

# COVID-19 Evidence Bulletin

# 25<sup>th</sup> October 2021

Details of new guidance and evidence relating to the response to COVID-19. Please check SaTH, NHS and Government guidance in conjunction with these resources where necessary.

## General

**COVID-19: Outpatient evaluation and management of acute illness in adults** [evidence summary from UpToDate]

[This topic will address the management of adult patients with acute COVID-19 in the outpatient setting (eg, <12 weeks after illness onset), including self-care advice, telehealth and outpatient clinic management, emergency department (ED) referral, and post-hospital discharge care.]

Available [here](#). Last updated 12<sup>th</sup> October

## Breastfeeding

**Using Tocilizumab or Sarilumab for hospitalised patients with COVID-19 who are breastfeeding**

[Specialist Pharmacy Service]

[Breastfeeding of full-term and healthy infants can continue if treatment with tocilizumab and sarilumab are required. If the infant was born prematurely, is unwell, or the mother is taking multiple medicines, the UK Drugs in Lactation Advisory Service should be contacted.]

Available [here](#)

**Breastfeeding with COVID-19 infection** [Specialist Pharmacy Service]

[It is recommended that breastfeeding should continue if the mother has COVID-19 infection. This page contains links to current advice and lists precautions that can be taken to reduce the risk of the infant becoming infected through close contact.]

Available [here](#)

## Complications

**Microcirculatory changes and thrombotic complications in COVID-19** [Das S. *British Journal of Community Nursing*]

[Key Points: The severity of the COVID-19 infection is related to the cytokine storm, hypoxic insult and activation of thrombosis; Patients with serious COVID-19 infections are mostly seen in the intensive care setting; Assessment of sublingual microcirculatory changes enables monitoring response to treatment and predict prognosis; There is evidence to suggest an increase in the incidence of venous and arterial thrombosis in patients with severe infection in the intensive care setting.]

Available [here](#). NHS OpenAthens account required.

## Convalescent Plasma

### **Results of the CAPSID randomized trial for high-dose convalescent plasma in severe COVID-19 patients**

[Körper S. *The Journal of Clinical Investigation*]

[COVID-19 convalescent plasma (CCP) added to standard treatment was not associated with significant improvement in the primary and secondary outcomes. A pre-defined subgroup analysis showed a significant benefit for CCP among those who received a larger amount of neutralizing antibodies.]

Freely available online

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## Diabetes

### **COVID-19, Hyperglycemia, and New-Onset Diabetes.**

Khunti K. *Diabetes Care* 2021;:dc211318.

[Article notes that the phenomenon of new-onset diabetes associated with COVID-19 is likely to be due to a number of complex interrelated processes including stress and steroid induced hyperglycaemia.

Authors state an urgent need for research to guide management pathways.]

Available [here](#)

### **Mortality Risk of Antidiabetic Agents for Type 2 Diabetes With COVID-19: A Systematic Review and Meta-Analysis**

[Kan C. *Frontiers in Endocrinology*]

[Metformin and sulfonylurea could be associated with reduced mortality risk in patients with T2DM who have COVID-19. Furthermore, insulin use could be associated with greater mortality, while DPP-4 inhibitor use could not be. The effects of antidiabetic agents in patients with T2DM who have COVID-19 require further exploration.]

Available [here](#)

## Digital Technologies

### **The role of contemporary digital tools and technologies in Covid-19 crisis: An exploratory analysis**

[Subramanian M. *Expert Systems*]

[The aim of this research is to look at possible technologies, processes, and tools for addressing Covid-19 issues such as pre-screening, early detection, monitoring infected/quarantined individuals, forecasting future infection rates, and more. We also look at the research possibilities that have arisen as a result of the use of emerging technology to handle the Covid-19 crisis.]

Available [here](#)

## Drug Therapy

### **COVID-19 rapid guideline: managing COVID-19**

[NICE]

[In October, NICE added new recommendations on casirivimab and imdevimab. New data on the use of heparins (from the REMAP-CAP trial results) does not change the current recommendations.]

Available [here](#)

**Combination therapies for COVID-19: an overview of the clinical trials landscape** [Akinbolade S. *British Journal of Clinical Pharmacology*]

[There are currently 744 therapeutics being tested in 2879 clinical trials globally, the majority (>90%) focused on monotherapies. This article reviews combination therapeutics targeting COVID-19, which have inherently complex clinical and regulatory development challenges.]

Freely available online

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**Antibiotics for the treatment of COVID-19** [Popp M. *Cochrane Database of Systematic Reviews*]

[OBJECTIVES: To assess the efficacy and safety of antibiotics compared to each other, no treatment, standard of care alone, placebo, or any other active intervention with proven efficacy for treatment of COVID-19 outpatients and inpatients. ]

Available [here](#)

**Efficacy and safety of ivermectin for the treatment of COVID-19: a systematic review and meta-analysis** [Deng J. *Quarterly Journal Of Medicine*]

[In review of 3 observational studies and 14 RCTs, the meta-analysis of RCTs found that ivermectin did not reduce time to viral clearance, duration of hospitalisation, incidence of mortality and incidence of mechanical ventilation. Evidence quality was very low to moderate.]

Available [here](#)

**Ruxolitinib and the Mitigation of Severe COVID-19: A Systematic Review and Meta-analysis** [Quiros JR. *Infection and Chemotherapy*]

[Review of 7 studies (n=168) found ruxolitinib had a higher likelihood of clinical improvement vs standard of care, but the difference was not statistically significant. Authors suggest further investigation is warranted into ruxolitinib as a treatment for severe COVID-19.]

Available [here](#)

**Effects of different corticosteroid therapy on severe COVID-19 patients: a meta-analysis of randomized controlled trials** [Tu J. *Expert Review of Respiratory Medicine*]

[Corticosteroid treatment did not convincingly improve survival in severe COVID-19 patients. Low-dose dexamethasone could be considered as a drug for the treatment of COVID-19 patients. More high-quality trials are needed to further verify this conclusion.]

Available [here](#)

**Safety and efficacy of different prophylactic anticoagulation dosing regimens in critically and non-critically ill patients with COVID-19: a systematic review and meta-analysis of randomized controlled trials** [Ortega-Paz L. *European Heart Journal - Cardiovascular Pharmacotherapy*]

[Review (7 RCTs; n=5,154) found escalated-dose prophylactic anticoagulation was associated with lower rates of VTE (2.5% vs. 4.7%; RR 0.55, 95% CI 0.41–0.74) but no benefit on other outcomes vs standard dose; and it increased risk of major bleeding (2.4% vs. 1.4%).]

Available [here](#)

**Colchicine for the treatment of COVID-19** [Mikolajewska A. *Cochrane Database of Systematic Reviews*]

[BACKGROUND: Colchicine is an anti-inflammatory medicine and is thought to improve disease outcomes in COVID-19 through a wide range of anti-inflammatory mechanisms.

OBJECTIVES: To assess the effectiveness and safety of Colchicine as a treatment option for COVID-19 in comparison to an active comparator, placebo, or standard care alone in any setting, and to maintain the currency of the evidence, using a living systematic review approach.]

Available [here](#)

### **Effect of antithrombotic therapy on clinical outcomes in outpatients with clinically stable symptomatic COVID-19: the ACTIV-4B randomized clinical trial** [*JAMA*]

[Among symptomatic clinically stable outpatients with COVID-19, treatment with aspirin or apixaban compared with placebo did not reduce the rate of a composite clinical outcome. However, the study was terminated after enrollment of 9% of participants because of an event rate lower than anticipated.]

Available [here](#)

### **Effectiveness of therapeutic heparin versus prophylactic heparin on death, mechanical ventilation, or intensive care unit admission in moderately ill patients with covid-19 admitted to hospital: RAPID randomised clinical trial** [Sholzberg M. *BMJ*]

[In moderately ill patients with covid-19 and increased D-dimer levels admitted to hospital wards, therapeutic heparin was not significantly associated with a reduction in the primary outcome but the odds of death at 28 days was decreased. The risk of major bleeding appeared low in this trial.]

Available [here](#)

## **Extracorporeal Membrane Oxygenation (ECMO)**

### **Extracorporeal membrane oxygenation for COVID-19: evolving outcomes from the international Extracorporeal Life Support Organization Registry** [Barbaro RP. *The Lancet*]

[Over the course of the COVID-19 pandemic, the care of patients with COVID-19 has changed and the use of extracorporeal membrane oxygenation (ECMO) has increased. Mortality after ECMO for patients with COVID-19 worsened during 2020. These findings inform the role of ECMO in COVID-19 for patients, clinicians, and policy makers.]

Available [here](#)

## **Health Services**

### **Agility: the missing ingredient for NHS productivity** [The Health Foundation]

[Some improvement approaches that can increase productivity, and how to make them happen]

Available [here](#)

## **HIV**

### **Associations between HIV infection and clinical spectrum of COVID-19: a population level analysis based on US National COVID Cohort Collaborative (N3C) data** [Yang X. *The Lancet HIV*]

[Given the COVID-19 pandemic's exacerbating effects on health inequities, public health and clinical communities must strengthen services and support to prevent aggravated COVID-19 outcomes among people with HIV, particularly for those with pronounced immunodeficiency.]

Available [here](#)

### **Sociodemographic, clinical, and immunological factors associated with SARS-CoV-2 diagnosis and severe COVID-19 outcomes in people living with HIV: a retrospective cohort study** [Nomah DK. *The Lancet HIV*]

[People living with HIV with detectable HIV viraemia, chronic comorbidities, and some subpopulations could be at increased risk of severe outcomes from COVID-19. These groups should be prioritised in clinical management and SARS-CoV-2 vaccination programmes.]

Available [here](#)

## Immunity

### **The durability of immunity against reinfection by SARS-CoV-2: a comparative evolutionary study**

[Townsend JP. *The Lancet Microbe*]

[The timeframe for reinfection is fundamental to numerous aspects of public health decision making. As the COVID-19 pandemic continues, reinfection is likely to become increasingly common. Maintaining public health measures that curb transmission—including among individuals who were previously infected with SARS-CoV-2—coupled with persistent efforts to accelerate vaccination worldwide is critical to the prevention of COVID-19 morbidity and mortality.]

Available [here](#)

### **Does infection with or vaccination against SARS-CoV-2 lead to lasting immunity?**

[Milne G. *The Lancet*]  
[This Personal View article reviews emerging data on cellular and humoral immunity to SARS-CoV-2, in response to natural infection and vaccination, and offers opinion on what the evidence means in terms of the longevity of protective immunity.]

Available [here](#)

## Long COVID

### **Post COVID syndrome referral pathways**

[Mak, V. *Primary Care Respiratory Update*]  
[PCS affects a significant proportion of people following acute COVID illness. The most common symptoms are fatigue, breathlessness, exertional malaise (mental and physical) and cognitive dysfunction. Patients presenting with these symptoms need a thorough assessment to exclude any treatable longterm complications following an acute COVID-19 illness.]

Available [here](#)

### **Addressing the post-acute sequelae of SARS-CoV-2 infection: a multidisciplinary model of care**

[Parker AM. *The Lancet Respiratory Medicine*]  
[Article highlights rigorous data characterising symptomology post-acute sequelae of SARS-CoV-2 infection are limited at present, but physical, psychological, cognitive, and respiratory domains are key among those affected. Authors recommend a multidisciplinary programme of care.]

Available [here](#)

### **A public health approach to estimating the need for long COVID services**

[Journal of Public Health]  
[This paper illustrates how a public health approach was used to influence and inform the development of post-COVID services across two Integrated Care Systems (ICSs). The findings have been valuable in informing early service developments, engaging with managers and clinicians, and supporting applications for funding at a local level.]

Available [here](#)

## Obstetrics and Gynaecology

### **Using Tocilizumab or Sarilumab for hospitalised patients with COVID-19 who are pregnant**

[Specialist Pharmacy Service]  
[This page signposts to current guidance on this off-label use of the two medicines from the UK Royal College of Obstetricians and Gynaecologists and UKTIS. Healthcare professionals are encouraged to contact UKTIS should they be considered for use.]

Available [here](#)

## Respiratory Care

### **Longitudinal respiratory subphenotypes in patients with COVID-19-related acute respiratory distress syndrome: results from three observational cohorts** [Bos LDJ. *The Lancet Respiratory Medicine*]

[At baseline, COVID-19-related ARDS has no consistent respiratory subphenotype. Patients diverged from a fairly homogenous to a more heterogeneous population, with trajectories of ventilatory ratio and mechanical power being the most discriminatory. Modelling these parameters alone provided prognostic value for duration of mechanical ventilation and mortality.]

Available [here](#)

### **The impact of COVID-19 on the sensitivity of D-dimer for pulmonary embolism** [Elberts SJ. *Academic Emergency Medicine*]

[Results from this multicenter retrospective study did not find a significant difference in sensitivity of D-dimer for PE due to concomitant COVID-19 infection. Further study is required to determine if PE can safely be excluded based on D-dimer results alone in patients with suspected or proven COVID-19 or if adjusted D-dimer levels could have a role in management.]

Available [here](#)

## Staff Wellbeing

### **"Surviving to thriving": a meta-ethnography of the experiences of healthcare staff caring for persons with COVID-19** [Agyei FB. *BMC Health Services Research*]

[Healthcare staff caring for persons infected with the Coronavirus disease are at risk of burnout and compassion fatigue and require ongoing mental health support commensurate to their needs. Staff who contract the disease may require additional support to navigate through the illness and recovery. Policies and concerted efforts are needed to strengthen support systems and build resilience among healthcare staff.]

Available [here](#)

### **'Fix the issues at the coalface and mental wellbeing will be improved': a framework analysis of frontline NHS staff experiences and use of health and wellbeing resources in a Scottish health board area during the COVID-19 pandemic** [Clarissa C. *BMC Health Services Research*]

[Our findings show that despite the provision of relaxational and cognitive behavioural interventions to support staff wellbeing during the early months of the COVID-19 pandemic, there were barriers to access, including heavy workload, understaffing, inconvenient locations and the stigma of being judged. Organisational factors were the most frequently reported support need amongst frontline staff across sites.]

Available [here](#)

## Speech and Language Therapy

### **Speech and language therapy during and beyond COVID-19: building back better with people who have communication and swallowing needs** [Royal College of Speech and Language Therapists]

[This RCSLT report shares people's experiences of accessing speech and language therapy during the first UK-wide lockdown. It also sets out what needs to happen to ensure that people with communication and swallowing needs can access the speech and language therapy that they need.]

Available [here](#)

## Supplementation

**Zinc supplementation as an adjunct therapy for COVID-19: Challenges and opportunities** [Chinni C. *British Journal of Pharmacology*]

[This article discusses the current literature on zinc supplementation challenges and highlights the importance of using an effective zinc delivery method to achieve its potential as a therapeutic agent against COVID-19 infection.]

Available [here](#)

## Transmissibility

**Transmissibility of COVID-19 Among Vaccinated Individuals: Targeted Literature Search** [SPOR Evidence Alliance]

[This rapid review examines transmissibility of COVID-19 by individuals who have been vaccinated but who still catch the virus. Researchers do not yet fully understand “asymptomatic” infection, and are looking to understand whether vaccinated people who catch COVID-19 are less infectious than unvaccinated people with the virus. The studies reviewed for this report suggest that being either partly or fully vaccinated reduces both the chance of asymptomatic infection and of infecting others.]

Available [here](#)

## Vaccination

**COVID-19 vaccination: women of childbearing age, currently pregnant or breastfeeding** [UK Health Security Agency]

[Information for all women of childbearing age, those currently pregnant or breastfeeding on coronavirus (COVID-19) vaccination. 8 October 2021: Updated 'COVID-19 vaccination: a guide on pregnancy and breastfeeding' and links to translated versions of the poster and social media cards.]

Available [here](#)

**Effectiveness of mRNA BNT162b2 COVID-19 vaccine up to 6 months in a large integrated health system in the USA: a retrospective cohort study** [Tartof SY. *The Lancet*]

[Our results provide support for high effectiveness of BNT162b2 against hospital admissions up until around 6 months after being fully vaccinated, even in the face of widespread dissemination of the delta variant. Reduction in vaccine effectiveness against SARS-CoV-2 infections over time is probably primarily due to waning immunity with time rather than the delta variant escaping vaccine protection.]

Available [here](#)

**COVID-19 hospital admissions and deaths after BNT162b2 and ChAdOx1 nCoV-19 vaccinations in 2.57 million people in Scotland (EAVE II): a prospective cohort study** [Agrawal U. *The Lancet Respiratory Medicine*]

[COVID-19 hospitalisations and deaths were uncommon 14 days or more after the first vaccine dose in this national analysis in the context of a high background incidence of SARS-CoV-2 infection. Sociodemographic and clinical features known to increase the risk of severe disease in unvaccinated populations were also associated with severe outcomes in people receiving their first dose of vaccine and could help inform case management and future vaccine policy formulation.]

Available [here](#). NHS OpenAthens account required

### **KnowledgeShare Evidence Alerts**

KnowledgeShare contains many updates on COVID-19 that can be accessed from the KnowledgeShare website without a password. If you'd like to receive these by email (along with updates on any other topics of interest) please complete the [form](#).

### **About this bulletin**

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