Anticoagulants in Older Adults

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Learning Objectives

- Review evidence to support anticoagulation in older adults
- Explain the unique challenges of anticoagulation including increased risks of bleeding, frailty, and comorbid conditions in older adults
- Discuss how to tailor anticoagulation therapy in older adults by applying risk assessment tools to balance bleeding and thrombotic risks
- Evaluate patient cases to differentiate between high-risk and low-risk older adults for anticoagulation, and analyze when to adjust or discontinue therapy based on clinical factors

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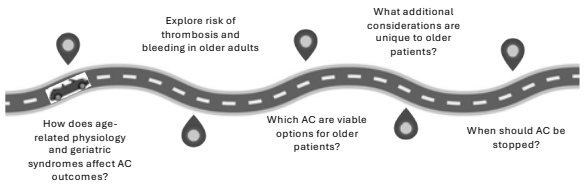
Roadmap for Our Discussion



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Age-related physiologic changes

Age-related physiologic changes	Potential impact on OAC and outcomes
Decreased skeletal muscle mass & total body water	• Increased plasma concentrations of apixaban and edoxaban if <60kg • Increased risk of major bleeding with edoxaban if body weight <60kg • Decreased hepatic clearance of warfarin
Decline in GFR	• Increased plasma concentrations of dabigatran>edoxaban>rivaroxaban>apixaban, esp if CrCl <30ml/min
Decrease in liver size and blood flow	• Increased DOAC plasma concentration if moderate (rivaroxaban) or severe (apixaban, edoxaban, dabigatran) hepatic dysfunction • Reduced warfarin clearance
Reduced activity in Vit K redox recycling symptom	• Increased warfarin sensitivity with about 20% lower warfarin dose requirements
Increased prevalence amyloid angiopathy, and cerebral atrophy	• Increased risk ICH
Increased prevalence of diverticular and peptic ulcer disease	• Increased risk of GI bleeding

Shybu et al. Thrombosis Research 238 (2024) 1–10

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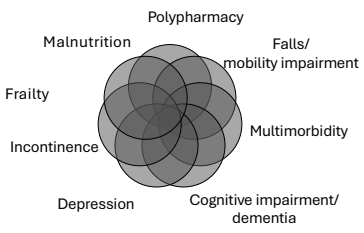
Geriatric syndromes



Small, if any, increase in absolute risk of fall-related major bleeding

Anticoagulation Forum

Shybu et al. Thrombosis Research 238 (2024) 1–10

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Case 1: Audience Response Question

87M to ER after fall

BP 154/85 HR ~95 bpm (irreg), wt 82kg

HTN, DM2, HLD, OA, macular degeneration

Hb 12.0 g/dL, INR 1.0 SCr 1.1mg/dL

Lisinopril, Metformin, Atorvastatin, Meloxicam, low dose aspirin

ECG - atrial fibrillation

A. Low dose aspirin
B. LMWH→ warfarin
C. Apixaban
D. Rivaroxaban
E. DOAC + ASA

What would you start this patient on to reduce the risk of AFib-related stroke?

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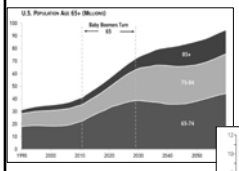
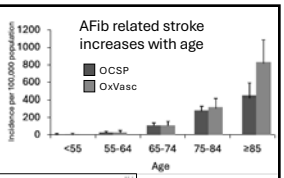
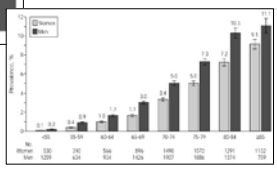
Why is this important to discuss?



US population is aging





AFib prevalence increases with age

OCSP: Oxfordshire Community Stroke Project; OXVASC: Oxford Vascular Study. Yiin GS, *et al. Circulation* 2014; 130(15):1236-44.

https://www.census.gov/en.html
Go et al. JAMA. 2001 May 9;285(18):2370-5.

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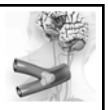
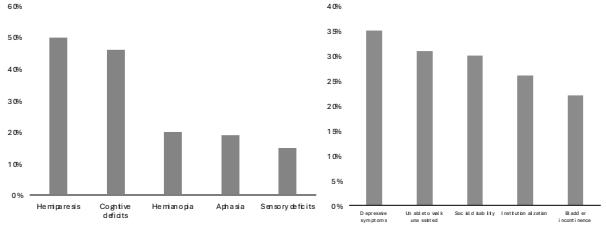
Stroke causes death and disability



30-day mortality up to 20%



Kelly-Hayes et al. J Stroke Cerebrovasc Dis. 2003 May-12(3):119-26. Grosiewicz Neurol Clin. 2008 Nov;26(4):871-95. Feigin et al. Lancet Neurol. 2003;2(1):43.

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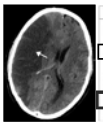
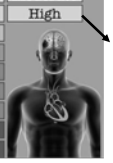
Stroke risk assessment in Afib: CHA_2DS_2-VASc score



	CHADS2 – VASc Score	
C	Congestive Heart Failure	1
H	Hypertension (>140/90 mmHg)	1
A	Age > 75	2
D	Diabetes Mellitus	1
S_2	Prior TIA or stroke	2
V	Vascular disease (MI, aortic plaque etc)	1
A	Age 65-74	1
Sc	Sex category (Female = 1 pt)	1

Score	Risk of stroke	
0	0.2%	Low
1	0.6%	Moderate
2	2.2%	High
3	3.2%	
4	4.8%	
5	7.2%	
6	9.7%	
7	11.2%	
8	10.8%	
9	12.2%	



No AC

Consider AC

Recommend AC

2020 ACC/AHA. 2021 Feb, 77 (5) 629–658

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VTE recurrence: risk assessment models

	Men and HERDOO2	Vienna Risk Model	DASH
Gender	X	X	X
D-dimer	X	X	X
Signs of Post-thrombotic syndrome	X		
Obesity	X		
Age	X		X
Location of DVT/PE		X	
Provoked?			X

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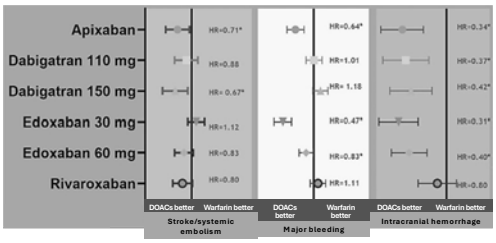
RCT Evidence for Anticoagulation in Older Patients with AFib

Network metanalysis of 28,135 patients >75 years with AFib



Malik AH, et al. Am J Cardiol. 2019 Jun 15;123(12):2051-2057.

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Stroke/Systemic embolism in age >_75yo: DOACs vs VKA in ARISTOPHANES registry

	apixaban vs. warfarin		dabigatran vs. warfarin		rivaroxaban vs. warfarin	
	incidence rate/ 100 person-years	HR (95% CI)	incidence rate/ 100 person-years	HR (95% CI)	incidence rate/ 100 person-years	HR (95% CI)
Stroke/SE						
75-79 years	1.03 v. 1.79	0.53 (0.42-0.66)	1.51 v. 1.75	0.86 (0.63-1.17)	1.33 v. 1.72	0.76 (0.64-0.9)
≥ 80 years	1.76 v. 2.59	0.62 (0.55-0.71)	2.14 v. 2.59	0.82 (0.66-1.03)	2.16 v. 2.57	0.79 (0.71-0.88)

Lip GYH, et al. Stroke. 2018;49:2933- 2944.

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Bleeding Risk Also Increases with Age

HAS-BLED Bleed Score

Clinical characteristic	Points
Hypertension	1
Renal or hepatic dysfunction	1 or 2
History of stroke	1
History of bleeding	1
Labile INR	1
Age >65	1
Drugs or alcohol	1 or 2

DOAC Bleed Score

Clinical characteristic	Points
Age 65-69	2
Age 70-74	3
Age 75-79	4
Age ≥ 80	5
CrCl 30-60 ml/min	1
CrCl <30 ml/min	2
BMI <18.5 kg/m2	1
Stroke/TIA/embolism	1
Diabetes	1
Hypertension	1
Single/Dual antiplatelet	2/3
NSAID use	1
Bleeding history	3
Liver disease	2

- Bleed risk scores should NOT be used in isolation to decide on prescribing anticoagulants
- Assess for & address modifiable bleed risk factors
- In our case patient
  - Need for aspirin?
  - Optimize BP
  - Minimize NSAID use
  - Assess fall risk with mac degen

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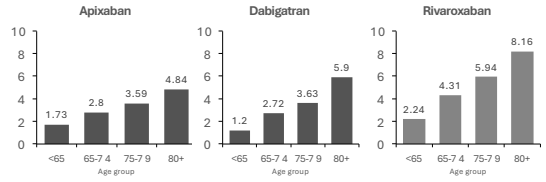
Real world evidence of Major bleeding on DOACs (ARISTOPHANES registry N=466,991)



Lip GY, et al. Stroke 2018; 49(12):2933-44.

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Major Bleeding in age >_75yo: DOACs vs VKA in ARISTOPHANES registry

	apixaban vs. warfarin		dabigatran vs. warfarin		rivaroxaban vs. warfarin	
	incidence rate/ 100 person-years	HR (95% CI)	incidence rate/ 100 person-years	HR (95% CI)	incidence rate/ 100 person-years	HR (95% CI)
Major bleeding						
75-79 years	3.59 v. 5.45	0.61 (0.54-0.69)	3.63 v. 5.34	0.68 (0.56-0.82)	5.94 v. 5.44	1.07 (0.98-1.16)
≥ 80 years	4.84 v. 6.88	0.65 (0.6-0.7)	5.9 v. 6.61	0.89 (0.78-1.02)	8.16 v. 6.52	1.17 (1.1-1.25)

Lip GYH, et al. Stroke. 2018;49:2933- 2944.

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Comment on: 2023 updated AGS Beers Criteria for potentially inappropriate medication use in older adults

	Key excerpts from Beers Criteria
Warfarin- avoid as initial therapy (unchanged)	A recommendation to "avoid" is not an absolute contraindication.
Dabigatran- use with caution (unchanged)	Medications listed in the Beer's Criteria are *potentially* inappropriate, not definitely inappropriate.
	The criteria are a blunt instrument, and it is not possible to delineate all specialized use cases and possible exceptions to the criteria.
Rivaroxaban- CHANGED from use with caution to avoid for long-term treatment	Prescribing for older adults is often a complex endeavor involving consideration of many factors , particularly the preferences and goals of the older person and their family.
	Rivaroxaban may be a reasonable option in select circumstances.

J Am Geriatr Soc. 2023;71(7):2052-2081. doi:10.1111/ jgs.18372
Burnett AE, et al. J Am Geriatr Soc. 2023. https://doi.org/10.1111/jgs.18579

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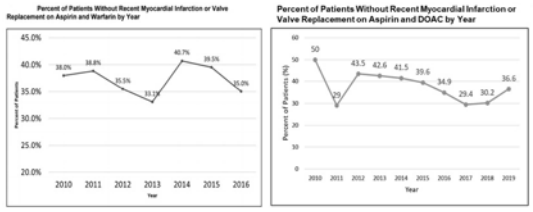
Anticoagulation + Antiplatelet Therapy: Common Practice

- 1/3 of patients on OAC are also on inappropriate antiplatelet therapy



Schaefer et al. 2019 Apr 1;179(4):533-541. 2. Schaefer JK et al. JAMA Internal Medicine. 2020;179(6)948-956. 3. Steinberg BA et al. Circulation. 2013 Aug 13;128(7):721-9. 4. So CH et al. J Thromb Thrombolysis. 2017 Jan;43(1):7-17. 5. Valeriani et al. J Thromb Haemost. 2020 Jul;18(7):1661-1671. 6. Kumar S et al. Cardiol Rev. 2016 Sep-Oct;24(5):218-23

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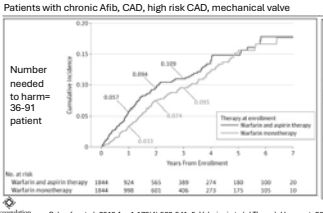
Anticoagulation + Antiplatelet Therapy: Risk vs Reward

- Addition of antiplatelet potentiate efficacy of OAC?
- No difference in thrombotic outcomes (exception mechanical heart valve)
- 2x increase in major bleeding

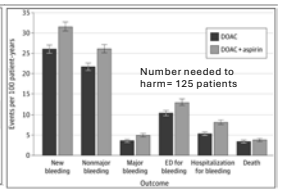
Patients with chronic Afib, CAD, high risk CAD, mechanical valve

Number needed to harm= 36-91 patient



Patient with Acute VTE

Number needed to harm= 125 patients



Schaefer et al. 2019 Apr 1;179(4):533-541. 5. Valeriani et al. J Thromb Haemost. 2020 Jul;18(7):1661-1671. 6. Dentali et al. Arch Intern Med. 2007;167(2):117–124

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Antiplatelet + Anticoagulant Use in NH residents

- Cross-sectional study
- 12 NH chains (709 facilities across 40 states)
- ≥100 days in a NH and had AF and a CHA2DS2-VASc (>1 men, > 2 women)
- Stratified:
  1) OAC plus antiplatelets (N=582)
  2) OAC only (N=1281)
  3) antiplatelets only (N=1523)
  4) no antithrombotic (N=1366)

12% receiving dual antithrombotic therapy and 45% receiving antiplatelets with no indication for use

Ko et al. *JAMA Intern Med*. doi:10.1001/jamainternmed.2024.1819

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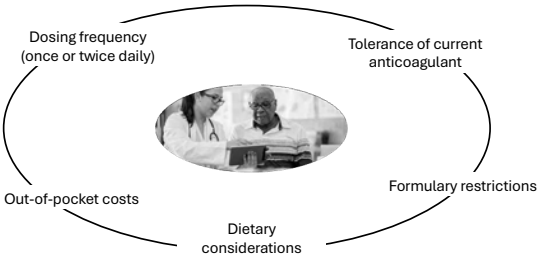
Key Considerations in Choosing an Anticoagulant WITH Your Older Patient



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Case 2: Audience Response Question

84-year-old man at his PCP office is diagnosed with new onset AFib.

He recently moved into an assisted-living facility after wife died 6 months ago.

HTN managed x 20 years with ACEI. **Severe OA** causing mobility limitations. **DM2** occasionally requiring medication adjustment. **Early-stage dementia** with mild memory impairment but still able to make decisions about his care.

Endorses mild fatigue and **has fallen once in the last year** (able to get up on his own and did not sustain serious injury)

Weight 72kg (5 kg↓) SCr 1.2 mg/dL INR 1.0 **CHA_2DS_2-Vasc= 4**

What would you start to prevent AFib-related stroke?

A. Low-dose ASA
B. LMWH→ VKA
C. DOAC
D. Withhold antiplatelets and anticoagulation

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Older patients less likely to be prescribed OAC

- Swedish registry (2009-2012) of 12,000 first-time stroke patients with AFib

Age group	Valid Observations	OAC Prescribing Frequency	Proportion (%)
18-69	1789	1098	61.4
70-79	2909	1531	52.6
80-89	5342	1551	29.0
90+	1993	209	10.5

Sjolander et al., Stroke 2015; 48: 2220-5.

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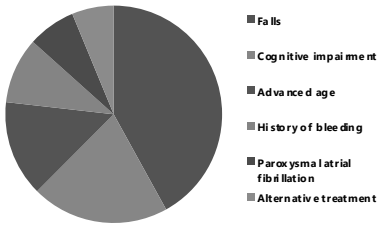
Prescriber criteria for withholding AC



Other reasons:
- Short life-expectancy
- Fear of bleeding
- Perceived harm>benefit
- Poor health
- Geriatric syndromes

Bo M et al. Eur J Intern Med. 2017;41:18-27 2. Bahri O et al., J Am Geriatr Soc 2015;63:71-76.

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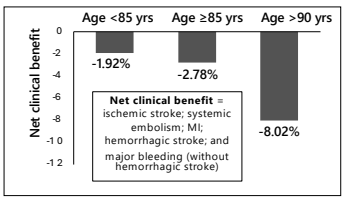
Net clinical benefit of OACs is higher in older age groups

Any OAC vs. No AC: PREFER-AF (European Registry) 2012-2014



Most OAC treatment in the registry was warfarin (~6% NOACs)

Patti G, et al. *Am Heart Assoc. 2017 Jul; 6(7): e005657*

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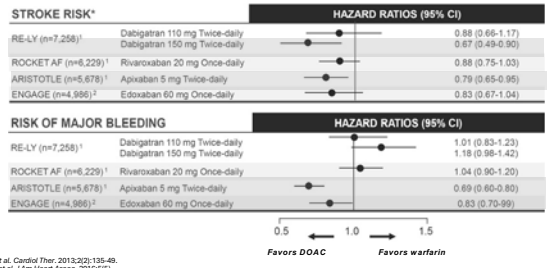
Net clinical benefit of DOACs preserved ≥ 75 years



Ng KH, *et al. Cardiol Ther.* 2013;2(2):135-49.
Kato ET, *et al. J Am Heart Assoc.* 2016;5(5).

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Case 3: Audience Response Question

82- year-old woman on **warfarin x 10 years** for AFib brought into anticoagulation clinic by her grandson

Increasingly reliant on others for help with ADLs, including transportation to medical appointments, because of vision, stamina and cognition issues

Weight 57 kg (5 kg↓) SCr 1.8 mg/dL INR 2.2 (TTR ~75%)

Her grandson asks you about "another blood thinner" he saw on TV that is "easier to use" and asks if this might be an option for her

How would you adjust this patient's anticoagulation regimen?

A. Switch to low-dose ASA
B. Switch to rivaroxaban
C. Switch to apixaban
D. Continue current therapy with warfarin

Anticoagulation ECHO Out

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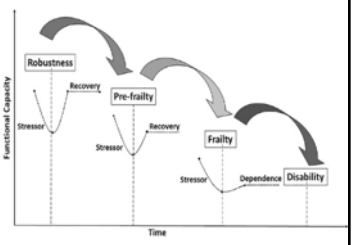
Frailty

Increased vulnerability due to aging-associated decline in reserve & function across multiple physiologic systems

Not well represented in RCTs

Multiple frailty scoring tools

Clinicians implicitly weigh multiple risk factors when deciding AC vs. no AC



Anticoagulation ECHO Out

Xue Q. Clin Geriatr Med. 2011 Feb; 27(1): 1–15.
Proietti M, et al Ageing Res Rev. 2022 Aug;79:101652.
Dent E, et al. J Nutr Health Aging. 2019;23(9):771-787.

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Meta-analysis of frailty in AFib (N=1,187,000)

Prevalence of Frailty: 40%
Prevalence of Pre-frailty: 35%

OAC under-prescription in frail patients vs prefrail/robust: OR 0.83 (0.61-1.06)

Frail >80yo → OAC significantly less prescribed

Frail patients at higher risk for major outcomes compared to robust patients

All-cause death
OR 5.56 (3.46-8.94)

Stroke
OR 1.59 (1.00-2.52)

Bleeding
OR 1.64 (1.11-2.41)

Proietti. Ageing Res Rev. 2022 Aug;79:101652.

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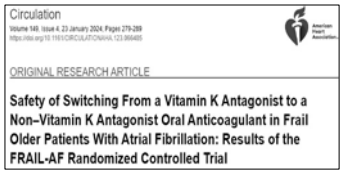
FRAIL-AF: Design



Circulation

ORIGINAL RESEARCH ARTICLE

Safety of Switching From a Vitamin K Antagonist to a Non–Vitamin K Antagonist Oral Anticoagulant in Frail Older Patients With Atrial Fibrillation: Results of the FRAIL-AF Randomized Controlled Trial

- 8 Dutch thrombosis clinics
- Nonvalvular AFib patients ≥ 75 yo on VKA, eGFR ≥ 30ml/min
- Groningen frailty score ≥ 3
- Randomized, open label
  - Continue VKA (n=661)
  - Switch to DOAC (n=662)
- Superiority trial with planned interim analysis at 160 events

Joosten LPT, et al. Circulation. 2024;149:279–289

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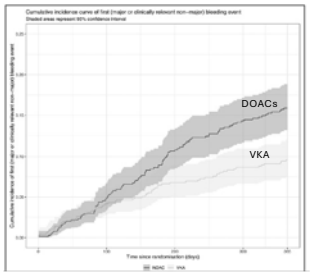
Cumulative incidence of bleeding DOACs vs VKA



Joosten. Circulation. 2024;149:279–289

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FRAIL-AF: Bleeding vs Thrombosis

Variable	Switch to NOAC		Continue with VKA		Hazard ratio (95% CI)
	n (%)	No. of events/100 patient-years (95% CI)	n (%)	No. of events/100 patient-years (95% CI)	
Primary outcome					
Major or CRNM bleeding	101 (15.3)	17.8 (14.5–21.6)	62 (9.4)	10.5 (8.0–13.4)	1.69 (1.23–2.32)
Secondary outcomes					
Bleeding outcomes separately					
Major bleeding	24 (3.6)	3.9 (2.5–5.9)	16 (2.4)	2.6 (1.5–4.2)	1.52 (0.81–2.87)
CRNM bleeding	84 (12.7)	14.6 (11.7–18.1)	49 (7.4)	8.2 (6.1–10.9)	1.77 (1.24–2.52)
Thromboembolic events	16 (2.4)	2.6 (1.5–4.3)	13 (2.0)	2.1 (1.1–3.6)	1.26 (0.60–2.61)
Composite of thromboembolic events plus major or CRNM bleeding	115 (17.4)	20.6 (17.0–24.7)	73 (11.0)	12.4 (9.8–15.6)	1.65 (1.23–2.21)
Composite of ischemic and hemorrhagic stroke	14 (2.1)	2.3 (1.3–3.8)	11 (1.7)	1.8 (0.9–3.2)	1.30 (0.59–2.87)
All-cause mortality	44 (6.7)	7.1 (5.2–9.5)	46 (7.0)	7.4 (5.4–9.8)	0.96 (0.64–1.45)

Joosten LPT, et al. Circulation. 2024;149:279-289

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FRAIL-AF: Discussion Points

Table 3. First Major or Clinically Relevant Nonmajor Bleeding* Location per Treatment Arm

Bleeding location	Major bleedings		CRNM bleedings	
	Switch to NOAC	Continue with VKA	Switch to NOAC	Continue with VKA
Skin, n (%)			23 (3.5)	10 (1.5)
Oropharyngeal, n (%)		1 (0.2)	19 (2.9)	16 (2.3)
Gastrointestinal, n (%)	9 (1.4)	1 (0.2)	8 (1.2)	3 (0.5)
Urogenital, n (%)			20 (3.0)	11 (1.7)
Brain,† n (%)	7 (1.1)	6 (0.9)		
Ophthalmic, n (%)		1 (0.2)	3 (0.5)	2 (0.3)
Musculoskeletal, n (%)	1 (0.2)		1 (0.2)	4 (0.6)
Lung, n (%)		1 (0.2)		
Other, n (%)	2 (0.3)	3 (0.5)	8 (1.2)	3 (0.5)

- Stopped early for futility (underpowered)
- Precludes drawing conclusions on differences between the groups
- VKA patients already tolerant
- DOAC choice not individualized or randomized (50% rivaroxaban)
- TTR not reported for VKA arm (likely >65-70% given setting)

Joosten LPT, et al. Circulation. 2024;149:279–289
Wallentin L, et al. Circulation. 2024;149:290–292

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Comorbidities to consider when choosing anticoagulant

- Renal insufficiency
  - dose reductions or avoidance for some DOACs
- Liver disease
  - Caution with VKA and DOACs based on Child-Pugh
- Underweight
  - Dose reduction with Apixaban/Edoxaban in AFib
- Cancer-associated VTE
  - Apixaban/Rivaroxaban/Edoxaban/LMWH > VKA
- Antiphospholipid syndrome
  - VKA > DOACs
- Mechanical Heart valves
  - VKA>DOACs

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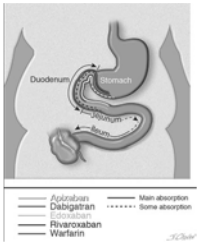
Comorbidities to consider when choosing anticoagulant

- Altered GI anatomy or enteral nutrition
  - Unpredictable absorption of OAC

DOACs for Enteral Administration

DOAC	Bioavailability	Safe to Crush?	Administer per NG/G Tube?
Apixaban	~50% (unaffected by food)	Yes	Yes
Rivaroxaban	>90% with food† (~66% without food)	Yes	Yes*
Dabigatran	***~5% (unaffected by food)***	***No***	***No***

*Doses ≤10 mg can be administered without regard to food
*Avoid administering post-pyloric



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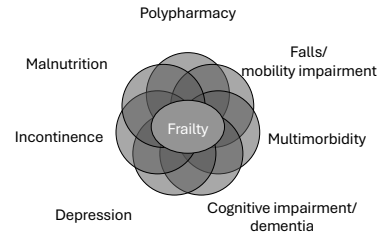
Geriatric Syndromes: Intersectionality of Multiple Conditions/Issues



- Most older AF patients have ≥ 1 geriatric syndrome
- ↑ # geriatric syndromes associated with ↓ anticoagulant use
- May be a key driver of undertreatment of AF
- Should be incorporated into decisions around stopping AC

Shah SJ, et al. Am Geriatr Soc. 2021 Feb;69(2):349-356.

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Key Considerations in Choosing an Anticoagulant WITH Your Older Patient

Switching from VKA to DOAC might be associated with similar benefits regarding major bleeds, stroke and mortality.

However, it may be associated with a higher rate of GI bleeding.

Weigh potential gains of simpler treatment with potential increased risk of GI bleeding.

Most important is maintaining long-term adherence, whether on VKA or DOAC.

Wallentin L, et al. Circulation. 2024;149:290–292

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Case 4: Audience Response Question

- **96 yo** woman on apixaban for atrial fibrillation
- Brought into ED from long-term care facility after a **fall event** that she does not remember
- Has **advanced Alzheimer's** and is **fully dependent** for ADLs
- Patient **intermittently refuses** oral medications at long-term facility
- Head CT is negative for any bleeding and ED resident is asking for recommendations on resuming apixaban

What would you recommend?

A. Continue twice daily apixaban
B. Switch to once-daily rivaroxaban
C. Switch to VKA
D. Stop all anticoagulation

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Stopping Anticoagulants: Need for a Patient-Centered Framework

Competing risk of death from non-stroke causes, such as advanced dementia, diminishes the net clinical benefit (NCB) of anticoagulant therapy

After age 87 years and 92 years, NCB of warfarin and apixaban, respectively, falls below the minimal clinically relevant threshold

Recent data suggests roughly 1/3 of nursing home residents with AF and advanced dementia remain on anticoagulation in last 6 months of life

More high-quality data is needed to inform decision-making and drive antithrombotic stewardship initiatives in these patient populations

"Drive to Deprescribe" initiative (https://paltc.org/drive-deprescribe)

Ouellet GM, et al. JAMA Intern Med. 2021;181(8):1121-1123.
Shah SJ, et al. Circ Cardiovasc Qual Outcomes. 2019 Nov;12(11):e006212
Parks A, et al. JAMA Intern Med. 2021;181(8):1123.

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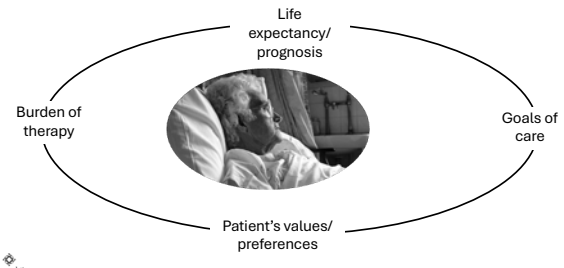
Key Considerations in Stopping an Anticoagulant WITH Your Older Patient



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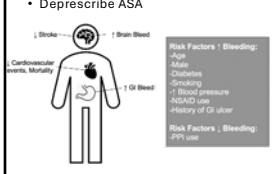
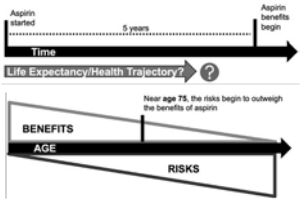
Antithrombotic Stewardship: Drive to Deprescribe (D2D) Initiative

- Post-Acute and Long-term Care Med Association (PALTmed) and American Society of Consultant Pharmacists (ASCP)
- Reduce polypharmacy and enhancing patient care
- Deprescribe ASA





https://paltc.org/drive-deprescribe

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Practical considerations when managing anticoagulation in older patients

Checklist of clinical parameters to assess when initiating AC and during follow-up
✓ Assess Thrombotic Risk (CHA_2DS_2-Vasc or VTE recurrence)
✓ Assess bleeding risk using RAMs and other risks specific to elderly
✓Check baseline labs- renal function, coagulation tests, liver function, CBC
✓Check for CI to DOACs or VKA. Alternatives to AC e.g. LAAO
✓Choose suitable AC and dose (QD vs BID) and dose reductions
✓Identify potential drug-drug interactions
✓Reduce unnecessary medications (ASA and others with antiplatelet properties)
✓Evaluate need for PPI
✓Tailor patient education to elderly and repeat as needed. Consider additional teaching/adherence tools
✓Provide anticoagulation card/medication alert tag
✓Determine appropriate frequency of follow-up (early initial F/U may be required in older patients)
✓Explore reasons for nonadherence
✓Explore options for dose reduction or discontinuation of anticoagulation

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Acknowledgements

Thanks to the Anticoagulation Forum for slides from a recent webinar on Anticoagulation in Older Patients
https://acforum.org/web/education-webinars.php

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