

## Venous Thromboembolism Sept-March 2021

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### Articles

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#### **[Antiplatelet and anticoagulant agents for secondary prevention of stroke and other thromboembolic events in people with antiphospholipid syndrome.](#)**

Bala MM. *Cochrane Database of Systematic Reviews* 2020;10:CD012169.

BACKGROUND: Antiphospholipid syndrome (APS) is a systemic autoimmune disease characterized by arterial or venous thrombosis (or both), and/or pregnancy morbidity in association with the presence of antiphospholipid antibodies. The prevalence of APS is estimated at 40 to 50 cases per 100,000 people. The most common sites of thrombosis are cerebral arteries and deep veins of the lower limbs. People with a definite APS diagnosis have an increased lifetime risk of recurrent thrombotic events.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012169.pub3/full>

#### **[Antithrombotic therapy for patients with chronic coronary syndromes.](#)**

Parker WA. *Heart* 2020;;doi: 10.1136/heartjnl-2020-316914.

In 2019, the European Society of Cardiology (ESC) published new guidelines on the management of CCS, including antithrombotic therapy. In this review, we evaluate the pathophysiology and pharmacology of atherothrombosis, highlight up-to-date evidence from randomised controlled trials (RCTs), and discuss the content and application of the the ESC 2019 CCS guidelines.

<https://heart.bmj.com/content/early/2020/10/30/heartjnl-2020-316914>

#### **[Arterial and venous thromboembolism in COVID-19: a study-level meta-analysis.](#)**

Tan BK. *Thorax* 2021;;doi: 10.1136/thoraxjnl-2020-215383.

Patients admitted in the ICU for severe COVID-19 had a high risk of VTE. Conversely, further studies are needed to determine the specific effects of COVID-19 on the risk of ATE or VTE in less severe forms of the disease.

*Freely available online*

<https://thorax.bmj.com/content/early/2021/02/22/thoraxjnl-2020-215383>

#### **[Arterial Thrombosis in Coronavirus disease 2019 \(COVID-19\) Patients: A Rapid Systematic Review.](#)**

Cheruiyot I. *Annals of Vascular Surgery* 2020;;doi.org/10.1016/j.avsg.2020.08.087.

Arterial thrombosis occurs in approximately 4% of critically-ill COVID-19 patients. It often presents symptomatically, and can affect multiple arteries. Further investigation of the underlying mechanism of AT in COVID-19 would be needed to clarify possible therapeutic targets.

*Freely available online*

<https://pubmed.ncbi.nlm.nih.gov/32866574/>

### **Association Between Preoperative Blood Transfusion and Postoperative Venous Thromboembolism: Review Meta-Analysis.**

Wang C. *Annals of Vascular Surgery* 2020;;doi: 10.1016/j.avsg.2020.11.033.

Our study indicated that preoperative blood transfusion was associated with higher odds of postoperative VTE. Further large-scale prospective cohort studies are needed to investigate the causality between preoperative blood transfusion and postoperative VTE.

<https://pubmed.ncbi.nlm.nih.gov/33383138/>

### **Beta-blockers versus placebo or no intervention for primary prophylaxis of oesophageal variceal bleeding in children with chronic liver disease or portal vein thrombosis.**

Cifuentes LI. *Cochrane Database of Systematic Reviews* 2021;1:CD011973.

OBJECTIVES: To determine the benefits and harms of beta-blockers compared with placebo or no intervention for primary prophylaxis of oesophageal variceal bleeding in children with chronic liver disease or portal vein thrombosis.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD011973.pub2/full>

### **Cardiac dysfunction and thrombocytopenia-associated multiple organ failure inflammation phenotype in a severe paediatric case of COVID-19.**

Latimer G. *The Lancet Child & Adolescent Health* 2020;;[https://doi.org/10.1016/S2352-4642\(20\)30163-2](https://doi.org/10.1016/S2352-4642(20)30163-2).

A 16-year-old male with chromosome 18q deletion and well controlled epilepsy presented to the Children's National Hospital (Washington, DC, USA) with haemodynamic shock after 4 days of fever and one generalised seizure at home. His initial infectious disease evaluation, including testing for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), did not detect an infectious aetiology; however, a second test for SARS-CoV-2 on day 3 after hospital admission was positive.

*Freely available online*

[https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642\(20\)30163-2/fulltext](https://www.thelancet.com/journals/lanchi/article/PIIS2352-4642(20)30163-2/fulltext)

### **Cerebral venous sinus thrombosis viewed as a postpartum complication.**

Koziołek W. *British Journal of Midwifery* 2020;29(1):52-54.

Cerebral venous sinus thrombosis (CVST) is a rare type of stroke caused by a clot forming in one of the cerebral sinuses and subsequent blockage in blood drainage. The clinical presentation of this disease can be atypical and diagnosis might be challenging. The patient in this case study was a 33-year-old woman admitted to the perinatology clinic at 39+5 weeks of gestation to perform a planned caesarean section, who had previously been discharged home in good condition.

<https://www.magonlinelibrary.com/doi/abs/10.12968/bjom.2021.29.1.52>

### **Compression stockings in addition to low-molecular-weight heparin to prevent venous thromboembolism in surgical inpatients requiring pharmacoprophylaxis: the GAPS non-inferiority RCT.**

Shalhoub J. *Health Technology Assessment* 2020;24(69):DOI: 10.3310/hta24690.

Low-dose low-molecular-weight heparin was non-inferior in reducing venous thromboembolism events in surgical patients at medium or high risk compared with use of graduated compression stockings in addition to heparin.

<https://www.journalslibrary.nihr.ac.uk/hta/hta24690#/abstract>

### **Control of cardiovascular risk factors with tailored recommendations: A randomized controlled trial.**

Barroso M. *Preventive Medicine* 2020;141:106302.

An intervention with tailored recommendations increased mean total cholesterol values. The intervention effect was higher in men who maintained blood lipids at optimal levels and had decreased BP values.

<https://www.sciencedirect.com/science/article/abs/pii/S0091743520303261>

### **[COVID-19 and coagulation dysfunction in adults: A systematic review and meta-analysis.](#)**

Lin J. *Journal of Medical Virology* 2021;93(2):934-944 .

Coagulation dysfunction is closely related to the severity of patients with COVID-19, in which low platelet, high d-dimer, and fibrinogen upon admission may serve as risk indicators for increased aggression of the disease.

*Freely available online*

<https://pubmed.ncbi.nlm.nih.gov/32706426/>

### **[Direct oral anticoagulants in treatment of cerebral venous thrombosis: a systematic review.](#)**

Bose G. *BMJ Open* 2021;11(2):e040212.

The evidence for DOAC use in CVT is limited although suggests sufficient safety and efficacy despite variability in timing and dose of treatment. This systematic review highlights that further rigorous trials are needed to validate these findings and to determine optimal treatment regimens.

*Freely available online*

<https://bmjopen.bmj.com/content/11/2/e040212>

### **[Early initiation of prophylactic anticoagulation for prevention of coronavirus disease 2019 mortality in patients admitted to hospital in the United States: cohort study.](#)**

Rentsch CT. *BMJ* 2021;372:n311.

Early initiation of prophylactic anticoagulation compared with no anticoagulation among patients admitted to hospital with covid-19 was associated with a decreased risk of 30 day mortality and no increased risk of serious bleeding events. These findings provide strong real world evidence to support guidelines recommending the use of prophylactic anticoagulation as initial treatment for patients with covid-19 on hospital admission.

<https://www.bmj.com/content/372/bmj.n311>

### **[Extending anticoagulation treatment for unprovoked venous thromboembolism.](#)**

Heneghan C. *BMJ Evidence-Based Medicine* 2020;25(5):184-186.

After a first unprovoked VTE, 36% of patients will have a recurrent VTE within 10 years after discontinuation of anticoagulation and 3.8% will die as a result. Evidence from published treatment trials suggests that extending treatment with DOACs and VKAs beyond 3 months reduces the risk of recurrent VTE, but only DOACs appear to reduce mortality.

<https://ebm.bmj.com/content/25/5/184>

### **[Fibrosis, atrial fibrillation and stroke: clinical updates and emerging mechanistic models.](#)**

Boyle PM. *Heart* 2020;;doi: 10.1136/heartjnl-2020-317455.

Review outlines the clinical knowledge in this setting, alongside computational modelling frameworks which may provide a mechanistic understanding of the clinical problem of thromboembolisation.

<https://heart.bmj.com/content/107/2/99>

### **[Incidence of Venous Thromboembolism in Hospitalized Coronavirus Disease 2019 Patients: A Systematic Review and Meta-Analysis.](#)**

Zhang C. *Frontiers in Cardiovascular Medicine* 2020;7:151 .

This meta-analysis revealed that the estimated VTE incidence was 25% in hospitalized COVID-19 patients. Higher incidence of VTE was observed in COVID-19 patients with a severe condition or with a low rate of pharmacologic thromboprophylaxis. Assessment of VTE risk is strongly recommended in COVID-19 patients, and effective measures of thromboprophylaxis should be taken in a timely manner for patients with high risk of VTE.

*Freely available online*

<https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7423832/>

**[Prediction models for recurrence and bleeding in patients with venous thromboembolism: A systematic review and critical appraisal.](#)**

de Winter MA. *Thrombosis Research* 2021;199:85-96.

Prognostic models for recurrence and anticoagulation-related bleeding risk often have important methodological limitations and insufficient predictive accuracy. These findings do not support their use in clinical practice to weigh risks of recurrence and bleeding when deciding on continuing anticoagulation after initial treatment of VTE.

*Freely available online*

<https://pubmed.ncbi.nlm.nih.gov/33485094/>

**[Prevalence and Risk Factors of Thromboembolism among Patients With Coronavirus Disease-19: A Systematic Review and Meta-Analysis.](#)**

Kefale B. *Clinical and Applied Thrombosis/Hemostasis* 2020;26:1076029620967083 .

The pooled prevalence of thrombotic events in COVID-19 patients was 33%. The prevalence of thrombotic events is variable on the basis of study design and study centers. Several risk factors such as elevated D-dimer, hospitalized in the intensive care unit and being under mechanical ventilation, were the most frequently reported risk factors identified. Therefore, healthcare professionals should consider these risk factors to optimally manage thromboembolism in COVID-19 patients.

*Freely available online*

<https://journals.sagepub.com/doi/full/10.1177/1076029620967083>

**[Primary prophylaxis for venous thromboembolism in ambulatory cancer patients receiving chemotherapy.](#)**

Rutjes AW. *Cochrane Database of Systematic Reviews* 2020;12:CD008500.

BACKGROUND: Venous thromboembolism (VTE) often complicates the clinical course of cancer. The risk is further increased by chemotherapy, but the trade-off between safety and efficacy of primary thromboprophylaxis in cancer patients treated with chemotherapy is uncertain.

OBJECTIVES: To assess the efficacy and safety of primary thromboprophylaxis for VTE in ambulatory cancer patients receiving chemotherapy compared with placebo or no thromboprophylaxis, or an active control intervention.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD008500.pub4/full>

**[Prophylaxis of thromboembolism during therapy with asparaginase in adults with acute lymphoblastic leukaemia.](#)**

Rank CU. *Cochrane Database of Systematic Reviews* 2020;10:CD013399.

BACKGROUND: The risk of venous thromboembolism is increased in adults and enhanced by asparaginase-based chemotherapy, and venous thromboembolism introduces a secondary risk of treatment delay and premature discontinuation of key anti-leukaemic agents, potentially compromising survival. Yet, the trade-off between benefits and harms of primary thromboprophylaxis in adults with acute lymphoblastic leukaemia (ALL) treated according to asparaginase-based regimens is uncertain.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD013399/full>

**[Prothrombin complex concentrate vs. fresh frozen plasma in adult patients undergoing heart surgery - a pilot randomised controlled trial \(PROPHECY trial\).](#)**

Green L. *Anaesthesia* 2020;;doi: 10.1111/anae.15327.

Haemostatic tests have provided useful insight into the haemostatic changes following prothrombin complex concentrate or fresh frozen plasma administration. A definitive trial is needed to ascertain the benefits and safety for each.

<https://pubmed.ncbi.nlm.nih.gov/33285008/>

**[Risk of venous thromboembolism in patients with COVID-19: A systematic review and meta-analysis.](#)**

Nopp S. *Research and Practice in Thrombosis and Haemostasis* 2020;;doi.org/10.1002/rth2.12439.

VTE occurs in 22.7% of patients with COVID-19 in the ICU, but VTE risk is also increased in non-ICU hospitalized patients. Patients developing VTE had higher D-dimer levels. Studies evaluating thromboprophylaxis strategies in patients with COVID-19 are needed to improve prevention of VTE.

*Freely available online*

<https://onlinelibrary.wiley.com/doi/10.1002/rth2.12439>

### **[Risk-assessment models for VTE and bleeding in hospitalized medical patients: an overview of systematic reviews.](#)**

Darzi AJ. *Blood Advances* 2020;4(19):4929-4944 .

Multiple risk-assessment models (RAMs) for venous thromboembolism (VTE) in hospitalized medical patients have been developed. To inform the 2018 American Society of Hematology (ASH) guidelines on VTE, we conducted an overview of systematic reviews to identify and summarize evidence related to RAMs for VTE and bleeding in medical inpatients.

*Freely available online*

<https://ashpublications.org/bloodadvances/article/4/19/4929/464328/Risk-assessment-models-for-VTE-and-bleeding-in>

### **[The Incidence, Prognosis and Laboratory Indicators of Venous Thromboembolism in Hospitalized Patients with COVID-19: A Systematic Review and Meta-analysis.](#)**

Liu Y. *Journal of Vascular Surgery. Venous and Lymphatic Disorders* 2021;;doi: 10.1016/j.jvsv.2021.01.012.The occurrence of VTE, DVT, and PE is substantial among hospitalized COVID-19 patients, especially severe COVID-19 patients. Severe COVID-19 patients with VTE have significantly higher mortality rate than do patients without VTE. Increased values of D-dimer may be indicators of the occurrence of VTE in COVID-19 patients.

*Freely available online*

<https://pubmed.ncbi.nlm.nih.gov/33529719/>

### **[The Use of Therapeutic-Dose Anticoagulation and Its Effect on Mortality in Patients With COVID-19: A Systematic Review.](#)**

Wijaya I. *Clinical and Applied Thrombosis/Hemostasis* 2020;;doi.org/10.1177/1076029620960797.

The incidence of venous thromboembolism (VTE) events in patients with COVID-19 treated with a standard thromboprophylaxis dose of anticoagulants remains high. We conducted a systematic review in order to explore the association between therapeutic-dose anticoagulation and its effect on mortality in patients with COVID-19. Of 8 studies in review, 3 retrospective cohort studies reported reduction in mortality rate, while 5 other studies showed no mortality benefits in this population.

*Freely available online*

<https://journals.sagepub.com/doi/full/10.1177/1076029620960797>

### **[Thrombolytic strategies versus standard anticoagulation for acute deep vein thrombosis of the lower limb.](#)**

Broderick C. *Cochrane Database of Systematic Reviews* 2021;1:CD002783.

OBJECTIVES: To assess the effects of thrombolytic clot removal strategies and anticoagulation compared to anticoagulation alone for the management of people with acute deep vein thrombosis (DVT) of the lower limb.

<https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD002783.pub5/full>

### **[Venous thromboembolism risk with JAK inhibitors: A Meta-analysis.](#)**

Yates M. *Arthritis and Rheumatology* 2020;;doi.org/10.1002/art.41580.

This meta-analysis of RCT data defines the VTE risk with JAKi as a class in IMiD patients. The pooled IRR do not support current warnings around VTE risk for JAKi. The findings will aid continued development of clinical guidelines for the use of JAKi in IMiDs.

<https://onlinelibrary.wiley.com/doi/abs/10.1002/art.41580>

### **[What factors should be considered when using LMWH to treat venous thromboembolism in patients with high body weight?](#)**

Specialist Pharmacy Service (SPS); 2020.

This Q&A offers guidance on what factors should be considered when calculating a LMWH treatment dose following a VTE in non-pregnant adult patients with a high body weight, defined as more than 120 kg.

<https://www.sps.nhs.uk/articles/what-factors-should-be-considered-when-using-lmwh-to-treat-venous-thromboembolism-in-patients-with-high-body-weight/>

## Guidelines

The following new guidance has recently been published:

### **[American Society of Hematology 2021 guidelines on the use of anticoagulation for thromboprophylaxis in patients with COVID-19.](#)**

Cuker A. *Blood Advances* 2021;5(3):872-888.

<https://ashpublications.org/bloodadvances/article/5/3/872/475154/American-Society-of-Hematology-2021-guidelines-on>

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. They will be updated using a living recommendation approach as new evidence becomes available.

*Freely available online*

### **[COVID-19 rapid guideline: reducing the risk of venous thromboembolism in over 16s with COVID-19.](#)**

National Institute for Health and Care Excellence (NICE); 2020.

<https://www.nice.org.uk/guidance/ng186>

This guideline covers pharmacological VTE prophylaxis for patients being treated for COVID-19 pneumonia. It includes patients receiving treatment in hospital or in a community setting such as a 'hospital at home' service or COVID-19 'virtual ward'. The guideline applies to all patients with COVID-19 pneumonia, including those who have other conditions.

*Freely available online*

### **[Therapeutic anticoagulation \(Heparin\) in the management of severe covid-19 patients](#)**

Department of Health and Social Care (DHSC); 2020.

<https://icmanaesthesiacovid-19.org/s/CEM-CMO-2020-042.pdf>

Therapeutic doses of either unfractionated heparin (UFH) or subcutaneous low molecular weight heparin (LMWH) should not be offered in the treatment of patients with COVID-19, unless there is a standard indication for therapeutic anti-coagulation, such as the acute management of acute deep vein thromboses or pulmonary emboli, or as part of a clinical trial.

*Freely available online*

### **[Venous thromboembolism in adults: diagnosis and management.](#)**

National Institute for Health and Care Excellence (NICE); 2021.

<https://www.nice.org.uk/guidance/gs29>

This quality standard covers diagnosing and treating venous thromboembolism (VTE) in adults. VTE includes deep vein thrombosis (DVT) and pulmonary embolism. It describes high-quality care in priority areas for improvement. In January 2021, statement 3 in this quality standard was updated to better reflect our guidance on interim therapeutic anticoagulation for suspected pulmonary embolism.

*Freely available online*

### **[Warfarin and other anticoagulants - monitoring of patients during the COVID-19 pandemic.](#)**

Medicines and Healthcare Products Regulatory Agency (MHRA); 2020.

<https://www.gov.uk/government/publications/warfarin-and-other-anticoagulants-monitoring-of-patients-during-the-covid-19-pandemic>

MHRA has published guidance following concerns over an apparent increase in the number of patients taking warfarin found to have elevated INR values during the pandemic; and reminds healthcare professionals and patients that continued close INR monitoring is crucial.

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