EVIDENCE SYNTHESIS BRIEFING NOTE

TOPIC: LOW MOLECULAR WEIGHT HEPARIN FOR THROMBOPROPHYLAXIS OF COVID-19-POSITIVE LONG-TERM CARE HOME RESIDENTS

Information finalized as of February 11, 2021.[a]

This Briefing Note was completed by the Evidence Synthesis Unit (Research, Analysis and Evaluation Branch, Ministry of Health) based on information provided by members of the COVID-19 Evidence Synthesis Network. Please refer to the Methods section for further information.

Purpose: To summarize the available evidence on whether low molecular weight heparin (LMWH) should be used for thromboprophylaxis of COVID-19-positive long-term care home residents.

Key Findings:

- **Long-Term Care Settings**:
  - No studies were identified on the effectiveness and safety of thromboprophylaxis with LMWH for long-term care residents with COVID-19.
  - Guidance from Canada (federal), Alberta, France, and the United Kingdom recommends the consideration of tailored thromboprophylaxis with LMWH for residents of long-term care homes. For example:
    - The Calgary Zone Long Term Care Pharmacy and Therapeutics Committee made the decision (December 1, 2020) to expedite coverage for LMWH when determined to be required by the attending physician. Instead of reviewing LMWH requests for coverage on a case-by-case basis, LMWH orders will automatically be approved for coverage when Health Canada guidance is met and documented.
- **Hospital Settings**:
  - Studies on the use of thromboprophylaxis with LWMH for hospitalized patients with COVID-19 have variable results and it is unclear how outcomes may have been affected by differences in study methods, thromboprophylaxis dosing regimens, patient profiles, and clinical settings.
  - Most Canadian and international guidance suggests using prophylactic dosing of pharmacologic thromboprophylaxis to prevent venous thromboembolism in patients who have been hospitalized with COVID-19, but does not suggest the routine use of extended-duration pharmacologic thromboprophylaxis.
- **Non-Hospital/Community Settings**:
  - International guidance recommends considering thromboprophylaxis with LMWH in COVID-19 patients under specific circumstances.

Implementation Implications: The importance of individual risk assessment for decisions on thromboprophylaxis are emphasized both in the scientific literature and available guidance. Clinical recommendations are primarily based on low certainty in the evidence, underscoring the need for high-quality, randomized controlled trials comparing different intensities of anticoagulation. These recommendations are likely to be updated, for example using a living recommendation approach, as new evidence becomes available from ongoing clinical trials. For example:

- Three international partners are collaborating in a multiple platform randomized controlled trial: the Randomized, Embedded, Multi-factorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) Therapeutic Anticoagulation; Accelerating COVID-19 Therapeutic Interventions and Vaccines-4 (ACTIV-4) Antithrombotics Inpatient; and Antithrombotic Therapy to Ameliorate Complications of COVID-19 (ATTACC). The common goal is to assess the benefit of full doses of blood thinners, including LMWH, to treat moderately ill or critically ill adults hospitalized for COVID-19, compared to a lower dose often used to prevent blood clots in hospitalized patients.

[a] This briefing note includes current available evidence as of the noted date. It is not intended to be an exhaustive analysis, and other relevant findings may have been reported since completion.

Context and Terminology

The Ontario Drug Benefit (ODB) Program provides drug coverage for eligible recipients, which includes residents of long-term care homes. One class of drugs covered under the ODB formulary are low molecular weight heparins (LMWHs), which are anticoagulants (blood thinners) that treat and prevent abnormal blood clots.[1,2] LMWHs are used both for treatment and prophylaxis of various thromboembolic disorders such as deep vein thrombosis, pulmonary embolism, and post-hip or knee replacement surgery. Other off-label indications are considered for funding under the Exceptional Access Program (EAP) on a case-by-case basis.[3]

Research suggests that COVID-19 is associated with significant inflammation and clinical and pathologic evidence of widespread blood clots.[4,5,6,7] According to the National Institutes of Health in the United States, clinical trials to test the effects of full doses of anticoagulants in COVID-19 patients were launched because clinicians have observed that many patients ill with COVID-19, including those who have died from the disease, formed blood clots throughout their bodies, even in their smallest blood vessels. This unusual clotting can cause multiple health complications, including lung failure, heart attack, and stroke.[8] Moreover, guidance by the Government of Canada on the care of long-term care home residents during the COVID-19 pandemic noted that residents with COVID-19 are at risk for coagulopathy and this appears to be correlated with disease severity.[9]

Supporting Evidence

Table 1 lists and describes scientific evidence and jurisdictional guidance on the role of LMWH for thromboprophylaxis of COVID-19-positive long-term care home residents. All of the information presented was identified and provided by members of the COVID-19 Evidence Synthesis Network. The majority of the information presented is taken directly from these sources.

- Limited information was identified from the long-term care sector. Information from the hospital and community sectors, as well as non-COVID-19 settings, was included where available.
- The majority of the information contains clinical guidance; these recommendations are those of the authors of the original sources and the Research, Analysis, and Evaluation Branch does not have the expertise to evaluate such recommendations.
- The methodological quality of most of the sources identified are unclear as they have not been assessed.

Table 1: Summary of Scientific Evidence and Jurisdictional Guidance on the Role of Low Molecular Weight Heparin (LMWH) in Thromboprophylaxis for COVID-19

Scientific Evidence	• A rapid review by Ontario Health (February 11, 2021)[b] did not identify any studies on the effectiveness and safety of thromboprophylaxis with LMWH for long-term care residents with COVID-19. The importance of individual risk assessment for venous thromboembolism and decisions on thromboprophylaxis are emphasized in the scientific literature.[10] ○ **Hospital Setting**: The rapid review identified two systematic reviews and 26 primary studies that examined the use of thromboprophylaxis with LWMH for hospitalized patients with COVID-19 and found the following: ▪ In the two systematic reviews, substantial heterogeneity was observed in the incidence of venous thromboembolism and mortality of hospitalized COVID-19 patients treated with LMWH. The authors stated heterogeneity was not mitigated by stratification of clinical setting (e.g., ward, intensive care unit) and may be related to different venous thromboembolism risk profiles and clinical severity of patients as well as differences in the methods used to identify venous thromboembolism across studies (e.g., clinical parameters, laboratory assessment, diagnostic imaging). ▪ In the primary studies (which were not included in the above-mentioned systematic reviews), prophylactic dose LMWH was most often compared with different doses of the same LMWH. Other comparators included other types of anticoagulants (e.g., fondaparinux) or no control group. Overall, the studies have variable direction of results and it is unclear how outcomes may have been affected by different thromboprophylaxis dosing regimens. ▪ Several factors limit the ability to draw conclusions from these studies, including: study design (most were observational, retrospective studies), small sample sizes, short follow-up periods, and lack of random assignment of dosing regimens. ▪ See Table 2 and Table 3 in the Appendix for further details about the findings on LMWH thromboprophylaxis in hospitalized patients with COVID-19 reported in each of the systematic reviews and primary studies, respectively.[11] ○ **Non-Hospital Setting**: In the ClinicalTrials.gov database, the rapid review did not identify any ongoing studies on LMWH within the long-term care population; however, the following ongoing randomized controlled trials within a non-hospitalized setting were identified: ▪ NCT04400799 (Switzerland): Enoxaparin vs. no enoxaparin in COVID-19 patients ≥50 years eligible for ambulatory treatment. Estimated completion date is April 2021. ▪ NCT04416048 (Germany): Rivaroxaban vs. standard of care (LMWH or unfractionated heparin) in moderate or severe COVID-19 patients >18 years. Estimated completion date is May 2021.

[b] The evidence summary by Ontario Health was developed within a few days using expedited systematic review methods without consultation with experts in the field, and it is not intended to be an exhaustive analysis. Three reviewers conducted an initial screening of titles and abstracts using the Covidence systematic review management software (Covidence, 2020) and then obtained the full texts of studies that appeared eligible for review according to the inclusion criteria. The three reviewers then examined the full-text articles and included eligible studies. Each abstract or study was reviewed by one of the three reviewers. The evidence presented is considered current as of the literature search date, but other relevant scientific findings may have been reported since completion (Ontario Health, Feb 11, 2021).

	▪ NCT04492254 (United Kingdom): Enoxaparin vs. standard of care (no enoxaparin) in confirmed COVID-19 patients ≥55 years with at least two additional risk factors. Estimated completion date is July 2021.[12] • Three international partners, spanning four continents (e.g., Canada, the United States, Australia, Mexico, Brazil) are collaborating in a multiple platform randomized controlled trial: the Randomized, Embedded, Multi-factorial Adaptive Platform Trial for Community-Acquired Pneumonia (REMAP-CAP) Therapeutic Anticoagulation; Accelerating COVID-19 Therapeutic Interventions and Vaccines-4 (ACTIV-4) Antithrombotics Inpatient; and Antithrombotic Therapy to Ameliorate Complications of COVID-19 (ATTACC). The trials have the common goal of assessing the benefit of full doses of blood thinners, including LMWH, to treat moderately ill or critically ill adults hospitalized for COVID-19, compared to a lower dose often used to prevent blood clots in hospitalized patients.[13] For example: ○ The results of the ATTACC trial will soon be publicly available. This randomized controlled trial is sponsored by the University of Manitoba, and the University Health Network in Toronto is a collaborator. There are 60 study locations across Canada, the United States, Mexico, and Brazil. This trial will determine whether therapeutic anticoagulation with heparin (subcutaneous LMWH or intravenous unfractionated heparin) versus usual care reduces the need for intubation or death in hospitalized patients with COVID-19 (n=1,203). The period covered by the study was May 20, 2020 to January 2021.[14] • A research article discussed whether aspirin can be used for prophylaxis of COVID-19-induced coagulopathy. The article discusses the mechanism of aspirin action, the current evidence of use of aspirin in COVID-19, and limitations of aspirin use in COVID-19. The article concluded that given many clinicians are already using aspirin and nonsteroidal anti-inflammatory drugs (NSAIDs) to treat viral infections including COVID-19 off-label, without recourse to robust evidence of safety or effectiveness, there is an urgent need for well-conducted, randomized clinical trials in this area. The results of such studies will help to guide clinical practice during this pandemic.[15] • Dr. Brian Hutton (Ottawa Hospital Research Institute) is leading a review on the incidence of thrombotic events and related risk factors for COVID-19. Results will be available soon. • A clinical review (December 2016) by the University of Ottawa Heart Institute assessed the comparative efficacy and safety of LMWH compared to unfractionated heparin (UFH) in medical and non-orthopedic surgical adult patients based on findings from randomized controlled trials published in or after 1995. The review found that: ○ Among medical patients, prophylaxis with LMWH reduced the risk of venous thromboembolism and deep vein thrombosis with no increased risk of bleeding or death, compared with UFH. There may be differences in the risk of an event between stroke and no stroke populations. ○ Among non-orthopedic surgical patients, prophylaxis with LMWH may increase the risk of bleeding, but not major bleeding, compared with UFH. There were no differences in the odds of venous thromboembolism, deep vein thrombosis, or pulmonary embolism. This finding was based on one trial and should be interpreted with caution.[16]
International Scan	• The rapid review by Ontario Health (February 11, 2021) identified limited guidance or information pertaining to thromboprophylaxis in long-term care residents with COVID-19 or non-hospitalized patients from international health authorities, organizations, and grey

literature. The importance of individual risk assessment for venous thromboembolism and decisions on thromboprophylaxis are emphasized in the available guidance.[17]

- **Long-Term Care Setting**: See Table 4 in the Appendix for further details.
  - United Kingdom: The British Geriatrics Society's guidance (November 16, 2020) recommended the consideration of tailored thromboprophylaxis for residents of care homes.[18]
  - France: The High Council for Public Health's guidance (April 8, 2020) recommended the consideration of thromboprophylaxis with LMWH for bedridden patients in residential facilities for the elderly.[19]
- **Hospital Setting**:
  - World Health Organization: The COVID-19 Clinical Management: Living Guidance (January 25, 2021) makes a conditional recommendation in favour of standard thromboprophylaxis dosing of anticoagulation, rather than intermediate or therapeutic dosing, in hospitalized patients with COVID-19 who do not have an established indication for higher dose anticoagulation.[20]
  - Canadian Agency of Drugs and Technologies in Health (CADTH): According to a CADTH report (June 11, 2020) on the state of the evidence for the use of LMWH prophylaxis in hospitalized COVID-19 patients, there is an increased risk of venous thromboembolism among hospitalized COVID-19 patients, especially those in intensive care units.
    - Most international guidance suggests using prophylactic dosing of pharmacologic thromboprophylaxis to prevent venous thromboembolism in patients who have been hospitalized with COVID-19.
    - International guidance does not suggest the routine use of extended-duration pharmacologic thromboprophylaxis. The use of extended-duration pharmacologic thromboprophylaxis in patients with COVID-19 who are being discharged from hospital may be considered based on the risk of venous thromboembolism and the risk of bleed.
    - The report also included a list of ongoing clinical trials assessing the effectiveness and safety of pharmacologic thromboprophylaxis to prevent venous thromboembolism.[21,22]
- **Non-Hospital Setting**: Guidance from the United States, Australia, Norway, and the United Kingdom recommends considering thromboprophylaxis with LMWH in COVID-19 patients under specific circumstances. See Table 5 in the Appendix for further details. For example:
  - United States: The National Institutes of Health's recommendations (December 17, 2020) state that anticoagulants and antiplatelet therapy should not be initiated in non-hospitalized patients with COVID-19 for the prevention of venous thromboembolism or arterial thrombosis unless the patient has other indications for the therapy or is participating in a clinical trial.[23]
  - Australia: The National COVID-19 Clinical Evidence Taskforce's guidelines (February 4, 2021) recommend using prophylactic doses of anticoagulants, preferably LMWH, in adults with moderate COVID-19 or other indications, unless there is a contraindication (e.g., risk for major bleeding).[24]

- The American Society of Hematology released a clinical guideline (February 8, 2021) on the use of anticoagulation for thromboprophylaxis in patients with COVID-19. A multidisciplinary

	guideline panel[c] made two conditional recommendations in favour of prophylactic-intensity anticoagulation over intermediate-intensity or therapeutic-intensity anticoagulation for patients with COVID-19-related critical illness or acute illness who do not have confirmed or suspected venous thromboembolism. These recommendations were based on very low certainty in the evidence, underscoring the need for high-quality, randomized controlled trials comparing different intensities of anticoagulation. The recommendations will be updated using a living recommendation approach as new evidence becomes available.[25]
Canadian Scan	• The rapid review by Ontario Health (February 11, 2021) identified limited guidance or information pertaining to thromboprophylaxis in long-term care residents with COVID-19 or non-hospitalized patients from national health authorities, organizations, and grey literature. The importance of individual risk assessment for venous thromboembolism and decisions on thromboprophylaxis are emphasized in the available guidance.[26] ○ **Long-Term Care Setting**: ▪ Government of Canada: According to Interim Guidance: Care of Residents in Long Term Care Homes during the COVID-19 Pandemic (July 17, 2020), medical or mechanical venous thromboembolism prophylaxis can be considered on a case-by-case basis for long-term care residents receiving active medical management, with consideration of disease severity, risks, benefits, goals of care, expressed wishes, and advance care plans.[27] ▪ Alberta Health Services: The Calgary Zone Long Term Care Pharmacy and Therapeutics Committee made the decision (December 1, 2020) to expedite coverage for LMWH when determined to be required by the attending physician in alignment with Health Canada interim guidance for long-term care residents with COVID-19. Instead of reviewing LMWH requests for coverage on a case-by-case basis in long-term care in Alberta, orders for LMWH will automatically be approved for coverage when Health Canada guidance is met and documented.[28] See Table 4 in the Appendix for further details. ○ **Hospital Setting**: ▪ CADTH: According to the CADTH report (June 11, 2020) on the state of the evidence for the use of LMWH prophylaxis in hospitalized COVID-19 patients, there is an increased risk of venous thromboembolism among hospitalized COVID-19 patients, especially those in intensive care units. ▪ Most Canadian guidance suggests using prophylactic dosing of pharmacologic thromboprophylaxis to prevent venous thromboembolism in patients who have been hospitalized with COVID-19. ▪ Canadian guidance does not suggest the routine use of extended-duration pharmacologic thromboprophylaxis. The use of extended-duration pharmacologic thromboprophylaxis in patients with COVID-19 who are being discharged from hospital may be considered based on the risk of venous thromboembolism and the risk of bleed.

[c] These guidelines are based on updated and original systematic reviews of evidence conducted under the direction of the McMaster University GRADE Centre with international collaborators. The panel used the Grading of Recommendations Assessment, Development and Evaluation (GRADE) approach to assess the certainty in the evidence and formulate recommendations (Cuker et al., 2021).

	▪ The report also included a list of ongoing clinical trials assessing the effectiveness and safety of pharmacologic thromboprophylaxis to prevent venous thromboembolism.[29,30] ▪ Alberta Health Services: A rapid evidence brief (January 11, 2021) by the COVID-19 Scientific Advisory Group highlighted an increased risk of venous thromboembolism among hospitalized COVID-19 patients, especially those who are admitted to intensive care and those with severe COVID-19 infection.[31] Recommendations included: ▪ COVID-19 patients in hospital should receive the usual preventative blood thinners recommended for hospitalized patients at risk of venous thromboembolism unless there are contraindications (usually once daily low-molecular weight heparin products such as tinzaparin). ▪ Further testing should be done if there are signs or symptoms suspicious for venous thromboembolism complications (e.g., unexplained high heart rate, low blood pressure, one sided leg swelling, worsening shortness of breath or low oxygen status) rather than relying on elevation in D-dimer blood tests. ▪ Higher than usual preventative doses of blood thinners (which have been suggested to prevent venous thromboembolism in COVID-19 patients) are not recommended as new evidence suggests that this increases bleeding risk without adding much benefit. COVID-19 patients should receive standard dosing for the usual length of therapy. Studies are continuing in this area and recommendations may change in the future.[32]
Ontario Scan	• No information identified.

Methods

The COVID-19 Evidence Synthesis Network is comprised of groups specializing in evidence synthesis and knowledge translation. The group has committed to provide their expertise to provide high-quality, relevant, and timely synthesized research evidence about COVID-19 to inform decision makers as the pandemic continues. The following members of the Network provided evidence synthesis products that were used to develop this Evidence Synthesis Briefing Note:

- Cochrane Canada. (February 8, 2021). Email Communications.
- Ontario Health. (February 11, 2021). Low Molecular Weight Heparin Thromboprophylaxis for Long-Term Care Residents With COVID-19: An Expedited Summary of the Evidence and Jurisdictional Scan.
- SPOR Evidence Alliance. (January 26, 2021). Email Communications.

For more information, please contact the Research, Analysis and Evaluation Branch (Ministry of Health).

APPENDIX

The following tables are from an evidence synthesis product produced by a member of the COVID-19 Evidence Synthesis Network:

- Ontario Health. (February 11, 2021). Low Molecular Weight Heparin Thromboprophylaxis for Long-Term Care Residents With COVID-19: An Expedited Summary of the Evidence and Jurisdictional Scan.

Table 2: Summary of Systematic Reviews on Low Molecular Weight Heparin for Hospitalized Patients with COVID-19[33]

Author (Year)	Population & Setting Age	Thromboprophylaxis Intervention	Comparison	Results	Limitations/Comments
Hasan et al 2020	COVID-19 patients admitted to intensive care units Age ranged from 59 to 70 years	LMWH or UFH either as prophylactic or therapeutic doses	Any	12 studies Pooled Incidence of VTE Prophylactic or therapeutic anticoagulation across all studies: 31% (95% CI 20–43%; I^2: 92%) Subanalyses: Prophylactic anticoagulation alone: 38% (95% CI 10–70%) Mixed therapeutic and prophylactic anticoagulation: 27% (95% CI 17–40%)	Literature search to 25 June 2020 Retrospective observational Substantial statistical heterogeneity in summary statistics. Lack of comparative studies
Chi et al 2020	Hospitalized patients with laboratory-confirmed COVID-19 infection. Mean age between 60 and 70 years	At least standard doses of thromboprophylaxis with UFH or LMWH	Any	Incidence of VTE (11 studies): 23.9% (95% CI, 16.2% to 33.7%) Mortality (6 studies): 21% (95% CI, 17.0% to 26.4%)	Literature search to 31 May 2020 Retrospective observational Substantial statistical heterogeneity in summary statistics Lack of comparative studies

Abbreviations: CI, confidence interval; LMWH, low molecular weight heparin; UFH, unfractionated heparin; VTE, venous thromboembolism.

Table 3: Summary of Primary Studies on Low Molecular Weight Heparin for Hospitalized Patients with COVID-19[34,d]

Author (Year) Study Design	Population & Setting Age	Thromboprophylaxis Intervention	Comparison	Results
Belgium				
Piagnerelli et al (2020) Retrospective case series	ICU patients Median (range) age: 58 (50–65) years	enoxaparin 60mg once daily n=19	none	ICU LOS – median (range): 9 (5–17) days Hospital LOS – median (range): 19 (11–23) days Deaths in ICU - n(%): 5 (26)
Stessel et al (2020) Retrospective observational	Adult patients with confirmed COVID-19 pneumonia admitted to ICU Median (IQR) age: Augmented LMWH: 69.5 (62.0, 76.0) years Nonaugmented LMWH: 62.0 (56.0, 73.0) years	Augmented (increased dose) LMWH prophylactic: n=26	Nonaugmented LMWH prophylactic: n=46	1 month mortality 39.13% (18/46) in the before group and 3.85% (1/26) in the after group ($p < 0.001$). ARDS n(%) Nonaugmented: 44 (97.78%) Augmented: 16 (80.00%), *P* = .03 Sepsis n(%) Nonaugmented: 35 (77.78%) Augmented: 7 (29.17%), *P* < .01 VTE n(%) Nonaugmented: 19 (41.30%) Augmented: 4 (15.38%), *P* = .03 LOS (ICU) (median [IQR] days) Nonaugmented: 13.00 (7.00, 32.00) Augmented: 11.00 (4.00, 20.00), *P* = .03 LOS (Hospital) (median [IQR] days) Nonaugmented: 21.00 (12.00, 34.00) Augmented: 18.50 (13.00, 23.00), *P* = .18
China				
Qin et al (2020) Retrospective observational	Hospitalized COVID-19 patients Mean (SD) age: 60 (15) years	Prophylactic LMWH dose: n=109 Therapeutic LMWH dose: n=77 No LMWH: n=563	None	LMWH (any dose) emerged as an independent factor for decreased 28-day death (HR 0.22, 95% CI: 0.09–0.55).
Shi et al (2020) Retrospective observational	Hospitalized COVID-19 patients Median (IQR) age LMWH: 69.0 (42.0–91.0) years	LMWH: n=21	No LMWH: n=21	Hospital length of stay, median (IQER): LMWH: 29.0 (17.0–42.0) days No LMWH: 27.0 (24.0–31.0) 0.41 days

[d] None of the primary studies in Table 3 were included in the systematic reviews in Table 2 (Ontario Health, Feb 11, 2021).

<table>
<tr><th>Author (Year)
Study Design</th><th>Population & Setting Age</th><th>Thromboprophylaxis Intervention</th><th>Comparison</th><th>Results</th></tr>
<tr><td></td><td>No LMWH:
69.0 (40.0–84.0) years</td><td></td><td></td><td></td></tr>
<tr><td colspan="5">Denmark</td></tr>
<tr><td>Dalager-Pedersen et al (2021)

Retrospective registry/chart review</td><td>Patients treated for SARS-CoV-2 at hospitals

Median age 69 years (range 54-78)</td><td>Ward patients on thromboprophylactic LMWH therapy: n=140</td><td>Ward patients not on thromboprophylactic therapy: n=310</td><td><u>Ward patients on thromboprophylactic therapy</u>
VTE: 3% (4/140) patients
Major bleeding: 1% (2/140) patients

<u>Ward patients not on thromboprophylaxis therapy</u>
VTE: 5% (15/310) patients
Major bleeding: 0% (0/310) patients

All patients admitted at the ICU received anticoagulant therapy and major bleeding was observed in 11% (15/132)</td></tr>
<tr><td colspan="5">France</td></tr>
<tr><td>Helms et al (2021)

Retrospective observational</td><td>Patients referred for COVID-19 in two ICUs from two centers of a French tertiary hospital

Median (IQR) age 62 [51; 70] years</td><td>Standard or reinforced prophylactic dosage of LMWH-enoxaparin— up to 6000 IU/12 h subcutaneously in obese patients or UFH 200 IU/kg/24 h if creatinine clearance <30 mL/min).

n=108</td><td>LMWH at curative dose (100 IU/kg/12 h SC based on actual weight, without exceeding 10,000 IU/12 h or UFH 500 IU/kg/24 h if creatinine clearance<30 mL/min)

n=71</td><td><table><tr><th>Thrombotic or Ischemic Events</th><th>Prophylactic Dose (n=108)</th><th>Therapeutic Dose (n=71)</th><th>OR (95% CI)</th></tr><tr><td>Thrombo-embolic complications - n (%)</td><td>42 (38.9)</td><td>15 (21.1)</td><td>0.38 [0.14–0.94]</td></tr><tr><td>Pulmonary embolisms – n (%)</td><td>22 (20.4)</td><td>3 (4.2)</td><td>0.19 [0.03–0.81]</td></tr><tr><td>Deep vein thrombosis—n (%)</td><td>10 (9.3)</td><td>1 (1.4)</td><td>0.13 [0.01–0.89]</td></tr><tr><td>Cerebral ischemic attack—n (%)</td><td>6 (5.6)</td><td>0</td><td>0.06 [0–0.68]</td></tr></table></td></tr>
<tr><td colspan="5">Greece</td></tr>
<tr><td>Poulakou et al (2021)

Retrospective observational</td><td>Consecutive patients admitted in two Hospitals for COVID-19

Mean (SD) age: 59.5 (19.1) years</td><td>LMWH or fondaparinux (dose depended on GFR and body weight)

Group B: Prophylactic dose (n=26)

Group C: Intermediate dose (n=42)

Group D: Therapeutic dose (n=12)</td><td>Group A = No anticoagulant (n=15)</td><td><u>Primary endpoint consisted of intubations or VTE or deaths during a follow-up of at least 14 hospitalization days:</u>
Observed 21 events (17 intubations, 4 deaths) during a median follow-up of 13 (6, 14) days.
Distribution of events per anticoagulation treatment group was:
Group A, 6 of 15 patients (40%) (including 1 death)
Group B, 5 of 26 patients (19%) (including 1 death)
Group C, 6 of 42 patients (14%)
Group D, 4 of 12 patients (33%) (including 2 deaths)

Rate of events in Group A (no anticoagulation) significantly higher than Group C (intermediate dose) (p=0.04)</td></tr>
<tr><td colspan="5">Italy</td></tr>
<tr><td>Albani et al (2020)

Retrospective observational</td><td>Adults (≥18 years) admitted to hospital and positive for SARS-CoV-2

Median age not reported</td><td>Patients (n=799) treated with enoxaparin at least once during hospital stay.
Median age 69 (60-77) years.</td><td>Admitted patients(n=604) who did not receive enoxaparin

Median age 72 (59-80) years</td><td>Prophylactic enoxaparin associated with lower in-hospital mortality compared with no enoxaparin:
OR 0.50 (95% CI 0.36-0.69)</td></tr>
</table>

<table>
<tr><th>Author (Year)
Study Design</th><th>Population & Setting Age</th><th>Thromboprophylaxis Intervention</th><th>Comparison</th><th>Results</th></tr>
<tr><td></td><td></td><td>Of 799 patients, 487 treated with prophylactic dose of ≤ 40 mg enoxaparin per day</td><td></td><td><table><tr><th>Thrombotic or Hemorrhagic Events</th><th>Prophylactic Enoxaparin (n=487)</th><th>No Enoxaparin (n=604)</th></tr><tr><td>Pulmonary embolism (n)</td><td>3</td><td>1</td></tr><tr><td>Venous thromboembolism (n)</td><td>1</td><td>2</td></tr><tr><td>Acute MI (n)</td><td>4</td><td>6</td></tr><tr><td>Cerebral infarction (n)</td><td>4</td><td>4</td></tr><tr><td>Hemorrhagic events (n)</td><td>6</td><td>13</td></tr></table></td></tr>
<tr><td>Bolzetta et al (2020)

Retrospective observational</td><td>Hospitalized adults (mean age 84.1 y)</td><td>Decision for treating with prophylactic (low) or therapeutic (high) dose was based on clinical, bio-humoral, radiological findings, giving higher doses of heparins to people at higher risk of mortality

No further data for doses reported

<u>Prophylactic (low) dose</u>
calciparin
fondaparinux
enoxaparin</td><td><u>Higher dose</u>
calciparin
fondaparinux
enoxaparin</td><td>Therapeutic doses were not associated with better survival rate (HR 1.06; 95% CI 0.47–2.60; P = 0.89), even after adjusting for 15 confounders related to mortality (HR 0.89; 95% CI 0.30–2.71; P = 0.84)</td></tr>
<tr><td>Chistolini et al, 2020

Observational study</td><td>Consecutive patients admitted to ICU swab culture-positive for COVID-19, affected by acute respiratory failure without active and diagnosed thromboembolic event, intubated and mechanically ventilated

Mean age (range): 66 y (38–85)</td><td>N = 14
Low-dose LMWH (100 IU kg/d)</td><td>N = 13
High-dose LMWH (100 IU kg/twice d)</td><td><u>Adverse events, low vs high dose</u>
PE: 2/14 vs 0/13
Acute myocardial ischemia: 1/14* vs 0/13
*Patient was previously on high-dose LMWH but switch to low-dose after tracheostomy site bleed</td></tr>
<tr><td>Di Castelnuovo et al (2020)

Retrospective observational</td><td>Patients who were hospitalised with confirmed SARS-CoV-2 infection

<u>Median (IQR) Age:</u>
Heparin: 68 (57-79)
No Heparin: 65 (53-77)</td><td>Heparin: n=1,804

The information on type of heparin used was missing for n=403 out of 1,804. In the others, LMWH and UFH were the types used in 99.5% and 0.5%, respectively.</td><td>No heparin: n=770</td><td><u>Hazard ratio (HR [95% CI]) for in-hospital mortality:</u>
Prophylactic doses vs no heparin 0.40 (0.30 to 0.52)
Therapeutic doses vs no heparin 0.65 (0.46 to 0.93)
Therapeutic vs prophylactic regimen 1.54 (1.06 to 2.25)</td></tr>
</table>

Author (Year) Study Design	Population & Setting Age	Thromboprophylaxis Intervention	Comparison	Results
		54.5% of the total heparin patients treated with prophylactic heparin		
Martinelli et al, 2020 Retrospective observational	Patients with COVID-19 admitted to 3 low- or high-intensity ICUs <u>Median age (IQR)</u> Standard dose group: 58 y (49–66) High dose group: 60 (51–69)	N = 151 Standard dose enoxaparin: 40 mg/d, increased to 60 mg/d in the obese	N = 127 High-dose enoxaparin: 0.7 mg/kg twice/d in high-intensity ICU 1 mg/kg/d in low-intensity ICU	<u>Adverse events, standard vs high dose incidence rate in patient–months (95% CI)</u> Death: 0.56 (0.36–0.84) vs 0.25 (0.13–0.43); adjusted HR 0.36 (0.18–0.76) Death or deterioration: 1.33 (1.00–1.73) vs 0.49 (0.32–0.72); adjusted HR 0.39 (0.23–0.62) VTE: 0.53 (0.33–0.80) vs 0.33 (0.20–0.52); adjusted HR 0.52 (0.26–1.05) Bleeding: 0 vs 0.08 (0.03–0.20)
Mattioli et al (2020) Retrospective observational	Consecutive hospitalized patients ≥ 18 y with confirmed COVID-19 Mean age (SD): 73.7 y (14.6)	N = 105 Enoxaparin (40, 80, or 100 mg/d depending on patient's renal function and body weight)	No comparator, analysis by age (< 85 y vs ≥ 85 y)	Median LOS (IQR): 12 d (7–16) <u>Adverse events, n (%)</u> Respiratory failure: 80 (76.2) Death: 22 (21) Thrombotic event: 1 (1) Bleeding event: 2 (1.9) Thrombocytopenia: 4 (3.8) Loss of hemoglobin ≥ 2 g/dl: 21 (21.2) Blood transfusions needed: 7 (6.7)
Paolisso et al (2020) Retrospective observational	Laboratory-confirmed COVID-19 patients admitted to hospital Median (IQR) age: 67 (55-79) years	N=361 Standard prophylactic LMWH enoxaparin dosage (subcutaneous enoxaparin 40–60 mg daily)	N=89 Intermediate LMWH enoxaparin dosage (subcutaneous enoxaparin 40–60 mg twice daily) for 7 days	**Outcome** / **Standard Prophylactic LMWH (40-60 mg daily)(n=361)** / **Intermediate LMWH (40-60 mg twice daily) (n=89)** / **P value** All cause death - n(%) / 75 (20.8) / 4 (4.5) / .001 ICU admission - n(%) / 57 (15.8) / 13 (14.6) / .8 Stroke - n(%) / 1/180 (0.56) / 0(0) / .5 AMI - n(%) / 4/180 (2.2) / 1/57 (1.8) / .8 Hospital LOS days - median (IQR) / 10 (6–13) / 8 (6–14) / .4
Pavoni et al (2020) Retrospective observational	Patients admitted to ICU Mean (±SD) age: 64.3 ± 12.1 years	Intermediate dose (enoxaparin 4000 UI or 6000 UI, if body mass index > 35, subcutaneously every 12 h) N=22	Therapeutic dose (Group 2) (enoxaparin 100 UI/kg b.i.d.) N=20	**Outcome** / **Intermediate Dose (n=22)** / **Therapeutic Dose (n=20)** / **P value** ICU mortality – n(%) / 2 (9.1) / 5(25) / .167 Hospital mortality – n(%) / 4(18.1) / 5(25) / .590 Minor bleedings – n(%) / 1(4.5) / 3(15) / .249 Major bleedings – n(%) / 0 / 0 / - VTE – n(%) / 3(13.6) / 13(65) / .001
Perazzo et al (2020)	16 elderly patients admitted to hospital with non-deferable	First 7 patients: standard prophylaxis 4000 IU/day	Subsequent 9 consecutive patients: escalated dose 4000 IU enoxaparin 2x/day	<u>No statistically significant difference in fatal cardiovascular events (*P* = .102)</u>

Author (Year) Study Design	Population & Setting Age	Thromboprophylaxis Intervention	Comparison	Results
Case series	femoral neck fractures and COVID-19 on PCR test. All COVID considered severity level 2: moderate symptoms, high fever, persistent dry cough, asthenia, dyspnoea, requires oxygen support (non-invasive) Mean age 86.4 years (SD 6.2)	LMWH (enoxaparin or nadroparin based on body weight)		Standard group: 4 events (57.1%) within a few days of admission (1 ischemic stroke, 2 cardiac arrests in heart failure, 1 pulmonary embolism) Escalated dose group:1 fatal ischemic stroke (11.1%) Discharged with recovery (*P* value not reported): Standard dose: 3 Escalated dose: 8 Hospital LOS (*P* value not reported): Standard: mean 10.4 days +/- 4.9 Escalated: mean 14.7 days +/- 8.6
Russo et al (2020) Retrospective observational	Consecutive symptomatic patients with laboratory-proven COVID-19 admitted to internal medicine units of 5 Italian hospitals Median age (IQR) Enoxaparin group: 63 y (55.3–73.76) Fondaparinux group: 65 y (53.6–77.7)	N = 74 Enoxaparin low-dose (4,000 units/d) or high-dose (6,000 units/d), choice of dosage was based on patient's VTE risk	N = 46 Fondaparinux 2.5 units/d	Median LOS (IQR) Enoxaparin vs fondaparinux: 31 d (14–51) vs 34 d (15–51), *P* = .90 Adverse events, enoxaparin vs fondaparinux N (%) VTE: 10 (13.5%) vs 3 (6.5%); OR 2.25 (0.58–8.61), *P* = .24 DVT: 5 (6.8%) vs 2 (4.3%); OR 1.59 (0.30–8.58) *P* = .54 PE: 4 (5.4%) vs 0 (0%) 5.94; OR (0.31–112.87), *P* = .24 Bleeding: 3 (4.1%) vs 3 (6.5%); OR 0.56 (0.11–2.91) *P* = .50 ARDS: 14 (18.9%) vs 7 (15.2%); OR 1.30 (0.48–3.51) *P* = .60 All-cause dead: 7 (9.5%) vs 5 (10.9%); OR 0.86 (0.25– 2.88) *P* = .80 Type of prophylaxis did not result in significantly increased risk of adverse events Net clinical benefit of fondaparinux over enoxaparin: +4.6
Sweden				
Jonmarker et al (2020) Retrospective observational study/chart review	Critically ill patients with respiratory failure admitted to ICU diagnosed as COVID-19 with PCR for SARS-CoV-2 Median age: 61 years (IQR 52 – 69)	N = 152 LMWH (tinzaparin or dalteparin) Low dose n = 67 Medium dose n = 48 High dose n = 37	Low dose (2500-4500 IU tinzaparin or 2500-500IU dalteparin) Medium dose (> 4500 IU < 175 IU/kg body weight tinzaparin or >500 IU < 200 IU/kg body weight dalteparin) High dose (≥175 IU/kg body weight tinzaparin or ≥ 200 IU/kg body weight dalteparin) *where dose was adjusted for reduced kidney function dose was classified as intended dose range	Lower 28-day Mortality in high-dose group (13.5%) compared with medium dose or low dose prophylaxis (25.0% and 38.8%, respectively *P* = .02) Hazard ratio for death: High vs low: 0.33 (95% CI: 0.13-0.87) Medium vs low: 0.88 (95% CI 0.43-1.83) Median days alive and out of ICU during the first 28 days (between groups comparison *P* =.07) Low dose: 0 (IQR 0-22) Medium dose: 11 (0-26) High dose: 18 (0-26) Cumulative proportion of thromboembolic events within 28 days of ICU admission (between groups comparison *P* = .04) Low dose: 17.9% Medium dose: 18.8% High dose: 2.7% Ischemic strokes: n= 4 in low dose group (6%) Cumulative proportion of bleeding events within 28 days of ICU admission (between groups comparison *P* = .16)

Author (Year) Study Design	Population & Setting Age	Thromboprophylaxis Intervention	Comparison	Results
				Low dose: 11.9% Medium dose: 14.6% High dose: 2.7% Minor intracranial hemorrhage 2 low dose Major or severe bleeding events 5 (low dose 3, medium dose 2) Other outcomes: levels of Fibrin-D-dimer
Turkey				
Arslan et al (2020) Retrospective observational	Hospitalized Covid-19 patients Mean age of all patients 50.6 ±16.7 years	Hospitalized Covid-19 patients treated with enoxaparin (n = 187) Low risk dose: 40 mg per day High risk dose: 0.5 mg/kg/12-hour hospitalization, and continuation for a month post-discharge	Hospitalized Covid-19 patients not treated with enoxaparin (n = 226)	LMWH treated patients had significantly shorter length of stay in hospital (mean ± SD): (8.2±3.6 vs 10.2±4.1 days; p<0.001).
Canoglu et al (2020) Retrospective observational	Adults (≥18 years) admitted to hospital with SARS-CoV-2 pneumonia Age ranged between 23 and 96 years, with a median (IQR) age of 60.0 (20.5) years.	Prophylactic dose LMWH (0.5 mg/kg twice daily) n=98	Therapeutic do se LMWH (1 mg/kg twice daily) n=56	44 (63.6%) patients treated with prophylactic dose died compared to 10(36.4%) patients treated with therapeutic dose. Mortality was 6.5-fold higher in the prophylactic dose group than in the therapeutic dose group (95% CI, 2.4-17.6).
Yormaz et al (2020) Retrospective chart review	Hospitalized patients at one hospital diagnosed with COVID-19 according to WHO guidelines/Health Commission of Turkey Average Age (Range) LMWH group: 53.3 years (40-68) Control group: 55.4 years (44-66)	N = 96 Intervention: LMWH (n = 48) thromboprophylactic dose of 4000 UI/day, for 7 days	Control (n = 48)	Days to conversion to negative (virus shedding) significantly shorted in the LMWH group compared with control: (5.2 days [IQR: 3.6 -6.3] vs 7.6 [IQR 6.5-9.7] *P* < .001) Hospital LOS significantly shorter in LMWH group compared with control (7.2 days [IQR 6.4-8.3] vs 9.6 [IQR 8.5-10.7] *P* < .001) Other outcomes: blood markers, lung CT-SS
United Arab Emirates				
Atallah et al (2020) Retrospective observational	Adult patients with confirmed SARS-CoV-2 infection admitted to ICU Median age (range): 49 (22–102) years	standard (enoxaparin 40 mg daily): n=83 (44 %) patients	high intensity thromboprophylaxis (enoxaparin 40 mg twice daily): n=75 (40%)	High-intensity thromboprophylaxis regimen associated with lower-risk of thrombotic events compared with the regular prophylactic regimen (OR = 0.20 [95% CI 0.06–0.69], *P* = 0.01). Among 75 patients who received high-intensity prophylactic regimen, 2 (2.7%) experienced major bleeding. No data reported for standard prophylaxis.
United States				
Billett et al (2020)	Adults (≥ 18 years) tested positive for COVID-19 for first	UFH (standard or high dose)	No anticoagulation	<u>Mortality – compared with no anticoagulation at baseline (OR, 95% CI)</u> Apixaban Prophylaxis: 0.52 (0.33-0.82), *P* = .005

Author (Year) Study Design	Population & Setting Age	Thromboprophylaxis Intervention	Comparison	Results
Retrospective observational	time within 24 hours of admission **Age, years (n=3625)** <50: n=708 (19.5%) 50-60: n=671 (18.5%) 60-70: n=836 (23.1%) 70-80: n=820 (22.6%) >80: n=590 (16.3%)	Apixaban Enoxaparin		Enoxaparin Prophylaxis: 0.50 (0·3 –0.77), *P* = .002 UFH Std Prophylaxis: 0.82 (0.55-1.23), *P* = .34 UFH High Prophylaxis: 0.84 (0.44-1.61), *P* = .60 Transfusion requirement - compared with no anticoagulation at baseline (OR, 95% CI) Apixaban Prophylaxis: 0·68 (0·31-1·50), P=0·34 Enoxaparin Prophylaxis: 0·68 (0·32-1·44), P=0·31 UFH Std Prophylaxis: 0·87 (0·43-1·74), P=0·69 UFH High Prophylaxis: 0·69 (0·26-1·79), P= 0·45
Daughety et al, (2020) Retrospective observational	Hospitalized adults with positive SARS-CoV-2 No overall age reported. Age (Median [Q1-Q3]) Survived: 61 (49–95) years Died: 76 (68–94) years	Severe COVID-19: Escalated-dose thromboprophylaxis (enoxaparin 0.5 mg/kg twice daily) Without severe COVID-19: standard-dose thromboprophylaxis (enoxaparin 40 mg daily if weight < 100 kg and 60 mg daily if weight > 100 kg)	No anticoagulant	<table><tr><th>Outcome</th><th>Prophylactic standard only (n=99)</th><th>Standard Prophylactic to Escalated (n=25)</th><th>No anticoagulant (n=13)</th></tr><tr><td>Died n (%)</td><td>24 (24)</td><td>4 (16)</td><td>4 (31)</td></tr><tr><td>Acute TE n (%)</td><td>0</td><td>1 (4)</td><td>16 (57)</td></tr><tr><td>Major hemorrhage n (%)</td><td>3(3)</td><td>2(8)</td><td>1(8)</td></tr></table>
Motta et al (2020) Retrospective observational	Adults ≥ 18 y admitted to hospital with COVID-19 Mean age (SD) Total: 64.7 (18.1) Prophylactic group: 64.2 (17.9) Therapeutic group: 66.9 (18.6)	N = 299 Prophylactic dose enoxaparin: 30 or 40 mg daily	N = 75 Therapeutic dose enoxaparin: 1 mg/kg twice/d or 1.5 mg/kg daily Therapeutic dose heparin	Risk of mortality, therapeutic vs prophylactic Deaths, n (%): 29 (38.7%) vs 43 (14.4%) Adjusted RR (95% CI): 2.3 (1.0–4.9), *P* = .04 Propensity-adjusted RR (95% CI): 2.4 (0.9–6.6), *P* = .09 Average treatment effect (95% CI): 0.11 (0.02–0.2), *P* = .01 Adverse events, prophylactic vs therapeutic Occlusive event: 1.3% vs 12.0% (significant difference) Significant bleeding requiring transfusion: 0.3% vs 2.7% (significant difference)
Rentsch et al, (2020) Retrospective observational	Hospitalized patients with laboratory-confirmed COVID-19 test result on or within 14 days before hospital admission Median age (IQR): 68 y (58–75)	Enoxaparin 40 mg/d or 30 mg twice/d) N = 2506 Also included: intravenous heparin, direct oral anticoagulants (apixaban, rivaroxaban, dabigatran)	No anticoagulation	IPT-weighted HR (95% CI) for enoxaparin 30-day mortality: 0.78 (0.68–0.89) Inpatient mortality: 0.72 (0.62–0.84) Initiate therapeutic anticoagulation: 0.79 (0.70–0.89)

Abbreviations: ARDS, acute respiratory distress syndrome; CI, confidence interval; d, day; DVT, deep vein thrombosis; HR, hazard ratio; inverse probability of treatment; IPT, inverse probability of treatment; IQR, interquartile range; LMWH, low molecular weight heparin; LOS, length of stay; OR, odds ratio; PE, pulmonary embolism; RR, risk ratio; UFH, unfractionated heparin; VTE, venous thromboembolism; y, year.

Table 4: Jurisdictional Guidance on Thromboprophylaxis in Long-Term Care Residents with COVID-19[35]

Jurisdiction(Date)	Target Population	Guidance	Link
Canada			
LMWH for VTE prophylaxis in LTC residents with COVID-19 infection *(December 1, 2020)*	LTC residents with COVID-19	Calgary Zone LTC Pharmacy and Therapeutics Committee made the decision to expedite coverage for LMWHs when determined to be required by the attending physician in alignment with Health Canada interim guidance for care of residents in LTC with COVID-19 infection In lieu of reviewing LMWH requests for coverage on a case-by-case scenario, orders for LMWHs will automatically be approved for coverage when the Health Canada guidance is met and documented Attending physician is required to specify a duration of therapy in the medication order LTC operators in Calgary may stock a small supply of one brand and one strength of commercially available prefilled LMWH syringes in their Statbox upon approval by the operators' medical advisory committee for the purposes of commencing therapy in a timely manner in urgent scenarios; subsequent doses should be provided patient-specific by the pharmacy service provider as per the service agreement	Alberta Health Services
France			
Notice relating to the care at home or in a care structure of suspected or confirmed cases of COVID-19 *(April 8, 2020)*	Residential facilities for the elderly, home hospitalization, medical practices or medical homes or health centres (excluding health institutions)	The following should be observed in every bedridden patient (residents of facilities for the elderly, or the elderly at home): • Prevention of thromboembolism (LMWH according to current recommendations) • Avoid discontinuation of any anticoagulant or antiplatelet agent in the context of infection because of the high risk of cardiovascular events	Haut Conseil de la santé publique[a]
United Kingdom			
Managing the COVID-19 pandemic in care homes for older people *(Version 4 updated November 16, 2020)*	Management and Treatment of COVID-19 in care homes for older people	**Thromboprophylaxis:** COVID-19 is commonly associated with thromboembolic events. For residents being treated in a care home setting, consideration of thromboprophylaxis may be necessary and should be tailored to the potential risks and benefits for an individual patient.	British Geriatrics Society

Abbreviations: LMWH, low molecular weight heparin; LTC, long-term care.
[a]Translated from French using Google Translate.

Table 5: Jurisdictional Guidance on Thromboprophylaxis in Non-Hospitalized Patients with COVID-19[36]

Jurisdiction (Date)	Target Population	Guidance	Link
Australia			
Australian guidelines for the clinical care of people with COVID-19 *(published Feb 4, 2021)*	Adults with moderate COVID-19 (regardless of hospitalization)	**VTE prophylaxis:** Use prophylactic doses of anticoagulants, preferably LMWH (e.g., enoxaparin 40 mg once daily or dalteparin 5000 IU once daily) in adults with moderate COVID-19 or other indications, unless there is a contraindication, such as risk for major bleeding. Where the estimated glomerular filtration rate (eGFR) (see below) is less than 30 mL/min/1.73m^2, unfractionated heparin or clearance-adjusted doses of LMWH may be used (e.g., enoxaparin 20 mg once daily or dalteparin 2500 IU once daily). (Consensus recommendation)	Australian National COVID-19 Clinical Taskforce
Norway			
COVID-19 and venous thromboembolism – prophylaxis and treatment *(published June 30, 2020)*	Prophylaxis for ambulant patients	**Proposed anticoagulant treatment:** Not generally indicated, but a prophylactic dose of LMWH may be considered for patients with a history of venous thrombosis, active cancer disease or obesity (BMI > 30 kg/m^2)	Kvåle et al, 2020 (Journal of the Norwegian Medical Association)
United Kingdom			
COVID-19 rapid guideline: reducing the risk of venous thromboembolism in over 16s with COVID-19 *(published November 2020)*	Adults (aged 16 years and older) who have had treatment for COVID-19 and are managed in community settings	For patients with COVID-19 pneumonia managed in community settings: • Assess the risks of VTE and bleeding • Consider pharmacological prophylaxis if the risk of VTE outweighs the risk of bleeding	National Institute for Health and Care Excellence guideline [NG186] COVID-19 rapid evidence review: reducing the risk of venous thromboembolism in over 16s
Guidance on venous thromboembolic disease in patients with COVID-19 *(February 2021)*	People discharged from hospital following COVID-19 pneumonia	Prophylactic thromboprophylaxis for up to 4 weeks may be considered for patients discharged following COVID-19 pneumonia who are deemed to be at high risk of VTE and low risk of bleeding	British Thoracic Society
Clinical guide for the prevention, detection and management of thromboembolic disease	COVID-19 patients in emergency department and ambulatory care COVID-19 patients discharged from hospital	Thromboprophylaxis should be considered in ambulatory COVID-19 patients and they should have a clinical risk assessment according to local protocols There is currently no specific evidence on the use of thromboprophylaxis following discharge from hospital following COVID-19 infection	Faculty of Intensive Care Medicine, Intensive Care Society, Association of Anaesthetists, Royal College of Anaesthetists

Jurisdiction (Date)	Target Population	Guidance	Link
in patients with COVID-19		Extended thromboprophylaxis may be considered on discharge in those patients who are high risk, including those with a critical care admission and reduced pre-admission mobility. 14 to 28 days of thromboprophylaxis with LMWH may be considered in such patients.	
United States			
Antithrombotic therapy in patients with COVID-19 (*Last Updated: December 17, 2020)*	Non-hospitalized patients with COVID-19	**VTE prophylaxis and screening:** For non-hospitalized patients with COVID-19, anticoagulants and antiplatelet therapy should not be initiated for the prevention of VTE or arterial thrombosis unless the patient has other indications for the therapy or is participating in a clinical trial	United States National Institutes of Health

Abbreviations: LMWH, low molecular weight heparin; VTE, venous thromboembolism.

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