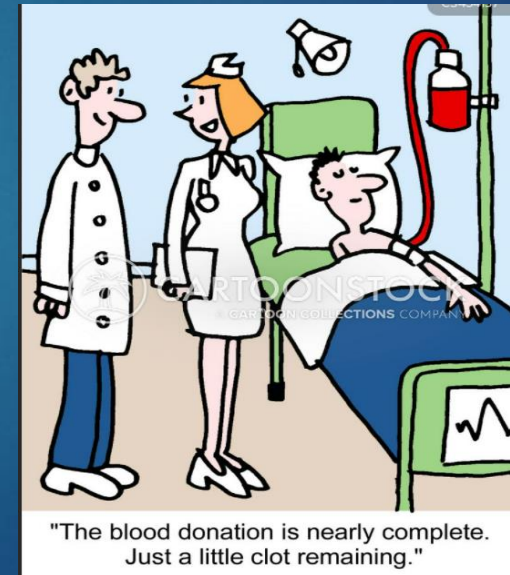


To Clot or Not to Clot:

A Pharmacist-Led Multidisciplinary Collaboration of Anticoagulation Management

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Disclosure & Disclaimer

- ▶ Disclosure
 - ▶ Neither Regina Tamon nor Patricia Schmidt
 - ▶ have any relevant financial relationships with any commercial interests

Disclaimer

- ▶ This informational presentation was developed by independent experts
- ▶ The information provided in this presentation is not the official position or recommendation of NCCHC but rather expert opinion. This information is not intended to be appropriate for every clinical situation nor does it replace clinical judgment.

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Learning Objectives

- ▶ Compare and contrast anticoagulation management in the community and the correctional setting
- ▶ Describe a clinical pharmacist anticoagulation management service collaborative practice agreement
- ▶ Evaluate Warfarin dosing using current guidelines and lessons learned

Pre-Test

- ▶ 50,000 people die of VTE annually in the USA,
- ▶ One-third (about 33%) of people with DVT/PE will have a recurrence within 10 years
- ▶ A pharmacist-Managed anticoagulation clinic is easy to establish and operate at every correctional facility
- ▶ VTE is the leading cause of death in the USA
- ▶ VTE is more common in >55 year old women
- ▶ Warfarin is the anticoagulant of Choice at most DOC's
- ▶ DOACs are a one size fit all

Overview

Why Worry About VTE

- ▶ Exact number unknown
- ▶ 1 in 4 people world wide die
 - ▶ pulmonary embolism-leading cause
- ▶ 900,000 Americans (or 1 to 2 per 1,000 people) are affected by DVT/PE according to CDC annually
- ▶ PE is fatal within 1 hr after onset of symptoms in 10% of case
- ▶ Untreated PE mortality rate is ~30%
- ▶ Up to 60 percent of VTE cases occur during or after hospitalization
 - ▶ making it a leading preventable cause of hospital death
- ▶ Most patients do well with therapy, but others don't



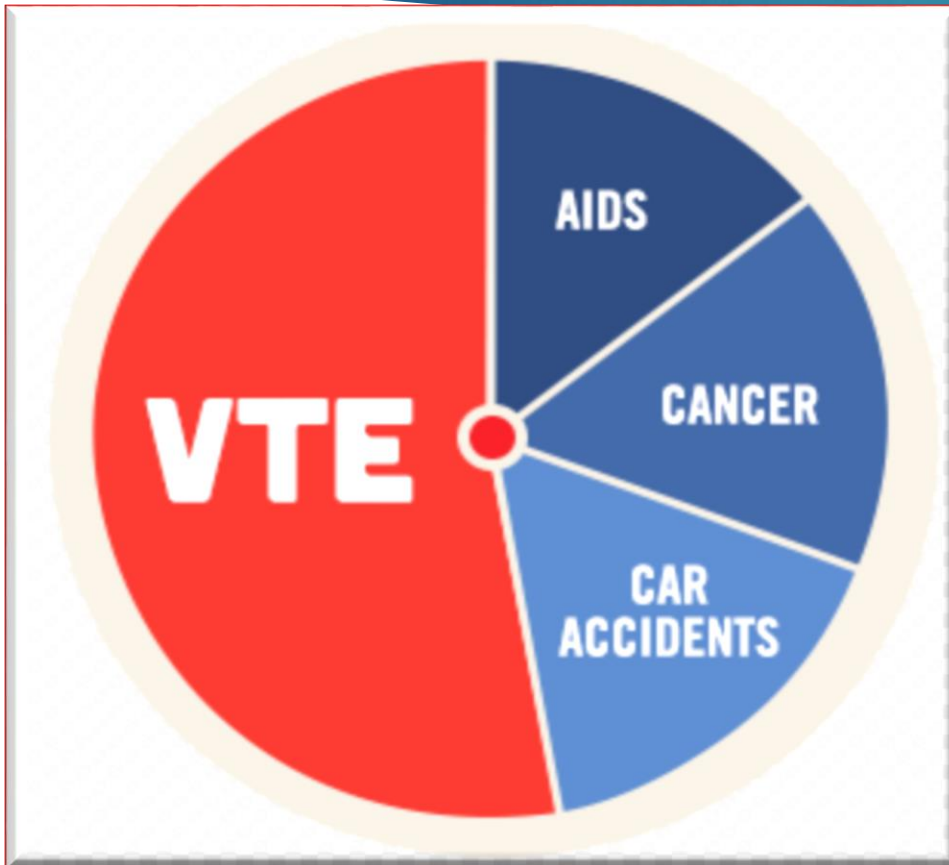
Overview

Why Worry About VTE

- ▶ 60,000-100,000 Americans die of DVT/PE (venous thromboembolism-VTE)
 - ▶ 10 to 30% of people will die within one month of diagnosis
 - ▶ Sudden death is the first symptom in about one-quarter (25%) of people who have a PE
- ▶ Long-term complications (post-thrombotic syndrome) include swelling, pain, discoloration, and scaling in the affected limb
- ▶ One-third (about 33%) of people with DVT/PE will have a recurrence within 10 years
- ▶ ~ 5 to 8% of the U.S. population has one of several genetic risk factors, inherited thrombophilias (genetic defect)
 - ▶ increases the risk for thrombosis.

Overview

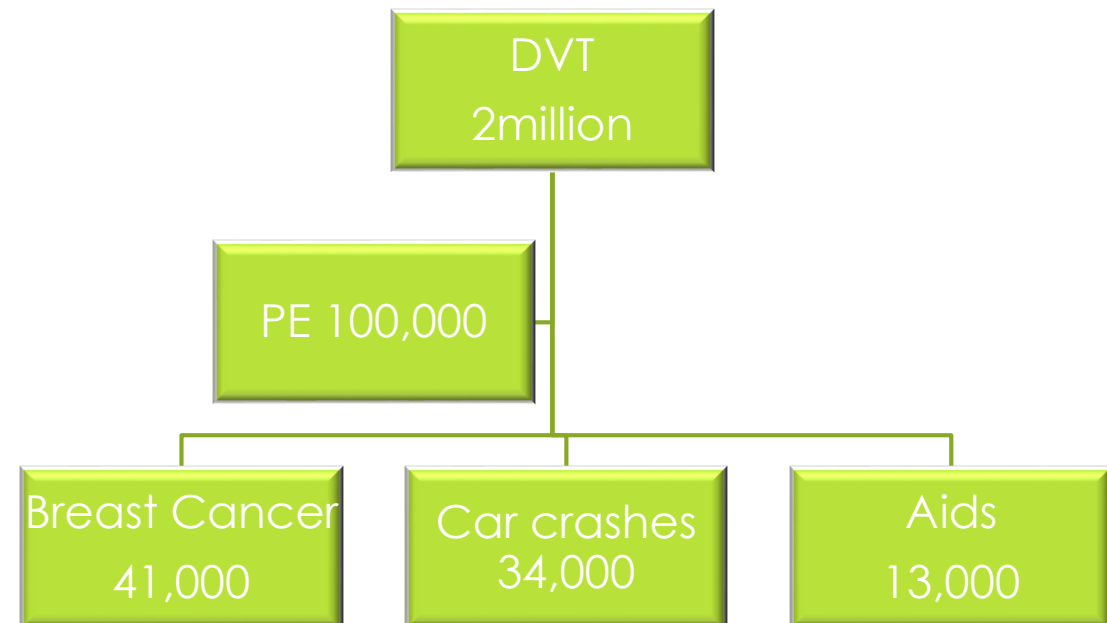
Why Worry About VTE Continued



Hirsh J & Hoak J. American Heart Association. 1996
Heit J et al. Blood 2005;106
Anderson FA et al. Am J Hematol 2007;82:777-82

► VTE

- Third leading cause of death than breast cancer, car crashes & Aids



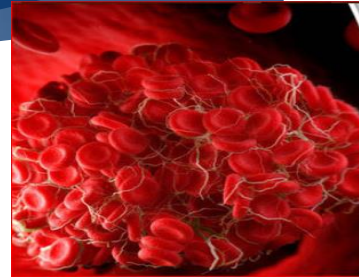
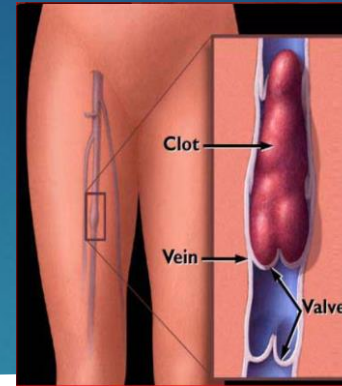
Economic Burden of VTE

- ▶ Significant global economic burden
- ▶ Multiple diagnostic tests and treatments, prolonged hospital stay and follow-up care - including recurrent VTE - can be extremely costly
- ▶ U.K.
 - ▶ VTE costs the National Health Service €640 (\$670) million per year
- ▶ U.S.
 - ▶ diagnosis and treatment of VTE costs \$15.5 billion per year
- ▶ Australia
 - ▶ VTE-related costs, including lost productivity, are estimated at \$1.72 billion a year
 - ▶ annual cost is \$19.99 billion (disability and premature death)

Thrombosis

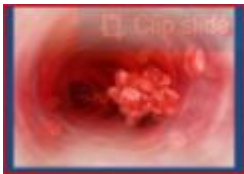
Definition

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Arterial Thrombosis

- ▶ Adherence of platelets to walls—"White" in color, associated with MI, stroke, and ischemia



Venous Thrombosis

- ▶ Develops in areas of stagnated blood flow (deep vein thrombosis) "Red" in color
- ▶ Associated with heart failure, cancer, surgery
- ▶ Maybe be provoked or unprovoked
- ▶ Embolus
 - ▶ Dislodged thrombus from arteries & veins
- ▶ Thromboembolism
 - ▶ Venous emboli may block arterioles in lung and pulmonary circulation

No one is immune
to PE or DVT

Who Is at Risk for VTE?

- Everyone is equally at risk for VTE
- Chances increase with age
- At 60 years old, **risk doubles every 10 years**
- There are also other factors that make you more susceptible to developing it, such as

RISK FACTORS

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<p>Cancer</p> <p>The onset of cancer can increase the production of certain substances in your body that make you more vulnerable to blood clots.</p> <p>Pancreatic, ovarian and lung cancers are typically associated with pulmonary embolism.</p>	<p>Surgery</p> <p>Blood clots are one of the main complications to watch out for after a surgery.</p> <p>This usually occurs because patients are typically bed-ridden for a long time. When you stop moving, blood flows slower in your deep veins, which can result in a clot.¹⁰</p>
<p>Smoking</p> <p>Cigarette smoking is closely associated with blood clots. Long-term abuse increases your chances of blood platelets sticking together and also damages the linings of your blood vessels, causing clots to form.¹¹</p>	<p>Pregnancy</p> <p>Pregnant women have a chance of developing blood clots due to the weight of the baby pressing on the pelvis, which can slow blood return from the legs.</p>
<p>Inactivity</p> <p>Long periods of bed rest due to an injury, surgery or other serious diseases causes the flow of blood in your legs to slow down. Long trips or flights contribute to this risk as well.</p>	<p>Obesity</p> <p>Obese people are at risk of blood clots because of genetic mutations related to blood coagulation factors caused by excess weight.¹²</p>

Clotting Disorders and Risk Factors

Inherited Disorders	Acquired Diagnoses	Miscellaneous Risks
<ol style="list-style-type: none">1. Protein C /S deficiency2. Factor V Leiden thrombophilia3. Prothrombin gene mutation4. Antiphospholipid syndrome5. Lupus anticoagulants	<ol style="list-style-type: none">1. Atrial Fibrillation2. HIV/AIDS3. Obesity4. Cancer5. Liver Disease6. Pregnancy	<ol style="list-style-type: none">1. Mechanical/Prosthetic Heart Valve2. History of an unprovoked clot3. Immobility4. Migraine with Aura5. Hormone Replacement therapy

Signs and Symptoms of an Embolism



Deep Vein Thrombosis

- Unilateral swelling, tender, warm, pain
- Calf, foot, leg, arm



Stroke

- Facial dropping, slurred speech, arm weakness
- Impaired vision, impaired balance



Pulmonary Embolism

- Sudden shortness of breath, chest pain, coughing up blood

Indications for Anticoagulation

- ▶ Venous thromboembolism (VTE)
 - ▶ Deep venous thrombosis
 - ▶ Pulmonary embolism
 - ▶ 3 types
 - ▶ Massive (PE with hypotension)
 - ▶ Submassive
 - ▶ Subsegmental
- ▶ Blocked central venous catheter
- ▶ Arterial thromboembolism
 - ▶ arterial ischemic stroke, Kawasaki disease, and after cardiac surgery
 - ▶ Arterial Fibrillation (A-Fib) (non-valvular)
 - ▶ Microbial Infarction
 - ▶ Cancer
 - ▶ Valve replacements (Bio prosthetic and Mechanical)

Common Anticoagulation Indications at our DOC

- ▶ Thromboembolism (Deep venous Thrombosis & Pulmonary Embolism)
- ▶ Atrial Fibrillation
- ▶ Atrial Flutter
- ▶ Mechanical valve Replacement
- ▶ Bioprosthetic Valve Replacement
- ▶ Mitral Valve replacement
- ▶ Ischemic Stroke
- ▶ Deficiency of Protein C, S or Anti Thrombin
- ▶ Homozygous Factor V Leiden
- ▶ Coagulation Factor deficiency
- ▶ Intracardiac Thrombosis

CHA₂DS₂VASc vs CHAD Score

The CHA₂DS₂-VASc scheme was adopted by the ESC to complement the CHADS₂ scoring system

CHADS ₂	Score	CHA ₂ DS ₂ -VASc	Score
Congestive heart failure	1	Congestive heart failure/left ventricular dysfunction	1
Hypertension	1	Hypertension	1
Aged ≥75 years	1	Aged ≥75 years	2
Diabetes mellitus	1	Diabetes mellitus	1
Stroke/TIA/TE	2	Stroke/TIA/TE	2
Maximum score	6	Vascular disease (prior MI, PAD, or aortic plaque)	1
		Aged 65–74 years	1
		Sex category (i.e. female gender)	1
		Maximum score	9

CHA₂DS₂-VASc:

- In patients with a CHADS₂ score of 0–1, or
- When a more detailed stroke risk assessment is indicated

Camm et al. Eur Heart J 2010;31:2369–429

- ▶ CHA₂DS₂VASc to complement CHADS₂ score
- ▶ More literature on CHADS₂ score
- ▶ Some providers have been slow to adopt CHA₂DS₂VASc
 - ▶ Sticking to the devil they know vs the angel they don't know

Important in establishing duration of anticoagulation for atrial fibrillation patients

Learning Objectives

- ▶ Compare and contrast anticoagulation management in the community and the correctional setting
- ▶ Describe a clinical pharmacist anticoagulation management service collaborative practice agreement
- ▶ Evaluate Warfarin dosing using current guidelines and lessons learned

Anticoagulation in the Community vs Correctional Setting

Community Setting	Correctional Setting
Physical barriers	Security barriers
Easily accessible	Need security details
Easier access to the Pharmacist	Pharmacist's face to face limited
Transportation to a healthcare setting	Easier access to health care (walking distance)

Same Anticoagulants available to both Settings

Anticoagulation in the Community vs Correctional Setting

Community Setting	Correctional Setting
Point-of-Care Testing	Not available or difficulty in calibrating Point-of-Care Testing
Same day INR values	Usually available next day except STAT orders
Patients keep their warfarin/DOAC prescriptions as KOP	Warfarin rx usually DOT and DOACS maybe KOP

Same Anticoagulants available to both Settings

Learning Objectives

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Pharmacist-Managed Warfarin Therapy (PMWT)

Rationale

“Systematic and coordinated fashion, incorporating patient education, systematic INR testing, tracking, follow-up, and good patient communication of results and adjustments”

American College of Chest Physicians Guidelines for the management of Antithrombotic and Thrombolytic Therapy (CHEST Supplement, 8th ed, 2008)

“Acceptable intervals for PT/INR determinations are normally within the range of 1 to 4 weeks after a stable dosage has been determined... Time in therapeutic range is significantly greater in patients managed by anticoagulation clinics, among self-testing and self-monitoring patients, and in patients managed with the help of computer programs”



Pharmacist-Managed Warfarin Therapy (PMWT)

Rationale

- ▶ Pharmacist managed anticoagulation has a role
- ▶ Anticoagulation management services are well known to improve
 - ▶ quality of patient care
 - ▶ reduce the rates of hospitalization and emergency department visits following adverse events related to anticoagulation therapy
 - ▶ The complexity of managing warfarin has led to the development of a variety of specialized models managed by pharmacists, physicians, nurses, and self-managed care

A systematic review on comparing 2 common models for management of warfarin therapy; pharmacist-led service versus usual medical care

- ▶ Of 758 potential articles identified, 24 studies (4 randomized controlled trials [RCT] and 20 non-RCT studies) with a population of 11,607
- ▶ The percentage of time in the therapeutic range (72.1% vs 56.7%; $P = .013$)
- ▶ Major bleeding events (0.6% vs 1.7%, $P < .001$), thromboembolic events (0.6% vs 2.9%; $P < .001$), hospitalization (3% vs 10%; $P < .001$)
- ▶ Emergency department visits (7.9% vs 23.9%; $P < .0001$) significantly favored PMWT
- ▶ Study supported PMWT regarding cost saving and patient satisfaction
- ▶ The results showed that the PMWT model is superior to UMC in managing warfarin therapy based on observational studies

Pharmacist-Managed Warfarin Therapy (PMWT)

Rationale

- ▶ Anticoagulation management should be:
 - ▶ Systematic
 - ▶ Standardized
 - ▶ Coordinated
 - ▶ Intensive
- ▶ Effective anticoagulation management results in:
 - ▶ Improved patient outcomes
 - ▶ Efficacy: Time within therapeutic range
 - ▶ Safety: Reduction in major bleeding events
 - ▶ Enhanced patient satisfaction

“High-quality anticoagulation management is required to keep these narrow therapeutic index medications as effective and safe as possible”

Pharmacist-Managed Anticoagulation in a Correctional Setting

- ▶ Michigan Department of Corrections
- ▶ Pilot started in 2017 with 4 high acuity Sites
- ▶ Collaborative Practice Agreement
- ▶ Team-Members (Team Work at its best)
 - ▶ Medical Providers (SMD, RMD, MPs, Hematology/Oncology Specialist)
 - ▶ Nursing staff (DONS, HUMs, RN13, Med room Staff)
 - ▶ Phlebotomist
 - ▶ Pharmacy staff
 - ▶ custody

**Clinical Pharmacist Anticoagulation Management Service Collaborative
Practice Agreement**

Date Reviewed/Revised: 10.22.2021

Clinical Pharmacist Anticoagulation Management Service Collaborative Practice Agreement

Date Reviewed/Revised: 10.22.2021

Signed Document that gives the Clinical Pharmacist warfarin prescribing/monitoring authority

Clinical Pharmacist Anticoagulation Management Service Collaborative Practice Agreement Date Reviewed/Revised: 10.22.2021	
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Clinical Pharmacist Anticoagulation Services

Ordering PT/INR labs (PT2) in COMS

Warfarin Dose changes to minimize adverse effects
DOAC Recommendation – via NF approval

Routine review of patients' pharmacotherapies for drug-drug interactions
Review history of diagnosis and determine duration of anticoagulation

Anticoagulation consultation services to other MDOC Sites

Duration of Anticoagulation Therapy

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Indication	INR (Range)	Duration	Comments
Thrombophilia with Thromboembolic Event			
Thromboembolism (DVT, PE) symptomatic or asymptomatic			
Provoked VTE event	2.5 (2-3)	3 months	dabigatran, rivaroxaban, apixaban, or edoxaban are recommended over VKA (2B) and VKA therapy is recommended over low molecular weight heparin (LMWH; (2C))
Unprovoked: 1st VTE event			
- Proximal or Distal DVT	2.5 (2-3)	3 months	Extend therapy for low or moderate risk of bleeding (Grade 2B) Continue with ASA after anticoagulation stops
- PE	2.5 (2-3)	3 months	Re-evaluate for longer therapy (2B)
Unprovoked: 2nd VTE event			
- DVT or PE	2.5 (2-3)	> 3 months	Consider Long-term
With malignancy	2.5 (2-3)	> 3 months	LMWH is recommended over VKA (2B) or any direct oral anticoagulants (2C) Consider Long-term
Acute Upper Extremity DVT			
- Associated with central venous catheter that was removed	2.5 (2-3)	3 months	
- Associated with central venous catheter that was NOT removed	2.5 (2-3)	extended	Continue anticoagulation until catheter removed
- Not associated with a central venous catheter	2.5 (2-3)	3 months	
Spontaneous superficial vein thrombosis	None	45 days	Prophylaxis LMWH or Fondaparinux
Thrombophilia with Thromboembolic Event			
Homozygous Factor V Leiden	2.5 (2-3)	indefinite	
Deficiency of Protein C, S or Anti-Thrombin	2.5 (2-3)	indefinite	
Antiphospholipid Syndrome			
No additional risk factor	2.5 (2-3)	indefinite (2B)	
Recurrent DVT/PE with therapeutic INR	3.0(2.5-3.5)	indefinite (2B)	
Atrial Fibrillation (AF)/ Atrial Flutter⁵			
CHA2DS2VASc = 0; Low stroke risk	None	May choose aspirin 75-325 mg daily	
CHA2DS2 VASc ≥ 1; Intermediate/High stroke risk	2.5 (2-3) or dabigatran	Chronic	Anticoagulation CI: aspirin 75-325 mg and clopidogrel 75 mg daily
CHA2DS2-VASc * ≥ 2 (high CVA risk)	2.5 (2-3) or dabigatran	long-term	
Thrombophilia with Thromboembolic Event			
Antiphospholipid Syndrome	2.5 (2-3)	long-term	
Homozygous Factor V Leiden	2.5 (2-3)	long-term	
Deficiency of Protein C, S or Anti-Thrombin	2.5 (2-3)	long-term	
Atrial Fibrillation (AF)/ Atrial Flutter⁵			
Pre-cardioversion (AF or flutter >48 hours)	2.5 (2-3)	3 weeks	
Post-cardioversion (in NSR)	2.5 (2-3)	4 weeks	
Ischemic Stroke⁶			
Non-cardioembolic stroke or TIA	None	long-term	Use antiplatelet therapy
Cardioembolic stroke or TIA		long-term	
-With warfarin CI	None	long-term	Aspirin 81-325 mg daily
Ischemic Stroke⁶			
-With cerebral venous sinus thrombosis	2.5 (2-3)	3-6 months	
- With patent foramen ovale	None	long-term	Use antiplatelet therapy

Indication	INR (Range)	Duration	Comments
Mechanical Heart Valve			
Aortic	2.0-3.0	long-term (1B)	
-AF, anterior-apical STEMI, enlarged left atrium, hypercoagulable state, or low ejection fraction	2.5-3.5	Long term	
-Caged ball/Cage disk mechanical valve	2.5 – 3.5	Long term	
Mitral	2.5-3.5	long-term (2C)	
Bioprosthetic Heart Valve			
Aortic	N/A		Aspirin 50-100mg (2C)
Thromboembolic complications while INR 2-3	2.5 – 3.5	Long term	
Mitral	2.0-3.0	3 months	Then switch to ASA (2C)
-history of systemic embolization	2.0-3.0	3 months	Then reassess
-left atrial thrombus at surgery	2.0-3.0		Until thrombus resolves
-risk factors (AF, hypercoagulable state, low ejection fraction)	2.0-3.0	Long term	
Valvular Disease⁸			
Rheumatic mitral valve disease			
- Left atrial diameter < 55 mm	None		
- With AF, left atrial thrombus, or left atrial diameter > 55 mm	2.5 (2-3)	Long term	
Rheumatic mitral valve disease			
- Left atrial diameter < 55 mm	None		
- With AF, left atrial thrombus, or left atrial diameter > 55 mm	2.5 (2-3)	Long term	
Valve Repair			
Aortic	None		Aspirin 81 mg daily
Mitral	None	3 months	Antiplatelet therapy
Valve Replacement - Bioprosthetic			
Aortic or TAVI*	None		Antiplatelet therapy
Mitral	2.5 (2-3)	3 months	Followed by aspirin 81 mg daily
Valve Replacement - Mechanical			
Aortic	2.5 (2-3)	Chronic	Low bleed risk: add aspirin 81 mg
Mitral	3 (2.5-3.5)	Chronic	Low bleed risk: add aspirin 81 mg
Dual Aortic and Mitral Valve	3 (2.5 -3.5)	Chronic	Low bleed risk: add aspirin 81 mg
Orthopedic Surgery⁹			
Total Knee or Hip Arthroplasty**	1.8-2.2	10-14 days	
Hip Fracture Surgery**	1.8-2.2	10-14 days	
Trauma Surgery**	1.8-2.2	35 days	

Pharmacist-Managed Anticoagulation in a Correctional Setting

Facility	Active Patients (Sept 2021)	D/C Patients
Site A	32	26
Site B	32	41
Site C	14	35
Site D(W)	11	12
Total	89	112

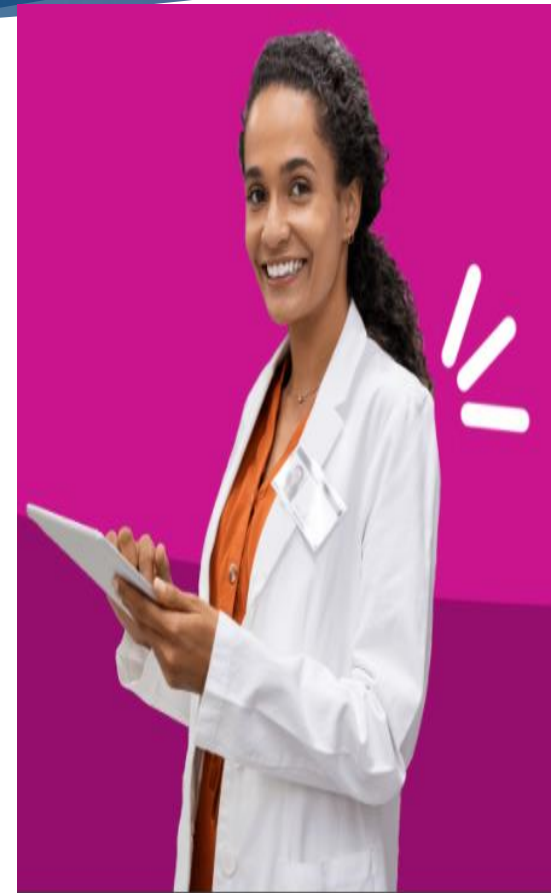
201 total
warfarin
patients
enrolled

Average
250 total
warfarin
patients per
month

Cost avoidance = \$1.5million
annually

How Does this work at our DOC

- ▶ Scheduled days for PT/INR lab draws
 - ▶ Values become available next day
- ▶ 5-10 hours per week needed for the clinical intervention
- ▶ Warfarin rx orders entered into the patient's profile along with a note
- ▶ Site notified of warfarin dose changes



Pharmacist-Managed anticoagulation

Positive Outcomes

- ▶ Safe and cost-effective anticoagulation therapy
 - ▶ Reduce toxicity with extended anticoagulation than required
- ▶ ↑ communication among team members
- ▶ Timely interventions resulting in reduction of drug-drug interactions, minimizing the risks of bleeding
- ▶ Reducing ER runs by stocking vit k (Phytonadione) on Site, fast reversal of supratherapeutic patients
- ▶ Non-Formulary approval by Pharmacist, ensuring DOACs are approved for the right patients
- ▶ INR therapeutic >70% of the time
- ▶ Minimize frequent dose changes by optimizing the current dose
- ▶ Improved patient, Provider and Client satisfaction
 - ▶ “Happy Providers” and Partners (clients)

Pharmacist-Managed anticoagulation

Down Side

- ▶ Very time consuming
- ▶ Lack face-to-face communication with the patients
- ▶ Unreported missed doses (non-adherence) & no notes in the EHR
- ▶ Missed labs or Stat labs not readily available in the patients chart

Learning Objectives

- ▶ Compare and contrast anticoagulation management in the community and the correctional setting
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Available Anticoagulants

- ▶ Warfarin
- ▶ DOACs

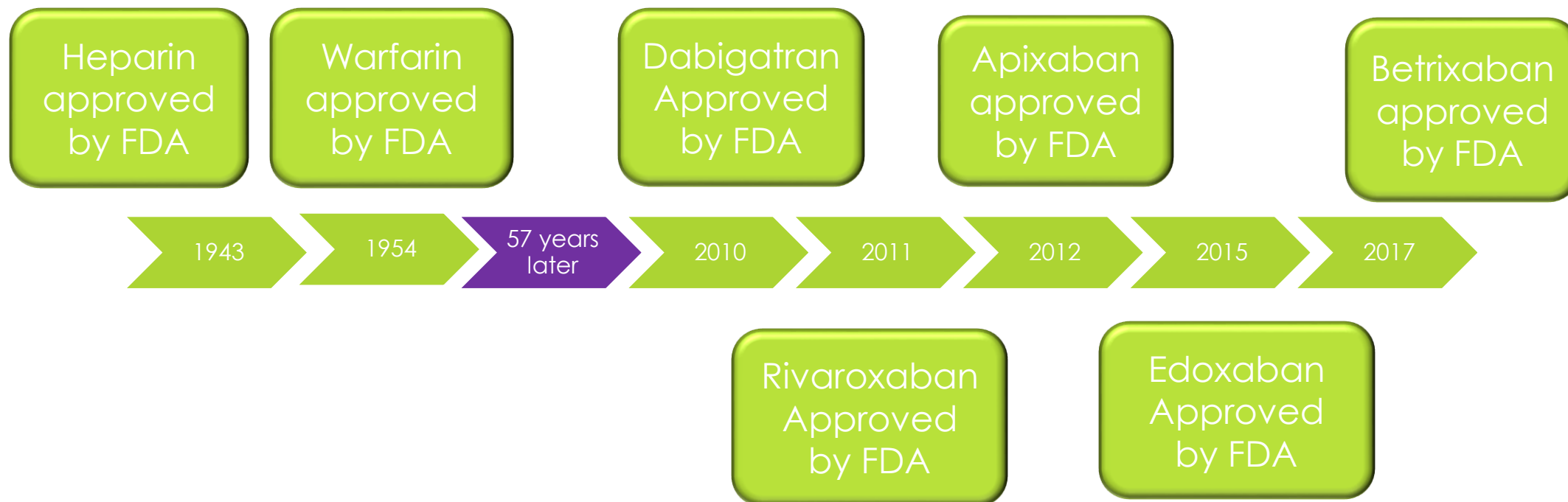


Pink	Lavender	Light Green	Tan	Blue	Peach	Teal	Yellow	White
1 mg	2 mg	2½ mg	3 mg	4 mg	5 mg	6 mg	7½ mg	10 mg

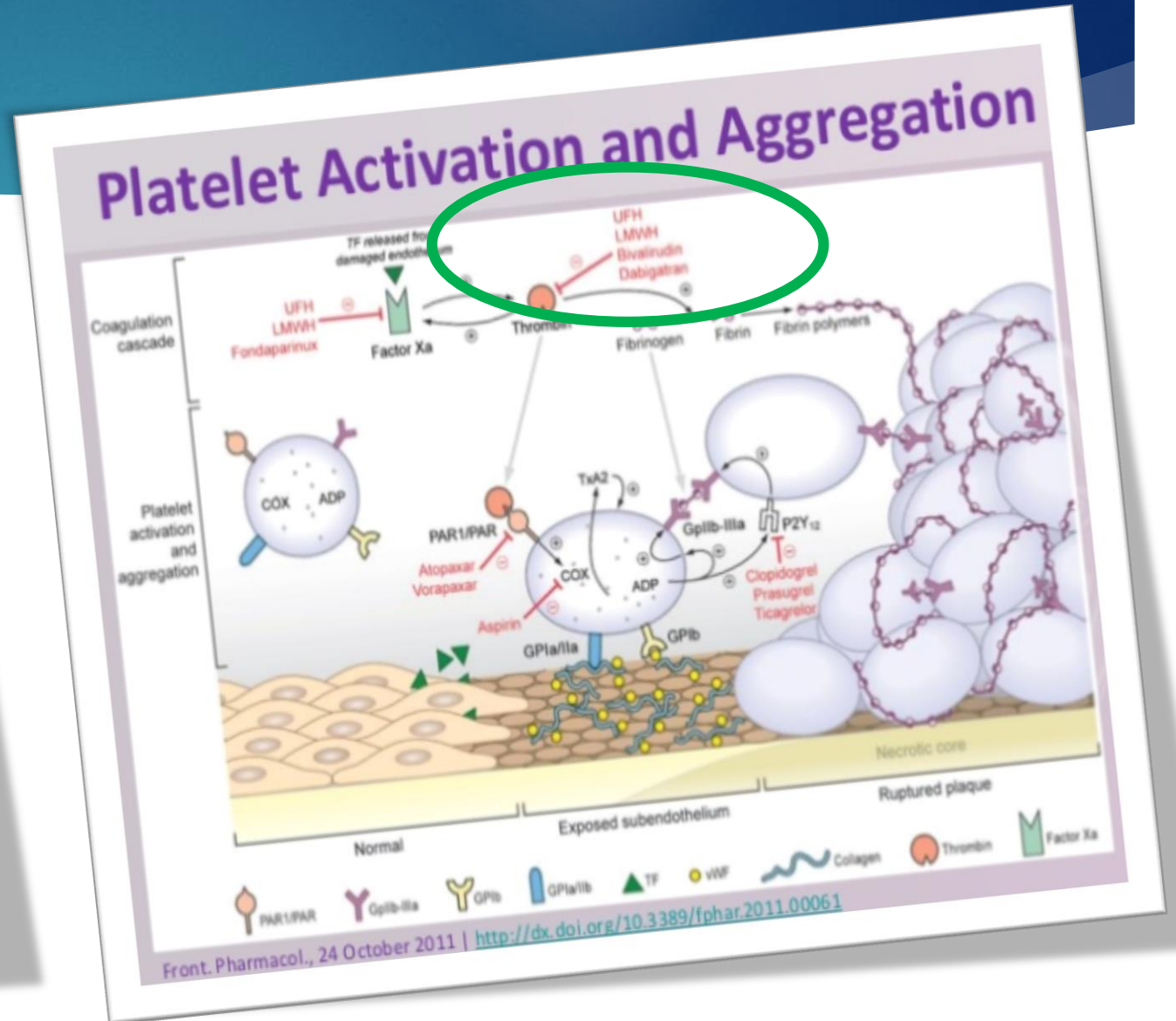
Warfarin Tablet Colors

1 mg	PLEASE	Pink
2 mg	LET	Lavendar
2.5 mg	GRANNY	Green
3 mg	BROWN	Brown
4 mg	BRING	Blue
5 mg	PEACHES	Peach
6 mg	TO	Teal
7.5 mg	YOUR	Yellow
10 mg	WEDDING	White

Anticoagulant Time line



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The Good Old Warfarin

WARFARIN

almost 70 years old and still causing problems...

Still we have to stick with it...

Mechanism of Action	Organ adjustments	Metabolic Interactions	Adverse Effects	Contraindications
Inhibits synthesis of vitamin K-dependent clotting factors (2, 7, 9 and 10, and proteins C and S)	No renal adjustments Hepatic caution (increases INR)	CYP3A4 substrates CYP1A2 substrates CYP2C9 substrates Vitamin K Alcohol intake	Hemorrhage Tissue Necrosis Hepatic injury Hair Loss Chills	Pregnancy Hemorrhagic tendencies or blood dyscrasias
Reversal Agent: Vitamin K				

Warfarin Review

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- ▶ Clearance is slow - 36 hrs
- ▶ Delayed onset 8 - 12 hrs
- ▶ Overdose - reversed by vitamin K infusion or PO
- ▶ Can cross placenta - do not use during late pregnancies

INR Goals for Warfarin

Standard: 2.0-3.0

Aortic or Mitral mechanical valve: 2.5-3.5

Thrombosis $2.0 < \text{INR} > 3.0$ Bleeding

Goal is also subject to adjustment based on patient risk factors

Warfarin

Pros vs Cons

Pros

- ▶ Many years of experience
 - ▶ Hypercoagulability
 - ▶ Heart valves
 - ▶ ESRD
- ▶ Measurable anticoagulation (can be monitored)
- ▶ Cost effective
- ▶ Can be reversed
- ▶ Once daily dosing

Cons

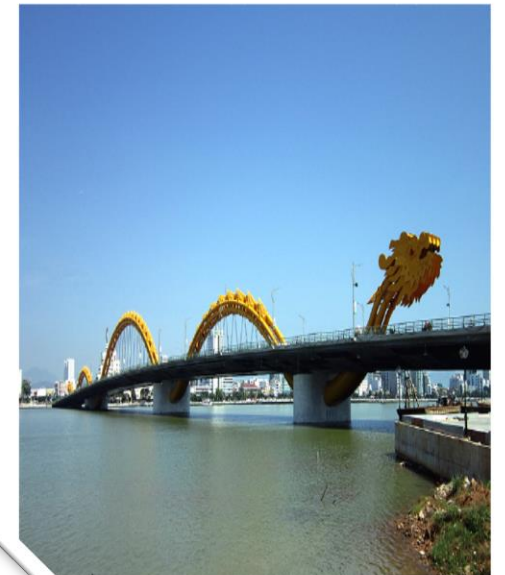
- ▶ Slow onset of action
- ▶ Many food/drug interaction
- ▶ More intracranial bleeds
- ▶ Monitoring requirements
- ▶ Varied dosing requirement
 - ▶ Elderly (>70 years), Malnourished, Active malignancy, High risk bleeding, Liver impairment, Low body weight (<50kg), ESRD, DDR

Warfarin

Limitations

- ▶ Unpredictable response
- ▶ Narrow therapeutic index (range 2-3)
- ▶ Need coagulation monitoring
- ▶ Frequent dose adjustment
- ▶ Slow onset of action (Bridge with LMWH)
- ▶ Numerous food-drug interactions and drug-drug interactions

Bridging



DOACs Comparison & Warfarin

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Parameters	Warfarin	Apixaban	Dabigatran	Edoxaban	Rivaroxaban
Bioavailability	>95%	50%	3-7% (Prodrug)	62%	10mg :80-100% 20mg: 66%
Time to Cmax	72-96 hours	3-4hours	1 hour	1-2 hours	2-4 hours
Half-Life	40 hours	12 hours	12-17 hours	10-14 hours	5-9 hours 11-13 hours (elderly)
Dosing frequency	Daily	BID	BID	Daily	Daily
Adjustments for renal Failure	No	Yes, adjust id Scr >1.5 (including ESRD w/HD if ≥80yo or ≤ 60Kg	Yes, avoid if CrCl <15mg/mL	Yes, avoid for NVAf if CrCl >95mg/ml or <15mg/ml	Yes, VTE: avoid for CrCl <30mg/ml NVAf: if CrCl <15mg/ml
Metabolism	Hepatic (2C9, 1A2, 2C19 & 3A4)	Hepatic	Renal: 80% Substrate P-gp	Largely uncharged (minimally CYP 450)	1/3 Renally unchanged 2/3 3A4 & P-gp
Elimination	92% renal	27%renal 63%fecal	80% renal 20% fecal	50% renal 50% biliaryand fecal	66% renal 33%fecal
Plasma protein binding	97%	87%	34-35%	55%	92-95%
Clinical Pearls	1. Cost effective	1. No food not needed for absorption 2. Concomitant chronic NSAIDS allowed in one study	1. Take with food 2. Not recommended if previous MI 3. 5-10days or parenteral tx recommended for new VTE	1. 5-10days or parenteral tx recommended for new VTE 2. CrCl <95mg/ml to initiate thx	1. Take with food 2. Concomitant clopidogrel allowed in studies

Direct Oral Anticoagulants (DOACs)

Agent	Mechanism of Action	Adverse Effects	Warnings/ Contraindication
Apixaban (Eliquis) 2.5, 5mg	Directly inhibits clotting factor Xa; resulting in decreased thrombin generation	Bleeding	CI: Active Pathological Bleeding Prosthetic Heart Valves Antiphospholipid syndrome
Rivaroxaban (Xarelto) 2.5, 10mg 15, 20mg			
Edoxaban (Savaysa) 15, 30, 60mg			
Dabigatran (Pradaxa) 75, 110, 150mg			

Rivaroxaban & Apixaban FDA Approved Reversal Agent: Andexaa (coagulation factor Xa (modified human recombinant))

FDA Approved Reversal Agent: Praxbind (idarucizumab) – binds to dabigatran to neutralize anticoagulative effect

Anticoagulants

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Generic Name	Brand Name	Strength	Dosage Forms	Dosing Frequency	Average Cost per 30 days
Warfarin	Coumadin	1mg, 2mg, 2.5mg, 3mg, 4mg, 5mg, 6mg, 7.5mg & 10mg	Tablets	QD	\$10
Heparin	Calcilean	10units, 100units	Inj	Varies	??
Enoxaparin	Lovenox	30-300mg	Inj	BID SQ	Varies
Rivaroxaban	Xarelto	10mg, 15mg & 20mg	Tablets	10-20mg PO QPM ± Food	\$500
Apixaban	Eliquis	2.5mg & 5mg	Tablets	2.5-5mg PO BID	\$530
Dabigatran	Pradaxa	75mg, 110mg & 150mg	Capsules	75-150mg PO BID	\$500
Edoxaban	Savaysa	15mg, 30mg & 60mg	Tablets	15-60mg QD	\$390
Betrixaban	Bevyxxa	40mg & 80mg	Capsules	40-80mg QD	\$1,800

DOACS: Pros vs Cons

Pros	Clinical Implication
Rapid onset of action	No need for Bridging
Specific coagulation enzyme target	Low risk of off-target adverse effect
Low potential for food and drug interactions	No dietary precautions and few drug restrictions
No frequent monitoring and dose adjustments	Increase adherence
Predictable dose response & predictable anticoagulant effect	Less major bleeding
Oral dosing	Increase adherence
Most have minimal/tolerable non-bleeding side effects	

Cons:

- ▶ Expensive
- ▶ ↑bleeding with advance age
- ▶ No data on special population
 - ▶ Prosthetic heart valve
 - ▶ Pregnancy
 - ▶ Pediatrics

Risk Factors for Bleeding Anticoagulation Therapy

- ▶ Age >65 yo
- ▶ History of bleeding
- ▶ Cancer
- ▶ Metastatic cancer
- ▶ Renal failure
- ▶ Liver failure
- ▶ Thrombocytopenia
- ▶ Previous stroke
- ▶ Diabetes
- ▶ Anemia
- ▶ Antiplatelet therapy
- ▶ Poor anticoagulant control
- ▶ Comorbidity and reduced functional capacity
- ▶ Recent surgery
- ▶ Alcohol abuse
- ▶ Nonsteroidal anti-inflammatory drug

What is on the Scale: Weighing the Risks vs Benefits of an Intervention

Balance the benefits
(Safety & Efficacy vs
risks (Bleeding or
other side effects)



- Lower major bleeding with Apixaban & dabigatran
- Rivaroxaban equivalent to warfarin

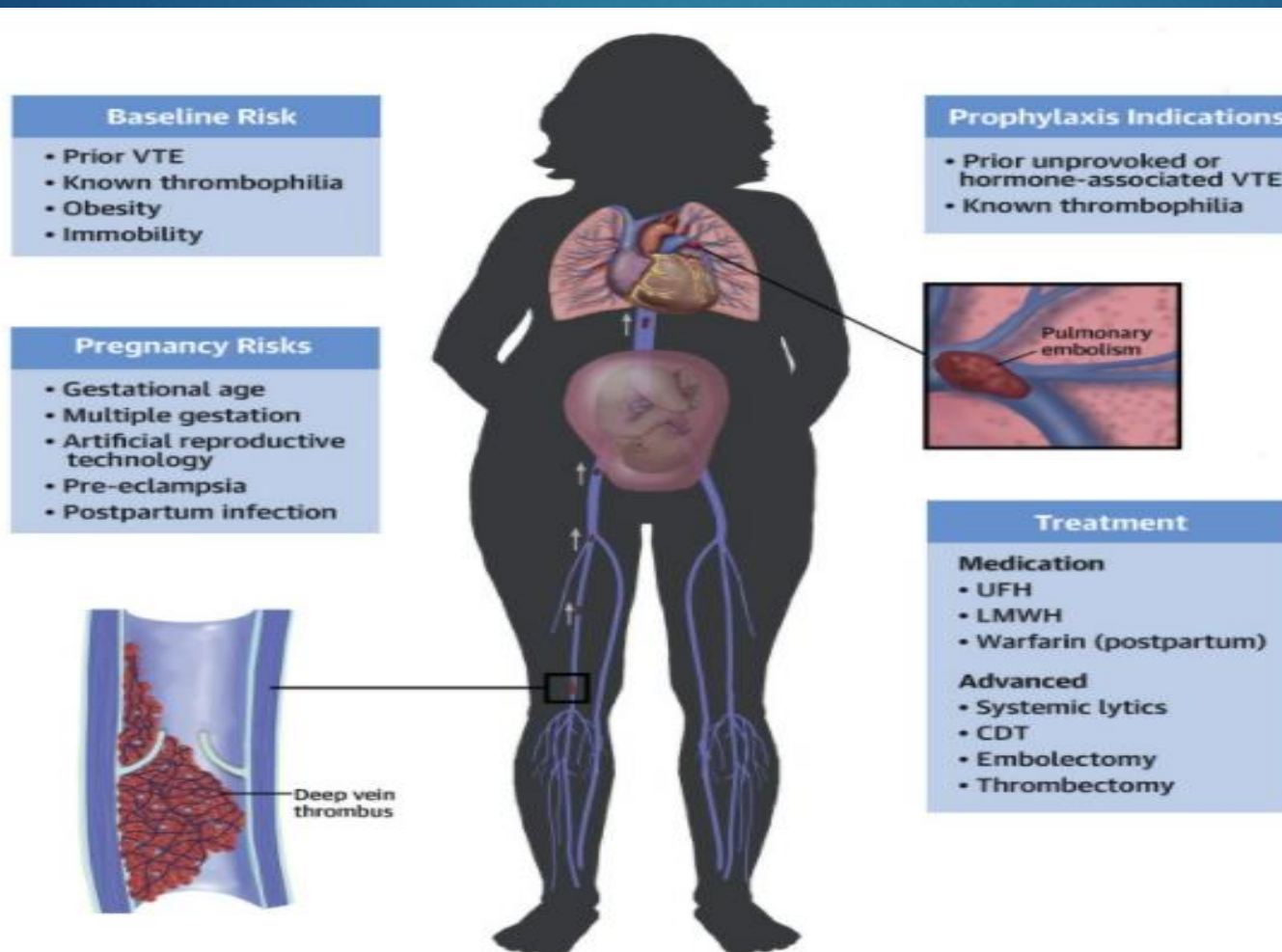
Duration of Anticoagulation

Indication	Duration of Therapy	Comments
First VTE episode secondary to a reversible or transient risk factor	3 months	Applies to proximal DVT and PE
First episode of unprovoked VTE	>3months	Evaluate the risk-benefit of indefinite therapy and reassess periodically
First episode of VTE with inherited or acquired thrombophilia	>3months	Evaluate the risk-benefit of indefinite therapy and reassess periodically
First Episode of cancer-associated VTE	>3-6 months and consider extending duration until cancer resolves and cancer treatment completed	LMWH, rivaroxaban, or edoxaban are preferred over other agents in this case, warfarin non-inferior
Second VTE (provoked or unprovoked)	Indefinite	Applies to patients who are not at high risk of bleeding

Anticoagulation Monitoring

- ▶ Important for Safety and efficacy
- ▶ Anticoagulant dosing may be adjusted based on
 - ▶ activated partial thromboplastin time (aPPT)
 - ▶ anti-factor Xa level (LMWH &)
 - ▶ prothrombin Time (PT)
 - ▶ international normalized ratio (INR)

Care of VTE in Pregnant Patients

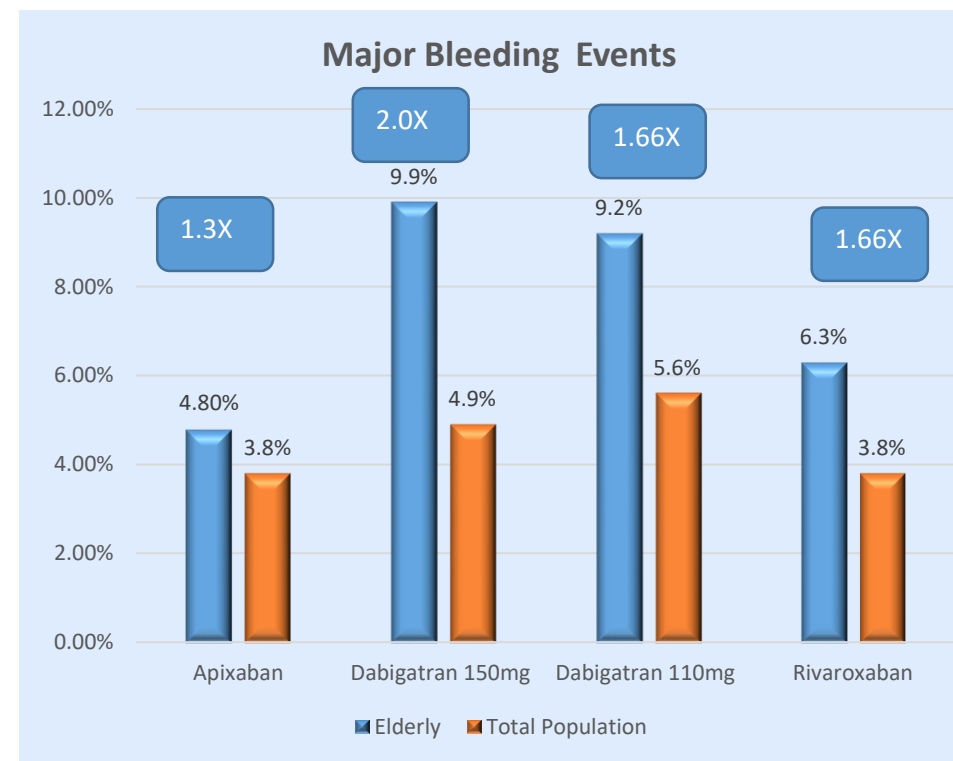


Anticoagulation in the Geriatric Population

- ▶ Systematic review and meta-analysis of randomized trials of DOACs for efficacy and safety outcomes compared to VKA in elderly participants (≥ 75 years) treated for acute VTE or stroke prevention in AF
- ▶ Efficacy in managing thrombotic risks for each DOAC was similar or superior to VKA in the elderly

Anticoagulation in the Geriatric Population

- ▶ Dabigatran
 - ▶ showed a significantly higher risk of gastrointestinal bleeding and a non significantly higher major bleeding risk than VKA
- ▶ Apixaban is slight safer for the elderly , but still with significant major bleeding



Lessons Learned

Critical Role of a Clinical Pharmacist in Anticoagulation Management

- ▶ Polypharmacy
 - ▶ Decreases therapeutic outcomes for anticoagulation
 - ▶ Pharmacist can play an important role here
- ▶ Duration of Anticoagulation Therapy
 - ▶ Thorough history and chart search
 - ▶ Appropriate duration of thx decrease toxicity to patients
- ▶ Non-Adherence
 - ▶ Communicate with the Provider and medroom staff
 - ▶ Minimize pill burden and frequent dose change

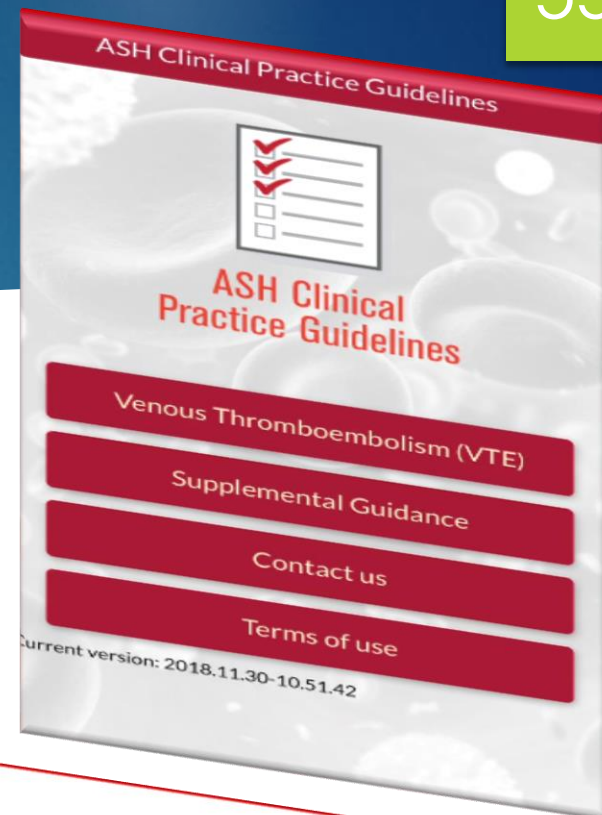


Current Guidelines

Management of Anticoagulation Therapy for Venous Thromboembolism Clinical Practice Guidelines (2019)

American Society of Hematology (ASH)

Reviewed and summarized by Medscape editors
January 31, 2019



ASH CLINICAL PRACTICE GUIDELINES VENOUS THROMBOEMBOLISM (VTE)

Current Guidelines

ACC.org | Guidelines | C

JACC
JOURNAL OF THE AMERICAN COLLEGE OF CARDIOLOGY

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JACC Journals **Issues** **Topics** **Multimedia** **Guidelines**

Journal of the American College of Cardiology

January 2019
DOI: 10.1016/j.jacc.2019.01.011
Just Accepted

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/American Heart Association Task Force on Clinical Practice Guidelines and the Heart Rhythm Society

Craig T. January, L. Samuel Wann, Hugh Calkins, Lin Y. Chen, Joaquin E. Cigarroa, Joseph C. Cleveland Jr., Patrick T. Ellinor, Michael D. Ezekowitz, Michael E. Field, Karen L. Furie, Paul A. Heidenreich, Katherine T. Murray, Julie B. Shea, Cynthia M. Tracy and Clyde W. Yancy

PDF Article

ELSEVIER Check for updates

Canadian Journal of Cardiology 34 (2018) 1371–1392

Society Guidelines

2018 Focused Update of the Canadian Cardiovascular Society Guidelines for the Management of Atrial Fibrillation

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AMERICAN COLLEGE of CARDIOLOGY

CHEST Guideline on Antithrombotics for Atrial Fibrillation

Aug 29, 2018 | Geoffrey D. Barnes, MD, MSc, FACC

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Authors:

Citation:

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ESC European Society of Cardiology

European Heart Journal (2018) 39, 1330–1393
doi:10.1093/eurheartj/ehy136

SPECIAL ARTICLE

The 2018 European Heart Rhythm Association Practical Guide on the use of non-vitamin K antagonist oral anticoagulants in patients with atrial fibrillation

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Document reviewers (ESC scientific document group): Gregory YH Lip (EHRA Review Coordinaor; UK, Denmark), Jeffrey Weitz (Canada), Laurent Fauchier (France), Deirdre Lane (UK), Giuseppe Boriani (Italy), Andreas Goette (Germany), Roberto Keegan (Argentina), Robert MacFadyen (Australia), Chern-En Chiang (Taiwan), Boyoung Joung (Korea), and Wataru Shimizu (Japan)

CHEST Guidelines Executive Summary (updated 2021)

- ▶ VTE recommend apixaban, dabigatran, edoxaban, or rivaroxaban over VKA as treatment-phase (first 3 months) anticoagulant therapy (strong recommendation, moderate-certainty evidence)
- ▶ Considerations for DOACs: comparable efficacy, improved safety, greater convenience
- ▶ Considerations for VKA: extremes of weight, severe renal impairment, presence of antiphospholipid syndrome, cost

Pause & Think: Case 1

- ▶ BB is a 55yo female with a history of DVT RLE for 2months. She is also no other prior history. BB is a very pleasant patient and likes to share personal stories with you when she visits. BB is here today for her next warfarin dose and mentions to you prior to her DVT, she had been involved in a car accident that resulted in fractured bones on both of her legs a few weeks before her DVT dx.
- ▶ Her wt.: 200lb & BP 133/85
- ▶ She is currently on warfarin 7.5mg daily (52.5mg weekly) and her INR a week ago was 1.58: range 2-3

Pause & Think: Question 1

- ▶ What is the appropriate duration of therapy for BB?
- A. BB has an unprovoked DVT continue Anticoagulation for 12months
- B. BB has a provoked DVT continue her anticoagulation for 12 months
- C. BB has an unprovoked DVT continue her therapy indefinitely
- D. BB has a provoked DVT continue her anticoagulation for another 3months
- E. BB has a unprovoked DVT continue her anticoagulation for another 3months

Pause & Think: Question 2

- ▶ You are the Pharmacist at the Anticoagulation Clinic today, how would you optimize BB warfarin therapy?
- A. Increase her Warfarin dose by 12mg weekly
- B. Increase her warfarin dose by 4mg weekly
- C. Decrease her dose by wartarin12mg weekly
- D. No change now, order her PT/INR labs for another week before adjusting her Warfarin dose

Pause & Think: Question 3

- ▶ At the clinic today, 1 week after her last warfarin dose change, her INR is 2.78, what should you do today?
- A. Increase her Warfarin dose by 2mg weekly to maintain within therapeutic limits
- B. Increase her dose by 5mg weekly
- C. Decrease her dose by 3mg weekly
- D. No change now, she is within therapeutic limits (2-3)

Pause & Think: Question 4

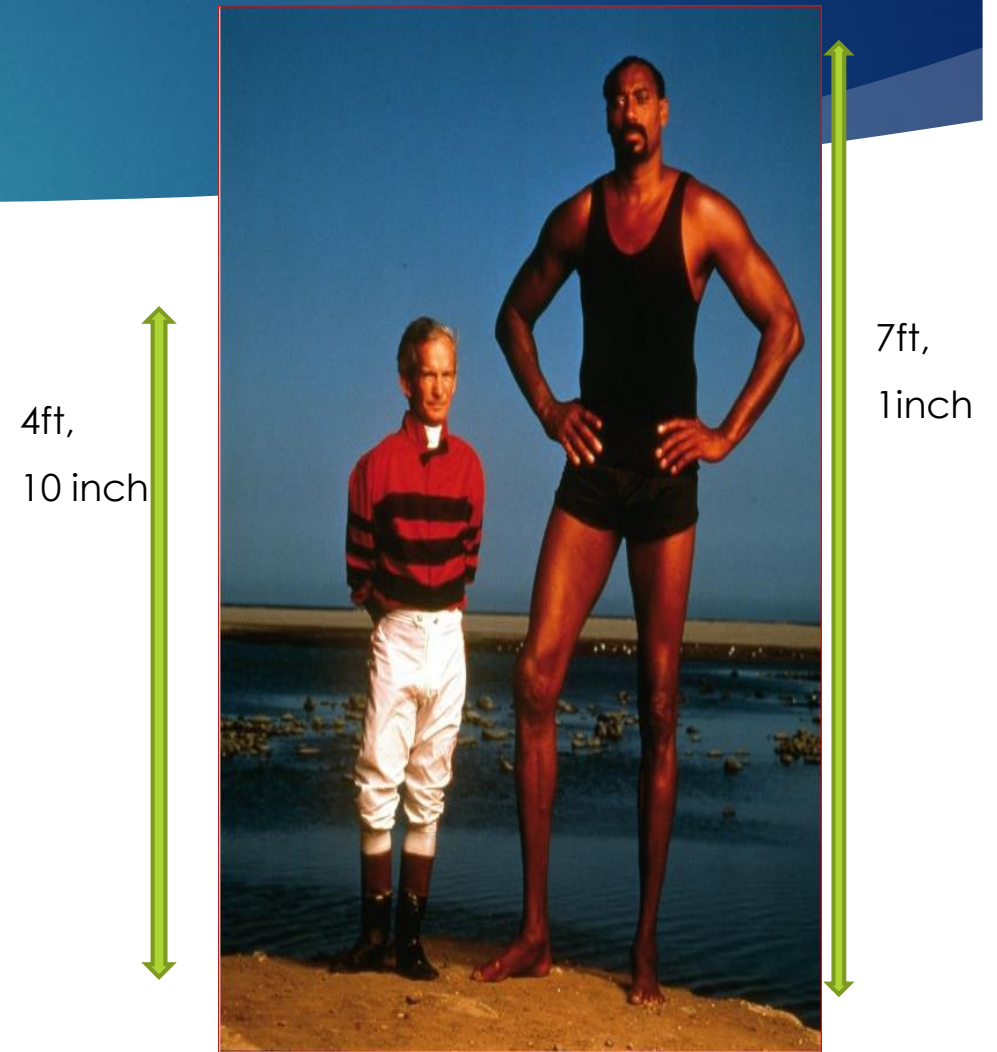
- ▶ Following your last recommendations of no dose change at the clinic today after a week her INR is 5.78, what should you do today?

What are you most concerned about her today and what are your recommendations?

- ▶ Diet? Addressed
- ▶ Bleeding?
- ▶ Adherence?
- ▶ Drug therapy-calcium carbonate (tums)TID PRN, sulfamethoxazole and trimethoprim (Bactrim DS) BID X10days from her other Provider
 - ▶ decrease warfarin dosing to 30% weekly dose till Bactrim DS is done

Anticoagulant Prescribing

- ▶ WC was diagnosed with acute proximal deep vein thrombosis. He is 7foot, 1 inch tall and weighs 330lbs (BSA = 3.0m^2)
 - ▶ WS was diagnosed with atrial fibrillation. He is 4 foot, 10 inch tall and weighs 90lbs (BSA = 1.29m^2)
 - ▶ What is the appropriate initial dose of Rivaroxaban for WS?
 - ▶ What is the appropriate correct initial dose of Rivaroxaban for WC?
- A. 15mg once daily
 - B. 15mg twice daily
 - C. 20mg once daily
 - D. 20mg twice daily
 - E. This is a \$\$\$\$ question



Willie Shoemaker & Wilt Chamberlain

Post-Test

- ▶ 50,000 people die annually of VTE in the USA, **No! 60,000-100,000**
- ▶ One-third (about 33%) of people with DVT/PE will have a recurrence within 10 years **YES**
- ▶ A pharmacist-Managed anticoagulation clinic is easy to establish and operate at every correctional facility, **No or maybe Yes**
- ▶ VTE is the leading cause of death in the USA. **It is the 3rd leading cause of death**
- ▶ VTE is more common in >55 year old women. **No one is immune to VTE**
- ▶ Warfarin is the anticoagulant of Choice at most DOC. **HMMM yes at mine**
- ▶ DOACs are a one size fit all. **No, evaluate patients for renal function and other factors**

Clinical Pearls and Take Away Message

- ▶ Anticoagulation management in the community and the correctional setting are different with more barriers to overcome in the correctional setting
- ▶ Different agents all have their place in therapy
- ▶ Clinical data, pharmacology, bleeding risk, and patient specific factors must be considered for safe use of anticoagulation
- ▶ Pharmacist-Managed anticoagulation in a correctional setting improves Patient outcomes
 - ▶ Improves quality of patient care
 - ▶ reduce the rates of hospitalization and emergency department visits following adverse events related to anticoagulation therapy
- ▶ DOACS May not be beneficial to the elderly
- ▶ Pharmacists may improve anticoagulation therapy by minimizing polypharmacy and non-adherence

AN OUNCE OF
PREVENTION IS
WORTH
A POUND OF CURE

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