NICE National Institute for Health and Care Excellence

2022 exceptional surveillance of chronic obstructive pulmonary disease in over 16s: diagnosis and management

Surveillance report
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Surveillance proposal

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

Reason for updating the exceptional review

A previous exceptional review (published 4 March 2020) assessed the impact of the PACE study (initial publication, Butler et al. [2019]) on the NICE guideline on COPD and concluded that no update was required. The PACE study team queried the decision, challenging several conclusions that had been made. As such a further exceptional review was initiated to look more widely at the current context for implementation of point of care testing (POCT) for people with COPD. The PACE team also highlighted that the associated health economic evaluation has now been published (Francis et al. 2020) Therefore, the outcome of the 2020 exceptional review has been reconsidered in light of this extra information.

Exceptional surveillance summary

Methods

The exceptional surveillance process consisted of:

- Evaluating the new health economic evidence.
- Searching for new evidence published since the last exceptional review, including any types of study examining POCT in primary care settings for people experiencing an exacerbation of COPD.
- Additional feedback from topic experts.
- Consulting on the proposal with stakeholders (this document).

For further details about the process and the possible update decisions that are available, see ensuring that published guidelines are current and accurate in developing NICE guidelines: the manual.

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Additional analyses from PACE study

The PACE study team conducted 3 further evaluations using the data from the Butler et al. (2019) publication; these focused on different aspects of the trial and are described briefly below.

Philips et al. (2020) reported a qualitative examination of the value of POCT for C-reactive protein (CRP) in patients with acute exacerbation of COPD (AECOPD) from both the patient and clinician perspective. This also included looking at potential care pathways, facilitators, and implementation barriers. Twenty patients and 20 clinicians selected from the PACE study participated in semi-structured telephone interviews and data was analysed with framework analysis.

The study was designed to include patients from different geographical locations and include both those who were prescribed antibiotics at consultation and those who were not. Different types of clinical staff were also included where possible such as nurses, healthcare assistants, research assistants and primary care doctors depending on who was responsible for performing the test at each location.

The results state that patient and clinician confidence in the CRP POCT was high and felt it helped guide antibiotic prescribing decisions and also reassured patients when antibiotics were not indicated. There was a difference in opinion between clinicians as to when the CRP POCT should be used, with some suggesting it should be routinely used and others felt strongly that it should only be used to help clarify when there was uncertainty in diagnosis following clinical examination. It was emphasised by clinicians that clinical skills should not be replaced by CRP POCT. Clinicians described the cost of the POCT machine and its associated supplies as "prohibitive under current funding arrangements" and stated that adoption would be unlikely on a larger scale unless additional funding was made available. Clinicians also highlighted the time to prepare the sample cartridge as a potential barrier as it took staff away from other clinical duties, and preparation of the sample cartridge was described as 'burdensome' (partly due to storage conditions of the cartridge and needing to come to room temperature before use), and the inability to use it for housebound patients.

Overall, the study confirmed that the CRP POCT has high acceptance with both patients and clinicians, however concerns remained about implementation in routine practice.

Gillespie et al. (2020) examined PACE study data to identify whether there was an

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association between the presenting features of a patient with AECOPD and antibiotic prescribing. Higher odds of receiving an antibiotic prescription were associated with patients presenting with clinician recorded crackles, wheeze, diminished vesicular breathing and clinician reported consolidation. However, increasing patient age and the presence of heart failure were associated with lower odds of antibiotic prescription.

Limitations of the study discussed by the authors, included the lack of a power calculation for this secondary analysis, potential confounding from clinicians' 'usual' antibiotic prescribing behaviour, and a difficulty in drawing causal conclusions from associations between presenting features and antibiotic prescribing. The authors also highlight that the finding of a lower odds of antibiotic prescribing in older age patients was inconsistent with other studies in this area and was likely due to older patients being inadvertently excluded from the PACE randomised controlled trial.

A fourth analysis from the PACE study (Francis et al. 2020) investigated the association between baseline clinical features, including CRP value in those randomised to testing, and the presence of pathogens in sputum. The only clinical feature with a significant association with 1 or more detectable bacterial pathogens was sputum purulence as assessed by the Bronkotest (now named Birmingham Sputum Colour Chart). Elevated CRP was associated with increased odds of finding bacterial pathogens, however this was not significant.

Non-PACE studies

No completed and published non-PACE studies were found in the search for new evidence but 1 study protocol (Thuy Do et al. 2021) was identified. This cluster randomised controlled trial will investigate the use of CRP POCT in primary care facilities in Vietnam for patients presenting with acute respiratory illness, which may include AECOPD. This study will be assessed for relevance to NICE's guideline when results are available. However, it may not be fully applicable due to the differences in healthcare systems between Vietnam and the UK NHS.

The Step-up study was highlighted to us by a topic expert. This is a UK study with a number of themes, including implementing point of care CRP testing in high antibiotic prescribing general practices. This study will be assessed when full results are available, however it does not focus solely on COPD.

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Health economic analysis - the PACE study (Francis et al. 2020)

The health economic evaluation of the PACE study, Francis et al. (2020), examined the cost-effectiveness of POCT for CRP to guide antibiotic prescribing in primary care for people experiencing AECOPD. The analysis was based on the co-primary outcome of antibiotic consumption at 4 weeks, and a cost–utility analysis at 6 months was performed. A cost–consequences analysis and a budget impact analysis were also conducted, and the robustness of the results was tested in sensitivity analyses. Importantly, the evaluations incorporated CRP POCT implementation costs in primary care and subsequent healthcare costs within the trial follow-up period of 6 months.

The health economic analysis considered the following:

Cost of the CRP POCT implementation in primary care

- Materials, consumables, staff time required and staff training information was obtained through interviews with general practice staff during the PACE trial.
- The CRP POCT manufacturer and wholesale catalogues were used to estimate consumables and machine costs, with the PACE trial data used to estimate how frequently consumables would be needed.
- Assumptions relating to staff or other costings were made by clinical expert opinion within the PACE study team.

Costs of medications prescribed

- This included prescriptions for antibiotics, oral steroids and inhaled medication, short- and long-acting beta-2 agonists, short- and long-acting muscarinic agonists, inhaled corticosteroids and combination inhalers.
- Unit costs for these medications were taken from the British National Formulary and the Monthly Index of Medical Specialities.
- Costs were based individually on prescribed medication dose and duration, or where not noted, the most common usage for that medication was used.
- If regularly used inhaled medication was increased at consultation, it was assumed a new prescription was also issued at that time.

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Cost of healthcare resource use

- This included primary care consultations, A&E visits, outpatient appointments and inpatient stays.
- The client service receipt inventory was adapted to monitor data on healthcare resource use and evaluated at both the 4-week and 6-month timepoints.
- Healthcare resource use was calculated individually using published unit costs based on the reason for contact, length of stay and speciality or department required.

The results were as follows:

Cost of the CRP POCT implementation in primary care

The estimated cost per POCT was £11.30, of which £5.40 was consumables and materials, £5.38 for staff to process the samples and report the results, £0.13 for capital expenditure and £0.10 for staff training. This costing also included quality control testing and an estimated cost for repeat tests required at £0.29.

At the 4-week timepoint 18 patients had received 20 CRP POCTs, increasing the average cost per test to £12.08.

Costs of medications prescribed

The PACE study demonstrated a 22% decrease in antibiotic use in the CRP guided group at initial consultation which was maintained at 4-week follow up. However, the economic evaluation found that the cost saving from the reduction in antibiotics at initial consultation was not maintained over the following 6 months because of a 5.4% increase in prescribed inhaled therapies in patients in the CRP guided group.

The results also state that there was a mean incremental cost-effectiveness ratio (ICER) of £222 per 1% reduction in antibiotic prescribing compared with usual care at 4 weeks, and a cost per quality adjusted life year (QALY) of £15,251 at 6 months.

Cost of healthcare resource use

When the cost of primary care visits (physical attendance) was examined, the number of patient visits was reduced at both 4 weeks and 6 months in the CRP guided group.

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However, authors stated the costs for secondary care were higher in the CRP guided group (26 patients with 35 hospitalisations) compared with the usual care group (28 patients with 34 hospitalisations). The authors state this may be due to the higher number of pneumonia cases in the CRP guided group, and as such was a non-COPD related cost.

Additional cost results from PACE

The authors reported the total cost per person to the NHS at 4 weeks was £17.59 higher in the CRP group and £126.26 higher at 6 months. The authors stated this was likely due to a combination of CRP tests and inpatient stays. They also state that, when comparing only COPD related costs, the usual care and CRP guided group were similar because the cost of the CRP test (£11.31) was slightly offset by a reduction in other resource use.

Patients in the CRP guided group also reported less time off work due to associated illness compared with the usual care group. However, the study also highlights clinician concerns that cost and time for using CRP POCT needed careful consideration.

Topic expert feedback

Topic experts were asked to comment on the implementation of the POCT for CRP. We contacted 10 topic experts and received 4 responses (all from general practitioners).

Staff training/availability

One topic expert felt that the use of POCT was unlikely to disrupt most practices as it would not require highly skilled staff; however, they also stated that even a minor disruption would increase workload. A second topic expert highlighted that the time to run the test would be logistically difficult in a busy surgery along with daily calibration times. A third expert felt the POCT represented a significant effort to train staff and have them maintain their skills given how infrequently they could be performing the test. They also commented that staff availability and the unpredictable nature of use could cause issues, as could the amount of time taken to perform the test in a busy/urgent clinic. It was also suggested that COPD nurses could be a good starting point for routine use of the POCT as it would highlight further implementation issues and help monitor usage of antibiotics. A topic expert also queried whether incentives for the practice would work because of difficulty in determining success, including that the economic argument needed to consider the amount of extra staff time for training, processing test and machine

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calibration.

Space – machine and reusables

Two topic experts felt that space would not be an issue as the machines are relatively small but mentioned that smaller branch surgeries may struggle. A third expert queried where the machine would be situated in a practice, and if that room was in use for other tasks as that would increase the wait time to access it.

Running costs and funding

All 4 topic experts commented that the machines would have to be provided and reusables be cost neutral for the practice or uptake would be very low. One expert commented that the relatively low number of exacerbations of COPD even in winter, at the smaller practices would not warrant the extra time and expense needed for the practice to fund the equipment. It was also queried whether clinical commissioning groups (CCGs) would fund equipment given the relatively low impact of the POCT on hospital admissions, even considering the impact on antibiotic stewardship. A third expert suggested that POCT should be viewed as a complex intervention and widespread uptake would only be likely with a fully funded and locally supported implementation plan over 1 to 2 years, and despite the POCT being under £20,000/QALY, there was not a gain in terms of hospital admissions/exacerbations.

Use during consultation

Three experts commented that use during a consultation would be limited. One estimated a maximum use of 1 to 2 patients per day in winter months in a moderate sized practice; another stated that having trialled similar equipment before it was rarely used and instead used sputum colour as an indicator for antibiotic prescribing. The third expert commented that the use would be different depending on surgery size; for example, branch surgeries are unlikely to have access to CRP machines, meaning patients would have to travel to a linked surgery to access. They also highlighted that most exacerbations are managed via telephone or patients self-medicate with rescue packs, more so since COVID-19, and that those with moderate to severe COPD would be less likely to attend surgery or out of hours and the machine could not be transported to them.

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Other implementation issues

The experts made additional comments around accessibility for patients.

One expert commented that COVID-19 would have a big impact on implementation of new testing practices such as the CRP POCT. This is due to the overlap in symptoms with COVID-19, as CRP tests were suspended earlier in the pandemic due to the inability to distinguish between COVID-19 and COPD exacerbations, which lead to a prescribing 'safety net' approach. They also felt that patients largely trusted their GP's decision on when to prescribe antibiotics in an exacerbation. A fourth expert felt that the main issue was patient access to the POCT and encouraging them to do so promptly. They stated that encouraging frail patients to have to travel to their surgery to do so would not improve their care when they are usually managed via telephone consultation at home.

Stakeholder consultation

We received consultation responses from 7 stakeholders including a pharmaceutical company, medical associations and royal colleges.

See appendix A for stakeholder consultation comments and our responses.

Six of the stakeholders agreed with our proposal not to update the guideline recommendations at this time. The stakeholder that did not agree stated reasons that were not related to CRP POCT for AECOPD, but rather changing in medication pricing which has been added to the guideline issue log for future consideration.

Of the 6 stakeholders who did agree with the proposal not to update, 3 of these stated that it should be reviewed as new evidence becomes available, as it is not the correct time for this level of implementation, however felt that the intervention had merit in theory, and if costing issues could be resolved would be more likely to be considered in practice. Concerns were also raised about the impact on antimicrobial prescribing, which will be added to the issue log and monitored for impact.

Equalities

Two stakeholders highlighted inequality in access to CRP as a concern; this was due to a number of factors such as which surgery would house the CRP machine within a satellite of surgeries, rural surgeries, housebound patients and that a large number of COPD

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patients are currently refusing face to face appointments given the current situation with COVID-19. These issues were also raised by topic experts.

Overall proposal

The economic evaluation by Francis et al. (2020) provided further evidence on the PACE study. Despite an initial cost saving from over 20% reduction in antibiotic prescribing in the CRP guided group, this was not maintained, because of an increase in inhaled therapies required over the following 6 months. Similarly, the reduction in cost due to fewer GP visits was also offset by a greater number of patients in the CRP guided group requiring secondary care over the 6 months.

The implementation and running costs may be prohibitive to implementation and a significant impact on important clinical outcomes was not seen. Topic experts highlighted similar concerns and felt that the new evidence is not sufficient to warrant an update of the guideline at this time.

Implementation may be further impacted by the increase in telemedicine use prompted by COVID-19, particularly in at risk groups such as those with COPD. Recommendations for minimising patient risk are described in NICE's COVID-19 rapid guideline: community-based care of patients with COPD; as such, patients would be less likely to visit a primary care facility during the management of their exacerbation and would therefore not have access to the CRP POCT. Topic experts also highlighted the above, stating that pre-COVID-19 those with moderate and severe COPD were largely managed at home to minimise the risk of infection presented by attending surgery.

Additional evaluation using PACE study data (Philips et al. 2020) also examined patient confidence in the use of CRP POCT and interviews found that there was a high degree of acceptability for both patients and clinicians. However, the clinicians still had differing opinions as to when the CRP POCT should be used and cautioned against it replacing clinical judgement, consistent with the section on managing exacerbations of COPD in the NICE guideline on COPD, which states that the diagnosis of an exacerbation should be made clinically and not based on the results of investigations.

Further 2 analyses using PACE study data also found that clinician reported chest crackles, wheeze, diminished vesicular breathing were associated with clinician reported consolidation and antibiotic prescribing across all groups (Gillespie et al. 2020). Sputum purulence was the only statistically significant variable for finding bacterial pathogens in

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sputum (Francis et al. 2020), and those with the most purulent sputum had almost 25 times the odds of finding a bacterial pathogen in the sputum compared with those with the least purulent sputum. Despite increased CRP levels being associated with the detection of more bacterial pathogens, this association was not significant.

Topic experts felt that although the use of a POCT had potential benefits, there were several issues such as staff training, staff availability, funding, little impact on hospital admission, impact of its use due to COVID-19 and its use in patients with the moderate-severe COPD. As such they concluded that uptake was likely to be very low and current methods of assessing the need for antibiotics such as sputum colour were more likely to be used. This is consistent with the recommendation on treatment in the NICE guideline on COPD (acute exacerbation): antimicrobial prescribing, which states that an increase in sputum purulence can be used to guide antibiotic prescribing in primary care.

The majority of stakeholders agreed with the proposal not to update the guideline recommendations at this time. Stakeholders largely echoed the views of topic experts, citing similar reasons why this intervention is unlikely to be possible at this time, however suggested that this be reviewed regularly.

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

Note

For information on the CRP POCT machine used in the PACE study see NICE's medtech innovation briefing on Alere Afinion CRP for C-reactive protein testing in primary care and for information on an alternative CRP POCT machine see NICE's medtech innovation briefing on QuikRead go for C-reactive protein testing in primary care.

Editorial amendments

The following errors were noted by the PACE study team in the 2019/2020 exceptional review, as such, the following editorial amendments will be made:

- The results from the EQ-5D-5L were converted to EQ-5D-3L in order to be comparable to other NICE products.
- Healthcare seeking behaviour data was detailed in the results section.

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- The average patient age in your study has also been shown to be similar in other large studies (Haughne et al. 2014).
- Medication usage was detailed in table S13 in the supplementary appendix.

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