Perioperative Thrombosis and Anticoagulation

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Disclosures

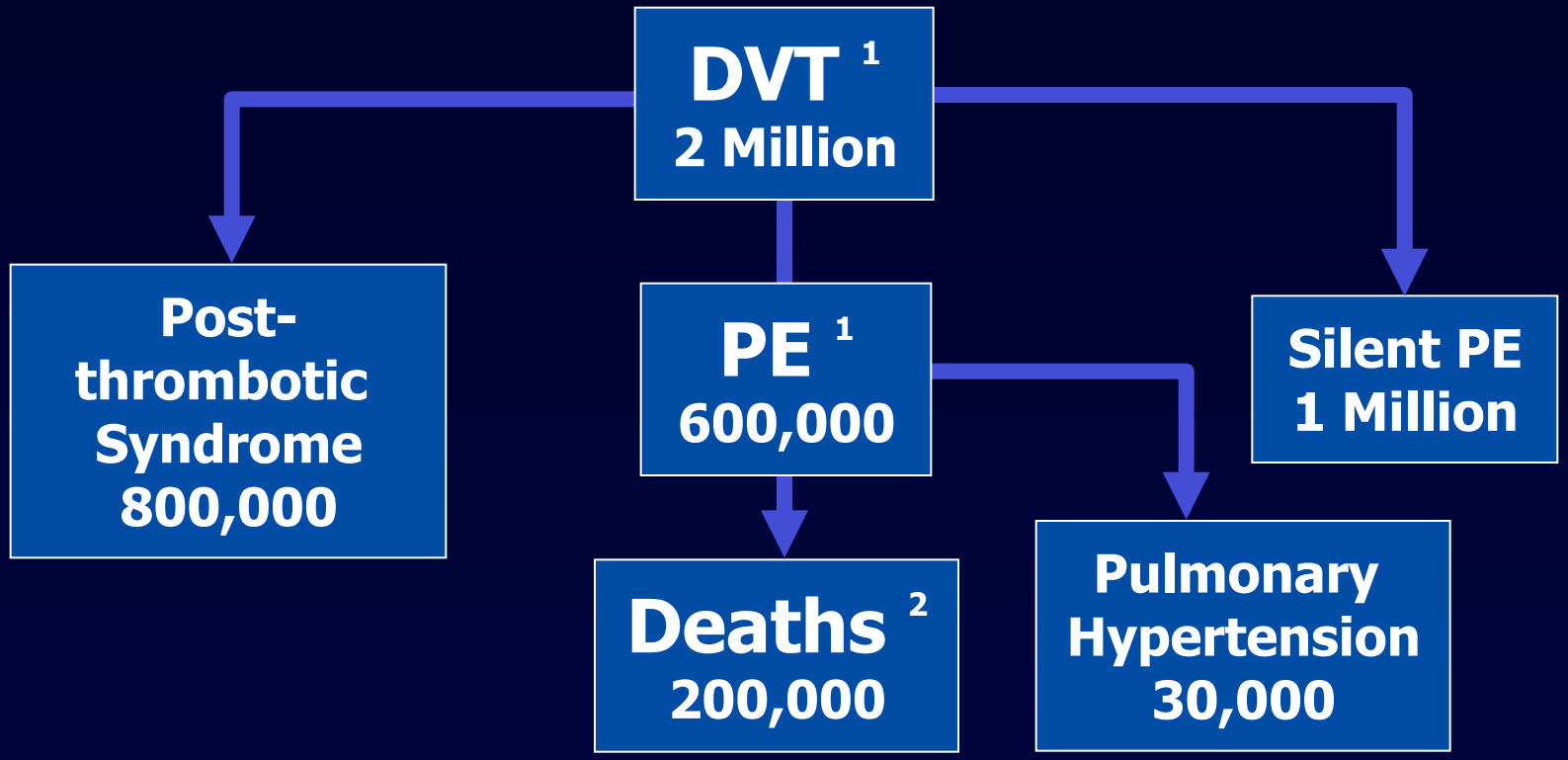
- Consultant
  - Boehringer-Ingelheim, Janssen, BMS, Daiichi Sankyo, Pfizer
- Research and Grant Support
  - NHLBI, Astra-Zeneca
- Board Member
  - Society of Perioperative Assessment and Quality Improvement (SPAQI)

Goals

1. What are the Key issues in DVT prophylaxis and the surgical patient?
2. How affective is ASA after Joint replacement surgery?
3. What is the role of mechanical compression devices in VTE prophylaxis?
4. Reversing DOACs for Emergent procedures?

Venous Thromboembolism

Third Leading cause of Cardiovascular Death



Estimated Cost of VTE Care $1.5 Billion/year

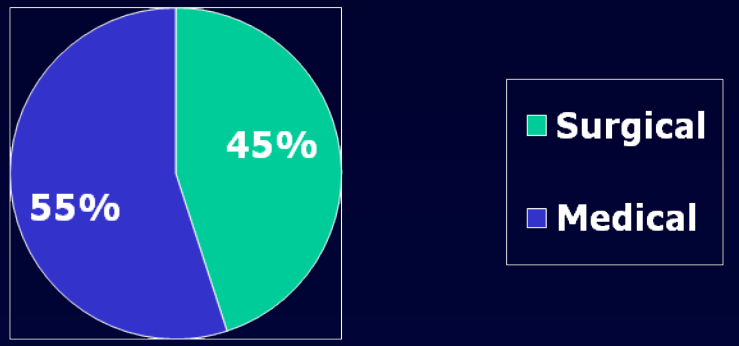
1. Hirsh J, Hoak J., "A Statement for Healthcare Professionals from the Council on Thrombosis, in Consultation with the Council on Cardiovascular Radiology, American Heart Association, 1996.
2. Anderson et al. Arch Intern Med. 1991;151:933-938

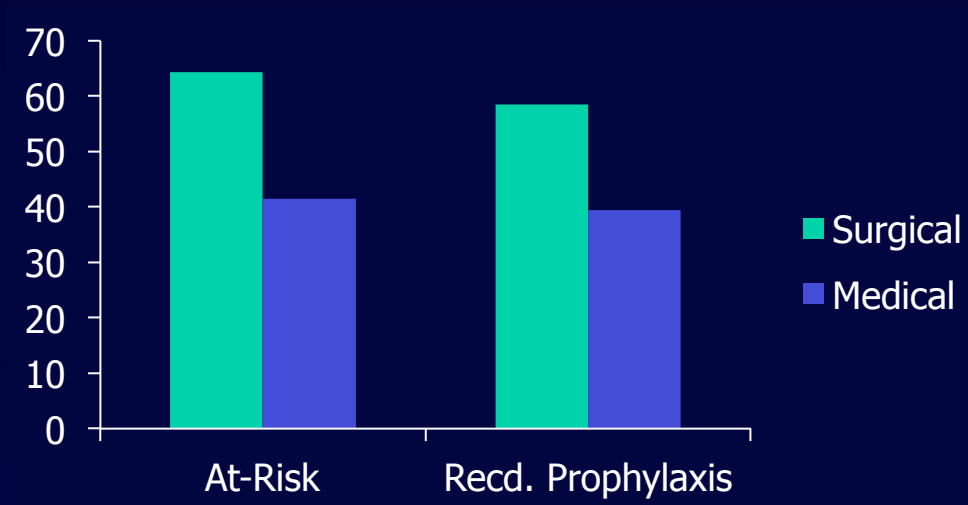
VTE Prevention as National Initiative

- Surgeon General Call to Action
  - Hospital-acquired VTE is now classified as medical error
  - Preventative treatment is most important to improve patient safety
  - Must address gap between evidence and implementation
- Joint Commission
  - Reduce patient harm associated with anticoagulation therapy (NPSG)
  - Focus on VTE Prevention and Treatment through core measures
- Medicare “Never Events”
  - Medicare will deny reimbursement for occurrence of DVT or PE following total knee or hip replacement

ENDORSE Registry

- Aug 2006-Jan 2007
- 68,183 patients
- 358 Hospitals
- 32 Countries
- Cross-sectional Survey

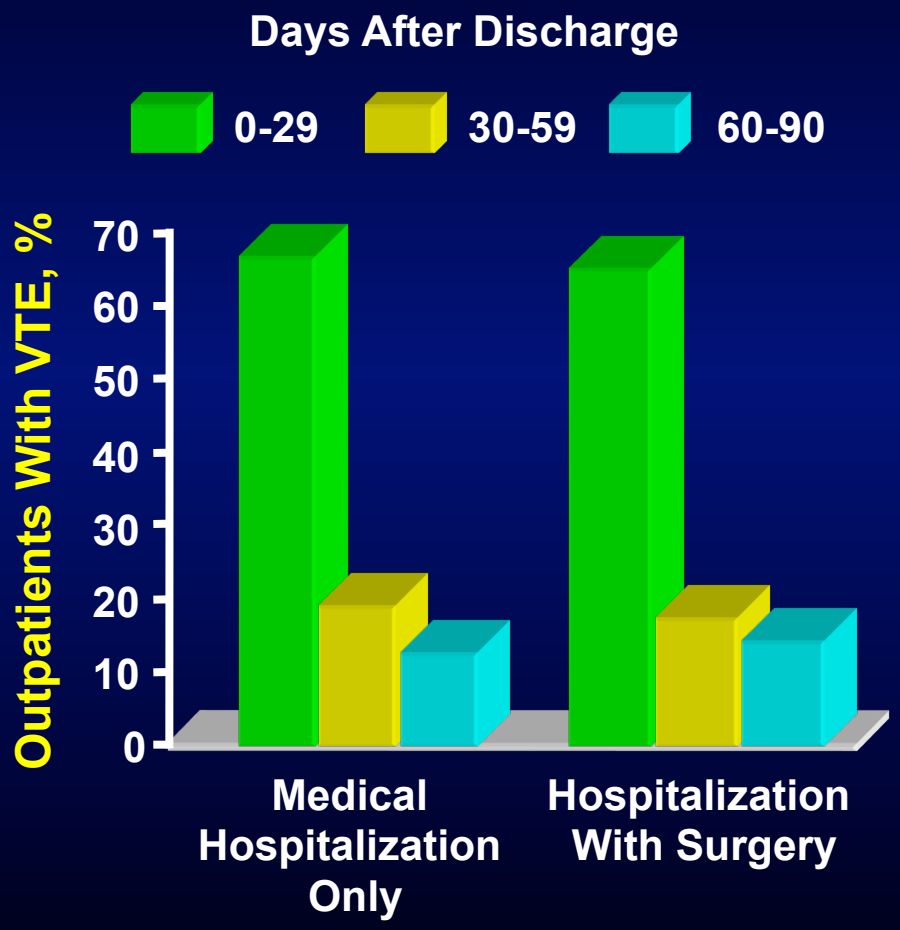




Cohen et al. Lancet 2008; 371:387

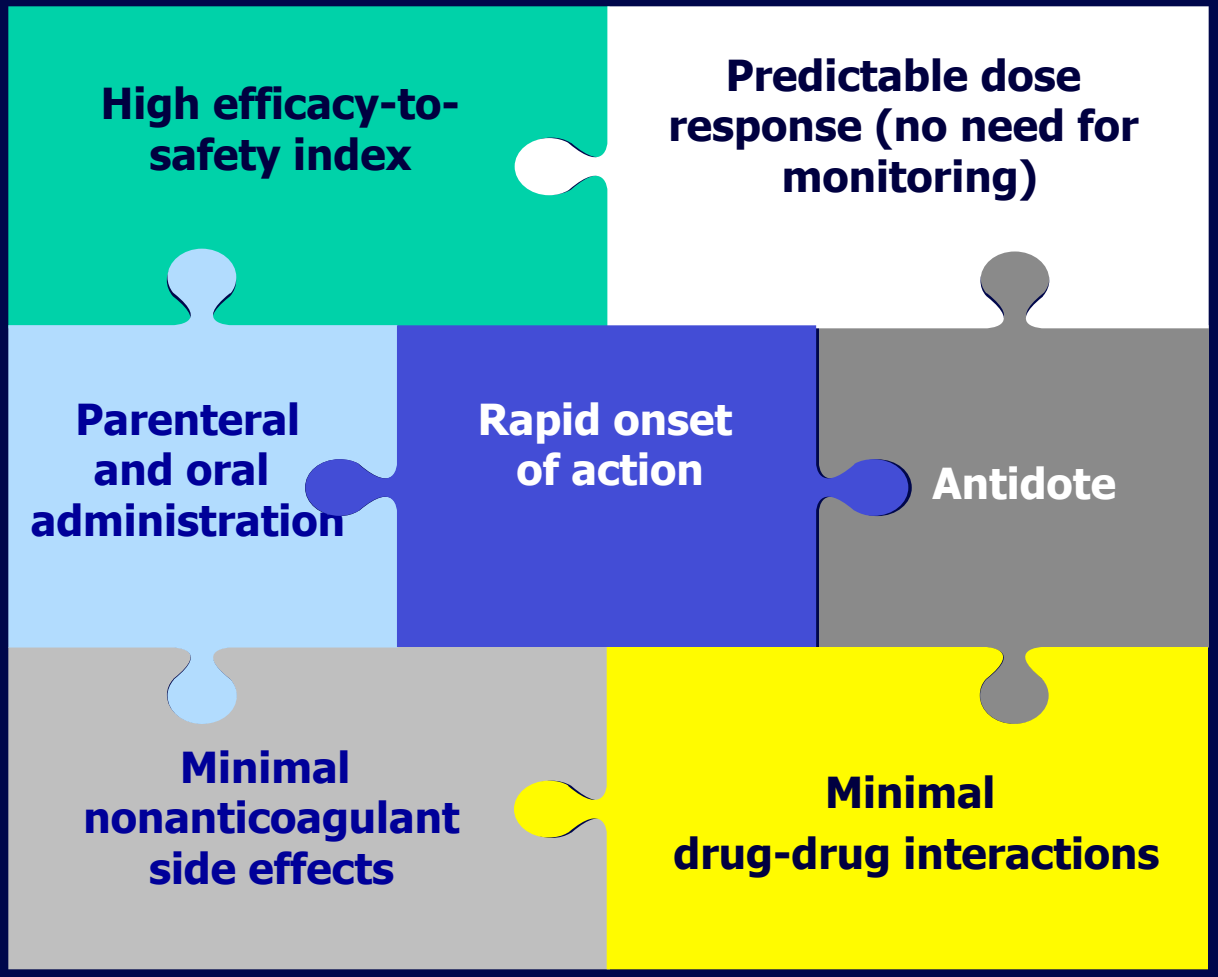
VTE Facts

- Outpatient VTE is 3-fold more common than inpatient VTE
- Almost half of the outpatients with VTE had been recently hospitalized
- Less than half of the recently hospitalized patients had received VTE prophylaxis during their hospitalizations



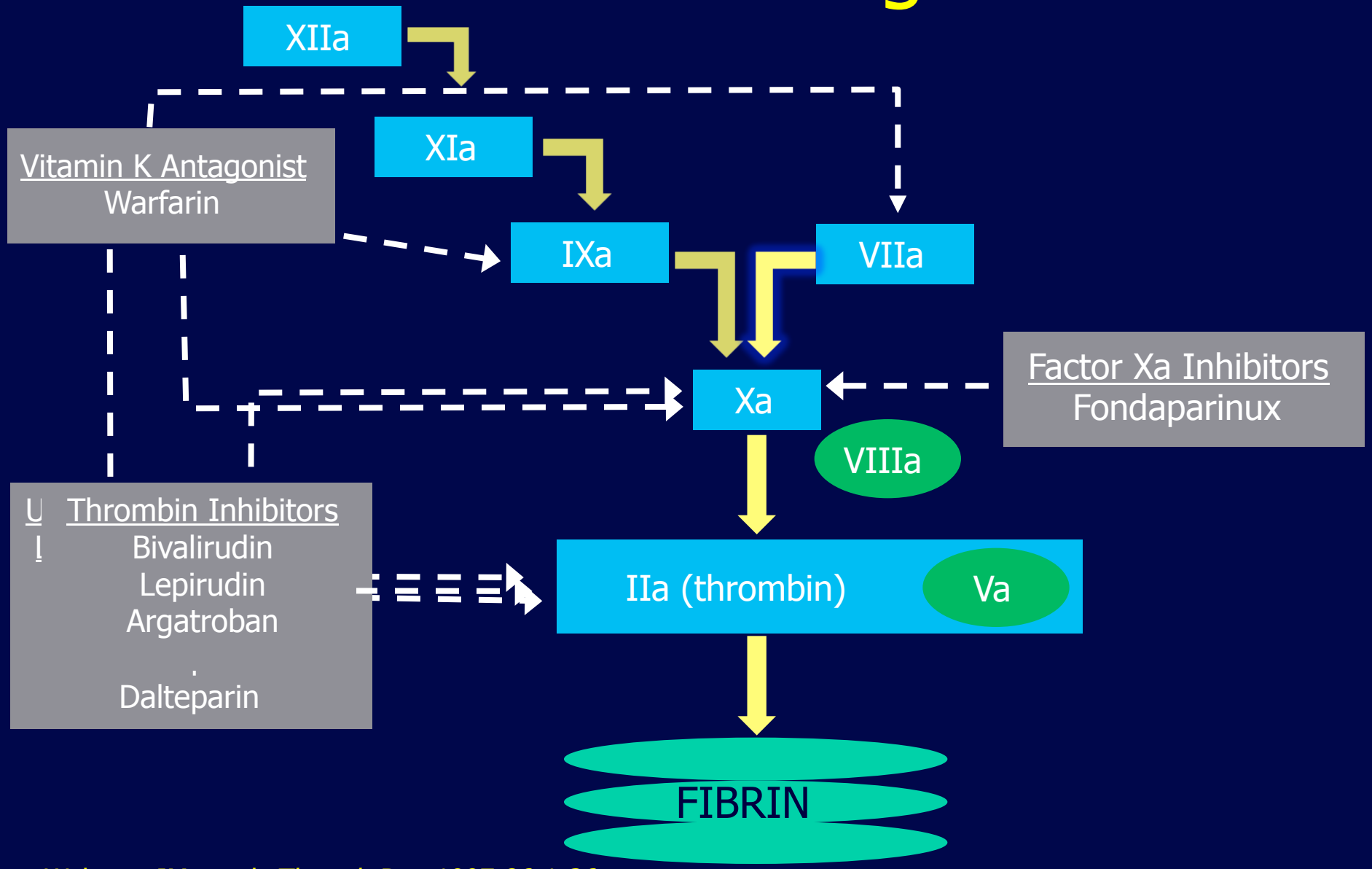
Goldhaber S. *Arch Intern Med.* 2007;167:1451-2.
Spencer FA et al. *Arch Intern Med.* 2007;167(14):1471-5.

Characteristics of an Ideal Anticoagulant



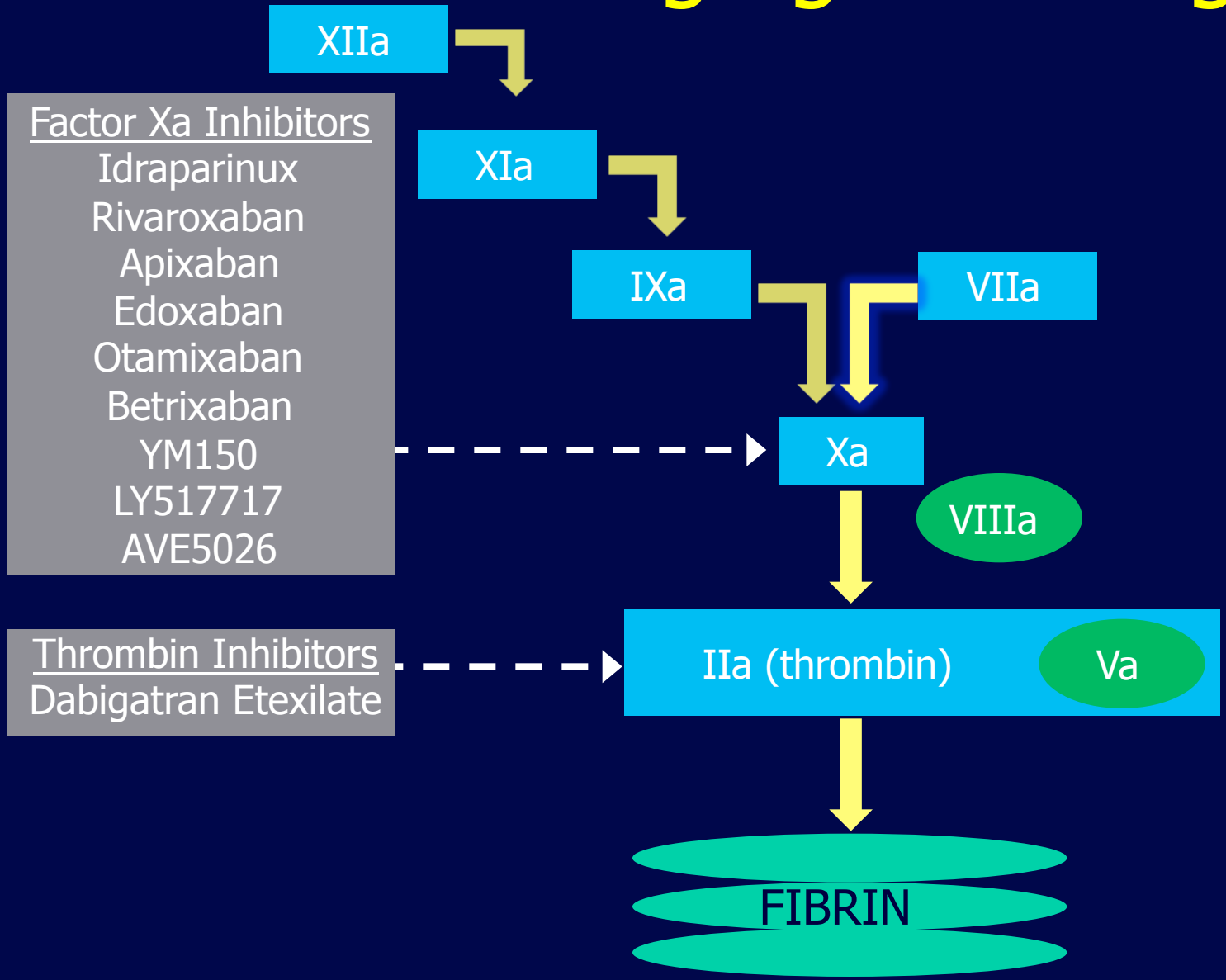
Hirsh J et al. *Blood*. 2005;105(2):453-461.

Current Anticoagulants



Walenga JM, et al. *Thromb Res*. 1997;86:1-36.

New and Emerging Anticoagulants



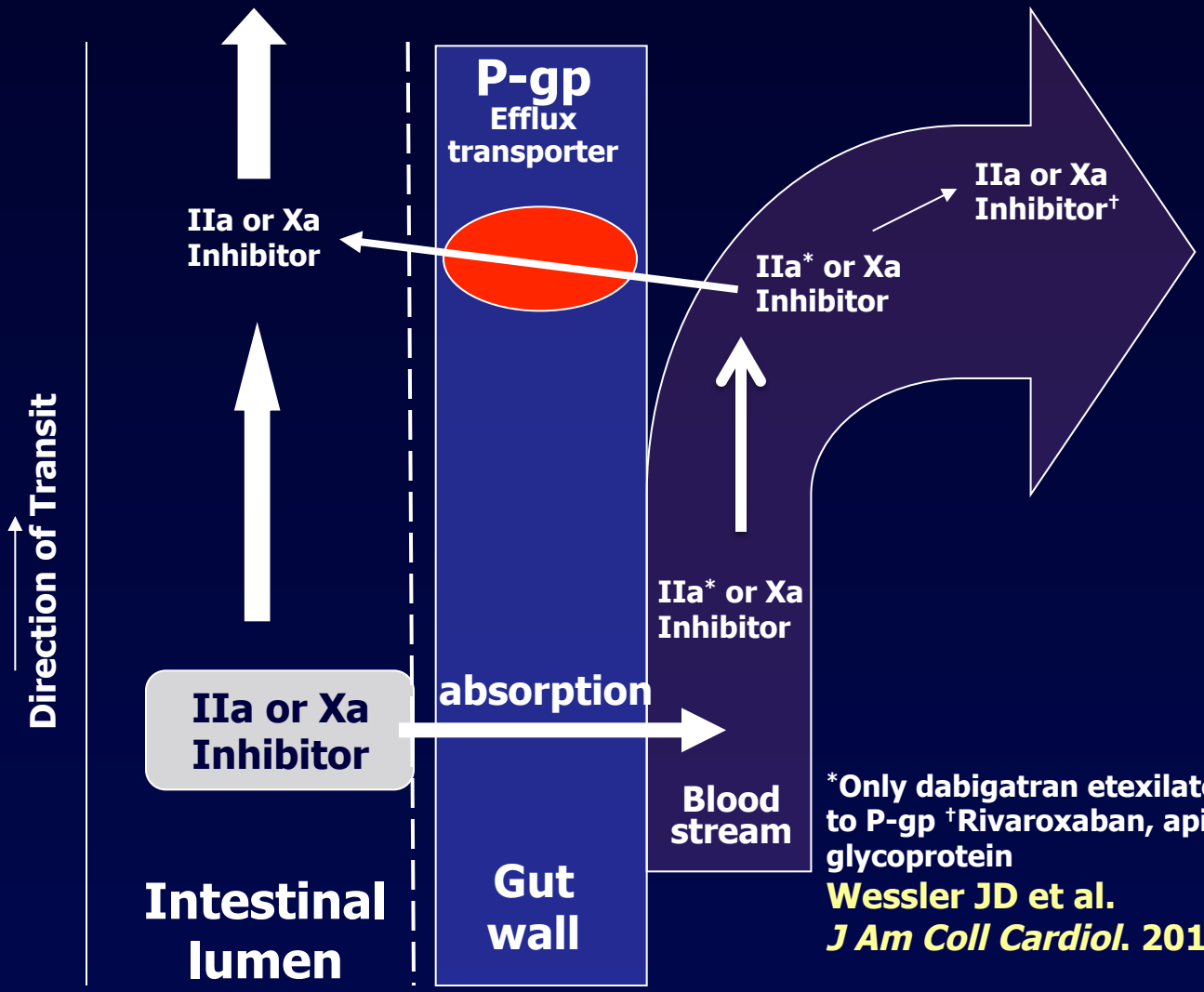
Walenga JM, et al. *Thromb Res*. 1997;86:1-36.

Pharmacokinetics of the Novel Oral Anticoagulants

Drug	Mechanism of action	Time to peak plasma concentration	Half-life	Dosing schedule	Clinically relevant interactions
Apixaban	FXa inhibitor	3-4 h	8-15 h	Twice daily	Avoid CYP3A4 inhibitors
Dabigatran	Thrombin inhibitor	1.5-2 h	15-17 h	Twice daily	Avoid inhibitors and inducers of p-GP
Edoxaban	FXa inhibitor	1-2 h	6-10 h	Once daily	Avoid inhibitors and inducers of p-GP
Rivaroxaban	FXa inhibitor	3-4 h	9-10 h	Once daily	Avoid inhibitors of CYP3A4 and p-GP

pGP, p-glycoprotein.

P-glycoprotein, an Efflux Transporter, Eliminates P-gp Substrates



Absorption of all agents is affected by P-gp, and varies based on enhanced or inhibited P-gp by other drugs

*Only dabigatran etexilate, and not dabigatran, is sensitive to P-gp †Rivaroxaban, apixaban, edoxaban P-gp, P-glycoprotein

Wessler JD et al.
***J Am Coll Cardiol*. 2013;61:2495-2502.**

Summary of PK Drug Interactions with TSOAs

Agent	Potential Drug Interaction	Potential Effect	US Package Insert Recommendations
Dabigatran	P-gp inhibitors*†	↑ dabigatran	Dronedarone or ketoconazole: dose reduction†
	P-gp inducers‡	↓ dabigatran	Rifampin: avoid use‡
Rivaroxaban	Combined P-gp inhibitors and strong CYP3A4 inhibitors	↑ rivaroxaban	Avoid use
	Combined P-gp inhibitors and weak/ moderate CYP3A4 inhibitors	↑ rivaroxaban	Use with caution in patients with moderate-to-severe renal impairment
	Combined P-gp inducers and strong CYP3A4 inducers	↓ rivaroxaban	Avoid use
Apixaban	Combined P-gp inhibitors and strong CYP3A4 inhibitors	↑ apixaban	N/A
	Combined strong P-gp inhibitors and CYP3A4 inhibitors	↑ apixaban	Reduce dose to 2.5 mg BID; avoid use in patients already taking 2.5 mg BID
	Combined strong P-gp inducers and CYP3A4 inducers	↓ apixaban	Avoid use

***Avoid all P-gp inhibitors in patients with severe renal impairment (CrCl <30 mL/min).**
†Reduce dose of dronedarone and ketoconazole to 75 mg BID in patients with moderate renal impairment (CrCl 30-50 mL/min); verapamil, amiodarone, quinidine, and clarithromycin do not require dose reduction, but avoid if CrCl <30 mL/min. ‡Due to lack of interactions data, avoid concomitant use of carbamazepine, dexamethasone, doxorubicin, nefazodone, paclitaxel, prazosin, St John's wort, tenofovir, trazodone, and vinblastine.

Hellwig T et al. *Ann Pharmacother*. 2013;47:1478-1487.

Case 1

You are asked to see a 65-year old AA obese male with h/o colon cancer for a preoperative evaluation on the medicine consult service.

What are your recommendations for VTE prophylaxis and for how long do you recommend therapy?

1. UFH 5000 U SC Bid while patient is hospitalized
2. UFH 5000 U SC tid plus mechanical prophylaxis while patient is hospitalized
3. Enoxaparin 40 mg SC or Dalteparin 5000IU plus mechanical prophylaxis in-house and then LMWH SC once-daily for total of 4 weeks
4. Fondaparinux 2.5 mg SC once-daily while patient is hospitalized

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Caprini Risk Assessment Model

1 Point	2 Points	3 Points	5 Points
Age 41-60 y	Age 61-74 y	Age ≥ 75 y	Stroke (<1 mo)
Minor surgery	Arthroscopic surgery	History of VTE	Elective arthroplasty
BMI >25 kg/m^2	Major open surgery (>45 min)	Family history of VTE	Hip, pelvis, or leg fracture
Swollen Legs			
Varicose Veins	Laparoscopic surgery (>45 min)	Factor V Leiden	Acute spinal cord (<1 mo)
Pregnancy or postpartum			
History of IBD	Malignancy	Prothrombin 20210A	
Medical Patient at bed rest	Confined to bed	Lupus anticoagulant/APLA	
Acute MI	(>72 h)	Elevated homocysteine	
History of unexplained or recurrent spontaneous abortion	Immobilizing plaster cast	HIT Thrombophilia	
Oral contraceptives or hormone replacement	Central venous access		
Sepsis (<1 mo)			
Serious lung disease, incl pneumonia (<1 mo)			
Abnormal pulmonary function			
Congestive heart failure (<1 mo)			

Total Score: _____

Gould et al. Chest 2012;141:e227s-277s

Categories of Risk for Venous Thromboembolism in Surgical Patients

Very Low risk (Caprini Score =0, VTE, 0.5%)

- No Specific pharmacologic or mechanical prophyalxis other than early ambulation

Low risk (Caprini Score=0-2, VTE ~1.5%)

- Mechanical prophylaxis preferably with IPCs

Moderate risk (Caprini Score=3-4, VTE~ 3%)

- LMWH, LDUH or IPCs (latter in patients with risk of bleeding)

High risk (Caprini Score $\geq$ 5, VTE ~ 6%)

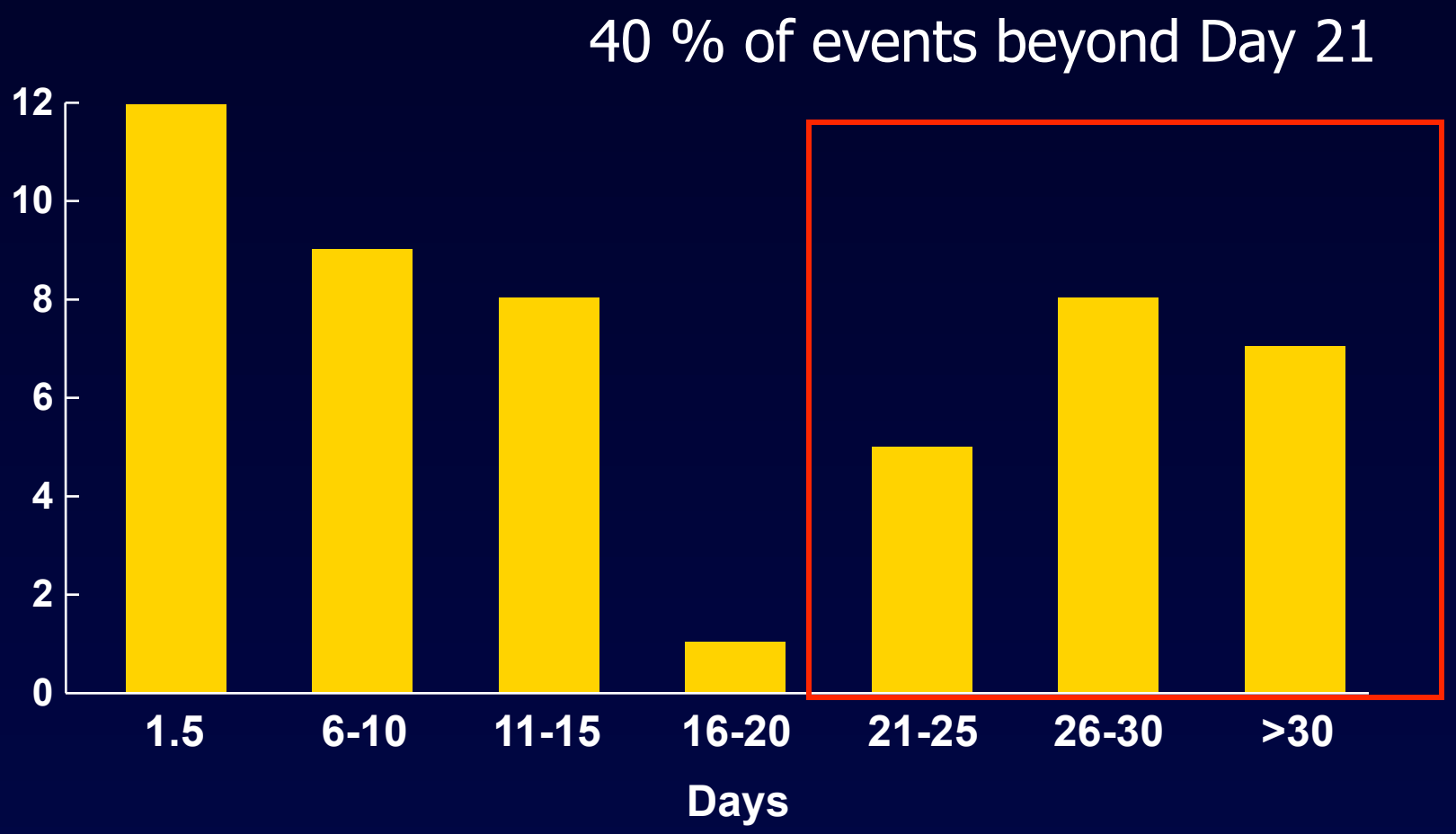
- LMWH or LDUH, ES or IPC should added
- If LMWH or LDUH are contraindicated then Fondaparinux or ASA can be used

High Risk Cancer Surgery

- LMWH or LDUH plus ES or IPC and extended prophylaxis with LMWH post-DC

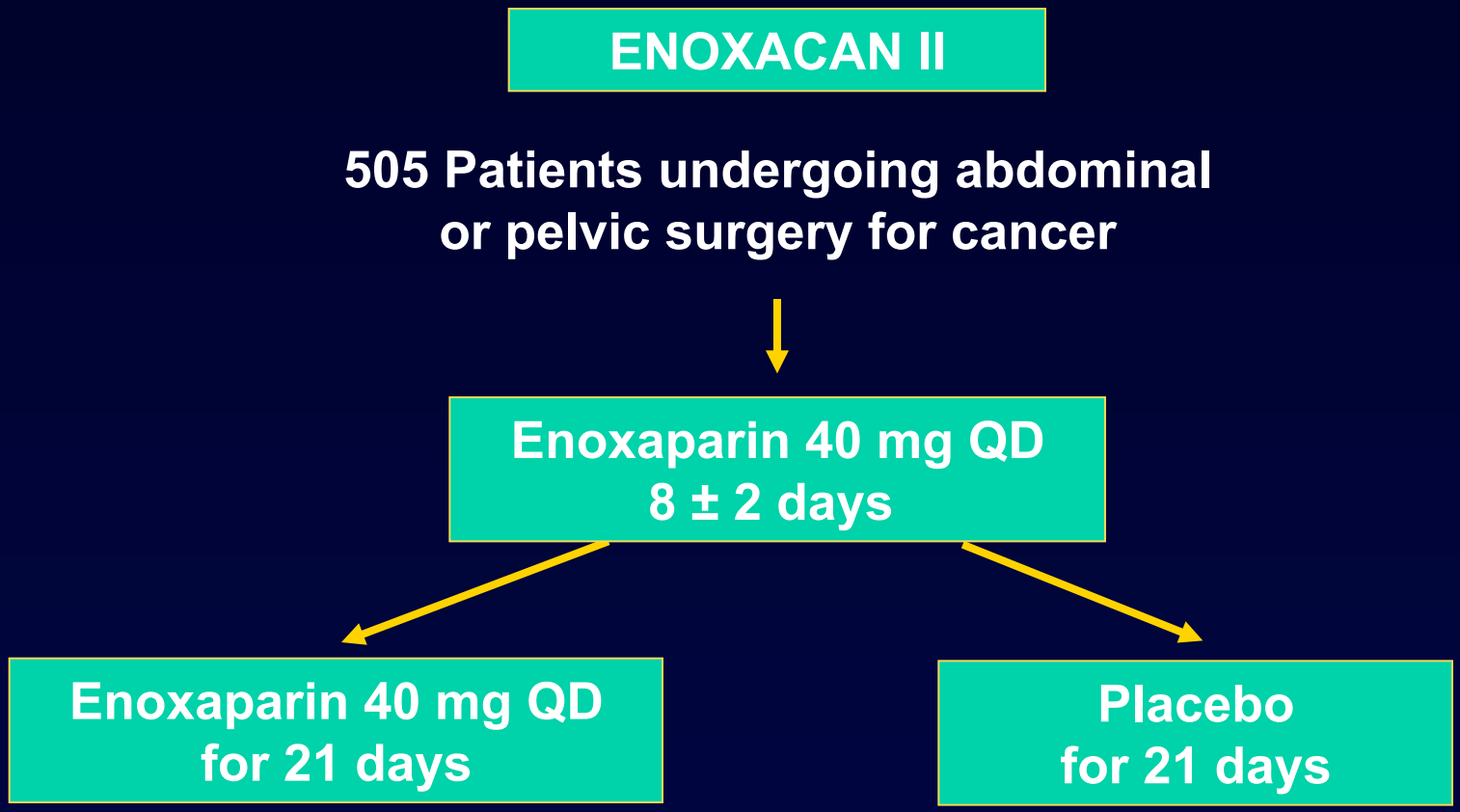
Gould et al. Chest 2012;141:141:e227S-277S

Time Distribution of VTE



Agnelli G et al. *Ann Surg* 2006;243:89-95

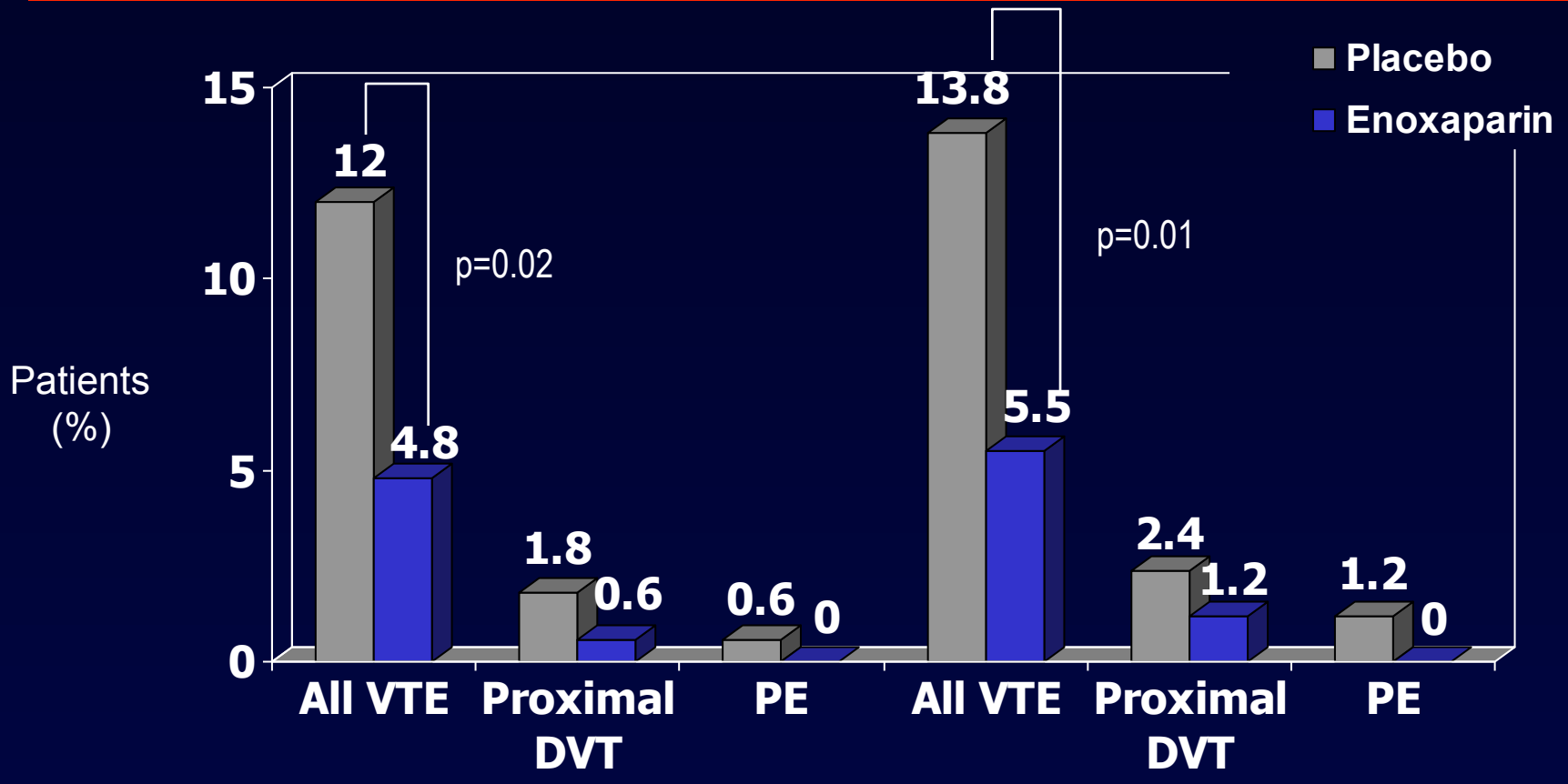
ENOXACAN II Study



Venogram at day 28 ±3

Bergqvist D et al. *NEJM*. 2002;346:975-980.

ENOXACAN II
Results



During Double-blind Period Cumulative Events at 3 Months

Bergqvist D et al. *NEJM*. 2002;346:975-980.

ENOXACAN II
Conclusions

- Prolonged post-operative prophylaxis with enoxaparin reduces VTE incidence by 60%
- Number needed to treat to prevent one VTE = 14
- Benefit maintained at 3 months
- Benefit comparable to that seen in orthopedic surgery

Bergqvist D et al. *NEJM*. 2002;346:975-980.

Case 2

You are consulted by orthopedics to see a 70- year old WF with h/o HTN, OA, ‘blood clot’ when she was on HRT about 10 years ago who is now scheduled for a hip replacement. She is particularly concerned about having another one and wants your recommendation.

What do you recommend and for how long?

1. Warfarin with target INR=1.8 for 2 weeks
2. Enoxaparin 40 mg SC daily for 1 week
3. Rivaroxaban 10 mg po daily for 4 weeks
4. Fondaparinux 2.5 mg SC daily until discharge
5. ASA 325 mg po bid for 4 weeks

What do you recommend and for how long?

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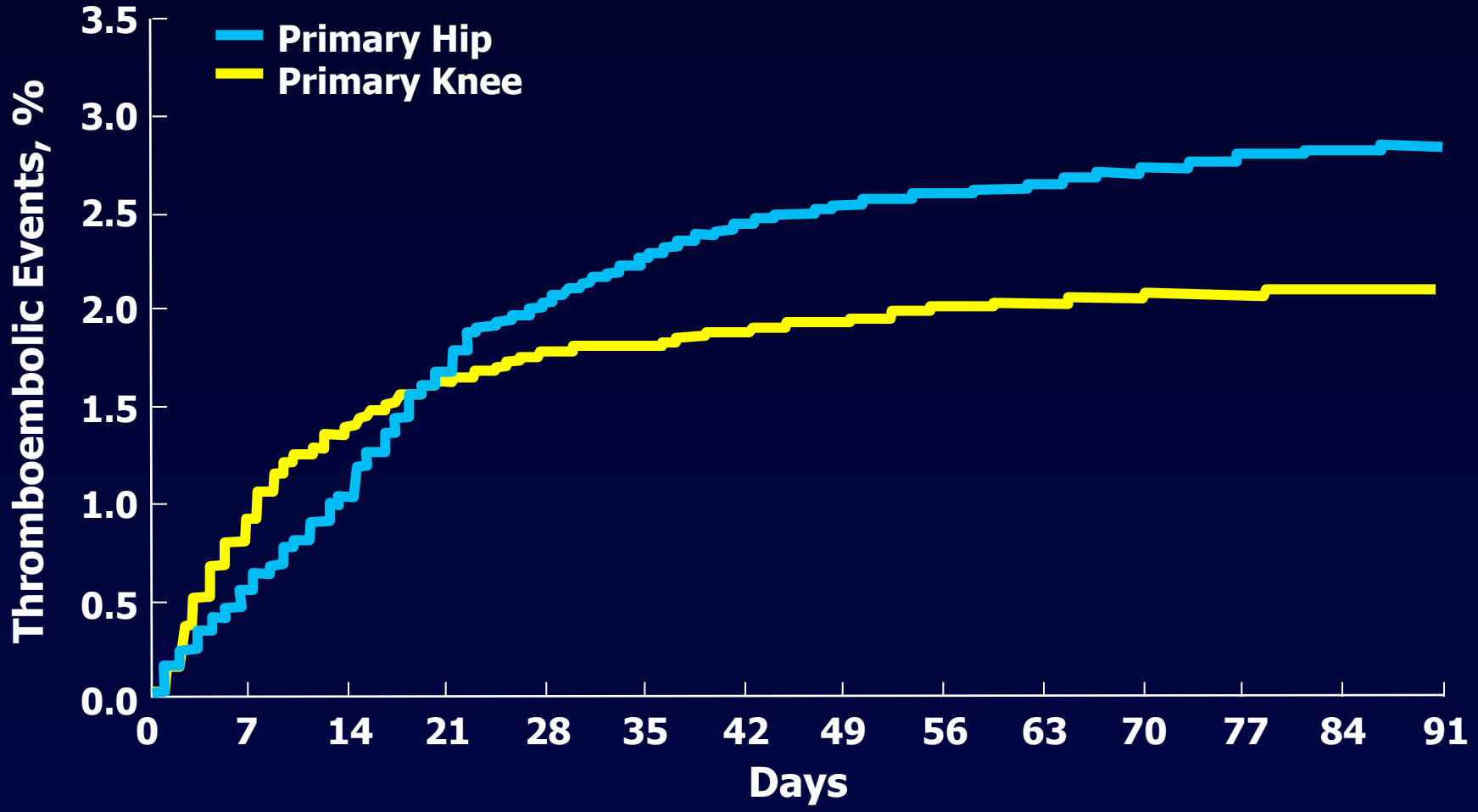
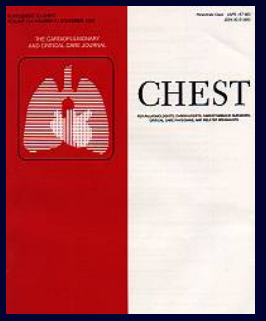
Temporal Patterns of Symptomatic VTE after THA and TKA



White et al. *Arch Intern Med.* 1998:1525-1531

Ninth ACCP Recommendations:

Total Knee or Hip Replacement



Grade 1B

Optimal duration of prophylaxis after THR and TKR at-least 10-14 days with

- LMWH (preferred)
- Adjusted-dose warfarin
- Fondaparinux
- Apixaban
- Dabigatran
- Rivaroxaban
- LDUH
- Aspirin
- IPC (grade 1C)

Dual Prophylaxis with Pharmacologic Prophylaxis and IPCs during hospital stay
(Grade 2B)

Yngve Falck-Yetter et al. Chest 2012;141:141: e278S-e325S

Duration of Prophylaxis

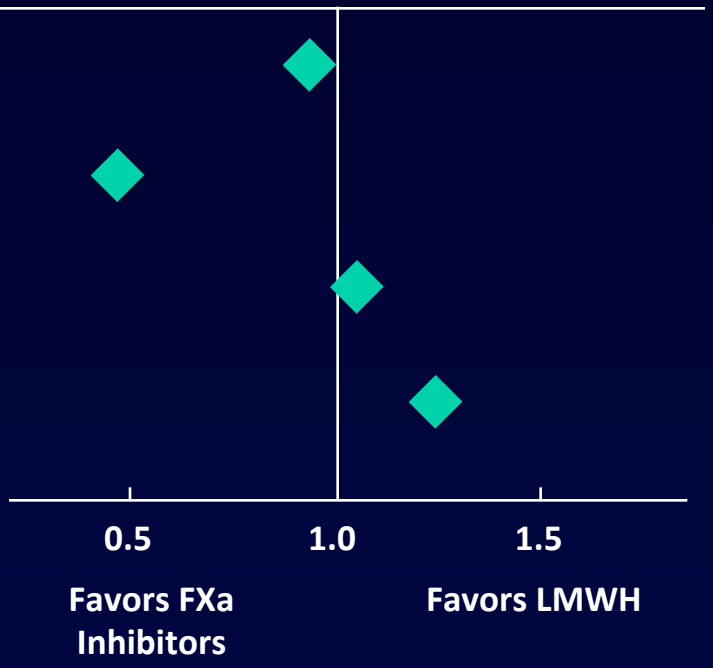
- Optimal duration of prophylaxis after major orthopedic surgery
  - at least 10-14 days of LMWH (grade 1B)
- Extended out-of-hospital prophylaxis for major orthopedic surgery up to 35 days from day of surgery (grade 2B)

Yngve Falck-Yetter et al. Chest 2012;141:141: e278S-e325S

Geerts, et al. Chest 2001;119:132S-175S.

FXa Inhibitors vs LMWH Systematic Review: THA and TKA

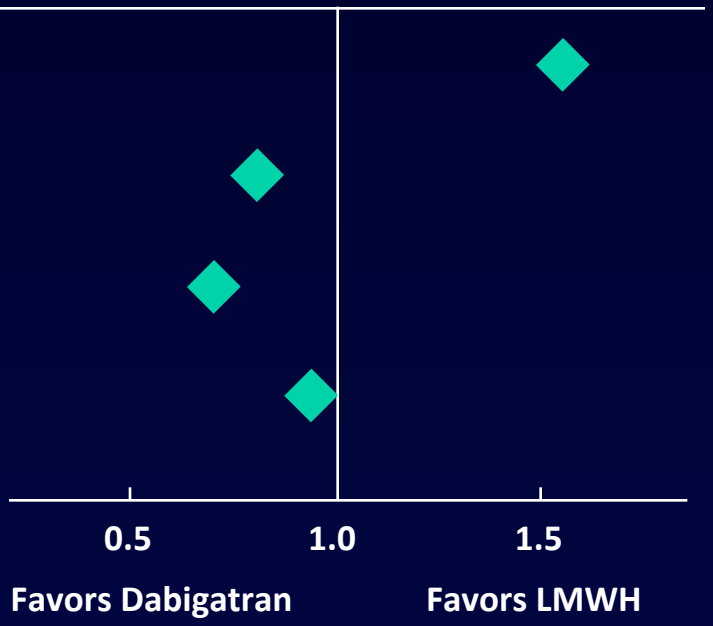
Variable	Total Studies Patients, (n)	Events/Total, n/N FXa Inhibitors	Events/Total, n/N LMWH	OR (95% CI)
Mortality	10 (22,838)	31/12394	26/10454	0.95 (0.55-1.63)
Symptomatic DVT	12 (22,877)	41/12991	57/10454	0.46 (0.3-0.7)
Non-fatal PE	30 (26,998)	44/15187	29/11811	1.07 (0.65-1.73)
Major bleeding	21 (31,424)	192/18307	26/13117	1.27 (0.96-1.65)



Adam et al. Ann Intern Med. 2013;159(4):275-284

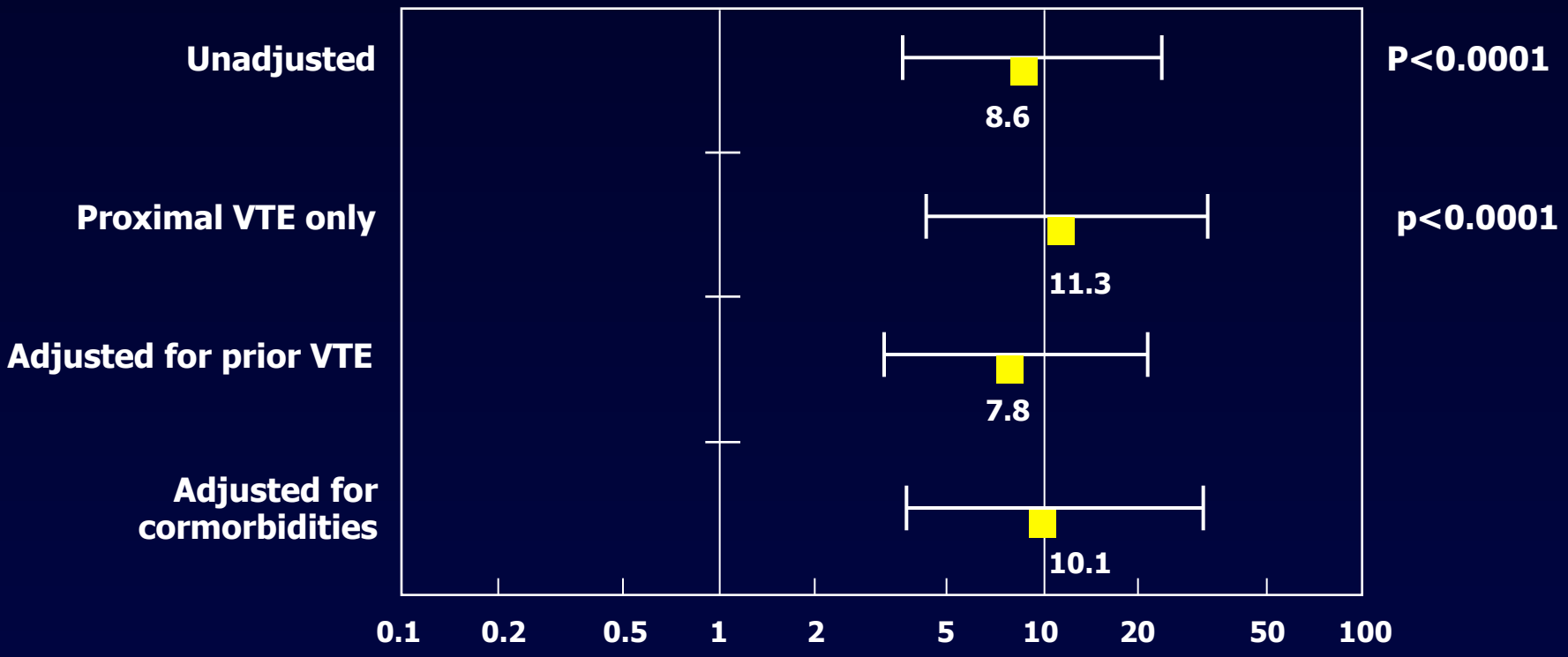
Dabigatran vs LMWH
Systematic Review: THA and TKA

Variable	Total Studies Patients, (n)	Events/Total, n/N		OR (95% CI)
		Dabigatran	LMWH	
Mortality	4 (10,264)	16/6500	2/3756	1.54 (0.38-6.33)
Symptomatic DVT	4 (10,264)	34/6500	18/3756	0.82 (0.17-1.99)
Non-fatal PE	4 (10,264)	14/6500	11/3756	0.69 (0.31-1.54)
Major bleeding	4 (10,264)	81/6500	48/3756	0.94 (0.58-1.57)



Adam et al. Ann Intern Med. 2013;159(4):275-284

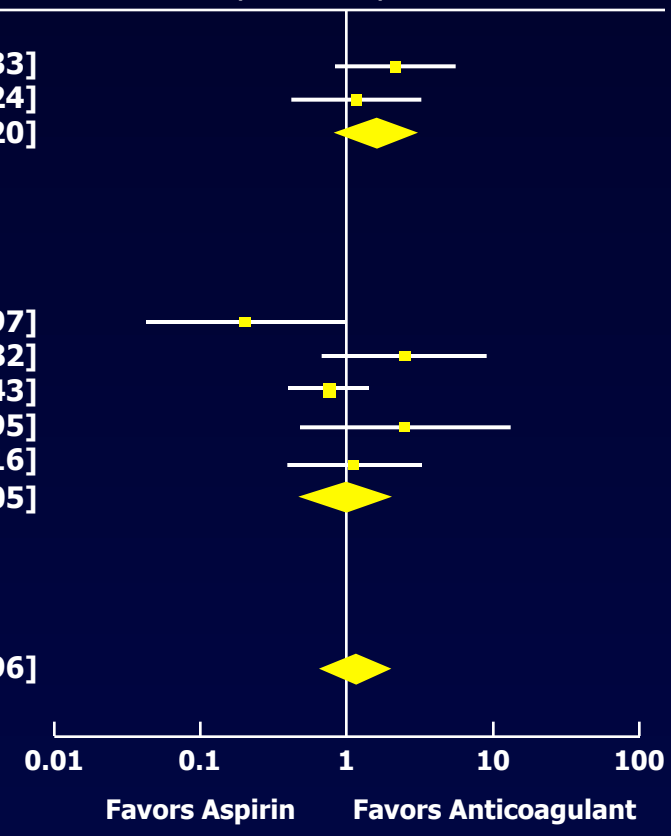
Warfarin Monotherapy Vs. Enoxaparin 30 mg SQ Twice daily



Brotman et al. *Thrombosis and Haemostasis* 2004

ASA vs. Anticoagulant after Hip Fx and Major Joint Arthroplasty on Rates of Proximal DVT

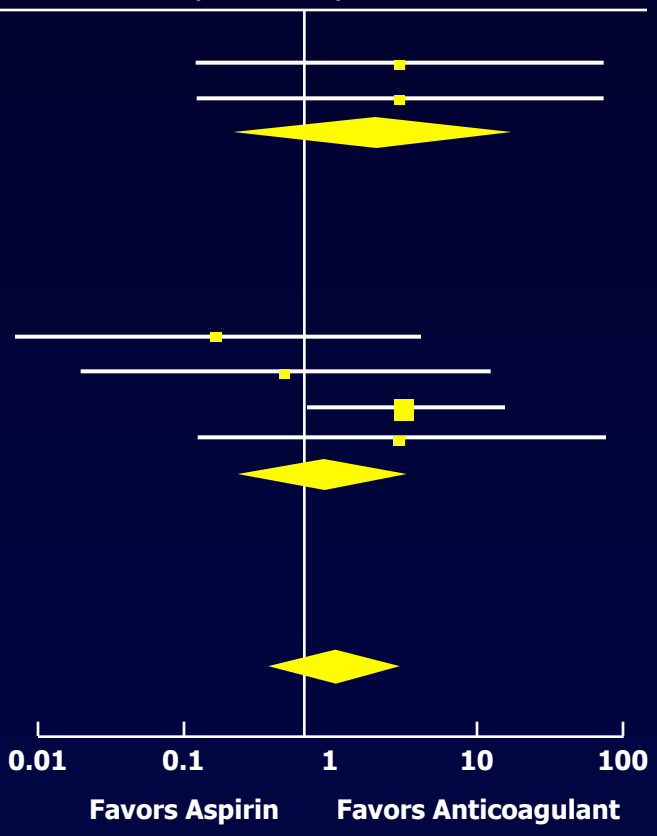
Study or subgroup	Aspirin Events	Aspirin Total	Anticoagulant Events	Anticoagulant Total	Weight	Risk Ratio M-H, Random, 95% CI
Hip fracture						
Gent 1996	12	84	6	88	17.1%	2.10 [0.82, 5.33]
Powers 1989	7	66	6	65	15.3%	1.15 [0.41, 3.24]
Subtotal (95% CI)		150		153	32.4%	1.60 [0.80, 3.20]
Total events	19		12			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.71$, df = 1 (P = 0.40); $I^2 = 0\%$						
Test for overall effect: Z = 1.33 (P = 0.18)						
Hip or knee arthroplasty						
Alfaro 1986	2	60	5	30	8.6%	0.20 [0.04, 0.97]
Josefsson 1987	7	40	3	42	11.7%	2.45 [0.68, 8.82]
Lotke 1996	16	172	18	146	23.9%	0.75 [0.40, 1.43]
Westrich 2006	5	136	2	139	8.3%	2.56 [0.50, 12.95]
Woolson 1991	7	72	6	69	15.2%	1.12 [0.40, 3.16]
Subtotal (95% CI)		480		426	67.6%	1.00 [0.49, 2.05]
Total events	37		34			
Heterogeneity: $Tau^2 = 0.31$; $Chi^2 = 7.86$, df = 6 (P = 0.10); $I^2 = 49\%$						
Test for overall effect: Z = 0.00 (P =1.00)						
Total (95% CI)		630		579	100.0%	1.15 [0.68, 1.96]
Total events	56		46			
Heterogeneity: $Tau^2 = 0.20$; $Chi^2 = 10.20$, df = 6 (P = 0.12); $I^2 = 41\%$						
Test for overall effect: Z = 0.52 (P = 0.60)						
Test for subgroup differences: $Chi^2 = 0.86$, df = 1 (P = 0.36); $I^2 = 0\%$						



Drescher et al. *JHM* 2014; 9:579-585

ASA vs. Anticoagulant after Hip FX and Major Joint Replacement on PE rates

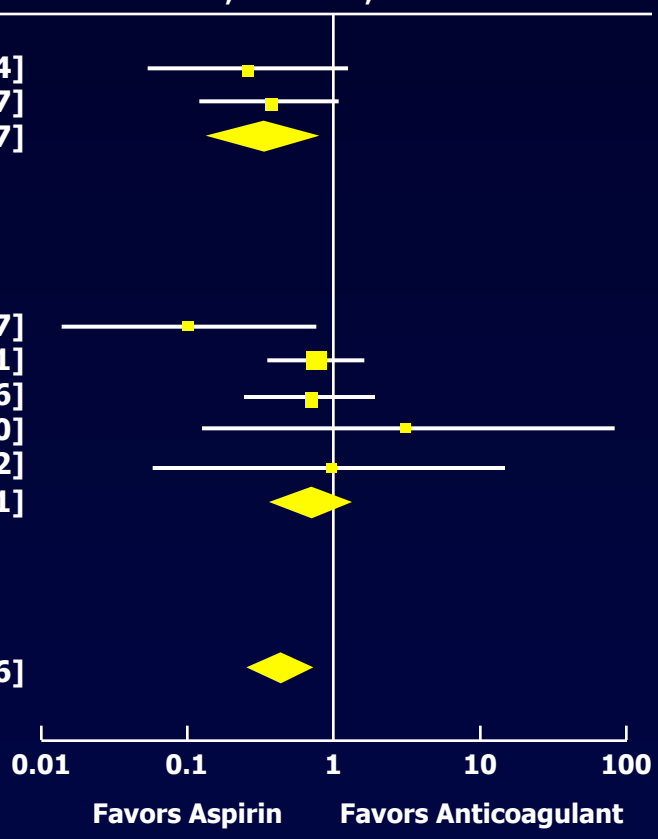
Study or subgroup	Aspirin Events	Aspirin Total	Anticoagulant Events	Anticoagulant Total	Weight	Risk Ratio M-H, Random, 95% CI
Hip fracture						
Gent 1996	1	126	0	125	10.7%	2.98 [0.12, 72.37]
Powers 1989	1	66	0	65	10.8%	2.96 [0.12, 71.24]
Subtotal (95% CI)		192		190	21.5%	2.97 [0.31, 28.23]
Total events	19		12			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.00$, df = 1 (P = 1.00); $I^2 = 0\%$						
Test for overall effect: Z = 0.95 (P = 0.34)						
Hip or knee arthroplasty						
Alfaro 1986	0	60	1	30	10.9%	0.17 [0.01, 4.04]
Harris 1982	0	51	1	75	10.8%	0.49 [0.02, 11.73]
Josefsson 1987	6	40	2	42	46.0%	3.15 [0.67, 14.70]
Woolson 1991	1	72	0	69	10.8%	2.88 [0.12, 69.44]
Subtotal (95% CI)		223		216	78.5%	1.47 [0.40, 5.42]
Total events	7		4			
Heterogeneity: $Tau^2 = 0.21$; $Chi^2 = 3.35$, df = 3 (P = 0.34); $I^2 = 10\%$						
Test for overall effect: Z = 0.58 (P =0.56)						
Total (95% CI)		415		406	100.0%	1.83 [0.64, 5.21]
Total events	9		4			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 3.57$, df = 5 (P = 0.61); $I^2 = 0\%$						
Test for overall effect: Z = 1.14 (P = 0.26)						
Test for subgroup differences: $Chi^2 = 0.28$, df = 1 (P = 0.60); $I^2 = 0\%$						



Drescher et al. *JHM* 2014; 9:579-585

ASA vs. Anticoagulant after Hip Fx and Major Joint Replacement on Any Significant Bleeding Rates

Study or subgroup	Aspirin Events	Aspirin Total	Anticoagulant Events	Anticoagulant Total	Weight	Risk Ratio M-H, Random, 95% CI
Hip fracture						
Gent 1996	2	128	8	125	10.3%	0.25 [0.05, 1.14]
Powers 1989	4	66	11	65	19.2%	0.36 [0.12, 1.07]
Subtotal (95% CI)		192		190	29.5%	0.32 [0.13, 0.77]
Total events	6		19			
Heterogeneity: $Tau^2 = 0.00$; $Chi^2 = 0.15$, df = 1 (P = 0.70); $I^2 = 0\%$						
Test for overall effect: Z = 2.54 (P = 0.01)						
Hip or knee arthroplasty						
Harris 1982	1	51	14	75	6.2%	0.11 [0.01, 0.77]
Josefsson 1987	9	40	13	42	37.4%	0.73 [0.35, 1.51]
Lotke 1996	6	166	8	146	21.0%	0.66 [0.23, 1.86]
Westrich 2006	1	136	0	139	2.5%	3.07 [0.13, 74.60]
Woolson 1991	1	72	1	69	3.3%	0.96 [0.06, 15.02]
Subtotal (95% CI)		465		471	70.5%	0.63 [0.33, 1.21]
Total events	18		36			
Heterogeneity: $Tau^2 = 0.09$; $Chi^2 = 4.63$, df = 4 (P = 0.33); $I^2 = 14\%$						
Test for overall effect: Z = 1.40 (P = 0.16)						
Total (95% CI)		657		661	100.0%	0.52 [0.31, 0.86]
Total events	24		55			
Heterogeneity: $Tau^2 = 0.04$; $Chi^2 = 6.52$, df = 6 (P = 0.37); $I^2 = 8\%$						
Test for overall effect: Z = 2.55 (P = 0.01)						
Test for subgroup differences: $Chi^2 = 1.47$, df = 1 (P = 0.23); $I^2 = 32.0\%$						



Drescher et al. *JHM* 2014; 9:579-585

Extended Prophylaxis: ASA vs LMWH after THA

Extended prophylaxis with aspirin vs dalteparin after total hip arthroplasty*

Outcomes	Aspirin	Dalteparin	At 90 d	
			ARR (95% CI)	RRR (CI)
PE or proximal DVT	0.3%	1.3%	1.0% (-0.5 to 2.5)†	79% (-34 to 97)
Clinically important Nonmajor bleeding	0.5%	1.0%	0.48% (-1.0 to 2.0)	48% (-141 to 89)
			ARI (95% CI)	RRI (CI)
Wound infection	3.1%	2.5%	0.6% (-1.8 to 3.2)	25% (-44 to 179)

*DVT = deep venous thrombosis; PE = pulmonary embolism; other abbreviations defined in Glossary. All RRR, RRI, and CI, and ARI and CI for wound infection, were calculated from event rates in article.
†P <0.001 for noninferiority.

Anderson DR et al. Ann Intern Med. 2013;158:800-6.

Ninth ACCP Recommendations
Hip Fracture Surgery

Grade 1B

- Fondaparinux
- LMWH (preferred)
- Adjusted-dose warfarin
- LDUH
- Aspirin

Grade 1C

- IPC

Geerts et al. Chest 2001;119:132S-175S.

Yngve Falck-Yetter et al. Chest 2012;141:141: e278S-e325S

Mechanical Compression Devices

- Nearly complication free
- Time worn = effectiveness
- Ensure do not actually impede ambulation

Portable Intermittent Compression Device

- Portable Intermittent Compression Device
- Miniature
- Portable
- Battery Powered
- Can be worn out of bed and out of hospital

Portable Intermittent Compression Device

- Triggers compression in synchronization with respiratory phase
- Provides natural phasic venous flow
- Patient compliance monitored by device
- Patient compliance clearly visible on device screen (LED)

DVT Prevention in Joint Replacement: Portable IPCs Vs. LMWH

Surgery	N	Portable Int. Device+ ASA	Enoxaparin	P- value
TJA	121	7% (4/61)	28% (17/60)	*0.002*
TKA	48	14% (4/28)	33% (13/40)	*NS*
THA	73	0% (0 / 33)	32.5% (13 / 40)	*<0.012*

- Conclusion: Portable Intermittent Compression Device + ASA is
  - Safe and effective in TJA
  - Significantly < DVT in TJA compared with enoxaparin

Gelfer et al. J Arthroplasty 2006, 21 (2) : 206-214

Large Prospective Randomized Multi-Centered Clinical Trial

Hosp Special Surg, NY

Siani Hosp, Baltimore, MD

Cleveland Clinic, OH

Indiana Research Found., IN

Mayo Clinic, MN

Ortho & Neuro Center of Cascades, OR

Loma Linda Univ, CA

Kerlan Jobe Ortho Clinic, CA

SCORE at Scripps Clinic, CA

Multi-Center Randomized Prospective Study

- All primary total hip arthroplasties
- Exclusion
  - Self-reported or documented hx DVT or PE
  - Routine use of anticoagulant or antiplatelet drug
- Patients signed HSC approved consent

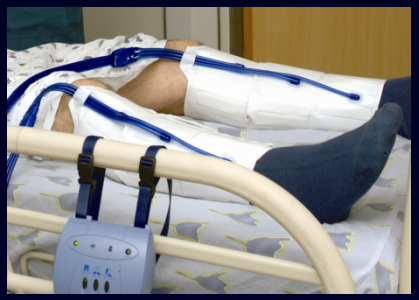
Colwell, et al. JBJS, 2010; 92:527-535

Methods

- Prospective randomized study
  - Portable Intermittent Compression Device group
    - Device ± aspirin 81 mg daily
  - LMWH group
    - Enoxaparin 30 mg twice daily in hospital
    - Enoxaparin 40 mg once daily after discharge

Colwell, et al. JBJS, 2010; 92:527-535

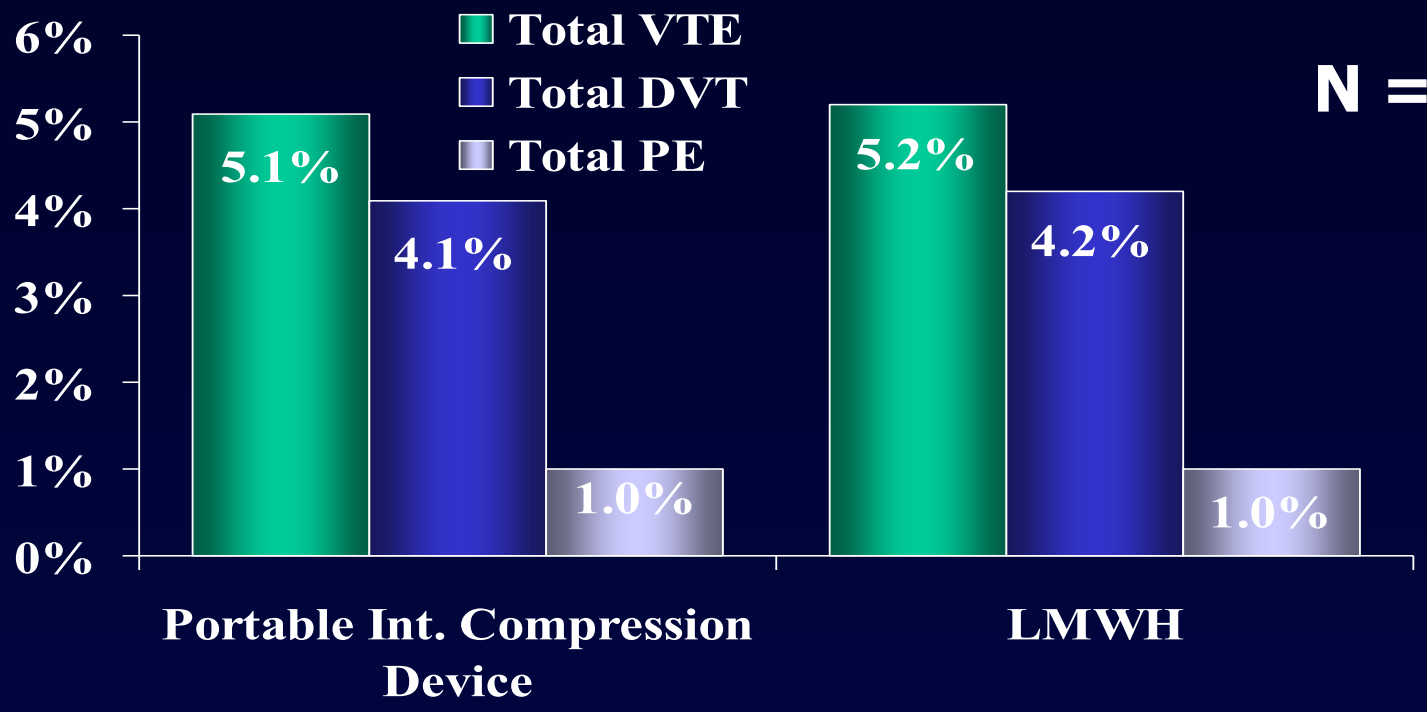
Methods



- Treatment for 10 days with Portable Intermittent Compression Device or LMWH
- Bilateral duplex ultrasound on day 10 – 12
- Compliance rate checked on Portable Intermittent Compression Device
- Portable Intermittent Compression Device placed on patient in OR
  - 53% received ASA 81 mg daily
- LMWH (enoxaparin) started 12 – 24 hours postop
- 3 months postop – clinical exam
- Signs and symptoms
  - DVT
  - PE

Colwell, et al. JBJS, 2010; 92:527-535

Results



N = 389

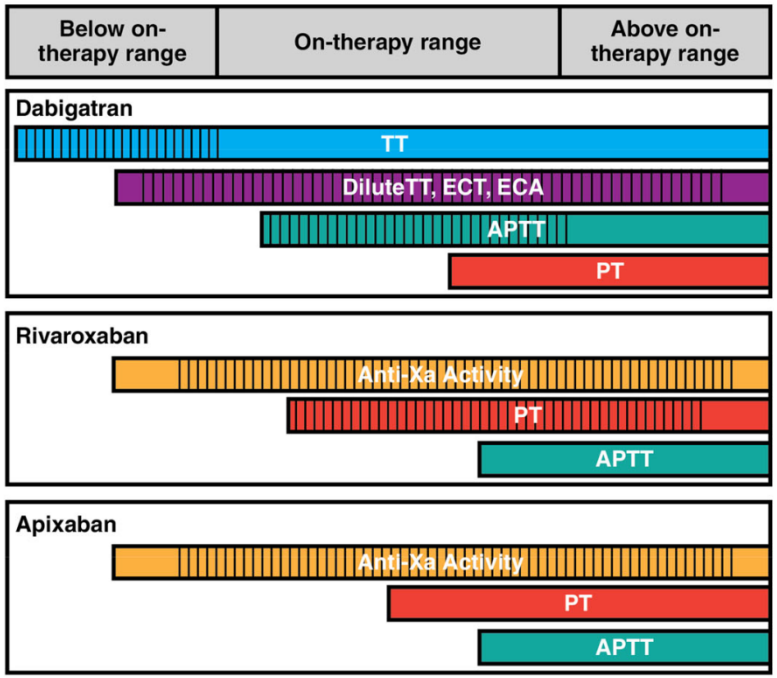
- **No fatal PE or deaths**
- **Major bleeding**
  - **Portable Int. Device 0%**
  - **LMWH 5.6%***
  - ***P=0.0007**

Colwell, et al. JBJS, 2010; 92:527-535

Case 3

75 yo female with h/o HTN and T2DM is on Rivaroxaban for Atrial Fibrillation. The patient's Crcl= 40ml/min. In preparation for Spine Surgery, the rivaroxaban is held for 2 days or 4 doses. In the morning of surgery, the anesthesia resident orders another PT/PTT. The PT is normal at 13s but the PTT is elevated at 38s. What do you do next?

Testing with DOACs

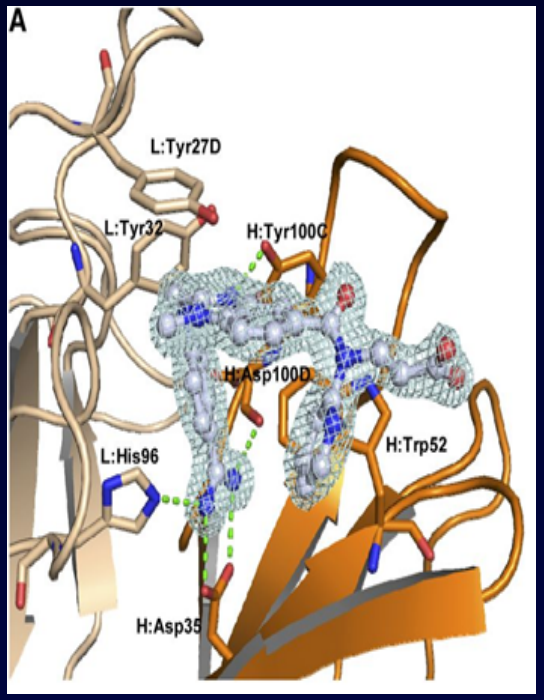


Horizontal bars and vertical hatching correspond to the approximate range of detectability (i.e., sensitivity) and linearity, respectively, of each assay to below, within, and above typical on-therapy concentrations of dabigatran, rivaroxaban, and apixaban. Ranges are approximations and may vary on the basis of choice of reagent.
APTT = activated partial thromboplastin time; ECA = ecarin chromogenic assay; ECT = ecarin clotting time; PT = prothrombin time; TT = thrombin time.

Burnett et al.
J of Thromb and Thrombolysis
2015: 41 (1) Issue 1 , 206-232

REVERSE-AD Interim Analysis

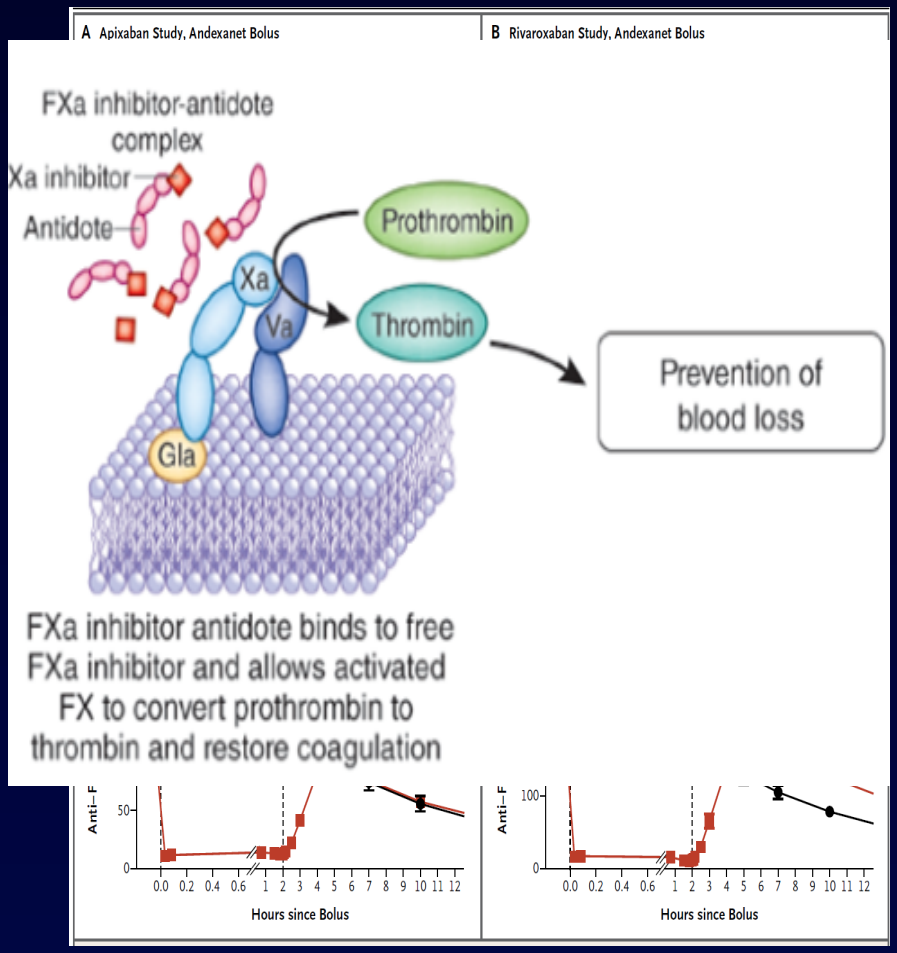
- 2.5 g IV of Idarucizumab (Praxabind) given in 2 doses
- 90 patients on Dabigatran {90% for Afib} (median age 76.5 years; 56% men; median creatinine clearance 58 mL/min)
- 51 patients in group A had serious bleeding (16 of them hemodynamically unstable) and 39 in group B (urgent procedure).
- Median patient-reported time from last dabigatran dose was 15.4 hours. Quick Reversal Confirmed
- Median maximum percentage reversal of anticoagulation (primary endpoint) was 100% (95% CI 100-100) in groups A and B, as assessed by both dilute thrombin time and ecarin clotting time. Reversal occurred soon after 1st dose
- Serious Adverse Events: 21 patients (13 in group A and 8 in group B). Plus Deaths: 18 deaths and 5 thrombotic events, these included GI hemorrhage in 2 patients and post-op wound infection, delirium, right ventricular failure, and pulmonary edema in 1 patient each.



Pollack et al. NEJM 2015; 373:511-20

Andexanet Alpha

- Half life 1-hr
- Dose dependent reversible anticoagulant effect
- Annexa A and Annexa R were RCTs
- Anti-Xa levels were reduced 94% vs 21% & 92% vs. 18% respectively
- Dose different for apixaban and rivaroxaban
- Andexanet reveresd the activity within minutes after adminsitration and without clinical toxic effects



Siegal DM. N Engl J Med. 2015 Dec 17;373(25):2413-24.

Conclusion

- VTE Prevention is an important patient Safety and Quality measure
- Surgical Patients should be risk stratified and prophlaxed paying attention to both risk of VTE and risk of major bleeding
- Extended prophylaxis should used for high risk cancer and major orthopedic surgery patients
- Idarucizumab may be an option to reverse patients needing emergent surgery on Dabigatran