ALLIANT HEALTH SOLUTIONS | HQIC Hospital Quality Improvement Contractors
CENTERS FOR MEDICARE & MEDICAID SERVICES
iQUALITY IMPROVEMENT & INNOVATION GROUP

HQIC Patient Safety: ADE

Welcome!

- All lines are muted, so please ask your questions in the Chat panel.
- For technical issues, chat to “All Panelists.”
- Please actively participate in polling questions that pop up on the lower right-hand side of your screen near the end of the presentation.

We will get started shortly!

HQIC Patient Safety: ADE

February 22, 2022

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Alliant Health Solutions

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Alabama Hospital Association

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Hospital Quality Improvement

Welcome from all of us!

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Adverse Drug Event Co-Leads

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Carol has over 20 years of experience in clinical nursing and quality improvement. She joined the Alabama Hospital Association as Quality Director in March 2021.

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Jennifer has 15 years of health care experience, including clinical pharmacy in the acute care hospital setting and in various roles at Alliant Health Solutions working on the CMS contract for the Quality Innovation Network–Quality Improvement Organization (QIN–QIO). She currently serves as the SME for Opioids and Adverse Drug Events for HQIC.

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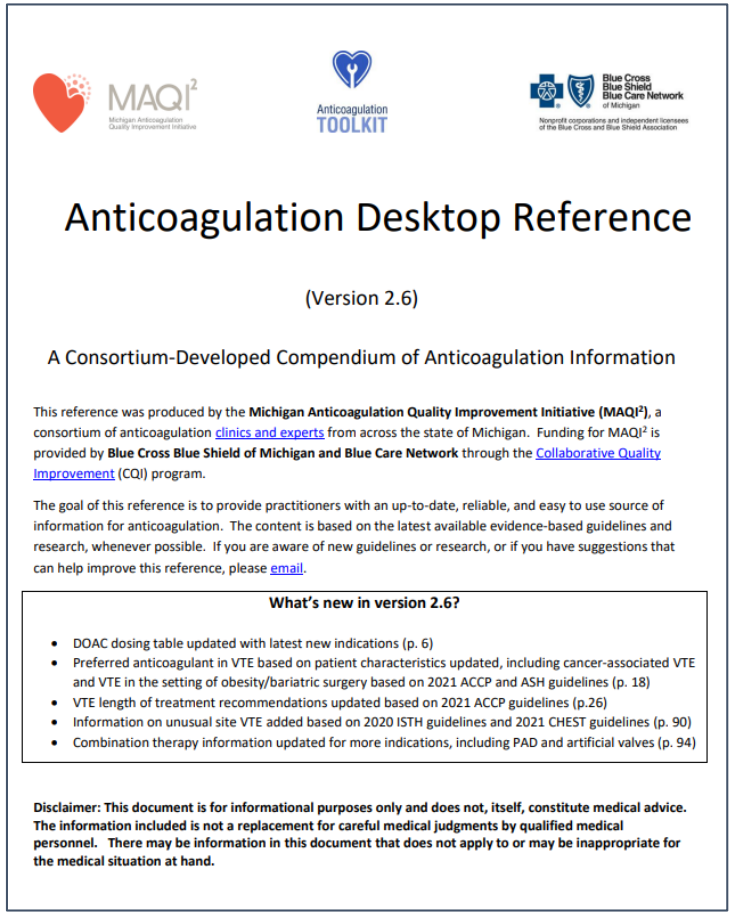
Learning Objectives

- Learn Today:
  - Going from RCA to change in practice using resources that are already available
    - Fishbone Diagram/Examples
    - Understand the Warfarin Adverse Event Analysis Form
    - Russell Medical Missed Opportunity Form
    - PDSA Cycle Example
- Use Tomorrow:
  - Post RCA tools and guidance

Anticoagulation Toolkit



MAQI² Michigan Anticoagulation Quality Improvement Initiative

Anticoagulation TOOLKIT

Blue Cross Blue Shield Blue Care Network of Michigan

Nonprofit corporations and independent licensees of the Blue Cross and Blue Shield Association

Anticoagulation Desktop Reference

(Version 2.6)

A Consortium-Developed Compendium of Anticoagulation Information

This reference was produced by the **Michigan Anticoagulation Quality Improvement Initiative (MAQI²)**, a consortium of anticoagulation clinics and experts from across the state of Michigan. Funding for MAQI² is provided by **Blue Cross Blue Shield of Michigan and Blue Care Network** through the Collaborative Quality Improvement (CQI) program.

The goal of this reference is to provide practitioners with an up-to-date, reliable, and easy to use source of information for anticoagulation. The content is based on the latest available evidence-based guidelines and research, whenever possible. If you are aware of new guidelines or research, or if you have suggestions that can help improve this reference, please email.

What's new in version 2.6?

- DOAC dosing table updated with latest new indications (p. 6)
- Preferred anticoagulant in VTE based on patient characteristics updated, including cancer-associated VTE and VTE in the setting of obesity/bariatric surgery based on 2021 ACCP and ASH guidelines (p. 18)
- VTE length of treatment recommendations updated based on 2021 ACCP guidelines (p.26)
- Information on unusual site VTE added based on 2020 ISTH guidelines and 2021 CHEST guidelines (p. 90)
- Combination therapy information updated for more indications, including PAD and artificial valves (p. 94)

Disclaimer: This document is for informational purposes only and does not, itself, constitute medical advice. The information included is not a replacement for careful medical judgments by qualified medical personnel. There may be information in this document that does not apply to or may be inappropriate for the medical situation at hand.

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(push Ctrl+F to search entire document for a keyword)

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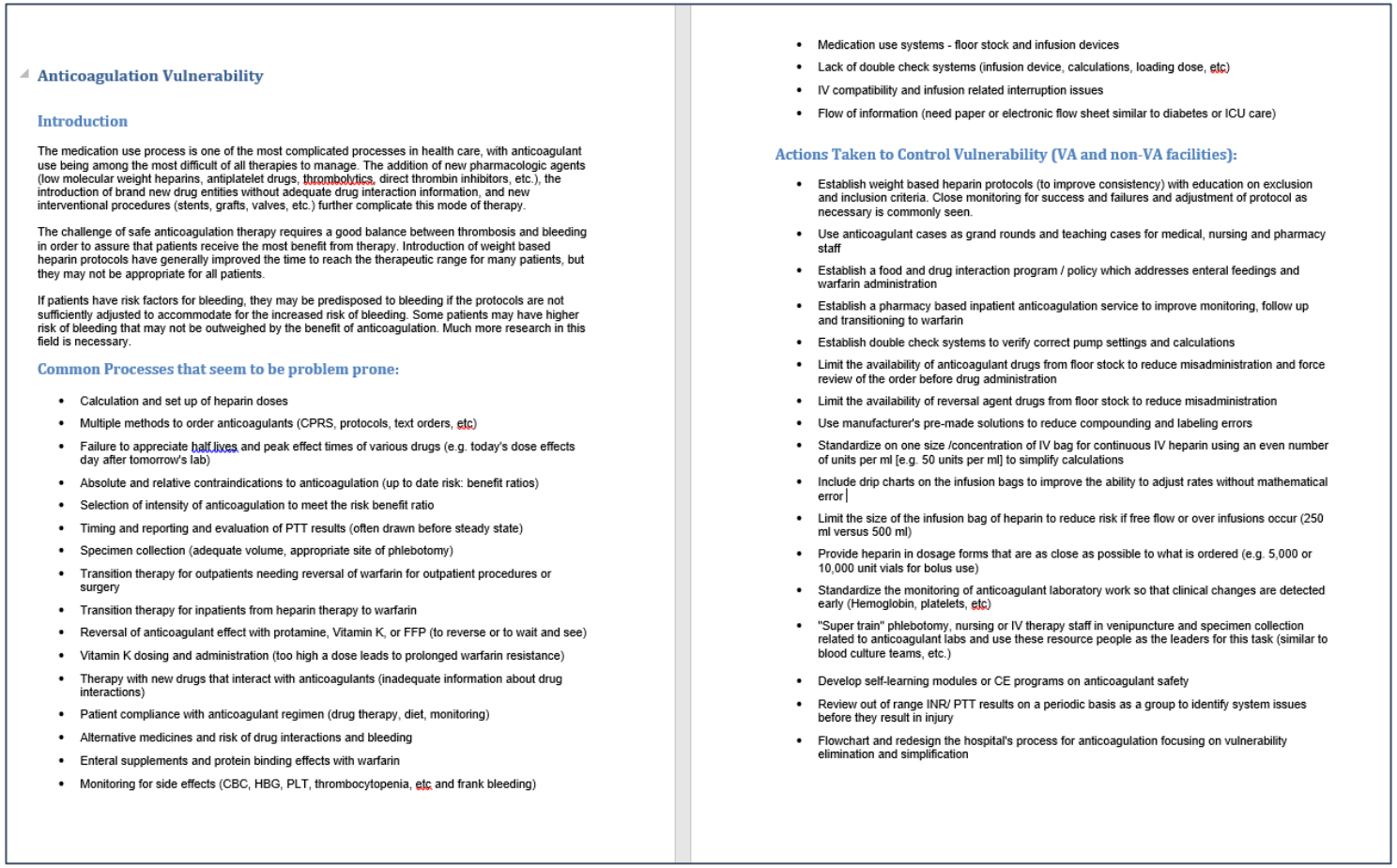
Anticoagulation Vulnerability Examples



Anticoagulation Vulnerability

Introduction

The medication use process is one of the most complicated processes in health care, with anticoagulant use being among the most difficult of all therapies to manage. The addition of new pharmacologic agents (low molecular weight heparins, antiplatelet drugs, thrombolytics, direct thrombin inhibitors, etc.), the introduction of brand new drug entities without adequate drug interaction information, and new interventional procedures (stents, grafts, valves, etc.) further complicate this mode of therapy.

The challenge of safe anticoagulation therapy requires a good balance between thrombosis and bleeding in order to assure that patients receive the most benefit from therapy. Introduction of weight based heparin protocols have generally improved the time to reach the therapeutic range for many patients, but they may not be appropriate for all patients.

If patients have risk factors for bleeding, they may be predisposed to bleeding if the protocols are not sufficiently adjusted to accommodate for the increased risk of bleeding. Some patients may have higher risk of bleeding that may not be outweighed by the benefit of anticoagulation. Much more research in this field is necessary.

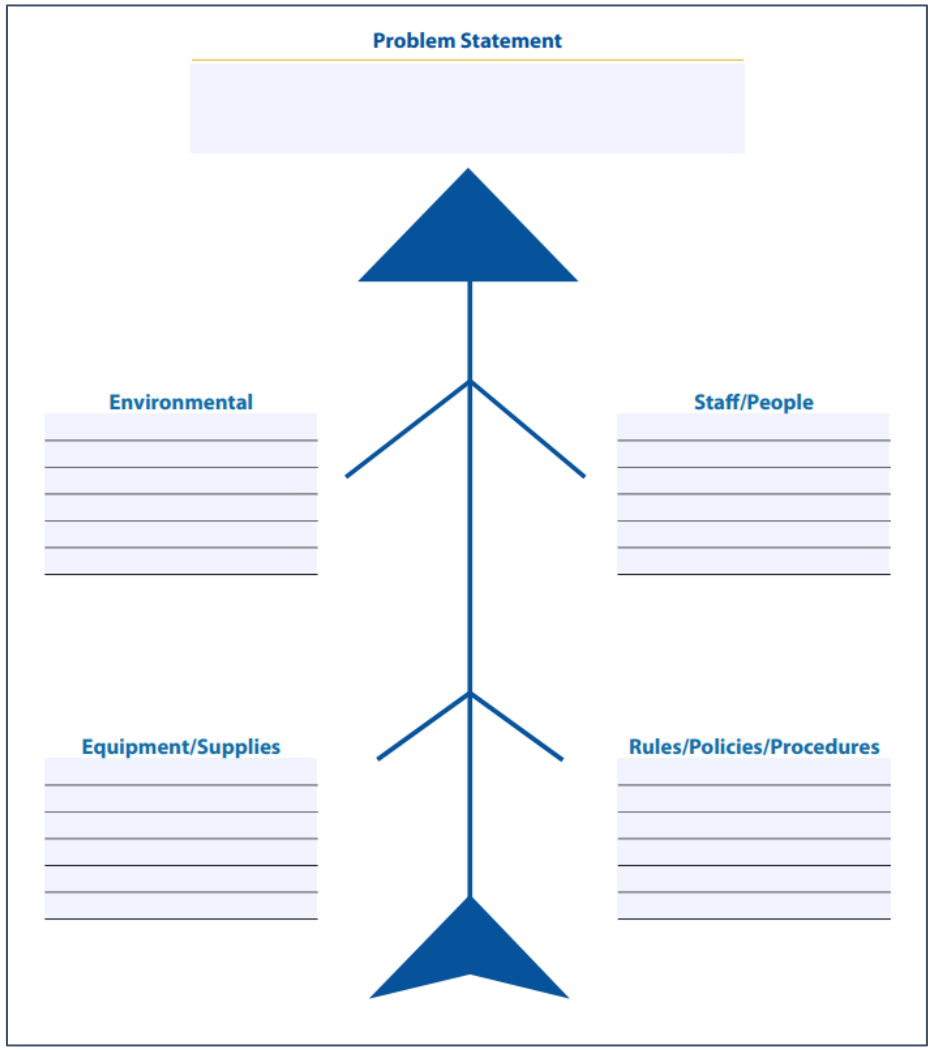
Common Processes that seem to be problem prone:

- Calculation and set up of heparin doses
- Multiple methods to order anticoagulants (CPRS, protocols, text orders, etc)
- Failure to appreciate half lives and peak effect times of various drugs (e.g. today's dose effects day after tomorrow's lab)
- Absolute and relative contraindications to anticoagulation (up to date risk: benefit ratios)
- Selection of intensity of anticoagulation to meet the risk benefit ratio
- Timing and reporting and evaluation of PTT results (often drawn before steady state)
- Specimen collection (adequate volume, appropriate site of phlebotomy)
- Transition therapy for outpatients needing reversal of warfarin for outpatient procedures or surgery
- Transition therapy for inpatients from heparin therapy to warfarin
- Reversal of anticoagulant effect with protamine, Vitamin K, or FFP (to reverse or to wait and see)
- Vitamin K dosing and administration (too high a dose leads to prolonged warfarin resistance)
- Therapy with new drugs that interact with anticoagulants (inadequate information about drug interactions)
- Patient compliance with anticoagulant regimen (drug therapy, diet, monitoring)
- Alternative medicines and risk of drug interactions and bleeding
- Enteral supplements and protein binding effects with warfarin
- Monitoring for side effects (CBC, HBG, PLT, thrombocytopenia, etc and frank bleeding)
- Medication use systems - floor stock and infusion devices
- Lack of double check systems (infusion device, calculations, loading dose, etc)
- IV compatibility and infusion related interruption issues
- Flow of information (need paper or electronic flow sheet similar to diabetes or ICU care)

Actions Taken to Control Vulnerability (VA and non-VA facilities):

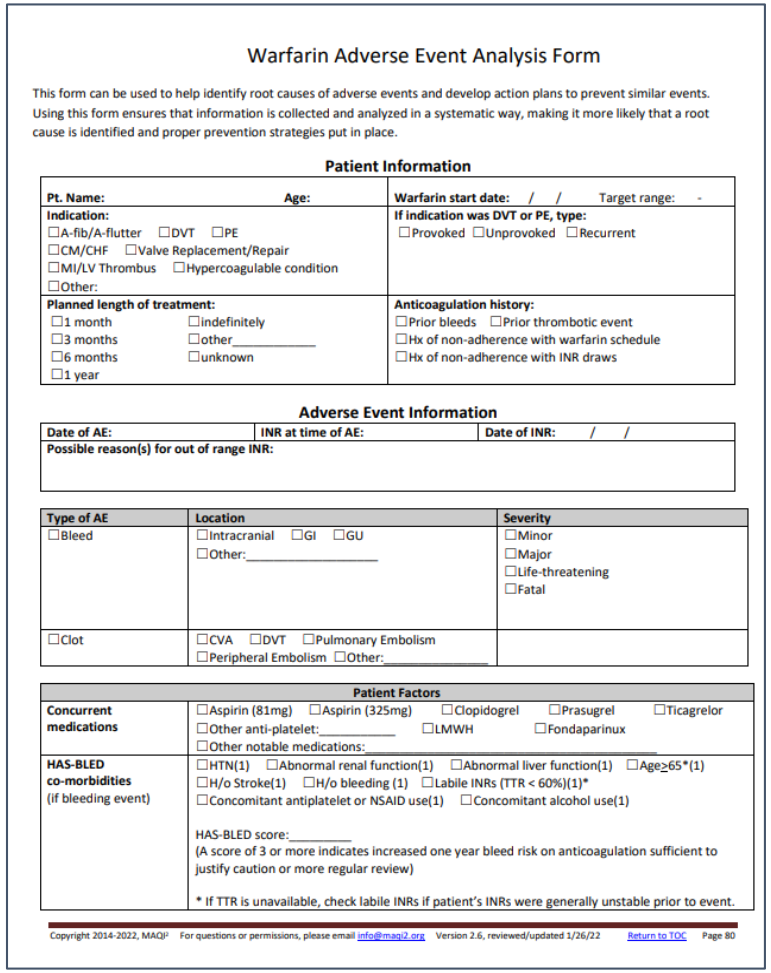
- Establish weight based heparin protocols (to improve consistency) with education on exclusion and inclusion criteria. Close monitoring for success and failures and adjustment of protocol as necessary is commonly seen.
- Use anticoagulant cases as grand rounds and teaching cases for medical, nursing and pharmacy staff
- Establish a food and drug interaction program / policy which addresses enteral feedings and warfarin administration
- Establish a pharmacy based inpatient anticoagulation service to improve monitoring, follow up and transitioning to warfarin
- Establish double check systems to verify correct pump settings and calculations
- Limit the availability of anticoagulant drugs from floor stock to reduce misadministration and force review of the order before drug administration
- Limit the availability of reversal agent drugs from floor stock to reduce misadministration
- Use manufacturer's pre-made solutions to reduce compounding and labeling errors
- Standardize on one size /concentration of IV bag for continuous IV heparin using an even number of units per ml [e.g. 50 units per ml] to simplify calculations
- Include drip charts on the infusion bags to improve the ability to adjust rates without mathematical error
- Limit the size of the infusion bag of heparin to reduce risk if free flow or over infusions occur (250 ml versus 500 ml)
- Provide heparin in dosage forms that are as close as possible to what is ordered (e.g. 5,000 or 10,000 unit vials for bolus use)
- Standardize the monitoring of anticoagulant laboratory work so that clinical changes are detected early (Hemoglobin, platelets, etc)
- "Super train" phlebotomy, nursing or IV therapy staff in venipuncture and specimen collection related to anticoagulant labs and use these resource people as the leaders for this task (similar to blood culture teams, etc.)
- Develop self-learning modules or CE programs on anticoagulant safety
- Review out of range INR/ PTT results on a periodic basis as a group to identify system issues before they result in injury
- Flowchart and redesign the hospital's process for anticoagulation focusing on vulnerability elimination and simplification

Defining the Problem



- Do an RCA on specific adverse drug events
- Don’t define the problem in terms of a solution
- Be clear and specific
- Change the major categories if needed

Warfarin Adverse Event Analysis Form



Warfarin Adverse Event Analysis Form

This form can be used to help identify root causes of adverse events and develop action plans to prevent similar events. Using this form ensures that information is collected and analyzed in a systematic way, making it more likely that a root cause is identified and proper prevention strategies put in place.

Patient Information

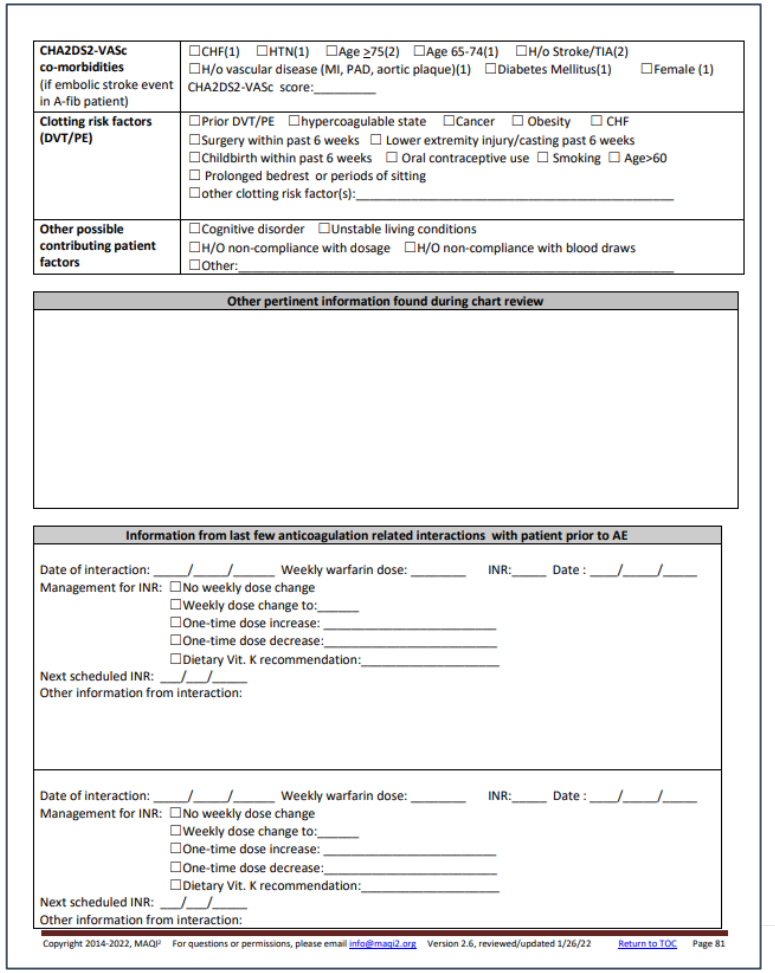
Pt. Name: **Age:**	**Warfarin start date:** / / Target range: -
Indication: ☐A-fib/A-flutter ☐DVT ☐PE ☐CM/CHF ☐Valve Replacement/Repair ☐MI/LV Thrombus ☐Hypercoagulable condition ☐Other:	**If indication was DVT or PE, type:** ☐Provoked ☐Unprovoked ☐Recurrent
Planned length of treatment: ☐1 month ☐indefinitely ☐3 months ☐other_____ ☐6 months ☐unknown ☐1 year	**Anticoagulation history:** ☐Prior bleeds ☐Prior thrombotic event ☐Hx of non-adherence with warfarin schedule ☐Hx of non-adherence with INR draws

Adverse Event Information

Date of AE:	**INR at time of AE:**	**Date of INR:** / /
Possible reason(s) for out of range INR:		

Type of AE	Location	Severity
☐Bleed	☐Intracranial ☐GI ☐GU ☐Other:_____	☐Minor ☐Major ☐Life-threatening ☐Fatal
☐Clot	☐CVA ☐DVT ☐Pulmonary Embolism ☐Peripheral Embolism ☐Other:_____	

Patient Factors	
Concurrent medications	☐Aspirin (81mg) ☐Aspirin (325mg) ☐Clopidogrel ☐Prasugrel ☐Ticagrelor ☐Other anti-platelet:_____ ☐LMWH ☐Fondaparinux ☐Other notable medications:_____
HAS-BLED co-morbidities (if bleeding event)	☐HTN(1) ☐Abnormal renal function(1) ☐Abnormal liver function(1) ☐Age≥65*(1) ☐H/o Stroke(1) ☐H/o bleeding (1) ☐Labile INRs (TTR < 60%)(1)* ☐Concomitant antiplatelet or NSAID use(1) ☐Concomitant alcohol use(1) HAS-BLED score:_____ (A score of 3 or more indicates increased one year bleed risk on anticoagulation sufficient to justify caution or more regular review) * If TTR is unavailable, check labile INRs if patient's INRs were generally unstable prior to event.



CHA2DS2-VASc co-morbidities (if embolic stroke event in A-fib patient)	☐CHF(1) ☐HTN(1) ☐Age ≥75(2) ☐Age 65-74(1) ☐H/o Stroke/TIA(2) ☐H/o vascular disease (MI, PAD, aortic plaque)(1) ☐Diabetes Mellitus(1) ☐Female (1) CHA2DS2-VASc score:_____
Clotting risk factors (DVT/PE)	☐Prior DVT/PE ☐hypercoagulable state ☐Cancer ☐Obesity ☐CHF ☐Surgery within past 6 weeks ☐Lower extremity injury/casting past 6 weeks ☐Childbirth within past 6 weeks ☐Oral contraceptive use ☐Smoking ☐Age>60 ☐Prolonged bedrest or periods of sitting ☐other clotting risk factor(s):_____
Other possible contributing patient factors	☐Cognitive disorder ☐Unstable living conditions ☐H/O non-compliance with dosage ☐H/O non-compliance with blood draws ☐Other:_____

Other pertinent information found during chart review

Information from last few anticoagulation related interactions with patient prior to AE

Date of interaction: ____/____/____ Weekly warfarin dose: _____ INR:____ Date : ____/____/____
Management for INR: ☐No weekly dose change
☐Weekly dose change to:_____
☐One-time dose increase: _____
☐One-time dose decrease:_____
☐Dietary Vit. K recommendation:_____
Next scheduled INR: ___/___/_____
Other information from interaction:

Date of interaction: ____/____/____ Weekly warfarin dose: _____ INR:____ Date : ____/____/____
Management for INR: ☐No weekly dose change
☐Weekly dose change to:_____
☐One-time dose increase: _____
☐One-time dose decrease:_____
☐Dietary Vit. K recommendation:_____
Next scheduled INR: ___/___/_____
Other information from interaction:

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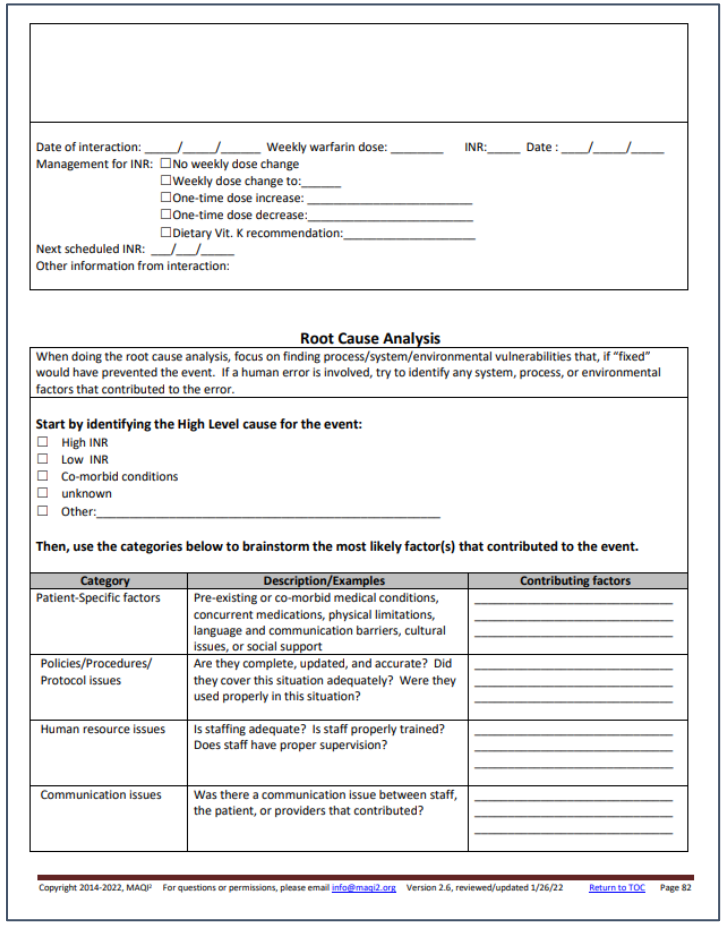
Warfarin Adverse Event Analysis Form Continued



Date of interaction: ____/____/_____ Weekly warfarin dose: _____ INR:____ Date : ____/____/_____
Management for INR: ☐No weekly dose change
☐Weekly dose change to:_____
☐One-time dose increase: _____
☐One-time dose decrease:_____
☐Dietary Vit. K recommendation:_____
Next scheduled INR: ___/___/_____
Other information from interaction:

Root Cause Analysis

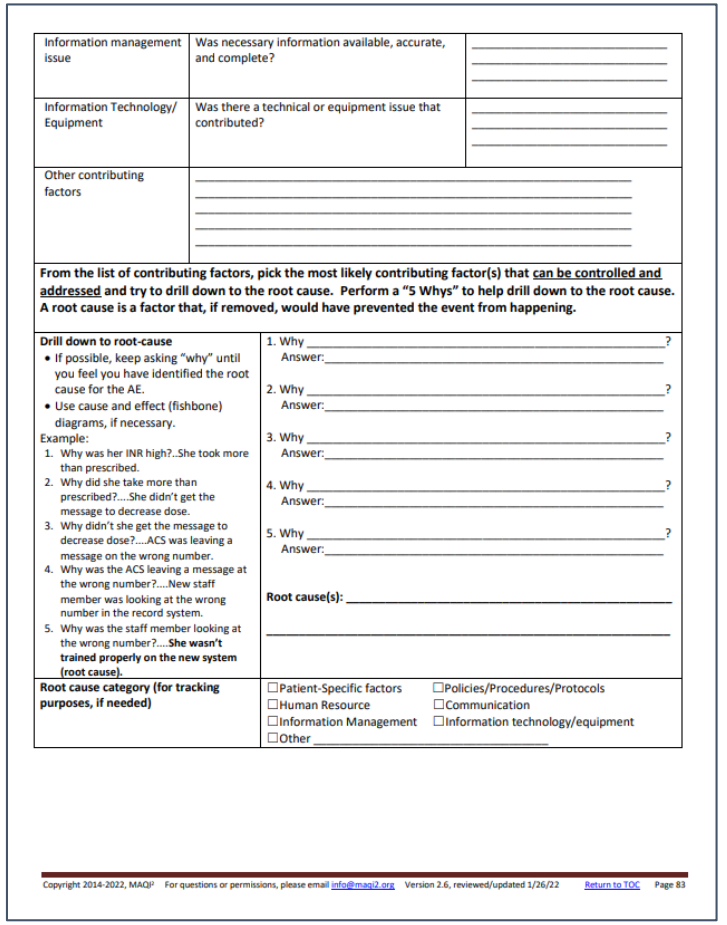
When doing the root cause analysis, focus on finding process/system/environmental vulnerabilities that, if "fixed" would have prevented the event. If a human error is involved, try to identify any system, process, or environmental factors that contributed to the error.

Start by identifying the High Level cause for the event:

- ☐ High INR
- ☐ Low INR
- ☐ Co-morbid conditions
- ☐ unknown
- ☐ Other:_____

Then, use the categories below to brainstorm the most likely factor(s) that contributed to the event.

Category	Description/Examples	Contributing factors
Patient-Specific factors	Pre-existing or co-morbid medical conditions, concurrent medications, physical limitations, language and communication barriers, cultural issues, or social support	_____ _____ _____
Policies/Procedures/ Protocol issues	Are they complete, updated, and accurate? Did they cover this situation adequately? Were they used properly in this situation?	_____ _____ _____
Human resource issues	Is staffing adequate? Is staff properly trained? Does staff have proper supervision?	_____ _____ _____
Communication issues	Was there a communication issue between staff, the patient, or providers that contributed?	_____ _____ _____



Information management issue	Was necessary information available, accurate, and complete?	_____ _____ _____
Information Technology/ Equipment	Was there a technical or equipment issue that contributed?	_____ _____ _____
Other contributing factors	_____ _____ _____ _____ _____	

From the list of contributing factors, pick the most likely contributing factor(s) that can be controlled and addressed and try to drill down to the root cause. Perform a "5 Whys" to help drill down to the root cause. A root cause is a factor that, if removed, would have prevented the event from happening.

Drill down to root-cause

- If possible, keep asking "why" until you feel you have identified the root cause for the AE.
- Use cause and effect (fishbone) diagrams, if necessary.

Example:

1. Why was her INR high?..She took more than prescribed.
2. Why did she take more than prescribed?....She didn't get the message to decrease dose.
3. Why didn't she get the message to decrease dose?....ACS was leaving a message on the wrong number.
4. Why was the ACS leaving a message at the wrong number?....New staff member was looking at the wrong number in the record system.
5. Why was the staff member looking at the wrong number?....**She wasn't trained properly on the new system (root cause).**

1. Why _____?
Answer:_____
2. Why _____?
Answer:_____
3. Why _____?
Answer:_____
4. Why _____?
Answer:_____
5. Why _____?
Answer:_____

Root cause(s): _____
_____

Root cause category (for tracking purposes, if needed)

☐Patient-Specific factors ☐Policies/Procedures/Protocols
☐Human Resource ☐Communication
☐Information Management ☐Information technology/equipment
☐Other _____

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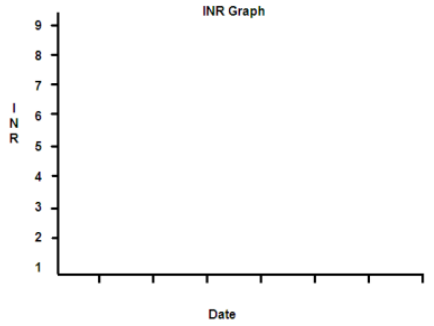
Warfarin Adverse Event Analysis Form Continued

Action Plan

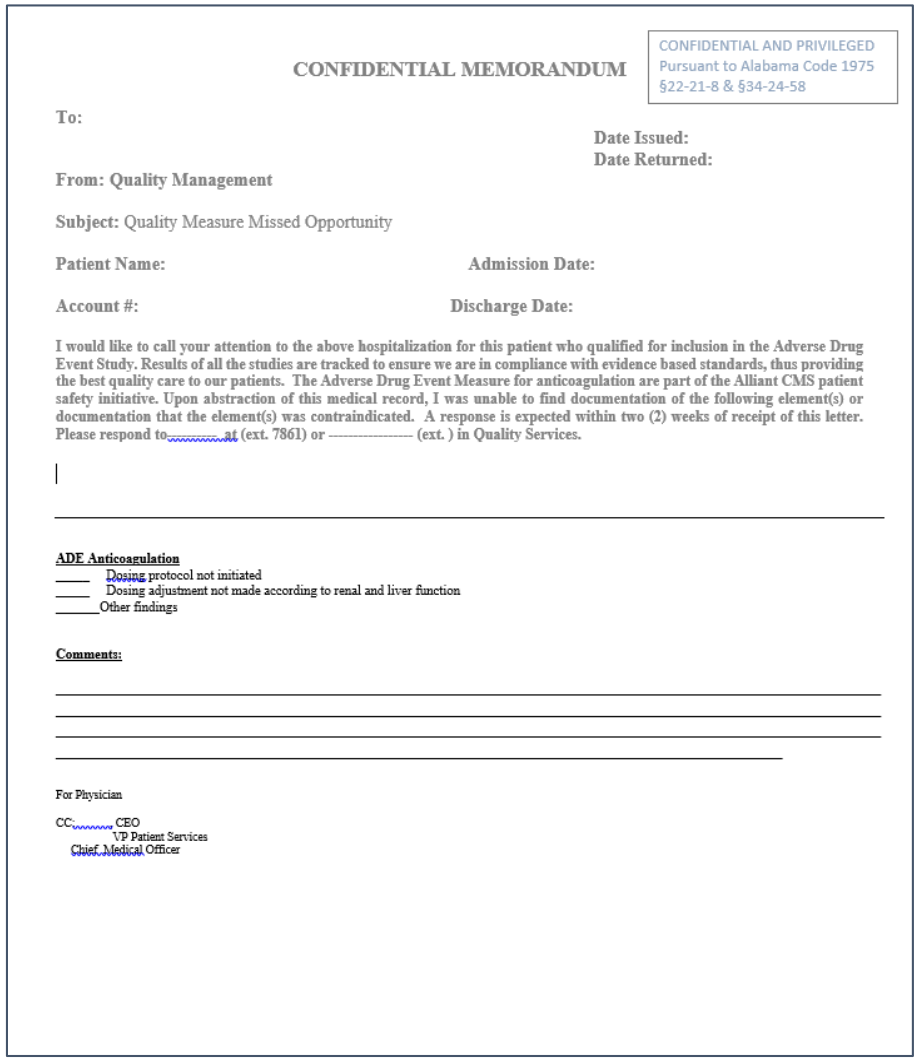
Is this an isolated incident or is this part of a larger trend?	☐Isolated incident ☐Part of a larger trend
What action(s) will be taken to address this root cause to prevent it from happening again?	☐No action clearly needed at this time. Will continue to monitor for trends indicating a need for system/process change. ☐Process/Workflow improvement: _____ ☐Structure/Staffing change:_____ ☐Protocol change:_____ ☐Communication change:_____ ☐Staff education:_____ ☐Other change:_____
Follow-up on plan	Date:____/____/_____ Status: _____ Date:____/____/_____ Status: _____ Date:____/____/_____ Status: _____

Timeline and INR Graph (if needed)

Date				
INR				
What happened?				



Russell Medical Missed Opportunity Form



CONFIDENTIAL MEMORANDUM

CONFIDENTIAL AND PRIVILEGED
Pursuant to Alabama Code 1975
§22-21-8 & §34-24-58

To:

Date Issued:
Date Returned:

From: Quality Management

Subject: Quality Measure Missed Opportunity

Patient Name: **Admission Date:**

Account #: **Discharge Date:**

I would like to call your attention to the above hospitalization for this patient who qualified for inclusion in the Adverse Drug Event Study. Results of all the studies are tracked to ensure we are in compliance with evidence based standards, thus providing the best quality care to our patients. The Adverse Drug Event Measure for anticoagulation are part of the Alliant CMS patient safety initiative. Upon abstraction of this medical record, I was unable to find documentation of the following element(s) or documentation that the element(s) was contraindicated. A response is expected within two (2) weeks of receipt of this letter. Please respond to_____ at (ext. 7861) or ---------- (ext.) in Quality Services.

ADE Anticoagulation
____ Dosing protocol not initiated
____ Dosing adjustment not made according to renal and liver function
_____Other findings

Comments:

For Physician

CC: CEO
VP Patient Services
Chief Medical Officer

- Positive Wording
- Form is not overwhelming
- Can be used for any missed opportunity
- Comment section and can add supporting documentation

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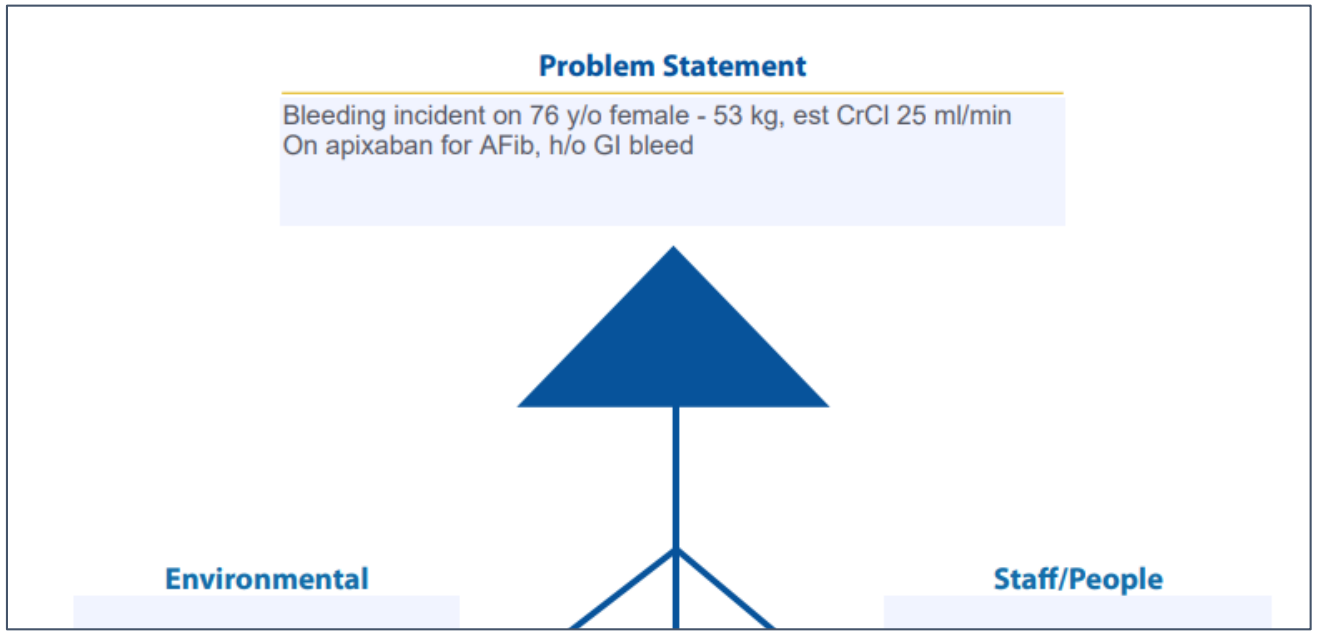
Anticoagulation Vulnerability

- Absolute and relative contraindications to anticoagulation (up to date risk: benefit ratios)
- Selection of intensity of anticoagulation to meet the risk benefit ratio



Resources to Define Bleeding Risk/Select Anticoagulant

Bleeding Risk Scores

Bleeding risk should be assessed at each patient contact and should initially focus on potentially modifiable risk factors. The HAS-BLED tool can be used to identify modifiable risk factors (in red). Patients with scores indicating high bleed risk (≥3) should be followed more closely.[1]

HAS-BLED Score (warfarin in atrial fibrillation patients)[2]
Estimates risk of major bleeding for patients on **warfarin** for **atrial fibrillation**.

	Condition	Points
H	Hypertension	1
A	Abnormal renal/liver function (1 pt each)	1 or 2
S	Stroke	1
B	Bleeding history or disposition	1
L	Labile INRs	1
E	Elderly	1
D	Current drugs (medication) or alcohol use (1pt each)	1 or 2
	TOTAL POINTS	

Total Points	Annual Major bleed risk (%)	Intracranial bleeds per 100-pt-yrs[3]	Major bleed risk category
0	1.13		Low
1	1.02		Low
2	1.88	0.6	Intermediate
3	3.74	0.7	High
4	8.7	1.0	High
5	12.5	1.2	High

Modifiable risk factors in red.

When evaluating the risk/benefit of anticoagulation in atrial fibrillation, it is important to consider the risks of ischemic stroke, intracranial hemorrhage and extracranial hemorrhage independently.

Condition	Definition
Hypertension	Systolic Blood Pressure >160
Abnormal renal function	Chronic dialysis, renal transplantation, serum creatinine ≥ 200 µmol/L, or CrCl<50
Abnormal liver function	Chronic hepatic disease/biochemical evidence of hepatic derangement (eg, bilirubin >2× upper limit of normal, with AST/ALT/Alk Phos >3× upper limit normal)
Stroke	Any previous history of Stroke
Bleeding history or disposition	Bleeding event history (defined below), genetic predisposition, anemia.
Labile INRs	<60% of time spent in therapeutic INR range (INR 2-3)
Elderly	Age ≥ 65 years
Current medication or alcohol use	Concomitant use of antiplatelet agent/aspirin, NSAIDs, or alcohol >16 beers/week, >10 glasses wine/week or equivalent
Bleeding event	Bleeding requiring hospitalization and/or causing a decrease in Hgb>2g/dL and/or requiring ≥2 unit blood transfusion.

[1]Lipp G, et al. Antithrombotic Therapy for Atrial Fibrillation CHEST Guideline and Expert Panel Report. CHEST 2018; 154(5):1121-1201

Comparison of Anticoagulants

Basic Characteristics of Warfarin and DOACs

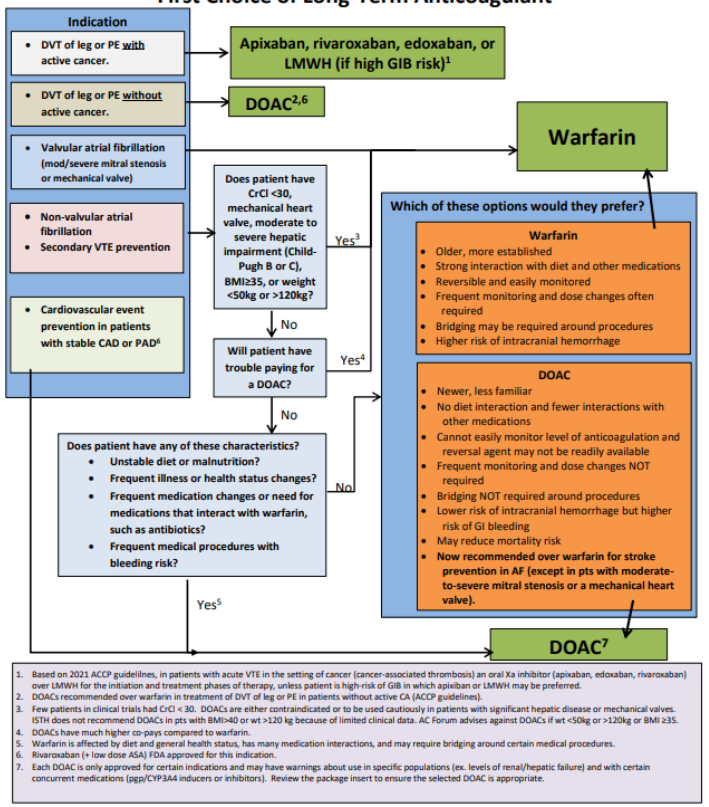
	Warfarin	DOACs
Onset	Slow	Rapid
Dosing	Variable	Fixed
Food effect	Yes	Rivaroxaban should be taken with largest meal of the day, otherwise no known food effects for DOACs
Medication interactions	Many	Few*
Therapeutic monitoring required	Yes	No
Offset	Long	Shorter

*Apixaban is contraindicated if patient has two or more of these factors (age≥80, weight ≤60kg, serum creatinine ≥1.5 mg/dL) AND is taking a strong dual CYP3A4 and P-gp inhibitor.

Safety, Efficacy, and Pharmacology

	Warfarin[a]	Rivaroxaban[a]	Apixaban[a]	Dabigatran[a]	Edoxaban[b]
FDA approved indications	• AF • VTE ○ treatment ○ secondary prevention ○ prophylaxis • Valve replacement • MI	• AF (non-valvular only) • VTE ○ treatment ○ secondary prevention ○ prophylaxis[1] • CV event reduction in stable CAD or PAD • VTE prophy in acutely ill medical patients	• AF (non-valvular only) • VTE ○ treatment ○ secondary prevention ○ prophylaxis[1]	• AF (non-valvular only) • VTE ○ Treatment[3] ○ secondary prevention ○ prophylaxis[2]	• AF (non-valvular only) • VTE ○ Treatment[3]
Administration	• Once daily with or without food	• Once or twice daily with largest meal of day[4]	• Twice daily with or without food	• Twice daily with or without food • Must be kept in original packaging • Can't be crushed	• Once daily with or without food
Safety in non-valvular atrial fibrillation	• Higher risk of intracranial hemorrhage compared to DOACs	• Higher risk of GI bleeding compared to warfarin	• Lower risk of major bleeding compared to warfarin	• Higher risk of GI bleeding compared to warfarin • Small increase in risk of MI compared to warfarin	• Lower risk of major bleeding compared to warfarin • Higher risk of GI bleeding (60mg dose)compared to warfarin
Efficacy in non-valvular atrial fibrillation[5]		• Non-inferior to warfarin	• Reduced all-cause mortality	• Lower risk of ischemic stroke (150mg dose only) • Trend towards reduced all-cause mortality	• Non-inferior to warfarin
Safety in VTE	• Increased risk of intracranial hemorrhage[d]	• Lower risk of major bleeding than warfarin[c] • May have higher risk of GI bleeding than warfarin[d]	• Potentially lower risk of major bleeding than warfarin, LMWH/dabigatran, and LMWH/edoxaban[c]	• May have higher risk of GI bleeding than warfarin[d]	• May have higher risk of GI bleeding than warfarin[d]
Efficacy in VTE	Similar reduction in risk of recurrence[c]	Similar reduction in risk of recurrence[c]	Similar reduction in risk of recurrence[c]	Similar reduction in risk of recurrence[c]	Similar reduction in risk of recurrence[c]
Initial parenteral	Yes	No	No	Yes	Yes

First Choice of Long-Term Anticoagulant



1. Based on 2021 ACCP guidelines, in patients with acute VTE in the setting of cancer (cancer-associated thrombosis) an oral Xa inhibitor (apixaban, edoxaban, rivaroxaban) over LMWH for the initiation and treatment phases of therapy, unless patient is high-risk of GIB in which apixaban or LMWH may be preferred.
2. DOACs recommended over warfarin in treatment of DVT of leg or PE in patients without active CA (ACCP guidelines).
3. Few patients in clinical trials had CrCl < 30. DOACs are either contraindicated or to be used cautiously in patients with significant hepatic disease or mechanical valves. ISTH does not recommend DOACs in pts with BMI>40 or wt >120 kg because of limited clinical data. AC Forum advises against DOACs if wt <50kg or >120kg or BMI ≥35.
4. DOACs have much higher co-pays compared to warfarin.
5. Warfarin is affected by diet and general health status, has many medication interactions, and may require bridging around certain medical procedures.
6. Rivaroxaban (+ low dose ASA) FDA approved for this indication.
7. Each DOAC is only approved for certain indications and may have warnings about use in specific populations (ex. levels of renal/hepatic failure) and with certain concurrent medications (pgp/CYP3A4 inducers or inhibitors). Review the package insert to ensure the selected DOAC is appropriate.

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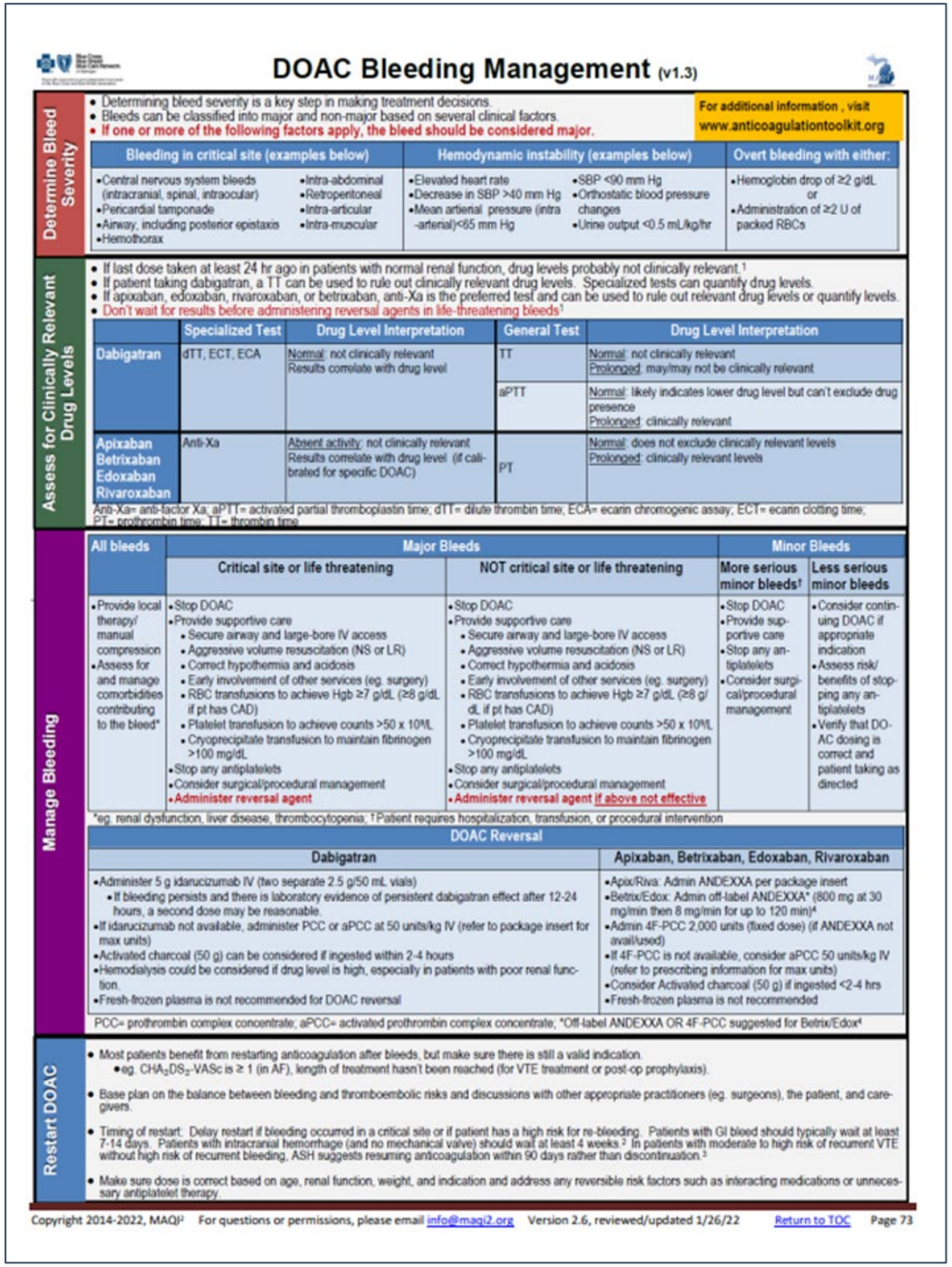


DOAC Bleeding Management (v1.3)

Determine Bleed Severity

- Determining bleed severity is a key step in making treatment decisions.
- Bleeds can be classified into major and non-major based on several clinical factors.
- **If one or more of the following factors apply, the bleed should be considered major.**

For additional information , visit www.anticoagulationtoolkit.org

Bleeding in critical site (examples below)	Hemodynamic instability (examples below)	Overt bleeding with either:
•Central nervous system bleeds (intracranial, spinal, intraocular) •Pericardial tamponade •Airway, including posterior epistaxis •Hemothorax •Intra-abdominal •Retroperitoneal •Intra-articular •Intra-muscular	•Elevated heart rate •Decrease in SBP >40 mm Hg •Mean arterial pressure (intra-arterial)<65 mm Hg •SBP <90 mm Hg •Orthostatic blood pressure changes •Urine output <0.5 mL/kg/hr	•Hemoglobin drop of ≥2 g/dL or •Administration of ≥2 U of packed RBCs

Assess for Clinically Relevant Drug Levels

- If last dose taken at least 24 hr ago in patients with normal renal function, drug levels probably not clinically relevant.[1]
- If patient taking dabigatran, a TT can be used to rule out clinically relevant drug levels. Specialized tests can quantify drug levels.
- If apixaban, edoxaban, rivaroxaban, or betrixaban, anti-Xa is the preferred test and can be used to rule out relevant drug levels or quantify levels.
- Don't wait for results before administering reversal agents in life-threatening bleeds[1]

	Specialized Test	Drug Level Interpretation	General Test	Drug Level Interpretation
Dabigatran	dTT, ECT, ECA	Normal: not clinically relevant Results correlate with drug level	TT	Normal: not clinically relevant Prolonged: may/may not be clinically relevant
			aPTT	Normal: likely indicates lower drug level but can't exclude drug presence Prolonged: clinically relevant
Apixaban Betrixaban Edoxaban Rivaroxaban	Anti-Xa	Absent activity: not clinically relevant Results correlate with drug level (if calibrated for specific DOAC)	PT	Normal: does not exclude clinically relevant levels Prolonged: clinically relevant levels

Anti-Xa= anti-factor Xa; aPTT= activated partial thromboplastin time; dTT= dilute thrombin time; ECA= ecarin chromogenic assay; ECT= ecarin clotting time; PT= prothrombin time; TT= thrombin time

Manage Bleeding

All bleeds	Major Bleeds: Critical site or life threatening	Major Bleeds: NOT critical site or life threatening	Minor Bleeds: More serious minor bleeds†	Minor Bleeds: Less serious minor bleeds
•Provide local therapy/ manual compression •Assess for and manage comorbidities contributing to the bleed*	•Stop DOAC •Provide supportive care • Secure airway and large-bore IV access • Aggressive volume resuscitation (NS or LR) • Correct hypothermia and acidosis • Early involvement of other services (eg. surgery) • RBC transfusions to achieve Hgb ≥7 g/dL (≥8 g/dL if pt has CAD) • Platelet transfusion to achieve counts >50 x 10⁹/L • Cryoprecipitate transfusion to maintain fibrinogen >100 mg/dL •Stop any antiplatelets •Consider surgical/procedural management •**Administer reversal agent**	•Stop DOAC •Provide supportive care • Secure airway and large-bore IV access • Aggressive volume resuscitation (NS or LR) • Correct hypothermia and acidosis • Early involvement of other services (eg. surgery) • RBC transfusions to achieve Hgb ≥7 g/dL (≥8 g/dL if pt has CAD) • Platelet transfusion to achieve counts >50 x 10⁹/L • Cryoprecipitate transfusion to maintain fibrinogen >100 mg/dL •Stop any antiplatelets •Consider surgical/procedural management •**Administer reversal agent if above not effective**	•Stop DOAC •Provide supportive care •Stop any antiplatelets •Consider surgical/procedural management	•Consider continuing DOAC if appropriate indication •Assess risk/ benefits of stopping any antiplatelets •Verify that DOAC dosing is correct and patient taking as directed

*eg. renal dysfunction, liver disease, thrombocytopenia; †Patient requires hospitalization, transfusion, or procedural intervention

DOAC Reversal

Dabigatran	Apixaban, Betrixaban, Edoxaban, Rivaroxaban
•Administer 5 g idarucizumab IV (two separate 2.5 g/50 mL vials) • If bleeding persists and there is laboratory evidence of persistent dabigatran effect after 12-24 hours, a second dose may be reasonable. •If idarucizumab not available, administer PCC or aPCC at 50 units/kg IV (refer to package insert for max units) •Activated charcoal (50 g) can be considered if ingested within 2-4 hours •Hemodialysis could be considered if drug level is high, especially in patients with poor renal function. •Fresh-frozen plasma is not recommended for DOAC reversal	•Apix/Riva: Admin ANDEXXA per package insert •Betrix/Edox: Admin off-label ANDEXXA* (800 mg at 30 mg/min then 8 mg/min for up to 120 min)[4] •Admin 4F-PCC 2,000 units (fixed dose) (if ANDEXXA not avail/used) •If 4F-PCC is not available, consider aPCC 50 units/kg IV (refer to prescribing information for max units) •Consider Activated charcoal (50 g) if ingested <2-4 hrs •Fresh-frozen plasma is not recommended

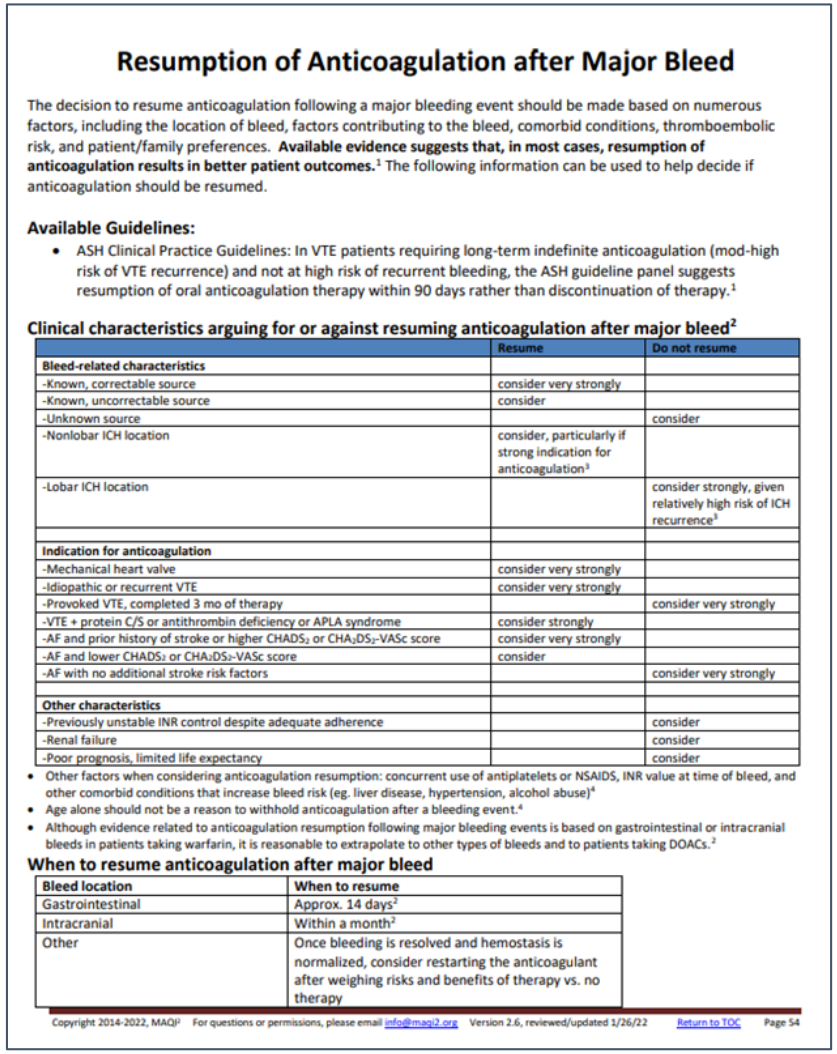
PCC= prothrombin complex concentrate; aPCC= activated prothrombin complex concentrate; *Off-label ANDEXXA OR 4F-PCC suggested for Betrix/Edox[4]

Restart DOAC

- Most patients benefit from restarting anticoagulation after bleeds, but make sure there is still a valid indication.
  - eg. CHA_2DS_2-VASc is ≥ 1 (in AF), length of treatment hasn't been reached (for VTE treatment or post-op prophylaxis).
- Base plan on the balance between bleeding and thromboembolic risks and discussions with other appropriate practitioners (eg. surgeons), the patient, and caregivers.
- Timing of restart: Delay restart if bleeding occurred in a critical site or if patient has a high risk for re-bleeding. Patients with GI bleed should typically wait at least 7-14 days. Patients with intracranial hemorrhage (and no mechanical valve) should wait at least 4 weeks.[2] In patients with moderate to high risk of recurrent VTE without high risk of recurrent bleeding, ASH suggests resuming anticoagulation within 90 days rather than discontinuation.[3]
- Make sure dose is correct based on age, renal function, weight, and indication and address any reversible risk factors such as interacting medications or unnecessary antiplatelet therapy.

- Determine Bleed Severity
- Assess for Clinically Relevant Drug Levels
- Manage Bleeding
- Restart DOAC

Resuming Anticoagulation after Major Bleed



Resumption of Anticoagulation after Major Bleed

The decision to resume anticoagulation following a major bleeding event should be made based on numerous factors, including the location of bleed, factors contributing to the bleed, comorbid conditions, thromboembolic risk, and patient/family preferences. **Available evidence suggests that, in most cases, resumption of anticoagulation results in better patient outcomes.**[1] The following information can be used to help decide if anticoagulation should be resumed.

Available Guidelines:

- ASH Clinical Practice Guidelines: In VTE patients requiring long-term indefinite anticoagulation (mod-high risk of VTE recurrence) and not at high risk of recurrent bleeding, the ASH guideline panel suggests resumption of oral anticoagulation therapy within 90 days rather than discontinuation of therapy.[1]

Clinical characteristics arguing for or against resuming anticoagulation after major bleed[2]

	Resume	Do not resume
Bleed-related characteristics		
-Known, correctable source	consider very strongly	
-Known, uncorrectable source	consider	
-Unknown source		consider
-Nonlobar ICH location	consider, particularly if strong indication for anticoagulation[3]	
-Lobar ICH location		consider strongly, given relatively high risk of ICH recurrence[3]
Indication for anticoagulation		
-Mechanical heart valve	consider very strongly	
-Idiopathic or recurrent VTE	consider very strongly	
-Provoked VTE, completed 3 mo of therapy		consider very strongly
-VTE + protein C/S or antithrombin deficiency or APLA syndrome	consider strongly	
-AF and prior history of stroke or higher $CHADS_2$ or CHA_2DS_2-VASc score	consider very strongly	
-AF and lower $CHADS_2$ or CHA_2DS_2-VASc score	consider	
-AF with no additional stroke risk factors		consider very strongly
Other characteristics		
-Previously unstable INR control despite adequate adherence		consider
-Renal failure		consider
-Poor prognosis, limited life expectancy		consider

- Other factors when considering anticoagulation resumption: concurrent use of antiplatelets or NSAIDS, INR value at time of bleed, and other comorbid conditions that increase bleed risk (eg. liver disease, hypertension, alcohol abuse)[4]
- Age alone should not be a reason to withhold anticoagulation after a bleeding event.[4]
- Although evidence related to anticoagulation resumption following major bleeding events is based on gastrointestinal or intracranial bleeds in patients taking warfarin, it is reasonable to extrapolate to other types of bleeds and to patients taking DOACs.[2]

When to resume anticoagulation after major bleed

Bleed location	When to resume
Gastrointestinal	Approx. 14 days[2]
Intracranial	Within a month[2]
Other	Once bleeding is resolved and hemostasis is normalized, consider restarting the anticoagulant after weighing risks and benefits of therapy vs. no therapy

Considerations for resuming anticoagulation after major bleed

- Bleed-related characteristics
- Indication for anticoagulation
- Other characteristics
  - Unstable INR
  - Renal Failure
  - Poor prognosis

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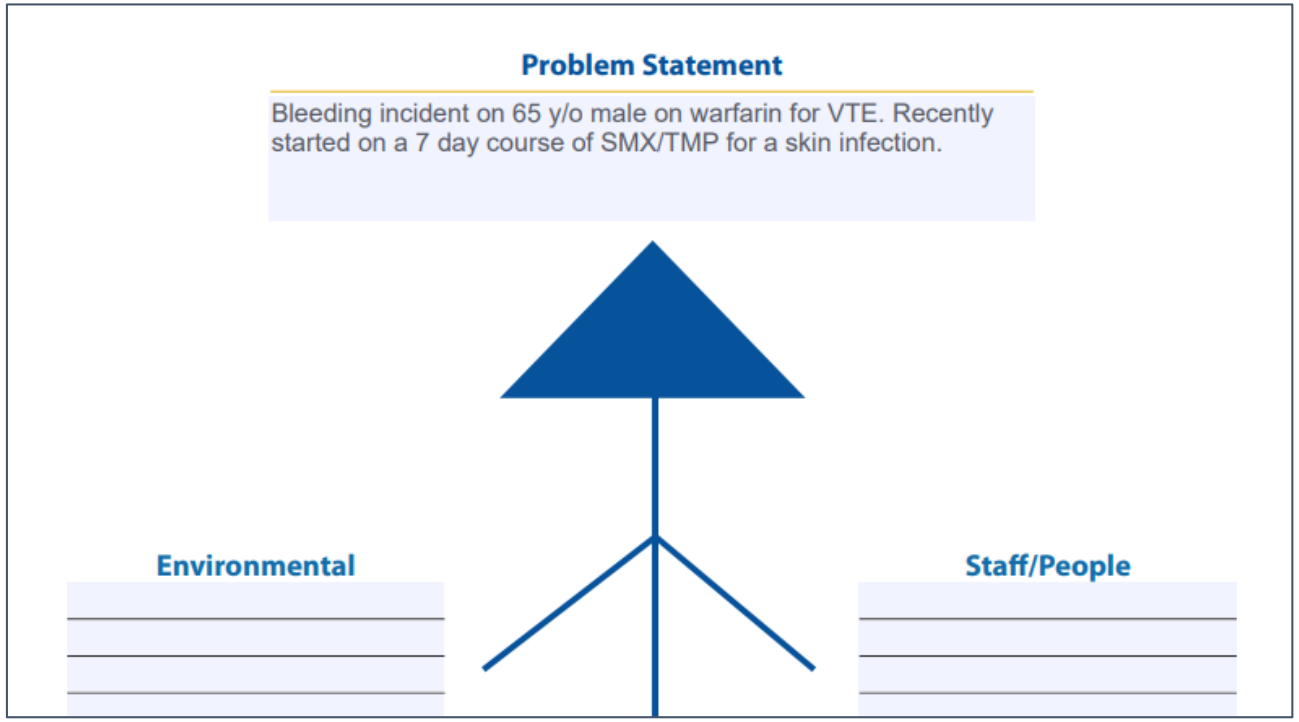
Anticoagulation Vulnerability

- Therapy with new drugs that interact with anticoagulants (inadequate information about drug interactions)
- Alternative medicines and risk of drug interactions and bleeding



Most Clinically Relevant Warfarin-Drug Interactions

Most Clinically Relevant Warfarin-Drug Interactions	
Potentiation of Drug Effect (Increased INR or increased bleed risk)	**Inhibition of Drug Effect (Decreased INR)**
Acetaminophen	Barbiturates
Allopurinol	Bosentan
Amiodarone	Carbamazepine
Amoxicillin	Cigarette Smoking
Aspirin	Chlordiazepoxide
Azithromycin	Ginseng
Bactrim(TMP-SMX)	Griseofulvin
Cimetadine	Mercaptopurine
Ciprofloxacin	Multivitamin Supplement
Citalopram	Nafcillin
Clarithromycin	Phenobarbital
Clopidogrel	Ribavarin
Cotrimoxazole	Rifampin
Diltiazem	Secobarbital
Entacapone	St. John's wort
Erythromycin	Phenytoin
Fenofibrate	
Fish Oil	
Fluconazole	
Fluvastatin	
Gemcitabine	
Gemfibrozil	
Levofloxacin	
Lovastatin	
Metronidazole	
Miconazole (Suppository and Gel)	
Omeprazole	
Propafenone	
Propanolol	
Simvastatin	
SSRI's	
Tamoxifen	
Tetracycline	
Tramadol	

For a more comprehensive list of potential drug, food, and dietary supplement interactions see Ageno et al. Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines http://journal.publications.chestnet.org/article.aspx?articleid=1159432

Sources:

- Holbrook AM, et al. Systematic Overview of warfarin and its drug and food interactions. Arch Intern Med. 2005 May 23;165(10):1095-106. doi:10.1001/archinte.165.10.1095
- Badyal DK, Dadhich AP. Cytochrome P450 and drug interactions. Ind J Pharmacol 2001;33:248-59.
- Stading JA, Faulkner MA, Skrabal MZ. Effect of tobacco on INR.[Letter]. Am J HealthSystem Pharm 2007;64:805.

Return to Things to Consider when Starting Patients on Warfarin

- Double check order entry system
- Alert Fatigue
- Build special warfarin/anticoag alert
- Review at least annually

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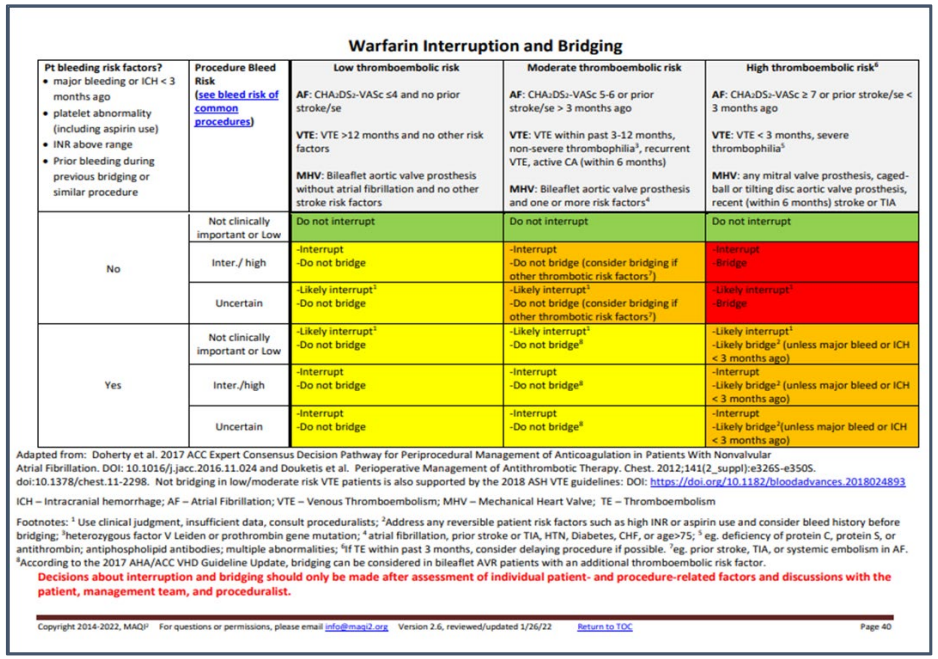
Anticoagulation Vulnerability: Interruption for Surgery



Warfarin Interruption and Bridging

Pt bleeding risk factors?	Procedure Bleed Risk (see bleed risk of common procedures)	Low thromboembolic risk	Moderate thromboembolic risk	High thromboembolic risk[6]
• major bleeding or ICH < 3 months ago • platelet abnormality (including aspirin use) • INR above range • Prior bleeding during previous bridging or similar procedure		**AF**: CHA_2DS_2-VASc ≤4 and no prior stroke/se **VTE**: VTE >12 months and no other risk factors **MHV**: Bileaflet aortic valve prosthesis without atrial fibrillation and no other stroke risk factors	**AF**: CHA_2DS_2-VASc 5-6 or prior stroke/se > 3 months ago **VTE**: VTE within past 3-12 months, non-severe thrombophilia[3], recurrent VTE, active CA (within 6 months) **MHV**: Bileaflet aortic valve prosthesis and one or more risk factors[4]	**AF**: CHA_2DS_2-VASc ≥ 7 or prior stroke/se < 3 months ago **VTE**: VTE < 3 months, severe thrombophilia[5] **MHV**: any mitral valve prosthesis, caged-ball or tilting disc aortic valve prosthesis, recent (within 6 months) stroke or TIA
No	Not clinically important or Low	Do not interrupt	Do not interrupt	Do not interrupt
	Inter./ high	-Interrupt -Do not bridge	-Interrupt -Do not bridge (consider bridging if other thrombotic risk factors[7])	-Interrupt -Bridge
	Uncertain	-Likely interrupt[1] -Do not bridge	-Likely interrupt[1] -Do not bridge (consider bridging if other thrombotic risk factors[7])	-Likely interrupt[1] -Bridge
Yes	Not clinically important or Low	-Likely interrupt[1] -Do not bridge	-Likely interrupt[1] -Do not bridge[8]	-Likely interrupt[1] -Likely bridge[2] (unless major bleed or ICH < 3 months ago)
	Inter./high	-Interrupt -Do not bridge	-Interrupt -Do not bridge[8]	-Interrupt -Likely bridge[2] (unless major bleed or ICH < 3 months ago)
	Uncertain	-Interrupt -Do not bridge	-Interrupt -Do not bridge[8]	-Interrupt -Likely bridge[2](unless major bleed or ICH < 3 months ago)

Adapted from: Doherty et al. 2017 ACC Expert Consensus Decision Pathway for Periprocedural Management of Anticoagulation in Patients With Nonvalvular Atrial Fibrillation. DOI: 10.1016/j.jacc.2016.11.024 and Douketis et al. Perioperative Management of Antithrombotic Therapy. Chest. 2012;141(2_suppl):e326S-e350S. doi:10.1378/chest.11-2298. Not bridging in low/moderate risk VTE patients is also supported by the 2018 ASH VTE guidelines: DOI: https://doi.org/10.1182/bloodadvances.2018024893

ICH – Intracranial hemorrhage; AF – Atrial Fibrillation; VTE – Venous Thromboembolism; MHV – Mechanical Heart Valve; TE – Thromboembolism

Footnotes: [1] Use clinical judgment, insufficient data, consult proceduralists; [2]Address any reversible patient risk factors such as high INR or aspirin use and consider bleed history before bridging; [3]heterozygous factor V Leiden or prothrombin gene mutation; [4] atrial fibrillation, prior stroke or TIA, HTN, Diabetes, CHF, or age>75; [5] eg. deficiency of protein C, protein S, or antithrombin; antiphospholipid antibodies; multiple abnormalities; [6]If TE within past 3 months, consider delaying procedure if possible. [7]eg. prior stroke, TIA, or systemic embolism in AF. [8]According to the 2017 AHA/ACC VHD Guideline Update, bridging can be considered in bileaflet AVR patients with an additional thromboembolic risk factor.

Decisions about interruption and bridging should only be made after assessment of individual patient- and procedure-related factors and discussions with the patient, management team, and proceduralist.

When to Interrupt and Restart DOAC (PAUSE Trial protocol[1])

DOAC	Procedure Bleed Risk (see next page for examples)	Peri-Procedural DOAC use*									
		Day -5	Day -4	Day -3	Day -2	Day -1	Day of proc.	Day +1	Day +2	Day +3	Day +4
Dabigatran (CrCl≥50 mL/min†)	High								Resume day 2 or 3 (1st dose ≥48 hrs post-procedure)		
	Low							1st dose ≥24 hrs post-procedure			
Dabigatran (CrCl<50 mL/min†)	High								Resume day 2 or 3 (1st dose ≥48 hrs post-procedure)		
	Low							1st dose ≥24 hrs post-procedure			
Rivaroxaban, apixaban, edoxaban‡	High								Resume day 2 or 3 (1st dose ≥48 hrs post-procedure)		
	Low							1st dose ≥24 hrs post-procedure			

[1]Douketis JD, Spyropoulos AC, Duncan J, et al. Perioperative management of patients with atrial fibrillation receiving a direct oral anticoagulant (PAUSE Trial). JAMA Intern Med. Published online August 5, 2019. doi:10.1001/jamainternmed.2019.2431

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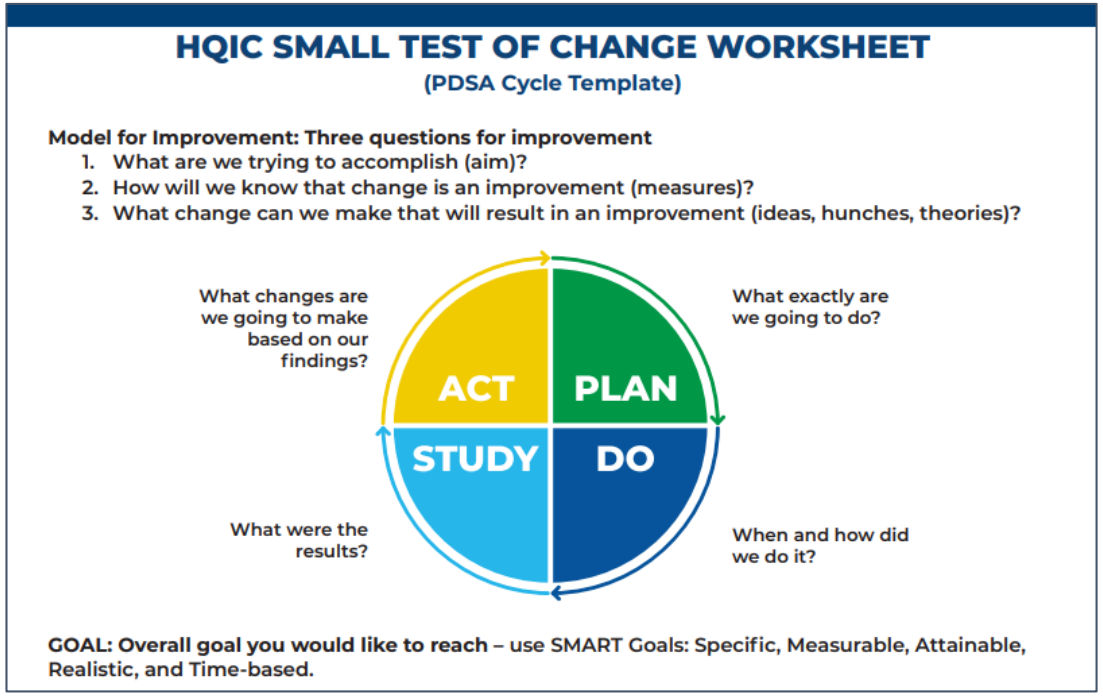
PDSA Cycle Example

ACT
- What needs to be changed again/tweaked?
- Review/revise policy for new drugs/indications/warnings
- Create decision making protocol for abx that interact with warfarin?

STUDY
- Continue RCA for all bleeding events – are there less bleeding events in this certain area?
- Feedback from physician/nurses/pharmacists



HQIC SMALL TEST OF CHANGE WORKSHEET

(PDSA Cycle Template)

Model for Improvement: Three questions for improvement

1. What are we trying to accomplish (aim)?
2. How will we know that change is an improvement (measures)?
3. What change can we make that will result in an improvement (ideas, hunches, theories)?

GOAL: Overall goal you would like to reach – use SMART Goals: Specific, Measurable, Attainable, Realistic, and Time-based.

PLAN
- Document bleeding risk prior to starting anticoagulation
- Create/revise policy around restarting anticoagulation after a major bleeding event
- Add new hard stop for certain drugs likely increase INR

DO
- Build new algorithm for determining bleeding risk in EHR in next 6 months
- Restarting Anticoag Policy revision – present at next P&T committee meeting
- Add hard stops to EHR – 3 months

Resources

- Michigan Anticoagulation Quality Improvement Initiative (MAQI^2)
  - toolkitfull_2.6.pdf (anticoagulationtoolkit.org)
- VHA National Center for Patient Safety: Anticoagulation Vulnerability
  - https://www.patientsafety.va.gov/professionals/hazards/anticoag.asp
- Alliant Health Solutions Root Cause/Fishbone Diagram
  - https://quality.allianthealth.org/wp-content/uploads/2021/07/Fishbone-Diagram-Worksheet_AHSHQIC-TO3H-21-871_11.5.21_508.pdf
- Alliant Health Solutions PDSA Cycle Template
  - https://quality.allianthealth.org/wp-content/uploads/2021/07/HQIC-Small-Test-of-Change-PDSA-Worksheet_AHSHQIC-TO3H-21-870-11.5.21_508.pdf

Key Takeaways

- Learn Today:
  - Going from RCA to change in practice using resources that are already available
    - Fishbone Diagram/Examples
    - Understand the Warfarin Adverse Event Analysis Form
    - Russell Medical Missed Opportunity Form
    - PDSA Cycle Example
- Use Tomorrow:
  - Post RCA tools and guidance

Questions?

Email us at HospitalQuality@allianthealth.org or call us 678-527-3681.

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HQIC Goals

Behavioral Health Outcomes & Opioid Misuse

- ✓ Promote opioid best practices
- ✓ Decrease high dose opioid prescribing and opioid adverse events in all settings
- ✓ Increase access to behavioral health services

Patient Safety

- ✓ Reduce risky medication combinations
- ✓ Reduce adverse drug events
- ✓ Reduce *C. diff* in all settings

Quality of Care Transitions

- ✓ Convene community coalitions
- ✓ Identify and promote optical care for super utilizers
- ✓ Reduce community-based adverse drug events

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Upcoming Events

March 22nd, 2022 12:30 p.m. EST

The Anticoagulation Forum

https://bit.ly/HQIC_ADE_Mar22

Darren Triller, PharmD
Director of Strategic Initiatives

Event registration and information:
www.quality.allianthealth.org

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How did we do today?

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