Advice Statement 008/18  May 2018

What is the clinical and cost-effectiveness of C-reactive protein point-of-care testing to guide antibiotic prescribing in patients presenting to primary care with symptoms of lower respiratory tract infection?

Advice for NHSScotland

Using C-reactive protein (CRP) point-of-care testing as part of the holistic clinical assessment of adult patients attending primary care with symptoms of lower respiratory tract infection shows potential as a cost-effective way to target antibiotic prescribing. However, the size of the reduction in antibiotic prescribing and the likely impact on clinical practice is unknown. There is little published evidence on the use of the test in children or older people. Additional piloting, with monitoring and evaluation, should be undertaken by the organisations in Scotland with responsibility for diagnostic testing, prior to any widespread implementation of CRP testing.

*NHSScotland is required to consider the Scottish Health Technologies Group (SHTG) advice.*

Why is SHTG looking at this topic?

Microbial resistance to antibiotics is a major public health issue. Improving the targeting of antibiotics to those patients who are most likely to benefit is one strategy for addressing this issue. Around 80% of medical antibiotic use is in primary care and, of that, 60% is for respiratory infections. Thus it is important to evaluate initiatives which have the potential to reduce unnecessary use of antibiotics for self-limiting respiratory infections.

The topic was prioritised for inclusion on the SHTG work programme following topic referrals from The Scottish Antimicrobial Prescribing Group (SAPG) and The Scottish Health Protection Network Public Health Microbiology Group.

Evidence Note 80 was produced by Healthcare Improvement Scotland in response to this request.
**Background**

- Experiencing symptoms of lower respiratory tract infection (LRTI) is a common reason for consulting with a primary healthcare clinician. Antibiotics are frequently prescribed, making this a clinical area where there may be potential to better target antibiotics.
- C-reactive protein (CRP) is released by the liver in response to tissue injury, including that due to bacterial infection.
- Measurement of elevation of this biomarker may have value in guiding prescription decisions where there is uncertainty around the presence of serious bacterial infection. There may be the potential to employ a point-of-care CRP test in primary care consultations to help reduce inappropriate use of antibiotics.
- At least 11 manufacturers have CE-marked products which provide rapid testing for CRP level using a finger-prick blood sample.

**Clinical effectiveness**

- In a meta-analysis of six randomised controlled trials (RCTs), the rate of antibiotic prescribing at the index consultation was lower where CRP testing was available for use in situations of uncertainty around antibiotic prescribing.
- Meta-analysis findings for the three cluster RCTs (relative risk (RR) 0.68, 95% CI 0.61 to 0.75, p<0.00001) were different from the three individual RCTs (RR 0.90, 95% CI 0.80 to 1.02 p=0.09). There is therefore uncertainty in the estimate of magnitude of effect.
- Cluster RCTs may most closely reflect everyday practice.
- Only one study incorporated in the meta-analysis included children so findings should only be considered to apply to adult patients.

**Safety**

- One of the studies in the meta-analysis identified an increased risk of hospitalisation in the CRP group (odds ratio (OR) 2.61, 95% CI 1.07 to 6.35, p=0.034). The number of events was low (22/2224 (1%) versus 8/2040 (0.40%) and the difference between groups was not statistically significant following adjusting for confounders. Full interpretation of this finding was limited due to lack of information on the number of hospital admissions in the CRP group related to patients not initially prescribed an antibiotic.

**Cost effectiveness**

- Four cost-effectiveness studies were identified. Two were UK-based and had an NHS perspective, both drawing on data from one of the remaining (non-UK) primary studies that had prospectively collected observational data on costs and EQ-5D® outcomes associated with CRP point-of-care testing, where used in routine practice. No longer-term implications were considered beyond a 3-year period.
- All four studies concluded that point-of-care CRP testing was cost-effective in terms of either QALYs gained or a proportionate reduction in antibiotic use (from the remaining non-UK study reporting a within-trial economic analysis from a cluster RCT). Three had explored uncertainty using sensitivity analyses but it did not change the overall conclusions.
- It is unclear whether the consistency of the results reflects that three of the studies utilised the EQ-5D® evidence from the same observational study, or that the value of CRP point-of-care testing is robust to the method of assessment used.
Context

- A wide range of potential interventions may help support antimicrobial stewardship including patient education campaigns and clinician communication skills training. The Scottish Antimicrobial Prescribing Group (SAPG) have collated resources to support reduction of unnecessary use of antibiotics for self-limiting respiratory tract infections. http://www.scottishmedicines.org.uk/SAPG/Optimising_antibiotic_use
- Advice around commissioning, implementation, evaluation and monitoring of diagnostic technologies and their impact is provided by:
  o Diagnostics Steering Group of the Scottish Government
  o Control of Antimicrobial Resistance Scotland (CARS)
  o UK antimicrobial resistance (AMR) strategy High Level Steering Group/UK AMR Diagnostic Collaborative.
- No information on the budget impact of introducing point-of-care CRP tests was identified and it is unclear how it would affect workflow in routine clinical practice in an NHS setting.

Further research

- Since the evidence to date is largely based on middle-aged participants, there is a need for RCTs investigating the clinical effectiveness and cost-effectiveness of the CRP point of care test in children and older people.
- Additional piloting, with monitoring and evaluation, should be undertaken by the organisations in Scotland with responsibility for diagnostic testing, prior to any widespread implementation of CRP testing.

Advice context:

The status of SHTG Advice Statements is ‘required to consider’.

No part of this advice may be used without the whole of the advice being quoted in full. This advice represents the view of the SHTG at the date noted.

It is provided to inform NHS boards in Scotland when determining the place of health technologies for local use. The content of this Advice Statement was based upon the evidence and factors available at the time of publication. An international evidence base is reviewed and thus its generalisability to NHSScotland should be considered by those using this advice to plan services. It is acknowledged that the evidence constitutes only one of the sources needed for decision making and planning in NHSScotland. Readers are asked to consider that new trials and technologies may have emerged since first publication and the evidence presented may no longer be current. This advice does not override the individual responsibility of health professionals to make decisions in the exercise of their clinical judgment in the circumstances of the individual patient, in consultation with the patient and/or guardian or carer.

SHTG Advice Statements will be considered for review if new evidence becomes available which is likely to materially change the advice. Stakeholders may submit a request, highlighting new evidence to shtg.hcis@nhs.net

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