

# BMJ Open Point-of-care measurement of C-reactive protein promotes de-escalation of treatment decisions and strengthens the perceived clinical confidence of physicians in out-of-hours outpatient emergency medical services

Anni Matthes,<sup>1,2</sup> Florian Wolf,<sup>1</sup> Elmar Wilde,<sup>3</sup> Jutta Bleidorn,<sup>1</sup> Robby Markwart <sup>1,2</sup>

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<sup>1</sup>Institute of General Practice and Family Medicine, Jena University Hospital, Friedrich Schiller University Jena, Jena, Germany

<sup>2</sup>InfectoGnostics Research Campus Jena, Jena, Germany

<sup>3</sup>Practice Network HiMed Hildesheim, Hildesheim, Germany

## Correspondence to

Dr Robby Markwart;  
roby.markwart@med.uni-jena.de

## ABSTRACT

**Objectives** Out-of-hours outpatient emergency medical services (OEMS) provide healthcare for patients with non-life-threatening conditions in need for urgent care when outpatient practices are closed. We studied the use of point-of-care-testing of C-reactive protein (CRP-POCT) at OEMS.

**Design** Cross-sectional questionnaire-based survey.

**Setting** Single centre OEMS practice in Hildesheim, Germany (October 2021 to March 2022).

**Participants** OEMS physicians answering a questionnaire immediately after performing CRP-POCTs (CUBE-S Analyzer, Hitado) on any patients.

**Primary and secondary outcomes** Impact of CRP-POCTs on clinical decision-making and perceived usefulness.

**Results** In the 6-month study period, 114 valid CRP-POCTs were performed in the OEMS practice by 18 physicians and the questionnaire was answered in 112 cases (response rate: 98.2%). CRP-POCTs were used in the diagnosis of inflammatory diseases of the gastrointestinal tract (60.0%), respiratory tract infections (17.0%), urinary tract infections (9.0%) and other non-gastrointestinal/non-specified infections (11.0%). The use of a CRP-POCT resulted in a change of the physicians' clinical decision in 83.3% of the cases. Specifically, in 13.6% and 35.1% of the cases, rapid CRP measurements led to decision changes in the (1) initiation of antimicrobial therapy and (2) other drug treatment, respectively. Notably, in 60% of all cases, the use of a CRP-POCT reportedly changed the decision on hospitalisation/non-hospitalisation of OEMS patients. In respect of antimicrobial therapy and hospitalisation, these decision changes primarily ( $\geq 73\%$ ) promoted 'step-down' decisions, that is, no antibiotic therapy and no hospital admission. In the great majority of CRP-POCT applications ( $\geq 95\%$ ), OEMS physicians reported that rapid CRP measurements increased the confidence in their diagnostic and therapeutic decision. In almost all cases (97%), physicians rated the CRP-POCT use as useful in the treatment situation.

**Conclusion** Quantitative CRP-POCT promotes step-down clinical decisions and strengthens the clinical confidence of physicians in out-of-hours OEMS.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

- ⇒ This study is the first evaluation with 'real-world' data on the effects of point-of-care-testing of C-reactive protein (CRP-POCT) use in outpatient emergency medical services in Germany with focus on physicians' decision-making and their experience of work.
- ⇒ Since we conducted a single centre study with physicians who have relatively large work experience, the external validity might be limited to some extent.
- ⇒ Since we only analysed cases where CRP-POCTs were actually used, we may have introduced selection bias towards physicians with a positive attitude towards CRP use.
- ⇒ Physicians were asked on their hypothetical clinical decision without CRP-POCT after they performed CRP testing, which may have led to biases associated with choice blindness.
- ⇒ We did not collect clinical patient data, so that we cannot judge whether the decision changes were clinically accurate.

## INTRODUCTION

In Germany, out-of-hours outpatient emergency medical services (OEMS) provide healthcare for patients with non-life-threatening conditions in need for urgent care when outpatient practices are closed. In 2019, there were 8.9million OEMS cases reported in Germany (82million inhabitants), with additional 10.2million patients using prehospital emergency care (including transported emergency care).<sup>1</sup> OEMS is provided in dedicated practices, sometimes in close proximity to hospitals, but usually has no laboratory facilities available. In emergency care settings, physicians from various disciplines face patients with a wide range of conditions<sup>2-4</sup> and a high workload.<sup>5</sup>

Due to their fast turnaround time, point-of-care laboratory tests (POCTs) have the potential to directly impact clinical decision-making during the physician–patient encounter,<sup>6 7 8</sup> which is particularly important in emergency medical services. C-reactive protein (CRP) is an acute-phase protein of hepatic origin, whose concentration in blood plasma increases in response to inflammation.<sup>9</sup> CRP has a diagnostic value (although limited in some cases) in differentiating between bacterial and viral infections<sup>9</sup> as well as estimating the severity of bacterial infections.<sup>10</sup> POCT measurement of CRP has been shown to safely reduce antibiotic prescriptions in respiratory tract infections (RTI) in primary care settings<sup>11 12</sup> as well as in nursing homes.<sup>13</sup> There is also evidence that CRP-POCTs can improve antibiotic prescriptions<sup>14</sup> and shorten the length of stay in emergency medical services.<sup>15–17</sup> However, in order to comprehensively understand potential benefits of POCTs, further aspects are important, such as impact on clinical routines and decision-making as well as acceptance among medical professionals.<sup>18</sup>

We therefore conducted an observational study to investigate the use of quantitative CRP-POCTs in a German OEMS practice and its impact on physician's clinical decision-making, experience of work and perceived usefulness in routine healthcare use.

## METHODS

This study followed the *Strengthening the Reporting of Observational Studies in Epidemiology* statement: guidelines for reporting observational studies.<sup>19</sup>

### Study design and outcomes

We conducted a single centre observational study on the application of a quantitative CRP-POCT (CUBE-S Analyzer, Hitado) in an OEMS practice located within a large hospital in Hildesheim (population approximately 100 000), Germany. The CRP-POCT was implemented prior to the start of the study, including training of the OEMS staff and was provided by the hospital (Helios Hildesheim). During the 6 months study period (October 2021 to March 2022), OEMS physicians had the sole discretion to use CRP-POCTs and were asked to answer a short questionnaire immediately after they performed a CRP-POCT. Eligible were all patient cases in the OEMS practice where CRP-POCT measurements were performed.

The primary outcomes were the impact of CRP-POCT measurements on clinical decision-making (decision on therapeutic measures and further diagnostics as well as certainty in diagnostic and therapeutic decisions after CRP-POCT use) and the perceived usefulness of CRP-POCT use in the treatment situation. Secondary outcomes were clinical indications and diagnostic goals for CRP-POCT use as well as the impact of CRP-POCTs on communication with patients.

### Questionnaire

The questionnaire was in German and was designed by an interdisciplinary research team consisting of experienced

outpatient care physicians with experience in OEMS (FW, EW and JB), a work and organisational psychologist (AM) and a healthcare researcher with focus on POCTs in outpatient care (RM). The questionnaire (see online supplemental material) included the following items: suspected diagnosis, diagnostic/therapeutic goal for CRP measurement, measured CRP value, clinical decisions taken, presumptive decision without CRP-POCT, perceived impact on clinical decision-making, communication with patients as well as items for physician's characteristics (ie, sex, specialisation and years since licence to practice medicine (approbation)) and a pseudonym code. In order to determine the impact on clinical decision-making, physicians were asked for their final clinical decisions after CRP-POCT use as well as for the (hypothetical) decisions they would have made without performing a CRP-POCT. Only anonymous data were collected and by returning the questionnaires, the physician's consent was implied.

### Data analysis

Raw data from the questionnaires were entered into Microsoft Excel 2010. Statistical analyses were performed using 'R' (V.4.0.2).<sup>20</sup> Open text answers (clinical indication, test goal) were categorised in an inductive approach by two researchers separately (AM and RM). A linear regression was calculated to predict the number of clinical decision changes after CRP-POCT use based on work experience on physician level. In this analysis and in the calculation of 95% CIs, we accounted for clustering at the physician level using the 'Survey' package (V.4.1.1).<sup>21</sup>

### Patient and public involvement

Patients were not involved in the study. However, since the study subjects were OEMS physicians, physicians were involved in the conceptualisation, planning, conduction of the study as well as in data interpretation.

## RESULTS

In the 6 months study period, 61 physicians worked in the OEMS practice, of whom 18 performed at least one CRP-POCT. The median number of performed tests per physician was 1.5 (IQR: 1.0–3.8). Among the 18 physicians, 16 were general physicians. Work experience of the included physicians was relatively high, as determined by years since receiving the licence to practice medicine (table 1).

In the study period, 115 CRP-POCTs were performed yielding 114 valid test results. In total, 112 questionnaires were answered immediately after CRP-POCT use on patients presenting at the OEMS practice, which results in a response rate of 98.2% (table 2).

### Clinical indications and diagnostic goals for CRP-POCT use

POCT of CRP was used as a diagnostic tool in the diagnosis of inflammatory diseases of the gastrointestinal tract (60.0%), RTI (17.0%), urinary tract infection (9.0%) and other non-gastrointestinal infections/non-specified

**Table 1** Characteristics of physicians performing CRP-POCTs

Number of OEMS physicians who performed at least one CRP-POCT and completed questionnaire(s)	18	
Sex (n, %*)		
Female	12	(66.7)
Male	6	(33.3)
Specialisation (n, %*)		
General physician	16	(88.9)
Other specialisation	2	(11.1)
Years since licence to practice medicine		
Median (IQR)	30	(26–40)

CRP, C-reactive protein ; OEMS, outpatient emergency medical services; POCT, point-of-care testing.

infections (11.0%) (table 2). In 75 cases, physicians reported a diagnostic goal for which a CRP-POCT was used. In nearly half (44.0%) of these cases, rapid CRP measurements were used for the exclusion of often severe conditions (eg, acute appendicitis, pneumonia), while in 26.7% CRP-POCTs were used for the confirmation of a suspected diagnosis. In 22.7% and 8.0% of the applications, the OEMS physicians reported that CRP-POCTs were used for the decision on hospitalisation and antibiotic therapy, respectively. In 68.6% (72/105) of the cases with reported CRP value the measured CRP value was not increased (ie, <1 mg/dL).

### Impact of CRP-POCT use on clinical decision-making

In 83% (65/78) of cases with POCT use, physicians reported a change in the clinical decision through CRP-POCT use. Specifically, in 13.6% and 35.1% of the cases, CRP-POCT measurements led to decision changes in the initiation of antimicrobial therapy and other drug treatment, respectively (figure 1A). Notably, in 60% of all cases, the use of a CRP-POCT reportedly changed the decision on hospitalisation/non-hospitalisation of the patients. On physician level, the work experience (determined by years since receiving the medical licence for practicing medicine) was not associated with the proportion of clinical decision changes after CRP-POCT use ( $R=0.46$ ,  $p=0.156$ ).

Importantly, In the great majority of cases when OEMS physicians reported that CRP-POCT use changed their clinical decision, it was a de-escalating ('step-down') decision in antimicrobial therapy (no antibiotic therapy), initiation of further diagnostics (no further diagnostics) and hospitalisation (no admission) (figure 1B). When CRP-POCT use resulted in decision changes on prescription of drugs other than antibiotics, OEMS physicians predominantly decided to initiate a drug prescription ('step-up').

**Table 2** Clinical indications and diagnostic goals for CRP-POCT use in out-of-hours outpatient emergency medical services

Number of completed questionnaires with valid CRP-POCT result	112	
Clinical indication (n, %*†)	100	(100)
Inflammatory diseases of the gastrointestinal tract	60	(60)
Infectious diseases	37	(37.0)
Respiratory tract infections	17	(45.9)
Urinary tract infections	9	(24.3)
Non-specified/other infection	11	(29.7)
Other‡	9	(9)
Not reported	12	–
CRP value (n, %*)	105	(100)
Not increased (<1 mg/dL)	72	(68.6)
Slightly increased (1–4 mg/dL)	13	(12.4)
Moderately increased (4–8 mg/dL)	12	(11.4)
Strongly increased (>8 mg/dL)	8	(7.6)
Not reported	7§	–
Mean (median; IQR)	2.3 mg/dL	(0.3, 0.2–1.8)
Diagnostic goal of CRP-POCT use (n, %*†)	75	(100)
Exclusion of often severe conditions	33	(44.0)
Confirmation of suspected diagnosis	20	(26.7)
Differential diagnosis	8	(10.7)
Decision on hospital admission (yes/no)	17	(22.7)
Decision on antimicrobial therapy (yes/no)	6	(8.0)
Not specified/reported	37	–

\*Percentage among reported answers (excluding 'Not reported').

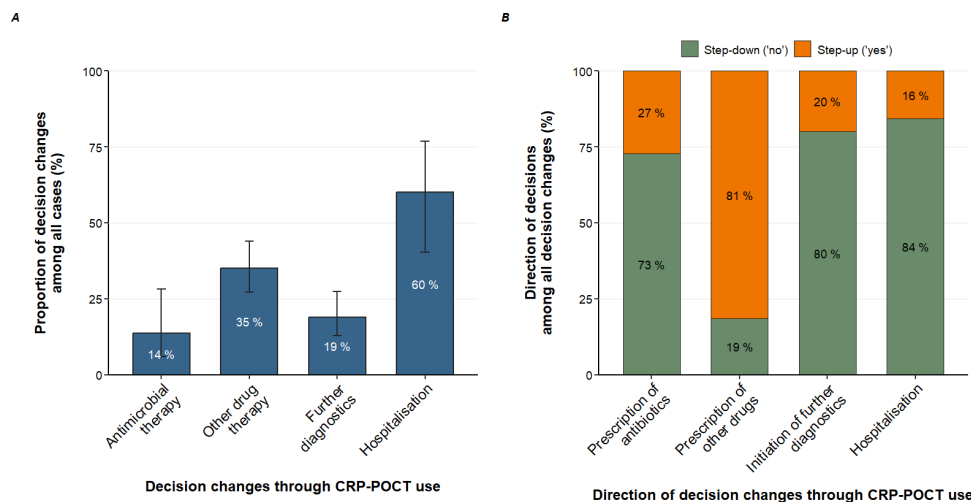
†In some cases more than one clinical indication or diagnostic goal was reported and therefore, the sum of percentages exceeds 100%.

‡Other include: stenocardia (2x), myocarditis (2x), intercostal neuralgia, vertebral blockage, bronchial asthma, transient ischaemic attack, sprained ligaments.

§We were not able to follow-up the CRP-POCT test results nor do we know why the physicians did not report these test results. CRP, C-reactive protein ; POCT, point-of-care testing .

### Impact of CRP-POCT use on clinical confidence and communication

In the great majority of CRP-POCT applications ( $\geq 95\%$ ), OEMS physicians reported that rapid CRP measurements increased the confidence in their diagnostic and therapeutic decision (figure 2). Moreover, physicians reported that in 89% of all cases, the CRP-POCT use improved the communication with the patient. In almost all cases



**Figure 1** Impact of CRP-POCT use on clinical decision-making in out-of-hours outpatient emergency medical services (OEMS). (A) Proportion of decision changes through CRP-POCT use among all cases as reported by OEMS physicians in %. Physicians were asked for their final clinical decisions after CRP-POCT use as well as for the (hypothetical) decisions they would have made without performing a CRP-POCT. Based on this information, decision changes were calculated. (B) Direction of decisions (ie, step-down ('no') and step-up ('yes')) among all decision changes as reported by OEMS physicians in %. CRP-POCT, point-of-care testing of C-reactive protein.

(97%), physicians rated the CRP-POCT use as useful in this situation and only in one case, the physician reported that the rapid CRP measurement was not useful.

## DISCUSSION

In this study we analysed 112 cases where rapid CRP-POCTs were performed on patients presenting with acute illness in an OEMS practice. Our results show that CRP-POCT use impacts clinical decision-making of physicians and supports de-escalating decisions ('step-down'), including decision against antibiotics prescription and hospital admission. Moreover, in the great majority of cases, physicians reported that CRP-POCT use increased their confidence in clinical decision-making

and improved communication with patients. Rapid CRP testing was rated as useful in almost all treatment situations in OEMS.

In our study, OEMS physicians predominantly used CRP-POCTs as diagnostic tools in (suspected) inflammatory diseases of the gastrointestinal tract, such as pancreatitis, appendicitis and diverticulitis. While CRP is an established marker in the diagnosis and prognosis of acute pancreatitis<sup>22-23</sup> and diverticulitis,<sup>24-25</sup> it has a limited diagnostic accuracy in appendicitis<sup>26-28</sup> indicating an ambivalent diagnostic value of CRP in inflammatory diseases of the gastrointestinal tract. Since CRP is a well-established biomarker in RTI, it is surprising that RTI accounted for only 17% of all CRP-POCT applications in



**Figure 2** Physician's rating of CRP-POCT use in out-of-hours outpatient emergency medical services. CRP-POCT, point-of-care testing of C-reactive protein. Percentages within the bars are only presented if  $\geq 5\%$ .

our study. This might be explained by the fact that the COVID-19 measures (eg, wearing masks, contact restrictions) during the study period led to a profound decrease in non-COVID-19 RTI in Germany.<sup>29–31</sup> Moreover, RTI may be more easily assessed by other clinical observable markers than CRP-POCTs, such as chest sounds and sputum purulence, which are commonly used to facilitate decisions on diagnosis and treatment of patients with RTI.

Physicians in emergency medicine face significant levels of stress, caused by high workload, uncomfortable working hours and patients in their most acute state of illness. Our results suggest that CRP-POCT use improves physicians' perception of situations in unclear cases of suspected inflammation/infection as rapid CRP testing increases the confidence in clinical decision-making and communication with patients. In particular, hospitalisation is one central decision in OEMS and is influenced by multiple clinical and non-clinical factors<sup>32–33</sup> and, therefore, is often associated with uncertainty among physicians. Our study shows that CRP-POCTs are frequently used to guide hospitalisation in OEMS and changed the physician's decision on hospitalisation/non-hospitalisation in over half of the cases. Importantly, OEMS physicians predominantly changed their decision towards non-hospitalisation indicating that CRP-POCT use increases the physicians' confidence to continue treatment in outpatient care. Rapid CRP tests therefore can be a tool to reduce hospital admissions in emergency care, which in turn may make CRP-POCT use cost-effective and improves patient healthcare.

In line with findings from primary care practices,<sup>11–12</sup> our results indicate that point-of-care CRP testing may have the potential to reduce antibiotic prescriptions in OEMS, which is especially important under the light of the rise of antibiotic resistance. The result of our study are also consistent with another primary care study showing that clinicians perceive that CRP-POCTs increase confidence, reduce diagnostic uncertainty and facilitate communication between patients and clinicians.<sup>34</sup> Although our results show that CRP-POCT use supported de-escalating ('step-down') clinical decisions, it frequently resulted in 'step-up' decision changes in regard to prescription of drugs other than antibiotics, in most cases analgesics, which were often used as an alternative therapy to hospital admission and antibiotic prescription.

### Strengths and limitations

From our knowledge, our study is the first evaluation of the effects of CRP-POCT use in OEMS in Germany with focus on physicians' decision-making and their experience of work. One strength of our study is that we evaluated CRP-POCT in routine healthcare provided in an OEMS practice, and therefore, our conclusions are based on 'real-world' data. Data were collected immediately after the CRP-POCT was performed minimising recall bias. However, our study has some limitations. First, we conducted a single centre study in an OEMS practice with participants who have relatively large work experience,

which may limit the external validity of our study. Second, since we only analysed cases where CRP-POCTs were actually used, we may have introduced selection bias towards physicians with a positive attitude towards CRP use. In our study, only one-third of the physicians who worked in the OEMS practice during the study period actually used the CRP-POCT. Third, physicians were asked on their hypothetical clinical decision without CRP-POCT after they performed CRP testing, which may lead to biases associated with choice blindness. Moreover, the results of the quantitative CRP-POCT measurements were not validated by central laboratory tests, as we were not primarily interested in the actual test accuracy. Lastly, we did not collect clinical patient data, so that we cannot judge whether the hypothetical decision changes were clinically accurate. However, the aim of this study was to give insights into the effects of point-of-care CRP testing on clinicians' decision-making and experience of work in a real-world emergency care setting, which was achieved successfully. Multicentre (quasi-)experimental study designs, also including patient outcome data, are necessary, preferably randomised controlled trials.

### CONCLUSION

Our prospective observational study provides evidence that CRP-POCT use in OEMS supports clinical decision-making and promotes step-down clinical decisions. Rapid CRP testing strengthens the clinical confidence of physicians and improves the physicians' experience of work. Moreover, CRP-POCT use may improve patient healthcare and may be cost-effective in OEMS. Interventional studies on the effectiveness of CRP-POCT use in OEMS are needed to confirm our findings.

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**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** The study complies with the declaration of Helsinki and Ethical approval was obtained from the Institutional Research Ethics Board of the Jena

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**Data availability statement** Data are available upon reasonable request. The data that support the findings of this study are available from the corresponding author, RM, upon reasonable request.

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#### ORCID iD

Robby Markwart <http://orcid.org/0000-0003-0338-3433>

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