

Point-of-care C-reactive Protein (CRP) for the management of patients with acute exacerbation of COPD in primary care

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Chronic Obstructive Pulmonary Disease

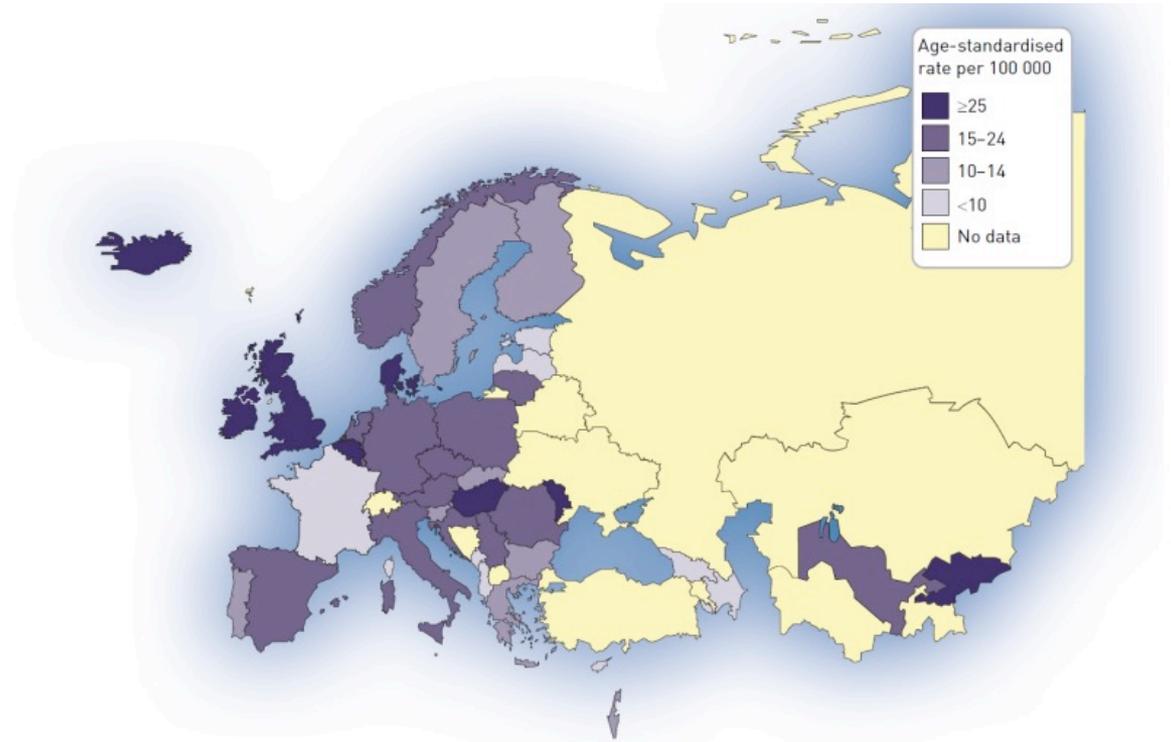


Figure 1 – Mortality rate for chronic obstructive pulmonary disease (COPD). Data from World Health Organization World and Europe Mortality Databases, November 2011 update. Data for some countries are missing because mortality data for asthma and COPD are not reported separately.

Antibiotic use

- Antibiotic prescribing for AECOPD in primary care is very high
 - Over 70% of patients, accounts for approx. 5% of all antibiotic prescriptions in primary care
 - Cochrane review in 2012: insufficient evidence to guide antibiotic prescribing for AECOPD in primary care
- Exacerbations have varied aetiology
 - 60% due to respiratory infections (including bacteria, atypical organisms, viruses)
 - 10% due to environmental pollution
 - 30% of unknown aetiology

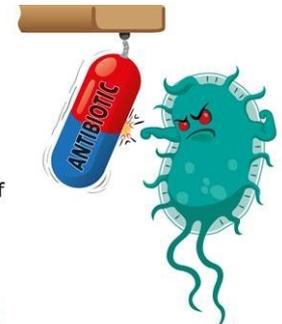


This week is World Antibiotic Awareness Week

The aim of this week is to increase awareness of antibiotic resistance. Antibiotics are a precious resource and we need to keep them working!

Up to 80% of winter illnesses affecting your nose, ears, throat and lungs are viral, so taking antibiotics will not make you feel better.

**#KeepAntibioticsWorking
#AntibioticGuardian #StopSuperbugs**



 **EICH MEDDYGINIAETHAU
EICH IECHYD
YOUR MEDICINES
YOUR HEALTH**

C-Reactive Protein point-of-care test

- CRP point-of-care test
 - A biomarker that rises in response to inflammation
 - Raised levels associated with bacterial infections
 - CRP management found to reduce antibiotic prescribing for other conditions (e.g. LRTI)
 - Antibiotic trial for patients with AECOPD found a differential effect by baseline CRP level (Llor et al, 2012)





The PACE Study

A UK multi-centre Randomised Controlled Trial of the **effectiveness** of CRP-POCT to **safely reduce antibiotic use** in patients presenting with acute exacerbation of COPD in primary care

- NIHR HTA funded study
- Co-Chief Investigators Professors Nick Francis and Chris Butler
- International collaboration

	CCQ worse in CRP-POCT arm	CCQ no worse in CRP-POCT arm
Antibiotic consumption higher in CRP-POCT arm	Intervention unsuccessful	Intervention unsuccessful
No evidence that antibiotic consumption is different in either arm	Intervention unsuccessful	Intervention unsuccessful
Antibiotic consumption lower in CRP-POCT arm	Intervention unsuccessful	Intervention successful

PACE: Guidance on interpretation of the CRP-POCT

CRP Guidance:	
CRP Measurement:	
CRP < 20	Antibiotics are unlikely to be beneficial and usually should not be prescribed.
CRP 20-40	Antibiotics may be beneficial – mainly if purulent sputum is present. You may decide to prescribe antibiotics after taking into account the patient’s underlying health status and the features of the current exacerbation.
CRP > 40	Antibiotics are likely to be beneficial. Consider prescribing antibiotics unless the patient is assessed as being at lower risk of complications and unlikely to have a bacterial infection (no increased sputum purulence and no features suggesting severe exacerbation).

Who did we aim to recruit?



Diagnosis of COPD in GP record



We did not confirm diagnosis with spirometry



≥ 40 years



AECOPD with at least one Anthonisen criterion



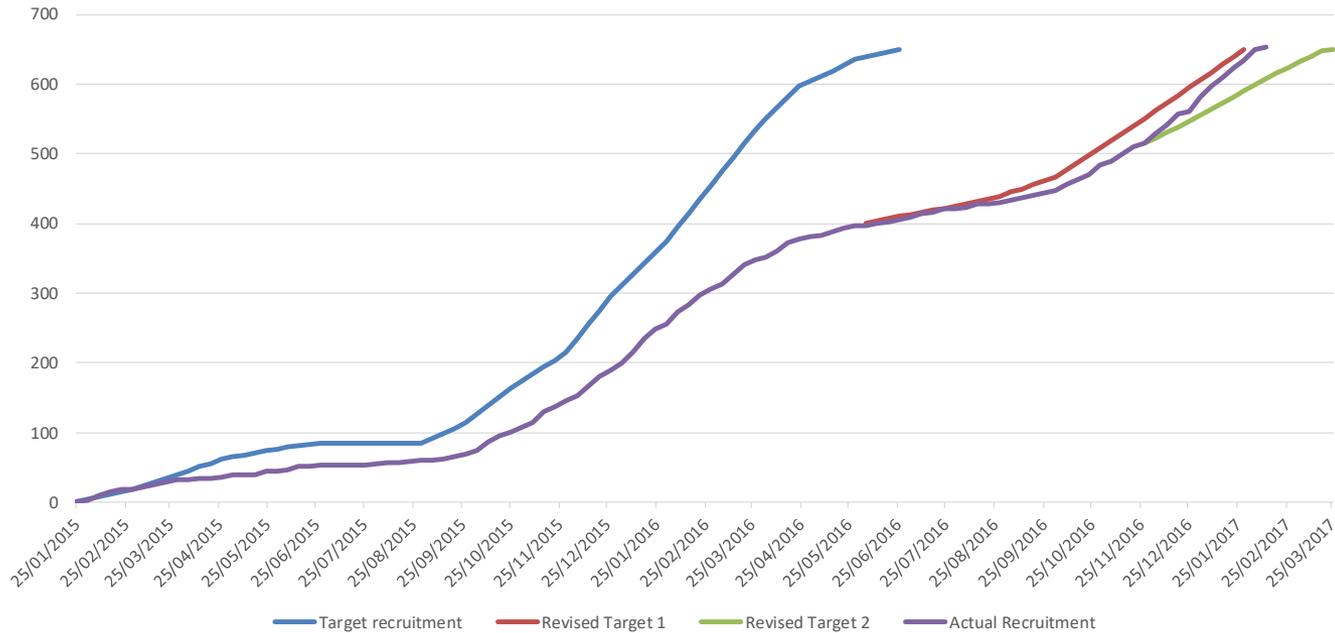
No suspicion of severe illness



No past history of respiratory failure; no active inflammatory condition; no cystic fibrosis; no tracheostomy; no bronchiectasis; not immunocompromised; not currently pregnant

How did we do?

PACE Recruitment Actual v Target



- ✓ 653 recruits across 86 practices
- ✓ 83% antibiotic outcome
- ✓ 87% CCQ outcome
- ✓ 98% randomised to CRP received it

Who did we recruit?

Mean age 68 years (range from 40 to 92 years)

48% female

55% with GOLD II (“moderate”) COPD

Unwell for median 5 days (IQR: 3 to 10 days)

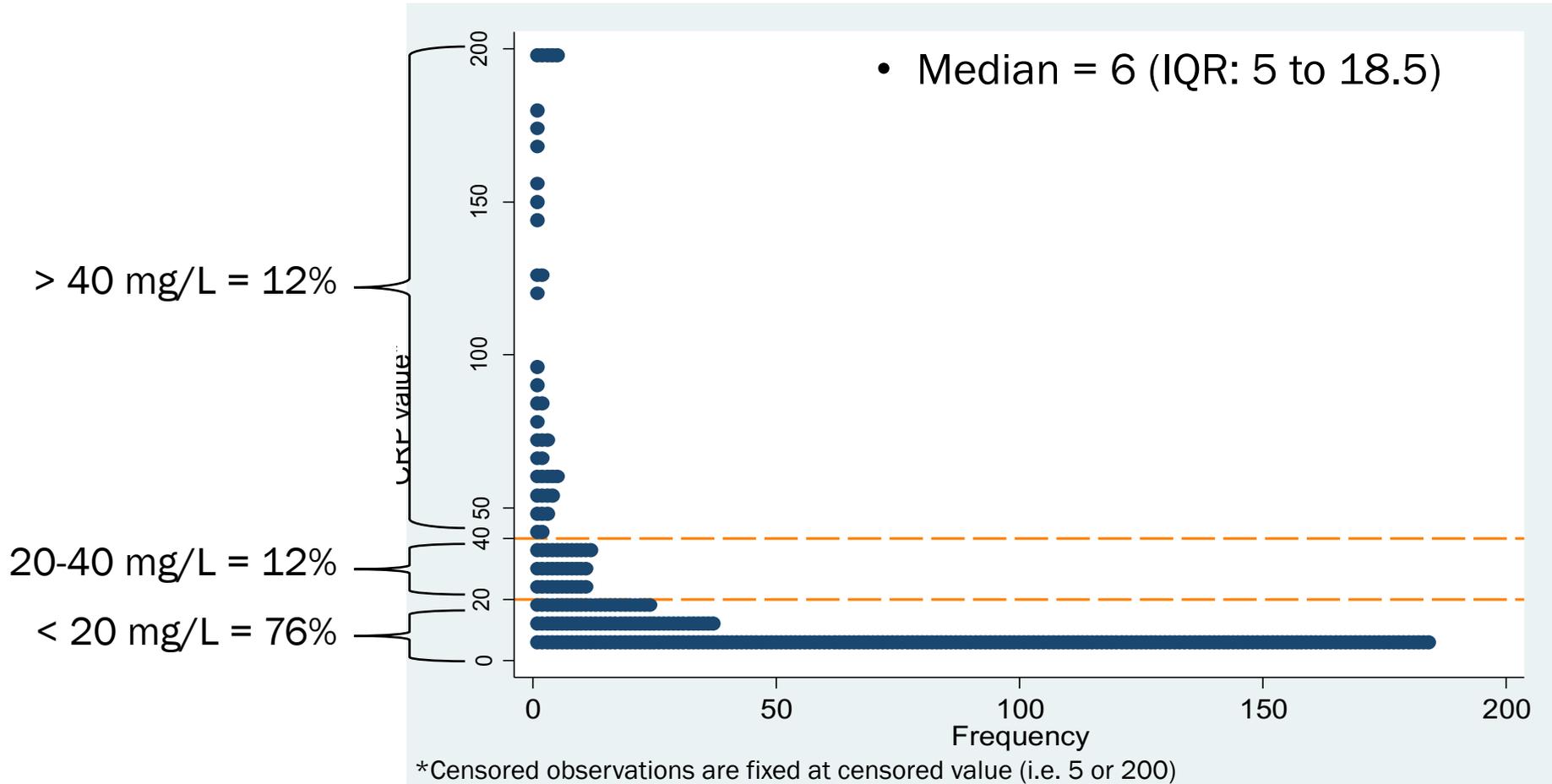
50% with crackles / wheezes

Few participants with evidence of consolidation

45% with all three Anthonisen criteria

44% had a bacterial pathogen cultured from sputum

What did we find?



What did we find?

Antibiotic consumption for AECOPD during the first four-weeks

Usual care: 212/274 (77%)

CRP-POCT: 150/263 (57%)

Adjusted OR: 0.31 (95% CI: 0.20 to 0.47)

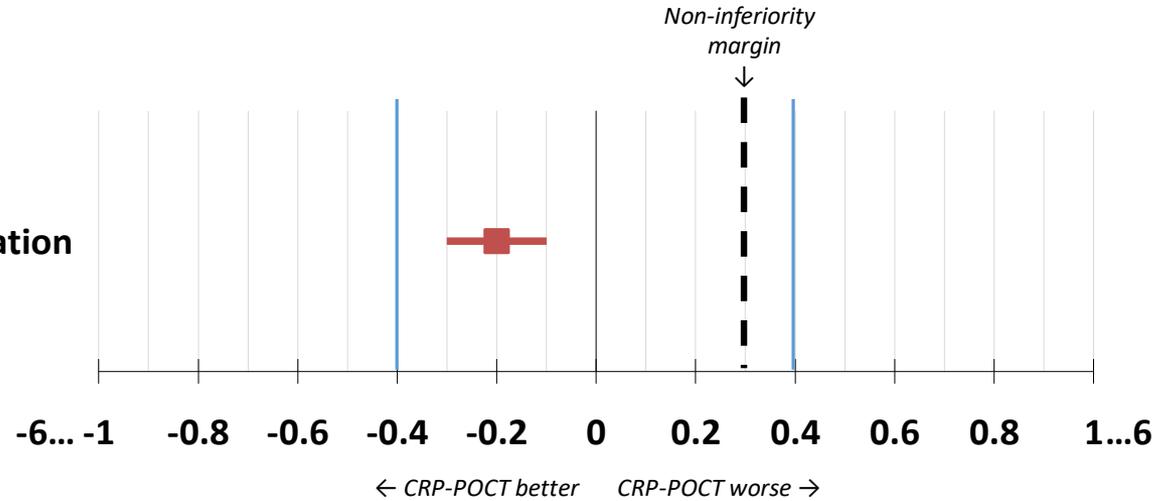
Similar results for all-cause antibiotic consumption and antibiotic *prescribing* outcomes.

Clinic COPD Questionnaire at two-weeks

- Scale from 0 (better health) to 6 (worse health)
- Established MCID of 0.4; *a priori* chosen non-inferiority margin of 0.3

What did we find?

CCQ at two-weeks post-randomisation



Adjusted mean difference (CRP-POCT minus Control)

	CCQ worse in CRP-POCT arm	CCQ no worse in CRP-POCT arm
Antibiotic consumption higher in CRP-POCT arm	Intervention unsuccessful	Intervention unsuccessful
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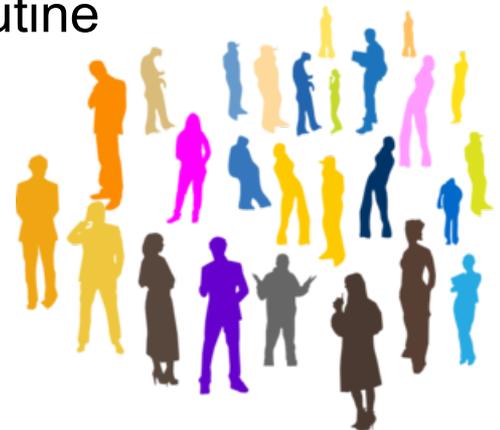
What did we find?

Outcome	Evidence of an effect of CRP-POCT?	Direction (if yes)
Other medication use	No	
Pneumonia diagnosis	No	
COPD health status	Yes	Patients managed with CRP-POCT had better COPD health status
Health-related quality of life	No	
Health service use	No	

Qualitative process evaluation

- What did patients and primary care teams think of the CRP-POCT?
 - Did they think it influenced antibiotic use?
 - Did they like it?
 - Did they understand what it was for?
 - Did they have confidence in the CRP-POCT?
 - Were there any problems with using it?
- How was the CRP-POCT used in practice?
- What did they think about using the test as part of routine care in the NHS?

Study Protocol: Bates, Francis, White et al (2017), *Trials*,
https://orca.cf.ac.uk/105131/1/Bates_et_al-2017-Trials.pdf



Who did we interview?

Table 1: Characteristics of qualitative process evaluation participants			
Patients	N	Prescribed antibiotics at index consultation (n)	Not prescribed antibiotics at index consultation (n)
CRP reading <20	14	4	10
CRP reading >20	6	5	1
Total patients	20	9	11
Primary care staff	N	Made prescribing decisions guided by CRP-POCT result (n)	Carried out the CRP-POCT (n)
General Practitioners	12	12	7
Nurse Practitioners	5	5	5
Non-prescribers			
<i>Practice nurse</i>	1	0	1
<i>Research assistant</i>	1	0	1
<i>Pharmacist</i>	1	0	1
Total primary care staff	20	17	15

How did the CRP-POCT work?

- Providing an objective sign of illness
- Reducing diagnostic uncertainty
- Improving confidence
- Enhancing clinician-patient communication
- Reinforcing prescribers' decisions

It gives something to justify to the patient that it's not just your clinical judgement on the signs and things. That you have actually done a test and that has, you know, given even more back up that the fact that you confidently don't need antibiotics.

(General Practitioner)

The value of the CRP-POCT

I think it's a great idea to measure really sort of how ill you are and whether you really need more treatment or not.

(Female patient, CRP <20, not prescribed antibiotics)



It's shown that we're not always right when we listen in, you know. There is a possibility that this may just be a viral crackle, as opposed to bacterial, but again it's very difficult without the reassurance of the, the CRP, to let the patient go away.

(Nurse Practitioner)

Using the CRP-POCT in routine NHS care



So I think it may help to standardise the treatments that we offer, I definitely think it's a good idea, I think it's something that we should be doing more of, because I think we probably would end up prescribing less antibiotics because of it.

(Nurse Practitioner)

I think where there was a great degree of uncertainty about what the right thing was to do, yeah there are definitely times when you'd be willing to invest that extra bit of time to do it.

(General Practitioner)

Using the CRP-POCT in routine NHS care



I think they're [GPs] doing their best, and I do think that the pinprick test is absolutely amazing and I should ... I would like it to be done as a regular thing if you get a flare up."

(Female patient, CRP<20, not prescribed antibiotics)

Barriers to implementation

*I wasn't happy to be honest, because, simply because they said the test that was OK and [I had] an ever [so] slight inflammation which they took because of this blood test she found and she gave me five days of the steroids, but after the five days I was back to square one.
(Male patient, CRP <20, no antibiotics)*

I'm not daft enough to think that this test was a right/no thing, a yes/no thing and I know that clinical suspicion and judgment and history is far more important"

(General Practitioner)



Barriers to implementation

I think that, you know, in theory that [using the CRP-POCT in routine care] could be very good, but the only thing I would say is that because it's so cumbersome within the consultation clinicians won't use it.

I'm just being honest with you, it takes, you know, 10 minutes to go and sort the machine and calibrate it, you know, how easy is that going to be?"

(General Practitioner)



Getting the CRP-POCT into routine use in the NHS

- **Clinical guidelines:** include use of CRP-POCT for AECOPD
- **Commissioning arrangements:** who will cover costs of equipment and test cartridges?
- **Improvements to technology:** quicker and more portable
- **Information for health professionals:** provide evidence for effectiveness and safety of CRP-POCT guided antibiotic prescribing to increase confidence
- **Information for patients:** how and why antibiotic treatment needs to be targeted, and the role this test can play
- **Clinician-patient communication:** ensure that patients still feel listened to, understand the risks and benefits of the CRP-POCT guided prescribing strategy, and that treatment decisions are made in a patient-centred way

Achieving Impact

- NEJM paper: page viewed >64,000 times, cited 13 times since July
 - <https://www.nejm.org/doi/full/10.1056/NEJMoa1803185>
 - Several more articles for peer-reviewed journals currently under review, in press, and in preparation
- Press release & media coverage
- Animations summarising key findings
 - English: <https://www.youtube.com/watch?v=AtZ7bnbpoNk>
 - Cymraeg: <https://www.youtube.com/watch?v=WHEXVFQ78LE>
- Infographics
 - PACE Infographics (English, Welsh, public dissemination version) available at: <http://www.pace-study.co.uk/>
- Stakeholder impact and dissemination event, June 2018, 52 attendees
 - Echoed findings of the qualitative work
 - Need to consider changes in how primary care services are delivered (e.g. role of nurses & pharmacists)
 - Funding & inclusion in national AMR strategy and COPD guidelines are key

What next?

- How and when should the tests be used to optimize effectiveness and cost-effectiveness?
 - With everyone?
 - When there is clinical ambiguity only?
- What happens when the test is widely implemented beyond the context of a clinical trial?
 - Is the test still used as intended?
 - Does it have an impact on health outcomes and antimicrobial resistance for people with COPD in the long-term?
- Are there other biomarkers that could be useful in this context?
- Could the CRP-POCT be used for other conditions in primary care?

Any questions?

Christopher Butler
Nick Francis
David Gillespie
Fasih Alam
Janine Bates
Rhiannon Phillips
Jonathan Bidmead
Jochen Cals
Brendan Delany
Micaela Gal
Katy Addison
Kerry Hood

Robin Howe
Nigel Kirby
Rachel Lowe
Carl Llor
Hasse Melbye
Gurudutt Naik
Christy Barlow
Helen Stanton
Emma Thomas-Jones
Patrick White
Mandy Wootton
Any many more...



Funding Acknowledgement: This project was funded by the National Institute for Health Research HTA programme (project number 12/33/12).

Department of Health Disclaimer: The views and opinions expressed therein are those of the authors and do not necessarily reflect those of the HTA programme, NIHR, NHS or the Department of Health.

