

ENASPOC

the European Network for Antibiotic Stewardship
at the Point-of-Care

**Guidance on
CRP POC testing and communication
to improve antibiotic prescribing
in children with acute RTIs**

8th November | 2023

ENASPOC

European Network
for Antibiotic Stewardship
at the Point of Care



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Effect of point-of-care tests on antibiotic prescribing rate in children in primary care



**Serious infections are rare (<1%)
but early detection
is important**



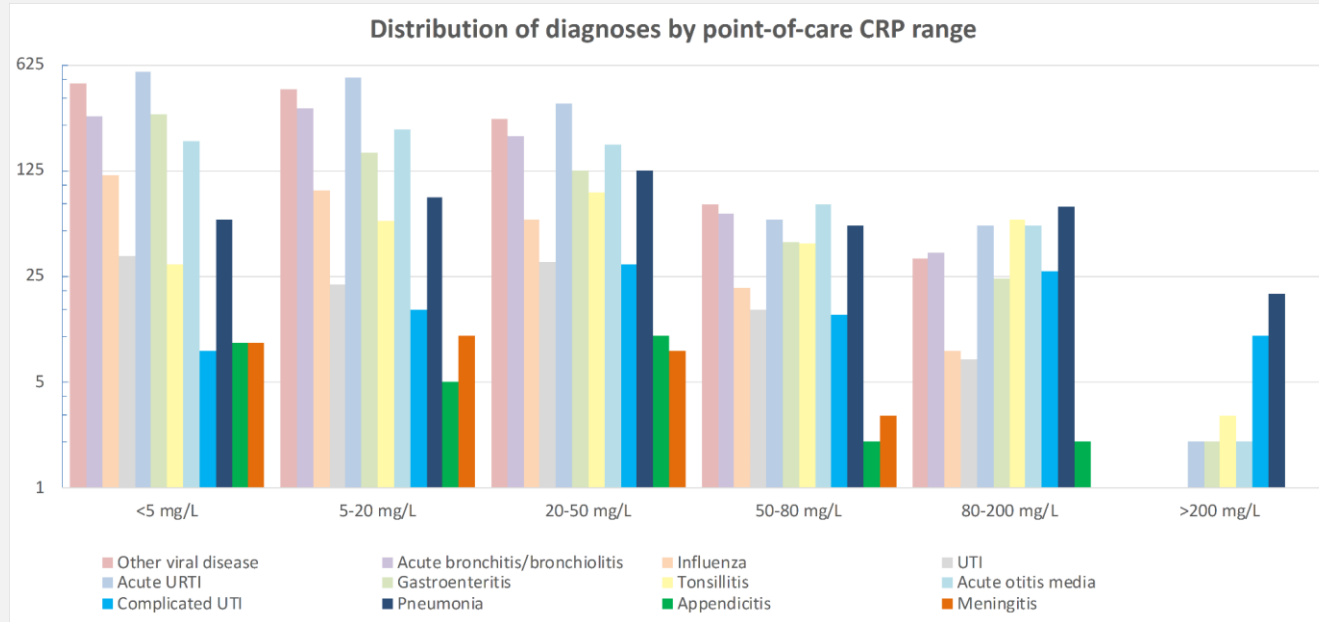
**High-risk for unnecessary
antibiotic prescribing due
to diagnostic uncertainty**



**In Belgium, almost every child
receives one antibiotic
prescription per year**

CRP POCT IN CHILDREN –THE STATE OF CLINICAL EVIDENCE

Point-of-care CRP in children

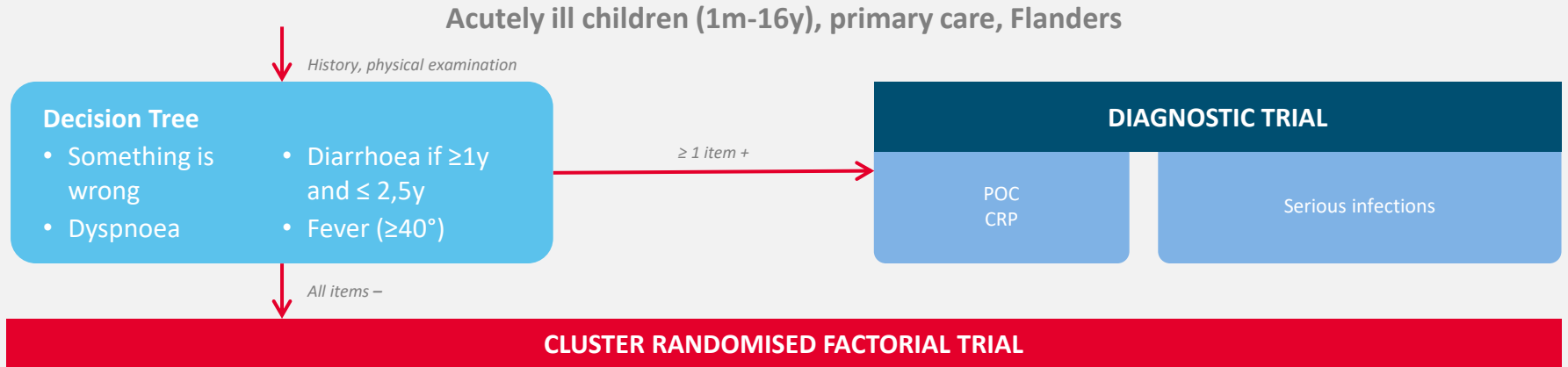


Distribution of frequency of diagnoses by point-of-care CRP range. X-axis displays 5 different point-of-care CRP ranges. Y-axis displays the frequency of the diagnoses on a logarithmic scale. CRP, C-reactive protein; URTI, upper respiratory tract infection; UTI, urinary tract infection

De Rop, L., *et al.* Point-of-care C-reactive protein test results in acute infections in children in primary care: an observational study.

BMC Pediatr **22**, 633 (2022). <https://doi.org/10.1186/s12887-022-03677-5>

Point-of-care CRP in children



Cluster = practice level

- I. POC CRP
- II. brief intervention & safety net
- III. POC CRP + brief intervention & safety net
- IV. usual care

- Antibiotic prescribing rate
- Parental concern
- Parental satisfaction
- Clinical recovery
- Use of medication, diagnostic tests, and medical services
- Health economic evaluation

ERNIE2 trial



Child with a serious infection (admitted to hospital >24 hours)



Children without serious infection



At clinical risk



At clinical risk & CRP \geq 5mg/L

Point-of-care CRP in children

SCANDINAVIAN JOURNAL OF PRIMARY HEALTH CARE
2018, VOL. 36, NO. 4, 423–436
<https://doi.org/10.1080/02813432.2018.1529900>



RESEARCH ARTICLE

OPEN ACCESS Check for updates

Point-of-care CRP matters: normal CRP levels reduce immediate antibiotic prescribing for acutely ill children in primary care: a cluster randomized controlled trial

Marieke B. Lemiengre^a, Jan Y. Verbakel^{b,c}, Roos Colman^a, Kaatje Van Roy^a, Tine De Burghgraeve^c, Frank Buntinx^{c,d}, Bert Aertgeerts^c, Frans De Baets^e and An De Sutter^a



Future research should focus on whether POC CRP can effectively identify children that benefit from antibiotics more accurately, without increasing the risks of under-prescribing



Normal CRP levels **discourage** immediate **antibiotic prescribing**, even when EBM practice guidelines advise differently.



Most likely, a normal CRP convinces FPs to withhold antibiotics when guidelines go against their own gut feeling.

Point-of-care CRP in children

PLOS ONE

RESEARCH ARTICLE

In-vitro diagnostic point-of-care tests in paediatric ambulatory care: A systematic review and meta-analysis

Oliver Van Hecke^{1*}, Meriel Raymond¹, Joseph J. Lee¹, Philip Turner¹, Clare R. Goyder¹, Jan Y. Verbakel², Ann Van den Bruel², Gail Hayward¹



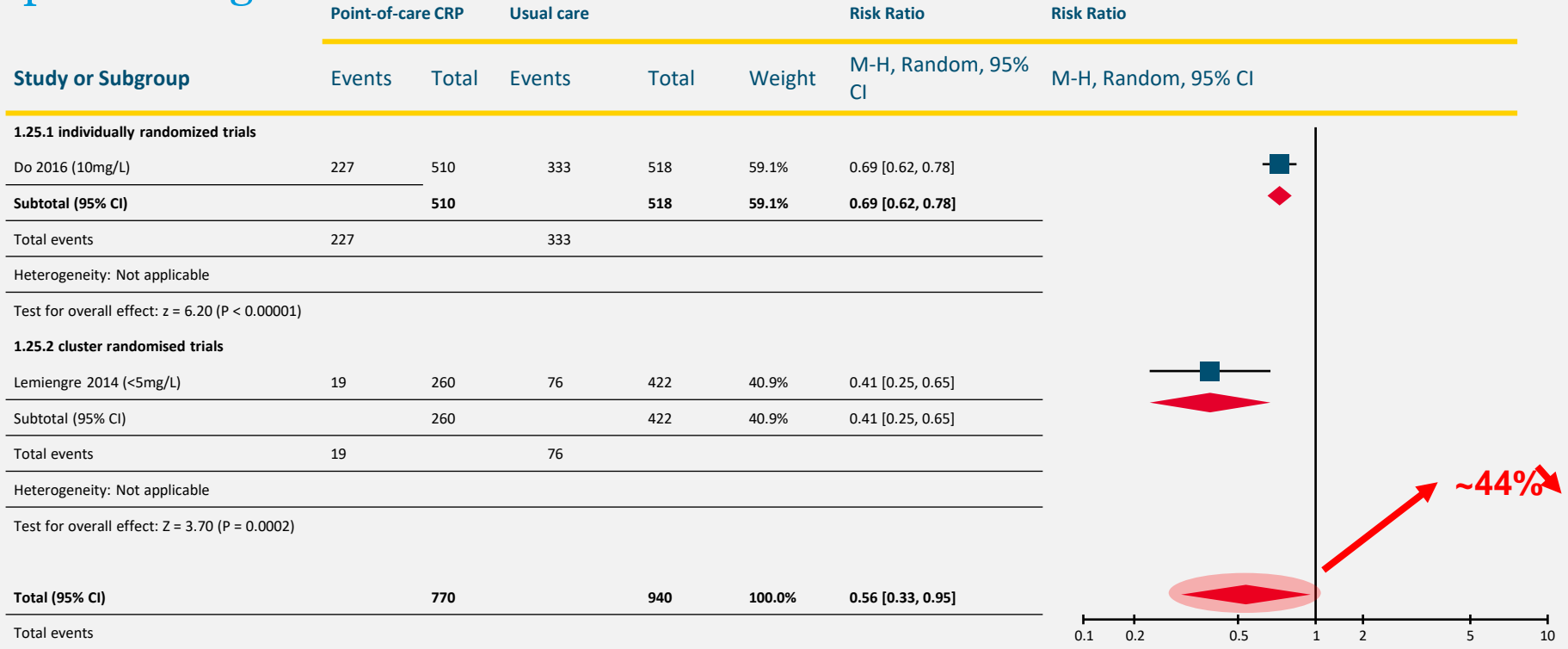
There is emerging evidence that POCT-CRP may better **target antibiotic prescribing** for children with acute RTIs



Research is **urgently needed** to understand where POCTs are likely to improve clinical outcomes in paediatric settings worldwide

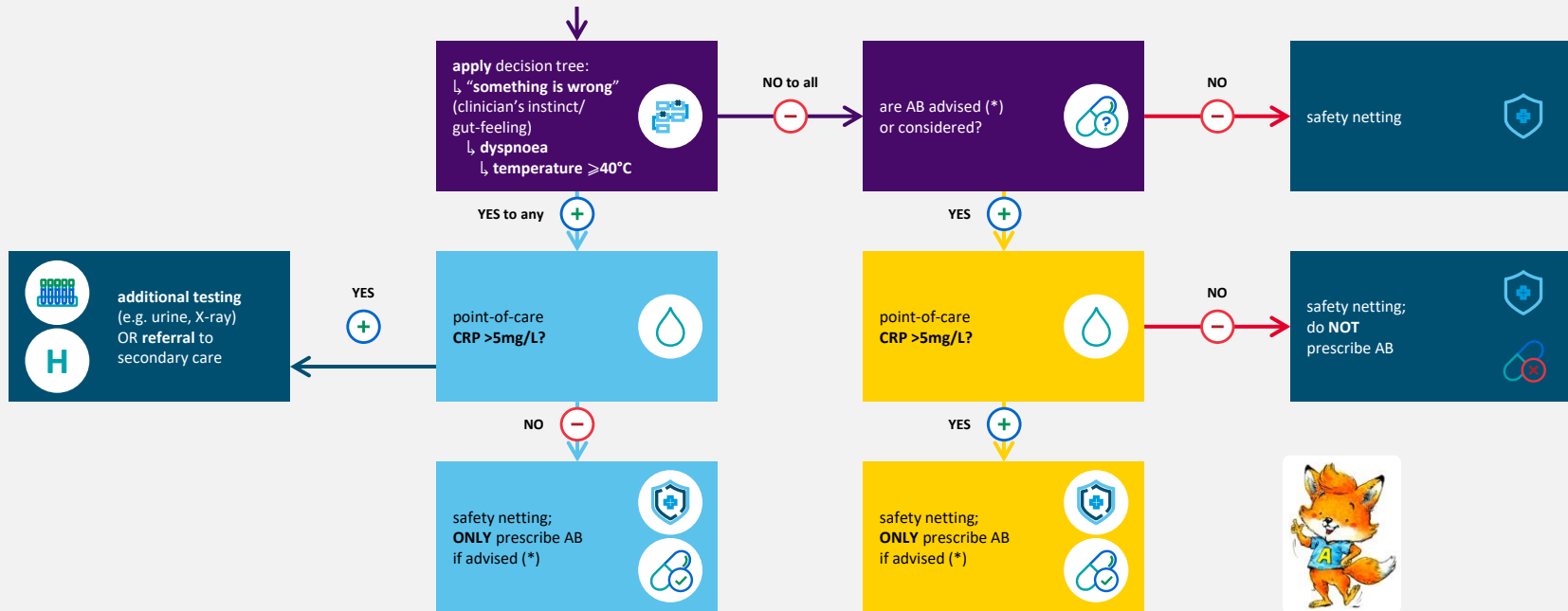
CRP POCT IN CHILDREN –THE STATE OF CLINICAL EVIDENCE

RCTs, children if cut-off guidance applied, immediate AB prescribing rate



The ARON trial: recruitment ongoing

1. Intervention group (diagnostic algorithm)



Ambulatory care

Effect of point-of-care C-reactive protein testing on antibiotic prescription in febrile patients attending primary care in Thailand and Myanmar: an open-label, randomised, controlled trial

- A multicentre, open-label, randomised, controlled trial
- 2410 enrolled patients, of whom 1200 children <12 years

THE LANCET
Global Health

Clinical characteristics and self-reported symptoms

Documented fever (>37.5°C)	200 (50%)	155 (38%)	203 (51%)	143 (35.5%)	223 (56%)	148 (37%)
Neurological symptoms†	62 (15%)	148 (37%)	39 (10%)	156 (39%)	40 (10%)	155 (39%)
Respiratory symptoms‡	326 (81%)	323 (80%)	315 (79%)	315 (78%)	327 (82%)	299 (75%)
Gastrointestinal tract symptoms§	104 (26%)	95 (23%)	124 (31%)	83 (21%)	109 (27%)	68 (17%)
Other symptoms¶	9 (2%)	25 (6%)	41 (10%)	37 (9%)	30 (8%)	43 (11%)

GROUP A

20 mg/L CRP
POCT CUT-OFF

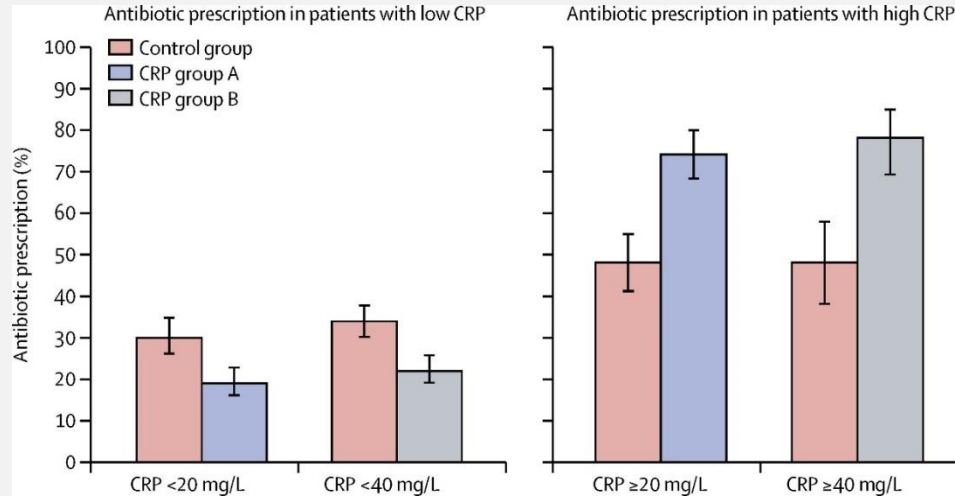
GROUP B

40 mg/L CRP
POCT CUT-OFF

GROUP C

NO CRP POCT

Primary outcome



- A significant difference of antibiotic prescription from day 0 up to day 5 between the control group (318 [39%] of 807) and patients in group B was observed (275 [34%] of 800), with a risk difference of – 5.0 percentage points (95% CI –9.7 to –0.3) and an adjusted odds ratio (aOR) of 0.80 (95% CI 0.65 to 0.98)

Emergency setting

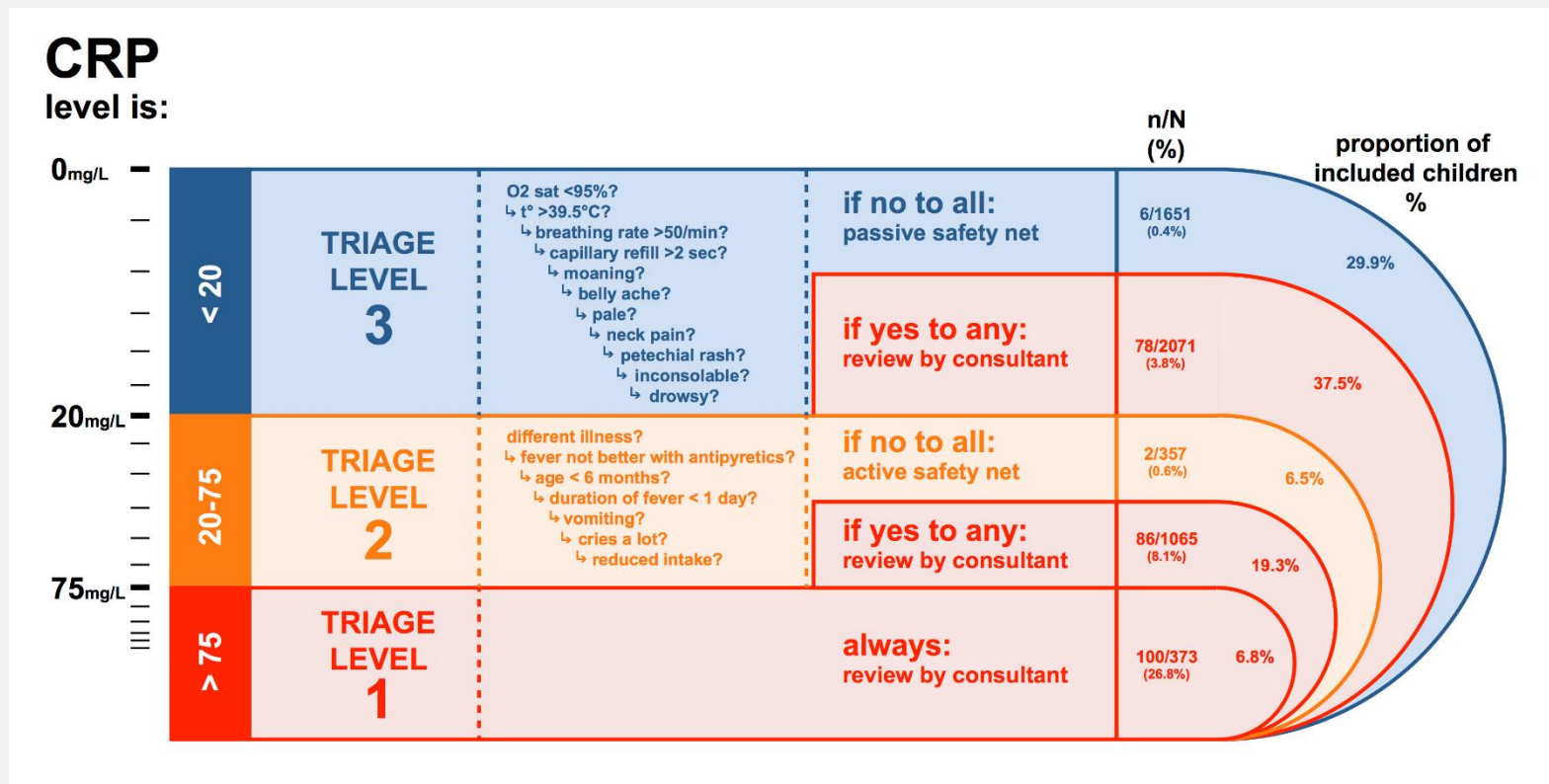
Point-of-care C reactive protein to identify serious infection in acutely ill children presenting to hospital: prospective cohort study

Table 2 Accuracy of POC CRP at different thresholds to diagnose serious infection

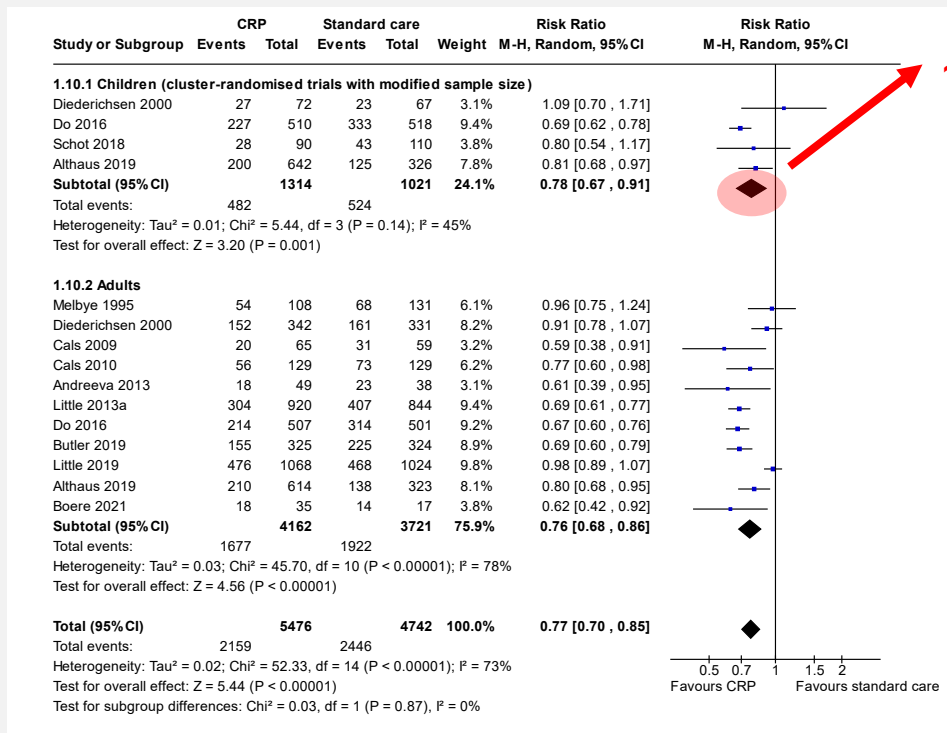
POC CRP threshold	Sensitivity (95% CI)	Specificity (95% CI)	Likelihood ratio (95% CI)		Predictive value (95% CI)	
			negative	positive	negative	positive
≥5 mg/L	90.8 (86.6 to 94.0)	33.4 (32.0 to 34.7)	0.3 (0.2 to 0.4)	1.4 (1.3 to 1.4)	98.5 (97.7 to 99.0)	7.1 (6.3 to 8.0)
≥20 mg/L	73.1 (67.2 to 78.4)	63.9 (62.5 to 65.2)	0.4 (0.3 to 0.5)	2.0 (1.9 to 2.2)	97.7 (97.1 to 98.2)	10.2 (8.9 to 11.7)
≥80 mg/L	35.0 (29.2 to 41.1)	94.8 (94.1 to 95.4)	0.7 (0.6 to 0.8)	6.7 (5.5 to 8.2)	96.3 (95.7 to 96.8)	27.3 (22.6 to 32.5)
≥200 mg/L	9.6 (6.3 to 13.9)	99.7 (99.5 to 99.9)	0.9 (0.9 to 0.9)	37.1 (18.9 to 37.1)	95.2 (94.5 to 95.7)	67.6 (50.2 to 82.0)

Arch Dis Child 2018;**103**:420–426.

Emergency setting



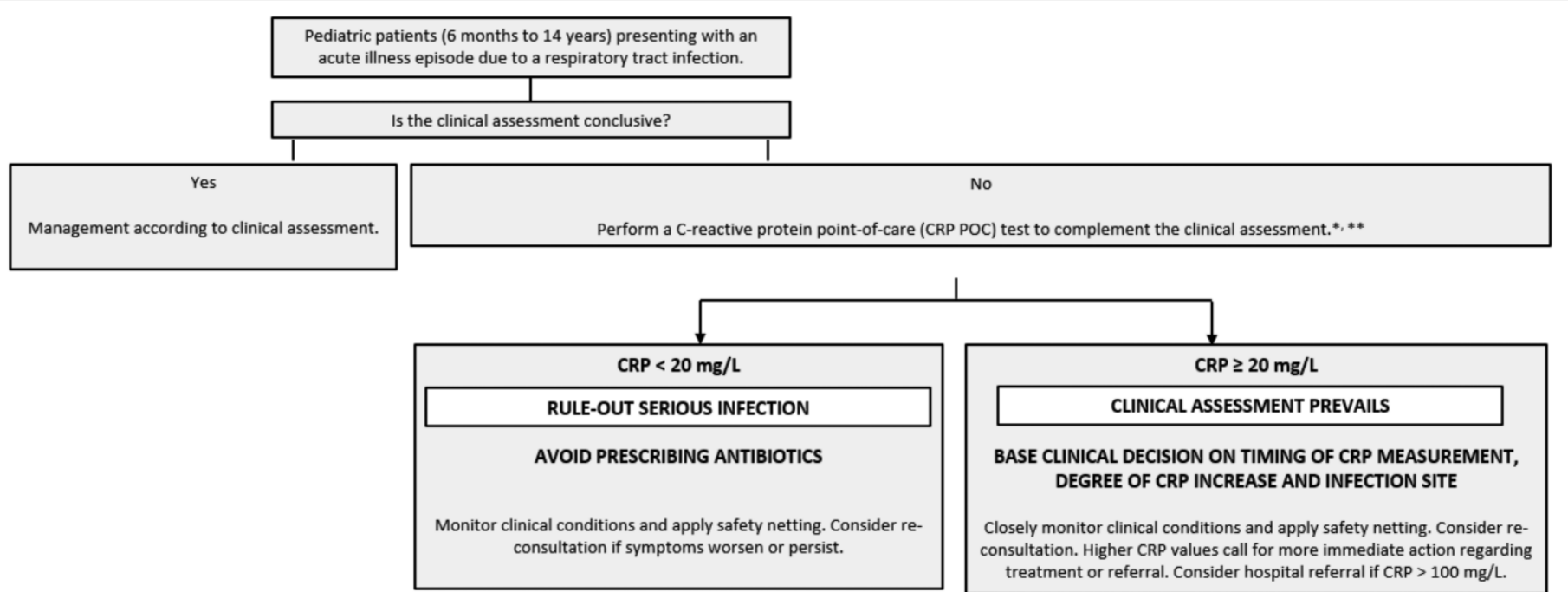
Cochrane update 2022



CONSENSUS STATEMENT #6

In the ambulatory care of febrile children presenting with symptoms of respiratory illness, CRP POCT can be useful to guide decisions regarding antibiotic prescribing and hospital referrals

Our proposed algorithm



* CRP should always be interpreted together with the clinical assessment

** Advise the patient/parents to reconsult, and consider repeating the CRP test, if symptoms worsen after a few days with mild respiratory symptoms

Guidance on CRP POCT cut-off values

CRP < 20 mg/L
RULE-OUT SERIOUS INFECTION
AVOID PRESCRIBING ANTIBIOTICS
Monitor clinical conditions and apply safety netting. Consider re-consultation if symptoms worsen or persist.

- Very high negative predictive value
- No antibiotics' prescription
- Careful monitoring of clinical conditions, particularly if the consultation occurs in the first 24-48 hours of infection

Guidance on CRP POCT cut-off values

CRP < 20 mg/L

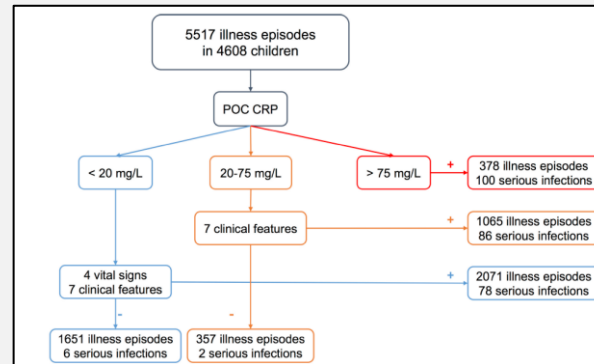
RULE-OUT SERIOUS INFECTION

AVOID PRESCRIBING ANTIBIOTICS

Monitor clinical conditions and apply safety netting. Consider re-consultation if symptoms worsen or persist.

- CRP < 20 mg had a negative predictive value of 99.6%
- 6 infections were missed of whom UTI and bronchopneumonia

- Very high negative predictive value
- No antibiotics' prescription
- Careful monitoring of clinical conditions, particularly if the consultation occurs in the first 24-48 hours of infection



The importance of clinical assessment

CRP \geq 20 mg/L

CLINICAL ASSESSMENT PREVAILS

**BASE CLINICAL DECISION ON TIMING OF CRP MEASUREMENT,
DEGREE OF CRP INCREASE AND INFECTION SITE**

Closely monitor clinical conditions and apply safety netting. Consider re-consultation. Higher CRP values call for more immediate action regarding treatment or referral. Consider hospital referral if CRP > 100 mg/L.

In this scenario the clinical assessment of the patient prevails, and CRP values can be used to complement clinical reasoning using the following parameters:

1. The timing of the CRP measurement
2. The degree of elevation of CRP values
3. The suspected type of infection plays an important role when making a management decision.

CONSENSUS STATEMENT #5

An effective implementation combining CRP POCT together with evidence-based complementary strategies, can increase the contribution to more appropriate antibiotic prescribing

- **Communication skills training for clinicians/physicians**
- **Safety netting advice**
- **Delayed prescribing techniques**
- **Decision aids**

Safety netting advice

Main message to parents	Explanation (more precise and with reasoning)
Antibiotics are great tools but if we do not use them appropriately, they can harm your child.	<ul style="list-style-type: none"> • Antibiotics have many side effects and affect the microbiome by selection of antimicrobial resistant strains. This means that over-use of antibiotics can over time lead to bacterial resistance in your child’s body. • On the long-term antibiotic use can increase the risk autoimmune and allergic diseases and increase the chances of more severe infections which last longer (47).
We need to make sure that antibiotics will work when your child really needs them, and so use them only when they are truly beneficial.	
The presence of cough and/or fever does not mean that your child needs antibiotics.	<ul style="list-style-type: none"> • A cough of 5–7 days is not at all abnormal or necessarily alarming. The average duration of a cough is 3–5 weeks (48). Sometimes, a cough can take a very long time (6–8 weeks), and antibiotics will not necessarily help. • Viral infections can cause cough and fever, and antibiotics do not work against viruses.
Antibiotic resistance is not a problem for some distant future, it’s a problem now.	<ul style="list-style-type: none"> • 1.27 Million deaths related to AMR in 2019. • 1 of 3 hospital deaths related to AMR (3). • AMR is a threat to neonate survival (5).
It is everyone’s responsibility to use antibiotics only when they are needed.	<ul style="list-style-type: none"> • Antibiotics do not help you when the infection is non-severe; The body can fight some RTIs (both bacterial and viral), and antibiotic treatment could reduce symptoms by less than a day, if at all (48).
An invitation to shared decision-making:	<ul style="list-style-type: none"> • Explain CRP predictive values and what certain levels of CRP would mean before reviewing the test results • Review a relevant leaflet or decision aid together • State that if CRP is low, it indicates a minor and self-limiting infection (often viral), and no antibiotics are needed.
I know that you are the parent and that you know your child better than anyone else. And I am a doctor and I know diseases and treatments, and I know my patients.	
Let’s use the CRP POCT to help us reach an agreement on the treatment together.	
Announcement method:	<ul style="list-style-type: none"> • Provide safety-netting advice: if your child’s symptoms get worse, if you feel insecure or your child’s condition changes, please come back for re-consultation
Let’s test the CRP level: if the value is low, it means that your child has a mild infection, so your child should not receive antibiotics.	

KEY MESSAGES



CRP POCT could be an effective strategy to safely reduce antibiotic prescribing in children



Skills training to communicate with parents is key



Safety netting advice is crucial



Decision aids can help reduce diagnostic uncertainty in managing acutely ill children