

# Respiratory Bulletin

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## General

### Articles

[Antihypertensive treatment and risk of cancer: an individual participant data meta-analysis.](#) - Copland E, et al. *The Lancet Oncology* 2021;22(4):P558-570.

This analysis (33 trials, n=260,447 with 15,012 cancer events) found no consistent evidence that antihypertensive medication use had any effect on cancer risk. Evidence for some comparisons was insufficient to entirely rule out excess risk e.g. calcium channel blockers.

[Disease burden and quality of life of patients with chronic cough in Japan: a population-based cross-sectional survey](#) - Kubo T, et al. *BMJ Open Respiratory Research* 2021;8:e000764.

Background: Cough lasting 3–8 and >8 weeks are defined as subacute/prolonged cough and chronic cough (CC), respectively. Studies have revealed that CC negatively impact patients' quality of life (QoL). In Japan, there is limited data on the impact of CC on health-related quality of life (HRQoL), work productivity and activity impairment (WPAI) and healthcare resource utilisation (HRU) using validated instruments. This study aimed to estimate the burden of CC and to compare the burden among patients with CC between subgroups.

[Journal club](#) - Thompson E. *Thorax* 2021;76:318.

[Racial microaggressions within respiratory and critical care medicine](#) - Babla K, et al. *Lancet Respiratory Medicine*, 2021, 9(3), ee.27-28.

The past year has seen much attention paid to racism and racial inequality in medicine, and in wider society. 1 In many countries, students and health-care professionals from ethnic minority backgrounds continue to have poor educational attainment, low pay and are under-represented in senior leadership roles. 234 But it has been the events surrounding the murder of George Floyd and the resulting protests that have brought racism and inequality in wider society, once again, to the top of the agenda. Impassioned dialogue around the world has occurred about racism, what qualifies as racism, and its definition including colourism, anti-Blackness in the Asian communities, and more recently, anti-Chinese sentiments in the wake of the COVID-19 pandemic.

[Short term associations of ambient nitrogen dioxide with daily total, cardiovascular, and respiratory mortality: multilocation analysis in 398 cities.](#) - Meng X, et al. *BMJ* 2021;372:n534.

This multilocation study provides key evidence on the independent and linear associations between short term exposure to NO<sub>2</sub> and increased risk of total, cardiovascular, and respiratory mortality, suggesting that health benefits would be achieved by tightening the guidelines and regulatory limits of NO<sub>2</sub>.

## Acute respiratory failure

### Articles

[High-flow nasal cannulae for respiratory support in adult intensive care patients.](#) - Lewis SR, et al. *Cochrane Database of Systematic Reviews* 2021;3:CD010172.

BACKGROUND: High-flow nasal cannulae deliver high flows of blended humidified air and oxygen via wide-bore nasal cannulae and may be useful in providing respiratory support for adults experiencing acute respiratory failure, or at risk of acute respiratory failure, in the ICU.

OBJECTIVES: To assess the effectiveness of HFNC compared to standard oxygen therapy, or non-invasive ventilation (NIV) or non-invasive positive pressure ventilation (NIPPV), for respiratory support in adults in the ICU.



## Articles

[Advanced glycation end products and wheeze: a plausible association?](#) - Grigg J. *Thorax* 2021;76:219.

In 1912 the French scientist Louis Camille Maillard, while attempting to synthesise proteins in his laboratory, ended up creating a byproduct that had a meaty aroma and flavour. The eponymous Maillard reaction produces many chemical compounds depending on the type of food, cooking time, temperature and presence of air. One class of Maillard-generated compounds receiving recent research attention is advanced glycation end products (AGEs), which are generated during high-temperature cooking. Animal-derived foods high in fat and protein are generally AGE-rich and prone to new formation of AGEs during cooking. Once ingested, AGEs act via engaging with the type I receptor for advanced glycation end-products (RAGE), and increasing evidence shows a role for RAGE in asthma pathogenesis. For example, Perkins et al<sup>1</sup> reported that the RAGE knockout mouse is resistant to airway inflammation induced by intranasal type 2 cytokines, and Brandt and Lewkowich<sup>2</sup> in a recent review of RAGE-induced asthma concluded that understanding the mechanisms by which RAGE inhibition attenuates Th2 cytokine signalling cascades might allow for development of novel therapeutics.

[Characterisation of patients with severe asthma in the UK Severe Asthma Registry in the biologic era](#) -

Jackson DJ, et al. *Thorax* 2021;76:220-227.

Background: The UK Severe Asthma Registry (UKSAR) is the world's largest national severe asthma registry collecting standardised data on referrals to UK specialist services. Novel biologic therapies have transformed the management of type 2(T2)-high severe asthma but have highlighted unmet need in patients with persisting symptoms despite suppression of T2-cytokine pathways with corticosteroids.

[Efficacy of one time per day, single-inhaler indacaterol/glycopyrronium/mometasone in patients with inadequately controlled asthma: post hoc analysis of IRIDIUM study in Asian population](#) - Sagara H, et al.

*BMJ Open Respiratory Research* 2021;8:e000856.

Background and objective: The 52-week IRIDIUM study demonstrated the efficacy of indacaterol acetate/glycopyrronium bromide/mometasone furoate (IND/GLY/MF) versus IND/MF and salmeterol xinafoate/fluticasone propionate (SAL/FLU) in patients with symptomatic asthma, despite long-acting  $\beta_2$ -agonist/inhaled corticosteroids (LABA/ICS) medium-dose or high-dose, predicted forced expiratory volume in 1 s (FEV1) <80% and at least one exacerbation in the previous year. Here, we present data from a post hoc analysis of the IRIDIUM study in the Asian subpopulation.

[Impact of COVID-19 national lockdown on asthma exacerbations: interrupted time-series analysis of English primary care data.](#) - Shah SA. *Thorax* 2021;;doi: 10.1136/thoraxjnl-2020-216512 .

There has been a significant reduction in attendance to primary care for asthma exacerbations during the pandemic. This reduction was observed in all age groups, both sexes and across most regions in England.

[Increased advanced glycation end product and meat consumption is associated with childhood wheeze: analysis of the National Health and Nutrition Examination Survey](#) - Wang JG, et al. *Thorax* 2021;76:292-294.

We examined 4388 children from the 2003 to 2006 National Health and Nutrition Examination Survey and used survey-design-adjusted multivariable logistic regression to evaluate associations between dietary advanced glycation end product (AGE) and meat consumption frequencies and respiratory symptoms. Higher AGE intake was significantly associated with increased odds of wheezing (adjusted OR 1.18; 95% CI 1.02 to 1.36), wheeze-disrupted sleep (1.26; 95% CI 1.05 to 1.51) and exercise (1.34; 95% CI 1.08 to 1.67) and wheezing requiring prescription medication (1.35; 95% CI 1.13 to 1.63). Higher intake of non-seafood



meats was associated with wheeze-disrupted sleep (2.32; 95% CI 1.11 to 4.82) and wheezing requiring prescription medication (2.23; 95% CI 1.10 to 4.54).

### [Onset of effect and impact on health-related quality of life, exacerbation rate, lung function, and nasal polyposis symptoms for patients with severe eosinophilic asthma treated with benralizumab \(ANDHI\): a randomised, controlled, phase 3b trial](#)

Harrison TW, et al. *Lancet Respiratory Medicine*, 2021, 9(3), pp.260-274.

Background: ANDHI was done to assess the efficacy of benralizumab, including onset of effect and impact on health-related quality of life (HRQOL), exacerbation rate, lung function, and nasal polyposis symptoms.

### [Relationship of Pneumocystis antibody responses to paediatric asthma severity](#)

Rayens E, et al. *BMJ Open Respiratory Research* 2021;8:e000842.

Background: Although asthma is the most commonly diagnosed respiratory disease, its pathogenesis is complex, involving both genetic and environmental factors. A role for the respiratory microbiome in modifying asthma severity has been recently recognised. Airway colonisation by *Pneumocystis jirovecii* has previously been associated with multiple chronic lung diseases, including chronic obstructive pulmonary disease (COPD) and severe asthma (SA). Decreased incidence of *Pneumocystis pneumonia* in HIV-infected individuals and reduced severity of COPD is associated with naturally occurring antibody responses to the *Pneumocystis* antigen, Kexin (KEX1).

### [Risks of and from SARS-COV-2 \(COVID-19\) infection in people with asthma - CEBM Oxford COVID-19 Evidence Service; 2021.](#)

In the context of the COVID-19 pandemic, WHO and WHO Member States are requesting information and guidance on key topics related to COVID-19 and the virus which causes the disease SARS-COV-2. This rapid review was commissioned to address specific key questions for WHO to provide high-quality, evidence-informed information products around COVID-19. This review presents a summary of the latest research evidence on the effects of COVID-19 in people with asthma (PWA).

### [Unnecessary antibiotic prescribing in children hospitalised for asthma exacerbation: a retrospective national cohort study.](#) - Jewell MJ, et al. *BMJ Quality & Safety* 2021;30(4):292-299.

Conclusions: These findings illustrate an opportunity to reduce unnecessary exposure to antibiotics in children hospitalised with asthma, particularly in general hospitals where three-quarters of children in the USA receive their hospital-based care.

## **Guidelines**

[Asthma: diagnosis, monitoring and chronic asthma management.](#) - National Institute for Health and Care Excellence (NICE); 2021.

This guideline covers diagnosing, monitoring and managing asthma in adults, young people and children. It aims to improve the accuracy of diagnosis, help people to control their asthma and reduce the risk of asthma attacks. It does not cover managing severe asthma or acute asthma attacks. In March 2021, we highlighted the importance of including advice in the personalised action plan on minimising indoor air pollution and reducing exposure to outdoor air pollution.



## What's New in Asthma from UpToDate

### [Lack of benefit for investigational TLR9 agonist in asthma \(March 2021\)](#)

Toll-like receptor 9 (TLR9), part of the innate immune system, recognizes cytosine guanine dinucleotide (CpG) motifs in microbial DNA and shifts T helper (Th) lymphocyte responses from Th2- to Th1-dominant. As asthma is generally a Th2-dominant disease, it was hypothesized that a shift towards Th-1 dominance would ameliorate asthma. In a randomized trial of 81 participants with moderate to severe asthma (using an inhaled glucocorticoid and long-acting beta agonist LABA as their only maintenance treatment), time to loss of asthma control after staged withdrawal of maintenance treatment was not significantly different for patients assigned to inhaled AZD1419, an investigational oligonucleotide containing CpG motifs known to activate TLR9, compared with placebo 1. A Th-1 response with a sustained reduction in markers of type 2 inflammation occurred in the treatment group and no deaths or serious adverse events were attributable to AZD1419. These findings do not support a benefit for TLR2 agonist therapy in adults with moderate to severe asthma.

## Bronchial diseases

### Articles

[‘It’s not one size fits all’: a qualitative study of patients’ and healthcare professionals’ views of self-management for bronchiectasis](#) - Kelly CA, et al. *BMJ Open Respiratory Research* 2021;8:e000862.

Background: Bronchiectasis is a chronic respiratory condition that impacts significantly on individuals and healthcare services. Self-management is recommended in clinical guidelines for bronchiectasis as an intervention to enable patients to manage their condition, yet there is little evidence to support it.

## Cancers of the respiratory tract

### Articles

[Camrelizumab plus carboplatin and pemetrexed versus chemotherapy alone in chemotherapy-naive patients with advanced non-squamous non-small-cell lung cancer \(CameL\): a randomised, open-label, multicentre, phase 3 trial](#) - Zhou C, et al. *Lancet Respiratory Medicine*, 2021, 9(3), pp.305-314.

Background: Immunotherapy combined with chemotherapy has been shown to be efficacious as treatment for advanced non-squamous non-small-cell lung cancer (NSCLC) without targetable genetic aberrations; however, there is scarce evidence of the effectiveness of the combinations in the Asian population. We evaluated camrelizumab plus chemotherapy against non-squamous NSCLC in China.

[Current Treatment Strategies and Future Directions for Extrapulmonary Neuroendocrine Carcinomas: A Review.](#) - Stelwagen J, De Vries EGE, Walenkamp AME. *JAMA Oncology* 2021

This review notes the introduction of immune checkpoint inhibitors signifies the first new systemic treatment option for small cell lung cancer in decades. Patients with EPNC need to be included in clinical trials to prove the value of these and other new drugs for these patients.

[Laryngeal Solitary Fibrous Tumor: A Case Report and Systematic Review.](#) - Yang J, Tamares S, Crawley BK. *Journal Of Voice* 2021;35(1):136-142.

Laryngeal solitary fibrous tumors are rare and are unlikely to recur in the absence of malignant findings. Complete surgical resection is an acceptable treatment for this lesion accompanied by appropriate follow-up.

[Managing employment among pre-retirement aged cancer survivors.](#) - Hunter EG, Rowles GD. *British Journal of Occupational Therapy* 2021;84(3):183-191.

Successfully maintaining (managing) paid employment can be a challenge as people negotiate the cancer care pathway and survivorship. Little research explores the influence of age on this situation. The purpose



of this project was to explore the role of age in managing employment for survivors from age 45 to 64 years.

[The oral microbiome and lung cancer risk](#) - Christiani DC. *Thorax* 2021;76:216-217.

The oral cavity is instrumental to the human body in several ways. It is the entry point for both ingested (to the GI tract) and inhaled (to the respirable tract) substances. The oral microbiome resides within biofilms throughout the oral cavity and forms an ecosystem that helps to maintain health. The breadth and depth of the oral microbiome is impressive: 1 mL of saliva contains 10<sup>8</sup> microbial cells and 700 distinct prokaryotic taxa. There are rich communities such as bacteria, fungi, viruses, archaea and protists, among which about 54% are cultivatable and identified, 14% are cultivatable, but not identified, and 32% are not even cultivatable.<sup>1</sup> Caselli et al defined the oral microbiome in 20 healthy individuals from Europe by whole genome sequencing (WGS) and reported that  $\alpha$ -diversity differed significantly among the different microsites in the mouth of each participant, but not among the participants, supporting the notion of a recognisable healthy oral microbiome.

[Variation in oral microbiome is associated with future risk of lung cancer among never-smokers](#) - Hosgood HD, et al. *Thorax* 2021;76:256-263.

Objective: To prospectively investigate whether diversity in oral microbiota is associated with risk of lung cancer among never-smokers.

## Guidelines

[Pembrolizumab with pemetrexed and platinum chemotherapy for untreated, metastatic, non-squamous non-small-cell lung cancer](#). - National Institute for Health and Care Excellence (NICE); 2021.

1 Recommendations 1.1 Pembrolizumab with pemetrexed and platinum chemotherapy is recommended as an option for untreated, metastatic, non-squamous non-small-cell lung cancer in adults whose tumours have no epidermal growth factor receptor (EGFR)-positive or anaplastic lymphoma kinase (ALK)-positive mutations. This is only if: it is stopped at 2 years of uninterrupted treatment, or earlier if the disease progresses and the company provides pembrolizumab according to the commercial arrangement.

## Websites

[Cancer in children and young people – what do the statistics tell us?](#) - Public Health Matters; 2021.

We have published the first UK-wide report on children, teenage and young adult cancers in almost a decade. The report combines data on cancer incidence, survival and mortality from cancer registries in the four UK countries and this blog looks at 5 of the key points.

[Cancer in children, teenagers and young adults](#) - National Cancer Registration and Analysis Service; 2021.

Data from the four UK national cancer registries to describe the incidence, survival and mortality from cancer diagnosed among children, teenagers and young adults resident in the United Kingdom. The analysis relates to children and young people who were diagnosed with cancer under the age of 25 during the 20-year period of 1997-2016.



## Chest imaging

### Articles

[Elderly Man With Chest Pressure](#). - Unold J, Olsen E. *Annals of Emergency Medicine* 2021;77(4):415-467. A 78-year-old man was rushed to the emergency department (ED) from an outpatient computed tomography (CT) imaging suite with complaints of chest pressure. The diagnosis was iatrogenic air embolism within the right ventricle from a peripheral intravenous catheter.

## COPD

### Articles

[Associations of CT evaluations of antigravity muscles, emphysema and airway disease with longitudinal outcomes in patients with COPD](#) - Tanabe N, et al. *Thorax* 2021;76:295-297.

Multiple CT indices are associated with disease progression and mortality in patients with COPD, but which indices have the strongest association remain unestablished. This longitudinal 10-year observational study (n=247) showed that the emphysema severity on CT is more closely associated with the progression of airflow limitation and that a reduction in the cross-sectional area of erector spinae muscles (ESMCSA) on CT is more closely associated with mortality than the other CT indices, independent of patient demographics and pulmonary function. ESMCSA is a useful CT index that is more closely associated with long-term mortality than emphysema and airway disease in patients with COPD.

[Chr15q25 genetic variant \(rs16969968\) independently confers risk of lung cancer, COPD and smoking intensity in a prospective study of high-risk smokers](#) - Hopkins RJ, et al. *Thorax* 2021;76:272-280.

Importance: While cholinergic receptor nicotinic alpha 5 (CHRNA5) variants have been linked to lung cancer, chronic obstructive pulmonary disease (COPD) and smoking addiction in case–controls studies, their corelationship is not well understood and requires retesting in a cohort study.

[Inspiratory crackles—early and late—revisited: identifying COPD by crackle characteristics](#) - Melbye H, et al. *BMJ Open Respiratory Research* 2021;8:e000852.

Background: The significance of pulmonary crackles, by their timing during inspiration, was described by Nath and Capel in 1974, with early crackles associated with bronchial obstruction and late crackles with restrictive defects. Crackles are also described as ‘fine’ or ‘coarse’. We aimed to evaluate the usefulness of crackle characteristics in the diagnosis of chronic obstructive pulmonary disease (COPD).

[Pharmacotherapy and Lung Function Decline in Patients with Chronic Obstructive Pulmonary Disease. A Systematic Review](#). - Celli BR, et al. *American Journal of Respiratory and Critical Care* 2021;203(6):689-698.

In chronic obstructive pulmonary disease, pharmacotherapy ameliorates rate of lung function decline. The relative benefit observed is within the range of those reported for health status and exacerbations in the same studies. Guidelines should be adjusted according to these findings.

[Transitions between COPD groups: A cross-sectional study in Turkey](#) - Turan PA, et al. *Respiratory Medicine*, 2021, 178, 106310.

Introduction: Since GOLD 2017 separates spirometry results from ‘ABCD’ groups, there have been some changes to the stages of COPD patients. Our aim was to investigate the shifts in COPD groups after GOLD 2017.





[Supervised pulmonary rehabilitation using minimal or specialist exercise equipment in COPD: a propensity-matched analysis](#) - Patel S, et al. *Thorax* 2021;76:264-271.

Background: Many trials supporting the benefits of pulmonary rehabilitation (PR) have used specialist exercise equipment, such as treadmills and cycle ergometers. However, access to specialist equipment may not be feasible in some settings. There is growing interest in delivering PR programmes with minimal, low-cost equipment, but uncertainty remains regarding their efficacy compared with programmes using specialist equipment.

[SZ alpha-1 antitrypsin deficiency and pulmonary disease: more like MZ, not like ZZ](#) - Franciosi AN, Carroll TP, McElvaney NG. *Thorax* 2021;76:298-301.

The ZZ genotype of alpha-1 antitrypsin deficiency (AATD) is associated with COPD regardless of smoking. Heterozygous MZ-AATD is recognised as a moderate deficiency state, increasing the risk of COPD only among smokers. The risk attributable to SZ-AATD remains debated. We compared 486 AATD-registry participants, to determine whether SZ-AATD was associated with pulmonary outcomes more comparable to MZ-AATD or ZZ-AATD. We found no significant differences between MZ and SZ individuals regardless of never-smoking/ever-smoking ( $p > 0.05$  for all). ZZ-AATD was associated with lower FEV<sub>1</sub>pp than SZ, regardless of never-smoking/ever-smoking, as well as an increased OR of lung-index status and visually defined emphysema on CT ( $p \leq 0.002$  for all). In our registry cohort SZ-AATD is associated with a risk of lung disease comparable to MZ, not ZZ-AATD.

[Validity and responsiveness of the Daily- and Clinical visit-PROactive Physical Activity in COPD \(D-PPAC and C-PPAC\) instruments](#) - Garcia-Aymerich J, et al. *Thorax* 2021;76:228-238.

Background: The Daily-PROactive and Clinical visit-PROactive Physical Activity (D-PPAC and C-PPAC) instruments in chronic obstructive pulmonary disease (COPD) combines questionnaire with activity monitor data to measure patients' experience of physical activity. Their amount, difficulty and total scores range from 0 (worst) to 100 (best) but require further psychometric evaluation.

## Cystic fibrosis

### What's New in COPD from UpToDate

#### [CFTR modulator therapy for advanced cystic fibrosis-related lung disease \(March 2021\)](#)

Cystic fibrosis transmembrane regulator (CFTR) modulators have clear benefits for most patients with cystic fibrosis (CF), but limited data are available regarding their safety and efficacy in those with advanced lung disease. In a new observational study of 245 patients with CF and advanced lung disease, treatment with elexacaftor-tezacaftor-ivacaftor for one to three months was associated with marked improvement in lung function (mean increase in forced expiratory volume in one second 15.1 percent predicted) and mostly mild adverse effects (primarily cutaneous rash and gastrointestinal symptoms) 10. In addition, the number of patients requiring enteral feeding, chronic oxygen, or noninvasive ventilation decreased by 50, 50, and 30 percent, respectively while mean body weight increased by 4.2 kg. In 45 patients, the rapid improvement in lung function was sufficient to remove them from lung transplant consideration during the study period. These findings support our recommendation to initiate CFTR modulator therapy in eligible patients with advanced lung disease, similar to the approach for other patients with cystic fibrosis; long term follow-up is needed to determine the duration of efficacy.





### General

#### Articles

[Ambient air pollution and risk of respiratory infection among adults: evidence from the multiethnic study of atherosclerosis \(MESA\)](#) - Kirwa K, et al. *BMJ Open Respiratory Research* 2021;8:e000866.

Background: Air pollution may affect the risk of respiratory infection, though research has focused on uncommon infections or infections in children. Whether ambient air pollutants increase the risk of common acute respiratory infections among adults is uncertain, yet this may help understand whether pollutants influence spread of pandemic respiratory infections like COVID-19.

[Effect of patient immunodeficiencies on the diagnostic performance of serological assays to detect Aspergillus -specific antibodies in chronic pulmonary aspergillosis](#) - Hunter ES, et al. *Respiratory Medicine*, 2021, 178, 106290.

Background: Prevalence of chronic pulmonary aspergillosis (CPA) is ~3 million patients worldwide, and detection of Aspergillus -specific antibody is a critical diagnostic component. Some patients with CPA have subtle immune deficits possibly contributing to poor Aspergillus antibody production and false negative results.

[Geographical and socioeconomic differences in compliance with and access to allergen immunotherapy in Denmark: A nationwide registry-based study – 1998-2016](#) - Borg M, Løkke A, Hilberg O. *Respiratory Medicine*, 2021, 178, 106332.

Background: Allergen immunotherapy (AIT) is a cost-effective treatment option in moderate-severe allergic rhino-conjunctivitis. Inequality in access to AIT and variation in compliance related to socioeconomic status or geographical location have not been described previously.

### COVID-19

#### Articles

[Association between influenza vaccination and hospitalisation or all-cause mortality in people with COVID-19: a retrospective cohort study](#) - Wilcox CR, Islam N, Dambha-Miller H. *BMJ Open Respiratory Research* 2021;8:e000857.

Introduction: Recent evidence suggests that influenza vaccination may offer protection against COVID-19 severity. Our aim was to quantify the association between influenza vaccination status and risk of hospitalisation or all-cause mortality in people diagnosed with COVID-19.

[Characteristics and outcomes in hospitalized COVID-19 patients during the first 28 days of the spring and autumn pandemic waves in Milan: An observational prospective study](#) - Radovanovic D, et al. *Respiratory Medicine*, 2021, 178, 106323.

Background: The therapeutic approach to COVID-19 and healthcare system preparedness improved during 2020. We compared characteristics and outcomes of hospitalized COVID-19 patients during the first 28 days of the March and October pandemic waves in Milan, Italy.

[Clinical characteristics and outcomes of adult patients admitted with COVID-19 in East London: a retrospective cohort analysis](#) - Cheng D, et al. *BMJ Open Respiratory Research* 2021;8:e000813.

Background: Descriptions of clinical characteristics of patients hospitalised with COVID-19, their clinical course and short-term inpatient and outpatient outcomes in deprived urban populations in the UK are still



relatively sparse. We describe the epidemiology, clinical course, experience of non-invasive ventilation and intensive care, mortality and short-term sequelae of patients admitted to two large District General Hospitals across a large East London National Health Service Trust during the first wave of the pandemic.

[Colchicine and SARS-CoV-2: Management of the hyperinflammatory state](#) - Vitiello A, Ferrara F. *Respiratory Medicine*, 2021, 178, 106322.

The global COVID-19 pandemic is currently underway. In December 2020, the European Agency of Medicine (EMA) licensed the first Sars-CoV-2 vaccine. Therapeutic management of the COVID-19 positive patient should primarily aim to avoid the severe complications and organ injury caused by generalized inflammation caused by a cytokine storm and occurring in the most severe stages of viral infection. Current knowledge of the pathophysiological mechanisms of SARS-CoV-2 suggests a central role for exaggerated activation of the innate immune system as an important contributor to the adverse outcomes of COVID-19. Several studies have shown that blocking the cytokine storm or acting early with prevention of it can be effective; studies are underway to evaluate agents that may be able to reduce this hyperinflammatory state. The search for effective management strategies for COVID-19 continues to evolve. The actions of colchicine, one of the oldest anti-inflammatory therapies, target multiple targets associated with excessive COVID-19 inflammation. Colchicine is easily administered, generally well tolerated, and inexpensive. This article reports the scientific and molecular rationale for the use of colchicine as monotherapy or in combination in the various stages of SARS-CoV-2 infection to modulate and control the inflammatory state. Low-dose colchicine may be considered safe and effective for the treatment and prevention of cytokine storm in patients with SARS-CoV-2 infection, particularly as an adjunctive remedy to other therapeutic agents. Well-organized clinical studies are needed in this direction.

[A comparison of characteristics and outcomes of patients with community-acquired and hospital-acquired COVID-19 in the United Kingdom: An observational study](#) - Shiwani HA, et al. *Respiratory Medicine*, 2021, 178, 106314.

Background and objectives: Reports comparing the characteristics of patients and their clinical outcomes between community-acquired (CA) and hospital-acquired (HA) COVID-19 have not yet been reported in the literature. We aimed to characterise and compare clinical, biochemical and haematological features, in addition to clinical outcomes, between these patients.

[Comparison of the characteristics, morbidity, and mortality of COVID-19 and seasonal influenza: a nationwide, population-based retrospective cohort study](#) - Piroth L, et al. *Lancet Respiratory Medicine*, 2021, 9(3), pp.251-259.

Background: To date, influenza epidemics have been considered suitable for use as a model for the COVID-19 epidemic, given that they are respiratory diseases with similar modes of transmission. However, data directly comparing the two diseases are scarce.

[Continuation versus discontinuation of renin–angiotensin system inhibitors in patients admitted to hospital with COVID-19: a prospective, randomised, open-label trial](#) - Cohen JB, et al. *Lancet Respiratory Medicine*, 2021, 9(3), pp.275-284.

Background: Biological considerations suggest that renin–angiotensin system inhibitors might influence the severity of COVID-19. We aimed to evaluate whether continuing versus discontinuing renin–angiotensin system inhibitors (angiotensin-converting enzyme inhibitors or angiotensin receptor blockers) affects outcomes in patients admitted to hospital with COVID-19.



[COVID-19: a heavy toll on health-care workers](#) - Mehta S, et al. *Lancet Respiratory Medicine*, 2021, 9(3), pp.226-228.

The COVID-19 pandemic has challenged and, in many cases, exceeded the capacity of hospitals and intensive care units (ICUs) worldwide. Health-care workers have continued to provide care for patients despite exhaustion, personal risk of infection, fear of transmission to family members, illness or death of friends and colleagues, and the loss of many patients. Sadly, health-care workers have also faced many additional—often avoidable—sources of stress and anxiety, and long shifts combined with unprecedented population restrictions, including personal isolation, have affected individuals' ability to cope.

[The COVID-19 ibuprofen controversy: A systematic review of NSAIDs in adult acute lower respiratory tract infections.](#) - Vaja R, et al. *British Journal of Clinical Pharmacology* 2021;87(3):776-784.

In this systematic review of NSAID use during acute lower respiratory tract infections in adults, we found that the existing evidence for mortality, pleuro-pulmonary complications and rates of mechanical ventilation or organ failure is of extremely poor quality, very low certainty and should be interpreted with caution.

[COVID-19 is not influenza](#) - Petersen E. *Lancet Respiratory Medicine*, 2021, 9(3), pp.219-220.

COVID-19 is often compared to influenza. In the middle of a pandemic with a new coronavirus transmitted from the respiratory tract, it is obvious to look at previous influenza pandemics and seasonal influenza for comparison. Yet it is important to understand that COVID-19 is not influenza. During the COVID-19 pandemic, several countries have struggled with overburdened intensive care unit capacity, whereas during the H1N1 pandemic in 2009, intensive care unit capacity was sufficient. For example, influenza never exceeded 4.5% of the total national intensive care unit (ICU) bed capacity in Denmark. 1 In the spring of 2020, mortality for COVID-19 in Lombardia, Italy, reached 159 per 100 000 population. 2 By contrast, a study of influenza deaths during the 2009 pandemic estimated the all-age mortality in the USA to be 4.1 per 100 000.

[Each person is a world in COVID-19](#) - Ely EW. *Lancet Respiratory Medicine*, 2021, 9(3), pp.236-237.

I believe it is our age-old acknowledgment of the dignity and self-worth of others that catapults us into caring enough to change health care for the better. From Aristotle to Boethius and down through the centuries, we recognise the unity of body, mind, and spirit in human beings. Medicine is a vocation of service, not merely a career by which to make money. It is about the relationship between people and is unavoidably an ethical and moral enterprise grounded in the promise to do our absolute best for those in need. I fulfill myself most completely by giving myself to another suffering person. As Whitman taught me in *Song of Myself*, “Hoping to cease not till death...The smoke of my own breath, Echoes, ripples buzz'd whispers...the passing of blood and air through my lungs...” I take myself to each person, thinking of how she is exposed emotionally, physically, and spiritually to me as her physician. This tethers us together in an intense healing relationship that is unparalleled and requires me to quash self-interest in favour of elevating the needs of her who is burdened, unwell, and weary.

[Factors associated with delayed viral shedding in COVID-19 infected patients: A retrospective small-scale study](#) - Cao HR, et al. *Respiratory Medicine*, 2021, 178, 106328.

Background: The outbreak of COVID-19 has caused ever-increasing attention and public panic all over the world. Until now, data are limited about the risk factors to virus shedding in COVID-19 infected patients.



[Implications of COVID-19 sequelae for health-care personnel](#) - Praschan N, et al. *Lancet Respiratory Medicine*, 2021, 9(3), pp.230-231.

The COVID-19 pandemic caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was initially described as causing a severe acute respiratory syndrome. Clinical studies have since shown that COVID-19 is a systemic illness with the potential for multiorgan complications. As the pandemic unfortunately continues, COVID-19 has the potential for a broader and more insidious effect, including the loss of skilled health-care personnel to post-COVID-19 disabilities.

[An issue of trust—vaccinating Black patients against COVID-19](#) - Okorodudu DO, Okorodudu DE. *Lancet Respiratory Medicine*, 2021, 9(3), pp.228-229.

2020 has brought unprecedented challenges to the field of medicine. At the forefront of it all is COVID-19. This disease has paralysed the globe, leading to closure of schools, religious establishments, and businesses worldwide. With the winter season upon us and hospitalisations reaching all-time highs, our level of concern for this disease rises. The estimated number of lives that will be lost and affected is unfathomable. If this holds true, achieving herd immunity must be a global priority, which in turn might mandate an effective vaccine deployment strategy. With the roll out of two vaccines achieving over 90% efficacy, an obvious question must now be answered. Which populations should be prioritised for immunisation?

[Long-term exposure to fine particulate matter and hospitalization in COVID-19 patients](#) - Mendy A, et al. *Respiratory Medicine*, 2021, 178, 106313.

Background: Ecological evidence suggests that exposure to air pollution affects coronavirus disease 2019 (COVID-19) outcomes. However, no individual-level study has confirmed the association to date.

[Managing intensive care admissions when there are not enough beds during the COVID-19 pandemic: a systematic review](#) - Tyrell CSB, et al. *Thorax* 2021;76:302-312.

The surge in cases of severe COVID-19 has resulted in clinicians triaging intensive care unit (ICU) admissions in places where demand has exceeded capacity. In order to assist difficult triage decisions, clinicians require clear guidelines on how to prioritise patients. Existing guidelines show significant variability in their development, interpretation, implementation and an urgent need for a robust synthesis of published guidance. To understand how to manage which patients are admitted to ICU, and receive mechanical ventilatory support, during periods of high demand during the COVID-19 pandemic, a systematic review was performed.

[My COVID-19 dream: training enough health workers](#) - Tulenko K. *Lancet Respiratory Medicine*, 2021, 9(3), e.26.

The past year has been a nightmare. As a health workforce expert, I felt that my concerns regarding the need to provide health workers with adequate personal protective equipment were dismissed while the US Occupational Safety and Health Administration and the Joint Commission (the US hospital accreditor), the very organizations that should have protected health workers, were silent and over 2900 health workers died and 8% of US physicians closed down their offices. I saw my fellow health workers suffering from overwork, fatigue, burnout, and psychological stress.

[Prevalence and risk factors for delirium in critically ill patients with COVID-19 \(COVID-D\): a multicentre cohort study](#) - Pun BT, et al. *Lancet Respiratory Medicine*, 2021, 9(3), pp.239-250.

Background: To date, 750 000 patients with COVID-19 worldwide have required mechanical ventilation and thus are at high risk of acute brain dysfunction (coma and delirium). We aimed to investigate the



prevalence of delirium and coma, and risk factors for delirium in critically ill patients with COVID-19, to aid the development of strategies to mitigate delirium and associated sequelae.

[Renin-angiotensin system inhibitors in hospitalised patients with COVID-19](#) - Williams B. *Lancet Respiratory Medicine*, 2021, 9(3), pp.221-222.

Following the onset of the COVID-19 pandemic, by February 2020, there was widespread speculation circulating on social media and in the medical press that treatment with medications that inhibit the renin-angiotensin system might increase susceptibility to COVID-19. <sup>1</sup> This concern was not insignificant because, globally, hundreds of millions of people are treated with renin-angiotensin system inhibitors, particularly angiotensin-converting enzyme inhibitors (ACEIs) or angiotensin-receptor blockers (ARBs) for hypertension, heart failure, or chronic kidney disease. Many wondered if they should discontinue these treatments, and inevitably some will have done.

[The right place for IL-1 inhibition in COVID-19](#) - Cavalli G, Dagna L. *Lancet Respiratory Medicine*, 2021, 9(3), pp.223-224.

The COVID-19 pandemic, caused by the spread of severe acute respiratory syndrome coronavirus 2, has resulted in more than 1.8 million deaths worldwide as of Jan 7, 2021, a figure that will grow indefinitely until effective vaccines become globally accessible. Two phases are generally recognised in the pathogenesis of COVID-19: an initial viral stage characterised by an appropriate host immune response, mild clinical symptoms, and self-resolution in most patients; and a later phase develops in a minority of patients, and is characterised by maladaptive hyperinflammation, rampant release of cytokines, acute respiratory insufficiency, and considerable mortality. Dampening hyperinflammation in patients with severe COVID-19 via inhibition of cytokines has emerged as a logical therapeutic option.

[Risk of adverse outcomes in patients with underlying respiratory conditions admitted to hospital with COVID-19: a national, multicentre prospective cohort study using the ISARIC WHO Clinical Characterisation Protocol UK](#). - Bloom CI. *The Lancet Respiratory Medicine* 2021; [https://doi.org/10.1016/S2213-2600\(21\)00013-8](https://doi.org/10.1016/S2213-2600(21)00013-8).

Inhaled corticosteroid use in those with asthma was associated with lower mortality than in patients without an underlying respiratory condition; patients with chronic pulmonary disease had significantly increased mortality compared to those with no underlying respiratory condition. Our results suggest that the use of inhaled corticosteroids, within 2 weeks of admission, improves survival for patients aged 50 years and older with asthma, but not for those with chronic pulmonary disease.

[Risks of lung transplantation in the SARS-CoV-2 era](#) - Meyer KC. *Lancet Respiratory Medicine*, 2021, 9(3), pp.224-226.

As the COVID-19 pandemic has swept the world, the provision of health care for conditions that are unrelated to COVID-19 has been extensively disrupted. This is especially the case for patients in need of solid organ transplantation, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infections have complicated the approach that transplant centres must take to ensure that recipients are not placed at risk of potentially fatal outcomes or severe allograft dysfunction should they become infected with SARS-CoV-2.

[Sedation in mechanically ventilated patients with COVID-19](#) - Page V. *Lancet Respiratory Medicine*, 2021, 9(3), pp.218-219.

Delirium in critical illness represents a considerable burden for individual patients, their family members, health-care services, and society. In the past decade, a number of initiatives have been launched with



some success in the UK and internationally, with the aim of educating and challenging clinicians to improve sedation practice. 12 Less sedation results in lower delirium prevalence, and lower prevalence of delirium is associated with better patient outcomes. 34 The Pan American and Iberian Federation of Critical Medicine and Intensive Therapy, German, and US sedation guidelines all recommend mechanically ventilated patients are kept awake or easily aroused, with effective pain control.

[Successful double-lung transplantation from a donor previously infected with SARS-CoV-2](#) - Ceulemans LJ, et al. *Lancet Respiratory Medicine*, 2021, 9(3), pp.315-318.

In late 2019, severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and its resulting respiratory disease, COVID-19, emerged. 1 As the pandemic continues, with more than 62 million people with documented SARS-CoV-2 infection, a growing number of potential organ donors will have been infected. Since SARS-CoV-2 resides primarily in the respiratory tract, lung transplantation has the highest concern in terms of donor-derived viral transmission and impaired graft quality. Therefore, graft acceptance for lung transplantation should carefully be balanced against the longer waiting time for the recipient. 23 So far, to our knowledge, there have been no published reports of lung transplantation from a donor with previous COVID-19. We describe a successful double-lung transplantation from a donor who recovered from SARS-CoV-2 infection with screening of different specimens for SARS-CoV-2 during procurement and transplantation ( figure 1 ; video). Approval for reporting was granted by the ethics committee of the University Hospitals Leuven (S52174).

## Websites

[International Society on Thrombosis and Haemostasis \(ISTH\) statement on the AstraZeneca COVID-19 vaccine and thrombosis.](#) - International Society on Thrombosis and Haemostasis (ISTH); 2021.

The ISTH recommends that all eligible adults continue to receive COVID-19 vaccinations, despite the recent decisions by some countries to at least temporarily suspend the use of the AstraZeneca vaccine due to reports of thrombosis.

## What's New in Critical Care from UpToDate

[Anticoagulation intensity in people hospitalized for COVID-19 \(March 2021\)](#)

Thromboembolic complications of severe COVID-19 are common in hospitalized patients, especially in the intensive care unit (ICU), but the optimal approach to venous thromboembolism (VTE) prophylaxis has been unclear. Limited data from the early months of the pandemic suggested that increased dosing intensity might be reasonable. However, recent randomized trials (one published and others in preprint) have found that prophylactic dose anticoagulation is equally effective as higher doses of anticoagulation in reducing VTE risk, including in patients in the ICU, with trends towards lower rates of bleeding 16,17. Based on currently available evidence, standard prophylactic dosing is appropriate for patients hospitalized for COVID-19 who do not have a VTE.

## Influenza

### Articles

[Improving Influenza Vaccination in Children With Comorbidities: A Systematic Review.](#) - Norman DA, et al. *Pediatrics* 2021;;e20201433.

Interventions were shown to consistently improve influenza vaccine coverage; however, no significant differences in coverage between different intervention types were observed. Future well-designed studies evaluating the effectiveness of different intervention are required to inform future optimal interventions.





## Interstitial lung diseases (pulmonary fibrosis)

### Articles

[Clinical improvement and effectiveness of exercise-based pulmonary rehabilitation in patients with idiopathic pulmonary fibrosis: a brief analytical review.](#) - Vainshelboim B. *Journal of Cardiopulmonary Rehabilitation and Prevention* 2021;41(1):52-57.

This review provides novel evidence with respect to clinical improvement and high effectiveness of EBPR among patients with IPF. The results suggest that the majority of patients would be expected to clinically improve by completing the EBPR program. The findings further support the prescription of EBPR as clinically effective therapy and implementation as standard of care for patients with IPF. Future studies examining effectiveness utilizing additional outcomes with the MCID are warranted.

[How IPF has changed our lives](#) - Flewett M, Flewett R. *Lancet Respiratory Medicine*, 2021, 9(3), pp.232-233. April 11, 2014, is the day that changed our lives completely. The day Ron was diagnosed with idiopathic pulmonary fibrosis (IPF) at the age of 53 years, and told that he had 3–5 years to live.

[Idiopathic pulmonary fibrosis and gastroesophageal reflux disease: A population-based, case-control study](#) Baqir M, et al. *Respiratory Medicine*, 2021, 178, 106309.

Background: It is unknown whether gastroesophageal reflux disease (GERD) is a risk factor or consequence of idiopathic pulmonary fibrosis (IPF). This study aimed to determine whether patients with IPF were more likely to have GERD compared with age- and sex-matched controls who either had 1) interstitial lung disease (ILD) other than IPF or 2) no diagnosed lung disease (population control).

[The microbiome in IPF: tissue is not the issue](#) - Molyneux PL. *Thorax* 2021;76:218.

The first line of defence in the airways is the epithelium. In health there are numerous mechanisms to repel invaders and facilitate repair of this barrier. However, when these mechanisms are ineffective, absent or simply become exhausted, fibrosis can ensue.<sup>1</sup> For many years epidemiological studies have highlighted potential environmental triggers which could target and damage the epithelium in idiopathic pulmonary fibrosis (IPF), but more recently we have come to understand the role of bacteria, and specifically the role of the ever-present respiratory microbiota in fibrogenesis.

[Quality of dying and death in patients with interstitial lung disease compared with lung cancer: an observational study](#) - Koyauchi T, et al. *Thorax* 2021;76:248-255.

Background: There is limited knowledge regarding the quality of dying and death (QODD) and end-of-life interventions in patients with interstitial lung disease (ILD). Hence, differences in QODD and end-of-life interventions between patients with ILD and those with lung cancer (LC) remain poorly understood.

[Real-world retrospective observational study exploring the effectiveness and safety of antifibrotics in idiopathic pulmonary fibrosis](#) - Wright WA, et al. *BMJ Open Respiratory Research* 2021;8:e000782.

Background: Pirfenidone and nintedanib are the only disease-modifying treatments available for idiopathic pulmonary fibrosis (IPF). Our aim was to test their effectiveness and safety in clinical practice.

[Role of extracellular vesicles in chronic lung disease.](#) - Trappe A. *Thorax* 2021;;doi: 10.1136/thoraxjnl-2020-216370.

This article provides an overview of the roles of extracellular vesicles in chronic lung diseases including



their role as intercellular communicators, and their potential as biomarker candidates or drug carriers.

[Telomere length and risk of idiopathic pulmonary fibrosis and chronic obstructive pulmonary disease: a mendelian randomisation study](#) - Duckworth A, et al. *Lancet Respiratory Medicine*, 2021, 9(3), pp.285-294.

Background: Idiopathic pulmonary fibrosis (IPF) is a fatal lung disease accounting for 1% of UK deaths. In the familial form of pulmonary fibrosis, causal genes have been identified in about 30% of cases, and a majority of these causal genes are associated with telomere maintenance. Prematurely shortened leukocyte telomere length is associated with IPF and chronic obstructive pulmonary disease (COPD), a disease with similar demographics and shared risk factors. Using mendelian randomisation, we investigated evidence supporting a causal role for short telomeres in IPF and COPD.

[Topographic heterogeneity of lung microbiota in end-stage idiopathic pulmonary fibrosis: the Microbiome in Lung Explants-2 \(MiLEs-2\) study](#) - Valenzi E, et al. *Thorax* 2021;76:239-247.

Background: Lung microbiota profiles in patients with early idiopathic pulmonary fibrosis (IPF) have been associated with disease progression; however, the topographic heterogeneity of lung microbiota and their roles in advanced IPF are unknown.

[Unravelling the risk of \(intermediate\) antitrypsin deficiency](#) - Quinn M, Turner AM, Mahadeva R. *Thorax* 2021;76:214-215.

The seminal observation of severe deficiency of alpha-1-antitrypsin (AAT) with premature emphysema over 50 years ago led to the elastase–antielastase hypothesis of lung disease. Subsequent research identified alpha-1-antitrypsin deficiency (AATD) as an inherited metabolic genetic condition caused by mutations on the SERPINA1 gene, resulting in a reduction in the serum concentration of AAT.<sup>1</sup> The role of AAT is to act as an inhibitor to the enzyme neutrophil elastase, and it is crucial in the homeostasis of elastase–antielastase activity, with an imbalance in this activity causing lung disease via a cycle of inflammation and proteolytic damage leading to premature emphysema, disability and death. There are over 100 mutations of SERPINA1 described in the literature, some of which are associated with AATD. The normal genotype is designated PiMM; the most common genotype resulting in severe deficiency is designated PiZZ. AATD is an autosomal codominant condition so heterozygosity can also create in genotypes resulting in mild and intermediate deficiency, such as PiMZ and PiSZ. The prevalence of AATD worldwide is estimated between 0.02% and 0.05%. Normal AAT serum concentration would be in the range 20–53 µmol/L, while deficient genotypes express varying levels, from 55% for PiMZ to 40% for PiSZ and <15% for PiZZ. While the risk of developing premature emphysema in PiZZ is beyond doubt, there has been considerable debate regarding the risk of SZ genotype (intermediate deficiency) and emphysema severity.

## What's New in Interstitial Lung Disease from UpToDate

### [Tocilizumab for systemic sclerosis-interstitial lung disease \(March 2021\)](#)

Tocilizumab is a humanized anti-interleukin (IL)-6 receptor antibody that has been approved by the US Food and Drug Administration for slowing the rate of decline in pulmonary function in adult patients with systemic sclerosis-interstitial lung disease (SSc-ILD) <sup>37</sup>. The approval is based on a randomized trial in 210 patients with SSc that found a reduced decline in forced vital capacity with subcutaneous tocilizumab compared with placebo at 48 weeks <sup>38</sup>. Tocilizumab had no benefit in the primary endpoint, a change in modified Rodnan skin score (mRSS). While awaiting additional long-term data, tocilizumab is a reasonable alternative for initial therapy in patients with SSc-ILD who are unable to take mycophenolate.



## Lifestyle interventions (diet, exercise, smoking)

### Articles

[Reduction of bronchial response to mannitol after partial switch from conventional tobacco to electronic cigarette consumption](#) - R  ther T, et al. *Respiratory Medicine*, 2021, 178, 106324.

Background: Regarding the multiple health effects of e-cigarettes, there are insufficient data on potential effects on bronchial reactivity (BHR). In the present study, we assessed the impact of a switch from conventional to e-cigarettes on BHR under realistic conditions over a period of 3 months.

### What's New in Critical Care from UpToDate

[Dexmedetomidine versus propofol sedation for mechanically-ventilated adults \(March 2021\)](#)

Dexmedetomidine and propofol are commonly used sedatives in the intensive care unit, but their differential effect on duration of mechanical ventilation when used to provide light sedation is unknown. One recent multicenter, randomized trial of 422 mechanically ventilated adults with sepsis (MENDS 2 trial) reported no significant difference in the number of ventilator-free days at 28 days in patients who received dexmedetomidine compared with propofol when a target goal of light sedation was set (median 23.7 to 24 ventilator-free days) 18. There was also no significant difference in days alive without delirium or coma, death at 90 days, cognitive status at 6 months, or measures of safety. These data support current practice and suggest that both propofol and dexmedetomidine are appropriate sedatives for mechanically ventilated adults with sepsis. Selection of an agent must be individualized according to patient characteristics and the clinical situation.

[Trial of baclofen for alcohol withdrawal prophylaxis in critically ill \(March 2021\)](#)

Some clinicians have advocated for baclofen as a treatment for alcohol withdrawal, but evidence is lacking. In a multicenter randomized trial, 314 patients on mechanical ventilation and at risk for alcohol withdrawal were treated with high-dose baclofen or placebo plus standard care 15. Although the trial reported a reduction in agitation events in the baclofen group, events were largely transient and not clearly related to withdrawal. Duration of intubation, ICU length of stay, and mortality were all higher in the baclofen group, although the mortality difference did not reach statistical significance. Benzodiazepines remain the primary medication for treatment and prophylaxis against alcohol withdrawal in critically ill patients; we recommend against the use of baclofen in this setting.

## Obstructive sleep apnoea

### Articles

[Validation of the STOP-Bang questionnaire as a screening tool for obstructive sleep apnoea in patients with cardiovascular risk factors: a systematic review and meta-analysis](#) Hwang M, et al. *BMJ Open Respiratory Research* 2021;8:e000848.

Background: Obstructive sleep apnoea (OSA) is highly prevalent in patients with cardiovascular risk factors and is associated with increased morbidity and mortality. This review presents the predictive parameters of the STOP-Bang questionnaire as a screening tool for OSA in this population.

## Pneumonia

### Articles

[Effect of anakinra versus usual care in adults in hospital with COVID-19 and mild-to-moderate pneumonia \(CORIMUNO-ANA-1\): a randomised controlled trial](#) - The Lancet Respiratory Medicine. *Lancet Respiratory Medicine*, 2021, 9(3), pp.295-304.

Background: Patients with COVID-19 pneumonia have an excess of inflammation and increased concentrations of cytokines including interleukin-1 (IL-1). We aimed to determine whether anakinra, a



recombinant human IL-1 receptor antagonist, could improve outcomes in patients in hospital with mild-to-moderate COVID-19 pneumonia.

[Hyperlipidaemia and mortality among patients hospitalised with pneumonia: retrospective cohort and propensity score matched study](#) - Yousufuddin M, et al. *BMJ Open Respiratory Research* 2021;8:e000757.  
Objective: To characterise the potential association of hyperlipidaemia (HLP) versus no HLP with all-cause mortality among patients hospitalised for pneumonia.

[Predictors of 30-day readmission following hospitalisation with community-acquired pneumonia](#) - Chakrabarti B, et al. *BMJ Open Respiratory Research* 2021;8:e000883.  
Background: There is a paucity of UK data to aid healthcare professionals in predicting which patients hospitalised with community-acquired pneumonia (CAP) are at greatest risk of 30-day readmission and to determine which readmissions may occur soonest.

[Provision of holistic care after severe COVID-19 pneumonia](#) - McPeake J, et al. *Lancet Respiratory Medicine*, 2021, 9(3), e.24.  
We read with interest the overview of a post-COVID-19 recovery service developed by Rebecca D'Cruz and colleagues in the UK. This multidisciplinary approach, implemented in response to the anticipated long-term burden of COVID-19 infection, will undoubtedly provide patient benefit. 1 The construction of this clinical pathway, alongside many others internationally, is based on previous knowledge pertaining to post-critical illness recovery and the previous severe acute respiratory syndrome pandemic. However, there are other crucial lessons that have been assembled in relation to critical care recovery, which require consideration in evolving services.

[Provision of holistic care after severe COVID-19 pneumonia – Authors' reply](#) - D'Cruz RF, et al. *Lancet Respiratory Medicine*, 2021, 9(3), e.25.  
We are grateful for the opportunity to respond to the Correspondence from Joanne McPeake and colleagues, which highlights the socioeconomic challenges that survivors of critical illness face, particularly with respect to returning to work. As the authors describe, these difficulties are undoubtedly applicable to the post-COVID-19 cohort. Indeed, the COVID-19 pandemic has magnified existing social inequalities, which render the economically disadvantaged more vulnerable, including to COVID-19 exposure and mortality, and to adverse employment implications.

## Pulmonary embolism

### Articles

[Incidence of pulmonary embolism in patients with non-invasive respiratory support during COVID-19 outbreak](#) - González-García JG, et al. *Respiratory Medicine*, 2021, 178, 106325.

While the incidence of thrombotic complications in critically ill patients is very high, in patients under non-invasive respiratory support (NIS) is still unknown. The specific incidence of thrombotic events in each of the clinical scenarios within the broad spectrum of severity of COVID-19, is not clearly established, and this has not allowed the implementation of thromboprophylaxis or anticoagulation for routine care in COVID-19. Patients admitted in a semi-critical unit treated initially with NIS, especially Continuous-Positive Airway Pressure (CPAP), were included in the study. The cumulative incidence of pulmonary embolism was analyzed and compared between patients with good response to NIS and patients with clinical deterioration that required orotracheal intubation. 93 patients were included and 16% required mechanical ventilation (MV) after the NIS. The crude cumulative incidence of the PE was 14% (95%, CI 8–22) for all group. In patients that required orotracheal intubation and MV, the cumulative incidence was



significantly higher 33% (95% CI 16–58) compared to patients that continued with non-invasive support 11% (CI 5–18) (Log-Rank,  $p = 0.013$ ). Patients that required mechanical ventilation were at higher risk of PE for a HR of 4.3 (95%CI 1.2–16). In conclusion, cumulative incidence of PE is remarkably higher in critically patients with a potential impact in COVID-19 evolution. In this context, patients under NIS are a very high-risk group for developing PE without a clear strategy regarding thromboprophylaxis.

[Outpatient Management of Patients Following Diagnosis of Acute Pulmonary Embolism.](#) - Westafer LM, et al. *Academic Emergency Medicine* 2021;28(3):336-345.

Despite guidelines promoting outpatient management, few patients are currently discharged home in the United States; however, practice varies widely across hospitals. Return visit rates were high but most did not result in hospitalization.

[Safety and efficacy of catheter directed thrombolysis \(CDT\) in elderly with pulmonary embolism \(PE\)](#)

Harrison E, et al. *BMJ Open Respiratory Research* 2021;8:e000894.

Introduction: Acute pulmonary embolism (PE) remains a common cause for morbidity and mortality in patients over 65 years. Given the increased risk of bleeding in the elderly population with the use of systemic thrombolysis, catheter-directed therapy (CDT) is being increasingly used for the treatment of submassive PE. Nevertheless, the safety of CDT in the elderly population is not well studied. We, therefore, aimed to evaluate the safety of CDT in our elderly patients.

## Pulmonary hypertension

### Articles

[Long-Term Outcomes in Patients With Connective Tissue Disease–Associated Pulmonary Arterial Hypertension in the Modern Treatment Era: Meta-Analyses of Randomized, Controlled Trials and Observational Registries.](#) - Khanna D, et al. *Arthritis & Rheumatology* 2021;:doi.org/10.1002/art.41669.

Modern therapy provides a similar reduction in morbidity/mortality risk in patients with CTD-PAH when compared to the PAH population overall. Risk of death is higher in CTD-PAH patients than in those with PAH overall, but survival has improved in the last 10 years, which may be related to increased screening and/or new treatment approaches. Early detection of PAH in patients with CTD and up-front intensive treatment are warranted.

[Riociguat treatment in patients with chronic thromboembolic pulmonary hypertension: Final safety data from the EXPERT registry](#) - Ghofrani HA, et al. *Respiratory Medicine*, 2021, 178, 106220.

Objective: The soluble guanylate cyclase stimulator riociguat is approved for the treatment of adult patients with pulmonary arterial hypertension (PAH) and inoperable or persistent/recurrent chronic thromboembolic pulmonary hypertension (CTEPH) following Phase 3 randomized trials. The EXPosurE Registry RiociguaT in patients with pulmonary hypertension (EXPERT) study was designed to monitor the long-term safety of riociguat in clinical practice.

## Respiratory interventions ( aspiration, chest drain, drug therapy, mechanical ventilation, oxygen therapy)

### Articles

[Changes in central venous to arterial carbon dioxide gap \(PCO<sub>2</sub> gap\) in response to acute changes in ventilation](#) - Shastri L, et al. *BMJ Open Respiratory Research* 2021;8:e000886.

Background: Early diagnosis of shock is a predetermining factor for a good prognosis in intensive care. An elevated central venous to arterial PCO<sub>2</sub> difference ( $\Delta$ PCO<sub>2</sub>) over 0.8 kPa (6 mm Hg) is indicative of low



blood flow states. Disturbances around the time of blood sampling could result in inaccurate calculations of  $\Delta\text{PCO}_2$ , thereby misrepresenting the patient status. This study aimed to determine the influences of acute changes in ventilation on  $\Delta\text{PCO}_2$  and understand its clinical implications.

[In vitro evaluation of disposable transport ventilators with combination aerosol therapy](#) - Eain MMG, et al. *BMJ Open Respiratory Research* 2021;8:e000739.

Background: The COVID-19 pandemic has highlighted the need for alternative short-term, reliable means to aid in the treatment of patients requiring ventilatory support. Concurrent aerosol drug delivery is often prescribed to such patients. As such, this study examines one such short-term option, the disposable gas-powered transport ventilator to effectively deliver aerosol therapy. Factors such as aerosol generator type, patient breathing pattern, humidification and nebuliser position within the respiratory circuit were also examined.

[Instrumental dead space in ventilator management](#) - Lellouche F, et al. *Lancet Respiratory Medicine*, 2021, 9(3), e.22.

Michela Botta and colleagues described ventilator management in a large cohort of patients with COVID-19 on mechanical ventilation. Their study provides important data on ventilator settings in this population and shows that high tidal volumes on the first day of ventilation are associated with a higher risk of 28-day mortality. These data reinforce the notion that low tidal volumes should be used in these patients, especially when low lung compliance is measured.

[Instrumental dead space in ventilator management – Authors' reply](#) - Schultz MJ, et al. *Lancet Respiratory Medicine*, 2021, 9(3), e.23.

We thank François Lellouche and colleagues for their Correspondence on our study on ventilation management and clinical outcomes in invasively ventilated patients with COVID-19.

[To drain or not to drain? Abscess or empyema?](#) - McDill H, et al. *Thorax* 2021;76:313-315.

We present a case posing the clinical dilemma of differentiating a large peripheral lung abscess from an empyema. A 71-year-old man attended the emergency department with a 1-week history of sudden onset left-sided chest pain, exacerbated by inspiration and movement. He reported a dry cough, exertional breathlessness and fatigue. He denied fever, weight loss or reduced appetite. He had no significant medical history, but was a 15 pack-year ex-smoker.

[Typical within and between person variability in non-invasive ventilator derived variables among clinically stable, long-term users](#) - Jeganathan V, et al. *BMJ Open Respiratory Research* 2021;8:e000824.

Background: Despite increasing capacity to remotely monitor non-invasive ventilation (NIV), how remote data varies from day to day and person to person is poorly described.

## What's New in Critical Care from UpToDate

[Ventilation of COVID-19 patients using anesthesia machines in operating rooms \(March 2021\)](#)

Due to shortages of ventilators and intensive care unit (ICU) beds, some patients with COVID-19 have been ventilated with anesthesia machine ventilators in operating rooms (ORs) or nearby areas. In a study in which individual ORs were used to accommodate multiple patients with COVID-19 who needed mechanical ventilation, the estimated probability of survival 30 days after admission (61 percent) was comparable to rates reported in other settings, suggesting conversion of ORs to ICU beds is a reasonable option during





critical shortages of ICU ventilators and beds 14. Challenges related to this practice included obtaining adequate medical gas supply and converting positive pressure ORs into negative pressure rooms.

## Respiratory rehabilitation

### Articles

[Feasibility of an online platform delivery of pulmonary rehabilitation for individuals with chronic respiratory disease](#) - Lewis A, et al. *BMJ Open Respiratory Research* 2021;8:e000880.

Introduction: SARS-CoV-2 has restricted access to face-to-face delivery of pulmonary rehabilitation (PR). Evidence suggests that telehealth-PR is non-inferior to outpatient PR. However, it is unknown whether patients who have been referred to face-to-face programmes can feasibly complete an online-PR programme.

## Sarcoidosis

### Articles

[Cardiac sarcoidosis: state-of-the-art review](#). - Kouranos V, Sharma R. *Heart* 2021;;doi: 10.1136/heartjnl-2019-316442.

Learning objectives: To improve knowledge of the epidemiology and clinical presentation of cardiac sarcoidosis. To understand the diagnostic approach in patients with suspected cardiac sarcoidosis and how to exclude important differential diagnoses which can mimic the condition. To understand the basic principles in the management of cardiac sarcoidosis.

[Optimizing routine screening for cardiac sarcoidosis through use of commonly available studies](#) - Holtzclaw AW, et al. *Respiratory Medicine*, 2021, 178, 106331.

Background: Sarcoidosis is a multisystem granulomatous disorder with unclear etiology. Morbidity and mortality vary based on organ involvement, with cardiac sarcoidosis (CS) associated with higher mortality; despite this, CS remains underdiagnosed. The Heart Rhythm Society (HRS) expert consensus statement recommends screening sarcoidosis patients for CS utilizing a symptom screen, EKG, and echocardiogram (TTE), while the American Thoracic Society (ATS) guideline recommends only EKG and symptom screening. These recommendations, however, are based on limited data with recommendations for further studies.

[Sequential FDG-PET in the management of multiorgan sarcoidosis](#) - Kelly A, et al. *Thorax* 2021;76:316-317.

A 32-year-old man presented with palpitations and central chest pain, examination was unremarkable and chest radiograph was normal. ECG demonstrated right axis deviation and inferolateral T-wave inversion; cardiac enzymes were normal. Cardiac MRI demonstrated multifocal, patchy subepicardial and mesocardial left ventricular late gadolinium enhancement, suggestive of cardiac sarcoidosis. Whole body and dedicated cardiac fluorodeoxyglucose (FDG)-positron emission tomography (PET) was performed 60 min after radiotracer injection following a special patient preparation to suppress physiological myocardial uptake of glucose.

## Tuberculosis

### Articles

[Using molecular testing and whole-genome sequencing for tuberculosis diagnosis in a low-burden setting: a cost-effectiveness analysis using transmission-dynamic modelling](#) - Mugwagwa T, Abubakar I, White PJ. *Thorax* 2021;76:281-291.

Background: Despite progress in TB control in low-burden countries like England and Wales, there are still diagnostic delays. Molecular testing and/or whole-genome sequencing (WGS) provide more rapid diagnosis but their cost-effectiveness is relatively unexplored in low-burden settings.

