



CRP AT  
POINT-OF-CARE

CRP & COVID-19:  
SEVERITY & OUTCOME

CRP & COVID-19:  
PRIORITIZATION OF  
HOSPITAL ADMISSION

CRP & COVID-19:  
MONITORING

ANTIBIOTIC  
RESISTANCE/AMR

ANTIBIOTIC  
PRESCRIBING  
& CRP POCT

ANTIBIOTIC  
PRESCRIBING  
DURING COVID-19

TAKE HOME  
MESSAGES



**Abbott**

# WHAT IS KNOWN ABOUT C-REACTIVE PROTEIN (CRP) AT THE POINT-OF-CARE IN THE CONTEXT OF COVID-19 & ANTIMICROBIAL STEWARDSHIP

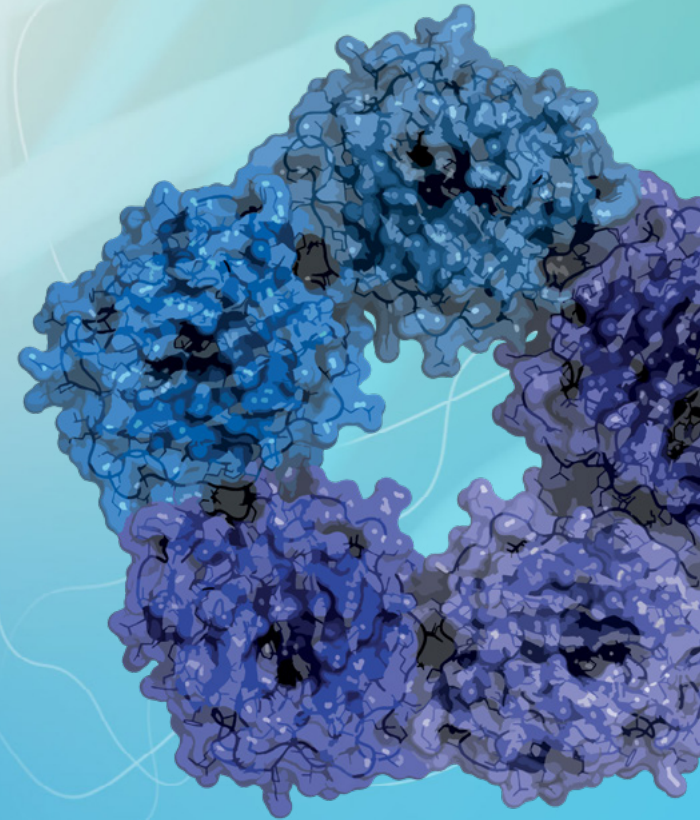




# C-REACTIVE PROTEIN (CRP)

- CRP is one of the cytokine-induced acute-phase proteins.
- CRP levels rise during a general, unspecific response to infections and non-infectious inflammatory processes.<sup>1,3</sup>
- **SINCE ELEVATED CRP LEVELS ARE TYPICALLY ASSOCIATED WITH PATHOLOGICAL CHANGES, THE CRP ASSAY PROVIDES INFORMATION FOR THE DIAGNOSIS, THERAPY AND MONITORING OF INFLAMMATORY DISEASES.**<sup>1-3,7</sup>
- While the CRP response is normally much higher for bacterial infections, specific viral infections can also cause elevated CRP levels.<sup>7</sup>
- Serum or plasma CRP levels:
  - In healthy persons < 5 mg/L.<sup>4-6</sup>
  - Within four to eight hours after an acute inflammatory event > 20 to 500 mg/L.<sup>7</sup>
- Abbott invented the first point-of-care (POC) CRP test in 1989.

1. Kushner et al. Baillieres Clin Rheumatol 1994; 2. Pepys et al. JCI 2003; 3. Van Leeuwen et al. Baillieres Clin Rheumatol 1994; 4. Claus et al. J Lab Clin Med 1976; 5. Dati et al. Eur J Clin Chem Clin Biochem 1996; 6. Dati et al. Clin Chem Lab Med 2001; 7. Morley et al. Acad Sci 1982





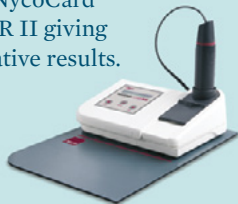
# PIONEERS IN CRP POC TESTING FOR 30 YEARS

Over the past three decades, Abbott has been dedicated to providing the very latest innovations in point-of-care testing – helping to improve diagnostic outcomes for both doctor and patient.

The semi-quantitative test NycoCard™ CRP Visual is launched.

1989

The NycoCard™ CRP Single Test is launched for the NycoCard® READER II giving quantitative results.



2000

The fully automated Afinion™ CRP point-of-care immunoassay is launched on the Afinion™ AS100 Analyzer.



2005

The Afinion™ 2 analyzer is launched, marking the next generation in diagnostic devices.



2017

The third generation Afinion™ CRP test is released, with improved precision.



2018



# AFINION™ CRP

Easy-to-use all-in-one  
cartridge.

No user calibration  
necessary.



Minimally invasive  
for the patient, 2.5 µL  
fingertick sampling.

Excellent agreement with  
laboratory methods.<sup>1-7</sup>

RESULTS IN  
**3** MINS



1. Verbakel et al. J Clin Pathol 2014 J; 2. Hughes et al. Clinical Pharmacist 2016; 3. Ivaska et al. PLOS ONE 2015; 4. Brouwer et al. Clin Chim Acta 2015; 5. Minnaard et al. Scand J Clin Lab In 2013; 6. Bukve et al. Clin Chem 2016; 7. Minnard et al. Scand J Clin Lab Invest 2015



# CRP IN THE ASSESSMENT OF PATIENTS WITH RESPIRATORY SYMPTOMS IN THE COVID-19 PANDEMIC

**CRP VALUES HIGHER  
THAN NORMAL LEVELS  
HAVE BEEN FOUND  
IN THE MAJORITY  
OF PATIENTS WITH  
COVID-19, ESPECIALLY  
IN SEVERE CASES.<sup>1-12</sup>**

While the CRP response is normally much higher for bacterial infections, specific viral infections can also cause elevated CRP-levels.<sup>13-15</sup>

Above-normal CRP values are often exceeded within 4-8 hours after an acute inflammatory event.<sup>16</sup>

1. CDC. 27. Oct. 2020. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease; 2. Luo et al. medRxiv preprint 2020; 3. Wang et al. Open Forum Infect Dis 2020; 4. Tan et al. ORCID iD: 0000-0002-2522-4524; 5. Li et al. Journal of Infection 2020; 6. Gao et al. J Med Virol 2020; 7. Guan et al. N Engl J Med 2020; 8. Zhu et al. ORCID iD: 0000-0001-7718-9591; 9. Chen et al. Lancet 2020; 10. Cao et al. medRxiv preprint 2020; 11. Zhang et al. Scandinavian J Clin Lab In 2020; 12. Dong et al. International Journal of Medical Sciences 2020; 13. Jeon et al. Korean J Clin Lab Sci 2017; 14. Vasileva et al. Inflammation Research 2019; 15. Wu et al. International Journal of Infectious Diseases 2016; 16. Morley et al. Acad Sci 1982





CRP at admission may reflect disease severity in COVID-19 patients and may be an independent predictor of adverse outcomes.<sup>1-7</sup>

## CDC<sup>1</sup>

“Lymphopenia, neutrophilia, elevated serum alanine aminotransferase and aspartate aminotransferase levels, elevated lactate dehydrogenase, high CRP, and high ferritin levels may be associated with greater illness severity.”

1. CDC, 27. Oct. 2020. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease; 2. Luo et al. medRxiv preprint 2020; 3. Wang et al. Open Forum Infect Dis 2020; 4. Tan et al. ORCID iD: 0000-0002-2522-4524; 5. Li et al. Journal of Infection 2020; 6. Zhang et al. Scandinavian J Clin Lab In 2020; 7. Stringer et al. Int J Epidemi 2021





# A SYSTEMATIC REVIEW & META-ANALYSIS<sup>1</sup>

28 and 7 studies were selected for a systematic review and a meta-analysis, respectively.

## 4,663

patients were  
included.

The most prevalent laboratory findings were:

- ↑ CRP (73,6%)
- ↓ albumin (62,9%)
- ↑ erythrocyte sedimentation rate (61,2%)
- ↓ eosinophils (58,4%)
- ↑ interleukin-6 (53,1%)
- ↓ lymphocytes (47,9%)
- ↑ lactate dehydrogenase (LDH) (46,2%)

A meta-analysis of seven studies with **1,905 patients** showed that **increased CRP (OR 3.0)**, lymphopenia (OR 4.5), and increased LDH (OR 6.7) **were significantly associated with severity.**

These results demonstrated that more attention is warranted when interpreting laboratory findings in patients with COVID-19. **Patients with elevated CRP levels, lymphopenia, or elevated LDH require proper management and, if necessary, transfer to the intensive care unit.**



# CRP in COVID-19: SEVERITY ASSESSMENT & OUTCOME PREDICTION<sup>1</sup>

1,564

patients were  
included.

271

patients were  
included in the  
validation cohort.

The study findings support the routine assessment of serum CRP as an adjunct in the early diagnosis and assessment of illness severity of hospitalized patients with COVID-19.

The distributional characteristics of CRP indicated an optimal cut-off of  $\geq 40$  mg/L was associated with mortality.

This threshold may assist clinicians in using CRP as an early trigger for enhanced observation, treatment decisions and advanced care planning.

$\geq 40$   
mg/L





# SEVERITY ASSESSMENT & OUTCOME PREDICTION

- In a UK study, String et al. demonstrated that **CRP of  $\geq 40$  mg/L on admission to hospital should be seen as a reliable indicator of disease severity and increased risk of death** (1,564 adult patients, validation cohort 271 patients).<sup>1</sup>
- In a group of 298 patients with COVID-19, Luo et al. identified **CRP at admission as an independent predictor of adverse outcome** (84 patients) with a significantly higher AUC than age, neutrophil count and platelet count (0.896 vs. 0.833, 0.820, 0.678).<sup>2</sup>
- Wang et al. found that **only CRP was significantly associated with the progression of COVID-19 patients** (16 of 209 patients). A multivariate analysis suggested that **for every 1-unit increase in CRP level, the risk of developing severe events increased by about 5%**.<sup>3</sup>
- Tan et al. found that **CRP in severe COVID-19 patients increased significantly at the initial stage, prior to CT findings**. CRP was associated with disease development and predicted early severe COVID-19 (27 patients; six developed severe disease).<sup>4</sup>
- The study of Li et al. with 132 COVID-19 patients indicated that **CRP is valuable in predicting the severity and distinguishing critically ill patients from mild ones**.<sup>5</sup>

Cut-off 40 mg/L

Sens: 84%

Spec: 33%

Cut-off 41,4 mg/L

AUC 0,896

Sens: 90,5%

Spec: 77,6%

Cut-off 26,9 mg/L

AUC 0,844

Sens 81,3%

Spec 79,3%

Cut-off 20,42 mg/L

AUC 0,87

Sens 83%

Spec 91%

Cut-off 24,65 mg/L

AUC 0,85

**AUC:** area under the receiver operating characteristic (ROC) curve



# MULTI-CRITERIA DECISION ANALYSIS TO PRIORITIZE HOSPITAL ADMISSION

of patients affected by  
COVID-19 in settings with  
hospital bed shortages.<sup>1</sup>

**MEWS:** Modified Early Warning Score (pulse and respiratory rates, systolic blood pressure, body temperature, neurological symptoms)

**96 experts from Italy** were asked to score the criteria's weights to prioritize hospital admission to be used in low- and middle-income countries in an online survey.

**They selected 11 criteria to prioritize hospital admission – among those CRP.**

“According to experts’ evaluation of COVID-19 patients, all ages are considered potentially at risk of rapid deterioration of clinical condition. Although PaO<sub>2</sub> – or alternatively O<sub>2</sub> saturation – are essential parameters, both MEWS and BMI should be considered to predict negative clinical outcome and not deferrable need of hospitalization.”

“In case of a large volume of patients entering healthcare facilities, point-of-care CRP testing can be adopted as a criterion in the proposed prioritization model.”



# MULTI-CRITERIA DECISION ANALYSIS TO PRIORITIZE HOSPITAL ADMISSION

of patients affected by  
COVID-19 in settings with  
hospital bed shortages.<sup>1</sup>

Selected 11 criteria to prioritize hospital admission <sup>1</sup>	Levels	Mean weights, summing to 100%
1. PaO2	<70 mmHg	16.3%
2. Peripheral O2 saturation	<92%	15.9%
3. Chest X-ray	bilateral interstitial lung abnormalities	14.1%
4. Modified Early Warning Score (MEWS) including pulse rate, respiratory rate, systolic blood pressure, body temperature, and neurological symptoms.	3-4	11.4%
5. Respiratory rate	>20 breaths/min	9.5%
6. Comorbidities	diabetes, pre-existing respiratory/ cardiovascular diseases, and onco-hematological diseases	6.5%
7. Living with vulnerable people	i.e. people with comorbidities, pregnant women, or immunosuppressed patients	6.4%
8. Body mass index (BMI)	>40	5.6%
9. Duration of symptoms before hospital evaluation	4-7 days	5.4%
<b>10. CRP</b>	<b>high by local cut off</b>	<b>5.1%</b>
11. Age	>70	3.8%



Clinical risk score to identify patients with COVID-19

# AT HIGH RISK OF CRITICAL CARE ADMISSION OR DEATH.<sup>1</sup>

1. Galloway et al. Journal of Infection 2020

Risk score incorporating 12 characteristics <sup>1</sup>	Mean weights, summing to 100%
1. Age	> 40
2. Male gender	
3. Non-white ethnicity	
4. Oxygen saturation	< 93%
5. Radiological severity score	> 3
6. Neutrophil count	> 8.0 x10 <sup>9</sup> /L
7. CRP	> 40 mg/L
8. Albumin	< 34 g/L
9. Creatinine	> 100 µmol/L
10. Diabetes mellitus	
11. Hypertension	
12. Chronic lung disease	

# 1,157

patients were included.

**Risk scores of 4** or higher corresponded to a 28-day cumulative incidence of **critical care admission or death** of **40.7% vs. 12.4%** for scores less than 4.



# CRP IN THE ASSESSMENT OF PATIENTS WITH RESPIRATORY SYMPTOMS IN THE COVID-19 PANDEMIC.

1. Feldt et al. STAKOB 2020; 2. Chinese National Health Commission; 3. March 2020. Chinese COVID-19 Management Guidelines 3. SIMEU. 12. March 2020. Covid-19 First Line Report PS/DEA management organisational structure as part of an epidemic or pre-epidemic outbreak; 4. Regional Council of Campania Directorate General for the Protection of Health. Feb. 2020. Operational guidelines identification/management of suspected and proven cases of suspected Coronavirus; 5. IFCC. 6. April 2020. Information Guide on COVID-19; 6. Chinese Center for Disease Control and Prevention. 20. Aug. 2020. Treatment Strategies to Prevent Mild to Severe Progression of COVID-19 Cases; 7. Shi et al. JAMA Cardiology 2020; 8. Guo et al. JAMA Cardiol 2020; 9. Madjid et al. JAMA Cardiol 2020; 10. Xu et al. medRxiv preprint 2020; 11. Mehta et al. Lancet 2020; 12. Huang et al. Lancet 2020; 13. Cao et al. medRxiv preprint 2020; 14. Zhou B. Research Square 2020

## Monitoring:

In patients with confirmed COVID-19, monitoring of inflammation markers such as CRP is recommended as part of a panel of chemistries by organizations in certain countries e.g. by Chinese and Italian guidelines, the Robert Koch Institute Germany and the IFCC.<sup>1-6</sup>

## Elevated CRP levels may reflect severe complications in COVID-19, e.g.:

- Cardiac complications, including myocardial infarction, induced by the high inflammatory burden of COVID-19.<sup>7-10</sup>
- Cytokine storm induced by viral invasion. As a result CRP increases.<sup>10-12</sup>
- Secondary bacterial infection also associated with poor clinical prognosis.<sup>13,14</sup>
- Germany and the IFCC.<sup>1-6</sup>



# ANTIMICROBIAL RESISTANCE

2014:

700,000

deaths per year.<sup>1</sup>

Estimate for

2050:

10 million

deaths per year. More than the  
number of people that currently  
die from cancer.<sup>1</sup>



“Antibiotics are a special category of antimicrobial drugs that underpin modern medicine as we know it: if they lose their effectiveness, key medical procedures (such as gut surgery, caesarean sections, joint replacements, and treatments that depress the immune system, such as chemotherapy for cancer) could become too dangerous to perform.”

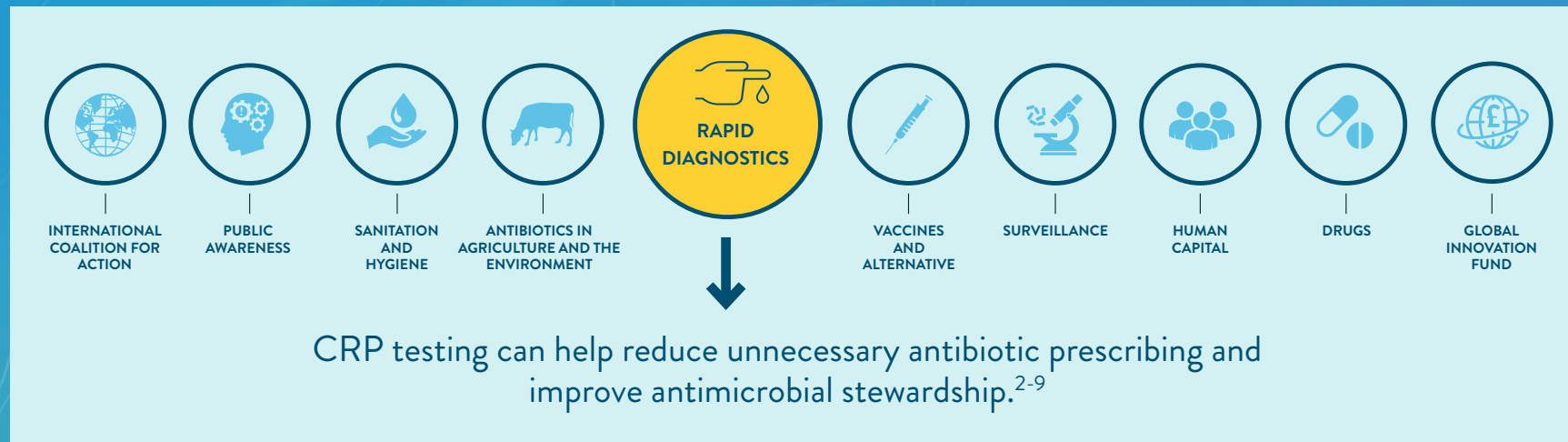
Review on Antimicrobial Resistance, 2016<sup>1</sup>





# WE CAN AVOID CRISIS WITH BETTER ANTIMICROBIAL STEWARDSHIP

A review commissioned by the British Government recommends the following strategies for promoting antimicrobial stewardship:<sup>1</sup>



1. O'Neill J. AMR Review 2016; 2. Cals et al. BMJ 2009; 3. Cals et al. The Annals of Family Medicine 2010; 4. Andreeva et al. BMC Family Practice 2014; 5. Little et al. The Lancet 2013; 6. Butler et al. N Engl J Med 2019; 7. Verbakel et al. BMJ Open 2019; 8. Cooke J et al. BMJ Open Resp Res 2020; 9. O'Brien et al. EUnetHTA Project ID: OTCA012. 2019





“ Today, antibiotics are rarely prescribed based on a definitive diagnosis. Diagnostic tests can show whether or not an antibiotic is actually needed.

*Having rapid, low-cost, and readily available diagnostics is an essential part of the solution to this urgent problem.”*

Dr. Margaret Chan,  
Director General of the World Health Organization<sup>1</sup>





# OVERPRESCRIBING OF ANTIBIOTICS FOR RESPIRATORY TRACT INFECTIONS (RTIs) IS A SERIOUS PROBLEM

- RTIs remain the most common reasons to prescribe antibiotics in primary care.<sup>1-2</sup>
- However, **90%** of RTIs are caused by a virus, meaning most patients are unlikely to benefit from this treatment.<sup>1,3</sup>



# ANTIBIOTIC PRESCRIBING & CRP POINT-OF-CARE TESTING

- Together with signs and symptoms, CRP at the point-of-care can be used to **differentiate between viral or self-limiting bacterial infections** and severe bacterial infections in patients presenting with **respiratory tract infections (RTIs)**.<sup>1-8</sup>
- Thus, it helps physicians to identify patients with RTIs who would benefit from antibiotics, and those who would not.<sup>1-8</sup>



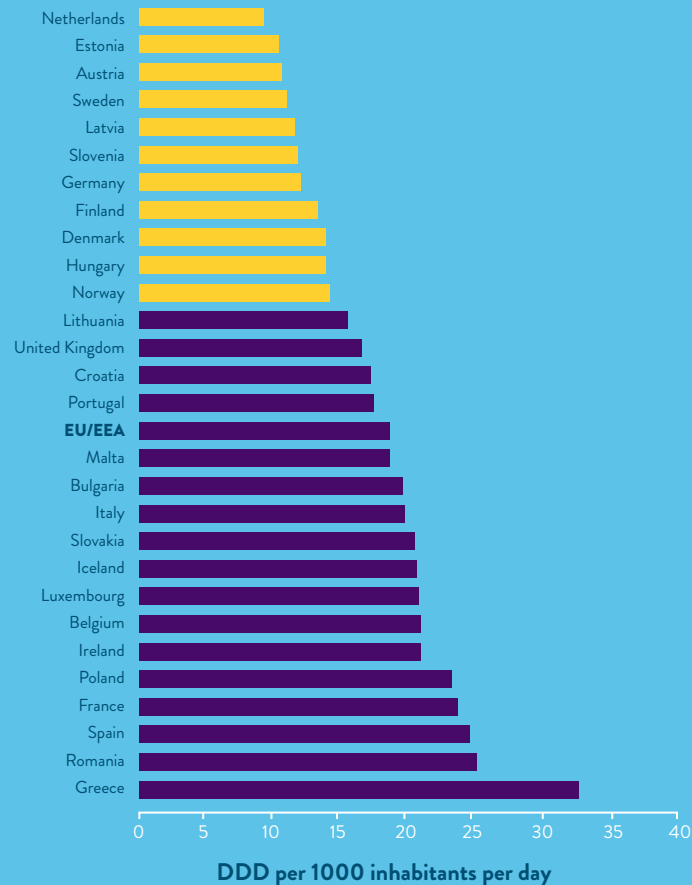


# CRP POINT-OF-CARE TESTING AND ANTIBIOTICS USAGE IN EU COUNTRIES

European countries that use point-of-care CRP testing have lower antibiotic prescribing rates.<sup>1</sup>

**The countries that used CRP POCT in 2015 to some or a wide extent were:** Finland, Netherlands, Denmark, Norway, Sweden, Germany, Czech Republic, Hungary, Austria, Slovenia, Latvia and Estonia.<sup>1</sup>

Interestingly, these countries are the lowest 12 prescribers of antibacterials in the ESAC survey 2018.<sup>1</sup>



ESAC: European Surveillance of Antimicrobial Consumption



# CRP POCT HAS AN ESTABLISHED ROLE IN THE REDUCTION OF ANTIBIOTIC PRESCRIBING AT PRIMARY CARE

The European Respiratory Guidelines of ERS and ESCMID for the Management of Adult Lower Respiratory Tract Infections recommend, beside several national guidelines, the measurement of CRP in patients with suspected pneumonia.<sup>1-6</sup>

1. Woodhead, et al. Euro. Resp. Guideline of ERS and ESCMID. Clin Micro Inf 2011; 2. NICE. Dec. 2014. Pneumonia in adults: diagnosis and management (CG191). Accessed January 2020; 3. Dutch College of General Practitioners (NHG) guideline M78. Acute cough. Update 2013: revision of the 2011 version; 4. André et al. Läkemedelsverkets expertgrupp. Läkartidningen 2009; 5. Norwegian Directorate of Health. 2012. National professional guideline for antibiotic use in the primary health service; 6. Krüger K et al. DEGAM-Leitlinie Nr. 11. 2021; 7. Van Vugt et al. BMJ 2013

## ERS AND ESCMID RECOMMEND THE USE OF CRP IN PATIENTS WITH SYMPTOMS OF LRTI<sup>1</sup>

Pneumonia suspected (new focal chest signs, dyspnoea, tachypnoea, pulse rate > 100 or fever > 4 days)

CRP rapid test

< 20  
mg/L

20-100  
mg/L

> 100  
mg/L

Pneumonia  
highly unlikely

Pneumonia  
likely

74%

23%

3%

NUMBER OF PATIENTS AFFECTED<sup>7</sup>



**CRP POCT HAS  
BEEN FOUND TO  
REDUCE ANTIBIOTIC  
PRESCRIBING BY UP  
TO 42% WITHOUT  
AFFECTING RECOVERY  
RATES OR THE  
DURATION OF ILLNESS.<sup>1-5</sup>**

Two large primary care studies in six European countries found that combining CRP POCT with enhanced communication skills for GPs resulted in a relative reduction of antibiotic prescribing by

**>60%<sup>1-4</sup>**

The European Network for Health Technology Assessment (EUnetHTA) concluded similarly as other recent reviews that CRP POCT may be used in the treatment of patients who present with symptoms of acute RTI, resulting in reduced antibiotic prescribing both at index consultation and up to 28 days follow-up without compromising patient safety.<sup>6-8</sup>

1. Cals et al. BMJ 2009; 2. Cals et al. The Annals of Family Medicine 2010; 3. Andreeva et al. BMC Family Practice 2014; 4. Little et al. The Lancet 2013; 5. Butler et al. N Engl J Med. 2019; 6. Verbakel et al. BMJ Open 2019; 7. Cooke J et al. BMJ Open Resp Res 2020; 8. O'Brien et al. EUnetHTA Project ID: OTCA012. 2019



# REPORT OF THE EUROPEAN NETWORK FOR HEALTH TECHNOLOGY ASSESSMENT (EU<sub>net</sub>HTA)

This collaborative assessment evaluated the relative effectiveness and safety of using CRP point-of-care testing to guide antibiotic prescribing in patients with acute respiratory tract infections in primary care settings.<sup>1</sup>

The systematic review included 12 studies, all performed with 3 different quantitative CRP POC tests.

“ Given the high prescribing rate for acute RTIs, this reduction is likely to be clinically important as it reduces an individual’s future risk of antibiotic resistance as well as reducing unnecessary antibiotic use for self-limiting RTIs when antibiotic-related harm is more likely than benefit.”

- The authors are moderately confident that **CRP POCT reduces antibiotic prescribing at index consultation in both upper and lower respiratory tract infections.**
- The authors are confident that **patient safety will not be compromised.**
- The reduction of antibiotic prescribing at index consultation was found to be **24%** in randomized studies and **39%** in observational studies.



# TWO IMPORTANT RECENT REVIEWS

Open access Research

**BMJ Open** Impact of point-of-care C reactive protein in ambulatory care: a systematic review and meta-analysis

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Jan Y Verbakel,<sup>1,2,3</sup> Joseph J Lee,<sup>1,3</sup> Clare Goyder,<sup>1,3</sup> Pui San Tan,<sup>3</sup>  
Thanusha Ananthakumar,<sup>1,3</sup> Philip J Turner,<sup>1,3</sup> Gail Hayward,<sup>1,3</sup> Ann Van den Bruel<sup>1,2</sup>

## Conclusions

Performing a point-of-care CRP test in ambulatory care **accompanied by clinical guidance on interpretation** reduces the immediate antibiotic prescribing in both **adults and children**.

Available evidence does not yet suggest an effect on other patient outcomes or healthcare processes.

If cut-off guidance was applied, immediate antibiotic prescribing could be reduced by **32% in adults** and by **44% in children**.


1. Verbakel et al. BMJ Open 2019<sup>3</sup>; 2. Cooke J et al. BMJ Open Resp Res 2020

Respiratory infection

**BMJ Open  
Respiratory  
Research**

**Respiratory tract infections (RTIs) in primary care: narrative review of C reactive protein (CRP) point-of-care testing (POCT) and antibacterial use in patients who present with symptoms of RTI**

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Jonathan Cooke <sup>1,2</sup> Carl Llor,<sup>3</sup> Rogier Hopstaken,<sup>4</sup> Matthew Dryden,<sup>5</sup>  
Christopher Butler<sup>6</sup>

## Conclusions

1. An overwhelming number of studies have demonstrated that the use of POC CRP tests in patients presenting with RTI symptoms reduces index antibacterial prescribing.
2. GPs and patients report a good acceptability for a CRP POCT.
3. Economic evaluations show cost-effectiveness of CRP POCT over existing RTI management in primary care.
4. POCT increases diagnostic precision for GPs in the better management of patients with RTIs.
5. Adopting systems that markedly reduce antibiotic consumption is a no-brainer for governments that are struggling to address the rise in AMR.





# ANTIBIOTIC PRESCRIBING IN AECOPD PATIENTS

- A study with 653 patients with acute exacerbations of COPD was conducted at 86 UK general practices in England and Wales.
- Patients were randomized to receive usual care or usual care guided by CRP point-of-care testing (Afinion™ CRP).

Antibiotic prescribing could be reduced in the point-of-care group by **26%** during the first four weeks of follow-up without negative effects on the outcome (57% vs. 77.4%; 20,4% absolute reduction).

## The NEW ENGLAND JOURNAL of MEDICINE

ESTABLISHED IN 1812

JULY 11, 2019

VOL. 381 NO. 2

### C-Reactive Protein Testing to Guide Antibiotic Prescribing for COPD Exacerbations

Christopher C. Butler, F.Med.Sci., David Gillespie, Ph.D., Patrick White, M.D., Janine Bates, M.Phil., Rachel Lowe, Ph.D., Emma Thomas-Jones, Ph.D., Mandy Wootton, Ph.D., Kerensa Hood, Ph.D., Rhiannon Phillips, Ph.D., Hasse Melbye, Ph.D., Carl Llor, Ph.D., Jochen W.L. Cals, M.D., Ph.D., Gurudutt Naik, M.B., M.S., M.P.H., Nigel Kirby, M.A., Micaela Gal, D.Phil., Evgenia Riga, M.Sc., and Nick A. Francis, Ph.D.

#### ALLAN S. BRETT AND MAJDI N. AL-HASAN - EDITORIAL COMMENT NEJM

*“In our view, the findings from this study are compelling enough to support CRP testing as an adjunctive measure to guide antibiotic use in patients with acute exacerbations of COPD.”<sup>2</sup>*



# ANTIBIOTIC PRESCRIBING AT LONG-TERM CARE FACILITIES

The UPCARE study is a pragmatic, cluster randomized trial. In total, 242 patients from 11 nursing home organizations in the Netherlands have been included by 84 physicians.

“*CRP POCT for suspected lower respiratory tract infection safely reduced antibiotic prescribing compared with usual care in nursing home residents.*

*The findings suggest that implementing CRP POCT in nursing homes might contribute to reduced antibiotic use in this setting and help to combat antibiotic resistance.”*

## Antibiotic prescribing at initial consultation:

- CRP 0-20 mg/L: seldom (6,4%)
- CRP 20-40 mg/L: not frequently (35%)
- CRP 40-60 mg/L: increasingly (67%)
- CRP  $\geq$ 60 mg/L: almost always
- Intervention group: 53.5%
- Control group: 82.3%

→ **Relative reduction 35%** (absolute reduction 28,8%).

- The low occurrence of hospital admission and mortality, and the relatively low between-group difference in full recovery at three weeks indicate safe use of CRP POCT.
- Because of the pragmatic trial design, the authors believe that the results can be generalized to other nursing homes and other countries with similar long-term care facilities.



# A GUIDELINE & A REVIEW FROM SOUTH AFRICA

## about the use of CRP in patients with lower RTI

### Guideline

#### South African guideline for the management of community-acquired pneumonia in adults

Tom H. Boyles<sup>1</sup>, Adrian Brink<sup>1,2</sup>, Greg L. Calligaro<sup>3</sup>, Cheryl Cohen<sup>4,5</sup>, Keertan Dheda<sup>1</sup>, Gary Maartens<sup>6</sup>, Guy A. Richards<sup>7</sup>, Richard van Zyl Smit<sup>1</sup>, Clifford Smith<sup>8</sup>, Sean Wasserman<sup>1</sup>, Andrew C. Whitelaw<sup>9,10</sup>, Charles Feldman<sup>11</sup>; South African Thoracic Society, Federation of Infectious Diseases Societies of Southern Africa

Boyles TH et al. Journal of thoracic disease 2017; 9(6).  
Open access: <http://dx.doi.org/10.21037/jtd.2017.05.31>

- Blood-based biomarkers (CRP and PCT) may be used to aid the diagnosis of community-acquired pneumonia (CAP) and to assist in severity assessment.

### SAMJ IN PRACTICE

#### CLINICAL PRACTICE

#### The role of appropriate diagnostic testing in acute respiratory tract infections: An antibiotic stewardship strategy to minimise diagnostic uncertainty in primary care

A J Brink,<sup>1</sup> MB ChB, MMed (Micro); J van Wyk<sup>2</sup> MB ChB, MMed (Clin Path); V M Moodley,<sup>2</sup> MB ChB, DTM&H, FCPATH (Micro) SA, MMed (Micro); C Corcoran,<sup>3</sup> MB ChB, FCPath (Viro), DTM&H, MMed (Viro); P Ekerimans,<sup>4</sup> MB ChB, DTMH, MMed (Clin Path); L Nutt,<sup>5</sup> MB ChB, MMed (Clin Path); T Boyles,<sup>6</sup> MA, BM BCh, MRCP, MD, DTM&H, Cert ID SA; O Perovic,<sup>7,8</sup> FC Path (SA) (Micro), MMed (Micro), DTM&H, MD; C Feldman,<sup>9</sup> MB BCh, DSc, PhD, FRCP, FCP (SA); G A Richards,<sup>10</sup> MB BCh, PhD, FCP (SA), FRCP; M Mendelson,<sup>11</sup> BSc, PhD, MBBS, FRCP, DTM&H

Brink AJ, Boyles T et al. S Afr Med J 2016;106(6):554-561.  
Access: <http://www.samj.org.za/index.php/samj/article/view/10857/7389>

- POCT CRP to be used to guide antibiotic treatment decisions in Lower RTI;
- and in patients with Acute Exacerbations of Chronic Obstructive Pulmonary Disease (AECOPD).



Suggested algorithm about the use of POCT CRP to distinguish CAP from acute bronchitis in the primary care setting in South Africa.

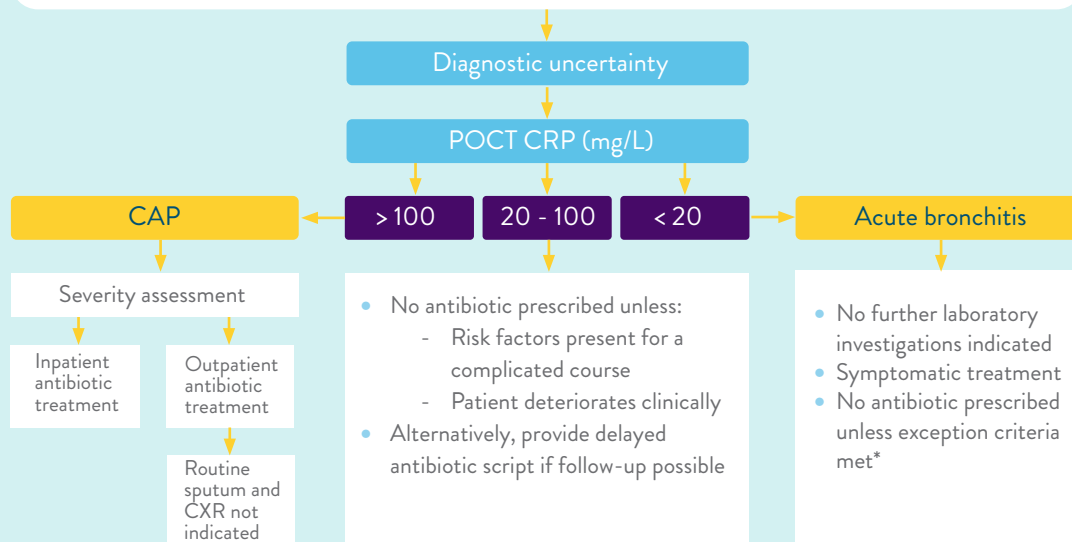
**CAP:** Community Acquired Pneumonia  
**POCT:** Point-of-Care Testing

## PATIENTS PRESENTING WITH ACUTE COUGH AND/OR OTHER LRTI SYMPTOMS

### CLINICAL EXAMINATION

#### The following features favor CAP over acute bronchitis:

- Fever  $\geq 38^{\circ}\text{C}$
- Tachypnoea  $\geq 24/\text{min}$
- Tachycardia  $\geq 100/\text{min}$
- Evidence of consolidation on examination:
  - Crackles
  - Bronchial breathing
  - Increased tactile fremitus or vocal resonance
  - Where there is diagnostic uncertainty, follow the algorithm





# MAKE EVERY MINUTE COUNT



**Afinion™ CRP Make Every Minute Count**  
Prof. Dr. Lars Olof Hansson



**Afinion™ CRP Make Every Minute Count**  
Prof. Dr. Dag Berild



**Afinion™ CRP Educational Video**  
Dr. Verena Gantner - Switzerland



# REDUCTION OF ANTIBIOTIC PRESCRIBING IN CHILDREN PRESENTING WITH LRTI

## A recent review concluded:<sup>1</sup>

“Performing a point-of-care CRP test in ambulatory care accompanied by clinical guidance on interpretation reduces the immediate antibiotic prescribing in both adults and children.”

## For children, this was true only when cut-off guidance was applied (5 or 10 mg/L):

- **< 5 mg/L:** do not routinely offer antibiotics/antibiotics unlikely to be beneficial and usually should not be prescribed.
- **≥5 mg/L:** consider clinical signs, symptoms, risk factors and CRP level before prescribing antibiotics.





# RULE OUT THE RISK OF SERIOUS INFECTION IN CHILDREN IN THE PRACTICE

In a large cluster randomized trial, CRP point-of-care testing was performed in 'high risk' acutely ill children presenting to 133 general practitioners (1 month - 16 years; 3,147 children).<sup>1</sup>

CRP was measured in the presence of one of the following clinical features: breathlessness, body temperature  $\geq 40^{\circ}\text{C}$ , diarrhea in children 12-30 months of age, or clinician concern.<sup>2</sup> CRP was measured with the Afinion™ System.

Results reveal adding CRP to the clinical prediction rule increases specificity from 80% to 89% while keeping sensitivity at 100%.<sup>1,2</sup>

*As with most other diagnostic tests, CRP results should always be combined with clinical findings when deciding upon treatment.*

“  
*A CRP < 5 mg/L rules out serious infection and could be used by GPs to avoid unnecessary hospital referrals.*”<sup>1</sup>



# LET'S NOT FORGET ABOUT ANTIMICROBIAL RESISTANCE (AMR)

## WHO<sup>1</sup>

“Despite the fact that antibiotics do not treat or prevent viral infections like COVID-19, the results of behavioural insight research conducted in nine countries and areas of the European Region showed antibiotic use increasing throughout the pandemic along with cases. Of those taking antibiotics, 79–96% reported not having been infected with COVID-19 but were taking antibiotics inappropriately, believing they would prevent infection.”

“Preventing the COVID-19 pandemic from causing an antibiotic resistance catastrophe.”

“Evidence indicates that up to 15% of severely affected COVID-19 patients develop bacterial co-infection and could need antibiotics, whereas 75% actually receive them.”

## AMR

2014: **700,000**  
deaths per year.

Estimate for 2050:

**10 million**  
deaths per year. More than the  
number of people that currently  
die from cancer.<sup>2</sup>





# LET'S NOT FORGET ABOUT ANTIMICROBIAL RESISTANCE (AMR)

**A panel of European physicians claims:<sup>1</sup>**

“

Don't neglect antimicrobial stewardship principles!”

“Despite the viral origin of COVID-19, a standard reflex by physicians is to start treatment with antibiotics since cough, fever and radiologic infiltrates are hallmarks of bacterial community-acquired pneumonia which requires antibiotic treatment.”

“Antibiotics should be reserved for the patients with the most severe presentations (e.g. those with high oxygen demands and rapidly progressing respiratory failure).”

**Jin YH and colleagues claim in a position article and guideline:<sup>2</sup>**

“The detection of CRP and PCT is of certain value to distinguish whether there was bacterial infection in the lung.”

“Avoid blind or inappropriate use of antibacterial drugs, especially the combination of broad-spectrum antibacterial drugs.”



# ANTIBIOTIC USE IN COVID-19 PATIENTS IN THE HOSPITAL

## Proposal from a UK study group:

“The absence of both admission WCC  $>8.2 \times 10^6/\text{ml}$  and a fall in CRP would support stopping antibiotics in almost 50% of COVID-19 patients during their admission, reducing total antibiotic prescriptions in this population by up to 25%.”<sup>1</sup>

1. Mason et al. medRxiv reprint 2020; 2. Rawson et al. Clin Infect Dis 2020; 3. Guan et al. N Engl J Med 2020; 4. Zhou et al. Lancet 2020; 5. Palmieri L et al. Characteristics of SARS-CoV-2 patients dying in Italy 2020; 6. Wang et al. J Antimicrob Chemo 2020; 7. Langford BJ et al. Clinical Microbiology and Infection 2020

		Antibiotic treatment	Bacterial infection
Rawson T et al.2	Review: publications 78% China, 22% USA	72%	8%
Guan W et al.3	1,099 patients, China	58%	
Zhou F et al.4	191 patients, China		15% 50% of those who died
Palmieri L et al.5	Report: 45,557 patients dying in Italy	86% those who died	
Mason BL et al.1	619 patients, UK	>90%	
Wang L et al.6	1,396 patients within 48 hours of admission, UK		2.7%
Langford BJ et al.7	3,338 patients, systematic review	71.9%	6.9%

Community-acquired pneumonia (CAP) was used as a benchmark to define the processes that occur in a bacterial pulmonary infection. The hypothesis was tested that baseline inflammatory markers and their response to antibiotic therapy could distinguish CAP from COVID-19. On admission all of 106 CAP and >90% of 619 COVID-19 patients received antibiotics. Blood samples collected 48-72 hours into admission revealed decreasing CRP in CAP but not COVID-19.

**The findings have been confirmed in an independent validation cohort population.**

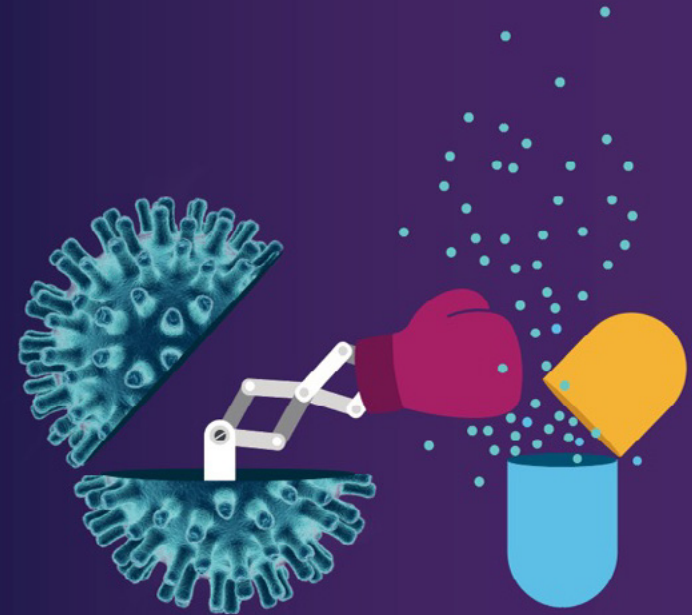


# ANTIBIOTIC USE IN COVID-19 PATIENTS IN PRIMARY CARE

## National Health Service (NHS) England numbers:<sup>1</sup>

- Absolute number of appointments (face-to-face plus virtual) decreased by **>20%** in 2020 compared to 2019
- Antibiotic prescribing decreased by **15%**
- However, given the decrease in absolute number of appointments over this time, this number of prescriptions is 6,71% higher than expected – **a statistically significant increase of antibiotic prescriptions ( $p < 0.0001$ )**

Findings from a review indicate higher prescribing rates in remote consultations than in face-to-face consultations.<sup>2</sup>



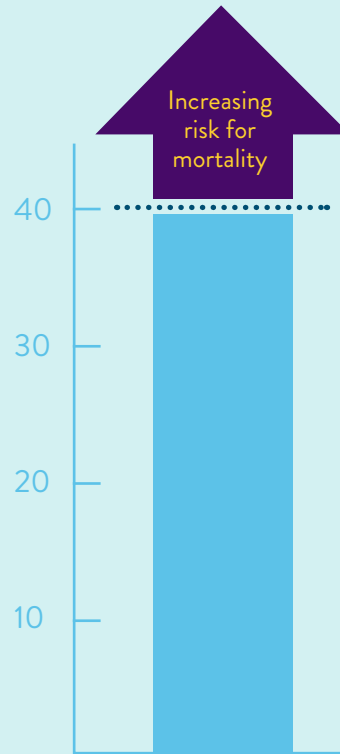


In just a **few minutes**,  
a rapid POC CRP test  
can deliver information  
regarding the inflammatory  
status of a patient.





**Increased CRP values above normal levels have been found in the majority of patients with COVID-19, especially in severe cases.<sup>1-12</sup>**



**CRP may therefore add valuable information:**

- For severity assessment and outcome prediction<sup>1-5, 11-13</sup>
- For prioritization of hospital admission<sup>14</sup>
- For monitoring<sup>15-20</sup>

**A CRP cut-off of  $\geq 40\text{mg/L}$**  has been shown to predict mortality and may assist clinicians in using CRP as an early trigger for enhanced observation, treatment decisions and advanced care planning.<sup>12\*</sup>

*\*evaluated in hospitalized COVID-19 adult patients*

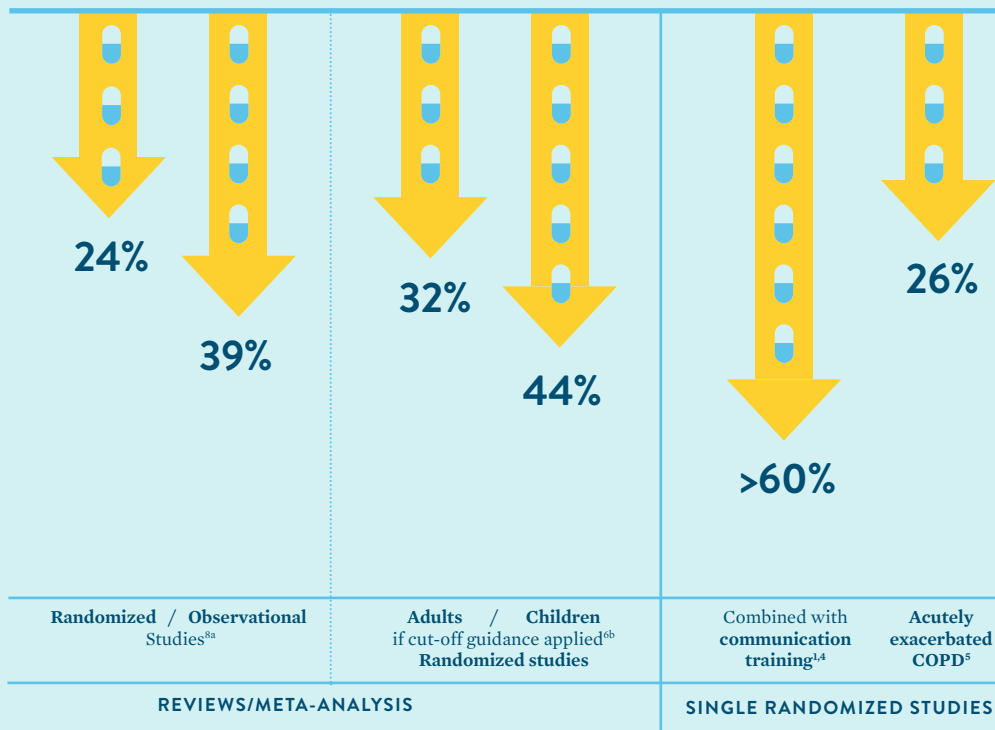
1. CDC. 27. Oct. 2020. Interim Clinical Guidance for Management of Patients with Confirmed Coronavirus Disease; 2. Luo et al. medRxiv preprint 2020; 3. Wang et al. Open Forum Infect Dis 2020; 4. Tan et al. ORCID iD: 0000-0002-2522-4524; 5. Li et al. Journal of Infection 2020; 6. Gao et al. J Med Virol 2020; 7. Guan et al. N Engl J Med 2020; 8. Zhu et al. ORCID iD: 0000-0001-7718-9591; 9. Chen et al. Lancet 2020; 10. Cao et al. medRxiv preprint 2020; 11. Zhang et al. Scandinavian J Clin Lab In 2020; 12. Stringer et al. Int J Epidemi 2021; 13. Liu et al. J Clin Virol 2020; 14. De Nardo et al. Int J Infect Dis 2020; 15. Feldt et al. STAKOB 2020; 16. Chinese National Health Commission. 3. March 2020. Chinese COVID-19 Management Guidelines; 17. Chinese Center for Disease Control and Prevention. 20. Aug. 2020. Treatment Strategies to Prevent Mild to Severe Progression of COVID-19 Cases; 18. SIMEU. 12. March 2020. Covid-19 First Line Report PS/DEA management organisational structure as part of an epidemic or pre-epidemic outbreak; 19. Regional Council of Campania Directorate General for the Protection of Health. Feb. 2020. Operational guidelines identification/management of suspected and proven cases of suspected Coronavirus; 20. IFCC. 6. April 2020. Information Guide on COVID-19



3

CRP POCT has been proven to reduce antibiotic prescribing in primary care without compromising patient safety.<sup>1-8</sup>

## REDUCTION of antibiotic prescribing with CRP POCT in primary care in respiratory tract infections



a. 12 studies, three of them included children; b. RTIs and other indications

1. Cals et al. BMJ 2009; 2. Cals et al. The Annals of Family Medicine 2010; 3. Andreeva et al. BMC Family Practice 2014; 4. Little et al. The Lancet 2013; 5. Butler et al. N Engl J Med 2019; 6. Verbakel et al. BMJ Open 2019; 7. Cooke J et al. BMJ Open Resp Res 2020; 8. O'Brien et al. EUnetHTA Project ID: OTCA012. 2019



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# AFINION™ CRP

Easy-to-use all-in-one  
cartridge.

No user calibration  
necessary.

Minimally invasive  
for the patient, 2.5 µL  
fingertick sampling.

Excellent agreement with  
laboratory methods.<sup>1-7</sup>



RESULTS IN  
**3** MINS



1. Verbakel et al. J Clin Pathol 2014 J; 2. Hughes et al. Clinical Pharmacist 2016; 3. Ivaska et al. PLOS ONE 2015; 4. Brouwer et al. Clin Chim Acta 2015; 5. Minnaard et al. Scand J Clin Lab In 2013; 6. Bukve et al. Clin Chem 2016; 7. Minnard et al. Scand J Clin Lab Invest 2015






# AFINION™ CRP IS IDEAL FOR PAEDIATRIC TESTING

**Afinion™ CRP is ideal use in children of all ages:**

- From drop to decision in just three minutes
- Easy-to-use all-in-one cartridge with no analytical steps
- Minimally invasive for the patient, 2.5 µL fingerstick sampling
- Excellent agreement with laboratory methods<sup>1-7</sup>
- No user calibration necessary



No matter what the diagnosis, young patients deserve to be handled with care.



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CRP AT  
POINT-OF-CARE

CRP & COVID-19:  
SEVERITY & OUTCOME

CRP & COVID-19:  
PRIORITIZATION OF  
HOSPITAL ADMISSION

CRP & COVID-19:  
MONITORING

ANTIBIOTIC  
RESISTANCE/AMR

ANTIBIOTIC  
PRESCRIBING  
& CRP POCT

ANTIBIOTIC  
PRESCRIBING  
DURING COVID-19

TAKE HOME  
MESSAGES

● COVID-19

● CRP

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