Antiplatelet Agents in ED: Tips, Tricks, Pearls, and Pitfalls

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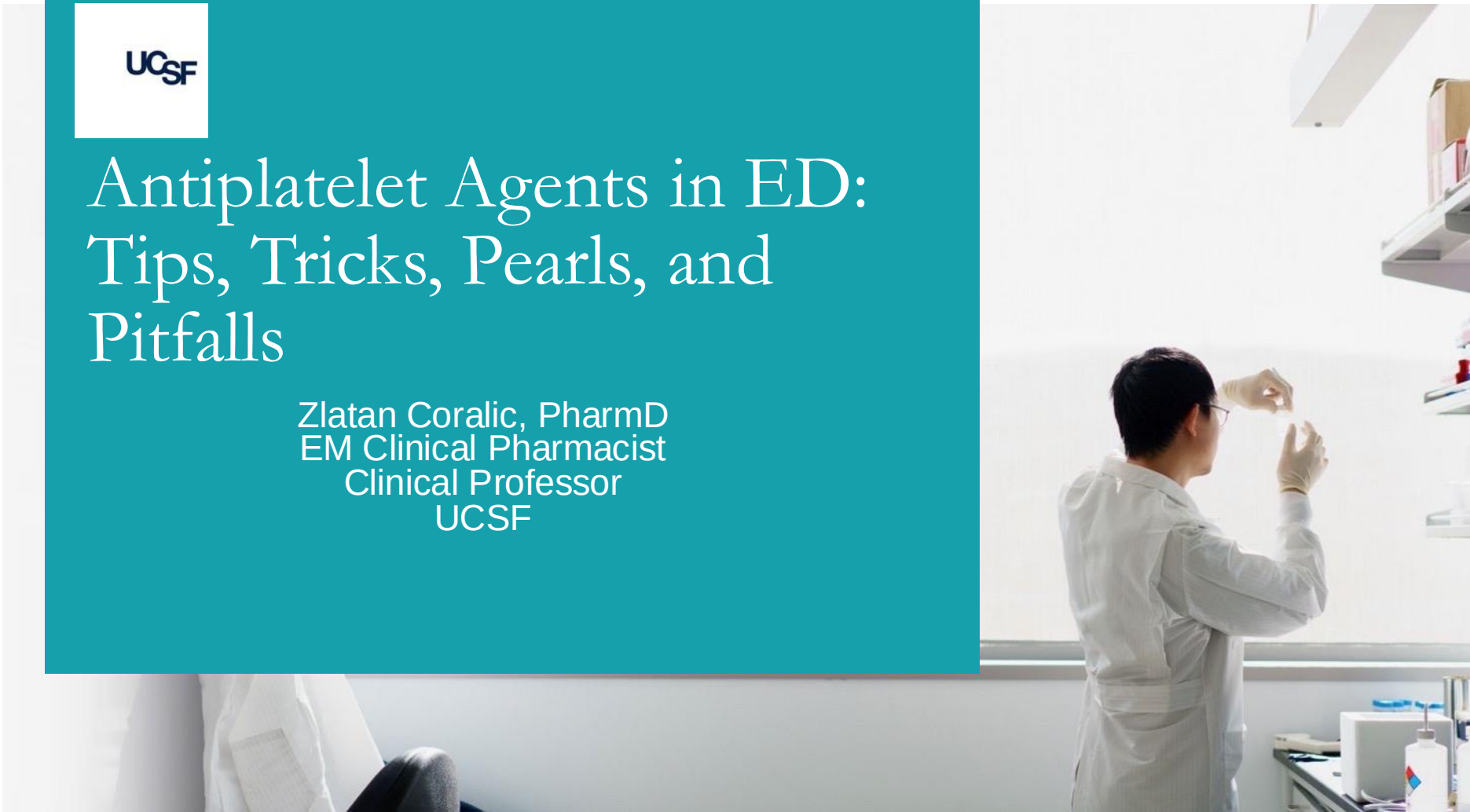

Disclosures

None

Antiplatelets in Emergency Medicine?

NSAIDs

STEMI/NSTEMI

CVA

New onset afib in patient on DAPT

Life-threatening bleeding

NSAIDs Cast of Characters

NSAID	Anti-inflammatory Potency	Antiplatelet Potency	COX-1 vs COX-2
Aspirin	Moderate	High (irreversible)	COX-1 > COX-2
Ibuprofen	Moderate	Low	COX-1 = COX-2
Naproxen	High	Moderate	COX-1 > COX-2
Meloxicam	High	Low	COX-2 > COX-1
Ketorolac	High	Low	COX-1 > COX-2
Celecoxib	High	Low	COX-2 >> COX-1

Cox 1 - gastroprotection, platelet function, kidney function
Cox 2 - pain, fever, inflammation

Ketorolac

- 60 mg IM x1 to 20 healthy EM residents
  - Measure Ivy bleeding time
  - Mean increase: 1 minute 46 seconds
- Less is more
  - 10-20 mg as good as 20 mg+
  - May require more rescue analgesia

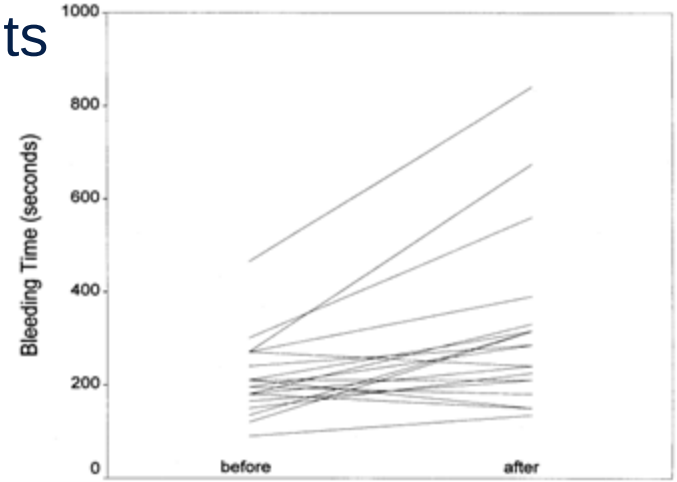

FIGURE 1. Individual baseline and post-Ketorolac bleeding times.

Am J Emerg Med . 2003 Sep;21(5):441-3
Ann Emerg Med. 2023 Nov;82(5):615-623

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Table 1. Risk of Serious Events Based on Duration of NSAID Therapy[7,24,25]

Days	**1-14**	**15-30**	**31-60**	**181-240**	**241-365**
RR of upper GI events	3.0	2.7	2.1	3.8	5.4
Days	**1-14**	**15-30**	**31-90**	**91-180**	
RR of first MI	1.39	1.22	1.25	1.54	
Days	**1-30**	**31-365**	**366-730**	**>730**	
RR of ARF	2.65	2.42	4.33	3.71	

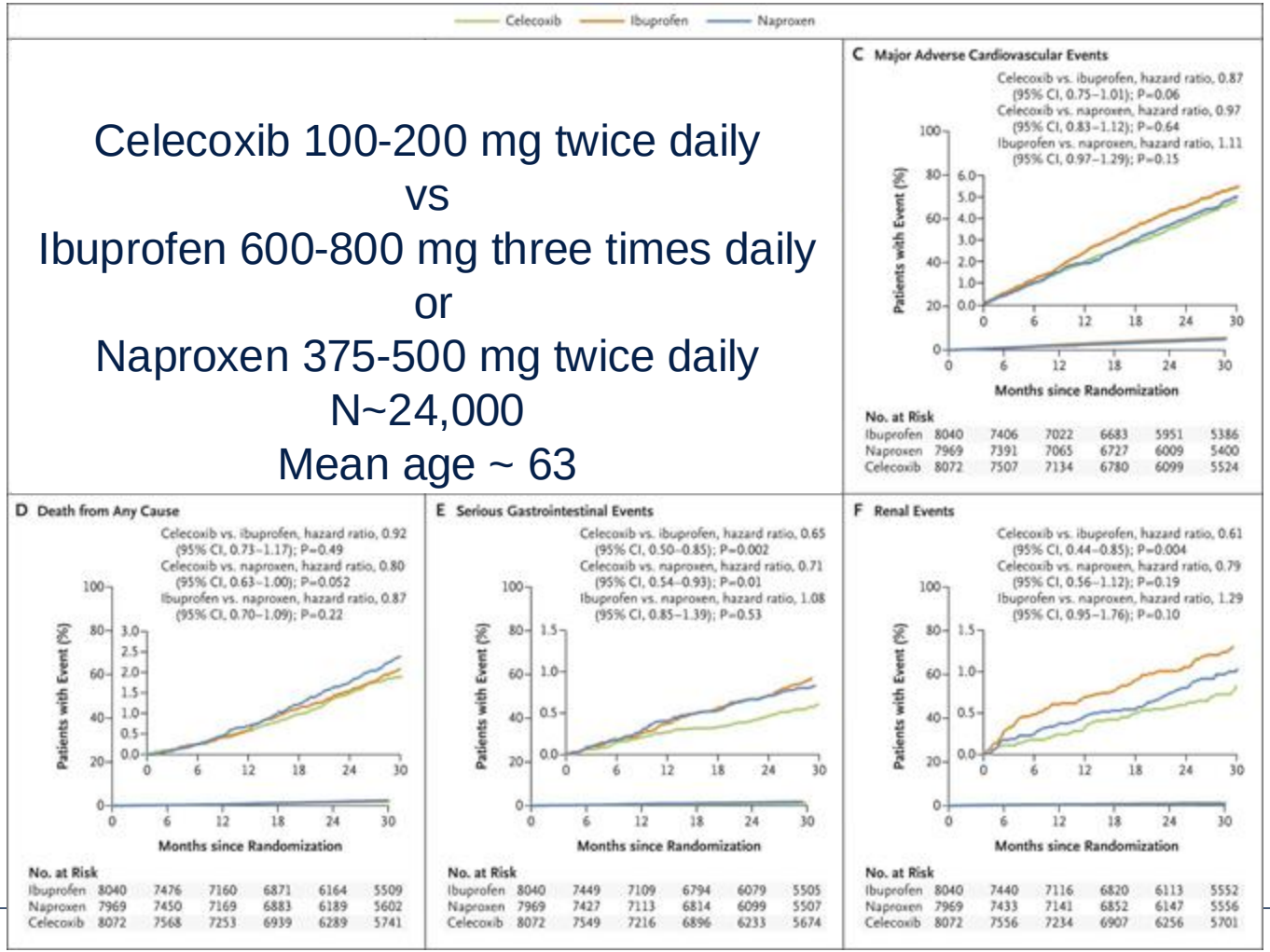
ARF indicates acute renal failure; GI, gastrointestinal; MI, myocardial infarction; NSAID, nonsteroidal anti-inflammatory drug; RR, relative risk.

Table 2. The Impact of Various Strategies on Serious Adverse Events[1,7,26-28]

	Serious GI Events	**Serious CV Events**	**Serious Renal Events**
Lower dose	↓	↓	↓
COX-2 selective inhibition	↓	↑	↑
NSAID + gastroprotective agents	↓	—	—

COX-2 indicates cyclooxygenase-2; CV, cardiovascular; GI, gastrointestinal; NSAID, nonsteriodal anti-inflammatory drug.

Celecoxib 100-200 mg twice daily
vs
Ibuprofen 600-800 mg three times daily
or
Naproxen 375-500 mg twice daily
N~24,000
Mean age ~ 63



Nissen SE et al. N Engl J Med 2016;:2519-2529

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Aspirin

- Hippocrates uses willow bark extract (salicin) for pain/fever
- 1899 Bayer markets Aspirin
- Ibuprofen competes for COX binding site
  - ASA first thing in AM if taken with ibuprofen
- ASA must be chewed for STEMI treatment
  - Can use EC or buffered, not ideal
  - AMS? -- > PR
- ASA can be used for pericarditis
- ASA allergy STEMI→ clopidogrel

NEJM 2001; 345: 1809-1817.

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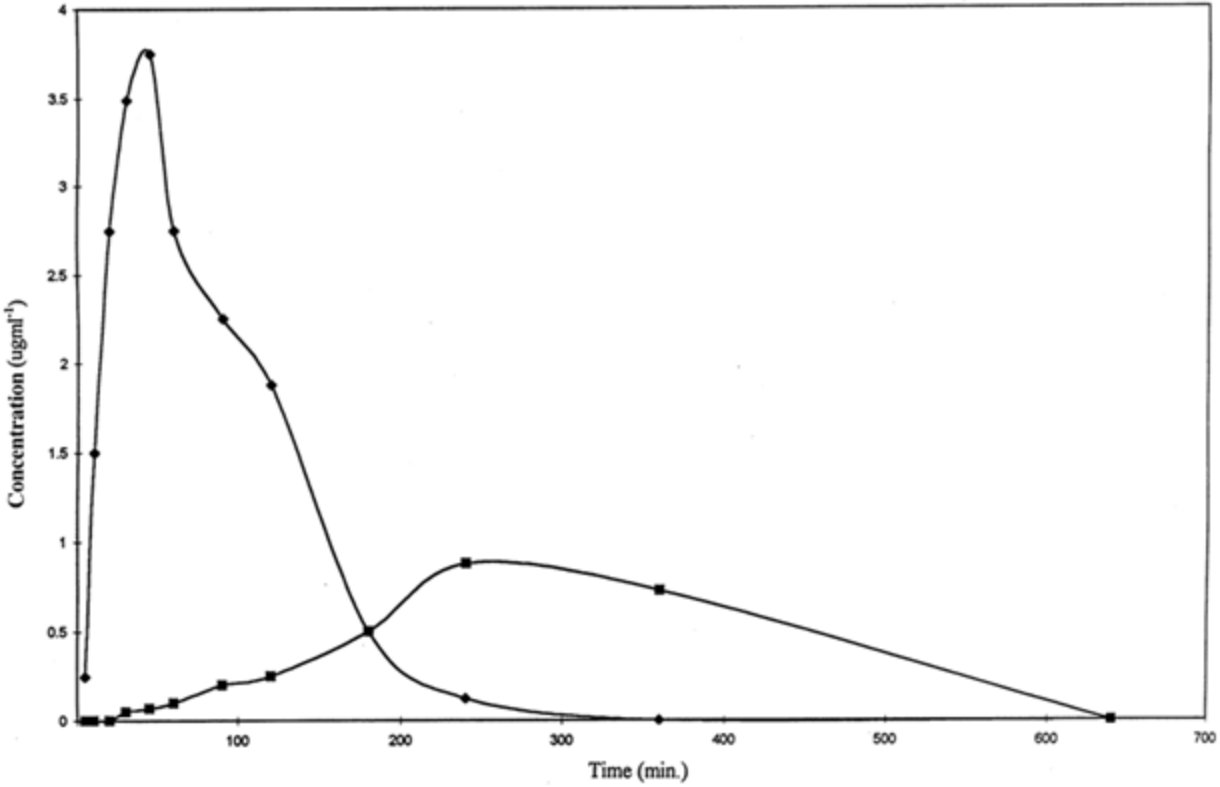
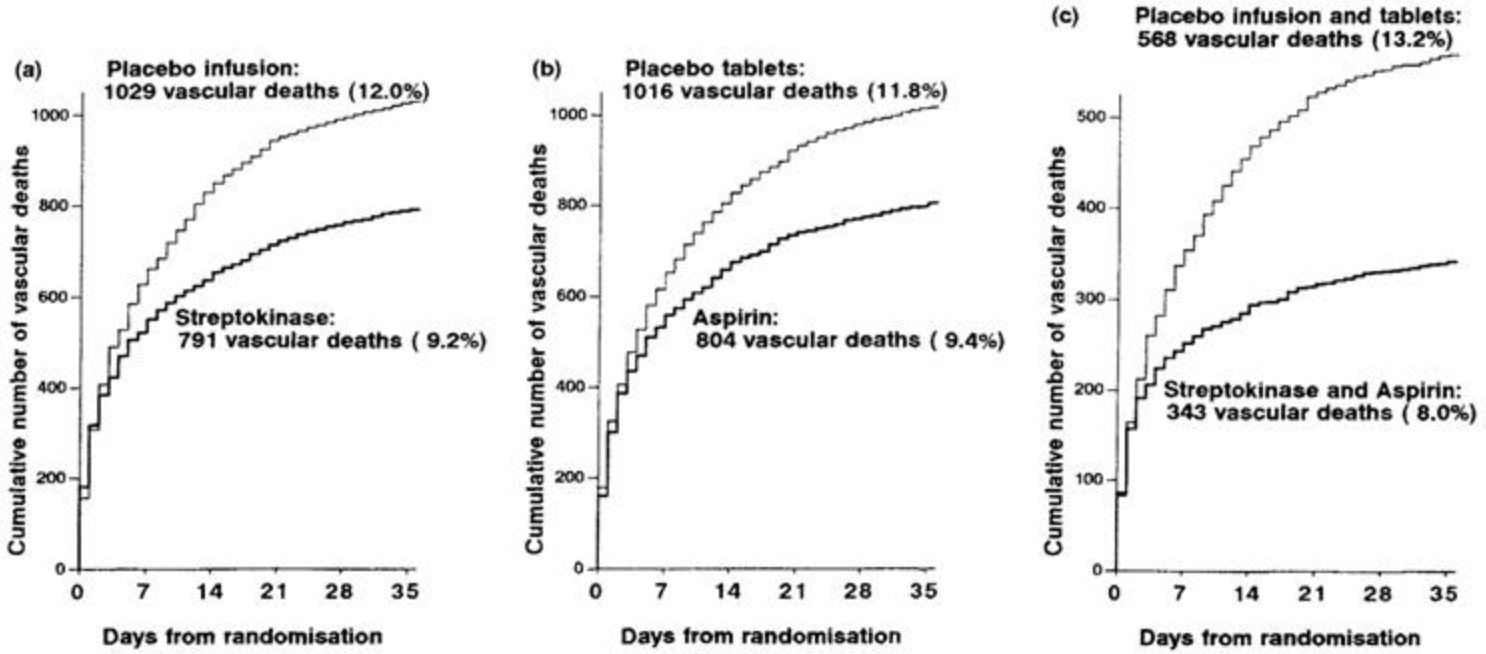


Fig. 6. Plasma level profile of plain (◆) and enteric-coated (■) aspirin.

J Pharm Biomed. 1999;21:383–392

Aspirin



NNT 35 NNT 40 NNT 20

Lancet. 1988 Aug 13;332(8607):349-60.

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Aspirin

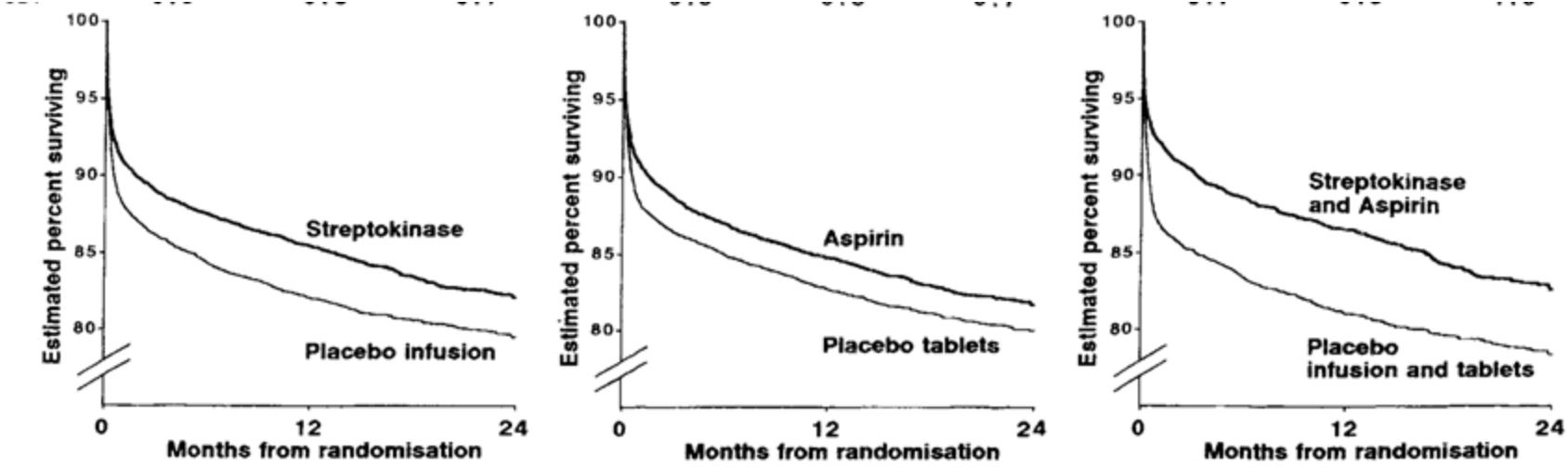

Fig 2—Life-table estimates of 12-month and 24-month survival.

Lancet. 1988 Aug 13;332(8607):349-60.

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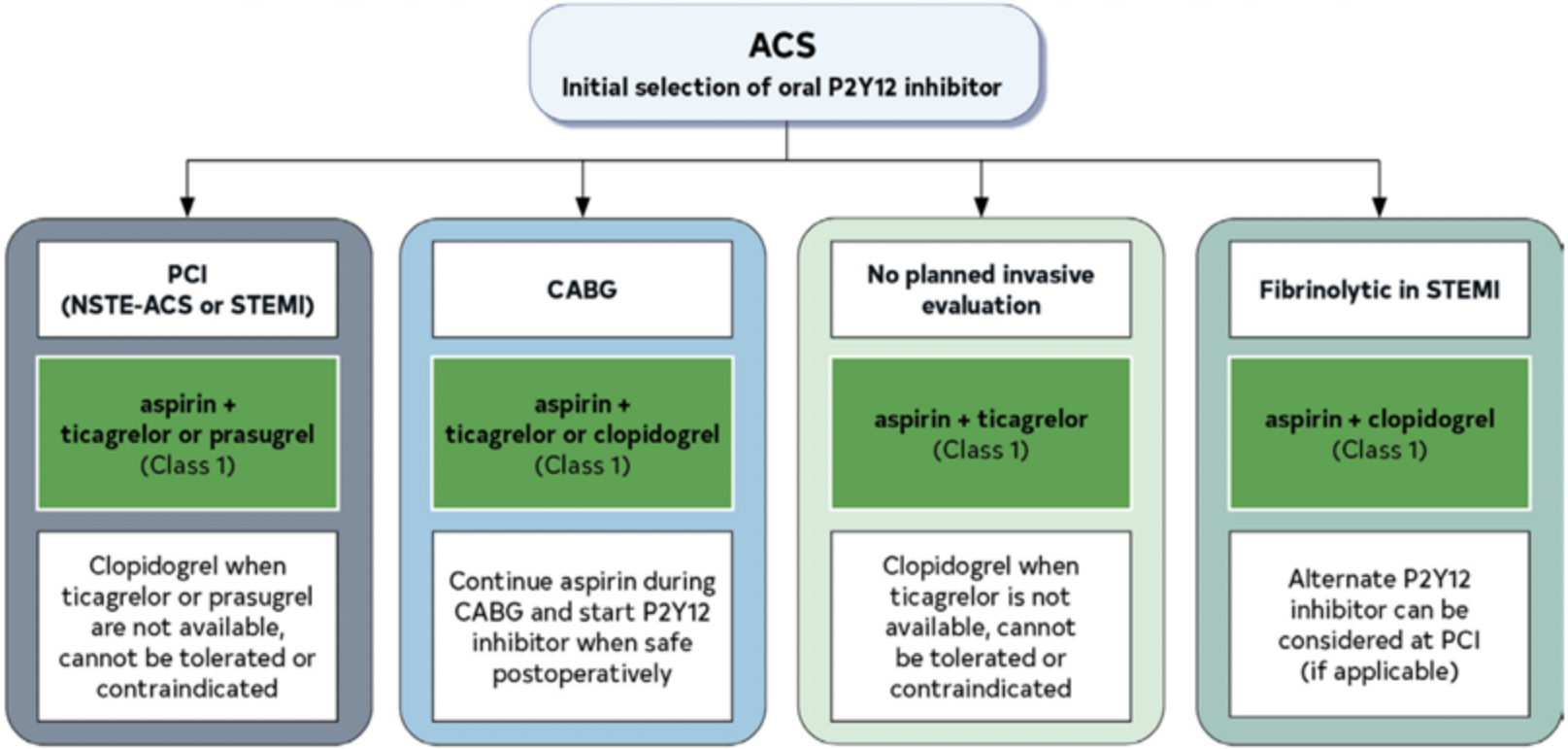
STEMI Upstream Therapy (in ED)

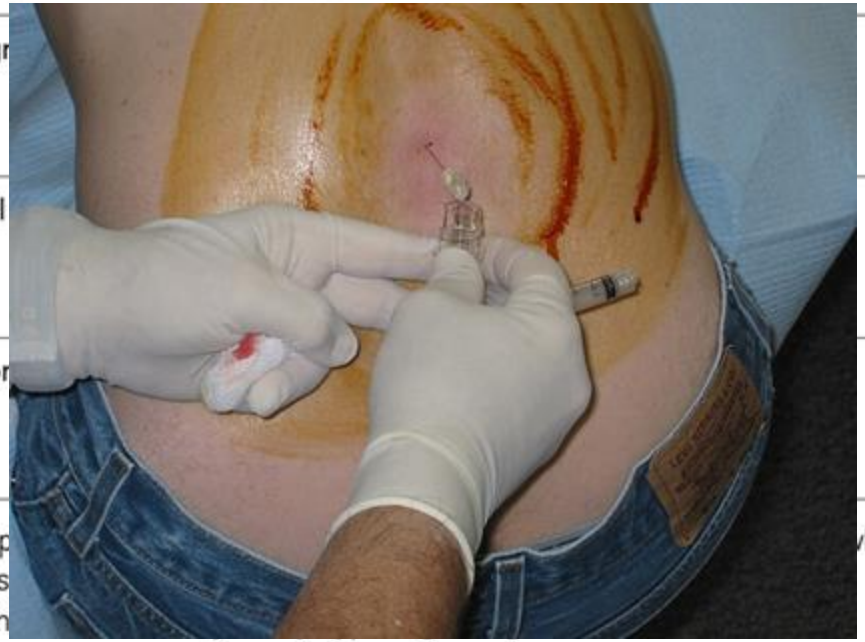
- Aspirin - ok
- Heparin - ok
  - Enoxaparin, fondaparinux - probably not
- Clopidogrel, Ticagrelor, Prasugrel - probably not
- Eptafibatide, tirofiban - no
  - Increased major bleeding (GI, ICH, arterial puncture site, blood transfusion)
  - No ischemic benefit
  - Prolonged ICU LOS
- Atorvastatin 40-80 mg - ok



Circulation. 2025;151:e00–e00.

Table 8. Management of Oral P2Y12 Inhibitors for Patients Who Require CABG Surgery*

Clopidogr	
Prasugrel	
Ticagrelor	



*For all p … when bleeding ris… CABG in…

Agent	Minimum Time Between Last Dose and Neuraxial Procedure	Minimum Time After Catheter Placement to Drug Start	Minimum Time Between Catheter Removal and Next Dose
ASA/NSAIDs/COX-I	No restriction	No restriction	No restriction
Clopidogrel	7 days	Contraindicated	2 hours
Prasugrel	9 days	Contraindicated	6 hours
Ticagrelor	5 days	Contraindicated	6 hours
Cangrelor	3 hours	Contraindicated	N/A

Anesth Pain Med. 2018. 43(3):225-62

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Agent	Onset of Action	Duration of Effect	Antiplatelet Effect
Clopidogrel	2-6 hours (depends on activation)	3-10 days (irreversible)	~40-60% platelet inhibition
Prasugrel	30-60 minutes	3-7 days (irreversible)	~70-80% platelet inhibition
Ticagrelor	30-60 minutes	3-5 days (reversible)	~70-80% platelet inhibition
Cangrelor	Within minutes (IV)	1-2 hours (reversible)	~90% platelet inhibition (fastest)

Note: vorapaxar -- excess bleeding, ~lasts for 2 weeks

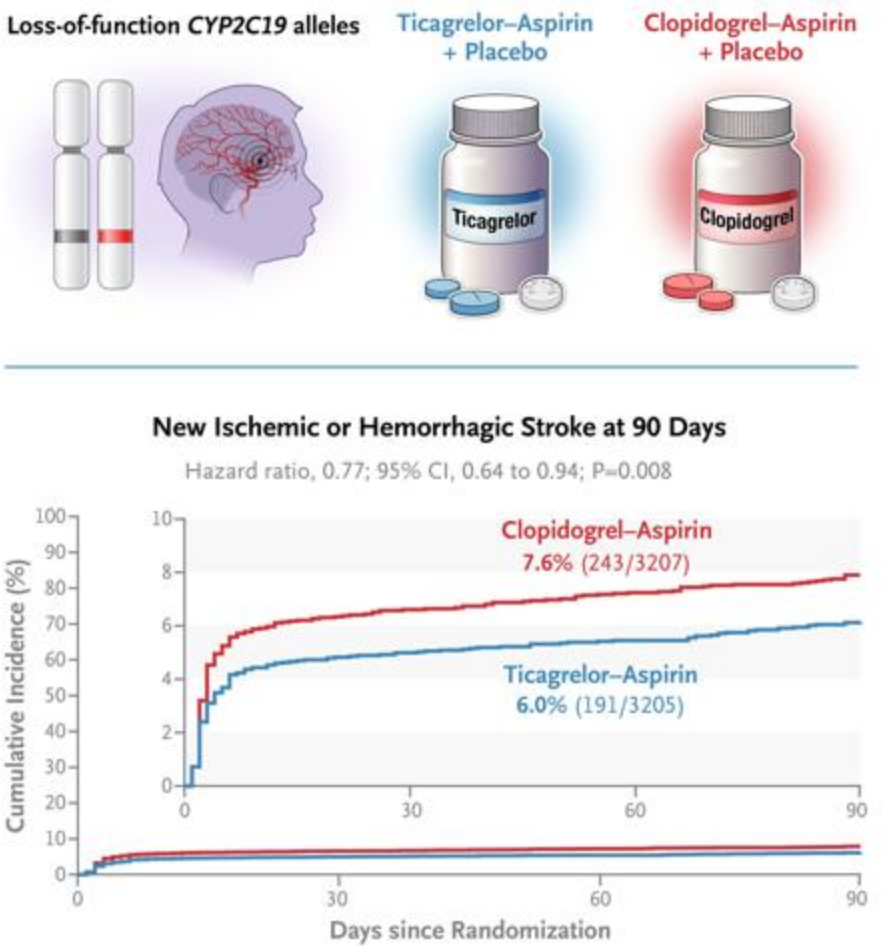
Trial*	Pts	Drug	Outcome	NNT	NNH
TRITON-TIMI	13,608 PCI	Prasugrel	↓CV death, MI, stroke (9.9% vs. 12.1%, HR 0.81, p<0.001)	46	167 *Hx of stroke/TIA =2.5 -fold ↑ major bleeding*
PLATO	18,624 ACS	Ticagrelor	↓CV death, MI, stroke (9.8% vs. 11.7%, HR 0.84, p<0.001)	52	Slightly more non-CABG bleeding
CHAMP/ PHOENIX	11,145 PCI	Cangrelor	↓Death, MI, ischemia-driven revascularization, stent thrombosis (4.7% vs. 5.9%, OR 0.78, p=0.005)	84	Slightly more non-CABG bleeding

*All vs. clopidogrel

N Engl J Med. 2007 Nov 15;357(20):2001-15
N Engl J Med. 2009 Sep 10;361(11):1045-57
N Engl J Med. 2013 Jun 13;368(14):1303-13.

Agent	Recommended Dosing	Pros	Cons	Place of Therapy
Clopidogrel $5 /tab	Loading: 300-600 mg PO, Maintenance: 75 mg PO daily	Well-studied, lower bleeding risk, available in generic form	Slow onset, requires metabolic activation, variable response, omeprazole	Preferred for fibrinolysis; alternative in PCI if prasugrel/ticagrelor unavailable
Prasugrel $15 /tab	Loading: 60 mg PO, Maintenance: 10 mg PO daily	More potent than clopidogrel, lower stent thrombosis risk in PCI	Bleeding risk, contraindicated in prior stroke/TIA	Preferred for PCI in patients without stroke/TIA history
Ticagrelor $10 /tab	Loading: 180 mg PO, Maintenance: 90 mg PO BID	Rapid onset, more potent than clopidogrel, superior in PLATO trial	Bleeding risk, dyspnea in ~10% of patients, BID dosing	Preferred for ACS and PCI, including medically managed NSTE-ACS
Cangrelor $1200 /bag	IV bolus 30 mcg/kg, then 4 mcg/kg/min infusion during PCI	Fastest platelet inhibition, useful in PCI when oral P2Y12 is not feasible	Requires IV administration, short-acting, expensive	Used in PCI when oral P2Y12 inhibitors cannot be administered

Ischemic St		Duration
High-Risk TIA (ABCD² S	*	21 days
Minor Ischemic Stroke	*	21 days
Large Artery Atherosc		Up to 90 days
Moderate to Severe St		N/A
Single Antiplatelet The		21 days
Atrial Fibrillation, Mec		N/A



*Ticagrelor alternative, BID, risk of

*Ticagrelor maybe better in Chines

Stroke. 2019;50(12):e344–e418.
N Engl J Med 2021;385:2520-2530

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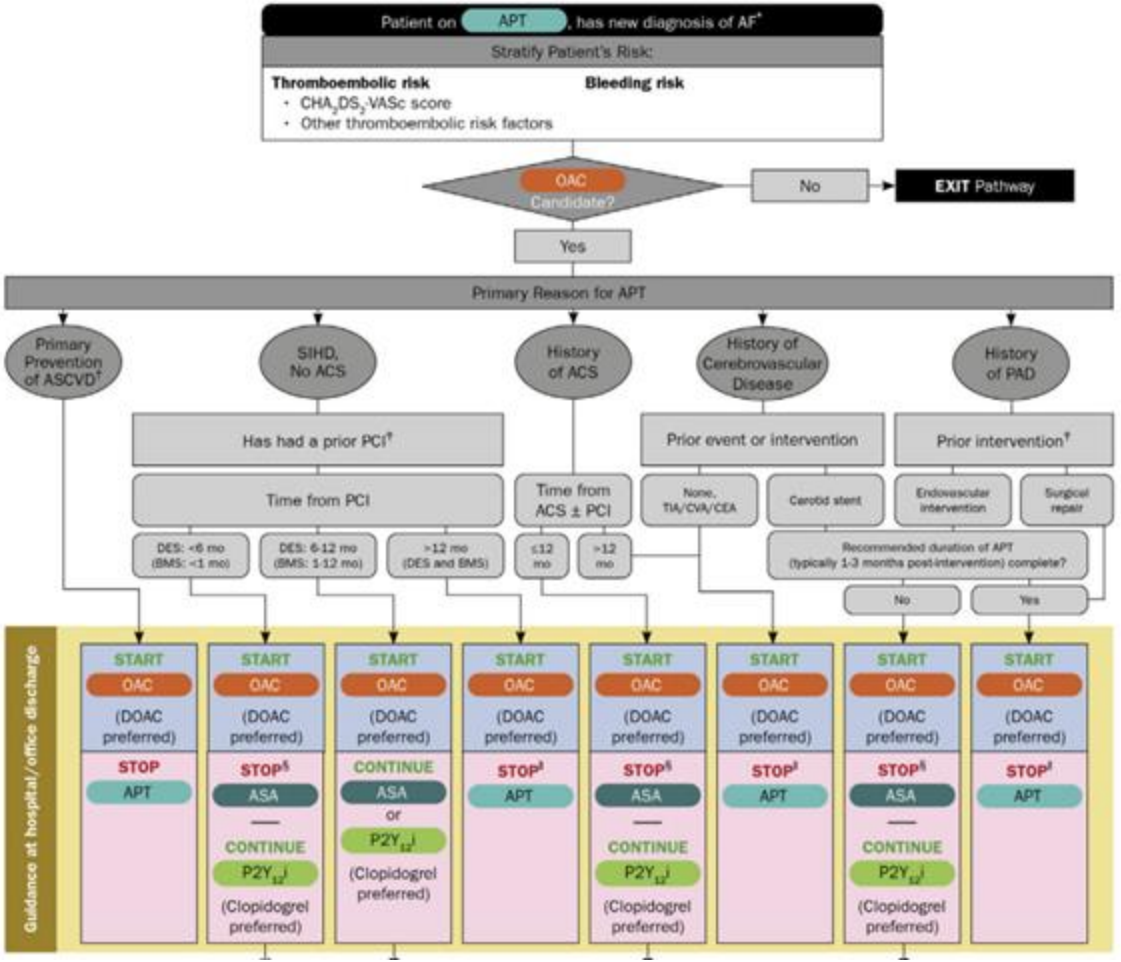
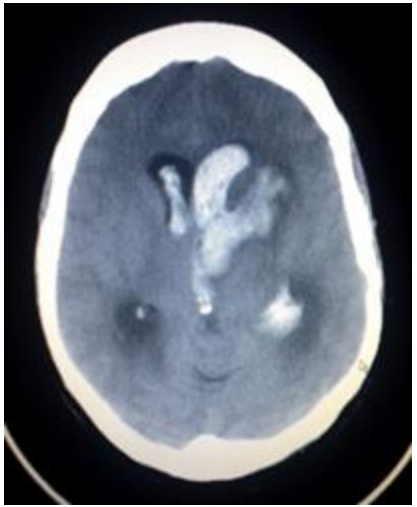
DAPT + AF/DVT/PE

"Triple therapy"



J Am Coll Cardiol. 2021 Feb 9;77(5):629-658.

Antiplatelet Reversal



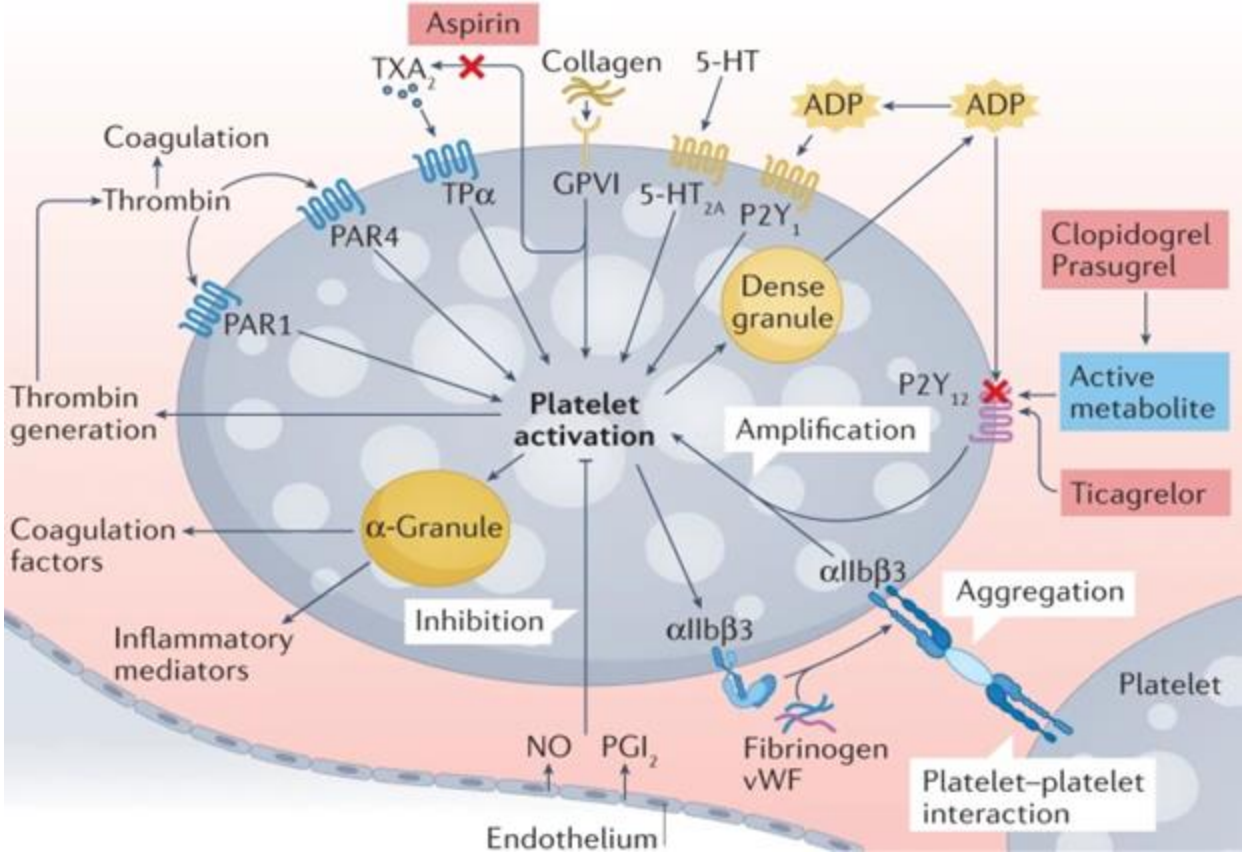
No clear reversal guidance

- Platelet transfusion
  - Post nsx bleeding - maybe
  - No nsx - ↑ mortality/dependence
  - Ticagrelor binds to transfused platelets (reversible)
- DDAVP
- TXA
- VIIa
- Bentracimab (ticagrelor reversal) - clinical trials

Stroke. 2022;53(7):e282–e361.
Lancet. 2016 Jun 25;387(10038):2605-2613.

Summary

- Antiplatelet medications are often seen and used in ED
- Harm from single doses/short courses of NSAIDs in ED is likely minimal
- P2Y12 inhibitors may cause complications with CABG/LP/major surgery
- No clear guidance on best reversal strategy with life-threatening bleeding in patients taking antiplatelet medications



Nature Reviews Cardiology volume 19, 829–844