XXXI Congreso Nacional de la Sociedad Española de Medicina Interna (SEMI)
II Congreso Ibérico de Medicina Interna
VII Congreso de la Sociedad Asturiana de Medicina Interna

Tratamiento extendido o prolongado de la Enfermedad Tromboembólica Venosa

VENOUS THROMBOEMBOLISM EXTENDED PROPHYLAXIS

Hospital Garcia de Orta, EPE.
Almada, Portugal

Hospital Garcia de Orta, E.P.E.

DISCLOSURES

- Scientific Consulting for Pfizer and Sanofi Aventis

VENOUS THROMBOEMBOLISM EXTENDED PROPHYLAXIS

A. Background
B. Scope
C. Key priorities for minimizing the problem

A. BACKGROUND

Hospital Interventions
Quality Improvement Organization
Support Center

- More than 900.000 Americans have VTE -each year
  -
  -
- **In ± 300.000 cases, PE is fatal;**
  -
  -

Gerotziafas and Samama. *Curr Opin Pulm Med*. 2004;10:356-365.

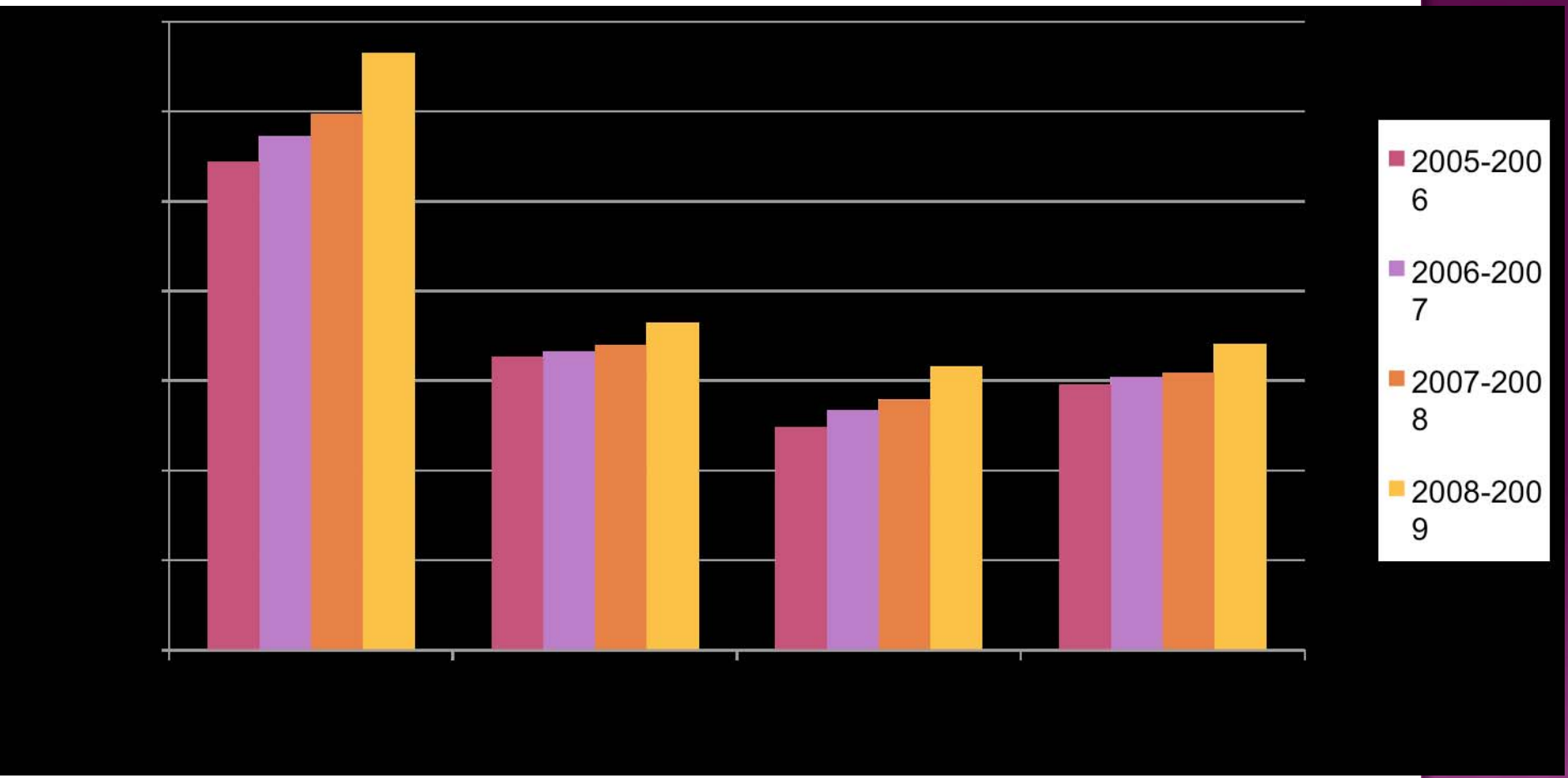
Heit et al., on behalf of the VTE impact assessment group. Poster #68. Presented at: 47th Annual Meeting and Exposition,
American Society of Hematology; December 10-13, 2005; Atlanta, Ga.

Murin et al. *Thromb Haemost*. 2002;88:407-414.

HESonline™
HOSPITAL EPISODE STATISTICS

Primary diagnosis: Pulmonary Embolism

ICD 10 (3 character)



http://www.hesonline.nhs.uk/ (accessed 20/10/2010)

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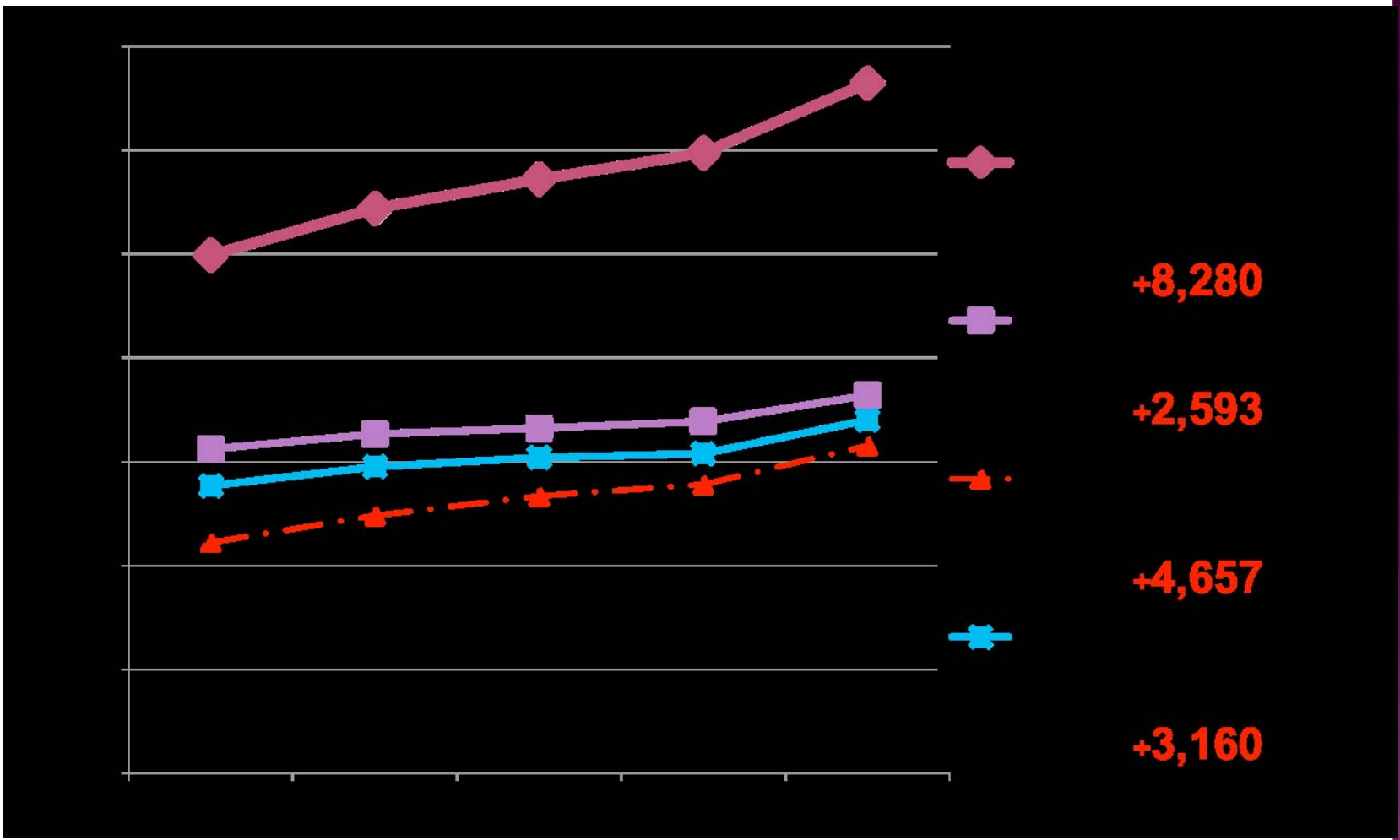
NHS
The Information Centre
for health and social care

NATIONAL STATISTICS



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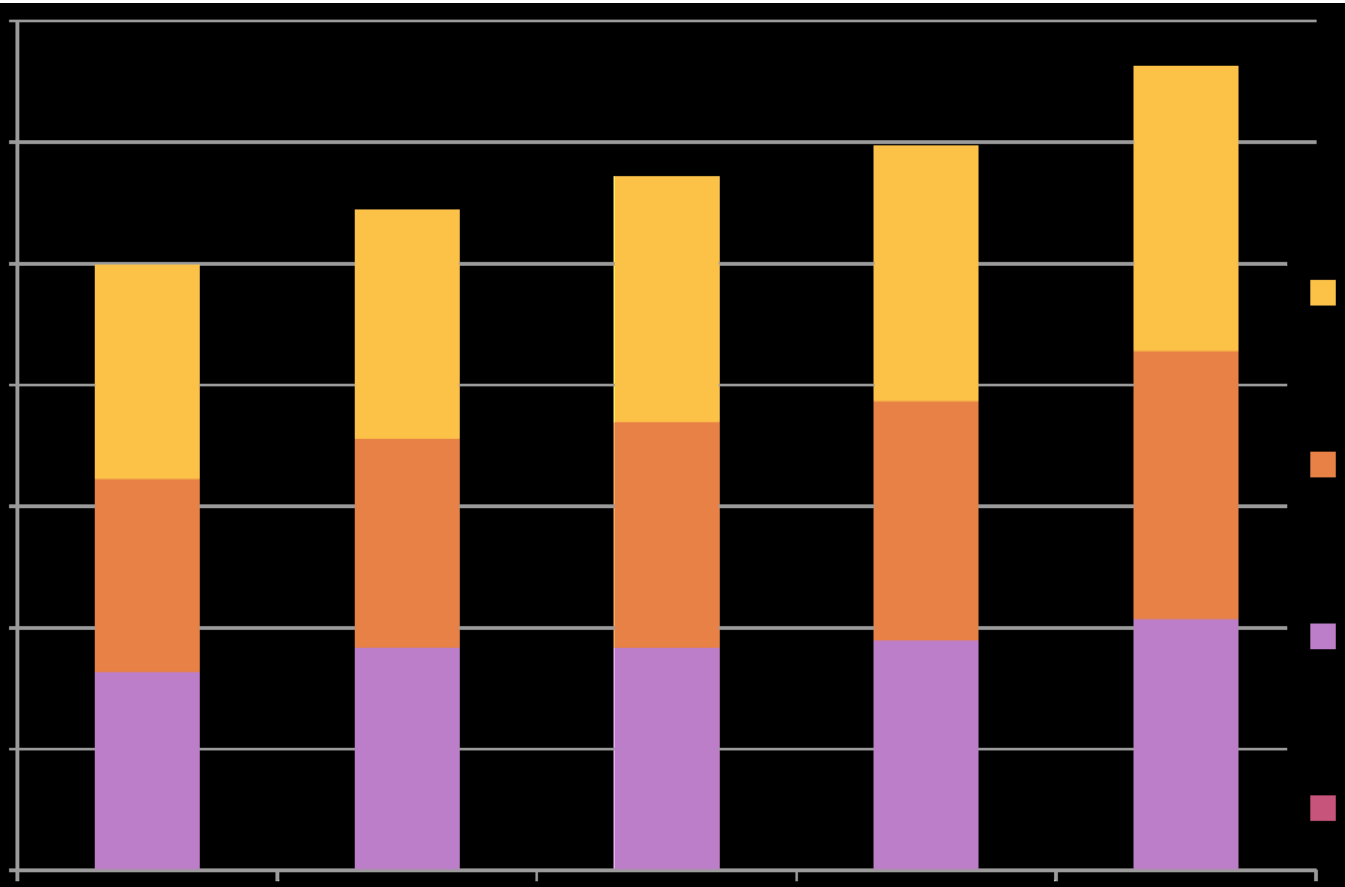


OUTPATIENT AND INPATIENT VTE ARE LINKED

1897 patients with a confirmed episode of VTE

- 74% of VTEs present in outpatients.
  - 42% of outpatient VTE patients have had recent surgery or hospitalization.
    - Only 40% had received VTE prophylaxis.

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

VENOUS THROMBOEMBOLISM EXTENDED PROPHYLAXIS

Scope

- medical illness
- cancer patients

REGISTRY DATA
HIGHLIGHT THE UNDERUSE OF THROMBOPROPHYLAXIS

Why??

DVT-FREE

RIETE

IMPROVE

Only a minority of hospitalized medical patients receive thromboprophylaxis

Goldhaber SZ, Tapson VF. *Am J Cardiol* 2004;93:259-62.
Monreal M, et al. *J Thromb Haemost* 2004;2:1892-8.
Tapson V, et al. *Blood* 2004;104:11. Abstract #1762.

RISK OF VTE IN MEDICAL PATIENTS

- **Nursing home residents are more than twice as likely as non-residents to develop DVT/PE[1]**
- **VTE prophylaxis remains underutilized or inadequate in hospitalized medical patients[2,3]**
  - **Underuse often occurs because of unwarranted safety concerns[4]**

1. Heit JA, et al. *Arch Intern Med.* 2002;162(11):1245-1248.
2. Goldhaber SZ, Tapson VF. *Am J Cardiol.* 2004;93(2):259-262.
3. Anderson FA Jr, et al. *Ann Intern Med.* 1991;115(8):591-595.
4. US Dept of Health and Human Services. *The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism*. Bethesda, MD: September 2008.

Why Underuse ?

Barriers to VTE Prophylaxis

Physicians have not accepted the data on VTE in the medically-ill hospitalized patient

Reasons

- Length of stay continues to shorten !
- Duration of prophylaxis ??
- **Iatrogenic complications of prophylaxis ??**

Acquired continuing risk factors and recurrent VTE

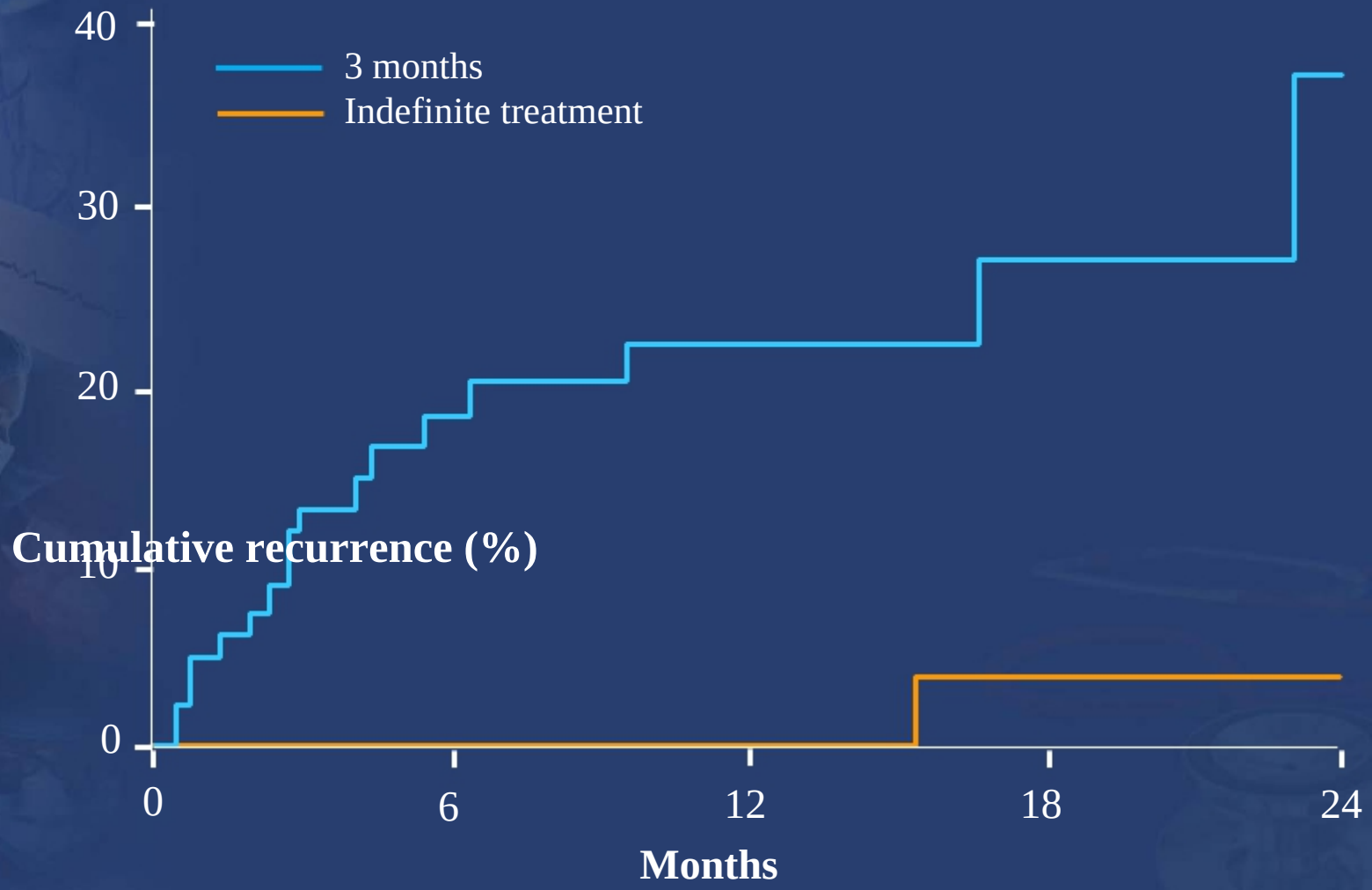
Risk Factors

BASELINE FEATURES	R.Recurrence.
Active cancer	approx. 3
- Metastatic vs non-metastatic	approx. 3
- Chemotherapy	approx. 2
Chronic medical diseases	approx. 2
Multiple (idiopathic) VTE	approx. 1.5
APLA syndrome	2-4

APLA=antiphospholipid ; VTE=venous thromboembolism

Kearon C, *Hematology* 2004

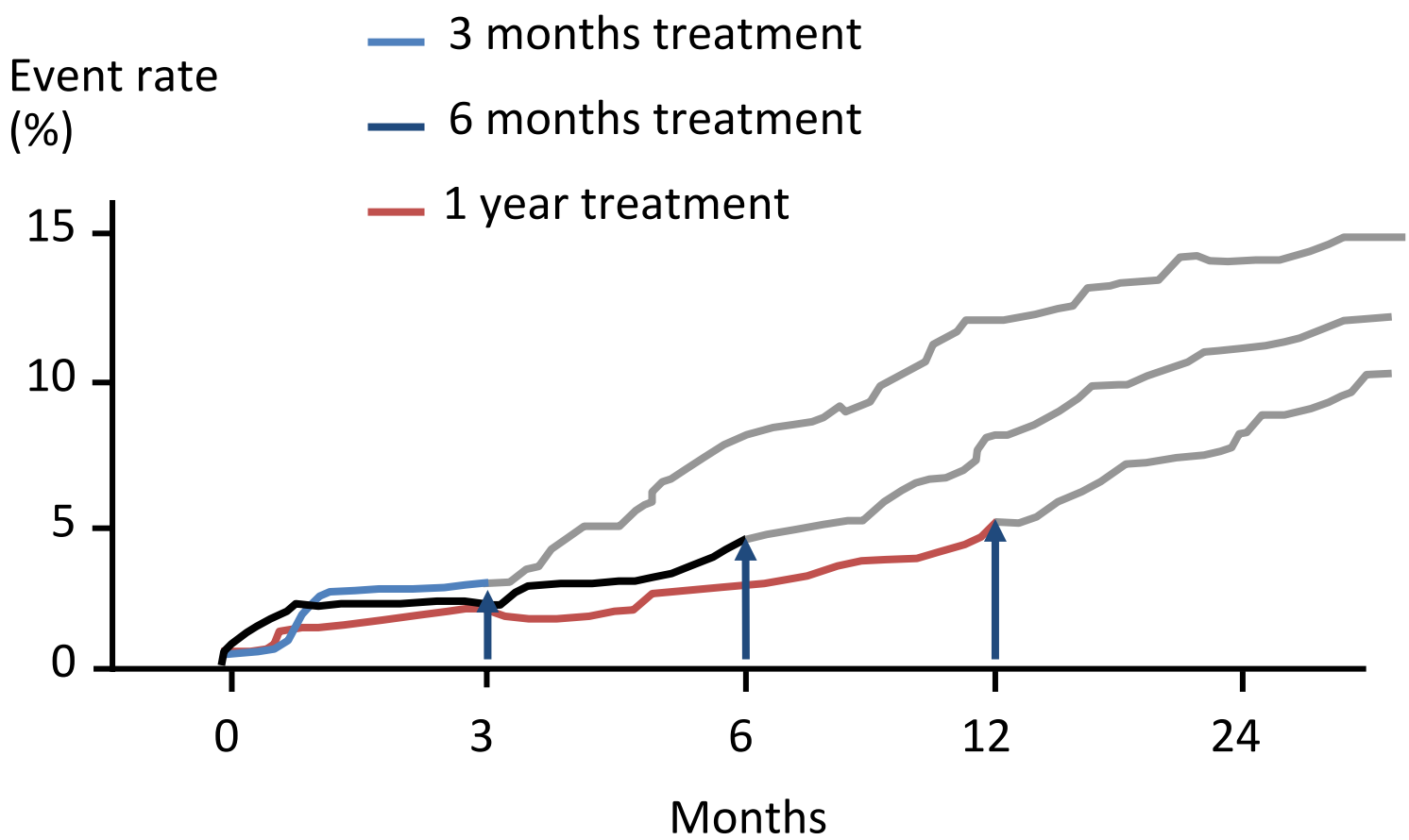
3 months versus indefinite oral anticoagulation for idiopathic DVT



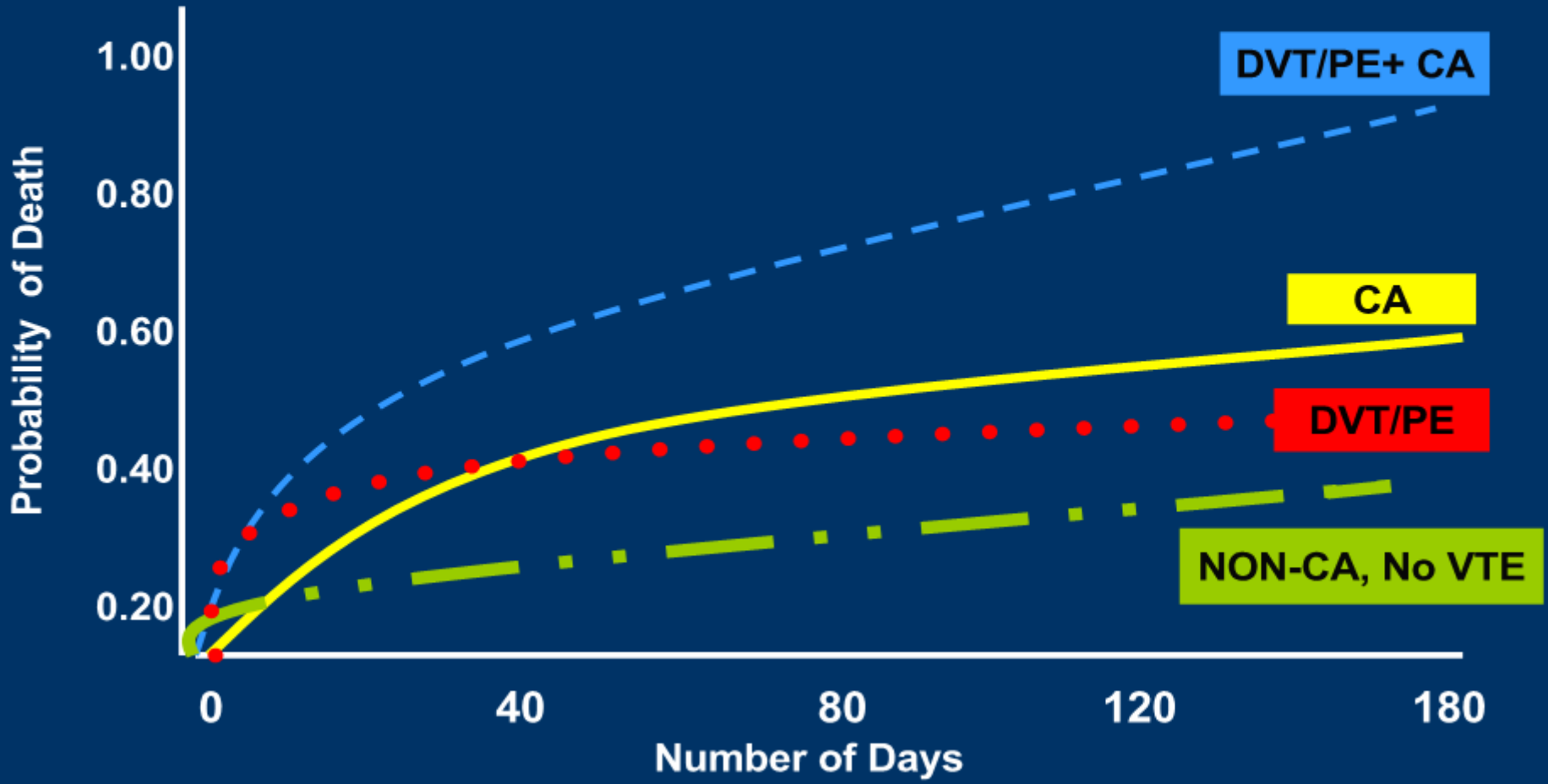
Kearon C, et al. N Engl J Med. 1999;340:901-7.

LIFEBLOOD THE Thrombosis CHARITY

Recurrence of VTE after stopping oral anticoagulation



Probability of Death Within 183 Days of Initial Hospital Admission in Cancer Patients With or Without Concurrent VTE



DVT/PE = deep vein thrombosis or pulmonary embolism; CA = cancer.

Levitan N, et al. *Medicine (Baltimore)*. 1999;78:285-91. Permission requested.

Prophylaxis

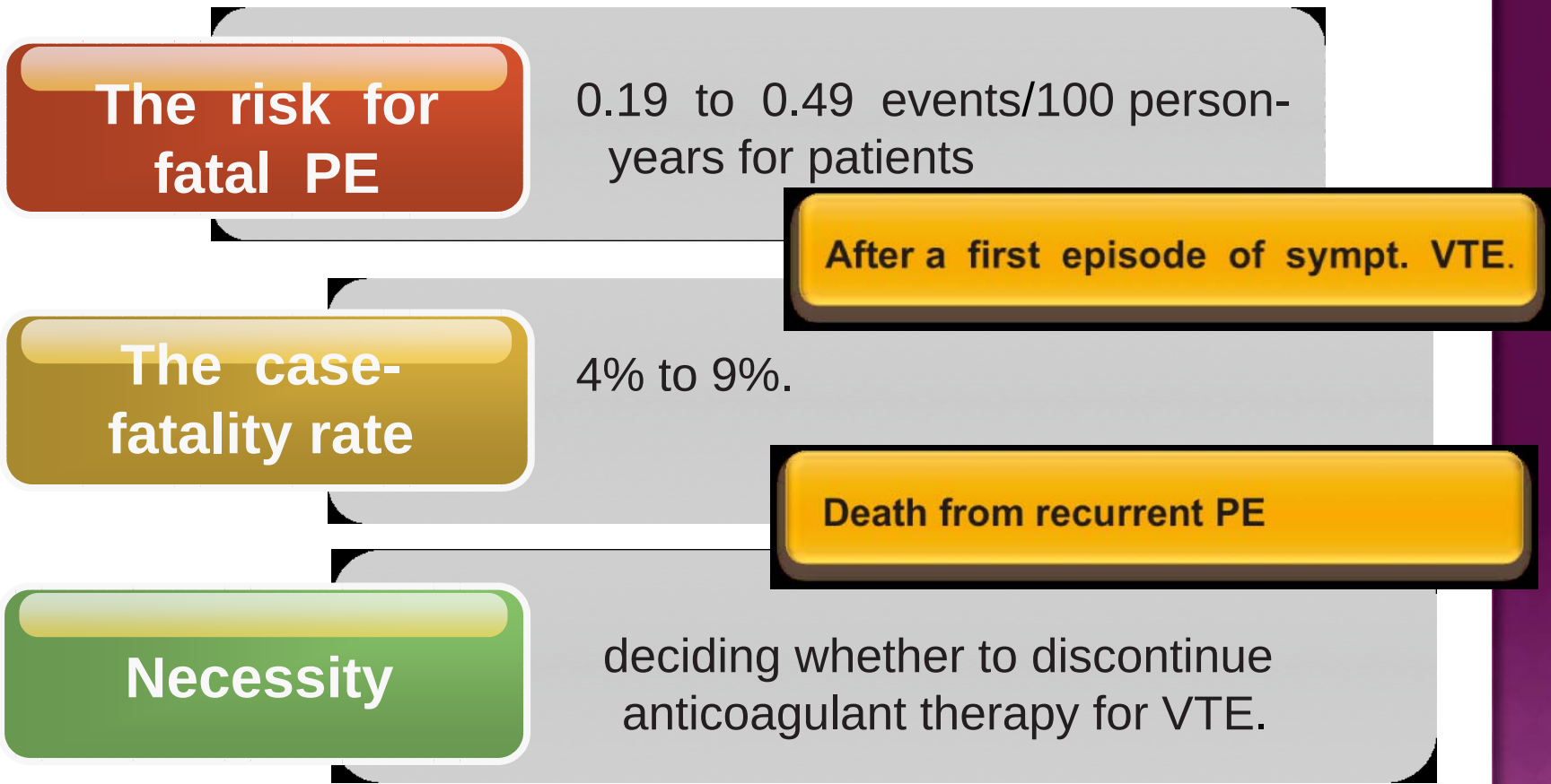
Controversies

Prophylaxis in Medical Patients: Ambulatory Cancer Patients

- The role of thromboprophylaxis in ambulatory cancer patients during chemotherapy and hormone therapy **is not established**

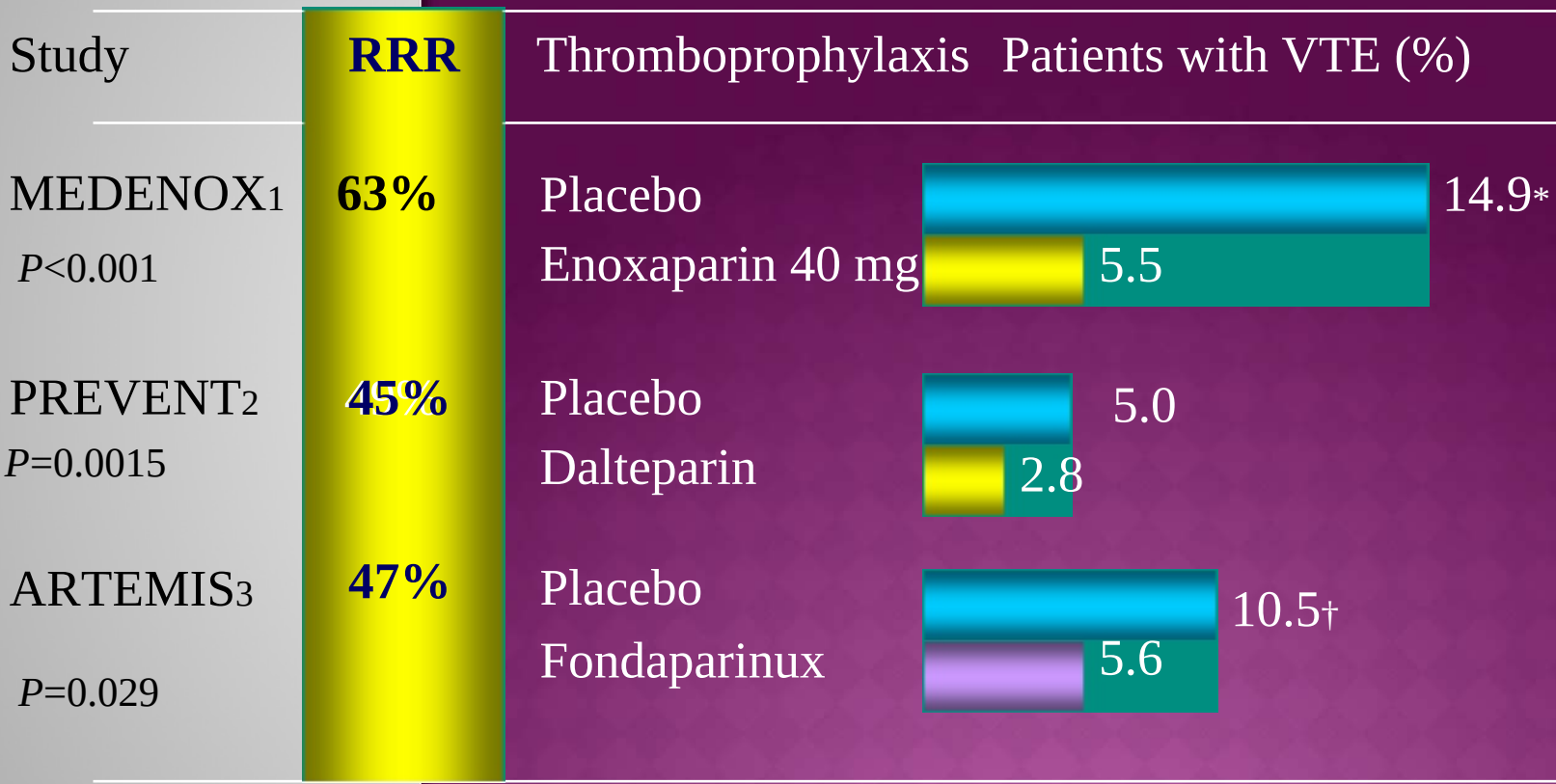
(8th ACCP Guidelines)

The Risk for Fatal Pulmonary Embolism after Discontinuing Anticoagulant Therapy for Venous Thromboembolism



Douketis,JD; Chu Shu Gu; Schulman,S; Ghirarduzzi,A; Pengo, V ; Prandoni,P
December 4, 2007 vol. 147 no. 11 766-774

LMWH: Clear benefits over placebo

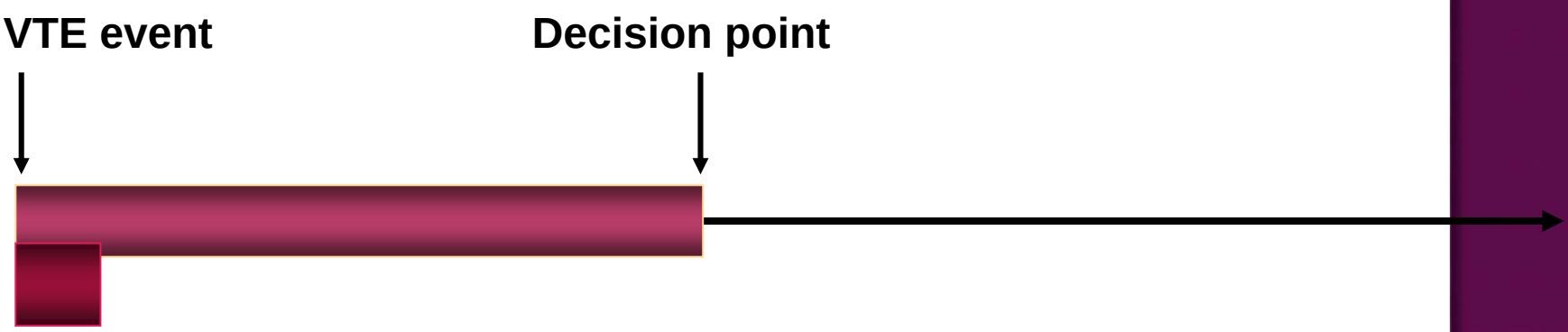


*VTE at day 14; †VTE at day 15. RRR = relative risk reduction

1Samama MM et al. *N Engl J Med*. 1999;341:793-800; 2Leizorovicz A et al. *Circulation*. 2004;110:874-879;Cohen AT et al. *BMJ*. 2006;332:325-329.

LifeBlood
The Thrombosis
Charity

Treatment and secondary prevention of VTE



Acute	Continue	How long?
Heparin or LMWH together with a VKA (e.g. warfarin) untill an INR of 2.0-3.0 is achieved	VKA (e.g. warfarin) INR 2.0-3.0	3-6-12 months or lifelong

Risk of VTE (5-7%/year)
vs.
Risk of bleeding (3-4%/year)

www.thrombosis-charity.org.uk (accessed 11/11/2010)

OPTIMAL DURATION OF ANTICOAGULATION AFTER VTE

OAC, oral anticoagulation

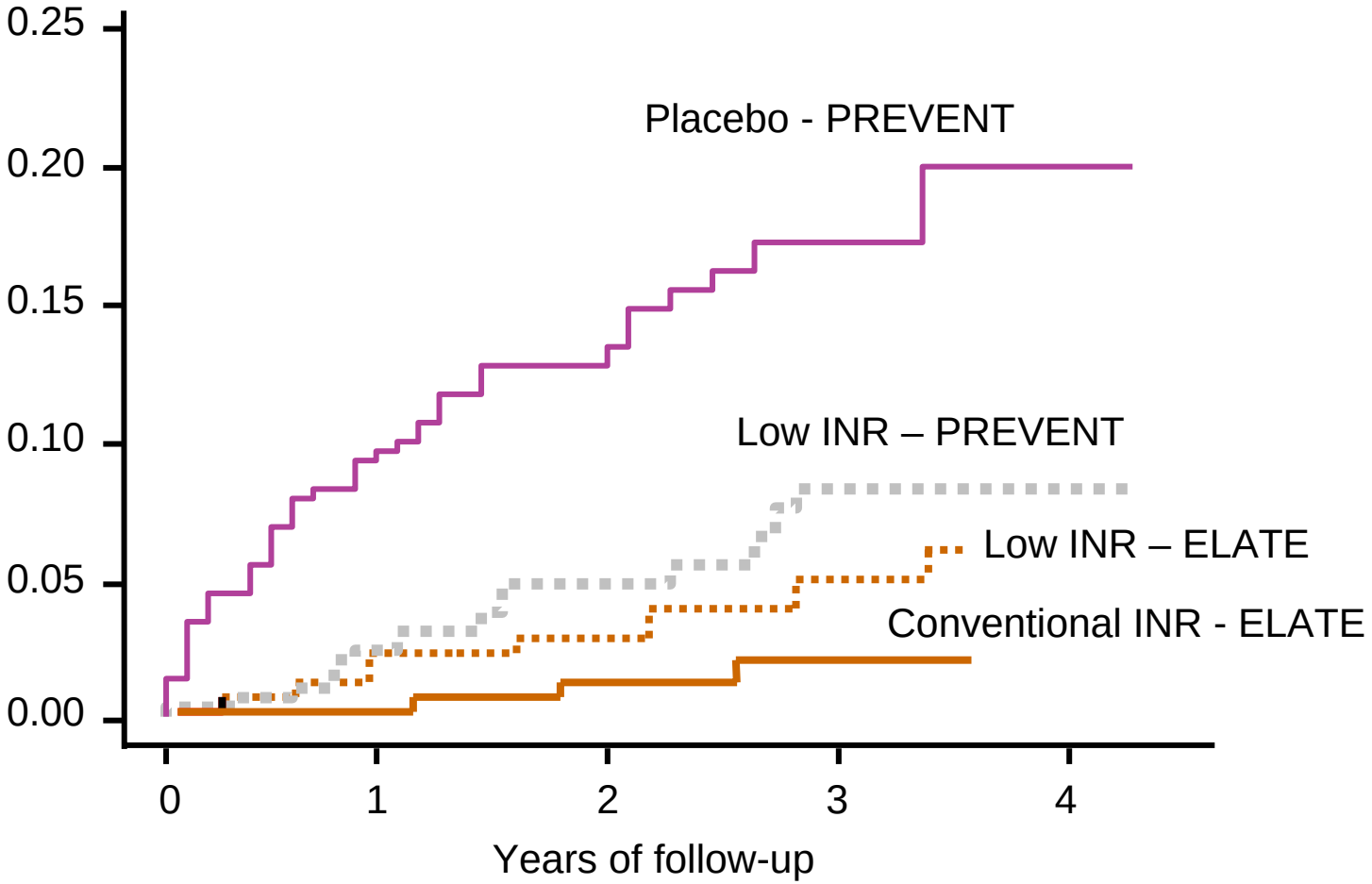
Reference	No. of patients	Long OAC months	Short OAC months	Follow up months	Recurrent VTE		Major bleeding	
					Long OAC	Short OAC	Long OAC	Short OAC
DURAC I	897	6	1.5	24	9.5%	18.1%	1.1%	0.2%
LAFIT	162	27	3	10	1.3%	27.4%	3.8%	0.0%
WODIT-DVT	267	12	3	12	3.0%	8.3%	3.0%	0.8%
WODIT-PE	326	6-12	3	32.7	4.1%	9.1%	1.8%	0.0%
DOTAVK	539	6	3	15	8.7%	8.1%	2.6%	1.9%
DURAC II	227	Indefinite	6	43	2.6%	20.7%	8.6%	2.7%

Schulman S, et al. (DURAC I). N Engl J Med 1995;332:1661-5.
Kearon Cet al. (LAFIT study). N Engl J Med 1999;340:901-7.
Agnelli G et al. N Engl J Med 2001;345:165-9.
Agnelli G, et al. Ann Intern Med 2003;139:19-25.
Pinede Let al. (DOTAVK study). Circulation 2001;103:2453-60.
Schulman Set al. (DURAC II). N Engl J Med 1997;336:393-8.

INTENSITY OF ANTICOAGULANT THERAPY

Recurrent VTE

Cumulative event rate (%)



Ridker PM et al. N Engl J Med 2003; 348:1425-34

Kearon C et al. N Engl J Med 2003;349:631-9

EXCLAIM: EXTENDED-DURATION ENOXAPARIN 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

NNT = 46 patients to avoid one VTE event.

NNT = 224 to result in one major bleeding event.

Hull RD, et al. Abstract presented at: ISTH, July 8-11, 2007, Geneva, Switzerland.

EXCLAIM

Conclusion

Reduction of VTE in acutely ill medical patients with:

- ✓ level I immobility,
- ✓ those older than 75 years, and
- ✓ women.

- Major bleeding not increased in elderly patients.

Hull RD et al. *Ann Intern Med*. 2010;153:8-18.

C. KEY PRIORITIES FOR MINIMIZING THE PROBLEM

1. **Assessing the risks of VTE vs bleeding**
2. **Reducing the risk of VTE**
3. **Patient information and planning for discharge**

1. Balancing

the risk of VTE recurrence and the risk of bleeding

- Is very difficult, because of the different entities
  - VTE is seen as a complication
  - **Meanwhile hemorrhage is an iatrogenic event**

Preventing VTE

2. *System of Care*

Admission

VTE Risk Assessment

SAFETY

Application of Prophylaxis

Methods

Order Sets

Reminder Stickers

Computer

Pharmacy Driven

Nurse Driven

Team

Metrics

TEAM
Physician + Nurse + Pharmacist + Patient

Education

Prophylaxis Ordered

Prophylaxis Given

Bleeding

DVT PE

Re-assess Risk

New Arena of Care

30 Days Post Discharge

3. ATTENTION TO TRANSITIONS OF CARE

- Ensure adequate training of the patient
  - **Education** on medications, diet, follow up appointments, lab monitoring, dietary precautions, and adverse reactions or drug-drug interactions
  - Education for family
  - Referral to anticoagulation clinic
  - Hospital must have explicit documentation of this training/education in the chart

PATIENT SAFETY
QUALITY IMPROVEMENT ORGANIZATION SUPPORT CENTER

NEW DRUGS

Patient preferences ???

Phase 3 Secondary Prevention (Extension) Trials

Study (Ongoing)	Oral Agent Tested	Comparator	N*	Treatment Duration
RE-MEDY	Dabigatran etexilate 150 mg BID	Warfarin PRN (INR 2.0-3.0) (All patients received 3-6 months of anticoagulation for symptomatic acute VTE before randomization)	2700	18 months
RE-SONATE	Dabigatran etexilate 150 mg BID	Placebo (All patients received 6-18 months of VKA for symptomatic acute VTE before randomization)	1462	6 months
AMPLIFY-EXT	Apixaban 2.5 mg BID 5.0 mg BID	Placebo (All patients completed intended treatment for DVT or PE before randomization)	2430	12 months
EINSTEIN-EXT (completed)	Rivaroxaban 20 mg QD	Placebo (All patients received 6-12 months of anticoagulant treatment for symptomatic acute VTE before randomization)	1197	6-12 months

*Estimated enrollment

Duration of Secondary Thromboprophylaxis:

Recommendations From the 8th ACCP Evidence-Based Clinical Practice Guidelines

Duration	Indication
3 months	• VTE secondary to a transient (reversible) risk factor *(grade 1A)* • 1st isolated, unprovoked distal DVT *(grade 2B)*
At least 3 months	• Unprovoked VTE *(grade 1A)* [more than 3 months, risk-benefit should be evaluated for long-term treatment *(grade 1C)*]
Long-term	• 1st unprovoked proximal VTE, absent risk factors for bleeding and good anticoagulant monitoring achievable *(grade 1A)* • 2nd unprovoked VTE *(grade 1A)* • DVT and cancer: LMWH for the first 3-6 months *(grade 1A)*; subsequent anticoagulant therapy with VKA or LMWH indefinitely or until cancer resolution *(grade 1C)*

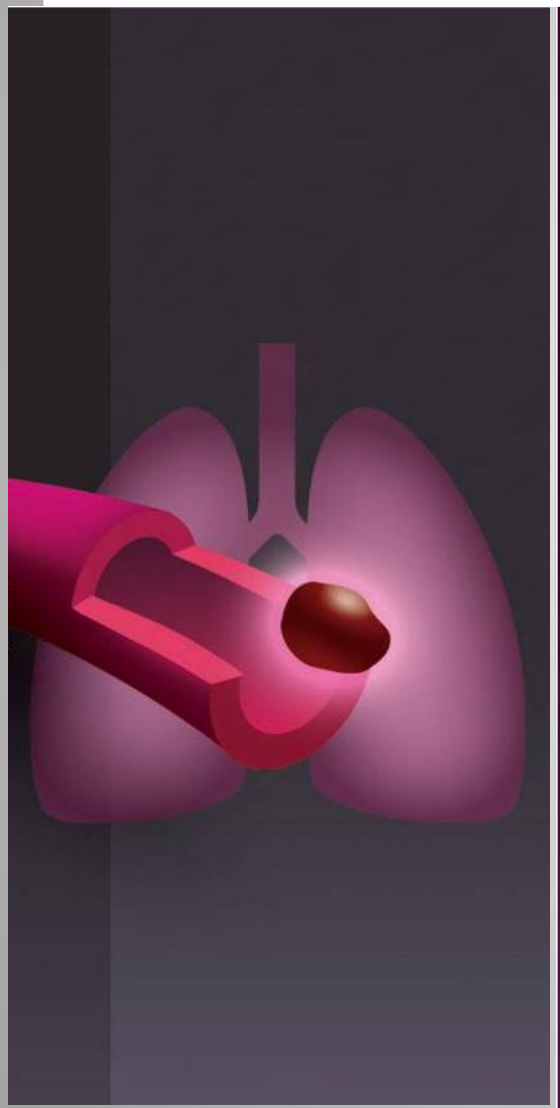
Thrombosis

Adapted from: Kearon C, et al. *Chest*. 2008;133;454S-545S.

theheart.org MedscapeCME

The future

THROMBOEMBOLISM EXTENDED PROPHYLAXIS



- Efficient prediction models
  - Identification of patients in whom anticoagulation can be safely px / withdrawn

✓**Availability of safer antithrombotic drugs**

Obrigada