

# Management of antithrombotic therapy in patients with LVADs

Lisa Baumann Kreuziger, MD, MS

Assistant Professor, Medical College of Wisconsin

Assistant Investigator, Blood Research Institute

Associate Medical Director, BloodCenter of Wisconsin

[Lisa.BaumannKreuziger@bcw.edu](mailto:Lisa.BaumannKreuziger@bcw.edu)

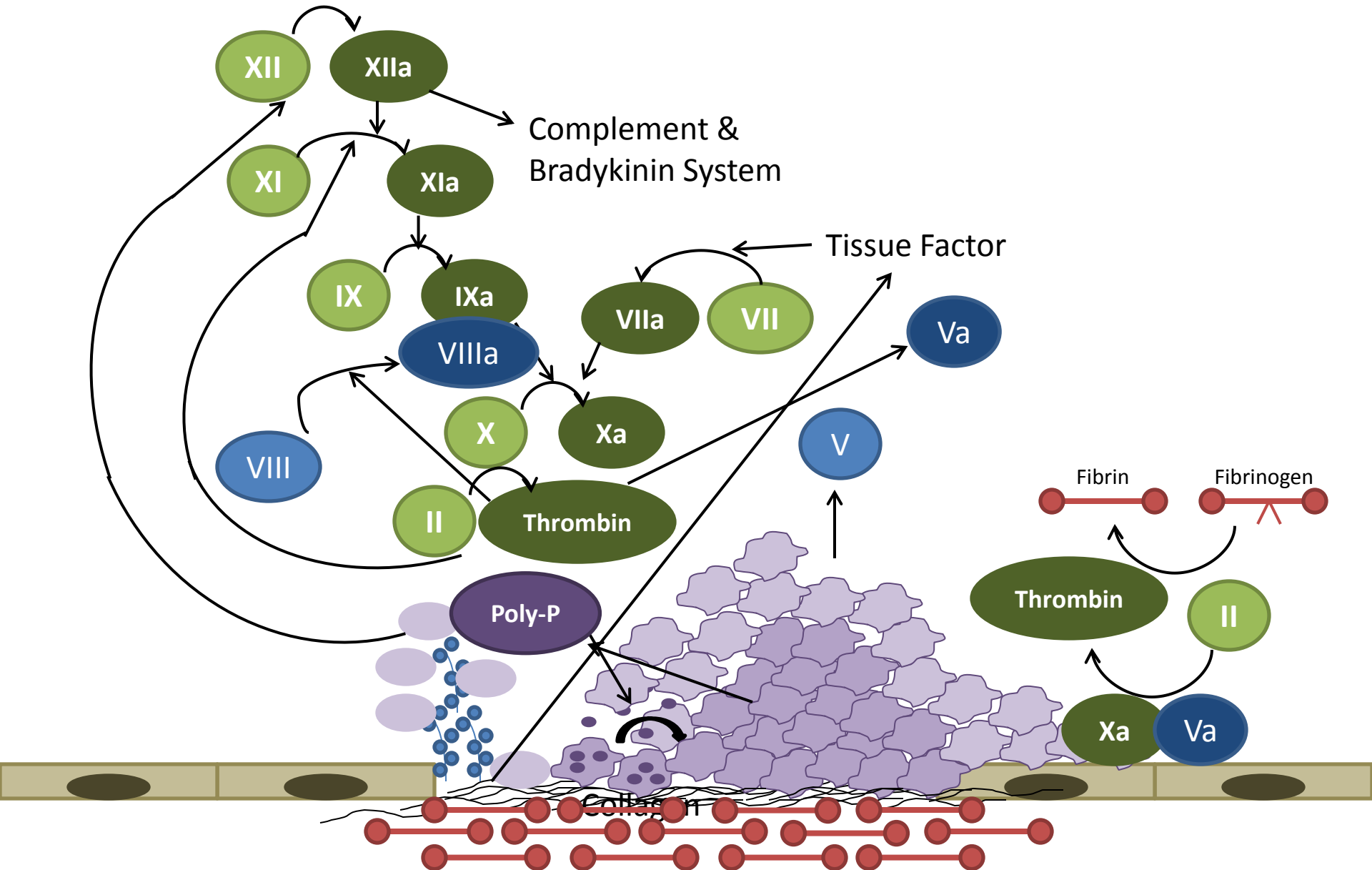
# Disclosures

- Research Funding
  - Blood Center Research Foundation
  - Clinical and Translational Science Institute of SE Wisconsin/Advancing Healthier Wisconsin Foundation
- Research Samples
  - Thoratec (St. Jude/Abbott)
- CME
  - American Society of Hematology
- Hematologist

# Outline

- Review coagulation cascade and effect of LVADs on coagulation
- Anticoagulation in patients with LVADs
- Antiplatelet therapy in patients with LVADs

# Coagulation system



# LVAD Effect on Coagulation System

## Normal

1. Platelets Bind to VWF
2. Platelets Activate
3. Coagulation Factors Activated
4. Thrombin → Fibrin
5. Fibrinolysis

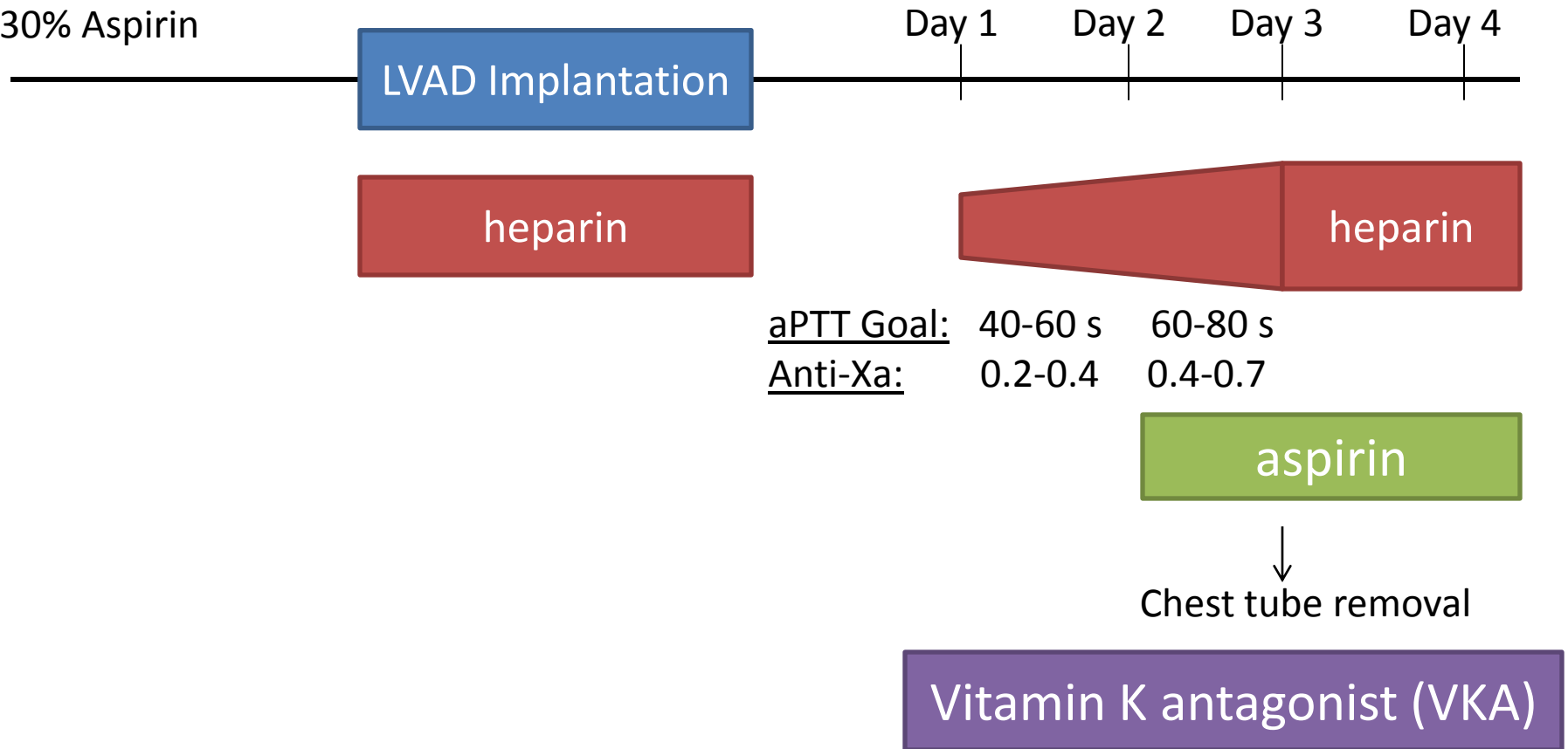
## LVAD

1. Impaired platelet/VWF binding  
Acquired VW Disease
2. Platelets Activated
3. Decreased Contact Pathway Factors
4. ↑ Thrombin formation
5. ↑ Fibrinolytic activation

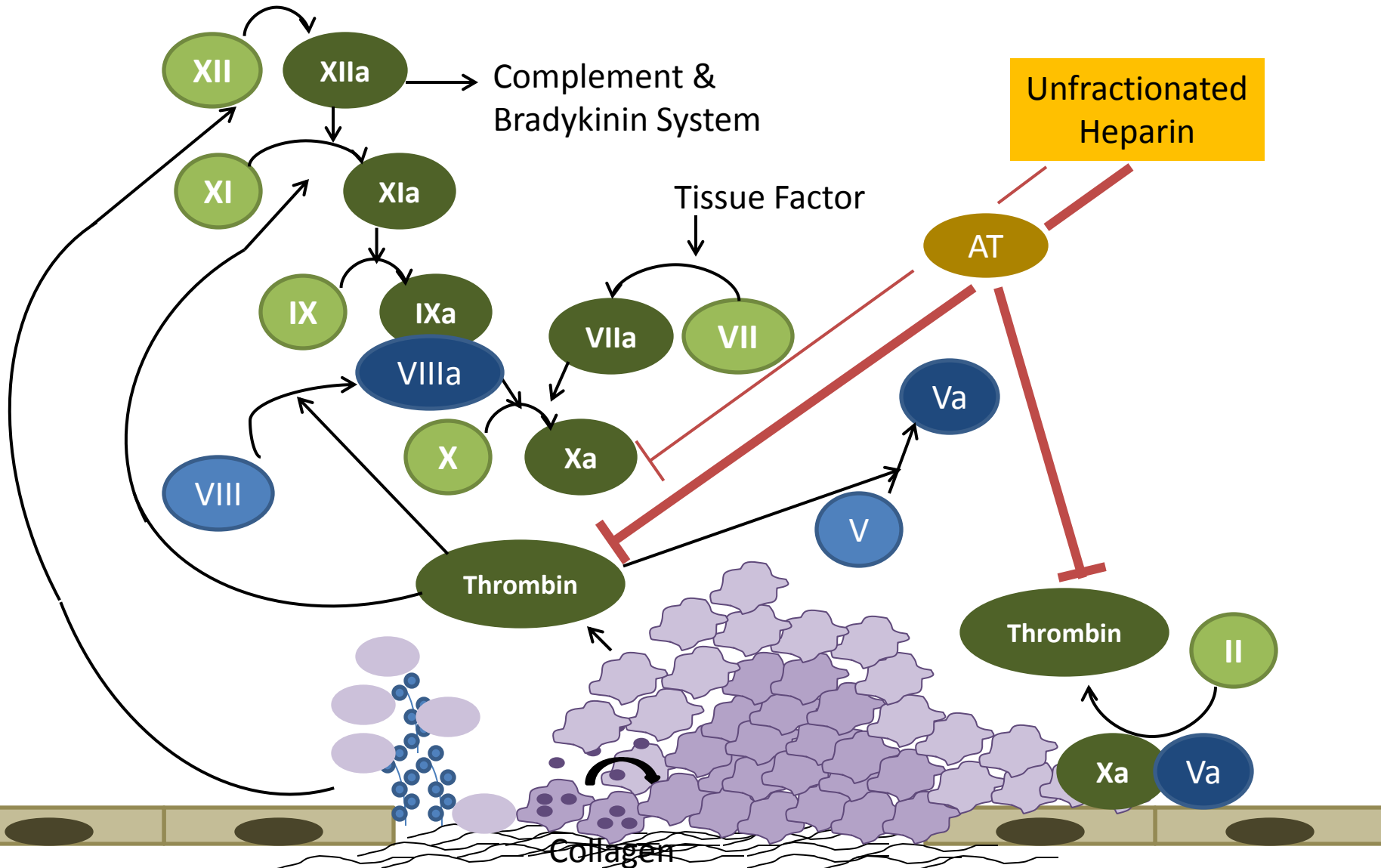
JACC 2009; 53 (23): 2162-7. J Am Coll Cardiol HF 2014;2:141-5; *Circ Heart Fail* 2010;3;675-681.; Ann Thorac Surg 2010;90:1263-9. J Thromb Thrombolysis (2014) 37:499-506; JHLT 2000;19:462-468. ASAIO 1995; 41:M790-94.; ASAIO 2008; 54:115-119.; Nat Clin Pract 2009; 6: 147-57; Ann Thorac Surg 2009;88:1171-9.

# Adult LVAD Antithrombotic Therapy

50% Anticoagulated  
30% Aspirin



# Heparin Mechanism of Action



# Perioperative Heparin

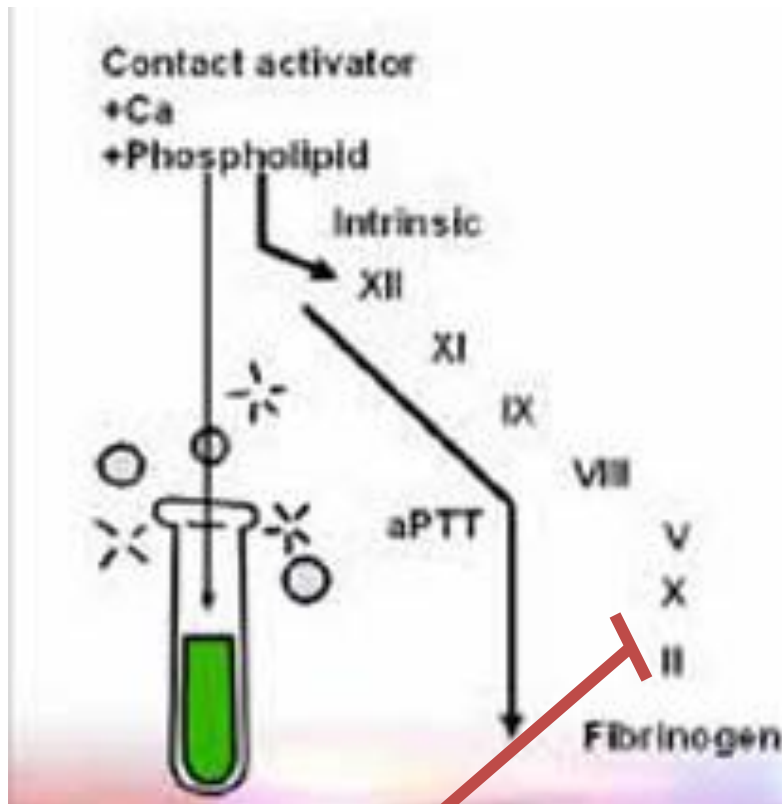
- HMII BTT retrospective review
  - Bridging: No difference in thrombosis rates
  - Less bleeding requiring transfusion in patients not treated with heparin
- Retrospective cohort, matched historical controls
  - Thrombosis: 4.9% heparin vs. 27.0% no bridging
  - Multivariate analysis: OR=0.10 (CI 0.01–0.85)
- PREVENT trial: standardized bridging
- Dr. Guglin: study of bridging around elective procedures



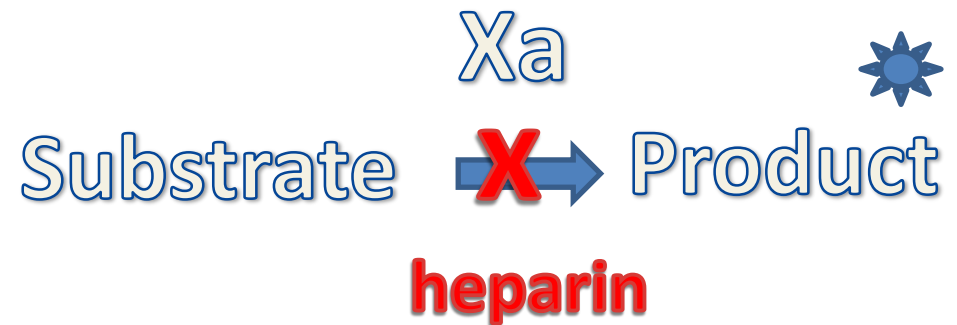
# Heparin Monitoring





## aPTT

## Anti-Xa



Heparin  
Antithrombin

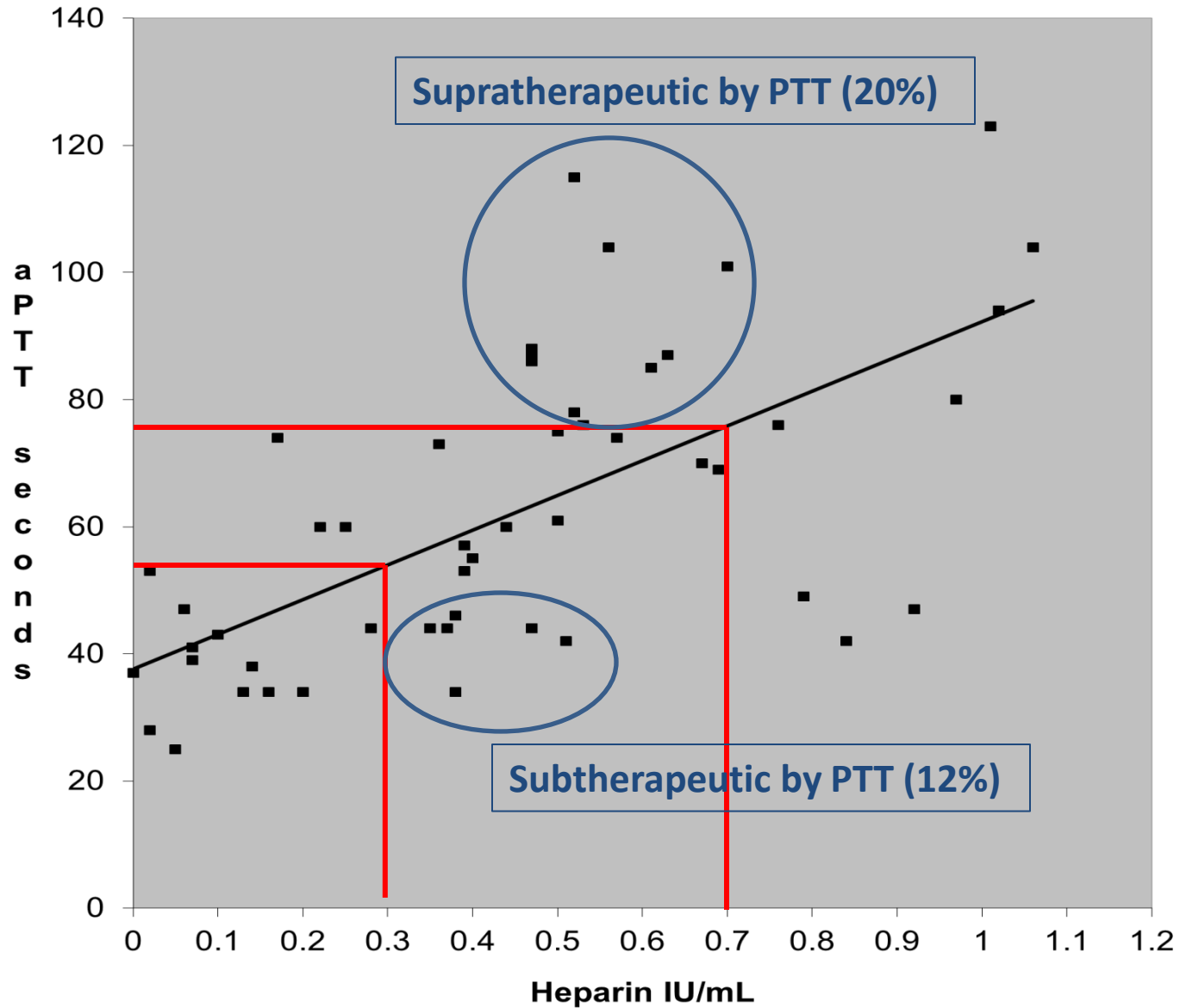


- More heparin = Less colored product 
- Less heparin = More colored product   

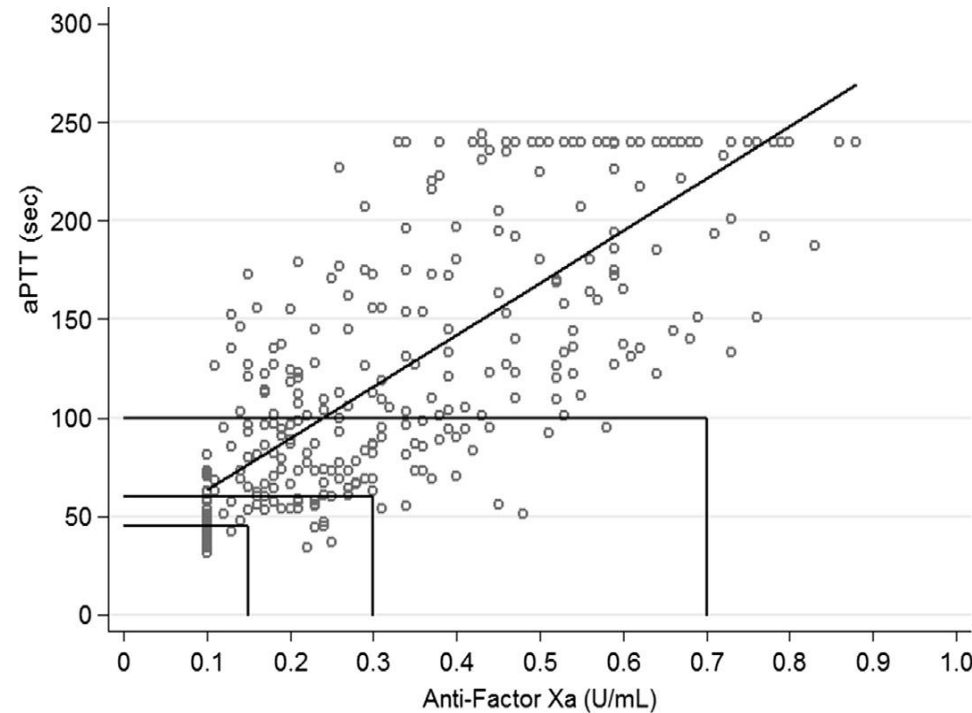
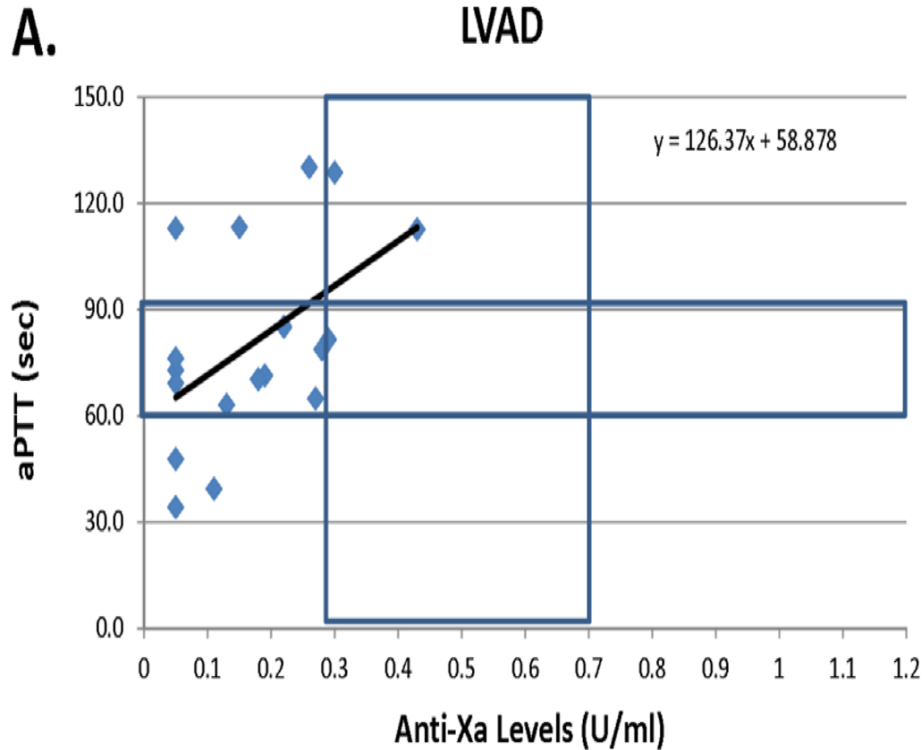
# Heparin Monitoring

- Determine if your lab adds anti-thrombin to anti-Xa assay
- aPTT assays not standardized between institutions
- aPTT activator (Kaolin) not standardized between manufactures or lots
- aPTT must be calibrated to measure anticoagulation with heparin against anti-Xa

# Heparin Xa Therapeutic Curve

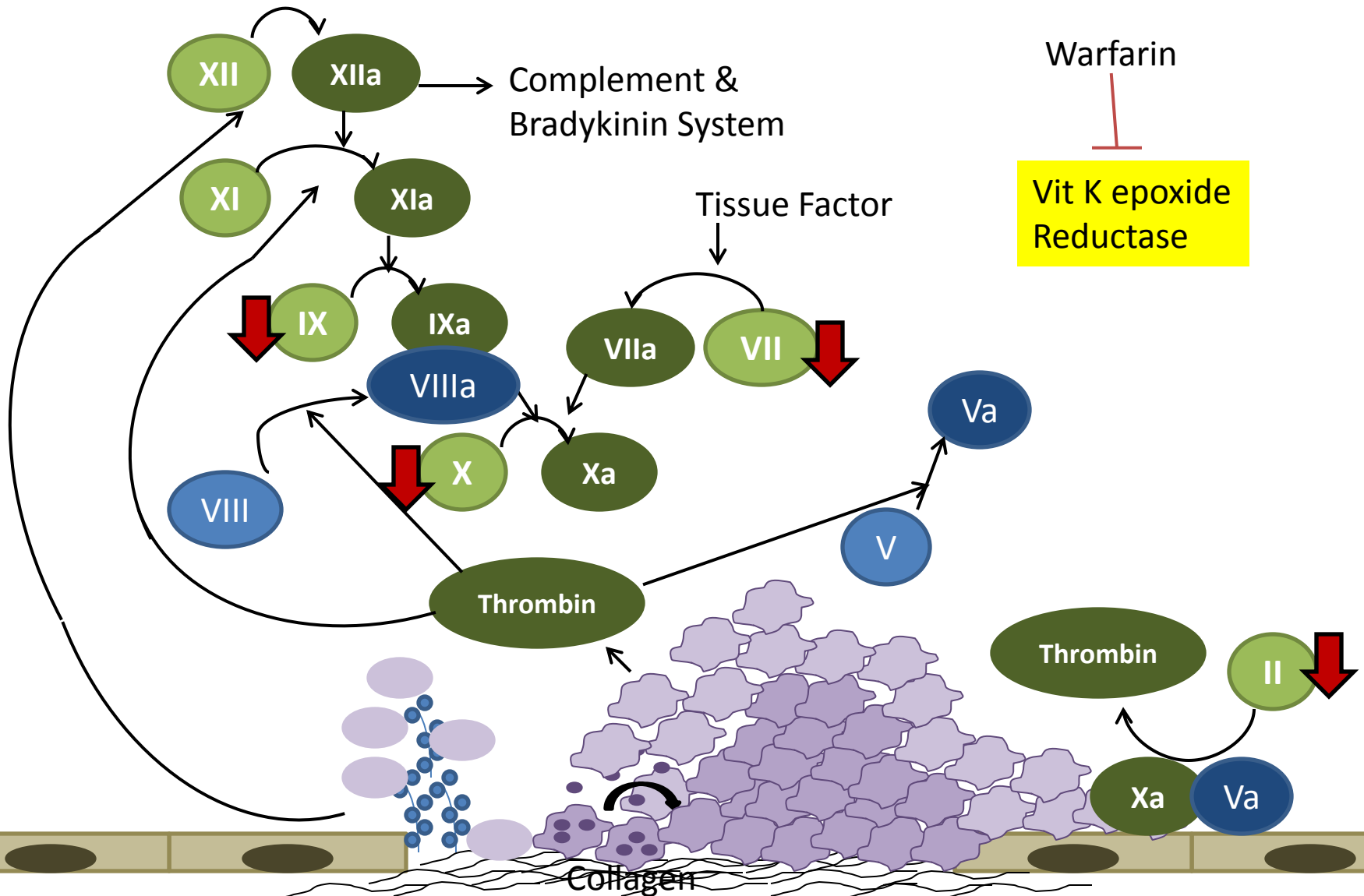


# PTT vs. anti-Xa monitoring



Discordance higher if INR > 1.5 and thrombosis/hemolysis

# Warfarin Mechanism of Action



# Long-term Antithrombotic Therapy

- Vitamin K antagonist treatment standard

	Axial	Centrifugal
<b>INR Goal</b> avg (range)	2-3 (1.5-3.5)	2-3 (2-3.5)

54% people changed warfarin dose

- 22% difference in weekly dose

- 70% decrease in dose

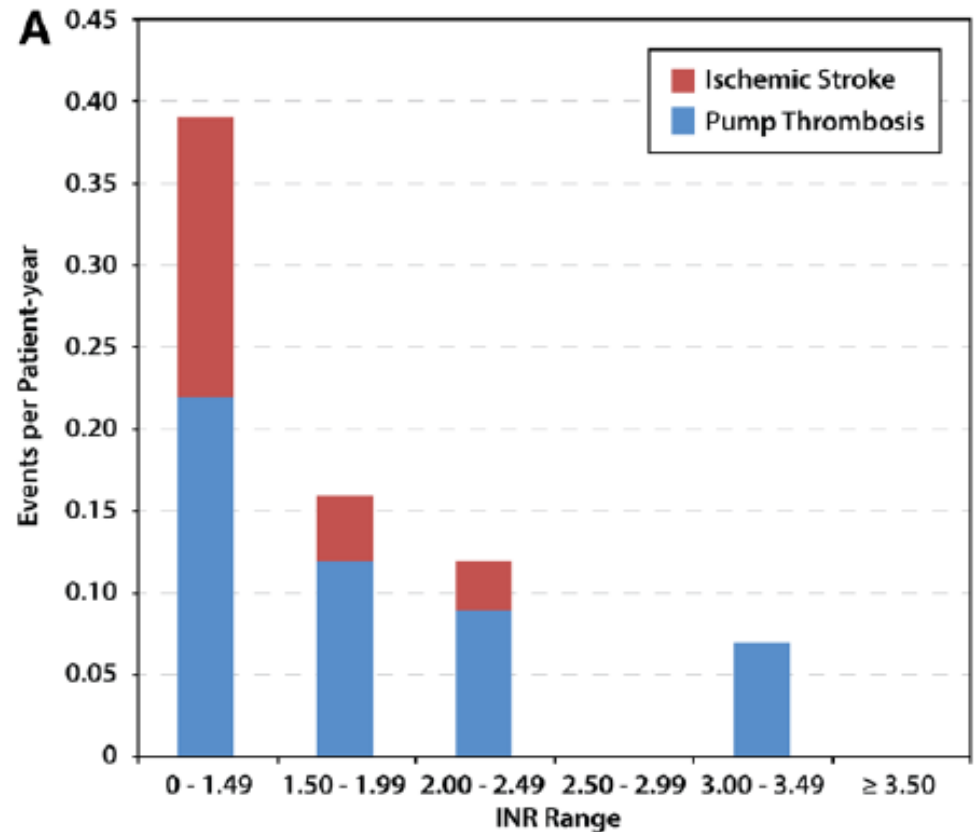
# Managing VKA therapy

Drug or Factor	Half-Life
Warfarin	40 hours
Phenprocoumon	144 hours
Factor VII	6 hours
Protein C	8 hours
Factor II	50 hours

- Will NOT see the effect of warfarin dose change for 24-36 hours

# INR Intensity

- Single center retrospective review
- 249 patients
- Median follow-up:  $17.6 \pm 13.6$  months
- Optimal INR 2.6





# Managing VKA therapy

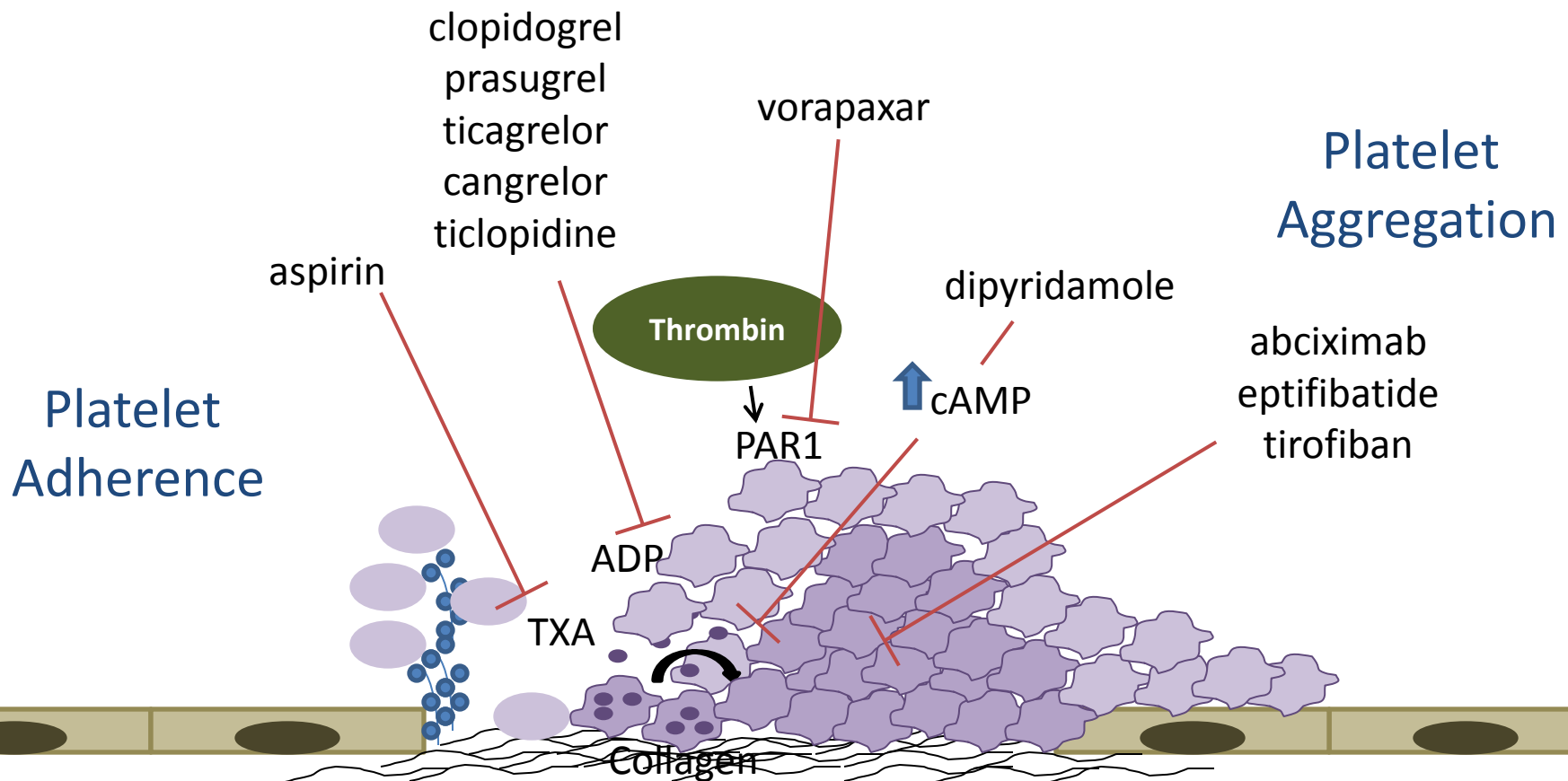
- Pharmacist Run Anticoagulation = Improved Time-In-therapeutic Range (TTR)
- Patient Self Management= Improved Time-In-therapeutic Range

	Pharmacist Management (n=11)	Usual Care (n=44)	P-value
<b>TTR</b>	<b>44.4%</b>	<b>30.6%</b>	<b>0.03</b>
Bleeding	0.23 ppy	0.33 ppy	0.55
Thrombosis	0.12 ppy	0.13 ppy	0.88

ppy=per-patient year

# Antiplatelet Mechanism of Action

## Platelet Activation



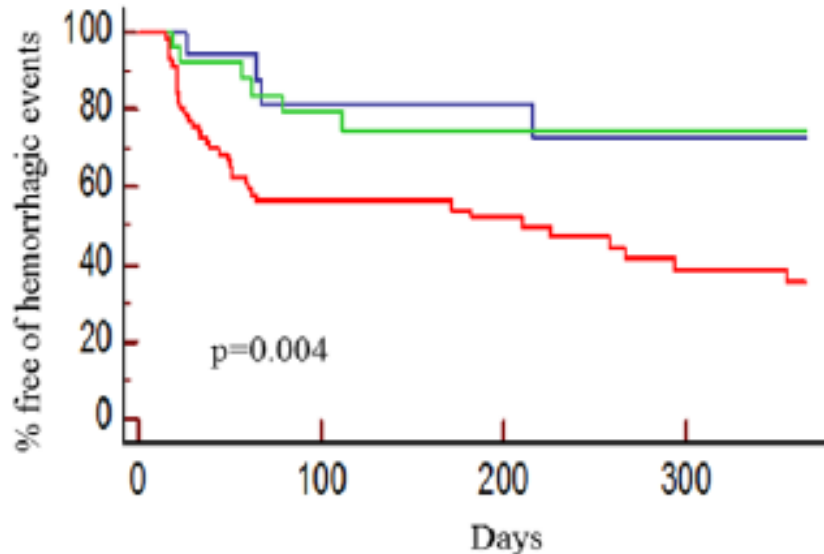
# Long-term Antithrombotic Therapy

- Meta-analysis: Antiplatelet therapy variable

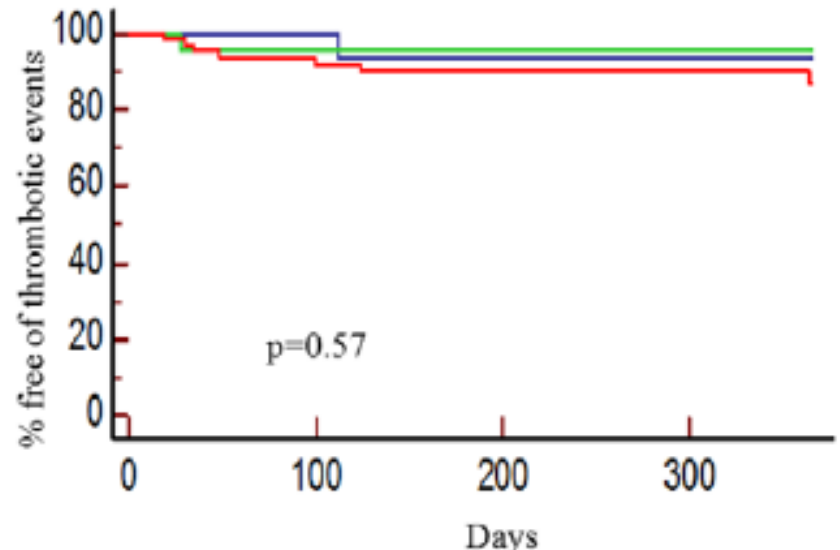
	Axial	Centrifugal
<b>Major Hemorrhage</b>		
Aspirin	6-58%	9-44%
Aspirin + Dipyridamole	16-40%	

# Aspirin Dose

## Hemorrhagic Events



## Thrombotic Events



Number at Risk					Number at Risk				
<b>ASA 81 +DPE</b>	26	17	13	10	<b>ASA 81 +DPE</b>	26	21	17	13
<b>ASA 81</b>	18	13	10	7	<b>ASA 81</b>	18	16	11	8
<b>ASA 325</b>	70	30	21	14	<b>ASA 325</b>	70	49	35	32

# TRACE

## EU-TRACE

- VKA therapy
- 91% Standard of Care
- 2-year rates (n=92)
  - Ischemic stroke=0.03 ppy
  - Device thrombosis=0.05 ppy
  - Bleeding= 0.10 ppy

## US-TRACE

- VKA alone, ASA alone, None
- 82% enrolled due to bleeding
- 1 year Rates
  - Ischemic stroke=0.07 ppy
  - Device thrombosis=0.08 ppy
- 52% Subsequent bleeding

# Monitoring Anti-Platelet Medications

- 8% “non-responders” based on aggregometry
- Retrospective cohort (n=57)
  - Goal: TEG-MA 60-70 mmHg
  - Regimen: aspirin 81 → 325 → 650 mg/day + Dipyridamole (DPE) max 1 g/day
  - 68% received DPE
    - 68% received ASA + DPE
  - Bleeding 0.21 events/py

# Summary

- Extreme variability in practice
- aPTT testing not standardized
- Consider use of anti-Xa testing especially in thrombosis
- VKA therapy with INR 2-3
- Limited evidence for modification of anti-platelet therapy based on testing