

ENASPOC

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

**Guidance on
CRP POC testing and communication
to improve antibiotic prescribing
in adults with lower RTIs**

26. October | 2023

ENASPOC

European Network
for Antibiotic Stewardship
at the Point of Care



www.ENASPOC.com

Dr. Rogier Hopstaken, MD PhD
Primary Health Care Center Hapert en Hoogeloon
Maastricht University Medical Centre
The Netherlands



Antimicrobial resistance and outpatient antibiotic use

2019

4.95m deaths associated with bact AMR

1.27m deaths attributable to bact AMR

Antimicrobial Resistance Collaborators; Lancet 2022

Outpatient antibiotic use

80%

AB prescribed by GPs
of AB are prescribed for RTI
of LRTI is non-severe, acute bronchitis
acute bronchitis is nevertheless treated with AB

Adverse events
Wrong message to patient
Bacterial resistance

2019

4.95m deaths associated with bact AMR

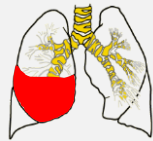
1.27m deaths attributable to bact AMR

Antimicrobial Resistance Collaborators; Lancet 2022

Why?



Diagnostic uncertainty



Pneumonia we learn



Pneumonia we see

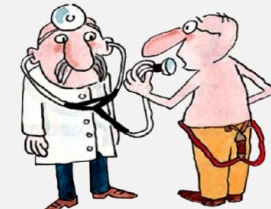


C-reactive protein (CRP) point of care testing

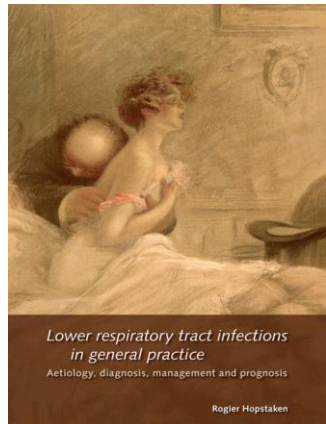
+

Patient and doctor related factors

Time pressure
Prescription as symbol
Patient expectations
Opinion on antibiotics
Worries

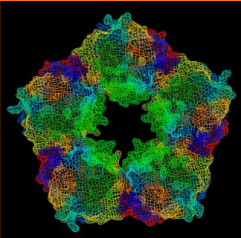


Enhanced consultation skills

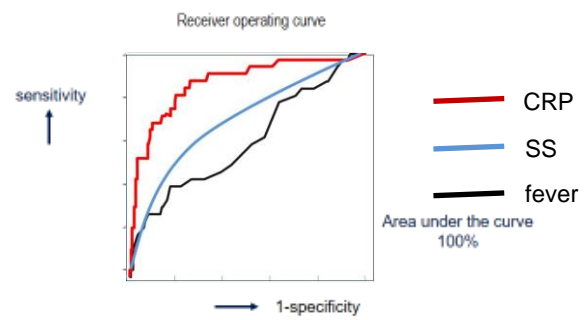


C-reactive protein

- Strongest predictor of pneumonia
- CRP < 20 mg/l excludes pneumonia
- Adds to history/physical exam
- POCT to change management



Diagnosing pneumonia



Data set	Change in AUC
Melbye et al., 1992 ²¹	0.11
Hopstaken et al., 2003 ²²	0.18
Flanders et al., 2004 ²⁸	0.05
Graffelman et al., 2007 ²⁹	0.02
Holm et al., 2007 ³⁰	0.05
Rainer et al., 2009 ⁷	0.05
Steurer et al., 2011 ⁸	0.15
van Vugt et al., 2013 ⁹	0.06
Overall	0.075 (0.044 to 0.107)

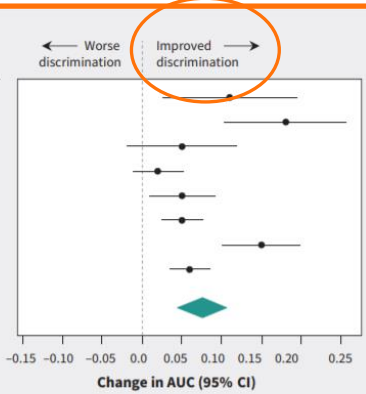
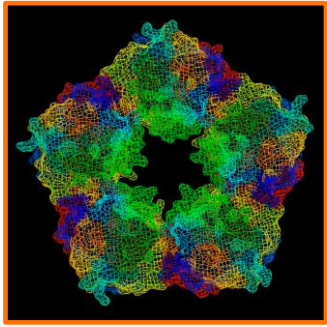


Figure 3: Effect of extended diagnostic prediction model (includes C-reactive protein measurement) in discriminating between patients with and without pneumonia in primary care, as shown by change in area under the curve (AUC). Values greater than zero indicate improvement in discrimination. CI = confidence interval.

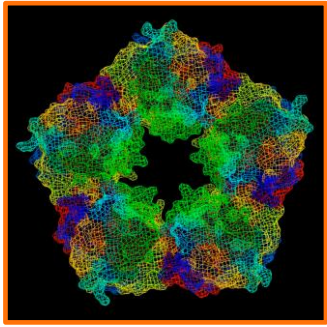


CRP POC test is...

sensitive

and

non-specific



CRP POC test is...

sensitive

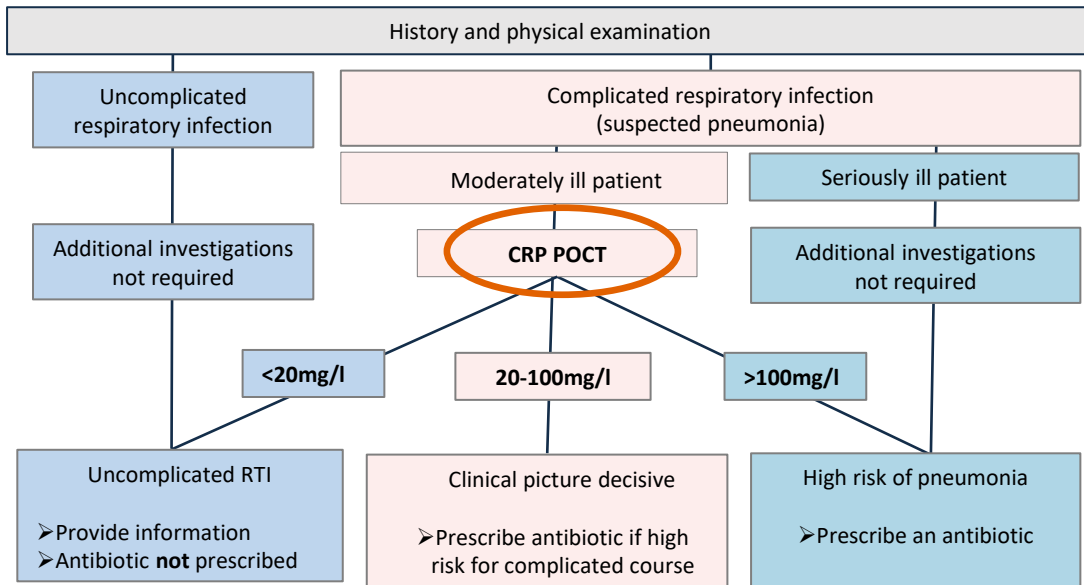
and

specific

in hands of a care professional

for severity of illness!

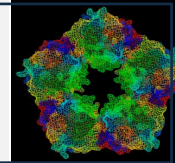
Guidelines for Acute Cough, Dutch College of GPs



Diagnostic studies and RCTs

C-reactive protein POCT

- Strongest predictor of pneumonia
- CRP < 20 mg/l excludes pneumonia
- Adds to history/physical exam
- POCT to change management



Hopstaken BJGP 2003, Minnaard CMAJ 2017 +

Enhanced consultation skills

- Simulated patients
 - Context-rich training
 - Combination of general and LRTI items
- Competence ++ → Performance?

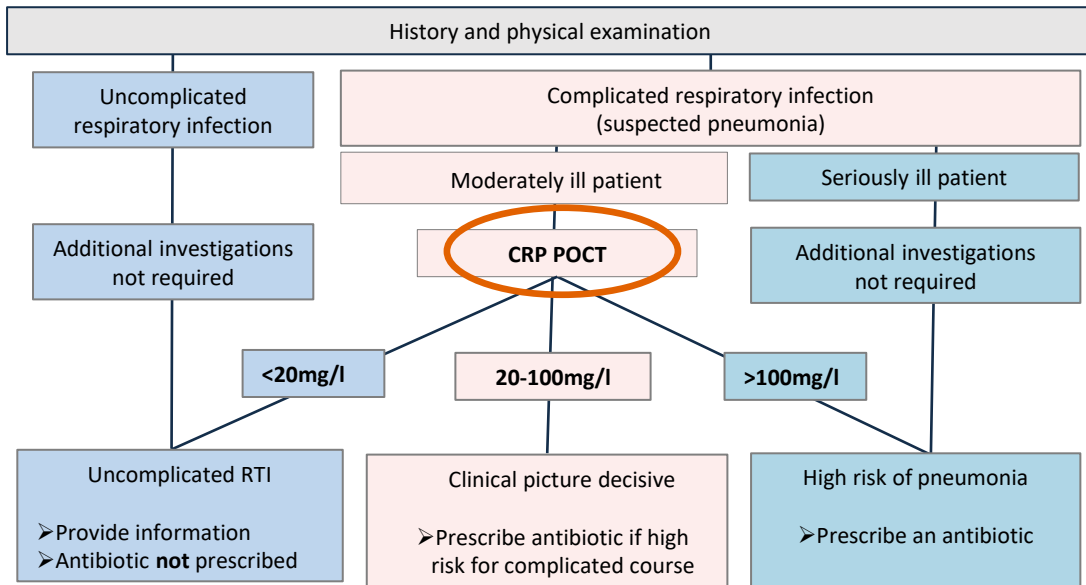
Cals Pat Educ Couns. 2007



22-44%
absolute reduction of antibiotics

Cals BMJ 2009, Little Lancet 2011

Guidelines for Acute Cough, Dutch College of GPs



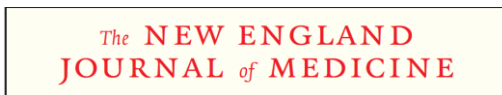
Smedemark 2022

Biomarkers as point-of-care tests to guide prescription of antibiotics in people with acute respiratory infections in primary care (Review)



Tonkin-Crine 2017

Clinician-targeted interventions to influence antibiotic prescribing behaviour for acute respiratory infections in primary care: an overview of systematic reviews (Review)



ESTABLISHED IN 1882 JULY 11, 2019 VOL. 381 NO. 2

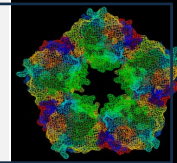
C-Reactive Protein Testing to Guide Antibiotic Prescribing for COPD Exacerbations

Butler 2019

Diagnostic studies and RCTs

C-reactive protein POCT

- Strongest predictor of pneumonia
- CRP <20 mg/l excludes pneumonia
- Adds to history/physical exam
- POCT to change management



Hopstaken BJGP 2003, Minnaard CMAJ 2017 +

Enhanced consultation skills

- Simulated patients
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- ➔ Competence ++ ➔ Performance?

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22-44%
absolute reduction of antibiotics

Cals BMJ 2009, Little Lancet 2011

RESEARCH

thebmj | BMJ 2021;374:n2198 | doi: 10.1136/bmj.n2198

OPEN ACCESS

Check for updates

Effect of C reactive protein point-of-care testing on antibiotic prescribing for lower respiratory tract infections in nursing home residents: cluster randomised controlled trial

Tjarda M Boere,¹ Laura W van Buul,¹ Rogier M Hopstaken,^{2,3,4} Maurits W van Tulder,⁵ Jos W M R Twisk,⁶ Theo J M Verheij,^{7,8} Cees M P M Hertogh^{1,7}



OPEN ACCESS

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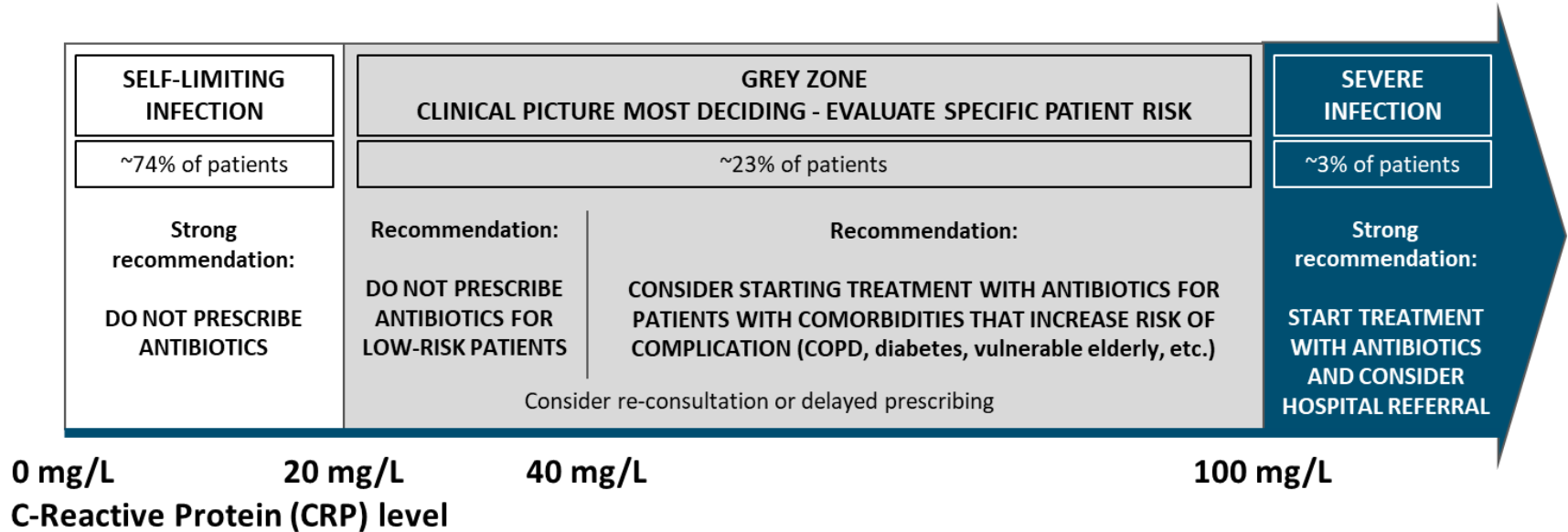
PUBLISHED 30 May 2023

Guidance on C-reactive protein point-of-care testing and complementary strategies to improve antibiotic prescribing for adults with lower respiratory tract infections in primary care

Oliver Van Hecke^{1,2*†}, Lars Bjerrum^{3†}, Ivan Gentile^{4†}, Rogier Hopstaken^{5†}, Hasse Melbye^{6†}, Andreas Plate^{7†}, Jan Y. Verbakel^{8,2†}, Carl Llor^{9†} and Annamaria Staiano^{10†}

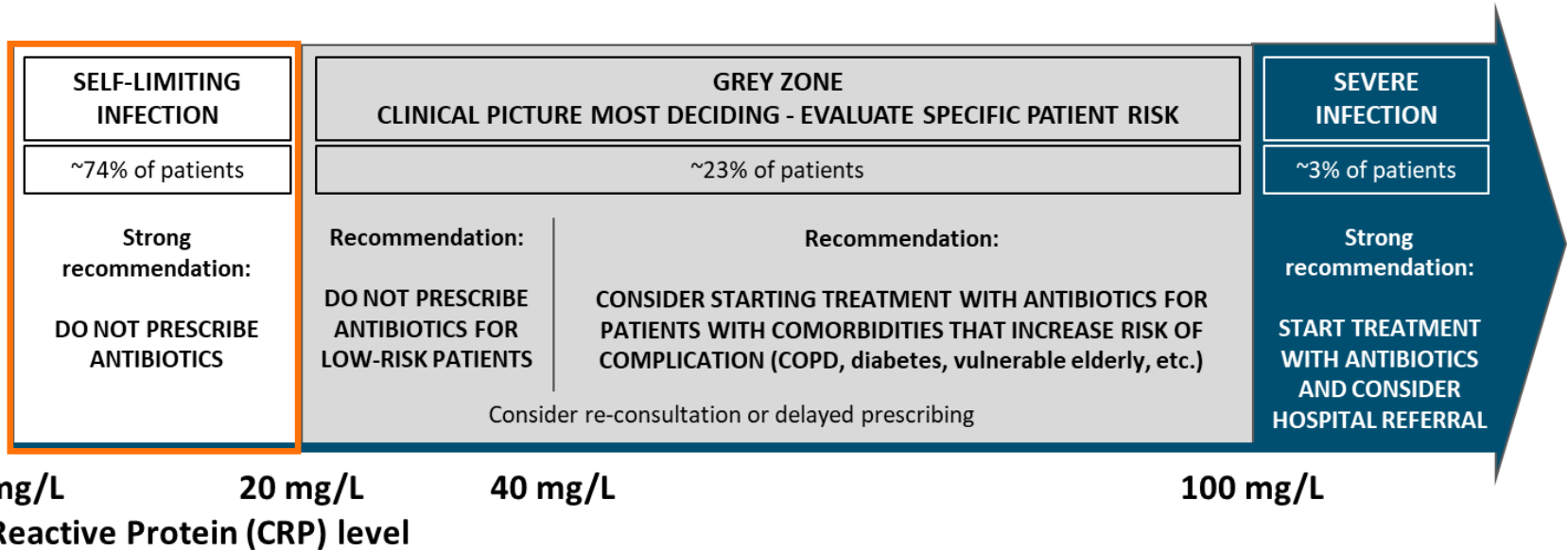


Interpretation CRP test result





Interpretation CRP test result





EXPERT GROUP ON CRP POINT OF CARE TESTING TO GUIDE ANTIBIOTIC PRESCRIPTIONS FOR RESPIRATORY ILLNESS

ENASPOC collaborators, *Frontiers in Medicine* (2023)

When to test CRP?

- Symptoms and signs of a LRTI
- Reduce diagnostic uncertainty: severe infection?
- To reassure and/or convince patients that AB are not helpful
- Monitor progression of illness

Physician's confidence versus appropriateness of AB prescribing decision

- GPs overconfident in clinical judgement and prescribing decision
- GPs overestimate pt expectations regarding antibiotics
- Testing before AB prescribing?



ENASPOC collaborators, *Frontiers in Medicine* (2023)

Main messages to be delivered by the physician to the patient	Explanation and additional details
<p>Our clinical assessment of your situation could benefit from a CRP test; if the value is low, it means that you have a mild infection (often viral).</p>	<ul style="list-style-type: none"> • Discuss leaflet or decision aid, and state that if • CRP is low, it indicates a minor infection (often viral) and no antibiotics are needed. • Consider delayed prescribing where applicable (ie: in the grey zone from Figure 1)
<p>Good news! Your CRP is low. ...So you should not take antibiotics. <i>(announcement method)</i></p>	<ul style="list-style-type: none"> • Practice safety-netting: if symptoms get worse or the condition changes, or if in doubt, re-consultation may be advised
<p>How do we know when we need to use antibiotics? The CRP value tells me if your inflammation is so severe, that you need an antibiotic today to help your body to fight.</p>	<ul style="list-style-type: none"> • Discuss CRP cut-off values, then explain: • The presence of cough or fever does not necessarily mean that you need antibiotics. • Antibiotics do not work for viruses. • Antibiotics may do more harm than good when an infection is non-severe.
<p>It is not abnormal for a cough to persist for quite a long time (up to 6 or even 8 weeks), and antibiotics will not help to shorten this period.</p>	<ul style="list-style-type: none"> • A cough of 5–7 days is not at all abnormal or necessarily alarming. • Average duration of a cough is 3 weeks, but is often up to 5 weeks; even up to 8 weeks is not necessarily alarming.

Performance of CRP devices

Scandinavian Journal of Clinical & Laboratory Investigation, 2013; 73: 627–634

informa
healthcare

ORIGINAL ARTICLE

Analytical performance, agreement and user-friendliness of five C-reactive protein point-of-care tests

MARGARETHA C. MINNAARD¹, ALMA C. VAN DE POL¹, BERNA D. L. BROEKHUIZEN¹,
THEO J. M. VERHEIJ¹, ROGIER M. HOPSTAKEN², SANNE VAN DELFT²,
ANTOINETTE M. J. KOOIJMAN-BUTTING², JORIS A. H. DE GROOT¹ & NIEK J. DE WIT¹

¹University Medical Center Utrecht, Julius Center for Health Sciences and Primary Care, Utrecht, the Netherlands
and ²Salto Diagnostic Center for Primary Care, Utrecht, the Netherlands

Scandinavian Journal of Clinical & Laboratory Investigation, 2015; Early Online: 1–5

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healthcare

ORIGINAL ARTICLE

The added diagnostic value of five different C-reactive protein point-of-care test devices in detecting pneumonia in primary care: A nested case-control study

MARGARETHA C. MINNAARD¹, ALMA C. VAN DE POL¹, JORIS A. H. DE GROOT¹,
NIEK J. DE WIT¹, ROGIER M. HOPSTAKEN², SANNE VAN DELFT²,
HERMAN GOOSSENS³, MARGARETA IJVEN³, CHRISTINE LAMMENS³,
PAUL LITTLE⁴, CHRIS C. BUTLER⁵, BERNA D. L. BROEKHUIZEN¹
& THEO J. M. VERHEIJ¹

¹University Medical Center Utrecht, Julius Center for Health Sciences and Primary Care, Utrecht, the Netherlands,
²Salto, Diagnostic Center for Primary Care, Utrecht, the Netherlands, ³University of Antwerp, Laboratory of Medical
Microbiology, Vaccine & Infectious Diseases Institute (VAXINFECTIO), Antwerp, Belgium, ⁴University of
Southampton Medical School, Primary Care Medical Group, Southampton, UK, and ⁵Institute of Primary Care
and Public Health, Cardiff University, Wales, UK

CRP POCT

Analytical performance

Clinical performance and effectiveness

Cost-effectiveness

Broader impact: **Better antibiotic stewardship**

- + Verbakel 2014
- + Matheussen 2018

Implementation study

GP

Nurse

✓ Patient

Collaboration
with laboratory



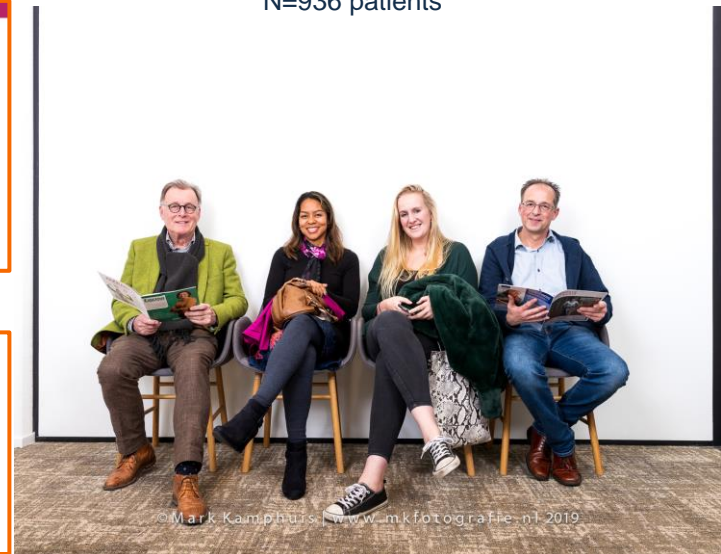
Rogier Hopstaken, Noortje Verdijk, Nicole van den Broek, Karen Verspaandonk, Marianne Meulepas, Conny Helder, Jules Keyzer

CRP-sneltest in de dagelijkse praktijk

Samenvatting
Hopstaken R, Verdijk N, Van den Broek N, Verspaandonk K, Meulepas M, Helder C, Keyzer J. CRP-sneltest in de dagelijkse praktijk. Huisarts Wet 2012;55(9):388-92.

INLEIDING
Bepaling van C-reactief proteïne (CRP) als sneltest, gecombineerd met goede algemene consultvaardigheden ('praten en prikken'), leidt bij patiënten met acute hoest in de Neder-

N=936 patients



Validation

✓ QC

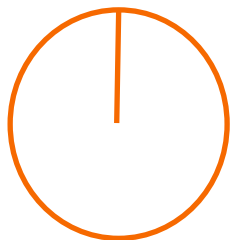
IT

Ned Tijdschr Klin Chem Labgeneesk 2012; 37: 238-244

Uit de laboratoriumpraktijk

Gecertificeerde CRP sneltest in de huisartspraktijk

N. van den BROEK, J. KEIJZER, R. HOPSTAKEN en K. NABBE



0% (1 GP)
↓
100% GP use in NL

Conclusion:

GPs, nurses, lab and patients were very satisfied with CRP POCT use

Implementation study

GP

Nurse

✓ Patient

Collaboration
with laboratory



Rogier Hopstaken, Noortje Verdijk, Nicole van den Broek, Karen Verspaandonk, Marianne Meulepas, Conny Helder, Jules Keyzer

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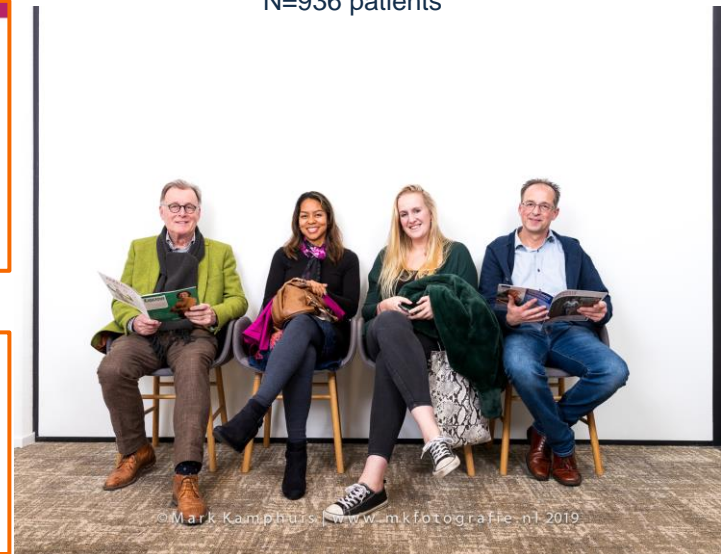
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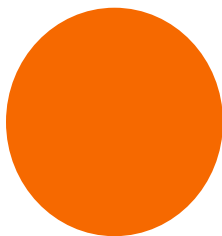
N=936 patients



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IT



0% (1 GP)
↓
100% GP use in NL

Conclusion:

GPs, nurses, lab and patients were very satisfied with CRP POCT use

Quality-assured POCT in general practice



Keypoints Guideline POCT in general practice

- Knowledge/EBM
- Quality
- Collaboration
- ISO 15189, ISO 22870
- General practice norms



RICHTLIJN POINT OF CARE TESTING (POCT) IN DE HUISARTSENZORG

Hopstaken RM¹, Kleinveld HA², Balen van JAM³, Krabbe JG⁴,
Broek van den S⁵, Weel F⁶, Slingerland RJ⁶, Bultter C⁷, Kusters GGM⁸
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³NHG Utrecht, ⁴Medlon Enschede/Almelo, ⁵Zore Leeuwarden,
⁶Isala Zwolle, ⁷NVVK Verenigingsbureau Utrecht,
⁸Jeroen Bosch Ziekenhuis 's-Hertogenbosch

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nederlands huisartsen
genootschap

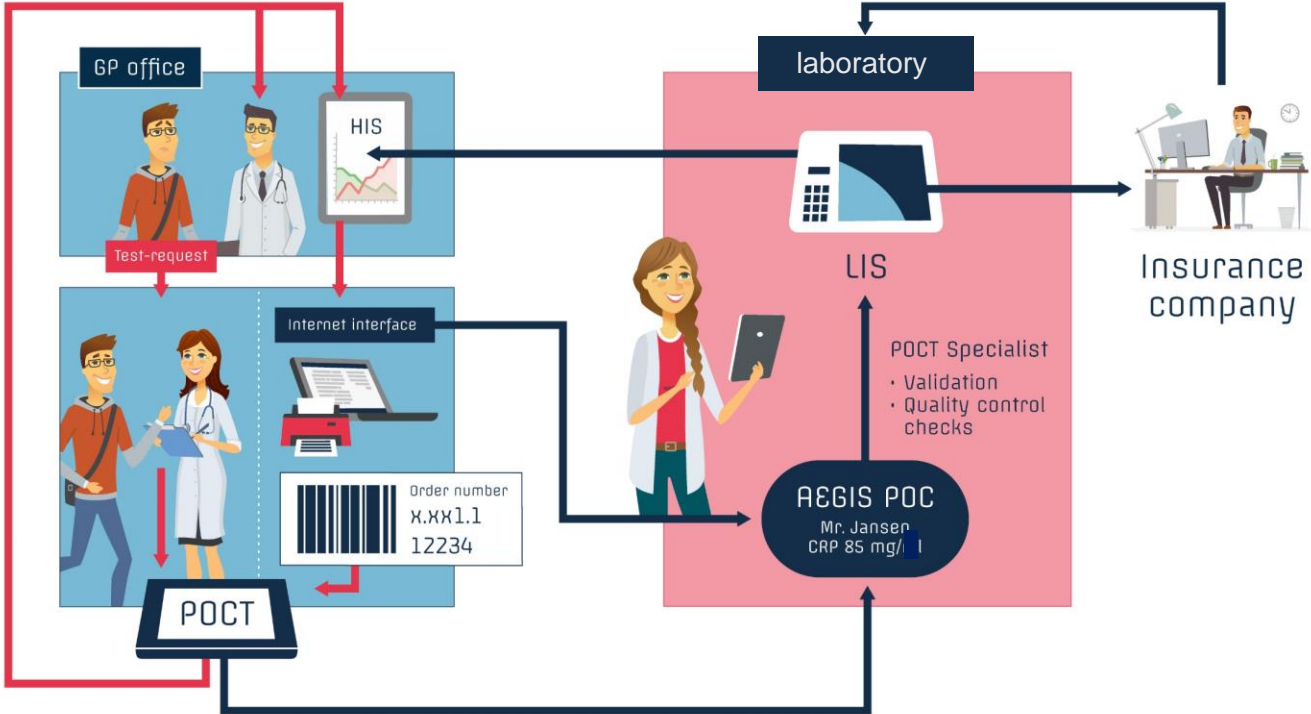
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Voor medische
diagnostiek

Nederlandse Vereniging
voor Klinische Chemie
en Laboratoriumgeneeskunde

Medische
Microbiologie

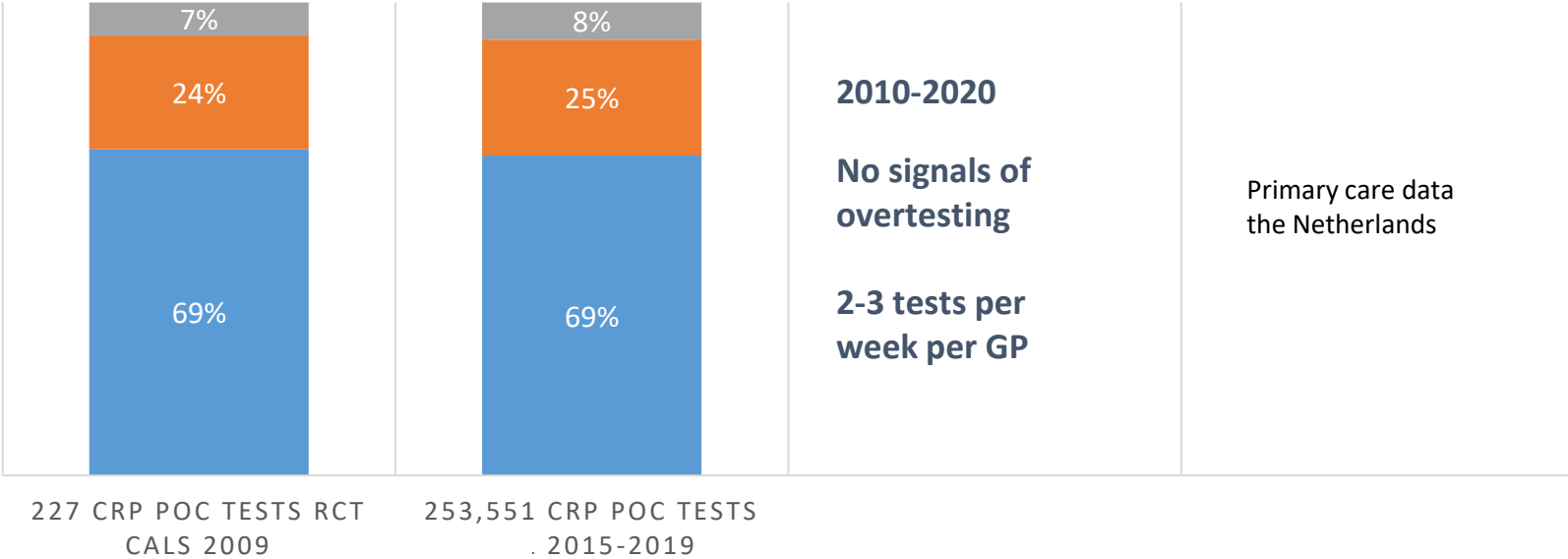
©NHG, NVVK, NVMM, SAN 2015

POCT process



CRP test result categories in RCT vs routine care

■ CRP <20 mg/l ■ CRP 20-100 mg/l ■ CRP >100 mg/l



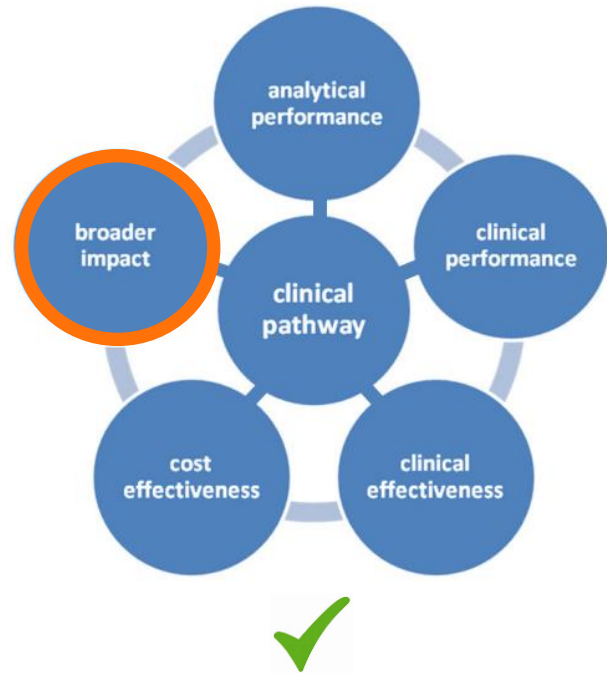
CRP POCT = routine care

Conny Helder
Minister of Health, The Netherlands

'CRP point-of-care testing has contributed a lot to the care of our patients in the Netherlands.

We highly recommend to follow our example, and to start building this innovative case to improve care in your country.

Dr. Hopstaken and others will be happy to help out.'



In general practice...

What takes him so long?



Mr Aziz, 38y



- Ill for 4 days, dry cough, some diarrhea
- ‘Can you check, do I have pneumonia?’
- General impression: pale, moderately ill
- T38.8
- Normal auscultation

No antibiotic?

80% chance

Hopstaken RM Fam Pract 2006

Mr van Gool, 72y



- COPD
- More dyspnea, productive cough
- 'To collect my antibiotic, like always'

- Dyspnea, BF24/min, SO2 89%, T37
- Crackles, rhonchi

Antibiotic?

>80% chance

Butler NEJM 2019

Mrs van den Boomgaard, 39y



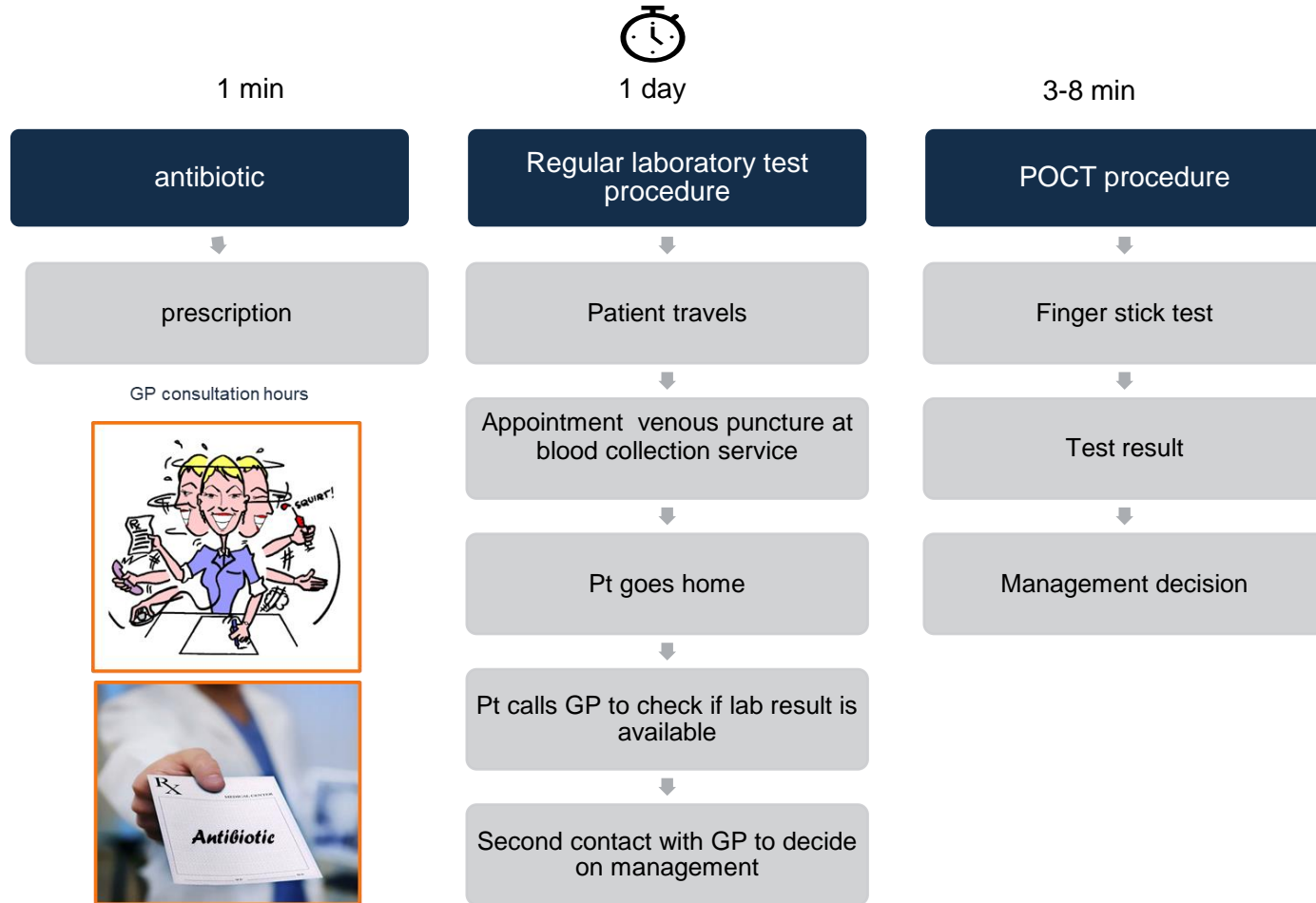
- Fever and cough 4 days.
- 'I guess it is time for an antibiotic'
- Not ill, T38.2
- Loud rhonchi chest

Antibiotic?

>80% chance

Hopstaken RM Fam Pract 2006

Antibiotic prescribing pitfall



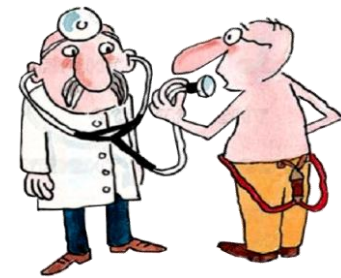
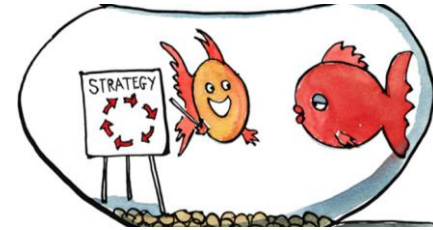
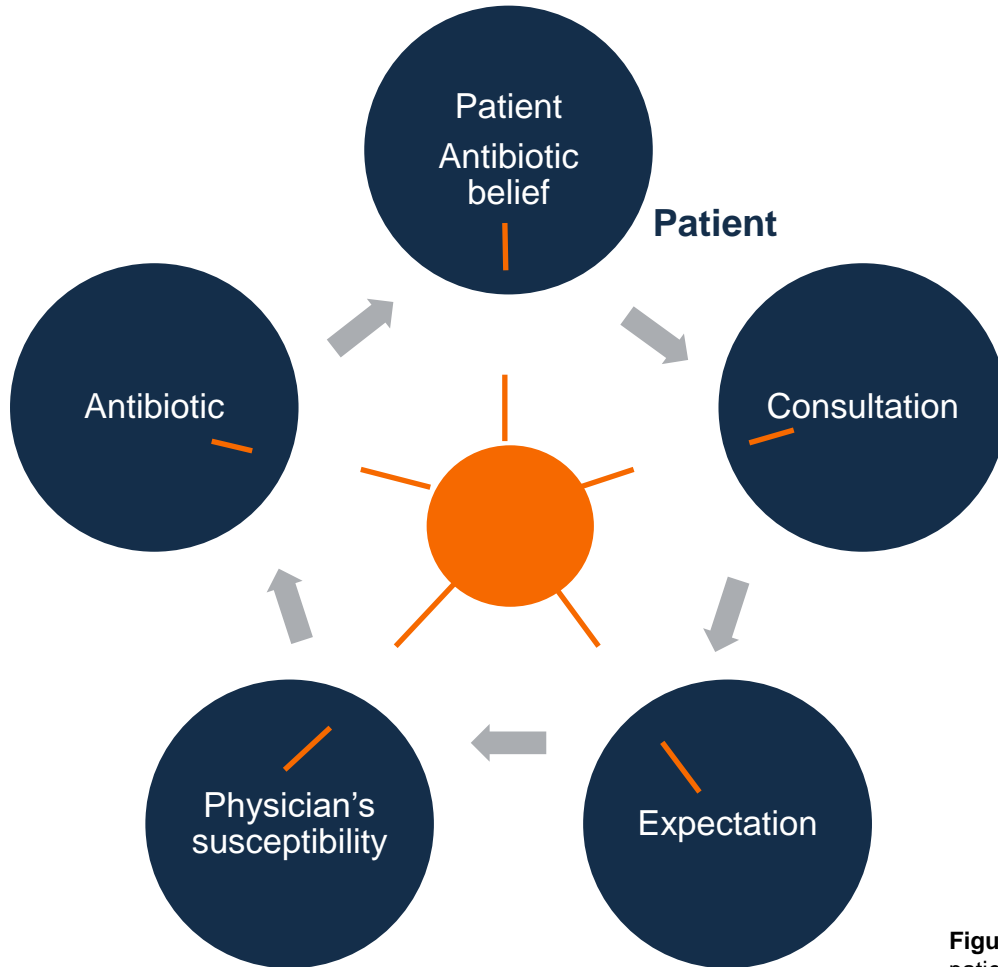


Figure. CRP POCT breaks ongoing AB prescribing enhancing patterns in patient-doctor contacts
Figure by R.Hopstaken

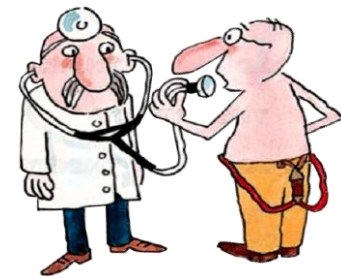
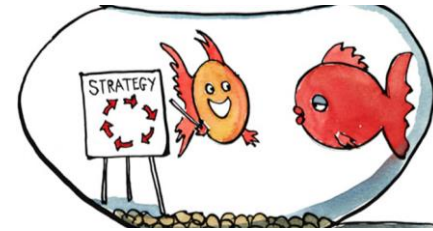
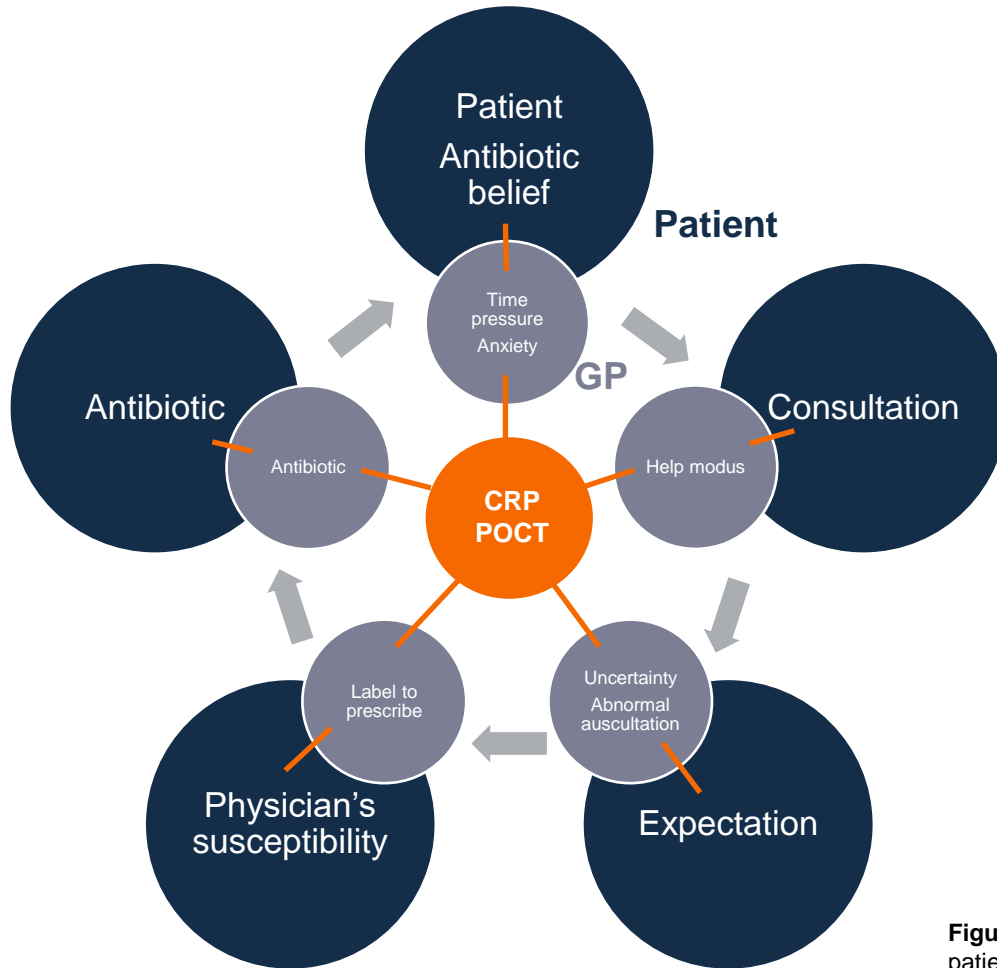
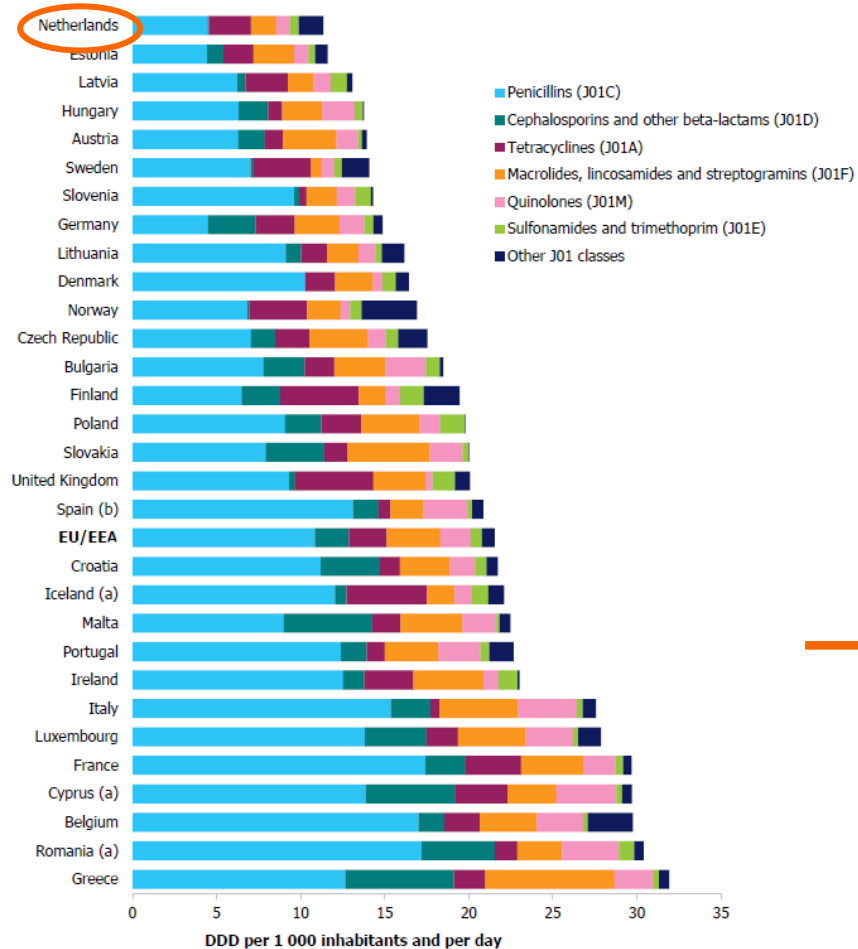


Figure. CRP POCT breaks ongoing AB prescribing enhancing patterns in patient-doctor contacts
Figure by R.Hopstaken

Figure 3.1. Consumption of antibacterials for systemic use (ATC group J01) at ATC group level 3 in the community, EU/EEA countries, 2012, expressed as DDD per 1 000 inhabitants and per day



Tigray, Ethiopia: 86% antibiotics for acute cough

CRP mg/l	%
<20	66.6
20-99	27,9
>100	5.5

Yebo 2016

Conclusion

Evidence



Into practice!

Rational use of CRP POCT in primary care

- Reduces diagnostic uncertainty
- Improves antibiotic stewardship
- Increases quality of care
- Increases satisfaction of patients and professionals
- Helps to combat AMR

If we want to combat AMR in primary care

- Focus on primary care
- Provide tools that instantly impact diagnostic uncertainty and patient concerns
- Upgrade the importance of severe vs non-severe infection
- Provide CRP POCT with guidance and QA
- CRP POCT for adults and children

Expert Group Consensus Statements – Overview

CONSENSUS STATEMENT 1:

Antimicrobial resistance is a global threat that must urgently be addressed.

CONSENSUS STATEMENT 2:

Antibiotic overprescribing for respiratory tract infections in primary care is a significant contributor to rising antimicrobial resistance.

CONSENSUS STATEMENT 3:

C-reactive protein point of care testing (CRP POCT) is an established tool that is proven to effectively and safely reduce overprescribing of antibiotics for lower respiratory tract infections (LRTIs) in adults presenting at primary care.

CONSENSUS STATEMENT 4:

To safely reduce antibiotic prescribing in primary care for patients presenting with respiratory illness, a broader application of CRP POCT globally is recommended.

CONSENSUS STATEMENT 5:

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

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.

CONSENSUS STATEMENT 7:

The use of CRP POCT for the management of patients presenting symptoms of LRTIs in primary care can be economically viable in several contexts.

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For further reading, please find an extensive list of related publications, including systematic reviews and meta-analysis, healthcare-economic analysis, guidelines, and more via the link below:

<https://www.enaspoc.com/publications>

Mr Aziz, 38y



- Ill for 4 days, dry cough, some diarrhea
- ‘Can you check, do I have pneumonia?’
- General impression: pale, moderately ill
- T38.8
- Normal auscultation
- **80% chance not receiving antibiotic**
- **CRP 145mg/l → antibiotic prescribed**

Mr van Gool, 72y



- COPD
- More dyspnea, productive cough
- 'To collect my antibiotic, like always'

- dyspnea, BF24, SO2 89%, T37.0
- Crackles, rhonchi
- **>80% chance to receive antibiotic**

- **CRP 11mg/l**
- **No antibiotic, prednisone**

Mrs van den Boomgaard, 39y



- Fever and productive cough 6 days.
- 'I guess it is time for an antibiotic'
- Not ill, T38.2
- Loud rhonchi chest

>80% chance to receive antibiotic

- **CRP 40mg/l → no antibiotic**
- Info, worries, when can antibiotics help?
Safety netting

Empty waiting room at last...



Disclaimer

- No real patients, but actors
- This is a real doctor, though atypical
- Photos: Mark Kamphuis

rogier.hopstaken@maastrichtuniversity.nl



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Thank you!