

# Oral Anticoagulation 102: Identifying and Managing Risks



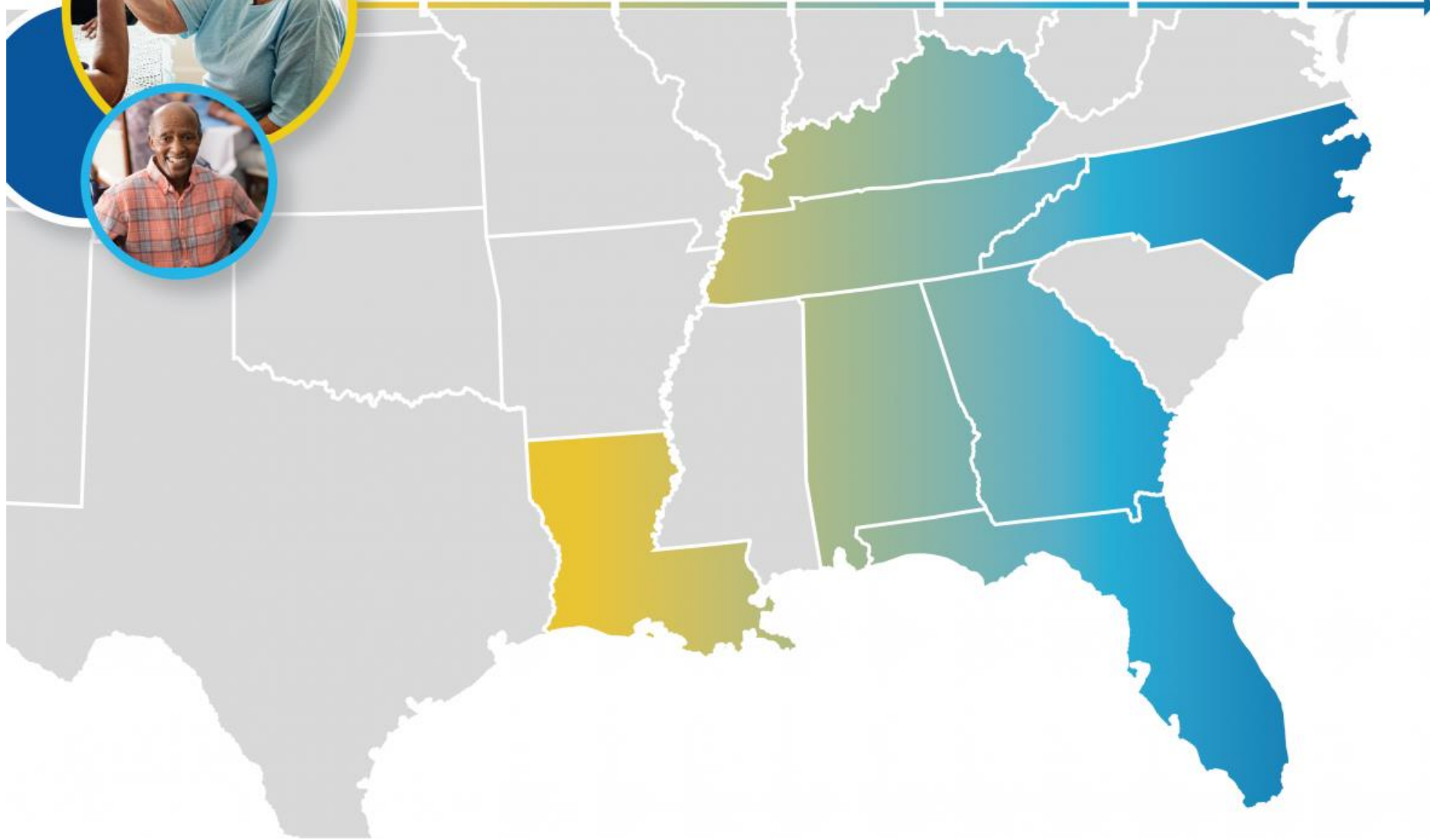
**Presented by:**  
Emily Persson, Pharm.D.

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# Objectives

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- Recall common indications for anticoagulation
- Recognize common drug-drug interactions with oral anticoagulants and the associated risks
- Identify ways to mitigate bleeding risk with oral anticoagulants
- Assess patient scenarios to identify medication-related problems in individuals taking oral anticoagulants

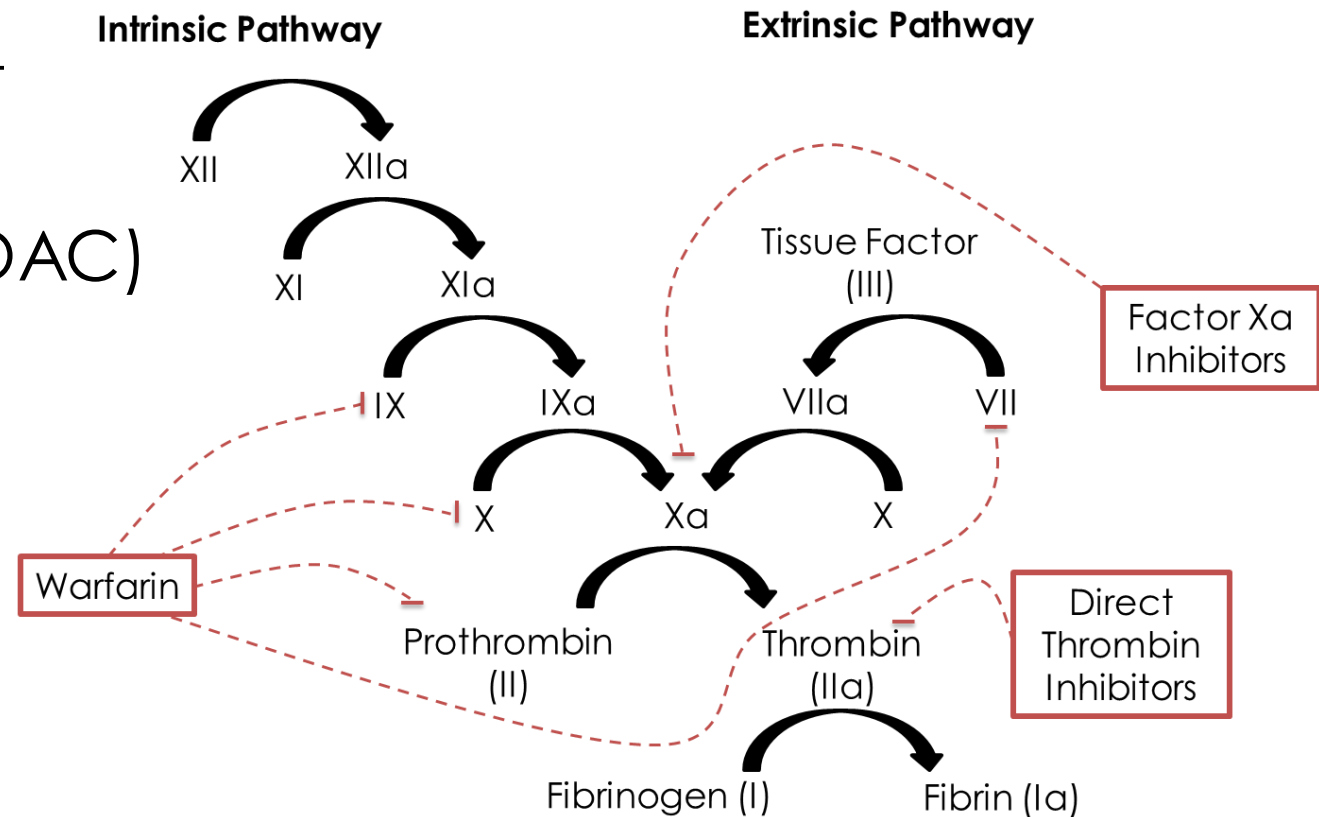
**The content in this presentation was current as of April 17, 2024.**

# Common Oral Anticoagulation Medications (OAC)

- Vitamin K antagonist (VKA):
  - Warfarin

## Direct oral anticoagulants (DOAC)

- Factor Xa inhibitors:
  - Apixaban (Eliquis®)
  - Rivaroxaban (Xarelto®)
  - Edoxaban (Savaysa®)
- Direct thrombin inhibitor:
  - Dabigatran (Pradaxa®)

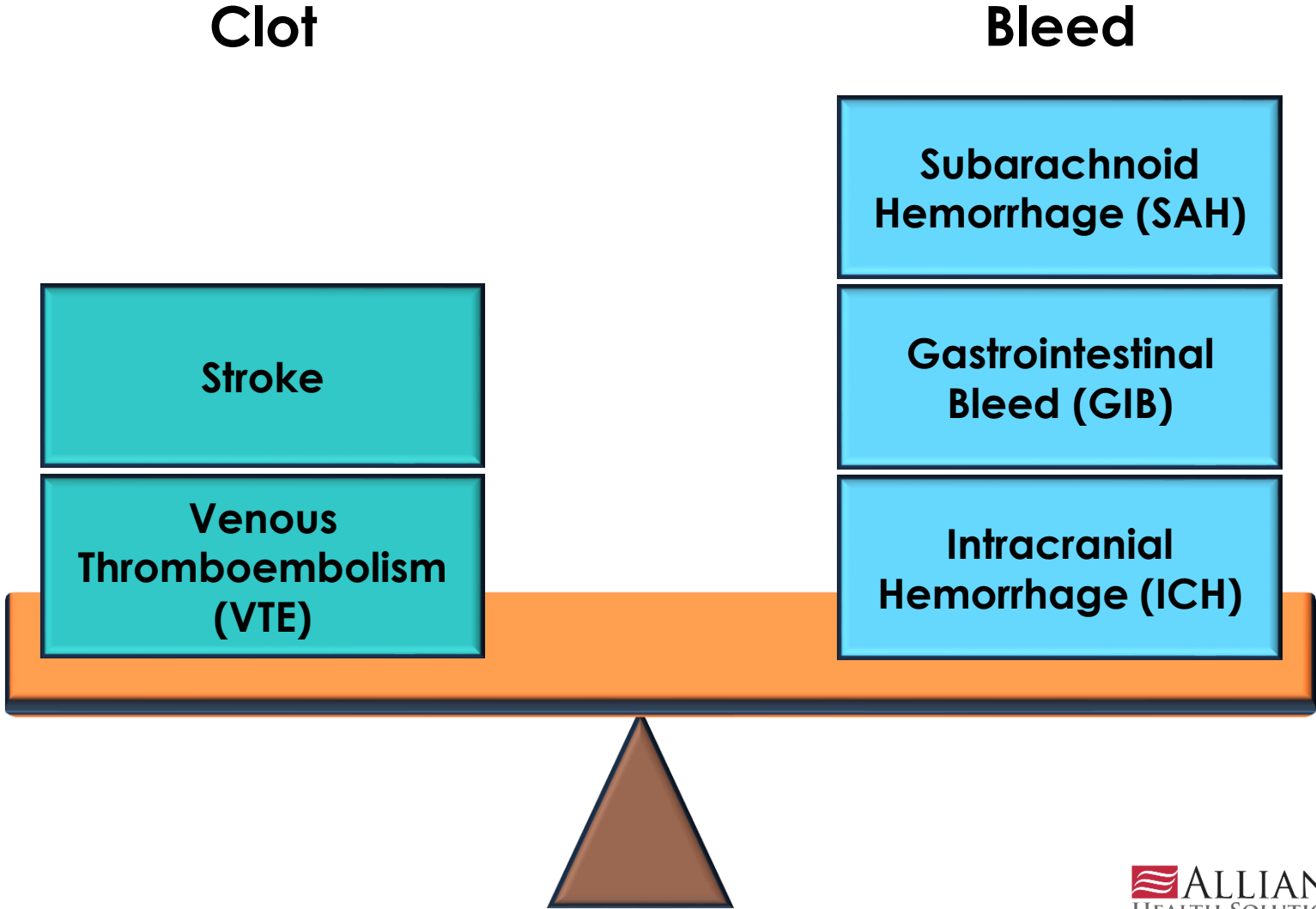


# Common Indications for OAC

Class	Drug	CAD/ ASCVD	Stroke (treatment & prevention)	VTE (treatment = X Prevention= #)
Vitamin K Antagonist	Warfarin		X	X/ #
Factor Xa Inhibitors	Apixaban		X	X/ #
	Rivaroxaban	X	X	X/ #
	Edoxaban		X	X
Direct Thrombin Inhibitor	Dabigatran		X	X/ #

Adapted from: Cabral K. Overview of Antithrombotic Therapeutics. Presentation at ACPHS, 2020.

# Clotting Versus Bleeding Risk





# Warfarin

# Warfarin: Box Warning

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## Box Warning:

Warfarin can cause major or fatal bleeding. Perform regular monitoring of international normalized ratio (INR) on all treated patients. Drugs, dietary changes, and other factors affect INR levels achieved with warfarin therapy. Instruct patients about prevention measures to minimize the risk of bleeding and to report immediately to their health care provider signs and symptoms of bleeding.

## Blood testing methods

- PT
- INR
- PTT

# INR Goal

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- Varies based on indication, patient history, and characteristics
- Dose of warfarin may be adjusted based on INR result
- For VTE and stroke prevention in atrial fibrillation:



INR can be affected by age, race/ethnicity, disease states, acute illnesses, diet and medications

# Warfarin: Diet Interactions

## Vitamin K-containing foods

- Brussel sprouts
- Collard greens
- Spinach
- Kale
- Parsley
- Broccoli
- Cabbage
- Liver
- Mayonnaise
- Oils

**Large portions over short periods of time may reduce anticoagulant effects**



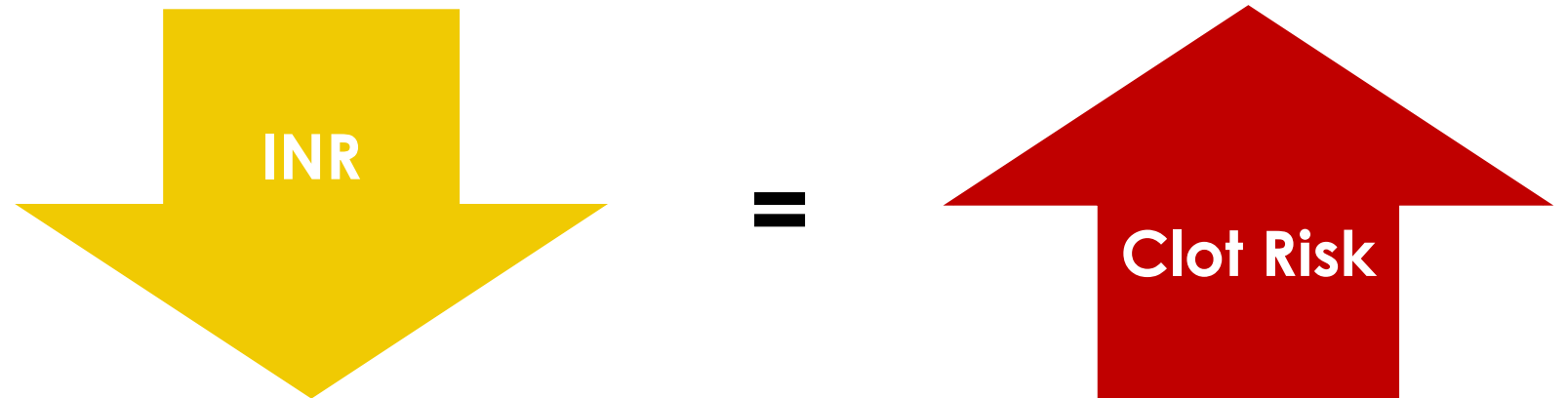
**Encourage consistent vitamin K intake**

# Warfarin: Drug Interactions – Decreases INR

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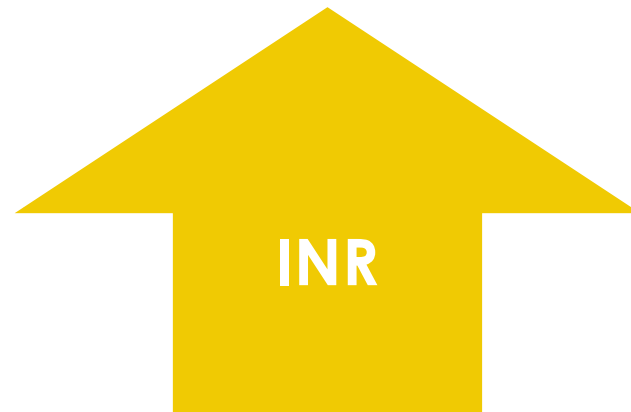
- Carbamazepine
- Phenytoin
- Rifampin
- Trazodone

- Sucralfate
- Cholestyramine



# Warfarin: Drug Interactions – Increases INR

- Anti-infective agents
  - Sulfamethoxazole/  
trimethoprim (Bactrim)
  - Metronidazole
  - Fluconazole
  - Fluoroquinolones
    - Ciprofloxacin
  - Macrolides
    - Erythromycin
    - Azithromycin
- Acetaminophen
- Alcohol
- Amiodarone
- Cimetidine
- Thyroid hormone



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# Warfarin: Drug Interactions – Neutral Effect on INR

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Some medications can increase the risk of bleeding without changing INR.

This is due to the synergistic effect of the medications together.

- COX-2 inhibitors (celecoxib)
- NSAIDS (ibuprofen, naproxen, indomethacin, ketorolac)
- Antiplatelets

# Warfarin: Monitoring – Efficacy and Adverse Events

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Frequent monitoring required

INR:

- Monitored at baseline and then about every few days (1-3)
- Once the dose is established and stable, can monitor less frequently
- If unstable or clinical changes, monitor more frequently
- At every INR draw, ask about
  - Adherence
  - Changes to medications
  - Changes to diet

Bleeding

- CBC (baseline and when warranted)



# Managing Elevated INR – Warfarin Reversal

Bleeding Status	INR	Reversal Strategy
Without bleeding	INR < 4.5	Lower or omit dose; monitor more frequently & resume warfarin at lower dose when INR therapeutic
	INR > 4.5 to ≤ 10	Omit next 1-2 doses; monitor more frequently. <b>OR</b> Omit dose & give <u>vitamin K (1-2.5 mg orally)</u> – low risk of thromboembolism and greater risk of bleeding  Resume an adjusted dose when INR in therapeutic range.
	INR > 10	Hold warfarin therapy & give a higher dose of <u>vitamin K (2.5-5 mg orally)</u> Monitor in 24-48 hours & administer more vitamin K if necessary.  Resume an adjusted dose when INR therapeutic.
Significant bleeding	Any elevation of INR	Hold warfarin & give <u>vitamin K (10 mg IV)</u> supplemented w/ <u>fresh frozen plasma (FFP)</u> or <u>4-factor prothrombin complex concentrate (PCC)</u> . Can repeat vitamin K in 12 hours.
Life-threatening bleeding		

# DOACs

# Box Warnings: DOACs

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Apixaban & rivaroxaban & dabigatran

- Premature discontinuation increases the risk of thrombotic events
- Spinal/Epidural hematomas

Edoxaban

- Same as above
- Reduced efficacy in nonvalvular atrial fibrillation patients with CrCl > 95mL/minute

# DOACs: Monitoring

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Routine coagulation testing is **not** required or necessary for DOACs. No FDA-approved assays or calibration reagents are currently available.

Labs (baseline and when clinically indicated)

- CBC
- Serum creatinine
- Liver function tests

# DOAC Dose Adjustments – Atrial Fibrillation

Class	Direct Thrombin Inhibitor	Factor Xa Inhibitor		
Name	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Renal dosing adjustments based on actual body weight	<b>CrCl &gt; 30 mL/min</b> 150 mg twice daily	<b>CrCl &gt; 50 mL/min</b> 20 mg daily with food	5 mg twice daily	<b>CrCl &gt; 95 mL/min</b> Avoid use
	<b>CrCl 51 - 95 mL/min</b> 60 mg daily			
	<b>CrCl 15-30 mL/min</b> 75 mg twice daily	<b>CrCl 15-50 mL/min</b> 15 mg daily with food	<b>If 2 of the following:</b> <b>age ≥80 y</b> <b>weight ≤60 kg</b> <b>SCr ≥1.5 mg/dL</b> 2.5 mg twice daily	<b>CrCl 15-50 mL/min</b> 30 mg daily
				<b>CrCl &lt; 15 mL/min</b> Avoid use

# DOAC Use in Special Populations

Class	Direct Thrombin Inhibitor	Factor Xa Inhibitors		
Name	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
<b>Dialysis</b>	Contraindicated	May be used in atrial fibrillation but not recommended for other indications	Follow dosing recommendation from previous slide for atrial	Avoid use
<b>Liver Function</b>				
Child-Pugh A	No dose adjustment needed			
Child-Pugh B	Use with caution	Avoid use	Use with caution	Use with caution
Child-Pugh C	Avoid use	Avoid use	Avoid Use	Avoid Use
<b>Obesity</b>	Patient weight > 120 kg or BMI ≥ 40 kg/m <sup>2</sup> : use other anticoagulants	No dose adjustments necessary	No dose adjustments necessary	Patient weight > 120 kg or BMI ≥ 40 kg/m <sup>2</sup> : use other anticoagulants Bariatric and other GI surgery patients: evaluate risk vs benefit
<b>Elderly</b>	Age ≥ 75 y: Use with extreme caution or consider other treatment options (increased risk of GIB)	Avoid* long-term treatment of VTE or atrial fibrillation; safer alternatives preferred	Preferred agent in elderly	Consider dose reduction in patients age ≥ 80 or body weight ≤ 60 kg plus risk factors

# DOAC: Drug Interactions

Class	Medication	Interactions	Effect
Oral factor Xa inhibitors	Apixaban	<ul style="list-style-type: none"> <li>Strong P-gp inhibitors and inducers</li> <li>CYP3A4 inhibitors and inducers</li> </ul>	<ul style="list-style-type: none"> <li>Dual CYP3A4 and P-gp inhibitors can increase effect</li> <li>CYP3A4 inducers and/or P-gp inhibitors can decrease effect</li> </ul>
	Rivaroxaban	<ul style="list-style-type: none"> <li>Strong P-gp inhibitors and inducers</li> <li>CYP3A4 inhibitors and inducers</li> </ul>	
	Edoxaban	<ul style="list-style-type: none"> <li>Strong P-gp inhibitors and inducers</li> </ul>	<ul style="list-style-type: none"> <li>P-gp inhibitors increase effect</li> <li>P-gp inducers decrease effect</li> </ul>
Direct thrombin inhibitor	Dabigatran	<ul style="list-style-type: none"> <li>Strong P-gp inhibitors and inducers</li> </ul>	

# DOAC: Drug Interactions – P-gp and CYP3A4

Class	Effect	Interactions	
P-gp	Inhibitors	<ul style="list-style-type: none"> <li>• Amiodarone</li> <li>• Clarithromycin</li> <li>• Cyclosporine</li> <li>• Erythromycin</li> <li>• Ticagrelor</li> </ul>	<ul style="list-style-type: none"> <li>• Itraconazole</li> <li>• Ketoconazole</li> <li>• Nicardipine</li> <li>• Ritonavir</li> <li>• Tacrolimus</li> </ul>
	Inducers	<ul style="list-style-type: none"> <li>• Carbamazepine</li> <li>• Dexamethasone</li> <li>• Phenytoin</li> <li>• Fosphenytoin</li> </ul>	<ul style="list-style-type: none"> <li>• Phenobarbital</li> <li>• Rifampin</li> <li>• St. John's Wort</li> </ul>
CYP3A4	Inhibitors	<ul style="list-style-type: none"> <li>• Clarithromycin</li> <li>• Erythromycin</li> <li>• Itraconazole</li> <li>• Diltiazem</li> </ul>	<ul style="list-style-type: none"> <li>• Cobicistat</li> <li>• Nefazodone</li> <li>• Ritonavir</li> <li>• Voriconazole</li> </ul>
	Inducers	<ul style="list-style-type: none"> <li>• Carbamazepine</li> <li>• Fosphenytoin</li> <li>• Phenobarbital</li> </ul>	<ul style="list-style-type: none"> <li>• Phenytoin</li> <li>• Rifampin</li> <li>• Primidone</li> </ul>



# Managing DOAC Bleeding

Agent	Reversal Strategy
Oral factor Xa inhibitors <ul style="list-style-type: none"><li>• Apixaban</li><li>• Rivaroxaban</li><li>• Edoxaban</li></ul>	<ul style="list-style-type: none"><li>• Andexanet alfa (AndexXa)</li></ul> OR <ul style="list-style-type: none"><li>• 4-factor PCC (Kcentra, Balfaxar)</li></ul>
Direct thrombin inhibitor <ul style="list-style-type: none"><li>• Dabigatran</li></ul>	<ul style="list-style-type: none"><li>• Idarucizumab (Praxbind)</li></ul> OR <ul style="list-style-type: none"><li>• 4-factor PCC (Kcentra, Balfaxar)</li></ul> Dialyzable

## Andexanet alfa boxed warning

- Thromboembolic risks, ischemic risks, cardiac arrest and sudden death

## 4-factor PCC boxed warning

- Arterial and venous thromboembolic complications

No boxed warning for idarucizumab

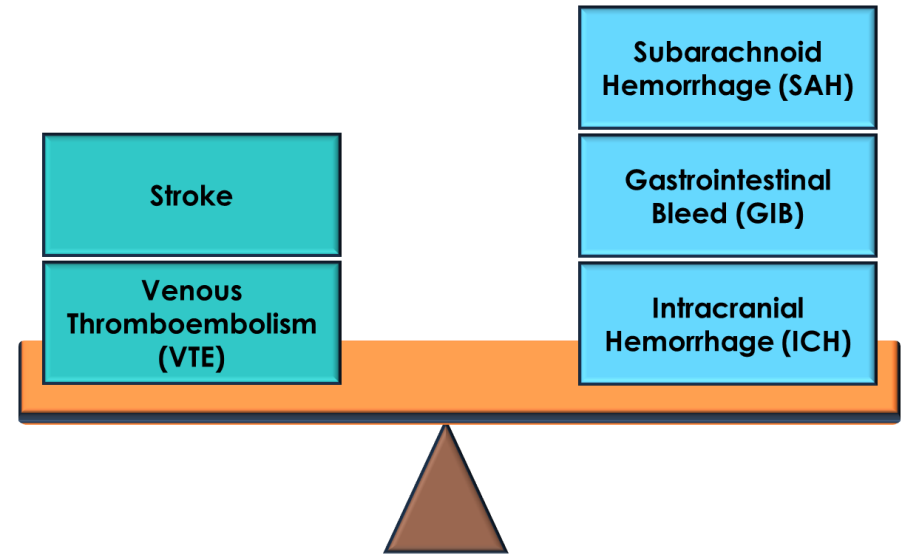
# Bleeding Risk

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- ISMP considers all anticoagulants as high-risk medications
- The Beers Criteria for potentially inappropriate medication use in older adults recommends the use of direct oral anticoagulants (calling out apixaban or dabigatran specifically) instead of rivaroxaban.
- Signs of bleeding due to anticoagulation:
  - Bruising
  - Blood in stool/urine
  - Coughing or vomiting up blood

# Mitigating Bleeding Risk

- Electric razors
- Non-slip socks/shoes
- Assisting patients with mobility issues
- Appropriate dosing
- Managing drug-drug interactions
- Periprocedural management
  - **When to stop** – based on the pharmacokinetics of the medications prior to the procedure
    - DOACs – usually two to three days prior to the procedure
    - Warfarin – varies; maybe five to six days prior to the procedure or based on INR
  - **When to start again** – based on the bleeding risk of the surgery
  - Appropriate use of bridging if necessary



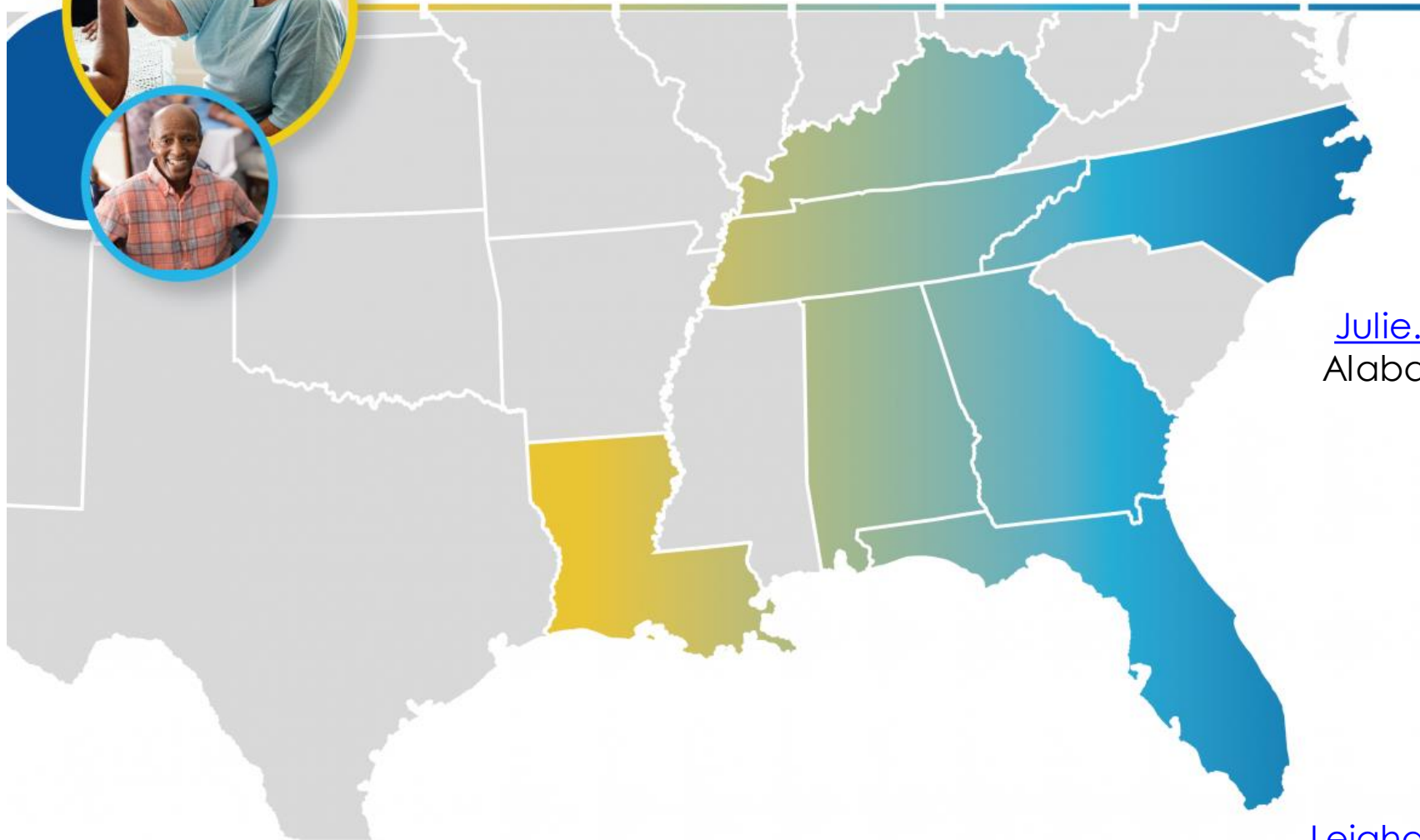
# Resources

- Warfarin. In: Lexi-drugs online [database on the Internet]. Waltham (MA): UpToDate Inc.; 2024 [updated 30 Apr 2024; cited 30 Apr 2024]. Available from: <http://online.lexi.com>. Subscription required to view.
- Apixaban. In: Lexi-drugs online [database on the Internet]. Waltham (MA): UpToDate Inc.; 2024 [updated 17 Apr 2024; cited 30 Apr 2024]. Available from: <http://online.lexi.com>. Subscription required to view.
- Rivaroxaban. In: Lexi-drugs online [database on the Internet]. Waltham (MA): UpToDate Inc.; 2024 [updated 24 Apr 2024; cited 30 Apr 2024]. Available from: <http://online.lexi.com>. Subscription required to view.
- Edoxaban. In: Lexi-drugs online [database on the Internet]. Waltham (MA): UpToDate Inc.; 2024 [updated 15 Apr 2024; cited 30 Apr 2024]. Available from: <http://online.lexi.com>. Subscription required to view.
- Dabigatran. In: Lexi-drugs online [database on the Internet]. Waltham (MA): UpToDate Inc.; 2024 [updated 24 Apr 2024; cited 30 Apr 2024]. Available from: <http://online.lexi.com>. Subscription required to view.
- Adexanet Alpha (Coagulation Factor Xa [Recombinant], Inactivated). In: Lexi-drugs online [database on the Internet]. Waltham (MA): UpToDate Inc.; 2024 [updated 24 Apr 2024; cited 30 Apr 2024]. Available from: <http://online.lexi.com>. Subscription required to view.
- Prothrombin Complex Concentrate (Human). In: Lexi-drugs online [database on the Internet]. Waltham (MA): UpToDate Inc.; 2024 [updated 4 Apr 2024; cited 30 Apr 2024]. Available from: <http://online.lexi.com>. Subscription required to view.
- Arnold M. J. (2024). Beers Criteria for Inappropriate Medication Use in Older Adults: Update From the American Geriatrics Society. *American family physician*, 109(4), 374–375.
- Hirsh J. (1998). Reversal of the anticoagulant effects of warfarin by vitamin K1. *Chest*, 114(6), 1505–1508. <https://doi.org/10.1378/chest.114.6.1505>

**Questions?**



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