

# Respiratory Bulletin

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## Contents

General	Acute respiratory distress syndrome	Acute respiratory failure
Asthma	Bronchial Diseases	Cancers of the respiratory tract
Chest Imaging	COPD	Cystic Fibrosis
Dyspnoea	Infections (including COVID-19)	Influenza
Interstitial lung diseases (pulmonary fibrosis)	Obstructive Sleep Apnoea	Pneumonia
Pulmonary Hypertension	Respiratory interventions (aspiration, chest drain, drug therapy, mechanical ventilation, oxygen therapy)	Respiratory Rehabilitation
Respiratory syncytial virus (RSV)	Sarcoidosis	Tuberculosis

## General

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### Articles

[180 degree shift](#) - Nolan A., Singer E. *Lancet Respiratory Medicine*, 2021, 9(2), pp.132-134.

Sat in one of the many lecture halls of Brunel University, London, in December, 2019, the concept of prone positioning seemed far detached from our reality. As we built up towards our final year physiotherapy exams, we knew this would be the last formal assessment before our final placements. Our physiotherapy lecturer, Dr Mandy Jones, discussed the PROSEVA trial and we listened attentively, knowing it could be assessed in the exam. However, what we did not know is that 4 months later, teams of health professionals termed “proning teams” would run from ward to ward turning patients onto their stomachs.

[Journal club](#) - Baker J. *Thorax* 2021;76:210.

### Guidelines

[Pregabalin \(Lyrica\): reports of severe respiratory depression](#). - Medicines and Healthcare Products Regulatory Agency (MHRA); 2021.

Drug Safety Update. Pregabalin has been associated with infrequent reports of severe respiratory depression, including some cases without the presence of concomitant opioid medicines. Patients with compromised respiratory function, respiratory or neurological disease, renal impairment; those using concomitant central nervous system (CNS) depressants; and people older than 65 years might be at higher risk of experiencing these events and adjustments in dose or dosing regimen may be necessary.

## Acute respiratory distress syndrome

### Articles

[Caution advised regarding lung recruitment before surfactant](#) - Kumar VHS. *Lancet Respiratory Medicine*, 2021, 9(2), e.11.

I read with interest the Article 1 by Giovanni Vento and colleagues on lung recruitment before surfactant administration in infants with extremely low birthweight. In a randomised controlled trial, the authors showed that lung recruitment just before surfactant administration improved the efficacy of surfactant treatment compared with the standard intubation-surfactant-extubation (IN-SUR-E) technique, without increasing the risk of adverse outcomes. However, in infants with extremely low birthweight, mechanical ventilation for the first 72 h is a poor surrogate marker for later adverse clinical outcomes. In the absence of any meaningful differences in clinically significant outcomes such as mortality, bronchopulmonary dysplasia, or neurodevelopmental impairment, the beneficial effects of an intubate-recruit-surfactant-extubate (IN-REC-SUR-E) procedure should be substantiated by larger trials.

[Caution advised regarding lung recruitment before surfactant – Authors’ reply](#) - Vento G. *Lancet Respiratory Medicine*, 2021, 9(2), e.12.

We thank Vasantha Kumar for his Correspondence on our study showing that a lung recruitment manoeuvre before surfactant administration IN-REC-SUR-E improves the efficacy of surfactant compared with the IN-SUR-E technique.

[Lung recruitment before surfactant administration in extremely preterm neonates with respiratory distress syndrome \(IN-REC-SUR-E\): a randomised, unblinded, controlled trial](#) - Vento G., et al. *Lancet Respiratory Medicine*, 2021, 9(2), pp.159-166.



Background: The importance of lung recruitment before surfactant administration has been shown in animal studies. Well designed trials in preterm infants are absent. We aimed to examine whether the application of a recruitment manoeuvre just before surfactant administration, followed by rapid extubation (intubate-recruit-surfactant-extubate IN-REC-SUR-E), decreased the need for mechanical ventilation during the first 72 h of life compared with no recruitment manoeuvre (ie, intubate-surfactant-extubate IN-SUR-E).

[Recruitment: the best way to IN-SUR-E surfactant delivery?](#) - Finer NN., Katheria A. *Lancet Respiratory Medicine*, 2021, 9(2), pp.119-120.

Surfactant therapy is a well established treatment for neonates with respiratory distress syndrome. However, the ideal method for delivery of surfactant remains under investigation. In *The Lancet Respiratory Medicine*, Giovanni Vento and colleagues report the results of a prospective, multicentre, randomised trial of a technique to improve surfactant delivery in 218 extremely premature neonates in 35 centres across Italy. <sup>1</sup> This unblinded study compared the approach of intubation-surfactant-extubation (IN-SUR-E) with intubate-recruit-surfactant-extubate (IN-REC-SUR-E), a technique which involved a lung recruitment manoeuvre after intubation before the administration of surfactant.

## Acute respiratory failure

### Articles

[Consensus on the referral and admission of patients with severe respiratory failure to the NHS ECMO service](#) - Camporota L., et al. *Lancet Respiratory Medicine*, 2021, 9(2), ee.16-17.

Respiratory extracorporeal membrane oxygenation (ECMO) in England and Scotland is provided by a multicentre service, which has been commissioned and regulated by the National Health Services (NHS) of England and Scotland since 2011. The respiratory ECMO service has consistently reported excellent patient survival rates (mean of 74% over the 6 years before the COVID-19 pandemic <sup>1</sup>) that remained unchanged during the first wave of COVID-19 in March to August, 2020, despite the unprecedented high number of concurrent patients treated with ECMO. During the first wave of the pandemic, the NHS England ECMO service treated 236 patients, with an overall survival rate of 74% at decannulation. This survival rate compares favourably with internationally reported data series.

[Prehospital continuous positive airway pressure for acute respiratory failure: the ACUTE feasibility RCT](#) Fuller GW., et al. *Health Technology Assessment* 2021;25(7):DOI: 10.3310/hta25070.

This study concluded that prehospital use of CPAP for Acute Respiratory Failure was not feasible for a full trial largely because it seems unlikely to materially reduce mortality.

## Asthma

### Articles

[Are women with asthma at increased risk for severe COVID-19?](#) - Fernando M., et al. *Lancet Respiratory Medicine*, 2021, 9(2), pp.125-126.

Although adults with asthma appear to have a reduced risk of severe COVID-19 compared with younger populations, <sup>1</sup> women with asthma might represent a somewhat susceptible subgroup for severe COVID-19 requiring hospitalisation. <sup>2</sup> A study by Atkins and colleagues established female sex as an independent risk factor for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) hospitalisation among patients with asthma in the UK. <sup>2</sup> This study and three additional studies from Paris, France, Illinois, USA, and New York, NY, USA, report that 37–53% of all individuals hospitalised with SARS-CoV-2 were women.



345 However, 56–71% of patients with asthma hospitalised for COVID-19 were women in these studies. 345 This increased proportion might be partially explained by the higher baseline prevalence of asthma in women than in men, because data from similar geographical areas suggest 51–65% of individuals with asthma are women. 6789 Several mechanisms might increase the risk of COVID-19-related hospitalisation in women with asthma. The recognition of these mechanisms might guide targeted management strategies.

#### [Association of asthma severity and educational attainment at age 6–7 years in a birth cohort: population-based record-linkage study](#) - Evans A., et al. *Thorax* 2021;76:116-125.

Background: There is conflicting research about the association between asthma and poor educational attainment that may be due to asthma definitions. Our study creates seven categories of current chronic and acute asthma to investigate if there is an association for poorer educational attainment at age 6–7 years, and the role of respiratory infections and school absence.

#### [Asthma in the anti-inflammatory reliever therapy era](#) - Baggott C., Beasley R. *Lancet Respiratory Medicine*, 2021, 9(2), pp.118-119.

The Global Initiative for Asthma recommendation that combination inhaled corticosteroid (ICS)–formoterol reliever therapy is preferred to short-acting  $\beta$  agonist (SABA) reliever therapy across the spectrum of asthma severity is arguably one of the greatest paradigm shifts in the management of asthma in decades. 1 This recommendation is based on evidence that ICS–formoterol reliever therapy reduces the risk of severe exacerbations compared with SABA reliever therapy in patients with moderate and severe asthma taking maintenance ICS–long-acting  $\beta$  agonist (LABA) treatment, and in patients with mild asthma on no maintenance therapy. 234 Understanding how titrating ICS through the vehicle of symptom-driven bronchodilator use leads to improved outcomes would help translation of these findings into clinical practice.

#### [Early life growth and associations with lung function and bronchial hyperresponsiveness at 11-years of age](#) Mikalsen IB., et al. *Respiratory Medicine*, 2021, 177, 106305.

Low birthweight and being born small-for-gestational age (SGA) are linked to asthma and impaired lung function. Particularly, poor intrauterine growth followed by rapid catch-up growth during childhood may predispose for respiratory disease. Bronchial hyperresponsiveness (BHR) is an essential feature of asthma, but how foetal and early childhood growth are associated with BHR is less studied. Our hypothesis was that children born SGA or with accelerated early life growth have increased BHR and altered lung function at 11-years of age. We studied the associations between SGA and early childhood growth with lung function and BHR at 11-years of age in a subgroup of 468 children from the Norwegian Mother, Father and Child Cohort Study (MoBa), and included data from the Medical Birth Registry of Norway (MBRN). Weight at 6 months of age was positively associated with forced vital capacity (adjusted Beta: 0.121; 95% Confidence interval: 0.023, 0.219) and negatively associated with the ratio of forced expiratory flow in first second/forced vital capacity (–0.204; –0.317, –0.091) at 11-years of age. Similar patterns were found for weight at 36 months and for change in weight from birth to 6 months of age. SGA or other various variables of early childhood growth were not associated with BHR at 11-years of age. Early life growth was associated with an obstructive lung function pattern, but not with BHR in 11-year old children. Foetal growth restriction or weight gain during early childhood do not seem to be important risk factors for subsequent BHR in children.

#### [Effect of a single day of increased as-needed budesonide–formoterol use on short-term risk of severe exacerbations in patients with mild asthma: a post-hoc analysis of the SYGMA 1 study](#) - O’Byrne PM., et al. *Lancet Respiratory Medicine*, 2021, 9(2), pp.149-158.



Background: In mild asthma, as-needed budesonide–formoterol reduces long-term exacerbation risk compared with as-needed short-acting  $\beta$  2 -agonist (SABA), with a similar or increased reduction versus maintenance with budesonide plus as-needed SABA, despite a lower budesonide dose. In this post-hoc analysis of the SYmbicort Given as needed in Mild Asthma (SYGMA) 1 study, we investigated the short-term risk of severe exacerbations after a single day with various levels of reliever use.

[Effect of vitamin D supplementation on asthma control in patients with vitamin D deficiency: the ACVID randomised clinical trial](#) - Andújar-Espinosa R., et al. *Thorax* 2021;76:126-133.

Background: The relationship between asthma and vitamin D deficiency has been known for some time. However, interventional studies conducted in this regard have shown conflicting results.

[Hormonal contraception and the risk of severe asthma exacerbation: 17-year population-based cohort study](#) - Nwaru BI., et al. *Thorax* 2021;76:109-115.

Background: Longitudinal studies investigating impact of exogenous sex steroids on clinical outcomes of asthma in women are lacking. We investigated the association between use of hormonal contraceptives and risk of severe asthma exacerbation in reproductive-age women with asthma.

[Mortality and morbidity in children with asthma: A nationwide study in Korea](#) - Sol IS., et al. *Respiratory Medicine*, 2021, 177, 106306.

Objective: Childhood mortality due to asthma remains problematic; however, asthma-related mortality in Korean children has not been previously described. This study aimed to estimate asthma mortality and morbidity and determine to what extent asthma contributes to childhood mortality in Korea.

[Poor outcome of SARS-CoV-2 infection in patients with severe asthma on biologic therapy](#) - Eger K., et al. *Respiratory Medicine*, 2021, 177, 106287.

Background: It is unclear whether asthma and asthma medications increase or decrease the risk of severe COVID-19, and this is particularly true for patients with severe asthma receiving biologics.

## Guidelines

[Mepolizumab for treating severe eosinophilic asthma](#). - NICE; 2021.

Evidence-based recommendations on mepolizumab (Nucala) for treating severe eosinophilic asthma in adults.

## Reports

[The Invisible Threat: how we can protect people from air pollution and create a fairer, healthier society](#). Asthma UK; 2021.

This invisible threat is a health emergency. It is harmful for everyone, but some groups are being hit hardest – pregnant women, children, older people, those living with lung conditions and those on the lowest incomes. This report sets out new analysis from Asthma UK that shows that people who are the most susceptible are being exposed in the places they should feel most safe. It calls for politicians to commit to air pollution health protection plans and stronger clean air laws.



## Bronchial diseases

### Articles

[Pseudomonas aeruginosa associated with severity of non-cystic fibrosis bronchiectasis measured by the modified bronchiectasis severity score \(BSI\) and the FACED: The US bronchiectasis and NTM Research Registry \(BRR\) study](#) - Choate R., et al. *Respiratory Medicine*, 2021, 177, 106285.

Rationale: Non-cystic fibrosis bronchiectasis (NCFB) is characterized by dilated bronchi, poor mucus clearance and susceptibility to bacterial infection. *Pseudomonas aeruginosa* (PA) is one of the most frequently isolated pathogens in patients with NCFB. The purpose of this study was to evaluate the association between presence of PA and disease severity in patients within the US Bronchiectasis and Nontuberculous mycobacteria (NTM) Research Registry (BRR).

[Updated prevalence, predictors and treatment outcomes for bronchiolitis obliterans syndrome after allogeneic stem cell transplantation](#) - Pham J., et al. *Respiratory Medicine*, 2021, 177, 106286.

Introduction: Bronchiolitis obliterans syndrome (BOS) after allogeneic haemopoietic stem cell transplant (HSCT) is an under-recognised and difficult to treat disease. This occurs in the context of limited clinical research and inconsistent diagnostic criteria.

## Cancers of the respiratory tract

### Articles

[Liverpool Lung Project lung cancer risk stratification model: calibration and prospective validation](#)

Field JK., et al. *Thorax* 2021;76:161-168.

Background: Early detection of lung cancer saves lives, as demonstrated by the two largest published low-dose CT screening trials. Optimal implementation depends on our ability to identify those most at risk.

[Nonpharmacological interventions for managing breathlessness in patients with advanced cancer: a systematic review.](#) - Gupta A., et al. *JAMA Oncology* 2020;doi:10.1001/jamaoncol.2020.5184.

Breathlessness is a frequent symptom in patients with advanced cancer. Often, in the context of breathlessness, aggressive cancer treatment is not beneficial, feasible, or aligned with goals of care. Targeted symptom-focused interventions may be helpful in this scenario. Findings include the safety and association with improved breathlessness of several nonpharmacological interventions. Guidelines and clinical practice should evolve to incorporate these interventions as first-line treatment.

### Guidelines

[Brigatinib for ALK-positive advanced non-small-cell lung cancer that has not been previously treated with an ALK inhibitor.](#) - National Institute for Health and Care Excellence (NICE); 2021.

1 Recommendations 1.1 Brigatinib is recommended, within its marketing authorisation, as an option for treating anaplastic lymphoma kinase (ALK)-positive advanced non-small-cell lung cancer (NSCLC) that has not been previously treated with an ALK inhibitor in adults. It is recommended only if the company provides brigatinib according to the commercial arrangement.

## Chest imaging

### Articles

[Metastases from tracheal adenoid cystic carcinoma](#) - Tan VSR., et al. *Thorax* 2021;76:208-209.

A 32-year-old female never smoker presented with dyspnoea and stridor. CT thorax showed a polypoidal mass obstructing the trachea. Bronchoscopy revealed a circumferential nodular tumour 4 cm from the vocal cords, removed using electro-surgical snare and thereby re-establishing trachea patency (figure 1A,B).





Histology showed adenoid cystic carcinoma (ACC). She underwent tracheal resection; as the resection margins showed ACC with perineural and fascia invasion, she received adjuvant radiation therapy 72 Gy. Yearly CT chest was performed for surveillance and CT 8 years after surgery showed enlarged subcarinal lymphadenopathy, bilateral pulmonary nodules and a left thyroid nodule (figure 1C,D). Thyroid ultrasound fine-needle aspiration confirmed 1 cm hypoechoic nodule due to ACC. Endobronchial ultrasound-guided transbronchial needle aspiration of subcarinal lymph node revealed metastatic ACC (figure 2), but no recurrence in the trachea.

## COPD

### Articles

[Are mesenchymal stem cells and derived extracellular vesicles valuable to halt the COVID-19 inflammatory cascade? Current evidence and future perspectives](#) - Monguió-Tortajada M., et al. *Thorax* 2021;76:196-200.

Clinical management of patients suffering from COVID-19 includes infection prevention, control measures and supportive care, including supplemental oxygen and mechanical ventilatory support.<sup>1 2</sup> If not expertly and individually managed with consideration for vasocentric features,<sup>3</sup> 20% of COVID-19 patients who exhibit acute respiratory distress syndrome (ARDS; 14.8% of hospitalised patients<sup>4</sup>) may eventually progress to multiorgan failure and death, even when not of advanced age or predisposed by pre-existing comorbidities or chronic diseases.<sup>5</sup> In these patients, infection by SARS-CoV-2 activates both the innate and adaptive immune responses, provoking the production of large amounts of pro-inflammatory cytokines and chemokines, resulting in a clinical presentation (ie, unremitting high fever, lymphadenopathy, hepatosplenomegaly, cytopenia, hyperferritinaemia, central nervous system abnormalities, hypoalbuminaemia and capillary leak) similar to other systemic, uncontrolled cytokine release syndromes (CRS)(figure 1).<sup>6 7</sup> Thus, at present, management of the potential inflammatory complications of COVID-19 by using appropriate immunosuppressive and immunomodulatory drugs is being explored.

[Characterisation of gas exchange in COPD with dissolved-phase hyperpolarised xenon-129 MRI](#)

Myc L., et al. *Thorax* 2021;76:178-181.

To investigate whether hyperpolarised xenon-129 MRI (HXeMRI) enables regional and physiological resolution of diffusing capacity limitations in chronic obstructive pulmonary disease (COPD), we evaluated 34 COPD subjects and 11 healthy volunteers. We report significant correlations between airflow abnormality quantified by HXeMRI and per cent predicted forced expiratory volume in 1 s; HXeMRI gas transfer capacity to red blood cells and carbon monoxide diffusion capacity (%DLCO); and HXeMRI gas transfer capacity to interstitium and per cent emphysema quantified by multidetector chest CT. We further demonstrate the capability of HXeMRI to distinguish varying pathology underlying COPD in subjects with low %DLCO and minimal emphysema.

[Comparative effectiveness of breathing exercises in patients with chronic obstructive pulmonary disease.](#)

Marotta N., et al. *Complementary Therapies in Clinical Practice* 2020;41

This study aims to determine the best choice of breathing exercises (BE) for patients with chronic obstructive pulmonary disease (COPD) via a network meta-analysis. Conclusion: Diaphragmatic breathing training and yoga seem to be the best choices for breathing exercises in people with COPD.



[COPD assessment test for the evaluation of COVID-19 symptoms](#) - Daynes E., et al. *Thorax* 2021;76:185-187.

There is evidence to demonstrate the ongoing symptoms of COVID-19; however, there are currently no agreed outcomes to assess these symptoms. This study examined the use of the chronic obstructive pulmonary disease (COPD) assessment test (CAT) for patients recovering from COVID-19. 131 patients who were admitted with COVID-19 were followed up over the phone to assess symptoms. The median (IQR) CAT score was 10 (5–16). Cough, phlegm and chest tightness domains were within range for healthy people, but there was evidence of significant breathlessness, loss of energy, and activity and sleep disturbance. The CAT is a useful tool to assess symptoms of COVID-19 recovery.

[COPD-Lower Respiratory Tract Infection Visual Analogue Score \(c-LRTI-VAS\) validation in stable and exacerbated patients with COPD](#) - Prins HJ., et al. *BMJ Open Respiratory Research* 2021;8:e000761.

Background: We developed the chronic obstructive pulmonary disease (COPD)-Lower Respiratory Tract Infection-Visual Analogue Score (c-LRTI-VAS) in order to easily quantify symptoms during exacerbations in patients with COPD. This study aimed to validate this score.

[The effect of Tai Ji and Qigong in patients with chronic obstructive pulmonary disease: a systematic review and meta-analyses.](#) - Yang TT., et al. *European Journal of Integrative Medicine* 2020;40

Exercise training is a core component of pulmonary rehabilitation (PR) and Tai Ji and Qigong (AJQ) are both traditional Chinese exercises. This review investigated the effectiveness of AJQ as an adjunct to PR for patients with COPD. The review demonstrated that AJQ may be useful as an adjunct to pulmonary rehabilitation of patients with COPD. Future studies should explore the differences between different types of AJQ to create tailor more effective exercise interventions for PR.

[Eosinophilic inflammation in COPD: from an inflammatory marker to a treatable trait](#) - David B., et al. *Thorax* 2021;76:188-195.

The heterogeneity of chronic obstructive pulmonary disease (COPD) creates many diagnostic, prognostic, treatment and management challenges, as the pathogenesis of COPD is highly complex and the underlying cellular and molecular mechanisms remain poorly understood. A reliable, easy-to-measure, clinically relevant biomarker would be invaluable for improving outcomes for patients. International and national guidance for COPD suggests using blood eosinophil counts as a biomarker to help estimate likely responsiveness to inhaled corticosteroids (ICS) and, potentially, to aid effective management strategies. However, with the mechanism underlying the association between higher eosinophil levels and ICS effect unknown, use of the blood eosinophil count in COPD continues to be widely debated by the respiratory community.

[Gene coexpression networks reveal novel molecular endotypes in alpha-1 antitrypsin deficiency](#) - Chu J., et al. *Thorax* 2021;76:134-143.

Background: Alpha-1 antitrypsin deficiency (AATD) is a genetic condition that causes early onset pulmonary emphysema and airways obstruction. The complete mechanisms via which AATD causes lung disease are not fully understood. To improve our understanding of the pathogenesis of AATD, we investigated gene expression profiles of bronchoalveolar lavage (BAL) and peripheral blood mononuclear cells (PBMCs) in AATD individuals.

[Non-invasive ventilation at home improves survival and decreases healthcare utilization in medicare beneficiaries with Chronic Obstructive Pulmonary Disease with chronic respiratory failure](#) - Frazier WD., Murphy R., Van Eijndhoven E. *Respiratory Medicine*, 2021, 177, 106291.





Background: Patients with Chronic Obstructive Pulmonary Disease with chronic respiratory failure (COPD-CRF) experience high mortality and healthcare utilization. Non-invasive home ventilation (NIVH) is increasingly used in such patients. We examined the associations between NIVH and survival, hospitalizations, and emergency room (ER) use in COPD-CRF Medicare beneficiaries.

[Oxygen therapy and inpatient mortality in COPD exacerbation](#) - Echevarria C et al. *Emergency Medicine Journal* 2021;38(3):170-177.

This shows that the practice of setting different target saturations based on carbon dioxide levels is not justified. Treating all patients with COPD with target saturations of 88%-92% will simplify prescribing and should improve outcome.

[Risk of incident dementia and cognitive impairment in patients with chronic obstructive pulmonary disease \(COPD\): A large UK population-based study](#) - Siraj RA., et al. *Respiratory Medicine*, 2021, 177, 106288.

Background: Although cognitive impairment and dementia are common comorbidities in patients with chronic obstructive pulmonary disease (COPD), estimates of incidence following a diagnosis of COPD are inconclusive.

## Cystic fibrosis

### Articles

[Downregulation of epithelial sodium channel \(ENaC\) activity in human airway epithelia after low temperature incubation](#) - Yadav S., et al. *BMJ Open Respiratory Research* 2021;8:e000861.

Introduction: The incubation of airway epithelia cells at low temperatures is a common in vitro experimental approach used in the field of cystic fibrosis (CF) research to thermo-stabilise F508del-CFTR and increase its functional expression. Given that the airway epithelium includes numerous ion transporters other than CFTR, we hypothesised that there was an impact of low temperature incubation on CFTR-independent ionoregulatory mechanisms in airway epithelia derived from individuals with and without CF.

[Effects of rehabilitation methods on lower-limb muscle function and functional performance in patients with cystic fibrosis: a systematic review.](#) - Poncin W., et al. *Clinical Rehabilitation* 2020;;doi: 10.1177/0269215520972941.

OBJECTIVE: To investigate the effects of rehabilitation methods on leg muscle function and functional performance in cystic fibrosis. CONCLUSION: Combined aerobic and resistance training enhances leg muscle strength in cystic fibrosis. There is insufficient data on other leg muscle outcomes, nor on alternative rehabilitation strategies.

## Dyspnoea

### Articles

[A rare cause of multiple airways narrowing in a 15-year-old girl](#) - Ghirardo S., et al. *Thorax* 2021;76:205-207.

Sergio Ghirardo (SG): a 15-year-old girl was first admitted to our unit, with significant dyspnoea and fatigue at rest. Her clinical history was uneventful until she was 14 years old when she was hospitalised twice for respiratory symptoms, interpreted as post viral wheezing. Treatment with intravenous corticosteroids, salbutamol and azithromycin was of little clinical benefit. In the last 6 months, she complained of progressive exercise-induced dyspnoea, and her lung function showed a moderate-to-severe obstructive pattern (forced expiratory volume in one second, FEV1/forced vital capacity, FVC 56.6%), with no response



to salbutamol. Her symptoms did not improve with inhaled corticosteroids, long-acting  $\beta_2$  agonists and montelukast treatment. Clinically, she reported moderate swelling of the nasal dorsum as a consequence of a blow with a ball received 5 months before admission. She had a bilateral transmissive mild hypoacusis and a significant weight loss of 18 kg in only 8 months.

## Infections (including COVID-19)

### COVID-19

#### Articles

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

[Assessing the importance of interleukin-6 in COVID-19](#) - Chen LYC., et al. *Lancet Respiratory Medicine*, 2021, 9(2), e.13.

The systematic review and meta-analysis of interleukin (IL)-6 in COVID-19, by Daniel Leisman and colleagues, 1 provides a crucial comparison with other inflammatory syndromes, showing that IL-6 is more markedly elevated in conditions such as sepsis and acute respiratory distress syndrome (ARDS). 1 We credit the authors for this key undertaking. However, we would like to raise two relevant considerations regarding aspects of the study design and the conceptualisation of hyperinflammatory syndromes in which IL-6 is elevated.

[Assessing the importance of interleukin-6 in COVID-19 – Authors' reply](#) -Leisman DE., et al. *Lancet Respiratory Medicine*, 2021, 9(2), ee.14-15.

We thank Luke Chen and colleagues for their interest in our study. 1 With respect to potential double counting of participants—this is a valid criticism. Indeed some participants could have been double counted if they were treated at the same hospital in overlapping time periods. Among the identified studies, only small fractions of the study periods overlap. Nevertheless, we recalculated our primary analysis using only one study—whichever was largest—from each group with potentially overlapping cohorts ( figure ). The results do not change.

[Assessment, Diagnosis, and Treatment of Dysphagia in Patients Infected With SARS-CoV-2: A Review of the Literature and International Guidelines.](#) - Vergara J., et al. *American Journal of Speech Language Pathology* 2020;29(4):2242-2253.

International associations have provided extensive guidance regarding the level of risk related to the management of dysphagia in this population. To date, there are no scientific papers offering disease and/or recovery profiling for patients with dysphagia and coronavirus disease 2019. As a result, research in this area is urgently needed.

[Assessment of SARS-CoV-2 infectivity of upper respiratory specimens from COVID-19 patients by virus isolation using VeroE6/TMPRSS2 cells](#) - Yamada S., et al. *BMJ Open Respiratory Research* 2021;8:e000830.

Background: An outbreak of novel coronavirus (SARS-CoV-2)-associated respiratory infectious diseases (COVID-19) emerged in 2019 and has spread rapidly in humans around the world. The demonstration of in vitro infectiousness of respiratory specimens is an informative surrogate for SARS-CoV-2 transmission from patients with COVID-19; accordingly, viral isolation assays in cell culture are an important aspect of laboratory diagnostics for COVID-19.



### [Could routine race-adjustment of spirometers exacerbate racial disparities in COVID-19 recovery?](#)

Anderson MA., Malhotra A., Non AL. *Lancet Respiratory Medicine*, 2021, 9(2), pp.124-125.

Minority populations disproportionately suffer from the effects of COVID-19, as evidenced by nearly three times the infection rate and one to two times the death rate among Black, Indigenous, and Latino people compared with White people. 1 Although some assume that these disparities are rooted in genetic differences between racial or ethnic groups, they are more likely a result of structural inequalities. Minority groups tend to live in densely populated areas, have limited access to health care, and have higher rates of comorbidities, among other factors, that put them at greater risk for infection. While long-term effects of COVID-19 on lung function have yet to be investigated, we predict that racial disparities will emerge. Disparities in recovery are likely to be influenced by preconceived ideas regarding racial differences within American medicine. 2 Specifically, we raise concern about racial biases built into the tools used to measure pulmonary dysfunction because they have the potential to exacerbate these disparities as minority patients recover from COVID-19.

### [COVID-19: the lessons learned amongst the losses - Szekely M. Lancet Respiratory Medicine, 2021, 9\(2\), pp.134-135.](#)

January, 2020. Only a few modules left of medical school before I am officially a doctor. Final exams, a medical elective, and transition to FY1. A simple trajectory, or so I thought, until March, 2020, when the pandemic began in the UK. To embark on my career in the midst of COVID-19 was something I could never have predicted. Nevertheless, the lessons I have learned and the losses I have experienced have moulded my clinical practice and greatly impacted my outlook on life not just in medicine.

### [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 CORIMUNO-19 Collaborative group. The Lancet Respiratory Medicine 2021;:https://doi.org/10.1016/S2213-2600\(20\)30556-7.](#)

Patients with COVID-19 pneumonia have an excess of inflammation and increased concentrations of cytokines including interleukin-1 (IL-1). Anakinra did not improve outcomes in patients with mild-to-moderate COVID-19 pneumonia. Further studies are needed to assess the efficacy of anakinra in other selected groups of patients with more severe COVID-19.

### [Functional respiratory imaging identifies redistribution of pulmonary blood flow in patients with COVID-19](#)

Thillai M., et al. *Thorax* 2021;76:182-184.

An increasing observation is that some patients with COVID-19 have normal lung compliance but significant hypoxaemia different from typical acute respiratory distress syndrome (ARDS). We hypothesised that changes in pulmonary blood distribution may be partially responsible and used functional respiratory imaging on CT scans to calculate pulmonary blood volume. We found that patients with COVID-19 had significantly reduced blood volume in the smaller calibre blood vessels (here defined as <5 mm<sup>2</sup> cross-sectional area) compared with matched ARDS patients and healthy controls. This suggests that using high levels of PEEP may not alone be enough to oxygenate these patients and that additional management strategies may be needed.

### [Functional respiratory imaging repurposed for COVID-19 - Van Es J., Meijboom LJ. Thorax 2021;76:107.](#)

Thillai and colleagues<sup>1</sup> describe a method of image analysis, functional respiratory imaging (FRI), which creates a three-dimensional reconstruction of both airways and the pulmonary vasculature from CT-scan images, in 10 patients with severe COVID-19 infection. They computed the distribution of pulmonary blood flow according cross-sectional vessel area size and compared the data to age, gender, height and premorbidity matched acute respiratory distress syndrome (ARDS) patients (n=7) and retrospective data from healthy volunteers (n=107).



[Herd immunity for COVID-19](#) - Burki TK. *Lancet Respiratory Medicine*, 2021, 9(2), pp.135-136.

In early October, 2020, three epidemiologists convened in Great Barrington, a small town in Massachusetts, USA. Jay Bhattacharya (Stanford University Medical School, Stanford, CA, USA), Sunetra Gupta (University of Oxford University, Oxford, UK) and Martin Kulldorff (Harvard University, Cambridge, MA, USA) were there to draft an argument for a new strategy to combat COVID-19. They called it the Great Barrington Declaration . It has since been endorsed by thousands of medical practitioners, researchers, and public health scientists.

[The impact of the COVID-19 pandemic on radiotherapy services in England, UK: a population-based study.](#)

Spencer K., et al. *The Lancet Oncology* 2021;:https://doi.org/10.1016/S1470-2045(20)30743-9.

Radiotherapy activity fell significantly, but use of hypofractionated regimens rapidly increased in the English NHS during the first peak of the COVID-19 pandemic. An increase in treatments for some cancers suggests that radiotherapy compensated for reduced surgical activity. These data will assist health-care providers in understanding the indirect consequences of the pandemic and the role of radiotherapy services in minimising these consequences.

[Nebulised interferon beta-1a for patients with COVID-19](#) - Peiffer-Smadja N., Yazdanpanah Y. *Lancet Respiratory Medicine*, 2021, 9(2), pp.122-123.

In *The Lancet Respiratory Medicine*, Phillip Monk and colleagues 1 report the results of a randomised, double-blind, placebo-controlled phase 2 pilot trial of nebulised interferon beta-1a in 101 adults admitted to hospital with COVID-19. The authors found that patients who received nebulised interferon beta-1a had significantly greater odds of clinical improvement across the WHO Ordinal Scale for Clinical Improvement than those who received placebo, both on day 15/16 (odds ratio OR 2.32 95% CI 1.07–5.04; p=0.033) and on day 28 (3.15 1.39–7.14; p=0.006). However, there was no significant difference between treatment groups in the odds of hospital discharge by day 28: 39 (81%) of 48 patients had been discharged in the nebulised interferon beta-1a group compared with 36 (75%) of 48 in the placebo group (OR 1.84 95% CI 0.64–5.29; p=0.26).

[New variant of SARS-CoV-2 in UK causes surge of COVID-19](#) - Kirby T. *Lancet Respiratory Medicine*, 2021, 9(2), ee.20-21.

For most of November, 2020, England was in lockdown to force down the incidence of COVID-19 cases that had steadily increased in the late summer and autumn. Other countries in the UK (Wales, Scotland, and Northern Ireland) had also been reimposing and subsequently lifting restrictions, since each of the four nations is in charge of its own COVID-19 control plans.

[A new year, but familiar challenges from COVID-19 in the USA](#) - Burki TK. *Lancet Respiratory Medicine*, 2021, 9(2), e.19.

On Jan 2, 2021, the USA registered 297 491 new cases of COVID-19. Three days earlier, the country saw 3750 deaths from the disease. Both figures represented record highs, though with cases trending upwards, and the effect of the holiday season yet to be fully quantified, further spikes are expected. “The pandemic is at its worst moment in the USA”, said Ashish Jha, dean of Brown University School of Public Health (Providence, RI, USA). “We are unlikely to see any improvement at least until the end of January, and even then it is going to take a while before the virus is brought under control.

[NICE guideline on long COVID](#) - Venkatesan P. *Lancet Respiratory Medicine*, 2021, 9(2), p.129.

As the global COVID-19 pandemic has progressed, evidence has emerged that some patients are experiencing prolonged multiorgan symptoms and complications beyond the initial period of acute



infection and illness. The list of persisting and new symptoms reported by patients is extensive, including chronic cough, shortness of breath, chest tightness, cognitive dysfunction, and extreme fatigue. Termed long COVID or post-COVID-19 syndrome, the implications and consequences of such ongoing clinical manifestations are a growing health concern.

[Pandemic thoughts from a British junior doctor in Melbourne](#) - Moini N. *Lancet Respiratory Medicine*, 2021, 9(2), pp.131-132.

We thought we got away lightly, the first time round. Early on I made myself available to return to clinical work from a long-awaited research role I had only just begun. I was on the ward the day we received our first COVID-positive patients and can remember all of those we admitted by name. They were not many, but we had no idea what to expect. We ended up with a small but significant number of cases, with every death poignant and tragic. It was nothing compared with the tidal wave hitting our colleagues in Europe and North America. Every day, even us non-believers had the words “there but for the Grace of God go we” hanging in our thoughts. By June, we felt victorious as our numbers were dwindling and business as usual became the mantra. I felt confident enough to ask my research supervisor for a return date and handed in my notice to the clinical team, who accepted it with grace. In any case, things were fine now, and the surge staffing we planned for was not necessary. I had worked hard in the 3 months until then, so the last weekend in June I escaped to the mountains with my partner and friends for some fresh air and exercise.

[Realising the potential of SARS-CoV-2 vaccines—a long shot?](#) - The Lancet Respiratory Medicine. *Lancet Respiratory Medicine*, 2021, 9(2), p.117.

The race to develop safe, effective vaccines against severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has produced impressive results. As of Jan 18, 2021, 64 vaccines were in clinical development according to the WHO COVID-19 candidate vaccine database. Phase 3 data for two RNA vaccines, BNT162b2 (Pfizer/BioNTech) and mRNA-1273 (Moderna), and the adenovirus-vectored vaccine ChAdOx1 nCoV-19 (Oxford University/AstraZeneca) have been published in peer-reviewed journals, and further phase 3 reports are expected imminently. Although the start of mass vaccination programmes should be celebrated, many challenges lie ahead in reaching eligible recipients and protecting those at risk from COVID-19-related morbidity and mortality.

[Remdesivir for COVID-19 in Europe: will it provide value for money?](#) - Dal-Ré R., et al. *Lancet Respiratory Medicine*, 2021, 9(2), pp.127-128.

Remdesivir is the first antiviral drug fully licensed for the treatment of patients with COVID-19. The use of remdesivir in 2020, can be summarised in five stages. First, between May and July, several regulatory agencies issued the authorisation—under emergency or conditional schemes—to treat selected patients hospitalised with COVID-19. 1 Second, the manufacturer, Gilead, set a price of US\$2340 for a 5-day treatment course in late June. 2 Third, in October, the US Food and Drug Administration (FDA) 3 granted full approval for use of remdesivir in adults and adolescent patients (aged 12 years or older; >40 kg) with COVID-19; it should be given intravenously for 5 days (six vials) to patients who do not need invasive mechanical ventilation or extracorporeal membrane oxygenation, or both, and 10 days (11 vials) in those who require this type of support. Fourth, the European Commission 4 signed a joint procurement contract in October for \$1.2 billion of remdesivir vials to treat 500 000 patients in 36 European countries, although the full marketing authorisation has not been granted yet. And fifth, the negative interim results on mortality from the largest randomised controlled trial (RCT), WHO Solidarity, 5 were reported.





[Safety and efficacy of inhaled nebulised interferon beta-1a \(SNG001\) for treatment of SARS-CoV-2 infection: a randomised, double-blind, placebo-controlled, phase 2 trial](#) - Monk PD., et al. *Lancet Respiratory Medicine*, 2021, 9(2), pp.196-206.

Background: Severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection carries a substantial risk of severe and prolonged illness; treatment options are currently limited. We assessed the efficacy and safety of inhaled nebulised interferon beta-1a (SNG001) for the treatment of patients admitted to hospital with COVID-19.

[Suggestions for lung function testing in the context of COVID-19](#) - Milanese M., et al. *Respiratory Medicine*, 2021, 177, 106292.

The 2019 coronavirus disease (COVID-19) pandemic is currently a challenge worldwide. Due to the characteristics of lung function tests, the risk of cross infection may be high between health care workers and patients. The role of lung function testing is well defined for the diagnosis of various diseases and conditions. Lung function tests are also indispensable in evaluating the response to medical treatment, in monitoring patient respiratory and systemic pathologies, and in evaluating preoperative risk in cardiothoracic and major abdominal surgeries. However, lung function testing represents a potential route for COVID-19 transmission, due to the aerosol generated during the procedures and the concentration of patients with pulmonary diseases in lung function laboratories. Currently, the opportunities for COVID-19 transmission remain partially unknown, and data are continuously evolving. This review provides useful information on the risks and recommendations for lung function testing, which have varied according to the phase of the pandemic. This information may support national and regional boards and the health authorities to which they belong. There is a need for rapid re-opening of lung function laboratories, but maximum safety is required in the COVID-19 era.

[Summary of COVID-19 medicines guidance: Respiratory disorders.](#) - Specialist Pharmacy Service (SPS); 2021.

This page summarises and signposts to medicine related guidance we're aware of from professional and government bodies relating to coronavirus and respiratory disorders.

[Ventilation management and clinical outcomes in invasively ventilated patients with COVID-19 \(PRoVENT-COVID\): a national, multicentre, observational cohort study](#) - Botta M., et al. *Lancet Respiratory Medicine*, 2021, 9(2), pp.139-148.

Background: Little is known about the practice of ventilation management in patients with COVID-19. We aimed to describe the practice of ventilation management and to establish outcomes in invasively ventilated patients with COVID-19 in a single country during the first month of the outbreak.

## Guidelines

[COVID-19 rapid guideline: delivery of radiotherapy.](#) - NICE; 2021.

12 February 2021: NICE added 3 recommendations for research following a review of the evidence on the effects of systemic anticancer treatment or radiotherapy on the risk of severe illness or death in patients with cancer and COVID-19.

[COVID-19 rapid guideline: delivery of systemic anticancer treatments.](#) - NICE; 2021.

12 February 2021: NICE reviewed the evidence on the effects of systemic anticancer treatment on risk of severe illness or death in patients with cancer and COVID-19 and made new recommendations.





## Practice Changing Update from UpToDate

### [Tocilizumab for COVID-19 \(February 2021\)](#)

Results from two recent open-label randomized trials of the interleukin-6 pathway inhibitor tocilizumab suggest a mortality benefit in severe COVID-19. In one of these trials, tocilizumab reduced 28-day mortality among over 4000 patients who were on oxygen support of any kind and had a C-reactive protein level  $\geq 75$  mg/L (29 versus 33 percent with usual care alone) 1. In the other, tocilizumab reduced in-hospital mortality among 800 patients who had started high-flow oxygen or more intensive respiratory support within the prior 24 hours (28 versus 36 percent with usual care alone) 2. These findings contrast with prior smaller trials, which had not identified a mortality benefit. Potential reasons for the difference include a higher baseline mortality and concomitant use of glucocorticoids in the more recent trials. Overall, tocilizumab does appear to have a clinical benefit, although optimal use remains uncertain. We suggest tocilizumab in addition to usual care for patients who recently initiated high-flow oxygen, noninvasive ventilation, or mechanical ventilation and for select patients on low-flow oxygen who are clinically progressing and have significantly elevated inflammatory markers.

## Influenza

### Articles

[Influenza infection](#). - BMJ Best Practice; 2021.

Update 03 February 2021: Baloxavir marboxil approved for post-exposure prophylaxis of influenza. The approved indication for baloxavir marboxil has been expanded in the US and in Europe to include post-exposure prophylaxis of influenza for patients 12 years of age and older.

## Interstitial lung diseases (pulmonary fibrosis)

### Articles

[CD4+T cells in ageing-associated interstitial lung abnormalities show evidence of pro-inflammatory phenotypic and functional profile](#) - Machahua C., et al. *Thorax* 2021;76:152-160.

Background: Interstitial lung abnormalities (ILA) occur in around 10% of subjects over 60 years, and are associated with a higher rate of all-cause mortality. The pathogenic mechanisms are unclear, and the putative contribution of alterations in the immune response has not been explored. Normal ageing is associated with immune deficiencies, including Naïve T-cell decrease and greater expression of the proliferative-limiting, co-inhibitory receptor killer-cell lectin-like receptor G1 (KLRG1).

[Living with idiopathic pulmonary fibrosis](#) - Kirby T. *Lancet Respiratory Medicine*, 2021, 9(2), pp.136-138.

John Conway grew up in small village close to Sligo town, in the west of Ireland, where his parents ran a small bar and grocery store, and reared poultry. He himself was drawn to maths and science at school, and studied electronics at a local college. However, the wider world beckoned, and 32 years ago John moved to London, UK, which has been his home ever since.

[MRI in interstitial lung disease \(M-ILD\): a momentum to innovate lung diagnostic](#) - Ciet P. *Thorax* 2021;76:108.

The prevalence of interstitial lung disease (ILD) is high and progressively increasing.<sup>1</sup> Mortality and morbidity vary according to ILD subtype, but overall median survival is poor, ranging from 5 to 14 years.<sup>2</sup> Irrespective of classification and cause of lung fibrosis, several patients present with progressive-fibrosing ILD (PF-ILD), characterised by a rapid decline in lung function.



[New reference atlas for pulmonary fibrosis severity score in systemic sclerosis](#) - Williamson L. *Lancet Respiratory Medicine*, 2021, 9(2), pp.130-131.

Of all the rheumatological diseases, systemic sclerosis has the highest morbidity and mortality rates. Also known as scleroderma, this autoimmune connective tissue disease, mostly affecting young and middle-aged women, is characterised by interstitial lung disease (ILD)—the most common cause of death. Although rare, it is associated with great uncertainty of outcome for patients. A key challenge remains amongst clinicians in quantifying ILD accurately and consistently. This challenge is one that a group of specialists from the Leiden University Medical Centre and the Haga Teaching Hospital in The Netherlands have recognised. Rheumatologists (Dr Anne Schouffoer and Dr Jeska de Vries-Bouwstra), Pulmonologist (Dr Maarten Ninaber), Radiologists (Dr Julie Korving and Dr Lucia Kroft), and Computer Specialist (Dr Berend Stoel) are involved in the clinical care of patients with systemic sclerosis. The *Lancet Respiratory Medicine* spoke to the group about the creation of their high-resolution Computer Tomography (HRCT) reference Atlas.

[Quantification of pulmonary perfusion in idiopathic pulmonary fibrosis with first pass dynamic contrast-enhanced perfusion MRI](#) - Weatherley ND., et al. *Thorax* 2021;76:144-151.

Introduction: Idiopathic pulmonary fibrosis (IPF) is a fatal disease of lung scarring. Many patients later develop raised pulmonary vascular pressures, sometimes disproportionate to the interstitial disease. Previous therapeutic approaches that have targeted pulmonary vascular changes have not demonstrated clinical efficacy, and quantitative assessment of regional pulmonary vascular involvement using perfusion imaging may provide a biomarker for further therapeutic insights.

[Serum angiotensin converting enzyme elevation in association with artificial stone silicosis](#) - Hoy RF., et al. *Respiratory Medicine*, 2021, 177, 106289.

Background: Silicosis is a rapidly emerging major health concern for workers in the artificial stone benchtop industry. The association between serum angiotensin converting enzyme (sACE) levels and artificial stone silicosis is unknown.

## Obstructive sleep apnoea

### Articles

[Reliability of automatic detection of AHI during positive airway pressure treatment in obstructive sleep apnea patients: A “real-life study”](#) - Fanfulla F., et al. *Respiratory Medicine*, 2021, 177, 106303.

Introduction: Automatic event detection (AED) of residual apnea-hypopnea index (AHI) by ventilators is a current practice in sleep and mechanical ventilation Units but this methodology has not been validated in an unselected population of OSA patients. Aim of the present study was to assess in a “real-life” condition the reliability of AED during PAP therapy by the in-built software compared to full polysomnography during follow-up.

### Reports

[Obstructive sleep apnoea—Effectiveness of different mandibular advancement devices.](#) - The Dental Elf; 2021.

This review of the effectiveness of different mandibular advancement devices (MADs) for obstructive sleep apnoea included 50 randomised controlled trials. While the findings suggest that mono-bloc MADs are more effective duo-bloc devices the quality of the available evidence is very low.



## 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 CORIMUNO-19 Collaborative group. *The Lancet Respiratory Medicine* 2021;:https://doi.org/10.1016/S2213-2600(20)30556-7.

Patients with COVID-19 pneumonia have an excess of inflammation and increased concentrations of cytokines including interleukin-1 (IL-1). Anakinra did not improve outcomes in patients with mild-to-moderate COVID-19 pneumonia. Further studies are needed to assess the efficacy of anakinra in other selected groups of patients with more severe COVID-19.

[Pneumococcal community-acquired pneumonia in the intensive care unit: Azithromycin remains protective despite macrolide resistance](#) - Shorr AF., et al. *Respiratory Medicine*, 2021, 177, 106307.

Background: Streptococcus pneumoniae (SP) remains the leading pathogen in community-acquired pneumonia (CAP). Despite the increasing prevalence of macrolide resistance in SP, guidelines recommend the use of macrolides as part of a combination regimen for intensive care unit (ICU) patients with CAP. We sought to describe if macrolide resistance affects outcomes in SP CAP in the ICU and if macrolides remain associated with a mortality advantage in an era of greater resistance.

[Severe organising pneumonia following COVID-19](#) - Vadász I., et al. *Thorax* 2021;76:201-204.

Various forms of diffuse parenchymal lung disease have been proposed as potential consequences of severe COVID-19. We describe the clinical, radiological and histological findings of patients with COVID-19-associated acute respiratory distress syndrome who later developed severe organising pneumonia including longitudinal follow-up. Our findings may have important implications for the therapeutic modalities in the late-phase of severe COVID-19 and might partially explain why a subgroup of COVID-19 patients benefits from systemic corticosteroids.

### Reports

[Oral hygiene for critically ill patients.](#) - The Dental Elf; 2021.

This Cochrane review updated assessing the impact of oral health measures on the incidence of ventilator associated pneumonia (VAP) in critically ill patients receiving mechanical ventilation in intensive care includes 40 randomised controlled trials and suggests that Chlorhexidine mouthwash or gel, as part of oral health measures, probably reduces the incidence of developing VAP.

## Pulmonary hypertension

### Articles

[Assessment of pinch force strength in patients with pulmonary arterial hypertension in the era of AOS® dry powder inhaler based therapies](#) - Sahay S., et al. *Respiratory Medicine*, 2021, 177, 106308.

Over the last two decades treatment options have drastically improved for patients with pulmonary arterial hypertension (PAH). In the recent times, there is renewed interest in dry powder inhaler (DPI) based inhaled therapies in the treatment of PAH. PAH patients are well known to have respiratory and other muscle weakness either related to the disease itself or due to the underlying diseases like connective tissue disease (CTD). CTD PAH patients are at particular disadvantage as there is a concern if they have enough strength to press the buttons on the inhaler device, needed to pierce the drug capsule inside the device. Additionally, CTD PAH patients develop hand deformities making it difficult to use devices. To our knowledge, this is the first study to systematically examine the pinch force strength needed to pierce the capsule in DPI devices in patients with PAH. We enrolled 35 patients and our results showed that all PAH patients were able to generate enough pinch strength needed to pierce the capsule regardless of the etiology of PAH.



## [Interventional and pharmacological management of chronic thromboembolic pulmonary hypertension](#)

Ghofrani HA., et al. *Respiratory Medicine*, 2021, 177, 106293.

Chronic thromboembolic pulmonary hypertension (CTEPH) is caused by obstruction of the pulmonary vasculature, leading to increased pulmonary vascular resistance and ultimately right ventricular failure, the leading cause of death in non-operated patients. This article reviews the current management of CTEPH. The standard of care in CTEPH is pulmonary endarterectomy (PEA). However, up to 40% of patients with CTEPH are ineligible for PEA, and up to 51% develop persistent/recurrent PH after PEA. Riociguat is currently the only medical therapy licensed for treatment of inoperable or persistent/recurrent CTEPH after PEA based on the results of the Phase III CHEST-1 study. Studies of balloon pulmonary angioplasty (BPA) have shown benefits in patients with inoperable or persistent/recurrent CTEPH after PEA; however, data are lacking from large, prospective, controlled studies. Studies of macitentan in patients with inoperable CTEPH and treprostinil in patients with inoperable or persistent/recurrent CTEPH showed positive results. Combination therapy is under evaluation in CTEPH, and long-term data are not available. In the future, CTEPH may be managed by PEA, medical therapy or BPA – alone or in combination, according to individual patient needs. Patients should be referred to experienced centers capable of assessing and delivering all options.

## [Riociguat treatment in patients with pulmonary arterial hypertension: Final safety data from the EXPERT registry](#) - Hoyer MM., et al. *Respiratory Medicine*, 2021, 177, 106241.

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 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.

### Reports

#### [National Pulmonary Hypertension Audit 11th Annual Report](#). - NHS Digital; 2021.

The National Audit of Pulmonary Hypertension is an audit of processes and outcomes and has the participation of all eight designated centres. The Audit uses national standards to measure clinical practice. This 11th Annual Report includes 10 year survival curves for diagnostic groups and reference tables, as well as results against the National Standards Publication Date:21 Jan 2021 Geographic Coverage:England, Scotland Date Range:01 Apr 2019 to 31 Mar 2020

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

### Articles

[Characteristics, physiology and mortality of intubated patients in an emergency care population in sub-Saharan Africa: a prospective cohort study from Kigali, Rwanda](#) - Mbanjumucyo G., Aluisio A., Cattermole GN. *Emergency Medicine Journal* 2021;38(3):178-183.

The first-attempt and overall success rates for intubation in this ED in Rwanda were comparable to those in high-income countries (HIC). Mortality postintubation is associated with lower postintubation SBP and higher postintubation shock index. The high complication and mortality rates suggest the need for better resources and training to address differences in compared with HIC.

[Effect of neuromuscular electrical stimulation on the duration of mechanical ventilation](#). - Gutiérrez-Arias RE., et al. *Respiratory Care* 2021;:doi.org/10.4187/respcare.08363.

Background: It has been proposed that neuromuscular or functional electrical stimulation may have effects on respiratory muscles through its systemic effects, similar to those produced by exercise training.



However, its impact on the duration of invasive mechanical ventilation has not been adequately defined. We sought to evaluate the effect of neuromuscular or functional electrical stimulation on the duration of invasive mechanical ventilation in critically ill subjects.

[Lung transplantation for silicosis and recovery: an Australian case study.](#) - McEwen K., Brodie L. *British Journal of Nursing* 2021;30(3):178–183.

Lung transplantation is a well-established treatment for a variety of end-stage pulmonary diseases. However, the journey of a lung transplant recipient is complex and multifaceted. Silicosis is a rare indication for lung transplantation, but no other treatment is yet available for this disease in its end stages. This Australian case study presents a 52-year-old man with silicosis who received bilateral lung transplantation. The patient was frequently noncompliant with noninvasive ventilation therapy and experienced the complication of type 2 respiratory failure. Patient education and support provided, particularly around medication management following transplantation surgery, are discussed here. The patient's social situation and its implications for both him and his family are also considered.

[Small airway loss in the physiologically ageing lung: a cross-sectional study in unused donor lungs](#) - Verleden SE., et al. *Lancet Respiratory Medicine*, 2021, 9(2), pp.167-174.

Background: Physiological lung ageing is associated with a gradual decline in dynamic lung volumes and a progressive increase in residual volume due to diminished elastic recoil of the lung, loss of alveolar tissue, and lower chest wall compliance. However, the effects of ageing on the small airways (ie, airways <2.0 mm in diameter) remain largely unknown. By using a combination of ex-vivo conventional CT (resolution 1 mm), whole lung micro-CT (resolution 150 µm), and micro-CT of extracted cores (resolution 10 µm), we aimed to provide a multiresolution assessment of the small airways in lung ageing in a large cohort of never smokers.

[Ventilation management and clinical outcomes in invasively ventilated patients with COVID-19 \(PRoVENT-COVID\): a national, multicentre, observational cohort study](#) - Botta M., et al. *Lancet Respiratory Medicine*, 2021, 9(2), pp.139-148.

Background: Little is known about the practice of ventilation management in patients with COVID-19. We aimed to describe the practice of ventilation management and to establish outcomes in invasively ventilated patients with COVID-19 in a single country during the first month of the outbreak.

## Respiratory rehabilitation

### Articles

[Capsaicin combined with ice stimulation improves swallowing function in patients with dysphagia after stroke: A randomised controlled trial.](#) - Cui F., et al. *Journal of Oral Rehabilitation* 2020;47(10):1297-1303. The combined use of capsaicin with ice stimulation is beneficial to the recovery of swallowing function of patients with dysphagia, which should be included into the clinical practice.

[Effects of rehabilitation methods on lower-limb muscle function and functional performance in patients with cystic fibrosis: a systematic review.](#) Poncin W., et al. *Clinical Rehabilitation* 2020;:doi: 10.1177/0269215520972941.

OBJECTIVE: To investigate the effects of rehabilitation methods on leg muscle function and functional performance in cystic fibrosis. CONCLUSION: Combined aerobic and resistance training enhances leg muscle strength in cystic fibrosis. There is insufficient data on other leg muscle outcomes, nor on alternative rehabilitation strategies.



## Respiratory syncytial virus (RSV)

### Articles

[National burden estimates of hospitalisations for acute lower respiratory infections due to respiratory syncytial virus in young children in 2019 among 58 countries: a modelling study](#) - Li Y., et al. *Lancet Respiratory Medicine*, 2021, 9(2), pp.175-185.

Background: Respiratory syncytial virus (RSV) is the predominant viral pathogen associated with acute lower respiratory infection (ALRI) in children who are younger than 5 years. Little is reported on the national estimates of RSV-associated ALRI hospitalisations in these children on the basis of robust epidemiological data. We aimed to generate national level estimates for RSV-associated ALRI hospitalisations in children aged younger than 5 years.

## Sarcoidosis

### Articles

[High expression of mTOR signaling in granulomatous lesions is not predictive for the clinical course of sarcoidosis](#) - Pizzini A., et al. *Respiratory Medicine*, 2021, 177, 106294.

Introduction: Sarcoidosis is a systemic granulomatous disease with a variable clinical presentation and disease course. There is still no reliable biomarker available, which assists in the diagnosis or prediction of the clinical course. According to a murine model, the expression level of the metabolic checkpoint kinase mechanistic target of Rapamycin complex 1 (mTORC1) in granulomas of sarcoidosis patients may be used as a clinical biomarker.

## Tuberculosis

### Articles

[Genome-wide association study of non-tuberculous mycobacterial pulmonary disease](#) - Cho J., et al. *Thorax* 2021;76:169-177.

Background: The prevalence of non-tuberculous mycobacterial pulmonary disease (NTM-PD) is increasing in South Korea and many parts of the world. However, the genetic factors underlying susceptibility to this disease remain elusive.

