PCC & ME: UPDATES IN REVERSAL OF ORAL ANTICOAGULANTS AND MAJOR BLEEDING

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Wake Forest® Baptist Health

DISCLOSURE STATEMENT

- I, H Andrew Wilsey, have no conflicts of interest to disclose.

OBJECTIVES

- Recognize the updated guideline recommendations for the management of bleeding in patient on oral anticoagulants.
- Analyze current literature pertaining to efficacy and safety of current reversal strategies for oral anticoagulant-related major bleeding.
- Devise an evidence-based treatment plan to manage major bleeding in patients taking oral anticoagulants.

Atrial Fibrillation & Oral Anticoagulation

TRENDS IN ATRIAL FIBRILLATION

- Ageing Population
- High BMI
- Hypertension
- Diabetes
- Chronic lung disease
- Enhanced detection

Hindricks *Eur Heart J* 2020 | Willliams *JAMA Netw Open* 2020

LIFETIME RISK FOR ATRIAL FIBRILLATION

1 in 3 individuals

of European ancestry at index age of 55 years

Hindricks *Eur Heart J* 2020 | Colilla *Am J Cardiol* 2013

$CHADS_2$ -> CHA_2DS_2VASc

CHADS2 Risk	Score
CHF	1
Hypertension	1
Age > 75	1
Diabetes	1
Stroke or TIA	2

From ESC AF Guidelines

http://www.escardio.org/guidelines-surveys/esc-guidelines/GuidelinesDocuments/guidelines-afib-FT.pdf

CHA2DS2-VASc Risk	Score
CHF or LVEF ≤ 40%	1
Hypertension	1
Age ≥ 75	2
Diabetes	1
Stroke/TIA/ Thromboembolism	2
Vascular Disease	1
Age 65 - 74	1
Female	1

ANTITHROMBOTIC CONSIDERATIONS

CHEST 2018	• Stroke prevention should be offered to those atrial fibrillation (AF) patients with **one or more non-sex** CHA_2DS_2-VASc stroke risk factors • *Strong recommendation, moderate quality of evidence*
ACC/AHA/HRS 2019	• CHA_2DS_2-VASc **score of 1 in men and 2 in women**, prescribing an oral anticoagulant to reduce thromboembolic stroke risk may be considered • *Class IIb recommendation*
ESC 2020	• Anticoagulation should be considered for stroke prevention in AF patients with a CHA_2DS_2-VASc score of **1 in men or 2 in women** • *Class IIa recommendation*

Lip *CHEST* 2018 | January ACC/AHA 2019 | Hindricks *Eur Heart J* 2020

ANTITHROMBOTIC CONSIDERATIONS

7. In patients with AF who are eligible for OAC, we recommend NOACs over VKA (Strong recommendation, moderate quality evidence).

2. **NOACs (dabigatran, rivaroxaban, apixaban, and edoxaban) are recommended over warfarin in NOAC-eligible patients with AF (except with moderate-to-severe mitral stenosis or a mechanical heart valve) (S4.1.1-8–S4.1.1-11).**

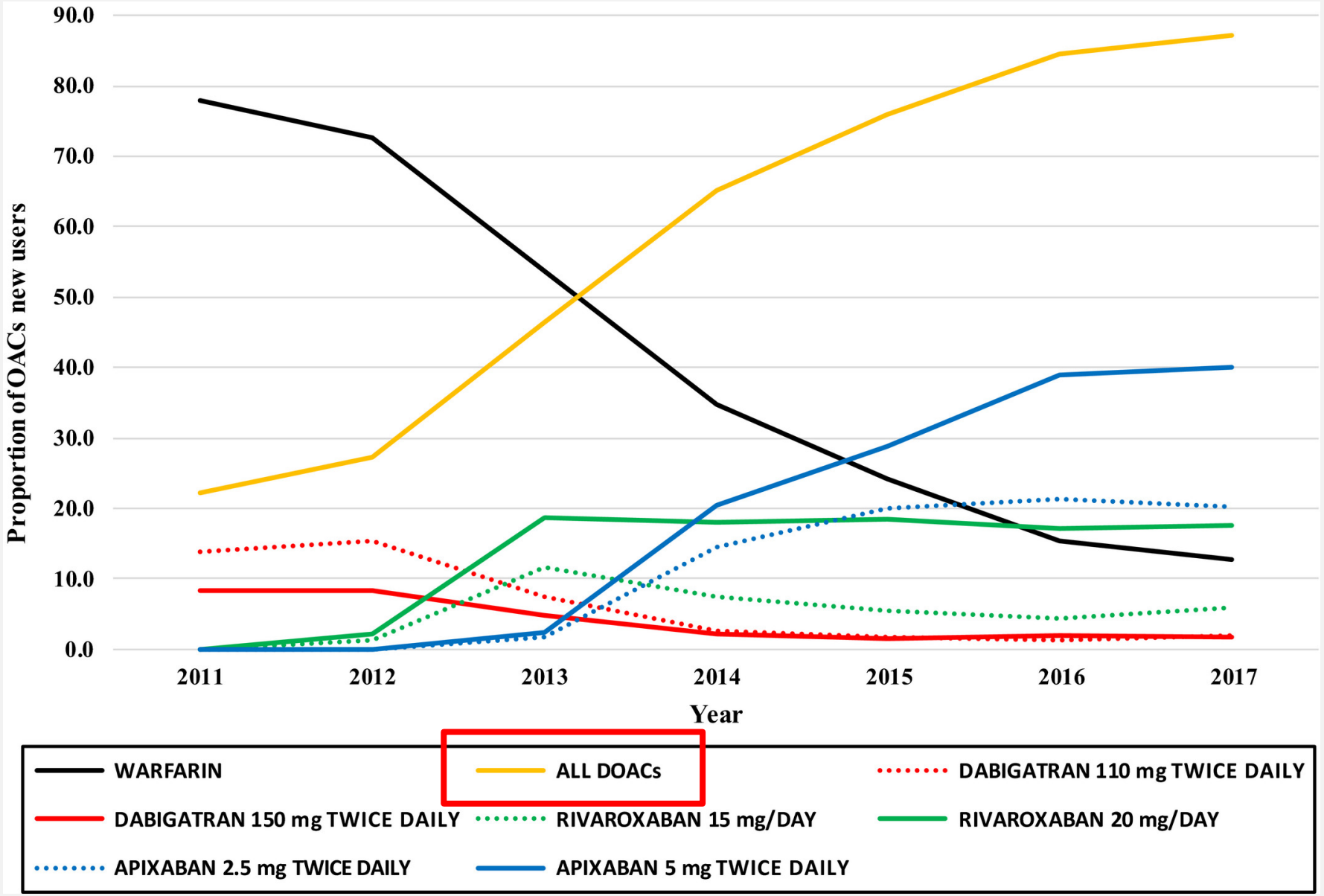
PK/PD

Monitoring

Outcomes

Lip *CHEST* 2018 | January ACC/AHA 2019 |Ruff *Lancet* 2014 | Kurogi *Neurology* 2018 | Hindricks *Eur Heart J* 2020

Oral Anticoagulant Prescription Trends, Profile Use, and Determinants of Adherence in Patients with Atrial Fibrillation



Perreault *Pharmcother* 2019

Assessing Bleeding Severity

DEFINING MAJOR BLEEDING

- Critical Site
- Hemodynamic Instability
- Overt Bleeding

Tomaselli *JACC* 2020

DEFINING MAJOR BLEEDING

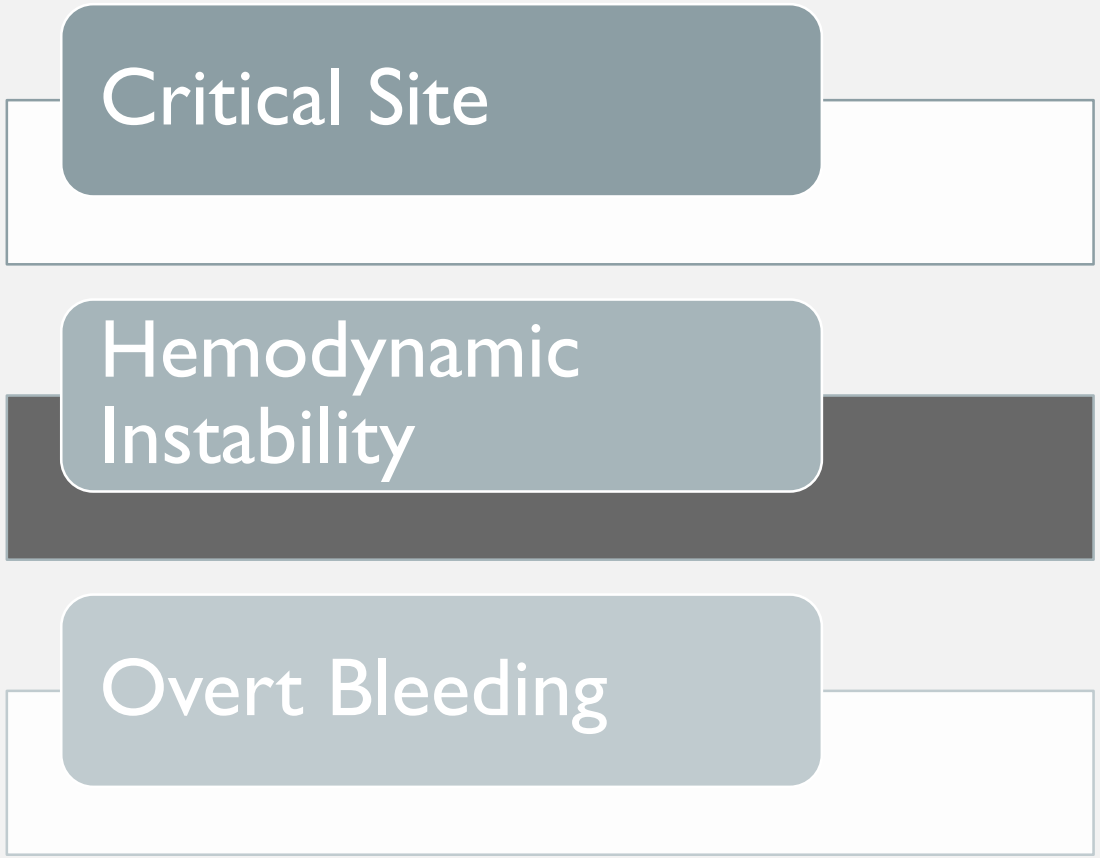
- Critical Site
- Hemodynamic Instability
- Overt Bleeding

Type of Bleed

- Intracranial
- Intraocular
- Spinal
- Pericardial tamponade
- Airway
- Intra-abdominal
- Retroperitoneal
- Intramuscular

Tomaselli *JACC* 2020

DEFINING MAJOR BLEEDING



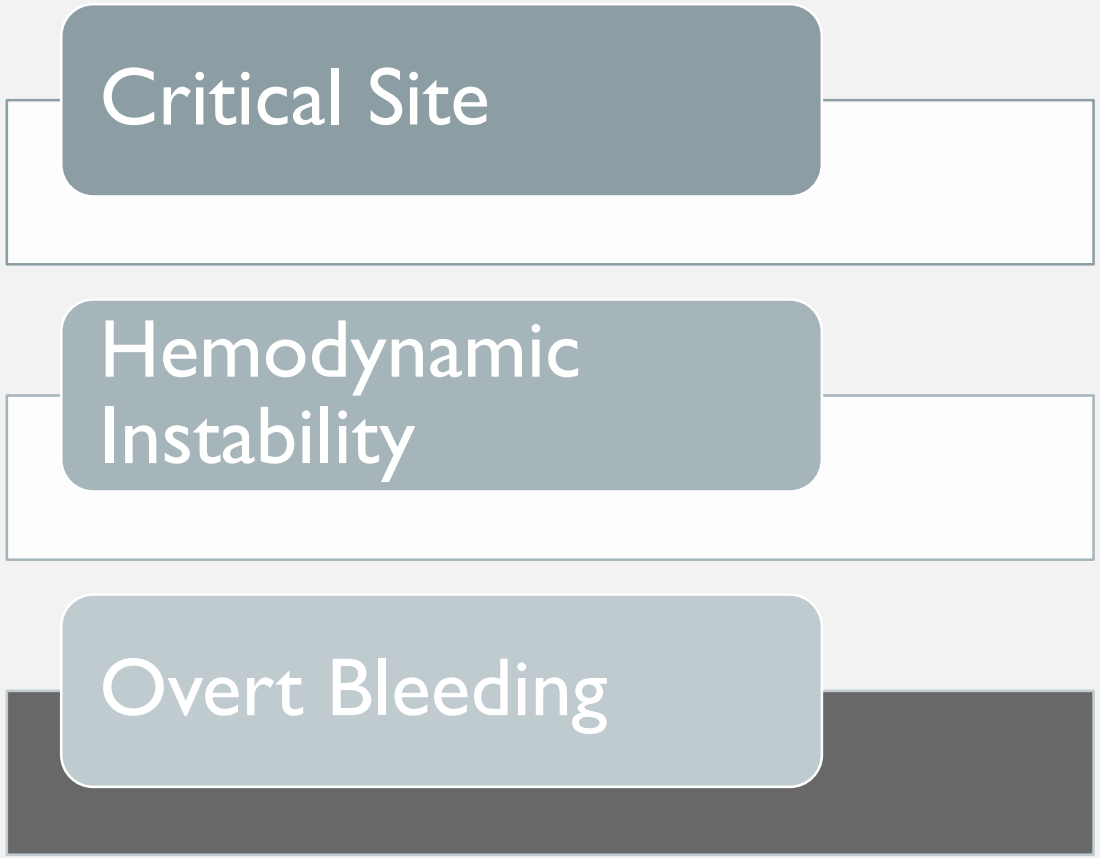
Signs of hemodynamic instability

- SBP < 90 mm Hg
- Decrease in SBP by >40 mm Hg
- MAP < 65 mm Hg
- Clinical signs (urine output)

* SBP, systolic blood pressure; MAP, mean arterial pressure

Tomaselli *JACC* 2020

DEFINING MAJOR BLEEDING



Overt bleeding with:

- Hemoglobin drop ≥ 2g/dL *or*
- ≥ 2 units of pRBC

* pRBC, packed red blood cells

Tomaselli *JACC* 2020

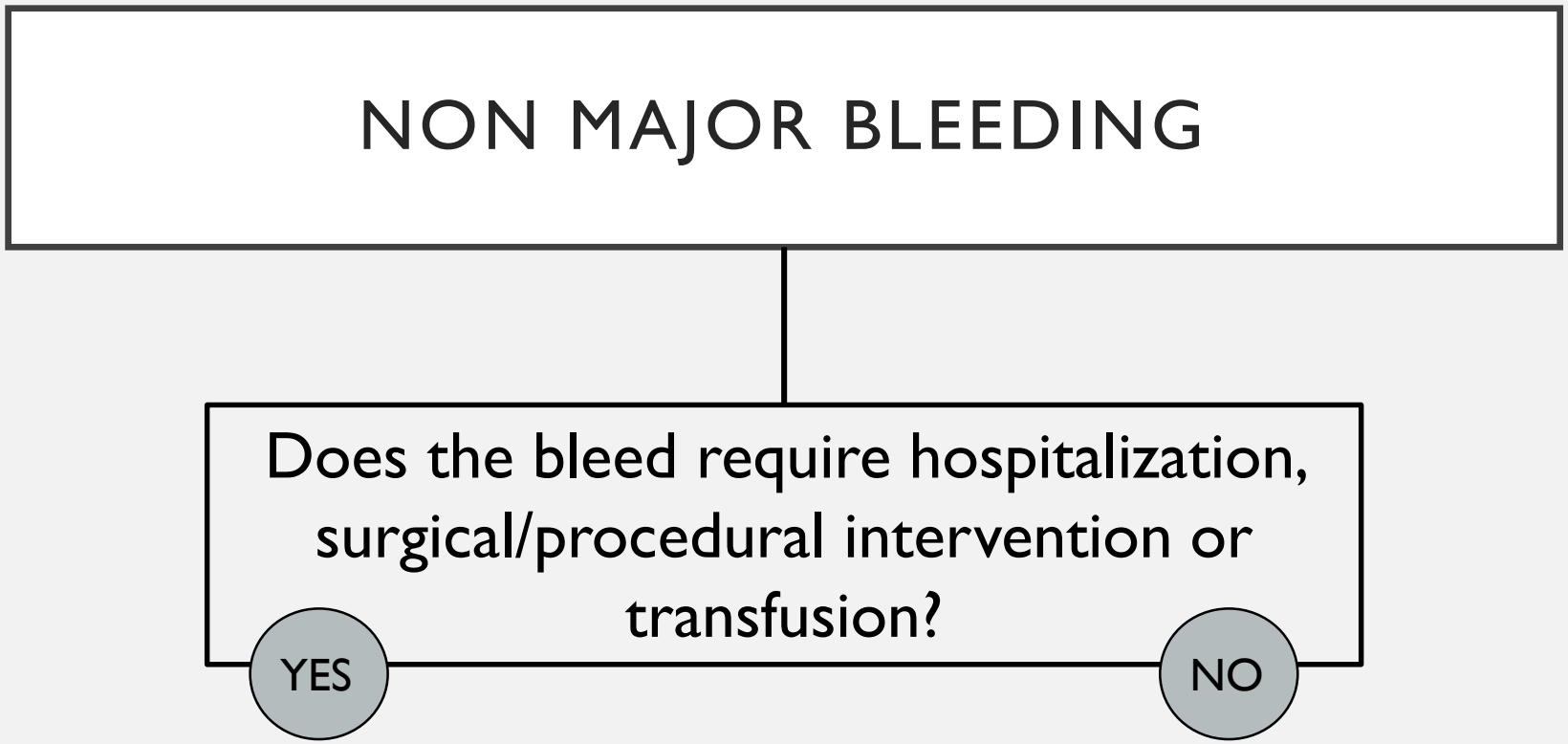
AUDIENCE RESPONSE QUESTION

LM is a 59 YOM admitted for coffee-ground emesis, with past medical history of peptic ulcer disease and atrial fibrillation (on apixaban).

- 132/88 mm Hg | 82 bpm
- Alert and oriented x 3
- Hgb 14.9 g/dL (no prior known)
- No blood products administer

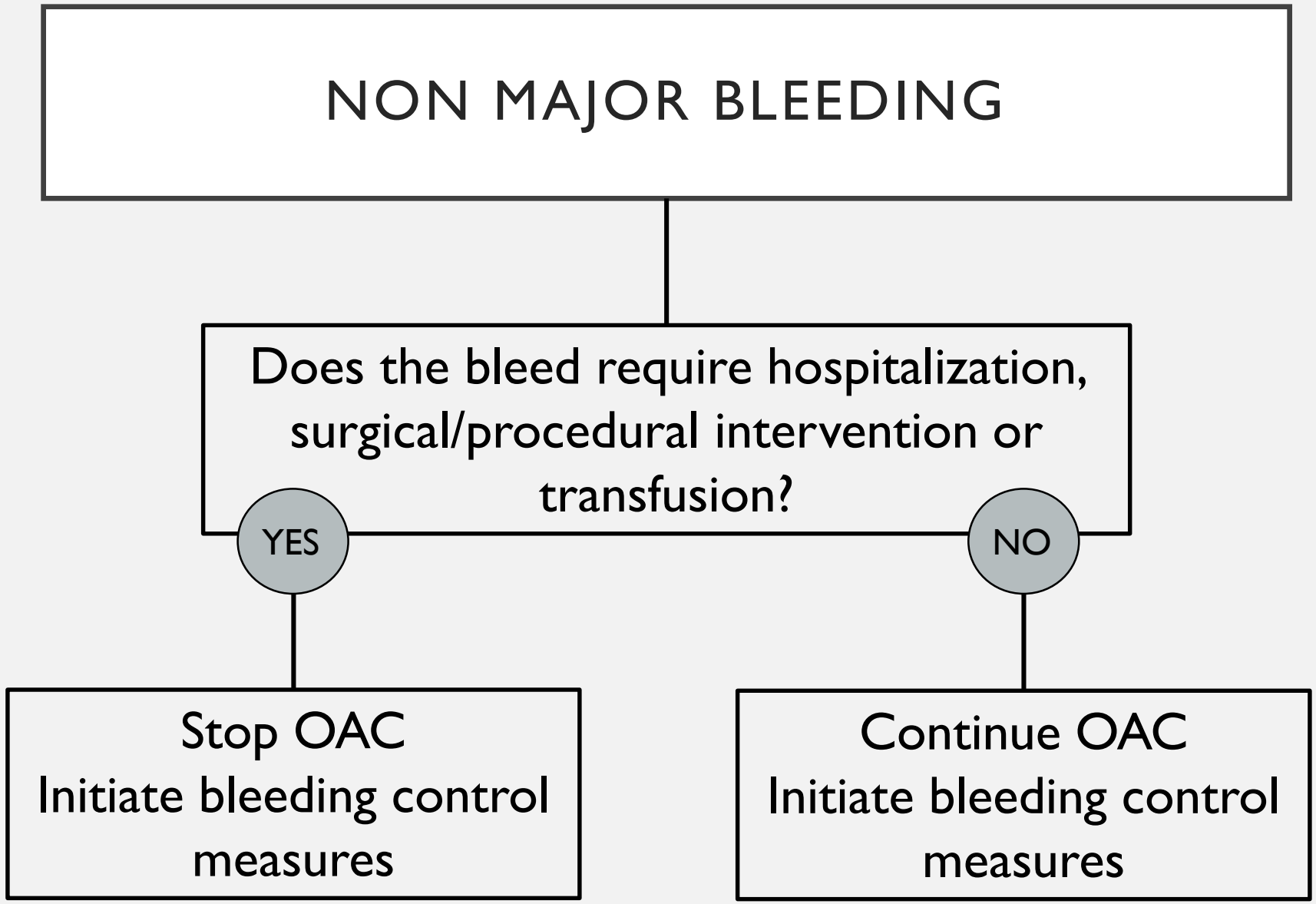
Which criteria does LM meet for a major bleed?

1. Critical site
2. Hemodynamic instability
3. Overt bleeding
4. None, this is a non-major bleed



* OAC, oral anticoagulation

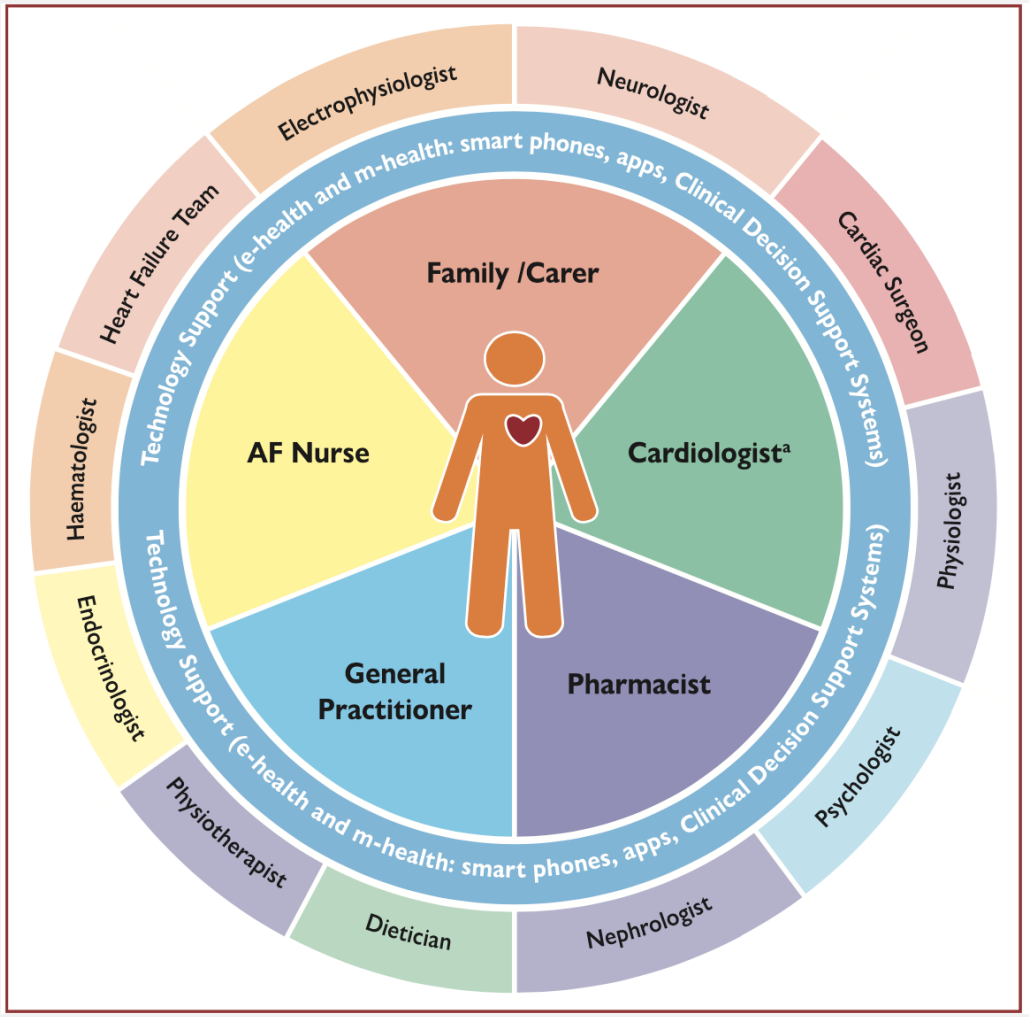
Tomaselli *JACC* 2020



* OAC, oral anticoagulation

Tomaselli *JACC* 2020

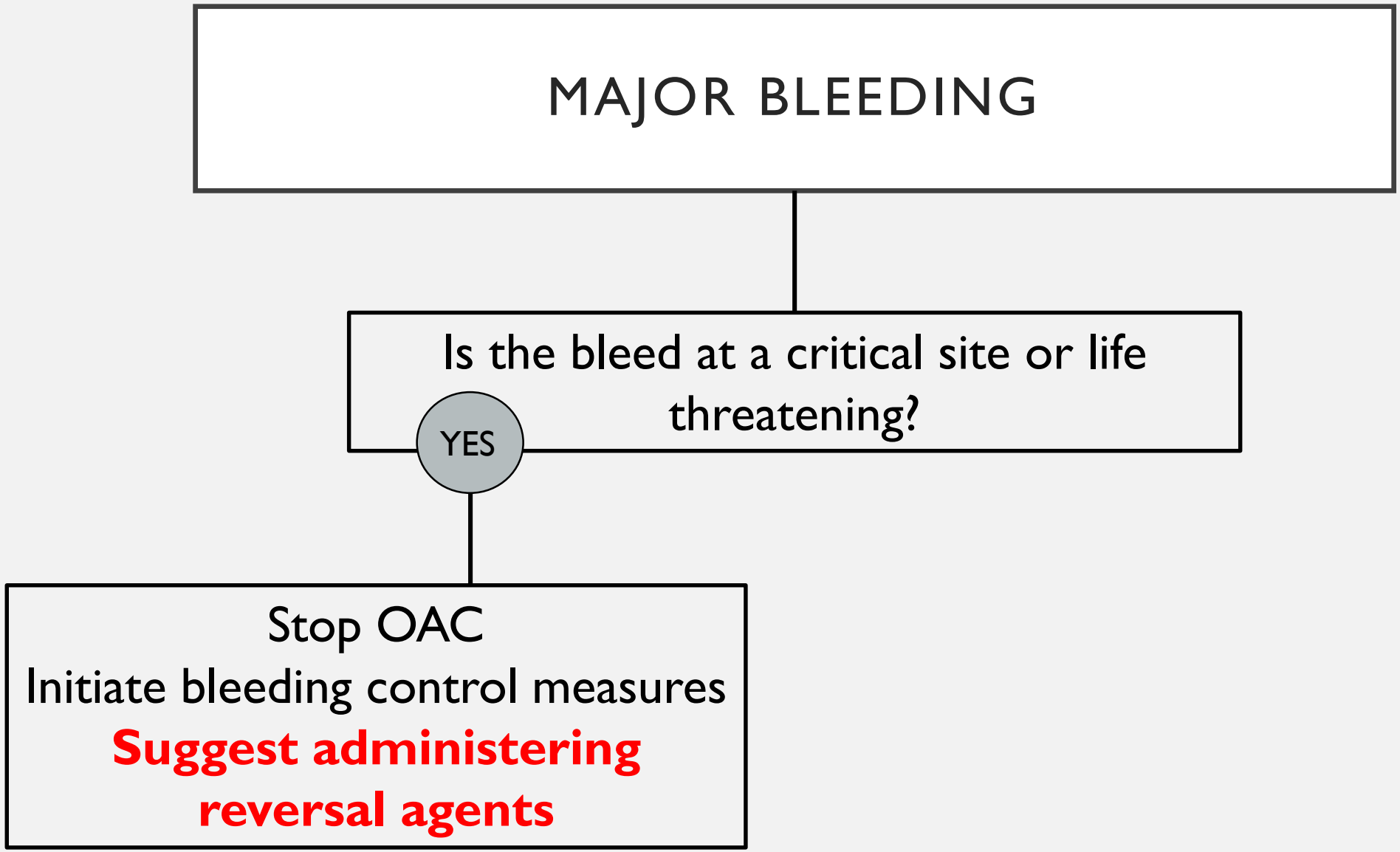
NON MAJOR BLEEDING



- Has patient's underlying bleeding risk changed?
- Dose appropriate?
- New medications or drug interactions?
- Patient education
- Goals of therapy
- Patient/Family wishes

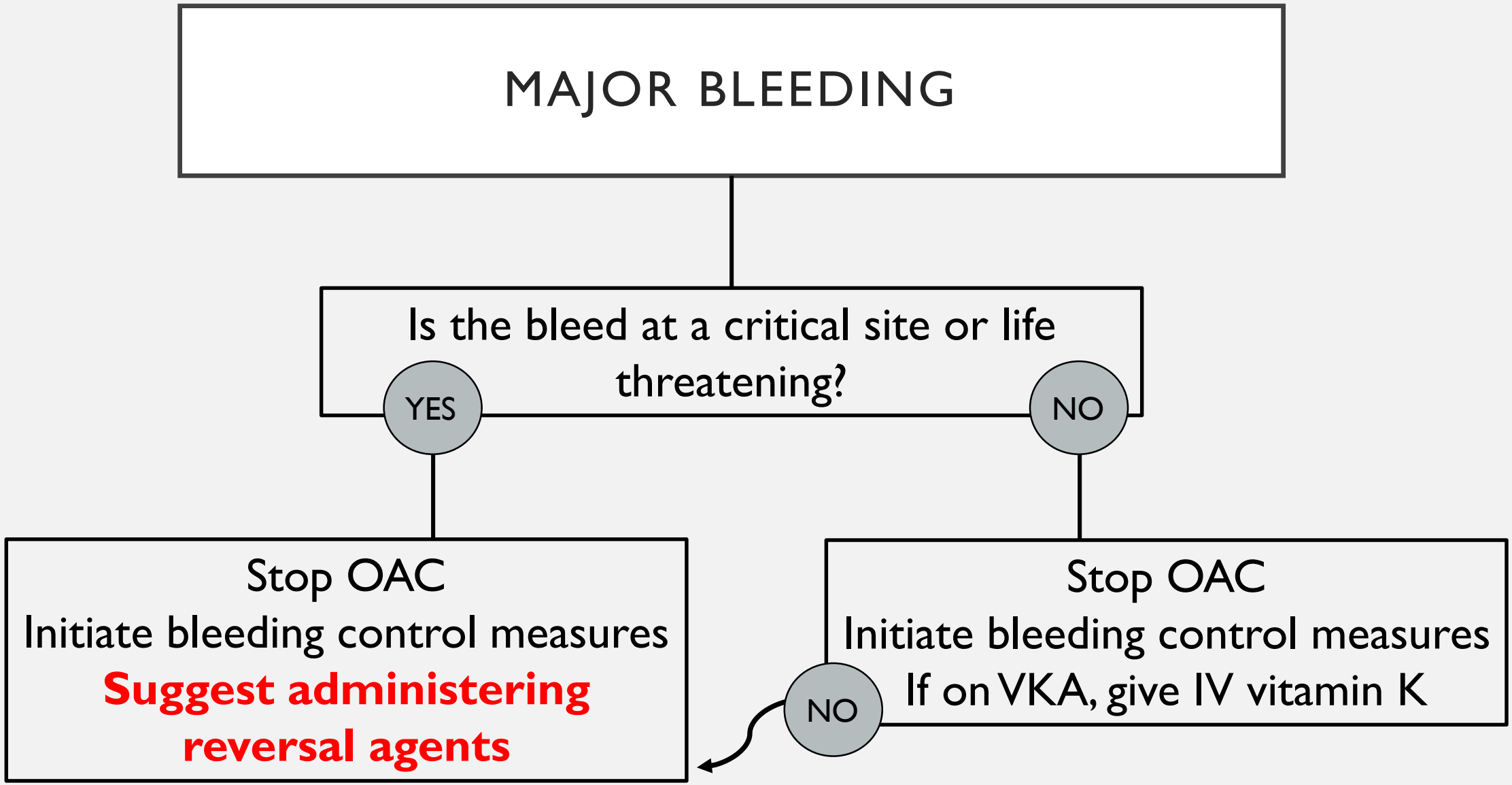
Hindricks *Eur Heart J* 2020 | Tomaselli *JACC* 2020

Reversal of Oral Anticoagulants & Major Bleeding



*VKA, vitamin K antagonist; OAC, oral anticoagulation

Tomaselli *JACC* 2020



*VKA, vitamin K antagonist; OAC, oral anticoagulation

Tomaselli *JACC* 2020

BLEEDING CONTROL MEASURES

- Airway and large-bore intravenous access secured
- Local pressure/packing
- Volume resuscitation
- Hypothermia/acidosis correction
- Early involvement of specialty service

Tomaselli *JACC* 2020

LABORATORY ASSESSMENT

TT	Anti-Xa	aPTT	PT	INR
• Normal TT excludes dabigatran • Prolonged does not discriminate	• Below limit "probably" excludes apixaban rivaroxban	• Normal does not exclude • Prolonged suggests dabigatran	• Normal does not exclude • Prolonged suggests apixaban rivaroxban	• Normal level excludes warfarin • Elevation in relation to exposure

* TT, thrombin time; aPTT activated partial thromboplastin time; PT, prothrombin time; INR, international normalized ratio

Tomaselli *JACC* 2020

AUDIENCE RESPONSE QUESTION

Patient labs

TT: 15 seconds (N: 14-19 seconds)

Anti-Xa LWMH assay: 1.1 IU/mL (N: undectable)

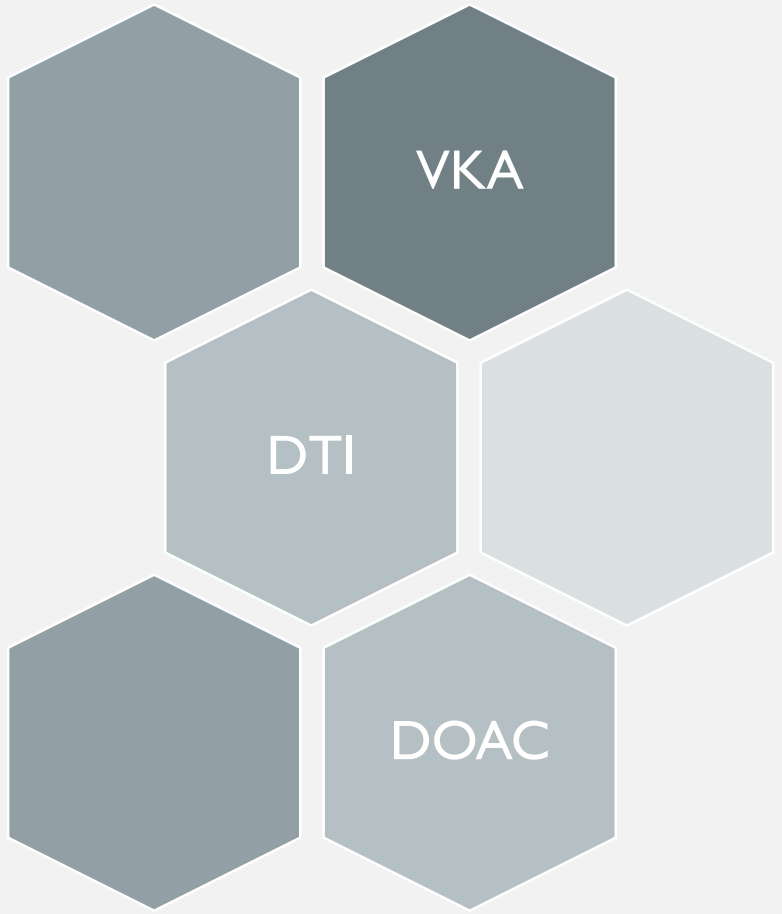
PT: 17 (N: 10-12 seconds)

INR: 1.5 (N: 0.8-1.2)

A patient is on an unknown OAC. Based on the labs below, which medication is the patient most likely taking?

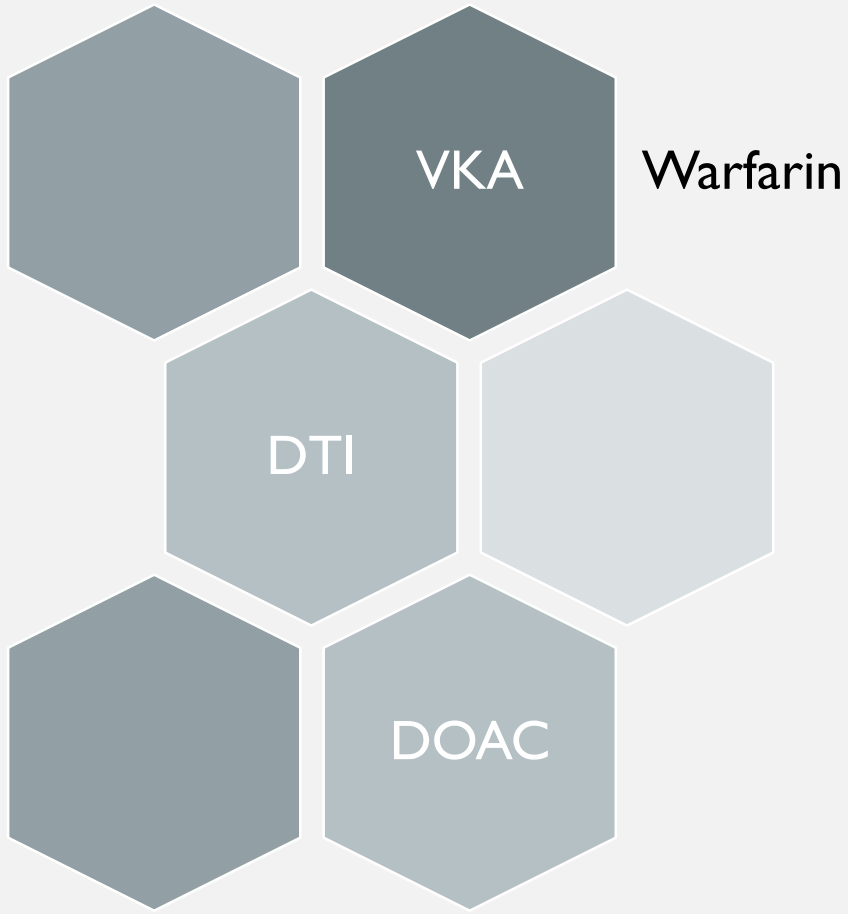
1. Warfarin
2. Rivaroxaban
3. Dabigatran
4. OAC unlikely present

AGENT-SPECIFIC REVERSAL CONSIDERATIONS



Witt *Blood Adv*. 2018 | Tomaselli *JACC* 2020

AGENT-SPECIFIC REVERSAL CONSIDERATIONS



Witt *Blood Adv*. 2018 | Tomaselli *JACC* 2020

VKA

BLEEDING MANAGEMENT

Give 5-10 mg IV vitamin K

- IV administration over 15-30 minutes
  - Onset 4-6 hours
- Subcutaneous route is NOT recommended

Administer 4F-PCC

- INR-based dosing
  - 2-4: 25 units/kg
  - 4-6: 35 units/kg
  - >6: 50 units/kg

~OR~

- Low fixed-dose
  - 1,000 units any non-ICH
  - 1,500 units for ICH

* 4F-PCC, four factor prothrombin complex concentrate; IV, intravenous; ICH, intracranial hemorrhage

Witt *Blood Adv.* 2018 | Tomaselli *JACC* 2020

VKA

PCC FIXED DOSING

Scott et al 2018

- Retrospective, single-center cohort study (n=61)
- 4F-PCC 1000 units vs per package insert in ICH patients
- No significant difference in reaching goal INR, repeat dosing, or in-hospital mortality

Scott *J Emerg Med* 2018 | Gilbert *Am J Emerg Med* 2019

VKA

PCC FIXED DOSING

Scott et al 2018

- Retrospective, single-center cohort study (n=61)
- 4F-PCC 1000 units vs per package insert in ICH patients
- No significant difference in reaching goal INR, repeat dosing, or in-hospital mortality

Gilbert et al 2019

- Retrospective, single-center cohort study (n=60)
- 4F-CC 1500 units ICH or 1000 units other vs per package insert
- No significant differences in reaching INR goal, hospital length of stay, or mortality

RCT completed, pending results
(NCT03064035)

Scott *J Emerg Med* 2018 | Gilbert *Am J Emerg Med* 2019

AUDIENCE RESPONSE QUESTION

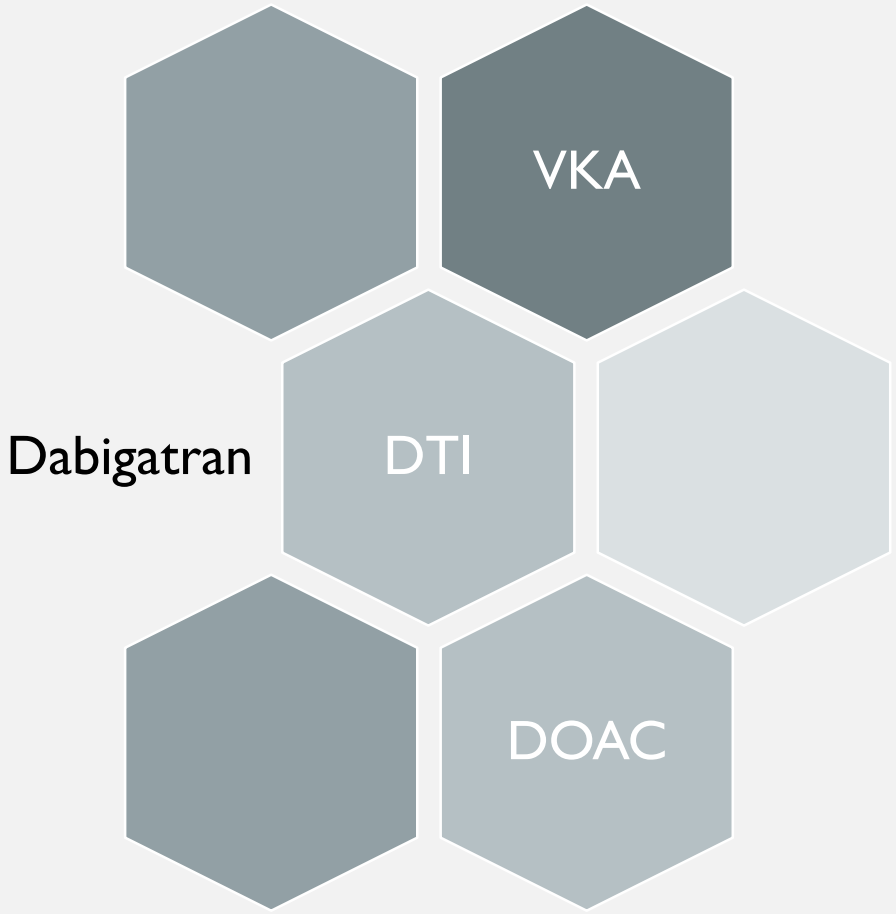
HG is a 54 YOF with PMH of mechanical MVR currently taking warfarin. She is admitted following a motor vehicle accident, found to have traumatic retroperitoneal bleeding.

- INR 3.3
- Weight: 75kg

Per the ACC 2020 guidelines, which is an appropriate 4F-PCC dosing strategy?

1. 800 units
2. 1000 units
3. 1500 units
4. 2600 units

AGENT-SPECIFIC REVERSAL CONSIDERATIONS



Witt *Blood Adv*. 2018 | Tomaselli *JACC* 2020

DTI

BLEEDING MANAGEMENT

In patients with dabigatran-associated major bleeding, whom a reversal agent is warranted, we suggest treatment with **idarucizmab 5 g IV.**

If unavailable:

- Administer aPCC (Anticoagulation Forum 2019)
- Administer either PCC or aPCC (ACC 2020)

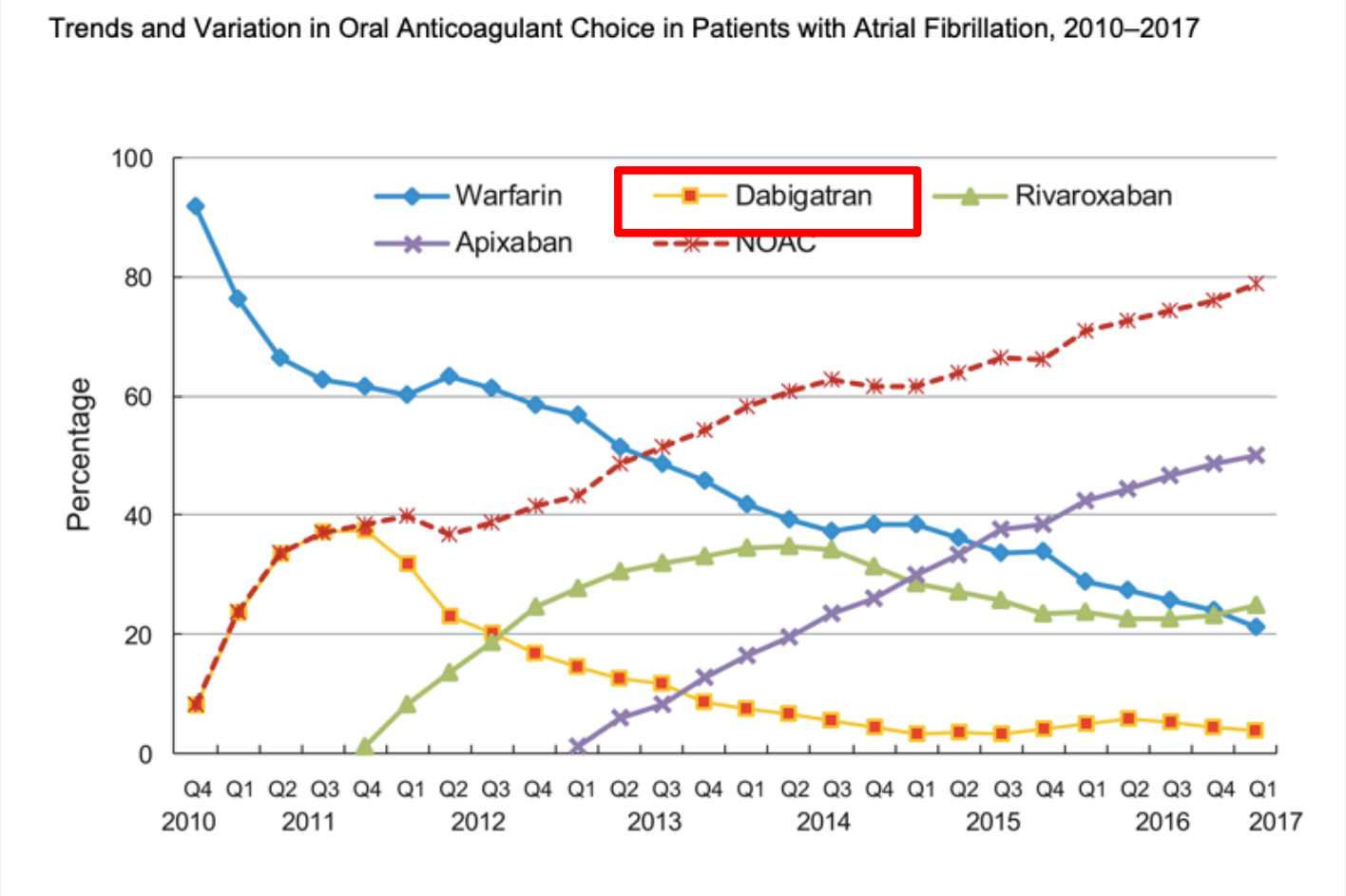
Hemodialysis	Activated charcoal	Rebound

Cuker *Am J Hematol* 2019 | Tomaselli *JACC* 2020

DTI

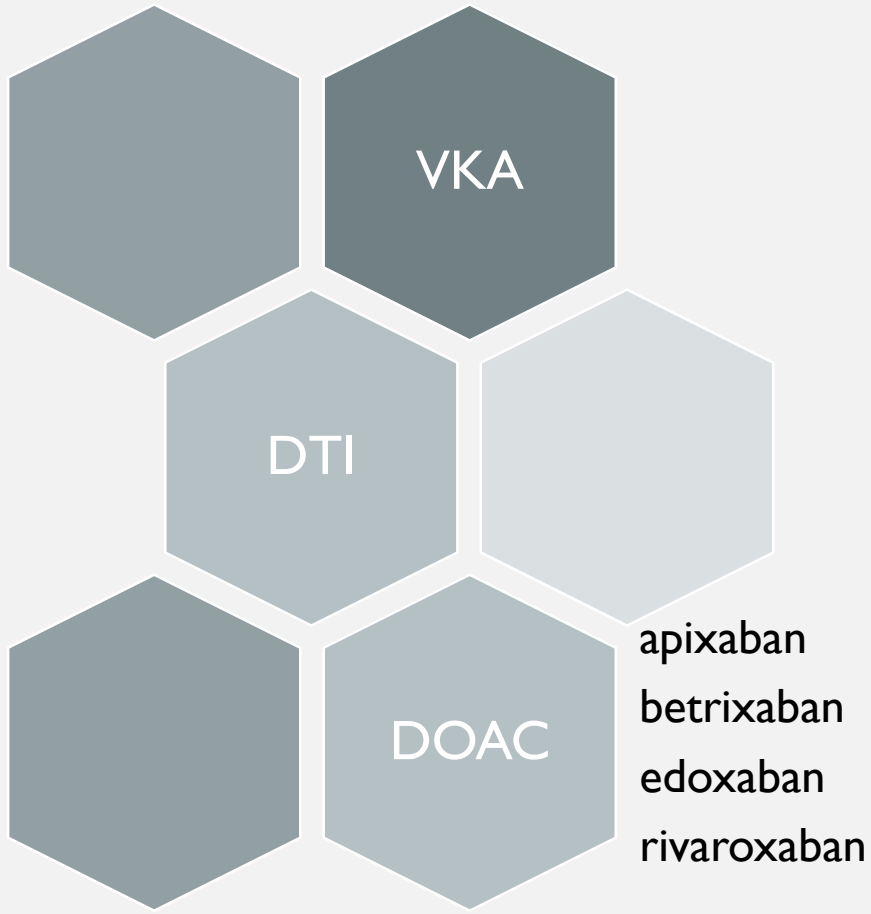
BLEEDING MANAGEMENT

- Clinical pharmacist should review appropriateness of dabigatran selection
- Dabigatran associated with **higher incidence of major bleeding**, regardless of anatomical site



Hernandez *JAMA Intern Med* 2015 | Zhu *Pharmcother* 2018

AGENT-SPECIFIC REVERSAL CONSIDERATIONS



apixaban
betrixaban
edoxaban
rivaroxaban

Witt *Blood Adv*. 2018 | Tomaselli *JACC* 2020

DOAC

DOAC GUIDELINE SUMMARY

ACC 2017

- Administer 4F-PCC 50 units/kg
- If unavailable, consider aPCC 50 units/kg

ASH 2018

- Panel suggests using **either** 4F-PCC or andexanet alfa

Anticoagulation Forum 2019

- Suggest treatment with andexanet alfa.
- If not available, suggest 2000 units 4F-PCC

ACC 2020

- Administer andexanet alfa
- If unavailable, administer PCC or aPCC.
- It is reasonable to dose 4F-PCC at fixed dose 2000 units

Tomaselli *JACC* 2017 Witt *Blood Adv.* 2018 | Cuker *Am J Hematol* 2019
Tomaselli *JACC* 2020

DOAC

DOAC GUIDELINE SUMMARY

ACC 2017	ASH 2018	Anticoagulation Forum 2019	ACC 2020
• Administer 4F-PCC 50 units/kg • If unavailable, consider aPCC 50 units/kg	• Panel suggests using **either** 4F-PCC or andexanet alfa		fixed dose 2000 units

In patients with edoxaban or betrixaban related bleeding, administer off-label treatment with **high-dose andexanet alfa**

Tomaselli *JACC* 2017 Witt *Blood Adv.* 2018 | Cuker *Am J Hematol* 2019
Tomaselli *JACC* 2020

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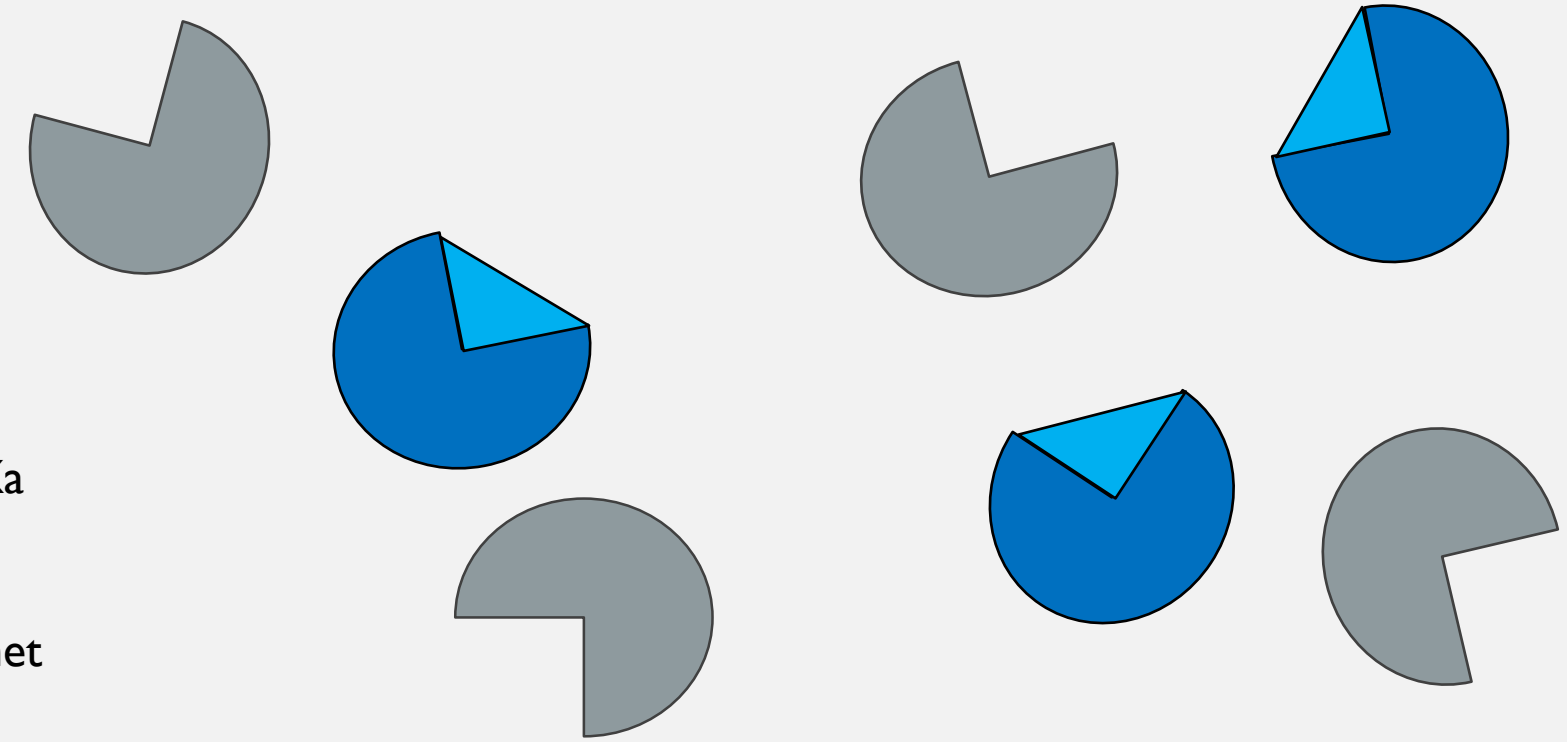
SPECIFIC REVERSAL STRATEGY

- Andexanet alfa is a recombinant, modified human factor Xa decoy protein
- Gained FDA approval May 2018

Andexanet alfa package inset. Portola Pharm. 2018

DOAC

ANDEXANET ALFA MECHANISM OF ACTION



Factor Xa inhibitor

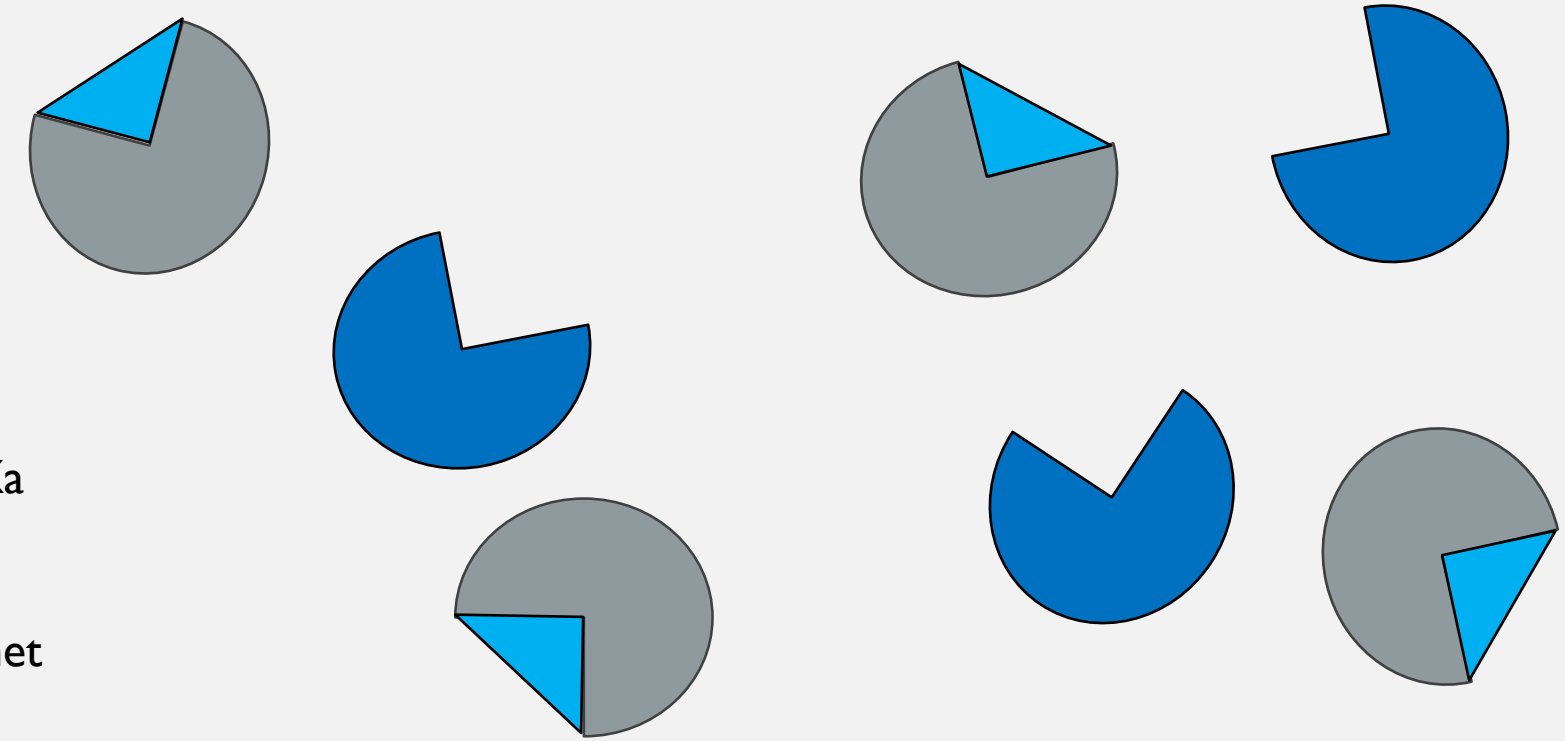
Andexanet alfa

Factor Xa

Andexanet alfa package inset. Portola Pharm. 2018

DOAC

ANDEXANET ALFA MECHANISM OF ACTION



Factor Xa inhibitor

Andexanet alfa

Factor Xa

Andexanet alfa package inset. Portola Pharm. 2018

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Full Study Report of Andexanet Alfa for Bleeding Associated with Factor Xa Inhibitors

S.J. Connolly, M. Crowther, J.W. Eikelboom, C.M. Gibson, J.T. Curnutte, J.H. Lawrence, P. Yue, M.D. Bronson, G. Lu, P.B. Conley, P. Verhamme, J. Schmidt, S. Middeldorp, A.T. Cohen, J. Beyer-Westendorf, P. Albaladejo, J. Lopez-Sendon, A.M. Demchuk, D.J. Pallin, M. Concha, S. Goodman, J. Leeds, S. Souza, D.M. Siegal, E. Zotova, B. Meeks, S. Ahmad, J. Nakamya, and T.J. Milling, Jr., for the ANNEXA-4 Investigators*

Connolly *NEJM* 2019

DOAC

PATIENT POPULATION

edoxaban n=4

- **Inclusion**:
- Reported to have received FXa inhibitor within the past 18 hours, experiencing acute major bleed*

- **Exclusion**:
- Surgery ≤ 12 hours after presentation
- GSC <7
- ICH volume >60mL
- Expected survival <1 month
- Major thrombotic event within 2 weeks

**Potentially life-threatening acute overt bleeding with signs and symptoms of hemodynamic compromise, Hgb drop >2g/dL or baseline <8g/dL, or symptomatic bleeding in critical site*

Connolly *NEJM* 2019

DOAC

ANNEXA-4

Acute major bleeding

↓

15-30 minute bolus & 2 hour infusion

Reported apixaban or >7 hours from last dose:
Bolus 400mg
+
Infusion of 480mg at 4mg/min

Reported enoxaparin, edoxaban, or rivaroxaban ≤ 7 hours from last dose OR unknown time:
Bolus 800mg
+
Infusion of 960mg at 8mg/min

Connolly *NEJM* 2016

DOAC

CO-PRIMARY ENDPOINTS

"Overall, there **was no significant relationship** between hemostatic efficacy and a reduction in anti-factor Xa activity during andexanet treatment"

Connolly *NEJM* 2019

DOAC

RESULTS

82% of the patients had excellent or good hemostasis at 12 hours after the infusion

10% of patients experienced thrombotic events

14% of patients died at 30 days

Connolly *NEJM* 2019

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SAFETY

Characteristic	Total (%)	<6 days	6-14 days	15-30 days
≥ 1 VTE within 30 days	30 (10)	11	11	12
Death within 30 days	49 (14)	8	21	20
Restart of any anticoagulation	220 (62)	145 (41)	46 (13)	29 (8)
Event after restart	8 (2)			
Restart of oral anticoagulation	100 (28)	31 (9)	37 (11)	32 (9)
Event after restart	0			

Connolly *NEJM* 2019

DOAC

ANNEXA-4 LIMITATIONS

- No comparator
- Time to administration
- Time to hemostatic effect
- Clinical evaluation timing
- Surgical population
- Reduced clearance and/or rebleeding

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ANDEXANET LIMITATIONS

Cost

For an unknown ingestion, average wholesale cost of $59,400 per 18 vials compared to $9,695 for 3,500U 4F-PCC

Centers for Medicare and Medicaid Services has granted cases involving Andexxa ® additional funding

Andexanet alfa Lexicomp 2021 | Prothrombin Complex Concentrates alfa Lexicomp 2021
https://www.andexxa.com/reimbursement/ | Frontera *Journal of Thrombosis and Thrombolysis* 2020

DOAC

REAL-LIFE ANDEXANET USE

Coagulation Factor Xa (Recombinant), Inactivated-Zhzo (Andexanet Alfa) Hemostatic Outcomes and Thrombotic Event Incidence at an Academic Medical Center

- Retrospective cohort study including ALL patients receiving andexanet alfa
- 13 patients included in analysis

Stevens *Clinical and Applied Thrombosis/Hemostasis* Nov 2019

DOAC

REAL-LIFE ANDEXANET USE

77% of the patients had excellent or good hemostasis at 12 hours after the infusion

Intracranial bleeding 50%

31% of patients experienced thrombotic events

15% of patients died at 30 days

Stevens *Clinical and Applied Thrombosis/Hemostasis* Nov 2019

DOAC

DOAC GUIDELINE SUMMARY

ACC 2017

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- If unavailable, consider aPCC 50 units/kg

ASH 2018

- Panel suggests using either 4F-PCC or andexanet alfa

Anticoagulation Forum 2019

- Suggest treatment with andexanet alfa.
- If not available, suggest 2000 units 4F-PCC

ACC 2020

- Administer andexanet alfa
- If unavailable, administer PCC or aPCC.
- It is reasonable to dose 4F-PCC at fixed dose 2000 units

Tomaselli *JACC* 2017 Witt *Blood Adv.* 2018 | Cuker *Am J Hematol* 2019
Tomaselli *JACC* 2020

DOAC

NON-SPECIFIC REVERSAL STRATEGY

- 4 factor prothrombin complex concentrates (4F-PCC)
- Activated prothrombin complex concentrates (aPCC)

Shaw *Res Pract Thromb Haemost.* 2018

DOAC

NON-SPECIFIC REVERSAL STRATEGY

Study Details	Drug	Population	Findings
Zhou et al. 2013	Rivaroxaban	Animal (rats)	• 4F-PCC and aPCC prevented hematoma expansion in dose-dependent fashion
Zahir et al. RCT, 2015	Edoxaban	Healthy human volunteers	• 4F-PCC dose-dependent effect on reversal of bleeding, with complete reversal seen at 50IU/kg
Dibu et al. Case series 2015	Rivaroxaban/ Apixaban	Intracranial hemorrhage (ICH)	• Those receiving 50IU/kg aPCC had no ICH expansion or thrombotic complications

*IU/kg = international units per kilogram, RCT= randomized controlled trial

Zhou *Sroke J Cereb Circl* 2013| Zahir *Circulation* 2015 | Dibu *Neurocrit Care* 2015

DOAC

4F-PCC: UPRATE

Management of rivaroxaban- or apixaban-associated major bleeding with prothrombin complex concentrates: a cohort study

Ammar Majeed,[1-4] Anna Ågren,[1,3] Margareta Holmström,[1,3] Maria Bruzelius,[1,3] Roza Chaireti,[3,5,6] Jacob Odeberg,[1,3,7] Eva-Lotta Hempel,[1,3] Maria Magnusson,[6,8,9] Tony Frisk,[10] and Sam Schulman[11,12]

- Prospective cohort study
- Predefined 4F-PCC dosing protocol
  - <65kg: 1500 units
  - ≥65kg: 2000 units

Majeed *Blood* 2017

Characteristic	Apixaban (n=39)	Rivaroxaban (n=45)	Total (n=84)
Age, median	77 (70-81)	73 (68-84)	75 (70-83)
Weight, kg	75 (67-89)	75 (65-80)	75 (66-88)
Indication (%)			
Atrial fibrillation (AF)	34 (87.2)	29 (64.4)	63 (75.0)
Venous thromboembolism (VTE)	2 (5.1)	1 (2.2)	3 (3.6)
AF & VTE	3 (7.7)	15(33.3)	18 (21.4)
Bleeding location (%)			
Intracranial	29 (74.4)	30 (66.7)	59 (70.2)
Gastrointestinal	5 (12.8)	8 (17.8)	13 (15.5)
Other	5 (12.8)	7 (15.6)	12 (14.3)

Majeed *Blood* 2017

DOAC

4F-PCC: UPRATE

69.1% of the patients had "effective" hemostasis based on ISTH criteria

2.4% of patients experienced thrombotic events

32% of patients died at 30 days

*ISTH= International Society on Thrombosis and Haemostasis

Majeed *Blood* 2017

DOAC

4F-PCC: SCHULMAN

Prothrombin Complex Concentrate for Major Bleeding on Factor Xa Inhibitors: A Prospective Cohort Study

- 2,000 unit 4F-PCC dose
- 66 patients included, with intracranial hemorrhage as primary type of bleed

Schulman *Thromb Haemost* 2018

DOAC

4F-PCC: SCHULMAN

76% of the patients had excellent or good hemostasis at 12 hours after the infusion

8% of patients experienced thrombotic events

14% of patients died at 30 days

Schulman *Thromb Haemost* 2018

DOAC

4F-PCC: ICH POPULATION

Circulation

ORIGINAL RESEARCH ARTICLE

Factor Xa Inhibitor-Related Intracranial Hemorrhage

Results From a Multicenter, Observational Cohort Receiving Prothrombin Complex Concentrates

- Multi-center, retrospective, observational cohort study of patients with DOAC-related ICH
- 433 patients evaluated for hemostatic efficacy

Jones *Circulation* 2020

DOAC

Characteristic	Safety Population (n=663)
Age, >75 years (%)	391 (59)
Body-mass index	28.1± 6.5
Estimated creatinine clearance <30mL/min (%)	52 (7.8)
Hospital presentation to drug administration, hours	2.6 (1.5-4.3)
Indication	
Atrial fibrillation (AF)	521 (78.6)
Venous thromboembolism (VTE)	102 (15.4)
Medical History (%)	
Myocardial infarction	62 (9.4)
Stroke	151 (22.8)
Diabetes mellitus	183 (27.6)

Jones *Circulation* 2020

Characteristic	Safety Population (n=663)	ANNEXA-4
Age, >75 years (%)	391 (59)	-
Body-mass index	28.1± 6.5	27.0± 5.9
Estimated creatinine clearance <30mL/min (%)	52 (7.8)	33 (9)
Hospital presentation to drug administration, hours	2.6	4.6
Indication		
Atrial fibrillation (AF)	521 (78.6)	280 (80)
Venous thromboembolism (VTE)	102 (15.4)	61 (17)
Medical History (%)		
Myocardial infarction	62 (9.4)	48 (14)
Stroke	151 (22.8)	69 (20)
Diabetes mellitus	183 (27.6)	23 (34)

Jones *Circulation* 2020 | Connolly *NEJM* 2019

DOAC

RESULTS

81.8% of the patients had excellent or good hemostasis at 12 hours after the infusion

3.8% of patients experienced thrombotic events

12.2% of patients died at 30 days

Jones *Circulation* 2020

DOAC

REVERSAL STRATEGY SUMMARY

Study	N	Age	ICH (%)	Effectiveness	VTE 30 days	Mortality 30 days
ANNEXA-4	254	77	67%	82%	10%	14%
Stevens	13	69	46%	77%	31%	15%
UPRATE	84	75	70%	73%	4%	32%
Shulman	66	77	55%	76%	8%	14%
Jones	433	-	100%	81.8%	3.8%	12%

Connolly *NEJM* 2019 | Majeed *Blood* 2017 | Schulman *Thromb Haemost* 2018 | jones *Circulation* 2020

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DOAC GUIDELINE SUMMARY

ACC 2017

- Administer 4F-PCC 50 unnits/kg
- If unavailable, consider aPCC 50 units/kg

ASH 2018

- Panel suggests using either 4F-PCC or andexanet alfa

Anticoagulation Forum 2019

- Suggest treatment with andexanet alfa.
- If not available, suggest 2000 units 4F-PCC

ACC 2020

- Administer andexanet alfa
- If unavailable, administer PCC or aPCC.
- It is reasonable to dose 4F-PCC at fixed dose 2000 units

Tomaselli *JACC* 2017 Witt *Blood Adv.* 2018 | Cuker *Am J Hematol* 2019
Tomaselli *JACC* 2020

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PCC DOSING

"On the basis of limited data, it is **reasonable to administer 4F-PCC at a fixed dose of 2,000 units** for severe or life-threatening bleeding" - ACC 2020

"We **prefer a fixed dose of 2000 units** because it has been studied in patients with FXa inhibitor-associated bleeding" and offers "greater simplicity for the ordering provider and pharmacy and reduced cost" – Anticoagulation Forum 2019

Cuker *Am J Hematol* 2019
Tomaselli *JACC* 2020

DOAC

PCC DOSING

Comparison of Low- Versus High-Dose Four-Factor Prothrombin Complex Concentrate (4F-PCC) for Factor Xa Inhibitor–Associated Bleeding: A Retrospective Study

- Retrospective cohort study comparing hemostasis between patients receiving low (20-34 units/kg) versus high-dose (35-55 units/kg) 4F-PCC for DOAC reversal
- 99 patients evaluated for efficacy

Wilsey *J Intensive Care* 2020

DOAC

PCC DOSING

Outcomes	20-34 U/kg (n = 57)	35 - 55 U/kg (n = 42)	P value
Hemostatic success	43 (75.4%)	33 (78.6)	0.72
Secondary outcomes			
Survival	46 (80.7%)	27 (64.3%)	0.07
Length of stay, days	11.3 ± 14.7	12.5 ± 8.7	0.71
Post reversal thrombosis	3 (5.3%)	1 (2.4%)	0.64

Wilsey *J Intensive Care* 2020

AUDIENCE RESPONSE QUESTION

RW is a 62 YOM admitted with acute onset of right-sided weakness and difficulty speaking. A head CT scan reveals right parietal intracerebral hemorrhage. The patient is taking edoxaban for stroke prophylaxis.

- Last dose 10 hours ago
- Weight 85 kg

Based on the ACC 2020 guidelines, which of the following is MOST appropriate for RM?

1. Andexanet alfa 400mg bolus + 480mg @ 4mg/min
2. IV vitamin K 10mg
3. 4F-PCC 2000 units
4. 4F-PCC 4250 units

MOVING FORWARD

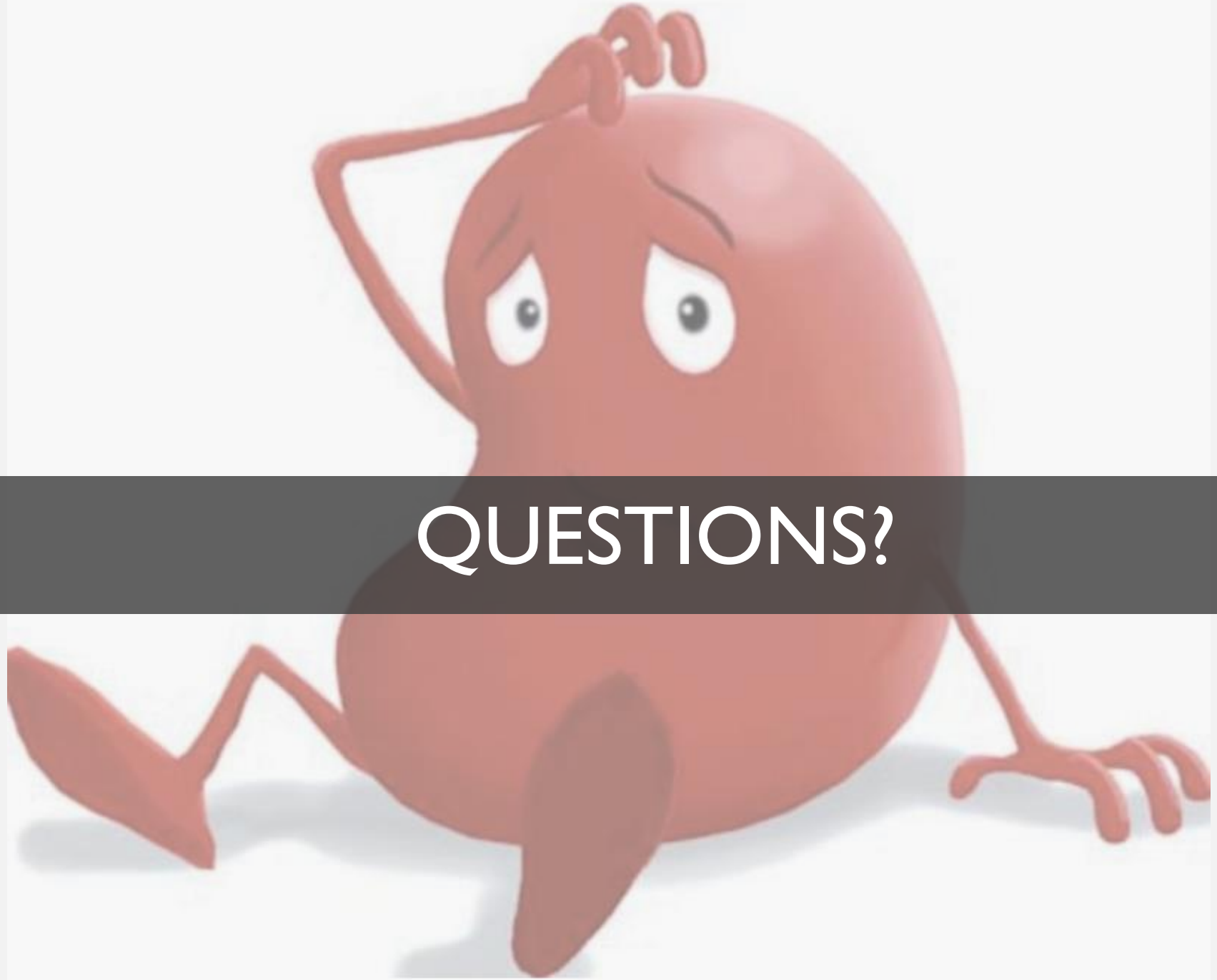
Head to head trials	Thrombotic risks	Hybrid strategies
New anticoagulants	New reversal agents	Ethical considerations

Buller *NEJM* 2014

Conclusions

CONCLUSIONS

- Atrial fibrillation remains the most common indication for oral anticoagulation, and prescribing rates of direct oral anticoagulants continues to climb.
- Assessing bleeding severity to determine appropriate of reversal is essential.
- Clinical pharmacists are vital to reversal agent appropriateness, selection, dosing, monitoring as well as medical profile review.
- Cost-effectiveness analysis and head to head analysis with our alternative strategies will strengthen our approach to reversal in this patient population.



QUESTIONS?

PCC & ME: UPDATES IN REVERSAL OF ORAL ANTICOAGULANTS AND MAJOR BLEEDING

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