

Approach to Stroke Prevention in Older Adults with Atrial Fibrillation (AF)

Determine the individual’s risk of stroke using the CHADS₂ or CHA₂DS₂VASc score.

Which validated stroke risk tool should I use – the CHADS₂ or CHA₂DS₂VASc?

Several analyses have compared the two; both appear similar for estimating risk of stroke, thromboembolism, and bleeding. The CHA₂DS₂VASc score, however, is better for estimating the risk of stroke in very low risk individuals, and is the most validated score. GARFIELD-AF, and ATRIA are newer scoring tools which consider variables including smoking, renal disease and dementia, but neither has been as rigorously evaluated as CHA₂DS₂VASc. [ACC/AHA’23](#)

CHADS ₂ Risk Criteria	Points	CHADS ₂ Score	Stroke Rate, %/year (95% CI)
Congestive Heart Failure (CHF) *	1	0	1.9 (1.2 – 3)
Hypertension (HTN) *	1	1	2.8 (2 – 3.8)
Age ≥75 years	1	2	4 (3.1 – 5.1)
Diabetes mellitus (DM) *	1	3	5.9 (4.6 – 7.3)
Stroke, Transient Ischemic Attack	2	4	8.5 (6.3 – 11.1)
		5	12.5 (8.2 – 17.5)
		6	18.2 (10.5 – 27.4)

CHA ₂ DS ₂ VASc Risk Criteria	Points	CHA ₂ DS ₂ VASc Score	Stroke Rate, %/year
Congestive Heart Failure *	1	0	0
Hypertension *	1	1	1.3
Age ≥75 years	2	2	2.2
Diabetes mellitus *	1	3	3.2
Stroke, Transient Ischemic Attack	2	4	4
Vascular disease *	1	5	6.7
Age 65 to 74 years	1	6	9.8
Sex – female	1	7	9.6
		8	6.7
		9	15.2

*CHF: moderate to severe systolic dysfunction, signs & symptoms of HF-REF, or recent HF hospitalization; HTN: resting BP >140/90mmHg x 2, or on antihypertensives; DM: FPG ≥7mmol/L, or on diabetes medications; Vascular disease: Coronary Artery Disease (CAD), Peripheral Vascular (PVD) Disease (PAD), or aortic plaque

Determine the individual’s risk of major bleeding using the HAS-BLED score. Address reversible bleeding risk factors when possible e.g. uncontrolled BP, concurrent ASA, NSAID, alcohol use.

HAS-BLED Risk Criteria	Points	HAS-BLED Score	Major Bleeds (%/year)
Hypertension (SBP>160 mmHg)	1	0	1.13
Abnormal renal (transplant, dialysis, SCr >200umol/L) or liver function (AST/ALT >3xULN, bilirubin>2x ULN)	1 to 2	1	1.02
Stroke (any stroke; ? 2 points if a hemorrhagic stroke)	1 ?2	2	1.88
Bleeding (hospitalization, ↓Hgb >20 g/L, transfusion)	1	3	3.74
Labile INRs (time in therapeutic range <60%)	1	4	8.70
Elderly (age >65 years)	1	5	12.50
Drugs (ASA/NSAID) or alcohol (≥ 8 drinks/week)	1 to 2		

HAS-BLED score ≥3=↑ risk of major bleed (intracranial, hospitalization, ↓ Hgb >20 g/L, transfusion)

Consider the predicted risk of stroke versus the predicted risk of major bleed.

- HAS-BLED score should not be used to identify if anticoagulation should be withheld, but rather, to identify modifiable risk factors which can be mitigated.
- Stroke has a higher risk of mortality & morbidity compared to major bleeds.
- Refer to the 3 tables in the column to the left for the risk of stroke/bleeds per year based on the CHADS₂, CHA₂DS₂VASc & HAS-BLED scores. There is also an atrial fibrillation stroke prevention risk tool available at www.sparctool.com.

Select an antithrombotic based on the individual’s risk of stroke & bleed.

- Oral Anticoagulants (OAC) used for AF:** **S** apixaban ^{ELIQUIS}, **S** dabigatran ^{PRADAXA}, **S** edoxaban ^{LIXIANA}, **S** rivaroxaban ^{XARELTO}, **B** warfarin ^{COUMADIN}
- DOACs are preferred over warfarin in non-valvular AF (NVAf) ^{CCS AF’20 SR, HQ; ACC/AHA/ACCP/HRS’23, ESC’20}
- Warfarin remains preferred over DOACs in AF with mechanical prosthetic valve or moderate-severe rheumatic mitral stenosis ^{CCS AF’20 SR, MQ; ACC/AHA/ACCP/HRS’23, ESC’20}
- Antiplatelets:** **ASA** ^{ASPIRIN} (± clopidogrel ^{PLAVIX}) as monotherapy or in combination are no longer recommended for stroke prevention due to unfavourable efficacy/harms compared to DOACs. ^{CCS AF’20 SR, MQ; ACC/AHA/ACCP/HRS’23; ESC’20}
 - Antiplatelets remain appropriate for patients with AF who have comorbid arterial vascular disease* (See Geri-RxFiles: [Antiplatelets & Anticoagulants](#) pg XX)
- The CHADS₂ & CHA₂DS₂VASc scores can be used to help select antithrombotic therapy. The Canadian Cardiovascular Guideline (CCS) recommends their own score, i.e. CHADS-65, which uses a predictive index and includes risk factors with a 1.5% annual risk of stroke or greater.

CHADS-65 (CCS Algorithm)	Canadian Cardiovascular Guideline (2020) Recommended Therapy
Age ≥65 years	OAC monotherapy - DOAC preferred (strong recommendation, high-quality evidence)
Age <65 years & CHADS ₂ score ≥1	
Age <65 years & CHADS ₂ score = 0 with stable arterial vascular disease* (CAD, PVD or aortic plaque)	Arterial Vascular Disease Management: ASA 81mg po daily <u>or</u> ASA 81mg po daily + clopidogrel 75mg po daily ^{DAPT} <u>or</u> ASA 81mg po daily + ticagrelor 60mg po BID ^{PEGASUS} <u>or</u> ASA 81mg po daily + rivaroxaban 2.5mg po BID ^{COMPASS} (strong recommendation, high-quality evidence)
Age <65 years & CHADS ₂ score = 0	No antithrombotic therapy (weak recommendation, moderate-quality evidence)

CHA ₂ DS ₂ VASc Score	European ^{ESC’20} & USA ^{ACC/AHA/ACCP/HRS’23} Guidelines Recommendations for OAC – DOAC preferred
0	No antithrombotic therapy (3B)
1	Male: consider OAC (2aA); Female: no OAC (2aB)
2	Male: OAC (1A); Female: consider OAC (2aA)
≥3	OAC (Level IA)

SB – See STOPP&Beers Criteria considerations on page XX

Approach to Stroke Prevention in Older Adults with Atrial Fibrillation

Beware of underutilizing, and under-dosing OAC in older adults

- With advancing age comes increased prevalence of AF and incidence of stroke. Despite this, older adults are less likely to be prescribed OAC even in the absence of contra-indications.²⁸⁻³³ Underutilization can be as high as 35-47% of eligible older adults, not receiving indicated OAC.³²⁻³³
- Frailty, advanced age, and fall risks do not outweigh the benefits of OAC in most older adults with AF. **CCS AF'20 SR, MQ** DOACs preferred over warfarin due to reduced bleed risk.
- Although the overtreatment of patients with higher than indicated DOACs dose is about 4%, the under-dosing of DOACs is 3-4x more common at 12-15%. This under-dosing is associated with increased risk of hospitalization, thromboembolic events, and death, without meaningfully reducing major bleeding. **CCS AF'20**

Which ANTICOAGULANTS are Available for Stroke Prevention in AF?

There are three classes of anticoagulants currently available:

- Direct Thrombin Inhibitor: **S B** dabigatran **PRADAXA**
- Factor Xa Inhibitor: **S** apixaban **ELIQUIS**, **S B** edoxaban **LIXIANA**, **S B** rivaroxaban **XARELTO**
- Vitamin K Antagonist: **B** warfarin **COUMADIN**

How Do the Various Anticoagulants Compare in Older Adults?

- **Determine which anticoagulant is best suited for the individual.**
- Consider factors that ↑ the risk of bleeding that apply to all anticoagulants, such as:
 - **≥65 YEARS** (concern further increases at **≥75 YEARS**)
 - **WITH CURRENT BLEEDING DISORDER, OR HISTORY OF PRIOR BLEED**
 - **ALCOHOL USE**
 - **COMBINATION WITH ASA OR NSAID** (without a PPI or misoprostol)
- **Warfarin** may be preferred over the other anticoagulants for individuals:
 - with mechanical heart valves, moderate to severe rheumatic mitral stenosis, or moderate & severe non-rheumatic mitral stenosis (where direct oral anticoagulants [DOAC] – apixaban, dabigatran, edoxaban & rivaroxaban, are contraindicated)
 - with very poor renal function (e.g. end-stage CKD, CrCl <15mL/min, dialysis)
 - when risk of dyspepsia &/or gastrointestinal bleeding is prominent, except apixaban
- ~20 to 40% of the patients included in the AF landmark trials with the direct oral anticoagulants were **≥75 years** of age:
 - apixaban **ARISTOTLE** 31% **AVERROES** 34%; dabigatran **RELY** 40%; edoxaban **ENGAGE** 40%; rivaroxaban **ROCKET** 18% (**≥80 years**)

For more complete **STOPP&Beers** (See Geri-RxFiles: [Antiplatelets & Anticoagulants](#) pg XX)

How Do the Various Anticoagulants Compare in Older Adults? - continued

- **Apixaban, dabigatran, edoxaban & rivaroxaban** had less intracranial bleeds compared to warfarin in the trials (NNT=96 to 477 over ~2 years).
- **Apixaban, dabigatran, edoxaban, and rivaroxaban** do not require INR monitoring, but all four require dose adjustments/caution in renal impairment. Assess CrCl at baseline and at least every 6 months in older adults. **General rule of thumb:** When lab reported eGFR is <50mL/min, be sure to calculate the CrCl for dose adjustment.
- Although no head to head RCTs exist to directly compare these agents, a recent meta-analysis of observational studies in AF suggests apixaban is at least as effective, and has lower risk of major bleeding compared to dabigatran and rivaroxaban. Apixaban also had lower risk of all cause mortality, ischemic stroke, and intracranial hemorrhage than rivaroxaban.³⁴ A multinational population-based cohort study of over 500,000 DOAC users found lower risk of GI bleed with apixaban compared to dabigatran, edoxaban, and rivaroxaban, with similar rates of systemic embolism or ischemic stroke.⁴⁰
- **Beers' 2023** leans towards apixaban as preferred DOAC in most older adults.
- Low dose edoxaban (15mg daily) has some limited evidence for use in **oldest older adults**. Based on ~ 13% of patients in the landmark **ENGAGE-AF** trial who were dosed at 15mg daily, the **ELDERCARE-AF** trial used this dose exclusively vs placebo.
 - **ELDERCARE-AF**, small (n=984) double-blind RCT compared edoxaban 15mg daily to placebo in Japanese patients **≥80 yrs** with NVAf, who were considered not appropriate for OAC (e.g. CrCl 15-30mL/min, history of GI bleed or from critical organ, low body weight ≤45kg, continuous NSAID use or current antiplatelet use.) Stroke or systemic embolism was 2.3%, per patient year, in edoxaban group vs 6.7% in placebo group (HR 0.34 CI 0.19-0.61) **NNT=23**. Major bleeding higher in edoxaban (3.3%) vs placebo (1.8%) but not statistically significant.³⁹
 - Applicability of this trial to a North American population is limited, and the **15mg dose** of edoxaban is not officially indicated for treatment of NVAf.

~Cost/month: Apixaban \$37, dabigatran \$98, edoxaban \$107 & rivaroxaban \$35. Warfarin \$40 (includes INR monitoring). The 4 DOACs are on the SK Drug Plan, and NIHB.

DOAC Monitoring Checklist <https://thrombosiscanada.ca/tools/?calc=vivomap329>

- A – adherence: ≥1 dose missed per week?
- B – bleeding (risk assessment): Severe epistaxis? Unusual bruising? Hematuria?
- C – creatinine clearance
- D – drug interactions: ASA? Antiplatelets? NSAID? Other?
- E – examination: Blood pressure (↑ or ↓). Risk of falls?

Dosing Considerations for Apixaban, Dabigatran, Edoxaban & Rivaroxaban

<p>S Apixaban <small>ELIQUIS</small></p> <ul style="list-style-type: none"> • 5mg BID, or • 2.5mg BID if ≥ 2 of the following: <ul style="list-style-type: none"> o ≥ 80 years o weight ≤ 60 kg o SCr ≥ 133 $\mu\text{mol/L}$ (CrCl < 25 mL/min) <p>STOPP: CrCl < 15 mL/min</p> <ul style="list-style-type: none"> • Limited efficacy / safety data for CrCl 15 - 25 mL/min <p>CAUTION: ≥ 75 yrs of age + unstable renal function</p> <ul style="list-style-type: none"> • Contraindicated with the concomitant use of strong inhibitors of both CYP3A4 & P-gp (e.g. ketoconazole, ritonavir) • Avoid with strong CYP3A4 inducers (phenytoin, CBZ) 	<p>S B Edoxaban <small>LIXIANA</small></p> <ul style="list-style-type: none"> • 60mg daily, or • 30mg daily if 1 of the following: <ul style="list-style-type: none"> o CrCl 30 to 50 mL/min o weight ≤ 60 kg o concomitant P-GP inhibitor except amiodarone or verapamil (e.g. cyclosporine, dronedarone, erythromycin, ketoconazole) <p>Beers: reduce dose (30mg daily) if CrCl 15 to 50 mL/min, and avoid if < 15 or > 95 mL/min</p> <p>STOPP: CrCl < 15 mL/min</p> <ul style="list-style-type: none"> • Limited efficacy / safety data for CrCl < 30 mL/min <p>CAUTION: ≥ 75 yrs of age + unstable renal function</p>
<p>S B Dabigatran <small>PRADAXA</small></p> <ul style="list-style-type: none"> • 150mg BID, or • 110mg BID if: <ul style="list-style-type: none"> o ≥ 80 years o ≥ 75 years + ≥ 1 bleeding risk factor: (e.g. CrCl 30 to 50 mL/min; recent GI bleed, combined use of dronedarone, amiodarone, quinidine, verapamil, NSAID, antiplatelet, SSRI) <p>Beers: \uparrow GI bleed vs warfarin (head to head trial) & \uparrow major bleed vs apixaban (observational trials & meta-analysis)</p> <p>STOPP: CrCl < 30 mL/min – use contraindicated</p> <p>CAUTION: ≥ 75 yrs of age + unstable renal function</p>	<p>S B Rivaroxaban <small>XARELTO</small></p> <ul style="list-style-type: none"> • 20mg daily with food, or • 15mg daily with food if: <ul style="list-style-type: none"> o CrCl 15 to 50 mL/min • Avoid with strong CYP3A4 inducers (phenytoin, CBZ) <p>Beers: Avoid long term use in AF, as appears to have \uparrow rates of major bleeding in older adults compared to other DOACs (S apixaban);</p> <ul style="list-style-type: none"> • Reduce dose if CrCl 15 to 50 mL/min, • Avoid if CrCl < 15 mL/min; <p>STOPP: CrCl < 15 mL/min</p> <ul style="list-style-type: none"> • Limited efficacy & safety data for < 30 mL/min; • Contraindicated when combined with strong inhibitors of both CYP3A4 & P-gp (e.g. ketoconazole, ritonavir)

How Do I Switch to/from Warfarin & the Direct Acting Oral Anticoagulants? Manufacturers' recommendations from the product monographs

Frail-AF RCT compared switching warfarin patients, age ≥ 75 , to a DOAC, vs remaining on warfarin. Switching was associated with increase bleeding (mostly non-major). However, study had many limitations, including: INR levels for warfarin patients were all managed by Dutch thrombosis services. Time in therapeutic range estimated 65-74%. This may not representative of most patients on warfarin.³⁶ In those with excellent warfarin management, there may not be a bleeding advantage to switching to a DOAC. A combination of patient preference and clinical considerations should guide decision making.

Warfarin → Apixaban	Warfarin → Dabigatran	Warfarin → Edoxaban	Warfarin → Rivaroxaban
Stop warfarin. Start apixaban when INR < 2 .	Stop warfarin. Start dabigatran when INR < 2 .	Stop warfarin. Start edoxaban when INR ≤ 2.5 .	Stop warfarin. Start rivaroxaban when INR ≤ 2.5 .
Apixaban → Warfarin	Dabigatran → Warfarin	Edoxaban → Warfarin	Rivaroxaban → Warfarin
Start warfarin. Stop apixaban when INR > 2 .	<ul style="list-style-type: none"> • If CrCl > 50 mL/min: start warfarin 3 days before stopping dabigatran • If CrCl 31-50 mL/min: start warfarin 2 days before stopping dabigatran • If CrCl 15-30 mL/min: start warfarin 1 day before stopping dabigatran 	Start warfarin. \downarrow edoxaban dose by 50%, & stop when INR > 2 .	Start warfarin. Stop rivaroxaban when INR ≥ 2 .

What are the antidotes for Warfarin & the Direct Acting Oral Anticoagulants? High quality studies somewhat lacking

Warfarin	Dabigatran	Apixaban or Edoxaban or Rivaroxaban
<ul style="list-style-type: none"> • Vitamin K 1 to 10mg PO/IV • Prothrombin complex concentrate (PCC) <small>OCTAPLEX, BERIPLEX</small> (4F-PCC) usually 1000-3000IU IV • Fresh frozen plasma if PCC unavailable • Recombinant factor VIIa 	<ul style="list-style-type: none"> • Idarucizumab <small>PRAXBIND</small> 5g IV infusion over 5-10 min • 4F-PCC <small>OCTAPLEX, BERIPLEX</small> • Activated charcoal if ≤ 2 to 4h of administration • Dialyzable 	<ul style="list-style-type: none"> • Andexanet <small>ONDEXXA</small> Bolus IV 400 to 800mg @30mg/min, then 4-8mg/min over 2 hr • 4F-PCC <small>OCTAPLEX, BERIPLEX</small> • Activated charcoal if ≤ 2 to 4h of administration • NOT dialyzable • ?Recombinant factor VIIa (for Apixaban)

Warfarin Tips & Dosing Nomograms for Older Adults

Initiating Warfarin in Older Adults

- Start with a lower dose (warfarin 2 to 3mg) if: >70 years of age, ↑ bleeding risk, taking medications known to ↑ INR, heart failure, liver disease or poor nutrition.
- The nomogram below may be helpful when starting warfarin in an older adult. The dose adjustments are extrapolated for a lower initial dose from a validated nomogram.

INITIATING WARFARIN NOMOGRAM (CONSERVATIVE DOSE)							
DOSE ADJUSTMENTS FOR 3MG DAY 1 & DAY 2 (TARGET INR 2 TO 3)							
DAY 3		DAY 4 (OPTIONAL INR)		DAY 5		DAY 6 (OPTIONAL INR)	
INR	DOSE (mg)	INR	DOSE (mg)	INR	DOSE (mg)	INR	DOSE (mg)
< 1.5	3 – 6	< 1.5	6	< 1.5	6	< 1.5	4.5 – 7.5
1.5 – 1.9	1.5 – 3	1.5 – 1.9	3 – 4.5	1.5 – 1.9	4.5 – 6	1.5 – 1.9	3 – 6
2 – 3	0 – 1.5	2 – 3	0 – 3	2 – 3	0 – 3	2 – 3	0 – 4.5
> 3	0	> 3	0	> 3	0	> 3	0

Frequency of INR Monitoring

- **Initiating Warfarin:** Week 1: Day 3 & 5. Week 2: 2 INRs. Week ≥3: 2 INRs/week until stable x 2 weeks, then every 2 weeks until stable x 1 month, then monthly INRs.
- **Maintaining Warfarin:**
 - Perform monthly INRs if no change in the individual’s health status, his/her drug therapy or INR results.
 - The frequency of INR monitoring may be extended to every 12 weeks in healthy older adults who have had stable INRs for ≥3 months, providing any medication changes are known/reported & the individual is compliant with the INR schedule. Avoid in frail adults.
 - **Warfarin Dose Changes:** check INR weekly until stable.
 - **Starting, Stopping or Changing the Dose of an Interacting Drug:** check the INR 4 to 6 days after change. ↑ monitoring duration for drugs with long t½ or onset (e.g. amiodarone).

Maintaining Warfarin Within Therapeutic Range

- The below validated nomogram can be used to adjust warfarin doses based on maintenance INR results.
- Do not routinely adjust warfarin doses based on **1 asymptomatic, unexplained, slightly out-of-range maintenance INR (≤0.5 ± target)**. Recheck INR in 1 to 2 weeks.
- Inquire about dietary changes & missed/extra doses, especially for individuals living independently.

MAINTENANCE OF WARFARIN NOMOGRAM

TARGET INR 2 TO 3	ACTION	TARGET INR 2.5 TO 3.5
<1.5	Extra dose, ↑ weekly dose by 10 to 20%	<2
1.5 – 1.9	↑ weekly dose by 5-10%	2 – 2.4
2 – 3	No Change	2.5 – 3.5
3.1 – 3.5	↓ weekly dose by 5-10%	3.6 – 4
3.6 – 4.9	Hold 1 dose, ↓ weekly dose by 10 to 20%	4.1 – 4.9
5 – 9	Hold 2 doses, ↓ weekly dose by 10 to 20%	5 – 9
>9	Urgent evaluation	>9

Warfarin and Food Interactions – Do Certain Foods Really Need to be Avoided?

- Higher than typical Vitamin K intake counteracts the effects of warfarin (a vitamin K antagonist). Foods contain varying levels of vitamin K (See food table below).
- Foods that contain vitamin K do not need to be avoided, but rather individuals taking warfarin should be encouraged to consume a consistent amount of vitamin K. A concern will exist when a major change in vitamin K intake occurs (very common during garden season), but normal daily variation in the foods consumed is okay.
- When an altered vitamin K intake occurs, the effects are unpredictable, & the warfarin dose should not be empirically changed – it is hard to get it right! If an INR result is below target below the 2 to 3 therapeutic range, inquire if there have been any changes in vitamin K intake, & whether it was a temporary or permanent change in consumption, or if it will continue (to know whether or not to adjust the dose). Do not adjust the warfarin dose based on 1 asymptomatic, abnormal INR that is only ±0.5 from the target. Recheck INR in 1 to 2 weeks in this scenario.

Vitamin K Content of Selected Foods

Low	Moderate ≤3 servings per day ^{Serving size}	High Only ONE serving per day ^{Serving size}
Beverages		Beverages
Coffee Cola Fruit juices	Milk Tea ^{Black}	Tea ^{Green*}
Dairy Products		
Milk		
Fats and Oils		Fats and Oils
Corn oil Peanut oil	Sesame oil Sunflower oil	Margarine Olive oil Canola oil Mayonnaise Soybean oil
Fruit		
Meats		
Vegetables		Vegetables (fresh or boiled)
Green beans Carrots Cauliflower Celery Corn Cucumber ^{Peel removed} Eggplant Mushrooms	Onions Green Pepper Potato Pumpkin Sauerkraut ^{Canned} Tomato	Asparagus Avocado Broccoli ^{Raw 1 cup} Brussels sprouts ^{½ cup} Endive ^{Raw 1 cup} Green leaf lettuce ^{1 cup} Green peas Pickle ^{Dill} Lettuce ^{Iceberg} Red cabbage Romaine lettuce ^{1 cup} Spinach ^{Raw 1 cup} Turnip Greens ^{Raw 1 cup}
		Broccoli Cabbage Collard greens ½ cup Parsley ^{Raw ½ cup} Spinach ^{½ cup} Kale ^{½ cup} Lettuce ^{Bib, Red leaf} Turnip Greens ^{½ cup} Watercress Swiss chard ^{½ cup}

*Effects of green tea on warfarin are controversial. The amount of vitamin K content or other constituents vary greatly among different products depending on their sources & processing; therefore, it is difficult to determine how much green tea consumption would have an effect on warfarin.

Alcohol and Warfarin

Alcohol can have varying effects on warfarin. Acute alcohol consumption can decrease warfarin metabolism and increase warfarin effect, whereas chronic alcohol consumption can induce warfarin metabolism and decrease warfarin effect.



Generic Taro-Warfarin

Acknowledgements: Originally written by Lynette Kosar. Edits provided by Eric Landry (2024). Thanks to our reviewers: Kelly Buxton, Darcy Lamb, Kirsten Tangedal, and Jeff Wilkinson.

Disclosures: No conflicts of interest are reported by the authors.

Disclaimer: RxFiles Academic Detailing is part of the College of Pharmacy and Nutrition at the University of Saskatchewan. The content of this work represents the research, experience and opinions of the authors and not those of the University of Saskatchewan. Neither the authors nor the University of Saskatchewan nor any other party who has been involved in the preparation or publication of this work warrants or represents that the information contained herein is accurate or complete, and they are not responsible for any errors or omissions or for the result obtained from the use of such information. Any use of the materials will imply acknowledgment of this disclaimer and release any responsibility of the University of Saskatchewan, its employees, servants or agents. Readers are encouraged to confirm the information contained herein with other sources.

Search Terms

Antithrombotics	13
ASA	13
ASPIRIN	13
Atrial Fibrillation	13
Bleed Risk	13
CHADS	13
HAS-BLED	13
Stroke	13
Anticoagulant	14
Apixaban	14
Atrial Fibrillation	14
COUMADIN	14
Dabigatran	14
DOACs	14
Edoxaban	14
ELIQUIS	14
LIXIANA	14
PRADAXA	14
Rivaroxaban	14
Warfarin	14
XARELTO	14
4F-PCC	15
Andexanet alfa	15
Anticoagulant	15
Apixaban	15
Atrial Fibrillation	15
BERIPLEX	15
Dabigatran	15
DOACs	15
Edoxaban	15
ELIQUIS	15
Idarucizumab	15
LIXIANA	15
OCTAPLEX	15
ONDEXXYA	15
PRADAXA	15
PRAXBIND	15
Prothrombin complex concentrate	15
Rivaroxaban	15
Vitamin K	15
Warfarin	15
XARELTO	15
Atrial Fibrillation	16
COUMADIN	16
Vitamin K	16
Warfarin	16

Geri-RxFiles Atrial Fibrillation References:

- 1) O'Mahony D, O'Sullivan D, Byrne S, O'Connor MN, Ryan C, Gallagher P. **STOPP/START** criteria for potentially inappropriate prescribing in older people: version 2. Age Ageing. 2014 Oct 16.
- 2) **2019 American Geriatrics Society Beers Criteria®** Update Expert Panel. American Geriatrics Society 2019 Updated AGS Beers Criteria® for Potentially Inappropriate Medication Use in Older Adults. J Am Geriatr Soc. 2019 Jan 29. [Epub ahead of print]
- 3) The American Geriatrics Society 2012 **Beers Criteria** Update Expert Panel. American Geriatrics Society updated Beers criteria for potentially inappropriate medication use in older adults. J Am Geriatr Soc 2012;60:616-31.
- 4) PL Detail-Document, Potentially Harmful Drugs in the Elderly: Beers List. Pharmacist's Letter/Prescriber's Letter. June 2012.
- 5) PL Detail-Document, STARTing and STOPping Medications in the Elderly. Pharmacist's Letter/Prescriber's Letter. September 2011.
- 6) Andrade JG, Verma A, Mitchell LB, et al; **CCS Atrial Fibrillation Guidelines** Committee. **2018** Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. Can J Cardiol. 2018 Nov;34(11):1371-1392.
- 7) Verma A, Cairns JA, Mitchell LB, et al. **CCS Atrial Fibrillation Guidelines Committee**. 2014 focused update of the Canadian cardiovascular society (CCS) guidelines for the management of atrial fibrillation. Can J Cardiol. 2014 Oct;30(10):1114-30.
- 8) You JJ, Singer DE, et al. Antithrombotic therapy for atrial fibrillation: antithrombotic therapy and prevention of thrombosis, 9th ed: **American College of Chest Physicians** (ACCP-AT9) evidence -based clinical practice guidelines. Chest. 2012;141(2)(suppl):e531S-575S.
- 9) Camm AJ, Lip GY, De Caterina R, et al. 2012 focused update of the **ESC Guidelines** for the management of atrial fibrillation: An update of the 2010 ESC Guidelines for the management of atrial fibrillation * Developed with the special contribution of the European Heart Rhythm Association. Europace. 2012 Aug 24. ESC Updated 2012 Management of Atrial Fibrillation Guidelines.
- 10) Camm AJ, Kirchhof P, Lip GY, et al; **European Heart Rhythm Association; European Association for Cardio-Thoracic Surgery**. Guidelines for the management of atrial fibrillation: the Task Force for the Management of Atrial Fibrillation of the European Society of Cardiology (ESC). Eur Heart J. 2010;31:2369-429.
- 11) De Caterina R, Husted S, Wallentin L, et al. New oral anticoagulants in atrial fibrillation and acute coronary syndromes. **ESC Working Group on Thrombosis—Task Force on Anticoagulants in Heart Disease** position paper. J Am Coll Cardiol 2012;59:1413-25.
- 12) Jin M, Kosar L. Atrial fibrillation. RxFiles 9th ed. Saskatoon, SK: RxFiles; 2012.
- 13) Kosar L, Jin M, Kamrul R, Schuster B. Oral anticoagulation in atrial fibrillation. Balancing the risk of stroke with the risk of bleed. Can Fam Physician 2012;58:850-8.
- 14) **ACTIVE A** Investigators, Connolly SJ, Pogue J, Hart RG, et al. Effect of clopidogrel added to aspirin in patients with atrial fibrillation. N Engl J Med. 2009 May 14;360(20):2066-78.
- 15) Dumont Z, Kosar L. Warfarin tips & dosing nomograms. Saskatoon, SK: RxFiles; 2013.
- 16) Gillis AM, Verma A, Talajic M, Nattel S, et al. and the **CCS Atrial Fibrillation Guidelines** Committee. Society Guidelines Canadian Cardiovascular Society Atrial Fibrillation Guidelines 2010: Rate and Rhythm Management. Can J Cardio 2011;27:47-59.
- 17) Frankel G, Kamrul R, Kosar L, Jensen B. Rate versus rhythm control in atrial fibrillation. Can Fam Physician 2013;59:161-8.
- 18) Whitbeck MG, Charnigo RJ, Khairy P et al. Increased mortality among patients taking digoxin - analysis from the **AFFIRM** study. Eur Heart J. 2013 May;34(20):1481-8.
- 19) Weiss, B. Diagnostic Evaluation of Urinary Incontinence in Geriatric Patients. Am Fam Physician. 1998 Jun 1;57(11):2675-2684.
- 20) Giardian EG. Therapeutic use & major side effects of sotalol. UpToDate®. Accessed: http://www.uptodate.com/contents/therapeutic-use-and-major-side-effects-of-sotalol?source=search_result&search=sotalol+elderly+female&selectedTitle=1~150#H21
- 21) Additional References:

- 22) Sardar P, Chatterjee S, Chaudhari S, et al. **New oral anticoagulants in elderly** adults: evidence from a meta-analysis of randomized trials. *J Am Geriatr Soc.* 2014 May;62(5):857-64.
- 23) Banerjee S, Picheca L. CHAD65 and CHA2DS2-VASc risk stratification tools for patients with atrial fibrillation: a review of clinical effectiveness and guidelines. Ottawa: CADTH; 2017, May.
- 24) Macle L, Cairns J, Andrade J, et al; CCS Atrial Fibrillation Guidelines Committee. The 2014 Atrial Fibrillation Guidelines Companion: A Practical Approach to the Use of the Canadian Cardiovascular Society Guidelines. *Can J Cardiol.* 2015 Oct; 31(10):1207-18.
- 25) Verma A, Cairns JA, Mitchell LB, et al; CCS Atrial Fibrillation Guidelines Committee. 2014 focused update of the Canadian Cardiovascular Society Guidelines for the management of atrial fibrillation. *Can J Cardiol.* 2014 Oct;30(10):1114-30.
- 26) Macle L, Cairns J, Leblanc K, et al; CCS Atrial Fibrillation Guidelines Committee. 2016 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation. *Can J Cardiol.* 2016 Oct;32(10):1170-1185.
- 27) Giugliano RP, Ruff CT, Braunwald E, et al; ENGAGE AF-TIMI 48 Investigators. Edoxaban versus warfarin in patients with atrial fibrillation. *N Engl J Med.* 2013 Nov 28;369(22):2093-104.
- 28) Andrade JG, Aguilar M, Atzema C, Bell A, Cairns JA, Cheung CC, Cox JL, Dorian P, Gladstone DJ, Healey JS, Khairy P. **The 2020 Canadian Cardiovascular Society/Canadian Heart Rhythm Society** comprehensive guidelines for the management of atrial fibrillation. *Canadian Journal of Cardiology.* 2020 Dec 1;36(12):1847-948.
- 29) Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, Deswal A, Eckhardt LL, Goldberger ZD, Gopinathannair R, Gorenek B. **2023 ACC/AHA/ACCP/HRS guideline for the diagnosis and management of atrial fibrillation:** a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice Guidelines. *Circulation.* 2024 Jan 2;149(1):e1-56.
- 30) ESC Scientific Document Group. **2020 ESC Guidelines for the diagnosis and management of atrial fibrillation** developed in collaboration with the European Association of Cardio-Thoracic Surgery (EACTS). *European Heart Journal.* 2020 Aug 29.
- 31) January CT, Wann LS, Calkins H, Chen LY, Cigarroa JE, Cleveland JC Jr, Ellinor PT, Ezekowitz MD, Field ME, Furie KL, Heidenreich PA, Murray KT, Shea JB, Tracy CM, Yancy CW. 2019 AHA/ACC/HRS focused update of the 2014 AHA/ACC/HRS guideline for the management of patients with atrial fibrillation: a report of the American College of Cardiology Foundation/ American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society. *J Am Coll Cardiol* 2019;
- 32) Steinberg, B.A., Greiner, M.A., Hammill, B.G., Curtis, L.H., Benjamin, E.J., Heckbert, S.R. and Piccini, J.P. (2015), Contraindications to Anticoagulation Therapy and Eligibility for Novel Anticoagulants in Older Patients with Atrial Fibrillation. *Cardiovasc Ther*, 33: 177-183. <https://doi.org/10.1111/1755-5922.12129>
- 33) Ekerstad N, Karlsson T, Söderqvist S, Karlson BW. Hospitalized frail elderly patients – atrial fibrillation, anticoagulation and 12 months’ outcomes. *Clin Interv Aging.* 2018;13:749-756 <https://doi.org/10.2147/CIA.S159373>
- 34) Douros A, Durand M, Doyle CM, Yoon S, Reynier P, Filion KB. Comparative Effectiveness and Safety of Direct Oral Anticoagulants in Patients with Atrial Fibrillation: A Systematic Review and Meta-Analysis of Observational Studies. *Drug Saf.* 2019 Oct;42(10):1135-1148. doi: 10.1007/s40264-019-00842-1. PMID: 31175610.
- 35) Connolly SJ, Eikelboom J, Joyner C, Diener HC, Hart R, Golitsyn S, Flaker G, Avezum A, Hohnloser SH, Diaz R, Talajic M. Apixaban in patients with atrial fibrillation. *New England Journal of Medicine.* 2011 Mar 3;364(9):806-17.
- 36) Joosten LP, van Doorn S, van de Ven PM, Köhler BT, Nierman MC, Koek HL, Hemels ME, Huisman MV, Kruip M, Faber LM, Wiersma NM. 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. *Circulation.* 2024 Jan 23;149(4):279-89.
- 37) **2023 American Geriatrics Society Beers Criteria® Update Expert Panel.** American Geriatrics Society 2023 updated AGS Beers Criteria® for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society.* 2023

- 38) O'Mahony D, Cherubini A, Guiteras AR, Denkinger M, Beuscart JB, Onder G, Gudmundsson A, Cruz-Jentoft AJ, Knol W, Bahat G, van der Velde N. **STOPP/START criteria** for potentially inappropriate prescribing in older people: version 3. *European Geriatric Medicine*. **2023** Aug;14(4):625-32.
- 39) Okumura K, Akao M, Yoshida T, et al. Low-dose edoxaban in very elderly patients with atrial fibrillation. *N Engl J Med* 2020;383:1735-45.
- 40) Lau WC, Torre CO, Man KK, Stewart HM, Seager S, Van Zandt M, Reich C, Li J, Brewster J, Lip GY, Hingorani AD. Comparative effectiveness and safety between apixaban, dabigatran, edoxaban, and rivaroxaban among patients with atrial fibrillation: a multinational population-based cohort study. *Annals of Internal Medicine*. 2022 Nov;175(11):1515-24.