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Evaluation of an elevated VTE thromboprophylaxis guideline for critically ill patients infected with COVID-19

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Disclosures

The authors of this study have no financials relationships related to this presentation to disclose

Objectives

Identify the current society and guideline recommendations for the prevention of venous thromboembolisms (VTE).

Identify the risk and benefits of thromboprophylaxis intensities higher than prophylactic-dose.

Background

Increase of risk of VTE suggested in critically ill patients infected with COVID-19.

What anticoagulation dose should be used for critically ill patients infected with COVID-19 to prevent a VTE?

Recommendations Overview

STATEMENT

Unless contraindicated, routine prophylactic dose anticoagulation is suggested/recommended for all patients who are hospitalized with a COVID-19 infection.

- American Society of Hematology
- National Institutes of health
- International Society of Thrombosis and Haemostasis

NIH. Covid19treatmentguidelines.nih.gov [Internet]. [Cited 2021 Apr 5]
Kreuziger LB, et al. Hematology.org [Internet]. [Cited 2021 Apr 5]
Spyropoulos AC, et al. J Thromb Haemost. 2020 Aug;18(8):1859–65.

Recommendations Overview - 2

STATEMENT

Critically ill patients infected with COVID-19 should receive routine prophylactic dose anticoagulation. Patients with high risk of VTE may be considered for intermediate intensity anticoagulation.

American Society of Hematology	
National Institutes of health	
International Society of Thrombosis and Haemostasis	

NIH. Covid19treatmentguidelines.nih.gov [Internet]. [Cited 2021 Apr 5]
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Recommendations Overview - 3

STATEMENT

Patients infected with COVID-19 with a high risk of VTE should receive treatment dose anticoagulation to prevent a VTE.

- **American Society of Hematology** 
- **National Institutes of health** 
- **International Society of Thrombosis and Haemostasis** 

NIH. Covid19treatmentguidelines.nih.gov [Internet]. [Cited 2021 Apr 5]
Kreuziger LB, et al. Hematology.org [Internet]. [Cited 2021 Apr 5]
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Takeaway

1. Unless contraindicated, hospitalized patients infected with COVID-19 should receive routine VTE prophylaxis
2. Anticoagulation higher than prophylactic dosing is controversial.
3. Treatment dosing at this time is not recommended by leading hematological organization or governmental agency.

NIH. Covid19treatmentguidelines.nih.gov [Internet]. [Cited 2021 Apr 5]
Kreuziger LB, et al. Hematology.org [Internet]. [Cited 2021 Apr 5]
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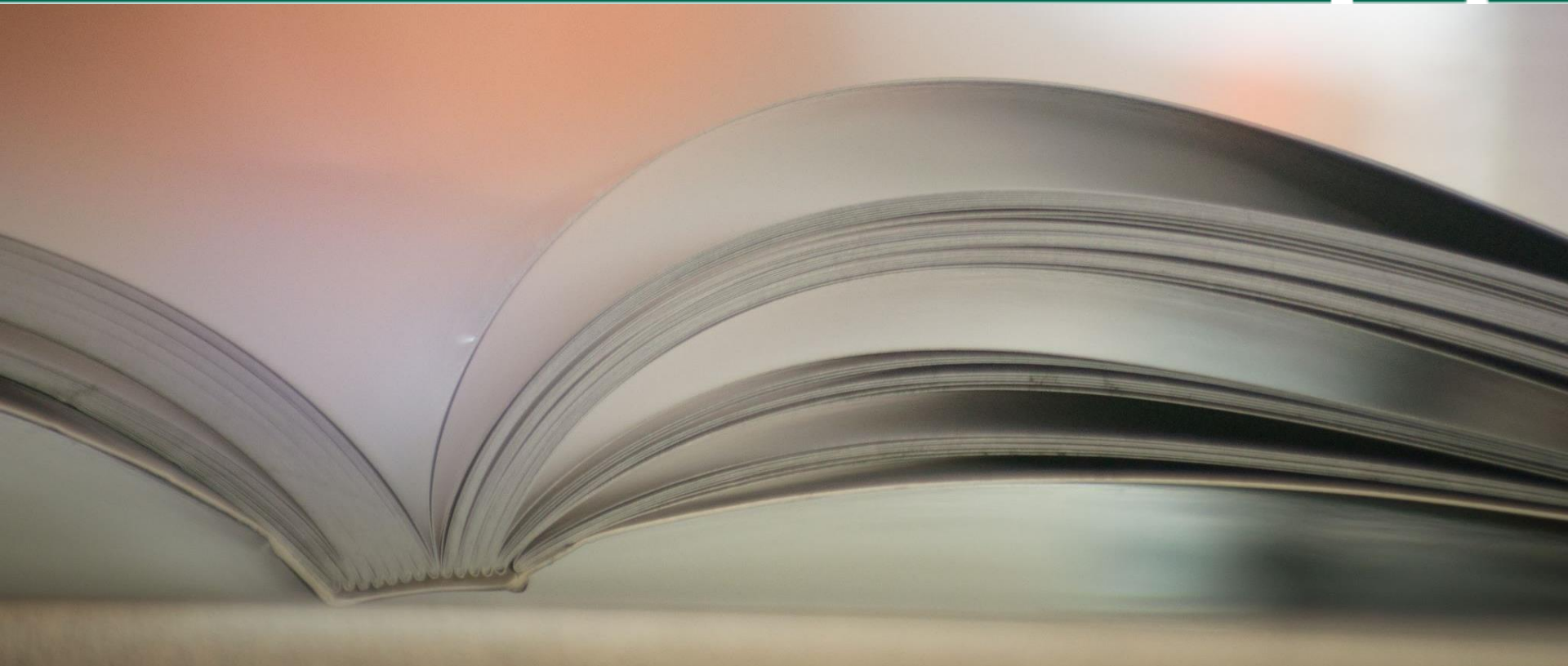
Purpose

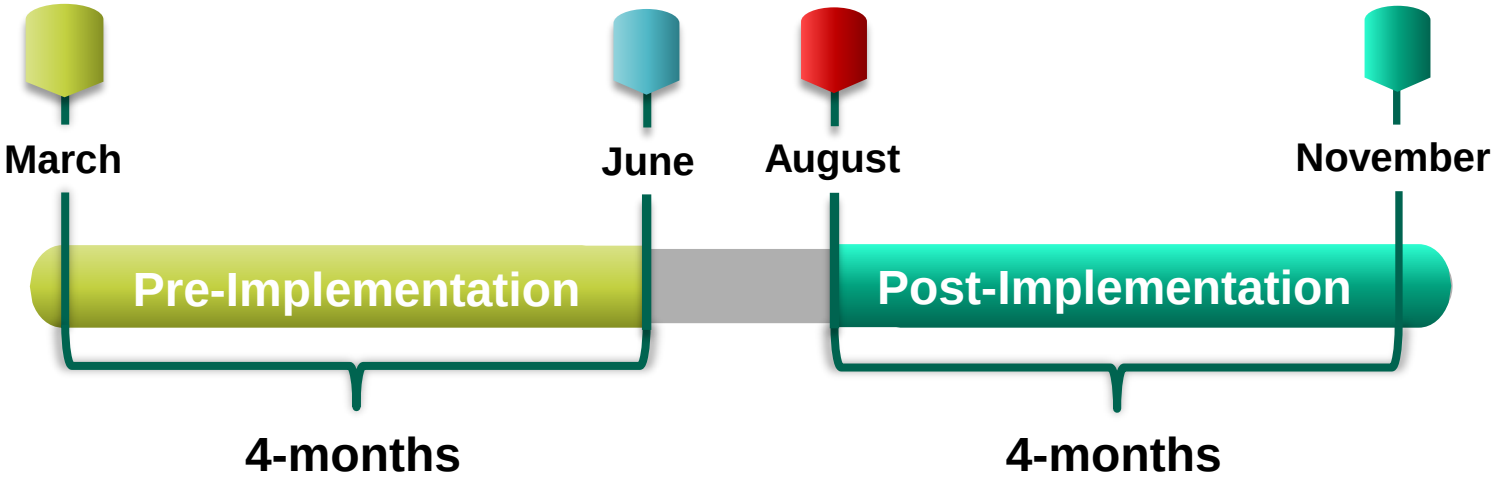
Evaluate the effects on clinical outcomes and ordering patterns of implementing an interim guidance document for thromboprophylaxis dosing in critically ill patients infected with COVID-19.

Methods



Design

Retrospective pre- and post-treatment guidance implementation study



Interim anticoagulation guidance document approved and communicated to stakeholders August 6th

Population

Inclusion

Adults with a COVID-19 infection admitted to the intensive care unit receiving anticoagulation for the primary prevention of a venous thromboembolism

Population

Exclusion

- Chronic anticoagulation prior to admission
  - › E.g., recent VTE, atrial fibrillation, valve replacement, etc.
- Admission for or new acute onset disease requiring treatment intensity anticoagulation
- Length of ICU stay < 72 hrs.
- Pregnancy
- Incarceration

ICU Intensive care unit

Intervention

Baptist Health South Florida

Guidelines for Anticoagulation in Adult Patients with COVID-19

BACKGROUND: COVID-19 patients with severe infection demonstrate a hypercoagulable profile. The recommendations below provide guidance, **and are not intended to substitute clinical judgement.** Optimal anticoagulant dosing for VTE prevention/treatment in COVID-19 patients is unknown. Patients on dual or single anti-platelet therapy should also be on chemical DVT prophylaxis.

ELEVATED DOSE PROPHYLAXIS: COVID-19 ICU patients or patients receiving ICU level of care WITHOUT known thrombus and have elevated D-Dimer > 3 mcg/mL (6XUNL), elevated CRP or IL6 who are at risk for Cytokine Release Syndrome, WITH **2 or more** independent risk factors for VTE (i.e., malignancy, immobility, injury) should receive elevated prophylactic doses of anticoagulation to prevent venous thromboembolism. If anticoagulation is contraindicated, we recommend sequential compression devices, and baseline and routine lower extremity doppler.

Elevated dose of DVT Prophylaxis	Patients with BMI greater than 40 kg/m^2	Low body weight patients (< 50 kg)
CrCl $\geq$ 30 mL/min, Enoxaparin (Lovenox) 40 mg SubQ BID CrCl < 30 mL/min, Heparin 7,500 units SubQ every 8 hours IF patient has a heparin allergy, consult with Hematology	CrCl $\geq$ 30 mL/min, Enoxaparin (Lovenox) 0.5 mg/kg SubQ BID, round per protocol (Max dose 100 mg SubQ BID) CrCl < 30 mL/min, Heparin 10,000 units SubQ every 8 hrs	CrCl $\geq$ 30 mL/min, Enoxaparin (Lovenox) 30 mg SubQ BID CrCl < 30 mL/min, Heparin 7,500 units SubQ every 8 hours

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Elevated dosing - Standard

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Elevated dose of DVT Prophylaxis	with BMI greater than 40 kg/m²	Low body weight patients (< 50 kg)
CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 40 mg SubQ BID	mL/min, Enoxaparin (Lovenox) 0.5 mg/kg SubQ	CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 30 mg SubQ BID
CrCl < 30 mL/min, Heparin 7,500 units SubQ every 8 hours	d per protocol (Max dose 100 mg SubQ BID)	CrCl < 30 mL/min, Heparin 7,500 units SubQ every 8 hours
IF patient has a heparin allergy, consult with Hematology	mL/min, Heparin 10,000 units SubQ every 8 hrs	

Tony Nguyen **Baptist Hospital of Miami**

Elevated Prophylaxis – Obese

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Elevated dose of DVT Prophylax		weight patients (< 50 kg)
CrCl ≥ 30 mL/min, Enoxaparin (L	Patients with BMI greater than 40 kg/m²	mL/min, Enoxaparin (Lovenox) 30 mg SubQ BID
CrCl < 30 mL/min, Heparin 7,500	CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 0.5 mg/kg SubQ BID, round per protocol (Max dose 100 mg SubQ BID)	mL/min, Heparin 7,500 units SubQ every 8
IF patient has a heparin allergy,	CrCl < 30 mL/min, Heparin 10,000 units SubQ every 8 hrs	

Elevated Prophylaxis - LBW

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Elevated dose of DVT Prophylaxis	Patients with BMI great
CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 40 mg SubQ BID	CrCl ≥ 30 mL/min, Enoxa
CrCl < 30 mL/min, Heparin 7,500 units SubQ every 8 hours	BID, round per protocol
IF patient has a heparin allergy, consult with Hematology	CrCl < 30 mL/min, Hepar

Low body weight patients (< 50 kg)
CrCl ≥ 30 mL/min, Enoxaparin (Lovenox) 30 mg SubQ BID
CrCl < 30 mL/min, Heparin 7,500 units SubQ every 8 hours

Clinical Outcomes

Incidence of VTEs in patients admitted to the ICU with COVID-19

Secondary Outcomes

- Clinically significant bleeding
- In-hospital mortality

Statistical Analysis

Baseline characteristics

- Descriptive statistics

Primary outcome

- Intervention success is defined as no difference in VTEs in the post-implementation group compared to pre-implementation group.
- Relative risk (RR) and 95% CI were calculated as supportive analysis
- The test statistic used was a two-sided x^2 test with a significance level of 0.05

Statistical Analysis (Continued)

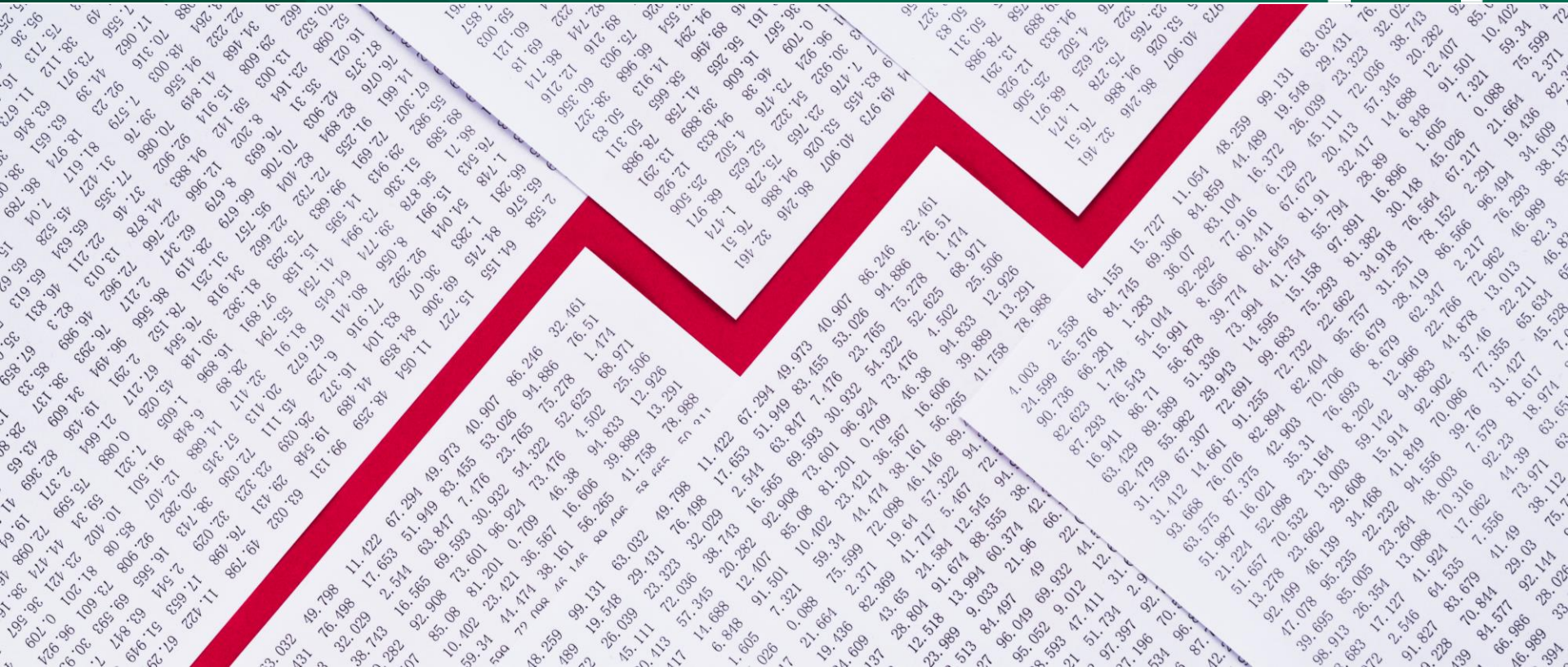
Secondary Outcomes

Incidence and relative risk of clinically significant bleeding, in-hospital mortality

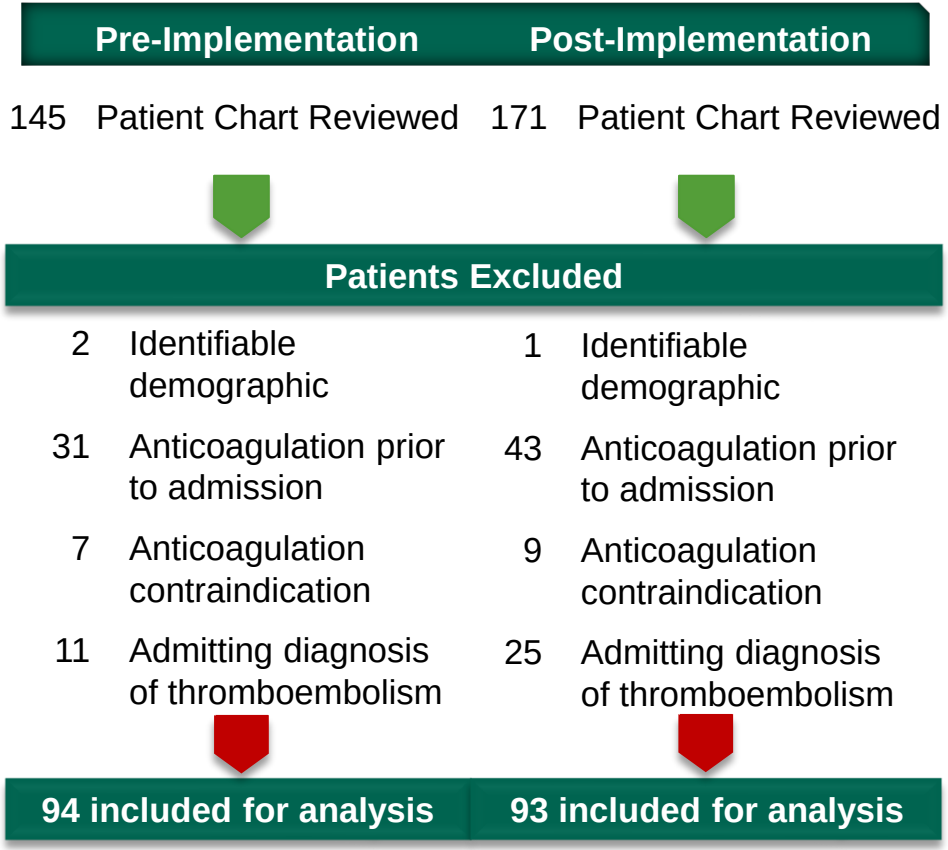
Sub-group analysis

Descriptive statistics

Results



Screening



Total 316 charts reviewed assessed for inclusion

Most % excluded were due to chronic anticoagulation prior to admission

Total: 187 patients

Baseline Characteristics

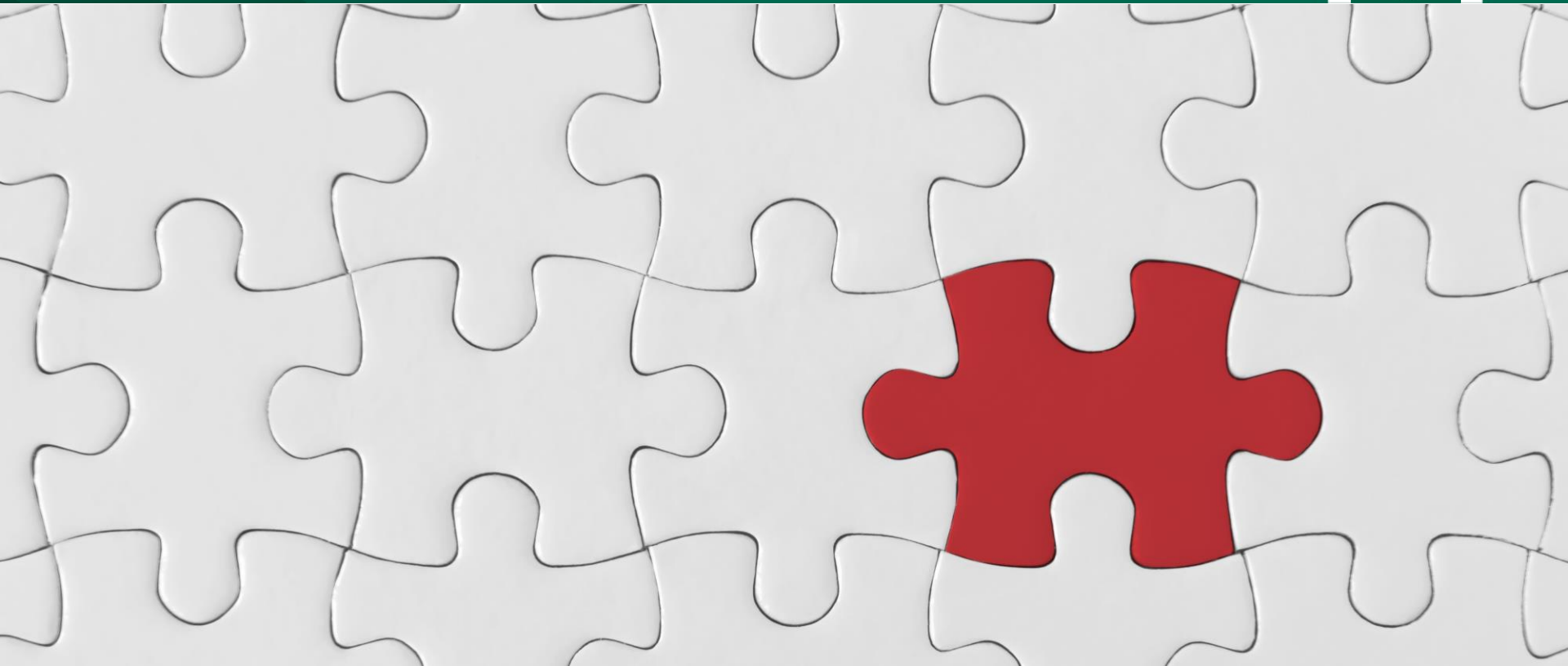


Table 1. Baseline Characteristics

Characteristics	Pre-implementation (N = 94)	Post-implementation (N = 93)
Age – yr	66 (55-75)	69 (59-69)
Male sex – no. (%)	62 (66.0)	62 (66.7)
White Hispanic – no. (%)	76 (80.9)	84 (90.32)
Weight – kg/m^2	30.3 ± 5.9	30.0 ± 5.8

BMI – Body mass index
*Comorbidities evaluated included: hypertension, diabetes, chronic kidney disease, hyperlipidemia, coronary artery disease, cancer, chronic obstructive pulmonary disease

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White Hispanic – no. (%)	76 (80.9)	84 (90.32)
Weight – kg/m^2	30.3 ± 5.9	30.0 ± 5.8
Weight Distribution – no. (%)		
BMI ≤ 30	49 (52.1)	47 (50.5)
BMI > 30-39.9	38 (40.4)	42 (45.2)
BMI ≥ 40	7 (7.5)	4 (4.3)
More than 3 Comorbidities	16 (17.0)	22 (23.7)
Concomitant antiplatelet – no. (%)	19 (20.2)	45 (48.4)

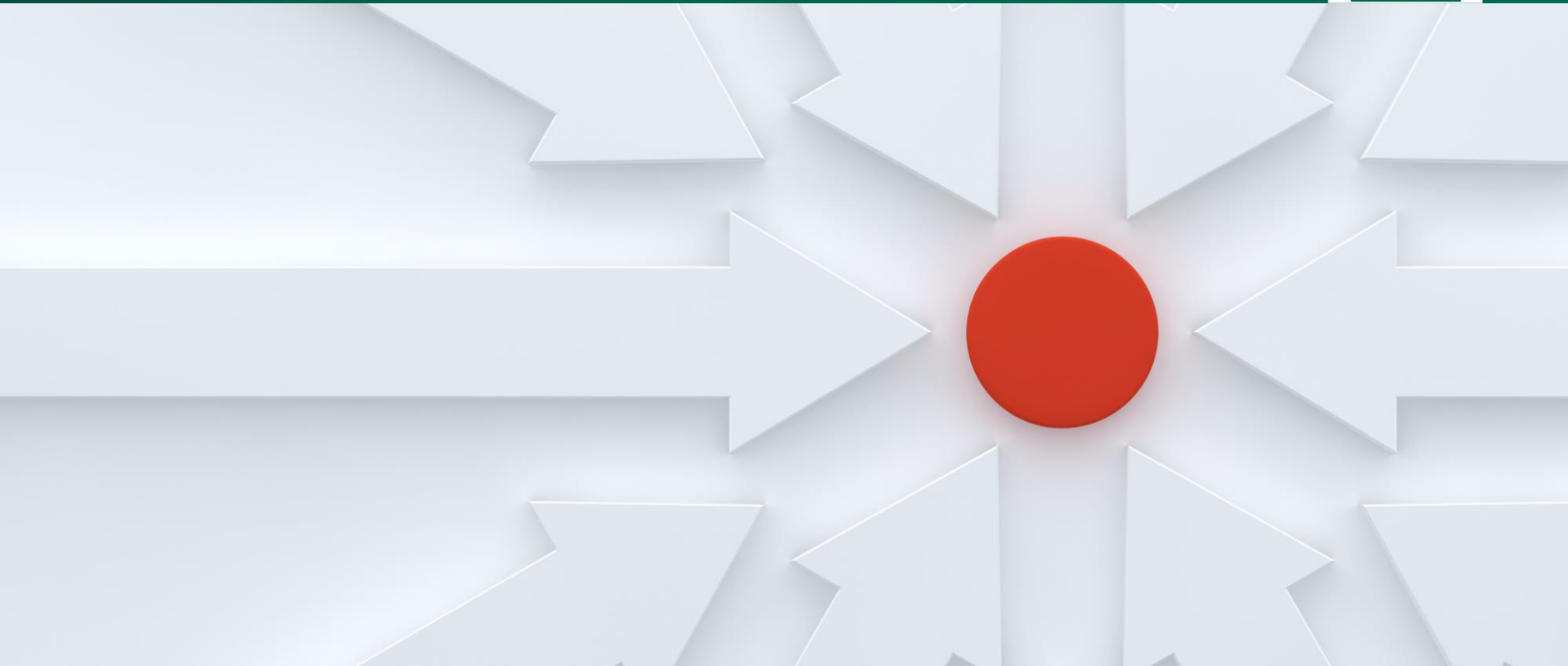
BMI – Body mass index
*Comorbidities evaluated included: hypertension, diabetes, chronic kidney disease, hyperlipidemia, coronary artery disease, cancer, chronic obstructive pulmonary disease

Table 1. Baseline Characteristics (Continued)

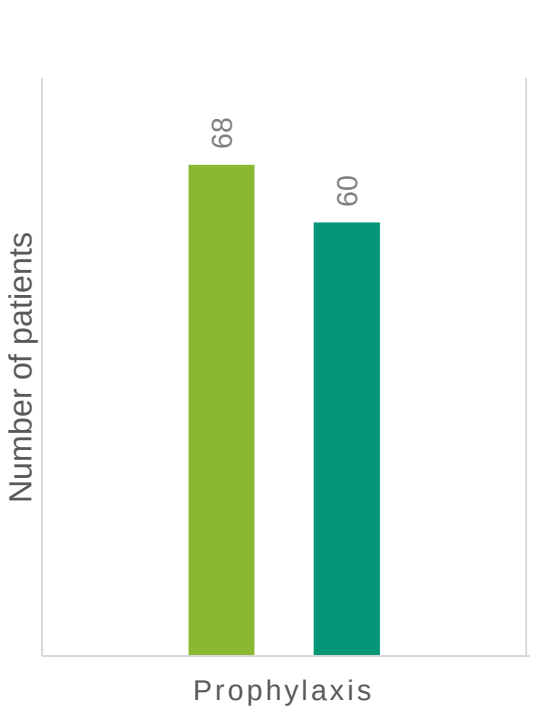
Laboratory Makers – mean (±SD)	Pre-Implementation (N = 94)	Post-Implementation (N = 93)
Hemoglobin, mg/dL	13.3 ± 1.8	13.4 ± 2.1
Platelet, count	212.3 ± 86.3	248.2 ± 103.7
INR*	1.1 (1.1-1.1)	1.1 (1.1-1.2)
Prothrombin time, ms	34.8 ± 20.5	31.1 ± 4.9
D-dimer, mcg/mL*	3.6 ± 10.3	2.8 ± 4.7
Ferritin, mcg/L	1468.2 ± 3337.4	811.4 ± 654.1

INR – International normalized ratio
*INR, D-dimer expressed as median with lower and upper quartile ranges

Clinical Outcomes



Anticoagulation Orders by Dose Intensity



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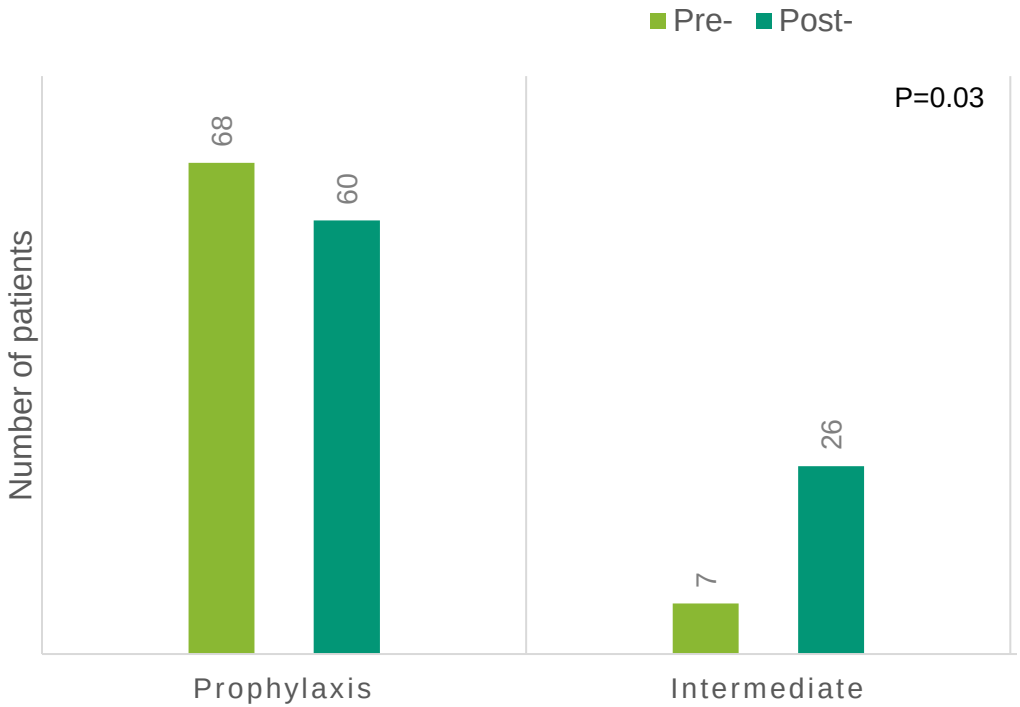

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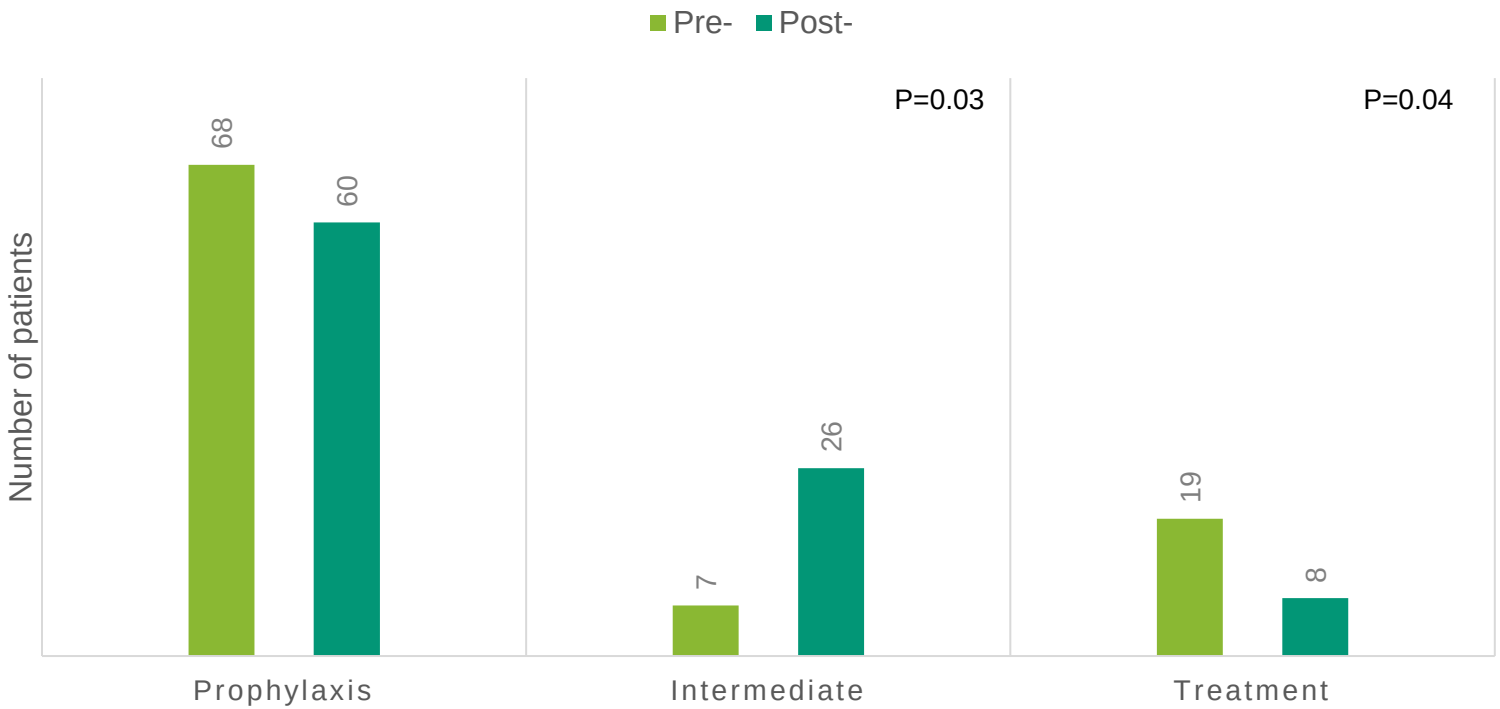

Table 2. Sub-group Analysis

Outcome – no. (%)	Prophylaxis Pre- N = 68	Prophylaxis Post- N = 60
Venous Thromboembolism	7 (10.3)	9 (15.0)
In-hospital mortality	23 (33.8)	20 (33.3)
Any bleeding	6 (8.8)	7 (11.7)

Table 2. Sub-group Analysis

Outcome – no. (%)	Prophylaxis		Intermediate	
	Pre- N = 68	Post- N = 60	Pre- N = 7	Post- N = 26
Venous Thromboembolism	7 (10.3)	9 (15.0)	0 (0)	4 (15.4)
In-hospital mortality	23 (33.8)	20 (33.3)	2 (28.6)	9 (34.6)
Any bleeding	6 (8.8)	7 (11.7)	1 (14.3)	2 (7.7)

Table 2. Sub-group Analysis

Outcome – no. (%)	Prophylaxis		Intermediate		Treatment	
	Pre- N = 68	Post- N = 60	Pre- N = 7	Pre- N = 26	Pre- N = 19	Post- N = 8
Venous Thromboembolism	7 (10.3)	9 (15.0)	0 (0)	4 (15.4)	0 (0)	2 (25)
In-hospital mortality	23 (33.8)	20 (33.3)	2 (28.6)	9 (34.6)	11 (58.9)	2 (25)
Any bleeding	6 (8.8)	7 (11.7)	1 (14.3)	2 (7.7)	3 (15.8)	3 (37.5)

Table 3. Clinical Outcomes

	Pre- (n= 94)
Primary Outcome – *no.* (%)	
Venous Thromboembolism	7 (7.5)
Pulmonary embolism	1 (1.1)
Deep vein thrombosis	6 (6.4)

Table 3. Clinical Outcomes

	Pre- (n= 94)	Post- (n= 93)
Primary Outcome – *no.* (%)		
Venous Thromboembolism	7 (7.5)	13 (14.0)
Pulmonary embolism	1 (1.1)	2 (2.2)
Deep vein thrombosis	6 (6.4)	11 (11.83)

Table 3. Clinical Outcomes

	Pre- (n= 94)	Post- (n= 93)	Relative Risk (95% CI)
Primary Outcome – *no.* (%)			
Venous Thromboembolism	7 (7.5)	13 (14.0)	1.88 (0.78 to 4.50)
Pulmonary embolism	1 (1.1)	2 (2.2)	
Deep vein thrombosis	6 (6.4)	11 (11.83)	

Figure 1. Relative Risk of Venous Thromboembolism in Pre- vs. Post-Implementation

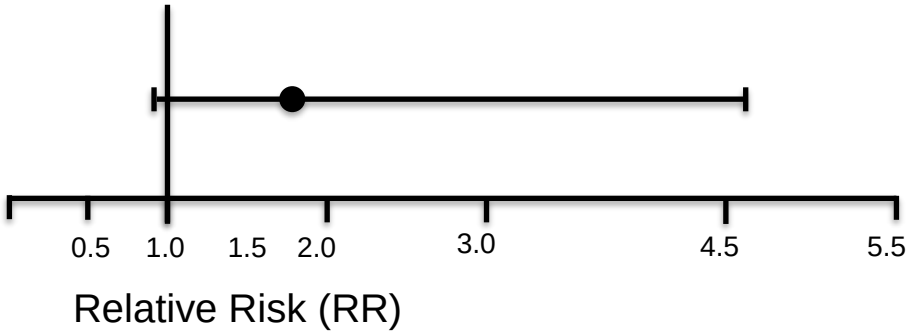

Table 2. Clinical Outcomes (Continued)

	Pre-implementation (n=94)	Post-implementation (n=93)
Secondary Outcomes – *no.*(%)		
Bleeding, any	10 (10.6)	12 (12.8)
In-hospital mortality	36 (38.3)	31 (33.0)

Conclusions

Implementation of an anticoagulation dosing guideline for the prevention of VTE in critically ill patients infected with COVID-19 had no observable difference on the incidence of VTE, however observed a statistically significant difference in the prescribing of intermediate and treatment dose orders.

Self-Assessment Questions

T/F: Unless contraindicated, routine prophylactic-intensity anticoagulation is recommended for all critically ill patients infected with COVID-19.

References

1. Spyropoulos AC, Levy JH, Ageno W, Connors JM, Hunt BJ, Iba T, et al. Scientific and Standardization Committee communication: Clinical guidance on the diagnosis, prevention, and treatment of venous thromboembolism in hospitalized patients with COVID-19. J Thromb Haemost. 2020 Aug;18(8):1859–65.
2. Covid-19 and vte-anticoagulation - hematology. Org [Internet]. [cited 2021 Apr 5]. Available from: https://www.hematology.org:443/covid-19/covid-19-and-vte-anticoagulation
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4. Piazza G, Morrow DA. Diagnosis, management, and pathophysiology of arterial and venous thrombosis in covid-19. JAMA. 2020 Dec 22;324(24):2548.

Acknowledgements

Heidi Clarke, PharmD BCCCP

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