

# The place of point of care testing for C-reactive protein in the community care of respiratory tract infections

Respiratory tract infections (RTIs) and infectious exacerbations of chronic obstructive pulmonary disease (IE-COPD) are frequent primary care presentations. Indeed, pneumonia seems to be increasingly common, partly reflecting changes in disease labelling.<sup>1</sup> Based on UK primary care records, the incidence of clinically diagnosed pneumonia increased from 1.50 cases per 1000 person-years in 2002 to 2.22 per 1000 in 2017. Rates of clinically suspected pneumonia rose from 23.7 cases in 2002 to 30.4 per 1000 in 2008 and then declined 18.2 per 1000 in 2017.<sup>1</sup>

Estimates of “rigorously measured” COPD prevalence vary from 4% and 10%.<sup>2</sup> Rayner *et al* estimated that the prevalence of definite COPD was 2.57% of the total population in England. COPD was most common in people aged 35 years or older (4.56%) and ex- or current smokers (5.41%). These estimates are higher than the prevalence of 1.9% based on the pay for performance disease register. The prevalence of definite and probable COPD was 3.02% of the total population, 5.38% in people aged 35 years or older and 6.46% in ex- or current smokers.<sup>3</sup>

Acute exacerbations of COPD are also common in primary care. A study that followed 2138 patients reported that 22%, 33% and 45% of people with mild, moderate and severe COPD respectively experienced at least two acute exacerbations during a year-long follow up.<sup>4</sup> Even mild acute exacerbations of COPD are associated with worsening lung function, reduced quality of life, lower levels of physical activity and increased mortality.<sup>4-7</sup>

Numerous factors can trigger acute exacerbations of COPD. The environment, such as pollution and weather, accounts for about 30% of acute exacerbations of COPD. Infections cause about 70% of exacerbations. Pathogenic bacteria, for instance, have been isolated from between 20% and 58% of people with IE-COPD. Pathogenic viruses are detected in about half of IE-COPD, sometimes alongside a bacterial infection.<sup>8,9</sup> Less commonly, fungi can cause RTIs, particularly in immunocompromised patients.<sup>10,11</sup>

The high prevalence of RTIs and IE-COPD helps account for the high rate of antibiotic use in primary care.<sup>12</sup> Across Europe, primary care accounts for between 80% and 90% of antibiotic prescriptions, mostly for RTIs.<sup>12,13</sup> As a result, several pathogens that cause RTIs, including *Streptococcus pneumoniae*, *Haemophilus influenzae*, *Pseudomonas aeruginosa* and *Mycobacterium tuberculosis*, show reduced susceptibility to several classes of antibiotics.<sup>14</sup> Inappropriate antibiotic use in primary care, therefore, contributes to the growing problem posed by antimicrobial resistance.

The Primary Care Respiratory Society (PCRS) takes the position that patients with diagnosed COPD who present with acutely worsening symptoms should receive antibiotics only when an exacerbation has been determined as the cause of the deterioration and then only when bacterial infection is considered to be the most likely trigger. In people with signs and symptoms consistent with RTIs, healthcare professionals should prescribe antibiotics only when bacteria, rather than viruses or fungi, are the most likely cause.

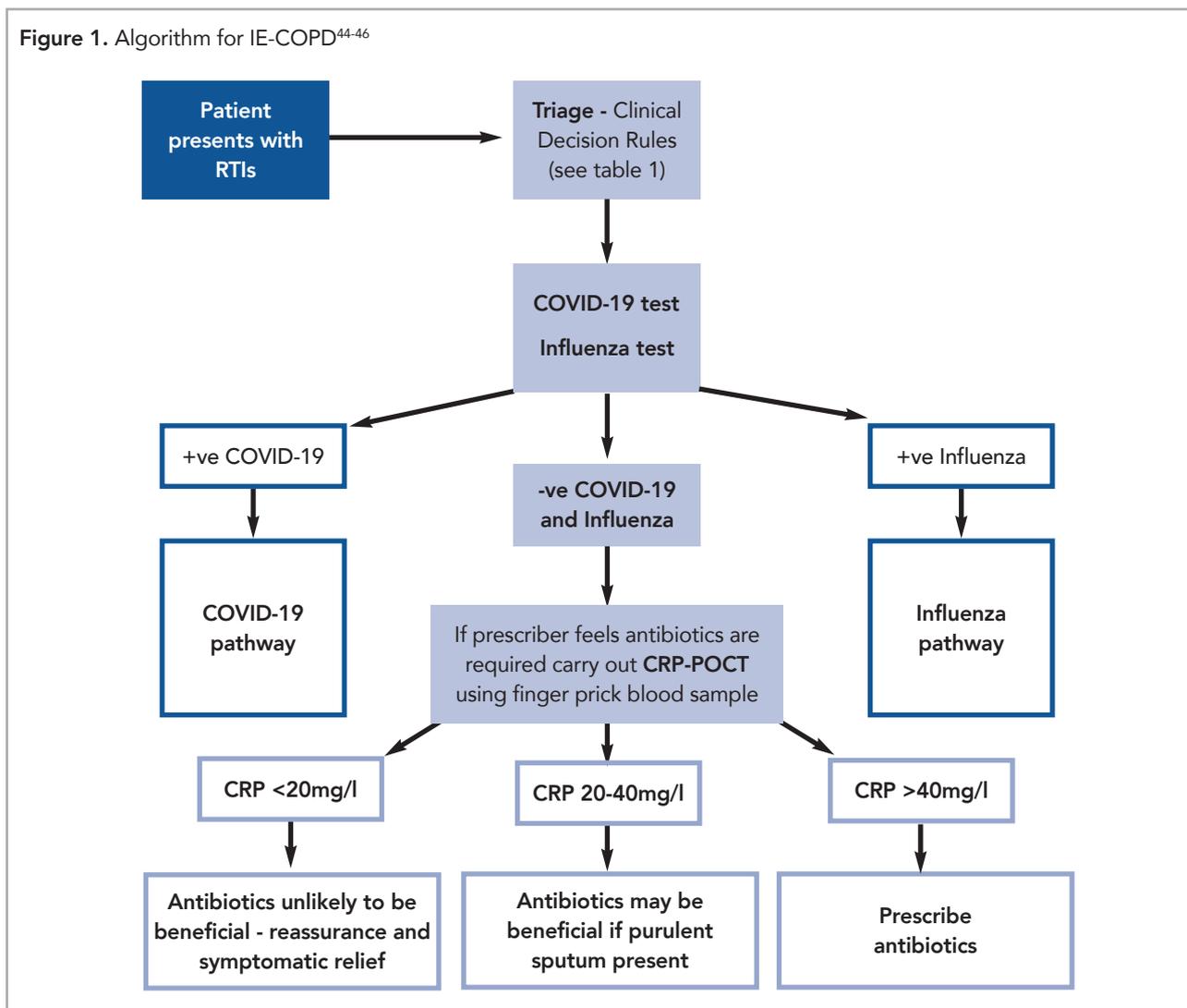
## Introduction to the pragmatic guide

A multidisciplinary panel of PCRS members developed this ‘pragmatic guide’, based around two algorithms, one for IE-COPD (figure 1) and one for RTIs that are not associated with COPD (figure 2), to help reduce inappropriate antibiotic prescribing. In particular, the algorithms and this document should help primary care teams implement point of care testing (POCT) for C-reactive protein (CRP). High-quality evidence

from various primary care settings shows that CRP POCT with guideline-based cut-offs and indications reduces antibiotic use for patients presenting with RTIs and IE-COPD.<sup>8,12,15-21</sup>

The Netherlands, for example, introduced robust antimicrobial stewardship, including CRP POCT for RTIs and uses fewer antibiotics for RTIs than any other European country.<sup>15,22</sup> This ‘pragmatic guide’ builds on this evidence and the Dutch experience. Fundamentally, the panel agreed that CRP POCT

Figure 1. Algorithm for IE-COPD<sup>44-46</sup>



addresses clinical uncertainty to support not prescribing antibiotics in appropriate low-risk patients. Conceptually, using CRP POCT to guide antibiotic use is similar to using fractional exhaled nitric oxide to guide asthma diagnosis. The panel also agreed that CRP POCT can educate and reassure patients that antibiotics are not needed.

## Biological background

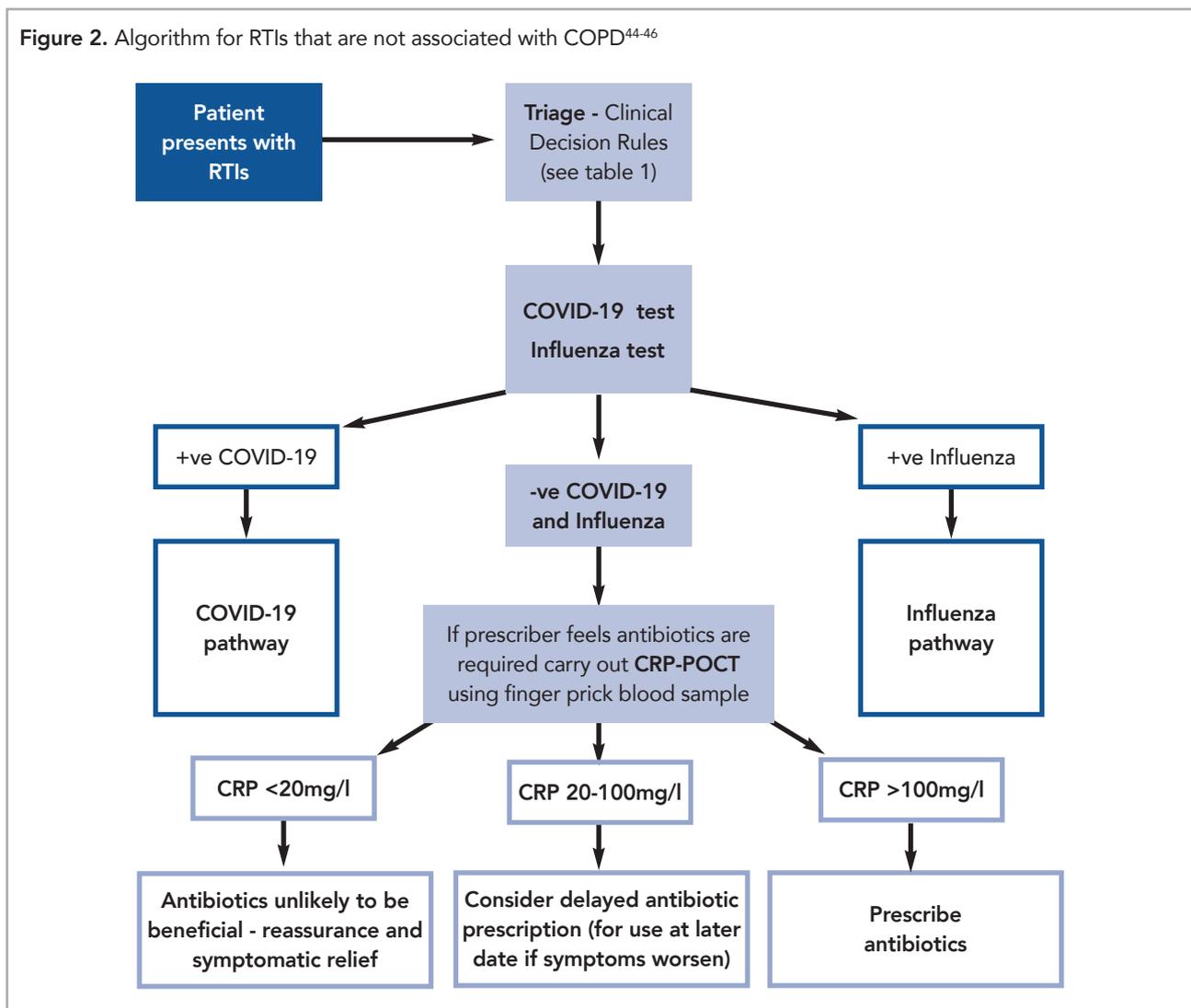
In 1930, Tillet and Francis reported that serum from people infected with *S. pneumoniae* contained a protein that could precipitate the C polysaccharide in bacterial cell walls. Levels of CRP, an acute phase reactant, rose in the early stages of *S. pneumoniae* infection.<sup>23,24</sup> Studies since then revealed that CRP has several actions that help initiate and sustain innate immune and inflammatory responses, such as activating the classical complement pathway, stimulating phagocytosis and binding to immunoglobulin receptors.<sup>24</sup>

CRP is a pattern recognition molecule. In other words,

CRP binds to specific molecular arrangements that are either exposed during cell death or present on the surfaces of pathogens. Levels of CRP, which is synthesised predominately by hepatocytes, increase within hours of tissue injury or infection and can rise more than 1000-fold during acute inflammation.<sup>24</sup> In addition to acting as a marker of bacterial infection,<sup>24</sup> increased baseline CRP levels are associated with early mortality and increases in exacerbations and hospitalisation in people with stable COPD.<sup>25</sup> This may partly reflect the systemic, musculoskeletal sequelae of COPD.<sup>25</sup>

## Evidence base

The PCRS believes that using CRP POCT in primary care may help reduce unnecessary prescribing of antibiotics by enabling a more considered diagnostic approach to people with suspected IE-COPD (figure 1) and RTIs (figure 2). Not only will a more considered diagnostic approach slow the spread of antibacterial resistance, but fewer people will experience



avoidable adverse events. For instance, beta-lactam antibiotics, such as amoxicillin, can cause: hypersensitivity reactions, including anaphylactic shock; changes to the gut microbiota allowing the overgrowth of pathogenic bacteria (eg *Clostridium difficile*); gastrointestinal disturbances; and nephrotoxicity with some cephalosporins (eg cefradine).<sup>26</sup>

A comprehensive review of the evidence supporting the use of CRP POCT in primary care to reduce unnecessary prescribing of antibiotics in people with IE-COPD and for RTIs is outside the scope of this pragmatic guide. Cooke *et al* offer a comprehensive overview.<sup>15</sup> The following examples, however, typify the evidence.

The PACE study analysed 653 patients who presented with acute exacerbations of COPD to 86 general practices in England and Wales. CRP-guided decisions reduced antibiotic prescribing and use, without any evidence of harm. Compared with usual care, 69% fewer patients in the CRP group reported using antibiotics: 77.4% and 57.0% respectively. Fewer pa-

tients in the CRP-guided group than in the usual-care group received an antibiotic prescription at the first consultation (47.7% and 69.7% respectively; adjusted odds ratio 0.31) and during the first four weeks of follow-up (59.1% and 79.7% respectively; adjusted odds ratio 0.30). After two weeks of follow-up, a statistically significant mean difference in the total score on the Clinical COPD Questionnaire, which evaluates health status in COPD patients, favoured the CRP-guided group.<sup>19</sup>

A study from South-East Asia randomised 2410 febrile patients attending primary care to usual care or to receive antibiotics if the CRP concentration exceeded either 20 mg/l or 40mg/l. By day 5, 39% of controls were prescribed an antibiotic, compared with 36% and 34% of those in the 20 mg/l and 40mg/l groups respectively. Allowing for confounders, patients in the 20 mg/l or 40mg/l groups were 14% and 20% respectively less likely be prescribed an antibiotic, although only the latter reached statistical significance. One patient (in

the 20 mg/l group) developed a serious adverse event (hospital admission) that was considered to be possibly related to the study.<sup>17</sup>

An audit from Spain found that GPs who could not access CRP testing prescribed antibiotics to significantly more patients (57.4%) than when guided by CRP (45.7%). In addition, GPs using POCT attached less weight to clinical criteria of infection and felt more confident not prescribing antibiotics despite patients' requests.<sup>20</sup>

Generally, healthcare professionals and patients are satisfied with diagnostic pathways for IE-COPD and RTIs that encompass CRP POCT irrespective of whether antibiotics are prescribed. Telephone interviews with 20 patients presenting with acute exacerbations of COPD and 20 primary care staff involved in the PACE study revealed that patients and clinicians felt that CRP POCT helped guide decisions about whether or not to prescribe antibiotics. Clinicians reported that CRP POCT enhanced their confidence in antibiotic prescribing decisions, reduced ambiguity around clinical decisions and aided patient education and communication.<sup>27</sup>

Opinions differed, however, regarding the place of CRP POCT in the diagnostic pathway. Some clinicians felt that CRP POCT should form part of the routine diagnostic work up of people presenting with acute exacerbations of COPD. Others felt that using CRP POCT is most appropriate when there is uncertainty about whether to prescribe antibiotics. The PCRS panel also differed in this regard and the algorithms in figures 1 and 2 reflect a consensus. The PCRS panel agreed with the PACE study's conclusion that "GPs should consider adopting CRP POCT in the routine management of acute exacerbations of COPD, but commissioning arrangements and further simplification of the point-of-care test need attention to facilitate this."<sup>27</sup>

## Using CRP POCT in primary care

### Clinical decision rules

Until the advent of CRP POCT, patients who presented with signs and symptoms (table 1) consistent with possible RTI or IE-COPD were diagnosed and treated empirically, based on, for example, sputum colour.<sup>9</sup> The PCRS panel felt that a chart could help promote consistent sputum evaluation. An example of such a chart can be viewed in the article by Channa, Gale and Lai *et al*, Colour vision deficiency and sputum colour charts in COPD patients: an exploratory mixed-method study (<https://rdcu.be/cJJrK>).<sup>28</sup>

In one study, for instance, coloured sputum was reported in 97.9% of 4089 samples from COPD patients with an acute exacerbation, while 46.4% were culture-positive for bacteria. Several factors predicted a positive bacterial culture including sputum purulence, which is more subjective than colour, increased dyspnoea, male sex and no fever. Sputum colour, however, emerged as the strongest predictor. Green (58.9% of samples) or yellow (45.5%) sputum samples were more likely to yield bacteria than rust-coloured (38.9%) or clear or white (18.4%) sputum. Green or yellow sputum showed a sensitivity of 94.7% and a specificity of 15.0% for the presence of bacteria compared with clear or white sputum. Sputum colour does not, however, necessarily predict the need for antibiotics.<sup>9</sup>

Other signs and symptoms can support an empirical diagnosis of IE-COPD and RTIs. For example, Htun and colleagues reported, based on a meta-analysis of 13 articles, the clinical features with the best pooled positive likelihood ratios for pneumonia among adults in primary care were: respiratory rate  $\geq 20$  per minute (3.47); temperature  $\geq 38^\circ\text{C}$  (3.21); pulse rate  $> 100$  per minute (2.79); and crackles on auscultation (2.42).<sup>10</sup> A systematic review of 11 randomised controlled trials and 8 non-randomised controlled studies encompassing

**Table 1: Clinical signs and symptoms that indicate possible bacterial causes of RTI or IE-COPD**

Chest crackles: In people with raised temperature, chest crackles could indicate the need for antibiotics irrespective of CRP levels

Cough: prescribers should exclude post-infective cough

History of recent antibiotic use

Increased breathlessness

Oxygen saturation  $< 95\%$

Possible fever ( $\geq 38^\circ\text{C}$ ); viral infections are more likely than bacterial pathogens to cause a fever

Raised heart rate  $> 100$  beats per minute

Raised respiratory rate  $\geq 20$  breathes per minute

Sputum colour (especially green or yellow)

Based on a consensus of the PCRS panel and Htun and colleagues<sup>10</sup>

**Figure 3.** Matrix showing clinical decision rules used in RTIs

	Confusion	Urea >7mmol/l	Resp Rate >30/min	Low systolic BP <90mmHg Diastolic <60mmHg	Age >65 years	
<b>CURB 65</b>	+	+	+	+	+	
<b>CRB 65</b>	+		+	+	+	Temp
	Inter-subcostal recession	Illness duration <4 days	Vomiting in last 24 hours	Wheeze present	Age <2 years	>37.8 in last 24 hours
<b>STARWAVE (children)</b>	+	+	+	+	+	+
	Pulse rate >100/min	Crackles	Resp Rate >20/min	Pro-Calcitonin	C-Reactive Protein	>38
<b>HTun</b>	+	+	+	+	+	+

16,064 patients concluded that CRP POCT in ambulatory care reduced immediate antibiotic prescribing by 19%. Including guidance on antibiotic prescribing based on the CRP level reduced immediate antibiotic prescribing by 32% in adults and 44% in children.<sup>21</sup>

Clinical decision rules (figure 3) encompass a number of signs and symptoms that indicate whether people with RTI require hospitalisation.<sup>15,28,29</sup> The CRB-65 rule, for example, includes confusion, respiratory rate, blood pressure and age to predict whether a person with pneumonia is probably suitable for home treatment or needs hospital referral.<sup>28</sup> A meta-analysis of 14 studies reported that CRB-65 accurately stratifies pneumonia severity and 30-day mortality when applied to hospitalised patients. In the community, however, CRB-65 appears to over-predict the probability of 30-day mortality especially in people at low (relative risk [RR] 9.41) and intermediate (RR 4.84 risk) as well as, to a lesser extent, high (RR 1.58) risk.<sup>29</sup>

Another clinical decision rule, STARWAVE, aims to improve antibiotic use in children who present with acute RTI and cough, by scoring: illness duration; temperature; age; intercostal or subcostal recession; wheeze; asthma; and vomiting. STARWAVE distinguishes children at very low, normal and high risk of hospital admission for RTI. STARWAVE also guides antibiotic use in children at very low risk of admission by reducing clinical uncertainty. The authors argue that halving antibiotic prescriptions in children at very low risk, staying unchanged in those at normal risk and increasing to 90% in those at high risk would reduce overall antibiotic prescribing by 10%, which, they point out, is a similar to the improvement with other antimicrobial stewardship interventions.<sup>30</sup>

Nevertheless, clinical decision rules still rely on non-specific clinical observations. Laboratory tests are associated with

higher pooled positive likelihood ratios for pneumonia among adults in primary care than clinical signs and symptoms: procalcitonin >0.25 ng/ml (7.61) and CRP > 20 mg/l (3.76).<sup>10</sup> This threshold differs, however, from that the panel suggests for starting antibiotics (>40 mg/l; figures 1 and 2).

During the PCRS panel's discussion, a grey area emerged in the case of COPD patients with purulent green sputum, but normal CRP POCT. The panel felt that most clinicians would prescribe antibiotics in this situation, but there is a lack of robust data. The panel also stressed that healthcare professionals should consider sputum culture testing early in the course of management to guide antibiotic choice and limit the spread of antimicrobial resistance driven by overuse of broad-spectrum antibiotics.

### Diagnostic work up

The PCRS panel agreed that a nasal antigen test or polymerase chain reaction should be used to exclude COVID-19 and influenza (figures 1 and 2) before considering other pathogens. In addition, when evaluating a patient with COPD experiencing worsening cough, breathlessness and other symptoms, healthcare professionals should consider all potential triggers including tobacco exposure, air quality, psychosocial factors, viruses and bacterial infection. CRP POCT should be performed if the prescriber feels that the presentation suggests bacterial infection as cause of a COPD exacerbation (figure 1) or antibiotics are needed for another RTI (figure 2).

The panel noted that in some circumstances (eg based on sputum purulence, auscultation, etc), antibiotics may be clinically indicated without CRP testing (table 1). CRP POCT will still be valuable in equivocal cases. Management depends on the CRP threshold and whether patients have RTI or COPD (figures 1 and 2).

## Follow up

CRP POCT can inform follow up. For example, the PCRS panel concurred that if CRP levels do not change or increase further after 72 hours, the prescriber should consider whether the antibiotic is appropriate. The panel also suggested that prescribers could consider the underlying CRP levels in COPD patients with history of recurrent exacerbations and purulent sputum to discuss whether further courses of antibiotics are needed or alternative strategies are more appropriate.

## Patient education

The PACE study showed that clinicians felt that CRP POCT aided patient education and communication.<sup>27</sup> The PCRS panel agreed, noting that the results of CRP POCT can be used as a patient education tool to facilitate shared decision making to determine whether antibiotics (bacterial exacerbation) or steroids (other causes of exacerbation) are the most appropriate treatment.

Healthcare professionals could also use the CRP POCT results to address other educational needs among patients and caregivers including, for example, the need for pulmonary rehabilitation and the early recognition of an impending exacerbation using sputum colour. The PCRS panel suggested that COPD rescue packs could include a sputum colour chart linked to advice about when to use antibiotics, which, currently, may not be used appropriately. Patients could, the panel suggested, visit a pharmacy offering CRP POCT to help decide if they need to use the antibiotics. In addition, improved communications skills could add value, such as by enhanced patient counselling, which, independently of CRP POCT, reduces inappropriate antibiotic use.<sup>31-34</sup>

## Overcoming barriers

A wealth of high-quality evidence shows that using CRP POCT in patients presenting with symptoms of RTI can significantly reduce the unnecessary use of antibiotics given at the index consultation.<sup>15,21</sup> The 2014 NICE guidelines for pneumonia for adults, which was withdrawn during the COVID-19 pandemic, included CRP POCT.<sup>35</sup> The PCRS panel noted, however, that numerous barriers potentially hinder implementation of CRP POCT in the management of RTIs and IE-COP. The panel stressed the value of considering new service models and performing a pilot study to determine the most effective and efficient way to implement CRP POCT into routine primary care practice.

## Barriers related to healthcare setting

CRP POCT for IE-COPD (figure 1) and RTIs (figure 2) need to be implemented in the right setting, delivered to the right patients and used in the right way to support clinical decision making to

not prescribe antibiotics in appropriate low-risk patients. For instance, to realise economies of scale and an adequate caseload to ensure quality, the CRP POCT needs to be used routinely and regularly in GP practices, pharmacies, diagnostic hubs and nursing homes. The panel noted that some POCT platforms can be used for tests other than CRP, eg D-dimer (thrombosis) and HbA<sub>1c</sub> (diabetes), which may offer economies of scale.

The setting implementing CRP POCT needs to offer good accessibility for patients, particularly given the functional limitations of some people with COPD, such as those who experienced deconditioning during the COVID-19 pandemic. In one model, a GP prescribes the antibiotic and refers the patient to the pharmacy team, who measure CRP and issues the antibiotic if CRP is elevated. This model may, however, be appropriate only for patients experiencing milder exacerbations, those without marked deconditioning or both. Nevertheless, in 2022 NHS England and NHS Improvement issued guidance for commissioners and community pharmacies delivering NHS services for running POCT services.<sup>36</sup>

A prospective pilot study in a rural community pharmacy used CRP POCT to evaluate 44 patients presenting with RTIs. GPs referred 25 of these patients. After testing, six patients were referred to the GP, five allocated to 'watch and wait', while pharmacists offered 33 self-care advice. None of the 'watch and wait' and self-care patients revisited the pharmacy or their GP. Overall, 42 patients receiving the test reported that they would have otherwise visited the GP and would have expected antibiotics.<sup>36</sup> While promising, this was a pilot study with a relatively small population and the most appropriate setting may depend on location, such as rural versus urban. Further studies are, therefore, needed.

A system needs to be in place to ensure the results are fed-back to responsible healthcare professionals and recorded in the medical records. The system also need to take account of the increasing use of remote consultations, which may be a barrier to the use of CRP POCT. The panel felt that remote consultations are likely to persist for the foreseeable future.

## Barriers related to staffing

Patients with possible IE-COPD or RTIs face a potential barrier accessing GPs in a timely fashion, especially given the pressures on the NHS arising from the COVID-19 pandemic. Limited work-force capacity, even aside from the pandemic, presents a barrier in terms of training (eg in using POCT equipment and clinical examination skills), reimbursement and having the staff to perform CRP POCT. Some centres have a relatively high staff turnover, which potentially exacerbates staffing issues. To help partly overcome barriers related to staffing, the panel suggested that CRP POCT could be encompassed by the increasing number of Clinical Support

Services, supported by an expansion of the range of health-care professionals eligible to prescribe antibiotics.

## Barriers related to finance

Introducing CRP POCT is associated with upfront costs in terms of equipment, training and External Quality Assessment system. A negative or subthreshold CRP value may also increase costs due to the greater need for inhaled therapies and step-up to triple therapy (inhaled corticosteroid, long-acting muscarinic antagonist and long-acting  $\beta$ 2-agonist) in people with COPD. Reduced prescribing of antibiotics, costs associated side effects of antibiotics and contribution to antimicrobial resistance may offset some of the additional expenditure. For example, an analysis of the PACE study found that higher total medication costs during the 6 months after presentation (mainly a 5.4% increase in prescribing of inhaled medication in the CRP POCT arm) offset the reduced antibiotic costs at the initial consultation.<sup>37</sup>

Such findings are, however, sensitive to changes in the antibiotic regimen. A recent study reported that in people with COPD exacerbations, clinical cure and bacterial eradication did not differ significantly between short (five days or fewer) and long (six days or longer) courses of antibiotic. The authors suggest that shorter antibiotic courses may reduce antimicrobial resistance and may become first-line regimens for ambulatory COPD patients.<sup>38</sup> While such changes may change the incremental cost-effectiveness, they do not change the other arguments for using CRP POCT to support not prescribing antibiotics in appropriate low-risk patients with IE-COPD or RTIs.

Improved diagnosis will also reduce healthcare encounters in primary care. CRP POCT is unlikely to impact hospitalisation rates, at least during a 6 month follow-up.<sup>19</sup> CRP POCT is, however, likely to reduce unscheduled reattendance, which can help build the business case supporting implementation. The PACE study showed that CRP POCT was associated with 2.7% fewer COPD-related GP contacts.<sup>37</sup>

Considering COPD-related health-care costs only, CRP POCT was associated with similar costs as usual care in the PACE study: savings in healthcare resource use slightly offset the cost of £11.31 per CRP POCT. The mean incremental cost-effectiveness ratio was £222 for each 1% reduction in antibiotic consumption compared with usual care at 4 weeks. The cost per quality-adjusted life-year (QALY) gained at 6 months was £15,251,<sup>39</sup> suggesting that CRP POCT is cost effective. NICE uses a cost-effectiveness threshold of £20,000 to £30,000 per QALY for reimbursing new drugs.<sup>40</sup>

The PCRS panel concluded that primary care should work with diagnostic companies to introduce CRP POCT as cost-effectively as possible, which may depend on the setting. In-

tegrated Care Systems should introduce incentives to adopt CRP POCT and other innovative diagnostic processes as soon as practicable in routine primary care.

## A pilot study could aid implementation

The PCRS panel recommended performing a pilot study to demonstrate the benefits of CRP POCT in terms of antibiotic prescribing, patient-reported outcomes and other measures. The pilot study could also explore how to overcome the barriers and offer a benchmark for future development. As part of this, the Medicine Management Team should work with diagnostic companies to identify the best model and CRP POCT system for a particular location. The panel suggested that identifying a local champion can help build a case for CRP POCT in primary care.

The panel noted that the OpenPrescribing website allows comparisons of antibiotic prescribing between practices in England. The pilot study should be based in a practice with at least one of the following to maximise patient enrolment: high users of antibiotics despite efforts to improve stewardship by the practice and local Medicine Management Team; a large cohort of COPD patients, which could be in areas of high socioeconomic deprivation; a large proportion of COPD patients attending accident and emergency departments; or a large proportion of COPD patients who frequently exacerbate.

## Future perspectives

### Political and managerial perspectives

The algorithms in figures 1 and 2 should help improve the integration of diagnostics into primary care, which aligns with government recommendations in the report *Rapid Diagnostics: Stopping Unnecessary Use of Antibiotics*.<sup>41</sup> The PCRS suggests that NICE should re-open the review of the current COPD management guideline and come to a position regarding the use of CRP POCT. The discussions should consider the growing body of high-quality data showing that testing can reduce unnecessary prescribing of antibiotics without compromising patient safety.<sup>8,12,15-21</sup> Without national guidance, the PCRS panel expressed concern that the NHS could face 'postcode diagnostics' and, possibly, differences in antimicrobial resistance patterns.

The NHS should consider planning to integrate technological advances (eg artificial intelligence) into RTI diagnosis to further reduce inappropriate use of antibiotics. The panel also noted that encouraging the use of CRP POCT aligns with the current pan-national environmental agenda by reducing the carbon footprint associated with antibiotic production and minimising environmental contamination with antibiotics and environmental levels of multidrug resistant bacteria.<sup>42,43</sup> Indeed, antibiotics and other pharmaceuticals account for 65% of primary care's greenhouse gas emissions.<sup>43</sup>

## Further research

The panel identified numerous areas for further research, including characterising cost-effectiveness encompassing the costs of antibiotics, changes in drug costs and the cost of antimicrobial resistance. Studies should, for example, characterise the proportion of patients with IE-COPD who subsequently develop exacerbations with 'resistant' bacteria in those managed based on CRP POCT compared with usual care. Economic analyses could also estimate the indirect costs associated with IE-COPD, RTI and antimicrobial resistance, such as absenteeism, presentism and environmental footprint.

Future studies also need to characterise the place of CRP POCT in the management of paediatric RTIs and the least distressing way to obtain a sample from children and adults with needle phobia. Capturing real-world epidemiologic data on the proportion of patients with a COPD exacerbation who have microbiologically confirmed bacterial infection at the various CRP levels could facilitate implementation and decision making. Finally, there is a pressing need to assess long-term outcomes associated with timely appropriate management and early referral to palliative care, the long-term implications for service utilisation and distinguishing true and frequent exacerbators from patients who need a different management approach.

## Summary

RTIs and IE-COPD are common in primary care, which partly accounts for the high rate of antibiotic use in this setting. Historically, patients presenting with signs and symptoms that indicate possible RTI or IE-COPD were diagnosed and treated empirically.<sup>9</sup> While valuable, clinical decision rules rely on non-specific observations. Laboratory tests allow more accurate predictions for pneumonia among adults in primary care with than clinical signs and symptoms.<sup>10</sup> Increasing evidence shows that CRP POCT with guideline-based cut-offs and indications reduces antibiotic use for patients presenting with RTIs and IE-COPD.<sup>8,12,15-20</sup> There is, however, a need for further research and analyses as well as co-ordinated action from local and nation policy makers. In the meantime, the PCRS hopes that this pragmatic guide will encourage the use of CRP POCT to support not prescribing antibiotics in appropriate low-risk patients. The PCRS anticipates that implementing the suggestion in this review will contribute to slowing the spread of antimicrobial resistance and improving management of these common conditions.

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