VTE Prophylaxis: Inpatient Management

Lori A. Porter

July 30, 2019

Learning Objectives

- Understand how to apply 'VTE Advisor Order-Set' to your patients
- Differentiate Between Low Risk vs. Moderate Risk vs. Highest risk for VTE
- Be able to figure out who in Moderate risk who needs VTE prophylaxis and who does not
- Review 'Strong VTE Risk Factors' vs 'Intermediate Risk Factors'
- Review Guidelines on VTE Prophylaxis for Surgical patients
- Review who is recommended to get extended prophylaxis



VTE in medical inpatients is common

Half of VTE events occur due to hospital admission for surgery (24%) or medical illness (22%)

40% of hospitalized patients have 3 or more risk factors for VTE

Risk factors for VTE in hospital include cancer, older age, prior VTE, central lines, immobility

Increase in thrombosis risk in medical inpatients persists 45 to 60 days after discharge



QUANTITATIVE RISK ASSESSMENT MODELS



Who is at risk for VTE in hospital?

• Risk Assessment Models (RAMs) can identify inpatients at high risk

Previous VTE

• Examples: Padua, IMPROVE-VTE Scores

These RAMs are not extensively validated for guiding decisions about prophylaxis

Padua RAM: Factors

Thrombophilia
Active cancer
Age > 70 years
Reduced mobility
Recent trauma/surgery
Heart or respiratory failure
Acute MI or stroke
Hormonal treatment

Obesity (BMI > 30)

Infection/rheumatologic

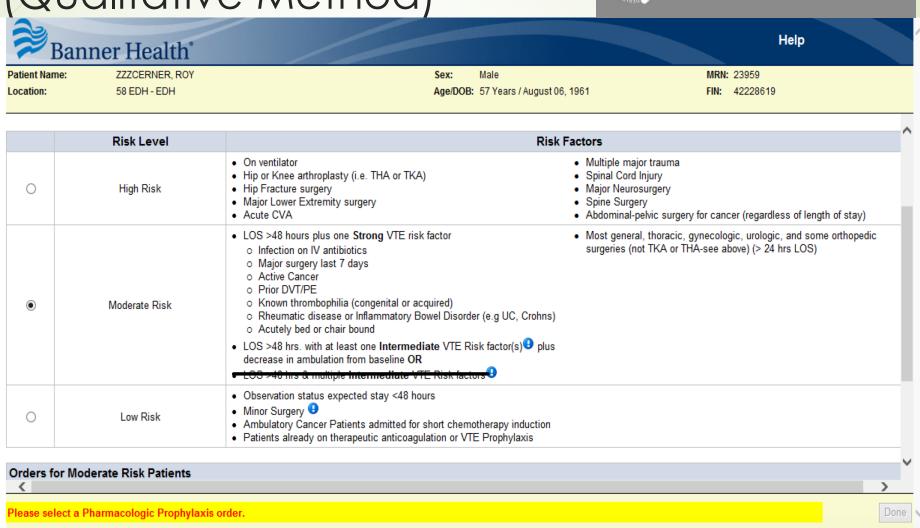
IMPROVE-VTE RAM: Factors

Previous VTE
Thrombophilia
Active cancer
Age > 60 years
Immobilization of ≥ 7 days
Lower limb paralysis
ICU/CCU stay

Spyropoulos Chest 2011 Leizorovicz Circulation 2004

VTE Prophylaxis: Three bucket Model (Qualitative Method)





Three largest Trials in medical patients 1999-2004

Rates of Asymptomatic DVT

MEDENOX (14 days)		PREVENT* (21 days)		ARTEMIS (14 days)	
Enoxaparin	Placebo	Dalteparin	Placebo	Fondaparinux	Placebo
5.2%	13.5%	1.8%	3.7%	5.6%	9.0%
Venography on days 6-14 or earlier if symptoms		Ultrasound on day 21 or earlier if symptoms		Venography on days 6-15 or earlier if symptoms	



^{*}proximal DVT only

Hospitals with High Rates of Prophylaxis vs. Low Prophylaxis

Hospital Performance for Pharmacologic Venous Thromboembolism Prophylaxis and Rate of Venous Thromboembolism A Cohort Study

Scott A. Flanders, MD; M. Todd Greene, PhD, MPH; Paul Grant, MD; Scott Kaatz, DO, MSc; David Paje, MD; Bobby Lee, MD; James Barron, MD; Vineet Chopra, MD, MSc; David Share, MD, MPH; Steven J. Bernstein, MD, MPH

JAMA Internal Medicine

October 2014
35 Michigan Hospitals
Medical patients with LOS ≥2 days and Caprini score ≥3



What were the results?

	High Performing Hospitals (n=5514)	Moderate Performing Hospital (n=7897)	Low Performing Hospitals (n=7383)
Rates of prophylaxis	86%	73%	56%
VTE in-hospital*	3.39	3.48	4.31
VTE after discharge*	1.15	1.31	0.97
*5			

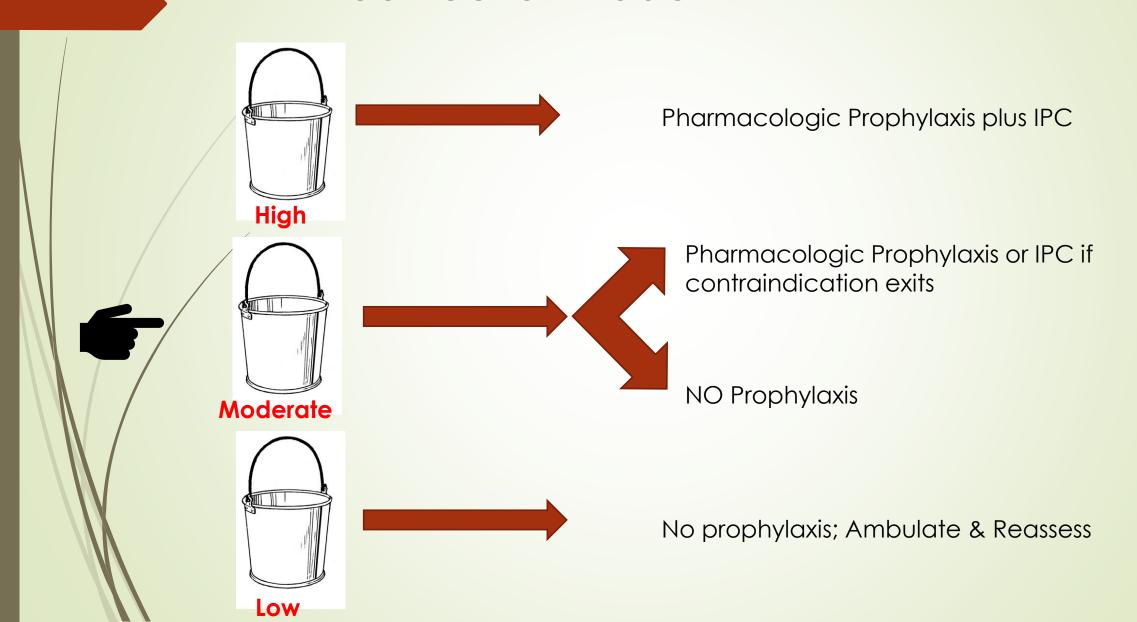
^{*}Rates are per 10,000 patient-days

This difference was the only one that met statistical significance.

Flanders et al. JAMA Intern Med. 2014;174(10):1577-84.



Three Bucket Model



What you need to navigate VTE order-set



Know High Risk Bucket (special populations)



Know Low Risk Bucket



Know Strong Risk factors for VTE (9)



Know intermediate Risk Factors VTE (10)

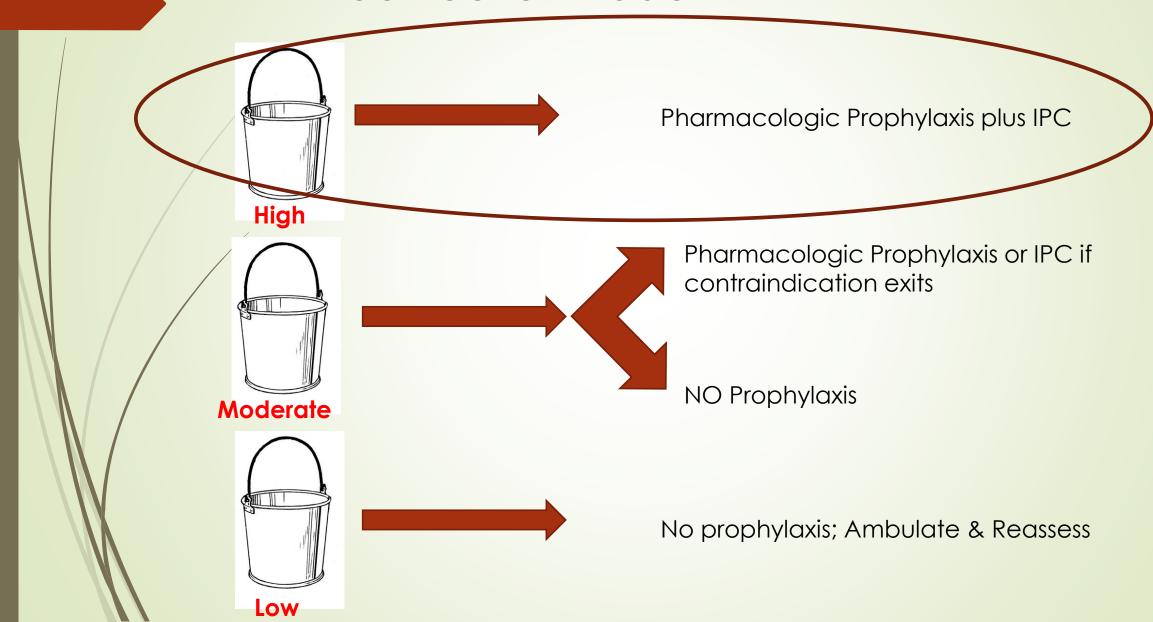


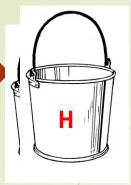
<u>Moderate Risk Equation #1</u>: Strong VTE RF + admission for >48 hrs = VTE Prophylaxis



Moderate Risk Equation #2: Intermediate VTE RF+ 48 hrs+ immobility from baseline= VTE Prophylaxis

Three Bucket Model





Highest Risk: MICU/SICU/NICU/Ortho

- 1. On Ventilator
- 2. CVA
- 3. THA (Hip Replacement)
- 4. TKA (Knee Replacement)
- 5. Hip Fracture Surgery
- 6. Major Lower extremity Surgery
- 7. Spine Surgery (not including elective spine surgery)
- 8. Multiple Major Truama
- 9. Abdominal-pelvic surgery for Cancer

Indication for extended VTE Prophylaxis

Extended Prophylaxis in Surgical Cases



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	Cancer surgery	LMWH for 4 wk
Orthopedic	Hip or knee arthroplasty ^d	IPC + LMWH, LDUH, aspirin, NOAC, fondaparinux, warfarin, or IPC alone if high bleeding risk; continue for 10-35 d
	Hip fracture repair ^d	IPC + LMWH, LDUH, warfarin, fondaparinux, or IPC alone if high bleeding risk; continue for 10-35 d
	Isolated lower leg fracture repairs	None
	Knee arthroscopy with no previous VTE	Early ambulation

For patients without increased bleeding risk, extended duration of postoperative prophylaxis for up to 35 days is recommended over shorter-duration prophylaxis of 10 to 14 days, which is the minimum recommended duration of pharmacologic VTE prophylaxis in orthopedic surgery.

FAIL FIRST AND FAIL FAST.... Gregory Maynard M.D.



This Photo by Unknown Author is licensed under <u>CC BY-SA</u>

Case 1

■ 35 y/o male rancher in northern Arizona with no PMHx who got kicked by horse resulting in right pelvic fracture. Presented to hospital with right pelvic fracture and underwent right hip fracture pinning surgery.

IM consulted for pain management and discharge planning for acute rehab placement and VTE Prophylaxis recommendations: Your orders for VTE Prophylaxis are:

- A. UFH until discharge to rehab facility
- B. Enoxaparin in hospital with IPC/GCS and with extended therapy 4 weeks after discharge
- C. Apixiaban for extended therapy up to 35 days
- D. Enoxaparin in hospital with IPC/GCS with extended prophylaxis for 35 days

Case 1:

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- C. Apixiaban (DOAC) for extended therapy up to 35 days
- D. Enoxaparin in hospital with IPC/GCS with extended prophylaxis for 35 days

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- For patients undergoing THA, TKA, or HFS, we recommend that pharmacologic prophylaxis is administered for a minimum of 10 to 14 days (**Grade 1B**). (See <u>'Duration'</u> above.)
 - For those undergoing THA, we suggest that pharmacologic prophylaxis is continued for up to 35 days after surgery (**Grade 2B**).
 - For those undergoing TKA, shorter courses at the 10 to 14 day end of the spectrum may be preferred.

Then...IM Made Friends With Orthopedics....



Original Research

Annals of Internal Medicine

Aspirin Versus Low-Molecular-Weight Heparin for Extended Wenous Censed under CC BY Thromboembolism Prophylaxis After Total Hip Arthroplasty

A Randomized Trial

David R. Anderson, MD; Michael J. Dunbar, MD; Eric R. Bohm, MD; Etienne Belzile, MD; Susan R. Kahn, MD; David Zukor, MD; William Fisher, MD; Wade Gofton, MD; Peter Gross, MD; Stephane Pelet, MD; Mark Crowther, MD; Steven MacDonald, MD; Paul Kim, MD; Susan Pleasance, BScN; Nicki Davis, BSc; Pantelis Andreou, PhD; Philip Wells, MD; Michael Kovacs, MD; Marc A. Rodger, MD; Tim Ramsay, PhD; Marc Carrier, MD; and Pascal-Andre Vendittoli, MD

EPCAT II TRIAL

Feb 2018

ORIGINAL ARTICLE

Aspirin or Rivaroxaban for VTE Prophylaxis after Hip or Knee Arthroplasty

David R. Anderson, M.D., Michael Dunbar, M.D., John Murnaghan, M.D., Susan R. Kahn, M.D., Peter Gross, M.D., Michael Forsythe, M.D., Stephane Pelet, M.D., William Fisher, M.D., Etienne Belzile, M.D., Sean Dolan, M.D., Mark Crowther, M.D., Eric Bohm, M.D., et al.

ASH GUIDELINES RECCOMENDATION Definitions

	STRONG Recommendation ("The panel recommends")	CONDITIONAL Recommendation ("The panel suggests")
For patients	Most individuals would want the intervention.	A majority would want the intervention, but many would not.
For clinicians	Most individuals should receive the intervention.	Different choices will be appropriate for different patients, depending on their values and preferences. Use shared decision making .





Recommendation

In critically ill medical patients, the panel suggests using LMWH over UFH (conditional recommendation, moderate certainty)

LMWH compared with **UFH** in critically ill patients:

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

Critically ill patients may require other prophylaxis options due to **hepatic or** renal dysfunction.

Dual VTE Prophylaxis: Is it indicated?

- Yes by Chest 2012 Guidelines for Surgical patients
- Yes in surgical cases (2019 Draft ASH Surgical Guidelines)

Question 3: Should pharmacological combined with mechanical prophylaxis vs. pharmacological prophylaxis alone be used for patients undergoing surgery?

The ASH guideline panel suggests using combined prophylaxis with mechanical and pharmacological methods over prophylaxis with pharmacological agents alone in surgical patients (conditional recommendation based on very low certainty of the evidence about effects).

No in Medical patients in ICU per ASH Guidelines 2018 (next slide)



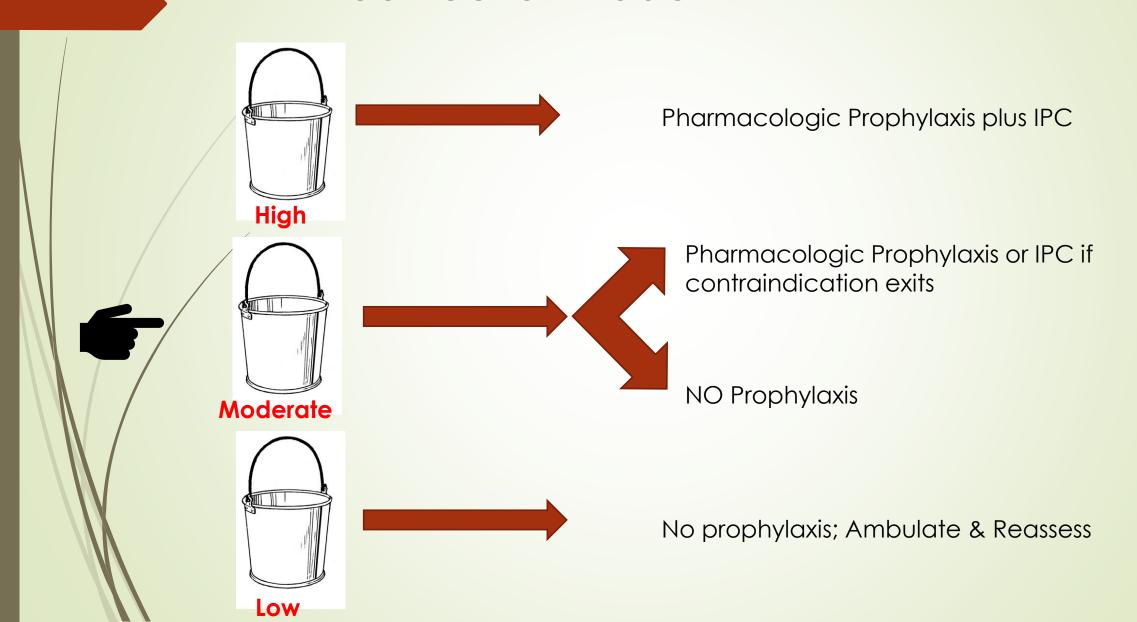
Recommendation

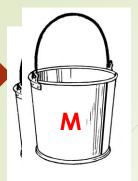
In acutely and critically ill medical patients, the panel suggests pharmacological VTE prophylaxis alone over mechanical combined with pharmacological VTE prophylaxis (conditional recommendation, very low certainty)

Mechanical combined with pharmacologic compared with pharmacologic alone:

	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)		
Outcomes		Risk with pharmacologic prophylaxis alone	Risk difference with combined prophylaxis	
Mortality	0.50 (0.05 to 5.30)	8 per 1,000	4 fewer deaths per 1,000 (8 fewer to 34 more)	
● PE	0.35 (0.05 to 2.22)	1 per 1,000	1 fewer PE per 1,000 (1 fewer to 1 more)	
Symptomatic proximal DVT	0.13 (0.04 to 0.40)	2 per 1,000	2 fewer DVT per 1,000 (2 fewer to 1 fewer)	
Major bleeding	2.83 (0.30 to 26.70)	28 per 1,000	51 more bleeds per 1,000 (20 fewer to 720 more)	

Three Bucket Model





Moderate Risk: Majority Med/Sx Patients!





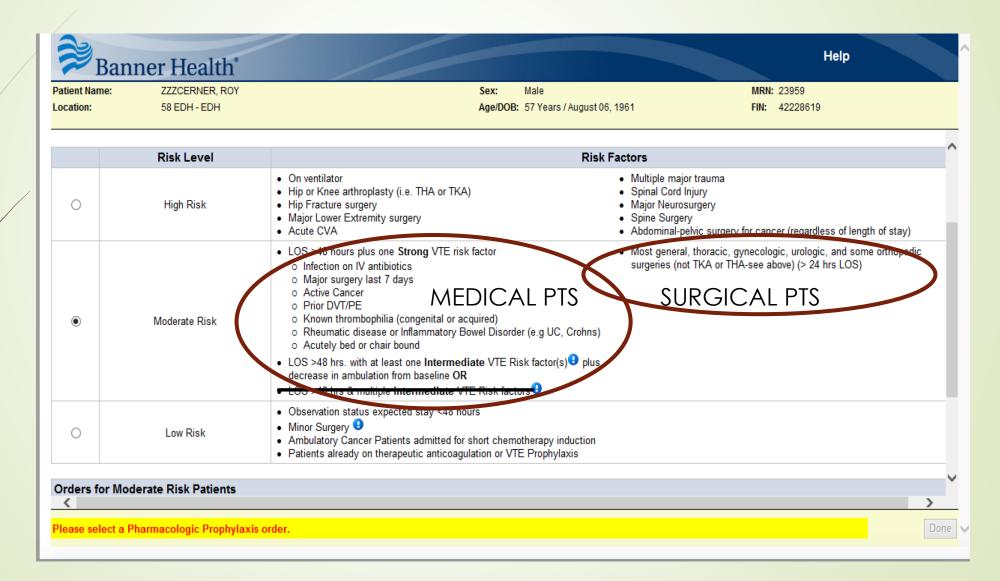
Recommendation

- In acutely ill medical patients, the panel suggests using UFH, LMWH, or fondaparinux rather than no parenteral anticoagulant (conditional recommendation, low certainty)
- The panel suggests using LMWH (low certainty) or fondaparinux (very low certainty) rather than UFH (conditional recommendation)

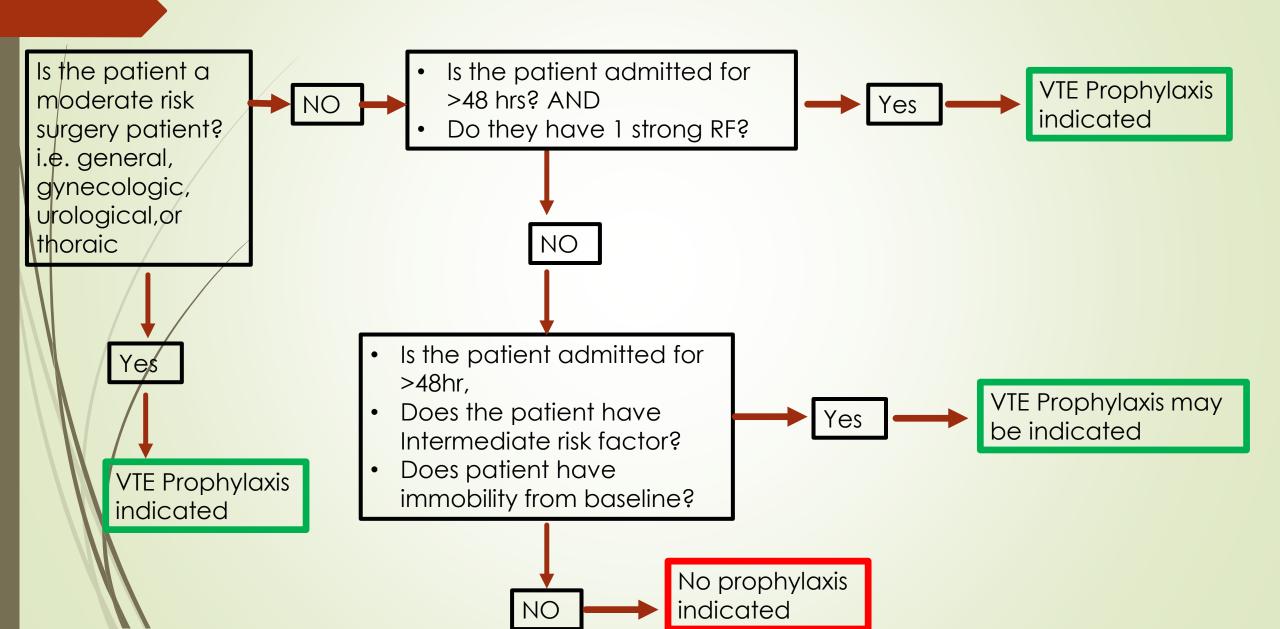
Parenteral anticoagulant compared with no parenteral anticoagulant:

	Relative effect: RR (95% CI)	Anticipated absolute effects (95% CI)		
Outcomes		Risk with no parenteral anticoagulant	Risk difference with parenteral anticoagulant	
Mortality	0.97 (0.91 to 1.04)	69 per 1,000	2 fewer deaths per 1,000 (6 fewer to 3 more)	
● PE	0.59 (0.45 to 0.78)	10 per 1,000	4 fewer PE per 1,000 (6 fewer to 2 fewer)	
Symptomatic proximal DVT	0.28 (0.06 to 1.37)	4 per 1,000	3 fewer DVT per 1,000 (4 fewer to 1 more)	
Major bleeding	1.48 (0.81 to 2.71)	7 per 1,000	3 more bleeds per 1,000 (1 fewer to 12 more)	

VTE Prophylaxis: Three bucket Model



Moderate Risk Bucket Algorithm



Approach to Surgical Patients

First Consider Procedure

- 1. Duration (greater than 45 minutes)
- 2. Position
- 3. Area
- 4. Cancer
- 5. ? emergency

Second consider Other Risk factors surrounding patients

- 1. Strong VTE Risk Factors
- 2. Intermediate Risk Factor

VTE Risk Factors

9 Strong Risk Factors

- Major Surgery in last 7 days
- Previous history of VTE
- Active infection on IV abx
- Thrombophilia (congenital or acquired)
- Rheumatic disease
- IBD
- Acute total immobility i.e. bedbound
- Active malignancy
- Postpartum

Intermediate Risk Factors

- M
- CHF
- Active infection
- COPD /Acute respiratory failure
- Severe dehydration
- Age greater than 65 y/o
- BMI>30
- Nephrotic syndrome
- Hormonal therapies
- CVL
- Previous CVA with paresis

Equation #1

Strong VTE RISK FACTOR + >48 hrs. = VTE Prophylaxis.

- Major Surgery in last 7 days
- Previous history of VTE
- Active infection on IV abx
- Thrombophilia (congenital or acquired)
- Rheumatic disease
- IBD
- Acute total immobility i.e. bedbound
- Active malignancy
- Postpartum

Equation #2

Intermediate Risk Factors + > 48 hrs. + immobility from baseline= VTE Prophylaxis

- MI
- Acute COPD/Acute respiratory Failure
- CHF
- Active infection
- Severe dehydration
- Age greater than 65 y/o
- BMI>30
- Nephrotic syndrome
- Hormonal therapies
- CVL
- Previous CVA with paresis

CASE 2

65 y/o male with PMHx CAD with CABG and chronic grade I diastolic CHF is transferred from outside hospital after 3 days on IV Zosyn for cholecystitis being evaluated for laparoscopic cholecystectomy.

Admission orders for VTE prophylaxis should include the following:

- A) SCDS
- B) Enoxaparin
- C) Combination of SCDS + LMWH
- D) Ambulate when tolerated

CASE 2

65 y/o male with PmHx CAD with CABG and chronic grade I diastolic CHF is transferred from outside hospital after 3 days on V Zosyn for aparoscopic cholecystectomy.

Admission orders for VTE prophylaxis should include the following:

- A) SCDS
- B) Enoxaparin
- C) Combination of SCDS + Enoxaparin
- D) Ambulate when tolerated

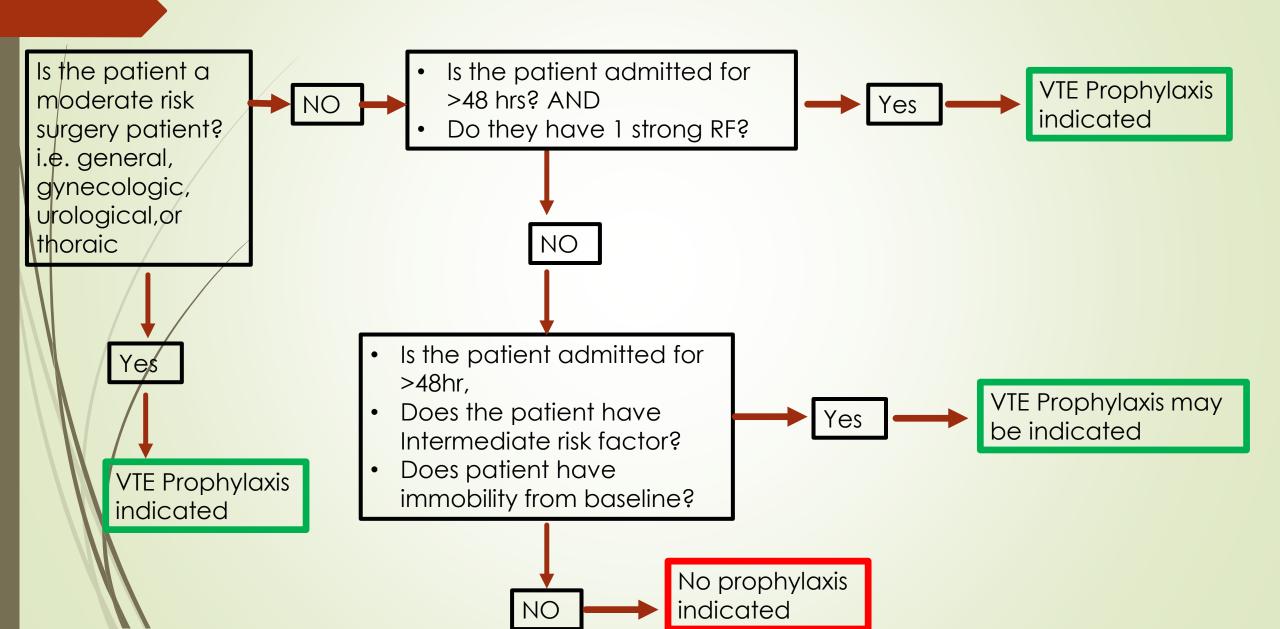
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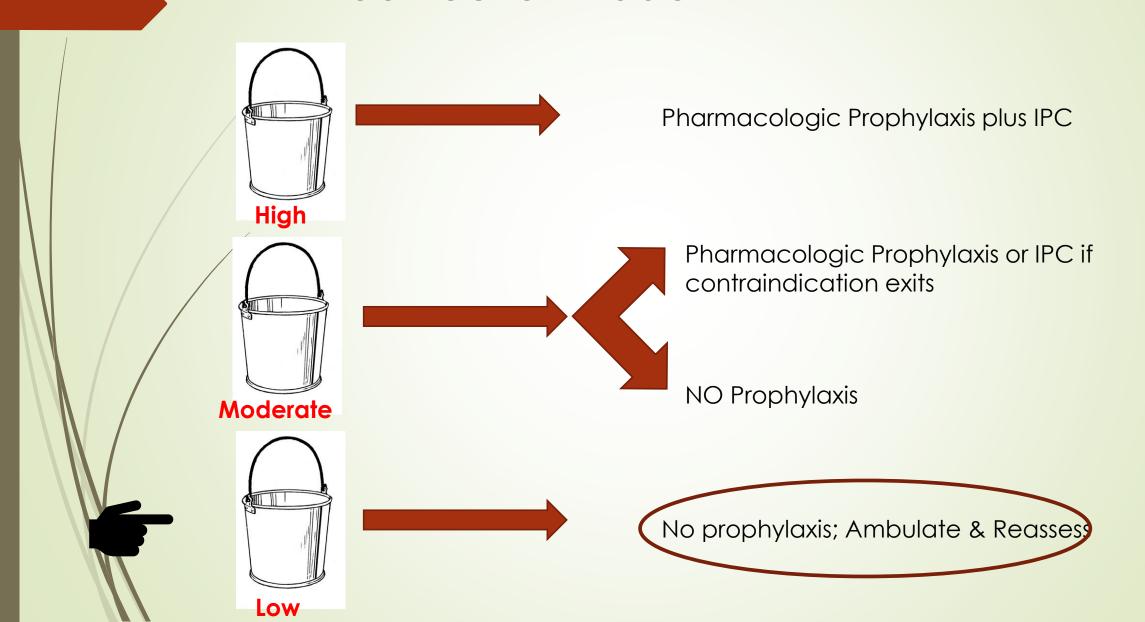
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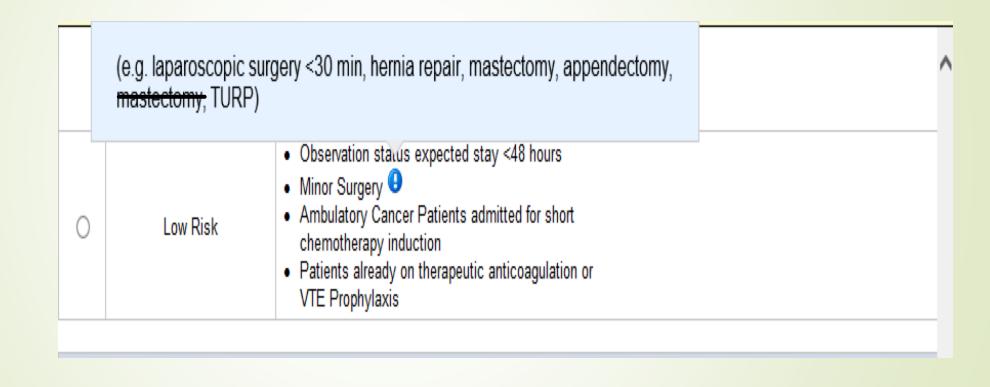
Moderate Risk Bucket Algorithm



Three Bucket Model



Minor Surgery





Lowest Risk: Obs/minor Sx/ Already on anticoagulated for other reasons

- 1. Minor Surgery (<30 min)
- 2. Laparoscopic surgery e.g. cholecystectomy, appendectomy
- 3. Already on anticoagulated (e.g afib)
- 4. Cancer patients for chemo induction or infusions
- 5. Observation Patients (<48 hours)
- Dynamic Process
- Consider how likely they will stay in observation
- Consider their VTE strong risk Factors

LOW RISK Nonorthopedic Surgery VTE RISK = 1.5%

- Low Risk (Caprini=1-2; Plastic/Reconstruction Caprini 3-4)
- 1. Minor elective abdominal-pelvic Surgery
 - Appendectomy
 - Laparoscopic cholecystectomy
 - Minor thoracic surgery (diagnostic thorascopy)
 - Vein ablation
 - Elective spine surgery (e.g. spinal fusion)

CASE 3

65 y/o male with PMHx CAD with CABG and chronic grade I diastolic CHF presents for laparoscopic cholecystectomy

Admission orders for VTE prophylaxis should include the following:

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- C) Combination of SCDS + Enoxaparin
- D) Ambulate when tolerated

CASE 3

65 y/o male with PmHx CAD with CABG and chronic grade I diastolic CHF presents for anticipated uncomplicated aparoscopic cholecystectomy; discharge is at <48 hours

Admission orders for VTE prophylaxis should include the following:

- A) SCDS
- B) Enoxaparin
- C) Combination of SCDS + Enoxaparin
- D) Ambulate when tolerated

CASE 3

65 y/o male with PMHx CAD with CABG and chronic grade I diastolic CHF presents for uncomplicated laparoscopic cholecystectomy

Admission orders for VTE prophylaxis should include the following:

- A) SCDS
- B) Enoxaparin
- C) Combination of SCDS + Enoxaparin
- D) Ambulate when tolerated

Guidelines on Low Risk Surgery

- ACCP 2012 for Low Risk Nonorthopedic surgery VTE Prevention is mechanical prophylaxis
- SAGES (Society of American Gastrointestinal and Endoscopic Surgeons) 2018 Recommendations:

"A meta-analysis on laparoscopic cholecystectomy indicated that routine use of VTE chemoprophylaxis was likely to be unnecessary and suggested considering its use only in higher risk patients based on risk stratification"

Rondelli F, Manina G, Agnelli G, Becattini C. <u>Venous thromboembolism after laparoscopic</u> <u>cholecystectomy: clinical burden and prevention.</u> Surg Endosc. 2013;27(6):1860-4.

■ **ASH** "Draft" Surgical VTE Prophylaxis Guidelines



ASH Draft Recommendations for VTE Prevention in Surgical Hospitalized Patients

Question 19: Should pharmacological prophylaxis vs. no pharmacological prophylaxis be used for patients undergoing laparoscopic cholecystectomy?

The ASH guideline panel suggests against pharmacological prophylaxis over no prophylaxis in patients undergoing laparoscopic cholecystectomy (conditional recommendation based on low certainty of the evidence about effects)

More Cases! Yes.....



Consulted on 45 y/o female with BMI 30 no PMhx other than diabetes with severe abdominal pain with abdominal mass anticipating laparoscopic hysterectomy.

Intraoperatively pathology preliminary read is adenocarcinoma of uterus. She had complication of intraoperative bleeding with some hypotension and ultimately underwent open TAHBSO. Bleeding vessel was clipped and hemostasis was achieved with resulting hemoglobin 10. and creatinine is 1.5 (CrCL>50)

- A. IPC
- B. UFH + IPC
- C. Fondaparinux
- D. Enoxaparin + IPC
- Enoxaparin + IPC/GCS with plans for Extended Prophylaxis after discharge x4 weeks
- F. Enoxaparin + IPC/GCS in hospital with plans for Extended Prophylaxis with Apixiban on discharge

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Apixaban to Prevent Venous Thromboembolism in Patients with Cancer

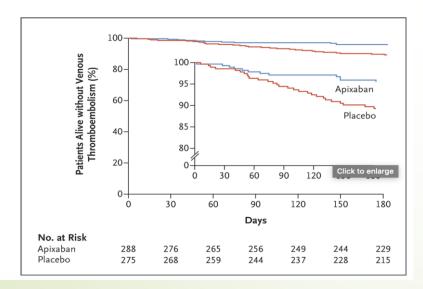
Marc Carrier, M.D., Karim Abou-Nassar, M.D., Ranjeeta Mallick, Ph.D., Vicky Tagalakis, M.D., Sudeep Shivakumar, M.D., Ariah Schattner, M.D., Philip Kuruvilla, M.D., Danny Hill, M.D., Silvana Spadafora, M.D., Katerine Marquis, M.D., Mateya Trinkaus, M.D., Anna Tomiak, M.D., et al., for the AVERT Investigators*

February 21, 2019 N Engl J Med 2019; 380:711-719

DOI: 10.1056/NEJMoa1814468 Chinese Translation 中文翻译

Apixaban for Thromboprophylaxis in Cancer

Published Feb 20, 2019 - Written by Carla Rothaus



- Advanced cancer with lymphoma, pancreas, and gynecologic cancers
- Few colorectal and prostate

65 y/o male admitted for CHF exacerbation and has been in ED overflow for 8 hours. PMhx significant for acute on chronic systolic dysfunction with ICM 40%. Repeat echo-pending. Other PMhx: DM, HTN,HLP, BMI >30. Your therapies include Lasix and is having a nice response. Oxygenation improved to 94% on RA and urine output is @ 1 Liter so far on Lasix.

- 1. Enoxaparin
- 2. UFH
- 3. Fondaparinux
- 4. SCDS only
- 5. Ambulate and Reassess

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- 5. Ambulate and Reassess

 65 y/o female with insulin dependent diabetes, HTN, and COPD admitted with UTI with septic shock with BP 70/50. Overnight she was started on CRRT due to anuria, pressors, and IV antibiotics

Appropriate VTE prophylaxis includes

- A. Enoxaparin with IPC
- B. Fondaparinux with GCS
- C. Unfractionated heparin with IPC
- D. Unfractionated heparin

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- C. Unfractionated heparin with IPC.
- D. Enoxaparin
- Unfractionated heparin





Banner Summary 2018 VTE Data

Facility & Year	Total Inpatient VTE (rate/1000 admits)	Total 30-day Readmit (rate/1000 admits)	Total VTE events (rate/1000 admits)
Univ. of Calif 2011-2014 Five academic centers			546/79565 <mark>(9.0→6.9</mark>)
Dignity Hospital (35 Community hospital system) 2011-2014	517 (1.84)	639 (2.28)	1584-→1156/280725 <mark>(5.25→4.12)</mark>
Banner System wide-2018	732/187152(<mark>2.44</mark>)	730/116802 (<mark>4.03</mark>)	1462/187152 <mark>(8.18)</mark>

Review of Learning Points

- Know how to navigate Cerner VTE Prevention Order-set
- Know how to navigate moderate risk patients and decipher who needs VTE prophylaxis and who does not
- Know 9 Strong VTE Risk factors
- Be familiar with Intermediate Risk Factors
- Know what populations of surgical patients need extended prophylaxis
- Be aware of possible future role for DOACS in VTE Prevention for Cancer patients
- Think outside the box and document

Park City, Utah 2019

The End.



