

UCSF

When and How to Reverse Anticoagulation: Best Practices

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Disclosures

None

Objectives

Discuss the benefits of anticoagulation

Review the available reversal agents

Discuss decision-making on initiating anticoagulation reversal

Review individual anticoagulation reversal agents and pearls

Over the next 5 years

76

people will have no stroke

8

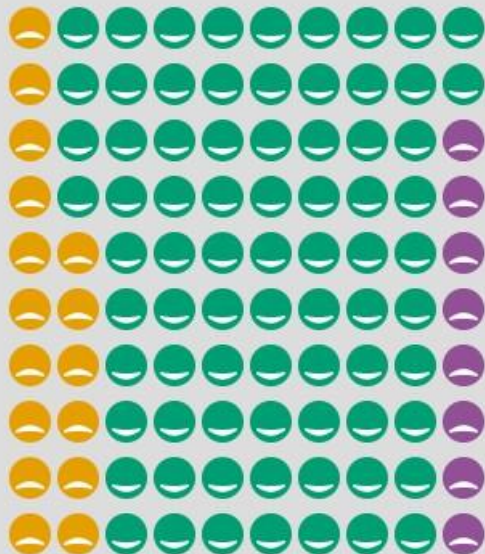
people will have a fatal or disabling stroke

16

people will have a non-disabling stroke

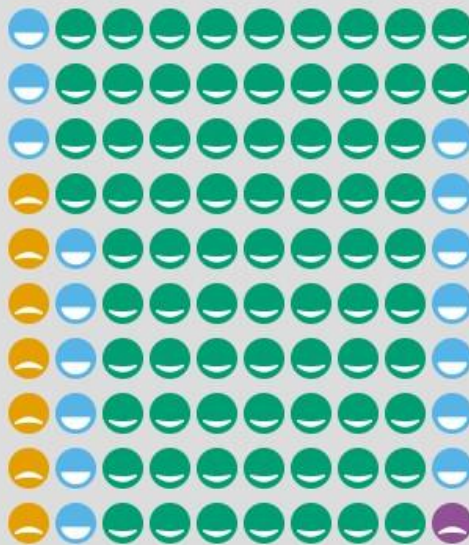
Current Risk of Stroke Without Anticoagulation

In 100 people like you who **are not** taking an anticoagulant, **at 5 years...**



Future Risk of Stroke With Anticoagulation

In 100 people like you who **are** taking an anticoagulant, **at 5 years...**



Over the next 5 years

92

people will have no stroke

1

person will have a fatal or disabling stroke

7

people will have a non-disabling stroke

16

people will avoid a stroke by taking anticoagulation

Cast of Characters

Medication Name (Route)	Brand Name	Class	FDA Approval Year
Heparin (IV/SQ)	N/A	UFH	1939
Warfarin (PO)	Coumadin	VKA	1954
Enoxaparin (SQ)	Lovenox	LMWH	1993
Dalteparin (SQ)	Fragmin	LMWH	1994
Fondaparinux (SQ)	Arixtra	FXaI	2001
Dabigatran (PO)	Pradaxa	DTI	2010
Rivaroxaban (PO)	Xarelto	FXaI	2011
Apixaban (PO)	Eliquis	FXaI	2012
Edoxaban (PO)	Savaysa	FXaI	2015

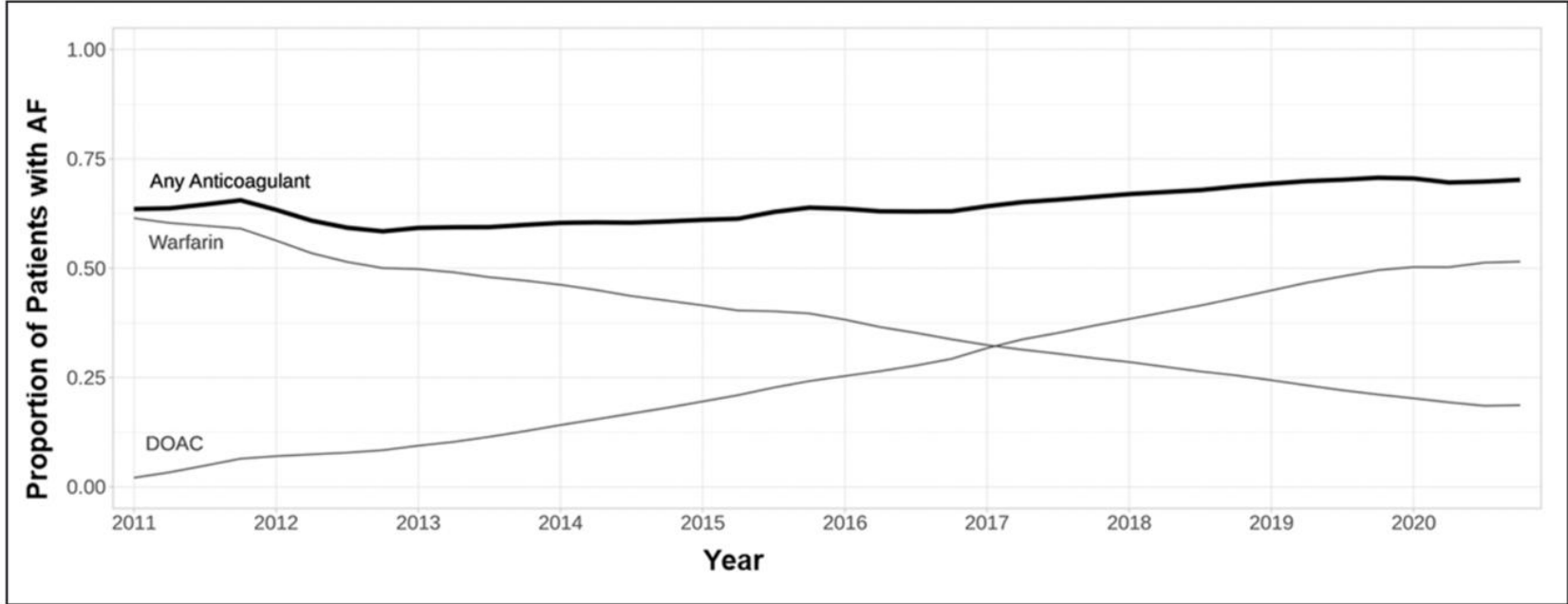
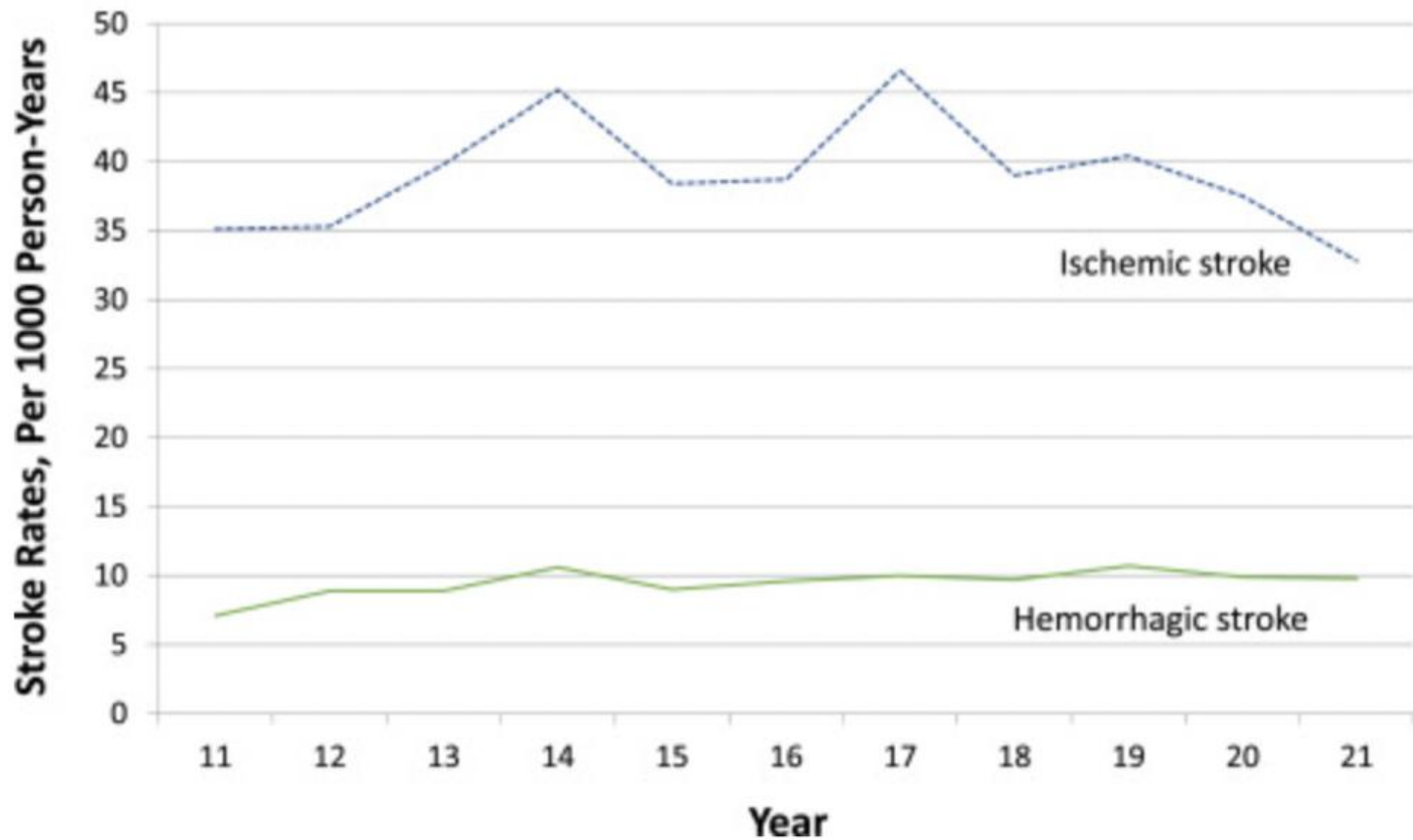



Figure 1. Rates of anticoagulation in patients with AF and CHA₂DS₂-VASc score ≥ 2 , 2011 to 2020.



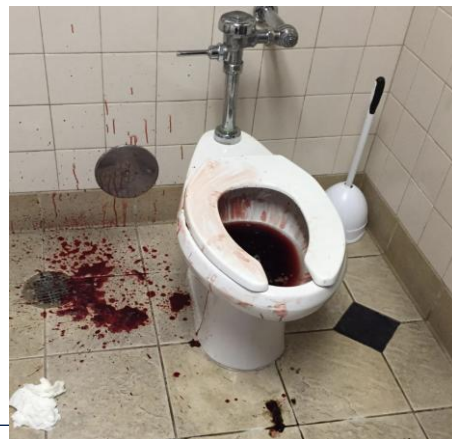
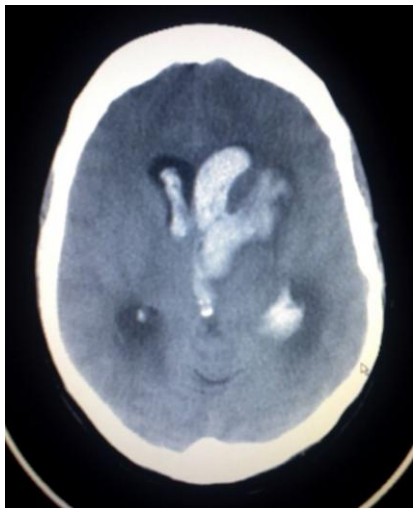
Medication Name (Route)	Class	Reversal Agent	Estimated AWP Cost per Reversal
Heparin (IV/SQ)	UFH	Protamine	\$ 15
Warfarin (PO)	VKA	Vitamin K, PCC, FFP	\$ 15,000 (PCC)
Enoxaparin (SQ)	LMWH	Protamine	\$ 15
Dalteparin (SQ)	LMWH	Protamine	\$ 15
Fondaparinux (SQ)	FXaI	PCC	\$ 15,000
Dabigatran (PO)	DTI	Idarucizumab	\$ 6,000
Rivaroxaban (PO)	FXaI	Andexanet, PCC	\$ 50,000
Apixaban (PO)	FXaI	Andexanet, PCC	\$ 50,000
Edoxaban (PO)	FXaI	PCC	\$ 15,000

Reversal Considerations & Sites of Bleeding

- ⌘ What agent?
 - ⌘ Last dose?
 - ⌘ Indication?
 - ⌘ How much? (charcoal?)
 - ⌘ Renal dysfunction?
 - ⌘ Hemodynamic stability?
 - ⌘ Acute vs. chronic?
 - ⌘ Goals of care?
- 
- ⌘ Intracranial
 - ⌘ Thoracic
 - ⌘ Intra-abdominal
 - ⌘ Retroperitoneal
 - ⌘ Intra-articular
 - ⌘ Intramuscular
 - ⌘ Hgb drop >2g/dL

Assay	Dabigatran	Rivaroxaban	Apixaban
aPTT	++	+	+
PT/INR	+	++	+/-
TT	+++	-	-
ECT	+++	-	-
Anti-Xa	-	++	++

Favaloro EJ, et al. Semin Thromb Hemost 2015;41:208-27
Hawes DM, et al. J Thromb Haemost 2013;11:1493-1502



Patients	OAC	Outcome
ICH + anticoag, n=9492	Warfarin: 3,178 (60.8%) Apixaban: 1,174 (22.5%) Rivaroxaban: 799 (15.3%) Dabigatran: 74 (1.4%) Edoxaban: 11 (0.2%)	DTT time was 82 (58-117) min DTT <60 min = ↓ mortality & hospice (0.82; 95% CI, 0.69-0.99) No diff in functional outcome (0.91; 95% CI, 0.67-1.24)

AHA/ASA Performance Measures

ICH on CT to Reversal: 90 min (likely move to 60 min in future)

How to decrease door to reversal?

Get an ED pharmacist!

Load reversal agents in ED

Create order sets



Am J Emerg Med. 2024 Jun;80:114-118.
Crit Care Med. 2024 Mar;52(3):215-222
Ann Pharmacother. 2024 Apr;58(4):307-312.

▶ Warfarin Reversal (Kcentra)

▶ Refractory Bleeding - Cardiothoracic Surgery (Kcentra)

▼ Factor Xa Inhibitor Reversal

- [Andexanet Alfa Criteria For Use](#)

- [Factor Xa Reversal Flowchart](#)

▼ Apixaban Reversal

Intracranial hemorrhage or life-threatening bleed

Non-life-threatening bleed, repeat reversal agent dosing, perioperative anticoagulant reversal, or last dose taken more than 24 hrs ago

▶ [Rivaroxaban Reversal](#) [Click for more](#)

▶ [Edoxaban Reversal](#) [Click for more](#)

▶ Heparin Reversal (Protamine)

▶ Enoxaparin (LOVENOX) Reversal (Protamine)

▶ Dabigatran Reversal (IdaruCIZUMAB)

▶ Kcentra - Other Indications

Ischemic Stroke on Anticoagulants, Reverse then Lyse?

🔗 AHA/ASA Guidelines - not recommended

🔗 Dabigatran

- 553 pts meta-analysis, idarucizumab → tPA
- Better 3-month fnx outcome

🔗 Warfarin

- 26 pts Kcentra → tPA (INR 2.6 → 1.3)
- No bleed in first 3 days, after 1 hemorrhoidal bleed in need of transfusion

🔗 Heparin

- 8 patients protamine → tPA
- No ICH at 3 months

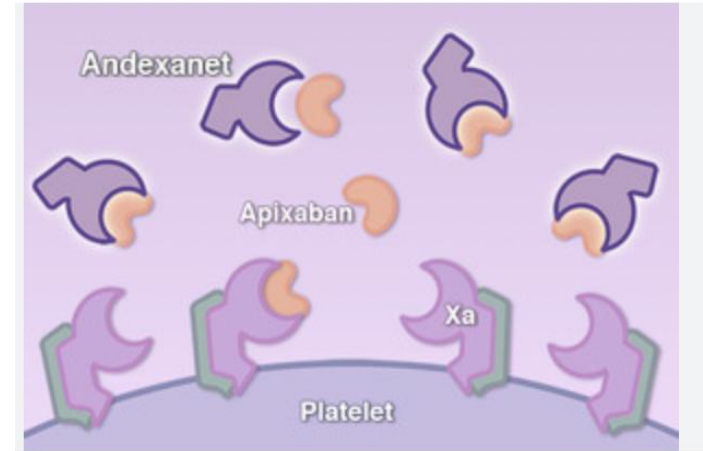
Neurology. 2024 Oct 8;103(7):e209862

Stroke . 2018 Oct;49(10):2526-2528

J Stroke Cerebrovasc Dis. 2019 Oct;28(10):104283

Andexanet alfa reversal

- ↳ Apixaban, rivaroxaban, edoxaban
- ↳ Mimic Xa molecule
- ↳ Bolus, followed by 2-hr infusion
- ↳ ANNEXA A, R, 4, & I trials
 - May 2018 FDA accelerated approval



Trial	Population	Intervention	Comparator	Outcome
ANNEXA-A (2015)	Healthy + apixaban	Andexanet (n=67)	Placebo (n=33)	94% reduction in anti-Factor Xa activity
ANNEXA-R (2015)	Healthy + rivaroxaban	Andexanet (n=40)	Placebo (n=20)	92% reduction in anti-Factor Xa activity
ANNEXA-4 (2019)	Acute major bleeding + apixaban, rivaroxaban, edoxaban, enoxaparin	Andexanet (n=352)	No control group	80% of patients achieved effective hemostasis; significant reduction in anti-Factor Xa activity
ANNEXA-I (2024)	ICH+apixaban, rivaroxaban, edoxaban	Andexanet (n=263)	Usual care (n=267) Most PCC	Thrombotic events (10.3% vs. 5.6%, P=0.048), Ischemic stroke (6.5% vs. 1.5%); Better hematoma expansion control (67.0% vs. 53.1%)

December 16, 2024 03:54 PM EST Updated [December 17, 09:16 AM](#) | Pharma, FDA+



AstraZeneca is denied full FDA approval of Andexxa following critical advisory meeting



Max Bayer
Pharma Reporter

AstraZeneca said the FDA declined to fully approve its anticoagulant reversal drug Andexxa, less than a month after an advisory committee meeting at which the ...

Medication Name (Route)	Class	Reversal Agent	Pearls
Heparin (IV/SQ)	UFH	Protamine	Maximum dose 50 mg over 10 minutes Allergy: fish, exposure to insulin NPH
Warfarin (PO)	VKA	Vitamin K, PCC, FFP	Give Vitamin K slowly Lower dose PCC may be as effective (e.g., 1500 units) Volume: PCC ~50ml, FFP 1-2L
Enoxaparin (SQ)	LMWH	Protamine	Match dose 1mg to 1mg up to 50 mg Based on when enoxaparin was last given ~60% reversal achieved
Dabigatran (PO)	DTI	Idarucizumab	Two 2.5 gm dose given over 15 minutes Consider aPTT or TT for monitoring
Rivaroxaban (PO)	FXaI	Andexanet, PCC	Andexanet likely going away PCC flat dose: 2000 units PCC weight based: 25-50 units/kg
Apixaban (PO)	FXaI	Andexanet, PCC	
Edoxaban (PO)	FXaI	PCC	

Conclusions

- ⌘ We see rare and catastrophic events associated with anticoagulation, but forget tremendous benefit
- ⌘ Reversal strategies for each anticoagulant exist, however, benefits remains modest (e.g., ICH)
- ⌘ Standard care: reverse AC with life-threatening bleeding
- ⌘ Risk of thromboembolism
- ⌘ Follow hospital protocols to avoid delay

