

Position Paper on Anti-Microbial Resistance Diagnostics

‘Major epidemiological challenge of the 21st Century’

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The government's Review on AMR suggested five approaches to tackle the problem:

- 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.**

Consumption of antibacterials for systemic use (ATC group J01) in the community (primary care sector) and the hospital sector expressed in DDD per 1000 inhabitants and per day in 2013

ATC group J01

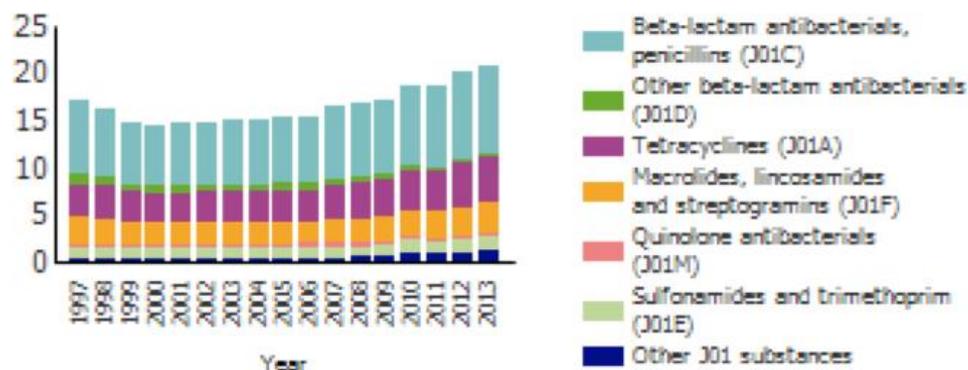
- Beta-lactam antibacterials, penicillins (J01C)
- Other beta-lactam antibacterials (J01D)
- Tetracyclines (J01A)
- Macrolides, lincosamides and streptogramins (J01F)
- Quinolone antibacterials (J01M)
- Sulfonamides and trimethoprim (J01E)
- Other J01 substances

Total

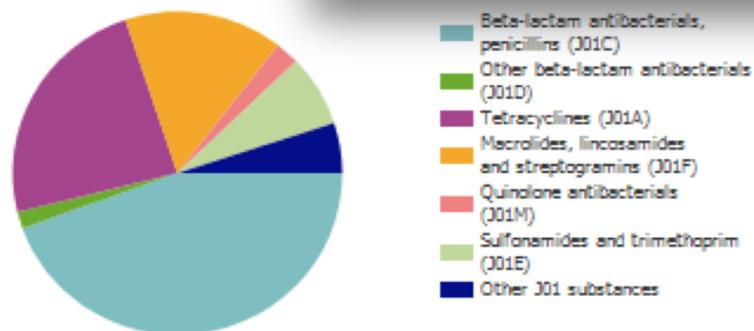
Community

Hospital sector

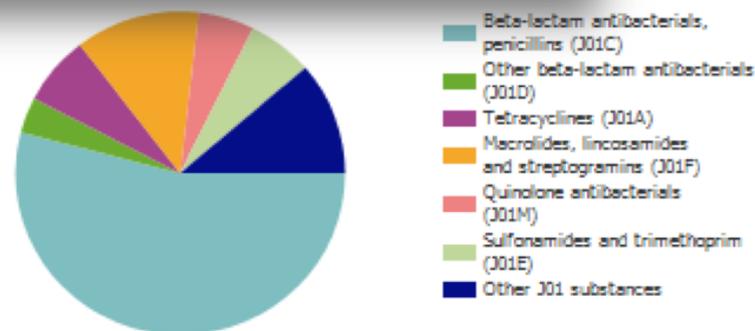
Trend of the consumption in the community (primary care sector) of ATC group J01 expressed in DDD per 1000 inhabitants and per day



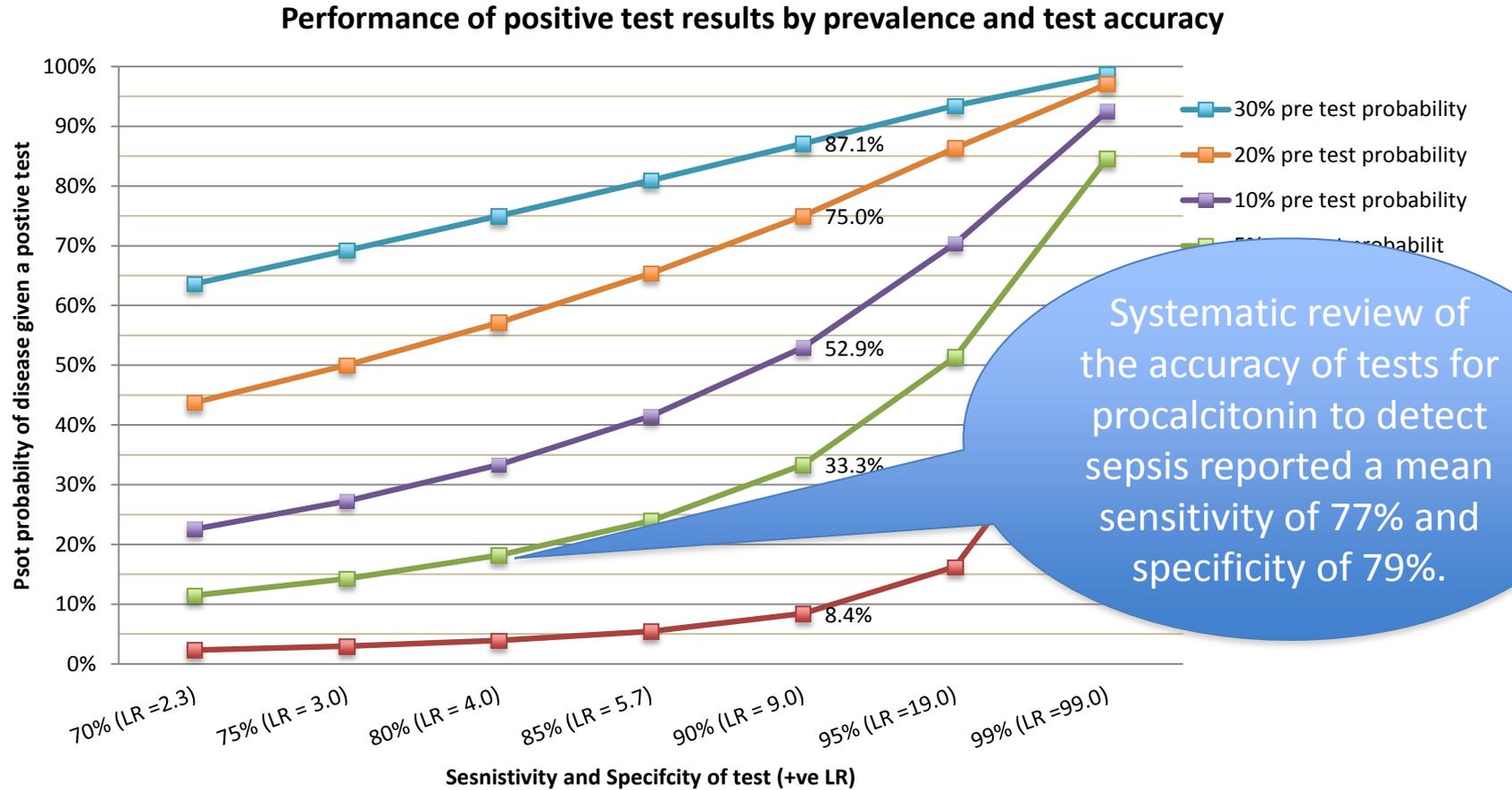
Distribution of the consumption in the community (primary care sector) of ATC group J01



Community (primary care sector) of ATC group J01

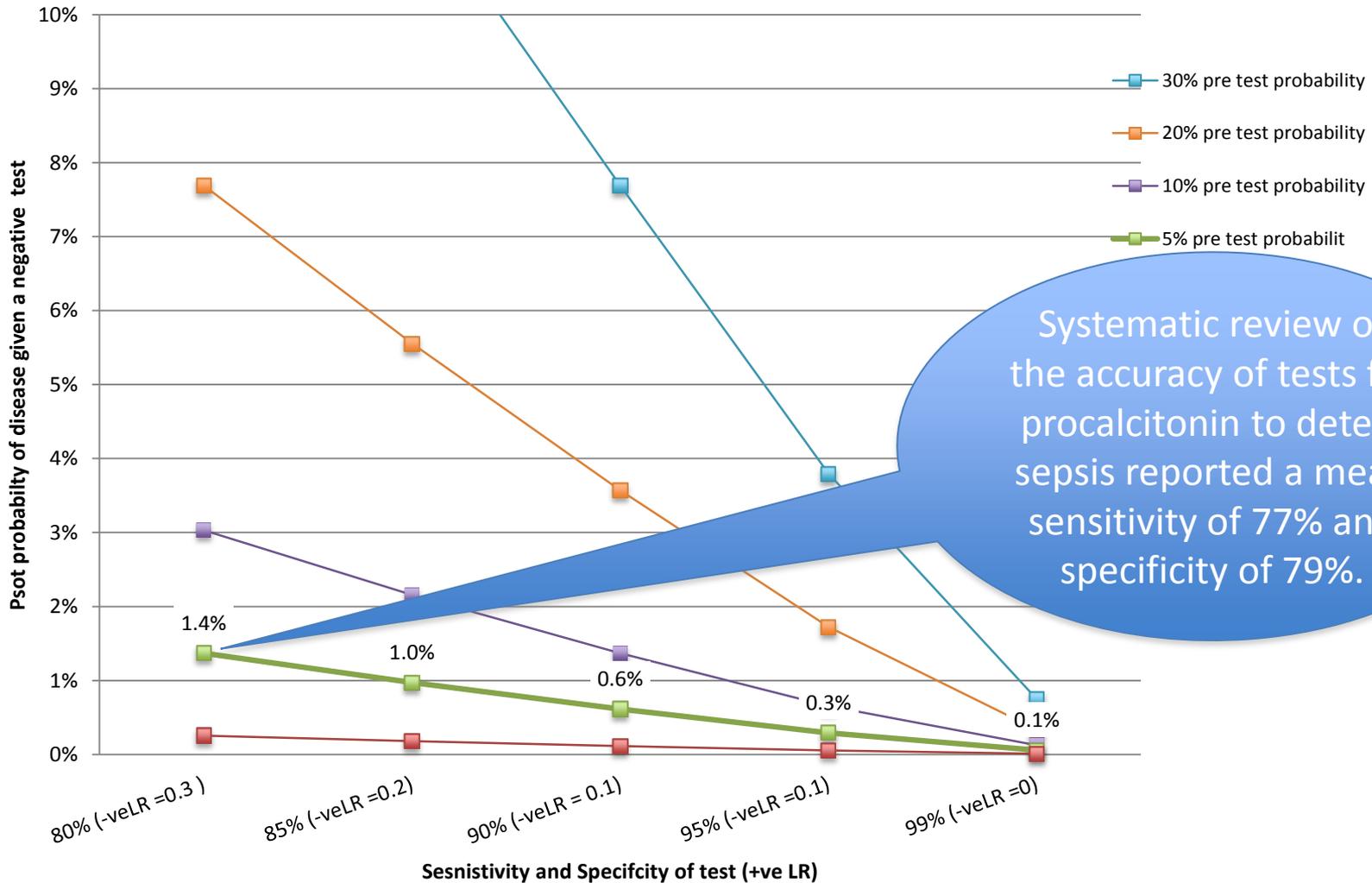


Test performance depends on the prevalence



Negative test

Performance of negative test results by prevalence and test accuracy



Systematic review of the accuracy of tests for procalcitonin to detect sepsis reported a mean sensitivity of 77% and specificity of 79%.



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June 2015

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NUFFIELD DEPARTMENT OF
PRIMARY CARE
HEALTH SCIENCES

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TECHNOLOGIES IN PRIMARY CARE (page 15)

SUMMARY OF KEY FINDINGS

- Overall a variety of multi-faceted interventions combining physician, **patient and public education** were the most successful in reducing inappropriate antibiotic prescribing.
- No single intervention could be applied to all settings, however a combination of methods including **patient-based interventions** and **physician reminders** show promise and require further investigation.
- Particularly the **use of delayed prescriptions** for infections, for which antibiotics are not immediately indicated, effectively reduced antibiotic use and associated morbidity.
- Many of the technologies are protein antigen based and do not have high **sensitivity**. Nucleic acid laboratory based tests have the sensitivity to influence clinical pathway/decision making.
- Protein based assays are likely to be supplanted by nucleic acid based assays and diagnostic agents. They are able to perform resistant organism detection.
- CRP testing is increasingly being used in primary care **however** the value of this point-of-care test is mixed.
- Overall there is a **lack of implementation research** in primary care and the cost-effectiveness of many of the technologies.

Table 3 (page 55)
Summary table of diagnostic technologies including company/research group, level of readiness ongoing UK-funded research

group A strains (Appendix 65).

For the diagnosis of influenza, there is a considerable array of point-of-care tests on the market and a meta-analysis has reported pooled sensitivity and specificity of 62% and 98%, respectively.

TECHNOLOGY: IMMUNOCHROMATOGRAPHIC TEST FOR COMMUNITY-ACQUIRED PNEUMONIA
CAUSED BY STREPTOCOCCAL PNEUMONIA

TABLE 3: Summary of evidence from clinical trials and systematic reviews of diagnostic accuracy for rapid point-of-care tests for community-acquired pneumonia caused by pneumococcal pneumonia.

| Technology | Condition |
|---|--|
| Rapid point-of-care blood and serum tests | Diagnosis of influenza |
| | Diagnosis of <i>Campylobacter</i> |
| | Diagnosis of syphilis |
| | Measurement of C-reactive protein |
| | Measurement of procalcitonin |
| | Measurement of white blood cell counts |
| Rapid point-of-care urine stick tests | Home measurement of white blood cell count |
| | Sepsis |
| | Diagnosis of <i>Helicobacter pylori</i> |
| | Diagnosis of urinary tract infection |
| Urinary culture and antibiotic susceptibility testing | ESBL urinary tract infection |
| | Diagnosis of chlamydia |

Bottom line: Immunochromatographic test could be a useful addition to the current diagnostic workup for community acquired pneumonia. However, a lack of clinical trials and cost-effectiveness information limit its application in the NHS.

Level of evidence

The immunochromatographic test could be a useful addition to the current diagnostic workup for CAP. However, evidence from the meta-analysis does not address whether rapid diagnosis with BinaxNOW-SP would impact the initial management of CAP patients.

**Level 1:
Systematic
review**

A summary of the implications for practice with regard to anti-microbial resistance

BinaxNow assay appears to have higher pooled sensitivity compared to culture, and it also has a high specificity. There is a need to determine its accuracy and effect on subsequent prescribing patterns in primary care alongside its cost effectiveness.

**Clinical
Relevance
Medium**

1. Definition

The BinaxNOW *Streptococcus pneumoniae* test is an immunochromatographic test (ICT) for the presence of the pneumococcal C-polysaccharide coat protein in urine. It is a rapid diagnostic test for *S. pneumoniae* infected patients producing a result within 15 minutes of a urine sample being obtained. ICT tests can be conducted in hospital/clinic laboratories; samples can be collected on admission or within 48 hours after admission.

2. Summary of the evidence

Twenty-seven studies were included (Sinclair et al, 2013). Participants in most studies were predominantly middle-aged or elderly, except for the studies which included HIV-positive or AIDS patients. No study had an overall low risk of bias, and none met the requirement for a perfect reference standard. After adjusting for the imperfect and variable nature of the reference standard, meta-analysis revealed a higher sensitivity of 74.0% (Credible interval (CrI), 66.6% to 82.3%) and specificity of 97.2% (CrI, 92.7% to 99.8%). There was substantial heterogeneity across studies, and this did not decrease with adjustment for covariates. The results were consistent with a previous meta-analysis of 24 studies (16 of which were included in the new report) (Boulware et al, 2007).

3. Requirements for further research

The meta-analysis does not address whether rapid diagnosis with BinaxNOW-SP would impact the initial management of CAP patients or changes to the initial management of CAP patients. Adequately powered randomized clinical trials are required to allow for a more robust assessment of the diagnostic accuracy and reliability of ICT.

4. References

- Sinclair A, Xie X, Teltscher M, Dendukuri N. Systematic review and meta-analysis of a urine-based pneumococcal antigen test for diagnosis of community-acquired pneumonia caused by *Streptococcus pneumoniae*. J Clin Microbiol. 2013 Jul;51(7):2303-10.
- Boulware DR, Daley CL, Merrifield C, Hopewell PC, Janoff EN. Rapid diagnosis of pneumococcal pneumonia among HIV-infected adults with urine antigen detection. J. Infect. 2007; 55:300-309

GPs should use point-of-care test to reduce antibiotic use for pneumonia

18 June 2014 | By [Caroline Price](#)

 [Print](#)  [Email](#)   [Comments \(8\)](#)

GPs should consider using a point-of-care test to determine if patients presenting with mild pneumonia need antibiotics, according to new guidance from NICE.

The [draft guidance](#) proposes GPs carry out the test if a patient is not clear from a clinical assessment whether an infection is present (see [box](#)).

They should then offer a five-day course of a single antibiotic for mild, low-severity pneumonia – but not a fluoroquinolone – if their symptoms do not improve within three days.

The guidance also advises GPs to use the CRB65 score to make their judgement about whether patients should be referred to hospital.

The CRB65 score assigns points based on aspects such as respiratory rate, low blood pressure and older age. Patients can be offered home-based care for patients with a score of zero or one, and hospital assessment for all other patients, particularly those with severe symptoms.

Professor Mark Baker, NICE's director of clinical practices, said: 'Pneumonia can be difficult to treat; it requires careful assessment and thoughtful treatment. These new draft recommendations make it very clear how to best test for pneumonia and when to consider treating with antibiotics.'

STRAIGHT
TO THE
POINT!

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

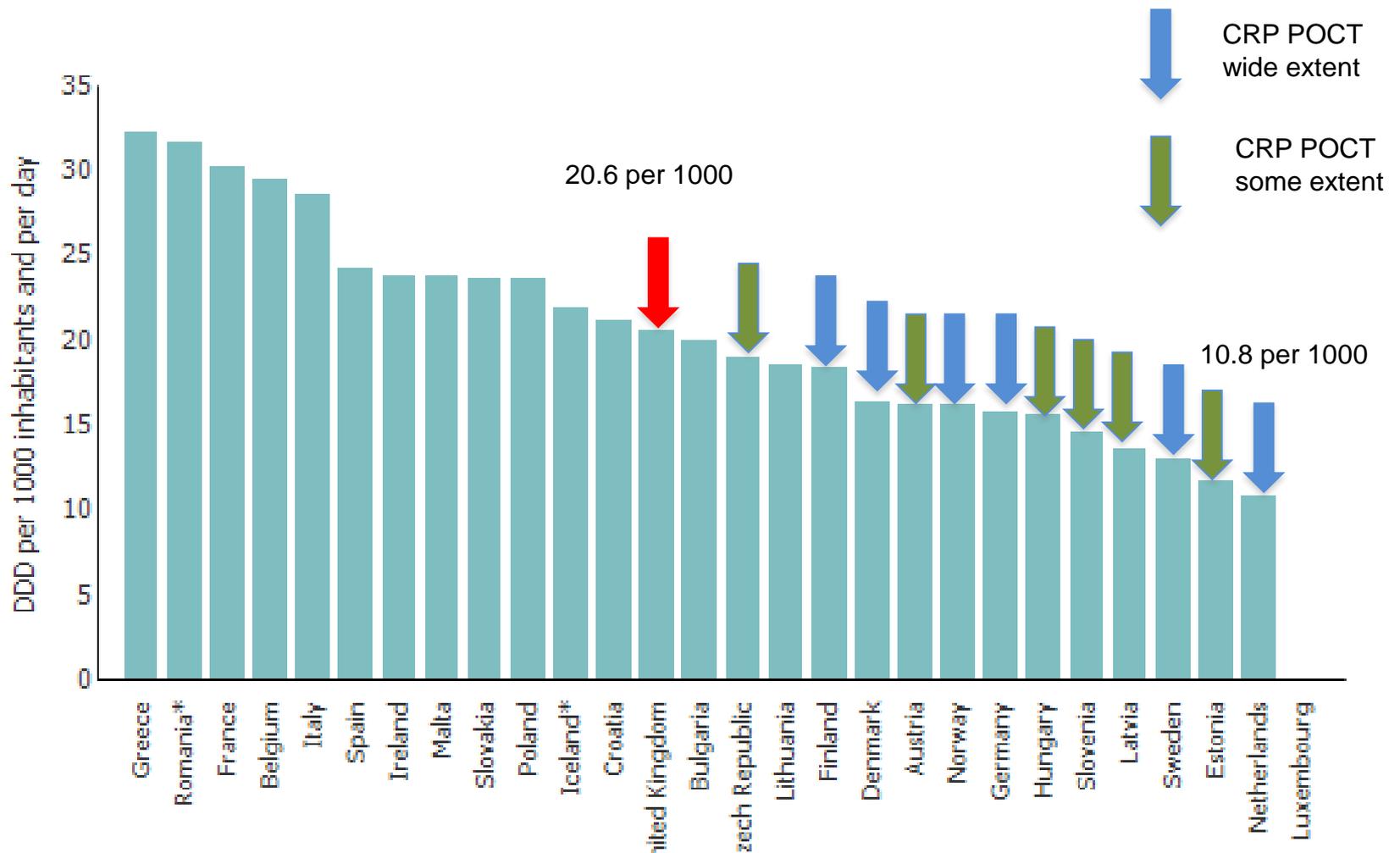
A Consensus Report

June 2015

30 June 2015

► **NICE plans for GP antibiotic**

Use of CRP POCT and antibiotic prescribing in Europe



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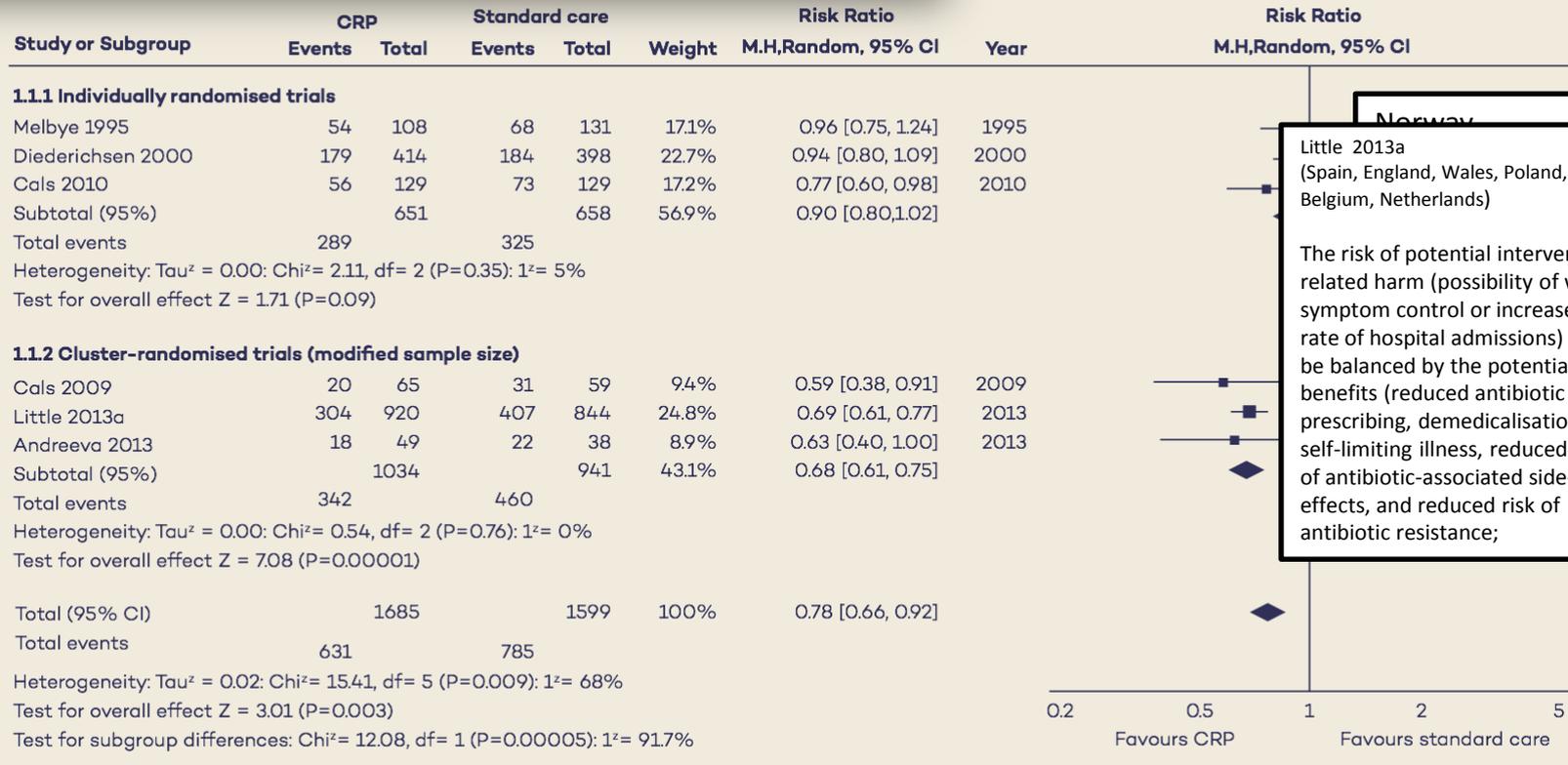
Database Home

Intervention Review

Biomarkers as point-of-care tests to guide prescription of antibiotics in patients with acute respiratory infections in primary care

 Rune Aabenhus^{1,*}, Jens-Ulrik S Jensen², Karsten Juhl Jørgensen³, Asbjørn Hróbjartsson³, Lars Bjerrum⁴

Database Title

[The Cochrane Library](#)


Norway

Little 2013a
 (Spain, England, Wales, Poland, Belgium, Netherlands)

The risk of potential intervention-related harm (possibility of worse symptom control or increased rate of hospital admissions) must be balanced by the potential benefits (reduced antibiotic prescribing, demedicalisation of self-limiting illness, reduced risk of antibiotic-associated side-effects, and reduced risk of antibiotic resistance;

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

Diagnostic classification by a simplified diagnostic score

Rounding of all regression coefficients in the model including symptoms signs and CRP >30 mg/L to 1 point resulted in the simplified diagnostic score presented in table 4. The proportions of pneumonia were 0.7%, 4%, and 18%, respectively, in the estimated low, intermediate, and high risk class.

Table 4 Diagnostic risk classification of pneumonia by simplified diagnostic score in 2820 patients with acute cough

| Score (risk category) | Symptoms and signs + CRP >30 mg/L* | |
|-----------------------|------------------------------------|---|
| | No of patients (% of 2820) | No with pneumonia (observed prevalence) |
| 0 (low) | 572 (20.3) | 4 (0.7) |
| 1-2 (intermediate) | 1902 (67.4) | 73 (3.8) |
| ≥3 (high) | 346 (12.3) | 63 (18.2) |
| All | 2820 (100) | 140 (0.05) |

*Score: 1×absence of runny nose+1×breathlessness+1×crackles+1×diminished vesicular breathing+1×raised pulse (>100/min)+1×fever (temperature >37.8°C) 1×raised CRP (>30 mg/L).

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assist. AMO. Severity scores, such as CURB-65, can be used once pneumonia has been diagnosed.

Do not routinely offer antibiotic therapy

Consider a delayed antibiotic prescription (a prescription for use at a later date if symptoms worsen)

Offer antibiotic therapy

Research

Use of serum C reactive protein and procalcitonin concentrations in addition to symptoms and signs to predict pneumonia in patients presenting to primary care with acute cough: diagnostic study

BMJ 2013 ; 346 doi: <http://dx.doi.org/10.1136/bmj.f2450> (Published 30 April 2013)
Cite this as: BMJ 2013;346:f2450

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Saskia F van Vugt, general practitioner¹, Berna D L Broekhuizen, assistant professor¹, Christine Lammens, analyst², Nicolaas P A Zuijthoff, assistant professor¹, Pim A de Jong, radiologist³, Samuel Coenen, assistant professor², Margareta Ieven, professor², Chris C Butler, professor⁴, Herman Goossens, professor², Paul Little, professor⁵, Theo J M Verheij, professor¹ on behalf of the GRACE consortium

[Author affiliations](#) ▼

TECHNOLOGIES IN SECONDARY CARE (Page 20)

SUMMARY OF KEY FINDINGS

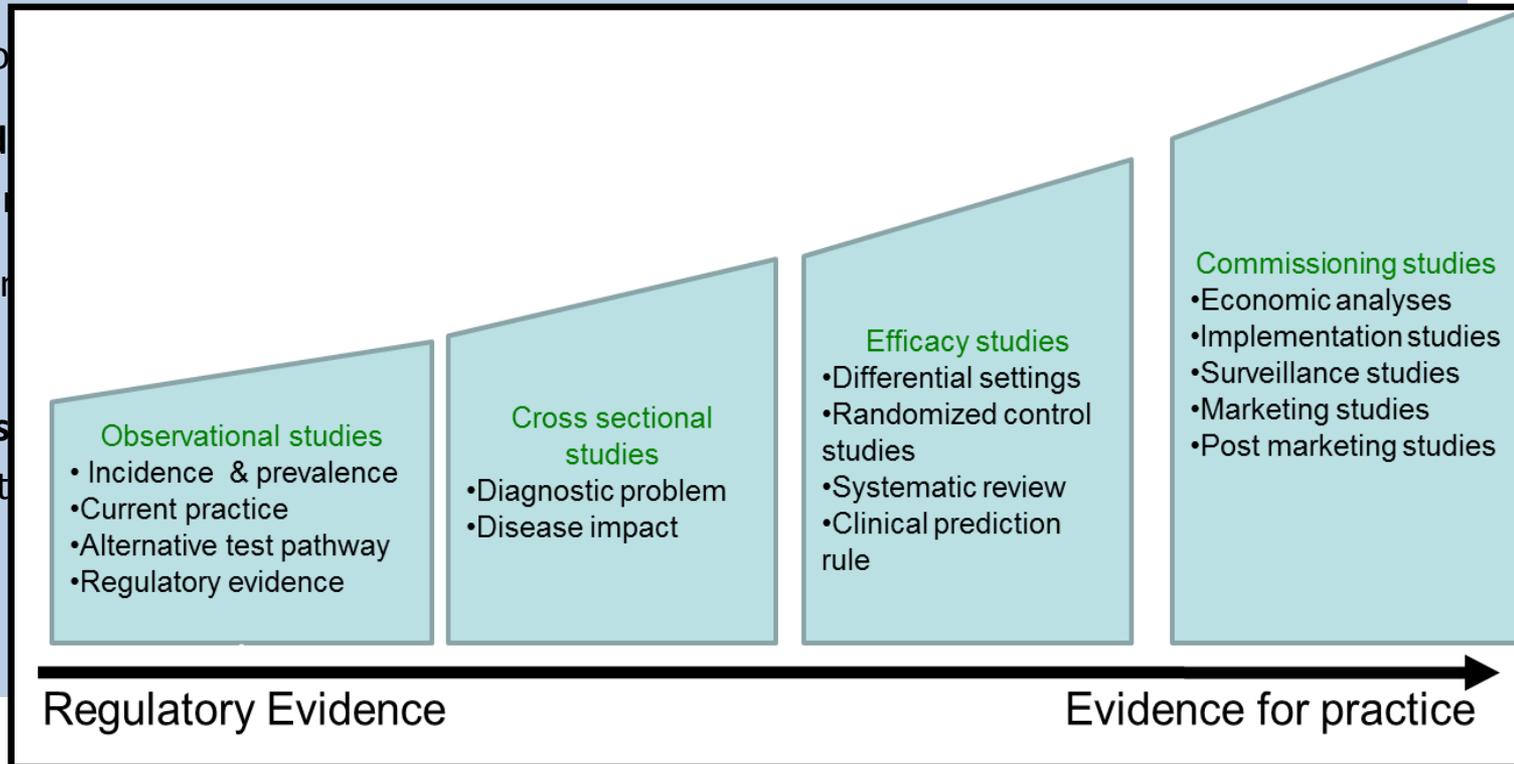
- Many technologies **lack clinical trial data**, validation and cost-effectiveness assessments.
- Current need to **streamline the development** of the evidence base for many tests and fast-track clinical trial data to aid implementation into clinical care.

• Better utilization

• **Hospital-based** associated with

• Studies assessing **result** reporting

• **Introducing tes** low risk of infect



OTHER INTERVENTIONS (page 30)

SUMMARY OF KEY FINDINGS

- No single quality improvement strategy was more effective than another
- **Academic peers** providing education on the guidelines and research evidence for acute respiratory tract infection had significant effects on prescribing.

• **Clinician education**

spectrum antibiotic

• **Interactive book**

been shown to

• **Internet training**

• **Automatic correction**

design of guideline

SUMMARY OF KEY FINDINGS

- Delayed prescription strategies were likely to provide similar benefits to immediate antibiotic prescription.
- Not prescribing any antibiotics (with the advice to return if symptoms did not improve) is likely to result in the least antibiotic use, while maintaining similar patient satisfaction and clinical outcomes to delayed antibiotics.
- Delayed antibiotic prescription was less effective than targeted use of antibiotics using a clinical score.

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Patient-Initiated Treatment of Uncomplicated Recurrent Urinary Tract Infections in Young Women

Kalpana Gupta, MD, MPH; Thomas M. Hooton, MD; Pacita L. Roberts, MS; and Walter E. Stamm, MD

Gold standard

Background: Recurrent urinary tract infections (UTIs) are a common outpatient problem, resulting in frequent office visits and often requiring the use of prophylactic antimicrobial agents. Patient-initiated treatment of recurrent UTIs may decrease antimicrobial use and improve patient convenience.

Objective: To determine the safety and feasibility of patient-initiated treatment of recurrent UTIs.

Design: Uncontrolled, prospective clinical trial.

Setting: University-based primary health care clinic.

Participants: Women at least 18 years of age with a history of recurrent UTIs and no recent pregnancy, hypertension, diabetes, or renal disease.

Intervention: After self-diagnosing UTI on the basis of symptoms, participating women initiated therapy with ofloxacin or levofloxacin.

Measurements: Accuracy of self-diagnosis determined by evi-

dence of a definite (culture-positive) or probable (sterile pyuria and no alternative diagnosis) UTI on pretherapy urinalysis and culture. Women with a self-diagnosis of UTI that was not microbiologically confirmed were evaluated for alternative diagnoses. Post-therapy interviews and urine cultures were used to assess clinical and microbiological cure rates, adverse events, and patient satisfaction.

Accuracy

Results: 88 of 172 women self-diagnosed a total of 172 UTIs. Laboratory evaluation showed a uropathogen in 144 cases (84%), sterile pyuria in 19 cases (11%), and no pyuria or bacteriuria in 9 cases (5%). Clinical and microbiological cures occurred in 92% and 96%, respectively, of culture-confirmed episodes. No serious adverse events occurred.

Conclusion: Adherent women can accurately self-diagnose and self-treat recurrent UTIs.

Ann Intern Med. 2001;135:9-16.

www.annals.org

For author affiliations, current addresses, and contributions, see end of text.

See related article on pp 41-50 and editorial comment on pp 51-52.

Series of patients

Index test

REDEsIgN 50/25

REsearch DEvelop ImplemeNt

Research

1. OOHs /Primary Care/ Secondary Care
2. The public understanding
3. Priority setting
4. Set parameters
5. Applied Evidence Base
6. Safety netting



Develop

1. Feasibility/acceptability
2. Test bed practice network
3. Benchmarking/Clinical audit
4. Improved use of Informatics
5. Develop an applied Evidence Base infrastructure

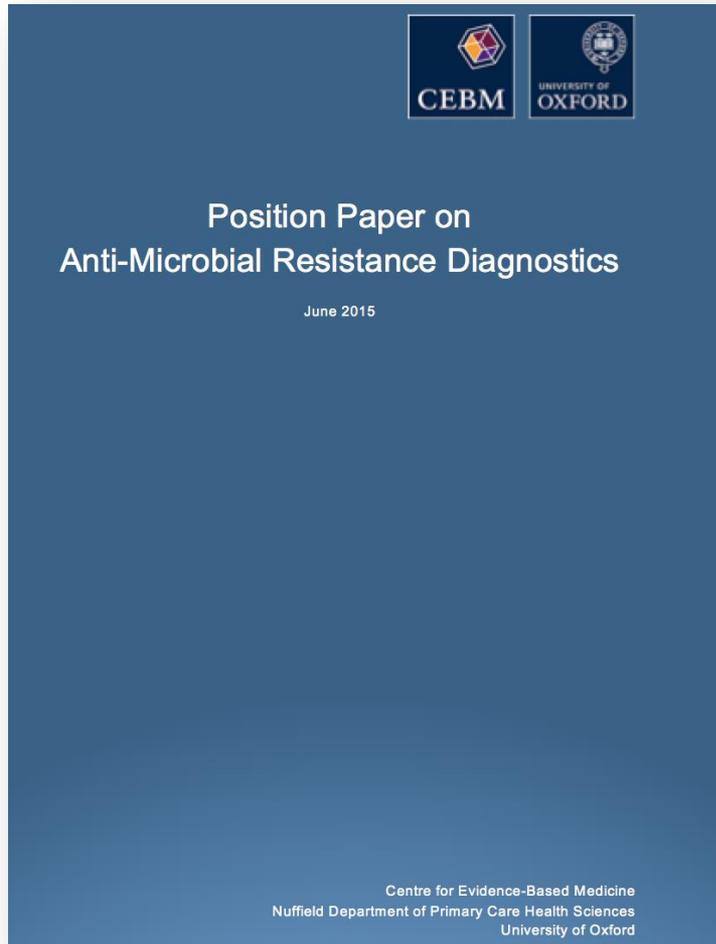


Implement

1. Cost effectiveness
2. Reimbursement schemes
3. Budget Silos
4. Decommissioning strategies
5. Dissemination

By 2025 we will set a target to reduce antibiotic prescriptions in the NHS by 50% without concomitant increases in harms

Thank You



This report presents independent research funded by the Department of Health. The views expressed are those of the authors and not necessarily those of the NHS or the Department of Health. The authors have received funding from the Medical Research Council, the National Institute for Health Research (NIHR), NIHR Diagnostic Evidence Co-operative, NIHR School for Primary Care Research, Wellcome Trust and the World Health Organization.