

NON-ST ELEVATION ACS

OPTIMIZING ANTI-THROMBOTIC THERAPY

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ISHNE- ISCP 2007

To make the the best or most effective use of antithrombotic drugs

PREVENT

Death, MI, revascularization

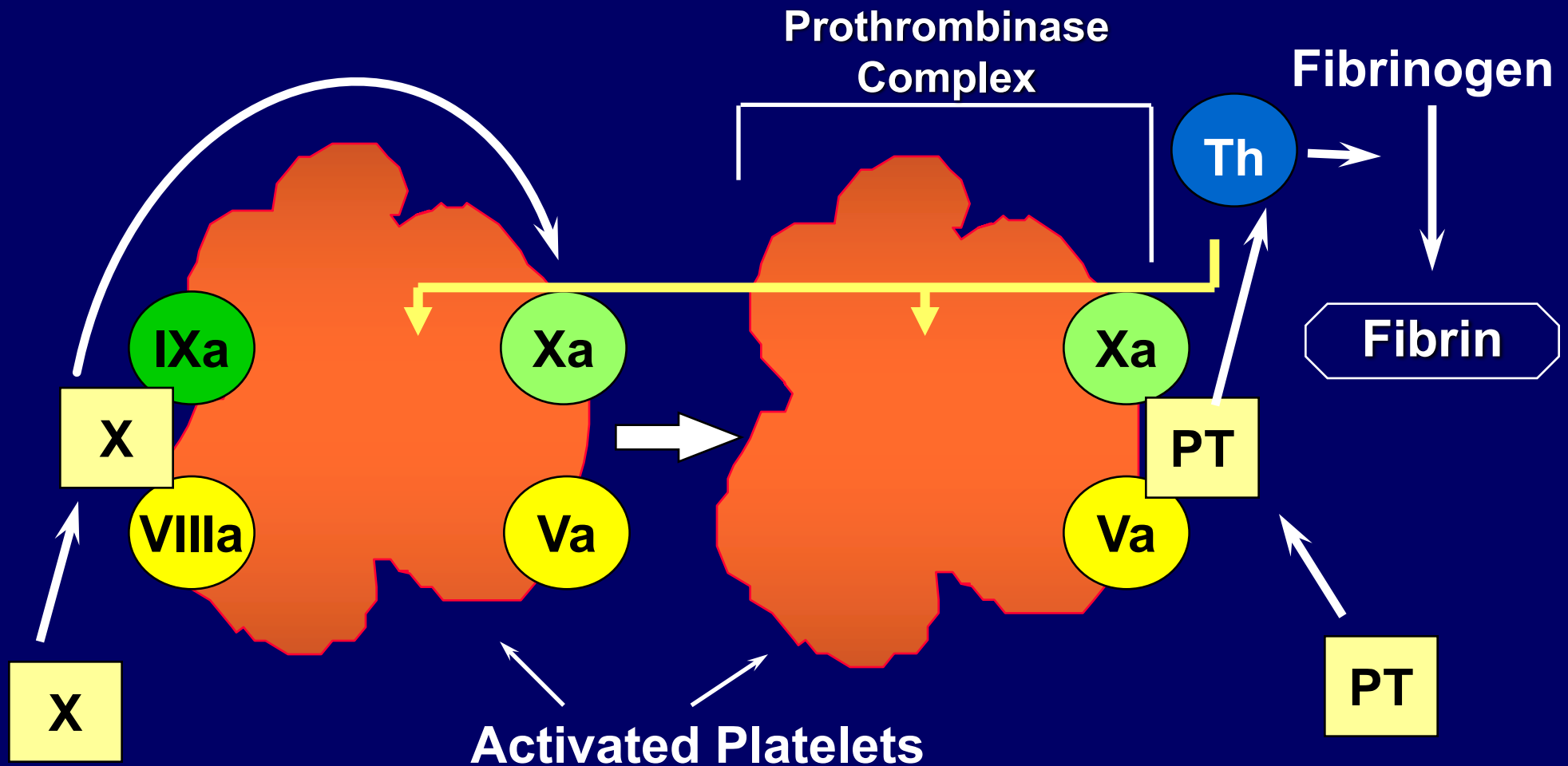
AVOID

Bleeding



- ***AVAILABLE DRUGS***
- ***PATIENTS SUBSETS***
- ***BLEEDING***
- ***CONCLUSIONS***

COAGULATION. PROPAGATION PHASE



COAGULATION INHIBITION

Tissue Factor

- None available for clinical use



Factor Xa

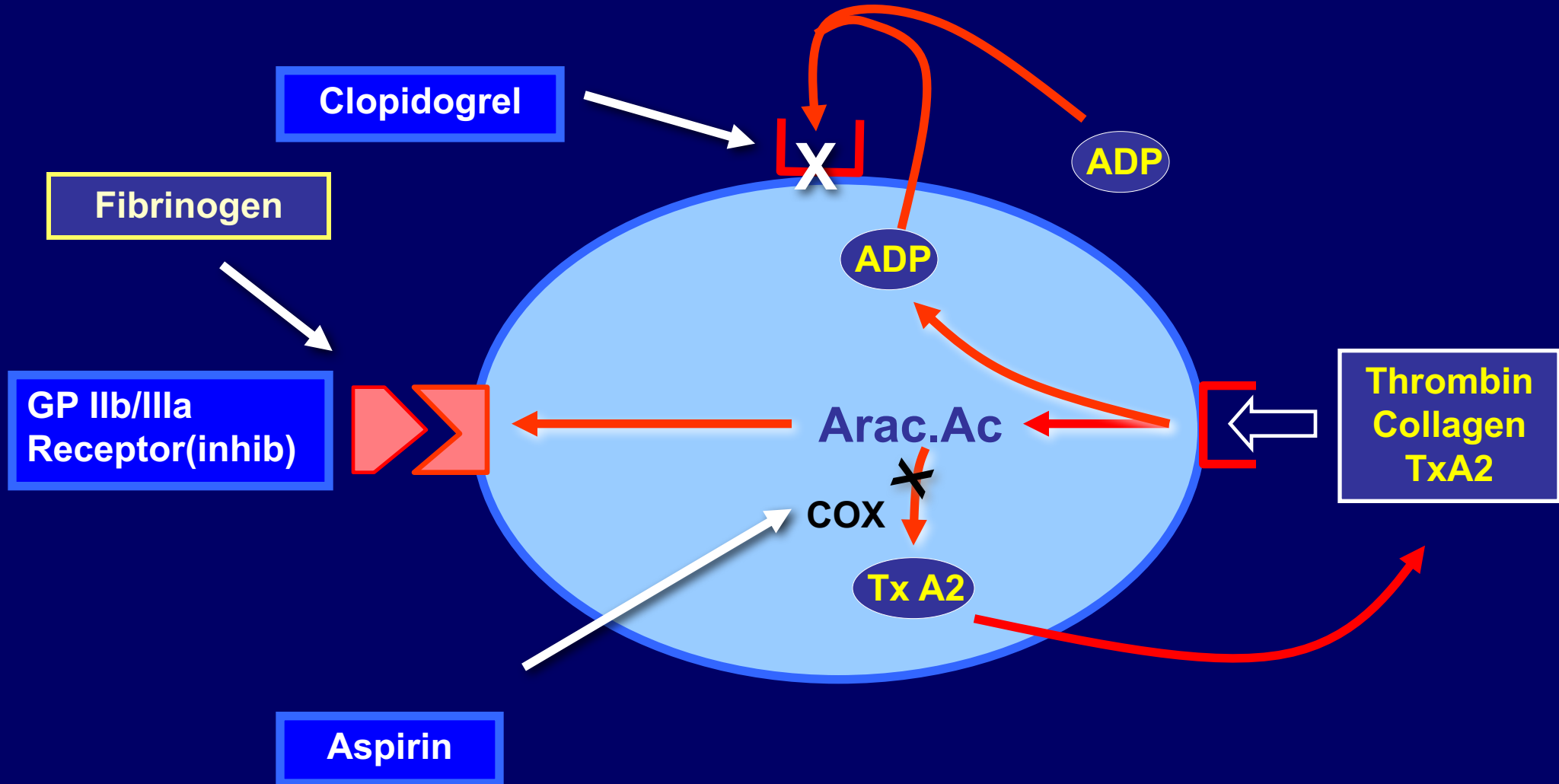
- LMWH
- Fondaparinux



Thrombin

- HNF
- Direct inhibitors: hirudin, bivalirudin

ANTIPLATELET DRUGS



ANTIPLATELET AGENTS

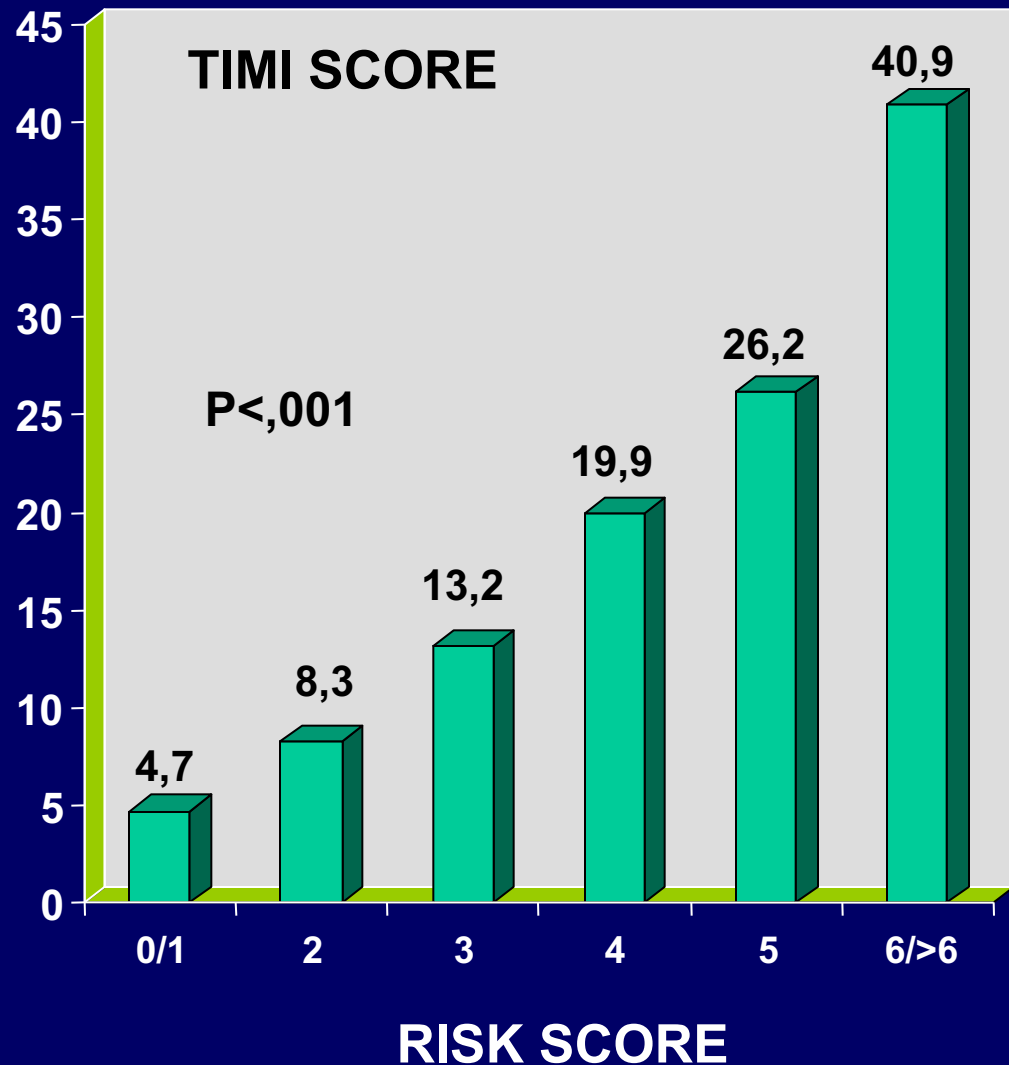
<u>DRUG</u>	<u>DOSE</u>	<u>DURATION</u>
Aspirin (1)	160-325 mg	Loading
	75-100 mg	Long-term
Clopidogrel (2)	300 mg (600?)	Loading
	75 mg	1-12 months
Abciximab (3)	0.25 mg/kg	Bolus
	0.125 μ /kg/m	12-24 h
Eptifibatide (3)	180 μ /kg/m	Bolus x 2
	2 μ /kg/m	72-96 h
Tirofiban (3)	0.4 μ /kg/m	30 minutes
	0.10 μ /kg/m	48-96 h

ANTICAOGULANT DRUGS

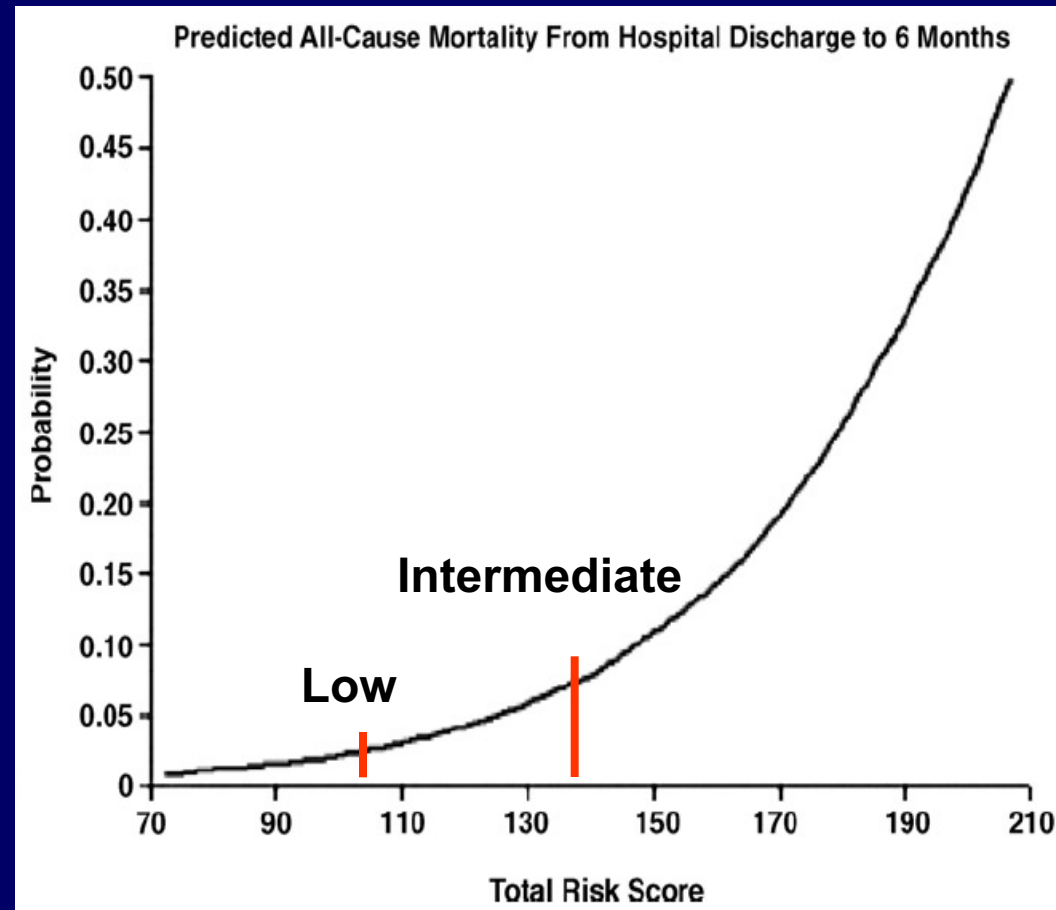
<u>DRUG</u>	<u>DOSE</u>	<u>DURATION</u>	<u>CATH LAB</u>
UFH	60 -70 UI / kg 12 - 15 UI / kg	Bolus ≥48h or revascul.	↓ACT when GP IIb/IIIa
Enoxaparin	1 mg/kg/12 h	Discharge or revascularization	0.3 mg iv, if ≥ 8h Previous dose
Fondaparinux	2.5 mg / d	Discharge or revascularization	Add UFH 50-70 UI/kg bolus
Bivalirudin	1 mg/kg 2.5 mg/kg/4h 0.2 mg/kg/20h	Bolus Until revascular.	Add 0.5 mg/kg ↑1.75mg/kg/h

TREATMENT ACCORDING TO RISK

DEATH, IM, Revascularization 14 d



All cause mortality discharge - 6 months



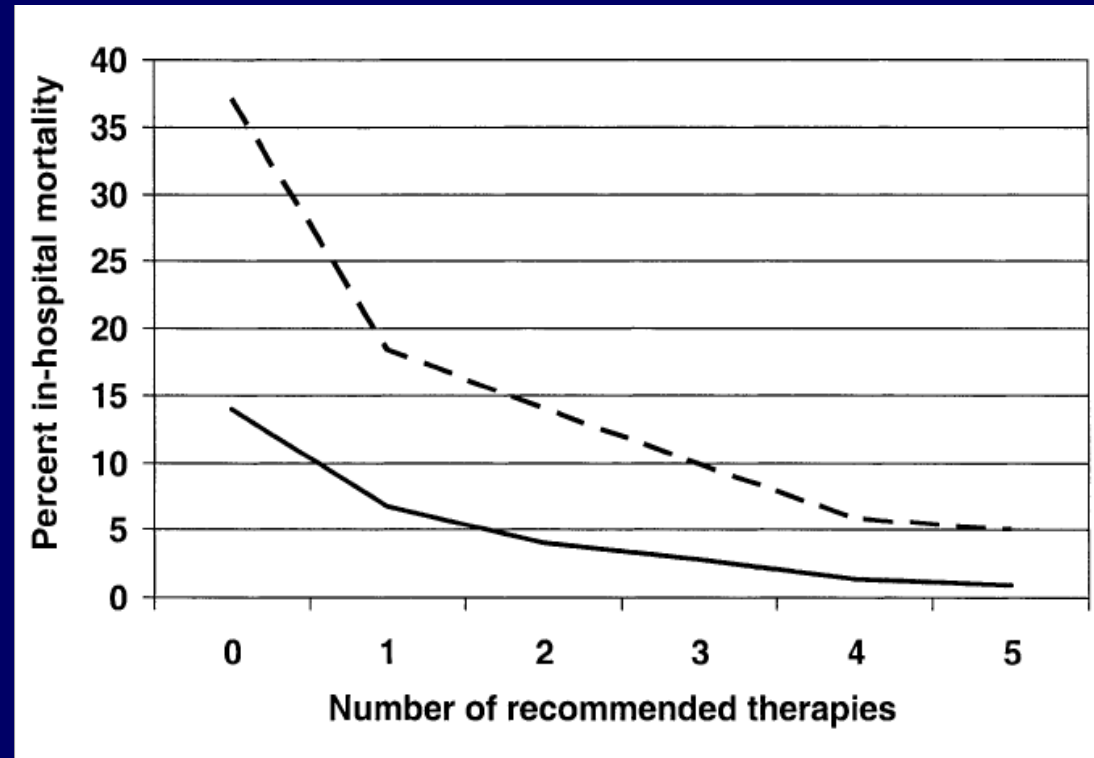
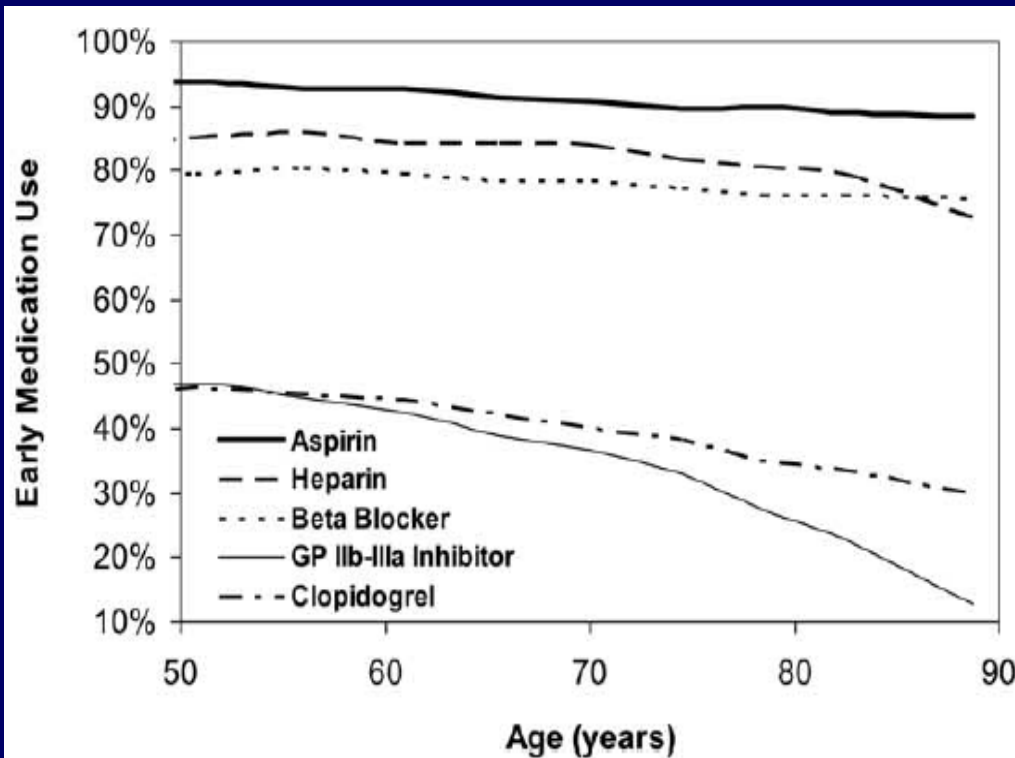
GRACE NOMOGRAM

POPULATION IN RANDOMIZED TRIALS vs SURVEYS

	ACUITY	ISAAR/REACT2	MASCARA	
			NST	Uncla
Age	63 (23-91)	66±11	69±11	75±10
Males (%)	70	76	70	61
Diabetes (%)	28	28	35	45
Insulin (%)	8	9	13	16
Renal fail. (%)	19	N/A	14	19
Stroke	N/A	excluded	9	9

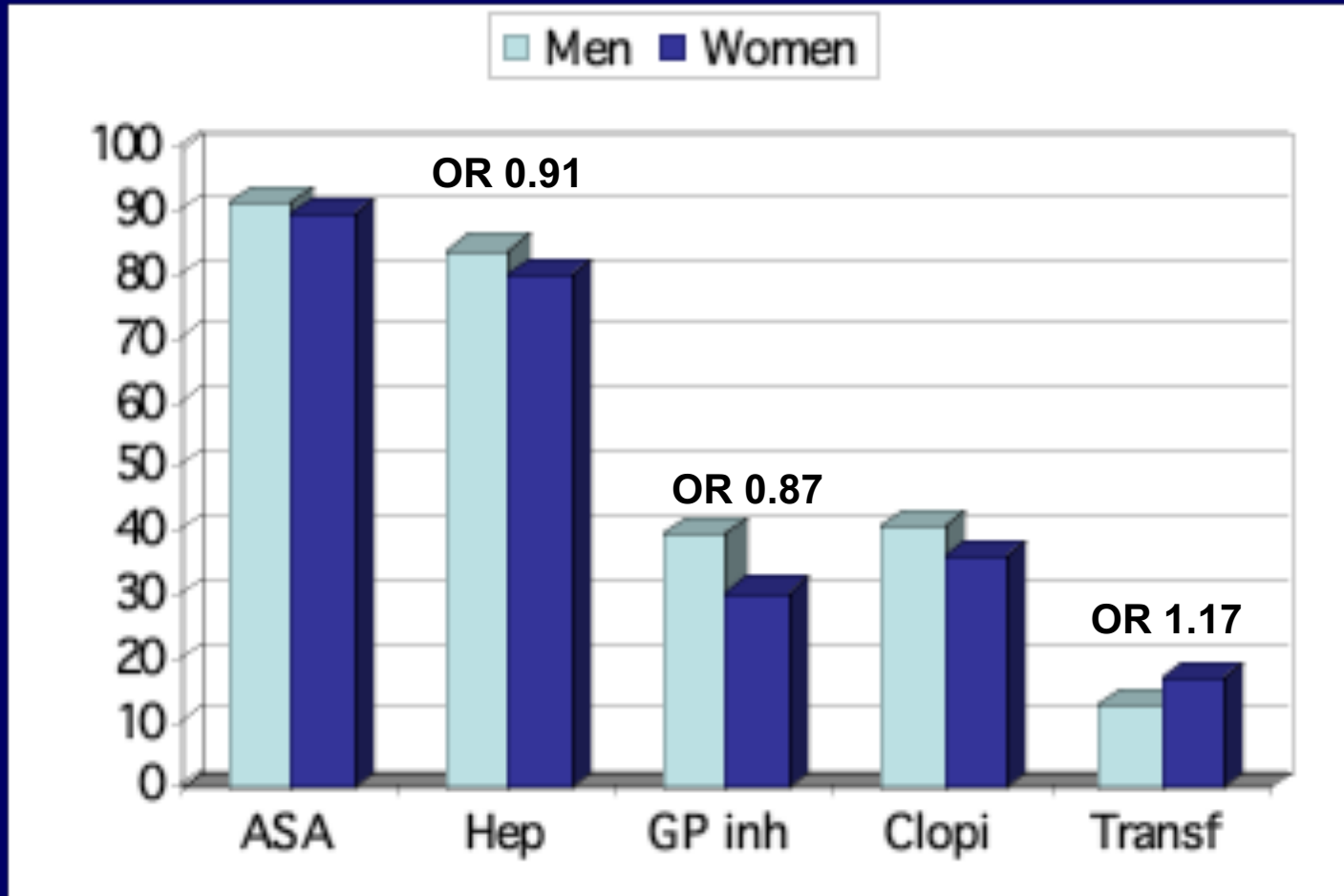
ANTITHROMBOTICS IN THE ELDERLY

THE CRUSADE DATABASE (n=56,963)
35% > 75 y, 11% > 85 y



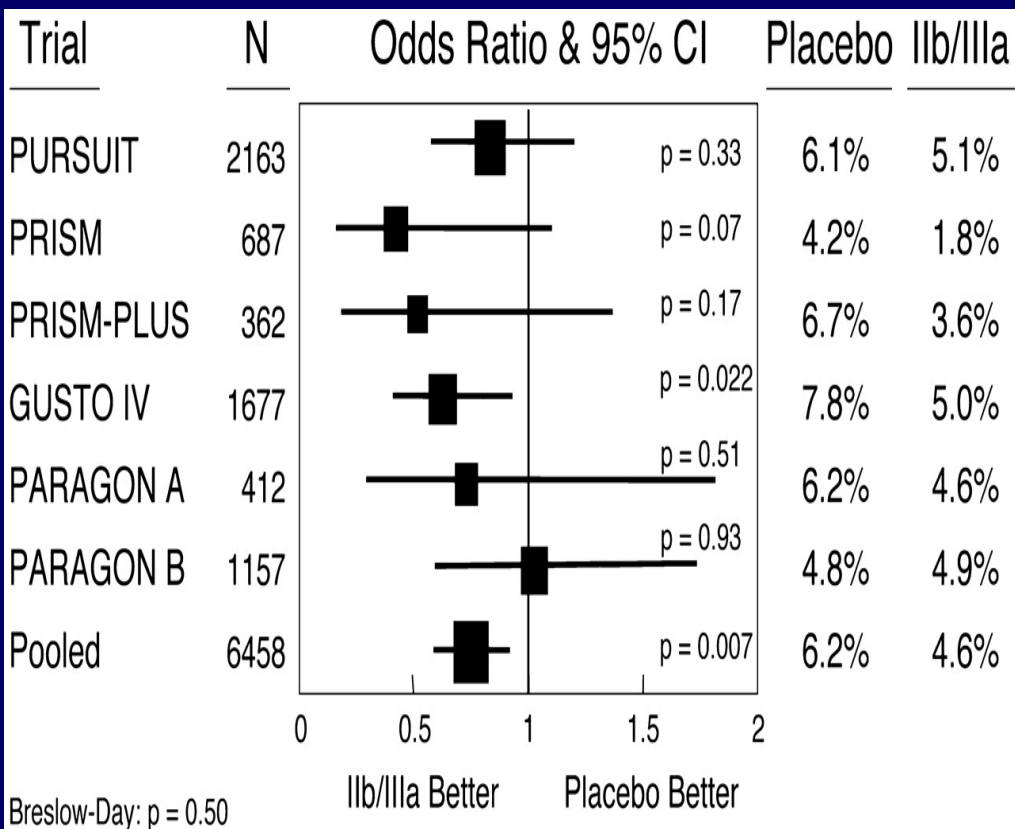
ANTITHROMBOTICS AND WOMEN

THE CRUSADE DATABASE (n= 35,875)
41% women. Older than men (73y vs 65y)

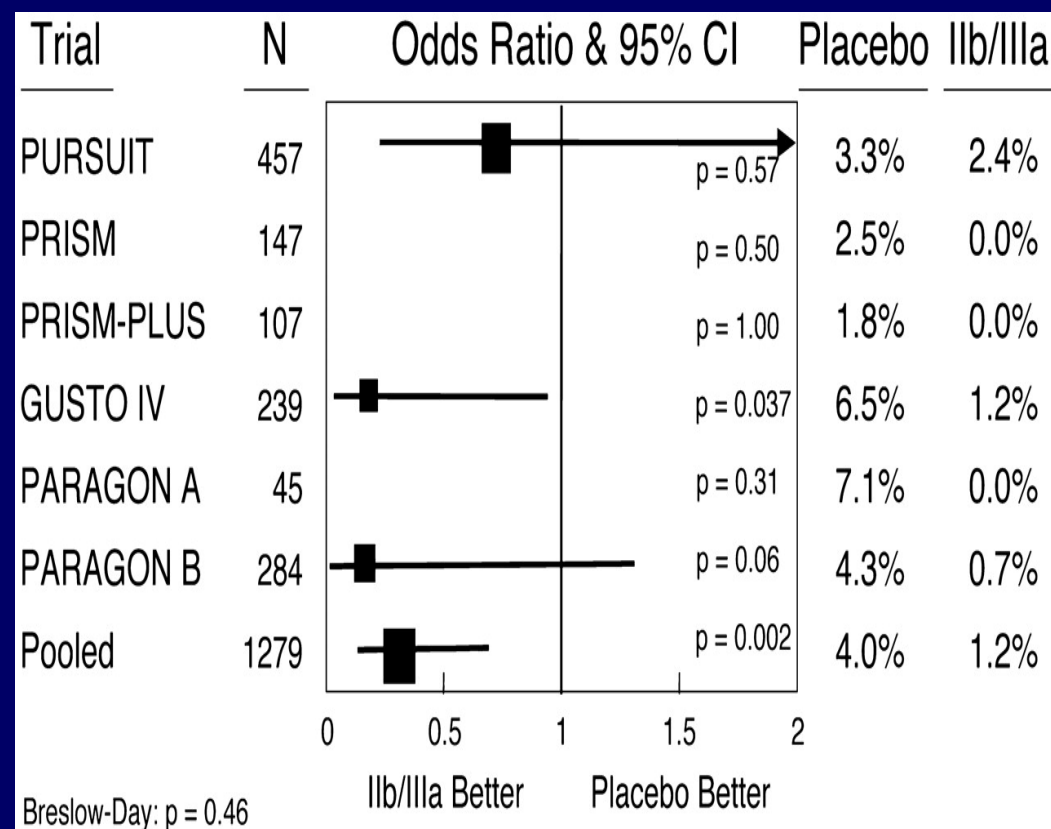


ANTITHROMBOTICS IN DIABETICS

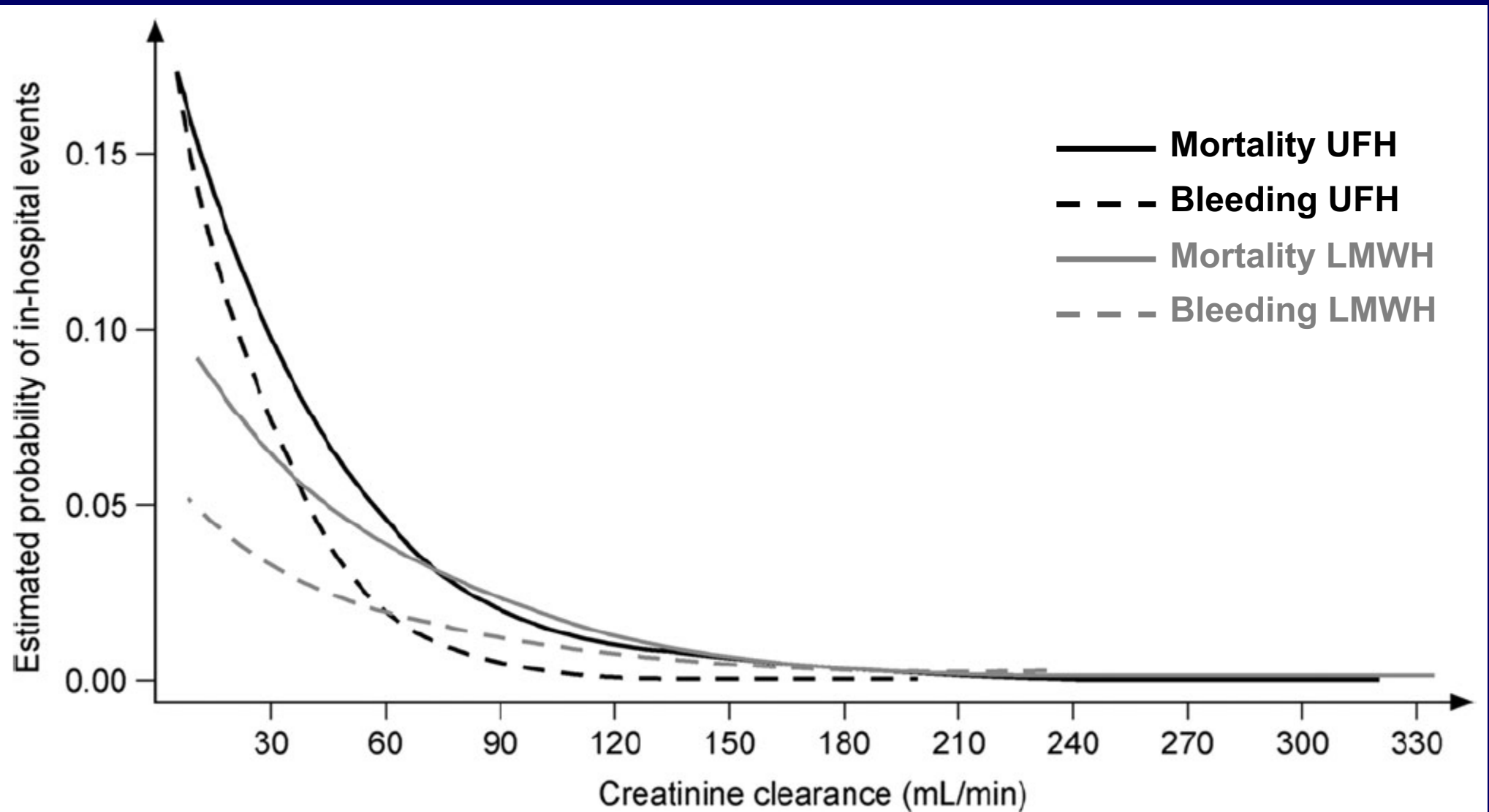
Death 30 d. Medical treatment



Death 30 d. PCI



ANTITHROMBOTICS AND RENAL FUNCTION



ANTITHROMBOTICS AND RENAL FUNCTION

CREATININE CLEARANCE (Cockcroft – Gault) WOMEN CHART

CREATININE (mg/dl)		AGE (y)											
WEIGHT (kg)	1,2	40	45	50	55	60	65	70	75	80	85	90	95
	45	44	42	40	38	35	33	31	29	27	24	22	20
	50	49	47	44	42	39	37	34	32	30	27	25	22
	55	54	51	49	46	43	41	38	35	32	30	27	24
	60	59	56	53	50	47	44	41	38	35	32	30	27
	65	64	61	58	54	51	48	45	42	38	35	32	29
	70	69	65	62	59	55	52	48	45	41	38	34	31
	75	74	70	66	63	59	55	52	48	44	41	37	33
	80	79	75	71	67	63	59	55	51	47	43	39	35
	85	84	79	75	71	67	63	59	54	50	46	42	38

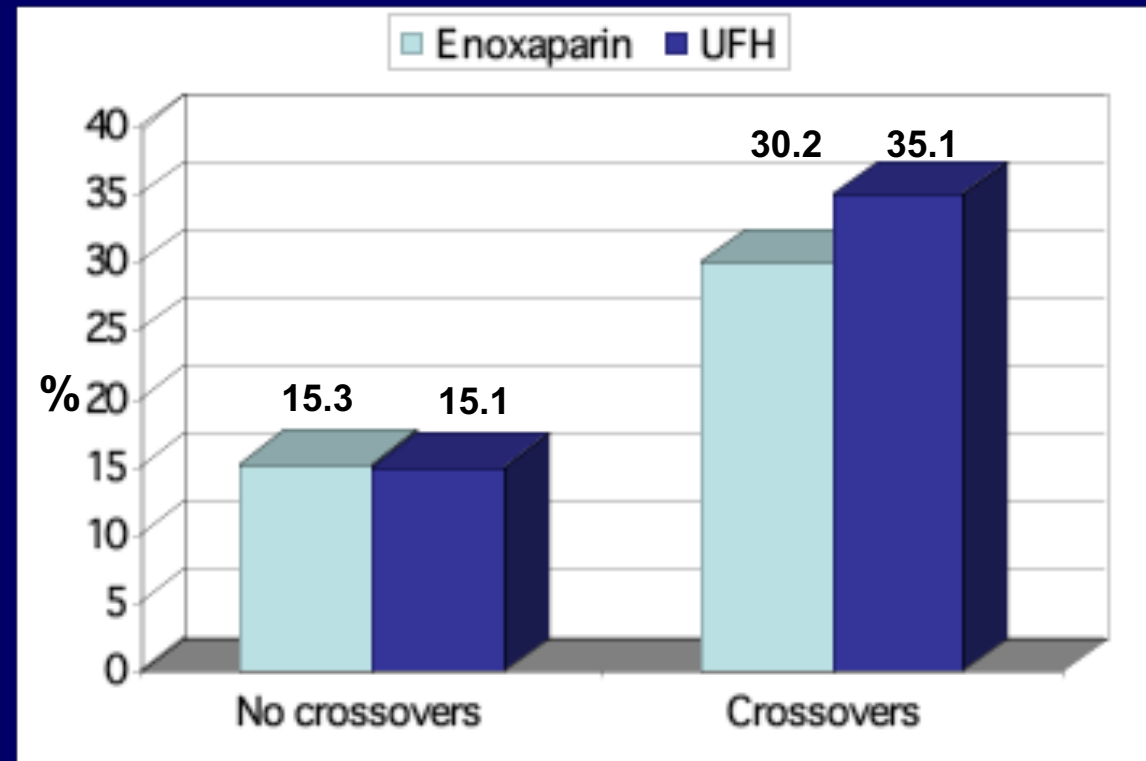
ANTITHROMBOTICS IN RENAL FAILURE

CLOPIDOGREL	No information
ENOXAPARIN	Not indicated if Cr Cl <30 mL/min
FONDAPARINUX	Not indicated if Cr Cl <30 mL/min
BIVALIRUDIN	If Cr Cl < 30 mL/min, ↓ infusion to 1mg/k/h
TIROFIBAN	↓ 50% dose if Cr Cl < 30 mL/min
EPTIFIBATIDE	If Cr Cl < 50 mL/min ↓ iv 1μg/k/m Not indicated if Cr Cl <30 mL/min
ABCIXIMAB	No specific recommendations Careful use in renal failure!

ANTITHROMBOTICS AND BLEEDING

<u>RISK FACTOR</u>	<u>OR</u>
Age (↑10 y)	1.22
Female	1.36
Renal failure	1.53
Bleeding	2.18
Diuretics	1.91
Gp IIb/IIIa	1.86
Inotropics	1.88
Use PCI	1.63
Right-heart kt	2.01

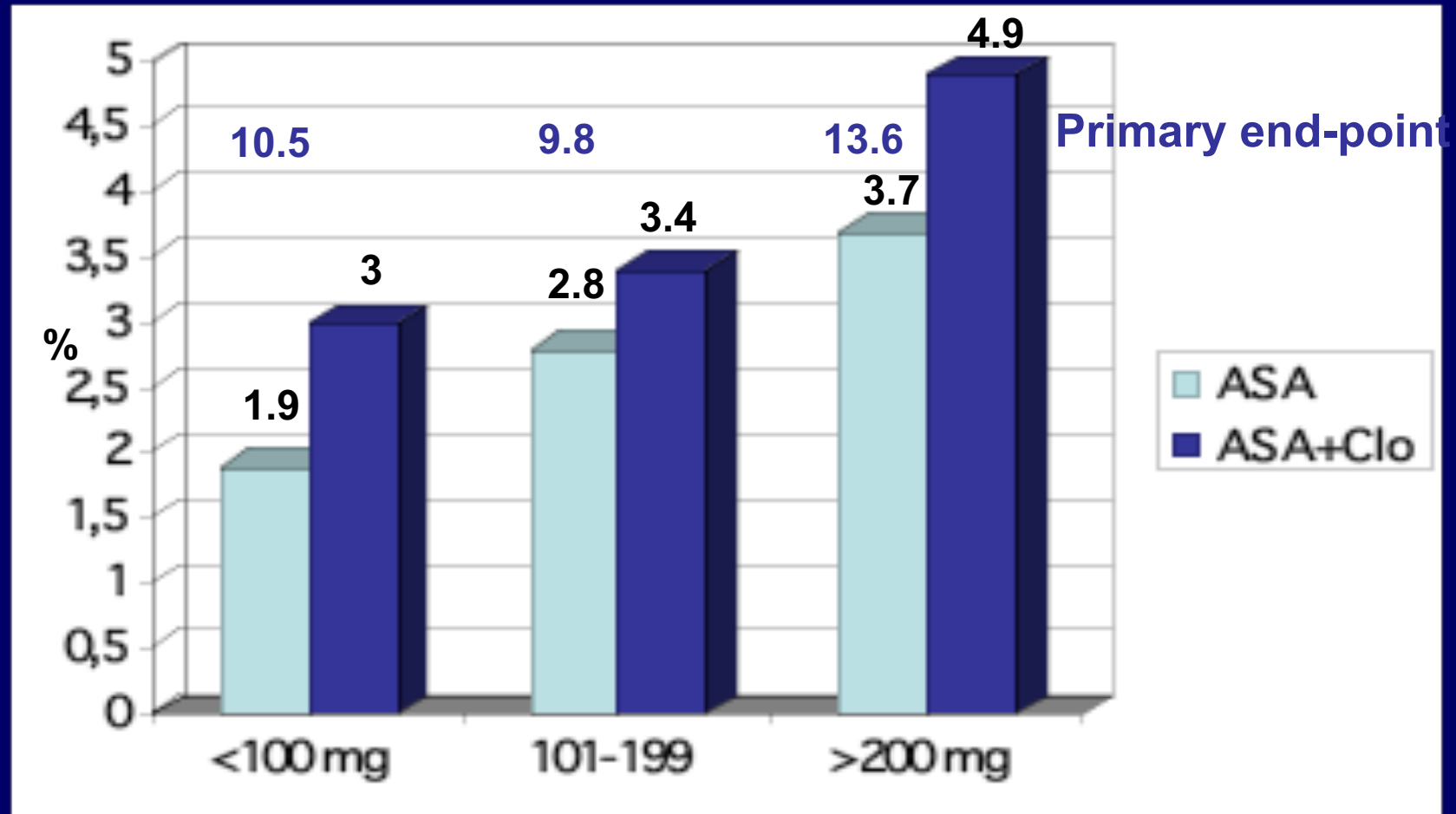
SYNERGY TRIAL ANY TRANSFUSIONS



Synergy Investigators. JAMA 2004;292:45-54

ANTITHROMBOTICS AND BLEEDING

MAJOR BLEEDING AND ASPIRIN DOSE



ANTITHROMBOTICS AND REVASCULARIZATION

CABG

- Discontinue clopidogrel 5 days before
- Discontinue abciximab 24h, eptifibatide & tirofiban 4h before
- Discontinue LMWH 12-24h, fondaparinux 24h, bivalirudin 3h

BMS

- Aspirin 162-325 mg / d for 1 month. Then, 75-100 mg
- Clopidogrel 75 mg/d for 1 month, ideally for 1 yr.

DES

- Aspirin 162-325 mg / d for 3-6 months. Then, 75-100 mg
- Clopidogrel 75 mg/d for at least 1 yr.
- Do not implant if long-term anticoagulation / surgery is needed

CONCLUSIONS

- In NSTEMACS, antithrombotic treatment must be used to prevent death, MI, revascularization
- Anticoagulants and antiplatelet agents have to be used simultaneously; the number of drugs and their combination depends on the risk and treatment strategy
- Bleeding is the most important complication. Major bleeding carries an adverse prognosis
- Guidelines recommendations are based on selected populations. The elderly, women, diabetics, renal failure are at higher risk of TE/bleed
- Important to adjust dosages when combining drugs and in invasive strategy