

COVID-19 CADTH HORIZON SCAN

Venous Thromboembolism Prophylaxis in Patients Hospitalized With COVID-19

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To produce this report, CADTH used a modified approach to the selection, appraisal, and synthesis of the evidence to meet decision-making needs during the COVID-19 pandemic. Care has been taken to ensure the information is accurate and complete, but it should be noted that international scientific evidence about COVID-19 is changing and growing rapidly.

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Bottom Line: Based on the evidence available as of June 8, 2020

- Individuals hospitalized with COVID-19, particularly critically ill patients admitted to intensive care units, are at an increased risk for venous thromboembolism (VTE).
- Most Canadian and international guidance suggests using prophylactic dosing of pharmacologic thromboprophylaxis to prevent VTE in patients who have been hospitalized with COVID-19.
- Canadian and international guidance does not suggest the routine use of extended-duration pharmacologic thromboprophylaxis. The use of extended-duration pharmacologic prophylaxis in patients with COVID-19 who are being discharged from hospital may be considered based on the risk of VTE and the risk of bleed.

Context

Acutely ill hospitalized patients, particularly those who are admitted to an intensive care unit (ICU) because they are critically ill, are at an increased risk for venous thromboembolism (VTE) because of endothelial injury, hypercoagulability, and immobilization resulting in venous stasis.¹ As such, the use of pharmacologic or mechanical thromboprophylaxis is recommended for acutely ill and critically ill hospitalized patients to reduce the risk for VTE.^{2,3} The decision to initiate prophylaxis, as well as the type of prophylaxis to be used, is based on the risk of VTE and the risk of bleed.^{2,3} When pharmacologic prophylaxis is indicated for acutely ill or critically ill medical patients, prophylactic dosing is recommended; however, the dose may be adjusted based on kidney function or body weight.^{2,3} In addition, continued use of pharmacologic thromboprophylaxis after discharge from hospital is not recommended in acutely ill medical hospitalized patients.²

Patients hospitalized with COVID-19 are also at an increased risk for VTE; however, it is unclear whether their risk for VTE is greater than acutely ill patients hospitalized for other reasons.⁴ In addition, for patients with COVID-19, it is unclear whether prophylactic doses of pharmacotherapy are adequate to manage VTE risk or whether these patients require a larger dose.⁴ Also, the ideal duration of pharmacotherapy is uncertain; it is unclear whether patients with COVID-19 require extended-duration pharmacologic thromboprophylaxis after discharge from hospital.

The purpose of this report is to, in patients hospitalized with COVID-19:

- describe the epidemiology of VTE
- report the available Canadian and international guidance regarding the dose and duration of the use of pharmacologic thromboprophylaxis for the prevention of VTE
- list the ongoing clinical trials evaluating pharmacologic thromboprophylaxis for the prevention of VTE.

Information on COVID-19 is rapidly developing; as such, this document reflects the guidance available at the time of publication and will be updated as information comes available.

About This Document

This publication summarizes information identified through a limited literature search. It is not a systematic review and does not include a critical appraisal of studies. It is not intended to provide recommendations.

Venous Thromboembolism in Patients Hospitalized With COVID-19

Seventeen studies reporting on 16 study populations were identified that reported the frequency of VTE in patients hospitalized with COVID-19. Locations of the study populations included China,⁵⁻⁷ France,⁸⁻¹¹ Italy,¹²⁻¹⁴ Mexico,¹⁵ the Netherlands,¹⁶⁻¹⁹ Switzerland,²⁰ the US,²¹ and one study that included patients from Canada, Europe, Japan, and the US.²² Study populations included patients admitted to ICUs and general medical wards with varying risks for VTE such as increasing age, obesity, active malignancy, and a previous history of VTE. The frequency of DVT ranged from 0% in a study from Italy that evaluated patients admitted to non-ICU wards¹² to 79.4% of patients in a study from France that evaluated patients admitted to the ICU.¹¹ The frequency of pulmonary embolism (PE) ranged from 1.6% in patients admitted to general non-ICU wards in the Netherlands¹⁹ to 35.3% in patients admitted to the ICU in a different study from the Netherlands.¹⁸ The use of pharmacologic thromboprophylaxis was inconsistently reported. Table 1 lists the details regarding the observational studies that have evaluated the frequency of VTE in people hospitalized with COVID-19.

Suggestions Regarding Pharmacologic Thromboprophylaxis for Venous Thromboembolism in Patients Hospitalized With COVID-19

Dose of Pharmacologic Thromboprophylaxis

Canadian and international organizations have released guidance regarding the use and dose of pharmacologic thromboprophylaxis for VTE prevention in patients who have been hospitalized for COVID-19. Their suggestions are listed in Table 2. Most organizations suggest the use of prophylactic dosing of pharmacologic thromboprophylaxis. Exceptions include the BC Centre for Disease Control that suggests using an intermediate dose of enoxaparin (30 mg subcutaneously twice daily) for all patients hospitalized with COVID-19,²³ and the American Venous Forum, the British Thoracic Society, the Italian Society on Thrombosis and Haemostasis, and the International Society on Thrombosis and Haemostasis suggest intermediate dosing of pharmacologic thromboprophylaxis for patients at higher risk of VTE.²⁴⁻²⁷ The Swiss Society of Hematology's Working Party on Hemostasis suggests the intermediate to therapeutic dosing of pharmacologic thromboprophylaxis in "patients in intensive care with a large increase in D dimers, severe inflammation, or signs of hepatic or renal dysfunction or imminent respiratory failure."²⁸

Duration of Pharmacologic Thromboprophylaxis

One Canadian and ten international guidance documents were identified that provided suggestions regarding the use of pharmacologic thromboprophylaxis in patients with COVID-19 after discharge from hospital.^{4,24-27,29-34} The organizations were consistent in that they suggested against the routine use of extended-duration pharmacologic thromboprophylaxis, but it may be considered in patients with an increased risk for VTE and a low risk of bleed. Table 3 lists the suggestions from Canadian and international organizations regarding the use of extended-duration thromboprophylaxis.

Ongoing Clinical Trials Evaluating Pharmacologic Thromboprophylaxis in Patients Hospitalized With COVID-19

Nine ongoing clinical trials were identified that are evaluating pharmacologic thromboprophylaxis for VTE prevention in patients with COVID-19; they are listed in Table 4.

Literature Search Methods

A limited literature search was conducted by an information specialist on key resources including MEDLINE and Embase via Ovid, PubMed, the Cochrane Library, the University of York Centre for Reviews and Dissemination (CRD) databases, the websites of Canadian and major international health technology agencies, as well as a focused internet search. The search strategy was comprised of both controlled vocabulary, such as the National Library of Medicine's MeSH (Medical Subject Headings), and keywords. The main search concepts were COVID-19 and thromboprophylaxis. No filters were applied to limit the retrieval by study type. Where possible, retrieval was limited to the human population. The search was also limited to English-language documents published between January 1, 2019 and May 11, 2020.

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Table 1: Observational Studies Reporting the Frequency of VTE in Patients Hospitalized With COVID-19

Study, location, and objective	Population and study time frame	Proportion with VTE	Proportion receiving VTE prophylaxis
<p>Beun et al. (2020)¹⁶ Netherlands Objective: “We provide data from our centre and provide guidance for treatment of perceived heparin resistance associated with the coagulopathy in patients with SARS-CoV-2 infection.”</p>	<p>n = 75 patients admitted to ICU Time frame: March 16, 2020 to April 9, 2020 Demographics of the study population: NR Demographics of patients diagnosed with VTE: NR</p>	<p>DVT: 3 (4.0%) PE: 20 (26.7%) Methods used for identifying VTE: NR</p>	NR
<p>Cattaneo et al. (2020)¹² Italy Objective: NR</p>	<p>n = 388 patients admitted to non-ICU wards Of the total 388 patients, n = 64 patients were screened for asymptomatic DVT Time frame: start of COVID-19 outbreak until April 14, 2020 Demographics of the study population: NR Demographics of 64 patients screened for asymptomatic DVT — median age: 70 years (IQR: 58 to 77.5) male: 35 (54.7%) obesity: 4 (6.3%) malignancy: 7 (10.9%) previous VTE: 0 (0%) median days of in-hospital bed rest: 9 (IQR: 4 to 15)</p>	<p>Symptomatic DVT: 0/388 (0%) Asymptomatic DVT: 0/64 (0%) Method used for screening for asymptomatic DVT: leg compression ultrasonography</p>	<p>Unclear how many patients received VTE prophylaxis “In our hospital we use 40mg enoxaparin daily, as recommended for high-risk, acutely ill medical patients.”</p>
<p>Cui et al. (2020)⁶ China Objective: “...the purpose of this study was to explore the incidence of VTE in such patients and to investigate the differences between VTE patients and non-VTE patients.”</p>	<p>n = 81 patients admitted to ICU Time frame: January 30, 2020 to March 22, 2020 Demographics of the study population — mean age: 59.9 years (range: 32 years to 91 years) male: 37 (45.7%) chronic medical conditions: 33 (40.7%) coronary heart disease: 10 (12.3%) diabetes: 8 (9.9%) hypertension: 20 (24.7%) history of smoking: 35 (43.2%)</p>	<p>Lower extremity venous thrombosis: 20 (24.7%) Method used for identifying lower extremity venous thrombosis: NR</p>	NR
<p>Goyal et al. (2020)²¹ US Objective: “...we characterize the first 393 consecutive patients with Covid-19 who were admitted to two hospitals in New York City.”</p>	<p>n = 393 patients admitted to hospital (both ICU and non-ICU patients) Time frame: March 3, 2020 to March 27, 2020 Demographics of the study population — median age: 62.2 years (IQR: 48.6 to 73.7) male: 238 (60.6%) obesity: 136/380 (35.8%) invasive mechanical ventilation:</p>	<p>VTE: 13/393 (3.3%) VTE in patients with invasive mechanical ventilation: 10/130 (7.7%) VTE in patients without invasive mechanical ventilation 3/263 (1.1%) Methods used for identifying VTE: NR</p>	NR

Study, location, and objective	Population and study time frame	Proportion with VTE	Proportion receiving VTE prophylaxis
	130 (33.1%) current smoker: 20 (5.1%) diabetes: 99 (25.5%) hypertension: 197 (50.1%) COPD: 20 (5.1%) asthma: 49 (12.5%) coronary artery disease: 54 (13.7%)		
Grein et al.(2020) ²² International Objective: “In this report, we describe outcomes in a cohort of patients hospitalized for severe Covid-19 who were treated with remdesivir on a compassionate-use basis.”	n = 53 patients who received at least one dose of remdesivir on a compassionate-use basis Time frame: January 25, 2020 to March 30, 2020 Locations of patients: Canada (1, 1.9%), Europe (21, 39.6%), Japan (9, 17.0%), and the US (22, 41.5%) Demographics of the study population — median age: 64 years (IQR: 48 to 71) male: 40 (75.5%) invasive ventilation (either mechanical ventilation or extracorporeal membrane oxygenation): 34 (64.2%) any coexisting condition: 36 (67.9%) asthma: 6 (11.3%) diabetes: 9 (17.0%) hypertension: 13 (24.5%) hyperlipidemia: 6 (11.3%)	DVT: 4 (7.5%) DVT in patients with invasive ventilation: 3/34 (8.8%) DVT in patients without invasive ventilation: 0/19 (1%) Method used for identifying DVT: NR	NR
Helms et al. (2020) ⁸ France Objective: “...we have aimed at describing the COVID-19-induced thrombotic complications and comparing them with non-COVID-19 ARDS patients.”	n = 150 COVID-19 patients with ARDS admitted to ICU n = 233 non-COVID-19 ARDS patients Time frame: March 3, 2020 to March 31, 2020 for COVID-19 patients; 2014 to 2019 for non-COVID-19 ARDS patients Demographics of patients with COVID-19 — median age: 63 years (IQR: 53 to 71) male: 122 (81.3%) malignancy: 9 (6.0%) cardiovascular diseases: 72 (48.0%) thromboembolic event: 8 (5.3%) diabetes: 30 (20.0%) respiratory disease: 21 (14.0%) Demographics of patients with non-COVID-19 ARDS — median age: 74 years (IQR: 63 to 81) male: 164 (70.4%) malignancy: 31 (13.4%) cardiovascular diseases: 143 (61.4%) thromboembolic event: 13 (5.6%)	PE in patients with COVID-19: 25 (16.7%) DVT in patients with COVID-19: 3 (2.0%) PE in patients with non-COVID-19 ARDS: 3 (1.3%) DVT in patients with non-COVID-19 ARDS: 3 (1.3%) Method used for identifying PE in patients with COVID-19: CT pulmonary angiography Method used for identifying DVT in patients with COVID-19: NR Methods used for identifying PE and DVT in patients with non-COVID-19 ARDS: NR	Patients with COVID-19 — prophylactic dosing of heparin: 105 (70.0%) therapeutic dosing of heparin: 45 (30.0%) Patients with non-COVID-19 ARDS — prophylactic dosing of heparin: 188 (80.7%) therapeutic dosing of heparin: 45 (19.3%)

Study, location, and objective	Population and study time frame	Proportion with VTE	Proportion receiving VTE prophylaxis
	diabetes: 51 (21.9%) respiratory disease: 49 (21.2%)		
Inciardi et al. (2020) ¹³ Italy Objective: "In this report, we describe the demographic characteristics, clinical presentation, and outcomes of consecutive patients with COVID-19 and cardiac disease, and compare them with patients with COVID-19 and no history of cardiac disease, hospitalized at the same hospital during the same time interval."	n = 99 patients hospitalized with COVID-19; 53 (53.5%) had a history of cardiac disease Time frame: March 4, 2020 to March 25, 2020 Demographics of study population — mean age: 67 years (SD: 12) male: 80 (80.8%) obesity: 18 (18.2%) smoker: 17 (17.2%) hypertension: 63 (63.6%) diabetes: 30 (30.3%) dyslipidemia: 29 (29.3%) COPD: 9 (9.1%) cancer: 17 (17.2%) ICU admission: 12 (12.1%) Demographics of patients with a history of cardiac disease (n = 53) — mean age: 68 years (SD: 12) male: 45 (84.9%) obesity: 13 (24.5%) smoker: 11 (20.8%) hypertension: 40 (75.5%) diabetes: 16 (30.2%) dyslipidemia: 23 (43.4%) COPD: 6 (54.5%) cancer: 13 (24.5%) ICU admission: 10 (52.6%)	VTE in study population: 12/99 (12.1%) VTE in patients with a history of cardiac disease: 9/53 (17.0%) Methods used for identifying VTE: NR	NR
Jin et al. (2020) ⁷ China Objective: "...this study was executed to evaluate the values of coagulation function for the prediction of severe COVID-19 patients."	n = 147 hospitalized patients Time frame: NR Demographics of study population — median age: 64 years (IQR: 54 to 73) male: 76 (51.7%) mild COVID-19: 105 (71.4%) severe COVID-19: 18 (12.2%) critical COVID-19: 24 (16.3%)	"Thrombotic disease": 37 (25.2%) Methods used for identifying "thrombotic disease": NR No definition of "thrombotic disease" provided	NR
Klok et al. (2020) ^{17,18} Netherlands Objective: "We evaluated the incidence of the composite outcome of venous thromboembolism (VTE) and arterial thrombotic complications in all COVID-19 patients admitted to the ICU of 2 Dutch university hospitals and 1 Dutch teaching hospital." ¹⁷	n = 184 patients admitted to ICU Time frame: March 7, 2020 – April 22, 2020 Demographics of study population — mean age: 64 years (SD: 12) male: 139 (75.5%) active cancer: 5 (2.7%) therapeutic anticoagulation at admission: 17 (9.2%)	PE: 65 (35.3%) DVT: 1 (0.5%) Method used for identifying PE: CTPA Method used for identifying DVT: ultrasonography	"All patients received pharmacological thromboprophylaxis according to local hospital protocols." Doses of nadroparin ranged from 2,850 IU per day to 5,700 IU twice daily depending on the hospital.

Study, location, and objective	Population and study time frame	Proportion with VTE	Proportion receiving VTE prophylaxis
Objective: To address questions raised about the Authors' initial analysis ¹⁷ examining the incidence of venous and arterial thromboembolism in patients admitted to ICUs with COVID-19. ¹⁸			
<p>Liitjos et al. (2020)⁹</p> <p>France</p> <p>Objective: "We here report our experience with systematic assessment of VTE using complete duplex ultrasound (CDU) in severe ICU COVID-19 patients."</p>	<p>n = 26 patients admitted to ICU</p> <p>Time frame: March 19, 2020 to April 11, 2020</p> <p>Demographics of study population — age: 68 years (unclear if mean or median) (51.5 to 74.5; unclear if range or IQR)</p> <p>male: 20 (76.9%)</p> <p>median BMI: 30.2kg/m² (IQR: 25.5 to 33.5)</p> <p>active cancer: 0 (0%)</p> <p>previous VTE: 1 (3.8%)</p> <p>hypertension: 22 (84.6%)</p> <p>tobacco: 7 (26.9%)</p> <p>anticoagulation prior to admission: 7 (26.9%)</p>	<p>DVT: 18 (69.2%)</p> <p>PE: 6 (23.1%)</p> <p>Method used for identifying DVT: CDU</p> <p>CDU performed after admission to ICU (between days 1 and 3) and at day 7</p> <p>Method for identifying PE: CTPA or transesophageal echocardiography when patient was unable to be transferred</p>	<p>n = 8 (25.8%) received prophylactic anticoagulation</p> <p>n = 18 (69.2%) received therapeutic anticoagulation</p> <p>Type and dose of pharmacologic thromboprophylaxis: NR</p>
<p>Lodigiani et al. (2020)¹⁴</p> <p>Italy</p> <p>Objective: "We aimed to describe the rate of venous and arterial thromboembolic complications in hospitalized patients with COVID-19."</p>	<p>n = 388 patients admitted to hospital</p> <p>n = 48 ICU cases closed at the time of analysis</p> <p>n = 314 general ward cases closed at the time of analysis</p> <p>Time frame: February 13, 2020 to April 10, 2020</p> <p>Demographics of study population — ICU admission: 61 (15.7%)</p> <p>median age: 66 years (IQR: 55 to 75)</p> <p>male: 264 (68.0%)</p> <p>obesity: 87/361 (24.1%)</p> <p>smoking: 45 (11.6%)</p> <p>hypertension: 183 (47.2%)</p> <p>diabetes: 88 (22.7%)</p> <p>dyslipidemia: 76 (19.6%)</p> <p>active cancer: 25 (6.4%)</p> <p>previous VTE: 12 (3.1%)</p>	<p>VTE in ICU patients: 4/48 (8.3%), of which 2 were PE (± DVT), 1 was isolated proximal DVT, and 1 was catheter-related DVT</p> <p>VTE in general ward patients: 12/314 (3.8%), of which 8 were PE (± DVT), 3 were isolated proximal DVT, and 1 was isolated distal DVT</p> <p>Method used for identifying DVT: two-point compression ultrasound in the ICU, whole-leg ultrasound on general wards</p> <p>Method used for identifying PE: "accepted imaging tests"</p>	<p>All ICU patients received thromboprophylaxis; 17 patients received weight-based dosage adjustments.</p> <p>Two patients on direct oral anticoagulants at home received therapeutic anticoagulation.</p> <p>n = 246 patients admitted to general wards received thromboprophylaxis (n = 133 received prophylactic dosing, 67 received intermediate dosing, and 74 received therapeutic dose anticoagulation)^a</p>
<p>Longchamp et al. (2020)²⁰</p> <p>Switzerland</p> <p>Objective: "...we evaluated the role of systematic deep vein thrombosis (DVT) screening with lower limb venous compression</p>	<p>n = 25 patients admitted to ICU</p> <p>Time frame: March 8, 2020 to April 4, 2020</p> <p>Demographics of study population — mean age: 68 years (SD: 11)</p> <p>male: 16 (64%)</p> <p>invasive mechanical ventilation: 23 (92%)</p> <p>mean BMI: 27.5 kg/m² (SD: 4.6)</p>	<p>VTE: 8 (32%)</p> <p>Proximal DVT: 6 (24%)</p> <p>PE: 5 (20%)</p> <p>Both DVT and PE: 3 (12%)</p>	<p>7/8 (87.5%) with VTE received thromboprophylaxis: n = 6 continuous heparin infusion (15,000 IU/24 hours or</p>

Study, location, and objective	Population and study time frame	Proportion with VTE	Proportion receiving VTE prophylaxis
ultrasound (CUS), and the prevalence of VTE among critically ill patients with Covid-19.”	active malignancy: 2 (8%) hypertension: 10 (40.0%) cardiovascular disease: 3 (12.0%) diabetes: 1 (4.0%) COPD: 2 (8.0%) asthma: 1 (4.0%) current or former tobacco smoker: 6 (24%) history of VTE: 0 (0%)	Method used for identifying DVT: lower limb venous compression ultrasound, performed between days 5 and 10 of the ICU admission Method used for identifying PE: CPTA	20,000 IU/24 hours for patients > 100 kg n = 1 enoxaparin 40 mg SC daily
Middeldorp et al. (2020) ¹⁹ Netherlands Objective: “...we report on the incidence and risk factors of VTE in COVID-19 patients admitted to the ICU or general ward.”	n = 198 admitted to ICU or general wards Time frame: March 2, 2020 to April 12, 2020 n = 74 (37.4%) ICU admission Demographics of study population — mean age: 61 years (SD: 14) male: 130 (65.7%) median BMI: 27kg/m ² (IQR: 24 to 31) history of VTE: 11 (5.6%) active cancer: 7 (3.5%)	VTE in study population: n = 33 (16.7%), including PE ± DVT (n = 11, 5.6%), proximal DVT (n = 13, 6.6%), distal DVT (n = 8, 4.0%), and upper extremity DVT (n = 1, 0.5%) VTE in ICU patients: n = 29/74 (39.1%), including PE ± DVT (n = 9, 12.2%), proximal DVT (n = 12, 16.2%), distal DVT (n = 7, 9.5%), and upper extremity DVT (n = 1, 1.4%) VTE in general ward patients: n = 4/124 (3.2%), including PE ± DVT (n = 2, 1.6%) and distal DVT (n = 2, 1.6%) Method used for identifying PE: CTPA Method used for identifying DVT: NR	n = 167 (84.3%) patients received thrombosis prophylaxis n = 19 (9.6%) received therapeutic anticoagulation Pharmacological thromboprophylaxis — Patients in ICU: nadroparin 2,850 IU twice daily for patients < 100 kg and 5,700 IU twice daily for patients ≥ 100 kg Patients on non-ICU units: 2,850 IU once daily for patients < 100kg and 5,700 IU once daily for patients ≥ 100 kg
Nahum et al. (2020) ¹¹ France Objective: “This case series reports a systematic assessment of deep vein thrombosis among patients in an intensive care unit (ICU) in France with severe COVID-19.”	n = 34 patients admitted to ICU Time frame: mid-March 2020 to beginning of April 2020 Demographics of study population — mean age: 62.2 years (SD: 8.6) male: 25 (73.5%) mechanical ventilation: 34 (100%) mean BMI: 31.4 kg/m ² (SD: 9.0) cancer: 1 (2.9%) COPD: 2 (5.9%) diabetes: 15 (44.1%) hypertension: 13 (38.2%)	n = 22 (64.7%) patients with DVT at admission n = 27 (79.4%) patients with DVT 48 hours after ICU admission Method used for identifying DVT: venous ultrasonogram of inferior limbs	“As recommended, all patients received anticoagulant prophylaxis at hospital admission.” Type and dose of pharmacologic thromboprophylaxis: NR
Poissy et al. (2020) ¹⁰ France Objective: NR	n = 107 patients admitted to ICU with COVID-19 n = 196 patients admitted to ICU during the same time interval in 2019	PE n = 22 (20.6%) in patients with COVID-19 PE n = 12 (6.1%) in patients admitted to ICU	“All our patients received thromboprophylaxis according to the current

Study, location, and objective	Population and study time frame	Proportion with VTE	Proportion receiving VTE prophylaxis
	<p>n = 40 patients admitted to ICU with influenza from January 1, 2019 to December 31, 2019</p> <p>Demographics for study population: NR</p> <p>Demographics for patients with COVID-19: NR</p> <p>Demographics for patients admitted in 2019: NR</p> <p>Demographics for patients with influenza: NR</p> <p>Demographics for patients with COVID-19 and PE (n = 22) — median age: 57 years (Range: 29 to 80) male: 13 (59.1%) median BMI: 30 kg/m² (Range: 22 to 53) intubation: 17 (77.3%)</p> <p>Demographics for patients admitted in 2019 and PE (n = 12) — median age: 66 years (Range: 30 to 72) male: 8 (66.7%) median BMI: 29 kg/m² (Range: 18 to 42) intubation: 8 (66.7%)</p> <p>Demographics for patients admitted with influenza and PE (n = 3) — median age: 71 years (Range: 57 to 72) male: 2 (66.7%) median BMI: 26 kg/m² (Range: 16 to 52) intubation: 3 (100%)</p>	<p>during the same time interval in 2019</p> <p>PE n = 3 (7.5%) in influenza patients</p> <p>DVT n = 5 (4.7%) in patients with COVID-19</p> <p>DVT n = 9 (4.6%) in patients admitted to ICU during the same time interval in 2019</p> <p>DVT n = 1 (2.5%) in influenza patients</p> <p>Method used for identifying PE: CTPA</p> <p>Method used for identifying DVT: doppler ultrasound</p>	<p>recommendations for critically ill medical patient.”</p> <p>Patients received unfractionated heparin or LMWH.</p> <p>Dose of pharmacologic thromboprophylaxis: NR</p>
<p>Valente-Acosta et al. (2020)¹⁵</p> <p>Mexico</p> <p>Objective: “We present a retrospective case series from a tertiary-level private medical centre in Mexico City, which we believe is of great value, since it represents one of the first experiences in Latin America of the clinical behaviour of the virus.”</p>	<p>n = 33 patients with COVID-19 and severe (n = 25) or critical (n = 8) pneumonia admitted to hospital</p> <p>Time frame: March 13, 2020 to April 13, 2020</p> <p>Demographics of study population — mean age: 60.6 years (SD: 12.7) males: 23 (69.7%) overweight or obese: 23 (69.7%) invasive mechanical ventilation: 33 (100%) hypertension: 12 (36.4%) diabetes: 8 (24.2%) COPD: 4 (12.1%) smoker: 13 (39.3%)</p>	<p>PE: n = 2 (6.1%)</p> <p>Method used for identifying PE: NR</p>	<p>Both patients who developed PE were receiving thromboprophylaxis with LMWH</p> <p>“...it is currently recommended that all patients (unless contraindicated) should receive thromboprophylaxis, and those with elevated coagulation markers (specifically D-dimer) should receive full dose anticoagulation, as it appears to be associated with lower mortality. Our patients were managed following these recommendations.”</p>

Study, location, and objective	Population and study time frame	Proportion with VTE	Proportion receiving VTE prophylaxis
<p>Xu et al. (2020)⁵ China Objective: “Our study aims to identify in-hospital VTE risk and bleeding risk in COVID-19 patients.”</p>	<p>n = 138 patients admitted to hospital Time frame: January 21, 2020 to February 21, 2020 Demographics of study population — mean age: 52.4 years (SD: 16.7) male: 81 (58.7%) malignancy: 4 (2.9%) obesity: 1 (0.7%) diabetes: 16 (11.6%) hypertension: 39 (28.2%) coronary heart disease: 7 (5.1%) critically ill: 15 (10.9%) Padua prediction score < 4: 115 (83.3%) Padua prediction score ≥ 4: 23 (16.7%)</p>	<p>DVT: n = 4 (2.9%) (3/15, 20.0% of critically ill patients; 1/123, 0.8% of non-critically ill patients) Method used for identifying DVT: compression ultrasound</p>	<p>n = 15 (100%) critically ill patients received thromboprophylaxis n = 26 (21.5%) non-critically ill patients received thromboprophylaxis “Routine thromboprophylaxis was provided to patients whose Padua score more than four points.” Type of pharmacologic thromboprophylaxis: unfractionated heparin or LMWH Dose of pharmacologic thromboprophylaxis: NR</p>

^a The corresponding author has been contacted to clarify the discrepancy between the total number of patients (n = 246) and the number of patients based on the category of thromboprophylaxis dosing (n = 274).

ARDS = acute respiratory distress syndrome; BMI = body mass index; CDU: complete duplex ultrasound; COPD: chronic obstructive pulmonary disease; CTPA: computed tomography pulmonary angiography; DVT = deep vein thrombosis; ICU = intensive care unit; IQR: interquartile range; IU = international units; LMWH= low-molecular-weight heparin; NR = not reported; PE = pulmonary embolism; SARS-Cov-2 = severe acute respiratory syndrome coronavirus 2; SC = subcutaneous; SD = standard deviation; VTE = venous thromboembolism.

Table 2: Canadian and International Guidance for the Dosing of Pharmacologic Thromboprophylaxis

Organization	Guidance
Guidance from Canada	
Alberta Health Services ³⁵	“All hospitalized patients with suspected or confirmed COVID-19 should receive pharmacologic thromboprophylaxis, preferably with low-molecular-weight heparin (LMWH). For prevention of VTE, LMWH should be given at prophylactic doses and follow weight-band dosing in SCM [electronic charting system] (i.e. tinzaparin 75 units/kg for patients >100 kg). LMWH prophylaxis is recommended over unfractionated heparin (UFH) to minimize complications such as HIT and health care provider exposure. UFH is recommended in patients who are in renal failure (creatinine clearance < 30 mL/min).”
BC Centre for Disease Control ²³	“Suggest enoxaparin 30 mg SC bid as the preferred dose for VTE prophylaxis in hospitalized patients with COVID-19. This dose was selected to reduce incident VTE and potentially save health care resources with patient transport and minimize risk of COVID-19 transmission to staff and others. Suggest even higher doses of enoxaparin for hospitalized patients with weight above 100 kg or BMI above 40 kg/m ² .”
Public Health Agency of Canada ³⁶	“Use pharmacological prophylaxis (low molecular-weight heparin [preferred] or heparin subcutaneously twice daily) in adolescents and adults without contraindications. For those with contraindications, use mechanical prophylaxis (intermittent pneumatic compression devices).”

Organization	Guidance
Thrombosis Canada ²⁹	<p>“All admitted COVID+ patients should receive standard weight-adjusted VTE prophylaxis; there are insufficient data at this juncture to recommend intensified empiric prophylaxis regimens (for high D-dimer, ICU patients) outside of clinical trials.”</p> <p>“All patients admitted to hospital (ward or ICU) with COVID, regardless of D-dimer, should receive standard LMWH prophylaxis. Consider dose adjustment in obese patients (>100-120 kg or BMI > 30).”</p>
International Guidance	
Bikdeli et al., endorsed by the International Society on Thrombosis and Haemostasis, the North American Thrombosis Forum, the European Society of Vascular Medicine, and the International Union of Angiology ⁴	<p>“Hospitalized patients with COVID-19 who have respiratory failure or co-morbidities (e.g., active cancer, or heart failure), patients who are bedridden, and those requiring intensive care should receive pharmacological VTE prophylaxis, unless there are contraindications.”</p>
Spyropoulos et al., for the Scientific and Standardization Committee, International Society on Thrombosis and Haemostasis ²⁷	<p>Non-ICU patients hospitalized with COVID-19:</p> <p>“a) A universal strategy of routine thromboprophylaxis with standard-dose UFH or LMWH should be used after careful assessment of bleed risk, with LMWH as the preferred agent. Intermediate-dose LMWH may also be considered (30% of respondents).</p> <p>b) VTE prophylaxis recommendations should be modified based on extremes of body weight, severe thrombocytopenia (i.e. platelet counts of 50,000 x 10⁹ per liter or 25,000 x 10⁹ per liter) or deteriorating renal function.”</p> <p>ICU patients with COVID-19:</p> <p>“a) Routine thromboprophylaxis with prophylactic-dose UFH or LMWH should be used after careful assessment of bleed risk. Intermediate-dose LMWH (50% of respondents) can also be considered in high risk patients. Patients with obesity as defined by actual body weight or BMI should be considered for a 50% increase in the dose of thromboprophylaxis. Treatment-dose heparin should not be considered for primary prevention until the results of randomized controlled trials are available.</p> <p>b) Multi-modal thromboprophylaxis with mechanical methods (i.e., intermittent pneumatic compression devices) should be considered (60% of respondents).”</p>
World Health Organization ³⁷	<p>“Use pharmacological prophylaxis (low molecular-weight heparin [preferred if available] or heparin 5000 units subcutaneously twice daily) in adolescents and adults without contraindications. For those with contraindications, use mechanical prophylaxis (intermittent pneumatic compression devices).”</p>
Guidance from the United States	
American College of Cardiology ³⁰	<p>“All patients hospitalized with COVID-19 should receive pharmacologic VTE prophylaxis unless a specific contraindication (e.g., active bleeding) exists. Strategies to minimize frequent interactions between patients and health care providers (e.g., use of daily low-molecular-weight heparin rather than thrice-daily unfractionated heparin injections) may help to minimize infection risk and use of personal protective equipment when clinically appropriate.”</p> <p>“Use of higher-intensity, non-standard VTE prophylaxis can be considered for patients with COVID-19, but ideally should be done within the context of a clinical trial given current lack of efficacy evidence.”</p>
American Society of Hematology ³¹	<p>“All hospitalized patients with COVID-19 should receive pharmacologic thromboprophylaxis with LMWH or fondaparinux (suggested over unfractionated heparin to reduce contact) unless the risk of bleeding is judged to exceed the risk of thrombosis. Dose adjustment for obesity may be used per institutional guidance. In patients with a history of heparin-induced thrombocytopenia, use fondaparinux. In patients where anticoagulants are contraindicated</p>

Organization	Guidance
	or unavailable, use mechanical thromboprophylaxis (e.g. pneumatic compression devices). Combined pharmacologic and mechanical prophylaxis is not generally recommended.”
American Venous Forum ²⁴	<ul style="list-style-type: none"> • Low molecular weight heparin (LMWH) – consider 30 mg BID or 40 mg QD with standard adjustments for renal insufficiency or obesity. • Morbid obese patients (BMI >35) and very-high risk patients (Caprini score >8) – consider twice the normal dose of anticoagulation (LMWH 60 mg BID). • If severe renal impairment (CrCl<30 mL/min) or acute kidney injury - Heparin 5000u SC TID. • If prior history or concern for Heparin induced thrombocytopenia use fondaparinux. • If platelets <30k, significant bleeding or other absolute contraindication to anticoagulation, use mechanical compression devices. • Direct oral anticoagulants (DOAC) should not be used for prophylaxis in the acute inpatient setting.”
Massachusetts General Hospital ³⁸	“Whether or not COVID-19 infected patients have a unique increased risk of VTE compared to other critical infections/processes is not currently known, and is an area of active research. At this time, we do not suggest escalating prophylactic dose of anticoagulation. A randomized controlled trial addressing this question will be available shortly.”
NIH–National Institutes of Health ³²	“Hospitalized adults with COVID-19 should receive VTE prophylaxis per the standard of care for other hospitalized adults (AIII) .”
Moore et al., for the CHEST Guideline and Expert Panel Report ³³	<p>“In the absence of a contraindication, in acutely ill hospitalized patients with COVID-19, we suggest anticoagulant thromboprophylaxis over no anticoagulant thromboprophylaxis.”</p> <p>“In the absence of a contraindication, in critically ill patients with COVID-19, we recommend anticoagulant thromboprophylaxis over no anticoagulant thromboprophylaxis.”</p> <p>“In acutely ill hospitalized patients with COVID-19, we suggest anticoagulant thromboprophylaxis with low-molecular-weight heparin (LMWH) or fondaparinux over anticoagulant thromboprophylaxis with unfractionated heparin (UFH); and we recommend anticoagulant thromboprophylaxis with LMWH, fondaparinux or UFH over anticoagulant thromboprophylaxis with a direct oral anticoagulant (DOAC).”</p> <p>“In critically ill patients with COVID-19, we suggest anticoagulant thromboprophylaxis with LMWH over anticoagulant thromboprophylaxis with UFH; and we recommend anticoagulant thromboprophylaxis with LMWH or UFH over anticoagulant thromboprophylaxis with fondaparinux or a DOAC.”</p> <p>“In acutely ill hospitalized patients with COVID-19, we recommend current standard dose anticoagulant thromboprophylaxis over intermediate (LMWH BID or increased weight-based dosing) or full treatment dosing, per existing guidelines.”</p> <p>“In critically ill patients with COVID-19, we suggest current standard dose anticoagulant thromboprophylaxis over intermediate (LMWH BID or increased weight-based dosing) or full treatment dosing, per existing guidelines.”</p>
Obi et al. ³⁹	<p>“All patients with COVID-19 or suspected COVID-19 should be treated with thromboprophylaxis. This statement places value on avoiding the need to reassess VTE risk when a patient has a change in status, and accepts overall low bleeding risk associated with use of anticoagulants used at thromboprophylactic doses.”</p> <p>“Thromboprophylaxis:</p> <ul style="list-style-type: none"> • Low molecular weight heparin 40mg qday (or 30mg bid) • Subcutaneous heparin 5000 units tid”
Guidance from Asia	

Organization	Guidance
<p>Zhai et al., on behalf of the Prevention Treatment of VTE Associated with COVID-19 Infection Consensus Statement Group, Pulmonary Embolism Pulmonary Vascular Diseases Group of the Chinese Thoracic Society, Pulmonary Embolism Pulmonary Vascular Disease Working Committee of Chinese Association of Chest Physicians, National Cooperation Group on Prevention Treatment of Pulmonary Embolism Pulmonary Vascular Disease, National Program Office for Prevention Treatment of Pulmonary Embolism Deep Vein Thrombosis, China Grade Center, Evidence-based Medicine Center of School of Basic Medical Sciences of Lanzhou University³⁴</p>	<p>“All severe and critically ill COVID-19 patients have a high risk of VTE, so prevention of VTE is strongly recommended in absence of contraindication.</p> <ul style="list-style-type: none"> • For mild or moderate COVID-19 patients, it is recommended to determine the risk of VTE by using PADUA or IMPROVE risk assessment models (RAM) for medical patients and CAPRINI RAM for surgical patients, leading to VTE prevention in high-risk and moderate-risk patients in absence of contraindications. • Pharmacological prevention with low molecular weight heparin (LMWH) is recommended as firstline treatment in [severe or critically ill COVID-19] patients at low or moderate risk of bleeding and with no contraindication to antithrombotic drugs. In patients with severe renal impairment (creatinine clearance rate: <30mL/min), it is recommended to use unfractionated heparin (UFH). • Mild and moderate COVID-19 patients presenting acute medical diseases and assessed to have a high or moderate risk of VTE (PADUA or IMPROVE RAM), pharmacological prevention should be prescribed and LMWH is recommended as firstline treatment, in absence of contraindication.”
<p>Guidance from Europe</p>	
<p>British Thoracic Society²⁵</p>	<p>“Possible approach to LMWH dosing: Standard Risk Patient: Standard weight-adjusted prophylactic dose LMWH (e.g. for a 70kg patient with CrCl>30mL/min: dalteparin 5,000 units od, enoxaparin 40mg od) High Risk Patient: Intermediate dose LMWH (e.g. for a 70kg patient with CrCl>30mL/min: dalteparin 5,000 units bd, enoxaparin 40mg bd)”</p>
<p>Casini et al., Working Party on Hemostasis, Swiss Society of Hematology²⁸</p>	<p>“• All in-hospital COVID-19 patients should receive pharmacological thromboprophylaxis according to a risk stratification score, unless contraindicated.</p> <ul style="list-style-type: none"> • In patients with creatinine clearance >30 mL/min, low molecular weight heparin (LMWH) should be administered according to the prescribing information. An increased dose should be considered in overweight patients (>100 kg). • In patients with creatinine clearance <30 mL/min, unfractionated heparin (UFH) subcutaneously twice or three times daily or intravenously should be administered according to the prescribing information. An increased dose should be considered in overweight patients (>100 kg). • In patients in intensive care with a large increase in D dimers, severe inflammation, or signs of hepatic or renal dysfunction or imminent respiratory failure, intermediate or therapeutic dosing of LMWH or UFH should be considered, according to the bleeding risk.”
<p>Marietta et al., Italian Society on Thrombosis and Haemostasis²⁶</p>	<p>“• The use of LMWH, UFH, or fondaparinux at doses indicated for prophylaxis of venous thromboembolism (VTE) is strongly advised in all COVID-19 hospitalised patients; patients with anticoagulant contraindications should be treated with limb compression.</p> <ul style="list-style-type: none"> • The use of intermediate-dose LMWH (i.e., enoxaparin 4,000 IU subcutaneously every 12 hours) can be considered on an individual basis in patients with multiple risk factors for VTE (i.e., BMI >30, previous VTE, active cancer, etc.). • The use of therapeutic doses of UFH or LMWH, although a reasonable approach, is currently not supported by evidence outside of established diagnoses of VTE or as a bridging strategy in patients on vitamin k antagonists (VKA), and cannot be recommended as a standard treatment for all COVID-19 patients. In this respect,

Organization	Guidance
	randomised clinical trials comparing efficacy/safety of higher doses of LMWH or UFH to those adopted for prophylactic use are urgently needed. To improve their clinical usefulness, it is advisable that these trials adopt simple and clear protocols, and that they are run by large collaborative efforts, hopefully supported by the Italian drug agency (AIFA)."
Oudkerk et al., National Institute for Public Health of the Netherlands ⁴⁰	"Prophylactic-dose low-molecular-weight heparin should be initiated in all patients with (suspected) COVID-19 admitted to the hospital, irrespective of risk scores (e.g. Padua score)."
Thrombosis UK ⁴¹	"The risk of venous thromboembolism (VTE) must be assessed in all patients admitted to hospital, and prevention should be given to all high-risk patients according to international guidance on thromboprophylaxis in medical patients (NICE/ASH). i.e. Pharmacological thromboprophylaxis should be given to all immobilised and severely ill patients with COVID-19 patients unless otherwise contraindicated. For CrCl > 30: Give LMWH or fondaparinux SC according to license. For CrCl < 30 or AKI: Unfractionated heparin 5000 units SC BD or TDS or dose reduced LMWH. All completely immobilised patients would benefit from intermittent pneumatic compression in addition to pharmacological thromboprophylaxis. Mechanical thromboprophylaxis should be used alone if platelets < 30,000 or bleeding."

AllI = strong evidence, expert opinion; AIFA = Italian Medicines Agency; AKI = acute kidney injury; ASH = American Society of Hematology; bD = British Thoracic Society; bid/BID = twice daily; BMI = body mass index; CrCl = creatinine clearance; DOAC = direct oral anticoagulant; HIT = heparin-induced thrombocytopenia; ICU = intensive care unit; LMWH = low-molecular-weight heparin; NICE = National Institute for Health and Care Excellence; QD/qd/od/qday = once daily; SC = subcutaneous; tid/TID = three times daily; u = unit; UFH = unfractionated heparin; VKA = vitamin K antagonist; VTE = venous thromboembolism

Table 3: Canadian and International Guidance for the Duration of Pharmacologic Thromboprophylaxis

Organization	Guidance
Guidance from Canada	
Thrombosis Canada ²⁹	<p>"Post-discharge prophylaxis: Patients with Moderate to Severe COVID</p> <ul style="list-style-type: none"> • Should not be offered routinely • Consider post-discharge pharmacologic prophylaxis for up to 45 days in those with VTE risk factors and low bleeding risk • Encourage ambulation and physical activity"
International Guidance	
Bikdeli et al., endorsed by the International Society on Thrombosis and Haemostasis, the North American Thrombosis Forum, the European Society of Vascular Medicine, and the International Union of Angiology ⁴	"After hospital discharge from acute medical illness, extended prophylaxis with LMWH or direct oral anticoagulants (DOACs) can reduce the risk of VTE, at the cost of increase in bleeding events, including major bleeding. While no data specific to COVID-19 exist, it is reasonable to employ individualized risk stratification for thrombotic and hemorrhagic risk, followed by consideration of extended prophylaxis (for up to 45 days) for patients with elevated risk of VTE (e.g., reduced mobility, co-morbidities such as active cancer, and [according to some authors in the writing group], elevated D-dimer >2 times the upper normal limit) who have low risk of bleeding."
Spyropoulos et al., for the Scientific and Standardization Committee, International Society on Thrombosis and Haemostasis ²⁷	"a) Either LMWH (30%) or a DOAC (i.e., rivaroxaban or betrixaban 30% of respondents) can be used for extended-duration thromboprophylaxis."

Organization	Guidance
	b) Extended post-discharge thromboprophylaxis should be considered for all hospitalized patients with COVID-19 that meet high VTE risk criteria. The duration of post-discharge thromboprophylaxis can be approximately 14 days at least (50% of respondents), and up to 30 days (20% of respondents)."
Guidance from the United States	
American College of Cardiology ³⁰	"Post-hospital VTE prophylaxis should be considered in patients with COVID-19. Experience from the MAGELLAN (https://www.nejm.org/doi/full/10.1056/NEJMoa1111096), APEX (https://www.nejm.org/doi/full/10.1056/NEJMoa1601747), and MARINER (https://www.nejm.org/doi/full/10.1056/NEJMoa1805090) studies suggest that in select patients without COVID-19, post-discharge thromboprophylaxis (particularly with a DOAC) may be beneficial if bleeding risk can be minimized. This may be even more important in COVID-19 because of the long duration of illness—a peak in symptoms around day 8-10 followed by a rather lengthy tail with increased likelihood of immobility and risk of superinfection. Use of a validated risk score (e.g., IMPROVE or IMPROVEDD score with D-dimer) may be particularly helpful in guiding decision-making."
American Society of Hematology ³¹	"Patients hospitalized for acute medical illness are at increased risk for VTE for up to 90 days after discharge. This finding should apply to COVID-19 patients, though data on incidence are not yet available. Therefore, it is reasonable to consider extended thromboprophylaxis after discharge using a regulatory-approved regimen (e.g., betrixaban 160 mg on day 1, followed by 80 mg once daily for 35-42 days; or rivaroxaban 10 mg daily for 31-39 days). Inclusion criteria for the trials studying these regimens included combinations of age, co-morbidities such as active cancer, and elevated D-dimer >2 times the upper normal limit. Any decision to use post-discharge thromboprophylaxis should consider the individual patient's VTE risk factors, including reduced mobility and bleeding risk as well as feasibility. "Home hospital" approaches for COVID-19 patients involving early discharge have been suggested to free up inpatient beds. Status at discharge should be considered in any decision to use VTE prophylaxis in these unique patients. Aspirin has been studied for VTE prophylaxis in low-risk patients after orthopedic surgery and could be considered for COVID-19 VTE prophylaxis if criteria for post-discharge thromboprophylaxis are met. Patients should be educated on the signs and symptoms of VTE at hospital discharge."
American Venous Forum ²⁴	"Patients that are very high-risk for VTE (morbid obesity, Caprini score >8) should be discharged on regular dose of chemical prophylaxis for six weeks."
NIH— National Institutes of Health ³²	"Hospitalized patients with COVID-19 should not routinely be discharged on VTE prophylaxis (AIII). Using Food and Drug Administration-approved regimens, extended VTE prophylaxis can be considered in patients who are at low risk for bleeding and high

Organization	Guidance
	risk for VTE as per protocols for patients without COVID-19 (see text for details on defining at-risk patients) (BI) .”
Moores et al., for the CHEST Guideline and Expert Panel Report ³³	“In patients with COVID-19, we recommend inpatient thromboprophylaxis only over inpatient plus extended thromboprophylaxis after hospital discharge.”
Guidance from Asia	
Zhai et al., on behalf of the Prevention Treatment of VTE Associated with COVID-19 Infection Consensus Statement Group, Pulmonary Embolism Pulmonary Vascular Diseases Group of the Chinese Thoracic Society, Pulmonary Embolism Pulmonary Vascular Disease Working Committee of Chinese Association of Chest Physicians, National Cooperation Group on Prevention Treatment of Pulmonary Embolism Pulmonary Vascular Disease, National Program Office for Prevention Treatment of Pulmonary Embolism Deep Vein Thrombosis, China Grade Center, Evidence-based Medicine Center of School of Basic Medical Sciences of Lanzhou University ³⁴	“Mild and moderate COVID-19 patients perceived to have a persistent risk of VTE at the time of discharge, a prolonged outpatient VTE prophylaxis care should be considered with LMWH over DOAC use, caution due to potential drug–drug interactions and/or frequent comorbidities.”
Guidance from Europe	
British Thoracic Society ²⁵	“Extended thromboprophylaxis on discharge can be considered if the patient is considered at high risk of VTE (e.g. past history VTE, cancer, significantly reduced mobility, critical care admission) and the risk of VTE is felt to outweigh the risk of bleeding. The nature and duration of thromboprophylaxis in patients recovering from COVID-19 pneumonia is not clear but a standard prophylactic dose of LMWH or DOAC for 4 weeks may be a reasonable approach.”
Marietta et al., Italian Society on Thrombosis and Haemostasis ²⁶	“Thromboprophylaxis should be administered for the entire duration of the hospital stay. This should also be maintained at home for 7-14 days after hospital discharge or in the pre-hospital phase, in case of pre-existing or persisting VTE risk factors (i.e., reduced mobility, body mass index (BMI) >30, previous VTE, active cancer, etc.).”

AIII = strong evidence, expert opinion; BII = moderate evidence, one or more well-designed, non-randomized trials or observational cohort studies; DOAC = direct oral anticoagulant; LMWH = low molecular-weight-heparin; VTE = venous thromboembolism.

Table 4: Ongoing Clinical Trials Evaluating Pharmacologic Thromboprophylaxis for VTE Prevention in Patients With COVID-19

Clinicaltrials.gov indicator	Title	Study details	Status as of June 1, 2020
NCT04344756 ⁴²	Cohort Multiple Randomized Controlled Trials Open-label of Immune Modulatory Drugs and Other Treatments in COVID-19 Patients: CORIMUNO-COAG Trial	RCT, open-label Target n = 808 patients Location: France Experimental group: Tinzaparin 175 IU/kg/24 hours for 14 days if CrCl ≥ 20mL/min, otherwise unfractionated heparin with an anti-	Posted to clinicaltrials.gov April 14, 2020 Not yet recruiting Estimated completion: September 30, 2020

Clinicaltrials.gov indicator	Title	Study details	Status as of June 1, 2020
		<p>Xa target between 0.5 and 0.7 IU/mL for 14 days</p> <p>Control group: standard of care and preventive anticoagulation for at least 14 days with enoxaparin 4,000 IU/24 hours, tinzaparin 3,500 IU/24 hours or dalteparin 5,000 IU/24 hours if CrCl ≥ 30mL/min or unfractionated heparin 5,000 IU/12 hours if CrCl < 30mL/min</p> <p>Primary outcome: Patients not admitted to ICU: Survival without ventilation at 14 days</p> <p>Patients admitted to ICU: ventilator-free survival at 28 days</p> <p>Secondary outcome: rate of clinically overt pulmonary embolism or proximal deep vein thrombosis (time frame: day 14 and day 90) confirmed by objective testing</p>	
NCT04373707 ⁴³	Effectiveness of Weight-adjusted Prophylactic Low Molecular Weight Heparin Doses Compared With Lower Fixed Prophylactic Doses to Prevent Venous Thromboembolism in COVID-2019. The Multicenter Randomized Controlled Open-label Trial COVI-DOSE	<p>RCT, open-label</p> <p>Target n = 602 patients</p> <p>Location: France</p> <p>Experimental group: weight-adjusted prophylactic dose of LMWH</p> <p>Control group: low prophylactic dose of LMWH</p> <p>Primary outcome: venous thromboembolism — risk of deep vein thrombosis or pulmonary embolism or venous thromboembolism-related death (time frame: 28 days)</p>	<p>Posted to clinicaltrials.gov May 4, 2020</p> <p>Recruiting</p> <p>Estimated completion: October 2020</p>
NCT04345848 ⁴⁴	Preventing COVID-19-associated Thrombosis, Coagulopathy and Mortality With Low- and High-dose Anticoagulation: a Randomized, Open-label Clinical Trial	<p>RCT, open-label</p> <p>Target n = 200 patients</p> <p>Location: Switzerland</p> <p>Experimental group: therapeutic doses of enoxaparin or unfractionated heparin</p> <p>Control group: prophylactic doses of enoxaparin or unfractionated heparin</p> <p>Primary outcome: composite of arterial or venous thrombosis, disseminated intravascular coagulation, and all-cause mortality at 30 days</p> <p>Secondary outcome: venous thromboembolism — risk of</p>	<p>Posted to clinicaltrials.gov on April 15, 2020</p> <p>Recruiting</p> <p>Estimated completion: November 30, 2020</p>

Clinicaltrials.gov indicator	Title	Study details	Status as of June 1, 2020
		symptomatic venous thromboembolism or asymptomatic proximal leg deep vein thrombosis at 30 days	
NCT04362085 ⁴⁵	Coagulopathy of COVID-19: A Pragmatic Randomized Controlled Trial of Therapeutic Anticoagulation Versus Standard Care as a Rapid Response to the COVID-19 Pandemic (RAPID COVID COAG)	RCT, open-label Target n = 462 patients Location: Canada Experimental group: Therapeutic anticoagulation with LMWH or UFH (high-dose nomogram). Control group: standard of care anticoagulation (LMWH, UFH, or fondaparinux at thromboprophylactic doses) Primary outcome: Composite outcome of ICU admission (yes/no), non-invasive positive pressure ventilation (yes/no), invasive mechanical ventilation (yes/no), or all-cause death (yes/no) up to 28 days Secondary outcome: number of participants with venous thromboembolism (time frame: up to 28 days)	Posted to clinicaltrials.gov April 24, 2020 Recruiting Estimated completion: December 2020
NCT04372589 ⁴⁶	Antithrombotic Therapy to Ameliorate Complications of COVID-19 (ATTACC)	RCT, open-label Target n = 3,000 patients Location: Canada Experimental group: therapeutic anticoagulation with LMWH (preferred) or UFH for 14 days Control group: usual care with thromboprophylactic dose anticoagulation based on local practice Secondary outcome: VTE (time frame: 30 days and 90 days)	Posted to clinicaltrials.gov May 4, 2020 Recruiting Estimated completion: January 2021
NCT04359277 ⁴⁷	A Randomized Trial of Anticoagulation Strategies in COVID-19	RCT, open-label Target n = 1,000 patients Location: US Experimental group: enoxaparin higher dose: <ul style="list-style-type: none"> • enoxaparin 1 mg/kg SC every 12 hours for patients weighing 50 kg to 150kg 	Posted to clinicaltrials.gov April 24, 2020 Recruiting Estimated completion: April 16, 2021

Clinicaltrials.gov indicator	Title	Study details	Status as of June 1, 2020
		<ul style="list-style-type: none"> • enoxaparin 0.75mg/kg SC every 12 hours for patients weighing > 150 kg or BMI > 40 kg/m² • unfractionated heparin IV titrated to a goal anti-Xa of 0.3 to 0.5 unit/mL (preferred in intubated patients and patients with CrCl < 30 mL/min) <p>Control group: lower-dose prophylactic anticoagulation:</p> <ul style="list-style-type: none"> • heparin 5,000 units SC every 8 or 12 hours, or 7,500 units every 8 hours, for BMI > 40 kg/m² or weight > 150 kg • enoxaparin 40 mg SC every 24 hours • enoxaparin 30 mg SC every 12 hours or every 24 hours in patients with CrCl < 30 mL/min • enoxaparin 60 mg SC every 12 hours for patients with BMI > 50 kg/m² <p>Primary outcomes include incidence of symptomatic DVT and incidence of PE (time frame: 21 days)</p>	
NCT04360824 ⁴⁸	COVID-19-associated Coagulopathy: Safety and Efficacy of Prophylactic Anticoagulation Therapy in Hospitalized Adults With COVID-19	<p>RCT, open-label</p> <p>Target n = 170 patients</p> <p>Location: US</p> <p>Experimental group: intermediate-dose enoxaparin (1 mg/kg SC daily or 0.5 mg/kg SC twice daily if BMI ≥ 40 kg/m²)</p> <p>Control group: standard prophylactic dose enoxaparin (40 mg SC daily if BMI < 40 kg/m² and 30 mg SC twice daily if BMI ≥ 40) kg/m²</p> <p>Secondary outcome: Risk of symptomatic venous thromboembolism (time frame: 30 days post-intervention)</p>	<p>Posted to clinicaltrials.gov April 24, 2020</p> <p>Not yet recruiting</p> <p>Estimated completion: April 16, 2021</p>
NCT04401293 ⁴⁹	Systemic Anticoagulation With Full Dose Low Molecular Weight Heparin (LMWH) Vs. Prophylactic or Intermediate Dose LMWH in High Risk COVID-19 Patients (HEP-COVID Trial)	<p>RCT, open-label</p> <p>Target n = 308 patients</p> <p>Location: US</p> <p>Experimental group: enoxaparin 1mg/kg SC twice daily for CrCl ≥ 30mL/min (or enoxaparin 0.5mg/kg SC twice daily for CrCl ≥ 15mL/min and < 30mL/min)</p>	<p>Posted to clinicaltrials.gov May 26, 2020</p> <p>Recruiting</p> <p>Estimated completion: April 26, 2021</p>

Clinicaltrials.gov indicator	Title	Study details	Status as of June 1, 2020
		<p>during the course of their hospitalization.</p> <p>Control group: UFH up to 22,500 IU daily in twice daily or three times daily doses, enoxaparin 30 mg and 40 mg SC daily or twice daily (the use of weight-based enoxaparin — i.e., 0.5mg/kg SC twice daily for this arm — is acceptable but strongly discouraged), dalteparin 2,500IU or 5,000IU daily</p> <p>Primary outcome: composite end point of the risk of arterial thromboembolic events (including myocardial infarction, stroke, systemic embolism), venous thromboembolism (including symptomatic DVT of the upper or lower extremity, asymptomatic proximal DVT of the lower extremity, non-fatal PE), and all-cause mortality at day 30 ± 2 days</p> <p>Secondary outcome: composite end point of arterial thromboembolic events (including myocardial infarction, stroke, systemic embolism), venous thromboembolism (including symptomatic DVT of the upper or lower extremity, asymptomatic proximal DVT of the lower extremity, non-fatal PE), and all-cause mortality at hospital day 10 + 4 days</p>	
<p>NCT04377997⁵⁰</p>	<p>A Randomized, Open-Label Trial of Therapeutic Anticoagulation in COVID-19 Patients with an Elevated D-Dimer</p>	<p>RCT, open-label Target n = 300 patients Location: US Experimental group: Therapeutic enoxaparin or unfractionated heparin in patients with morbid obesity or moderate to severe kidney dysfunction Control group: Standard of care anticoagulation (enoxaparin or unfractionated heparin in patients with morbid obesity or moderate to severe kidney dysfunction) based on the Massachusetts General Hospital guidelines Primary outcome: Number of patients with the</p>	<p>Posted to clinicaltrials.gov May 7, 2020 Not yet recruiting Estimated completion: January 1, 2022</p>

Clinicaltrials.gov indicator	Title	Study details	Status as of June 1, 2020
		composite efficacy outcome of death, cardiac arrest, symptomatic deep venous thrombosis, pulmonary embolism, arterial thromboembolism, myocardial infarction, or hemodynamic shock (time frame: 12 weeks)	

BMI = body mass index; CrCl = creatinine clearance; DVT = deep vein thrombosis; ICU = intensive care unit; IU = international unit; LMWH = low-molecular-weight heparin; min = minute; PE = pulmonary embolism; RCT = randomized controlled trial; SC = subcutaneously; UFH = unfractionated heparin; VTE = venous thromboembolism.