# CLARION CALL

***A section for passionate calls for action to further develop the contribution that pharmacy can make to healthcare***

## C-Reactive Protein (CRP) As A Point Of Care Test (POCT) To Assist In The Management Of Patients Presenting With Symptoms Of Respiratory Tract Infection - A New Role For Community Pharmacists?

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## Summary

- Antimicrobial resistance is a global threat to all healthcare systems.
- Health services and governments worldwide recognise that tackling antimicrobial resistance means combining stewardship, education, legislation, clinical and technological innovation.
- Respiratory tract infections are the reason for 60 per cent of all antibiotic prescribing in general practice - this constitutes a significant cost to the NHS.
- However, most acute uncomplicated respiratory tract infections are viral or self-limiting bacterial infections, which can be self-managed and for which antibiotics are inappropriate.
- A Cochrane review of randomised or cluster randomised trials reported that CRP POCT significantly reduced GP antibiotic prescriptions for acute RTIs. In one of these studies, the use of CRP POCT showed a difference in GP antibiotic prescribing in RTIs of 43.4 per cent.
- Community Pharmacists are ideally placed to offer CRP POCT to patients presenting with symptom of RTI.

## Background

Antimicrobial resistance (AMR) is a global healthcare and economic problem, and should be a priority for all the World's governments.[1] The Director General of the WHO, Margaret Chan, has stated with respect to AMR that 'No action today means no cure tomorrow'.[2] In the UK, Chief Medical Officer Sally Davies has repeatedly emphasised the threat of AMR.[3]

The UK Strategy for AMR[4] has three aims of:

1. improving knowledge and understanding of AMR;
2. conserving and stewarding the effectiveness of existing treatments; and
3. stimulating the development of new antibiotics, diagnostics and novel therapies.

Prescribing of antibacterial medication in the community varies considerably across Europe (Figure 1), with a strong association between high prescribing countries having a higher level of AMR[5] (Figure 2).

Respiratory Tract Infections (RTIs) are the most common infections in patients presenting to GPs and most patients presenting to a GP with a simple RTI still receive an antibiotic, with many doctors and patients believing that this is the 'right thing' to do.[6]

However, it is well known that:

- most RTIs are viral
- there is only limited evidence to support the use of antibiotics in acute bronchitis, sore throat, sinusitis and otitis media, and
- evidence from systematic reviews and other studies suggests little benefit is achieved from the prescription of antibiotics, except in elderly patients at high risk of pneumonia.[7,8,9,10,11]

A Cochrane review of randomised and cluster randomised clinical trials concluded that CRP POCT could assist the clinical assessment, guide antibiotic treatment of acute respiratory infections in primary care and significantly reduce antibiotic use.[13] Indeed, evidence from these and other studies show that there is improved patient satisfaction with the clinical consultation even when no antibiotics are issued (Figure 3).

A recent report, 'Straight to the Point', summarises the compelling evidence that measuring CRP using point-of-care testing helps to differentiate self-limiting RTIs from more serious infections that

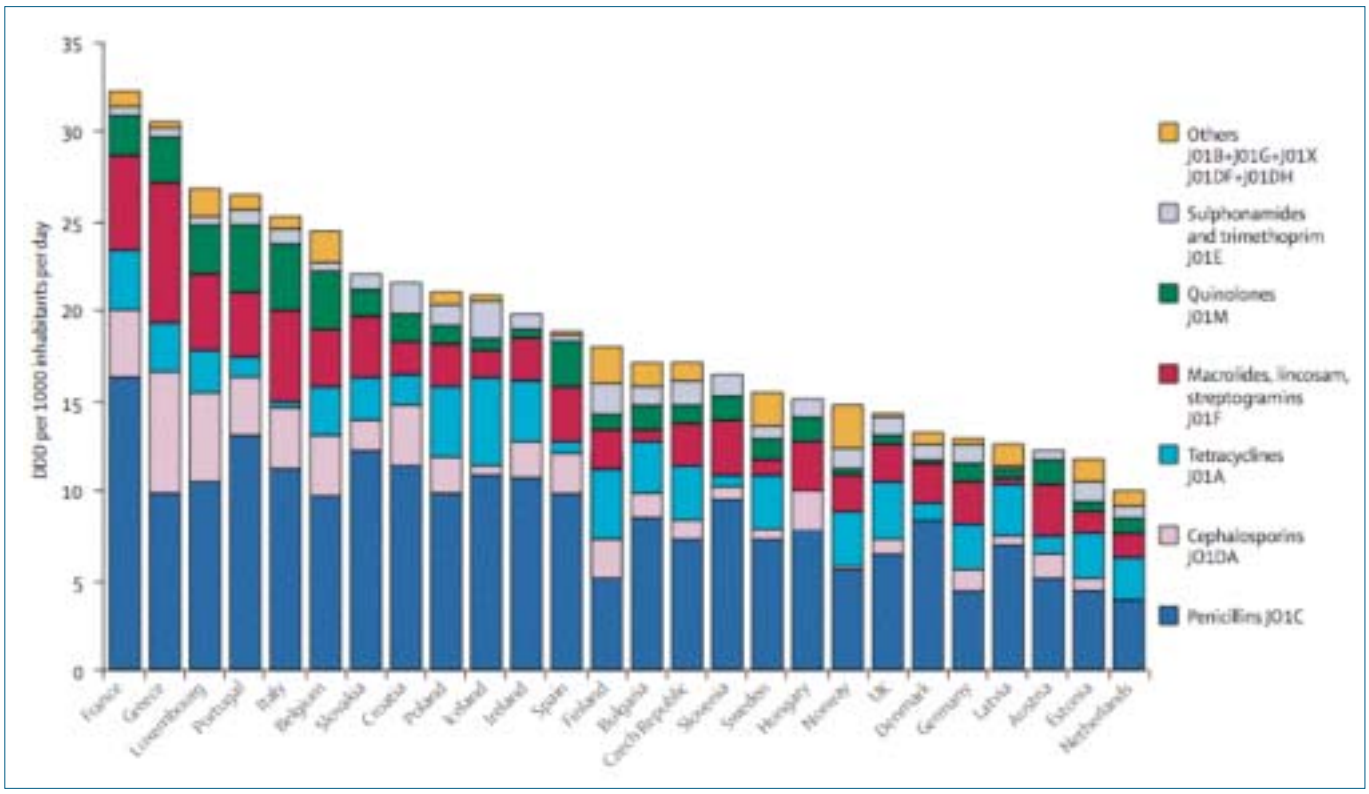


*Figure 1: Total outpatient antibiotic use in 26 European countries in 2002. Goosens et al 2005.5*

require antibiotics. The report makes recommendations targeted at policy makers, clinical commissioning groups (CCGs) and healthcare professionals, including suggesting ways in which CRP POCT can be used by Community Pharmacists to deliver enhanced services that optimise the use of antibiotics.[14] CRP POCT appears to be a clinically and cost-effective intervention in reducing antibiotic prescribing for patients presenting in primary care with symptoms of RTI (Figure 4).

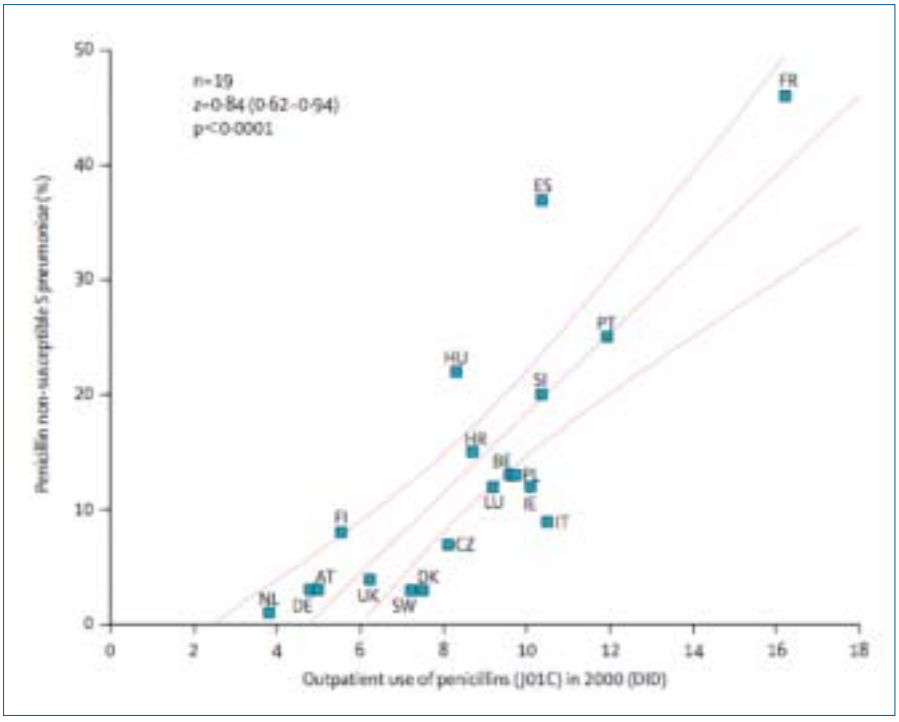


*Figure 2: Correlation between penicillin use and prevalence of penicillin non-susceptible S pneumoniae. AT, Austria; BE, Belgium; HR, Croatia; CZ, Czech Republic; DK, Denmark; FI, Finland; FR, France; DE, Germany; HU, Hungary; IE, Ireland; IT, Italy; LU, Luxembourg; NL, The Netherlands; PL, Poland; PT, Portugal; SI, Slovenia; ES, Spain; UK, England only. Goosens et al 2005.[5]*

## What are Point of Care Tests (POCT)?

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

- Small amounts of blood (finger stick – typically 1.5 to 20µl for CRP POCT) without the need for venipuncture or phlebotomy or sampling of other biological fluids (such as urine or nasal or throat swabs).
- Point-of-care analysers are often straightforward to use and do not require users to manipulate the sample or use complex and complicated calibrations.
- Many point-of-care analysers provide real-time results – levels of CRP are usually available in less than 5 minutes,

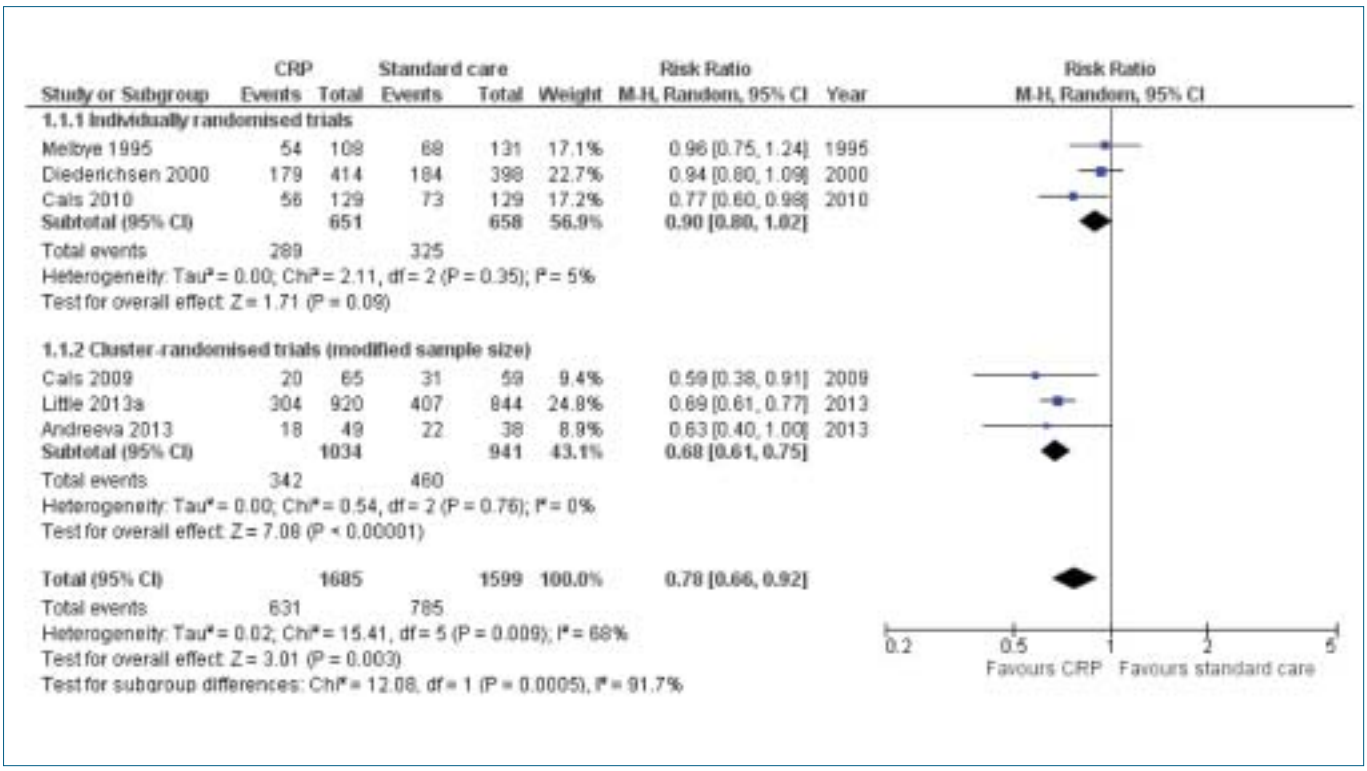


*Figure 3: Forest plot of comparison: 1 C-reactive protein - antibiotic prescribing: all trials, outcome: 1.1 C-reactive protein - antibiotics prescribed at index consultation. All trials (cluster-RCTs modified sample size).*[13]

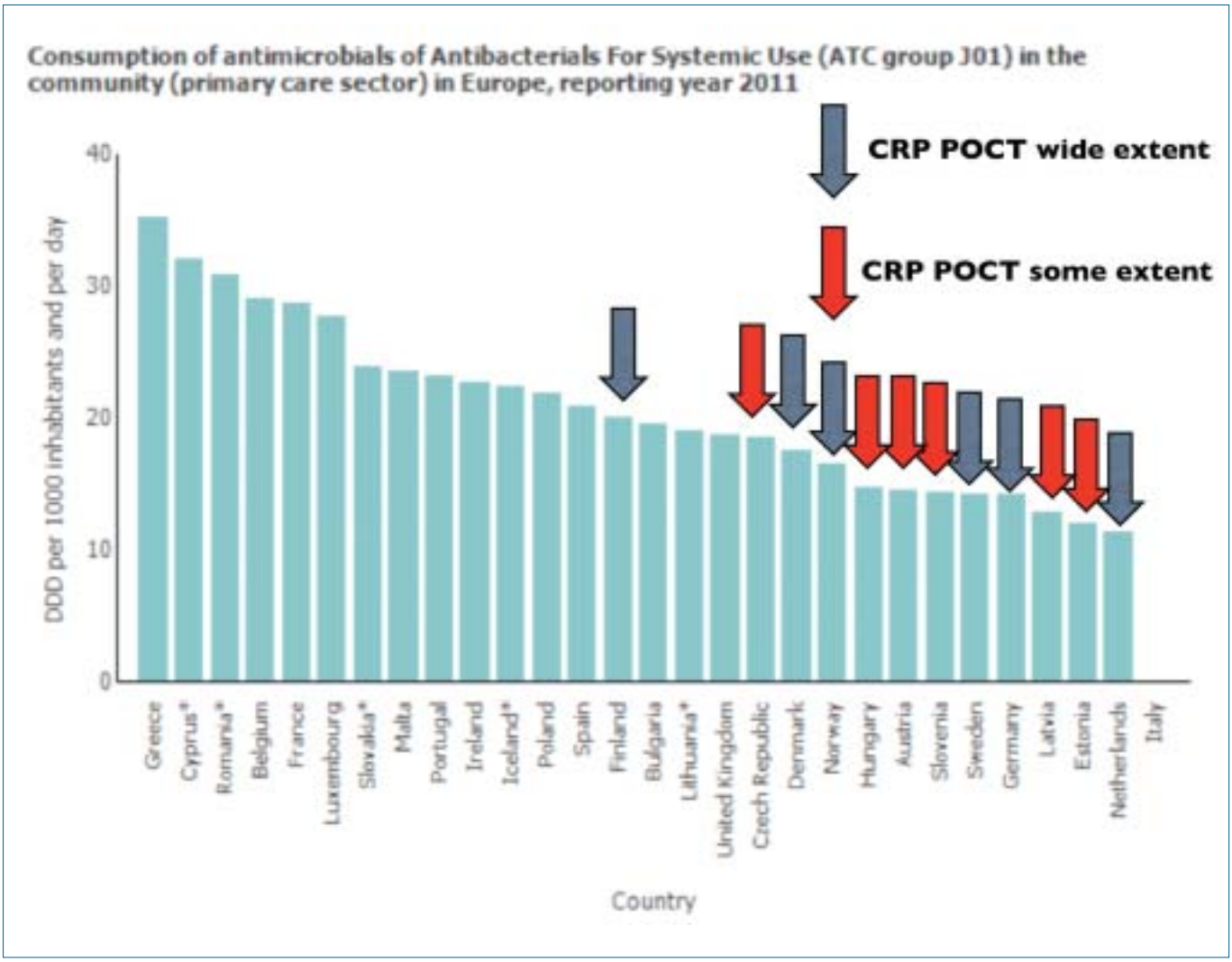


*Figure 4: Antimicrobial use by country*

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 are quite small and compact and can be easily situated on a bench in the dispensary. 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 and in line with MHRA requirements.[12]

The availability of POCT for blood biomarkers of infection such as CRP offers a new dimension into clinical decision making for practioners in primary care. CRP is an acute-phase plasma protein which is produced in response to infection or tissue injury. The main biological function of CRP is determined by this ability to recognise pathogens and damaged host cells. CRP is normally present in small levels in serum, but increases rapidly and dramatically in response to a variety of infectious or inflammatory stimuli and its levels typically are highest in patients with a bacterial infection and lower in those with viral infection.

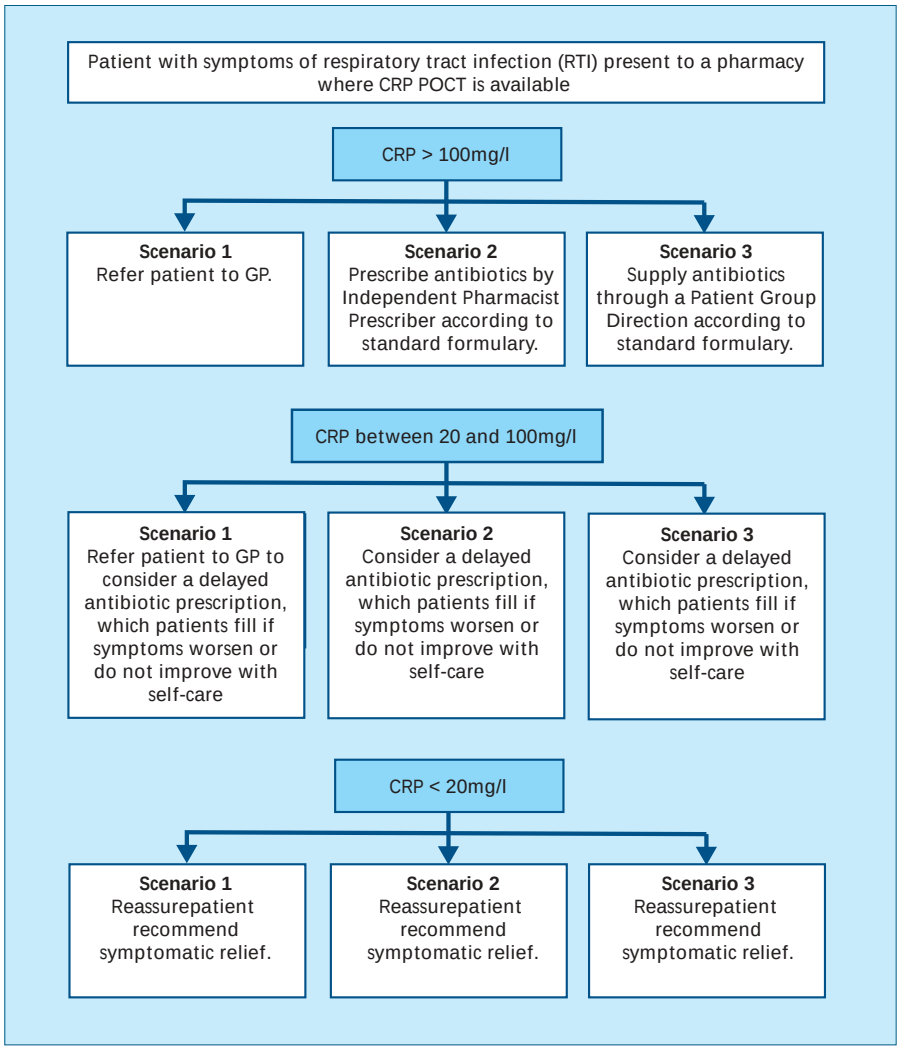


*Figure 5: Algorithm for options facing Community Pharmacies that have POCT CRP testing facilities*

## How can CRP POCT be undertaken in Community Pharmacies?

In a joint document, 'Building the Workforce – the New Deal for General Practice',[15] eight new ways of working are described. One of these recommends that 'NHS England, Health Education England (HEE) and others should work together to identify key workforce initiatives that are known to support general practice - including e.g. physician associates, medical assistants, clinical pharmacists, advanced practitioners (including nursing staff), healthcare assistants and care navigators.'

A shared programme of key pilots at scale in primary care seeks to invest in and trial new ways of working for these roles; demonstrating how they work across the community, hospitals and within GP surgeries to support safe and effective clinical services for patients. This is intended to support current GPs in managing their workload, as well as piloting new ways of working for the future. See http://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/building-the-workforce-new-deal-gp.pdf .

## Using the NHS standard contract to innovate with providers

The aspirations of NHS England's Five-Year Forward View depend on more imaginative and flexible contracting to overcome the problems posed by existing primary care contracts.[16]

The NHS standard contract is the tool that should be used to contract with new models and systems of care. This new approach will require understanding of the mechanics of the contract and how it can be used to influence and change behaviours.

'Straight to the Point' recommends that CCGs should work with pharmacists and other HCPs to assess CRP POCT in pharmacies and other community settings to reduce pressure on general practices.[14]

## Scenarios for CRP-POCT in Community Pharmacies

These are shown as an algorithm in Figure 5.

### Scenario 1

Offering CRP-POCT in the Community Pharmacy for patients presenting with symptoms of respiratory tract infection. Options are for referral to a local GP for prescribing or offering symptomatic relief depending on CRP levels.

### Scenario 2

As Scenario 1 but Independent Pharmacy Prescribers can prescribe an antibiotic as appropriate or symptomatic relief depending on clinical assessment of the patients and with the assistance of CRP blood levels.

### Scenario 3

As Scenario 1 but antibiotics may be supplied through a Patient Group Direction (PGD),[17] which is legally embodied in The Human Medicines Regulations 2012.[18]

## Conclusion

Antimicrobial resistance is a global problem for all healthcare systems and is directly related to the overuse of antibiotics. Unnecessary antibiotic use can be reduced by more accurate diagnosis of common infections. Biomarkers, such as CRP, offer greater precision for diagnosing respiratory tract infections that will respond to antibiotic treatment and those where antibiotics are inappropriate. CRP POCTs offer a simple way of determining whether a patient needs an antibiotic or not from a 5-minute test using a finger prick blood sample. CRP POCT devices can be easily used in Community Pharmacies, which can offer other NHS health screening tests at the same time.

### Declaration of interests

- The author has chaired the Antimicrobial Stewardship Sub-Group of the Department of Health Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (travel expenses only) and has chaired, presented and received honoraria at meetings supported by Astellas, Alere, Matoke Holdings and Basilea.

*"CRP POCTs offer a simple way of determining whether a patient needs an antibiotic or not from a 5-minute test using a finger prick blood sample. CRP POCT devices can be easily used in Community Pharmacies . . ."*


REFERENCES

1. WHO Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR). Antimicrobial resistance: global report on surveillance. 2014.
2. Chan M. Antimicrobial resistance: no action today, no cure tomorrow. World Health Day 2011 Combat antimicrobial resistance. Geneva. Director-General of the World Health Organization. 2011.
3. Davies SC. Annual Report of the Chief Medical Officer. Volume Two, 2011. Infections and the rise of antimicrobial resistance. Department of Health, London. 2013.
4. Department of Health. UK 5 Year Antimicrobial Resistance Strategy 2013 to 2018. In: Department of Health, ed. London. 2013.
5. Goossens H, Ferech M, Vander Stichele R, Elseviers M. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. Lancet 2005;365:579-87.
6. National Institute for Health and Clinical Excellence. Respiratory tract infections – antibiotic prescribing. Prescribing of antibiotics for self-limiting respiratory tract infections in adults and children in primary care. NICE clinical guideline 69. 2008.
7. Smith SM. Fahey T. Smucny J. Becker LA. Antibiotics for acute bronchitis. Cochrane Database Syst Rev 2014.
8. Spinks A, Glasziou PP, Del Mar CB. Antibiotics for sore throat. Cochrane Database Syst Rev 2013;11:CD000023.
9. Ahovuo-Saloranta A, Rautakorpi UM, Borisenko OV, Liira H, Williams JW, Jr., Makela M. Antibiotics for acute maxillary sinusitis in adults. Cochrane Database Syst Rev 2014;2:CD000243.
10. Venekamp RP, Sanders S, Glasziou PP, Del Mar CB, Rovers MM. Antibiotics for acute otitis media in children. Cochrane Database Syst Rev 2013;1:CD000219.
11. Petersen I, Johnson AM, Islam A, Duckworth G, Livermore DM, Hayward AC. Protective effect of antibiotics against serious complications of common respiratory tract infections: retrospective cohort study with the UK General Practice Research Database. BMJ (Clinical research ed) 2007;335:982.
12. (MHRA). MaHPRA. Management and use of IVD point of care test devices. 2013.
13. Aabenhus R, Jensen Jens-Ulrik S, Jørgensen Karsten J, Hróbjartsson A, Bjerrum L. Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care. Cochrane Database of Systematic Reviews: John Wiley & Sons, Ltd; 2014.
14. Munro and Forster. Staight to the Point - Ensuring the Rational Use of Antibiotics in Primary Care using C-Reactive Protein Testing A Consensus Report: Munro and Forster. 2015. Available at: http://www.patients-association.org.uk/wp-content/uploads/2015/06/straight-to-the-point.pdf.
15. Royal College of General Practitioners, The British Medical Association, NHS England and Health Education England. Building the Workforce – the New Deal for General Practice. 2015.
16. NHS England. Five Year Forward View. 2014.
17. National Institute for Health and Clinical Excellence. Patient Group Directions. NICE guidelines [MPG2]. 2013.
18. UK Parliament. The Human Medicines Regulations 2012 In: UK Parliament, ed. 2012 No 1916 Norwich: The Stationary Office. 2012.