

	Study group	Design	Outcomes	Key results
Systematic reviews				
Verbakel 2019 ³⁸	11 RCTs and 8 non-randomised trials (16,064 Adults and children)	Systematic review (Cochrane review)	Reduction in antibiotic prescribing.	Based on 10 RCTs, performing a CRP POCT resulted in a significant reduction of antibiotic prescriptions issued at the index consultation with a pooled effect estimate RR of 0.81 (95% CI 0.71 to 0.92). Performing a POC CRP test in ambulatory care accompanied by evidence-based clinical guidance on interpretation reduces the immediate antibiotic prescribing rate in both adults and children.
Kochling et al 2018 ³⁹	17 RCTs	Systematic review	Reduction in antibiotic prescribing.	Clinical skills training and CRP POCT alone or as adjunct can reduce antibiotic prescriptions for RTI. Five of 17 trials reported a statistically significant reduction. Pre-intervention antibiotic prescription rates varied between 13.5% and 80% and observed reductions ranged from 1.5 to 23.3%. Trials with initially lower prescription rates were less likely to be successful.
O'Connor et al 2018 ⁴⁰	139 papers	Narrative review	Factors that affect primary care providers' prescribing decisions	Strategies proven to reduce inappropriate prescribing include appropriately aimed multifaceted educational interventions for primary care providers, mass media educational campaigns aimed at healthcare professionals and the public, use of good communication skills in the consultation, use of delayed prescriptions especially when accompanied by written information, POCT and, probably, longer less pressurised consultations.
Htun et al 2019 ²⁶	13 papers were included.	Systematic review	Effectiveness of prognostic indicators for pneumonia compared with chest radiography.	Clinical features with the best pooled positive likelihood ratios were respiratory rate ≥ 20 min ⁻¹ (3.47; 1.46–7.23), temperature ≥ 38 °C (3.21; 2.36–4.23), pulse rate > 100 min ⁻¹ (2.79; 1.71–4.33), and crackles (2.42; 1.19–4.69). Laboratory testing showed highest pooled positive likelihood ratios with PCT > 0.25 ng/ml (7.61; 3.28–15.1) and CRP > 20 mg/l (3.76; 2.3–5.91). Cough, pyrexia, tachycardia, tachypnoea, and crackles are limited as a single predictor for diagnosis of radiographic pneumonia among adults. Development of clinical decision rule that combine these clinical features together with molecular biomarkers may further increase overall accuracy for diagnosis of radiographic pneumonia among adults in primary care.
Tonkin-Crine et al 2017 ⁴¹	44 clinical trials	Cochrane overview of 11 Systematic Reviews	Reduction in antimicrobial prescribing	Evidence that CRPPOCT, shared decision making, and procalcitonin-guided management reduce antibiotic prescribing for patients with ARIs in primary care. These interventions may therefore reduce overall antibiotic consumption and consequently antibiotic resistance. There do not appear

				to be negative effects of these interventions on the outcomes of patient satisfaction and re-consultation, although there was limited measurement of these outcomes in the trials.
Clinical studies				
Little et al 2019 ⁴²	A total of 246 general practices in 6 countries	Cluster-randomized to usual care	Reduction in antibiotic prescribing for RTIs after 12 months.	Clinical Skills and CRP training reduced antibiotic prescribing for RTIs decreased with usual care (from 58% to 51%), but increased with CRP training (from 35% to 43%) and with both interventions combined (from 32% to 45%); at 12 months, the adjusted RRs compared with usual care were 0.75 (95% CI, 0.51-1.00) and 0.70 (95% CI, 0.49-0.93), respectively. Between 3 months and 12 months, the reduction in prescribing with communication training was maintained (41% and 40%, with an RR at 12 months of 0.70 [95% CI, 0.49-0.94]). Although materials were provided for free, clinicians seldom used booklets and rarely used CRP POCT.
Althaus et al 2019 ⁴³	Febrile patients in Thailand and Myanmar	open-label, randomised, controlled trial	Reduction in antibiotic prescribing, with patients with high CRP being more likely to be prescribed an antibiotic, and no evidence of a difference in clinical outcomes	Reduction in antibiotic prescribing, with patients with high CRP being more likely to be prescribed an antibiotic, and no evidence of a difference in clinical outcomes. This study extends the evidence base from lower-income settings supporting the use of CRP tests to rationalise antibiotic use in primary care patients with an acute febrile illness
Minnaard et al 2016 ³¹	1473 eligible patients presenting with acute cough, 348 (24%) were recruited	Cross-sectional observational study	Reduction in antibiotic prescribing	POC CRPT were conducted and antibiotics prescribed more frequently as compared to non-recruited patients (81% versus 6% and 44% versus 29%, respectively). The ORs were 18.2 (95%CI: 9.6-34.3), 30.5 (95%CI: 13.2-70.3) and 3.8 (95%CI: 0.9-14.8) respectively in all eligible patients, the recruited and the non-recruited patients. Having POC CRP results available influences the decision of GPs to prescribe antibiotic treatment in patients with an acute cough, but not in GPs with a low antibiotic prescribing rate.
Haldrup et al 2017 ³²	Data linkage	Data linkage - nationwide health care databases to assess POCT use	POCT	The overall use of POCT in Denmark increased by 45.8% during 2004-2013, from 147.2 per 1,000 overall consultations to 214.8. CRP tests increased by 132%. In 2013, 44% of all antibiotic prescriptions were preceded by POCT but testing rates vary greatly across individual GPs.
Llor et al 2019 ⁴⁴	1906 Patients presenting to GP practices with LRTI	Audit-based study	Reduction in antibiotic prescribing	A low POCT result was negatively associated with antibiotic prescribing, with odds ratios ranging from 0.09 to 0.23. GPs using POCTs attached less weight to clinical criteria. GPs using rapid tests are mainly influenced by

				POCT results in the decision to prescribe antibiotics. However, antibiotic prescribing is still observed with negative POCT results.
Cooke et al 2019 ⁴⁵	Setting GP Practice and Community Pharmacy with 40 patients	Feasibility and observational study	Reduction in antibiotic prescribing Time for CRP POCT Patient satisfaction	Patients who had a CRP of less than 100 were given a leaflet and told to visit the GP if symptoms did not resolve within 3 weeks. 63% of patients had a CRP value of <5 mg/l and were deemed to have self-limiting illness and not requiring an antibiotic. 10% of the patients had a CRP over 100 mg/l and were recommended to receive an antibiotic. Most CRP tests took an additional 5–10 min from the initial consultation with the GP to the patient's total consultation time. Almost all patients found the test useful and would recommend it as it provided reassurance that the symptoms were not serious.
Wakeman et al 2019 ⁴⁶	52 Patients accessed the scheme via referral from GPs, pharmacy staff or self-referral.	Pilot study	Reduction in antibiotic prescribing	Immediate GP referral: 1 (subsequent antibiotic prescription) Self-care recommended: 7. CRP test: 44. CRP test result > 100 mg/ml-5. CRP test result 20–100 mg/ml-4. CRP test result <20 mg/ml-35. Action taken GP referral: 6 (subsequent antibiotic prescription). Watch and wait: 5 (no subsequent GP referral). Self-care: 33 (no subsequent GP referral). Antibiotic prescriptions avoided: 38 Community pharmacy can effectively deliver an efficient CRP POC service with high degrees of patient satisfaction, significantly diminishing the burden of RTIs in general practice with concurrent reduction in unnecessary antibiotic prescribing; in this case by 86%.
Johnson et al 2018 ⁴⁷	19 including healthcare commissioners, pharmacists, primary and secondary care clinicians and public health professionals.	Mixed-methods study including a qualitative survey and quantitative analysis of results from a real-world implementation study.	Value and barriers to CRP POCT adoption Survey respondents confirmed costs and funding as important barriers in addition to physical and operational constraints and cited training and the value of a local champion as enablers.	Survey respondents highlighted the clinical benefits of CRP POCT, but funding remains a barrier to implementation in UK primary care and appears not to be alleviated by the existing financial incentives available to commissioners. The potential to meet incentive targets using lower cost methods, a lack of policy consistency or competing financial pressures and commissioning programmes may be important determinants of local priorities. An implementation champion could help to catalyse support and overcome operational barriers at the local level, but widespread implementation is likely to require national policy change. Successful implementation may reproduce antibiotic prescribing reductions observed in research studies.
Paediatrics				
Schot et al 2018 ⁴⁸	Children between 3	Open, pragmatic,	Reduction in antibiotic prescribing	No statistically significant reduction in antibiotic prescriptions in the CRP group (30.9% versus 39.4%; odds ratio [OR] 0.6; 95% confidence interval

	months and 12 years of age with acute cough and fever	randomised controlled trial		[CI] = 0.29 to 1.23). Only the estimated severity of illness was related to antibiotic prescription. Forty-six per cent of children had POC CRP levels <10mg/L.
COPD				
Butler et al 2019 ⁴⁹	653 COPD patients randomized to receive usual care guided by CRP point-of-care testing (CRP-guided group) or usual care alone	Multicentre, open-label, randomized, controlled trial	Antibiotic reduction	Fewer patients in the CRP-guided group reported antibiotic use than in the usual-care group (57.0% vs. 77.4%; adjusted odds ratio, 0.31; 95% confidence interval [CI], 0.20 to 0.47). A lower percentage of patients in the CRP-guided group than in the usual-care group received an antibiotic prescription at the initial consultation (47.7% vs. 69.7%, for a difference of 22.0 percentage points; adjusted odds ratio, 0.31; 95% CI, 0.21 to 0.45) and during the first 4 weeks of follow-up (59.1% vs. 79.7%, for a difference of 20.6 percentage points; adjusted odds ratio, 0.30; 95% CI, 0.20 to 0.46). CRP-guided prescribing of antibiotics for exacerbations of COPD in primary care clinics resulted in a lower percentage of patients who reported antibiotic use and who received antibiotic prescriptions from clinicians, with no evidence of harm.
Cost-effectiveness studies				
Holmes et al 2018 ⁵⁰	94 patients in UK GP practice	Cost-effectiveness decision analysis model	Resource utilisation	Incremental cost-effectiveness ratios of CRP testing were £19,705 per quality-adjusted-life-year (QALY) gained and £16.07 per antibiotic prescription avoided. Following clinical guideline, CRP testing in patients with LRTIs cost £4390 per QALY gained and £9.31 per antibiotic. At a threshold of £20,000 per QALY, the probabilities of POC CRP testing being cost-effective were 0.49 (ARTI) and 0.84 (LRTI). POC CRP testing as implemented in routine practice is appreciably less cost-effective than when adhering to clinical guidelines
Fawsitt et al 2019 ⁵¹	Network meta-analysis	Probabilistic decision tree	Budget impact	Budget impact more costly with CRP POCT against savings of prescriptions avoided. No assessment of AMR avoided, or CDI avoided
Qualitative studies				
Eley et al 2018 ⁵²	11 intervention practices (eight accepting CRPs;	A qualitative methodology	Views on use of CRP POCT	Participants reported that CRP POCT can increase diagnostic certainty for acute cough, inform appropriate management, manage patient expectations for antibiotics, support patient education and improve

	three declining CRPs) and the eight control practices	including interviews and focus groups		appropriate antibiotic prescribing. Reported barriers to implementing CRP POCT included: CRP cost, time, easy access to the POCT machine and effects on clinical workflow. Participants with greater CRP use usually had a dedicated staff member with the machine located in their consultation room.
Hardy et al 2017 ⁵³	Five family medicine clinics across two US states. 30 clinicians	Qualitative study	Barriers and facilitators to use of C-reactive protein (CRP) point-of-care tests (POCT) in US family medicine clinics for the management of acute respiratory tract infections (ARTIs) in adults.	Clinicians believed CRP POCT could support decision-making for some presentations of ARTIs and patient populations when used in conjunction with clinical criteria. Clinicians had concerns about possible overuse and inaccuracy of CRP POCT which they believed might increase antibiotic prescribing rates. Other concerns identified included integration of the test with clinic workflows and cost-effectiveness. Incorporating CRP POCT with clinical guidelines may strengthen utility of this test, when there is diagnostic uncertainty
Van Hecke et al 2019 ⁵⁴	23 clinicians in South Africa	Qualitative study	Prescribing influencers	Clinicians working in publicly funded clinics in the Western Cape Metro of South Africa saw POCTs as potentially useful for positively addressing both clinical and social drivers of the overprescribing of broad-spectrum antibiotics. They were concerned about the resource implications and disruption of existing patient workflows.
Barriers and facilitators to CRP POCT				
Lamas-Fernandez et al 2019 ⁵⁵		Mathematical modelling	Access to CRP POCT	Different implementation models where POCTs were placed at either GP surgeries, pharmacies or both analysed the trade-offs between cost and travel, and it is possible to achieve a meaningful reduction in the number of necessary POCT facilities to serve a region by referring some patients to be tested at nearby GP surgeries or pharmacies.

Table 1. The most relevant studies included systematic reviews of randomised controlled trials, cluster randomised controlled trials, observational and economic evaluations