- Systems do not support automation of assessment and administration of prophylaxis
- Ambulation is enough???????
- Disagreement among guidelines

A survey of barriers to prophylaxis: The Canadian Perspective

- 2007 Survey of 1601 Canadian healthcare professionals in Ontario, Canada
- Purpose: identify barriers for prophylaxis in the medical patient.
- Most common barriers:
  - "Increased risk of bleeding with anticoagulants"
  - "Lack of clear indications"
  - "Concern for contraindications for anticoagulants"
  - "Lack of time to consider VTE prophylaxis in every patient."

Llyod N, et al. abst. ASH 2009, submitted for publication

Despite Evidence – Hospitalized Patients at Risk Remain Unprotected

	Medical	Surgical
No. of patients	37,356	30,827
At risk for VTE	42%	64%
Receiving ACCP Tx	40%	59%

	United States	Other Countries
No. of patients	3,410	11,746
VTE prophylaxis	1852 (54%)	5788 (49%)
LMWH	476 (14%)	4657 (40%)
UFH	717 (21%)	1014 (9%)

Quality Organizations Driving VTE Prevention and Treatment Measures

- Agency for Healthcare Research and Quality (AHRQ)
- Centers for Medicare and Medicaid Services (CMS)*
- Institute of Medicine (IOM)
- The Joint Commission (TJC)*
- The Leapfrog Group*
- National Institute of Clinical Excellence (NICE)
- National Quality Forum (NQF)*
- Medicare Modernization Act (MMA)

QuickTime™ and a decompressor are needed to see this picture.

- **1.2 VTE Prophylaxis Policy**

1.2.1 We recommend that **every general hospital** develop a **formal, <u>active</u> strategy** that addresses the prevention of VTE [Grade 1A]

What is the Evidence?

- Hundreds of **randomized trials over 35 yrs:**
  - Thromboprophylaxis reduces DVT, PE, Mortality and costs
- Thromboprophylaxis is the **number 1 ranked patient safety strategy** in hospitalized patients
- More than 25 published **evidence-based guidelines** since 1986 showing clear evidence of benefit and safety

Current Prophylaxis Regimens

- UFH - Unfractionated Heparin (5000 IU b.I.d. versus t.I.d.)
- LMWH - Low Molecular Weight Heparin
  - Enoxaparin 40 mg once daily
  - Dalteparin 5000 IU once daily
  - Tinzaparin 4500 IU once daily*
- Fondaparinux 2.5 mg once daily*
- Mechanical Prophylaxis Strategies
  - Graduated Compression Devices
  - Pneumatic Compression Devices
  - Foot pumps
  - Inferior Venal Caval Filters

* Not FDA approved for prophylaxis in nonsurgical patients

CLOTS Trial

- Design: Two-part, multi-center, randomized, partially blinded, control trial with planned enrollment of ~ 5000
- Inclusion Criteria: patients presenting within 7 days with incapacitating stroke.
  - Trial 1: Clinician unsure about the value of GCS
    - Pts randomized to GCS vs. nothing (n=2,518)
  - Trial 2: Clinician about the optimal length of GCS
    - Pts randomized to full-length vs. knee-length GCS (stopped early)
- Primary outcome: incidence at 30d of pDVTs (DUS or veonography)

The Lancet, 2009;373:1958 - 1965

CLOTS Trial

- Results (ClOTS 1):
  - Thigh-high GCS 126 events or 10% VTEs
  - Avoid GCS 133 events or 10.5% VTEs
    - ARR = 0.5% (95% CI -1.9 to 2.9%)
  - Adverse events = skin breaks, blisters, and skin necrosis
    - TH-GCS 64[5%] vs. Nothing 16[1%]
    - OR = 4.18 (95% CI2.40 - 7.27)

The Lancet, 2009;373:1958 - 1965

The Rationale Against Mechanical Devices

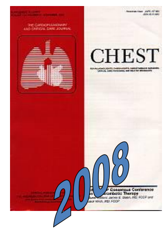
- No established standards for size, pressure, or physiologic features.
- No data to demonstrate reduction in mortality from VTE.
- Studies for mechanical devices were often unblinded and subject to significant bias.
- Compliance from both patients and staff is poor - may inhibit walking.
- Head-to-head less effective than pharmacologic strategies in high risk patients.
- Significant cost associated with purchase, storage, as well as ensuring optimal compliance.

Important Caveats for Mechanical Methods

- GCS not recommended for the foundation for VTE prophylaxis in any at-risk patient group
- Pneumatic sleeves must be worn at least 18 hours/24 hour period (comparative efficacy shown in GYN patients with LMWHs)
- Foot pumps must be used for ~ 19 hours/24 hour period (Orthopedic surgery)
- Physiology changes in fibrinolysis observed with possible increased risk of bleeding
- Precautions/contraindications to use of mechanical devices
- No controlled or RCT data in the Medically ill population
  - Some data in Stroke patients (CLOTS study)

Current ACCP Recommendations

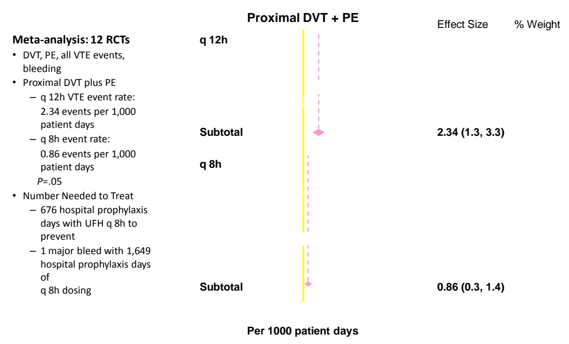
- We recommend that mechanical methods of prophylaxis be used primarily in patients who are at high risk of bleeding (Grade 1C+)
- We recommend that aspirin not be used for VTE prophylaxis in any patient group (1A)



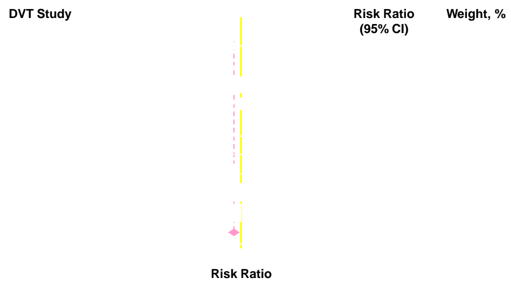
New Anticoagulants & their targets

Initiation	VIIa	Tifacogin NAPc2 FVIIai
Propagation	IXa VIIIa/Va Xa	TTP889 Protein C ART-123 Idraparinux Rivaroxaban Apixaban
Fibrin Formation	Thrombin	Dabigatran

Unfractionated Heparin Prophylaxis: q 12h vs q 8h



VTE Prophylaxis: LMWH vs UFH



Study Populations

	PREVENT 2003	
- Age ≥ **40** yrs (avg~74), expected hospital stay ≥ 6 days	- Age ≥ **40** yrs (avg~68), expected hospital stay ≥ 6 days	- Age ≥ **60** yrs (avg~75), expected hospital stay ≥ 4 days
and	**and**	**and**
- CHF (NYHA III/IV)	- CHF (NYHA III/IV)	- CHF (NYHA III/IV)
- acute respiratory illness	- acute respiratory failure	- acute or chronic lung disease
-infection **or** bone/joint **or** inflamed bowel	- acute severe systemic disease	- acute infectious or inflammatory disease
plus 1 risk factor	**plus** 1 risk factor	- **no other risks**

Proximal DVT + Symptomatic VTE at D14-21

Enox.	**2.1 %**	Dalte.	**2.6 %**	Fond.	**1.5 %**
Placebo	**6.6 %**	Placebo	**5.0 %**	Placebo	**3.4 %**

VTE Prophylaxis: 19,958 Medical Patients
9 Studies (Meta-analysis)

- studies - 53% reduction in symptomatic DVT;
  - RR = .47 (.22-1.00); P=.05
- 5 studies - 62% reduction in fatal PE;
  - RR = .38 (.21 – 0.69); P<.01
- 8 studies - 57% reduction in fatal or nonfatal PE;
  - RR = .43 (.26-0.71); P<.01

Translating "Relative" into "Absolute"

Outcome	RR	ARR (%)	NNT
DVT			
Any asymptomatic	0.51 (0.39-0.67)	2.6	36
Proximal asymp.	0.45 (0.31-0.65)	1.8	55
Proximal Symp.	0.47 (0.33-0.69)	0.43	232
Pulmonary Embolism			
All Symptomatic	0.43 (0.26-0.71)	0.29	345
Fatal PE	0.38 (0.21-0.69)	0.25	400
Major bleeding	1.32 (0.73-2.37)	NA	NA

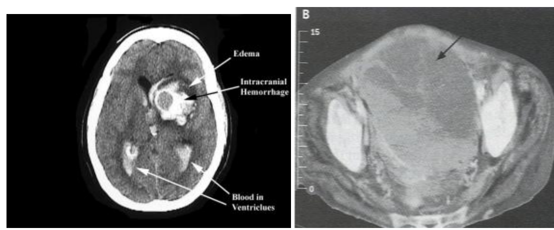
Dentali F, et al. *Ann Intern Med.* 2007;146:278-288

What about the risk?

Bleeding and H.I.T.

VTE Carries Long-Term Consequences

: Bleeding



Bleeding risk and VTE Prophylaxis

- Overall risk of major bleeding not increased in meta-analysis (range 0.2 - 5.6% depending on definition)
- Case fatality rate for major bleed is 9%
- Overall risk of Major bleed 0.02 - 0.5%.
- Who's at increased risk:
  - Active bleeding
  - At high risk for bleeding (ie. recent bleed < 4 weeks)
  - Impaired hemostasis (INR > 1.5, PTT > 40 s, Plt < 75K

Risk of H.I.T.

- Type of Heparin
  - Size, sulfation, source
- Route of administration
- Dose
- Duration
- Patient population
  - Gender, clinical population
- Previous exposure

What are the principle factors contributing to this disease?

Which hospitalized patients should receive prophylaxis?

Rudolf Ludwig Karl Virchow
1821-1902

- "Changes in pattern of blood flow. . ."
- "Changes in vessel wall . . ."
- "Changes in constituents of blood . . ."

Virchow RLK (translated by: Matzdorff, et al. Thrombose und Emolie. Canton, MA: Science History Publications; 1998

Model for Venous Thrombosis

Lopez JA et al. Hematology Jan 2004:439-456

Acquired Risk Factors for VTE

ACCP[1]

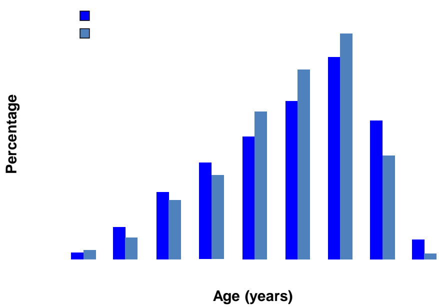
- Increasing age
- Immobility, paresis
- Previous VTE
- Cancer and/or its treatment
- Surgery
- Trauma (major or lower limbs)
- Obesity
- Central venous catheters
- Inflammatory bowel disease
- Nephrotic syndrome
- Pregnancy and postpartum
- Estrogen therapy or estrogen-containing oral contraceptives
- Acute medical illness

THRIFT[2]

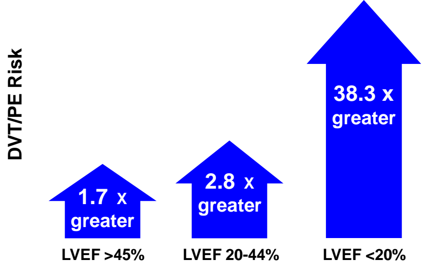
- Increasing age
- Immobility (>4d), limb paralysis
- Previous VTE
- Malignancy
- Surgery
- Trauma (pelvis, hips, legs)
- Obesity
- Varicose veins
- Heart failure
- Recent myocardial infarction
- Inflammatory bowel disease
- Nephrotic syndrome
- Pregnancy
- High-dose estrogen therapy
- Infection

1. Geerts WH, et al. *Chest.* 2008;133:381S-453S.
2. THRIFT Consensus Group. *BMJ.* 1992;305:567-574

Distribution of Patients With DVT by Age



The Importance of DVT Prophylaxis in Congestive Heart Failure



Risk of VTE Varies by Ethnic Group

- California claims database

Ethnic Group	Incidence per	RR (95% CI)
Caucasian	230	Reference
Black	293	1.27 (1.07 -1.51)
Hispanic	139	0.60 (0.54-0.67)
Asian/Pacific	60	0.26 (0.22-0.30)

White RH Ann Intern Med 1998

Independent Risk Factors for First Lifetime Definite VTE Within Olmsted County

RISK FACTOR[a]	AR[b]	95% CI
Hospitalization or nursing home	58.8	53.4-64.2
Hospitalization with surgery	23.8	20.3-27.3
Hospitalization without surgery	21.5	17.3-25.6
Nursing home	13.3	9.9-16.8
Active malignant neoplasm	18.0	13.4-22.6
Trauma	12.0	9.0-14.9
Congestive heart failure	9.5	3.3-15.8
Prior central venous catheter or pacemaker	9.1	5.7-12.6
Neurological disease with extremity paresis	6.9	3.5-10.2
Prior superficial vein thrombosis	5.4	3.0-7.7

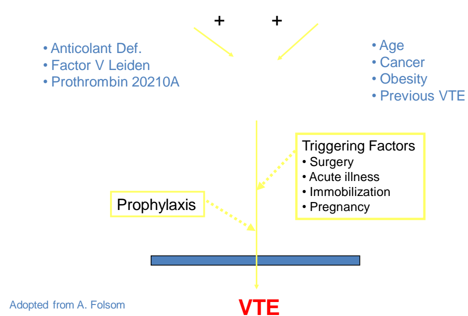
Heit JA, et al. *Arch Intern Med.* 2002;162:1245-1248.

Two-thirds of VTE Cases are Hospital Acquired . . .

Acute illness/major surgery leading to hospitalization is the most important risk factor for VTE.

1. Heit J, et al. *Blood.* 2005;106:Abstract 910.
2. Anderson FA Jr, et al. *Am J Hematol.* 2007;82:777-782.

VTE Risk Factor Model



How should providers assess risk of VTE in each patient?

Is the risk dichotomous or continuous?

I. RISK FACTOR ASSESSMENT	
Risk Factor (One point each unless otherwise noted)	Risk Factor (One point each unless otherwise noted)
❑ Documented history of DVT or PE **(3 points)** ❑ Hypercoagulable states **(3 points)** ❑ Visceral malignancy **(3 points)** ❑ Age > 40 years ❑ Obesity (BMI ≥ 27)) ❑ History of, or anticipated bed confinement/immobilization > 12 hours ❑ Confining air/ground travel > 4 hours within 1 week of admission ❑ Leg swelling, ulcers, stasis, varicose veins ❑ History of pelvic or long bone fracture ❑ Lower extremity arthroscopy in patient > 50 years ❑ Spinal cord injury with paralysis ❑ Stroke with paralysis ❑ Pneumonia ❑ Acute exacerbation of COPD	❑ Mechanical ventilation ❑ MI/CHF (class III and IV) ❑ Non-hemorrhagic myeloproliferative disorders including polycythemia vera ❑ Severe systemic infection or sepsis ❑ Estrogen hormone replacement or use of contraceptives ❑ Major surgery (general anesthesia time > 2 hours) ❑ Pregnancy or postpartum < 1 month ❑ Multiple trauma (major or lower extremity) ❑ Acute inflammatory disorders ❑ Nephrotic syndrome ❑ Indwelling central venous catheter **TOTAL RISK FACTOR SCORE:**

III. RISK ASSESSMENT CATEGORY AND SUGGESTED REGIMEN FOR DVT PROPHYLAXIS			
Low Risk	Moderate Risk	High Risk	Very High Risk
❑ **Score of 1 or less OR:** ❑ Minor surgery in patients < 40 years and no additional risk factors	❑ **Score of 2 OR:** ❑ Major surgery in patients < 40 years with no additional risk factors ❑ Minor procedures with additional risk factor ❑ Non-major surgery in patients 40-60 years with no additional risk factors	❑ **Score of 3 OR:** ❑ Non-major surgery in patients > 60 years or with additional risk factors ❑ Major surgery in patients > 40 years or with additional risk factors	❑ **Score of 4 or greater OR:** ❑ Major surgery in patients > 40 years with any of the following: 1. History of venous thromboembolism 2. Hip fracture (ORIF) total joint, procedure of the leg* 3. Spinal cord injury 4. Visceral malignancy 5. Hypercoagulable states 6. Additional risk factors

A Popular Risk Assessment Tool

The Caprini Score

- **The Caprini Score**

- Originally published in 1991

- Developed in a surgical patient group and adapted to other groups

- No prospective validation of tool.

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 (< I 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 ☐

Please see Following Page for Prophylaxis Safety Considerations

Revised November 4, 2006

VTE Risk Assessment (≥ 4 pts)

VARIABLE	POINTS
Major:	
Malignancy	**3**
Previous DVT or PE	**3**
Hypercoagulability	**3**
Intermediate:	
Major surgery(duration >1 hour)	**2**
Minor:	
Advanced age (>70)	**1**
Obesity (BMI >29)	**1**
Bed rest (ordered)	**1**
HRT or oral contraceptives	**1**

Kucher N, wet al. N Engl J Med. 2005;352(10):969-77.

Levels of Thromboembolism Risk and ACCP Recommendations for Prophylaxis in Hospital Patients[a]

Levels of Risk	Approximate DVT Risk Without Thromboprophylaxis %[b]	Suggested Thromboprophylaxis Options
Low risk		
Minor surgery in mobile patients	< 10	No specific thromboprophylaxis
Medical patients who are fully mobile		Early, “aggressive” ambulation
Moderate risk		
Most general, open gynecologic, or urology surgery patients	10-40	LMWH (at recommended doses), LDUH bid or tid, fondaparinux
Medical patients, bed rest or sick		“OR → IF”
Moderate VTE risk plus high bleeding risk		Mechanical thromboprophylaxis
High risk		
Hip or knee arthroplasty, HFS Major trauma, SCI	40-80	LMWH (at recommended doses), fondaparinux, oral vitamin K antagonist (INR 2-3)
High VTE risk plus high bleeding risk		Mechanical thromboprophylaxis[c]

Recommendations for Prophylaxis in Medical Patients

- In acutely ill medical patients who have been admitted to the hospital with:[1,2]
  - Congestive heart failure or severe respiratory disease
  - Or who are confined to bed and have ≥1 additional risk factors, including active cancer, previous VTE, sepsis, acute neurologic disease, or inflammatory bowel disease
    - LMWH (Grade 1A; IUA: enoxaparin 40 mg qday or dalteparin 5000 qday)
    - Low-dose UFH (Grade 1A; IUA: 5000 IU tid)
    - Fondaparinux 2.5 mg q day(Grade 1A)*

Definitions of Immobility Or "Bed Rest"

Study	Definition
MEDENOX	Autonomous walking distance of <10 m[1]
THE-PRINCE	Confined to bed for >2/3 of the day[2]
PRIME	Expected immobilization for >1/2 day[3]

MEDENOX=Prophylaxis in MEDical Patients with ENOXaparin; THE-PRINCE=THromboEmbolism-PRevention IN Cardiac or Respiratory Disease with Enoxaparin; PRIME=THromboEmbolism PRophylaxis in Internal Medicine with Enoxaparin

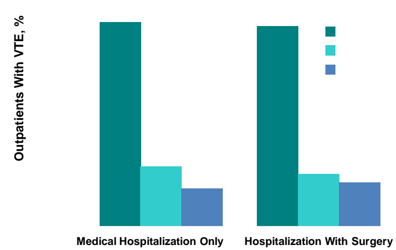
Transitioning from Inpatient to Outpatient

- At risk hospital patients are discharged with continued risk and immobility
- Specific groups have proven benefit from extended prophylaxis - supported by Evidence-based guidelines (ACCP)
  - Trauma and high-risk orthopedic patients
  - Patients undergoing cancer surgery
  - At-risk medical patients with continued decreased mobility.
- All patients should be reassessed for the need for appropriate ongoing prophylaxis.
- Evidence-based therapy for PX is 6 - 11 days regardless of setting.
  - "Complete the course" vs. "Extended prophylaxis"

Hospital Stays Are Often Shorter Than Approved Prophylaxis Duration

Thrombosis prophylaxis indications	Average length of hospital stay	FDA Approved length of prophylaxis for LMWH
Medical illness (acute)	**2-8 days**	**6-11 days**
Abdominal surgery	**2-7 days**	**7-10 days**
Total hip-replacement surgery	**2-6 days**	**7-10 days or 3 weeks (extended therapy)**
Total knee-replacement surgery	**2-5 days**	**7-10 days**

Outpatient and Inpatient VTE Are Linked

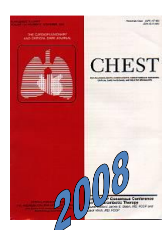


- 74% of VTEs present in outpatients
- 23% of outpatient VTE patients have had recent surgery; 37% recently hospitalized
- Only 43% had received VTE prophylaxis

Spencer FA, et al. *Arch Intern Med.* 2007;167:1471-1475.

Current ACCP Recommendations

- For each of the anti-thrombotic agents, “Clinicians should follow the manufacturer-suggested dosing guidelines” (Grade 1C)
  - How long were agents given in RCTs that led to FDA approval?



EXCLAIM: Extended-duration LMWH Prophylaxis in High-risk Medical Patients

End points	Extended prophylaxis n=2013 (%)	Placebo n=2027 (%)	RR reduction (%)	*P* value
VTE events	2.8	4.9	44	.001
Symptomatic	0.3	1.1	73	.004
No symptoms	2.5	3.7	34	.032

EXCLAIM: Extended-duration LMWH Prophylaxis in High-risk Medical Patients

Additional findings:

- Benefit of extended prophylaxis post-discharge was equal regardless of diagnosis (CHF, respiratory illness, infection etc.)
- Benefit of prophylaxis across mobility groups:
  - Level 1 (total bedrest/sedentary) and Level 2 (with bathroom privileges).
  - Overall incidence of VTE 3.2%
    - Level 1 - 4.8% vs. 2.6% (P=0.007)
    - Level 2 - 4.6%vs. 1.9% (P<0.0001)

Yusen RD, et al. ASH 2007. Abstract #1862
Schellong SM, et al. ASH 2007. Abstract #1870.

What is meant by "Appropriate Prophylaxis"?

It means:

- The *right* Agent/modality . . .
- The *right* Dose/way . . .
- The *right* Duration . . .

- Used In the *right* Patient!

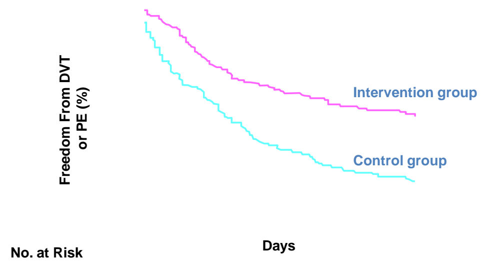
- This decision must be made while considering the balance of risk and benefit to the individual patient - It must "Add Up"

Strategies to increase prophylaxis rates: how well do they work?

- Passive strategy
  - Passive dissemination
    - Adherence to guidelines poor; not effective alone
- Active strategies: better improvements in prophylaxis practices
  - Documentation aids, quality assurance activities, audit and feedback
    - Appropriate prophylaxis rates approximately 80%
  - Computer-based decision aids
    - Most effective, appropriate prophylaxis rates approach 100%

Tooher et al. *Ann Surg*. 2005;241(3):397-415.

Electronic Alerts to Prevent VTE in Hospitalized Patients



No. at Risk

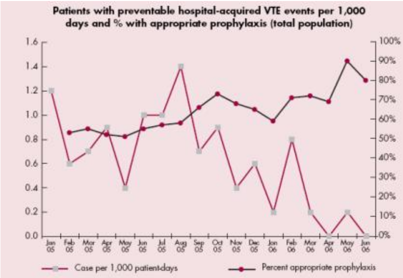
Days

Kucher N, et al. *N Engl J Med*. 2005;352:969-977.

The Human Alerts Trial

Kucher N, et al. *N Engl J Med*. 2005;352:969-977.

What A Successful Program Can Achieve



Maynard GA, et al. J Hosp Medicine 2009

Learning Objectives

1. Recognize the importance of VTE in hospitalized patients (medical) and why it is a healthcare priority
2. Identify the main factors contributing to the risk of VTE and methods for risk stratification
3. Critically review and assess the underlying evidence for prophylactic management strategies as it relates to both safety and efficacy.
4. Review the latest guidelines from the ACCP (2008), particularly with regard to the development of a formal prevention strategy at all hospitals