

Primary Care Call to Action for VTE Management

Sharpening Skills in Recognition, Treatment, and Secondary Prevention

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Fadi Elias Shamoun, MD, has no financial interests/relationships or affiliations in relation to this activity.

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Housekeeping Notes

Thank you to PeerView for providing this session, and Bristol Myers Squibb and Pfizer Alliance for providing the educational grant for this symposium.

You should have received a link to an online program evaluation.

Post-test and Evaluation: **[PeerView.com/VTE-Survey-TFY](https://www.peerview.com/VTE-Survey-TFY)**

Your evaluation of the program is very important in helping us to better meet your current and future medical education needs. We welcome your opinions and comments.

Educational Objectives

- Apply appropriate evidence-based clinical decision tools in an interprofessional manner to identify patients in primary care at risk for VTE
- Compare the efficacy and safety profile and dosing regimens of available treatment options for VTE
- Implement the most up-to-date evidence-based guidelines in the management of VTE to determine an individually appropriate treatment strategy for each patient
- Explain the indications and rationale for standard vs extended treatment for the secondary prevention of VTE
- Educate patients on the heightened risk of VTE recurrence, and the importance of treatment adherence

Recognizing and Assessing VTE Risk in the Primary Care Setting

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The Epidemiology and Consequences of VTE in the United States: Fast Facts¹⁻⁴

Things to Know



Blood clots can happen to anyone.



They are often preventable.

Blood Clots Affect Many People

900,000
EACH YEAR

VTE affects as many as 900,000 Americans each year.



3 IN 10

3 in 10 people who have a blood clot will have another episode within 10 years.

Blood Clots Can Be Deadly

100,000
PEOPLE DIE EACH YEAR



As many as 100,000 people die of blood clots each year.

SUDDEN DEATH



1 of 4 people who have a PE die without warning.



Blood clots are a leading cause of death in people with cancer after the cancer itself.

PE is a leading cause of death in a woman during pregnancy or just after having a baby.



- ~50% of all VTE cases occur during or shortly after hospital admission for surgery or acute medical illness
- Mortality rates are unchanged since 2000; early diagnosis is critical to prevent death

VTE Provoking Factors by Risk Category^{1,a}

Minor Transient and Persistent Risk Factors

Minor transient

- Immobilization
- Lower limb trauma with transient impairment of mobility
- Pregnancy, puerperium
- Air travel >8 hours
- Use of estrogen therapy

Minor persistent

- BMI >30 kg/m²
- HF
- CrCl <50 mL/min
- Family history of VTE or known thrombophilia
- IBD
- Lower extremity paralysis or paresis

Major Transient and Persistent risk factors

Major transient

- Major surgery or trauma
- Cesarean section

Major persistent

- Active cancer at baseline diagnosis or treatment <6 months or recurrent or metastatic cancer

Classification of risk factor by category is important to determine treatment duration in patients with VTE

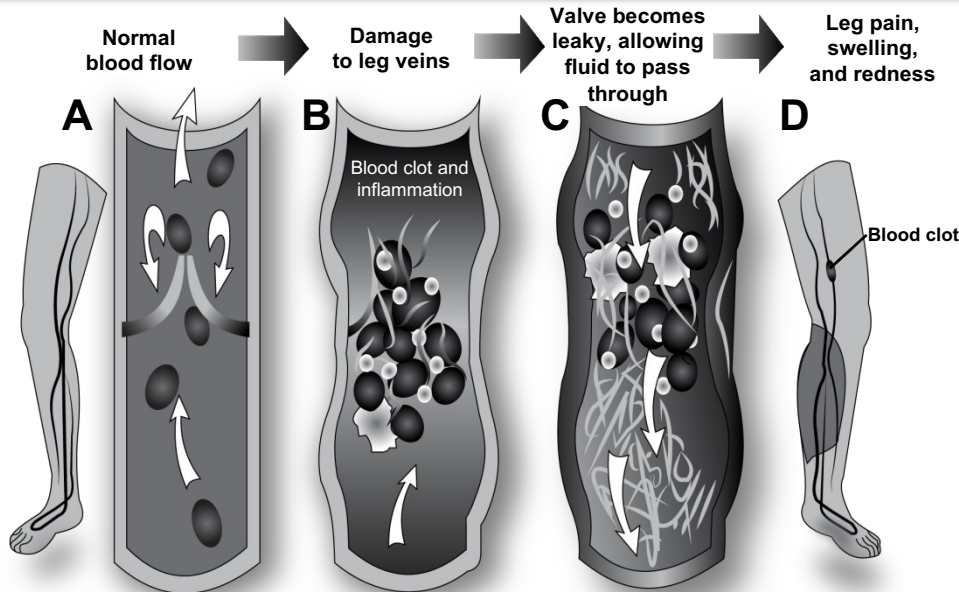
^a VTE provoking factors by category were obtained from the EINSTEIN EXT/EINSTEIN CHOICE baseline risk factor pooled analysis.

1. Schindewolf M, Weitz JI. *Thromb Haemost.* 2020;120:14-26.

Long-Term Consequences of VTE¹⁻³

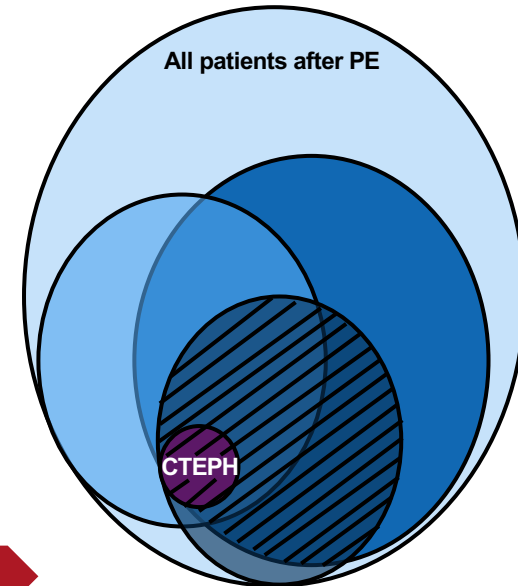
Post-Thrombotic Syndrome

Develops in 20% to 50% of patients with DVT, even when appropriate anticoagulant therapy is used



Post-PE Syndrome and CTEPH

- All patients after PE
- Reported symptoms of reduced functional status
- Persistent thrombi
- Measurable limitations in cardiopulmonary function
- CTEPH
- Post-PE syndrome



Anxiety and depression are also long-term consequences of VTE

Post-Thrombotic Syndrome: Treated DVT

Author and Year	N	Journal	2-Year, %
Prandoni 1996	355	<i>Ann Intern Med</i>	23
Brandjes 1997	96	<i>Lancet</i>	23
Prandoni 2004	90	<i>Ann Intern Med</i>	25
Partsch 2004	37	<i>Int Angiol</i>	46
Van Dongen 2005	244	<i>J Thromb Haemost</i>	30

What Does DVT Look Like in Primary Care?^{1,2}

Common Symptoms

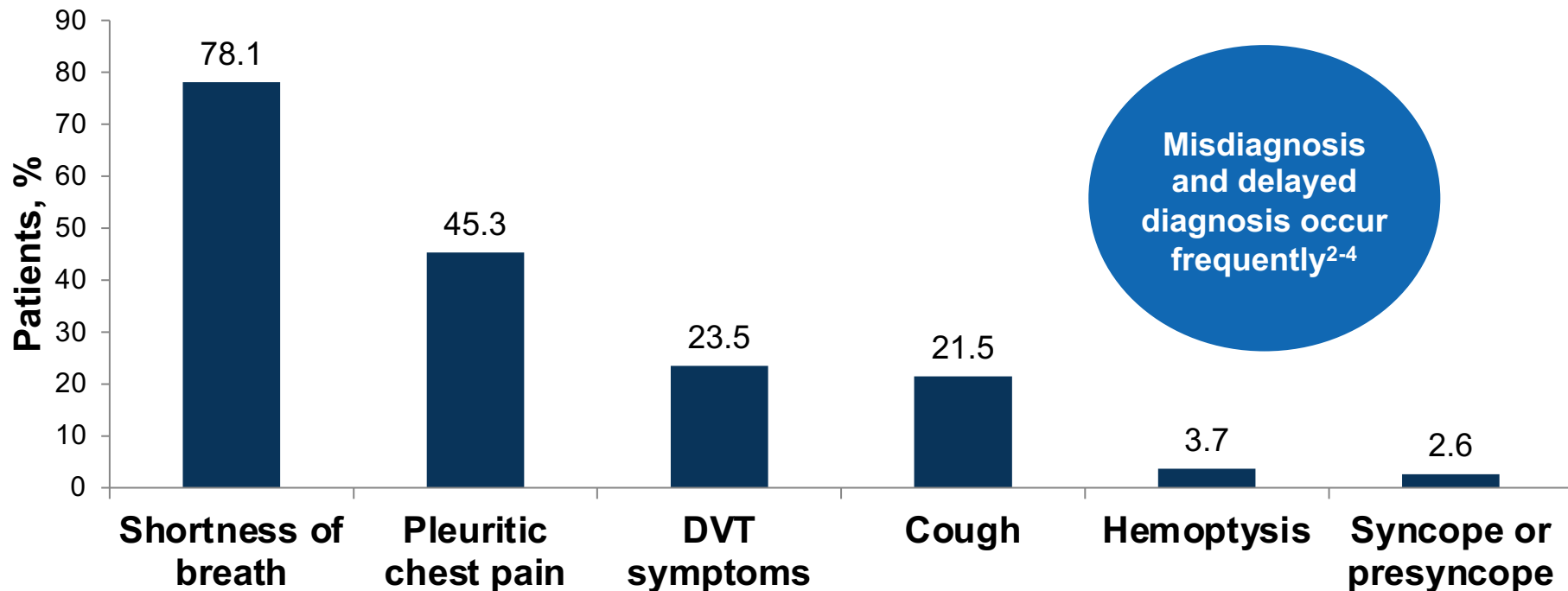
- Unilateral leg discomfort
- Warmth
- Swelling
- “Heaviness”

Common Exam Signs

- Unilateral edema
 - Larger calf circumference
- Dilated superficial veins
- Skin discoloration
- Warmth or erythema
- Pain and tenderness along course of vein

What Does PE Look Like in Primary Care Practice?

Cohort of 652 Patients Diagnosed With Acute PE in Primary Care¹



1. Vinson DR et al. *J Gen Intern Med*. 2022 Jan 12 [Epub ahead of print]. 2. Hunter R et al. *Br J Health Psychol*. 2017;22:8-25.
3. Golemi I et al. *Int Angiol*. 2019;38:284-290. 4. Van Maanen R et al. *BMJ Open*. 2020;10:e039913.

Helpful Tools to Establish a VTE Diagnosis^{1,2}

- Pretest probability
 - Wells score
 - Avoid underdiagnosis or overtreatment
 - Different scores are used for DVT and PE
 - There are many other pretest probability scores: check population before use!
- Confirmatory testing
 - D-dimer
 - Useful only if Wells score is low/unlikely (high negative predictive value)
 - Negative if $<500 \mu\text{g/L}$ or $<10\times$ age
 - Imaging
 - Compression ultrasound
 - CT/MR venogram

Wells Scores for Predicting the Probability of VTE

DVT (Nonpregnant Adult Outpatients)¹

Clinical Characteristic(s)	Score
Active cancer	+1
Paralysis, paresis, or recent plaster immobilization of the lower extremities	+1
Recently bedridden for 3 days or major surgery within the last 12 weeks	+1
Localized tenderness along the deep venous system	+1
Entire leg swollen	+1
Calf swelling ≥ 3 cm larger than asymptomatic side	+1
Pitting edema confined to symptomatic leg	+1
Collateral superficial veins	+1
Previously documented DVT	+1
Alternative diagnosis at least as likely as a DVT	-2
Clinical probability of DVT	Total score
Likely	≥ 2
Unlikely	< 2

PE (Nonpregnant Adult Inpatients and Outpatients)²⁻⁴

Clinical signs and symptoms compatible with DVT	3
PE judged to be the most likely diagnosis	3
Surgery or bedridden for more than 3 days during the past 4 weeks	1.5
Previous DVT or PE	1.5
Heart rate > 100 min	1.5
Hemoptysis	1
Active cancer (treatment ongoing or within previous 6 months or palliative treatment)	1

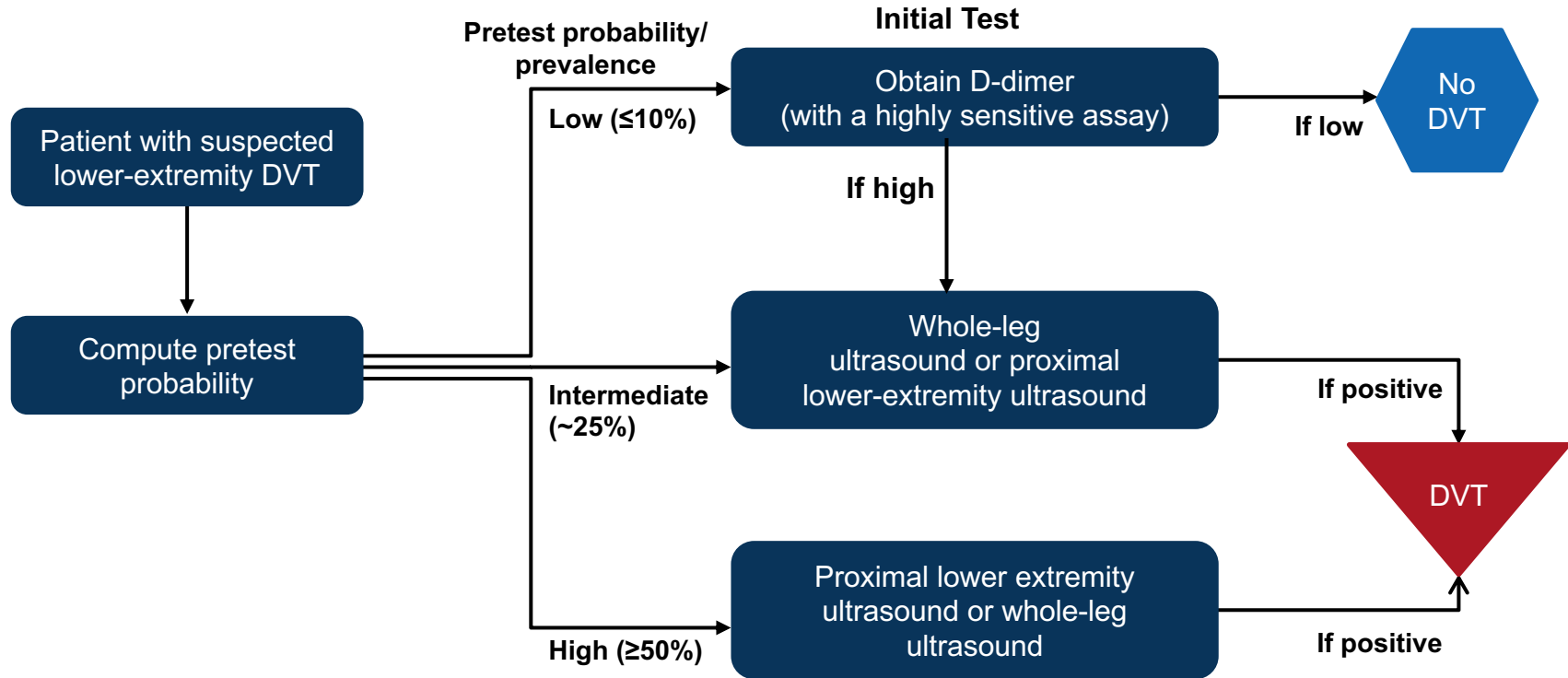
**≤ 4 : low (or PE unlikely) pretest probability;
4.5-6: moderate pretest probability; > 6 : high pretest probability**

<https://www.mdcalc.com/wells-criteria-dvt>

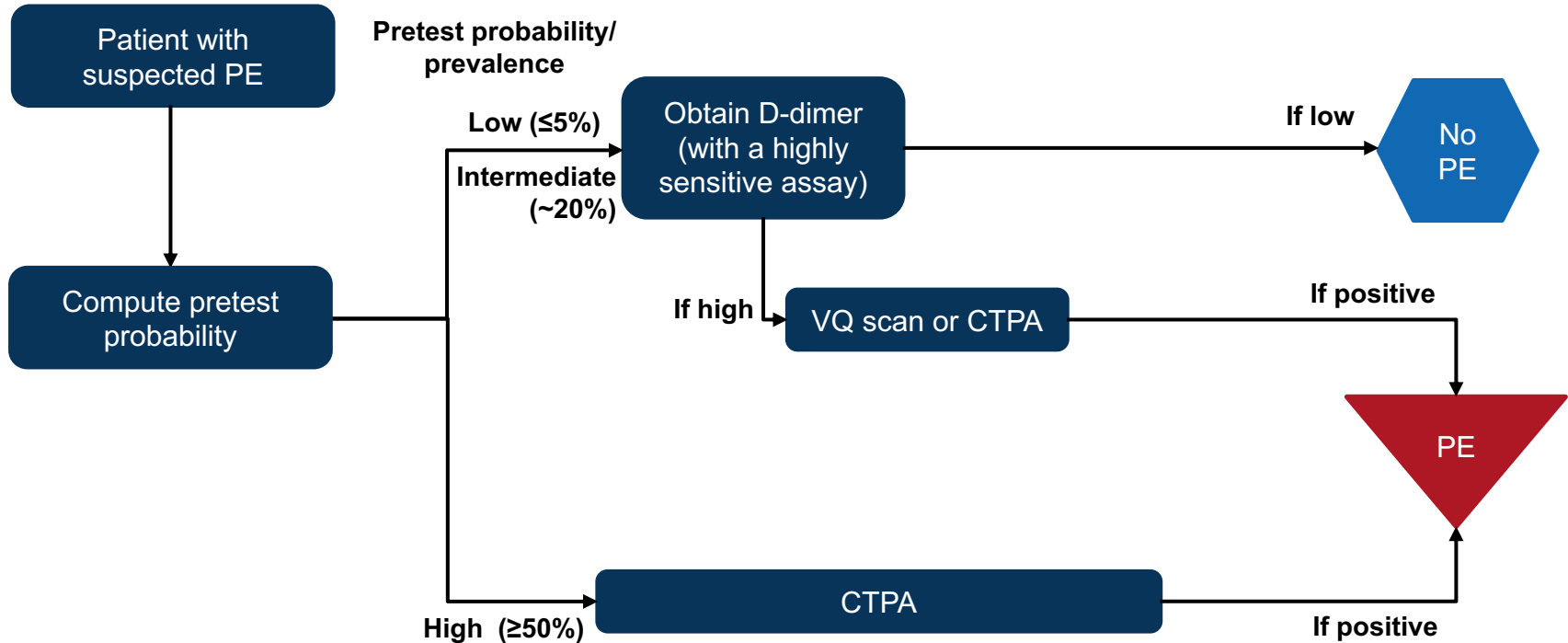
<https://www.mdcalc.com/wells-criteria-pulmonary-embolism>

1. Wells PS et al. *N Engl J Med*. 2003;349:1227-1235. 2. Wells PS et al. *Ann Intern Med*. 1998;129:997-1005.
3. Wells PS et al. *Thromb Haemost*. 2000;83:416-420. 4. Kearon C et al. *Ann Intern Med*. 2006;144:812-821.

Evaluating Suspected Lower-Extremity DVT: ASH 2018 Guidelines¹



Evaluating Suspected PE: ASH 2018 Guidelines¹



Pulmonary Embolism Severity Index (PESI)¹

Predictors	Points
Age	+1/year
Male sex	+10
HF	+10
Chronic lung disease	+10
Arterial oxygen saturation <90%	+20
Pulse ≥110 beats per minute	+20
Respiratory rate ≥30 breaths per minute	+20
Temperature <36°C	+20
Cancer	+30
SBP <100 mmHg	+30
Altered mental status	+60

PE Severity Score (sum of points)	Risk Class	30-Day Mortality Rate
≤65	I	0%-1.6%
66-85	II	1.7%-3.5%
86-105	III	3.2%-7.1%
106-125	IV	4.0%-11.4%
>125	V	10.0%-24.5%

Low-risk PESI → candidate for outpatient treatment

www.mdcalc.com/pulmonary-embolism-severity-index-pesi

Patient Profile: Jackie

**57-year-old
female
patient**

- Routine follow-up visit 1 week after cholecystectomy
- Notes new leg discomfort since surgery

**Physical
exam and
laboratory
results**

- HR = 86; RR = 20; O₂ sat = 97%; temp = 98.0°F; BP = 142/77 mmHg; BMI = 31.2 kg/m²; weight = 123 kg; oriented x4
- Normal work of breathing, right leg swollen, edematous and erythematous
- No history of VTE or cancer; postmenopausal and a nonsmoker
- Current medications
 - Oxycodone/acetaminophen for pain following surgery
 - Losartan/HCTZ and rosuvastatin

Patient Case Assessment: Jackie¹

Wells' Criteria for DVT ☆
Calculates risk of DVT based on clinical criteria.

INSTRUCTIONS

- **Note:** The Wells' Score is less useful in hospitalized patients (Silveira PC, 2015).
- There are a few versions of this criteria with minor differences based on the study; this set is the most widely validated, based on Wells 2003.

When to Use ▼ Pearls/Pitfalls ▼ Why Use ▼

Active cancer Treatment or palliation within 6 months	No 0	Yes +1
Bedridden recently >3 days or major surgery within 12 weeks	No 0	Yes +1
Calf swelling >3 cm compared to the other leg Measured 10 cm below tibial tuberosity	No 0	Yes +1
Collateral (nonvaricose) superficial veins present	No 0	Yes +1
Entire leg swollen	No 0	Yes +1
Localized tenderness along the deep venous system	No 0	Yes +1
Pitting edema, confined to symptomatic leg	No 0	Yes +1
Paralysis, paresis, or recent plaster immobilization of the lower extremity	No 0	Yes +1
Previously documented DVT	No 0	Yes +1
Alternative diagnosis to DVT as likely or more likely	No 0	Yes -2

4 points
High risk group for DVT. "Likely" according to Wells' DVT studies.

Copy Results 📄 Next Steps >>>

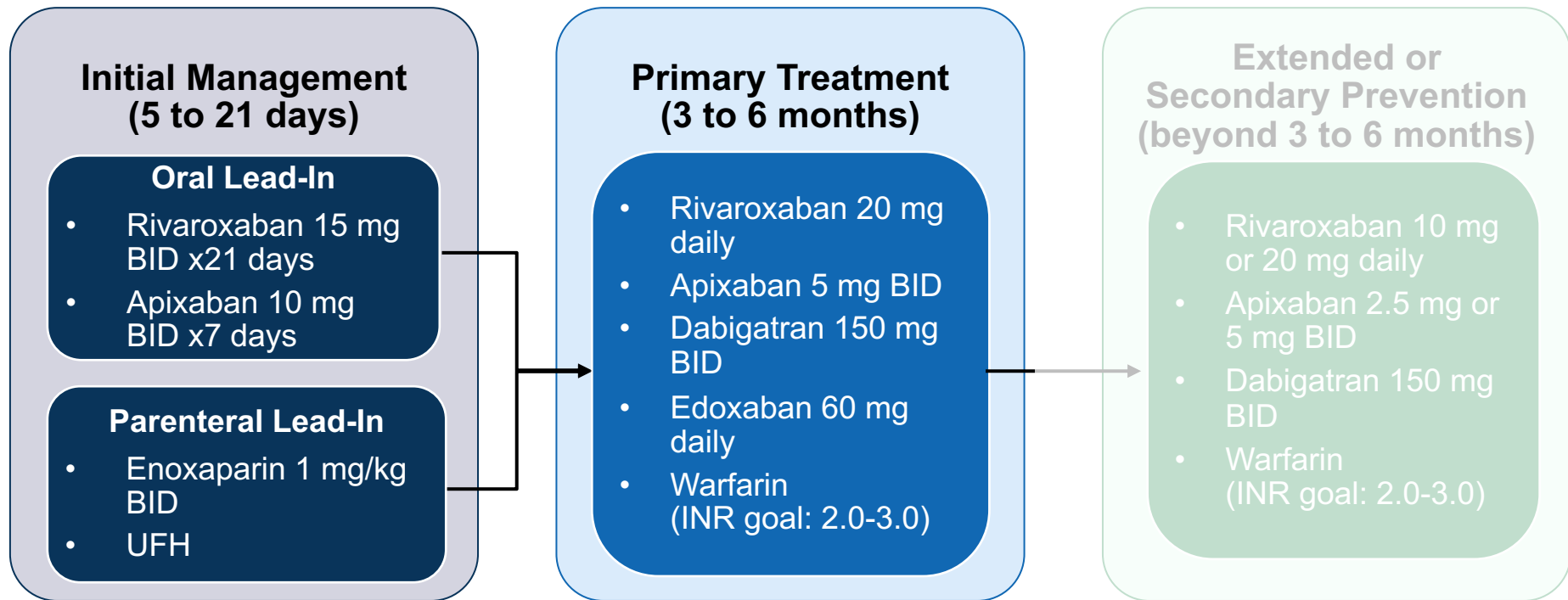
High pretest probability → no D-dimer needed

LE ultrasound scan:
acute right popliteal DVT

Strategies for Individualizing Anticoagulation Therapy in Patients With or at Increased Risk of VTE

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Choices in Anticoagulation Treatment by Stage of VTE¹



Note: There is not a renal dosing adjustment for VTE

Pharmacologic Characteristics of Anticoagulants for VTE¹

	Warfarin	Dabigatran	Rivaroxaban	Apixaban	Edoxaban
Onset	Slow Several days	Fast A few hours	Fast A few hours	Fast A few hours	Fast A few hours
Food effects	Yes Vitamin K interactions	No	Yes Take with food	No	No
Drug interactions	Many	Few	Few	Few	Few
Routine drug monitoring	Yes	Routine drug monitoring not needed Labs recommended annually and should include CBC and renal/liver function tests; consider more frequent lab monitoring for elderly or frail patients			
Reversal agents^a	Yes PCC, vitamin K, FFP	Yes Idarucizumab	Yes Andexanet alfa	Yes Andexanet alfa	Not yet

^a If FDA-approved agents are not available, 4-factor PCC can be used.

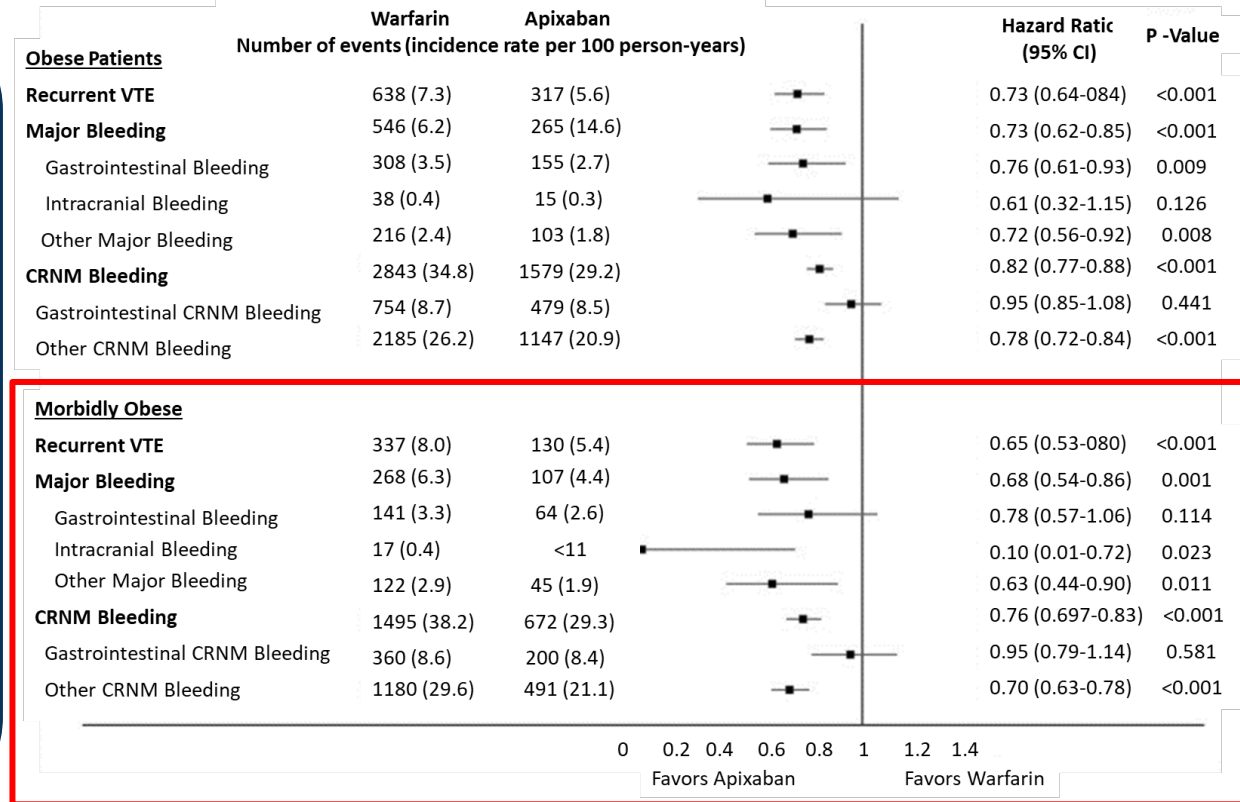
1. <https://thrombosis.org/wp-content/uploads/2021/09/NATF-ACC-Healthcare-Providers-Sept-2021.pdf>.

DOACs and Obesity¹

Data From Five US Healthcare Claims Databases

- ~112K patients at normal weight
- ~ 43K patients with obesity
- ~ 20K patients morbidly obese (BMI >40 kg/m²)

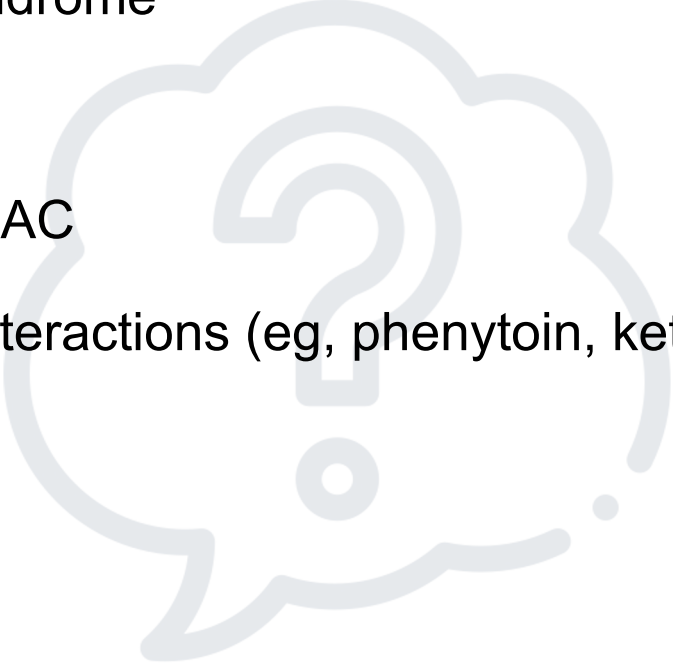
VTE indication for DOAC prescription



ISTH 2021 Updated Guidance on DOAC Use in Patients With Obesity

- Standard doses of apixaban and rivaroxaban are acceptable for acute VTE treatment *regardless* of weight/BMI
 - Anti-Xa peak and trough levels do *not* need to be checked
- Dabigatran and edoxaban have unconvincing or insufficient data to recommend their use if BMI >40 kg/m² or weight >140 kg

When Should LMWH/Warfarin Be First-Line Therapy?

- Antiphospholipid syndrome
 - Mechanical valve
 - Inability to afford DOAC
 - Severe drug–drug interactions (eg, phenytoin, ketoconazole, HIV medications)
 - Severe liver disease
- 

Patient Case Discussion: Jackie

**57-year-old
female patient**

- Found to have right popliteal (proximal) DVT 1 week after surgery

**Anticoagulant
considerations**

- What were her risk factors for VTE?
- Which agent? Is weight a consideration?
- What dose?
- When to follow up?
- When to refer?

Patient Profile: Arielle

**47-year-old
female
patient**

- Severe calf pain began 2 days ago in her right leg
- Flew from Bangkok, Thailand to New York City 3 days ago

**Medical
history
and physical
exam**

- HR = 92; RR = 20; O₂ sat = 97%; temp 97.4°F; BP = 132/77 mmHg; BMI = 24.2 kg/m²; eGFR = 45 mL/min/1.73 m²; oriented x4
- Calf measurements: left, 34 cm; right, 39 cm
 - Entire right leg swollen
 - Localized tenderness with pitting edema
 - No history of DVT or cancer; nonsmoker (12 years)
- Current medications
 - Oral contraceptive (drospirenone/ethinyl estradiol) and an oral multivitamin with iron

Wells Score for Predicting the Probability of DVT¹⁻⁴

Active cancer Treatment or palliation within 6 months	No 0	Yes +1
Bedridden recently >3 days or major surgery within 12 weeks	No 0	Yes +1
Calf swelling >3 cm compared to the other leg Measured 10 cm below tibial tuberosity	No 0	Yes +1
Collateral (nonvaricose) superficial veins present	No 0	Yes +1
Entire leg swollen	No 0	Yes +1
Localized tenderness along the deep venous system	No 0	Yes +1
Pitting edema, confined to symptomatic leg	No 0	Yes +1
Paralysis, paresis, or recent plaster immobilization of the lower extremity	No 0	Yes +1
Previously documented DVT	No 0	Yes +1
Alternative diagnosis to DVT as likely or more likely	No 0	Yes -2

4 points
High risk group for DVT. "Likely" according to Wells' DVT studies.

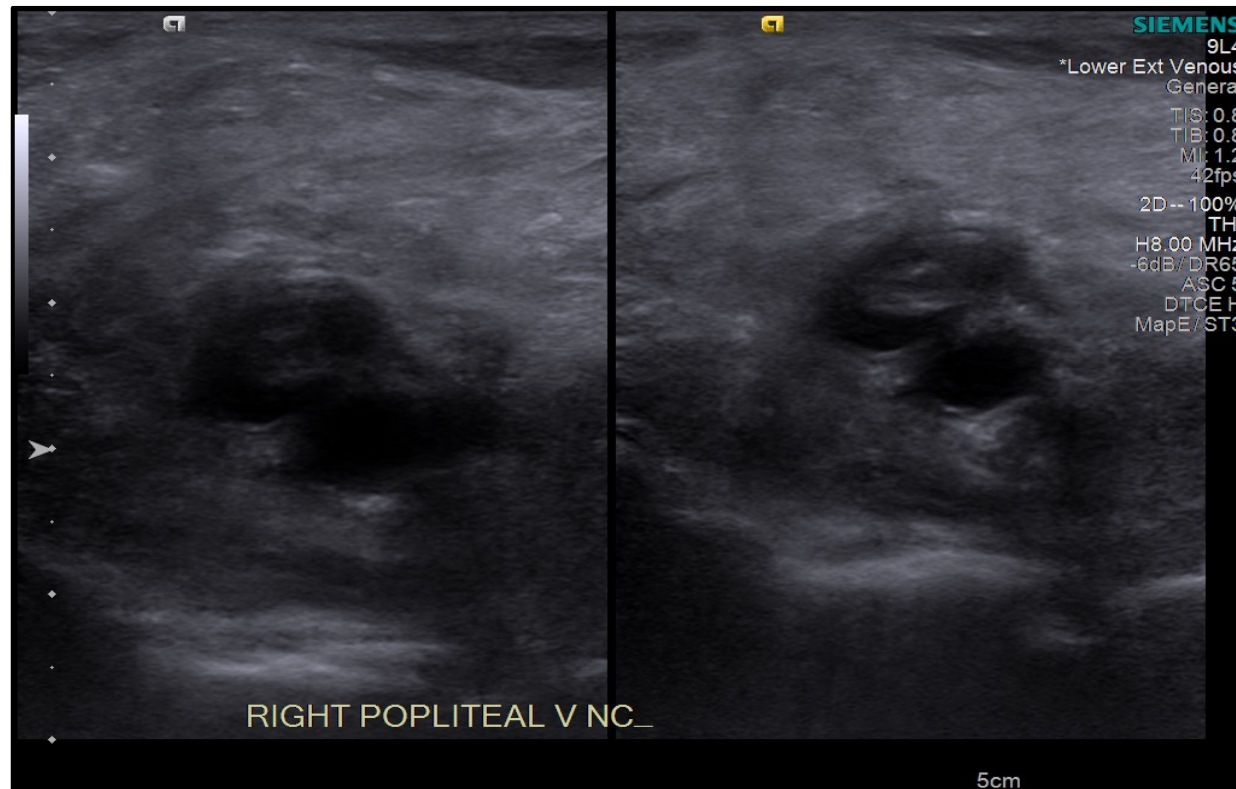
Copy Results

Next Steps >>>

- What are her risk factors for VTE?
- Should she get D-dimer testing or go straight to ultrasound?
- If ultrasound is negative, what is the next step?

<https://www.mdcalc.com/wells-criteria-dvt>

Patient Imaging Results: Arielle^a



Ultrasound shows
DVT in the right
superficial femoral
vein, popliteal vein,
and posterior
tibial vein

^a Image courtesy of Geoffrey Barnes, MD, MSc.

Patient Case Discussion: Arielle

**47-year-old
female patient**

- Severe calf pain began 2 days ago in right leg
- Flew from Bangkok, Thailand to New York City 3 days ago
- Diagnosed with DVT in right leg

**Anticoagulant
considerations**

- Which agent?
- Should dose be reduced given her eGFR?
- Can she be treated as an outpatient?
- How long would you continue anticoagulation?

Risk Factors for VTE Recurrence After Anticoagulation Is Stopped¹

Increased Risk

Risk Factors	Risk ratio
Antiphospholipid syndrome: yes vs no	1.5-3.0
Cancer vs unprovoked	1.5-3
Elevated D-dimer (after unprovoked VTE): yes vs no	1.5-2.5
Noncancer persistent risk factor	1.5-2
Hereditary thrombophilia: yes vs no	1.2-2.0
Male vs female (after unprovoked VTE): yes vs no	1.75
Previous VTE: yes vs no	1.5
Proximal DVT vs PE without proximal DVT	1.4
Residual DVT on ultrasound	1.4

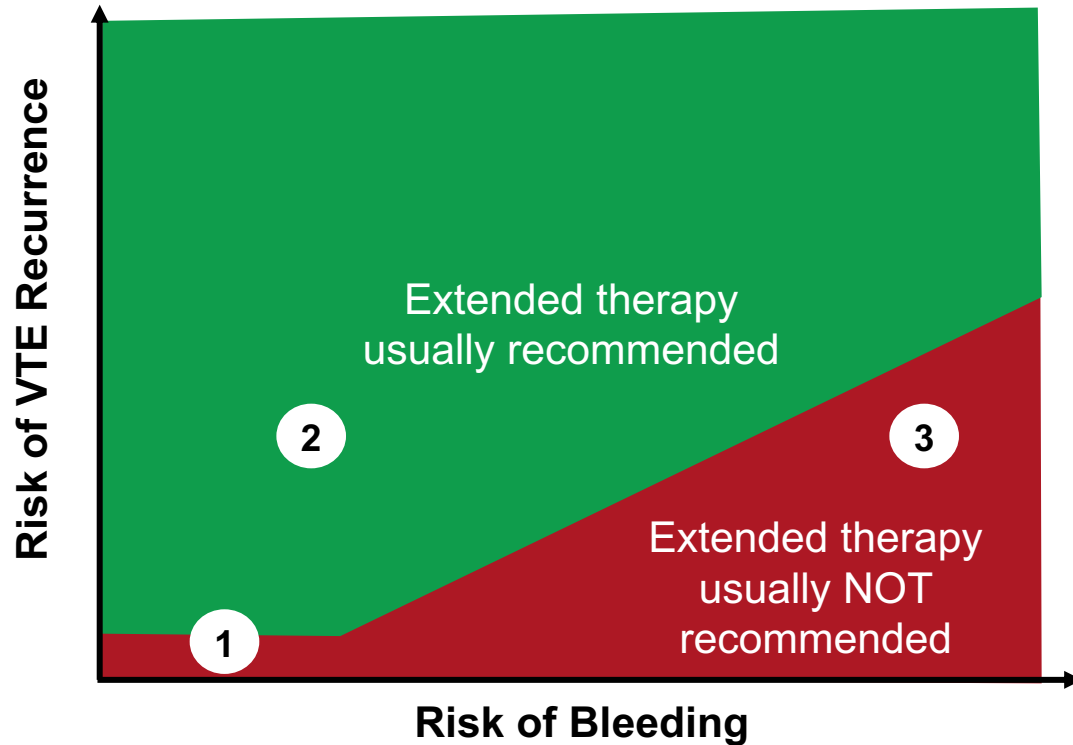
Decreased Risk

Risk Factors	Risk ratio
Asian vs White or Black	0.8
Minor transient risk factor vs unprovoked	0.5
Isolated distal DVT vs proximal DVT	0.2-0.5
Major transient risk factor vs unprovoked	0.2

Risk of VTE Recurrence After Anticoagulation Is Stopped^{1,2}

Characteristic	Recurrence at 1 Year, %	Recurrence at 5 Years, %
Major provoked (transient)	1	3
Minor provoked (transient)	5	15
Unprovoked	10	30
Cancer	20	—

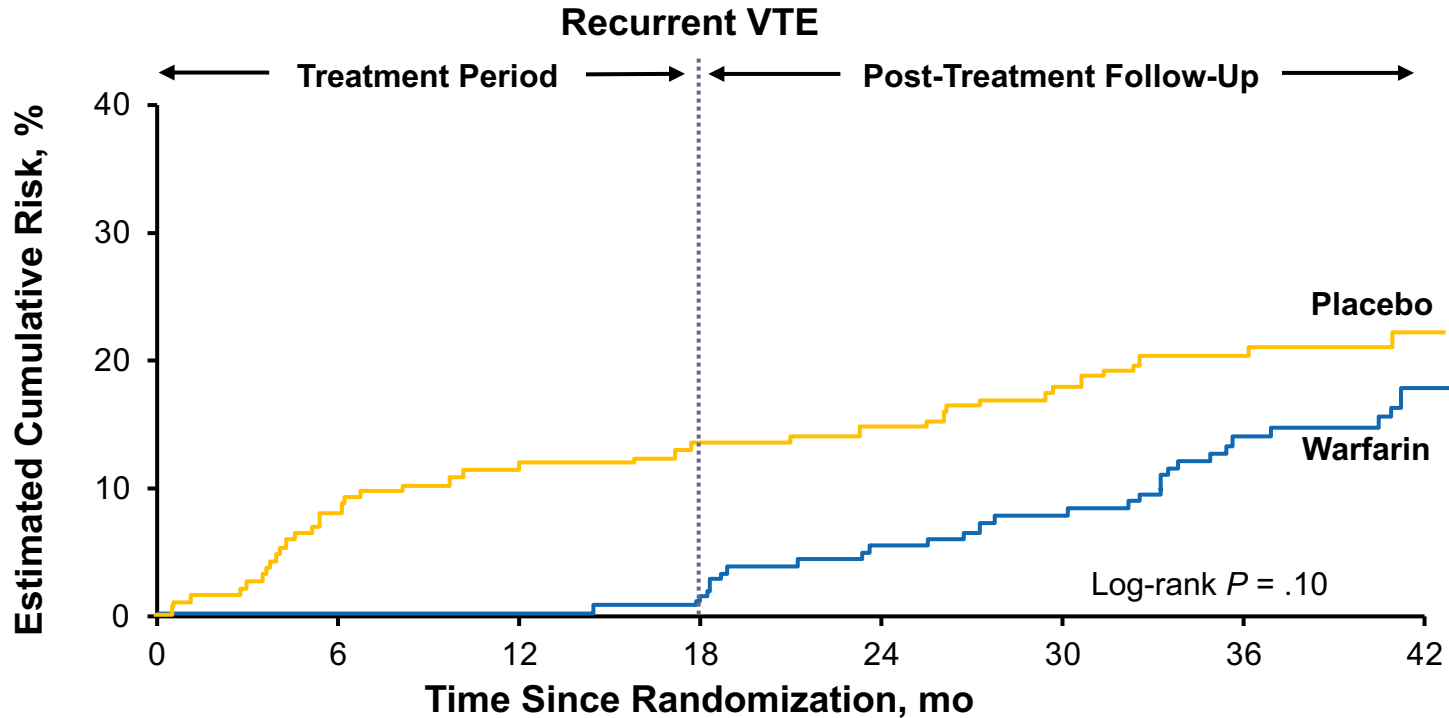
Risk of Bleeding Versus Risk of VTE Recurrence^{1,a}



1. Reversible risk factor clot, only needs a short course of anticoagulation
2. First unprovoked clot, no cancer, low risk of bleeding; extended therapy makes sense
3. Person with same risk of recurrence as #2 but much higher risk of bleeding

^a Figure courtesy of Geoffrey Barnes, MD, MSc.
1. Cohen AT et al. *PLoS One*. 2016;11:e0160064.

Duration of Extended Anticoagulation¹



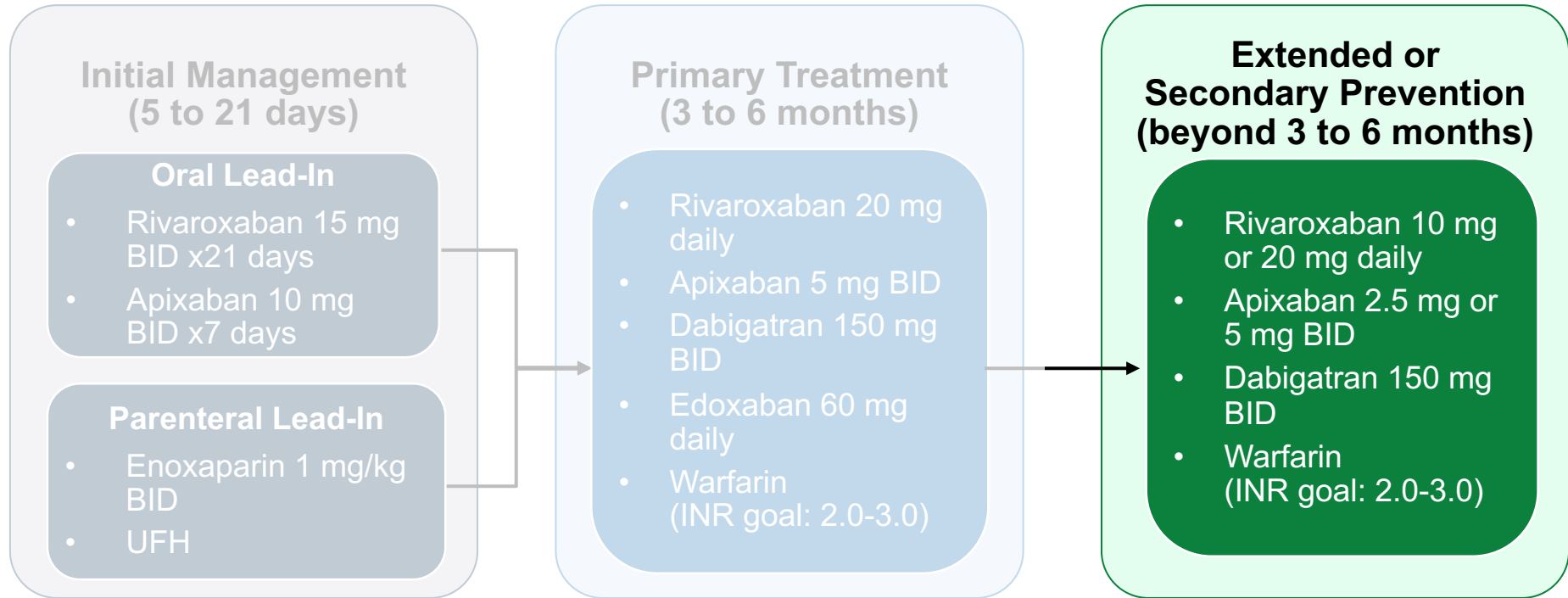
No. at Risk

Placebo	187	170	162	158	155	141	117	105
Warfarin	184	182	180	174	168	150	120	110

Duration of Anticoagulation for VTE: 2021 CHEST and 2020 ASH Guidelines^{1,2}

Indication	CHEST 2021	ASH 2020
First provoked VTE (transient risk factor)	3 months	3-6 months
First unprovoked VTE or chronic risk factor	Extended	Extended
Recurrent VTE	Extended	Extended (even if provoked)
VTE + cancer	Extended	Extended

Choices in Anticoagulation Treatment by Stage of VTE¹



Note: There is not a renal dosing adjustment for VTE

Patient Case Resolution: Arielle

**47-year-old
female patient**

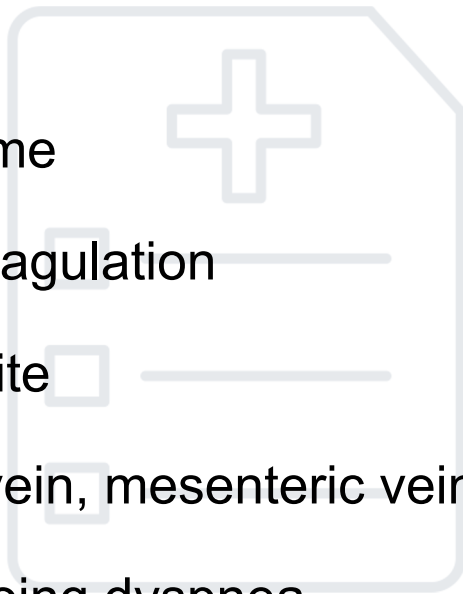
- Severe calf pain began 2 days ago in right leg
- Flew from Bangkok, Thailand to New York City 3 days ago
- Acute DVT femoral → posterior tibial vein

**Anticoagulant
considerations**

- What if this patient had advanced CKD?
- How long would you continue anticoagulation?
- Would you order a thrombophilia panel?

When Should Patients Be Referred to a Specialist?

- Upper extremity DVT that is *not* associated with a catheter
- Severe proximal DVT
- Antiphospholipid syndrome
- Recurrent VTE on anticoagulation
- Thrombosis in unusual site
 - Portal vein, hepatic vein, mesenteric vein, cerebral sinus vein
- PE with evidence of ongoing dyspnea



Patient Profile: Tom

65-year-old man with lung cancer

- Recently completed chemotherapy
- Has routine CT chest for staging

Exam and studies

- BP = 130/80 mmHg; HR = 61; O₂ sat = 98%
- Found to have a RUL segmental PE
- RV/LV ratio <1.0
- Completely asymptomatic

Key questions

- Should he receive anticoagulation?
- If so, what anticoagulant to use?

Transitioning Patients With or At Risk for VTE From Acute to Outpatient Care

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Common Pitfalls With VTE Transitions in Care¹

- Transitions between drug therapies and across care settings (eg, medical ward to operating room and back, discharge to long-term care facility) are high-risk periods for medical errors
- Care transitions require thoughtful consideration and planning
- While DOACs do not require routine outpatient monitoring, a standardized follow-up strategy must be delineated to facilitate periodic patient evaluation for clinically relevant issues

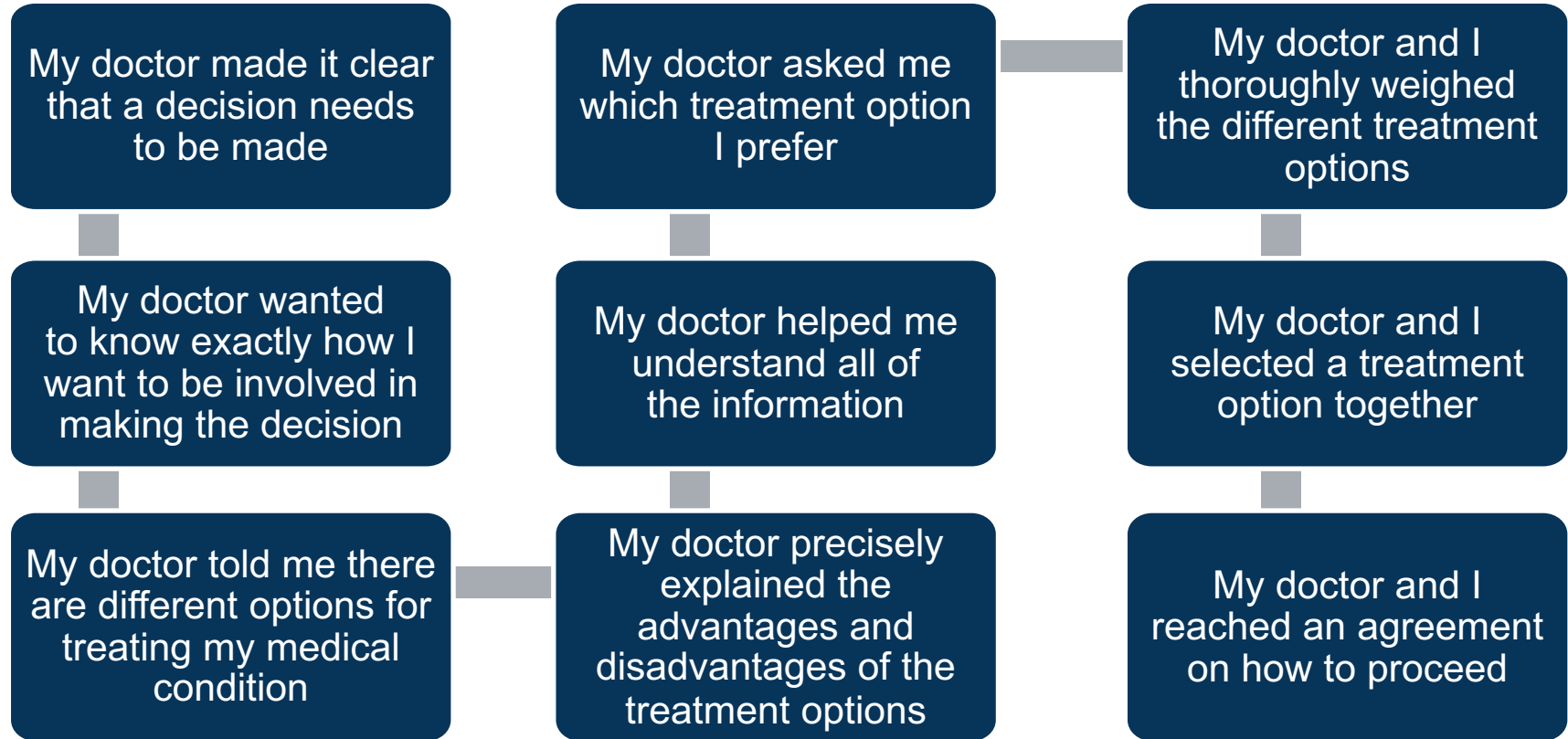
Transitioning From Warfarin, LMWH, or UFH to DOACs¹

Switching	Warfarin to DOAC	LMWH to DOAC	UFH to DOAC	DOAC to Another DOAC
Dabigatran	Start when INR <2.0	Stop LMWH; start DOAC ≤2 hours before the time of next scheduled dose of LMWH	Start DOAC immediately after stopping IV UFH	Stop current DOAC; at time of next dose of current DOAC, begin the new DOAC
Rivaroxaban	Start when INR <3.0			
Apixaban	Start when INR <2.0	Stop LMWH; start DOAC at the time the next dose of LMWH is due	Start edoxaban 4 hours after stopping IV UFH	
Edoxaban	Start when INR ≤2.5			

As a general rule, as INR drops below 2.5, a DOAC can be started, and each DOAC can be started within 30 minutes of stopping IV UFH

1. https://acforum-excellence.org/Resource-Center/downloads/DOAC%20Playbook%20_07-2021.pdf.

Using the SDM-Q-9 Tool Ensures the Patient Is Included in Decision-Making¹



Transitions of Care: Key Points for Primary Care

- Reinforce diagnosis *and* medication education
 - Signs and symptoms of bleeding
 - Signs and symptoms of progressive thrombosis
- Ensure access to medication (current and future)
- Remind patients to get refills *at least* 3 to 5 days before current medication runs out
- Assess for anxiety/depression symptoms about VTE diagnosis
 - Refer to stoptheclot.org for patient resources
- If PE, ensure rapid follow-up (phone-based is acceptable) and need for follow-up testing (eg, ECG at 3 months)

Resources for Anticoagulation Care

- **Anticoagulation Forum Centers of Excellence**
 - <https://acforum-excellence.org/Resource-Center/>
- **MAQI² Anticoagulation Toolkit**
 - www.anticoagulationtoolkit.org
- **Drug–Drug Interaction Reference**
 - https://acforum-excellence.org/Resource-Center/resource_files/-2021-04-28-132351.pdf
 - <https://depts.washington.edu/anticoag/home/content/rivaroxaban-drug-interaction-potential>
 - <https://depts.washington.edu/anticoag/home/content/apixaban-drug-interaction-potential>
- **Medication Access**
 - Consult pharmaceutical company websites for patient medication assistance programs

Key Takeaways

VTE occurs frequently and can have serious consequences when it is not treated appropriately

Many cases can be appropriately managed in the outpatient setting

Selection of anticoagulation for VTE treatment and prevention, as well as the duration of therapy, should be patient-specific

Transitions of care represent high-risk times for patients on anticoagulation: Close communication and follow-up are key

Audience Q&A



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**Please remember to complete and submit
your Evaluation.**

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Thank you and have a good day.

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