# VTE Prophylaxis in Acutely Ill Medical Patients

Arunab Mehta, MD, MEd, FHM, FACP Assistant Professor of Medicine



## No Financial Disclosures



- Gap: lack of adherence to latest evidence for VTE prophylaxis in the inpatient setting
- Need: lack of education on latest evidence for VTE prophylaxis in the inpatient setting





# Learning Objectives

- Use risk assessment models for VTE prophylaxis
- Use appropriate pharmacologic and mechanical prophylaxes for patients in the hospital
- ➤ Identify patients who could benefit from VTE prophylaxis on discharge



## **Expected Outcome**

 You will be able to use evidence-based techniques for VTE prophylaxis for acute care medicine patients

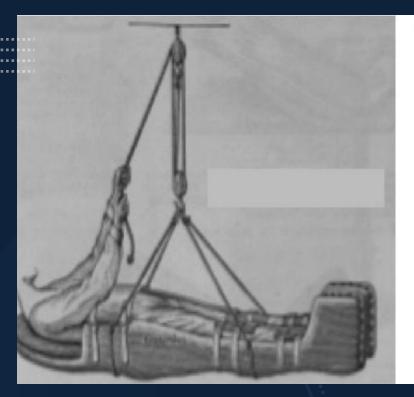


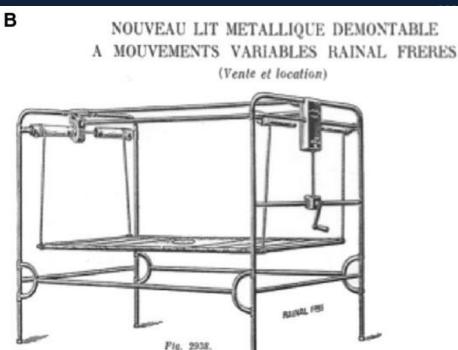
## History of VTE prophylaxis



1271: Raoul - first likely reported case of DVT







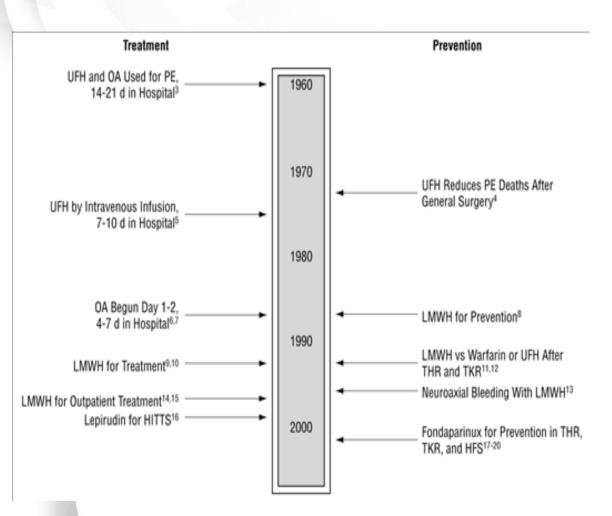
## History

• 1793: Hunter hypothesized blood clots cause DVT

Modèle déposé,

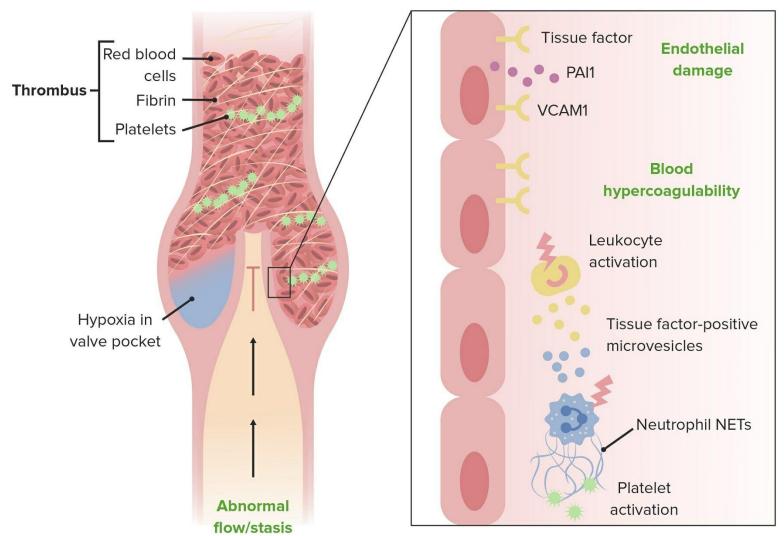
- 1856: Virchow finds relationship between DVT and PE
- 1941: Wright proposes DVT ppx in hospitals (early ambulation, avoidance of dehydration, elastic compression)

### History



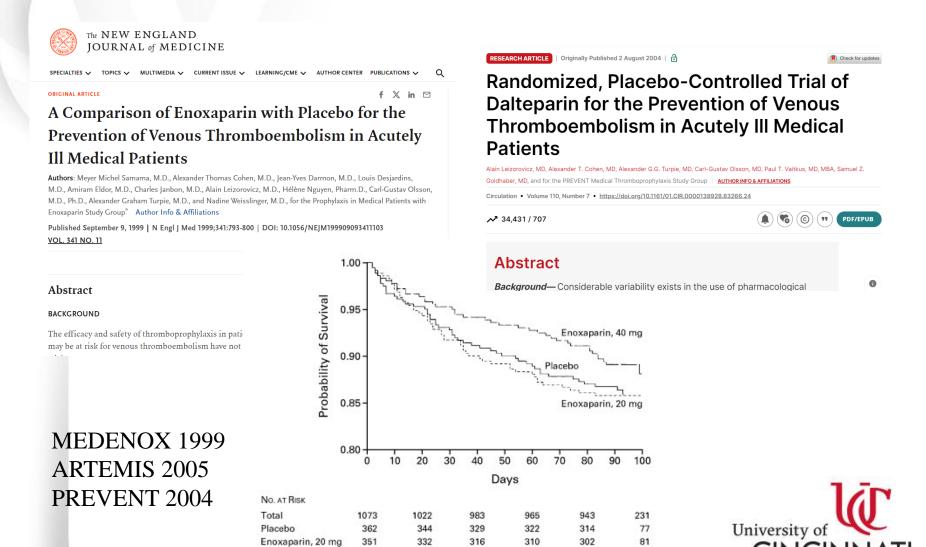
1911: heparin discovered by Doyon/McLean/
Howell
1935: purified, could be used on humans- for post-surgical DVT prophylaxis
1940: Swiss surgeon recommended heparin ppx







### LMWH in Acutely III Medical Patients



Enoxaparin, 40 mg

# 2005: Joint Commission & National Quality Forum

'National Consensus Standards for the Prevention and Care of Deep Vein Thrombosis (DVT)' project



# 2008- Surgeon General Call to Prevent DVT/PE

The Surgeon General's Call to Action to Prevent Deep Vein Thrombosis and Pulmonary Embolism 2008U.S. Department of Health and Human Services

- VTE-1
- VTE-2
- VTE-6
- CMS does not pay for HA-VTE since 2008



## **Questions for thought**

- Does every admitted patient need heparin ppx?
- Is heparin better than LMWH?
- What about DOACs?
- What about my high bleeding risk patients?
- What about mechanical ppx?
- After discharge VTE ppx?





# Case: Medical Inpatient Admission

72-year-old male

**Past Medical History:** COPD, type 2 diabetes, obesity (body mass index [BMI] of 42 kg/m<sup>2</sup>), provoked DVT 20 years ago (after cholecystectomy)

Medications: Tiotropium, metformin, amlodipine,

lisinopril

Admitted to: Internal Medicine Ward with cellulitis

**Treated with:** antibiotics

He is not ambulating on the ward due to generalized weakness.



## Which ONE of the following options would you suggest for thromboprophylaxis during this medical inpatient's hospital admission?

- A. Subcutaneous low molecular weight heparin (LMWH)
- B. Direct oral anticoagulant (Betrixaban, Rivaroxaban, or Apixaban)
- C. Graduated compression stockings
- D. No prophylaxis because patient is low thrombosis risk



## Which ONE of the following options would you suggest for thromboprophylaxis during this medical inpatient's hospital admission?

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- D. No prophylaxis because patient is low thrombosis risk



### Does everyone hospitalized need pharmacologic prophylaxis?

Home > Journal of Thrombosis and Thrombolysis > Article

Benefits versus risks of pharmacological prophylaxis to prevent symptomatic venous thromboembolism in unselected medical patients revisited. Meta-analysis of the medical literature

No benefit in unselected patient population (odds ratio [OR], 0.59; 95% CI, 0.29 - 1.23

FREE

Published: 20 April 2012

Small benefit

in higher risk

Volume 34, pages 11–19, (2012) Cite this article

**Original Investigation** 

July 23, 2007

#### Pharmacological Venous Thromboembolism **Prophylaxis in Hospitalized Medical Patients**

A Meta-analysis of Randomized Controlled Trials

Lironne Wein; Sara Wein; Steven Joseph Haas, BPharm, BPharmSci(Hons), MSHPA; et al.

> Author Affiliations | Article Information

Arch Intern Med. 2007:167(14):1476-1486. doi:10.1001/archinte.167.14.1476

population NNT: 345 to

prevent PE

patient



#### Heparin for the prevention of venous thromboembolism in acutely ill medical patients (excluding stroke and myocardial infarction)

Raza Alikhan, Rachel Forster, Alexander T Cohen Authors' declarations of interest

Version published: 07 May 2014 Version history

Increase in major hemorrhage in VTE ppx patients (OR, 1.81; 95% CI, 1.10-2.98; P = .02) NNH= 336

https://doi.org/10.1002/14651858.CD003747.pub4 3

ORIGINAL ARTICLE | VOLUME 22, ISSUE 3, P765-774, MARCH 2024

▲ Download Full Issue

Association of pharmacologic thromboprophylaxis with clinically relevant bleeding and hospital-acquired anemia in medical inpatients: the risk stratification for hospital-acquired venous thromboembolism in medical patients study

Damien Choffat ス □ • Jean-Benoît Rossel • Drahomir Aujesky • Peter Vollenweider • Christine Baumgartner •

Published: December 08, 2023 • DOI: https://doi.org/10.1016/j.jtha.2023.11.021

#### **Abstract**

Background

Pharmacologic thromboprophylaxis (pTPX) might exacerbate the risk of clinically relevant bleeding (CRB) and acquired anemia (HAA) in older multimorbid inpatients.

Hospital acquired Anemia

Prospective Cohort-Study in 3 Swiss Hospitals

Primary Outcome: **HAA** 

rates

1305 patients (90% low bleeding risk)  $\rightarrow$  809 (62%) received pTPX

**Results:** 

➤ <u>CRB rates</u> (2.2% vs 2.2%)

**►** HAA rates (23.2% vs

**15.3%**) (OR 1.4; CI 1.0-2.1)

➤ Median drop in Hgb (0.7)

University of

vs 0.2 g/dl)

# Journal of Hospital Medicine



Choosing Wisely®: Things we do for no Reason™ ☐ Full Access

#### Things We Do for No Reason<sup>™</sup>: Universal Venous Thromboembolism Chemoprophylaxis in Low-Risk Hospitalized Medical Patients

Brooke Barlow PharmD X, Ashley Barlow PharmD, Anthony C Breu MD

First published: 01 May 2021 | https://doi.org/10.12788/jhm.3502



# Who will most benefit from VTE prophylaxis?





High Risk VTE risk?

Low Bleeding Risk?



### Who is at risk of developing VTE?

#### Padua and IMPROVE VTE RAMs

#### Risk

Assessment Models (RAMs) will help risk stratify medically ill patients.

#### **□**Examples:

Padua score, Improve score

3
3
3
3
3
2
1
1
1
1
1
1

IMPROVE VTE RAM: Score ≥2 Indicates Increased VTE Risk†	
Risk factor(s)	Points
Previous VTE	3
Known thrombophilia	2
Lower limb paralysis <sup>b</sup>	2
Active cancer	2
Immobilization of ≥7 days	1
ICU/CCU stay	1
Age > 60 years	1
Abbreviations: ICU, intensive care unit; CCU, coronary care unit.	
a. Congenital or acquired thrombophilic condition (e.g., factor V Leiden,	
lupus anticoagulant, protein C or protein S deficiency)	1
<ul> <li>Leg falls to bed by 5 seconds but has some effort against gravity</li> </ul>	1
utilizing NIH stroke scale	1
†Risk level:	1
Score of 0 -1 low risk	
Score of 2 – 3 moderate risk	
Score of ≥ 4 high risk	

Barbar, S., Noventa, F., Rossetto, V., Ferrari, A., Brandolin, B., Perlati, M., ... & Prandoni, P. (2010). A risk assessment model for the identification of hospitalized medical patients at risk for venous thromboembolism: the Padu Prediction Score. Journal of Thrombosis and Haemostasis, 8(11), 2450-2457.

<sup>2.</sup> Spyropoulos, A. C., Anderson Jr., F. A., FitzGerald, G., Decousus, H., Pini, M., Chong, B. H., ... & Monreal, M. (2011). Predictive and associative models to identify hospitalized medical patients at risk for VTE. Chest, 140(3), 706-71



### Many other risk assessment models

Development and validation of a risk model for hospital-acquired venous thrombosis: the Medical Inpatients Thrombosis and Hemostasis study

Venous thrombosis risk assessment in medical inpatients: the medical inpatients and thrombosis (MITH) study

N.A. Zakai A ■ • P.W. Callas • A.B. Repp • M. Cushman

Rogers <sup>53</sup>	Intermountain <sup>55</sup>	IMPROVE <sup>56</sup>	Premier <sup>58</sup>
142	22	52	374
U.S.	U.S.	12 countries	U.S.
Prospective	Retrospective	Prospective	Retrospective
Surgical	Medical	Medical	Medical



#### Guidelines from Societies favor RAM









Volume 141, Issue 2, Supplement, February 2012, Pages e419S-e496S

Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physician Evidence-Based Clinical Practice Guidelines Online Only Articles

Antithrombotic Therapy for VTE Disease: Antithrombotic Therapy and Prevention of Thrombosis, 9th ed: American College of Chest Physicians Evidence-Based Clinical Practice Guidelines

#### **ASH Clinical Practice Guidelines on Venous Thromboembolism**



### Circulation

**CURRENT IS** 



REVIEW ARTICLE | Originally Published 7 May 2020 | 🙃



#### Call to Action to Prevent Venous **Thromboembolism in Hospitalized Patients:** A Policy Statement From the American **Heart Association**

"The AHA recommends a central steward for data tracking VTE risk assessment, application of VTE prophylaxis, and VTE rates for all hospitals such as the Core Quality Measures Collaborative."



### Implementation of Risk Assessment

>400 pts: prospective and retrospective cohort study over 1 year

No change in VTE and bleeding rates

Decreased VTE ppx rates (saved €1.67 / pt (27.2% decrease))

Clinical impact of application of risk assessment models (Padua Prediction Score and Improve Bleeding Score) on venous thromboembolism, major hemorrhage and health expenditure associated with pharmacologic VTE prophylaxis: a "real life" prospective and retrospective observational study on patients hospitalized in a Single Internal Medicine Unit (the STIME study)

IM - ORIGINAL | Published: 03 March 2018

RESEARCH ARTICLE | Originally Published 6 February 2024

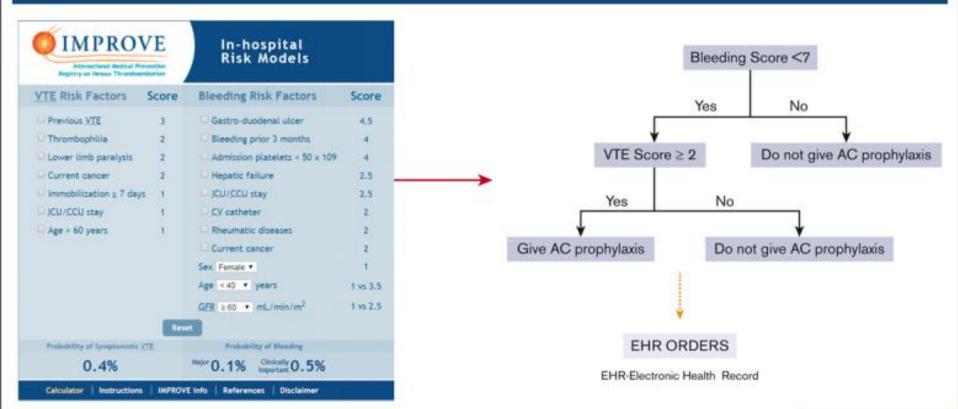
Impact of Embedding a Venous
Thromboembolism Risk Assessment Model
in the Electronic Health Record Versus
Usual Care: A Cluster-Randomized Trial

Adding VTE risk calculator (Padua) did **not** change **VTE** and **bleeding rates** (reduced VTE ppx from 73→65%)

Limitation: use 24%



# Converting IMPROVE bleeding and VTE predictive models into FFT (T) for implementing most optimal hospital VTE prophylaxis at the point of care



**Proposed decision tree**: Djulbegovic B et al. Converting IMPROVE bleeding and VTE risk assessment models into a fast-and-frugal decision tree for optimal hospital VTE prophylaxis. Blood Adv. 2024 Jun 25;8(12)





#### **INTERVENTIONS (How)**(Active, Completed, Future) **KEY DRIVER DIAGRAM** Project Name: VTE prophylaxis project Project Leader: Arunab Mehta, MD Add Risk Assessment calculator to admission order **Revision Date:** 03/15/2024 set **KEY DRIVERS (What) GLOBAL AIM** Make standardized orderset organizing preferred Inclusion of standard risk assessment Increase appropriate VTE VTE ppx by renal function/weight method available for providers to use prophylaxis for medical admitted patients Inclusion of standardized option to Educating providers about importance of VTE risk help provider order appropriate ppx **SMART AIM** stratification - email vs annual training module in orderset Increase the appropriate VTE prophylaxis rates in Awareness of providers to risk stratify Nursing education about ambulation and VTE ppxmedical admitted patient patients for VTE on admission email from 50 to 75% to help align this practice with guideline and joint commission Nursing awareness for patient Nursing education module on VTE ppx and standards by November 30, ambulation and documentation documentation 2023. System to re-address change in VTE **POPULATION** Add VTE risk calculator led reassessment during risk throughout hospitalization every transfer Medical, non-surgical, non-ICU patients on general Improve patient awareness on medicine services. BPA alert frequently or change in Storyboard importance of VTE ppx (refusals) Add patient education on admission (in room) on importance of VTE ppx



#### **VTE Prophylaxis Project**



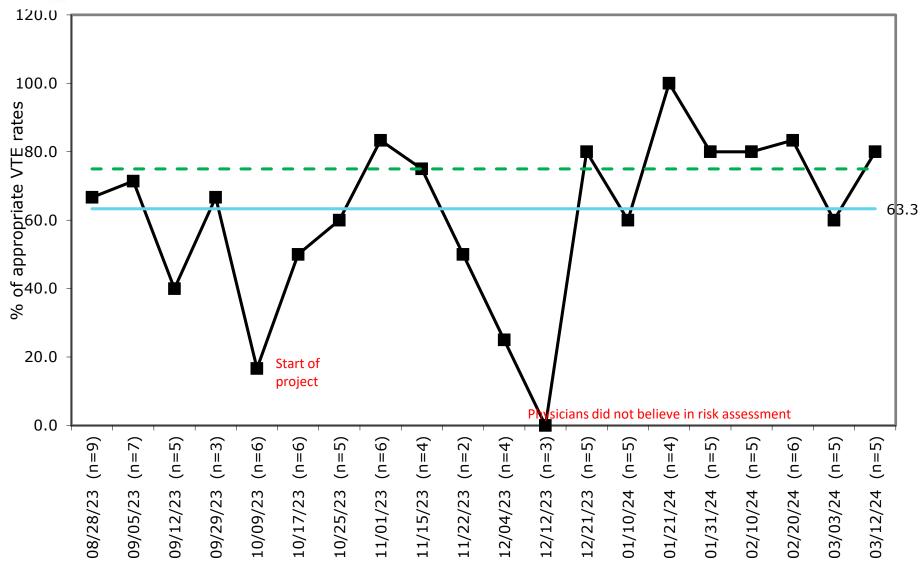


Chart prepared by: Arunab

Mehta

Data source: Collected data

Dates

**─**■ Percentage of patients who met outcome

### What is the best pharmacologic ppx?

August 9, 2022

# Low-Molecular-Weight Heparin Outperforms Other Options for Inpatient VTE Prophylaxis

Bruce Soloway, MD and Daniel D. Dressler, MD, MSc, MHM, FACP, reviewing Eck RJ et al. BMJ 2022 Jul 4

A meta-analysis supports current guidelines and demonstrates that LMWH balances benefits and risks better than unfractionated heparin or direct-acting oral anticoagulants.

- LMWH (40 mg daily) (>20,000 pts in 20 studies) & fondaparinux (850 pts in 1 study) reduced symptomatic VTE rates compared to placebo.
- UFH (3x daily) and DOACs increased bleeding rates (ORs 2.63 and 2.31 respectively)
- LMWH is <u>once daily</u>
- LMWH has <u>lower rates of HIT</u>



# LMWH outweighs heparin in critically ill patients

0.4	Relative effect:	Anticipated	d absolute effects (95% CI)
Outcomes	RR (95% CI)	Risk with UFH	Risk difference with LMWH
Mortality	<b>0.90</b> (0.75 to 1.08)	243 per 1,000	24 fewer deaths per 1,000 (61 fewer to 19 more)
PE	<b>0.80</b> (0.44 to 1.46)	11 per 1,000	2 fewer PE per 1,000 (6 fewer to 5 more)
Symptomatic proximal DVT	<b>0.87</b> (0.60 to 1.25)	25 per 1,000	3 fewer DVT per 1,000 (10 fewer to 6 more)
Major bleeding	<b>0.98</b> (0.76 to 1.27)	53 per 1,000	1 fewer bleeds per 1,000 (13 fewer to 14 more)
Heparin-induced thrombocytopenia	<b>0.42</b> (0.15 to 1.18)	6 per 1,000	4 fewer episodes per 1,000 (5 fewer to 1 more)



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### Our Patient's Risk factors for VTE

#### **Padua RAM: Factors**

Previous VTE

Thrombophilia Active cancer

 $\triangle$  Age > 70 years

Reduced mobility

Recent trauma/surgery

Heart or respiratory failure

Acute MI or stroke

Hormonal treatment

Obesity (BMI > 30)

Infection/rheumatologic

#### **IMPROVE-VTE RAM:**

#### **Factors**

Previous VTE

Thrombophilia

Active cancer

Age > 60 years

Immobilization of  $\geq 7$  days

Lower limb paralysis

ICU/CCU stay



#### Could you use DOACs for VTE ppx?

**†** bleeding rate

expense

Clearance issues with renal impairment

August 9, 2022

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A meta-analysis supports current guidelines and demonstrates that LMWH balances benefits and risks better than unfractionated heparin or direct-acting oral anticoagulants.



#### LMWH > DOACs

	Relative effect:	Anticipated absolute effects (95% CI)		
Outcomes	RR (95% CI)	Risk with prophylactic LMWH	Risk difference with any DOAC	
Mortality	<b>0.64</b> (0.21 to 1.98)	1 per 1,000	0 fewer deaths per 1,000 (1 fewer to 1 more)	
PE	<b>1.01</b> (0.29 to 3.53)	1 per 1,000	0 fewer PE per 1,000 (1 fewer to 3 more)	
Symptomatic proximal DVT	1.03 (0.34 to 3.08)	2 per 1,000	0 fewer DVT per 1,000 (1 fewer to 4 more)	
Major bleeding	<b>1.70</b> (1.02 to 2.82)	2 per 1,000	2 more bleeds per 1,00 (0 fewer to 4 more)*	



# High bleeding risk but high VTE risk?

Could you use heparin 5000 units BID instead of TID?





# Unfractionated Heparin BID vs TID

- VTE rate (BID, 5.4; vs TID, 3.5; p = 0.87)
- PE rate [BID, 1.5; vs TID, 0.5; p = 0.09]
- Proximal DVT and PE rate (BID, 2.3; vs TID, 0.9; p = 0.05)
- Bleeding rate (BID, 0.35; vs TID, 0.96; p < 0.001)</li>

Assess bleeding risk in your patient!



## Back to our patient:

Your patient developed some redness in his stools. You suspect GI bleeding. You decide to withhold pharmacologic prophylaxis to ensure hemostasis.

Which of the following options for thromboprophylaxis would you suggest at this time?

- A. Graduated compression stockings
- B. Pneumatic compression devices
- C. Calf exercises
- D. No mechanical prophylaxis is needed



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Can't use pharmacologic agents? What about mechanical thromboprophylaxis?



MARIA PLATT - EVANS / PHOTO RES

# Types of mechanical thromboprophylaxis

Graduated Compression Stockings (GCS)



Intermittent Pneumatic Compression Devices
 (IPC)





# Mechanical prophylaxis

Pneumatic Compression devices compared to graduated compression stockings (10 RCTs)

Outcome	Relative effect	Risk difference
Mortality	3.43	0 fewer per 1,000
PE	0.38	27 fewer per 1,000
Symptomatic proximal DVT	0.16	110 fewer per 1,000

ASH recommends using either methods AAFP recommends using PCD



#### Pharmacologic + mechanical prophylaxis?

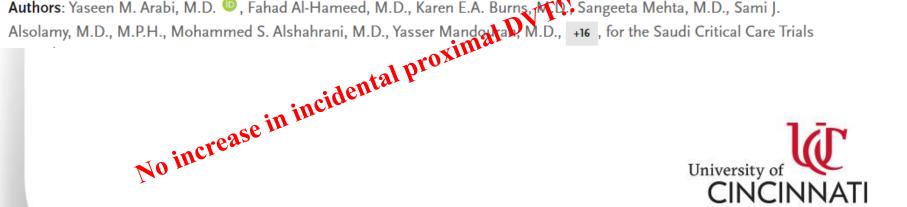


SPECIALTIES V MULTIMEDIA V CURRENT ISSUE > LEARNING/CME V

**ORIGINAL ARTICLE** 

#### **Adjunctive Intermittent Pneumatic Compression for** Venous Thromboprophylaxis

Authors: Yaseen M. Arabi, M.D. D, Fahad Al-Hameed, M.D., Karen E.A. Burns, M.D., Sangeeta Mehta, M.D., Sami J.



You are discharging your patient after an acute medical illness. He has received prophylaxis with LMWH in hospital for 9 days. He is ambulatory and back on his usual medications.

#### What would you recommend on discharge for VTE prophylaxis?

- A. Stop LMWH on the day of discharge
- B. Extend LMWH for 3 weeks post-discharge
- C. Switch LMWH on discharge to a DOAC, and continue the DOAC for 3 weeks post-discharge
- D. Graduated compression stockings for 3 weeks post-discharge



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- D. Graduated compression stockings for 3 weeks post-discharge



## Extended VTE Prophylaxis



#### Trials for extended prophylaxis

Study	Extended Prophylaxis
EXCLAIM <sup>9</sup>	Enoxaparin 40 mg/d 28 d after initial open-label enoxaparin 10 ± 4 days
ADOPT 10	Apixaban 2.5 mg twice/d 30 days
MAGELLAN <sup>11</sup>	Rivaroxaban 10 mg/d 35 ± 4 days
PEX <sup>12</sup>	Betrixaban 80 mg/d 35-42 days
MARINER <sup>13</sup>	Rivaroxaban 10 mg/d 45 days after in-hospital LMWH or unfractionated heparin
	Univ

#### Summary of trials

PE	<b>0.67</b> (0.41 to 1.09)	4 per 1,000	1 fewer PE per 1,000 (2 fewer to 0 fewer)
Symptomatic proximal DVT	<b>0.62</b> (0.36 to 1.05)	6 per 1,000	2 fewer DVT per 1,000 (4 fewer to 0 fewer)
Major bleeding	1.99 (1.08 to 3.65)	4 per 1,000	4 more bleeds per 1,000 (0 more to 10 more)

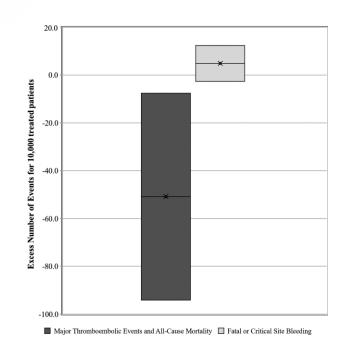
American Society of Hematology: In acutely ill hospitalized medical patients, the panel recommends inpatient VTE prophylaxis with LMWH only, rather than inpatient and extended duration outpatient VTE prophylaxis with DOACs (strong recommendation, moderate certainty)



# Pooled cohort analysis of Magellan/Mariner trials

NNT: 197 NNH: 2045

(FDA Approval for Rivaroxaban= 31-39 days post-hospitalization; exceptions for recent bleeding, active duodenal ulcer bleeding, cancer, pulmonary cavitation.)

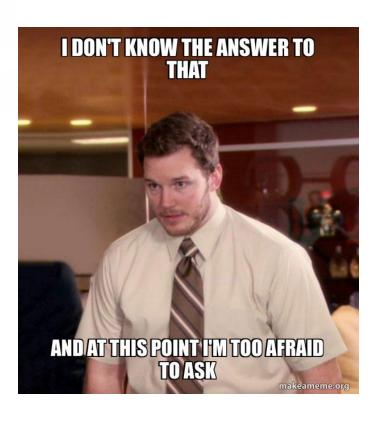


#### **NATF**

recommends extended VTE prophylaxis with DOAC for high-risk patients



# Final Answer?



• Risk assess your patient!!



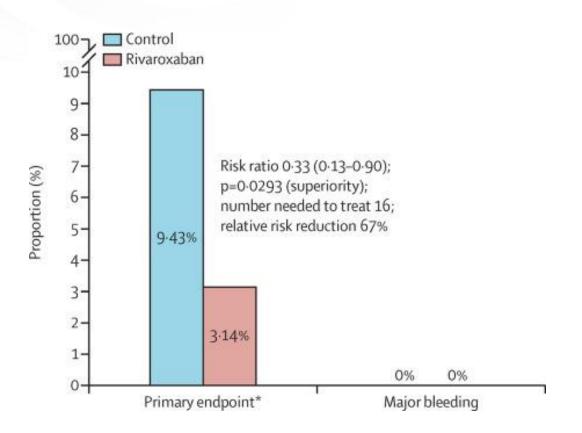
#### IMPROVEDD risk score calculator

Please check the boxes that apply to you to get your individualized IMPROVEDD Risk score for VTE at 42 days after hospitalization:

Prior episode of VTE				
Thrombophilia				
Paralysis of the lower extremity during the hospitalization				
Current malignancy				
D-dimer ≥ 2x Upper Limit of Normal (ULN)				
Immobilization for at least 7 days				
ICU or CCU admission				
Age more than 60 years				
Score: 8				
Predicted VTE risk through 3 months is 2.2%				



# MICHELLE trial (2022): Extended VTE ppx in COVID-19 patients (high risk!)



Primary Outcome= composite of symptomatic or fatal venous thromboembolism, asymptomatic venous thromboembolism on bilateral lower-limb venous ultrasound and CT pulmonary angiogram, symptomatic arterial thromboembolism, and cardiovascular death at day 35



Universal clinical decision support tool for thromboprophylaxis in hospitalized COVID-19 patients: post hoc analysis of the IMPROVE-DD cluster randomized trial

```
\underline{\mathsf{Mark}\,\mathsf{Goldin}} \overset{\mathsf{C}}{\overset{\mathsf{1,2,3}}{\overset{}\boxtimes}} \overset{\underline{\mathsf{Mark}}}{\overset{}{\overset{}\boxtimes}} \cdot \mathsf{Nikolaos}\,\mathsf{Tsaftaridis}\,^{\mathsf{1,2}} \cdot \mathsf{Ioannis}\,\mathsf{Koulas}\,^{\mathsf{1,2,4}} \cdot \dots \cdot \mathsf{Kanta}\,\mathsf{Ochani}\,^{\mathsf{1,2}} \cdot \mathsf{Thomas}\,\mathsf{McGinn}\,^{\mathsf{7,8}} \cdot \mathsf{Alex}\,\mathsf{C.}\,\mathsf{Spyropoulos}\,^{\mathsf{1,2,3}} \dots \mathsf{Show}\,\mathsf{more}
```

#### CDS vs no CDS

Primary outcome: rates of appropriate VTE ppx Secondary outcomes: rates of major thromboembolism, all-cause and VTErelated readmissions and death, major bleeding, and all-cause mortality 30 days after discharge

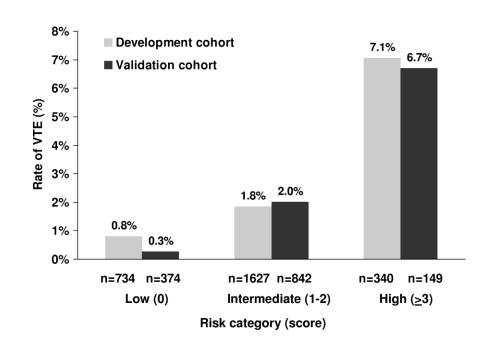
- At-discharge VTE ppx: 42.6% vs 28.8%
- VTE rates (OR, 0.54; 95% CI, 0.39-0.75; P < .001)</p>
- $\blacksquare$  Arterial thromboembolism (OR, 0.10; 95% CI, 0.01-0.81; P = .01)
- Total thromboembolism (OR, 0.50; 95% CI, 0.36-0.69; *P* < .001)
- $\blacksquare$  30-day all-cause readmission/death (OR, 0.78; 95% CI, 0.62-0.99; P = .04)
- Major Bleeding



#### VTE prophylaxis in cancer patients



Khorana Score  $\geq 2 = \text{consider}$ VTE ppx in ambulatory settings



For ambulatory patients with cancer at intermediate risk for thrombosis receiving systemic therapy, the ASH guideline panel suggests thromboprophylaxis with a DOAC (apixaban or rivaroxaban) or no thromboprophylaxis (conditional recommendation, moderate certainty in the evidence of effects  $\oplus \oplus \oplus \bigcirc$ ).

For ambulatory patients with cancer at high risk for thrombosis receiving systemic therapy, the ASH guideline panel *suggests* thromboprophylaxis with a DOAC (apixaban or rivaroxaban) over no thromboprophylaxis (conditional recommendation, moderate certainty in the evidence of effects  $\oplus \oplus \oplus \bigcirc$ ).

### Take home points

- ✓ Use Risk Assessment Models to help identifying who needs pharmacologic VTE prophylaxis in the hospital
- ✓ LMWH works best for most patients as a pharmacologic agent for VTE prophylaxis
- ✓ Most patients do not need VTE prophylaxis on discharge (but a few might!)





