Management of chronic obstructive pulmonary disease

Abstract

Chronic obstructive pulmonary disease is a prevalent condition in the UK, associated with high morbidity and mortality. Hospital physicians manage a significant portion of acute chronic obstructive pulmonary disease admissions to hospital and readmissions after discharge.

Optimal management of exacerbations requires controlled oxygen therapy and ventilatory support where necessary, and careful administration of bronchodilators, steroids and antibiotics. Holistic care for these patients includes nutritional supplementation and palliative support for those with advanced disease.

To reduce the chance of readmission, chronic obstructive pulmonary disease care bundles can be used, along with a review of inhaled and oral therapies. Where available, hospital-at-home discharge schemes can safely facilitate early discharge.

Most importantly, high quality evidence-based smoking cessation support must be offered to smokers. Exercise improves the physiological and psychological condition of people with chronic obstructive pulmonary disease and should be encouraged, with referral to a pulmonary rehabilitation service if available.

Key words: Chronic obstructive pulmonary disease; COPD; Discharge; Exacerbation; Pulmonary rehabilitation; Readmission; Smoking cessation

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Introduction

Chronic obstructive pulmonary disease is a chronic and preventable condition, characterised by persistent airflow obstruction caused by small airways inflammation (chronic bronchitis) and alveolar destruction (emphysema). It is most commonly caused by tobacco smoking but is also associated with indoor and outdoor air pollution and occupational exposures. The diagnosis can be made in a patient who has a relevant exposure history and symptoms of dyspnoea, chronic cough, sputum production and lower respiratory tract infections, with airflow obstruction defined as post-bronchodilator forced expiratory volume in 1 second/forced vital capacity <0.70 (Global Initiative for Chronic Obstructive Lung Disease, 2020).

There are an estimated 1 200 000 people in the UK with a diagnosis of chronic obstructive pulmonary disease. It is the second most common reason for emergency hospital admissions and accounts for almost 30 000 deaths each year (British Lung Foundation, 2020). Rates of readmission to hospital after discharge with a chronic obstructive pulmonary disease exacerbation are as high as 30% (Harries et al, 2017). Hospital physicians are therefore exposed to high numbers of inpatients with chronic obstructive pulmonary disease. This review collates key points from the literature, with particular focus on management of acute exacerbations, interventions to reduce readmissions and smoking cessation.

Management of exacerbations

A chronic obstructive pulmonary disease exacerbation is an acute deterioration in respiratory symptoms requiring additional treatment (Wedzicha and Seemungal, 2007). Viral infections, particularly rhinovirus, appear to trigger most exacerbations, although bacterial infections and environmental factors such as pollution and air temperature play a role as well (Woodhead et al, 2005). A subgroup of patients have elevated levels of eosinophils in the

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airways, lungs and blood, which may increase their susceptibility to viral infections (Papi et al, 2006), but also suggest a greater response and clinical improvement with systemic steroids (Bafadhel et al, 2012).

The management of exacerbations aims to both reduce the severity and duration of a current illness, and reduce the risk of future events. This is important as exacerbations cause progression of chronic obstructive pulmonary disease and are associated with poor health status (Wedzicha and Seemungal, 2007).

The best predictor of exacerbations is a history of frequent exacerbations (>2 per year) (Hurst et al, 2010), but low lung function, poor health status and gastro-oesophageal reflux (Ingebrigtsen et al, 2015) are also associated with increased risk. Low levels of markers of systemic inflammation in the stable state indicate low risk (Thomsen et al, 2013).

Inpatient management

More than four out of every five exacerbations are treated in the community, but sometimes patients need to be admitted for ongoing care. A hospital admission with chronic obstructive pulmonary disease is a prognostic indicator, associated with approximately 50% 5-year survival (Hoogendoorn et al, 2011). Triggers for hospital assessment include (Global Initiative for Chronic Obstructive Lung Disease, 2020):

1. Severe symptoms of breathlessness, high respiratory rate, low oxygen saturations, confusion or drowsiness
2. Respiratory failure
3. Failure of treatment in the community
4. Serious comorbidity, eg worsening heart failure or arrhythmia
5. Insufficient support to be managed in the community.

It is critical to identify patients with respiratory failure requiring ventilatory support, as this has a well-documented effect on survival. Patients should be assessed after starting initial management which includes supplemental controlled oxygen, bronchodilators and often corticosteroids and/or antibiotics.

Controlled oxygen

Before performing a blood gas in a patient with chronic obstructive pulmonary disease, target peripheral oxygen saturations of 88–92% should be achieved. If the partial pressure of carbon dioxide ($PaCO_2$) is normal this can be adjusted to 94–98%, unless there is a previous episode requiring a ventilator (non-invasive or invasive) (O'Driscoll et al, 2017). Oxygen should be administered via a Venturi mask in an unstable patient or nasal cannulae in a stable patient, with a repeat blood gas measurement taken after 30–60 minutes.

Bronchodilators

Combined $beta_2$-agonist and anticholinergic bronchodilators are most conveniently delivered as metered dose inhalers via a spacer or nebulised. Side effects (tremor, tachycardia, inner unrest and low potassium levels) are frequent, especially in patients on nebulisers, and should be monitored.

Corticosteroids

In patients with <2% eosinophils in peripheral blood, there is likely no benefit of giving oral prednisolone 0.5 mg/kg and possible harm associated with using corticosteroids (Camp et al, 2018). Prednisolone should be given for 5 days with no tapering (Walters et al, 2018). Even a short course of prednisolone is associated with risks of sepsis, pneumonia and death (Waljee et al, 2017), so its use should always be considered carefully.

Antibiotics

Patients requiring ventilatory support should be given antibiotics, as should patients with increased sputum volume and purulence. Low levels of procalcitonin can identify patients where antibiotics are not required (Mathioudakis et al, 2017). The most frequent pathogen is *Haemophilus influenzae* and the drug of choice is often doxycycline or amoxicillin + clavulanic acid.

Ventilatory support

Patients with chronic obstructive pulmonary disease exacerbations and decompensated type 2 respiratory failure (pH<7.35, $PaCO_2$>6.5) that persists despite 60 minutes of optimal medical therapy should be given ventilatory support, preferably as non-invasive ventilation (Davidson et al, 2016). In practice, initiation of non-invasive ventilation is often delayed significantly beyond 60 minutes (as a result of slight improvement in their symptoms or blood gas parameters, adjustment of their oxygen or administration of more medical therapy), with consequently poorer outcomes (National Confidential Enquiry into Patient Outcome and Death, 2017).

Patients with life-threatening acute respiratory failure who are unable to tolerate or are deteriorating with non-invasive ventilation will, if clinically appropriate, require admission to an intensive care unit for invasive ventilation.

Intubation and ventilation may not be appropriate in many patients because of disease severity and functional status. Plans for the event of treatment failure, including cardiopulmonary resuscitation and escalation in care, should be made before starting treatments such as non-invasive ventilation. A full discussion on non-invasive ventilation is beyond the scope of this article, but there are detailed guidelines from the British Thoracic Society (Davidson et al, 2016).

Reducing chronic obstructive pulmonary disease readmissions

The days and weeks following a hospital discharge are the most vulnerable for patients with chronic obstructive pulmonary disease, as there is a high likelihood of rehospitalisation and death (Lindenauer et al, 2018). The latest National Asthma and COPD Audit programme report showed that, in 2017, 24.8% and 43.1% of patients with chronic obstructive pulmonary disease were readmitted at least once within 30 days and 90 days respectively of their index discharge date, with chronic obstructive pulmonary disease or emphysema being the most common cause for readmission (Hurst et al, 2019). Frequent hospital admissions for chronic obstructive pulmonary disease exacerbations can lead to poor quality of life, depression, increased mortality risk, societal burden and significant healthcare costs (Press et al, 2019).

The managing team may reduce chronic obstructive pulmonary disease readmissions by providing patient education, optimising inhaled and oral medications, and ensuring good inhaler technique, smoking cessation support and appropriate referrals for long-term oxygen assessment and/or non-invasive ventilation on discharge (Freedman, 2019). Patients who are at high risk for further exacerbations should also have early outpatient clinic follow up.

Chronic obstructive pulmonary disease discharge bundles

Care bundles are evidence-based, structured interventions that are used to reduce readmissions and improve patient outcomes (Calvert et al, 2014). An expert panel from the British Thoracic Society and NHS Improvement developed the bundle content for the management of acute exacerbations of chronic obstructive pulmonary disease at discharge (Turner et al, 2015). This aims to reduce the number of readmissions following discharge after an exacerbation of chronic obstructive pulmonary disease and ensure that all aspects of the patient's care are considered. This care bundle identifies five high impact actions to ensure the best clinical outcome for patients admitted with an acute exacerbation of chronic obstructive pulmonary disease.

1. Review patient's medications and demonstrate use of inhalers
2. Provide written self-management plan and emergency drug pack
3. Assess and offer referral for smoking cessation
4. Assess for suitability for pulmonary rehabilitation
5. Arrange follow-up call within 72 hours of discharge.

A checklist is completed by the respiratory specialist nurse on discharge. The details included in the discharge care bundle may differ between hospitals according to their needs and preferences (eg regarding emergency drug packs), but the British Thoracic Society's high impact actions are essential components.

Medication review: escalation and de-escalation strategies

It is essential that patients are discharged home on optimal pharmacological treatment. The Global Initiative for Chronic Obstructive Lung Disease (2020) strategy for chronic obstructive pulmonary disease provides an algorithm for changing therapy in these patients. Pharmacological management should be guided by the principles of first review and assess, then adjust if needed:

- Review symptoms (breathlessness) and risk of exacerbations
- Assess inhaler technique and adherence, and the role of non-pharmacological therapy
- Adjust pharmacological treatment: escalation or de-escalation, change of inhaler device, plan subsequent review of clinical response.

Inhaled therapy for chronic obstructive pulmonary disease contrasts that of asthma. All patients with asthma should be on inhaled corticosteroids. For chronic obstructive pulmonary disease the first-line therapies are bronchodilators (long-acting beta-agonists and long-acting muscarinic antagonists), starting with a single drug and escalating to combined long-acting beta-agonists and long-acting muscarinic antagonists (Global Initiative for Chronic Obstructive Lung Disease, 2020), although the most recent National Institute for Health and Care Excellence (2018) guidance differs slightly and recommends immediate use of combined long-acting beta-agonists and long-acting muscarinic antagonists in patients requiring more than a short-acting bronchodilator. Addition of inhaled corticosteroids should only be considered in patients with frequent (≥ 2/year) or severe exacerbations or elevated blood eosinophil levels (Singh et al, 2019) (Figure 1). Inhaled corticosteroids can be de-escalated if the patient develops pneumonia as an adverse effect or fails to respond. Most patients admitted with chronic obstructive pulmonary disease are already on inhaled treatment and the admission is an opportunity to review their medication (Chalmers et al, 2020).

Additional medications, including azithromycin and roflumilast, can be trialled by respiratory physicians in patients on maximal inhaled therapy who continue to have frequent exacerbations.

Hospital-at-home and assisted-discharge schemes

The 2018 National Institute for Health and Care Excellence guideline on chronic obstructive pulmonary disease management recommends that hospital-at-home and assisted-discharge

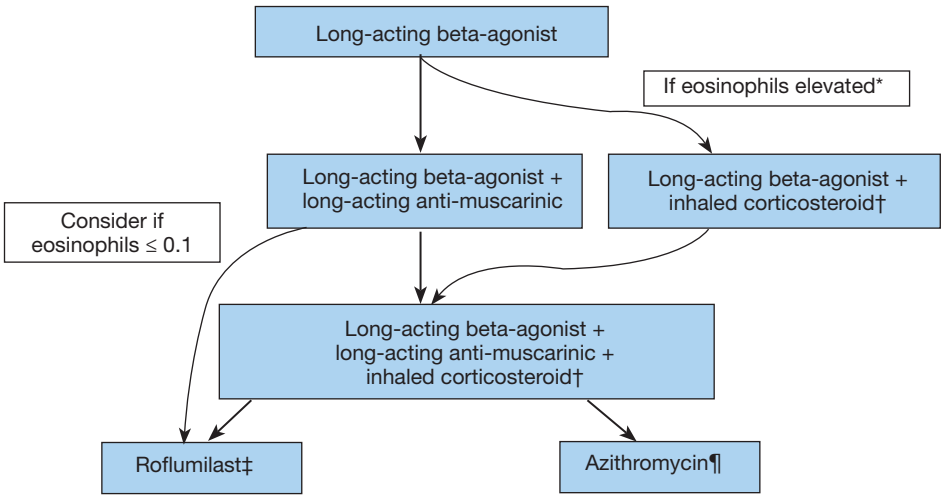

Figure 1. Stepwise escalation of medical management of chronic obstructive pulmonary disease. Initial treatment is with a long-acting beta-agonist, followed by addition of a long-acting anti-muscarinic, followed by addition of an inhaled corticosteroid. If further escalation is required then roflumilast or azithromycin may be added by a respiratory physician. *Consider earlier addition of inhaled corticosteroid if eosinophils are ≥0.3x10^9/litre or ≥0.1x10^9/litre and ≥2 moderate exacerbations or one hospitalisation. †Consider de-escalation of inhaled corticosteroids if pneumonia, lack of response or inappropriate initial indication. ‡Consider roflumilast if forced expiratory volume in 1 second ≤50% and chronic bronchitis. ¶Azithromycin can be trialled by respiratory physicians in patients with frequent and severe exacerbations, despite optimisation of other medications, in line with British Thoracic Society guidelines (Smith et al, 2020). From Global Initiative for Chronic Obstructive Lung Disease (2020).

schemes are safe and effective and should be used as an alternative way of caring for people with exacerbations of chronic obstructive pulmonary disease who would otherwise need to be admitted or stay in hospital.

Hospital-at-home may be an effective alternative for a small group of patients and may be more cost effective than acute admission to hospital, while maintaining similar outcomes (Shepperd et al, 2008). However, there are no firm recommendations for patient selection, which should consider available resources, patient preference and the absence of poor prognostic factors (National Institute for Health and Care Excellence, 2018).

In assisted discharge, selected patients with a chronic obstructive pulmonary disease exacerbation may be discharged home with nebulised therapy, oral steroids and regular home visits until the exacerbation resolves. This can reduce the length of hospital stay and associated healthcare costs.

Pulmonary rehabilitation

Pulmonary rehabilitation can be defined as 'a comprehensive intervention based on thorough patient assessment followed by patient-tailored therapies that include, but are not limited to, exercise training, education, self-management intervention aiming at behaviour change, designed to improve the physical and psychological condition of people with chronic respiratory disease and to promote the long-term adherence to health-enhancing behaviours' (Spruit et al, 2013).

A typical pulmonary rehabilitation programme is delivered as a minimum of twice weekly supervised sessions for 8–12 weeks in an outpatient (hospital or community) setting (Bolton et al, 2013).

Patients who are functionally limited by breathlessness should be referred for outpatient pulmonary rehabilitation. The duration of effect is 6–18 months and most patients will benefit from repeated courses of pulmonary rehabilitation. Referrals for pulmonary rehabilitation should be made regardless of smoking status, as patients can be offered smoking cessation advice and referred to smoking cessation services. Patients admitted with an exacerbation of chronic obstructive pulmonary disease should be offered pulmonary rehabilitation on discharge, ideally within 1 month (Bolton et al, 2013; National Institute for Health and Care Excellence, 2018).

Nutrition

Patients with chronic obstructive pulmonary disease commonly have unintentional weight loss and malnutrition which have been associated with increased healthcare use, reduced functional capacity and poorer clinical outcomes. Referral to a dietician may be beneficial. Nutritional support, via oral supplements, can overcome energy and protein deficiencies leading to improved nutritional status and functional capacity (Collins et al, 2019). Patients with low body mass index should be encouraged to exercise to augment the effects of nutritional supplementation (National Institute for Health and Care Excellence, 2018).

Vaccination

All patients with chronic obstructive pulmonary disease should be offered pneumococcal and annual influenza vaccinations in line with current National Institute for Health and Care Excellence (2018) guidelines.

Long-term oxygen therapy

Long-term oxygen therapy refers to use of oxygen for at least 15 hours per day in chronically hypoxaemic patients. This offers survival benefit and improves pulmonary haemodynamics in selected patients with chronic obstructive pulmonary disease (Hardinge et al, 2015).

Long-term oxygen therapy is indicated in patients with a resting arterial partial pressure of oxygen of ≤7.3 kPa, or ≤8 kPa with one or more of polycythaemia (haematocrit ≥55%), peripheral oedema or pulmonary hypertension (Hardinge et al, 2015). The assessment should be made 8 weeks after an exacerbation and reproduced on two measurements 3 weeks apart.

Patients who have frequent exacerbations are often unable to achieve a sufficient period of stability and may need to be assessed at an earlier stage after exacerbation. Hospitalised patients who are breathless with SaO_2 ≤92% and unable to manage off oxygen may rarely

require long-term oxygen therapy ordering at discharge. In these cases, patients should be counselled that at follow-up assessment the long-term oxygen therapy may no longer be required and may be removed.

Long-term non-invasive ventilation assessment

Chronic hypercapnia increases the likelihood of hospital admissions, rapid clinical deterioration and is a determinant of increased mortality. Managing hypercapnia may be an important intervention for improving the health outcome of chronic obstructive pulmonary disease patients with chronic respiratory failure (Ergan et al, 2019).

National Institute for Health and Care Excellence (2018) recommends referral of patients who are adequately treated but have chronic hypercapnic failure and need assisted ventilation (invasive or non-invasive) during an exacerbation, or who are hypercapnic or acidotic on long-term oxygen therapy, to a specialist centre for consideration of long-term domiciliary non-invasive ventilation.

Palliative care

Patients with advanced chronic obstructive pulmonary disease often benefit from involving the multidisciplinary palliative care team in their management. This helps reduce frequent hospital admissions. Admission to hospice is an option for management of end-stage chronic obstructive pulmonary disease. These patients may also have intractable breathlessness unresponsive to usual treatment and may benefit from opioids, benzodiazepines, tricyclic antidepressants and oxygen if appropriate. Handheld fans, an inexpensive intervention, are often helpful for relieving breathlessness (National Institute for Health and Care Excellence, 2018). The opportunity for early planning for end-of-life and holistic support for the patient, family members and carers is often missed during hospital admissions.

Smoking cessation

The importance of smoking cessation in the management of chronic obstructive pulmonary disease cannot be overstated. In the UK 14.4% of adults smoke, with significant variation between regions and social class (NHS Digital, 2019). Smoking is responsible for almost half a million hospital admissions and 77 800 deaths each year in the UK (NHS Digital, 2019). Smoking cessation is the most important intervention that can influence the progression of chronic obstructive pulmonary disease (World Health Organization, 2019).

Structural changes for tobacco control include increased taxation, advertising bans, pack warnings, smoke-free environments and cessation programmes (World Health Organization, 2019). Between 2011 and 2018 the prevalence of smoking in the UK declined from 19.8% to 14.4% yet, paradoxically, 68% fewer prescription items for smoking cessation were dispensed over that time (NHS Digital, 2019). Almost 60% of smokers want to quit but continue to smoke because of addiction (Office for National Statistics, 2019). Prescribing healthcare professionals should offer every smoker evidence-based interventions to support them. Smokers are four times more likely to successfully quit when using smoking cessation services (Office for National Statistics, 2019) and hospital-initiated smoking cessation support is a cost-effective way to reduce morbidity, mortality and hospital readmissions (Mullen et al, 2017; Cartmell et al, 2018).

Pharmacotherapy consists of nicotine replacement therapy, bupropion (a noradrenaline-dopamine reuptake inhibitor), and varenicline (a partial nicotine receptor agonist) which is the most commonly used non-nicotine replacement therapy cessation medication in the UK (NHS Digital, 2019) and the most effective (Mills et al, 2012).

Concerns about varenicline being associated with an increased risk of suicide have been thoroughly addressed by powerful studies and shown to be unfounded. However, smoking cessation and nicotine withdrawal is associated with an increased risk of adverse neuropsychiatric effects in those with and without a history of psychiatric disorders. This should not discourage smokers from quitting as the benefits for physical and mental health outweigh the risks, but clinicians and patients should be cognisant of this.

A double-blind randomised placebo-controlled trial of 8144 smokers with and without a history of psychiatric disorders found varenicline to be effective for smoking cessation

without a significantly increased risk of neuropsychiatric side effects compared to placebo, bupropion and nicotine patches (Anthenelli et al, 2016). A systematic review and meta-analysis (Thomas et al, 2015) of 39 randomised control trials with 10 761 participants found no evidence of increased risk of suicide, suicide attempts, suicidal ideation, depression or death with varenicline. A Swedish population-based cohort study of 7 917 436 people aged 15 years and over, including 67 757 people treated with varenicline between 2006 and 2009, found no evidence for increased risk of suicidal behaviour, although there was a small increase in anxiety and mood conditions in people with pre-existing psychiatric disorders (Molero et al, 2015).

Varenicline should be prescribed as part of a programme of behavioural support. All hospital patients who smoke and are motivated to quit should be offered a referral to the local smoking cessation service for counselling, medical therapies and follow-up contact and prescriptions after discharge. The patient may decline counselling or a local referral service may not be available, but this should not preclude a patient from being prescribed this effective treatment (National Institute for Health and Care Excellence, 2007).

Electronic cigarettes, so-called e-cigarettes or vapes, are devices that heat up glycerine and propylene glycol liquid into a vapour which is inhaled, and can be used with or without nicotine or flavourings. They are not licenced medications, but there are minimum standards for safety and quality from the European Union Tobacco and Related Products Regulations 2016. They have gained popularity over the last decade with an estimated 5% of the UK population using them, most being smokers or recent ex-smokers (McNeill et al, 2018; Action on Smoking and Health, 2019).

A review by Public Health England concluded that, while electronic cigarettes should not be considered 'safe', they are about 95% less harmful than smoking (McNeill et al, 2018). However, the International Forum of Respiratory Societies' position is that comparing the relative harms of electronic cigarettes to tobacco, the most lethal product in history, is flawed (Ferkol et al, 2018). National Institute for Health and Care Excellence recommends offering all smokers support from a cessation service including counselling and pharmacotherapy but, as a harm reduction strategy, does not recommend discouraging people from using electronic cigarettes as an aid to smoking cessation. This UK stance on electronic cigarettes is opposed by the European Respiratory Society (Pisinger et al, 2019), the International Forum of Respiratory Societies (Ferkol et al, 2018) and the World Health Organization (2020).

The Centers for Disease Control in the USA reported an outbreak of acute lung injury in 2019 with 2807 patients hospitalised and 68 deaths as a result. There was evidence linking this outbreak mainly to the cannabinoid tetrahydrocannabinol and vitamin E acetate additives to the vape liquid. As a result, the Centers for Disease Control (2020) recommends avoiding these additives, and discourages any electronic cigarette user going back to tobacco cigarettes. They also recommend choosing Food and Drug Administration approved medications for smoking cessation. As a relatively new product the safety and effectiveness of electronic cigarettes is still unclear.

Conclusions

The authors started writing this review before the COVID-19 pandemic. Undoubtedly medicine will be affected by this for a significant time. With many services for patients with chronic obstructive pulmonary disease being provided virtually, postponed or unavailable, from outpatient clinics to pulmonary rehabilitation and smoking cessation support, the options are now more limited. Patients with chronic obstructive pulmonary disease are a vulnerable cohort, especially in the midst of a viral pneumonia pandemic. It is important to maintain focus on what can be done for these patients. For patients who continue to smoke, providing compassionate advice and support through nicotine replacement therapy and varenicline remains a very high impact intervention. Pulmonary rehabilitation may not be available, but emphasising the importance of physical exercise is critical. Indoor exercise or socially distanced outdoor exercise should be encouraged. Optimising inhaled medication is easy to do by following the Global Initiative for Chronic Obstructive Lung Disease guidelines, as is checking inhaler technique. These core principles of chronic obstructive pulmonary disease management should always be kept in mind, but they are now more important than ever until something resembling normal service resumes.

Key points

- Despite declining smoking rates in the UK, chronic obstructive pulmonary disease remains a common problem in patients presenting to hospital.
- Managing acute hospital admissions for chronic obstructive pulmonary disease includes careful use of medication, oxygen and non-invasive ventilation.
- Measures to reduce readmission rates include optimising medication, hospital-at-home schemes, pulmonary rehabilitation, long-term oxygen and ventilation and, where appropriate, palliative care.
- Providing effective smoking cessation support to patients admitted with chronic obstructive pulmonary disease is critical in slowing the progression of disease, improving quality of life and reducing readmissions to hospital.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

References

Action on Smoking and Health. Use of e-cigarettes (vaporisers) among adults in Great Britain. 2019. https://ash.org.uk/information-and-resources/fact-sheets/statistical/use-of-e-cigarettes-among-adults-in-great-britain-2019/ (accessed 13 May 2021)

Anthenelli RM, Benowitz NL, West R et al. Neuropsychiatric safety and efficacy of varenicline, bupropion, and nicotine patch in smokers with and without psychiatric disorders (EAGLES): a double-blind, randomised, placebo-controlled clinical trial. Lancet. 2016;387(10037):2507–2520. https://doi.org/10.1016/S0140-6736(16)30272-0

Bafadhel M, McKenna S, Terry S et al. Blood eosinophils to direct corticosteroid treatment of exacerbations of chronic obstructive pulmonary disease: a randomized placebo-controlled trial. Am J Respir Crit Care Med. 2012;186(1):48–55. https://doi.org/10.1164/rccm.201108-1553OC

Bolton CE, Bevan-Smith EF, Blakey JD, British Thoracic Society Pulmonary Rehabilitation Guideline Development Group, on behalf of the British Thoracic Society Standards of Care Committee et al. British Thoracic Society guideline on pulmonary rehabilitation in adults: accredited by NICE. Thorax. 2013;68(Suppl 2):ii1–ii30. https://doi.org/10.1136/thoraxjnl-2013-203808

British Lung Foundation. Chronic obstructive pulmonary disease (COPD) statistics. 2020. https://statistics.blf.org.uk/copd (accessed 13 May 2021)

Calvert J, Lim WS, Rodrigo C, Turner A, Welham S. British Thoracic Society Pilot Care Bundle Project: a care bundles-based approach to improving standards of care in chronic obstructive pulmonary disease and community acquired pneumonia. British Thoracic Society Reports. 2014;6(4):1–56

Camp J, Cane JL, Bafadhel M. Shall we focus on the eosinophil to guide treatment with systemic corticosteroids during acute exacerbations of COPD?: PRO. Med Sci. 2018;6(3):74. https://doi.org/10.3390/medsci6030074

Cartmell KB, Dismuke CE, Dooley M et al. Effect of an evidence-based inpatient tobacco dependence treatment service on 1-year postdischarge health care costs. Med Care. 2018;56(10):883–889. https://doi.org/10.1097/MLR.0000000000000979

Centers for Disease Control and Prevention. Outbreak of Lung Injury Associated with the use of E-cigarette, or Vaping, Products. 2020. https://www.cdc.gov/tobacco/basic_information/e-cigarettes/severe-lung-disease.html (accessed 7 June 2021)

Chalmers JD, Laska IF, Franssen FM et al. Withdrawal of inhaled corticosteroids in COPD: a European Respiratory society guideline. Eur Respir J. 2020;55(6):2000351. https://doi.org/10.1183/13993003.00351-2020

Collins PF, Yang IA, Chang YC, Vaughan A. Nutritional support in chronic obstructive pulmonary disease (COPD): an evidence update. J Thorac Dis. 2019;11(S17):S2230–S2237. https://doi.org/10.21037/jtd.2019.10.41

Davidson AC, Banham S, Elliott M et al. BTS/ICS guideline for the ventilatory management of acute hypercapnic respiratory failure in adults. Thorax. 2016;71(Suppl 2):ii1–ii35. https://doi.org/10.1136/thoraxjnl-2015-208209

Ergan B, Oczkowski S, Rochwerg B et al. European Respiratory Society guidelines on long-term home non-invasive ventilation for management of COPD. Eur Respir J. 2019;54(3):1901003. https://doi.org/10.1183/13993003.01003-2019

Ferkol TW, Farber HJ, La Grutta S et al. Electronic cigarette use in youths: a position statement of the Forum of International Respiratory Societies. Eur Respir J. 2018;51(5):1800278. https://doi.org/10.1183/13993003.00278-2018

Freedman N. Reducing COPD readmissions: Strategies for the pulmonologist to improve outcomes. Chest. 2019;156(4):802–807. https://doi.org/10.1016/j.chest.2019.06.005

Global Initiative for Chronic Obstructive Lung Disease. Global strategy for prevention, diagnosis and management of chronic obstructive pulmonary disease. 2020. https://goldcopd.org/wp-content/uploads/2019/11/GOLD-2020-REPORT-ver1.0wms.pdf (accessed 18 March 2021)

Hardinge M, Annandale J, Bourne S, British Thoracic Society Home Oxygen Guideline Development Group et al. British Thoracic Society guidelines for home oxygen use in adults: accredited by NICE. Thorax. 2015;70(Suppl 1):i1–i43. https://doi.org/10.1136/thoraxjnl-2015-206865

Harries TH, Thornton H, Crichton S et al. Hospital readmissions for COPD: a retrospective longitudinal study. NPJ Prim Care Respir Med. 2017;27(1):1–6

Hoogendoorn M, Hoogenveen RT, Rutten-van Molken MP, Vestbo J, Feenstra TL. Case fatality of COPD exacerbations: a meta-analysis and statistical modelling approach. Eur Respir J. 2011;37(3):508–515. https://doi.org/10.1183/09031936.00043710

Hurst JR, Vestbo J, Anzueto A et al. Susceptibility to exacerbation in chronic obstructive pulmonary disease. N Engl J Med. 2010;363(12):1128–1138. https://doi.org/10.1056/NEJMoa0909883

Hurst J, Stone RA, McMillan V, National Asthma and Chronic Obstructive Pulmonary Disease Audit Programme (NACAP) et al. Outcomes of patients included in the 2017 COPD clinical audit (patients with COPD exacerbations discharged from acute hospitals in England and Wales between February and September 2017). London: Royal College of Physicians, 2019

Ingebrigtsen TS, Marott JL, Vestbo J et al. Gastro-esophageal reflux disease and exacerbations in chronic obstructive pulmonary disease. Respirology. 2015;20(1):101–107. https://doi.org/10.1111/resp.12420

Lindenauer PK, Dharmarajan K, Qin L et al. Risk trajectories of readmission and death in the first year after hospitalization for chronic obstructive pulmonary disease. Am J Respir Crit Care Med. 2018;197(8):1009–1017. https://doi.org/10.1164/rccm.201709-1852OC

Mathioudakis AG, Chatzimavridou-Grigoriadou V, Corlateanu A, Vestbo J. Procalcitonin to guide antibiotic administration in COPD exacerbations: a meta-analysis. Eur Respir Rev. 2017;26(143):160073. https://doi.org/10.1183/16000617.0073-2016

McNeill A, Brose LS, Calder R, Bauld L, Robson D. Evidence review of e-cigarettes and heated tobacco products 2018. A Report Commissioned by Public Health England. London: Public Health England. 2018;6

Mills EJ, Wu P, Lockhart I et al. Comparisons of high-dose and combination nicotine replacement therapy, varenicline, and bupropion for smoking cessation: a systematic review and multiple treatment meta-analysis. Ann Med. 2012;44(6):588–597. https://doi.org/10.3109/07853890.2012.705016

Molero Y, Lichtenstein P, Zetterqvist J, Gumpert CH, Fazel S. Varenicline and risk of psychiatric conditions, suicidal behaviour, criminal offending, and transport accidents and offences: population based cohort study. BMJ. 2015;350:h2388–h2388. https://doi.org/10.1136/bmj.h2388

Mullen KA, Manuel DG, Hawken SJ et al. Effectiveness of a hospital-initiated smoking cessation programme: 2-year health and healthcare outcomes. Tob Control. 2017;26(3):293–299. https://doi.org/10.1136/tobaccocontrol-2015-052728

National Confidential Enquiry into Patient Outcome and Death. Inspiring change. A review of the quality of care provided to patients receiving acute non-invasive ventilation. 2017. https://www.ncepod.org.uk/2017niv.html (accessed 13 May 2021)

National Institute for Health and Care Excellence. Varenicline for smoking cessation. Technology Appraisal Guidance [TA 123]. 2007. https://www.nice.org.uk/guidance/ta123 (accessed 18 March 2021)

National Institute for Health and Care Excellence. Chronic obstructive pulmonary disease in over 16s: diagnosis and management (NG 115). 2018. https://www.nice.org.uk/guidance/ng115 (accessed 18 March 2021)

NHS Digital. Statistics on smoking, England – 2019. 2019. https://digital.nhs.uk/data-and-information/publications/statistical/statistics-on-smoking/statistics-on-smoking-england-2019 (accessed 18 March 2021)

O'Driscoll BR, Howard LS, Earis J, Mak V. British Thoracic Society Guideline for oxygen use in adults in healthcare and emergency settings. BMJ Open Respir Res. 2017;4(1):e000170. https://doi.org/10.1136/bmjresp-2016-000170

Office for National Statistics. Adult smoking habits in the UK: 2018. 2019. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/healthandlifeexpectancies/bulletins/adultsmokinghabitsingreatbritain/2018#%20toc (accessed 18 March 2021)

Papi A, Bellettato CM, Braccioni F et al. Infections and airway inflammation in chronic obstructive pulmonary disease severe exacerbations. Am J Respir Crit Care Med. 2006;173(10):1114–1121. https://doi.org/10.1164/rccm.200506-859OC

Pisinger C, Dagli E, Filippidis FT et al. ERS and tobacco harm reduction. Eur Respir J. 2019;54(6):1902009. https://doi.org/10.1183/13993003.02009-2019

Press VG, Au DH, Bourbeau J et al. Reducing chronic obstructive pulmonary disease hospital readmissions. An official American Thoracic Society workshop report. Ann Am Thorac Soc. 2019;16(2):161–170. https://doi.org/10.1513/AnnalsATS.201811-755WS

Shepperd S, Doll H, Angus RM et al. Admission avoidance hospital at home. Cochrane Database Syst Rev. 2008;9(9):CD007491. https://doi.org/10.1002/14651858.CD007491.pub2

Singh D, Agusti A, Anzueto A et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive lung disease: the GOLD science committee report 2019. Eur Respir J. 2019;53(5):1900164. https://doi.org/10.1183/13993003.00164-2019

Smith D, Du Rand IA, Addy C et al. British Thoracic Society guideline for the use of long-term macrolides in adults with respiratory disease. BMJ Open Respir Res. 2020;7(1):e000489. https://doi.org/10.1136/bmjresp-2019-000489

Spruit MA, Singh SJ, Garvey C et al. An official American Thoracic Society/European Respiratory Society statement: key concepts and advances in pulmonary rehabilitation. Am J Respir Crit Care Med. 2013;188(8):e13–e64. https://doi.org/10.1164/rccm.201309-1634ST

Thomas KH, Martin RM, Knipe DW, Higgins JP, Gunnell D. Risk of neuropsychiatric adverse events associated with varenicline: systematic review and meta-analysis. BMJ. 2015;350:h1109. https://doi.org/10.1136/bmj.h1109

Thomsen M, Ingebrigtsen TS, Marott JL et al. Inflammatory biomarkers and exacerbations in chronic obstructive pulmonary disease. JAMA. 2013;309(22):2353–2361. https://doi.org/10.1001/jama.2013.5732

Turner AM, Lim WS, Rodrigo C, Welham SA, Calvert JM. A care-bundles approach to improving standard of care in AECOPD admissions: results of a national project. Thorax. 2015;70(10):992–994. https://doi.org/10.1136/thoraxjnl-2015-206833

Waljee AK, Rogers MA, Lin P et al. Short term use of oral corticosteroids and related harms among adults in the United States: population based cohort study. BMJ. 2017;357:j1415. https://doi.org/10.1136/bmj.j1415

Walters JA, Tan DJ, White CJ, Wood-Baker R. Different durations of corticosteroid therapy for exacerbations of chronic obstructive pulmonary disease. Cochrane Database Syst Rev. 2018;3(3):CD006897. https://doi.org/10.1002/14651858.CD006897.pub4

Wedzicha JA, Seemungal TA. COPD exacerbations: defining their cause and prevention. Lancet. 2007;370(9589):786–796. https://doi.org/10.1016/S0140-6736(07)61382-8

Woodhead M, Blasi F, Ewig S et al. Guidelines for the management of adult lower respiratory tract infections. Eur Respir J. 2005;26(6):1138–1180. https://doi.org/10.1183/09031936.05.00055705

World Health Organization. WHO report on the global tobacco epidemic 2019: Offer help to quit tobacco use. 2019. https://www.who.int/tobacco/global_report/en/ (accessed 18 March 2021)

World Health Organization. E-cigarettes. 2020. https://www.who.int/news-room/q-a-detail/e-cigarettes-how-risky-are-they (accessed 18 March 2021)