Practitioners' Guide for Improving Oral Anticoagulant Use

Welcome to Practitioners' Guide for Improving Oral Anticoagulant Use.

Learning Objectives

The learning objectives for this course are:

- Discuss the prevalence and types of adverse drug events related to oral anticoagulants.
- Review the drug classifications of oral anticoagulants.
- Compare characteristics of oral vitamin K antagonists and direct acting oral anticoagulants.
- Identify pathophysiological states for utilization of oral anticoagulation therapy.
- Review barriers to proper oral anticoagulant use.
- List steps that clinicians can take to reduce the risk of adverse drug events from oral anticoagulants.

For your convenience, all clinician tools and references can be located and downloaded from the "Handouts and Resources" section of the course launch page.

Acronyms and Abbreviations

Here you'll find some of the acronyms and abbreviations that will be used throughout this course.

Acronym/Abbreviation	Full Term
AFib	atrial fibrillation
ADE	adverse drug event
CBC	complete blood count
DOAC	direct acting oral anticoagulant
DVT	deep vein thrombosis
ED	emergency department
FFP	fresh frozen plasma
GI	gastrointestinal
INR	international normalized ratio
PCC	prothrombin complex concentrate
PE	pulmonary embolism
PST	patient self-testing
PT	prothrombin time
SDM	shared decision-making
SNF	skilled nursing facility
VTE	venous thromboembolism

Background

First, let's discuss some background on oral anticoagulants.

Why the Focus on Oral Anticoagulants?

So, why is it important to focus on the proper use of oral anticoagulants? There is a high prevalence of oral anticoagulants being prescribed. Some examples of oral anticoagulants are warfarin, dabigatran, rivaroxaban, edoxaban, apixaban, and betrixaban. But oral anticoagulants are underused in at-risk patients. Despite the fact that oral anticoagulants can be efficacious for stroke prevention in patients with atrial fibrillation, or AFib, less than 60% of AFib patients at high-risk for stroke are treated with oral anticoagulants. Providers may have trouble identifying situations in which oral anticoagulation therapy outweighs the bleeding risk associated with these drugs. Improper use of oral anticoagulants can be harmful. There are misconceptions about the proper use and burdens associated with anticoagulant use. For example, many providers are unaware that patient self-testing options are available for

warfarin international normalized ratio (or INR) monitoring. And lastly, there's a high number of emergency department visits resulting from anticoagulant adverse drug events.

What Is an Adverse Drug Event (ADE)?

What is an adverse drug event, or ADE? An adverse drug event is an injury resulting from medical intervention related to a drug. This includes medication errors, adverse drug reactions including drug therapeutic failure, allergic reactions, and overdoses. Drug therapeutic failure could be considered as an adverse drug reaction in which the expected drug effects do not occur following a prescribed pharmacological treatment, including any clinical event that could be related to a low prescribed dose or lack of compliance.

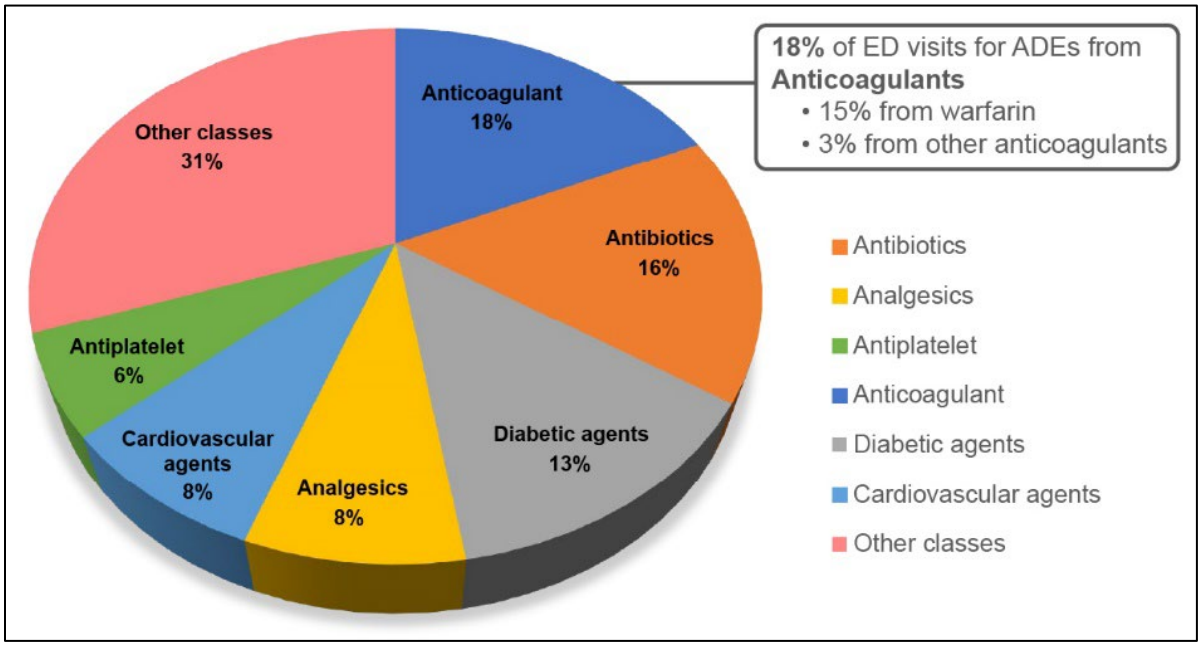
Outpatient Adverse Drug Event Results 2013-2014

From 2013 to 2014, outpatient ADEs in the United States resulted in 3.5 million physician office visits. The prevalence of emergency department visits for ADEs was 1.3 million, which translates to four per 1000 individuals. And, of those 1.3 million ED visits, 27 percent, or a total of 350,000, resulted in a hospitalization. More current data reveal slightly higher numbers in all three categories, but the data have not yet been published.

ED Visits for ADEs by Medication Class

Looking at all emergency department visits related to adverse drug events, 18% were related to anticoagulants.

Of the 18%, warfarin accounted for the largest portion with 15%.



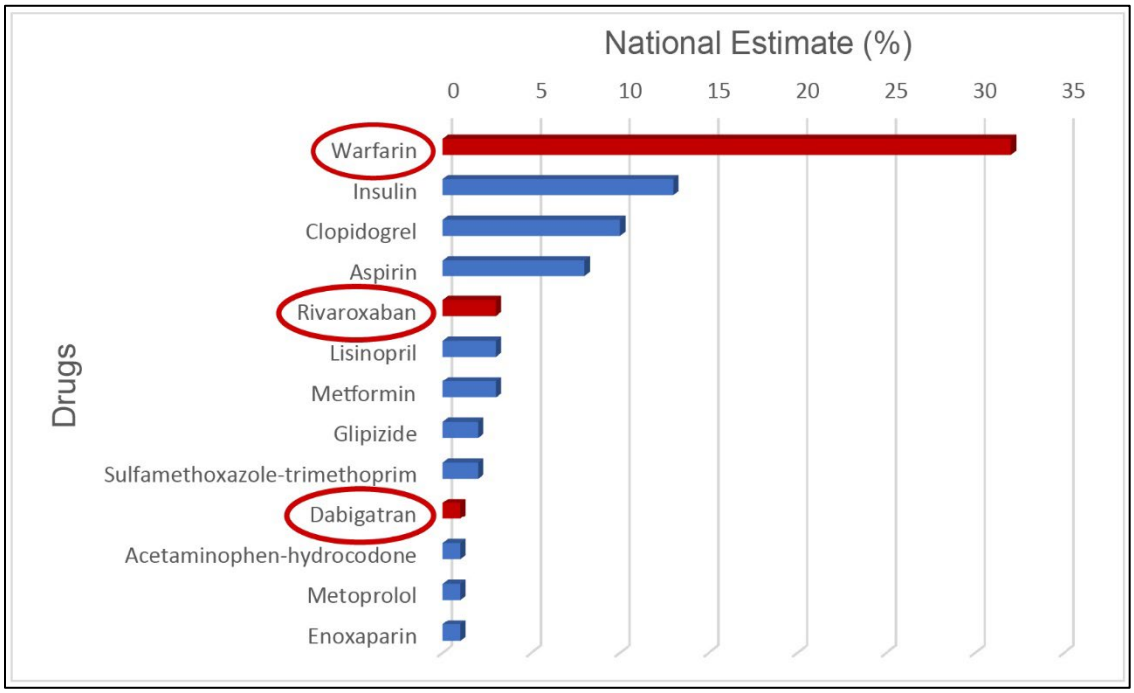
Alt Text: Pie chart representing ED visits for ADEs by medication class. 18% Anticoagulant. 16% Antibiotics. 13% Diabetic agents. 8% Analgesics. 8% Cardiovascular agents. 6% Antiplatelet. 31% Other classes.

ADE ED Visits in Adults ≥ 65 years, 2013-2014

In adults 65 years and older, warfarin was the most commonly implicated drug causing 32% of all ED visits due to ADEs.

Rivaroxaban was fifth, and dabigatran was tenth.

Anticoagulant-related ADEs are also common in skilled nursing facilities and rehabilitation hospitals.



Alt Text: Bar graph for ADE Visits in Adults ≥ 65 years, 2013-2014. Drugs on y axis, National Estimate percentage on x axis. Warfarin caused 32% of ED visits. Insulin, approx. 13%, Clopidogrel, approx. 9%, Aspirin, approx. 7%, Rivaroxaban, approx. 3%, Glipizide and Sulfamethoxazole-trimethoprim, approx. 2%, Dabigatran, Acetaminophen-hydrocodone, Metoprolol and Enoxaparin approx. 1-2%.

What Is the Most Common ADE Due to an Anticoagulant in the ED?

What is the most common ADE due to an anticoagulant in the emergency department, or ED? The most commonly seen ADE in the emergency department from anticoagulants were hemorrhages – about 80%. The most common hemorrhage was gastrointestinal, followed by skin and wound, epistaxis or nose bleed, genitourinary, central nervous system, and pulmonary hemorrhages. The most common type of ADE in hospitalized Medicare patients was excessive bleeding due to anticoagulants. Excessive bleeding related to anticoagulants is also the most common cause of death from adverse events in hospitalized Medicare patients. Excessive bleeding is the second most common type of ADE in skilled nursing facility residents and in rehabilitation hospitals.

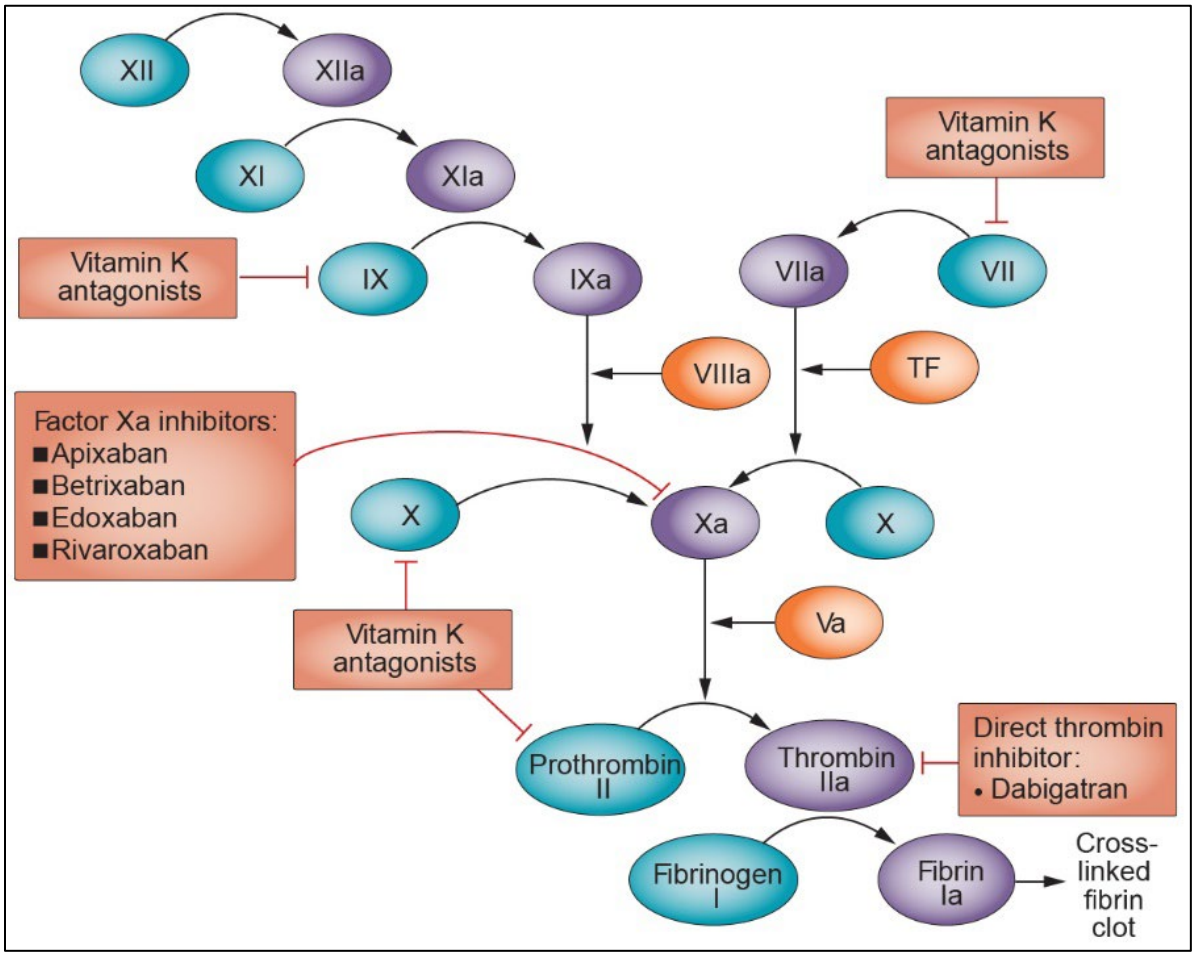
Adverse Event Manifestation	No. of Cases	National Estimate, % (95% CI)
Hemorrhage	5101	79.4 (75.2-83.6)
Central nervous system[d]	262	2.8 (1.4-4.2)
Pulmonary	149	2.3 (1.7-3.0)
Gastrointestinal	1577	27.0 (21.0-32.9)
Genitourinary	547	9.5 (6.6-12.4)
Epistaxis	815	15.0 (11.7-18.3)
Skin, wound, or other minor	1418	18.8 (13.2-24.4)
Other hemorrhage types	333	4.1 (2.5-5.6)

Drug Classifications of Oral Anticoagulants: DOACs and Vitamin K Antagonists

Now that we're aware of the prevalence and severity of ADEs associated with anticoagulants, let's look at the different drugs in this class and how they differ from one another. In this part of the course, we'll identify the different oral anticoagulants, we'll learn how they interact with the coagulation cascade, and we'll compare the characteristics of the different drugs.

Direct Acting Oral Anticoagulants (DOACs) and Vitamin K Antagonists

Here we have a graphic of the coagulation cascade and the specific targets acted upon by the oral anticoagulants. Let's begin with the direct acting oral anticoagulants, or the DOACs, first. Dabigatran directly inhibits thrombin or factor IIa. Apixaban, betrixaban, edoxaban, and rivaroxaban all inhibit factor Xa. Vitamin K antagonists, such as warfarin, inhibit factors II, VII, IX, and X. Currently warfarin is the only oral vitamin K antagonist available in the United States.



Alt Text: Coagulation Cascade and specific targets acted upon by oral anticoagulants. Factors XII impacts XIIa. Factors XI impacts Xia. Vitamin K antagonists: Factors IX impact IXa, VIIIa. Vitamin K antagonists: Factor VII impacts VIIa. Thrombin Factor (TF) impact VIIa. Factor Xa inhibitors: Apixaban, Betrixaban, Edoxaban, Rivaroxaban: X impacts Xa. Vitamin K Antagonists: X and Prothombin III impacts Thrombin IIa. Direct thrombin inhibitor: Dabigatran. Fibrongen I impacts Fibrin Ia which is cross-linked with fibrin clot

The "Ideal" Oral Anticoagulant

If there was an ideal oral anticoagulant, it may have characteristics like the ones listed here. Other desirable characteristics would be a quick onset and no bleeding risk.

- Once daily dosing
- Minimal monitoring required
- Reversal agent available
- Wide therapeutic index
- Low cost
- Easy dose adjustments for renal function and age

Indications for Oral Anticoagulation

The FDA-approved indications for oral anticoagulants include treatment of existing thrombosis such as acute venous thromboembolism, or VTE. Primary prevention of thrombosis includes AFib with an increased risk of stroke, mechanical heart valves, and extended VTE prophylaxis following major orthopedic surgeries. Warfarin is the only oral anticoagulant labeled for thromboembolic prophylaxis in patients with a mechanical heart valve. Secondary prevention includes a history of VTE for which the benefits outweigh the risks, patients with both AFib and a history of cardioembolic stroke, and reduction in the risk of death, recurrent myocardial infarction, and thromboembolic events such as stroke or systemic embolization after myocardial infarction. The most recent indication is a reduction in the risk of major cardiovascular events in patients with coronary artery disease and peripheral artery disease.

VA and NIH Recommendations

The Department of Veterans Affairs, or VA, and the National Institutes of Health, or NIH, among other institutions and professional organizations provide clinicians with recommendations for baseline and on-going laboratory testing, whenever a patient is started on an oral anticoagulant.

Clinical Lab Recommendations Prior to and During Oral Anticoagulant Therapy

Here are the recommended lab tests that should be performed for both warfarin and the DOACs. For warfarin, tests should include a complete blood count, or CBC, prothrombin time, or PT, and international normalized ratio, or INR. It is recommended that the INR be measured at the clinic initially rather than have the patient self-test his or her INR. For DOACs, tests should include a CBC, serum creatinine to assess renal function, and liver function tests if there is a history or risk of hepatic insufficiency. Additional testing, such as a baseline full coagulation panel, may be indicated for both warfarin and the DOACs based on the patient's clinical situation.

Warfarin	DOACs
• CBC (complete blood count) • PT (prothrombin time) • INR (international normalized ratio) *NOTE: Initial INR should not be performed using patient self-testing (PST) devices.*	• CBC • Serum creatinine • Liver function tests (if history or risk of hepatic insufficiency)

CHA2DS2-VASc

Before we compare the characteristics of the different oral anticoagulants, we must first understand two important assessments related to stroke and bleeding risk. The first scoring assessment, called the CHA2DS2-VASC, is used to understand the patient risk factors that would necessitate stroke prevention with an anticoagulant in patients with atrial fibrillation. Points are assigned to each clinical characteristic and added up for a total score. The far-right column gives you a predicted unadjusted stroke rate, percent per year, for each risk factor. The higher the total score, the higher the risk of stroke in that patient. An interpretation of the CHA2DS2-VASC score is as follows: A male patient with a score of zero or a female patient with a score of one, does not require aspirin or an oral anticoagulant. A patient with a score of one or higher (non-gender related) has a higher risk of stroke and should be started on aspirin or an oral anticoagulant. A patient with a score of two or greater should be started on aspirin or an oral anticoagulant because their risk for stroke is high.

Risk	Points
Congestive Heart Failure (CHF) or Left ventricular ejection fraction (LVEF) < 40%	1
Hypertension	1
Age > 75 years	2
Diabetes	1
Stroke/Transient ischemic attack (TIA)/ Thromboembolism	2
Vascular disease	1
Age 65-74 years	1
Female	1

CHA2DS2-VASc Score	Unadjusted Ischemic Stroke Rate (% / year)
0	0.2
1	0.6
2	2.2
3	3.2
4	4.8
5	7.2
6	9.7
7	11.2
8	10.8
9	12.2

HAS-BLED

Letter	Clinical Characteristic	Points
H	Hypertension (> 160mm Hg systolic)	**1**
A	Abnormal Liver or Renal Function (one point for each)	**1 or 2**
S	Stroke (previous history)	**1**
B	Bleeding (history of predisposition)	**1**
L	Labile INR (time in therapeutic range < 60%)	**1**
E	Elderly (age > 65 years)	**1**
D	Drugs or Alcohol (1 point for each) (one point for antiplatelet or nonsteroidal anti-inflammatory drugs and one point for alcohol excess)	**1 or 2**

Maximum Score: 9

The second assessment is called HAS-BLED, and it focuses on the bleeding risk of AFib patients being treated with anticoagulants. These patients should be evaluated for bleeding risk at every visit. Providers should initially focus on modifiable risk factors, including uncontrolled hypertension; labile or unstable INRs which we'll discuss later in the course; excess alcohol use; concomitant use of NSAIDs, aspirin or antiplatelets and a bleeding predisposition (for example, treating a gastric ulcer); and optimizing renal or liver function. The HAS-BLED bleeding risk score was derived from the EURO Heart Survey on Atrial Fibrillation to measure the risk of bleeding in patients with AFib taking systemic anticoagulants. The score assigns points for nine different clinical characteristics as noted on the slide: Low risk for bleeding is a score of zero, moderate risks have scores of one, two or three, and patients at high risk for bleeding have scores greater than three.

HEMORR$_2$HAGES

The HEMORR$_2$HAGES bleeding risk score was validated in AFib patients in a combined Medicare inpatient dataset from seven states. The score assigns two points for a prior bleed and one point for each additional clinical characteristic listed on the slide. Patients can be categorized into low, intermediate, and high bleeding risk according to scores of 0 to 1, 2 to 3, and greater than or equal to 4, respectively. The higher the HEMORR2HAGES score, the higher the risk of bleed in patients.

Letter	Clinical Characteristic	Points
H	Hepatic or Renal Disease	1
E	Ethanol Abuse	1
M	Malignancy	1
O	Older Age	1
R	Reduced Platelet Count or Function	1
R	Rebleeding Risk	2
H	Hypertension	1
A	Anemia	1
G	Genetic Factors	1
E	Excessive Fall Risk	1
S	Stroke	1

Maximum Score: 12

Case Study

It is important for providers to be able to recognize the likely causes of a gastrointestinal, or GI, bleed. Here we have a case study with JR, a 62-year-old male, with a history of hypertension, type 2 diabetes, arthritis, and alcoholism, and previously had a GI bleed. His current medications include: 200 mg ibuprofen as needed, 81 mg aspirin daily, 20 mg lisinopril daily, and 500 mg metformin twice daily. Using the HAS-BLED bleeding risk assessment, which of these factors would you identify as contributing to the cause of the GI bleed?

Case Study

JR is a 62-year-old man with a history of hypertension, type 2 diabetes, arthritis, alcoholism, and previously had a gastrointestinal (GI) bleed. His current medications include 200 mg ibuprofen as needed, 81 mg aspirin daily, 20 mg lisinopril daily, and 500 mg metformin twice daily.

Which of these factors increases JR's risk of a bleeding event?

Letter	Clinical Characteristic	Points
H	Hepatic or Renal Disease	1
E	Ethanol Abuse	1
M	Malignancy	1
O	Older Age	1
R	Reduced Platelet Count or Function	1
R	Rebleeding Risk	2
H	Hypertension	1
A	Anemia	1
G	Genetic Factors	1
E	Excessive Fall Risk	1
S	Stroke	1

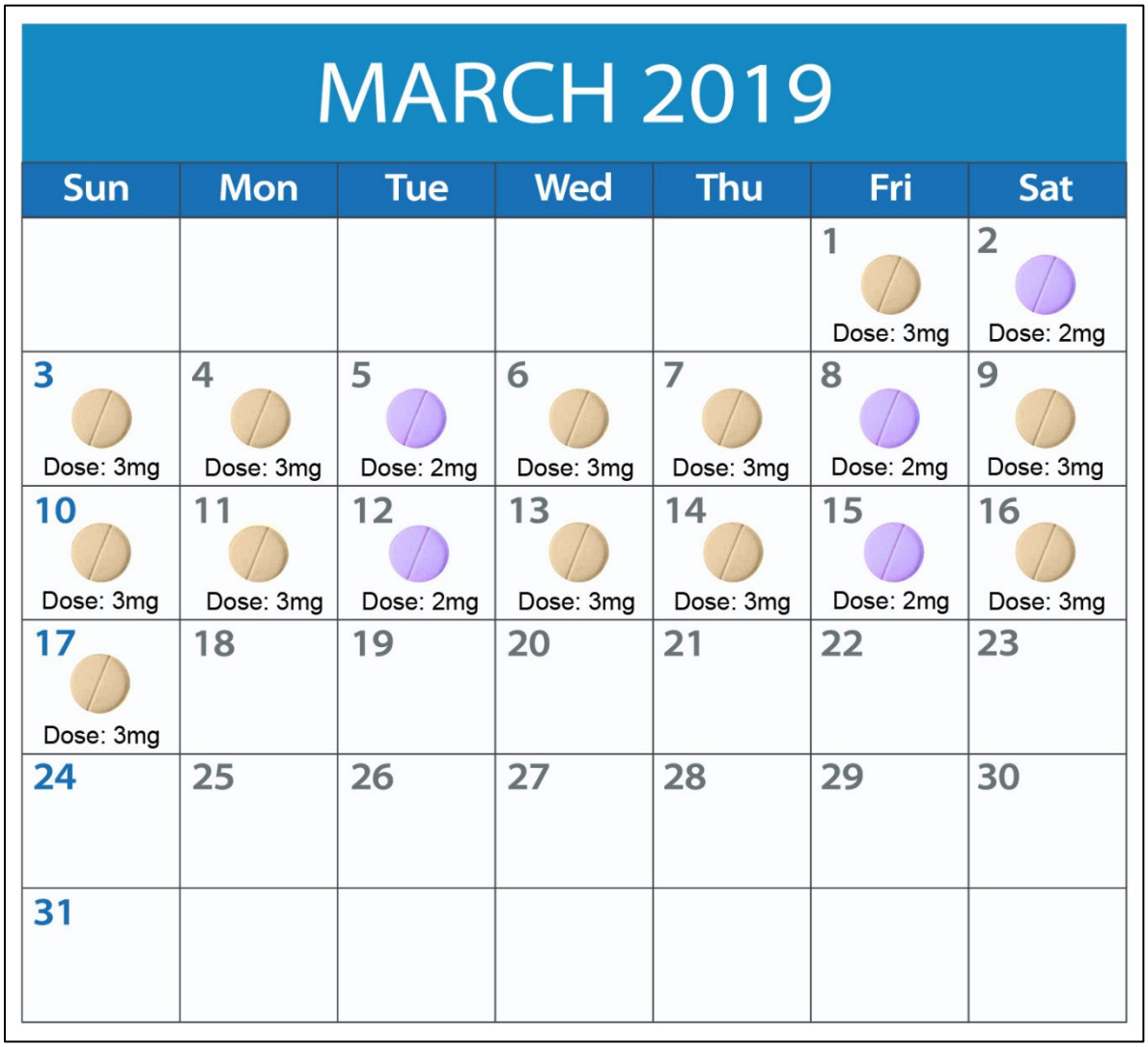
Maximum Score: 9

Using the HAS-BLED bleeding risk assessment, you will notice the following four factors put JR at a higher risk for bleeding: Previous GI bleed, Excessive alcohol consumption, Anti-platelet and NSAID use

such as ibuprofen and aspirin, and Hypertension, having a systolic pressure greater than 160 millimeters of mercury.

Warfarin

Some clinical aspects to consider when prescribing and monitoring patients taking warfarin include the following: Warfarin has a narrow therapeutic index and dosing is critical. There are many food, drug, and disease state interactions, and the dosing schedule can be very complicated both for clinicians and patients. The calendar shows an example of the warfarin dosing for a patient throughout a series of weeks, and the dose is different each day or every few days. It is critical that patients understand their dosing schedule.



Alt Text: March 2019 calendar. Images of small pills on March 1 through March 17 indicating doses ranging from 2mg to 3 mg.

Warfarin Dosing and INR

Some considerations before starting warfarin treatment are: Measure baseline INR prior to starting therapy. Initiation of warfarin in patients for the treatment of acute thrombosis needs to be bridged with a parenteral anticoagulant such as heparin, low molecular weight heparin or fondaparinux until a therapeutic INR is reached. Initial dose of warfarin is usually between 2 to 5 mg once daily, and maintenance doses range from 2 to 10 mg once daily. Smaller starting doses should be considered for high risk patients such as the elderly, and patients with low body weight, abnormal liver function, or those who are at a high risk for bleeding.

Warfarin Monitoring Parameters

The INR should be checked daily until the therapeutic range has been reached and sustained for 2 consecutive days, then it should be checked 2 or 3 times weekly for 1 to 2 weeks, then less often, according to the stability of the results. In healthy people, an INR of 1.1 or below is considered normal. An INR range of 2.0 to 3.0 is generally an effective therapeutic range for disorders such as AFib, deep vein thrombosis, or pulmonary embolism. With an INR that is higher than the recommended range, the blood clots more slowly. With an INR that is lower than the recommended range, the blood clots more quickly than desired. Once the INR becomes consistently stable, the frequency of testing can be reduced to intervals as long as 12 weeks. When dose adjustments are required, frequent monitoring is resumed.

Long-Term Warfarin Therapy

Some patients on long-term warfarin therapy experience unexpected fluctuations in dose-response due to changes in diet, concurrent medication changes, poor compliance, alcohol consumption, or new or worsening disease states (such as hepatic deterioration, malnutrition). On such occasions there may be instances requiring daily INR monitoring. The safety and effectiveness of warfarin therapy depends critically on maintaining the INR within the therapeutic range.

Patient Self-Testing (PST)

Besides having blood drawn in a clinic, patients may also self-monitor their INR. An INR test meter is a portable, battery-operated device, used to monitor a patient's response to warfarin. It is used similarly to a blood glucose meter. Effective management of patients using warfarin is resource-intensive, requiring frequent in-clinic testing of the INR. Patient self-testing, or PST, has emerged as a convenient alternative to in-clinic testing without sacrificing quality of life as observed in The Home INR, or THINRS, Study.

Warfarin INR Interactions

Let's review some of the dietary, disease states, and drug interactions with warfarin that affect the INR.

Warfarin INR Interactions

Dietary interactions include vitamin K, alcohol, and enteral tube feeding. A common misconception for patients on warfarin is that green, leafy vegetables high in vitamin K should be avoided. Providers should stress that while this drug-food interaction with warfarin does exist, patients do not necessarily need to avoid these foods if they are already an integral part of their diet. Patients should understand that if

they do eat foods high in vitamin K, the amount consumed should stay as consistent as much as possible. This will help prevent large ups and downs in patients' INR. Alcohol consumption can increase the INR in the short term and decrease it over the long term. Several studies have assessed the influence of enteral tube feeding and co-administration with warfarin. Mechanisms include higher concentrations of vitamin K, as well as protein-binding, resulting in decreased drug levels. To prevent these interactions, health care providers should avoid warfarin co-administration with enteral feeding. Enteral feeding should be withheld 1 hour before and after warfarin administration.

Warfarin INR Interactions

Disease state interactions include thyroid and liver dysfunction.

Warfarin INR Interactions

Drug interactions include acetaminophen, amiodarone, antimicrobials, herbals and clopidogrel among others. Acetaminophen is usually the first analgesic drug choice in patients taking anticoagulants due to an increased bleeding risk associated with NSAIDs. A meta-analysis revealed significant increases in INR in concomitant acetaminophen administration. Possible mechanisms of interaction include inhibition of the CYP3A4 and CYP1A2 enzymes. Patients treated with warfarin and acetaminophen should be monitored for elevated INR and dose adjustment

Potentiation of Warfarin

You can access a table of the different types of drugs, food products, and herbal supplements that may potentiate the action of warfarin on The American College of Chest Physicians (CHEST) website. The INR should be monitored, and warfarin dose adjusted as necessary. A PDF handout of this table is also available in the Resources section of the course launch page. For the full table of drugs listed, please refer to The American College of Chest Physicians, or CHEST, Guidelines. A link to the CHEST Guidelines is provided in the Resources section.

Level of Causation	Anti-infectives	Cardiovascular	Analgesics, Anti-inflammatories, Immunologics	CNS Drugs	GI Drugs and Food	Herbal Supplements	Other Drugs
Highly Probable	Ciprofloxacin Co-trimoxazole Erythromycin Fluconazole	Amiodarone Clofibrate Diltiazem	Phenylbutazone Piroxicam	Alcohol (if concomitant liver disease) Citalopram Sertraline	Cimetidine Fish oil Mango Omeprazole	Boldo-fenugreek Quilinggao	Anabolic steroids Zileuton
Probable	Amoxicillin/ clavulanate	Aspirin	Acetaminophen Aspirin	Disulfiram Chloral hydrate	Grapefruit	Danshen Dong quai	Fluorouracil Tamoxifen
Possible	Amoxicillin	Amiodarone-induced toxicosis	Celecoxib	Felbamate	Orlistat	Danshen/ Methyl salicylate	Acarbose
Highly Improbable	Cefamandole Cefazolin	Bezafibrate Heparin	Levamisole Nabumetone	Fluoxetine Diazepam			Levonorgestrel

Inhibition of Warfarin

You can access a table of the different types of drugs, food products, and herbal supplements that may inhibit the action of warfarin on The American College of Chest Physicians (or CHEST) website. The INR should be monitored, and warfarin dose adjusted as necessary. A PDF handout of this table is also available in the Resources section of the course launch page. For the full table of drugs listed, please refer to the CHEST Guidelines. A link to the CHEST Guidelines is provided in the Resources section.

Level of Causation	Anti-infectives	Cardiovascular	Analgesics, Anti-inflammatories, Immunologics	CNS Drugs	GI Drugs and Food	Herbal Supplements	Other Drugs
Highly Probable	Griseofulvin	Cholestyramine	Mesalamine	Barbiturates	High vit. K content foods Avocados (lg. amts)		Mercaptopurine
Probable	Dicloxacillin	Bosentan	Azathioprine	Chlordiaze-poxide	Soy milk Sucralfate	Ginseng	Chelation Therapy Multi-vitamins
Possible	Terbinafine	Telmisartan	Sulfasalazine		Seaweed		Cyclosporine
Highly Improbable	Cloxacillin	Furosemide		Propofol		Green tea	

Warfarin Reversal Agent

Vitamin K is indicated in patients treated with warfarin when reversal of the anticoagulant effects is needed due to life-threatening or uncontrolled bleeding. Professional societies have published guidelines on management of bleeding in patients taking oral anticoagulants. For example, the American College of Chest Physicians recommends an oral dose of vitamin K for warfarin reversal for nonbleeding patients only if the INR is greater than 10. The onset of action can be expected within 6 to 12 hours, with its peak effect at 24 hours. Vitamin K is available in both oral and intravenous dosage forms. Intravenous vitamin K is recommended over the oral route for bleeding patients because it has a more rapid onset of action of within 2 hours, and its peak effect occurs within 6-12 hours. The treatment of intracerebral hemorrhage due to warfarin includes replacing clotting factors within 90 minutes of emergency department arrival for patients that present within 12 hours of time last known to be well. Treatment must include intravenous vitamin K along with prothrombin complex concentrates, which is preferable, or fresh frozen plasma, which is acceptable. Recombinant Factor 7a is not recommended for reversal in intracerebral hemorrhage. Use of IV vitamin K alone is insufficient for reversal in the first hours but should be part of all acute reversal strategies.

Supratherapeutic Warfarin Management

There may be situations where the warfarin dose should be held or decreased, or reversal agents given to prevent loss of life from bleeding. Several products are used in the treatment of major bleeding due to vitamin K antagonists such as warfarin. These products include vitamin K, in combination with prothrombin complex concentrate, fresh frozen plasma, or recombinant factor 7a. Fresh frozen plasma has the disadvantage of potential allergic reaction, or transmission of infection, preparation time, and higher volume. Prothrombin complex concentrate, also known as PCC, and recombinant factor 7a, are more rapidly concentrated with less infection transmission risk, but they have not been compared with fresh frozen plasma in adequately powered randomized clinical trials. Vitamin K is indicated in patients treated with warfarin when reversal of the anticoagulant effect is needed. Some examples for using reversal agents include life-threatening or uncontrolled bleeding, or in cases when urgent surgery is required and there's no time to wait for the INR to normalize.

INR	Clinical Scenario	Management
Between 4.5-10	No bleeding	Hold warfarin until INR in therapeutic range and resume at lower dose Do not administer vitamin K
> 10	No bleeding	Hold warfarin until INR in therapeutic range and resume at lower dose Consider 2.5 mg oral vitamin K
Any	Life threatening bleeding or urgently needed surgery	Hold warfarin Vitamin K 5 to 10 mg slow IV infusion AND Four-Factor prothrombin complex concentrate (PCC)

Knowledge Check

It's time for a knowledge check. Refer to the Potentiation and Inhibition of Warfarin tables.

Please select the correct drug-drug interaction and its effect on bleeding:

a. Amiodarone and warfarin interact to cause an inhibition of warfarin effect
b. Phenytoin and warfarin interact to cause a potentiation of warfarin's effect
c. Citalopram and warfarin interact to cause a potentiation of warfarin's effect or
d. Azole antifungals and warfarin interact to cause an inhibition of warfarin effect

Knowledge Check

The correct answer is c. Citalopram and warfarin interact to cause a potentiation of warfarin's effect. The efficacy of warfarin is increased and therefore risk of bleeding is increased.

Contraindications to Warfarin

Some contraindications to using warfarin include: Active bleeding, imminent hemorrhage, patient with a high bleeding risk, and pregnancy. Warfarin is contraindicated in women who are pregnant except in pregnant women with mechanical heart valves, who are at high risk of thromboembolism. Warfarin exposure during pregnancy causes a recognized pattern of major congenital malformations known as warfarin embryopathy and fetotoxicity, fatal fetal hemorrhage, and an increased risk of spontaneous abortion and fetal mortality. If warfarin is used during pregnancy or if the patient becomes pregnant while taking this drug, the patient should be informed of the potential hazard to a fetus. There are several bleeding risk assessments for AFib patients including HAS-BLED, HEMORR2HAGES, and ATRIA. Of these three, the HAS-BLED has a superior performance for predicting the risk of a major bleed.

Knowledge Check

Now it's time for another knowledge check question. Select the best answer:

According to the CHEST guidelines, what is the recommended INR monitoring frequency in patients receiving warfarin with consistently stable INRs?

a. 4 weeks
b. 6 weeks
c. 8 weeks
d. Up to 12 weeks
e. At every doctor's visit

Knowledge Check

The correct answer is d. Up to 12 weeks.

DOACs and Approved Indications

Now that we understand some considerations for warfarin, let's explore the FDA-approved indications for the direct acting oral anticoagulants, or DOACs. Apixaban, dabigatran, and rivaroxaban are approved for the following indications: primary VTE prophylaxis in hip and knee replacement surgery, non-valvular AFib, deep vein thrombosis and pulmonary embolism, or DVT/PE, treatment, and secondary prevention of recurrent deep vein thrombosis and pulmonary embolism, or DVT/PE. Dabigatran is limited for use in primary VTE prophylaxis with hip replacement surgery only. Betrixaban and rivaroxoban are indicated in primary VTE prophylaxis of adult patients hospitalized for an acute medical illness who are at risk for VTE but not at high risk for bleeding. Edoxaban is approved for non-valvular AFib and deep vein thrombosis and pulmonary embolism treatment. A recently approved indication for rivaroxaban, in combination with aspirin, is the reduction in the risk of major cardiovascular events such as cardiovascular death, myocardial infarction, and stroke in patients with coronary artery disease or peripheral artery disease.

DOAC	Primary VTE Prophylaxis in Hip/Knee Replacement Surgery	Non-Valvular Atrial Fibrillation	DVT/PE Treatment	Secondary Prevention of Recurrent DVT/PE	Primary VTE Prophylaxis of Adult Patients Hospitalized for an Acute Medical Illness	Reduce Risk of Major Cardiovascular Events in CAD and PAD patients (in combination with aspirin use)
Apixaban	X	X	X	X		
Betrixaban					X	
Dabigatran	X (Hip)	X	X	X		
Edoxaban		X	X			
Rivaroxaban	X	X	X	X	X	X

Knowledge Check

It's time for another Knowledge check question. True or False? All of the DOACs are indicated for prophylaxis of stroke in patients with AFib?

Knowledge Check

The correct answer is False. Betrixaban is not indicated for the prophylaxis of stroke in patients with AFib.

DOAC	Primary VTE Prophylaxis in Hip/Knee Replacement Surgery	Non-Valvular Atrial Fibrillation	DVT/PE Treatment	Secondary Prevention of Recurrent DVT/PE	Primary VTE Prophylaxis of Adult Patients Hospitalized for an Acute Medical Illness	Reduce Risk of Major Cardiovascular Events in CAD and PAD patients (in combination with aspirin use)
Apixaban	X	X	X	X		
Betrixaban					**X**	
Dabigatran	X (Hip)	X	X	X		
Edoxaban		X	X			
Rivaroxaban	X	X	X	X	X	X

DOAC Dosing for Stroke Prophylaxis in Nonvalvular AFib

Here you'll find the dosing schedules of the different DOACs when treating nonvalvular AFib patients for stroke prophylaxis. Dabigatran and apixaban are both dosed twice daily, and rivaroxaban and edoxaban are dosed once a day. Betrixaban is not indicated for stroke prophylaxis in patients with AFib. DOACs are not recommended in patients with severe renal or hepatic impairment. Dose adjustments should be made with patients having mild to moderate renal impairment or taking certain medications.

DOAC	Dosing for Stroke Prophylaxis in Nonvalvular Atrial Fibrillation	Dose Adjustment
Dabigatran	150 mg **twice daily**	CrCl 15-30 mL/min: 75 mg twice daily CrCl 30-50 mL/min with concomitant P-gp inhibitors: 75 mg twice daily
Apixaban	5 mg **twice daily**	Decrease to 2.5 mg twice daily if at least **2** of the following are present: age ≥ 80 years, weight ≤ 60 kg, or serum creatinine ≥ 1.5 mg/dL Moderate to severe hepatic impairment: not recommended
Rivaroxaban	20 mg **once daily** with evening meal	CrCl 15-50 mL/min: 15 mg once daily with evening meal Moderate to severe hepatic impairment: not recommended
Edoxaban	60 mg **once daily**	CrCl > 95 mL/min: not recommended CrCl 15-50 mL/min: 30 mg once daily Moderate to severe hepatic impairment: not recommended
Betrixaban	Not indicated for Stroke Prophylaxis in Nonvalvular Atrial Fibrillation	Not indicated for Stroke Prophylaxis in Nonvalvular Atrial Fibrillation

DOAC Dosing for VTE Treatment

Now we'll discuss the DOAC dosing for the treatment of venous thromboembolism. Dabigatran and apixaban are both dosed twice daily. Rivaroxaban is dosed twice daily for 3 weeks, then once daily afterwards. Edoxaban is dosed once daily and betrixaban is not indicated for treatment of patients with venous thromboembolism. Most DOACs are not recommended in patients with moderate to severe hepatic impairment, and dose adjustments or avoidance should be determined according to the patient's creatinine clearance levels and other patient factors.

DOAC	Dosing for VTE Treatment	Dose Adjustment
Dabigatran	150 mg **twice daily** (prior bridging with parenteral anticoagulation required for 5-10 days)	CrCl ≤ 30 mL/min: not recommended CrCl < 50 mL/min with concomitant P-gp inhibitor: avoid use
Apixaban	10 mg **twice daily** for 1 week, then 5 mg twice daily	CrCl < 15 mL/min: not studied Moderate to severe hepatic impairment: not recommended
Rivaroxaban	15 mg **twice daily** with evening meal for 3 weeks, then 20 mg **once daily** with evening meal	CrCl < 30 mL/min: not recommended Moderate to severe hepatic impairment: not recommended
Edoxaban	60 mg **once daily** (prior bridging with parenteral anticoagulation required for 5-10 days)	CrCl 15-50 mL/min or weight ≤ 60 kg or concomitant P-gp inhibitors: 30 mg once daily Moderate to severe hepatic impairment: not recommended
Betrixaban	Not indicated for VTE treatment	Not indicated for VTE treatment

DOAC Dosing for VTE Prophylaxis Following Knee or Hip Replacement Surgery

Three DOACs are approved for the prophylaxis of venous thromboembolism following knee or hip surgery: dabigatran, apixaban, and rivaroxaban. The duration of treatment is dependent on the type of surgery performed on the patient. Hip replacement surgery requires a longer duration of treatment than knee replacement surgery in most cases. Dabigatran is given once daily for 28 to 35 days only for hip replacement surgery. It should not be used in patients on dialysis or having a creatinine clearance of less than or equal to 15 milliliters per minute. Apixaban requires twice daily dosing for 12 to 35 days and should not be used in patients with moderate to severe hepatic impairment. Rivaroxaban is given once daily for 12 to 35 days. It is not recommended for use in patients with a creatinine clearance of less than or equal to 30 milliliters per minute or with moderate to severe hepatic impairment. Apixaban and rivaroxaban are indicated for prophylaxis use following both knee and hip replacement surgery. Edoxaban and betrixaban are not indicated for VTE prophylaxis following knee or hip surgery.

DOAC	Dosing for VTE Prophylaxis After Hip or Knee Replacement	Dose Adjustment
Dabigatran	110 mg within 1-4 hours after surgery, then 220 mg **once daily** for 28-35 days for hip replacement surgery If not started on the first day, then treatment can be started at 220 mg **once daily** for hip replacement surgery	Dialysis or CrCl ≤ 15 mL/min: not recommended
Apixaban	2.5 mg **twice daily** within 12-24 hours after surgery For knee replacement, the recommended duration is 12 days For hip replacement, the recommended duration is 35 days	Moderate to severe hepatic impairment: not recommended
Rivaroxaban	10 mg **once daily** within 6-10 hours after surgery For knee replacement, the recommended duration is 12 days For hip replacement, the recommended duration is 35 days	CrCl ≤ 30 mL/min: not recommended Moderate to severe hepatic impairment: not recommended
Edoxaban	Not indicated for VTE Prophylaxis after hip or knee replacement	Not indicated for VTE Prophylaxis after hip or knee replacement

Betrixaban	Not indicated for VTE Prophylaxis after hip or knee replacement	Not indicated for VTE Prophylaxis after hip or knee replacement

DOAC Safety Considerations and Interaction Examples

There are several safety considerations and interactions with DOACs, though fewer than with warfarin. Some dietary interactions to consider include the following: Dabigatran capsules must be swallowed whole and not opened due to the risk of increased absorption. Rivaroxaban (in 15 milligram and 20 milligram doses) should be taken with food for adequate absorption.

DOAC Safety Considerations and Interaction Examples

Disease state interactions include renal function. Renal elimination differs among DOACs.

DOAC Safety Considerations and Interaction Examples

Drug interactions due to pharmacokinetic and pharmacodynamic interactions can increase or decrease DOAC exposure (for example, strong Pgp and CYP3A4 inhibitors increase exposure; while strong Pgp and CYP3A4 inducers decrease exposure). Pharmacokinetic interactions occur when one drug alters the absorption, distribution, metabolism or excretion of the other drug. Examples include strong p-glycoproteins and cytochrome P 450-3A4 inhibitors or inducers. Pharmacodynamic interactions occur between drugs with similar or opposite pharmacological effects and can increase bleeding risk. The effects are generally common to related drugs. Examples include aspirin, NSAIDS, and antiplatelet agents. Each DOAC has different drug interactions, and practitioners should check the prescribing information before initiating patients on DOACs.

DOAC Reversal

DOACs have relatively short half-lives. Major bleeding that occurs in patients taking DOACs is often able to be managed by temporarily discontinuing the anticoagulant and providing supportive measures. These supportive measures include compression, surgical repair, and fluid and/or blood replacement. Rates of severe and fatal bleeding associated with DOACs in the pivotal registry trials were low in the absence of reversal agents. High quality data on the impact of reversal agents on clinical outcomes in DOAC associated bleeding are lacking. There is no randomized clinical trial evidence demonstrating that the administration of reversal agents improves outcomes.

DOAC Reversal

Reversing anticoagulation places patients at their baseline elevated risk of thromboembolism. Consider restarting anticoagulation as soon as medically appropriate. The use of a reversal agent should only be considered if the bleed is life threatening, in a critical organ, or is not controlled with supportive measures. There should be reasonable certainty that therapeutic anticoagulant levels are present.

DOAC Reversal Agents

There are reversal agents available for dabigatran, apixaban, and rivaroxaban to reverse the anticoagulant effect in life-threatening or uncontrolled bleeding. Idarucizumab is indicated in patients treated with dabigatran when reversal of the anticoagulant effects is needed, for emergency surgery, for urgent procedures, or in life-threatening or uncontrolled bleeding. The route of administration is intravenous only with a dose of 5 grams (2 vials, each containing 2.5 grams) as two consecutive infusions or bolus injection by injecting both vials consecutively one after another via syringe into I.V. line. In the REVERSE-AD study, investigators observed reversal effects within 30 minutes, and a median of 11.4 hours for time to bleeding cessation.

DOAC Reversal Agents

In May 2018, FDA approved the first Factor Xa inhibitor antidote, Andexanet Alfa, which is indicated for patients treated with apixaban and rivaroxaban when reversal of anticoagulation is needed due to life-threatening or uncontrolled bleeding. The route of administration is an I.V. bolus dose, with a target rate of 30 mg per minute, followed by continuous infusion for up to 120 minutes. The Andexanet Alfa dose is based on the specific DOAC, dose, and time that the DOAC dose was last given. Reversal activity was observed within 2 to 5 minutes following bolus administration and maintained throughout the duration of continuous infusion. There are no FDA approved reversal agents for patients treated with betrixaban or edoxaban.

Advantages and Disadvantages of Warfarin

Some advantages of using warfarin include: A long track record with predictable benefits and results, Once daily dosing, and The ability to readily measure anticoagulant effect with INR test. Some disadvantages of using warfarin include: A narrow therapeutic window that can be affected by factors such as diet. Diet, disease states, and drugs may significantly alter INR. INR must be monitored regularly, sometimes daily, weekly or monthly. Maintaining INR target range optimizes the balance of efficacy and safety. For AFib and VTE patients, the range is between 2 and 3. For patients with certain types of heart valves, the range may be higher, between 2.5 to 3.5. INRs outside the target ranges can increase the risk for adverse events such as bleeding or ischemic events. Dosing schedules can be complicated, and warfarin is contraindicated in pregnant women.

Advantages of DOACs

Some advantages of using DOACs include: No regular laboratory monitoring for anticoagulant effect, Rapid onset and offset of action, Fewer drug interactions, Predictable pharmacokinetics, The efficacy and safety are at least as good as warfarin for stroke prevention in atrial fibrillation, and treatment and secondary prevention of venous thromboembolism, and There are lower rates of stroke caused by bleeding in the brain and of major bleeding events.

Disadvantages of DOACs

Some disadvantages of using DOACs include: No regular laboratory monitoring for an anticoagulant effect which can be viewed as both an advantage and a disadvantage. Upset stomach. Shorter half-life than warfarin, making missed doses more consequential. Higher incidence of major bleeding events in those aged 75 years or older with certain agents. There are no adequate and well-controlled studies

with DOACs in pregnant women. DOAC treatment is likely to increase the risk of hemorrhage during pregnancy and delivery. It should only be used during pregnancy if the potential benefit outweighs the potential risk to the mother and fetus.

Knowledge Check

It's time for our knowledge check question. Select the best answer:

Which of the following is not a risk factor for both risk of stroke and risk of bleeding for patients with AFib?

a. Hypertension
b. History of stroke
c. Age >65 years
d. Female gender
e. All of the above are risk factors for both risk of stroke and risk of bleeding for patients with AFib

Knowledge Check

The correct answer is d. female gender. Hypertension, history of stroke, and older age are all factors that can be found on the CHADS2-VASC and HAS-BLED scoring systems and can increase a patient's risk for both a stroke or a bleed.

Challenges in the Use of Oral Anticoagulants

Now, we'll address some challenges in using oral anticoagulants.

Barriers to Oral Anticoagulant Use

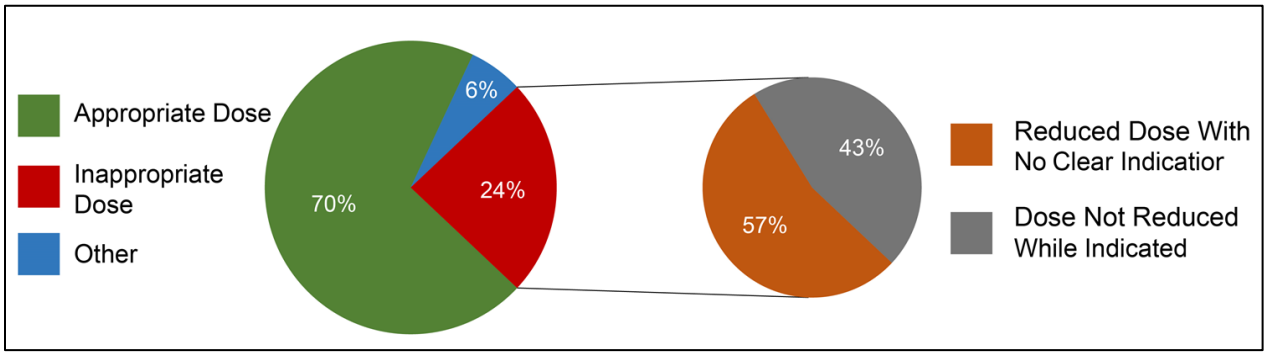
Some barriers to anticoagulant use include narrow therapeutic index, especially for warfarin, availability of continuous monitoring, perceived risk of bleeding, patient preferences, cost, and the availability of reversal agents.

Improper Use of DOACs

Let's look at some of the ways DOACs are being prescribed and used improperly. A retrospective analysis investigating the appropriateness of DOAC prescriptions was conducted in the province of Quebec, Canada. Adult patients hospitalized between October 2011 and October 2014, with a diagnosis of Afib and taking a DOAC prescription for apixaban, dabigatran, or rivaroxaban were included in the study. The study included a total of 500 patients. Data retrieved from the electronic medical records and prescriptions were evaluated according to appropriateness criteria.

Study Results: Improper Use of DOACs

The study reported that: Overall only 70% of DOAC prescriptions were considered appropriate, 24% of patients received an inappropriate dose. Of this 24%, 57% of patients received a reduced dose with no clear indication, and 43% received a dose that was not reduced while indicated. This data is not representative of Canada or the United States' population, but it indicates a need for clarification in dosing recommendations.



Alt Text: 70% of DOAC prescriptions were appropriate. 6% of patient of DOAC prescriptions were classified as "other." 24% of DOAC doses were inappropriate. Of this 24%, 57% received a reduced dose with no clear indication, and 43% received a dose that was not reduced while indicated.

Improper Use of DOACs

Two retrospective U.S. AFib cohort registries showed that while most patients are receiving appropriate doses of DOACs, a significant minority of patients receive off-label dosing (under or over dosing). Off-label dosing of DOACs in the AFib population is associated with worse outcomes such as: Increased all-cause mortality and cardiovascular hospitalizations Increased major bleeding in overdosing and increased stroke in under dosing in patients with kidney disease It's important to evaluate renal function and other factors for indications of reduced dosing, and off-label use of lower than recommended doses may be harmful.

Underutilization of Anticoagulation

Findings from a 2012 study which focused on adherence to guidelines for approximately 20,000 elderly patients with AFib, found the following causes of anticoagulation underutilization, and its clinical outcomes. During 40 to 48 percent of observed patient days, there was no antithrombotic protection, and older females with a high number of comorbidities were especially at risk for underutilization of oral anticoagulation.

Steps for Clinicians to Optimize Oral Anticoagulant Use

Here are some steps for clinicians to take to optimize oral anticoagulant use.

Use Shared Decision-Making Tools

The first step is to use shared decision-making tools. Shared decision-making is a collaborative process between a patient and his or her provider, and it's a core strategy to promote patient-centered

healthcare. It helps patients weigh the pros and cons of treatments and leads to more realistic expectations. Shared decision-making has been shown to improve treatment adherence in many areas of clinical practice such as diabetes and pain treatment.

AHRQ SHARE Approach

Alt Text: S Seek your patient's participation, H Help your patient explore and compare treatment options, A Assess your patient's values and preferences, R Reach a decision with your patient, E Evaluate your patient's decision

AHRQ SHARE Approach

Step 1: Seek your patient's participation. The provider could say, "I would like to work with you on preventing another stroke."

AHRQ SHARE Approach

Step 2: Help your patient explore and compare treatment options. For example, "Here are a few treatments that are available to lower your risk of having another stroke. Let's work together to identify one that might be best for you."

AHRQ SHARE Approach

Step 3: Assess your patient's values and preferences. The clinician might say, "Warfarin is an option, and when managed appropriately, is effective at reducing your chances of having another stroke. Are you available for weekly blood monitoring so that we can adjust your doses?" The patient could respond, "Transportation to the clinic is very difficult for me. I do not have a car and am not able to easily use public transportation."

AHRQ SHARE Approach

Step 4: Reach a decision with your patient. The patient and provider should continue to exchange information. The clinician considers the patient's preference for frequency of lab monitoring. The clinician might ask the patient about DOACs, which do not require frequent monitoring, but may be more expensive. After engaging in further conversation and weighing the risks versus the benefits, the patient may agree that a DOAC would be best.

AHRQ SHARE Approach

Step 5: Evaluate your patient's decision. The clinician and patient reach an agreement on an evidence-based treatment plan, and the clinician follows the proper steps to ensure that the patient understands his or her anticoagulant regimen.

Solicit Patient Preferences

Soliciting patient preferences will provide patients and their caregivers with the pros and cons of warfarin compared to DOACs. We need to identify what is important to the patient to enable us to prescribe an effective medication therapy with a high expected rate of adherence. Identify your patients' values before selecting an anticoagulant and allow patients to actively participate in the decision-making process. One patient may prefer warfarin over a DOAC without a reversal agent, even though there is more INR testing involved, because of the availability of a reversal agent. Other patients may prefer the simplicity of dosing with a DOAC compared to a more complex warfarin dosing schedule. Cost is also a factor for most patients.

Patient Preferences

Since the introduction of DOACs, there have been many studies looking at patient preferences in deciding which oral anticoagulant to use for treatment. Several studies showed that prevention of stroke was the most important factor in their treatment. Factors that were important to patients were prevention of stroke, lack of interactions with drugs and food, the availability of a reversal agent, and the ease of administration.

Patient Preferences

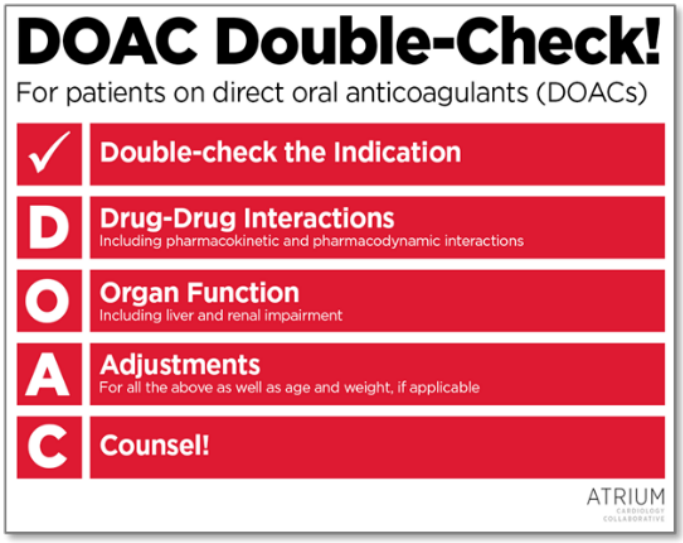
Only a few studies compared patient preferences for vitamin K antagonists and DOACS. DOACS were generally preferred over vitamin K antagonists due to the absence of INR monitoring and lower risk of bleeding. However, cost can be a factor in driving patient and provider preferences of a vitamin K antagonist over a DOAC. Healthcare plan reimbursements and co-pays may dictate one drug over another and may also factor into this decision.

Tools for the Safe Use of Oral Anticoagulants

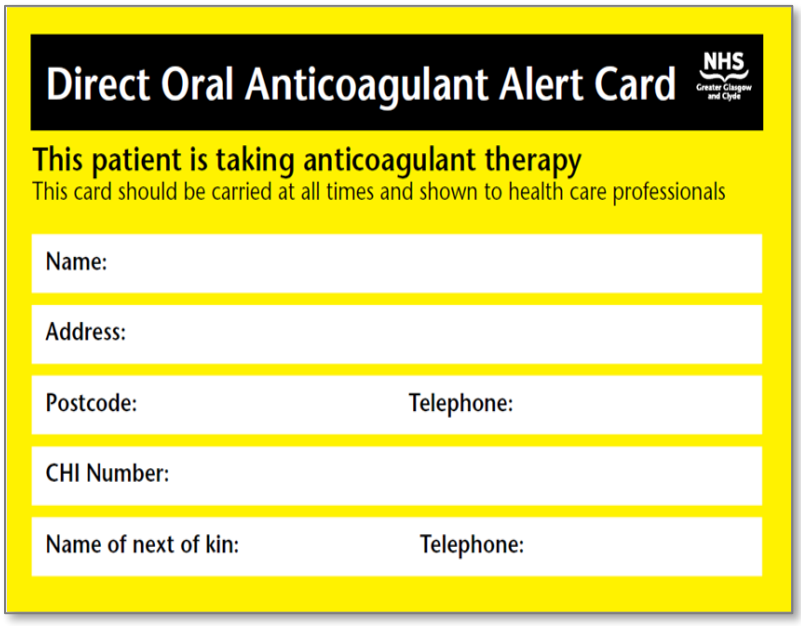
Now, we'll review some tools that patients and clinicians can use for the safe use of oral anticoagulants.

Patient Tools

Here are two patient tools that can be accessed by patients and healthcare providers online or printed and handed to patients at the office during a visit. The DOAC Double Check and the DOAC Alert Card.



Alt Text: DOAC Double-Check! For patients on direct oral anticoagulants (DOACs). Check: Double-check the indication. D: Drug-Drug Interactions, including pharmacokinetic and pharmacodynamic interactions. O: Organ Function, including liver and renal impairment. A: Adjustments for all the above as well as age and weight, if applicable. C: Counsel!



Alt Text: Direct Oral Anticoagulant Alert Card. NHS Seal. This patient is taking anticoagulant therapy. This card should be carried at all times and shown to health care professionals. Name. Address. Postcode. Telephone. CHI Number. Name of next of kin. Telephone.

ISMP's Patient Handout on Warfarin

Warfarin is considered a high-alert medication by the Institute for Safe Medication Practices (ISMP). The ISMP has created patient handouts for high-alert medications, as these medications can cause serious injury if extra precautions are not taken. It is important that patients have all the information they need to take this medicine exactly as intended. This information can be printed out and handed to patients in the office or accessed by the patient online. A link to this patient handout is available in the Resources section on the course launch page.

Patient Handouts on DOACs

As part of a study funded by the FDA Safe Use Initiative, ISMP developed three patient handouts for the DOAC oral anticoagulants– Eliquis, Pradaxa, and Xarelto. The handouts are available for both healthcare providers and consumers.

Clinician Tools

The Michigan Anticoagulation Quality Improvement Initiative, or MAQI², is a multicenter collaborative of anticoagulation clinics across the state of Michigan. MAQI² seeks to improve the safety, quality of care, and outcomes for patients requiring anticoagulation. An anticoagulation toolkit for providers and patients was produced by the MAQI² with the goal of providing practitioners and patients with an up-to-date, reliable, and easy to use source of information for anticoagulation.

MAPPP App for Peri-Procedural Management

The Management of Anticoagulation in the Peri-Procedural Period, or MAPPP, App is a guide intended to assist clinicians in evaluating procedure-related bleeding risk and underlying risk of thrombosis, guide decision-making regarding the interruption of anticoagulation and the use of anticoagulant "bridging," provide drug dosing and laboratory monitoring guidance in the peri-procedural period, and encourage clear communication between clinicians involved in prescribing anticoagulants and performing invasive procedures.

Patient Order Sets

The Anticoagulation Forum has several Patient Order Sets available for use in initiating oral anticoagulant therapy for AFib and acute VTE care transition in adults. Patient order sets take into consideration individual patient characteristics and can be helpful in identifying the best drug therapy and dose, and which lab tests should be run before and during the treatment. This screen and the next contain two pages taken from the patient order set for initiation of oral anticoagulation in patients with atrial fibrillation.

Patient Order Sets

A link to this Patient Order Set is available in the Resources section of the course landing page.

Patient Order Sets

This screen and the next show the first two pages of the Patient Order Set to be used for adult patients needing acute VTE care transition.

Patient Order Sets

A link to this Patient Order Set is available in the Resources section of the course landing page.

Clinical Guidelines

American Society of Hematology. (n.d.). *ASH Clinical Practice Guidelines*. https://www.hematology.org/Clinicians/Guidelines-Quality/Guidelines.aspx

American College of Chest Physicians. (n.d.). *Guidelines & Resources*. https://www.chestnet.org/Guidelines-and-Resources

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European Society of Cardiology. (n.d.). *Novel Oral Anticoagulants for Atrial Fibrillation: EHRA Practical Guide to NOAC* Use in AF. https://www.escardio.org/Guidelines/Recommended-Reading/Heart-Rhythm/Novel-Oral-Anticoagulants-for-Atrial-Fibrillation

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Knowledge Check

It's time for your final knowledge check! Consider this case study: MJ is a 66-year-old woman with a history of hypertension and diabetes mellitus. She is currently taking lisinopril and metformin ER once daily. MJ's mother died after suffering a stroke 10 years ago. She is interested in starting oral anticoagulation but is concerned over the increased risk of bleeding. She finds it inconvenient to come to the doctor's office every week or take medicine more than once a day.

Which oral anticoagulant would you recommend for MJ?

a. Aspirin
b. Warfarin
c. Rivaroxaban
d. None of the above

Knowledge Check

The best answer in this case is c. rivaroxaban. Aspirin is not indicated for stroke prophylaxis in patients with atrial fibrillation. Warfarin is indicated for stroke prophylaxis. However, MJ states that it's inconvenient and she prefers not to have to come to the doctor's office for frequent monitoring. Rivaroxaban is the best choice, given MJ's preferences and needs. Rivaroxaban is dosed once daily and does not require regular INR monitoring. The dose of rivaroxaban should be adjusted according to MJ's renal function.

Summary

In summary, oral anticoagulants are beneficial in the treatment of existing thrombosis and the prevention of primary and secondary thrombosis, and there is a high prevalence of oral anticoagulants being prescribed. However, oral anticoagulants also make up a significant amount of adverse drug event related visits to the emergency department. Therefore, pharmacokinetic and pharmacodynamic differences between DOACs and oral vitamin K antagonists, along with patient-specific factors, should be considered when choosing the appropriate oral anticoagulant agent. Clinicians should use strategies such as shared decision-making, patient preferences, and other evidence-based tools to help guide their oral anticoagulant choices.

Conclusion

You should now be able to:

- Discuss the prevalence and types of adverse drug events related to oral anticoagulants.
- Review the drug classifications of oral anticoagulants.
- Compare characteristics of oral vitamin K antagonists and direct acting oral anticoagulants.
- Identify pathophysiological states for utilization of oral anticoagulation therapy.
- Review barriers to proper oral anticoagulant use.
- List steps clinicians can take to reduce the risk of adverse drug events from oral anticoagulants.

Thank you for completing this course. We hope you take what you've learned today and use it in your daily practice to improve the use of oral anticoagulants among your patients.