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EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT

Comments by external experts on the 2nd draft rapid assessment on OTCA12: C-reactive protein point-of-care testing (CRP POCT) to guide antibiotic prescribing in primary care settings for acute respiratory tract infections (RTIs)

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Elizabeth Beech, NHS Improvement	Document Title		Suggest consider defining the population in the title to ensure clarity to the reader/user: C-REACTIVE PROTEIN POINT-OF-CARE TESTING (CRP POCT) TO GUIDE ANTIBIOTIC PRESCRIBING IN PRIMARY CARE SETTINGS FOR ACUTE RESPIRATORY TRACT INFECTIONS (RTIS) in adults and children.		Thank you. Unfortunately unable to amend the name of the REA at this point.
Elizabeth Beech, NHS Improvement	3		Elizabeth Beech, National Project Lead - Healthcare Acquired Infection and Antimicrobial Resistance, NHS Improvement, England		Changed thank you
Summary					
Elizabeth Beech, NHS Improvement	8	14-17	'How does the analytical performance of the commercially available CE-marked CRP point of-care tests marketed for use in primary care compare with standard laboratory CRP measurement and with each other? That is, are they likely to have equivalent effectiveness in terms of changes in antibiotic prescribing? (SR3 – analytical performance)' There are 2 different questions here that have been linked in a slightly confusing statement that relates to a single question 1. Diagnostic accuracy between tests 2. Impact of use of CRP testing on antibiotic prescribing It would be helpful to rephrase the content in these lines to clarify the question		Agreed – have rephrased this in the summary and elsewhere in the document to provide clarity as to the questions that would be answered by the three systematic reviews and in particular the distinction between diagnostic test accuracy (of CRP) and the analytical performance (which addressed the performance of the devices)
Nuala O'Connor,ICGP' GP Lead HSE Clinical	8	30-34	Consider reword in the context of CRP as a rule-out test: 'In the context of patients presenting to primary care with acute RTIs, the aim of CRP POCT is to rule out serious bacterial infections thereby		Reworded as suggested

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Programme, HCAI-AMR			supporting a decision not to prescribe an antibiotic for those who are unlikely to benefit from treatment.'		
Elizabeth Beech, NHS Improvement	9	15-16	'It is estimated that LRTIs were the fifth leading cause of death and the leading infectious cause of death worldwide in 2015' This is a somewhat misleading statement in this EU HTA context, and it would be more accurate to detail the cause of death, age of people, and country of death as a large proportion of these deaths are in children in Low Income Countries for whom vaccination and antibiotics have reduced accessibility. Advise rephrase to reflect this and note the following sentence reports a lack of EU data. NICE CG 191 report incidence of community acquired pneumonia in context of primary care RTI presentations and associated mortality rates https://www.nice.org.uk/guidance/cg191/chapter/Introduction		Rephrased as follows to reflect data from high income countrie: Worldwide, LRTIs, and in particular, pneumonia are associated with substantial morbidity and mortality. While the disease burden is lower in high-income countries, reflecting better access to vaccines and antibiotics, LRTIs still contribute to increased morbidity and mortality particularly in children aged < 5 years and the elderly.
Elizabeth Beech, NHS Improvement	9	17-21	Missing data reporting the RTI activity in primary care in UK NICE CG 69 report in 1.3.1 a quarter of the population will visit the GP due to an RTI each year - incidence of RTI consultations in primary care from this reference: Ashworth M, Charlton J, Ballard K et al. (2005) Variations in antibiotic prescribing and consultation rates for acute respiratory infection in UK general practices 1995-2000. British Journal of General Practice 55: 603-8 https://www.nice.org.uk/guidance/cg69/evidence/full-guideline-pdf-196853293 and more recently rates of RTIs in England		Thank you. Have limited the country-specific data included in the summary due to recommended word count restrictions.

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			https://www.bmj.com/content/354/bmj.i3410 Advise consider inclusion of this data in addition to that already reported		
Elizabeth Beech, NHS Improvement	9	39	The number of current deaths due to AMR are stated; it would be useful to include the (newly published) EU predictions of deaths in the future also to add context to why reducing unecessary antibiotic use matters		Added text as suggested: AMR contributed to an estimated 33,000 deaths in the EU in 2015, with the highest burden in infants (aged < one year) and those aged 65 years or older. AMR is estimated to cost the EU €1.5 billion each year due to extra healthcare costs and productivity losses. Prudent use of antibiotics to prevent development of AMR is an important component of the 2017 EU action plan against antimicrobial resistance
Martin Cormican, Consultant Microbiologist National Lead for HCAI/AMR.	10		With the exception of AMR, there is no reference to the harms associated with antibotic treatment. While antibiotic-related adverse events (AEs) are common, serious AEs are rare. This could be explained in terms of the relative NNT to NNH for a particular RTI. By prescribing an antibiotic to a patient with a viral RTI, there is no benefit, but there is the prospect of harm through adverse drug events and it will potentially contribute to increased antimicrobial resistance at both the individual and community level.		Thank you – text added to this effect, both in the summary and to Health Burden chapter [A0006]
Elizabeth Beech, NHS	11	14 + 21	It would be useful to include brief statement about the countries in which the studies occurred; both effectiveness and analytic performance		Added note that 10/12 effectiveness studies undertaken in Europe

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Improvement					
Elizabeth Beech, NHS Improvement	12	7	'Two studies (one RCT and one non-randomised study) provided information on whether antibiotics' It would be consistent to include the N= data to this section as has been done previously		Added thank you
Elizabeth Beech, NHS Improvement	12	20	'Studies showed point estimates in favour of usual care when considering the number of patients' It would be consistent to include the number (N) of studies that reported re-consultation		The number (RCTs n=4524) is included along with the RR.
Elizabeth Beech, NHS Improvement	12	24	'None of the included studies reported on physician satisfaction with CRP POCT. Patients were' It would be consistent to include the number (N) of studies that reported patient satisfaction		Added thank you.
Elizabeth Beech, NHS Improvement	12	29	'Only two studies included children and in each case the effect of CRP POCT on the prescription of antibiotics was similar in both adults and children' This phrasing could be confusing. Suggect rephrase as 'All studies included adults, with 2 studies also including children aged (state age range)'		Rephrased. Three studies included children (n=1 age >1 year; n=2 all ages) in addition to adults. In the two studies for which data could be extracted for meta-analysis, the effect of CRP POCT on prescribing of antibiotic was similar in both adults and children. However, one study found a significant effect in both groups while the other reported no effect in

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					both groups. Information on the included studies is also reported in the 'Available evidence section'.
Elizabeth Beech, NHS Improvement	12	30	'None of the retrieved studies assessed the effect of CRP POCT exclusively in older adults (>65 years)' It would be useful to add that N studies included adults aged >65 years but did not report effect by age. Note this then begs the question were patients allocated to active and control/usual care by age? If not bias?		Thank you. Detail on the number studies added. Only one study included an upper age limit (65 years). However, it was not possible to do a planned sub-group analysis for older adults (≥65 years) as none of the retrieved studies assessed the effect of CRP POCT exclusively in this cohort.
Elizabeth Beech, NHS Improvement	13	17	'In LRTI, antibiotics are generally only recommended for the treatment of pneumonia' This statement placing is inconsistent with preceeding syndrome sections which do not have a similar statement. In addition what guidance is this statement based on, as guidelines vary by country? In England non-pneumonia LRTI in older people with co-morbidities advise use of antibiotics if a bacterial infection is suspected. In contrast new NICE guidance advises no antibiotics for acute sinusitis. Advise consider need to include current management guidance (and if so which/whose guidance), and reason for inclusion. If this were a country specific report I would advise inclusion of current		Have removed this sentence from this section as is out of context here. Clarity added to later text in the document around this point and specifically: For LRTI, the use of antibiotics is recommended in patients with pneumonia and in those at higher risk of complications, but antibiotics

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			URTI/LRTI guideline advice as this is very helpful context for considering need for diagnostic test in clinical practice		are not otherwise recommended to treat acute bronchitis.
Elizabeth Beech, NHS Improvement	14	14	'current guidelines for antibiotic prescribing in pneumonia that recommend a cut point of ≥100 mg/L for antibiotic prescribing. [D1001, D1008]' Requires clearer wording as this implies that antibiotics are not prescribed for pneumonia if a CRP <100. NICE CG191 advise antibiotic treatment for all cases of CAP		Have removed this sentence here as context given in the discussion in greater detail.
Elizabeth Beech, NHS Improvement	14	32-33, 44-45	Conflicting reporting of Smart Eurolyser performance 32 the Smart Eurolyser had unacceptably high imprecision. 44 The Smart Eurolyser had acceptable accuracy and precision in the laboratory and at the POC, but had better performance in the laboratory		Agreed – the data for the different studies conflict. This is highlighted in the discussion section.
Elizabeth Beech, NHS Improvement	15	2-3	'Accuracy and precision therefore appear to be negatively impacted when the device is used at the point of care by healthcare professionals. [D1007]' Does this statement apply to all products? It would be useful to report this at the start of the section and then follow onto evidence. This section was hard to read and pull intelligence from; the content is complicated but it would be helpful to reword, or tabulate, to improve clarity for the reader who may have little expert knowledge at a summary level		Agree – it is a little difficult as have to adhere to REA layout of presenting only the findings in the results section.The implications of the findings are then included in the discussion. Text amended to reflect that there were limited studies comparing device performance in a number of settings and that data were only available for a small number of the devices.

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					Sentence rephrased as: Accuracy and precision therefore **may** be negatively impacted when the device is used at the point of care by healthcare professionals.
Elizabeth Beech, NHS Improvement	22	Discussion	'Two studies provided data to suggest that CRP POCT does not lead to an increase in delayed antibiotic prescribing; however, based on the findings of a single study, patients who received a delayed prescription may be less likely to redeem it' The patient numbers associated with these 2 studies are very small. Advise add a comment to this effect in the discussion		Comment added as suggested. Thank you.
Elizabeth Beech, NHS Improvement			'The addition of an educational or communications component may enhance the effect of CRP POCT to inform antibiotic prescribing decisions; however, removal of such studies from the meta-analysis had a minimal impact on the pooled estimate suggesting that the observed effect is largely due to CRP POCT alone' This is the first comment on educational component as a co-intervention – needs to be included in the clinical effectiveness section of the summary.		Due to word count limits in the executive summary, this section of text removed from here as not related to a primary outcome.
Elizabeth Beech, NHS Improvement	23		'In pharyngitis/tonsillitis' Note an absence of reference to diagnostic scoring (centor / FeverPAIN) although reference to RADT is included. Is this an oversight?		The text alludes to the use of CRP as part of a clinical prediction rule. The clinical prediction rule used in the studies were based on the

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					Centor score.
Elizabeth Beech, NHS Improvement	23		'Pneumonia' the scope of this review is primary care management; is CRP use included in CAP guidelines? In England, NICE CG 191 guidance does not advise use of CRP POCT in primary care if there is a clinical diagnosis of pneumonia as antibiotics are prescribed. It would be helpful to report variation in current CAP guidance in EU countries to place CRP use / potential use		Text amended to note that CRP POCT only indicated if uncertainty. The review of guidelines is not complete, so the level of variation is ncertain. Countries for which information on CRP POCT reimbursement was obtained is included.
Elizabeth Beech, NHS Improvement	24	Conclusion	The report summary started with 3 questions, and these are not clearly answered in the summary conclusion; Q1 Does the use of CRP POCT in primary care lead to a significant reduction in antibiotic prescribing without compromising patient safety? (SR1 – effectiveness and safety) Part of this Q is – see comment below		Amended to make this clear
Elizabeth Beech, NHS Improvement	24	Conclusion	'Given the high prescribing rate for acute RTIs, this reduction is likely to be clinically important given the association between antibiotic use and antimicrobial resistance' suggest rephrase to align to the prior content in page 9 lines 27-39 about **individual** AMR risk associated with antibiotic use as this was reported to have the more robust evidence of associated with antibiotic use, than evidence of clinically significant harm Propose Reducing unecessary antibiotic use for self limiting RTIs is likely to reduce		Amended to reflect this point.

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			an individuals future risk of antibiotic resistance		
Elizabeth Beech, NHS Improvement	24	Conclusion	Omission – any ref to the comprimising patient safety part of the above SR1 although note the sepcific ref to safety in children and older adults later in the section		Amended to address this point.
Elizabeth Beech, NHS Improvement	24	Conclusion	Q2 What is the diagnostic test accuracy (DTA) of CRP POCT in relation to acute RTIs? (SR2 – DTA) 'There is very limited evidence for the use of CRP POCT to diagnose acute RTIs in primary care. In patients with ambiguous clinical findings, CRP testing may be useful when used in conjunction with clinical examination or as part of a clinical decision rule to identify those patients most likely to benefit from antibiotic therapy, particularly where there is diagnostic uncertainty based on clinical examination alone. However, further validation of prediction rules incorporating CRP measurement is required' This does not answer the question about accuracy very clearly		Amended to address this point.
Description and technical characteristics of the technology					
Nuala O'Connor,ICGP' GP Lead HSE Clinical Programme, HCAI-AMR	51	B009	Differences in pre-analytical and analytical handling time as well as overall test turn around time are important and would have implications for the acceptability of these devices in primary care		Agreed – have added text to discussion to ensure and to the organisational domain to ensure that this point is reflected.
Nuala O'Connor,ICGP'	53	B009	Smaller primary care practices (single GP) may find it difficult tocomply with the quality assurance requirments for CRP POCT and could represent		Agreed – have noted the requirements for QA in the

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GP Lead HSE Clinical Programme, HCAI-AMR			an important barrier to uptake.		discussion and in the organisational domain to reflect the need for careful planning and an implementation plan that also addresses requirements for quality assurance
Elizabeth Beech, NHS Improvement		Discussion	There is potential learning from Wales where POCT was recently adopted. There was a substantial learning curve for providers and therefore there is a need for careful planning to support implementation.		Thank you. Noted added to organisational domain.
Elizabeth Beech, NHS Improvement		Discussion	Given wide variation between countries in prescribing guidelines, patient access and pathways, and cultures, it is noted that CRP values could be used to change the conversation between clinician and patient, rather than reduce diagnostic uncertainty and subsequent management. If this is the case, and clinicians already have high clinical certainty of diagnosis, the value of the CRP value may be around patient education rather than just clinician behaviour change.		Thank you. Text added to the social domain.
Elizabeth Beech, NHS Improvement			Suggested that there may be potential learning from Norway, as they have developed a substantial quality service around POCT. Wales has introduced a CRP POCT programme.		Text added to organisational domain around the need for careful planning inclusing use of a quality management system is required to support implementation at a regional or national level.
Nuala O'Connor,ICGP'	52	B0009	The volume of consumables used is an important pratical consideration. As considered biohazardous waste, the additional waste generated and		Agreed. The issue of disposal of consumables is included as point in

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GP Lead HSE Clinical Programme, HCAI-AMR			the cost of its disposal will contribute to practice costs		chapter, plus in the organisational domain. This may be relevant for any economic evaluation
Martin Cormican, Consultant Microbiologist National Lead for HCAI/AMR.		Summary / Anaytical performance	While analytical performance of device is important, the level of accuracy to inform good clinical decision making may differ to requirements at a hospital level. The interpretation of the performance will need to be in the context of any cut-points being used and the extent to which it would impact clinical decision making.		Agreed – text added to the discussion to strengthen and clarify this point.
Martin Cormican, Consultant Microbiologist National Lead for HCAI/AMR.			Baseline CRP levels may be elevated in patients with ongoing inflammatory disease, so that the utility / interpretation of CRP test results may be complicated for these patients.		Agreed - noted that elevated CRP levels in inflammatory disease in B0001. SR2 – DTA included data on mean CRP levels to provide context also to this discussion.
Martin Cormican, Consultant Microbiologist National Lead for HCAI/AMR.			The test itself introduces a hazard as it required as it requires skin puncture which in a healthcare setting is associated with risk of transmission of blood borne virus. It is rare but a very significant event when it occurs – experience for example in acute hospitals unless there is a lot of audit glucometers tend to be blood stained and sharps may not always be safely disposed of. Skin puncture /sharps are also associated with risk for staff.		Agree – reviewed in safety chapter (although no data found) and ethical summary.
Health problem and current use					
Elizabeth			It is important to note that a proporation of RTIs are vaccine preventable		Thank you. Text added to A0025:

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Beech, NHS Improvement			and variation in vaccine policy, access and uptake may account for differences in the burden of RTIs in different countries. Vaccines form an important part of the antimicrobial stewardship. For the seasonal influenza accine, it is also important to note that variation in the effectiveness of the vaccine may impact antibiotic prescribing rates. In some years, it is well publicised that the vaccine is less effective, so clinicians will be aware that a larger number of RTI could be viral rather than bacterial origin.		Seasonal influenza is a vaccine-preventable disease and annual Influenza vaccination remains the most effective preventive strategy for severe influenza. While the ECDC recommend the vaccine for all Europeans, it is noted to be especially important for those at higher risk of serious influenza complications: individuals with specific chronic medical conditions, pregnant women, and children aged 6-59 months, the elderly and healthcare workers. Text added to A0023 A proportion of RTIs are vaccine-preventable, with variation in vaccination policy, and access to and uptake of vaccine, contributing to differences in disease burden. As noted in (A0025) seasonal influenza is a vaccine-preventable disease and annual influenza vaccination remains the most effective preventive strategy for severe influenza.

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Nuala O'Connor,ICGP' GP Lead HSE Clinical Programme, HCAI-AMR			Important to identify also evidence that redution in antibiotic usage is not associated with increases in serious complications of RTI (peritonsillar abscess. This is an important clinical consideration; these events are now paticularly rare in developed countriesThese data will not be captured in the shorter term RCTs, but there are data from long term short studies. Reference Gulliford 2016.		Thank you. Text added in relation to this point in the summary, A0006, and in discussing the findings of the safety review.
Nuala O'Connor,ICGP' GP Lead HSE Clinical Programme, HCAI-AMR			Include also reference regarding contribution of antibiotics to multi-drug resistance (for example, fluoroquinolone usage and C diff).		Thank you – Text added to A0003
Nuala O'Connor,ICGP' GP Lead HSE Clinical Programme, HCAI-AMR			Vaccination policies re 'flu, pneumococcus, uptake and efficacy (influenza) also impact disease burden and are an important preventive form of antimicrobial stewardship		Thank you – Text added to A00024/25 and to the discussion
Martin Cormican, Consultant Microbiologist National Lead for HCAI/AMR.			A lot of the discussion and text is framed on reducing antibiotic use to prevent resistance or becaues it is unlikely to be effective. The link between antibiotic use and adverse effects (which are very common) for the individual patient should be fleshed out as these are important given the limited potential to benefit from treatment for most patietns.		Thank you – text added to health burden chapter, safety discussion and the summary to reflect this important point
Martin			With the exception of pneumonia, the majority of RTIs are self-limiting and,		Thank you – text added to health

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Cormican, Consultant Microbiologist National Lead for HCAI/AMR.			even if bacterial in origin, do not warrant antibiotic treatment. Previously clinician were concerned regarding serious complications of RTIs, but these are very rare in the developed world – should include the more recent evidence in relation to these.		burden chapter, safety discussion and the summary to reflect this point.
Clinical effectiveness					
Elizabeth Beech, NHS Improvement			Of interest, a recent systematic review and meta-analysis of CRP to tailor antibiotic use was published in the BMJ open, although noting that it is not limited to CRP POCT. https://bmjopen.bmj.com/content/8/12/e022133		Thank you. We have cross-checked this to ensure we have not omitted relevant studies from our review.
Elizabeth Beech, NHS Improvement			In publication report of 12 month follow up from Little P et al GRACE consortium will provide evidence of sustained impact of use of CRP POCT +/- communication skills. Suggest contact the authors for pre publication information https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(13)60994-0/fulltext		Thank you. We have contacted the authors who have confirmed that the paper has been accepted for publication, but is currently only available as a confidential abstract. As such we cannot include it in the REA. The discussion highlighted that additional data were required to support the long term efficacy of this intervention. We will highlight that this study is in the publication process.
Elizabeth Beech, NHS Improvement			The studies all have a short follow-up for the intervention. It is important to highlight the absence of long term data. If the device stays, does it continue to impact practice?		Thank you – this important clarification has been added.

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			Unpublished reporting from Sunderland (UK) CRP POCT has been introduced into GP care for a fixed 6 month period as a catalyst for behaviour change, and is removed after this time period. Suggest consider this model of use.		General statement included in organisational domain around the need for planning to support implementation.
Elizabeth Beech, NHS Improvement			'The addition of an educational or communications component may enhance the effect of CRP POCT to inform antibiotic prescribing decisions; however, removal of such studies from the meta-analysis had a minimal impact on the pooled estimate suggesting that the observed effect is largely due to CRP POCT alone' It is not clear that this statement is fully supported by the very small number of published studies and appears to be at odds with the findings from the Cals 2009 study which found a substantial effect for the educational/communications trial arm.		Agreed. This systematic review did not evaluate the effectiveness of education / communications as a separate intervention, so the text was written in the context of this being used in conjunction with CRP POCT only. The text has been amended, to omit the end of the sentence: (*suggesting that the observed effect is largely due to CRP POCT alone*)
Elizabeth Beech, NHS Improvement			Important to emphasise that the context is important; CRP POCT is not the only antimicrobial stewardship initiative, rather it is part of a range of initiatives. Delayed prescribing is a very effective intervention for the GP. Use intended only where there is clinical uncertainty to support the findings of the clinical assessment. Noted that it may also have a role in supporting the GPs decision not to prescribe where there is a strongly held		Text added to discussion to reflect this imporant point.

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			patient/carer belief regarding the need for an antibiotic. The relevance of the trial results to the primary care setting will be heavily dependent on a good implementation plan.		
Nuala O'Connor,ICGP' GP Lead HSE Clinical Programme, HCAI-AMR	SR 2 discussion		In terms of interpretation of evidence in CRP in the diagnostic test accuracy review, clarify its value is as a rule-out tool to support reduce prescribing with the overall aim of reducing antimicrobial resistance		Thank you – text added to discussion and summary to reflect this point.
Nuala O'Connor,ICGP' GP Lead HSE Clinical Programme, HCAI-AMR	SR 2 discussion		While the results of SR1 (that CRP POCT is effective at reducing antibiotic prescribing) and the DTA results (SR2) appear to be at odds, it is important to note that CRP POCT is not a diagnostic test for an RTI and there is no good gold standard for diagnosing acute RTIs that require antibiotic treatment in primary care. The importance of the CRP POCT may lie in the fact that it is used to support decision making; to reduce uncertainty and possibly to facitiate a discussion with a patient as to why an antibiotic may not be needed.		Agreed – text amended to reflect this point more strongly.
Nuala O'Connor,ICGP' GP Lead HSE Clinical Programme, HCAI-AMR	SR 3 discussion		The point about the impact of poor accuracy is well made – it is only important in the context of whether the reading is so inaccurate that it would change the prescibing decision – from no antibiotic / delayed antibtioic /immediate antibiotic. Therefore the inaccuracy at the cut-points used is what is important rather than inaccuracy at the extremes (CRP <10 or CRP >>100).		Agreed – text amended to reflect this point more strongly.

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Nuala O'Connor,ICGP' GP Lead HSE Clinical Programme, HCAI-AMR	SR3 - discussion		The evidence that device accuracy is lower /more variable when used in primary care is important. It is also noted that the ease of use data suggest some devices are easier to use and require less pre-handling that others. Both these points are important in terms of practical application in a GP practice setting – devices that are complex or tricky or more time consuming to use or if they require a lot of additional quality assurance will reduce their acceptability in primary care, particularly for single operator GPs		Agreed –this point also discussed in the organisational domain and also in the discussion of the various chapters.
Martin Cormican, Consultant Microbiologist National Lead for HCAI/AMR.			Acknowledge the difficulty summarising the DTA data and their limitations as on the face of it, the sensitivity and specificity are not great, so the results are not convincing. The results do not conflict with the findings from the review looking at its effectiveness in reducing prescribing. It is is possible that the test itself is not useful, but that it still has the desired effect because it is part of a process that encourages consideration and a discussion that an antibiotic might not be needed, despite the uncertainty, it is likelty that CRP POCT supports a culture of appropriate antimicrobial prescribing.		Agreed - thank you.Text added to discussion to reflect this point.
Martin Cormican, Consultant Microbiologist National Lead for HCAI/AMR.			There is a concern that the decision to perform the test becomes one of habit or defensive medicine rather than because the test results are needed to inform a decision. We have seen a proliferation of testing for all conditions which is leading to increased costs, but not necessarily leading to an improvement in the quality of care. There is also a concern that clinicians will start to treat the test rather than the patient. While it can be		Thank you. Text added to reflect that no long term evidence found in relation to the effect of CRP POCT on prescribing behaviour. Text clarified to reflect that indication for CRP POCT is when there is still uncertainty as to the need for an

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			useful to have an objective measure for some patients as part of an education drive to confirm that an antibiotic is not ncessary, driving the process of testing can undermine the confidence of the doctor (and the patient) in their ability to make a clinical diagnosis.		antibioic following a clinical diagnosis.
Martin Cormican, Consultant Microbiologist National Lead for HCAI/AMR.			From a behavioural perspective, there is a concern that patients may transfer their dependency on antibiotic for every RTI to having to have a test to confirm that they don't need an antibiotic – it increases the cost of care and also the concern that there may be treatment of the test, particularly for borderline results.		Thank you. Text added to reflect that further research required to assess the effect of CRP POCT on patient consultation behaviour .
Martin Cormican, Consultant Microbiologist National Lead for HCAI/AMR.			Again, earlier point is relevant. A degree of inaccuracy may be acceptable as it is the accuracy at the cut-points that is important or the extent to which inaccuracies lead to a different decision.		Text added to clarify this point.
Safety					
Elizabeth Beech, NHS Improvement			It is important to highglight that the data in this systematic review do no capture adverse events associated with antibiotic treatment unless result in a reconsultation or a hospital admission. NICE clinical guidelines outline the number needed to harm for different conditions. Findings could be discussed in this context.		Text added to the discussion to reflect this point.
Nuala O'Connor,ICGP'	Discussion		Note earlier point in relation to CRP POCT as a decision support tool. RCT data will not capture rare serious events, so evidence from long term		Agreed – text added to discussion to reflect hte limitiations of the

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GP Lead HSE Clinical Programme, HCAI-AMR			cohort studies important to support the safety of CRP POCT in treatment decisions for patients presenting with acute RTIs, Similarly, the trials capture a limited range of safety issues. The findings should be discussed in the context of the potential for other harms (common ADR etc) associated with antibiotic treatment and the data regarding relative NNT / number needed to harm for various RTIs		evidence.
Martin Cormican, Consultant Microbiologist National Lead for HCAI/AMR.			The data in this systematic review are limited to short term patient follow-up (up to 28 days) and only include side-effects that result in a reconsultation or an admission to hospital. Less serious adverse events are very common with antibiotics – it should be acknowledged that the reduction in these events associated with reduced prescribing was not captured. Rare serious adverse events associate with treatment will also not be captured given the trial sizes. Given that the majority of RTIs are self-limiting, this is an important point – see earlier point about NNT vs NNH.		Text added to acknowledge and clarify this point.
Appendix					
Elizabeth Beech, NHS Improvement	178 and 182		NICE guidance published for antibiotic prescribing for acute otitis media NG91 and sore throat NG84 contain information on NNT and NNH which are useful to quantify the potential benefit		Thank you – these have been updated and this information added to the discussion.

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