2019 exceptional surveillance of chronic obstructive pulmonary disease in over 16s: diagnosis and management (NICE guideline NG115)

Surveillance report
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Surveillance decision

We will not update the NICE guideline on chronic obstructive pulmonary disease (COPD) in over 16s.

Reasons for the decision

This exceptional review examined any impact on NICE’s guideline on COPD in over 16s following the publication of a National Institute for Health Research funded trial on C-reactive protein (CRP) testing to guide antibiotic prescribing for COPD exacerbations.

This randomised controlled trial investigated the use of point of care testing (POCT) in GP practices in England and Wales for people with a diagnosis of COPD experiencing an acute exacerbation. Fewer patients in the CRP guided group received antibiotic prescriptions both at the initial consultation and during the 4-week trial period, compared with those in the non-CRP guided group. Additional studies, including a Cochrane review, also showed reduced antimicrobial prescribing in some groups but studies were small and heterogeneous and might not represent the general population of COPD patients. Overall, topic experts considered that the study has promising preliminary results, but further studies are needed to clarify the role of POCT in the management of COPD exacerbations; funding and feasibility were noted as concerns for wider adoption in general practice.
Exceptional surveillance summary

Methods


- A focused search for new evidence related to point of care testing (POCT) for acute exacerbations of chronic obstructive pulmonary disease (AECOPD) identified any randomised control trials (RCT), systematic reviews and diagnostic studies specifically relating to POCT in primary care for AECOPD published between 1 January 2015 (publication of the guideline) and 21 January 2020. Databases searched included Cochrane, Central, Medline and Embase.

- We obtained views from topic experts.

- We considered whether any new information has equalities implications.

Information considered in this surveillance review

Clinical evidence

Butler et al. (2019), RCT comparing usual care with and without POCT

The RCT prompting this exceptional review (Butler et al. 2019), examined POCT in 649 adults presenting with an AECOPD at 86 UK primary care practices. Participants were eligible to enter the trial if they were 40 years or older with a diagnosis of chronic obstructive pulmonary disease (COPD) including a minimum of 1 Anthonisen criteria and were then randomised to usual care with and without POCT. Details of 'usual care' were not reported in the paper but is assumed to have been normal clinical examination with antibiotic prescribing where deemed clinically necessary.

The trial used the following criteria for interpretation of C-reactive protein (CRP) results which were adapted from NICE's guideline and the Global Initiative for Chronic Obstructive Lung Disease.
- CRP less-than 20 mg/l antibiotics unlikely to be useful.
- CRP 20 mg/l to 40 mg/l antibiotics may be beneficial (if purulent sputum present).
- CRP greater-than 40 mg/l antibiotics likely to be beneficial.

The GP practices all used the Afinion CRP rapid in vitro diagnostic test (Abbott Diagnostics). Abbott Diagnostics were not involved in the trial other than to loan the POCT equipment to the GP practices.

Participants completed the clinical COPD questionnaire (CCQ) and the EuroQol 5-dimension questionnaire (EQ-5D-5L) at baseline. (Note that NICE currently recommend the previous version of this questionnaire, EQ-5D-3L due to a lack of value sets for England, see NICE’s position statement on the use of the EQ-5D-5L value set for England October 2019).

Participants received follow-up telephone calls at week 1 and week 2 (which involved completing the CCQ and EQ-5D-5L and reporting any adverse events) followed by a consultation in person at week 4 including a sputum sample and throat swab where possible. Additional questionnaires were also sent to participants after 6 months: the EQ-5D-5L and chronic respiratory disease questionnaire, self-administered, standardised (CRQ-SAS).

The primary outcomes were patient reported antibiotic use 4 weeks post examination, and COPD-related health status at 2 weeks post examination. Three prespecified subgroups were included, severity of COPD, severity of COPD exacerbation (measured by Anthonisen criteria type 1, type 2 and type 3) and presence of potentially pathogenic bacteria from sputum culture.

Patients in the CRP guided group reported significantly lower antibiotic use (57.0% compared to 77.4%) and better COPD-related health scores on the CCQ compared with the usual care group. However, the authors also state that differences in reported antibiotic use were only observed when patients had at least 2 of the Anthonisen criteria.

For the secondary outcome of antibiotic prescribing decisions, at baseline, the CRP guided group received fewer antibiotic prescriptions (47.7%) compared with the usual care group (69.7%). This was also seen at the 4-week time point with 158 prescriptions compared with 235 prescriptions issued in the CRP guided and usual care groups, respectively. The CRP results following the baseline assessment were also included, showing that antibiotic prescriptions were given to over 30% of people that had a CRP of less-than 20 mg/l.
was no difference in the number of adverse events or hospitalisations between the 2 study groups. The study concludes that both antibiotic prescribing and antibiotic use may be reduced by primary care based CRP tests.

**Additional studies**

The literature search identified 2 more studies examining POCT for management of AECOPD.

**Strykowski et al. 2015** (n=952) examined the impact of CRP testing on over- or under-prescribing of antibiotics by GPs in Spanish primary care clinics. The definitions of over and under-prescribing were not disclosed in this secondary analysis. Criteria for patient enrolment included those with exacerbations of chronic bronchitis but did not require a spirometric diagnosis of COPD (n=952). Based on clustering of practices, the GPs had access to either a multifaceted intervention with rapid CRP testing (full intervention group n=210) or the intervention without rapid CRP testing (partial intervention group n=70). A comparison group of GPs had no access to the intervention and as such applied usual care alone.

GPs allocated to the full intervention group received: follow up meetings for feedback on test results, clinical guideline information, antibiotic use training courses and workshops on the use of the CRP rapid test. GPs were asked to only use the CRP test when they were unsure about the diagnosis, not as a standalone test, all used the NycoCard CRP apparatus (Axis-Shield, Norway). After CRP testing, patients with levels less-than 20 mg/l did not receive a prescription for antibiotics and patients with levels more-than 100 mg/l received a prescription. No detail is given regarding CRP results that fell into the 20 mg/l to 99 mg/l group. GPs in the partial intervention group received the same training but not the CRP rapid test workshop and did not have access to CRP testing.

After adjusting for clustering of GP practices and for patient age and sex, over-prescribing was significantly reduced in the full intervention group (odds ratio=0.35; 95% confidence interval 0.18 to 0.68) and under-prescribing was not significantly increased. There were no statistically significant changes in prescribing habits in the partial intervention group.

A Cochrane review (**Schuetz et al. 2017**; n=6,708 participants, 26 trials) assessed procalcitonin guided antibiotic stewardship for people with acute respiratory infection (ARI) in any setting. The primary outcomes for this review were all cause mortality and length of hospital stay. For all patients, significantly lower mortality was seen in the
procalcitonin guided group compared with the control group when any type of ARI was considered, with a greater reduction in number of days with antibiotic treatment and lower risk of antibiotic related side effects. For patients with COPD (n=1,252), 30-day mortality, treatment failure and antibiotic related side effects were lower in the procalcitonin guided group compared with the control group, however the differences were not statistically significant. Although the primary outcome was hospital length of stay which is not relevant to this exceptional review, for the secondary outcomes of antibiotic initiation and duration of antibiotics for all participants with ARI in any setting, results were significantly lower for the procalcitonin group compared with the control group. However, for primary care alone, only initiation of antibiotics was significantly lower, no difference was found for duration of antibiotics between the control and procalcitonin group. The results are also detailed for the subgroup of participants with an AECOPD, which was significantly lower for initiation of antibiotics in the procalcitonin group but not for duration of antibiotics.

One limitation of this Cochrane review is that despite giving data on various subgroups, we cannot view the data by setting for AECOPD or any outcome/condition, as such it is difficult to interpret the impact of these results specifically for COPD investigation in the primary care setting. The authors also stated that the outcome of mortality in the primary care subgroup could not be estimated. The test used in this review was a POCT for procalcitonin, rather than CRP guided antibiotic stewardship as used in Butler et al. and Strykowski et al., making comparison of results difficult to interpret.

**Views of topic experts**

Five topic experts expressed their views on the Butler et al. study and commented on its relevance to NICE's guideline.

Two topic experts suggested a potential impact on the guideline, first noting that the Butler et al. study reported that a third of exacerbations had a bacterial cause which reflects the current guideline as it states that bacterial infection is a common cause of COPD exacerbation. One expert felt that the study provided much needed support for clinicians in emergency departments (outside the scope of this guideline) and general practice to assist in a diagnosis of a patient presenting with worsening respiratory symptoms. A second expert stated that the findings of Butler et al. were consistent with NICE's guideline on pneumonia in adults, which includes a recommendation on CRP testing for people presenting with lower respiratory tract infections (LRTI) symptoms to guide antibiotic prescribing when a diagnosis of pneumonia has not been made following clinical assessment. The expert also commented that near patient testing is widely used in
Denmark, and as such is feasible for use in the UK although there are likely to be issues regarding funding and commissioning group compliance.

However, the other 3 topic experts felt that the study would not impact on NICE's guideline. One felt that Butler et al. was a good preliminary study but given the number of people who have COPD in the UK, felt that a much larger study size was both achievable and required in order to confirm the results. The expert noted that although a reduction was seen in the CRP guided group, antibiotic prescriptions were still high, and also highlighted that data were not collected on healthcare seeking behaviour by participants, such as a follow up visit or accessing their rescue packs of antibiotics at home. The topic expert added that a missing but crucial piece of information was whether or not the CRP result significantly affected prescribing behaviour, highlighting particular concern that a low CRP result may offer false reassurance to clinicians. It was also raised that the demographics of the CRP guided group in this study may not represent the wider COPD population as they were generally younger and likely to have fewer exacerbations per year. The topic expert concluded that it would be difficult to justify the use of a CRP POCT in every patient with the current available evidence.

Several topic experts suggested that the funding and practicality of having a CRP POCT available in every GP practice was unlikely to be feasible. They also raised the question of how POCT would work with housebound patients. One expert highlighted potential limitations of the Butler et al. study such as that the patient group selected were unlikely to be those with previous COPD hospitalisations, which would be the group most likely to require antibiotic prescriptions from primary care. They also raised concern around other treatment received for those in the CRP guided group who did not require an antibiotic prescription, such as a potential increase in oral corticosteroids, as other medication use was not recorded.

Ongoing studies

A brief search for ongoing studies was undertaken on 5 February 2020, with 2 potentially relevant protocols found. These were:

Delayed antibiotic prescribing for respiratory tract infections: protocol of an individual patient data meta-analysis. The methods for deciding who should have a delayed prescription may include a POCT and as such this study will be tracked and assessed for relevance when it publishes.
Impact

The study by Butler et al. provides new evidence on the potential for a POCT in primary care, which has shown to reduce antimicrobial prescribing in patients experiencing an exacerbation of COPD. A second study also found antimicrobial prescribing was reduced when CRP testing was used in combination with a multifaceted intervention. These findings are supported by several topic experts; however, funding and feasibility were noted as concerns about adoption in every general practice. Some important concerns were also raised by topic exerts, such as the severity of COPD in the study groups, healthcare seeking behaviour of patients following the initial appointment, use of rescue packs of antibiotics, prescribing of non-antibiotic treatments and the impact on housebound COPD patients. Several topic experts felt that this study was important preliminary work, however given the large population of people with COPD, they thought that further studies were needed to support and confirm these findings. The additional studies found in this review showed improvements in antimicrobial prescribing in some groups, however differences in references ranges and test used make it difficult to combine the results.

The NICE guideline on antimicrobial stewardship: systems and processes for effective antimicrobial medicine use includes recommendation 1.1.30 for the use of POCT in LRTI, as described in NICE's guideline on pneumonia in adults. However the full guideline expresses concern regarding healthcare utilisation such as repeat GP visits and appropriateness of hospital admissions. The use of CRP POCT was considered in detail by the guideline development group for the guideline on pneumonia in adults, who stated that the high cost of implementation was not currently supported by the evidence for the UK setting; specifically more data were required regarding hospital admission from primary care and length of hospital stay. NICE's guideline on pneumonia in adults also mentions that the recommendations in the guideline should not be inappropriately applied to other conditions and highlights concern regarding the elderly population and their lack of high level CRP response to infection.

Based on topic expert feedback, further studies would be helpful, focussing on areas such as use of rescue pack antibiotics, type and duration of antibiotic prescribing, and including
further details regarding severity of COPD and outcomes for housebound patients. It would also be important for studies to include prescribing information for any medication related to a COPD exacerbation to see if a reduction in antimicrobial prescribing was increasing the use of steroids for example. Studies that investigate the effect of CRP level in the elderly COPD population and in those on other medications such as statins would be helpful. POCT is a growing area of interest but currently there are few studies in primary care specific to this population, and the available studies often include patient self-reported outcomes. This is important but subjective data, and future studies should use validated measures of health-related quality of life to allow combining and comparison of data across studies.

Based on the currently available evidence, topic expert feedback and little robust information specific to COPD such as uncertainties over subgroups (older age, higher number of exacerbations and the reliability of CRP in some groups) no impact is anticipated on the guideline at this time.

**Equalities**

No equalities issues were identified during the surveillance process.

**Overall decision**

After considering all evidence and other intelligence and the impact on current recommendations, we decided that no update is necessary.