Perspectives on Deep Vein Thrombosis

Satellite Conference and Live Webcast
Wednesday, January 10, 2007
1:00-2:30 p.m. (Central Time)

Learning Objectives

- **This session is designed to:**
  - **Identify the signs and symptoms of DVT and pulmonary emboli (PE) and their prevention**
  - **Detail the efforts of the Coalition to Prevent DVT**
  - **Highlight perspectives of the patient, family, physician and nurse on the impact of DVT**
  - **Provide an opportunity for discussion of DVT**

Nursing Perspective

Rita Munley Gallagher, PhD, RN

DVT Assessment

Clinical Variable	Score
Active cancer (treatment ongoing or within previous 6 months or palliative)	1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	1
Recently bedridden for 3 days or more, or major surgery within the previous 12 weeks requiring general or regional anesthesia	1
Localized tenderness along the distribution of the deep venous system	1

DVT Assessment

Clinical Variable	Score
Entire leg swelling	1
Calf swelling at least 3 cm larger than that on the asymptomatic leg (measured 10 cm below the tibial tuberosity). In patients with symptoms in both legs, the more symptomatic leg was used.	1
Pitting edema confined to the symptomatic leg	1
Collateral superficial veins (nonvaricose)	1
Previously documented DVT	1
Alternative diagnosis at least as likely as DVT	-2

The Importance of Educating the Public About DVT

Melanie Bloom

41 Organizations Joined To Date

- Academy of Managed Care Providers (AMCP)
- American Academy of Home Care Physicians (AAHCP)
- American Academy of Nurse Practitioners (AANP)
- American Academy of Physicians Assistants (AAPA)
- American Academy of Physical Medicine and Rehabilitation (AAPM&R)
- American Association of Managed Care Nurses (AAMCN)

41 Organizations Joined To Date

- American Board of Managed Care Nursing (ABMCN)
- American College of Health Care Administrators (ACHA)
- American College of Chest Physicians (ACCP)
- American College of Physicians (ACP)
- American Geriatric Society (AGS)

41 Organizations Joined To Date

- American Nurses Association (ANA)
- American Obesity Association (AOA)
- American Osteopathic Association (AOA)
- American Pharmacists Association (APhA)
- American Public Health Association (APHA)
- American Society for Aesthetic Plastic Surgery (ASAPS)
- American Society for Bariatric Surgery (ASBS)
- American Society of Consultant Pharmacists (ASCP)
- American Society of Health Risk Managers (ASHRM)

41 Organizations Joined To Date

- American Society of Health-System Pharmacists (ASHP)
- American Society of Hematology (ASH)
- American Venous Forum (AVF)
- Association of Black Cardiologists (ABC)
- Barnes Jewish Hospital
- Case Management Society of America (CMSA)
- ClotCare Online Resource Center (www.clotcare.com)
- Hematology/Oncology Pharmacy Association (HOPA)

41 Organizations Joined To Date

- Emergency Nurses Association (ENA)
- The Leapfrog Group
- National Association of Managed Care Physicians (NAMCP)
- National Association of Orthopedic Nurses (NAON)
- National Alliance for Thrombosis and Thrombophilia (NATT)
- National Business Coalition on Health (NBCH)
- National Medical Association (NMA)
- National Quality Forum (NQF)

41 Organizations Joined To Date

- Society of Hospital Medicine (SHM)
- Society of Critical Care Medicine (SCCM)
- Visiting Nurse Associations of America (VNAA)
- Vascular Disease Foundation (VDF)

Making a Difference

- More than 80,000 letters and emails of support have been received
- "We watched the news about David and cried along with everyone. We loved him. He did great work. But my husband had a pain in his leg. And when we saw this about David, he decided to go get it checked. He had a deep-vein thrombosis."
- More than 2,000 people have shared their story with the Coalition

DVT is…

…a common but serious medical condition that occurs when a thrombus (blood clot) forms in one of the large veins, usually in the lower limbs, leading to either partially or completely blocked circulation which may result in complications, such as a pulmonary embolism (PE) and even death if not diagnosed and treated effectively.

Risk Factors for DVT

- Increasing age
- Immobility
- Stroke
- Paralysis
- Previous VTE
- Cancer and its treatment
- Major surgery (particularly involving the abdomen, pelvis or lower extremities)

Risk Factors for DVT

- Respiratory failure
- Trauma (especially pelvis, hip or leg fractures)
- Obesity
- Varicose veins
- Congestive heart failure
- Myocardial infarction
- Indwelling central venous catheters

Risk Factors for DVT

- Inflammatory bowel disease
- Nephrotic syndrome
- Pregnancy
- Oral contraceptives
- Hormone replacement
- Inherited clotting predisposition

Symptoms of DVT

- Pain
- Swelling
- Tenderness
- Discoloration/redness of the affected area
- Skin warm to the touch

DVT Statistics

- Two million Americans suffer from DVT
  - That is more than those who will die annually from breast cancer and AIDS combined
- 600,000 people are hospitalized in the US each year for DVT
- Pulmonary embolism (PE), claims up to 200,000 lives

DVT Statistics

- Fatal PE may be the most common preventable cause of hospital death in the US
  - Only one-third of hospitalized patients with risk factors for blood clots received preventive treatment
- Up to 60 percent of patients who undergo total hip replacement surgery may develop DVT

DVT Statistics

- More than 15 million Americans experience postphlebitic syndrome (PTS)
- The estimated cost for DVT/PE/PTS is $2.8-$4.8 billion each year

DVT Can Impact Anyone…

Jimmy Stewart

Richard Nixon

Jesse Ventura

Derrick Thomas

Lainie Kazan

…and is a *MAJOR* public health risk.

Coalition to Prevent DVT Mission Statement

To reduce the immediate and long-term dangers of deep-vein thrombosis (DVT) and pulmonary embolism (PE), which together comprise one of the nation's leading causes of death…the Coalition will educate the public, healthcare professionals and policy-makers about risk factors, symptoms and signs associated with DVT, as well as identify evidence-based measures to prevent morbidity and mortality from DVT and PE.

Steering Committee Members

- Georges Benjamin, M.D.
  - American Public Health Association
- Morgan Downey, J.D.
  - American Obesity Association
- Rita Munley Gallagher, Ph.D., R.N.
  - American Nurses Association
- Samuel Goldhaber, M.D.
  - Brigham and Women's Hospital
- Craig Kessler, M.D.
  - Georgetown University Medical Center ~ Representating National Quality Forum
- Robert Lavender, M.D.
  - University of Arkansas for Medical Sciences ~ Representing American College of Physicians

Steering Committee Members

- Geno Merli, M.D.
  - Thomas Jefferson University Medical Center
- Franklin Michota, M.D.
  - Cleveland Clinic Foundation ~ Representing Society of Hospital Medicine
- Ruth Morrison, B.S.N., R.N., C.V.N.
  - Brigham and Women's Hospital
- Victor Tapson, M.D.
  - Duke University Medical Center ~ Representing American College of Chest Physicians
- Jeffrey Weitz, M.D.
  - McMaster University ~ Representing American Society of Hematology

Venous Thromboembolism Future Challenges

Geno J. Merli, MD, FACP

Director Jefferson Center for Vascular Diseases

Jefferson Medical College

Thomas Jefferson University Hospital

VTE Future Challenges

- **Duration of VTE prophylaxis in the acute postoperative period**
- **Duration of secondary VTE prophylaxis in orthopaedic surgery**
- **Duration of Secondary VTE prophylaxis in cancer surgery**

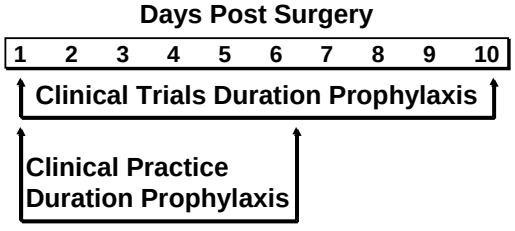
VTE Future Challenges

- **Improving the application of VTE prophylaxis in the hospitalized medically ill patient**
- **Duration of secondary VTE prophylaxis in the patient with Idiopathic DVT/PE or cancer patient with DVT/PE**

Postoperative Duration of VTE Prophylaxis

- **Clinic Trials: Prophylaxis studied for 7 to 10 days**
- **Clinical Practice: Prophylaxis applied for the time of hospitalization**
- **Challenge: Physician acceptance and application of evidence based duration of VTE prophylaxis**

Postoperative Duration of VTE Prophylaxis



Future Challenges Duration Acute VTE Prophylaxis Surgery

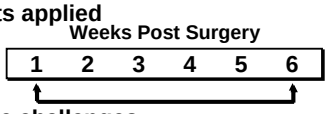
- Physician acceptance: duration acute VTE prophylaxis
- Standardize VTE prophylaxis through specialty societies
- Infrastructure which supports duration of VTE prophylaxis

Future Challenges Duration Acute VTE Prophylaxis Surgery

- Insurance and government support of duration of VTE prophylaxis
- New Oral Xa and IIa agents will impact management

Extended VTE Prophylaxis
Orthopaedic Surgery

- Clinical trials: Orthopaedic surgery data support Extended Prophylaxis
- Clinical practice: Variation in duration and agents applied



- Future challenges:
  - Standardize duration of VTE prophylaxis in orthopaedic surgery
  - Standardize the use of VTE prophylaxis regimens

Future Challenges Extended VTE Prophylaxis Orthopaedic Surgery

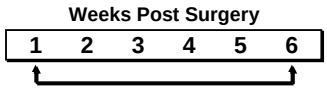
- Physician Acceptance: Extended VTE Prophylaxis in orthopaedic surgery
- Standardize VTE prophylaxis through orthopaedic societies
- Establish the infrastructure which supports extended VTE prophylaxis

Future Challenges Extended VTE Prophylaxis Orthopaedic Surgery

- Insurance and government support of extended VTE prophylaxis
- New Oral Xa and IIa agents will impact management

Extended VTE Prophylaxis
Cancer Surgery

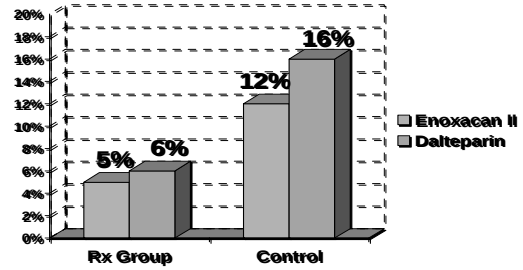
- Clinical trials: Cancer surgery data beginning to support Extended Prophylaxis
- Clinical practice: Inconsistent application of VTE prophylaxis



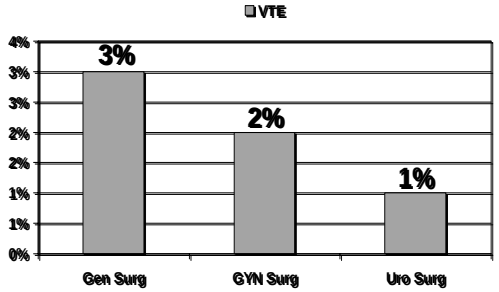
- Future challenges:
  - More data on duration of VTE prophylaxis in cancer surgery
  - Diversity of cancer patient populations

Extended VTE Prophylaxis
Cancer Surgery

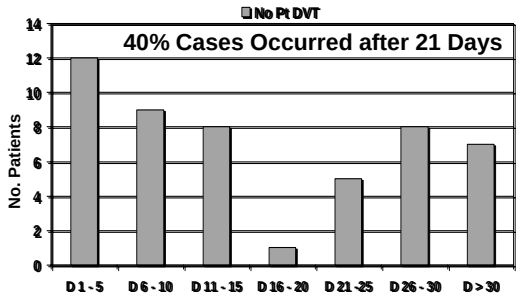
Enoxaparin 40 mg, Q24 hrs x 30 days
Dalteparin 5000 U, Q24hrs x 30 days



Clinical Outcome Cancer Surgery
Incidence VTE
@RISTOS Project



Incidence VTE
@RISTOS Project



Risk Factors Cancer Surgery
@RISTOS Project

Risk Factors VTE	Odds Ratio	95% CI
Age > 60 years	2.63	1.27 5.71
Previous VTE	5.98	2.13 16.80
Advance Cancer	2.68	1.37 5.24
Anesthesia > 2 hrs	4.50	1.06 19.04
Bed Rest > 3 days	4.37	2.45 7.78

The Odds Ratio were the same for late VTE

Extended VTE Prophylaxis
Cancer Surgery

- **In Selected High-Risk General Surgery patients including those who have undergone major cancer surgery, suggested post-hospital discharge prophylaxis with LWMH [2A]**
  - **Enoxaparin 40mg, SC, Q24hrs**
  - **Dalteparin 5,000 IU, SC, Q24hrs**

2A = RCTs without important limitations, Risk/Benefit not clear
2C= Observational Studies, Risk Benefit not clear

Extended VTE Prophylaxis
Cancer Surgery

- **Patients undergoing GYN Cancer Surgery and who are > 60 years of age or have previously experienced a VTE recommend continuing prophylaxis for 2 to 4 weeks [2C]**
  - **Enoxaparin 40mg, Q24hrs**
  - **Dalteparin 5,000 IU, Q24hrs**

2A = RCTs without important limitations, Risk/Benefit not clear
2C= Observational Studies, Risk Benefit not clear

Future Challenges Extended VTE Prophylaxis Cancer Surgery

- Well designed clinical trials in extended VTE prophylaxis in cancer surgery
- Establish the infrastructure which supports extended VTE prophylaxis
- Insurance and government support of extended VTE prophylaxis
- New Oral Xa and IIa agents will impact management

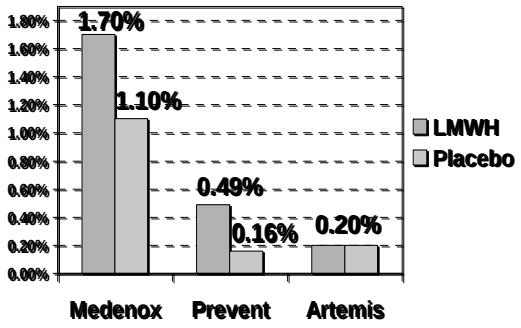
Medically-ill Patient

Low-Molecular-Weight Heparin Clear Benefits over Placebo

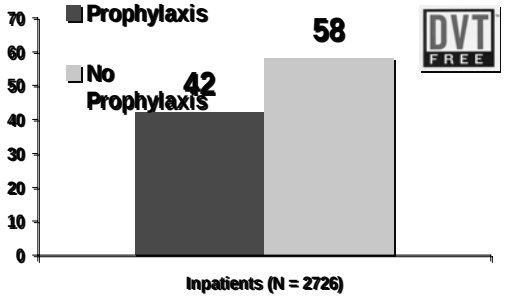
Study	RRR	Thromboprophylaxis	Patients with VTE (%)
MEDENOX	63%	Placebo	14.9*
		Enoxaparin 40mg	5.5
P<0.001 PREVENT	45%	Placebo	5.0
		Dalteparin	2.8
P=0.0015 ARTEMIS	47%	Placebo	10.5†
		Fondaparinux	5.6

*VTE at day 14; †VTE at day 15
RRR= Relative Risk Reduction

Major Bleeding



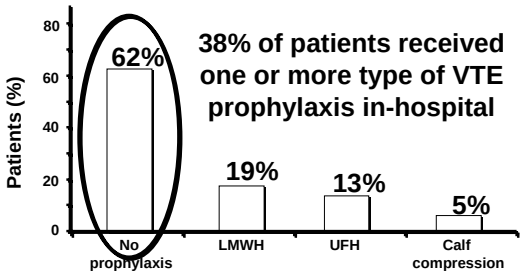
DVT FREE Study



DVT FREE Study

- Patient status at the time of diagnosis (5451)
  - Outpatient 2725 (50%)
  - Inpatient 2726 (50%)
- Inpatient status at diagnosis (2726)
  - Non-ICU 2118 (78%)
  - ICU 605 (22%)
  - Mechanical ventilation 441 (16%)

IMPROVE Registry Results



38% of patients received one or more type of VTE prophylaxis in-hospital

DVT Incidence and Thromboprophylaxis

étape	Incidence of DVT,n (%)	Thromboprophylaxis Received (%)
Patients at major risk	58 (1.9)	55.8
Patients at moderate risk	36 (0.9)	38.4
Patients at low risk	70 (0.7)	26.7

Computer Reminder System

- Computer program linked to patient database to identify consecutive hospitalized patients at risk for VTE
- Patient randomized to intervention group or control group
- In the intervention group the physicians were alerted to the VTE risk and offered the option to order VTE prophylaxis

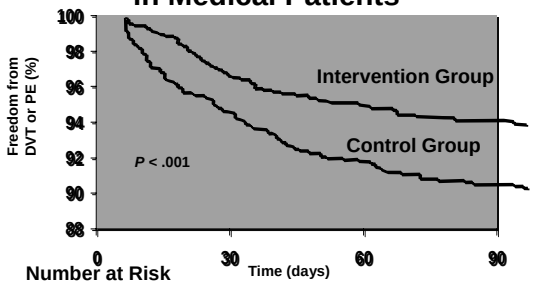
Computer Reminder System

- Point scale for VTE risk
  - Major risk: cancer, prior VTE, hypercoagulability (3 points)
  - Intermediate risk: major surgery (2 points)
  - Minor risk: advanced age, obesity, bedrest, HRT, use of oral contraceptives (1 point)
- VTE prophylaxis (graduated elastic stockings, IPC, UFH, LMWH, warfarin)

Electronic Alerts to Prevent VTE in Medical Patients

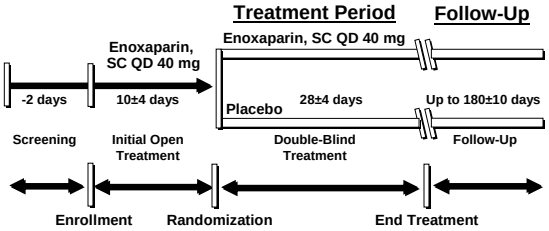
Measure	Intervention Group (n = 1255)	Control Group (n = 1251)	*P* Value
Mechanical	125 (10.0)	19 (1.5)	< .001
compression stockings	52 (4.1)	7 (0.6)	< .001
pneumatic boots	73 (5.8)	12 (1.0)	< .001
Pharmacological	296 (23.6)	163 (13.0)	< .001
UFH	213 (17.0)	81 (6.5)	< .001
warfarin	28 (2.2)	41 (3.3)	.11
enoxaparin	55 (4.4)	41 (3.3)	.18

Electronic Alerts to Prevent VTE in Medical Patients



Number at Risk				
Intervention Group	1255	977	900	853
Control Group	1251	876	893	839

Exclaim Study



- A double blind, placebo controlled, parallel, multicenter study on extended VTE prophylaxis in acutely ill medical patients with prolonged immobilization.

ACCP Recommendations At-Risk Medical Patients

- In acutely ill medical patients who have been admitted to the hospital with CHF or severe respiratory disease, or who are confined to bed and have 1 or more additional risk factors, including active cancer, previous VTE, sepsis, acute neurologic disease, or IBD, ACCP recommends.

ACCP Recommendations At-Risk Medical Patients

- Low-molecular-weight heparin (1A)
  - Enoxaparin 40 mg, SC, QD
  - Dalteparin 5000 U, SC, QD
  - Fondaparinux 2.5 mg, SC, QD
- Low-dose UFH (1A)
  - 5000 U, SC, q8, or 12h

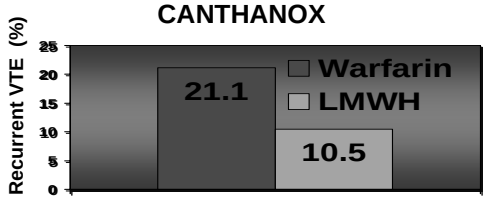
Future Challenges VTE Prophylaxis Medically-ill Patient

- Physician acceptance VTE prophylaxis in medically-ill patient.
- Standardize VTE prophylaxis through medical societies and publications.
- Establish system which supports VTE prophylaxis (computer or paper systems).
- New oral Xa and IIa agents will impact management.

Duration Secondary VTE Prophylaxis Cancer Patient Idiopathic DVT/PE

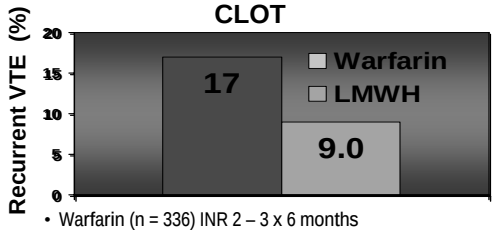
LMWH in Cancer Patient

CANTHANOX



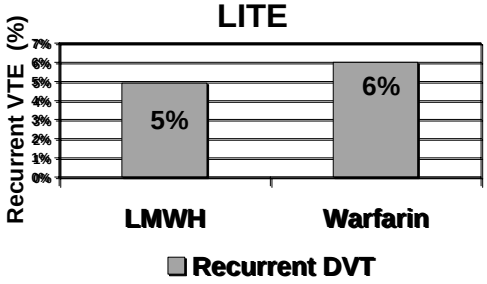
- Warfarin (n = 71) INR 2 – 3 x 3 months
- Warfarin major bleeding = 8%
- LMWH (n = 67) enoxaparin 1.5 mg/kg SC QD x 3 months
- LMWH major bleeding = 0%

LMWH in Cancer Patients
CLOT



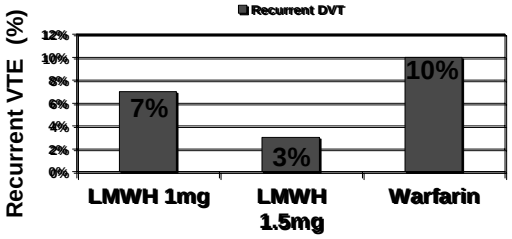
- Warfarin (n = 336) INR 2 – 3 x 6 months
- Warfarin major bleeding = 4%
- LMWH (n = 336) dalteparin 200 IU/kg SC QD x 1 month,
- then 150 IU/kg SC QD x 5 months
- LMWH major bleeding = 6%

LMWH in Cancer Patients
LITE



Tinzaparin 175mg/kg/Q24hrs
UFH followed by warfarin INR 2-3
Treatment 84 days

LMWH in Cancer Patients
ONCENOX



Enoxaparin 1mg/kg/Q12hrs then 1mg/kg/Q24hrs
Enoxaparin 1mg/kg/Q12hrs then 1.5mg/kg/Q24hrs
Enoxaparin 1mg/kg/Q12hrs the warfarin 2-3
Treatment 175 days

ACCP Recommendations 2° DVT Prevention

- **DVT and Cancer:**

  LMWH for 3 – 6 months [1A] then

  WARFARIN (INR 2 – 3) for indefinite

  period [1C]

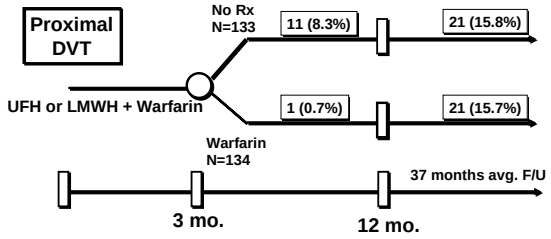
Future Challenges Secondary VTE Prophylaxis Cancer Patient

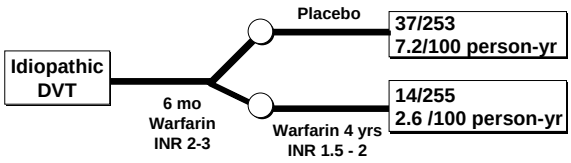
- **Physician acceptance of LMWH for secondary VTE Prophylaxis**
- **Insurance and Government support of treatment modality**
- **Infrastructure to support this approach to treatment**

Future Challenges Secondary VTE Prophylaxis Cancer Patient

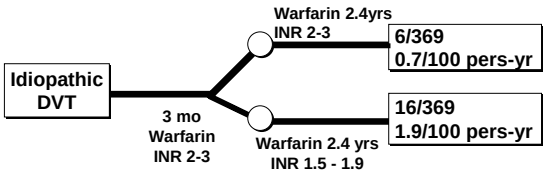
- **Demonstration of greater safety and efficacy**
- **Demonstration of improved survival**
- **New Oral Xa and IIa agents will impact management**

Idiopathic DVT: 3 Months vs 1 Year Treatment



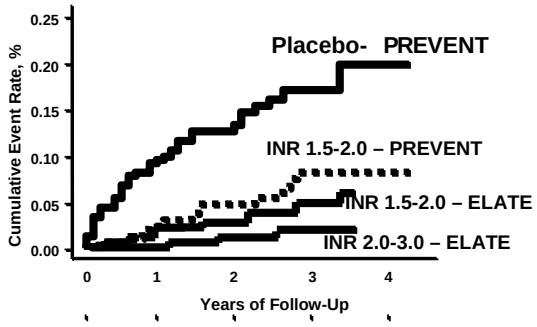


	No./100 person on-yr		
	Placebo	Warfarin	*P*
Major bleeding	2 (0.4)	5 (0.9)	0.25
Deaths	8 (1.4)	4 (0.7)	0.26



	No Events(No./100 person-yr)		
	Warfarin 2 3	Warfarin 1.5 19	*P*
Major bleeding	8 (0.9)	9 (1.1)	0.25
Deaths	8 (0.9)	16 (1.9)	0.26

PREVENT and ELATE
Recurrent VTE



ACCP Recommendations 2° DVT Prevention

- Recommend adjusted INR to 2 – 3 range for all 2° prevention [1A]
- Recommend against low-intensity warfarin at INR of 1.5 – 1.9 [1A]
- First DVT idiopathic: 6 – 12 months INR 2 – 3 [1A]

ACCP Recommendations 2° DVT Prevention

- First DVT idiopathic: Indefinite treatment at INR 2 – 3 [2A]
- Patients should be assessed periodically during anticoagulation to evaluated risk benefit [1C]

Future Challenges Secondary VTE Prophylaxis Idiopathic VTE Patient

- **Physician acceptance of duration of treatment of idiopathic VTE**
- **More specific risk assessment methods to predict continued VTE secondary prophylaxis**
- **New Oral Xa and IIa agents will impact management**