

PCRS Position Statement

Point-of-care testing of C-reactive protein (CRP) for acute assessment in COPD

Point-of-care testing of C-reactive protein (CRP) for the acute assessment of worsening symptoms in people known to have COPD can safely reduce the use of antibiotics and could help improve the diagnostic approach towards someone presenting in such a crisis. New high-quality evidence has emerged since the last NICE COPD update and we encourage re-opening and review of the current guideline to enable clinicians and system leaders to understand whether and how to implement this promising diagnostic aid.

Background

Exacerbations of chronic obstructive pulmonary disease (COPD) account for 115,000 hospitalisations in the UK each year.¹ COPD exacerbations can be caused by environmental triggers and bacterial or viral airways infection.² In an era of antibiotic guardianship, it is essential to ensure that patients only receive antibiotics when clinically warranted. However, determining whether an exacerbation is caused by a bacterial infection, a viral infection or another trigger can be challenging in the primary care setting and the default approach is often to prescribe an antibiotic to treat a presumed underlying bacterial infection.

Currently, an estimated 80% of patients presenting in primary care with moderate exacerbations of COPD are treated with antibiotics.³ However, not all patients prescribed an antibiotic for an acute COPD exacerbation will benefit from such treatment.⁴⁻⁶ Unnecessary antibiotic prescribing can contribute to increases in the prevalence of drug-resistant bacteria and result in a delay in patients receiving potentially more effective interventions when their exacerbation is not driven by an underlying bacterial infection. Identifying patients most likely to benefit from antibiotic therapy, and conversely, those unlikely to benefit from antibiotic therapy, has the potential to reduce unnecessary antibiotic use, preserve the patients airway microbiome, reducing the risk for colonisation by drug-resistant bacteria, and for adverse events such as colitis caused by *Clostridioides difficile*.

Current clinical guidelines for antibiotic prescribing in COPD

Antibiotic prescribing for patients presenting with a COPD exacerbation is still essentially guided by the criteria set out by Anthonisen and colleagues in 1987, with antibiotics recommended for those with increased breathlessness, increased sputum volume and increased sputum purulence.^{7,8}

The current NICE guidelines were issued in December 2018⁹ and recommend that antibiotic therapy should be considered for patients presenting with an acute exacerbation of COPD only after taking into account:

- the severity of symptoms, particularly sputum colour changes and increases in volume or thickness beyond the person's normal day-to-day variation,
- whether they may need to go into hospital for treatment,
- previous exacerbation and hospital admission history, and the risk of developing complications,
- previous sputum culture and susceptibility results,

- the risk of antimicrobial resistance and repeated courses of antibiotics.

While point-of-care CRP testing is not included in the algorithm for COPD exacerbation management, point-of-care CRP testing is included in the clinical guidance recommendation for the diagnosis and management of community and hospital acquired pneumonia.¹⁰ In this setting, the guidance is not to routinely offer antibiotic therapy if the CRP is <20 mg/L, consider a delayed antibiotic prescription for use at a later date should symptoms worsen if the CRP is between 20 and 100 mg/L and to offer antibiotics if the CRP is >100 mg/L.

Point-of-care testing to guide antibiotic prescribing for COPD exacerbation

A single drop of blood from a finger prick test is required to perform the test using an assay kit and analyser instrument (quantitative measurement) or disposable single-use test strips (semi-quantitative measurement) with results available within a few minutes.

Patients with raised levels of CRP in their blood are those most likely to benefit from antibiotics to treat an underlying bacterial infection.⁴ The PACE study was a multicentre trial conducted at 86 primary care clinics in England and Wales.³ The study included 653 patients with an acute exacerbation of COPD who were randomised to receive usual care guided by point-of-care CRP testing via a rapid finger prick test or usual care only. For CRP-guided care, clinicians were advised that antibiotics were unlikely to be beneficial when the CRP level was <20 mg/L, likely to be beneficial when the CRP level was >40 mg/L and possibly beneficial when the CRP level fell between 20 and 40 mg/L and purulent sputum was present. Prescribing decision were to be based on a comprehensive assessment of likely risks and benefits. Antibiotic prescribing was 20% lower among those patients who received usual care guided point-of-care CRP testing compared with those who received usual care only (57% vs 77%, respectively). Importantly, this reduction in antibiotic use did not have a negative effect on patients' recovery over the first two weeks after their consultation at their GP surgery, or on their well-being or use of health care services over the following 6 months. The results of the study show that CRP-guided prescribing of antibiotics for COPD exacerbations presenting in primary care can reduce the proportion of patients prescribed an antibiotic

with no evidence of harm in terms of COPD-related health status or of increased visits to GPs or a greater need for antibiotics over the following 6 months.

PCRS position

- Patients presenting with acutely worsening symptoms and known to have COPD should receive antibiotics only when COPD exacerbation has been determined as the cause of the change and then when bacterial infection is considered to be the most likely trigger.
- Point-of-care testing of C-reactive protein (CRP) in primary care may help reduce unnecessary prescribing of antibiotics for people with COPD by enabling a more considered diagnostic approach to people with COPD in crisis.
- When evaluating a patient with COPD experiencing a symptomatic exacerbation, such as cough and worsening breathlessness, all potential triggers should be considered including tobacco exposure, air quality, psychosocial factors, viral infection, and bacterial infection.
- PCRS encourage NICE to re-open the review of the current COPD management guideline and come to a position on the use of CRP point-of-care testing given the emerging data that such testing can reduce unnecessary prescribing of antibiotics without compromising patient safety.

References

- NHS England. Overview of potential to reduce lives lost from Chronic Obstructive Pulmonary Disease (COPD). Available at: <https://www.england.nhs.uk/wp-content/uploads/2014/02/rm-fs-6.pdf>. Accessed February 2020.
- Barnes PJ, Burney PG, Silverman EK, *et al*. Chronic obstructive pulmonary disease. *Nat Rev Dis Primers* 2015;1:15076.
- Butler CC, Gillespie D, White P, *et al*. C-reactive protein testing to guide antibiotic prescribing for COPD Exacerbations. *NEJM* 2019;381:111-120.
- Miravittles M, Moragas A, Hernández S, Bayona C, Llor C. Is it possible to identify exacerbations of mild to moderate COPD that do not require antibiotic treatment? *Chest* 2013;144:1571-7.
- Vollenweider DJ, Jarrett H, Steurer-Stey CA, Garcia-Aymerich J, Puhan MA. Antibiotics for exacerbations of chronic obstructive pulmonary disease. *Cochrane Database Syst Rev* 2012;12:CD010257.
- van Velzen P, Ter Riet G, Bresser P, *et al*. Doxycycline for outpatient-treated acute exacerbations of COPD: a randomised double-blind placebo-controlled trial. *Lancet Respir Med* 2017;5:492-9.
- Anthonisen NR, Manfreda J, Warren CP, Hershfield ES, Harding GK, Nelson NA. Antibiotic therapy in exacerbations of chronic obstructive pulmonary disease. *Ann Intern Med* 1987;106:196-204.
- Global Initiative for Chronic Obstructive Lung Disease (GOLD). 2020 Global Strategy for Prevention, Diagnosis and Management of COPD. Available at: <https://goldcopd.org/gold-reports/>. Accessed December 2019.
- NICE. Chronic obstructive pulmonary disease (acute exacerbation): antimicrobial prescribing. Available at: www.nice.org.uk/guidance/ng114 Accessed December 2019.
- NICE. Pneumonia in adults: diagnosis and management. Available at: <https://www.nice.org.uk/guidance/cg191>. Accessed December 2019.

Approved by PCRS Executive policy lead on committee: 25 February 2020

The Primary Care Respiratory Society UK Registered office Miria House, 1683b High Street, Knowle, Solihull B93 0LL Registered Charity 1098117
Company No 4298947 VAT Registration Number 866 1543 09 Telephone +44 (0)1675 477600 Email info@pcrs-uk.org Website <http://www.pcrs-uk.org>

We are grateful to our corporate supporters including AstraZeneca UK Ltd, Boehringer Ingelheim Ltd, Chiesi Ltd, Cipla EU Ltd, Circassia Ltd, Napp Pharmaceuticals and Novartis UK for their financial support which supports the core activities of the Charity and allows PCRS to make its services either freely available or at greatly reduced rates to its members.