



STRAIGHT
**TO THE
POINT!**

Ensuring the Rational Use
of Antibiotics in Primary
Care using C-Reactive
Protein Testing

A Consensus Report

June 2015



Antimicrobial resistance...
is just as important and
deadly as climate change
and international terrorism

Chief Medical Officer
Dame Sally Davies¹



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ABOUT THIS REPORT

Antimicrobial resistance (AMR) represents a major, current and future danger to the foundations of modern medicine, dramatically increasing mortality and morbidity from many common infections and resulting in marked, and potentially unsustainable, increases in healthcare expenditure.¹⁻³ Clinicians, policymakers and governments worldwide agree that urgent action is needed to slow the spread of AMR. However, tackling AMR requires a coherent, co-ordinated multifaceted approach crossing international boundaries, market segments (e.g. medicines and agriculture; diagnostics and pharmaceuticals), and interfaces between professional groups.

Against this background, diagnostics are an increasingly important element of antimicrobial stewardship (AMS) allowing healthcare professionals (HCPs) to target antibiotics to each patient and pathogen. This, in turn, reduces inappropriate and unnecessary antibiotic prescribing in primary care, an important driver of AMR. For instance, a growing body of robust evidence supports using point of care testing (POCT) for C-reactive protein (CRP) to help control the rise of AMR in primary care. Indeed, guidelines from several European countries now suggest using CRP POCT to augment history taking and consideration of the signs and symptoms when diagnosing respiratory tract infections (RTIs) in primary

care.⁴⁻¹⁰ CRP POCT is especially effective when combined with enhanced consultation skills to help HCPs address the patient's agenda, including worries, misconceptions about antibiotics, and the appropriate management when patients express intermediate CRP levels.

Several studies¹¹⁻¹⁹ show that by resolving diagnostic uncertainty, CRP POCT can reduce antibiotic prescribing for RTIs in primary care by up to 42% (in suspected lower RTIs with a cough lasting less than four weeks together with one focal and one systemic symptom),¹⁸ without a clinically significant increase in complications or missed diagnoses.¹⁵ CRP POCT is cost effective,^{4,20-22} does not markedly increase workflow in most practices^{23,24} and had no effect on the rate of RTI consultations during long-term follow-up.²⁵ Indeed, giving patients evidence-based information improves their satisfaction with the consultation and could lead to fewer visits through improved self-management of future RTIs.²⁵ However, despite being recognised by Public Health England (PHE)²⁶ and National Institute for Health and Care Excellence (NICE) in pneumonia⁴ and AMS⁵ guidelines, CRP POCT is less widely used in the UK than in other European countries, many of which have lower rates of antibiotic usage.

In response, a multidisciplinary panel of leading HCPs, researchers and healthcare

experts met to reach a consensus about the most effective and efficient means to implement CRP POCT in the NHS. This report is the result of the panel's deliberations.

The panel estimates that as a first approximation, CRP POCT in primary care could reduce the number of antibiotic prescriptions by up to 10 million each year, which would make a significant contribution to the UK's AMR strategy. In addition, CRP POCT in primary care could save £56 million a year in prescription and dispensing costs alone.

In addition, the Academy of Medical Royal Colleges recently launched a Choosing Wisely programme in collaboration with other organisations. As part of the Choosing Wisely programme, doctors are encouraged to "provide patients with resources that increase their understanding about potential harms of interventions and help them accept that doing nothing can often be the best approach".²⁷ This report provides evidence that CRP POCT in primary care provides this resource with respect to antibiotic use in RTIs. The report also makes suggestions for clinicians, commissioners and policymakers to ensure that CRP POCT can help the NHS meet the challenges posed by AMR.



FOREWORD

Antimicrobial resistance is a ticking time bomb not only for the UK but also for the world.

Dame Sally Davies

“Antimicrobial resistance (AMR) is a ticking time bomb not only for the UK but also for the world,” the Government’s Chief Medical Officer Dame Sally Davies noted in her 2011 Annual Report. Indeed, Dame Sally has described the risk posed by AMR as being “just as important and deadly as climate change and international terrorism”.

Currently, resistant bacteria kill some 25,000 people across Europe each year, close to the number that die in road accidents. Unless something happens soon this toll could rise. For instance, the National Risk Register for Civil Emergencies notes that a widespread outbreak of a bacterial blood infection could affect 200,000 people and, if it could not be treated effectively with existing drugs, approximately 80,000 could die.

Against this background, there is an increasing recognition that tackling AMR means taking global, multifaceted, concerted action to address the overuse of antibiotics and inappropriate prescribing. However, antimicrobial stewardship begins at home. In 2013, healthcare professionals prescribed some 41.6 million antibiotic items. Indeed, according to the survey for the European Antibiotic Awareness Day (EAAD) 2013, 41% of UK residents had taken antibiotics in the last 12 months compared to a European average of 35%. Approximately 60% of these antibiotic prescriptions

were probably for respiratory tract infections (RTIs). In this survey, RTIs (flu, bronchitis, cold, and sore throat) accounted for four of the top five reasons for taking antibiotics in the UK (Urinary tract infections were the remaining reason). However, most acute uncomplicated RTIs are viral or self-limiting bacterial infections and antibiotic confer marginal benefits. We need to address professional and public behaviour to reduce the volume of antibiotics expected and prescribed. In turn, inappropriate antibiotic prescribing fuels the rise in AMR. The continuing high use of antibiotics suggests that a radical shift is needed in the way healthcare professionals diagnose and manage RTIs and other infections.

Improved diagnosis is one way we can reduce inappropriate and unnecessary antibiotic prescribing. Public Health England (PHE) supports CRP POCT for lower respiratory infection when antibiotics are being considered. Interestingly, while UK residents were more likely to receive antibiotics, the EAAD report found that they were also more likely that the European average to know that antibiotics are ineffective against viruses, cold and flu. This report argues that POCT also offers an opportunity to help bridge the existing gap between understanding and professional and public behaviour, and help augment healthcare professionals’ communication and consultation skills.

Integrating current and future point-of-care diagnosis into routine care, supported by effective communication, is a keystone of antimicrobial stewardship. The recommendations in this report help place diagnosis and, in turn, rational prescribing at the centre of primary care decision making about when and in whom to suggest antibiotics. With the number of diagnostic technologies likely to increase dramatically over the next few years, implementing CRP POCT for RTIs offers a test case to ensure timely, effective and efficient implementation and uptake of the other diagnostic technologies.

We believe that improved diagnosis is one element of the multifaceted approach needed to tackle AMR – especially as, in the short and medium term at least; relatively few antibiotics are in development. The wider use of modern diagnostic technologies, when properly integrated into the consultation, optimises prescribing of appropriate antibiotics and facilitates the good prescribing practice that will ensure the preservation of effective treatments for our children and grandchildren.

Professor Michael Moore

Professor of Primary Health Care Research at University of Southampton and RCGP National Clinical Champion for Antimicrobial Stewardship (2012-2015)

RECOMMENDATIONS FOR

HEALTHCARE PROFESSIONALS

- Healthcare professionals (HCPs) should routinely use C-reactive protein (CRP) point of care testing (POCT) in primary care, combined with clinical observations of signs and symptoms and consideration of the patient's history, in the diagnosis of RTIs, including pneumonia.^{4,5,26} CRP POCT helps HCPs, especially GPs, 'rule out' need for antibiotics in low-risk patients, while 'ruling in' antibiotics for high-risk patients.
- HCPs should ensure CRP POCT is properly integrated into the consultation and is supported by appropriate consultation and communication skills.
- HCPs should recognise that CRP POCT could help Clinical Commissioning Groups (CCGs) attain the Quality Premium and meet the NHS quality agenda more widely. HCPs should develop procedures and protocols to enable CRP POCT to optimise performance against quality indicators.
- HCPs should follow NICE guidance for pneumonia, which supports combining primary care CRP POCT with clinical diagnosis and history taking when deciding whether to prescribe antibiotics for lower RTIs⁴ and as part of antimicrobial stewardship.⁵
- HCPs should use CRP POCT as an opportunity to improve communication during the consultation, such as educating and informing patients about self-management and the appropriate use of antibiotics as well as addressing any concerns.
- HCPs (including GPs, pharmacists, nurses and public health doctors) must work together locally and nationally to influence clinical and business plans that implement diagnostics and other advances that improve antimicrobial stewardship.
- Pharmacists should work with CCGs to develop clinical and business plans to implement CRP POCT as part of the proposed Common Ailments Scheme and any equivalent local schemes and as a triage to reduce pressure on general practice. HCPs and commissioners should also consider implementing CRP POCT in out-of-hours services.
- HCPs (including GPs, pharmacists and nurses) should collaborate with commissioners to develop local guidelines that support accurate differential diagnosis for RTIs.
- Local pathology services should be organised and commissioned in a way that allows pathologists to support GPs, pharmacists and nurses who are providing community based CRP POCT. In particular, pathologists should focus on quality control, education and compliance.
- CRP POCT leads to less diagnostic uncertainty while improving patient satisfaction through quicker diagnosis, better management and better service. HCPs should attempt to capture and communicate these factors to increase the likelihood of widespread implementation of CRP POCT.

RECOMMENDATIONS FOR

COMMISSIONERS

- CCGs should use the new quality premium for antibiotic prescribing as opportunity to review current RTI diagnostic pathways and implement CRP POCT in primary care.
- CCGs should ensure that healthcare professionals are adequately trained in CRP POCT, including consultation and communication skills. This may include commissioning local pathology services to support CRP POCT in the community.
- CCGs should explore opportunities for implementing CRP POCT within the Quality, Innovation, Productivity and Prevention (QIPP) programme.
- CCGs should explore alternative funding mechanisms that encourage uptake of diagnostics, while avoiding disincentives. These funding mechanisms should address the issue of economic benefits associated with fewer resistant infections (e.g. reduced hospitalisation, reduction in *Clostridium difficile*, benefits to the economy) that do not accrue to the CCG or HCP budget.
- Each CCG should determine the most effective and efficient means to implement the NICE guidelines.^{4,5} Each CCG should develop guidelines and procedures that integrate primary care CRP POCT with clinical diagnosis and history taking when deciding whether to prescribe antibiotics for lower RTIs.⁴ These initiatives should form part of the antimicrobial stewardship programme.⁵
- CCGs should work with a multidisciplinary group of local HCPs and the medicines optimisation teams to develop local guidelines and antimicrobial stewardship programmes that support accurate differential diagnosis and explain how CRP POCT could help HCPs engage with and educate patients about appropriate antibiotic use and self-management of RTIs.
- CCGs should use data collected (for instance, to meet requirements of the Care Quality Commission) to audit primary care CRP POCT to drive continual improvements in patient care, antimicrobial stewardship and to meet the NHS quality agenda. CCGs should also implement optimal quality assurance across all CRP POCT users to ensure patient safety.
- CCGs could consider developing locally incentivised enhanced services or patient group directives to increase implementation and use of CRP POCT in primary care.
- CCGs should actively promote and encourage primary care CRP POCT for suspected RTIs and other infections.
- CCGs planning the implementation of primary care CRP POCT should assess the impact on HCPs. Trusts and other organisations should use these assessments to plan services, education and training.
- CCGs should develop policies and organisational structures that allow local pathology services to support CRP POCT in the community. In particular, pathology services should focus on quality control, training and supply.
- Antibiotic use by out-of-hours services is rising more rapidly than in other parts of the NHS.³³ Further studies should ascertain if the increase is clinically justified and determine the role of CRP POCT in reducing antibiotic prescriptions and referrals to hospital by out-of-hour services.
- CCGs should work with pharmacists and other HCPs to assess CRP POCT in pharmacies and other community settings to reduce pressure on general practices.

RECOMMENDATIONS FOR

POLICY MAKERS

- The NHS should encourage uptake and implementation of CRP POCT as part of the ‘quality agenda’.
- The NHS should include CRP POCT in their strategic and tactical plans for antimicrobial stewardship.
- The NHS should use CRP POCT as a ‘pilot’ to ensure smooth implementation and uptake of the other diagnostic technologies in primary care relevant to antimicrobial stewardship that are likely to reach the market in the next few years.
- The proposed Common Ailments Scheme and any equivalent local schemes should advocate CRP POCT to identify low-risk patients.
- Code of practices for antimicrobial stewardship, and for the prevention and management of healthcare-acquired infections, should encompass CRP POCT.
- The NHS, professional bodies, medical, pharmacy and nursing schools, and manufacturers should raise awareness of POCT generally and CRP POCT in particular. Stakeholders running the Choosing Wisely programme should consider advocating CRP POCT as a resource that helps patients understand the harms of interventions and accept the value of watchful waiting.
- Monitor, NHS England, Public Health England (PHE), NICE and the Care Quality Commission should promote and encourage POCT for pneumonia and other infections. The equivalent organisations in Northern Ireland, Scotland and Wales should also consider promote and encourage POCT in primary care.
- Consensus groups should consider the relevance of CRP POCT when developing guidelines, documents and tools.
- Comprehensive clinical and economic research programme should examine expanded roles for CRP POCT (e.g. in pharmacies) as a keystone of antimicrobial stewardship.
- The Royal College of General Practitioners (RCGP) and PHE should include information about CRP POCT in the TARGET (Treat Antibiotics Responsibly, Guidance, Education, Tools) Antibiotic Toolkit.
- NICE Guidelines should align with the latest advice and evidence supporting CRP POCT in primary care.
- Policy makers should ensure that CCGs implement optimal quality assurance.
- CRP POCT leads to less diagnostic uncertainty while improving patient satisfaction through quicker diagnosis, better management and better service. The NHS and public health services should attempt to capture and communicate these factors to increase the likelihood of widespread implementation of CRP POCT.
- Quality Statements and CCG Outcomes Indicators should be developed to encourage CRP POCT in primary care covering pneumonia and antimicrobial stewardship.

SUMMARY FOR

PATIENTS

Antibiotics can prevent infections that result from simple scratches and sore throats, or chest and ear infections, developing in to fatal septicaemia (blood poisoning.) These medications can save countless lives from once-feared diseases such as scarlet fever and tuberculosis. Without effective antibiotics, cancer treatments, childbirth and many operations would be far riskier.³ However, widespread inappropriate antibiotic prescribing is driving a rise in antimicrobial resistance that threatens our ability to treat many infections. Therefore, governments, healthcare professionals (HCPs) and industry are working together to tackle the problem.

Viruses cause most coughs, colds and other respiratory tract infections. Antibiotics do not work against viruses and will not reduce symptoms. However, when antibiotics are used there is still the potential for adverse events – including allergies, diarrhoea and rash – and inappropriate use like this, causes our bodies to develop resistance. Resistance causes antibiotics to become ineffective at treating infection even when they are being prescribed correctly.³

Measuring the level of C-reactive protein (CRP) in the blood, which occurs as part of the body's natural response to infection, can help HCPs determine whether a patient needs antibiotics. Used alongside signs, symptoms and history taking, the test can help HCPs prescribe antibiotics more effectively, reducing the risk of resistance. The test itself takes only a few minutes and can be performed during a HCP consultation. Only a tiny drop of blood from the finger is needed, of which the retrieval process is very quick and painless. Other European countries already use CRP tests to decide whether antibiotics are needed when patients have coughs, colds and chest infections, and a lot of these nations have a lower occurrence of antibiotic resistance than the UK.

INTRODUCTION

Antibiotics can prevent infections resulting from simple scratches, sore throats, ear infections and so on from developing into fatal septicaemia. Antibiotics save countless lives from once-feared diseases, such as scarlet fever, postpartum infections and tuberculosis. Without effective antibiotics, some cancer treatments, childbirth and orthopaedic operations would be far riskier.³ However, widespread inappropriate antibiotic prescribing is driving a rise in AMR that threatens our ability to treat many infections. Indeed, AMR is one of the top seven threats to the human race (figure 1).³⁴



AMR threatens many of the most important medical advances we have made.

The O'Neill Review on Antimicrobial Resistance³

Overall, infections and infectious diseases cost the UK about £30 billion a year.²⁸ However, the O'Neill Review on Antimicrobial Resistance estimated that by 2050, AMR in just three bacteria (*Klebsiella pneumoniae*, *Escherichia coli* and *Staphylococcus aureus*) could cause more than 10 million additional deaths worldwide every year, than if resistance remained at today's level. The cumulative cost could reach US\$100 trillion.³⁵

AMR could dramatically increase the morbidity, mortality and costs associated with bacterial infections. Infections accounted for 4% of potential years of life

lost in England in 2010, caused 7% of deaths and were the primary reason for admission for 8% of hospital bed days. Indeed, AMR was recently added to the National Risk Register for Civil Emergencies. The Register notes that: "The numbers of infections complicated by AMR are expected to increase markedly over the next 20 years. If a widespread outbreak were to occur, we could expect around 200,000 people to be affected by a bacterial blood infection that could not be treated effectively with existing drugs, and around 80,000 of these people might die."²⁹

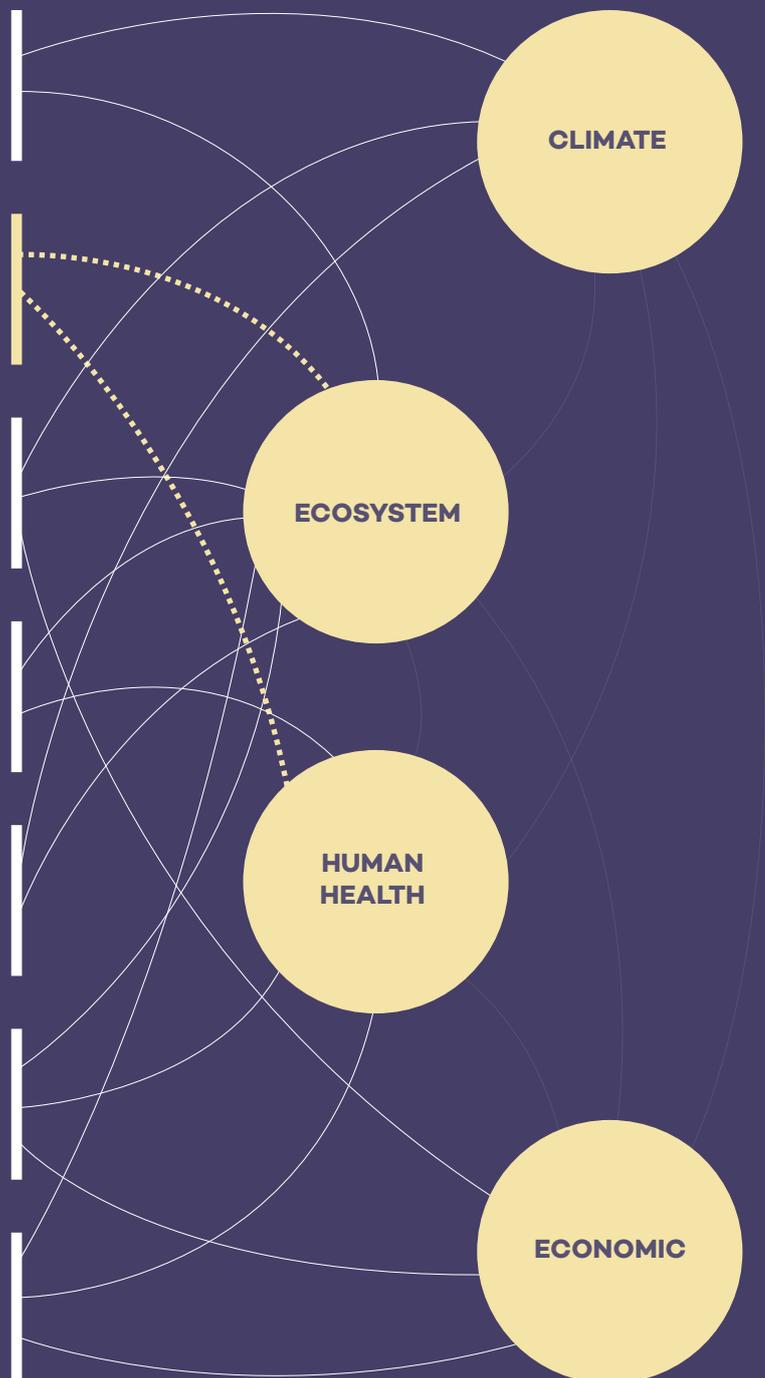
Figure 1: The top seven threats to the human race³⁴

Source adapted from: *Science*, Vol 325, September 2009

GLOBAL DRIVERS

- 1 Changed carbon nitrogen cycles and rising atmospheric greenhouse gas concentration
- 2 **Increasing antibiotic resistance**
- 3 Increasing connectivity (economic, social, ecological)
- 4 Rising human numbers and urbanisation
- 5 Increasing per capita resource use
- 6 Nuclear proliferation
- 7 International terrorism

UNWANTED OUTCOMES





We are losing the battle against infectious diseases. Bacteria are fighting back and are becoming resistant to modern medicine. In short, the drugs don't work.

Davies et al¹

1.1

A co-ordinated, sustained response

Tackling AMR requires a co-ordinated, sustained response encompassing:

- Responsible use (“stewardship”) of antibiotics in humans and animals.
- Improved design of healthcare environments and processes.
- Greater investment in HCPs, researchers and support staff.
- Greater investment in basic and applied research.
- Challenging entrenched behaviours and attitudes towards treatment and use of diagnostics among patients, HCPs and in society more generally. For instance, patients need to be aware that viruses cause most RTIs. Therefore, antibiotics will not alleviate symptoms, but will expose patients to potential adverse events as well as driving AMR.

Despite widespread recognition of the problem posed by AMR among HCPs, several factors hinder more rational antibiotic prescribing. Currently, for example, some doctors worry that denying patients antibiotics without sufficient justification could undermine their clinical relationship. Understandably, some HCPs worry about missing people with developing infections and, therefore, prescribe antibiotics as a safety net or to aid diagnosis.

Additional training and improved diagnostic support can help HCPs generally (including hospital doctors, nurses, pharmacists and

dentists), and GPs in particular, resist pressure from patients and carers to prescribe antibiotics for simple, self-limiting infections. For instance, the present report argues that rapid, accurate differentiation of low- and high-risk infections:

- Encourages appropriate antibiotic prescribing.
- Facilitates patient education and self-management.
- Will slow the spread of AMR.
- Potentially results in savings to the NHS and society more widely from fewer prescriptions and AMR-related costs.

Over the next few years, advances in genetic and molecular technologies will allow HCPs to diagnose bacterial and viral infections more quickly and accurately than sending a sample to a microbiology laboratory. Indeed, several point-of-care diagnostic tests for specific antigens and pathogens (including *Streptococcus pneumoniae*, Group A streptococcus, Respiratory Syncytial Virus, Legionella and influenza) are already available and are used in secondary care. In the present report, the consensus panel focused on CRP POCT for patients presenting with symptoms of RTI in primary care.

CRP is a marker for inflammation and infection. High levels of CRP in the blood are often associated with potentially serious bacterial infections. In contrast, CRP does not usually increase to high levels in viral or self-limiting bacterial infections. HCPs combine CRP POCT with clinical observations of signs and symptoms and

consideration of the patient's history to improve diagnosis of RTI. This, in turn, allows HCPs to identify both ‘low risk’ patients who do not require antibiotics and those at high-risk of having a bacterial infection that need antibiotics. Indeed, NICE supports combining CRP POCT with clinical diagnosis and history taking when deciding whether to prescribe antibiotics for suspected lower respiratory tract infections (LRTIs). CRP POCT is also part of the draft guidance for antimicrobial stewardship (AMS)^{4,5} Public Health England (PHE) supports CRP POCT for RTIs.²⁶ CRP POCT is also routinely used in general practice in several other European countries.⁶⁻¹⁰

Essentially, CRP POCT helps resolve diagnostic uncertainty and, therefore, can help GPs prescribe antibiotics where appropriate and, importantly, justify the reason to patients. As such, CRP POCT can help resolve perceived conflicts between patients, public health and the NHS. For instance, CRP POCT can reassure patients who are very worried or are demanding an antibiotic.¹⁵ In some cases, HCPs might issue a prescription for an antibiotic that patients fill only if self-care fails to improve symptoms (delayed prescribing). Over time, CRP POCT that is well integrated into the consultation could help engender behaviour change and greater understanding of rational antibiotic prescribing among HCPs, patients and the general public.

THE GROWING BURDEN IMPOSED BY AMR

“

Drug resistance appears to be a simple case of adaptation via natural selection: The use of antimicrobials in medicine and agriculture imposes selective pressure on microorganisms, favoring the persistence and spread of bacteria with resistant phenotypes.

Perron et al³⁶

AMR emerged almost as soon as penicillin and tetracyclines reached the clinic in 1944 and 1945 respectively.¹ Indeed, Alexander Fleming predicted that antibiotic-resistant bacteria would evolve soon after he discovered penicillin in 1929.³⁶ In response, pharmaceutical companies developed new antibiotics (figure 2), including launching methicillin in 1960. However, microbiologists discovered methicillin-resistant *Staphylococcus aureus* (MRSA) within a year of the antibiotic's launch.³⁷ For several years, glycopeptides (e.g. vancomycin) remained the final-line antibiotic against Gram-positive bacteria.¹ Microbiologists once believed that glycopeptide resistance was impossible.¹ Yet vancomycin-resistant *Staphylococcus aureus* (VRSA) emerged in 1995.³⁷

Experience over the last 70 years demonstrates that even appropriate and conservative use of antimicrobials contributes to AMR. Genes encoding resistance have existed since bacteria first evolved. However, antibiotics used in medicine and agriculture enhanced the expression and prevalence of genes encoding AMR. Indeed, at the time of writing, The Comprehensive Antibiotic Resistance Database included 2978 genes specially linked with AMR (arpcard.mcmaster.ca) and the number is growing. Furthermore, bacteria are increasingly multidrug-resistant. Infectious staphylococcal strains resistant to penicillin and tetracycline emerged in the early 1950s. Today, multiple drug-resistant bacteria account for between 20% and 80% of healthcare-associated infections worldwide.³⁶

Despite the rise in AMR generally and multidrug-resistant bacteria in particular, few novel antibiotics, especially from new classes, have reached the market over the last few years. The Food and Drug Administration (FDA) in the USA approved 19 new antibiotics between 1980 and 1984. Antibiotic approvals fell to just three between 2005 and 2009 and one in 2010–12.³⁸ While several new classes of antibiotic are in development, infection control strategies and antimicrobial stewardship (AMS) focus on 'protecting' existing antibiotics rather than relying on pharmacological innovation to overcome AMR. Indeed, new antibiotics should be reserved for infections that are resistant to current drugs.

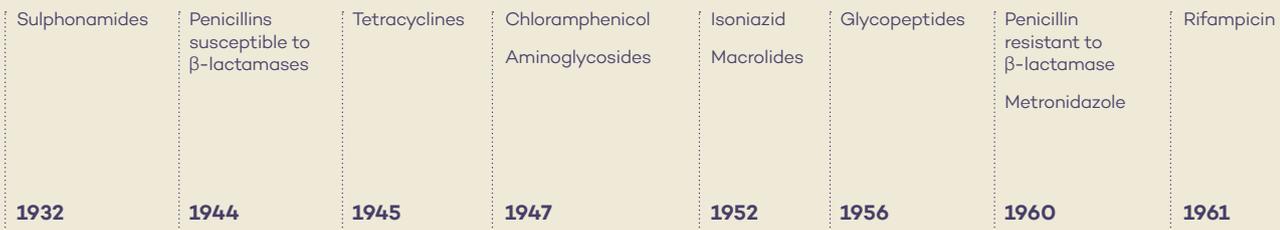


Figure 2: Timeline of antibiotic introduction into clinical use¹

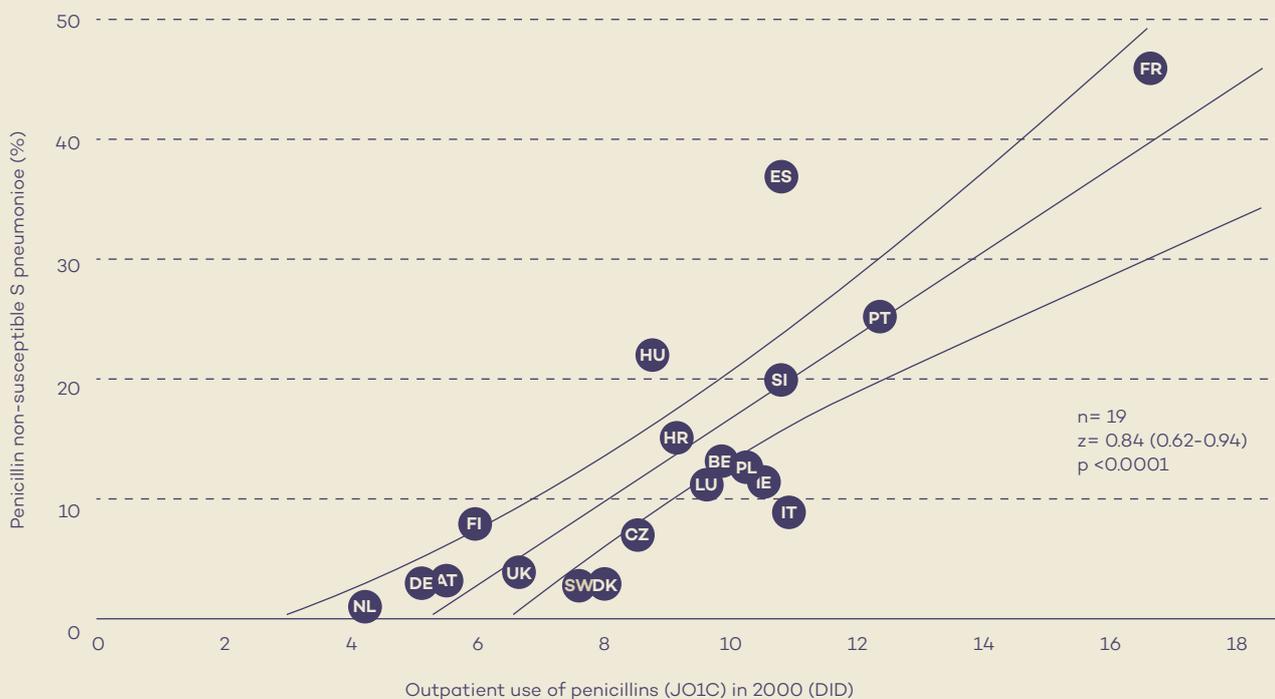
Source adapted from: Davies S, Grant J, Catchpole M. *The Drugs Don't Work: A Global Threat* Penguin Specials 2013.



When we look at our successes in controlling methicillin-resistant *Staphylococcus aureus* ... and *C. difficile* ... we can see that action with political will behind it can have a tremendous effect.

Certainly, concerted infection control strategies and AMS can reduce the clinical burden imposed by AMR. For example, the number of cases of MRSA bacteraemia declined by 84.7% between 2003/4 and 2011. *Clostridium difficile* cases fell by 53% between 2008 and 2011.²⁸ However, HCPs, commissioners and policy makers need to make further efforts to develop educational platforms, tools, incentives and guidelines to ensure rational antibiotic prescribing.

Annual Report of the Chief Medical Officer Volume Two 2011²⁸



AT Austria, BE Belgium, HR Croatia, CZ Czech Republic, DK Denmark, FI Finland, FR France, DE Germany, HU Hungary, IE Ireland, IT Italy, LU Luxembourg, NL The Netherlands, PL Poland, PT Portugal, SI Slovenia, ES Spain, UK England only

Figure 3: Relationship between primary care antibiotic prescribing and resistance in penicillin non-susceptible *Streptococcus pneumoniae*³⁹

Cephalosporins Fusidic acid	Trimethoprim	Carbapenems	Penicillins combined with a β -lactamase inhibitor	Fluoroquinolones	Mupirocin	Oxazolidinones	Lipopeptides
1962	1969	1975	1976	1982	1983	2001	2006

2.1

Antibiotic prescribing drives AMR

Excessive antimicrobial use promotes AMR's emergence, persistence and transmission. A study from 26 European countries found a significant linear correlation between outpatient antibiotic prescribing and AMR for *Streptococcus pneumoniae* (Figure 3). In addition, antibiotic prescribing showed marked seasonal fluctuations, peaking during the winter.³⁹ This pattern may reflect the increase in RTIs during the winter.

In the UK, approximately 79% of antibiotics are prescribed in primary care, mainly by GPs.³³ As a result, numerous initiatives aim to reduce inappropriate antibiotic prescribing in primary care. For example, the *When Should I Worry?* leaflet (whenshouldiworry.com) aims to educate parents of children suffering RTIs about self-management and appropriate use of antibiotics. The TARGET (Treat Antibiotics Responsibly, Guidance, Education, Tools) antibiotics toolkit—developed by the Royal College of General Practitioners (RCGP), PHE and The Antimicrobial Stewardship in Primary Care Collaboration—aims to inform GPs and commissioners about safe, effective and appropriate antibiotic prescribing.

The TARGET toolkit includes:⁴⁰

- Antibiotic management guidelines.
- Audit tools.
- Patient information leaflets.
- Resources for clinicians and links to external resources.
- Self-assessment checklists.
- Training resources.

Unfortunately, there is little evidence that these and other educational initiatives aimed at HCPs and the public have markedly altered antibiotic prescribing in the UK, which remains considerably higher than

in many other northern European countries.¹⁵ Indeed, between 2010 and 2013, antibiotic use in primary care in England increased by 4%, while total use increased by 6% (figure 4).³³ Furthermore, the likelihood that GPs in England would prescribe antibiotics for coughs and colds increased by 40% between 1999 and 2011.⁴¹ A study of 452 people with RTIs found that GPs or nurses refused only 3.5% of requests for antibiotics. Seventy four per cent of the patients were prescribed antibiotics after some discussion and 23% without any discussion.⁴²

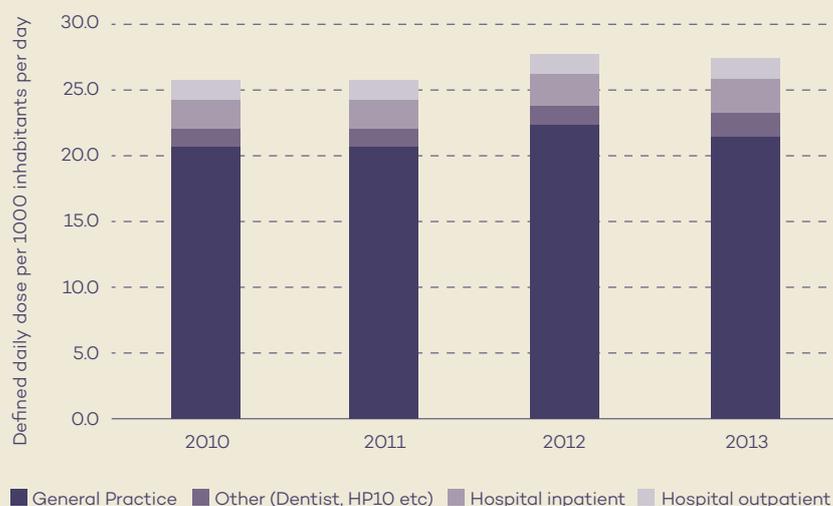


Figure 4: Consumption of total antibiotics in England, 2010-2013³³

Reproduced with permission from: Public Health England, English surveillance programme for antimicrobial utilisation and resistance Report 2014.

2.2

Inappropriate antibiotic prescribing for RTIs

More than half of antibiotics prescribed in general practice are for RTIs.⁴⁰ Indeed, acute uncomplicated RTIs are among the most common acute presentations in primary care:⁴³⁻⁴⁵

- The crude overall incidence of LRTIs in the UK is 123 episodes per 1000 person-years.⁴⁶
- Between 24 and 46 per 1000 of the population develop acute bronchitis each year.¹⁷
- The annual incidence of community-acquired pneumonia is approximately 5-11 per 1000 patients.¹⁷

RTIs become increasingly common with advancing age. People aged 85-89 years had twice as many LRTIs and seven times more episodes of community-acquired pneumonia as those aged 65 to 69 years.⁴⁶ Infective exacerbations of chronic obstructive pulmonary disease (COPD) are also especially common among elderly people and the prognosis declines with advancing age.⁴⁸ Therefore, RTIs could impose a growing burden with the larger numbers of elderly people in the population over the next few years. This underscores the importance of implementing strategies to ensure effective AMS, including enhanced diagnosis of RTIs in primary care.

Most acute uncomplicated RTIs are viral or self-limiting bacterial infections. Therefore, antibiotics are inappropriate. For instance, viruses cause approximately 90% and 70% of cases of pharyngitis in adults and children respectively.⁴⁹ Patients can self-manage most acute uncomplicated RTIs with symptomatic and supportive

treatments at home.^{12,50,51} Indeed, systematic reviews show the paucity of evidence supporting antibiotics for people with acute bronchitis,⁵⁰ sore throat,⁵² sinusitis⁵³ and otitis media.⁵⁴

The exception may be elderly patients, who are at high risk of pneumonia. Among patients aged ≥65 years who present with an LRTI, 4% of those not prescribed antibiotics were diagnosed with pneumonia in the next month. This rate is more than twice that of those prescribed antibiotics (1.5%).⁴⁵

Despite this evidence base, GPs in one analysis prescribed antibiotics to three-quarters of patients with LRTIs on the day of diagnosis.⁴⁶ Another study found that doctors prescribed antibiotics to 79.1% of 6771 patients with RTIs.¹² In a recent study from the Netherlands, 46% of antibiotic prescriptions for RTIs were for conditions not indicated by the guidelines. Overprescribing was most common:

- For patients between 18 and 65 years of age.
- When GPs felt under pressure from a patient for an antibiotic.
- For patients presenting with fever.
- For those with symptoms lasting more than a week.⁵⁵

These figures seem to be excessive given antibiotics' relatively limited clinical role for RTIs. Some antibiotics are prescribed unnecessarily for clinical reasons that are unsupported by evidence, such as the colour of nasal discharge, sputum or both. This is often to reduce re-attendance, because the HCP feels under pressure from patients to prescribe antibiotics,³² or, in the consensus panel's experience, as a safety net or a diagnostic aid.

A COMMON PROBLEM

RTIs are common presentations in primary care in England and Wales. In 2011, the mean weekly incidence of 'pneumonia and pneumonitis' (inflammation of lung tissue) was 0.96 per 100,000 of the population of all ages. The incidences of 'tonsillitis and sore throat' were 55.8 per 100,000 and 10.1 per 100,000 for 'influenza and flu-like illness'. The mean weekly incidences of upper RTIs and LTRIs were 208.5 per 100,000 and 100.6 per 100,000. So, upper RTIs and LTRIs were more than 100 times more common than, for instance, breast cancer in women (1.14 per 100,000), prostate cancer in men (1.13 per 100,000) and osteoarthritis of the hip (1.24 per 100,000). In addition, upper RTIs and LTRIs were at least five times more common than atopic eczema and dermatitis (18.6 per 100,000), episodes of anxiety (17.2 per 100,000) and migraine (7.8 per 100,000).⁴⁷

2.3

Beyond resistance

Antibiotics are associated with several other adverse consequences other than AMR. For example, about 1-in-10 people taking antibiotics develop side effects, commonly gastrointestinal disturbances.⁵⁶ Gastrointestinal adverse events may be even more common in some settings. For instance, in the placebo arm of a study assessing a probiotic, 44% of inpatients developed antibiotic-associated diarrhoea that lasted, on average, 6.4 days.⁵⁷

In addition, approximately 1-in-15 people taking an antibiotic develops an ‘allergic’ reaction to it. Penicillins and cephalosporins are especially prone to trigger hypersensitivity reactions⁵⁶ and some of these allergic reactions are fatal. A study from the USA showed that antibiotics may contribute to 19.3% of all emergency department visits for drug-related adverse events.⁵⁸ Allergic reactions seem to account for the majority (79%) of emergency visits for antibiotic-associated adverse events.⁵⁸ We propose that this should be studied in the UK to ascertain the incidence of emergency visits for antibiotic-associated adverse events in this country. Antibiotics can also cause rare, serious adverse reactions such as Stevens-Johnson Syndrome.

2.3.1

The effect on the microbiota

Antibiotics disrupt the body’s natural colonies of bacteria and other microorganisms (the microbiota, also called the microbiome), which may have long-term health consequences. For instance, approximately 30,000 strains of bacteria colonise the lower gastrointestinal tract. (In comparison, an acre of undisturbed tropical rainforest might contain 15,000 species.⁵⁹) These bacteria break down foods that we cannot digest, boosting the energy released from our diets by about 10%, make vitamin K (involved in blood clotting), shape our immune responses, and reduce the risk of colorectal cancer and obesity.⁶⁰⁻⁶³

Unfortunately, antibiotics kill beneficial as well as harmful bacteria, which can allow pathogens—including those resistant to antibiotics—to become more prominent.⁵⁹ For example, a healthy microbiota controls *Clostridium difficile* numbers. However, *Clostridium difficile* levels can increase rapidly in people taking antibiotics, causing severe diarrhoea, bleeding and even death. The most important risk factor for *Clostridium difficile* infection remains antibiotic use.⁶⁴

The microbiota also controls populations of the yeast *Candida albicans*. As a result, in one study, vaginal candidiasis was up to 11 times more frequent in women taking antibiotics than in a control group of women taking antidepressants.⁶⁵ Antibiotics may also increase the risk of bacterial vaginosis, caused by disruptions to the vaginal microbiota. Bacterial vaginosis appears to be a risk factor for HIV infection.⁶⁶

Increasing evidence also suggests that the intestinal microbiota shape immune responses. So, disruptions to gastrointestinal microbiota, especially in infancy, may increase the risk of atopic conditions, obesity, metabolic syndrome, insulin resistance, and other conditions in later life.⁶⁷⁻⁶⁹ Indeed, treating young mice with low-dose penicillin produces long-lasting effects on metabolism and immunity.⁶⁹ The implications for older patients are less well characterised, although recent studies link repeated course of antibiotics, especially penicillin, with an increased risk of colorectal cancer. Again, changes to the microbiota seem to mediate the association.⁷⁰

Antibiotics can also select resistant bacteria on the skin and in the gut, which can pass between family members, pets and other close contacts. The gastrointestinal tract is a reservoir for pathogens, such as *Escherichia coli*, that can cause urinary tract infections (UTIs). The rising rate of AMR is now limiting antibiotic choice for UTIs.⁷¹ Moreover, the growing problem posed by gonorrhoea resistance prompted the *Gonorrhoea Resistance Action Plan* for England and Wales introduced in 2013, which seems to have had some success in controlling the spread of resistance.⁷² It seems reasonable to assume that the increasing resistance in UTIs and gonorrhoea, in part, reflects more widespread colonisation with resistant bacteria in the gastrointestinal tract following antibiotic use. Clinical and economic analyses rarely assess the burden that these effects place on patients, the NHS and society more widely.

DIAGNOSTICS: CENTRAL TO TACKLING AMR

The Government's Review on Antimicrobial Resistance suggested five approaches to tackle the problem posed by AMR and protect antibiotics:⁷³

- Increased funding for basic research to tackle AMR.
- Protect current antibiotics through effective and efficient AMS.
- Investment in scientific, clinical and other staff to tackle AMR.
- Modernise AMR surveillance resistance globally.
- Support the development and use of relevant diagnostic technologies.

Essentially, enhancing diagnostic accuracy would reduce unnecessary antibiotic prescriptions and would allow the NHS to save more powerful antibiotics for infections that are resistant to other options.⁷³

Future diagnostic technologies might use genetic targets—such as antibiotic resistance genes, virulence factors and phylogenetic markers⁷⁴—to identify pathogens and discriminate antibiotic susceptibility.

In the meantime, CRP POCT, used alongside consideration of the patient's history, signs and symptoms, helps HCPs differentiate viral and self-limiting bacterial infections from more serious infections that require antibiotics. In addition, future diagnostic technologies are also likely to be more expensive than CRP POCT. Therefore, CRP POCT is still likely to have a role 'screening' patients before moving to more expensive diagnostic approaches.



If we could diagnose bacterial infections and resistance more quickly and accurately, even if only for certain types of infection, we could 'save' our most powerful antibiotics by using them only for cases resistant to other options. This would make our drugs last longer.

O'Neill Review on Antimicrobial Resistance⁷³



If we had the right diagnostics, more patients would receive the right antibiotic to treat their infection, but fewer antibiotics would be prescribed unnecessarily.

The O'Neill Review on Antimicrobial Resistance⁷³



The main diagnostic challenge of general practitioners (GPs) facing patients with acute community-acquired lower respiratory tract infections (LRTIs) is selecting the right patients for antibiotic treatment... GPs have the difficult task of balancing the fear of missing the diagnosis of pneumonia against their duty not to contribute to the growing problem of bacterial resistance by routine prescription of antibiotics.

Hopstaken et al¹⁷

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Diagnostic dilemmas in RTIs

Despite being common, RTIs can pose diagnostic dilemmas. Clinicians can use six clinical criteria to predict pneumonia in patients presenting with acute cough:

- Absence of runny nose.
- Breathlessness.
- Crackles.
- Diminished breath sounds on auscultation.
- Tachycardia (>100 beats per minute).
- Fever ($\geq 37.8^{\circ}\text{C}$).

However, these clinical criteria correctly identified only 26% of patients with a “low” (<2.5%) or “high” (>20%) risk of RTI. In the 74% of patients in whom diagnostic doubt remained, measuring CRP (using a threshold of >30 mg/l) helped to correctly exclude pneumonia.⁷⁵ Adding CRP values to symptoms and signs improved the probability of predicting pneumonia significantly better than symptoms and signs alone. The negative predictive value in the low-risk group was 97%. The risk of missing pneumonia was between 2.5% and 4%.^{17,75}

Several studies suggest that clinical diagnosis of pneumonia in general practice correlates poorly with radiographic evidence

of infection.^{17,76,77} In one study, for example, only 15% of adults treated with antibiotics for suspected pneumonia showed the condition on chest x-ray.⁷⁶ Another study reported that only 13% of patients with clinically suspected pneumonia showed a positive radiograph.¹⁷

During an investigation that enrolled 2810 patients presenting with acute cough in primary care, GPs recorded whether they believed pneumonia was present based on history and physical examination. Radiographers performed chest x-rays within a week of the clinical diagnosis. The authors reported that:

- Just 5% of the patients had radiographic pneumonia.
- GPs had diagnosed 29% of those with radiographic pneumonia.
- 1% had a clinical diagnosis of pneumonia that was not confirmed by radiography.
- X-rays confirmed 57% of diagnoses based on clinical criteria.

The results highlight the “need to further support the detection of clinically relevant pneumonia in primary care”.⁷⁷ CRP testing appears to predict radiographic pneumonia more accurately than clinical criteria alone and, therefore, meets this need.^{17,76}

CRP POCT: CENTRAL TO ANTIBACTERIAL STEWARDSHIP

CRP is a marker for inflammation rather than being a definitive test for bacterial infections that need antibiotics. Patients with serious bacterial infections usually show high CRP levels. In contrast, CRP levels are rarely high in viral or self-limiting bacterial infections. This makes CRP POCT a valuable adjunct to clinical observation of signs and symptoms, and the patient’s history, when deciding whether to prescribe antibiotics particularly for RTIs.

4.1 A brief introduction to CRP

Normally, blood contains only trace amounts of CRP, a protein discovered in 1929. The liver rapidly increases CRP production following infection or injury. CRP binds to phosphocholine, which is found in bacterial and fungal polysaccharides and most cell membranes.¹⁵ This ‘tags’ infective or injured cells, and helps the immune system recognise and remove pathogens and damaged host cells.

Figure 5 shows the time course of CRP levels following upper RTI with bacteria and viruses. Signs and symptoms of an upper RTI generally peak on days 3 to 4.⁷⁸ Therefore, CRP tends to be highest when patients experience the most severe symptoms. A viral infection commonly causes moderately elevated CRP (10–60mg/l) after less than 7 days of symptoms, peaking on days 2–4. CRP that remains elevated after 7 days suggests secondary bacterial infection.⁷⁸

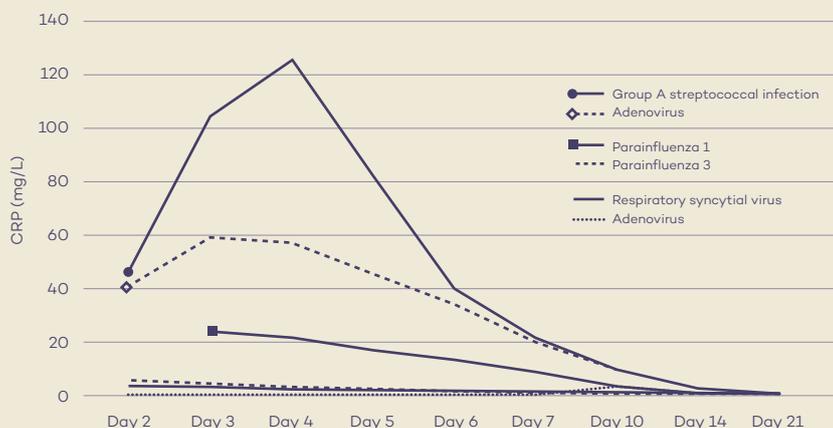


Figure 5: CRP values in 6 subjects with untreated upper RTI, showing duration of illness and pathogen⁷⁸



The patient is the ‘great winner’ with CRP POCT. Management decisions are more evidence-based, the service is much better—faster and more convenient—and there is a greater likelihood of appropriate shared-decision making with skilled HCPs.

Rogier Hopstaken, a GP from Utrecht, the Netherlands and POCT expert

CRP levels correlate with the severity of the infection or the extent of the injury and are higher in patients with a potentially serious bacterial infection, than in those with viral or self-limiting bacterial infections.¹⁵ Therefore, used alongside clinical observation of signs and symptoms, and the patient's history, CRP is a sensitive and specific test^{77,79} (table 2) that helps resolve diagnostic uncertainty and, in turn, allows HCPs to prescribe antibiotics more accurately.

Table 2: Diagnostic accuracy of CRP⁷⁷

CRP concentration	Positive predictive value	Negative predictive value
Diagnosing pneumonia in patients presenting with acute cough		
<20 mg/l	11.8%	97.4%
> 100 mg/l	35.4%	96.1%

Several studies have examined the diagnostic thresholds that offer the greatest clinical utility for differentiation low-risk from high-risk RTIs. These studies led to the conclusions that:

- <20mg/L is optimal for identifying people at low risk of serious RTI (negative predictive value 97.4%).
- >100mg/L as the high-risk threshold, when considered alongside clinical signs and symptoms (table 2).^{17,77}
- Measuring CRP can aid the differential diagnosis of pneumonia⁷⁶ and bacterial acute exacerbations of COPD and chronic bronchitis.^{19,80}
- In one study, the 'classic' clinical indicators of pneumonia—such as cough (positive predictive value [PPV] 0.17), sore throat (PPV 0.20), yellow (PPV 0.14) and bloody (PPV 0.30) sputum, and dyspnoea (PPV 0.15)—had a relatively poor predictive value. In contrast, CRP levels >50 mg/l showed a high predictive value (PPV 0.80).⁷⁶
- Another study defined patients at 'low-risk' of pneumonia as having a maximum of one positive score on three items (diarrhoea, dry cough, and temperature >38°C) with CRP<20 mg/l. In this low-risk group, the three items were associated with a predictive value of not having pneumonia of 97%. This approach missed between 2.5% and 4% of cases of pneumonia.¹⁷ As figure 6 shows, the probability of predicting pneumonia (90% AUC 0.9) was better by adding CRP values to symptoms and signs than with symptoms and signs alone (70% AUC 0.7), a statically significant difference.¹⁷ In this figure, a perfect diagnostic test would form a right angle up the Y axis at 0, then run along the top parallel to the x axis.

4.2

CRP POCT reduces antibiotic use

CRP POCT used alongside history taking and evaluation of signs and symptoms reduces antibiotic prescribing without producing a clinically significant increase in the risk of complications or missed diagnoses (table 3).¹⁶⁻¹⁸

For example, using a threshold of <20 mg/l to define a low-risk patient potentially avoided 41% of antibiotic prescriptions.¹⁷ Furthermore, in randomised or cluster randomised controlled trials (RCTs), using CRP POCT was associated with reductions on antibiotic prescribing of:

- 41.78% in patients presenting with suspected LRTI with a cough lasting less than four weeks together with one focal and one systemic symptom.¹⁸
- 36.16% in patients presenting with acute cough/LRTI (including acute bronchitis, pneumonia, and infectious exacerbations of COPD or asthma).¹¹
- 31.25% in patients with upper and lower RTI.¹²
- 23.3% in lower RTIs or rhinosinusitis.¹⁴

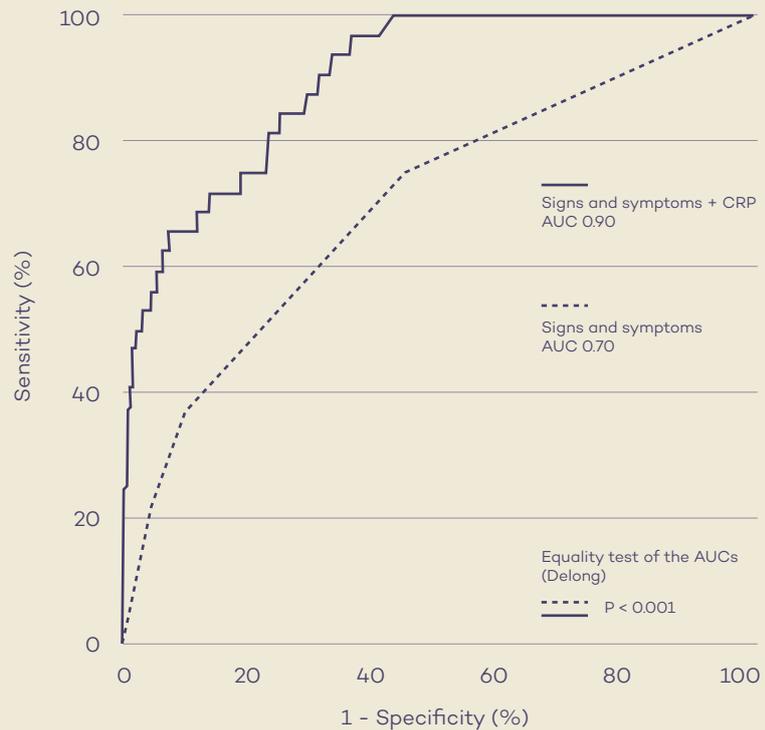


Figure 6: Receiver operating characteristic curves comparing symptoms and signs alone combined CRP model for predicting pneumonia¹⁷

Reproduced with permission from: Hopstaken R, Contributions of symptoms, signs, erythrocyte sedimentation rate, and C-reactive protein to a diagnosis of pneumonia in acute lower respiratory tract infection. *Br J Gen Pract.* 2003;53(490):358-364.

In another study, 31.5% of patients managed with CRP POCT received antibiotics during their index visit. This compared to 54.5% in those who were not tested. During the 28-day follow up, 45.3% and 59.7% respectively received antibiotics.²⁵

Paper	Setting	RTI	Number of patients	% antibiotics no CRP	% antibiotics with CRP	% relative difference	% absolute difference
Cals 2009 ¹⁸	Netherlands	LRTI	431	53	31	41.51	22
Cals 2010 ¹⁴	Netherlands	LRTI or rhinosinusitis	258	56.6	43.4	23.32	13.2
Little 2013 ⁹¹	6 EU countries	LRTI or URTI	6771	48	33	31.25	15
Andreeva 2014 ¹¹	Russia	Acute cough or LRTI	179	58.9	37.6	36.16	21.3

Table 3: Antibiotic prescribing rates for RTIs with and without CRP POCT



CRP POCT could help with one of the really big challenges in RTIs: Identifying the patients who are really sick while avoiding unnecessary antibiotic use.

A member of the consensus panel

4.2.1

A view from Cochrane

A Cochrane review of CRP POCT encompassed six RCTs or cluster RCTs that enrolled 3284 participants, including 139 children. While the review identified some limitations in the study designs, significantly fewer antibiotics were prescribed in the CRP POCT group (37.4%) versus standard of care (49.1%). The pooled results (figure 7) showed that CRP POCT significantly reduced the number of antibiotic prescriptions issued in primary care for acute RTIs by 22%. The number needed to test (NNT) to save one antibiotic prescription at the index consultation ranged from 6 to 20 depending on the study design.¹⁶

No difference in clinical recovery (defined as at least a substantial improvement at day 7 and 28 or re-consultation by day 28) emerged between patients managed using CRP POCT and standard care. No deaths or serious complications were reported in any of the studies.¹⁶

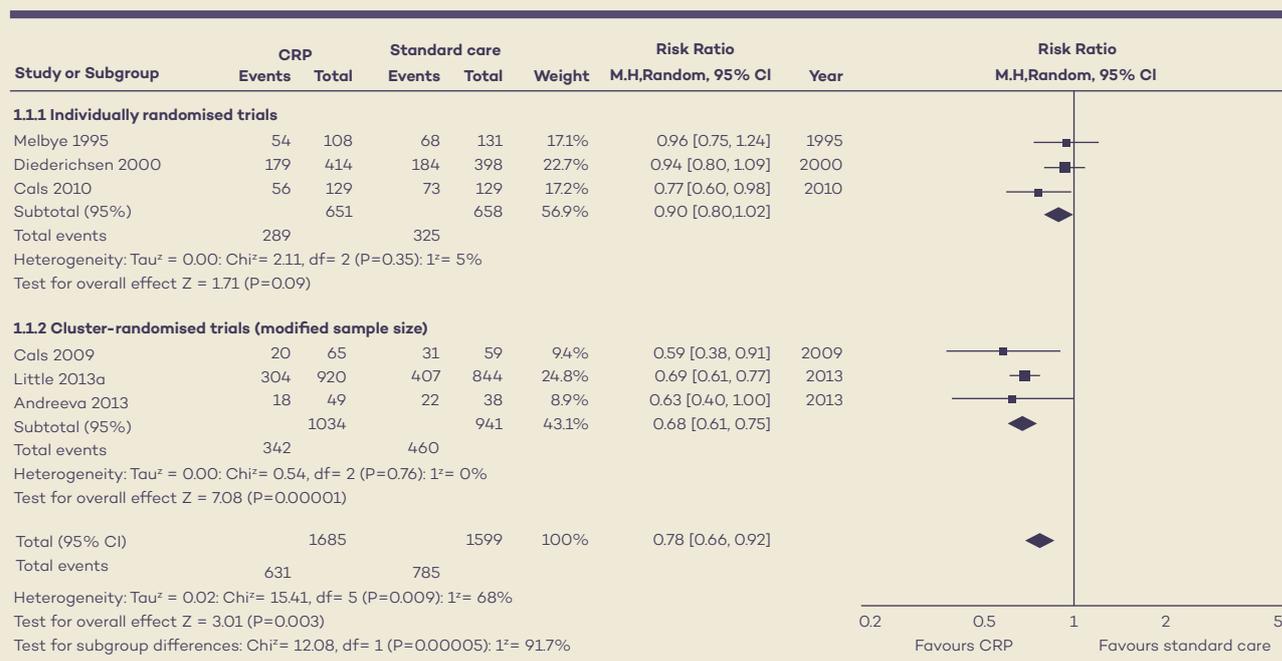


Figure 7: Forest plot of the impact of measuring CRP on antibiotic prescribing¹⁶

4.3

An international perspective

The likelihood of prescribing antibiotics for a RTI varies widely between and within countries. For example, depending on the country, between 15% and 83% of people presenting with an acute cough receive antibiotics.⁶ However, most countries that use CRP POCT widely—such as Denmark, Norway, Sweden, Germany, The Netherlands and Switzerland—use fewer antibiotics in primary care than in England (figure 8). In Switzerland, for example, just 22% of adults presenting to primary care receive an antibiotic prescription. In this study, the CRP level, the white blood cell count and symptom duration emerged as statistically significant predictors of antibiotic prescription.⁶



Figure 8: Use of CRP POCT and antibiotic prescribing in Europe

Adapted from: European Centre for Disease Prevention and Control http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/esac-net-database/Pages/Antimicrobial-consumption-rates-by-country.aspx June 2015

Obviously, CRP POCT is not solely responsible for the lower antibiotic use in these countries. However, clinicians in several countries, including the Netherlands, regard CRP POCT as an important element in their decision-making.⁸² Furthermore, widespread use of CRP POCT could reflect primary care's commitment to addressing the problems posed by inappropriate antibiotic prescribing

EXAMPLE OF THE BENEFITS OFFERED BY POCT

Point-of-care diagnostics range from simple urine dipsticks, such as for nitrites and leucocytes used for UTIs, to sophisticated diagnostic and management tools covering, for example, lipid, glucose and HbA1C and infections generally (e.g. CRP) and for some specific pathogens. The benefits offered by POCT vary depending on the test, condition and setting, but include:

- Many point-of-care analysers use small amounts of blood (finger stick – typically 1.5 to 20 µl for CRP POCT) without the need for venopuncture or phlebotomy or sampling of other biological fluids (such as urine or nasal or throat swabs).
- Many point-of-care analysers are straightforward to use and do not require users to manipulate the sample or use complex and complicated assays.
- Many point-of-care analysers provide real-time results – levels of CRP are usually available in less than 5 minutes, depending on the device. This rapid analysis means that patients do not need follow-up visits to receive a diagnosis and begin treatment.
- Rapid diagnoses avoid delayed or unnecessary treatments, which is especially beneficial for infections, and allows HCPs to counsel patients.
- A single device can perform multiple tests (for example, by changing cartridges), which reduces the need for training and space. Some systems are portable allowing their use in care homes, pharmacies, workplaces and doctors' offices.
- The devices' footprints are relatively small, especially as some of the POC CRP tests use the same devices as other essential community-based tests, such as lipids (NHS Health Check), HbA1c (diagnosing and monitoring diabetics) and urine albumin-to-creatinine ratio (diabetic nephropathy).
- Point-of-care machines are supported by robust quality control and standards and show good correlation with laboratory methods.

WHAT THE GUIDELINES SAY

Several European guidelines advocate CRP POCT to differentiate viral and self-limiting infections from those that need antibiotics.^{4,7-9} In the UK, NICE advocates CRP POCT in some people presenting with symptoms of LRTI in primary care.⁴ Draft NICE guidelines on AMS also note that CRP POCT reduced use of antimicrobials in adults with acute respiratory infections without increasing re-consultations or reducing patient satisfaction. The NICE guideline development group agreed that CRP POCT might assist decisions about antimicrobial use and, therefore, support AMS.⁵ PHE now suggests considering CRP POCT as part of the differential diagnosis of community-acquired pneumonia.²⁶

5.1

IMPAC3T and GRACE

Table 4 and figure 9 summarise guidelines developed by the Improving Management of Patients with Acute cough by C-Reactive Protein Point of Care Testing and Communication Training (IMPAC3T) Programme and the Genomics to Combat Resistance against Antibiotics in Community-acquired LRTI in Europe (GRACE) consortium.^{12,83}

CRP levels	Interpretation	Action
<20mg/l	Self-limiting lower RTI	Withhold antibiotics
21–50 mg/l	Most patients have self-limiting lower RTI	Assessment of signs, symptoms, risk factors and CRP is important Withhold antibiotics, in most cases
51–99 mg/l		Assessment of signs, symptoms, risk factors and CRP is crucial Withhold antibiotics in most cases Consider delayed antibiotics in the minority of cases
100 mg/l	Severe infection	Prescribe antibiotics

Table 4: Actions based on CRP levels

5.2

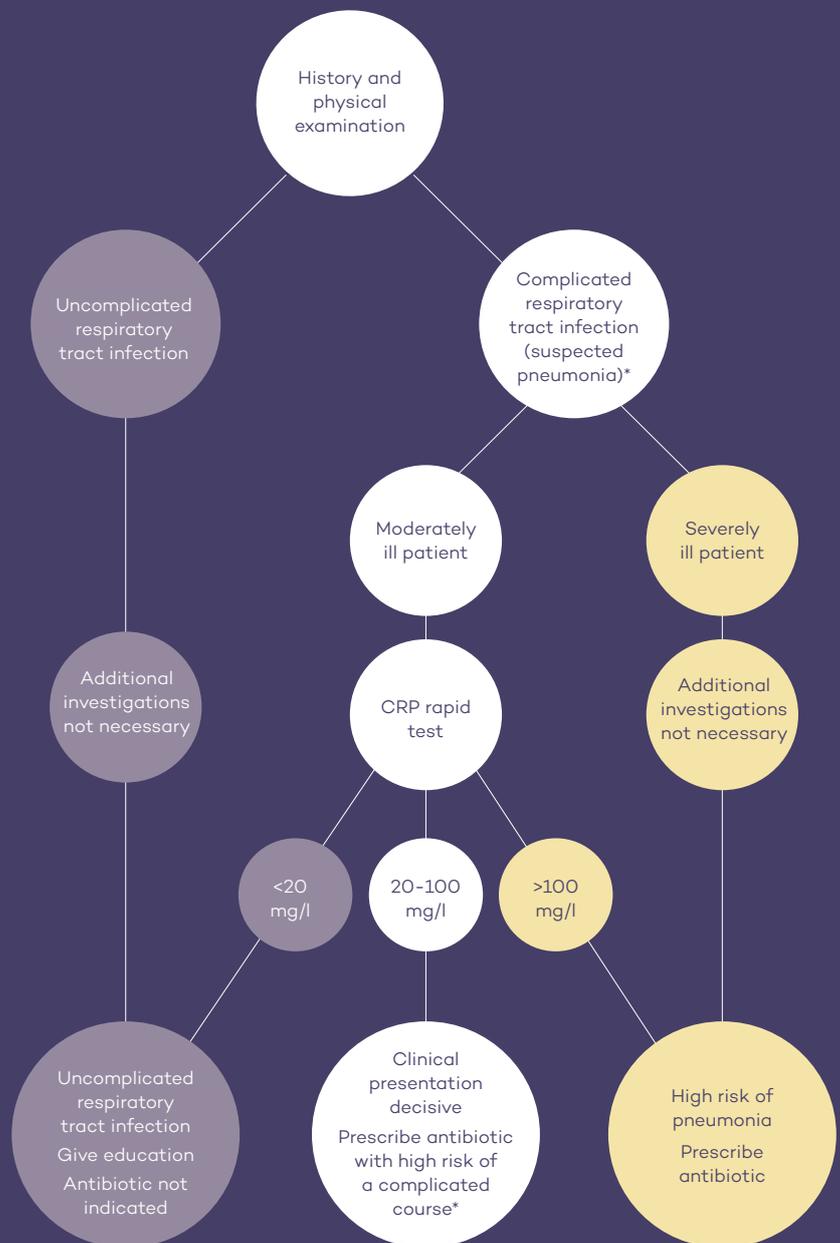
European Respiratory Society

The European Respiratory Society's guidelines for the management of LTRIs in adults recommend CRP testing in patients with suspected pneumonia:

- A CRP level of <20 mg/L at presentation, with symptoms for >24 hours, makes pneumonia “highly unlikely”.
- A CRP level of >100 mg/L makes pneumonia likely.⁸

Figure 9: Dutch algorithm for using CRP POCT in primary care⁹

Reproduced with permission from: Rogier Hopstaken (c) 2013, Dutch College of General Practitioners



* In addition to the patient having pneumonia, the management (antibiotic or not) also depend on the presence of other risk factors (age, relevant co-morbidity, refer to main text).



The possibility of bringing these tests (including CRP) into the community has the potential to radically improve diagnostic certainty in primary care.

Department of Health and Public Health England⁸⁴

5.3

National Institute for Health and Care Excellence (NICE) and Public Health England (PHE)

NICE advocates CRP POCT in people presenting with symptoms of LRTI in primary care if pneumonia cannot be diagnosed on clinical grounds and it is unclear whether antibiotics should be prescribed (figure 10). NICE suggests:

- Not offering antibiotic therapy routinely if the CRP concentration is less than 20 mg/l.
- Considering a delayed antibiotic prescription (which patients fill if symptoms worsen or do not improve with self-care) when the CRP level is between 20 mg/l and 100 mg/l.
- Offering antibiotic therapy if the CRP concentration is greater than 100 mg/litre.⁴

PHE now suggests considering CRP POCT as part of the differential diagnosis of community-acquired pneumonia.²⁶ As mentioned above, draft NICE guidelines also concluded that CRP POCT might assist AMS.⁵ Severity scores, such as CURB-65, can be used once pneumonia has been diagnosed.

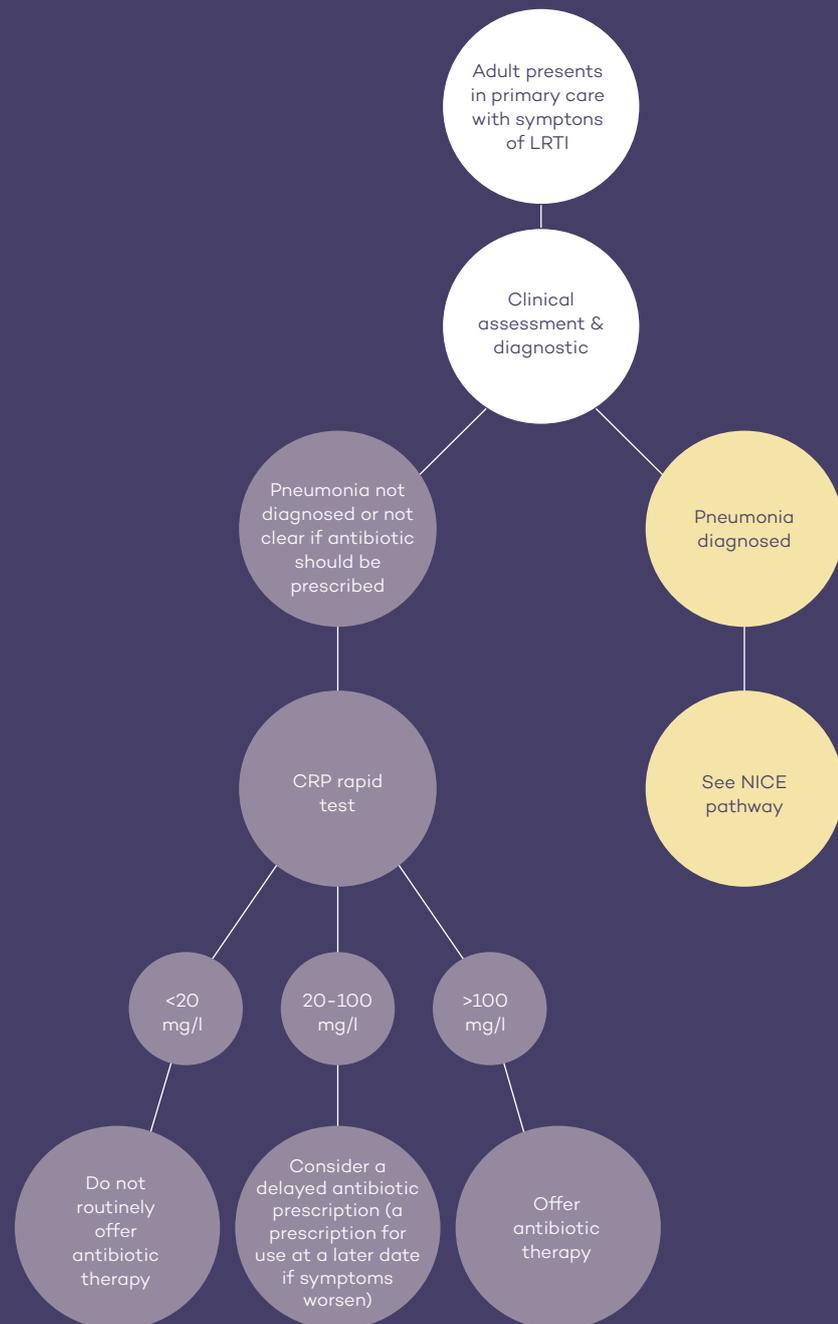


Figure 10: NICE recommendations for use of CRP POCT in patients with symptoms of LRTI

CRP POCT SUPPORTS PATIENT EDUCATION

Despite several educational initiatives aimed at patients and carers, many people still request inappropriate antibiotic prescriptions for viral or self-limiting bacterial infections. There is clearly a need to improve patients' and carers' understanding of the role of antibiotics and the need to limit, as far as possible, their contribution to the rise in AMR. Indeed, several studies now show that training doctors in enhanced communication skills can reduce antibiotic prescriptions.

Enhanced communication is especially beneficial when combined with CRP POCT.^{12,18}

In one study:

- GPs using CRP POCT prescribed antibiotics to 30.8% of patients presenting with symptoms of LRTI compared with 52.9% by those who did not use the test.
- GPs trained in enhanced communication skills prescribed antibiotics to 27.4% of patients compared with 53.5% by those without training.
- GPs combining CRP POCT and enhanced communication skills prescribed antibiotics to 23% of patients compared with 67% of patients receiving “usual care”.

Patients' recovery and satisfaction were similar in all the groups.¹⁸

Another study confirmed the value of supporting CRP POCT with enhanced communication skills:

- CRP POCT reduced antibiotic compared to no testing (33% and 48% respectively). This was a difference of 31%.

- Enhanced-communication training, delivered over the internet, reduced antibiotic prescribing compared to no training (36% and 45% respectively). This was a difference of 31%.
- Combining CRP POCT and enhanced-communication training resulted in a difference in antibiotic prescribing of 62%.¹²

Qualitative studies suggest that most GPs feel that patients would welcome POCT for infections.⁸⁵ In a multinational study, clinicians felt that technology that augmented clinical assessment reassured patients when antibiotics were not clinically indicated.⁸⁶ However, there is a need for education about POCT in general and CRP POCT in particular. For instance, some clinicians worry that patients might demand POCT when not clinically relevant.⁸⁵ Patients need to understand that CRP POCT can add precision to a standard clinical examination, but they are not 100% accurate⁷⁷ or a substitute for self-management when clinically warranted.

Surveys suggest that patients would trust and accept the result from CRP POCT. However, some felt that the CRP POCT result should be interpreted in conjunction with clinical findings. A few patients expressed anxiety about waiting for a result or an aversion to needles and having blood samples taken. Overall, however, patients were satisfied if doctors provided a low CRP POCT result rather than an antibiotic prescription.⁸⁵ Indeed, 23% of people managed with the aid of CRP POCT filled their delayed prescriptions compared to 72% of controls.¹⁴

Therefore, several studies show that CRP POCT facilitates effective communication with patients about self-management and antibiotic prescribing. Clinicians and patients recommend considering the CRP level in conjunction with the overall assessment and caution against over reliance on CRP results without clinical assessment.^{85,86}

Against this background, a recent literature review from Department of Health and PHE identified behaviours that contribute to AMR and drivers that might be “amenable to change”. The report notes that “real-time near-patient testing” – such as POCT – could have a “substantial” impact on the diagnosis of infections. The document adds

that the possibility of bringing markers such as CRP “into the community has the potential to radically improve diagnostic certainty in primary care”.⁸⁴

The report also notes that CRP POCT offers “proof of concept” of the approach and when used “in primary care shows an association with prescribing and redemption behaviour” – as discussed above.⁸⁴ Moreover, the consensus panel believes that CRP POCT in primary care helps address on the drivers of behaviour mentioned in the report: automatic motivation.

The literature review comments that emotion and the need for reassurance from medical professionals, particularly regarding children, influences patient’s decision making about antibiotics. The TARGET antibiotic toolkit developed by RCGP and PHE trains GPs to negotiate and manage patient’s emotional needs, but notes that there is “little else of an organised nature active in this space”.⁸⁴

In the panel’s view, CRP POCT moves the discussion on antibiotic prescribing to a more rational basis and offers reassurance, if necessary, supported by delayed prescribing. Therefore, CRP POCT could help address the need for additional ways to modify the behavioural drivers of automatic motivation.

“

There is a slight fear among some of my GP colleagues that POCT in RTIs could lead to the over-medicalisation of a condition that should be self-managed. It’s important that the testing is introduced in a way that minimises this risk.

A member of the consensus panel

ECONOMIC BENEFITS OF CRP POCT

Estimates of additional cost imposed by AMR vary from less than \$5 to more than \$55 000 per patient episode, depending on the type of resistance and the method of including productivity losses. However, the costs of AMR could be much higher than these estimates suggest.² On the other hand, because of the frequency of consultations for RTIs, small and sustainable changes in AMS (such as those gained by CRP POCT) can have a disproportionate clinical and economic impact.

As discussed previously, CRP POCT in primary care can reduce antibiotic prescribing for RTIs in primary care up to 41.51% (in suspected LRTI with a cough lasting less than four weeks together with one focal and one systemic symptom),¹⁸ without a clinically significant increase in complications or missed diagnoses¹⁵ as well as improving patient satisfaction.¹² This, in turn, reduces the risk of AMR and adverse events. Several studies now show that the approach is either cost effective or cost saving.²⁰⁻²²

For example, a Dutch economic evaluation showed that CRP POCT and communication skills training are cost-effective interventions to reduce antibiotic prescribing for LRTI. The total mean cost per patient was:

- €35.96 with the usual antibiotic prescribing rate of 68%.
- €37.58 per patient managed by GPs using CRP POCT, which reduced antibiotic prescribing to 39%.
- €25.61 per patient managed by GPs trained in enhanced communication skills, which reduced antibiotic prescribing to 33%.
- €37.78 per patient managed by GPs using CRP POCT and interventions enhanced communication skills, which reduced antibiotic prescribing to 23%.

The analysis found that CRP POCT and communication skills training are cost effective in their own right and in combination.²⁰

Other analyses confirmed that CRP POCT is cost effective.^{21,22} For instance, CRP POCT costs more per patient in the short term (€11.27 per patient) based on data from Norway and Sweden. However, a 10% reduction in antibiotic prescriptions (€112.70 per prescription avoided) and improved quality of life offsets the short-term cost. The cost per quality-adjusted life year (QALY) gain was €9391,²¹ which is lower than the current NICE threshold for cost-effectiveness. This study did not include costs associated with antibiotic adverse events or the costs of AMR and is, therefore, likely to underestimate the full economic benefits.

7.1

The UK perspective

The NICE guideline development group for AMR estimated that the recurrent costs associated with CRP POCT are £13.50 per test.⁵ However, reduced consultations for infections and antibiotic prescriptions seem to offset this additional cost.²²

A recent study evaluated the cost-effectiveness of CRP POCT for RTIs in primary care in England over 3 years. The evaluation compared the costs and benefits of:

- GP consultation plus CRP POCT.
- Practice nurse consultation plus CRP POCT.
- GP consultation plus CRP POCT and communication training.

Compared with current standard practice, CRP POCT delivered by a GP or practice nurse resulted in increased Quality Adjusted Life Years (QALYs) and reduced costs (table 5). GP consultations plus CRP testing and communication training increased costs and reduced QALYs. All three CRP arms led to fewer antibiotic prescriptions and infections presenting to primary care over 3 years.²²

Over the 3 years, the Net Monetary Benefit offered by CRP POCT when delivered by a GP or practice nurse dominated over current strategies.²² Again, however, this is likely to represent a conservative estimate of the benefits of CRP POCT: The analysis did not include the costs associated with antibiotic adverse events or the costs of AMR.

“

The additional cost per patient of the CRP test is outweighed by the associated cost savings and QALY increment associated with a reduction in infections in the long term.

Hunter²²

Statistic	Current practice	GP and CRP POCT	Practice nurse and CRP POCT	GP and CRP POCT and communication
Total cost (discounted)	£18,081	£18,039	£17,401	£18,431
QALYs				
(discounted)	255.630	255.764	255.761	255.588
Antibiotic courses prescribed	184	136	167	137
Infections (consultations)	217.89	202.97	202.97	199.98
Per patient Net Monetary Benefit*	£50,945	£50,972	£50,978	£50,933

*The highest Net Monetary Benefit is considered the most favourable option. Net Monetary Benefit is calculated as the total QALYs, multiplied by the willingness to pay for a QALY (£20,000), minus the total cost.

Table 5: Costs and consequences of using CRP POCT for 100 patients with RTIs over three years

ESTIMATING THE ECONOMIC IMPACT

According to the Health and Social Care Information Centre (HSCIC), 41,618,000 antibiotic items were dispensed in 2013.³⁰ Approximately 60% of these (24,970,800) were probably for RTIs, according to NICE.³² CRP POCT can reduce antibiotic prescribing by 41%.¹⁸ Therefore, CRP POCT could reduce the number of antibiotic prescriptions each year by up to 10,238,028, which would make a significant contribution to the UK's AMR strategy.

The Net Ingredient Cost for antibiotic prescriptions is £191,984,000,³⁰ suggesting that the average cost for the 41,618,000 prescriptions is £4.61. Dispensing costs are at least £0.90,³⁷ suggesting that the average total cost for an antibiotic prescription is £5.51. Based on the above assumptions, CRP POCT could, as a first approximation, save £56 million a year.

In addition, adding CRP POCT does not markedly increase workflow in most practices.²³ A recent study by National Institute for Health Research (NIHR) Diagnostic Evidence Co-operative London described the experience of three participants who discussed the impact of CRP POCT on clinic flow. One described no effect, one described a change in the clinical flow with no overall consequences and one suggested CRP POCT can influence work flow, but a robust process testing can mitigate this.²⁴

Each practice needs to implement bespoke processes to minimise any effect on clinic flow. In some case, GPs could undertake CRP POCT during the consultation. Other process include the patient leaving the consultation to have CRP POCT undertaken by a practice nurse, health care assistant or in-house primary care laboratory technician while the practitioner sees the next patient. Decision-making is based on written instructions from the practitioner or a second consultation being undertaken (figure 11).²⁴

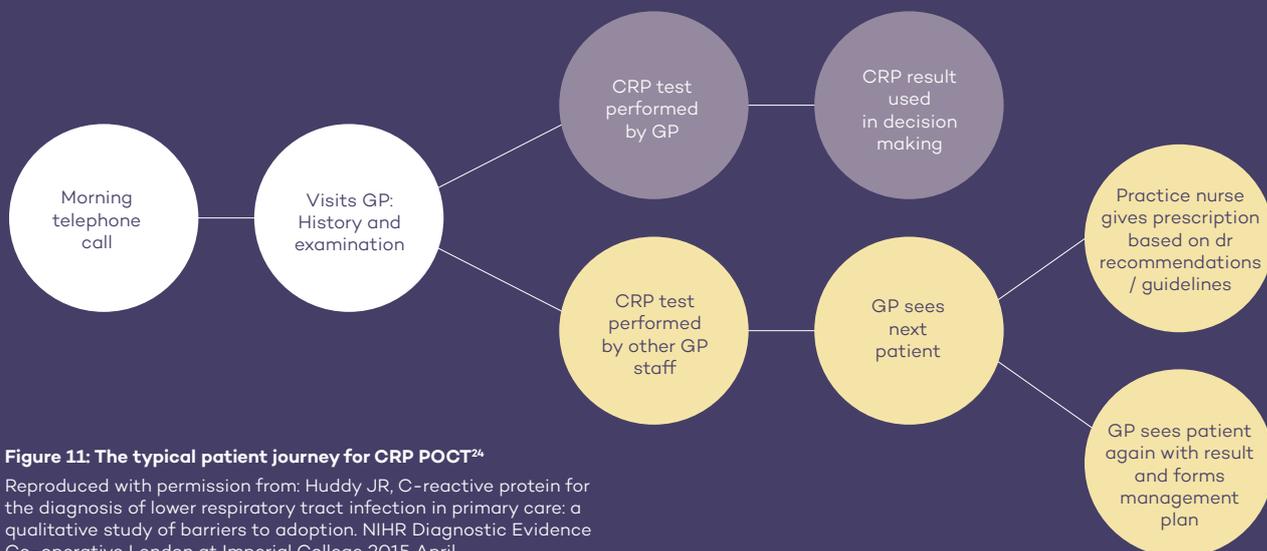


Figure 11: The typical patient journey for CRP POCT²⁴

Reproduced with permission from: Huddy JR, C-reactive protein for the diagnosis of lower respiratory tract infection in primary care: a qualitative study of barriers to adoption. NIHR Diagnostic Evidence Co-operative London at Imperial College 2015 April.

As discussed below, pharmacists could use CRP POCT to offer low-risk patients symptomatic self-care advice and refer high-risk patients or those with red-flag symptoms to their GP or an out-of-hours service. Pharmacists could also prescribe antibiotics according to a patient group directive (PGD).

CRP POCT can also reduce fulfilment of delayed prescriptions. In one study, 23% of people managed with the aid of CRP POCT filled their delayed prescriptions compared to 72% of control group.¹⁴ In addition, a single visit with a GP that included CRP POCT had no effect on the rate of visits for RTI episodes during the subsequent 3.5 years. So, there is no evidence to support concerns about the potential medicalisation of CRP POCT, such as patients demanding the test regardless of whether it is clinically relevant.⁸⁵ Indeed, giving patients evidence-based information by physicians trained in illness-focused communication skills could theoretically lead to fewer visits through improved self-management of future RTI.²⁵

CASE STUDY

CRP POCT IN UK PRIMARY CARE

Preliminary results of a UK pilot study that used CRP POCT to aid diagnosis and educate and reassure patients enrolled 100 patients presenting with a cough to primary care. Of these, 41 patients answered 'yes' or 'possibly' to the question 'were you expecting antibiotics?'. Only 15 received antibiotics. Specifically:

- 47 patients had a CRP score of <5 mg/l; 36% of these were expecting antibiotics. None were given antibiotics after CRP POCT.
- 70 patients had CRP <20 mg/l; 40% of these were expecting antibiotics. After CRP POCT, one patient (1.5%) received antibiotics.
- 38 patients had CRP levels between 20 and 100 mg/l; 44% of these were expecting antibiotics. After CRP POCT, 41% received an antibiotic prescription.
- 3 patients had CRP levels >100 mg/l and all were given antibiotics.

Overall, 27% of patient presenting who expected an antibiotic prescription were given one based on clinical signs and POC CRP level.

Provided CRP POCT is performed early in the consultation, it is very easy to fit into time available. All patients reported that performing the test was useful, with the main reasons being reassurance and peace of mind, speed of result, and a preference not to take antibiotics unless necessary. The test was particularly useful as an educational device and for reassuring patients. The testing process provided an opportunity to educate patients about the nature of viral coughs and the need to avoid antibiotics if necessary.

POLICY BACKGROUND



Quality assurance of POCT is central to the safe introduction and continuous use of POCT. A multidisciplinary approach to quality-assured POCT use, including feasible IT support, is invaluable.

Rogier Hopstaken, GP from Utrecht, the Netherlands and POCT expert

Several mutually reinforcing policies aim to drive innovation to tackle AMR and to encourage better AMS. The UK Antimicrobial Resistance Strategy, in particular, aims to conserve the effectiveness of existing treatments by:

- Optimising prescribing practice by implementing AMS programmes that promote rational prescribing.
- Better use of existing and new rapid diagnostics.
- Improving professional education, training and public engagement to improve clinical practice and promote wider understanding of the need for more sustainable use of antibiotics.⁸⁸

The UK strategy aligns with the EU Action plan against the rising threats from AMR.⁸⁹ The wider adoption of CRP POCT in primary care represents a significant opportunity to enable these strategic aims. Indeed, several quality initiatives are underway to improve antibiotic prescribing. For instance, practice-level data on antibiotic prescribing is available to the public and the Care Quality Commission's (CQC) reports now include Quality Indicators on antibacterial prescribing:

- The number of antibacterial prescription items prescribed per Specific Therapeutic group Age-sex Related Prescribing Unit.
- Percentage of cephalosporins and quinolones as a proportion of antibiotics prescribed.

Improving antibiotic prescribing in primary and secondary care accounts for 10 per cent of quality premium for CCGs. There are two elements to this quality premium. Firstly, CCGs should reduce the number of antibiotics prescribed in primary care by at least 1%. Each CCG can decide on the reduction for individual practices. Secondly, CCGs should reduce prescriptions for co-amoxiclav, cephalosporins and quinolones by 10% from each CCG's 2013/14 value, or to below the 2013/14 median proportion for English CCGs (11.3%), whichever is smaller.⁹⁰

Such quality initiatives are part of a trend in AMS to shift focus from which antibiotic to prescribe to when to prescribe. CRP POCT can help GPs reduce antibacterial prescribing, thereby contributing to national AMR strategies and augmenting performance against these indicators.

8.1

Funding models

Currently, GPs would have to meet the additional costs associated with CRP POCT. Therefore, the NHS generally and Clinical Commissioning Groups (CCGs) in particular need to develop alternative funding mechanisms, such as using ‘enhanced service’ contracting arrangements or co-commissioning. These alternative mechanisms could fund several ways to deliver the services locally, including:

- Local procurement to support pilot studies.
- Trust-wide or local procurement of a full service provided by a hospital trust covering purchase, quality control (QC), training, compliance, education, troubleshooting, maintenance, etc.
- Trust-wide or local procurement using a mixed model: the hospital provides QC, compliance and training for a monthly fee. The GP purchases the equipment and tests.
- Privately managed diagnostic services: a full service model provided by a private company implanted trust-wide or locally.
- Hospital-private hybrid. In this model, a private company and hospital working together implanted trust-wide or locally to deliver the entire suite of services relevant to CRP POCT in primary care.
- Trusts or individual GPs buy kit and tests, and manages QC. The diagnostics company supports initial training.

ENHANCED SERVICES AND CO-COMMISSIONING

Currently, ‘enhanced service’ contracts cover services such as childhood vaccination and immunisation schemes, extended hours access and improving patient online access.

Co-commissioning describes arrangements when two or more organisations commission healthcare services. NHS England sees co-commissioning as “a key enabler in developing seamless, integrated out-of-hospital services based around the diverse needs of local populations”. NHS England also hopes that co-commissioning will “drive the development of new models of care such as multispecialty community providers and primary and acute care systems”.⁹¹



Community pharmacy has an important responsibility in ensuring appropriate use of antimicrobials. POCT is already part of many pharmacists’ offering, for example during health checks. CRP POCT is a natural evolution of the pharmacists’ clinical role.

Ashok Soni, community pharmacist and RPSGB President, the Network Lead for Pharmacy at NHS Lambeth CCG and Local Professional Network Pharmacy Chair for London

ENSURING A HIGH-QUALITY SERVICE

Rogier Hopstaken, a GP from Utrecht, helped pioneer CRP POCT in the Netherlands. Based on 11 years' experience, he stresses the importance of quality assurance and "data connectivity" among all groups using CRP POCT to ensure maximal patient safety. He suggests that this includes:

- Clinical chemists, local pathology services and other POCT experts need to check the technical quality of devices and the CRP tests, and act on the results.
- Contracts, guidelines, standard operating procedures and so on between suppliers, pathology services, CCGs and HCPs need to ensure a consistently high-quality CRP POCT service.
- Users need training in the clinical (background, indications, interpretations) and technical aspects of CRP POCT; skills should be regularly revalidated.
- Local pathology services should be organised and commissioned in a way that allows pathologists to support HCPs providing community based CRP POCT. In particular, pathologists should focus on quality control, education and compliance.
- HCP accreditation programmes should address these issues for all primary care diagnostics.

8.2

A growing role for pharmacists and other community providers

As CRP POCT illustrates, technological advances allow a growing number of diagnostic tests to be performed in GP surgeries, nurse consultation rooms, Emergency Multidisciplinary Units, community clinics or pharmacies by a HCP that would once have occupied a bench in a medical laboratory and required an experienced technician.

Pharmacists, for example, have a growing role in AMS and the management of self-limiting conditions. Pharmacists could use CRP POCT to offer low-risk patients symptomatic self-care advice and refer high-risk patients or those with red-flag symptoms to their GP or an out-of-hours service. Pharmacists could also prescribe antibiotics (or other medications) according to a PGD.



Health policy makers need to begin considering now how to establish clear incentives to promote the uptake and usage of point-of-care diagnostics once they are available. This is particularly important in settings where the costs of deploying new diagnostics will fall on individual providers, but the benefits accrue to health systems and society more broadly. They also need to consider how to encourage the behaviour change that will be needed to ensure that these devices are used appropriately... and that the results are acted upon.

O'Neill Review on Antimicrobial Resistance⁷³

CASE STUDY

EMERGENCY MULTI- DISCIPLINARY UNIT

Abingdon Emergency Multidisciplinary Unit, an out of hospital ambulatory care triage and treatment unit aimed at older patients living with frailty, uses CRP POCT as well as other point-of-care tests for rapid diagnosis and management. From their data, 51% of patients have an infection. The Alere Afinion CRP POCT gave a result in 4 minutes compared to waiting for results the next day with central hospital laboratory testing. The results of Alere Afinion CRP POCT correlated very well with laboratory values (correlation coefficient 0.95).

RECOMMENDATIONS

Increasing evidence shows that CRP POCT is a valuable adjunct to clinical observation of signs and symptoms and the patient's history when assessing patients presenting with symptoms of RTIs in primary care. CRP POCT in primary care helps resolve diagnostic uncertainty and, therefore, helps ensure that GPs prescribe antibiotics only when necessary. In addition, CRP POCT in primary care will help inform discussions with patients about their self-management. As such, CRP POCT can make an important contribution to AMS in primary care.⁵

The O'Neill Review on Antimicrobial Resistance points out that health providers must ensure they are ready to implement diagnostic technologies. Health policy makers, the report says, should consider how to establish clear incentives to promote uptake and use of point-of-care diagnostics.⁷³ In some ways, implementing existing point-of-care technologies can act as a 'test case' for the new generation diagnostics.

Nevertheless, using point-of-care technologies more widely requires a culture change in the NHS. The NIHR Diagnostic Evidence Co-operative London, for example, identified several barriers that hinder implementation of CRP POCT in primary care. The Co-operative grouped these into eight themes: reimbursement and incentivisation; quality control and training; laboratory services; practitioner attitudes; patient attitudes; effects on clinic flow and workload; use in pharmacy and gaps in evidence.²⁴

Against this background, we have made several recommendations to help encourage implementation of CRP POCT in primary care. At the front of the present document, we suggested recommendations for different stakeholders. In this section, we present recommendations arising from the five main themes that emerged during the report's development.



CCGs should develop innovative ways to fund primary care CRP POCT

- CCGs should use the new quality premium for antibiotic prescribing as opportunity to review current RTI diagnostic pathways in primary care and implement CRP POCT.
- CCGs should ensure CRP POCT is properly integrated into the consultation and is supported, if necessary by enhanced consultation and communication skills.
- CCGs should explore alternative funding mechanisms that encourage uptake of diagnostics in primary care, while avoiding disincentives, such as GPs having to meet the additional costs of CRP POCT and current contractual arrangements.
- CCGs should develop innovative funding mechanisms that address the issue of economic benefits (e.g. reduced hospitalisation, reduction in *C. difficile*, benefits to the economy) that do not accrue to the CCG or GP budget.
- While reducing the spread of AMR is the most important benefit, CCGs should remain cognisant of the other benefits of reduced antibiotic prescriptions (such as the reduced risk of adverse events and protecting the microbiota) when drawing-up their business cases. GPs can use such arguments during patient consultations to support appropriate antibiotic prescribing.
- CCGs should consider implementing CRP POCT in out-of-hours clinics, where antibiotic use is rising more rapidly than in other parts of the NHS.³³
- CCGs should engage with local pathology services to support GPs, pharmacists and other HCPs providing CRP POCT in primary care, especially to optimise quality control and compliance.



Ensuring access to CRP POCT is an issue and it will be interesting to see how quickly people implement the NICE guidance. I suspect that these issues are not yet on many area's radars.

A member of the consensus panel.

2

The NHS should consider ensuring the uptake and implementation of CRP POCT in primary care

- CCGs, GPs and other stakeholders should recognise that CRP POCT in primary care can help meet the NHS quality agenda, including the CCG quality premium. Therefore, CRP POCT should be included in strategic and tactical plans.
- The CQC collects data on antibiotic prescribing and scrutiny of antibiotic prescribing is set to intensify. Therefore, CCGs and GPs should increase use of diagnostics to optimise performance against these indicators.
- The proposed national pharmacy-led Common Ailments Scheme and any equivalent local schemes should advocate using CRP POCT to identify low-risk patients.
- NICE should consider adding CRP POCT to other relevant guidelines to ensure alignment.
- CCGs should explore opportunities for CRP POCT within the Quality, Innovation, Productivity and Prevention (QIPP) programme.
- CCGs could consider developing locally incentivised enhanced services or PGDs to increase implementation and use of CRP POCT in primary care.
- Quality Statements and CCG Outcomes Indicators should be developed to encourage CRP POCT in primary care covering pneumonia and antimicrobial stewardship.

3

Each clinical commissioning group should adopt the NICE and PHE guidelines for RTIs and antimicrobial stewardship

- Each CCG should determine the most effective and efficient implementation the NICE guidelines^{4,5} and CRP POCT as a central part of their local AMS programmes.
- CCGs and GPs should use data collected (for instance, to meet requirements of the Care Quality Commission) to audit primary care CRP POCT to drive continual improvements in patient care, AMS and to meet the NHS quality agenda. CCGs should also implement optimal quality assurance across all CRP POCT users to ensure patient safety. These data would also provide evidence of implementation of the NICE guidance and compliance with the code of practice for the AMS elements of preventing healthcare-acquired infections.
- CRP POCT leads to less diagnostic uncertainty while improving patient satisfaction through quicker diagnosis, better management and better service. CCGs and HCPs should attempt to capture and communicate these factors to increase the likelihood of widespread implementation of CRP POCT.
- Local guidelines and AMS programmes for primary care should include CRP POCT to improve appropriate antibiotic prescribing for RTI, and engage with and educate patients about appropriate antibiotic use.
- CCGs could consider working with medicines optimisation teams to improve uptake and implementation of CRP POCT in primary care in line with NICE and other guidelines.
- Each practice should determine the most appropriate workflow to optimise the use of CRP POCT in primary care.
- CCGs should ensure that healthcare professionals are adequately trained in CRP POCT, including, if necessary, further training in consultation and communication skills.



The NHS, professional bodies, medical, and pharmacy and nursing schools and manufacturers should raise awareness of POCT generally and primary care CRP POCT in particular among doctors, commissioners and other HCPs

- All these stakeholders should educate HCPs and commissioners about POCT. Point-of-care diagnostic technologies, other than simple dipstick tests or using glucose meters, are a relatively recent advance for primary care. Inevitably, diagnostics and other devices do not receive the same attention as innovative pharmaceuticals, although their impact can be just as marked.
- Monitor, NHS England, PHE, CQC and CCGs must actively promote and encourage CRP POCT in primary care for pneumonia and other infection scenarios. The equivalent organisations in Northern Ireland, Scotland and Wales should also promote and encourage CRP POCT in primary care.
- Other consensus groups should consider the relevance of CRP POCT in primary care when developing other guidelines, documents and tools, such as for abdominal infections (e.g. diverticulitis, appendicitis), sepsis and COPD. CRP POCT reduces antibiotic overprescribing for acute exacerbations of chronic bronchitis and COPD as part of a multifaceted approach.¹⁹
- Stakeholders planning implementation of CRP POCT in primary care should assess the impact on nurses and other healthcare professional. Trusts and other organisations should use these assessment to plan services, education and training.
- Commissioners and HCPs should agree policies covering testing, competence and equipment management, including working with local pathology services and in line with MHRA guidance.



A comprehensive clinical and economic research programme should examine expanded roles for primary care CRP POCT as a keystone of antimicrobial stewardship

- Studies should assess the ease of use, clinical impact and cost-effectiveness of CRP POCT in a variety of primary care settings, including late-night pharmacies, out-of-hours services and as part of the proposed national pharmacy-led Common Ailments Scheme and any equivalent local schemes.
- Antibiotic use by out-of-hours services is rising more rapidly than in other parts of the NHS.³³ Further studies should ascertain if the increase is clinically justified.
- Further studies should address the value of CRP POCT in COPD patients and children. Most participants in the trials of CRP POCT were middle-aged adults. The ongoing PACE (www.nets.nihr.ac.uk/projects/hta/123312) and ERNIE 2 enrolled COPD patients and children.⁹²
- Further economic analyses should consider a larger range of costs and consequences as well as providing stratified analyses (e.g. by age group and length of stay if patients are admitted to hospital⁵).
- Pharmacoepidemiological studies should be undertaken to ascertain the contribution that antibiotics make to admissions to hospital following side effects in the UK.

MEMBERS OF THE CONSENSUS PANEL

Jonathan Cooke

Jonathan currently holds an honorary Chair in the Manchester Pharmacy School at the University of Manchester and is a Visiting Professor in the Infectious Diseases and Immunity Section, Division of Infectious Diseases, Department of Medicine, Imperial College London. Jonathan was, until 2011, Director of Research and Development and Clinical Director for Medicines Management and Pharmacy at the University Hospital of South Manchester NHS Foundation Trust. His research interests include antimicrobial usage, medication safety and health economics, and he is the author of more than 160 peer-reviewed publications, reviews and chapters of standard textbooks. Jonathan has served as a Member of the Department of Health Specialist Advisory Committee on Antimicrobial Resistance (SACAR) as Chair of the Prescribing sub-Committee. He is currently Chair of the Antimicrobial Stewardship Group of Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI).

Helen Bosley

Helen qualified as a registered general nurse in 1989. Her career has involved broad and varied experience across several specialised fields, including paediatric and adult critical and intensive care. She has worked abroad, gaining an insight into different health care systems and challenges, and as a tutor for pre-registration nursing students with the Open University. Helen has worked for the last 13 years in infection prevention and control. This included working in an acute Trust and latterly as Head of Infection Prevention and Control in a large combined community and Mental Health Foundation Trust. Her interests include developing effective collaborative partnerships across health economies to improve outcomes.

Chris Butler

Chris is Professor of Primary Care at the Nuffield Department of Primary Care Health Sciences at the University of Oxford and Professor of Primary Care Medicine at Cardiff University, Wales. His main research interests are in common infections (especially the appropriate use of antimicrobials and AMR), and health behaviour change (especially motivational interviewing). He is Clinical Director of the University of Oxford Primary Care Clinical Trials Unit and practices as a general practitioner in Mountain Ash in South Wales.

Rose Gallagher

Rose has been the professional lead at the Royal College of Nursing (RCN) for infection prevention and control (IPC) since August 2007. She started her career in infection control in 1998, collecting data for the national surgical site surveillance scheme. After completing a BSc (Hons) in infection control, she became senior nurse position at Stoke Mandeville Hospital in 2002, leading the infection control nursing team through the outbreak of *Clostridium difficile* and subsequent investigations. Rose now works at the local, regional, UK and European levels providing leadership and guidance for RCN members as well as working with or supporting professional, governmental and patient advocacy stakeholders. The RCN IPC network offers a forum for the exchange of information and provides opportunities for its members to get involved in the work of the College. Rose works closely with other professional advisers in the Nursing Department as well as Employment Relations team on issues relating to health and safety and patient safety. Rose is currently the RCN's Interim Head of Knowledge, Standards and Innovation Services.

Philip Howard

Philip is the Consultant Pharmacist in Antimicrobials at the Leeds Teaching Hospitals NHS Trust, an Honorary Senior Lecturer at Leeds University, an NHS England Healthcare-associated infection Project Lead, and a spokesman for the Royal Pharmaceutical Society of Great Britain (RPSGB) on antimicrobials. He has been involved in many AMS activities since 2008: Development of national AMS guidelines for hospitals (Start Smart then Focus), General Practice (TARGET), NICE AMS guidelines, and led the first global survey of AMS in hospitals. Philip has lectured and run workshops on AMS throughout the world. He is a committee/council member of the United Kingdom Clinical Pharmacy Association (UKCPA) Pharmacy Infection Network, British Society of Antimicrobial Chemotherapy (BSAC), and the European Society of Clinical Microbiology and Infectious Diseases Study Group for Antibiotic Policies (ESCMID:ESGAP).

Katherine Murphy

Katherine, who has a background in nursing, joined The Patients Association in 2003 as head of communications and was appointed Chief Executive in 2008. As Chief Executive, Katherine has been at the forefront of most of the recent campaigns at The Patients Association, and launched a number of other high profile initiatives. Katherine has a very strong interest in the rights and responsibilities of the patient. Katherine is also a member of the Equality and Diversity Forum. Katherine sits on many committees and boards to represent patient views and ensure politicians' rhetoric is translated into reality for patients and the public. The Evening Standard's 1000 Most Influential People ranked Katherine 11th in 2011 and 19th in 2012, and the HSJ's Most Influential in Health survey saw her placed 82nd.

Dilip Nathwani OBE

Dilip is a Consultant Physician of Infectious Diseases and Honorary Professor of Infection at Ninewells Hospital and Medical School. He is also Chairman of the Scottish Antimicrobial Prescribing Group (a sub-group of the Scottish Medicines Consortium), ESCMID:ESGAP and the BSAC Outpatient Parenteral Antimicrobial Therapy Group (OPAT). Dilip is Director of Medical Education for NHS Tayside and National Specialty Adviser for Infectious Diseases to the Scottish Government Health Department. He has authored more than 225 peer-reviewed publications and contributed to 20 national and international infection guidelines and consensus statements, including those for the Scottish Intercollegiate Guidelines Network, the British Thoracic Society and BSAC.

Graham Phillips

Graham is a second-generation pharmacist and Managing Director of the award-winning Manor Pharmacy Group. He has worked with GPs and in primary care more widely for fifteen years. Graham has been a Primary Care Trust (PCT) Prescribing Lead, and a Professional Executive Committee and Board member. He has been involved in pharmacy politics at the local and national level, for 15 years including four years on the Council of the RPSGB – three as chair of the Education Committee. Graham also sat on the RPS English Pharmacy Board. Graham has a long-term interest in Public Health: he has been involved with the NHS cancer-reform strategy and sat on the board of the National Obesity Forum. Graham was also a member of the Healthy Living Pharmacy reference group. The Manor Pharmacy Group has won numerous local and national awards – notably runners-up in the Pharmaceutical Journal "Care Awards" 2009. In November 2012, Graham was awarded Leader of the Year at the Pharmacy Business awards. Graham was made a Fellow of the RPSGB in 2009.

Ashok Soni OBE

Ashok graduated from Portsmouth School of Pharmacy. Over the last 30 years, Ash has held a number of positions from owning and operating his own pharmacy to working for Lambeth Southwark and Lewisham Local Pharmaceutical Committee, sessional work with the local GP practice and consultancy work for a number of pharmaceutical companies. Ash has also held positions on boards including Lambeth PCT, RPSGB English Pharmacy Board, Pharmaceutical Services Negotiating Committee and National Pharmacy Association. He was appointed as a member of the NHS Future Forum to review the Health & Social Care Bill. Ash was a member of the Clinical Advice and Leadership workstream in the first phase. In the second phase, he jointly led the workstream on 'The NHS's Role in the Public's Health'. In the third phase, he was involved in the review of the NHS Constitution. Ash is a Fellow of The Royal Pharmaceutical Society and Honorary Fellow of The University College London School of Pharmacy. He was awarded an OBE for services to pharmacy and the NHS. He is a Board member of the South London Local Education & Training Board and is the Network Lead for Pharmacy at NHS Lambeth CCG and Local Professional Network Pharmacy Chair for London. Ash was recently appointed President of the RPSGB.

Doris-Ann Williams MBE

Doris-Ann has been Chief Executive of British In Vitro Diagnostics Association (BIVDA) since October 2001. She has more than 30 years' experience in the in vitro diagnostic (IVD) sector. She has had a variety of experience; initially in R&D and subsequently in commercial roles including international responsibilities. She is on the editorial board of *IVD Technology* and on a number of steering groups for organisations, such as the Technology Strategy Board and is currently on the NHS Implementation Board for Innovation, Health and Wealth. She also works closely with European Diagnostic Manufacturers Association and other global IVD industry associations. She was awarded an MBE in January 2011 and was recognised as a Friend of the Royal College of Pathologists in November 2012.

CHAPTER 11

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