

**Date:** October 1, 2021

**To:** All Physicians, Pharmacists and Nursing Staff

**From:** Dr. Elizabeth Mackay and Micheal Guirguis, on behalf of the AHS VTE Prophylaxis Working Group

**RE:** Updated VTE Prophylaxis Guidance for Admitted COVID-19 Patients

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### Interim Recommendations:

1. Current evidence supports that patients admitted with an acute COVID-19 respiratory infection to a non-critical care setting and with the exception of those with high bleeding risk should be considered for weight – based therapeutic dose tinzaparin to prevent COVID-19 complications including the progression to high flow oxygen, critical care, organ support, ventilation or death. High Bleeding risk is defined as a HASBLED score greater than 2.
2. At this time, there is insufficient evidence to recommend higher doses of tinzaparin for COVID-19 patients admitted directly to critical care, given an increased risk of bleeding and lack of improvement in these primary outcomes. COVID-19 Patients admitted to a critical care setting should continue to receive weight based LMWH prophylaxis.

Rationale: Based on the recently published RCT studies by the ATTACC, ACTIV-4a, and REMAP-CAP Investigators, for every 1000 hospitalized patients with moderate disease, an initial strategy of therapeutic-dose anticoagulation, as compared with usual-care thromboprophylaxis, would be anticipated to result in the survival of 40 additional patients until hospital discharge without organ support at the expense of 7 additional major bleeding events. (N Engl J Med 2021;385:790-802. DOI: 10.1056/NEJMoa2105911)

### Background:

Patients with a severe COVID-19 infection may have a hypercoagulable state. Patients often have an elevated fibrinogen and D-dimer levels that correlate with other markers of inflammation (e.g., CRP, LDH, ferritin). There may be other signs of coagulopathy such as an elevated aPTT, INR or mild thrombocytopenia (platelet count  $> 100 \times 10^9/L$ ). The incidence of acute VTE in patients with COVID is high in critically ill patients, and also appears to be higher than the general medical population. In a recently completed AHS audit, a prevalence of VTE was 3.7% for hospitalized COVID-19 patients. While the typical Alberta prevalence of VTE in all hospitalized patients, ranges from 2.0 -2.3%.

It is clear from the evolving evidence that **all admitted COVID-19 patients** should receive at least standard weight-adjusted VTE prophylaxis, tinzaparin 4,500 IU s/c or 75 unit/kg for patients with weight  $> 80$  kg or  $< 40$  kg for the duration of their illness, unless contraindicated (as outlined in the [AHS Formulary](#)). There is no evidence to suggest the superiority of one LMWH over another; once daily weight-adjusted VTE prophylaxis tinzaparin ideally limits unnecessary interaction with Patients with a severe COVID-19 infection.

D-dimer elevations are common (50-60%) in COVID-19 patients. Studies have shown that a markedly elevated D-Dimer is associated with mortality from COVID-19. This may be a reflection of either a pro-inflammatory or hypercoagulable state.

An elevated D-dimer alone does not warrant investigation or treatment for VTE. Pulmonary embolism should be considered for admitted patients with COVID-19 who have unexplained worsening respiratory status/hypoxia, unexplained hypotension or tachycardia, or signs of DVT regardless of their anticoagulation. Patients with high D-dimer who are admitted to ICU should be followed closely for signs of VTE and considered for empiric therapeutic anticoagulation pending investigations.

Based on a recent article published in NEJM, an open-label, adaptive, multiplatform, controlled trial completed by the ATTACC, ACTIV-4a, and REMAP-CAP Investigators, showed that among 2219 patients with moderate covid-19, admitted and requiring low flow oxygen and not requiring critical care and randomized to therapeutic anticoagulation with heparin, had a 4% lower risk of death or the requirement for organ support when compared to those randomized to prophylactic heparin therapy. (adjusted odds ratio, 1.27; 95% credible interval, 1.03 to 1.58) This finding was irrespective of the presence of a d-dimer level that was greater than or equal to 2 times the upper limit of normal.

The current evidence does not support the use of **extended prophylaxis** for patients post hospitalization for COVID-19 infection. There has been some evidence of an increased rate of VTE in ambulatory or non-hospitalized patients with COVID-19. Consideration should be given for providing VTE prophylaxis for **patients/residents of LTC with moderate to severe COVID -19 infection** who are not admitted to hospital but provided with care in place. This is suggested in particular for those without a major bleeding risk and who have additional risk factors for VTE including prior VTE, active cancer or other chronic inflammatory conditions. This should continue to include usual dosage of LMWH at tinzaparin 4,500 IU s/c or 75 unit/kg for patients with weight > 100 kg or < 40 kg for the duration of their illness. The risk of HITT with provision of LMWH prophylaxis is not high enough in the LTC or subacute care settings to warrant platelet monitoring in the community.

An update of the Scientific Advisory Group Rapid Evidence Brief, Evidence for screening and preventing venous thromboembolic events in patients with COVID-19, is underway and should be available in October, 2021.

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