Diagnostic Stewardship to reduce antibiotic use in a GP setting

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Pilot study of C-reactive protein point-of-care testing

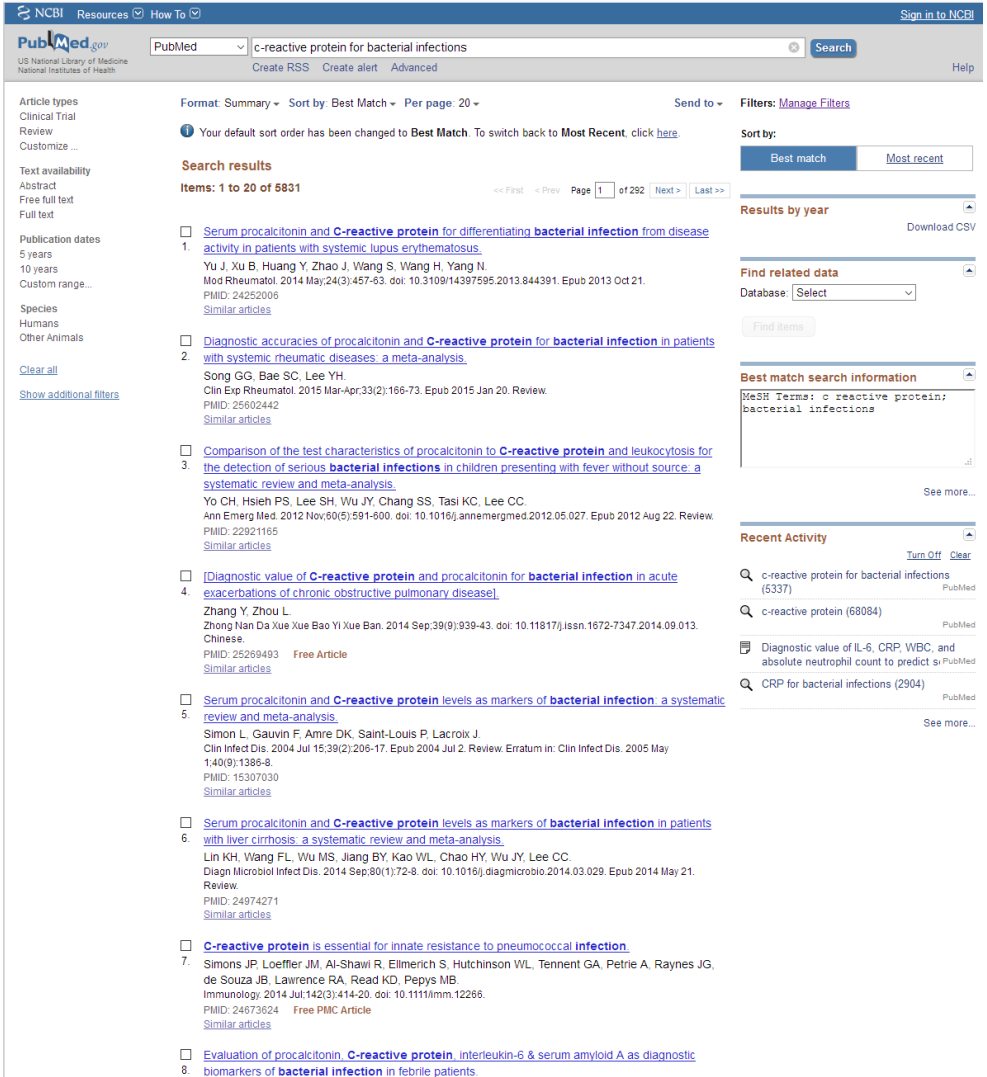
- First three months of 2016
- Assess its practicality and results

► **Using point of care CRP for patients with lower respiratory tract infection**

NICE introduces the use of point of care diagnostics to aid identification of more serious lower respiratory tract infections. While these are not currently used routinely in the UK, they are part of day-to-day practice in many European countries and there has been a growing body of data regarding their use.

Practices will need an analyser that can measure CRP – these cost around £700. The idea is that this is something that would be funded on a locality level, not individual practice level. NICE estimates that approximately 2500 practices already have a suitable analyser which they are using for NHS health check tests such as cholesterol profiles – these are usually multi-purpose and will be able to also use CRP kits. NICE estimate the cost per test is around £13.50 which includes the cost of time to conduct the test.

NB Check any evidence for CRP (near patient) use? *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1. Serum procalcitonin and C-reactive protein for differentiating bacterial infection from disease activity in patients with systemic lupus erythematosus.
Yu J, Xu B, Huang Y, Zhao J, Wang S, Wang H, Yang N.
Mod Rheumatol. 2014 May;24(3):457-63. doi: 10.3109/14397595.2013.844391. Epub 2013 Oct 21.
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2. Diagnostic accuracies of procalcitonin and C-reactive protein for bacterial infection in patients with systemic rheumatic diseases: a meta-analysis.
Song GG, Bae SC, Lee YH.
Clin Exp Rheumatol. 2015 Mar-Apr;33(2):166-73. Epub 2015 Jan 20. Review.
PMID: 25602442
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3. Comparison of the test characteristics of procalcitonin to C-reactive protein and leukocytosis for the detection of serious bacterial infections in children presenting with fever without source: a systematic review and meta-analysis.
Yo CH, Hsieh PS, Lee SH, Wu JY, Chang SS, Tasi KC, Lee CC.
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Zhang Y, Zhou L.
Zhong Nan Da Xue Xue Bao Yi Xue Ban. 2014 Sep;39(9):939-43. doi: 10.11817/j.issn.1672-7347.2014.09.013. Chinese.
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Simon L, Gauvin F, Amre DK, Saint-Louis P, Lacroix J.
Clin Infect Dis. 2004 Jul 15;39(2):206-17. Epub 2004 Jul 2. Review. Erratum in: Clin Infect Dis. 2005 May 1;40(9):1386-8.
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6. Serum procalcitonin and C-reactive protein levels as markers of bacterial infection in patients with liver cirrhosis: a systematic review and meta-analysis.
Lin KH, Wang FL, Wu MS, Jiang BY, Kao WL, Chao HY, Wu JY, Lee CC.
Diagn Microbiol Infect Dis. 2014 Sep;80(1):72-8. doi: 10.1016/j.diagmicrobio.2014.03.029. Epub 2014 May 21. Review.
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7. C-reactive protein is essential for innate resistance to pneumococcal infection.
Simons JP, Loeffler JM, Al-Shawi R, Ellmerich S, Hutchinson WL, Tennent GA, Petrie A, Raynes JG, de Souza JB, Lawrence RA, Read KD, Pepys MB.
Immunology. 2014 Jul;142(3):414-20. doi: 10.1111/imm.12266.
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8. Evaluation of procalcitonin, C-reactive protein, interleukin-6 & serum amyloid A as diagnostic biomarkers of bacterial infection in febrile patients.
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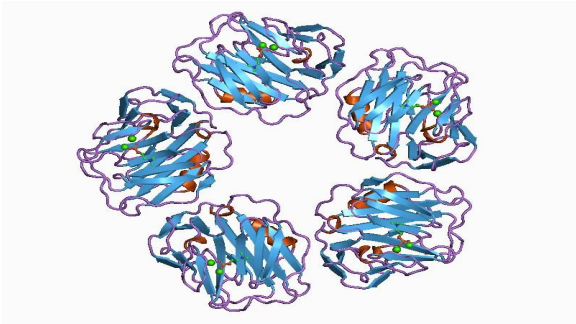
C-reactive protein



- C-reactive protein is an annular pentameric protein found in blood plasma, the levels of which rise in response to inflammation.
- CRP is synthesized by the liver in response to interleukin-6 and other cytokines released by macrophages and fat cells.

- CRP binds to the phosphocholine expressed on the surface of dead or dying cells and some bacteria. This activates the complement system, promoting phagocytosis by macrophages, which clears necrotic and apoptotic cells and bacteria.

- Normal concentration in healthy human serum is usually lower than 10 mg/L, slightly increasing with aging. Higher levels are found in late pregnant women, mild inflammation and viral infections (10–40 mg/L), active inflammation, bacterial infection (40–200 mg/L), severe bacterial infections and burns (>200 mg/L).
- It has a constant half-life of 18 hours.

Some Research

- In The American journal of emergency medicine, vol. 31, no. 1, p. 137-144 (January 2013), there was a paper on C-reactive protein as predictor of bacterial infection among patients with an influenza-like illness.
- There was a significant difference between the bacterial group, and both the influenza and other viral infection groups ($P < .001$). The receiver operating characteristic curve for CRP as a determinant of bacterial infection had an area under the curve of 0.978, whereby a CRP value of <20 had a sensitivity of 100% and >80 had a specificity of 100%. C-reactive protein is both a sensitive and specific marker for bacterial infection in patients presenting with Influenza-like illness during the influenza season.

Some More Research

- In Age and ageing, vol. 39, no. 5, p. 559-565 (September 2010) Serum C-reactive protein as a biomarker for early detection of bacterial infection in the older patient was looked into.
- They concluded CRP and temperature had higher sensitivity and specificity than white cell count and neutrophil count in the diagnosis of infection. For every 1-mg/l increment in CRP, the risk of bacterial infection increases by 2.9%. CRP is a convenient and useful biomarker to predict early bacterial infection in older patients.

Even More Research

- In The Journal of Paediatrics, vol. 153, no. 4, p. 570-574 (October 2008), a Systematic review of the diagnostic accuracy of C-reactive protein to detect bacterial infection in non-hospitalized infants and children with fever was conducted.
- They concluded CRP provides moderate and independent information for both ruling in and ruling out serious bacterial infection in children with fever at first presentation.

Yet More Research

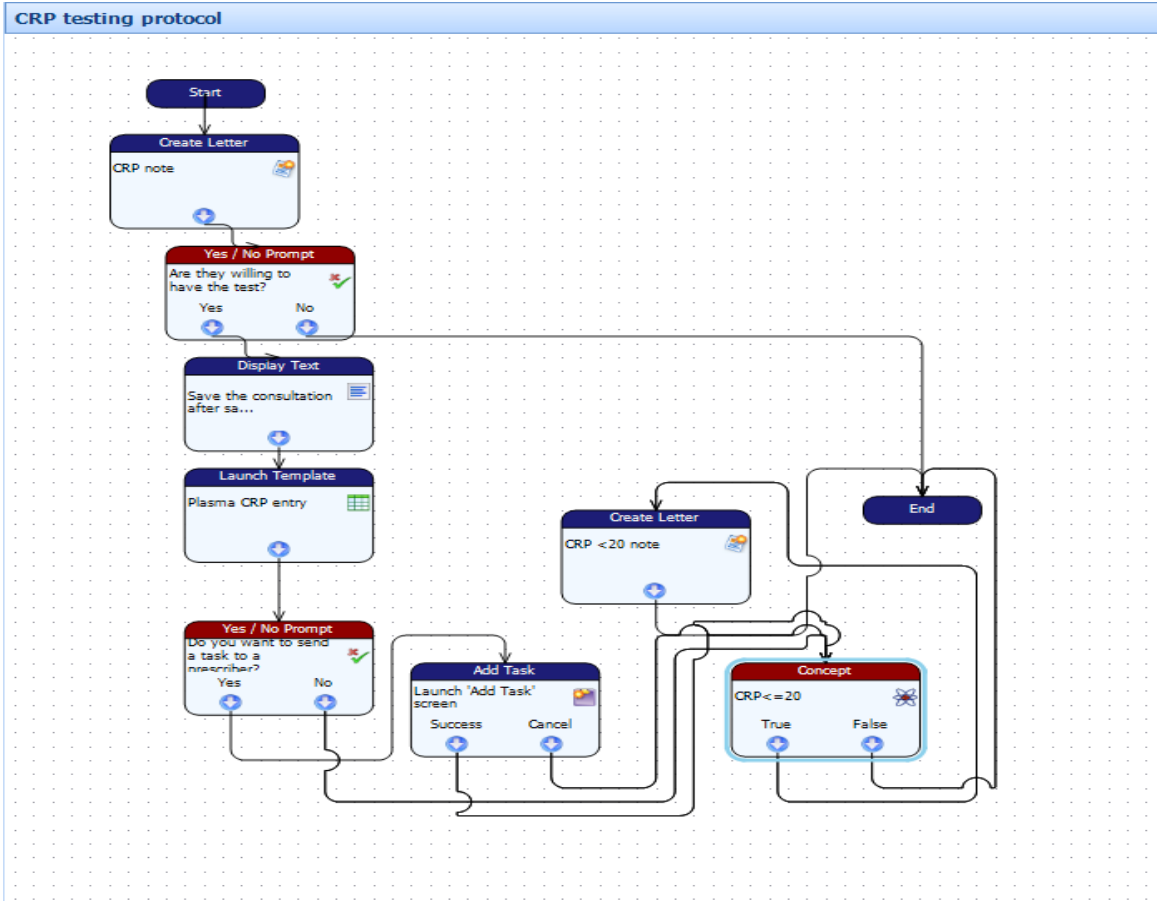
- As long ago as 1991 The New Zealand medical journal, vol. 104, no. 909, p. 138-139, 0028-8446 reported ‘CRP estimation could potentially help reduce unnecessary antibiotic prescription and shorten hospitalisation in febrile children' and was therefore a good thing.

NICE Guidance

- Pneumonia: Diagnosis and management of community- and hospital-acquired pneumonia in adults 2015

- For people presenting with symptoms of lower respiratory tract infection in primary care, consider a point of care C-reactive protein test if after clinical assessment a diagnosis of pneumonia has not been made and it is not clear whether antibiotics should be prescribed. Use the results of the C-reactive protein test to guide antibiotic prescribing in people without a clinical diagnosis of pneumonia as follows:
- Do not routinely offer antibiotic therapy if the C-reactive protein concentration is less than 20 mg/litre.
- Consider a delayed antibiotic prescription (a prescription for use at a later date if symptoms worsen) if the C-reactive protein concentration is between 20 mg/litre and 100 mg/litre.
- Offer antibiotic therapy if the C-reactive protein concentration is greater than 100 mg/litre.

- We used an EMIS web protocol to streamline the process:



Results

- We checked the CRP levels in most patients for whom we would probably have prescribed antibiotics, apart from suspected UTIs, and where there was not a contra-indication or pre-existing condition which would have rendered the result unhelpful eg RA, IBD etc.
- We would not normally offer antibiotics to anyone with a CRP of less than 20, and would definitely prescribe for anyone with a value over 80.
- We gave a written guidance sheet before doing the test and a sheet with the value and the usual viral advice if the result were less than 20.

Long date letter merged

Full Name(inc. middle) Date of Birth NHS Number

The C-reactive protein test detects inflammation in the body. We will be using it to tell the difference between infections caused by bacteria, which are normally susceptible to antibiotics, and infections caused by viruses, which are not.

The test only requires a small amount of blood obtained using a tiny lancet causing mild discomfort and takes about 4 minutes to run.

If the test demonstrates a viral cause for the illness then antibiotics would be of no benefit and might cause complications.

EMIS: EMIS Number

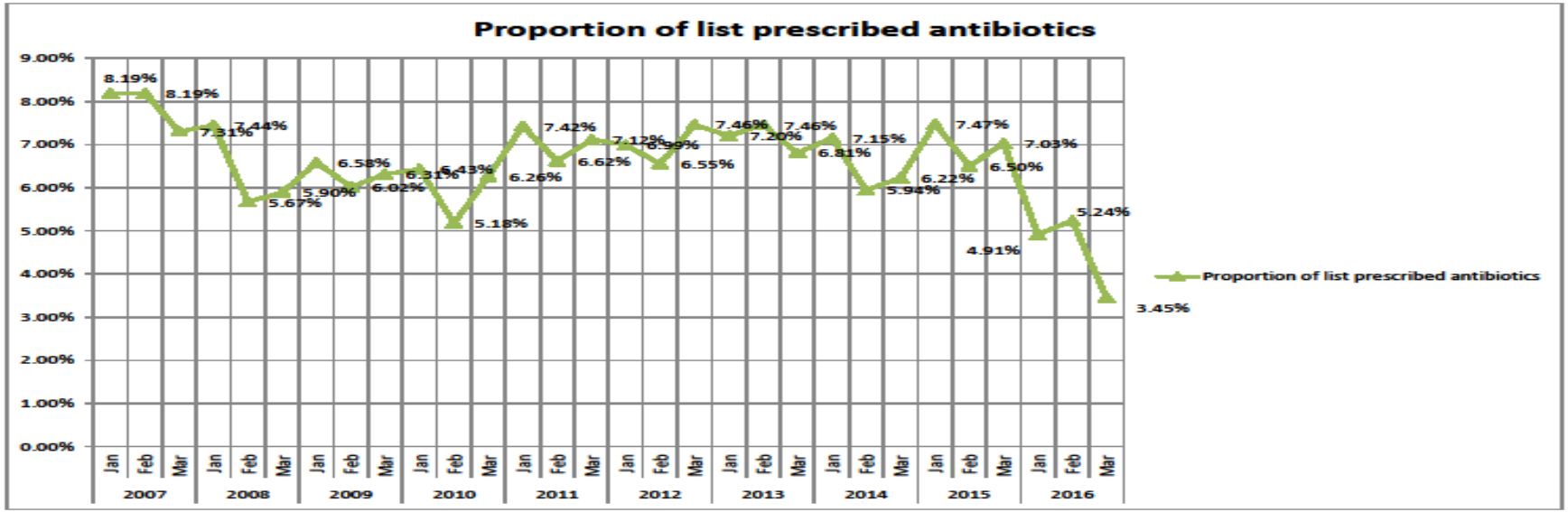
The CRP level of Full Name(inc. middle) Date of Birth NHS Number on Short date letter merged atTime letter merged was Single Code Entry: Plasma C reactive protein

Therefore the cause of the infection is almost certainly viral and treatment with rest, plenty of fluids and over-the-counter medications such as paracetamol is appropriate.

This sort of infection may take a couple of weeks to resolve.

- We did a total of 606 tests between 6/1/16 and 31/3/16 of which:
  - 5 or less 291
  - Between 6 & 20 175
  - 21 to 80 123
  - More than 80 17
- So it looks like 466 patients were saved from being prescribed antibiotics.

- I had a look at our antibiotic (except urinary antibiotics) prescribing historically:



- You will note the dramatic drop in antibiotic prescribing in the first three months of this year; in fact 960 patients received antibiotics from 6/1/16 to 31/3/16, compared with 1383 in the same period last year. These are raw figures with no weighting.
- Mark Galloway kindly supplied me with Antibacterial items per 1000 STAR-PUs:

Locality	Dec 14 – Feb 15	Dec 15 – Feb 16	Change
Westside	7,272	7,135	-1.88%
Rugby	7,676	7,660	-0.21%
Coventry and Rugby	8,099	8,089	-0.12%
England	8,363	8,452	+1.06%

- This would suggest that CRP testing has had a positive impact on antibacterial prescribing volume as our fall was significantly higher than that seen across Rugby and the CCG as a whole.

Costs

- The normal cost of the instrument was (at 24 August 2015) £2,350 or £800 pa for a 3 year rental, although this would be negotiable for large volumes across the CCG.
- Each cartridge costs £4 and we allowed 5 minutes per test, so depending on the pay grade of the person doing the test, we calculated that the cost of each test, excluding capital costs, is about £6.

Workload

Number of tests:

Day	*Total*	*Avg*	*Max*	*Min*
Mon	163	13	22	7
Tues	126	10	17	5
Wed	110	9	15	4
Thur	113	9	16	5
Fri	108	9	14	5

- 474 patients had 1 test
- 55 had 2
- 6 had 3
- 1 had 4

The Future

- We had the machine for slightly under a quarter, so we might calculate that we would do 2424 tests in a year, at a cost of about £14,544. Given our list size, this works out at £1.32 per patient per year.
- C&W CCG covers about 450,000 patients, so rolling out the CRP analyser to all practices would cost £594,981 plus the capital cost of the machines at £800 p.a. for each of the 75 practices, £60,000, a grand total of £654,981.81 cheap.

- NHS England announced that, from April 2016, CCGs will receive extra funding if they reduce the number of antibiotics prescribed in primary care either by 4% or down to the average performance level of 2013-14. A CCG with a population of 450,000 might receive a maximum of £225,000 a year.
- A mere £429,981.82 to find.
- C&W CCG has a budget of £553,000,000.
- 0.08%