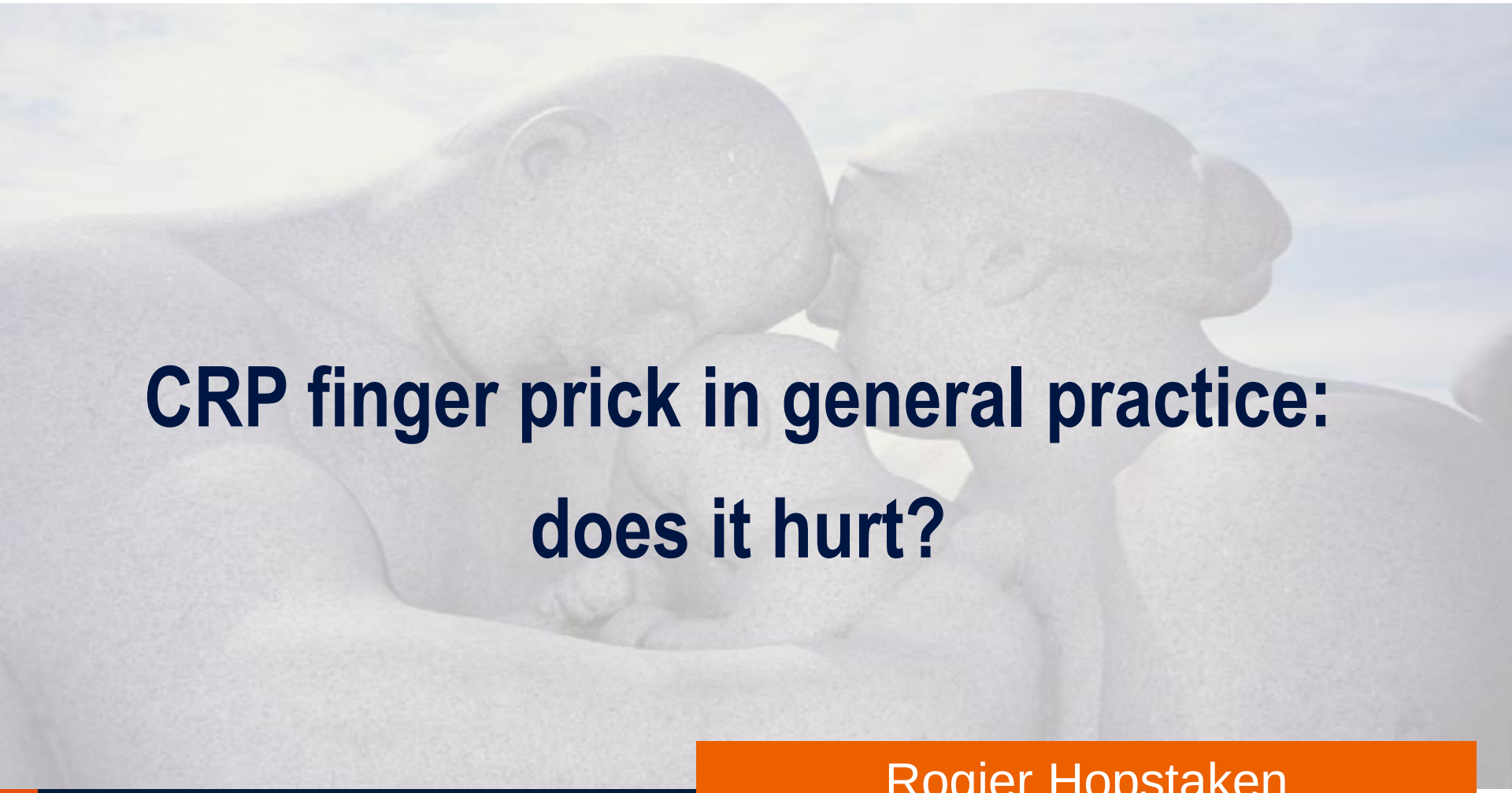
Slovak Society of GP Bojnice 16 Oct 2009



CRP finger prick in general practice: does it hurt?

Rogier Hopstaken

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Universiteit Maastricht

I am great

I am a

great

pneumonia expert

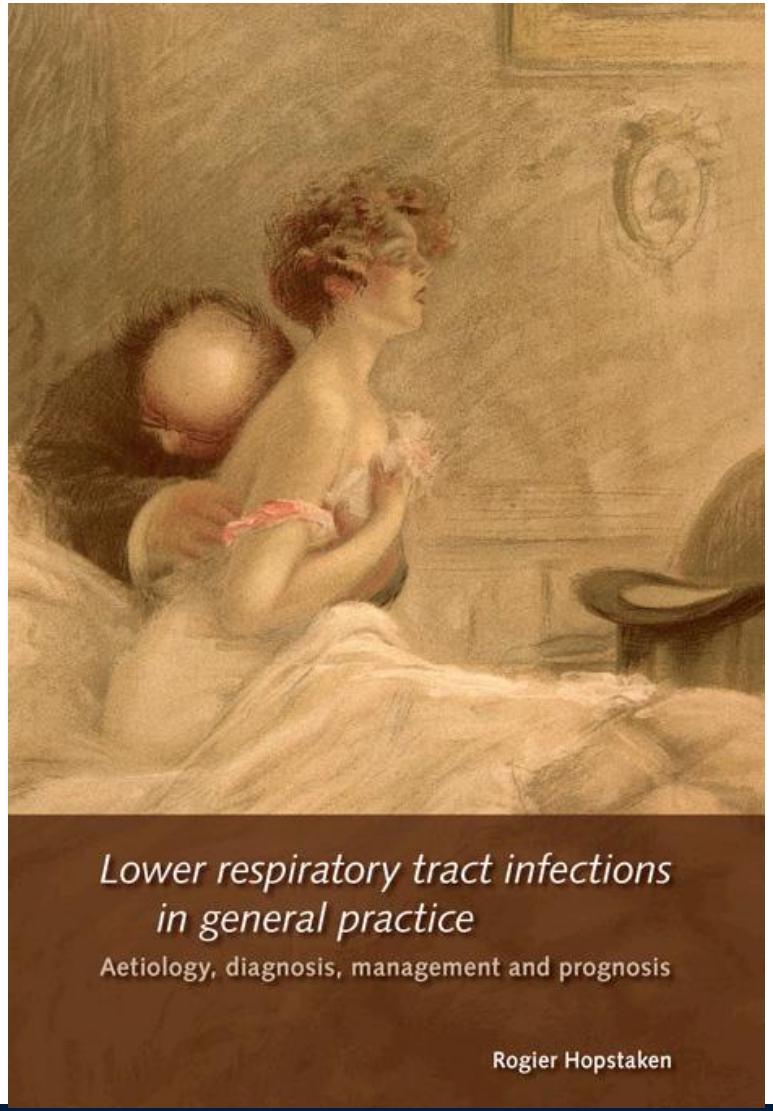
Patient

Mr X: 3 weeks dry cough, fever, chills, generally ill

Physical examination	no abnormalities
Sputum/blood, serology	no pathogen
Pulmonary infiltrate right lower lobe	
CRP	430 mg/l

Patient… pneumonia expert!

2005 thesis



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Who am I?

Family physician (GP)	1800 pts
PHC centre Eindhoven, NL	7000 pts, 40 prof.
Found Prim Health Care Centres	50 GPs

Research: RTI, antibiotics, CRP poc testing

The Netherlands

Top 20 incidence

1	URTI (R74)	51 /1000
2	Cough (R05) 	34/1000
8	Acute sinusitis (R75) 	22/1000
9	Acute bronchitis (R78) 	22/1000
12	Otitis media (H71)	16/1000

Overuse of antibiotics

- antibiotics by GPs
- for RTI
- of LRTI is acute bronchitis
- acute bronchitis treated with antibiotics

80%

Bacterial resistance

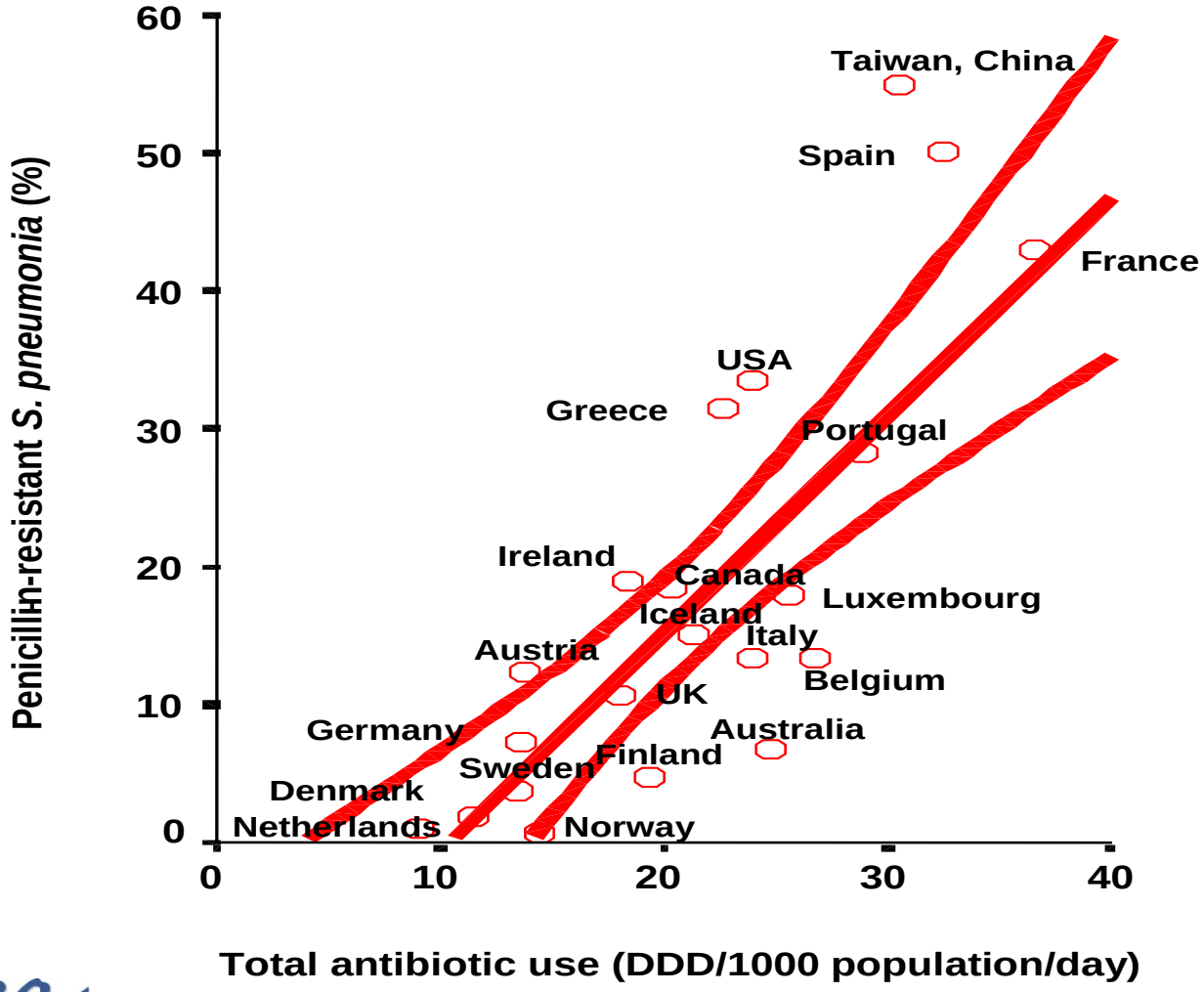
Causes of resistance

Animals

Crowding

Antibiotic overuse

Resistance and antibiotic use



Source: Albrich. Emerg Infect Dis 2004

Antibiotics for acute cough

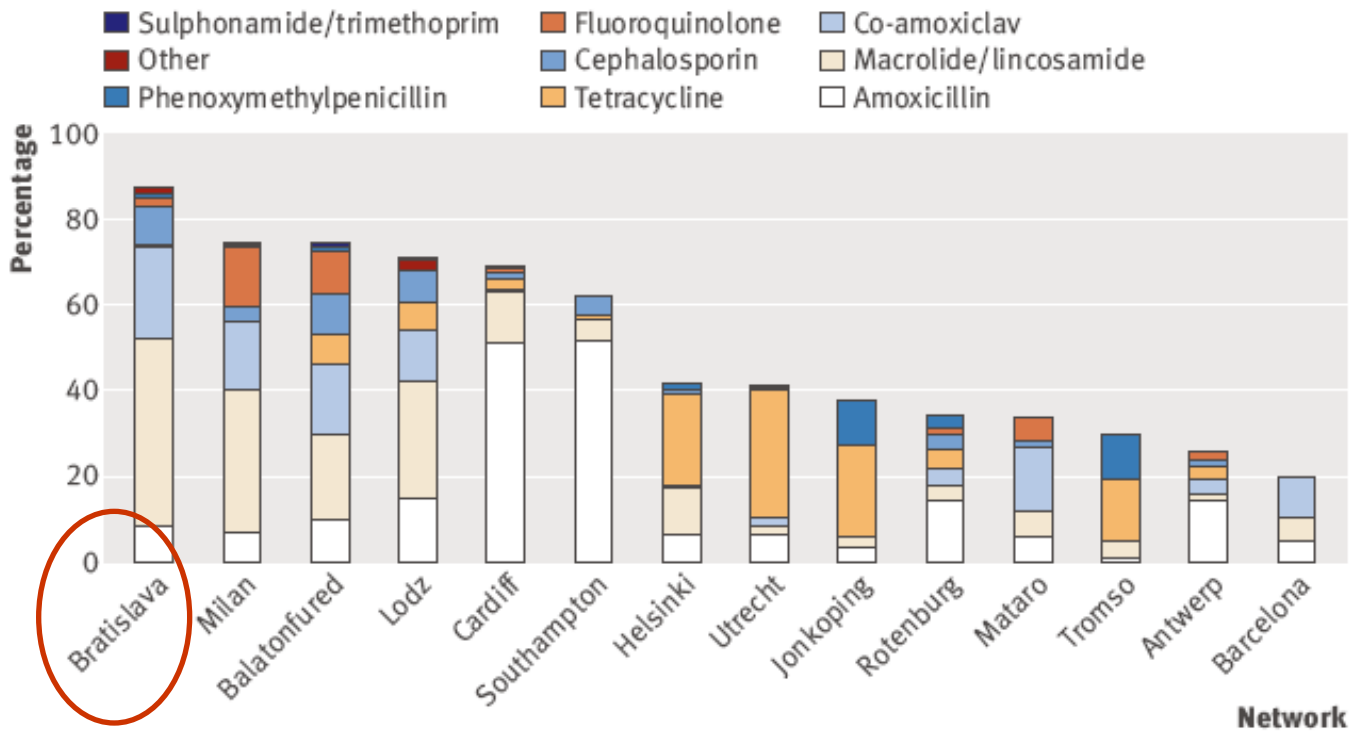


Fig 2 | Choice of antibiotic by network

N=3402

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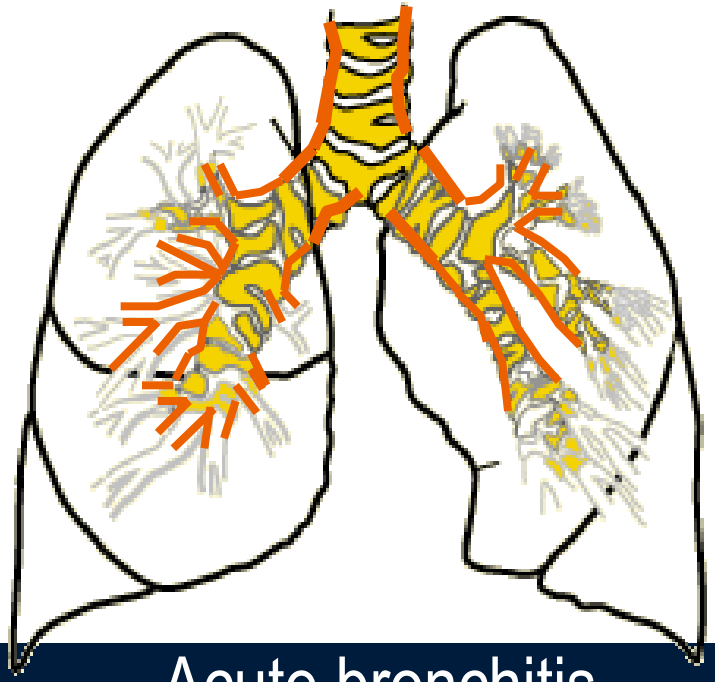
Butler BMJ 2009

Lower respiratory tract infections

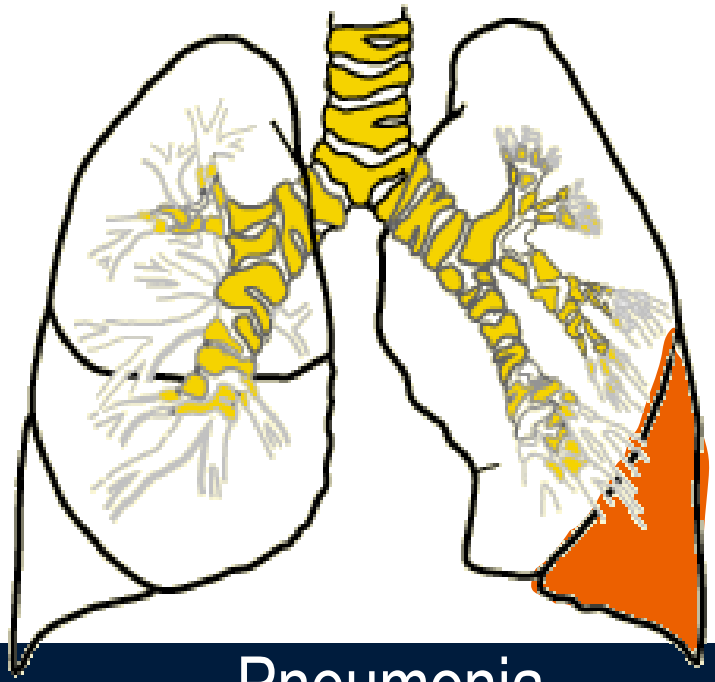
Antibiotics?

No



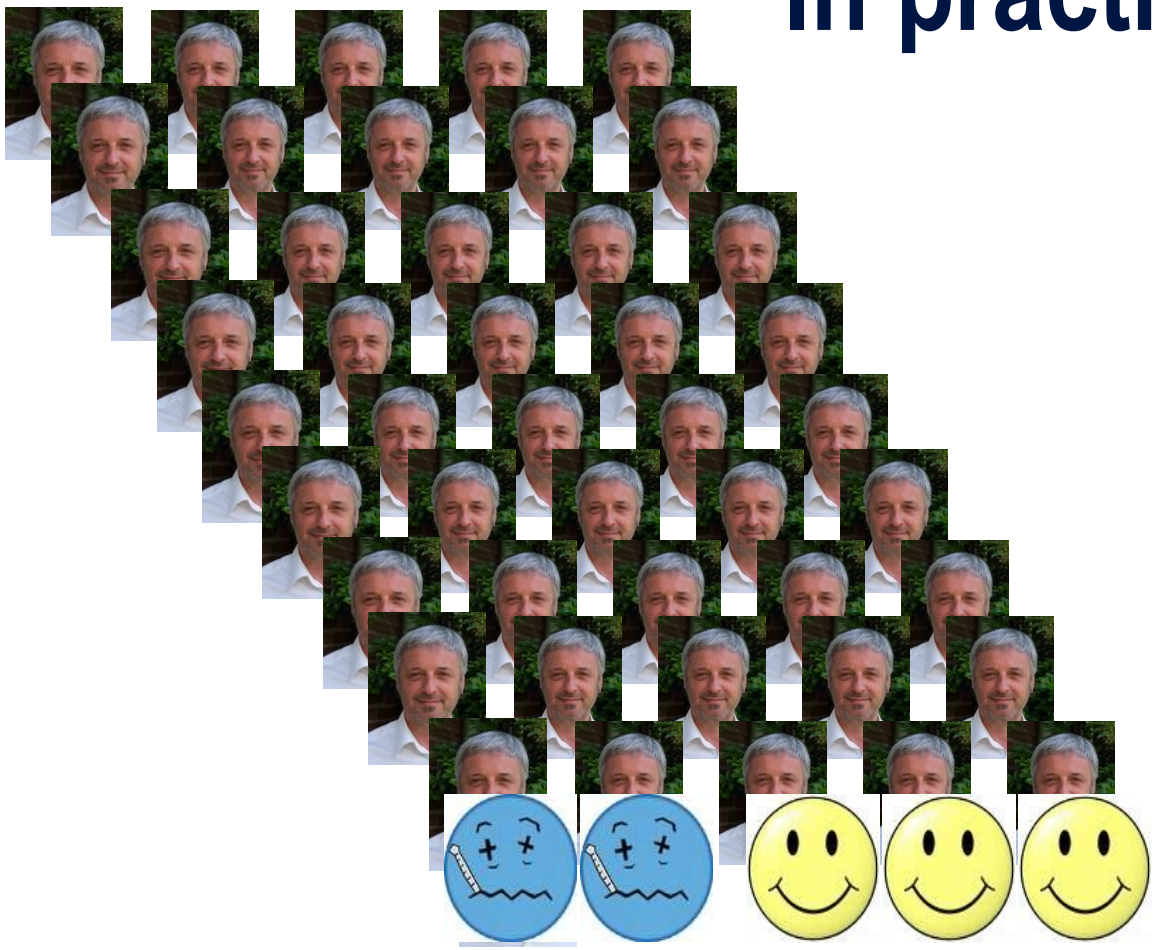
Acute bronchitis

Yes



Pneumonia

In practice



NNT 17 NNH 33

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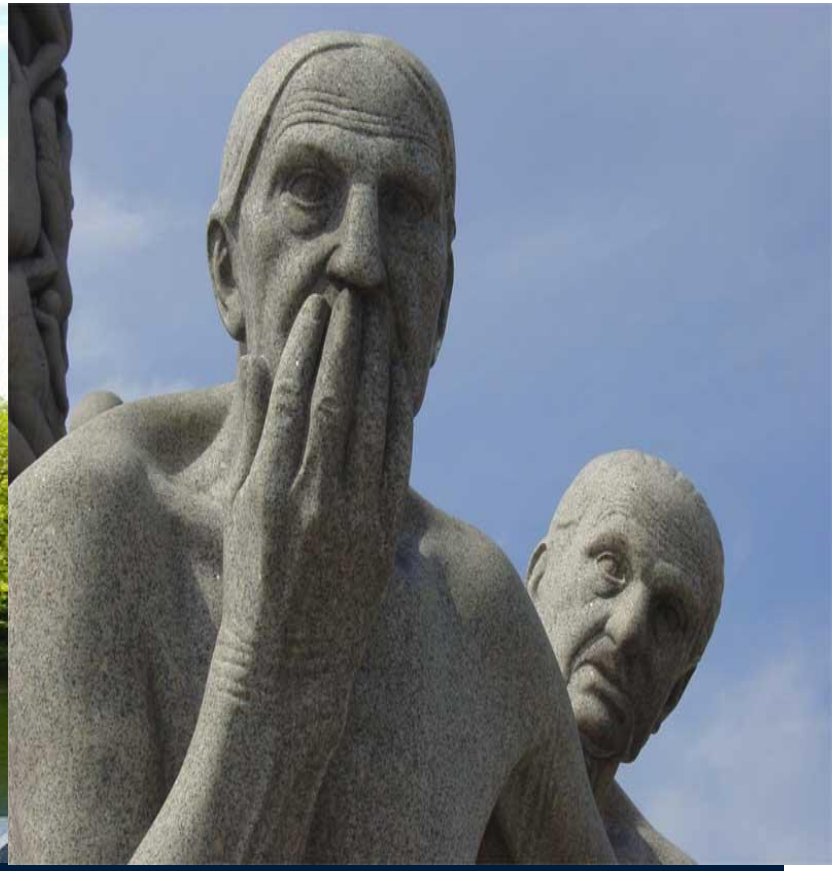
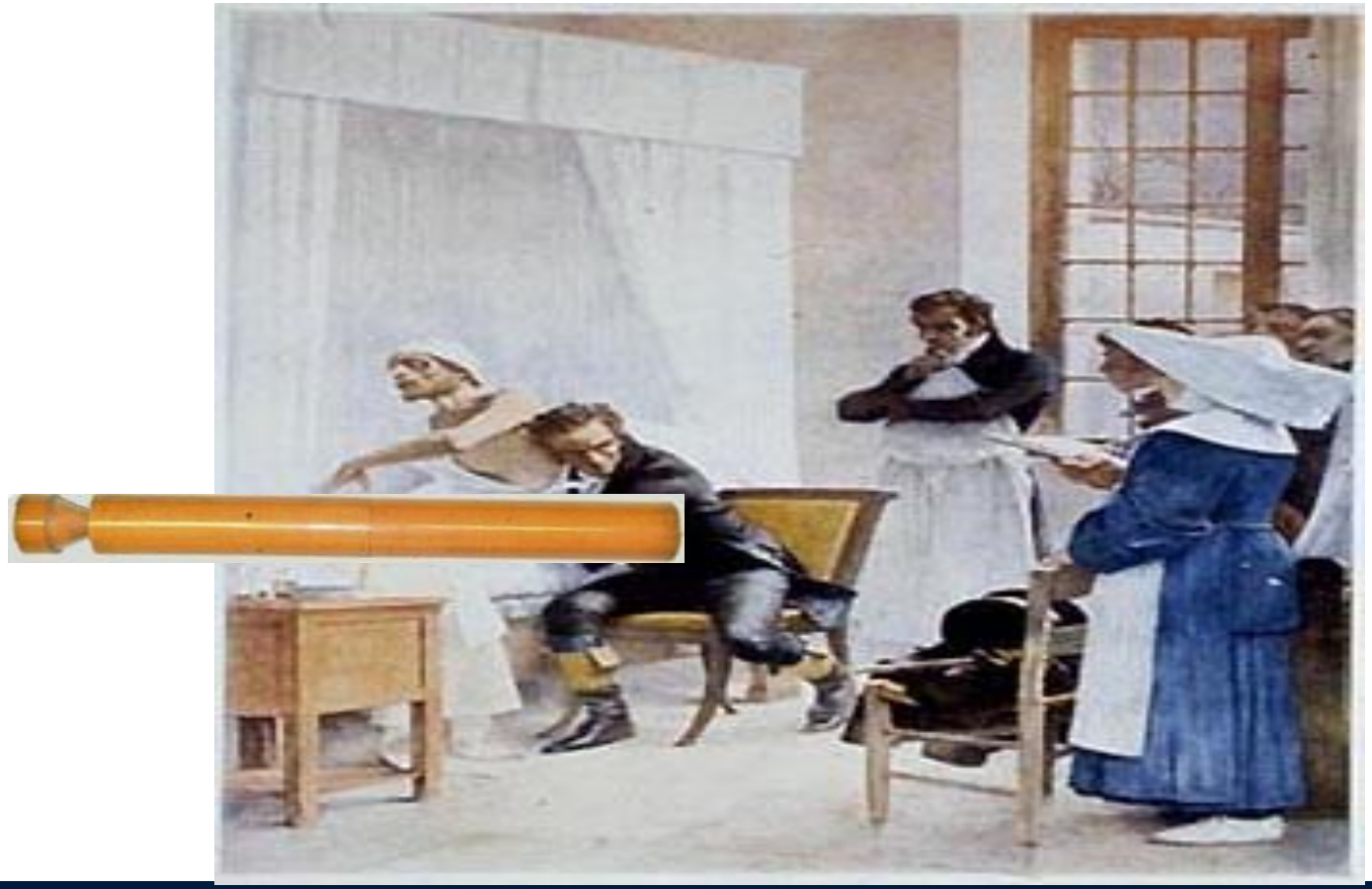
High risk groups?



Laennec at work

With or without stethoscope?



Diagnostic studies: clinical predictors of pneumonia

weak, varying predictors of pneumonia

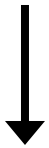
fever

physical exam contributes little

Auscultation abnormalities

are present in

pneumonia AND acute bronchitis

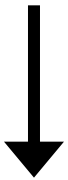


low predictive value for pneumonia

Hopstaken Brit J Gen Pract 2003

Auscultation abnormalities

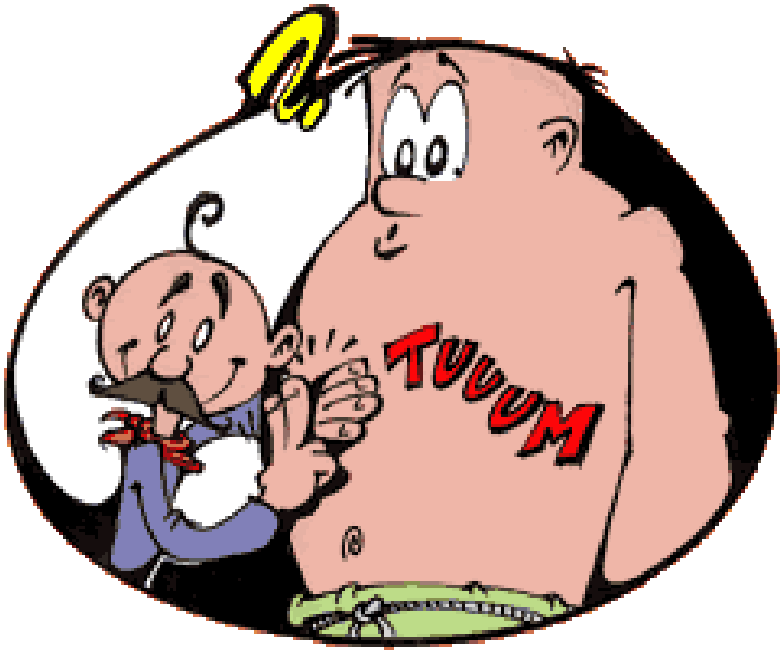
most important clinical reason for GPs to prescribe antibiotics



unnecessary antibiotic prescriptions

Hopstaken, Fam Pract 2005

Percussion



Does not predict pneumonia in general practice

J Chron Dis 1984, J Emerg Med 1989, Ann Int Med 1990, Br J Gen Pract 2003

Chest x-rays (expert panel)

Clinical diagnosis

	pneumonia	bronchitis	
pneumonia	7	22	29
bronchitis	13	360	373
	20	382	402

Melbye, Scand J Prim Health Care 1992

Chest x-rays (2-3 interpretations)

Clinical diagnosis

	pneumonia	bronchitis	
pneumonia	4	17	21
bronchitis	28	194	222
	32	211	243

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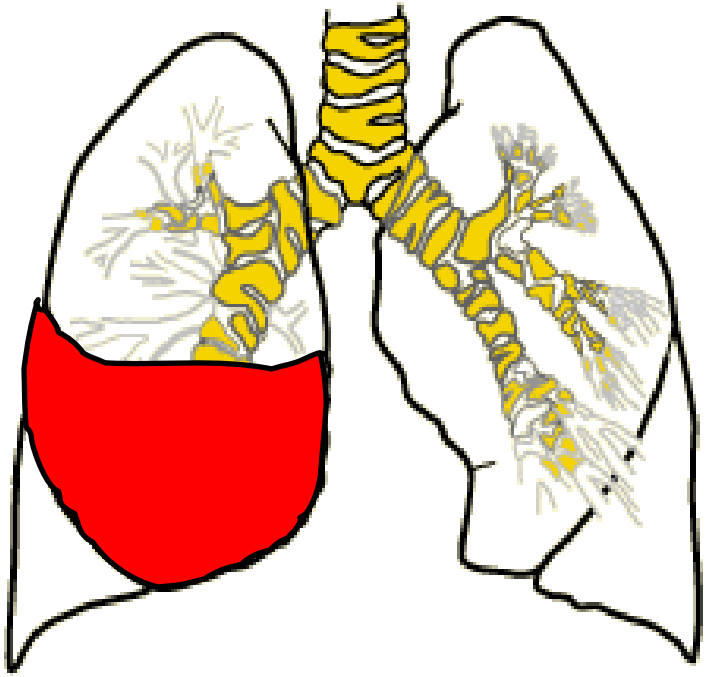
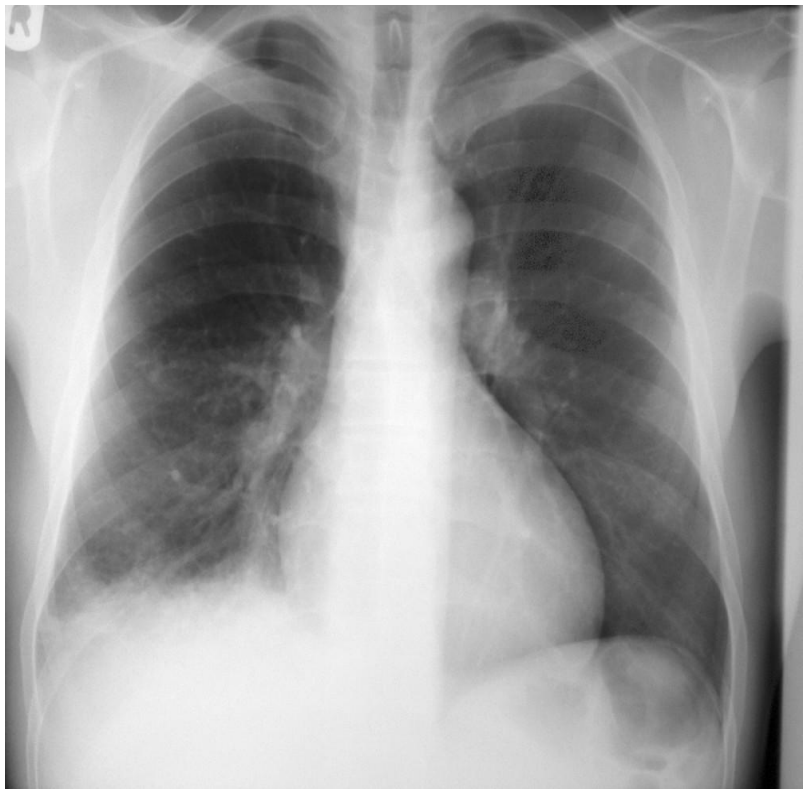
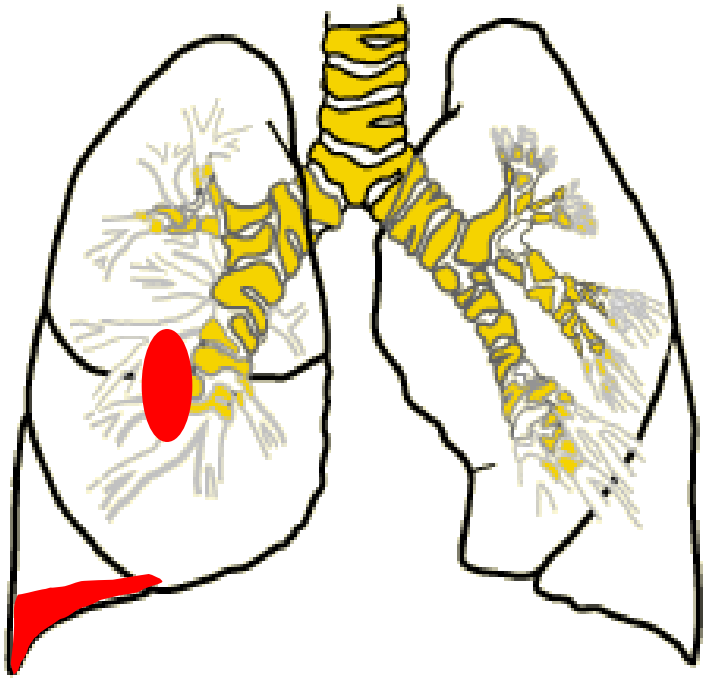
Hopstaken, Br J Gen Pract 2003

Pneumonias we were taught…

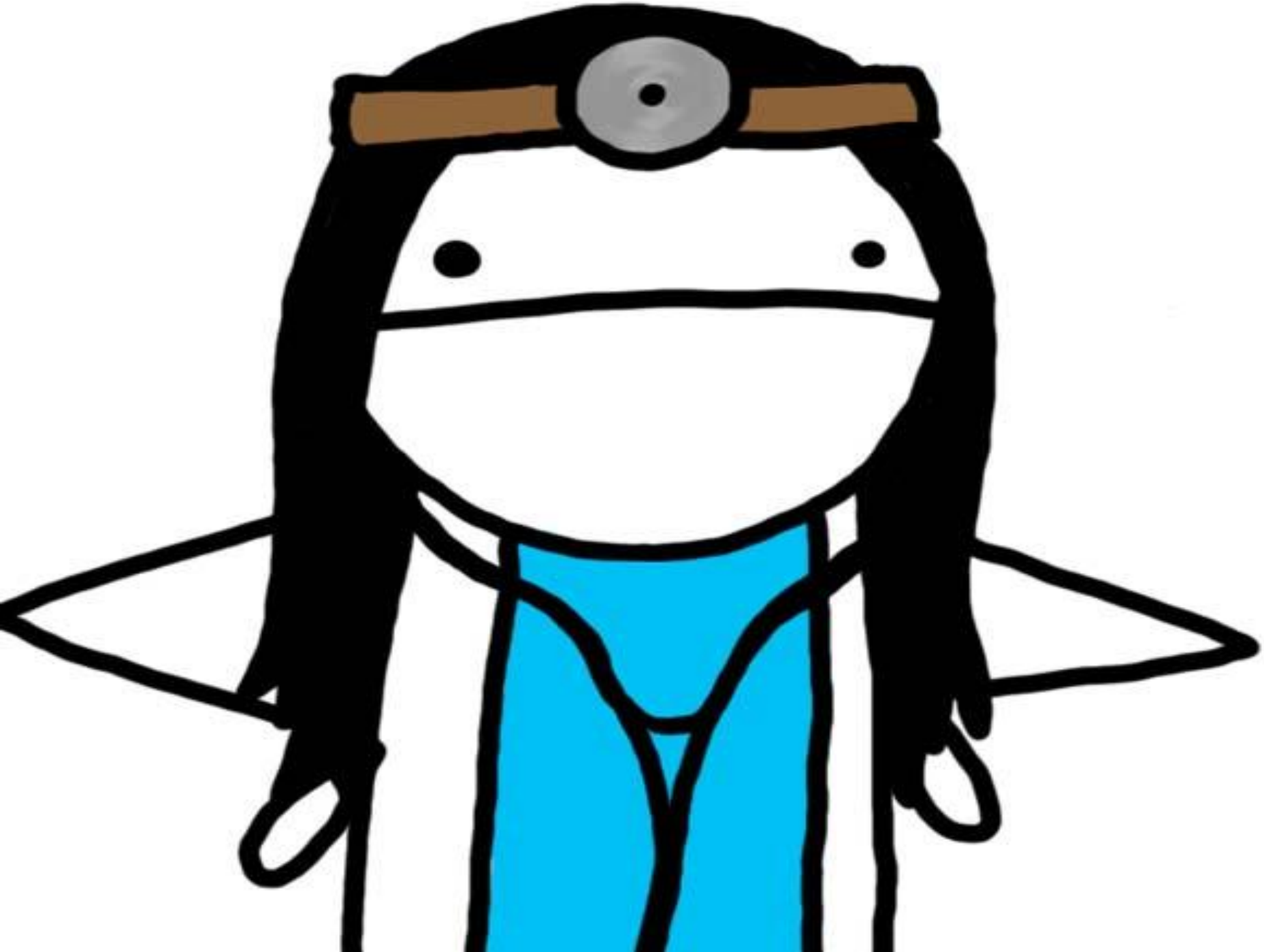


Pneumonias we see!





Practical ‘solution’



Acknowledge…

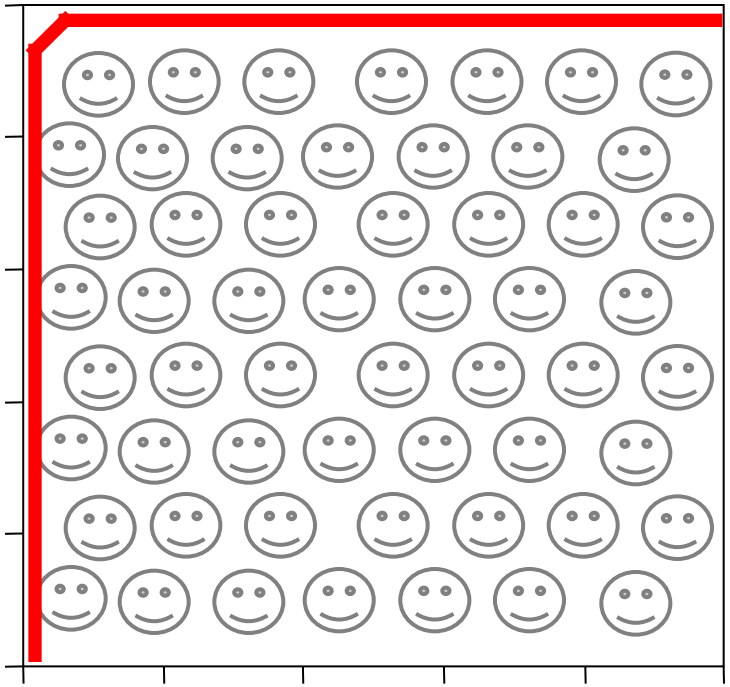
- the problem of bacterial resistance
- limitations of clinical skills
- clinical diagnosis of pneumonia is poor

CRP and pneumonia according to researchers

Perfect test

Receiver operating curve

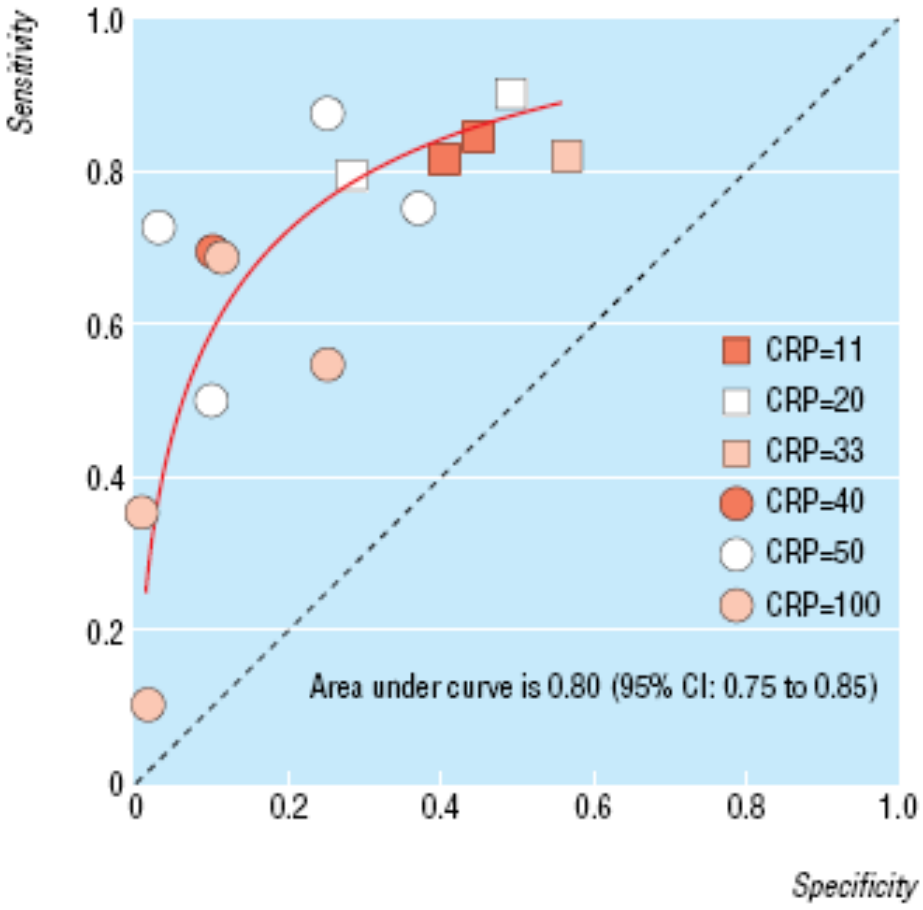
sensitivity



Area under the curve
100%

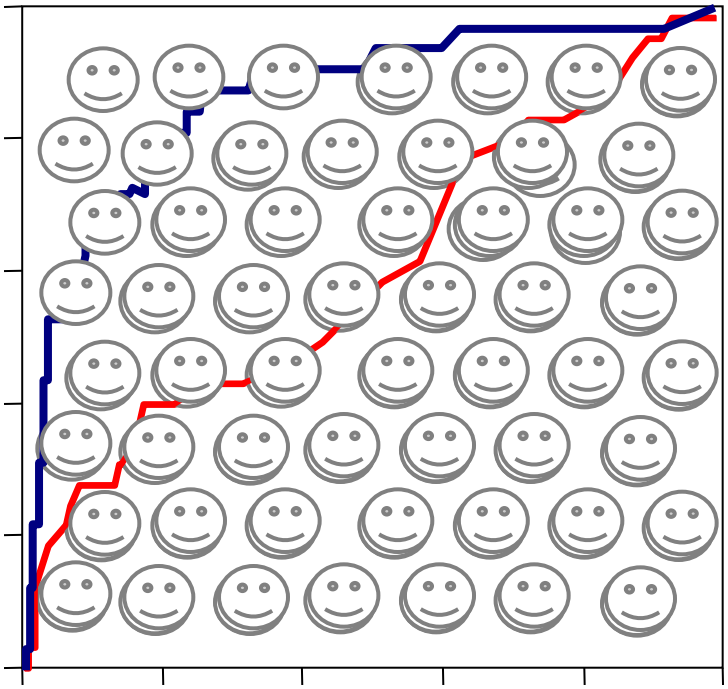
1-specificity

No test is perfect



Van der Meer BMJ 2005

No test is perfect

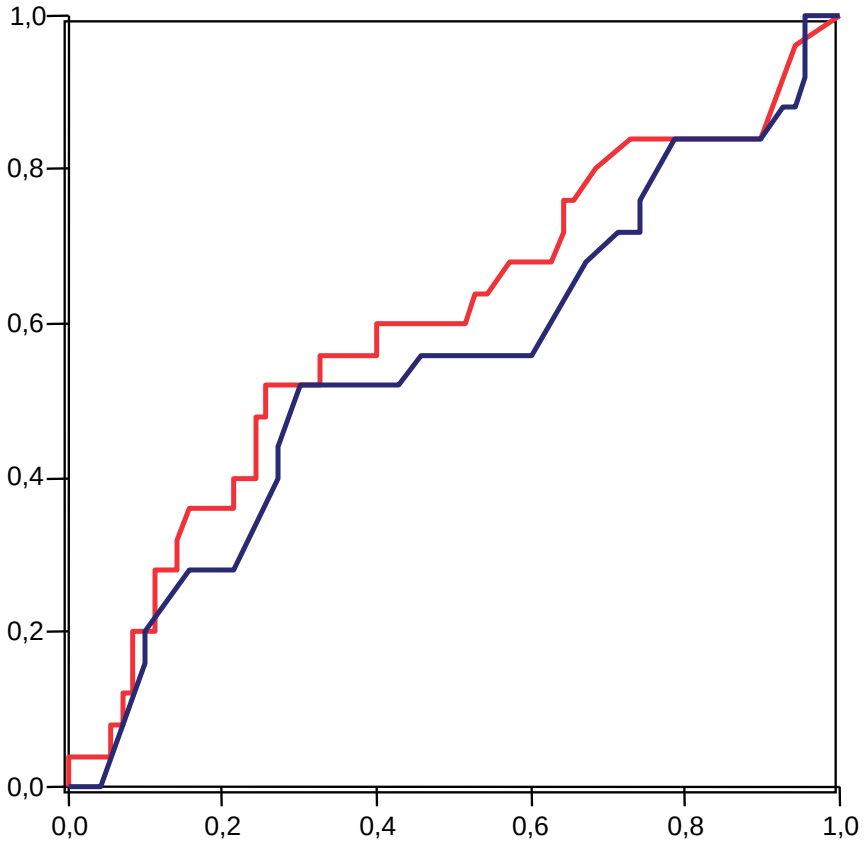


fever

CRP

Hopstaken Brit J Gen Pract 2003

CRP predicting bacterial infection?



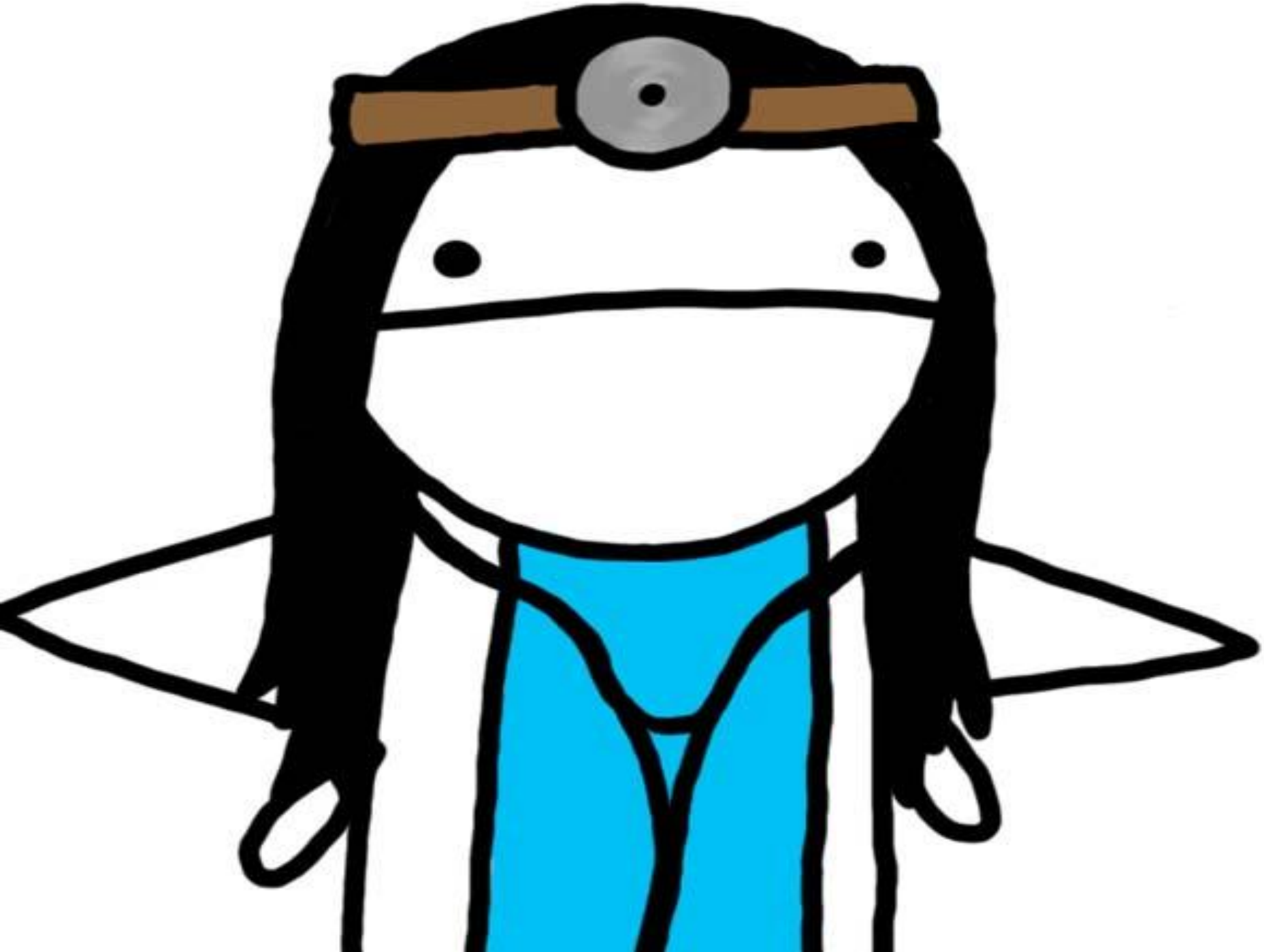
CRP
auc 0.601

Fibrinogen
auc 0.548

Hopstaken, Prim C Resp J 2009

CRP test results interpretation

CRP	
< 20	Very low probability of pneumonia
20 – 50	Low probability of pneumonia
50 – 100	Clear infection most probably acute bronchitis possibly pneumonia
> 100	Serious infection consider pneumonia



Value of CRP

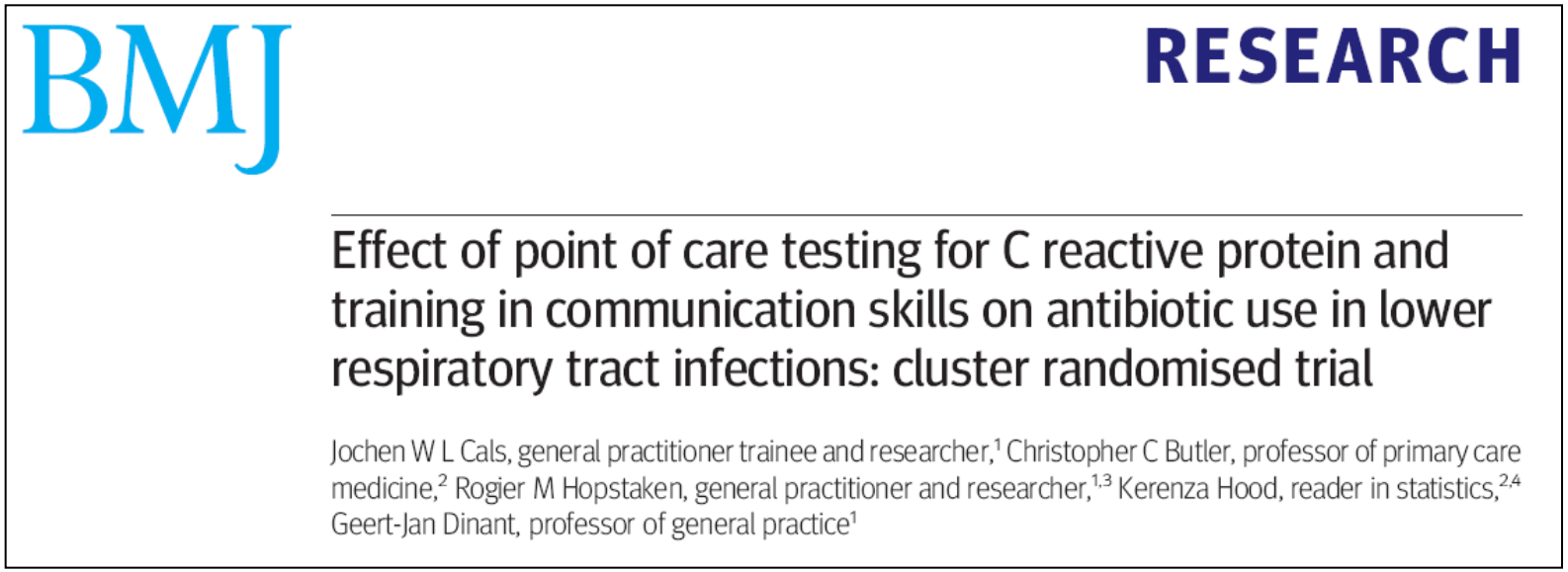
- strong predictor of pneumonia
- <20 mg/l to exclude pneumonia
- adds to history and physical exam!
- confuses researchers and doctors
- but…evidence is clear!

Less antibiotics with CRP testing?

if **not** point of care forget it!

LRTI

IMPAC^{3}T study

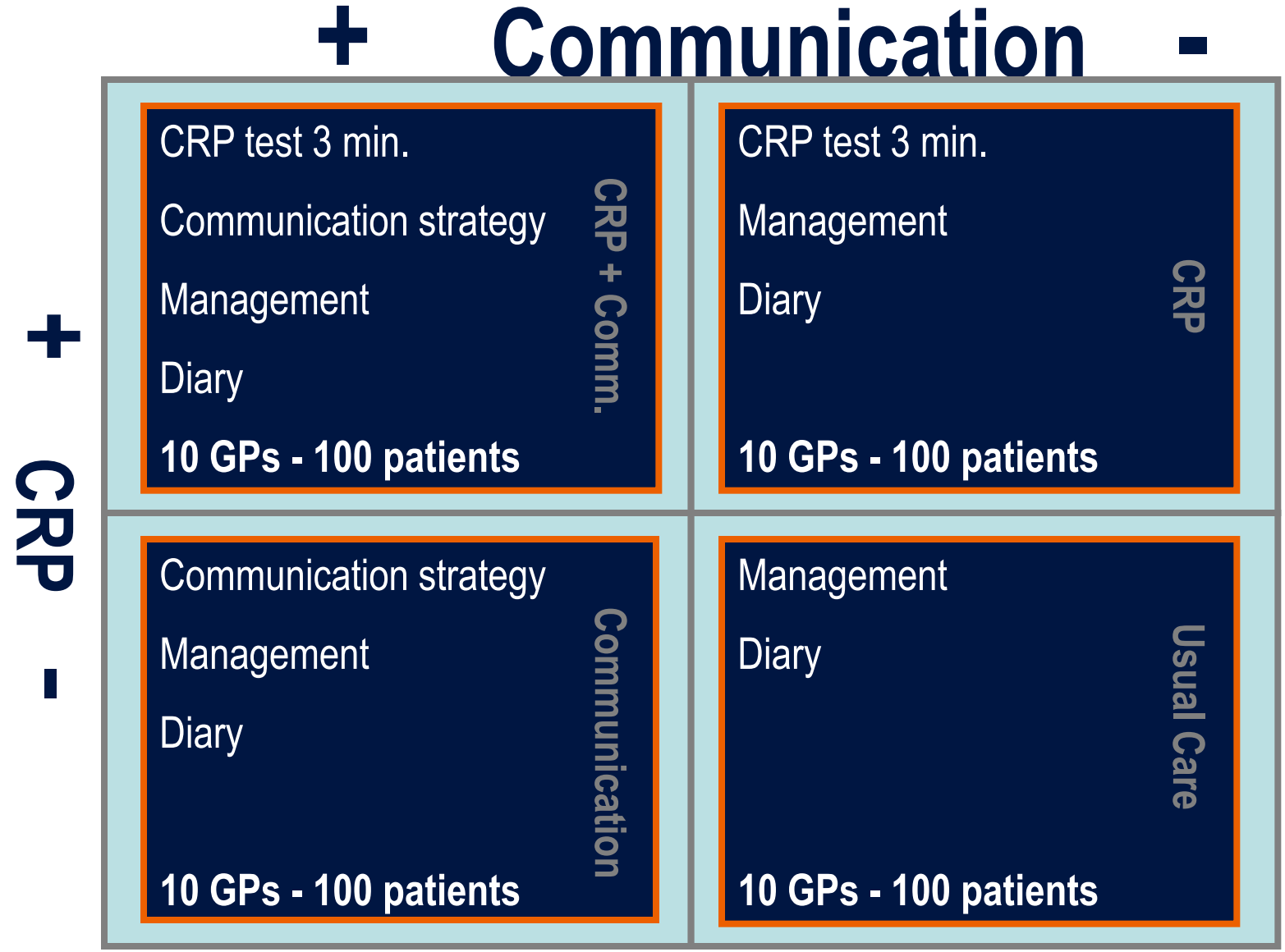


BMJ

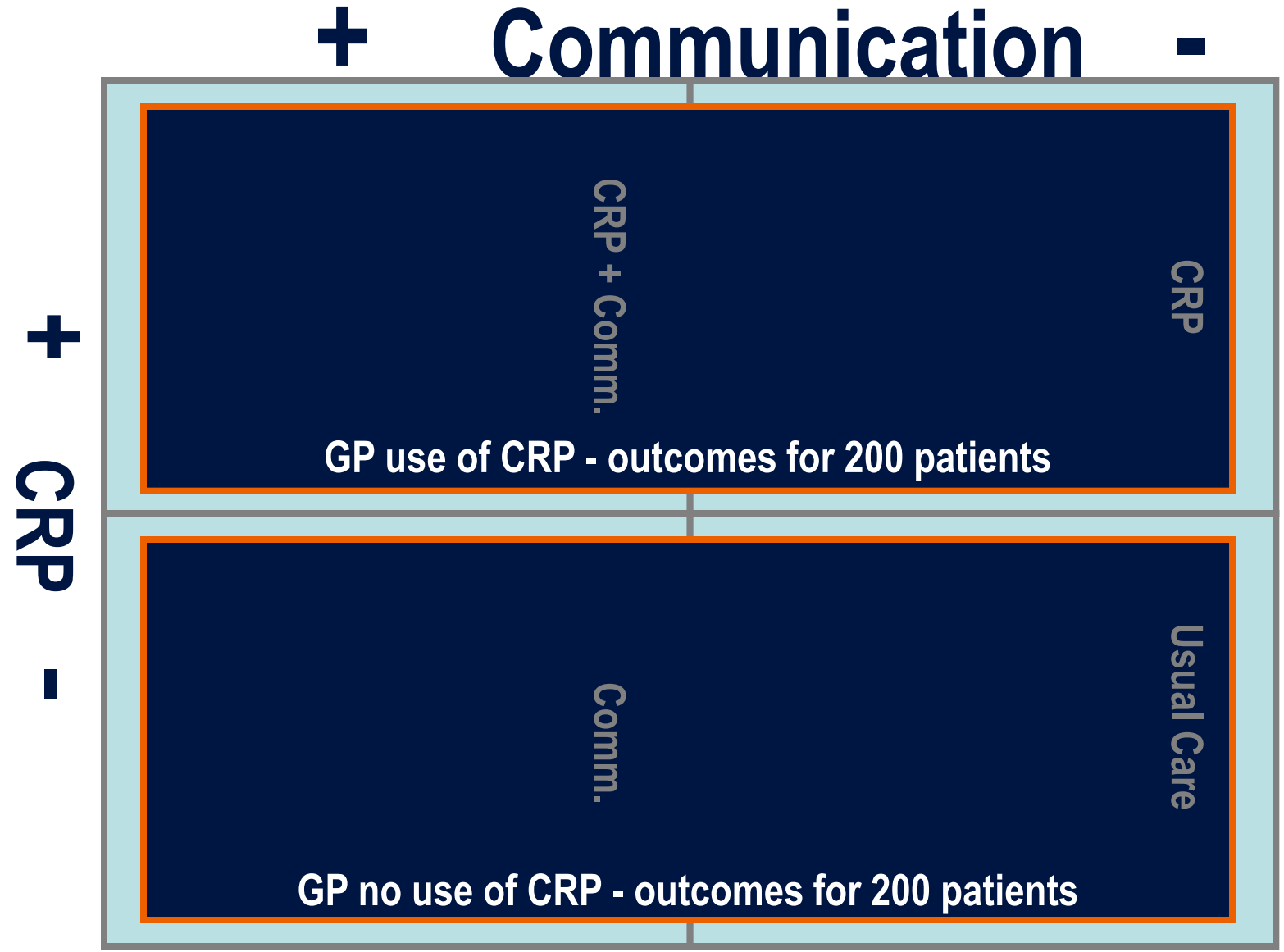
RESEARCH

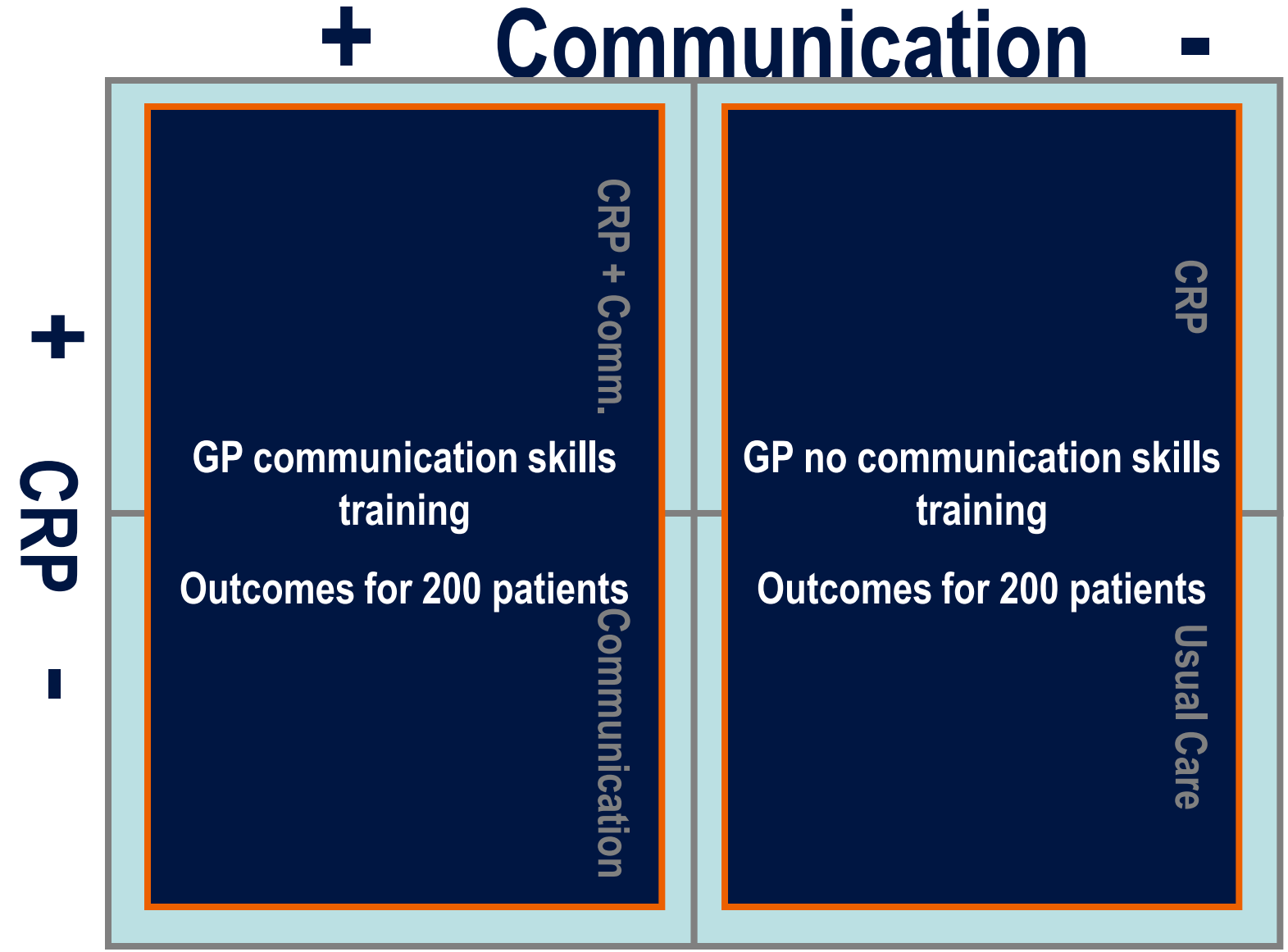
Effect of point of care testing for C reactive protein and training in communication skills on antibiotic use in lower respiratory tract infections: cluster randomised trial

Jochen W L Cals, general practitioner trainee and researcher,[1] Christopher C Butler, professor of primary care medicine,[2] Rogier M Hopstaken, general practitioner and researcher,[1,3] Kerenza Hood, reader in statistics,[2,4] Geert-Jan Dinant, professor of general practice[1]



Cals Brit Med J 2009


+ Communication -
+ CRP -
CRP + Comm.
CRP
GP use of CRP - outcomes for 200 patients
Comm.
Usual Care
GP no use of CRP - outcomes for 200 patients


+ Communication -
+ CRP -
CRP + Comm.
GP communication skills training
Outcomes for 200 patients
Communication
CRP
GP no communication skills training
Outcomes for 200 patients
Usual Care

Communication training

- reason for encounter
- concerns/worries
- explore expectations
- pt beliefs of illness and AB
- discuss long duration, but positive outcome
- safety net

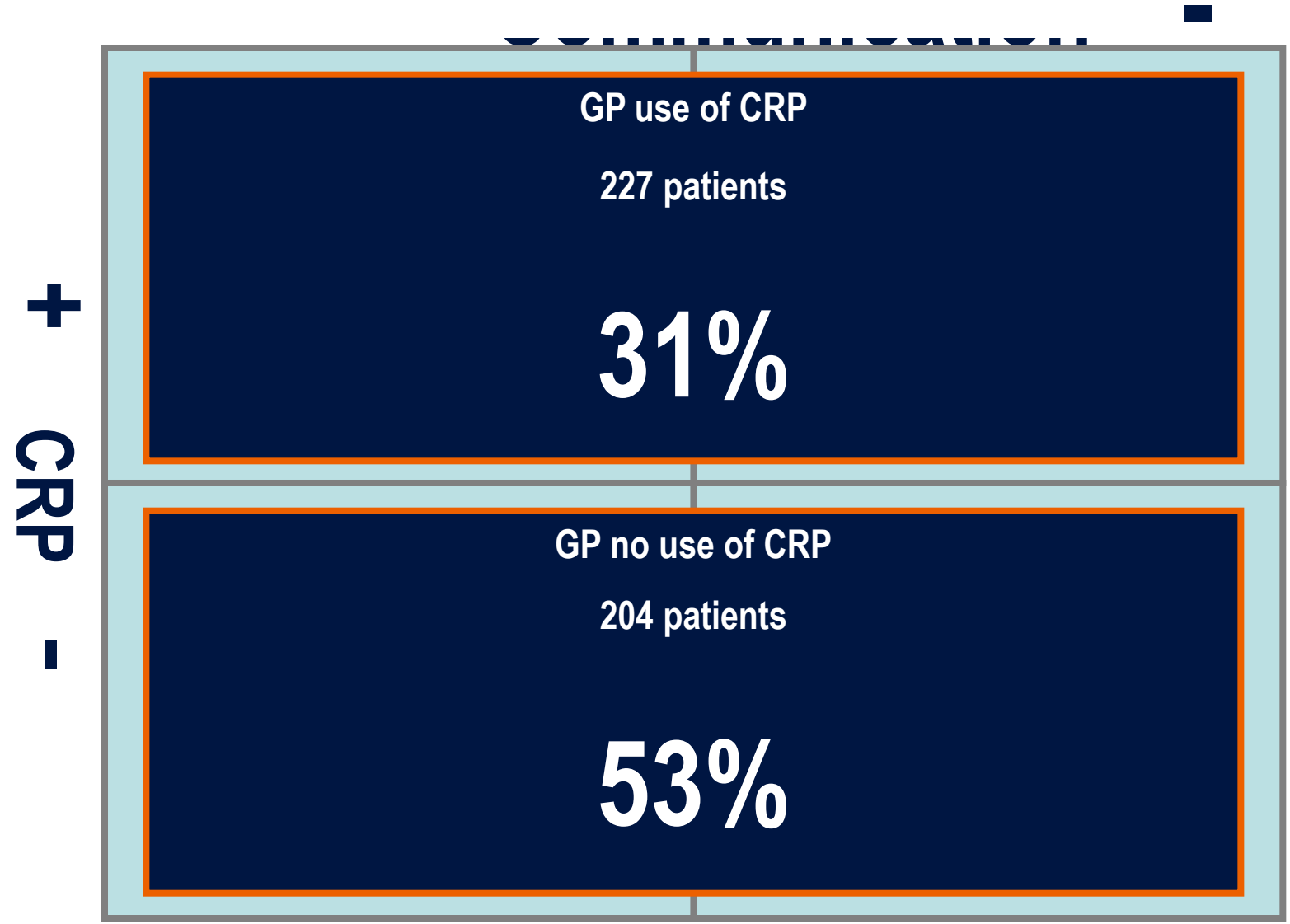
Cals, Patient Educ Couns 2007

CRP point of care

- One drop of blood
- Result < 3 minutes
- <8 tot 250 mg/L

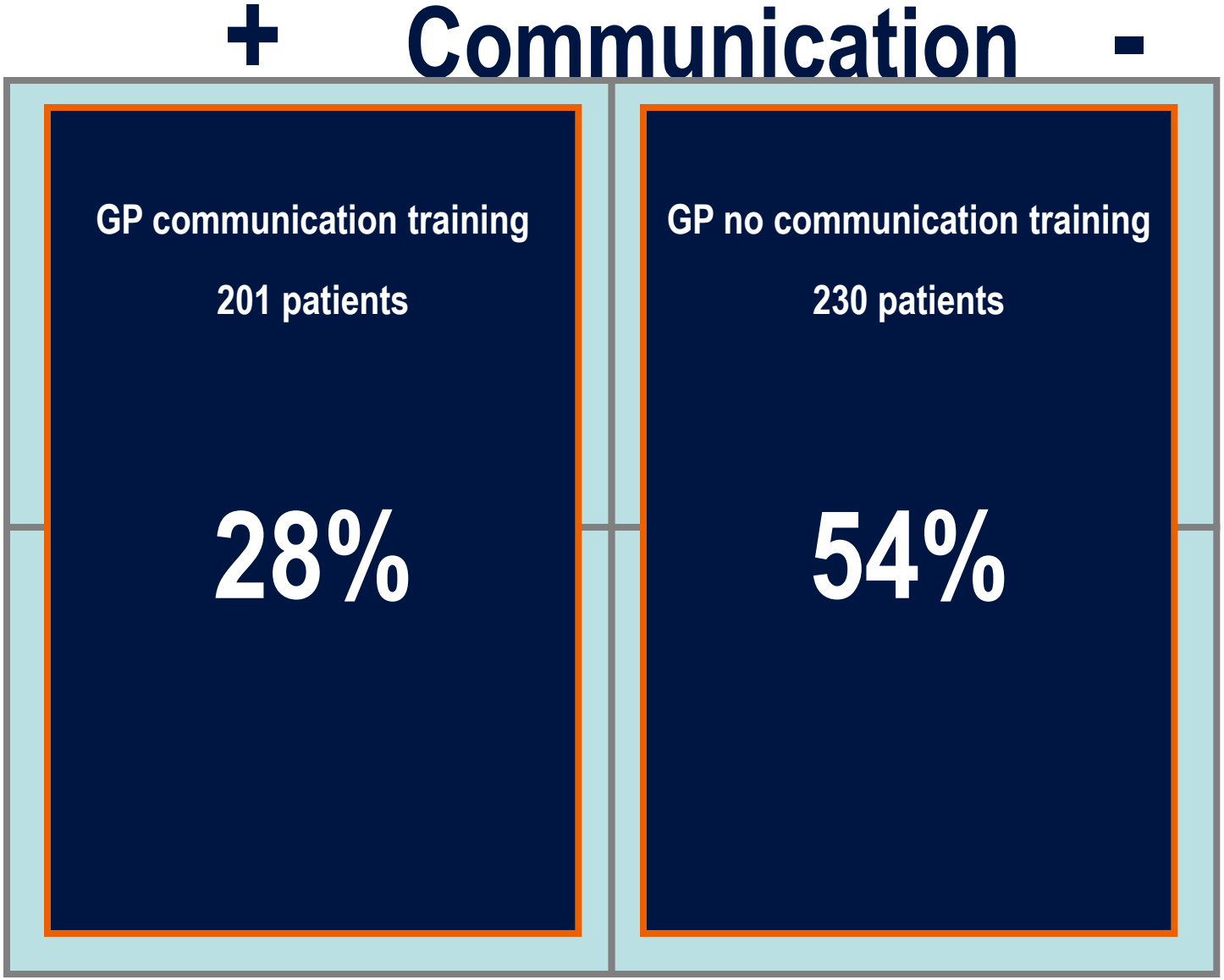
Axis-Shield

Universiteit Maastricht



AB prescribing day 1

p = 0.02*



AB prescribing day 1

$p < 0.01$*

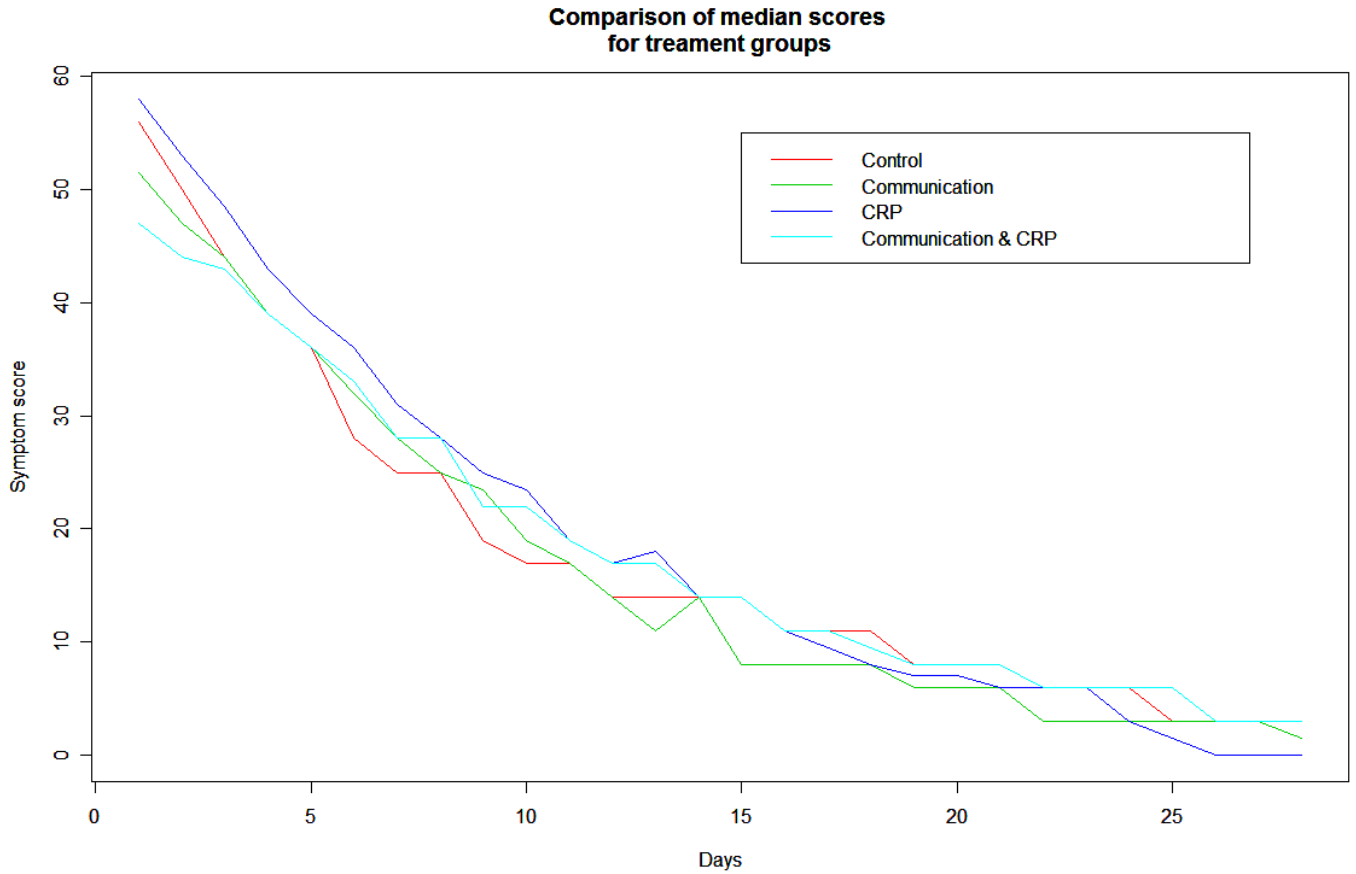
Secondary outcomes

	CRP		Communication	
	Yes (n=227)	No (n=204)	Yes (n=201)	No (n=230)
Reconsultation	35%	30%	27%	37%
Satisfaction	77%	76%	79%	74%
Consultation intention	75%	79%	74%	80%
Enablement, median (IQR)	3 (4)	3 (4)	3 (4)	3 (4)
Patient reported time to recovery, median (25-75 IQ)	**22 days (14-28)**			

STICHTING GEZONDHEIDSCENTRA EINDHOVEN sge

All n.s.*

Recovery


Comparison of median scores
for treament groups
Control
Communication
CRP
Communication & CRP
Symptom score
0
10
20
30
40
50
60
0
5
10
15
20
25
Days

IMPAC^{3}T

Reduced antibiotic prescribing

without compromising GP and patient relevant outcomes

(reconsultation, clinical recovery, patient satisfaction and enablement)

IMPAC^{3}T

Economic evaluation IMPACT study

Conclusion

The two strategies, both singly and combined, are cost effective measures to reduce antibiotic prescribing for LRTI

Submitted for publication

BJGP
The British Journal of General Practice

Predictors of patient-initiated reconsultation for lower respiratory tract infections in general practice

Jochen WL Cals, Kerenza Hood, Nienke Aaftink, Rogier M Hopstaken, Nick A Francis, Geert-Jan Dinant and Christopher C Butler

- Patient reported dyspnoea
- Post-consultation worries
- Intermediately elevated CRP values (20-99 mg/l)

GPs' opinions on CRP PoC testing

- positive attitudes for LRTI in particular
- reimbursement essential
- CRP uptake in guidelines requested
- concern: dealing with intermediate elevated test results

Fam Practice (accepted for publication)

Maastricht University

CRP Assisted Prescribing for REspiratory tract infections to Stimulate Antibiotic stewardship (CAPRESA)

RCT in primary care

Jochen Cals and Rogier Hopstaken

These days in practice…

- Time pressure
- Expectations (patient)
- Perceived expectations (GP)
- Knowledge of AB
- physician – patient relation

Serious

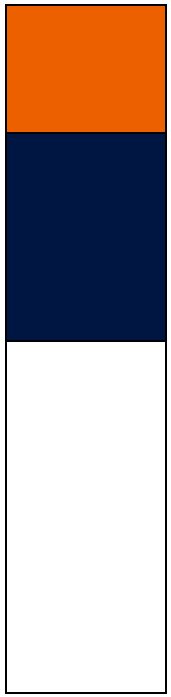
Very ill — AB — AB

moderately ill — ? — AB

Not ill — No AB — (No) AB

Self-limiting

CAPRESA



High CRP — AB

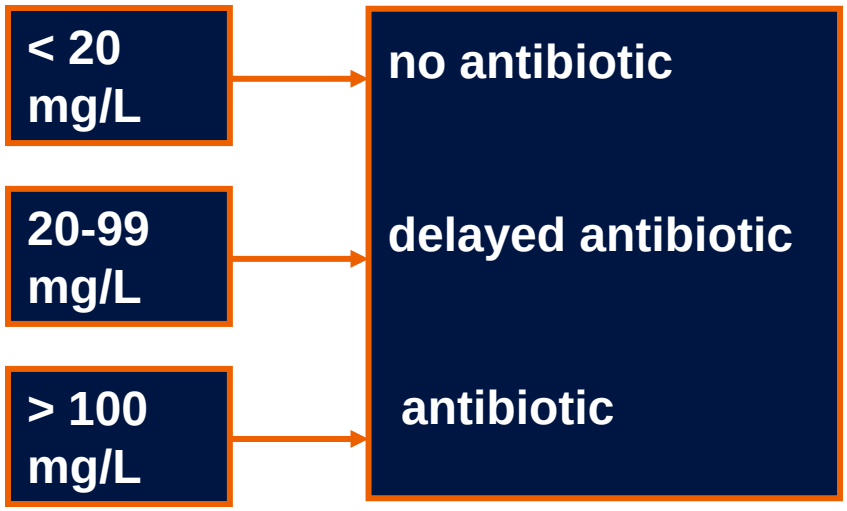
Moderately elevated CRP — Delayed AB

Low CRP — No AB

Reduces antibiotic use
Shared decision
Safety net

Arroll BJGP 2003, Little JAMA 2005

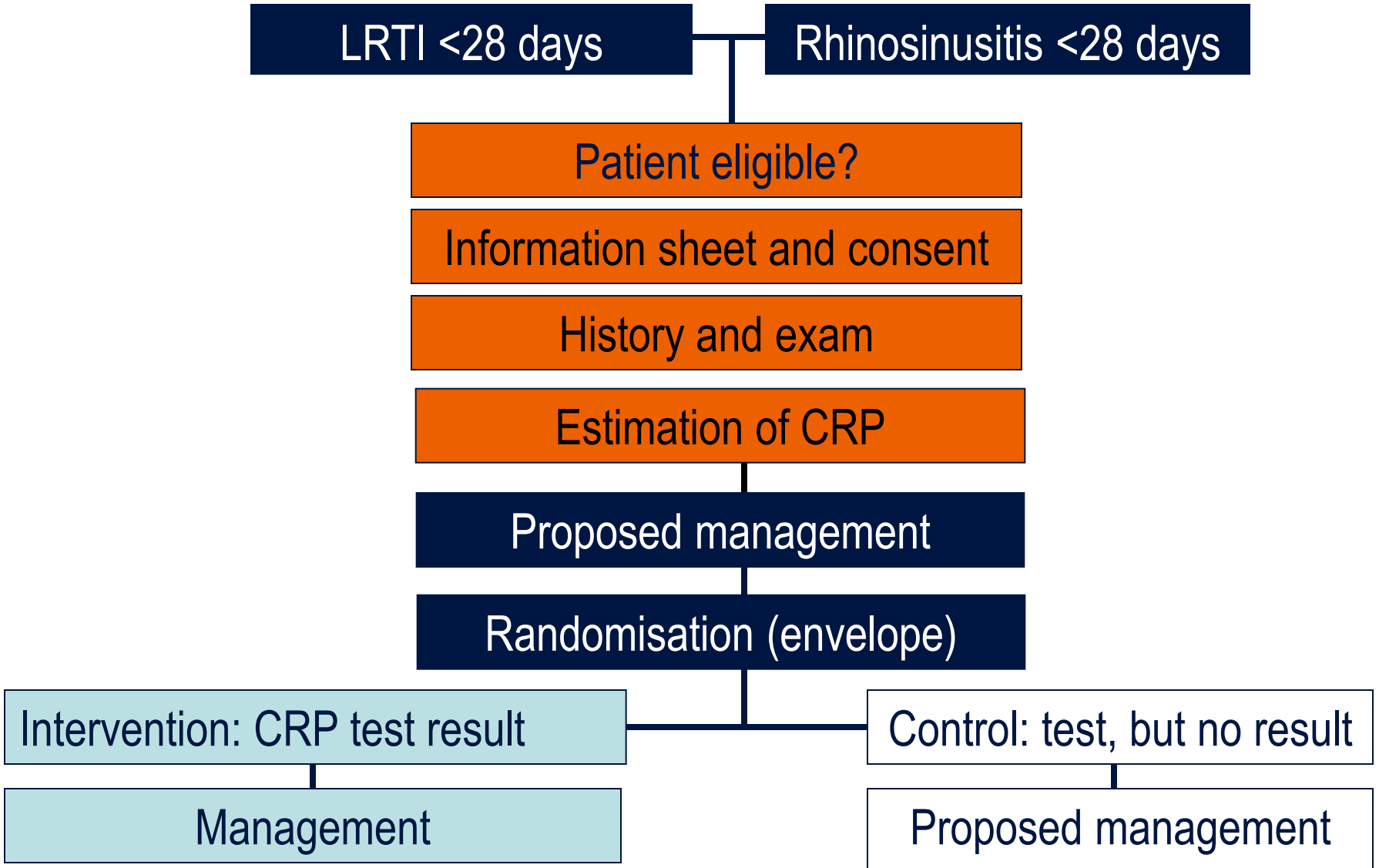
Guiding the GPs

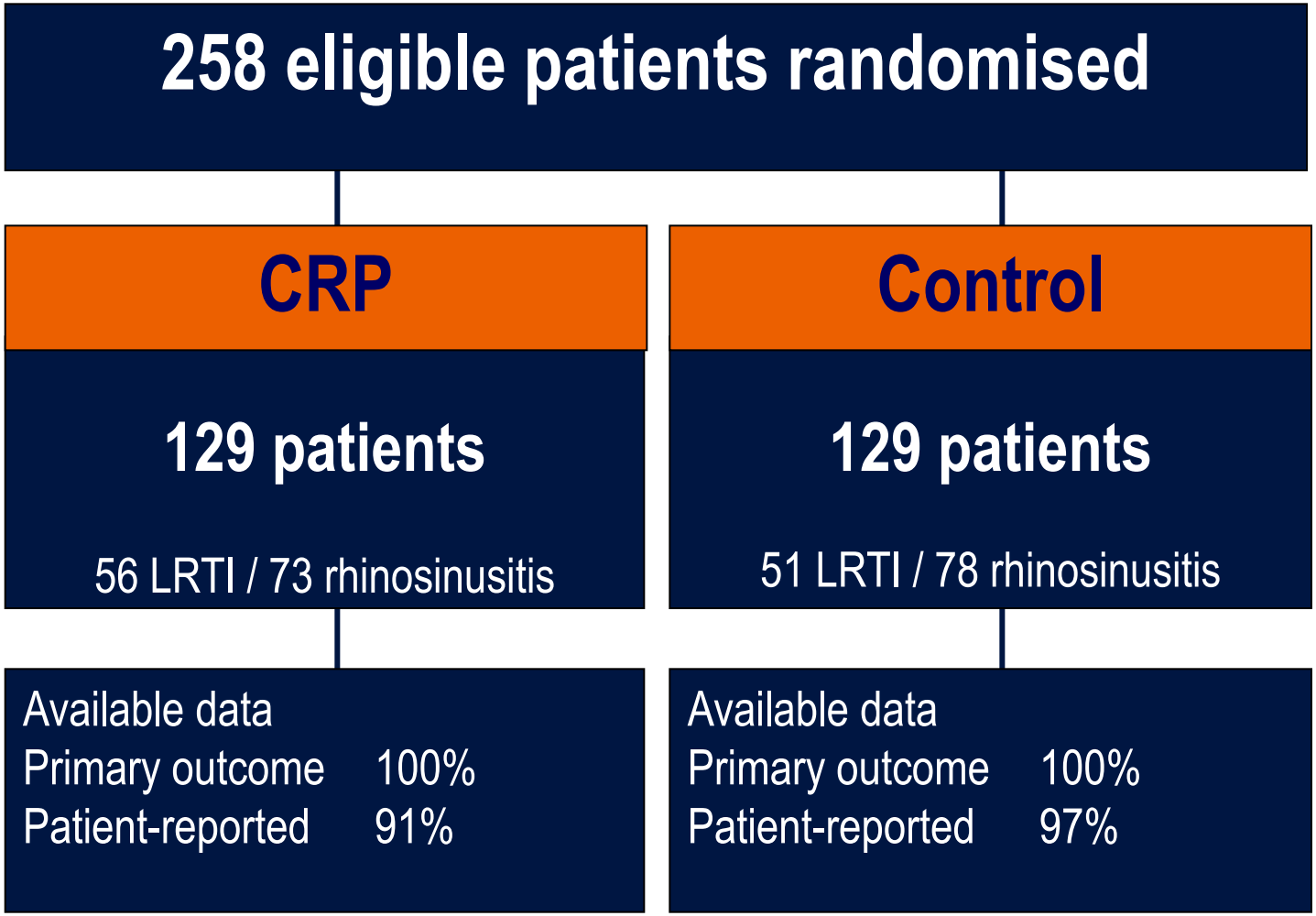


Add CRP to findings from history and physical exam!

CAPRESA - Objective

Determine effect of guided PoC CRP testing on antibiotic prescribing for LRTI and rhinosinusitis

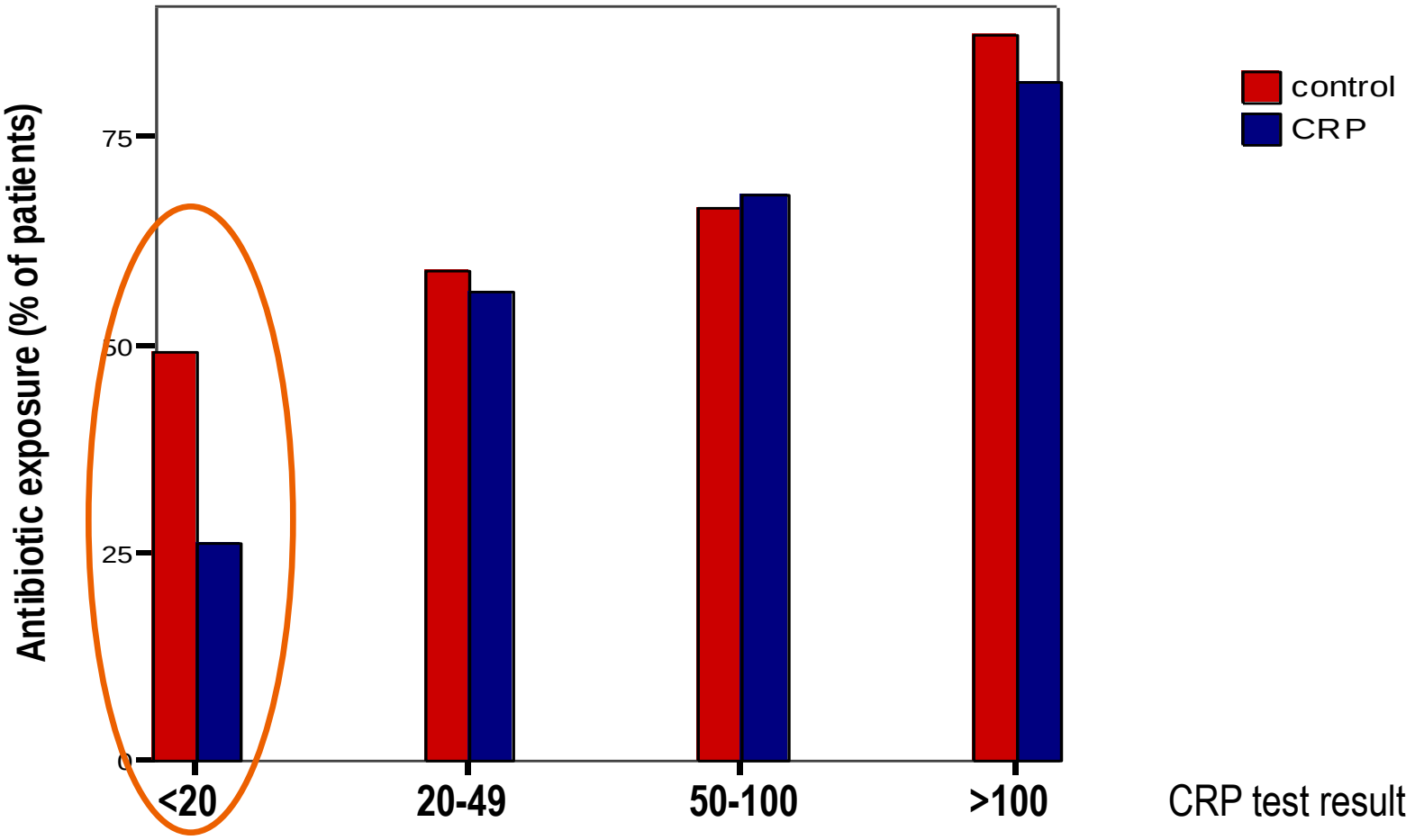

LRTI <28 days
Rhinosinusitis <28 days
Patient eligible?
Information sheet and consent
History and exam
Estimation of CRP
Proposed management
Randomisation (envelope)
Intervention: CRP test result
Control: test, but no result
Management
Proposed management
= actual management


258 eligible patients randomised
CRP
Control
129 patients
56 LRTI / 73 rhinosinusitis
129 patients
51 LRTI / 78 rhinosinusitis
Available data
Primary outcome 100%
Patient-reported 91%
Available data
Primary outcome 100%
Patient-reported 97%

Results – primary outcome

	CRP assistance		
	Yes n=129	No n=129	P-value
Antibiotic use on day 1	56 (43.4%)	73 (56.6%)	0.03
Antibiotic use days 1-28	68 (52.7%)	84 (65.1%)	0.04
Use of delayed prescription	5/22 (23%)	21/29 (73%)	

Antibiotic exposure by CRP categories

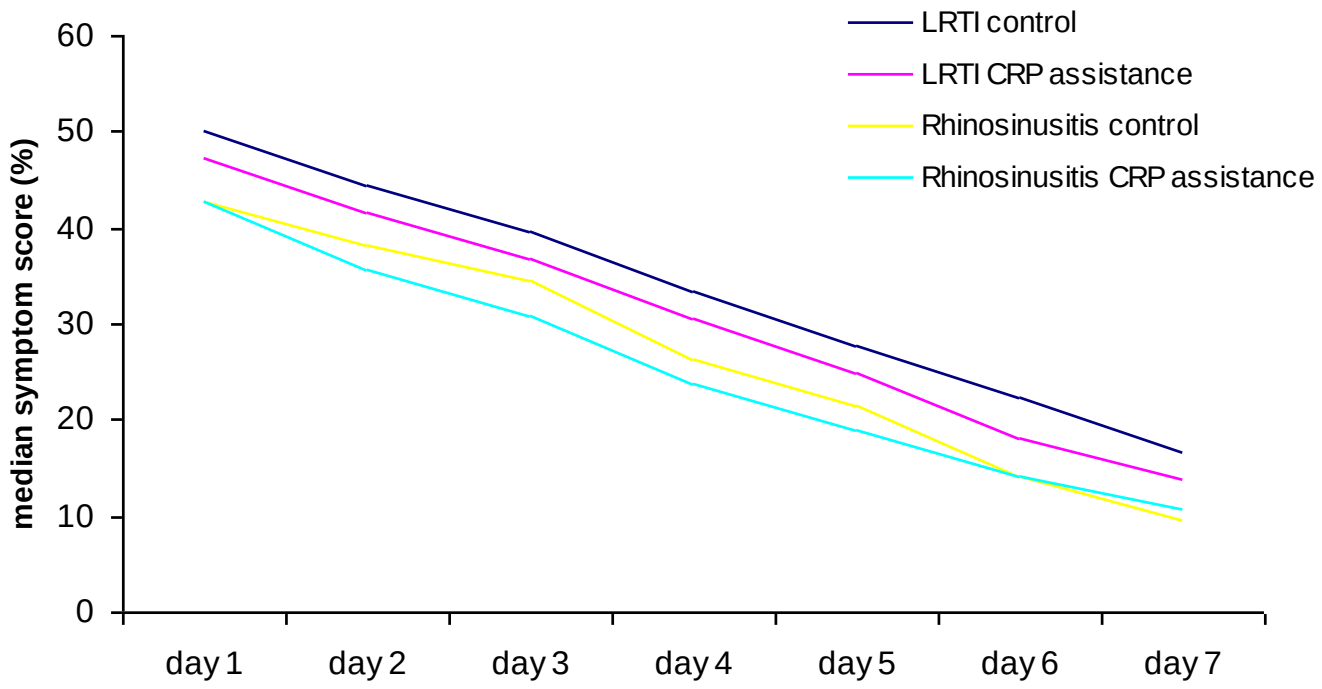


<20	20-49	50-100	>100
140 (54%)	62 (24%)	37 (14%)	19 (7%)

Results – other outcomes

	CRP guidance		
	Yes n=129	No n=129	P-value
Pt reported time to recovery (median, 25-75 IQ, days)	14 (10-28)	15 (7-30)	ns
Reconsultaton	33 (25.6%)	23 (17.8%)	ns
Satisfaction	83 (77.6%)	70 (65.4%)	<0.05

Recovery – symptom scores per day



CAPRESA

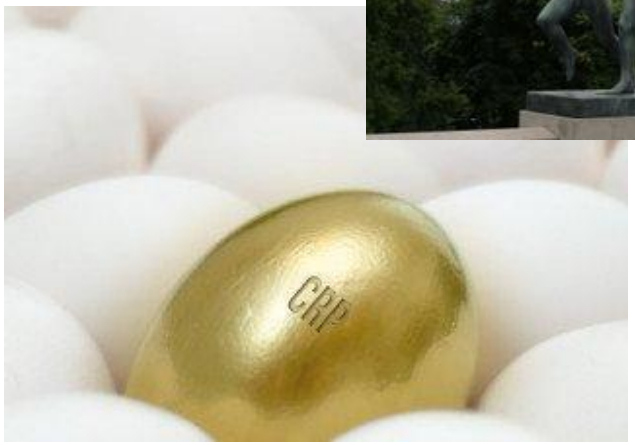
Reduced antibiotic prescribing

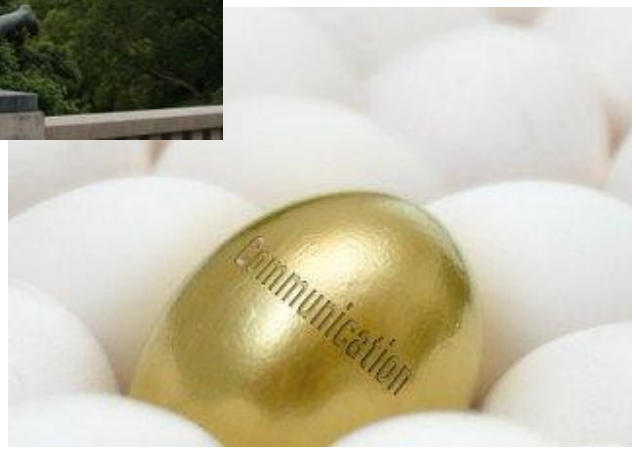
for LRTI and rhinosinusitis
with greater patient satisfaction and
without compromising other outcomes

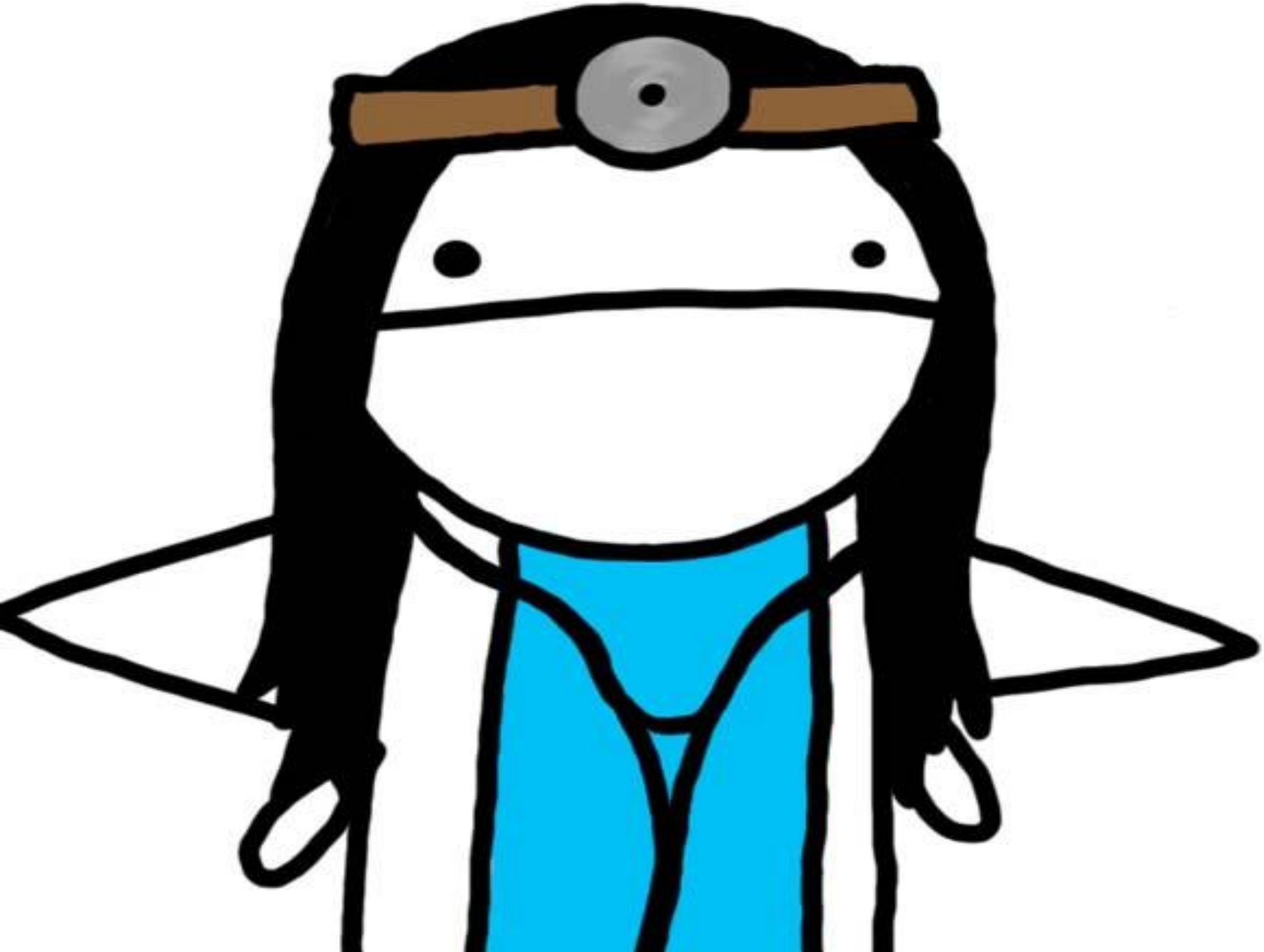
Targeting the right prescribing strategy at the right patient

IMPAC^{3}T

CAPRESA





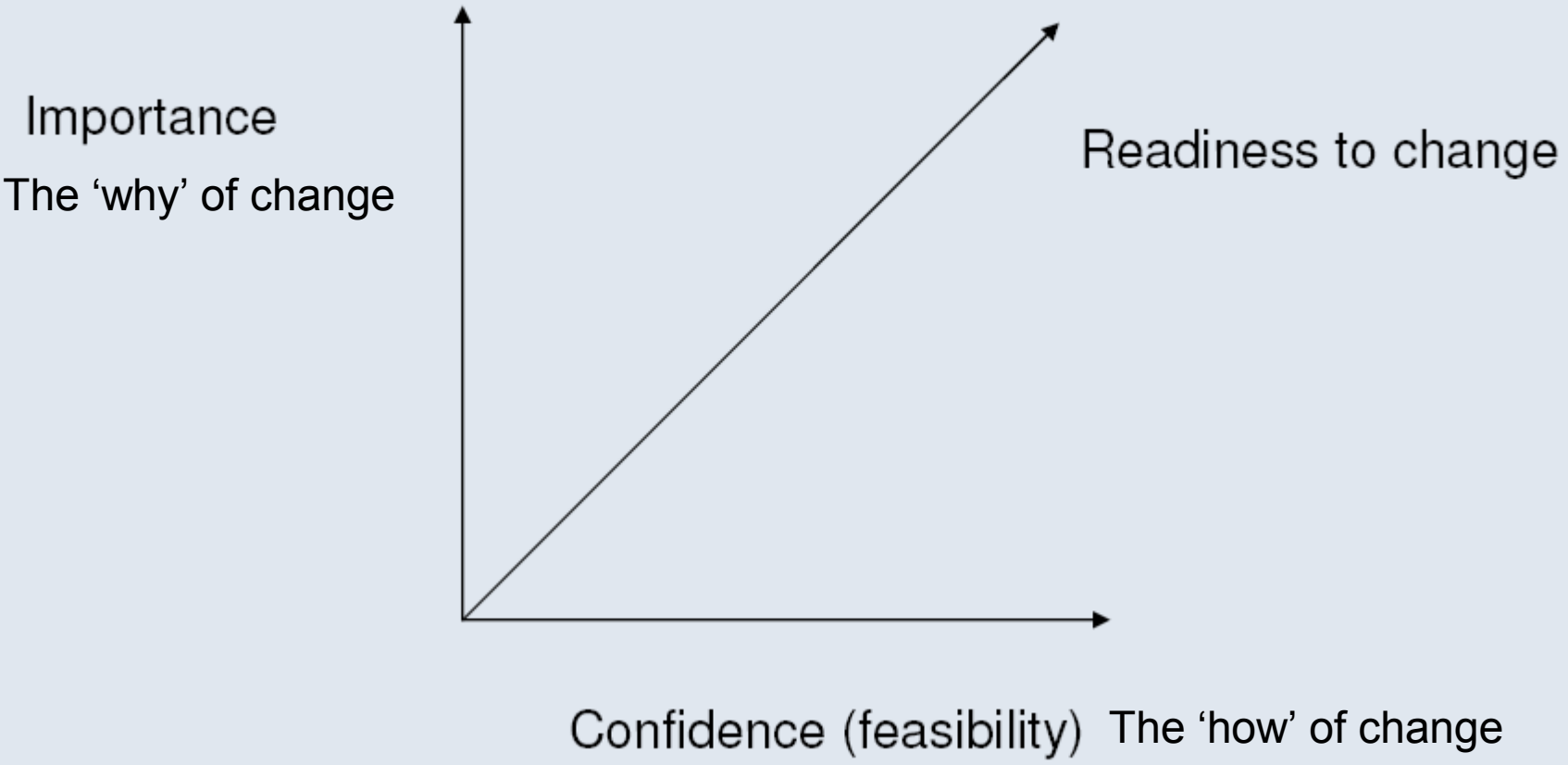


CRP PoC testing

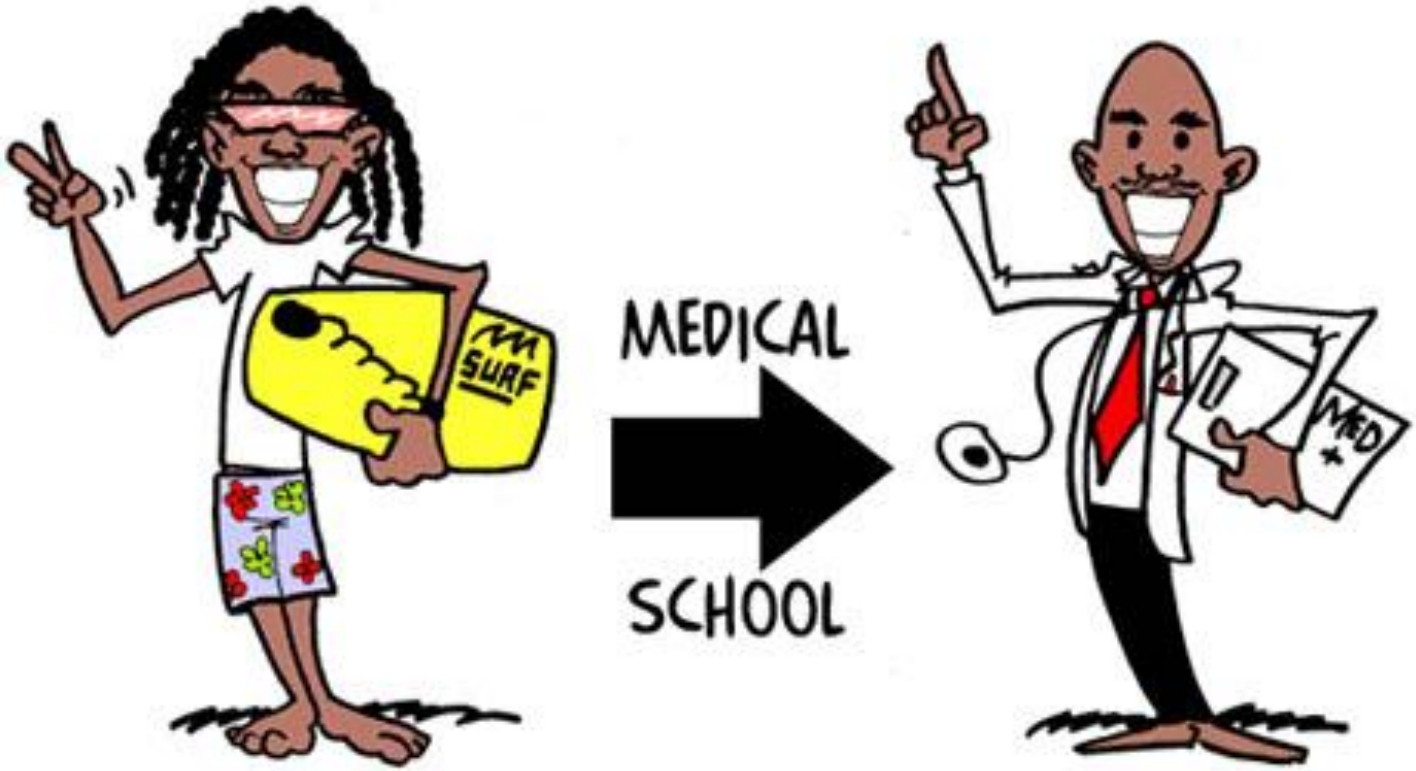
- CRP is the best PoC test to differentiate pneumonia from other (L)RTI
- may guide the discussion between doctor and pt
- Leads to better antibiotic stewardship
- CRP and communication: 1+1=3
- But:

- be aware of limitations
- proper instructions
- prevent overuse of CRP testing

Changing prescribing behaviour



Secrets of the doctor



…just a human being!

Secrets of the doctor

Secrets of the doctor

- uncertainties
- well informed/educated pt
- fear of getting sued

↓

defensive mechanisms

↓

unjustified antibiotic prescribing

Secrets of the doctor

- Time pressure

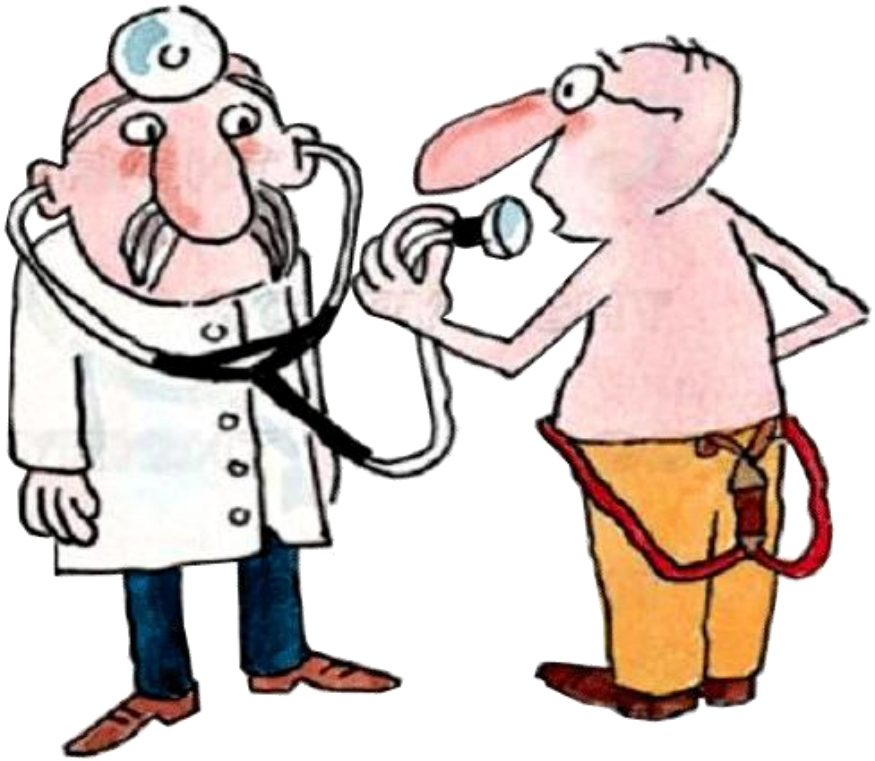
- Act

- Recepy
- clear
- symbol of helping a pt
- defines end of consult

Confidence in habits

'I'll pass you on to the nurse'

Communication



‘Do you hear me?’

Does a CRP finger prick hurts?

YES just a little for the patient

YES for doctors who believe their diagnostic skills are perfect

NO for the other doctors

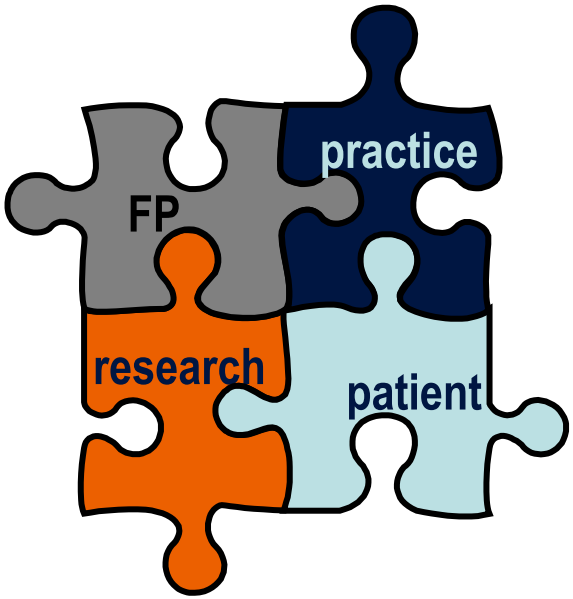

CRP TESTING
BEYOND THIS POINT!

Thank you

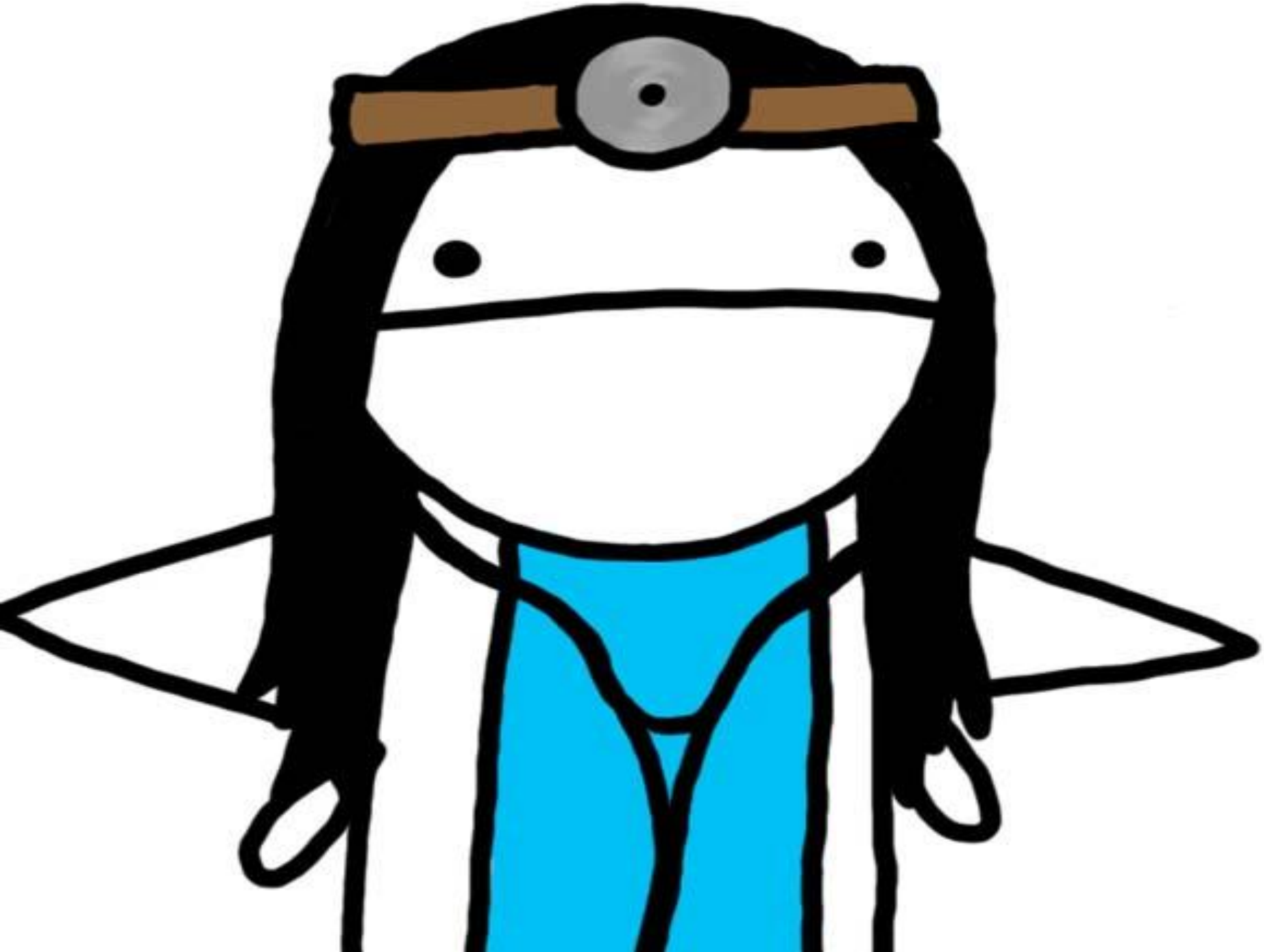
C areful use

R educes

P rescribing

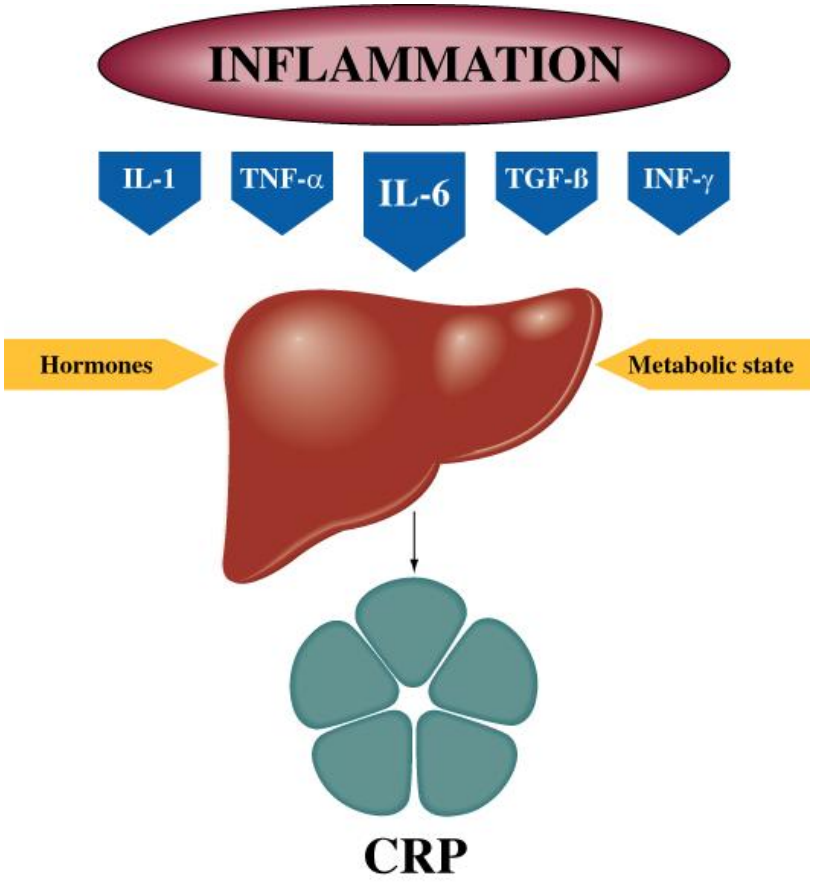


r.hopstaken@sge.nl



C-reactive proteïn

- Acute phase protein
- Rises in 4-6 hours
- Rapid fall
- Sensitive, non-specific

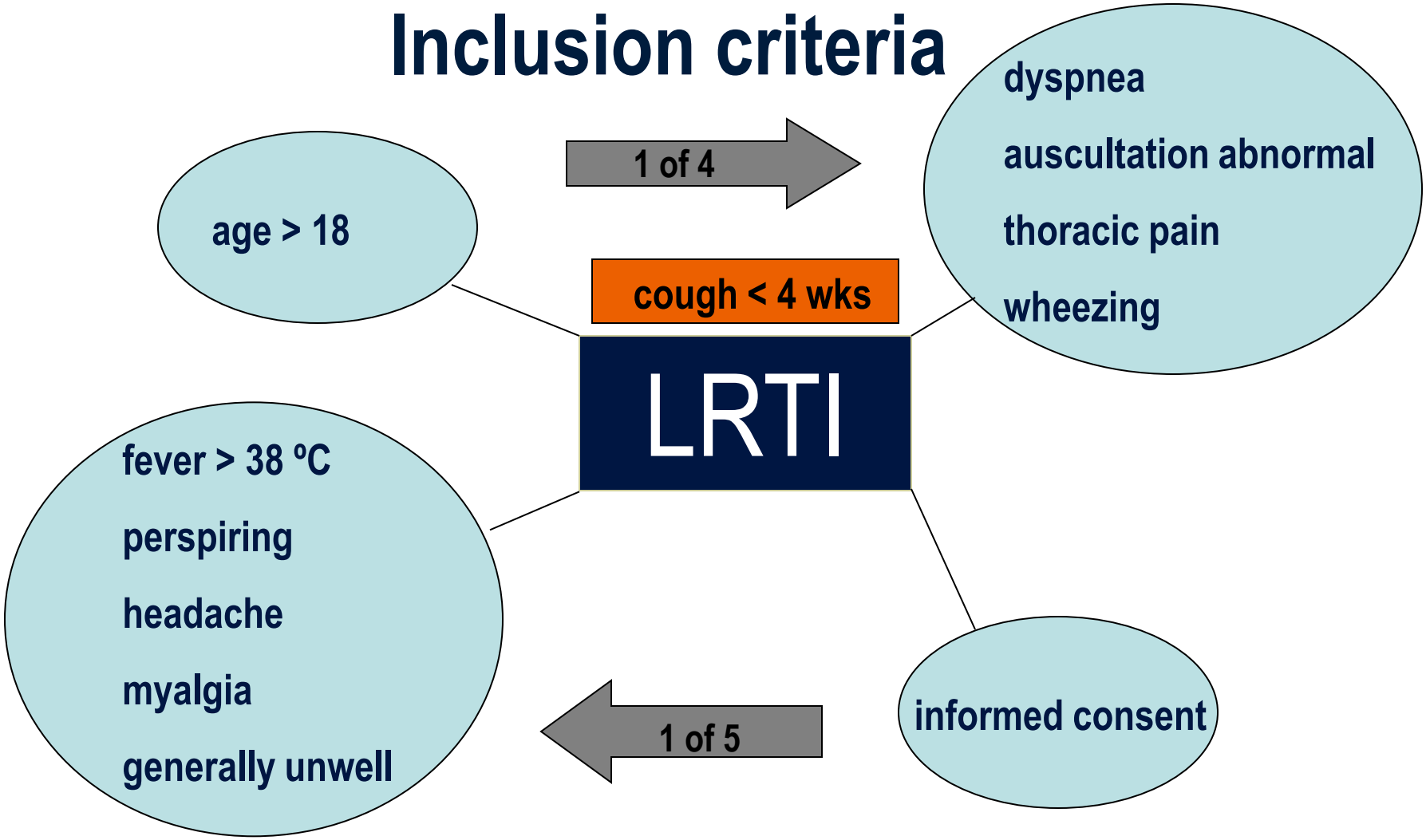


AB1 per CRP category

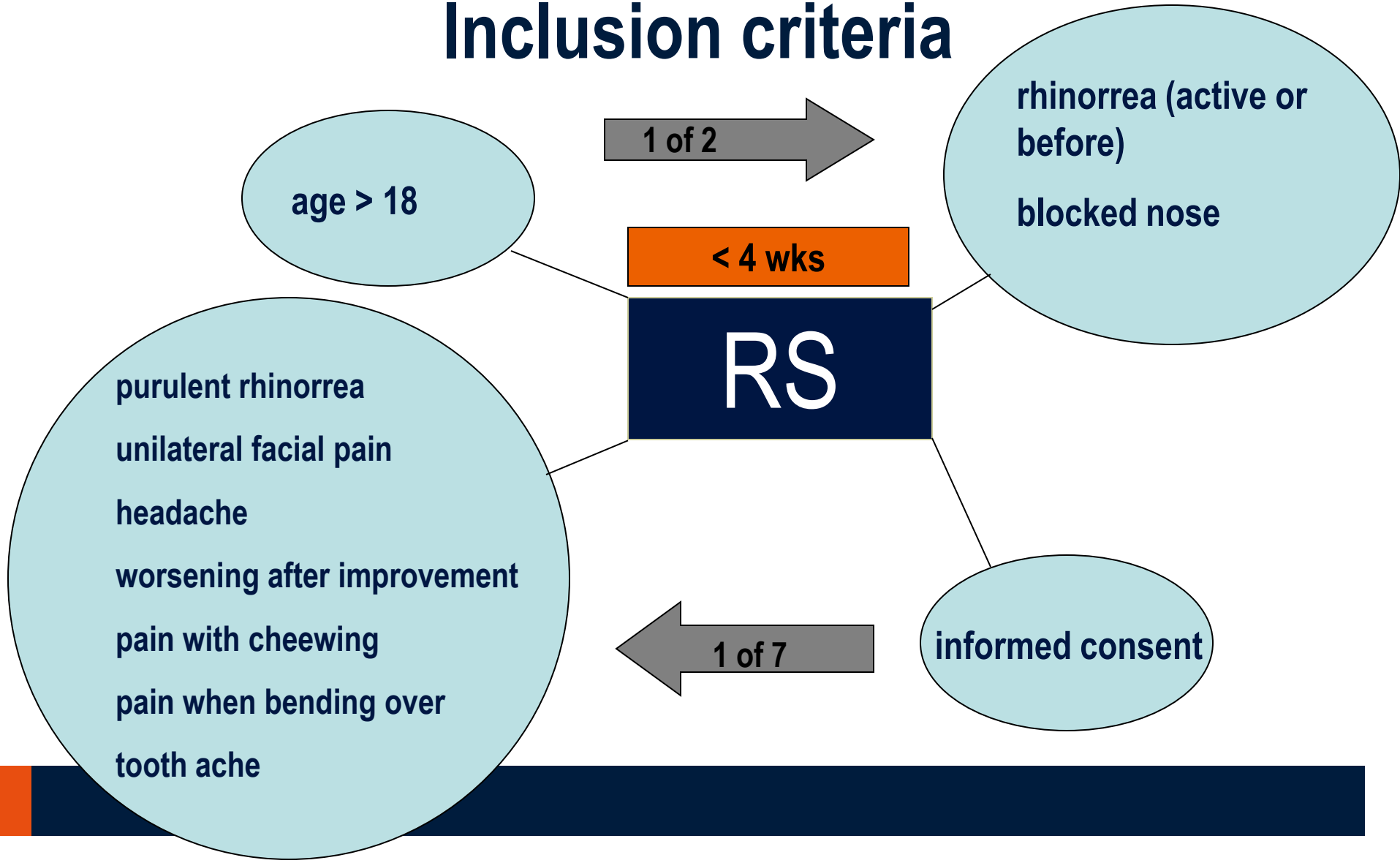
crpcat * ABday1 Crosstabulation

			ABday1		
			yes	no	Total
crpcat	<9	Count	17	96	113
		% within crpcat	15,0%	85,0%	100,0%
	9-20	Count	10	33	43
		% within crpcat	23,3%	76,7%	100,0%
	21-50	Count	15	20	35
		% within crpcat	42,9%	57,1%	100,0%
	51-100	Count	14	5	19
		% within crpcat	73,7%	26,3%	100,0%
	>100	Count	14	1	15
		% within crpcat	93,3%	6,7%	100,0%
Total		Count	70	155	225
		% within crpcat	31,1%	68,9%	100,0%

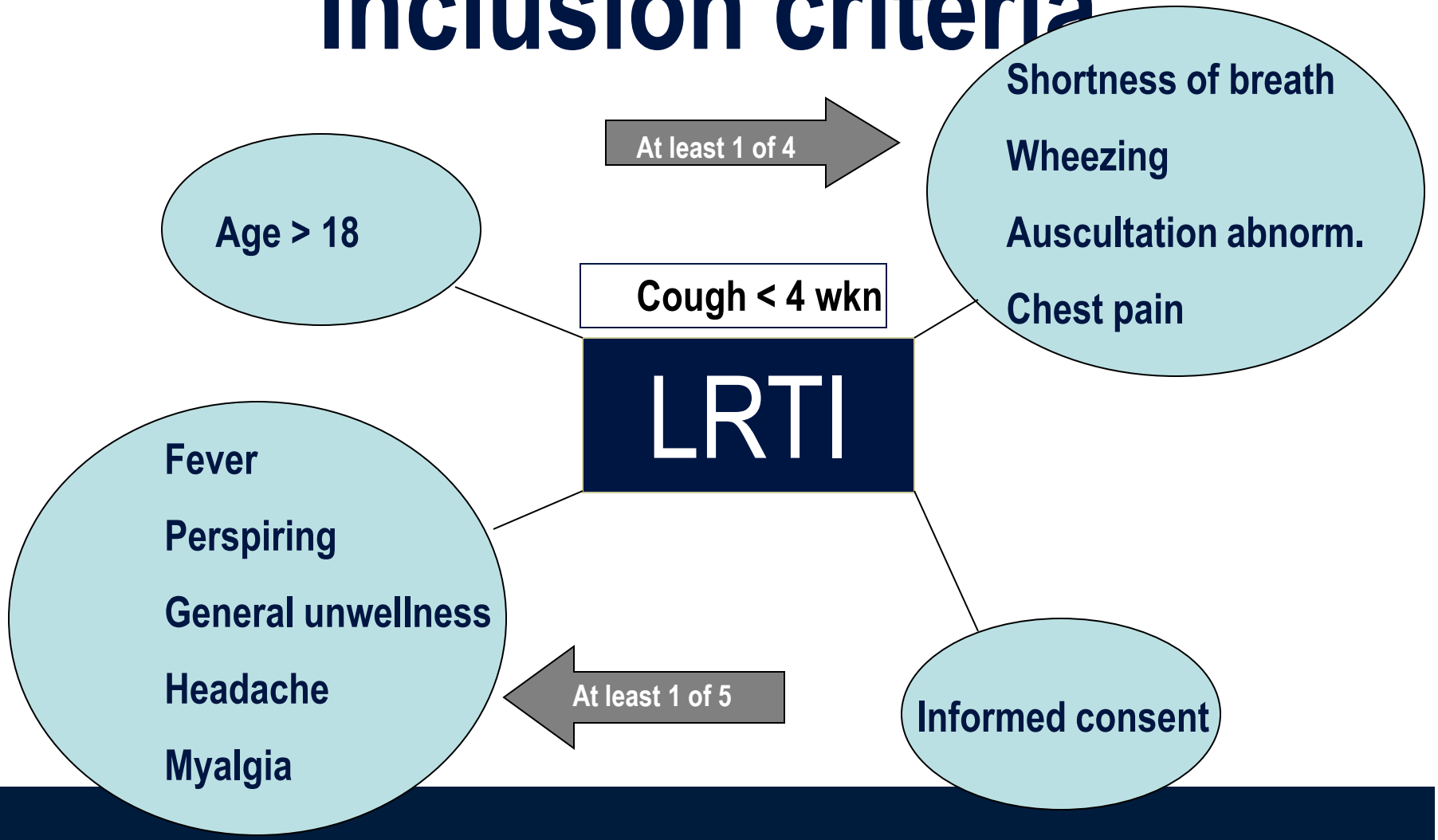
Inclusion criteria



Inclusion criteria



Inclusion criteria



Rhinosinusitis Inclusieformulier CAPRESA

Naam patiënt: *Janssen*

Geboortedatum: *03-07-1957* Geslacht: M / V

	JA	
Verdenking Rhinosinusitis	☐	
Leeftijd ≥ 18 jaar	☐	
Eerste consult voor deze episode	☐	
Duur van de klachten ≤ 4 weken, namelijk	☐	dagen
Welke van de volgende 2 symptomen		☐ (doorgemaakte) rinorroe ☐ verstopte neus
Ten minste 1 van de 2 bovenstaande	☐	
Welke van de volgende 7 symptomen		☐ purulente rinorroe ☐ unilaterale aangezichtspijn ☐ hoofdpijn ☐ tandpijn ☐ pijn bij kauwen ☐ maxillaire of frontale pijn bij bukken ☐ verslechtering van symptomen na initiële verbetering
Ten minste 1 van de 7 bovenstaande	☐	
Toestemmingsformulier getekend?	☐	
Voldoet NIET aan exclusie criteria - acute opname ziekenhuis - ziekenhuisopname in laatste 6 weken - antibiotica gebruik in laatste 2 weken - eerdere deelname aan deze studie - onvoldoende begrip Nederlandse taal	☐	

→ **Inclusie indien alle antwoorden JA**

Datum inclusie: _____ / _____ / _____

Ernst van de rhinosinusitis **Niet ziek** ——— **Ernstig ziek**

Heeft CRP bij deze patiënt aanvullende diagnostische waarde? ja / nee

Hoe hoog schat u de CRP waarde bij deze patiënt op basis van anamnese en LO? _____mg/L

Wat is op dit moment op basis van anamnese en lichamelijk onderzoek uw voorgenomen beleid tav antibiotica?

☐ geen antibiotica ☐ uitgesteld recept voor antibiotica ☐ antibiotica

Open nu de envelop en volg de stappen op het randomisatieformulier

Follow-up

- Diary 7 days, than repeated CRP test
- SMS or phone call reminder
- 28 days, incl data from patient records

Baseline characteristics (1)

Patients	CRP guidance	
	Yes n=129	No n=129
Female sex (%)	88 (68.2)	91 (70.5)
Age (SD)	43.0 (13.4)	45.5 (14.0)
Smoking (%)	33 (30.8)	27 (25.5)
COPD	5 (3.9)	3 (2.3)
asthma	10 (7.8)	9 (7.0)
diabetes	9 (7.0)	4 (3.1)

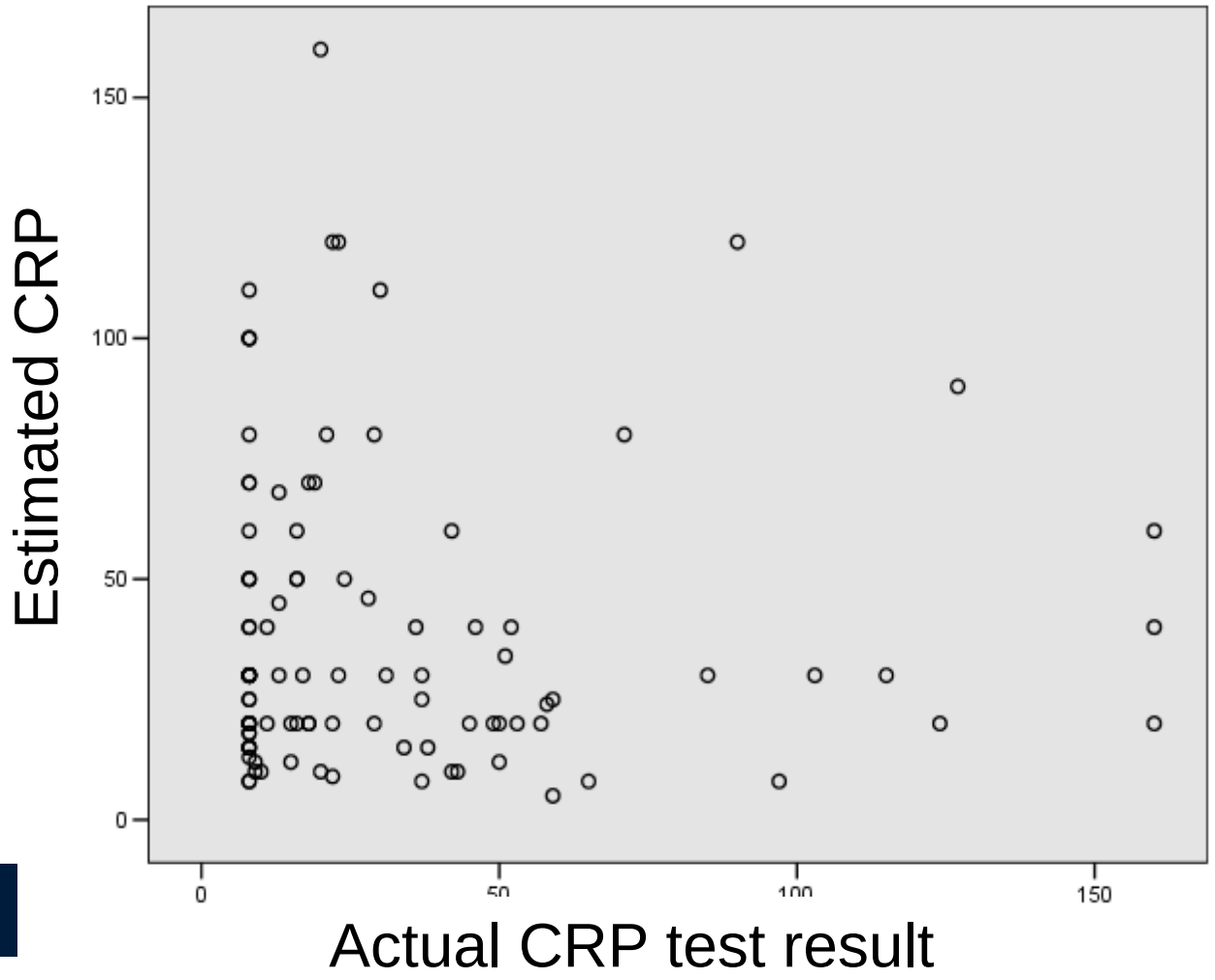
Baseline characteristics (2)

LRTI	CRP guidance	
	Yes	No
	n=56	n=51
Fever	27 (48.2)	25 (49.0)
Shortness of breath	37 (66.1)	30 (58.8)
Auscultation abnormalities	25 (44.6)	21 (41.2)
Generally feeling unwell	42 (75.0)	40 (78.4)
Duration of symptoms (SD)	8.1 (5.1)	8.8 (6.2)
VAS illness severity	46.2 (22.9)	42.1 (23.1)

Baseline characteristics (3)

Rhinosinusitis	CRP guidance	
	Yes n=73	No n=78
Purulent rhinorroe	38 (52.1)	44 (56.4)
Blocked nose	57 (78.1)	59 (75.6)
Unilateral facial pain	39 (53.4)	44 (56.4)
Pain when bending over	44 (60.3)	52 (66.7)
Duration of symptoms (SD)	9.3 (6.7)	10.0 (6.9)
VAS illness severity	40.6 (22.3)	40.5 (21.1)

Results - Estimated vs actual CRP

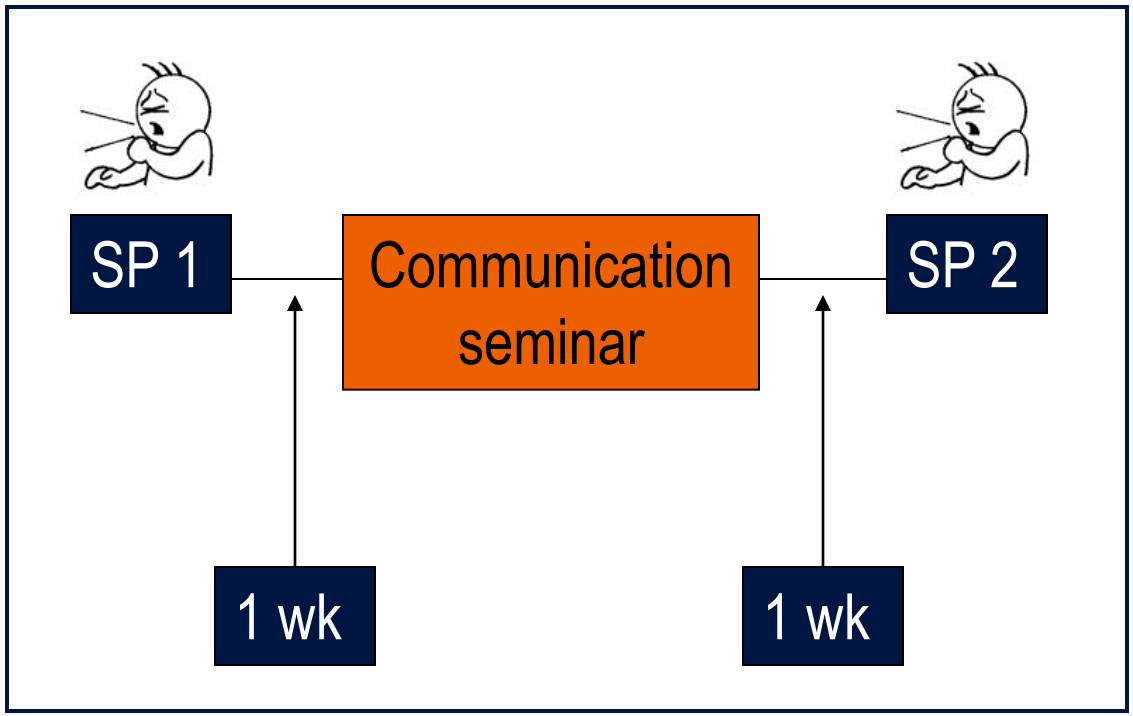


Enhanced communication

Patient centred strategy to achieve shared decision about investigation and treatment of acute infection

- Simulated patients
- Context-rich training
- Peer-review transcripts

- Combination of general and LRTI items



Communication items

- Main concern/worries
- Expectations
- **Opinion on AB**
- Natural course (>4 weeks)
- Self-limiting
- Balance of benefits and side effects
- Self-management strategies
- Alarm symptoms (safety net)
- Understanding
- Agreement

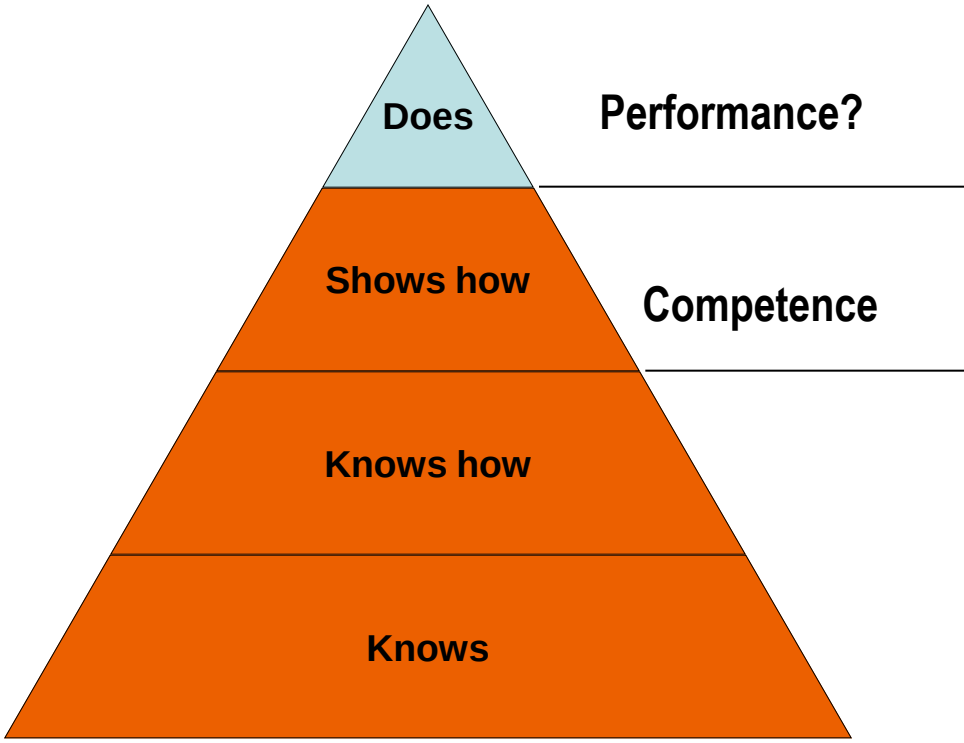
Enhanced communication

Competence

- Short term +
- Longer term +
- Time-efficient

Performance

- AB prescribing
- Patient satisfaction / enablement



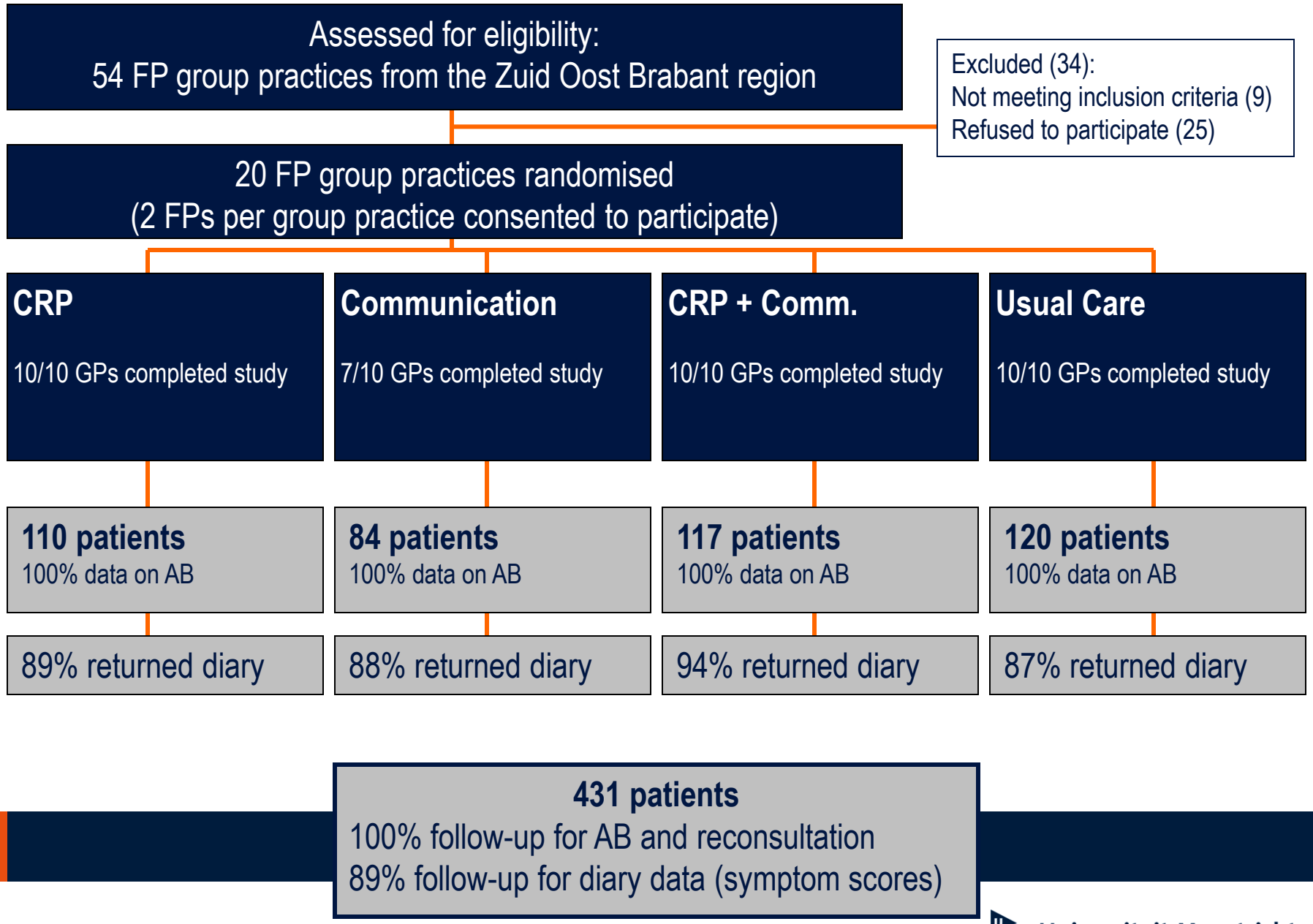
Outcome measures

Primary outcome

- AB prescribing at index consultation

Secondary outcomes

- Prescribing within 28 days
- Reconsultation
- Clinical recovery
- Patient satisfaction/enablement and future consultation intention
- Cost-effectiveness



Universiteit Maastricht

Baseline characteristics

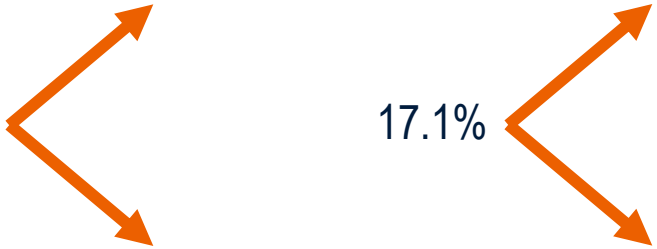
	CRP		Communication	
	Yes (n=227)	No (n=204)	Yes (n=201)	No (n=230)
Female sex (%)	134 (59.0)	131 (64.2)	130 (64.7)	135 (58.7)
Age (SD)	49.4 (14.7)	50.3 (16.0)	51.4 (15.3)	48.5 (15.1)
Cough duration, days (SD)	10.1 (6.6)	10.3 (6.5)	11.0 (6.7)	9.4 (6.2)
Smoking (%)	49 (23.7)	61 (34.3)	47 (25.8)	63 (31.0)

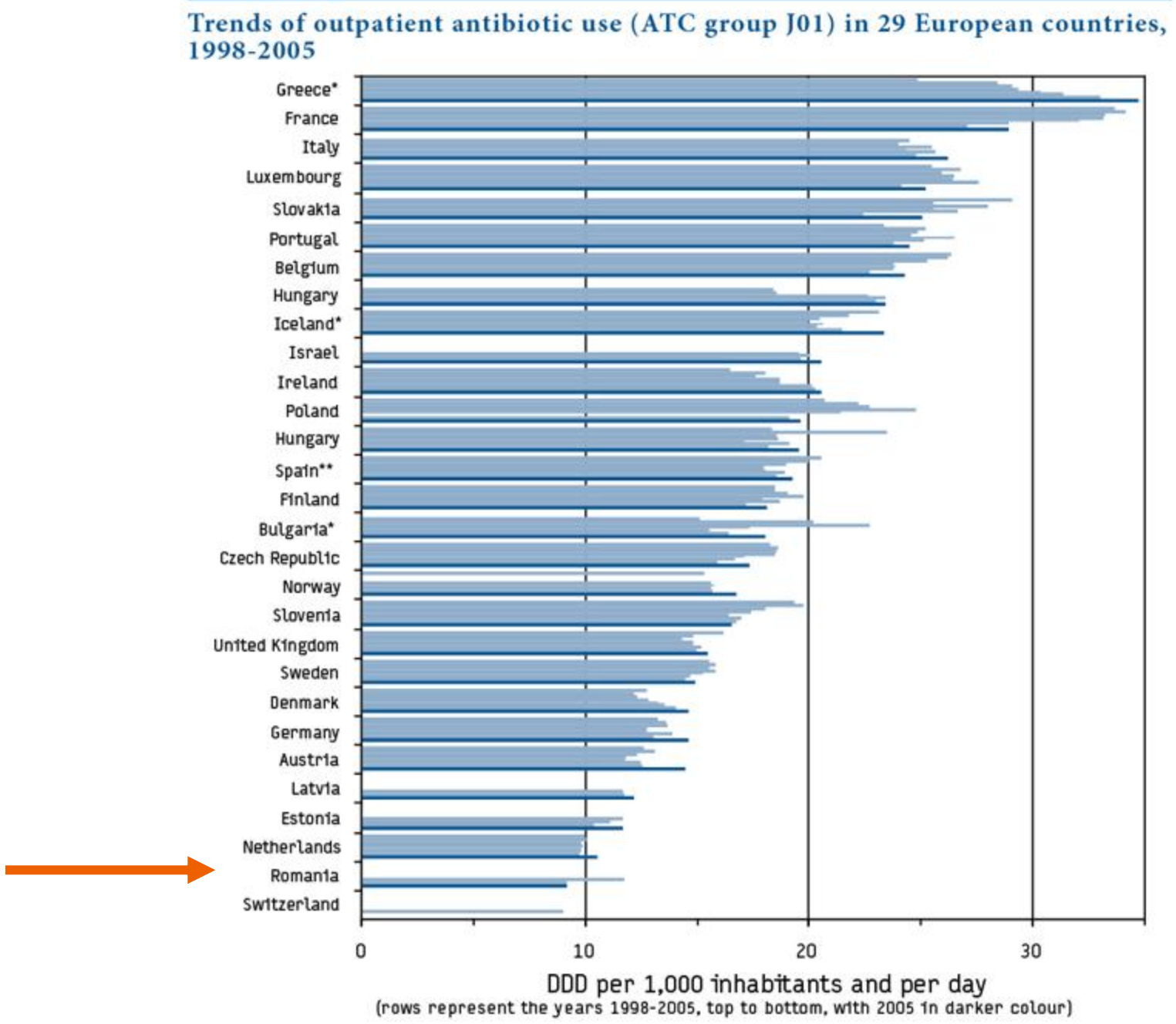
Table 3. Sensitivities, specificities, positive and negative predictive values (PPV, NPV;%) of C-reactive protein (CRP), lipopolysaccharide-binding protein (LBP), fibrinogen and fever at different cut-off values for patients with pneumonia.

	Sensitivity	Specificity	PPV	NPV
CRP >10	100	36.1	17.2	100
CRP >20	100	50.6	21.2	100
CRP >100	81.8	84.3	40.9	97.2
LBP >10	100	33.7	16.7	100
LBP >20	81.8	79.5	34.6	97.1
LBP >30	72.7	90.4	50.0	96.2
Fibrinogen >4	90.9	54.9	21.3	97.8
Fibrinogen >5	81.8	89.0	50.0	97.3
Fever (≥38°C)	36.4	83.1	22.2	90.8

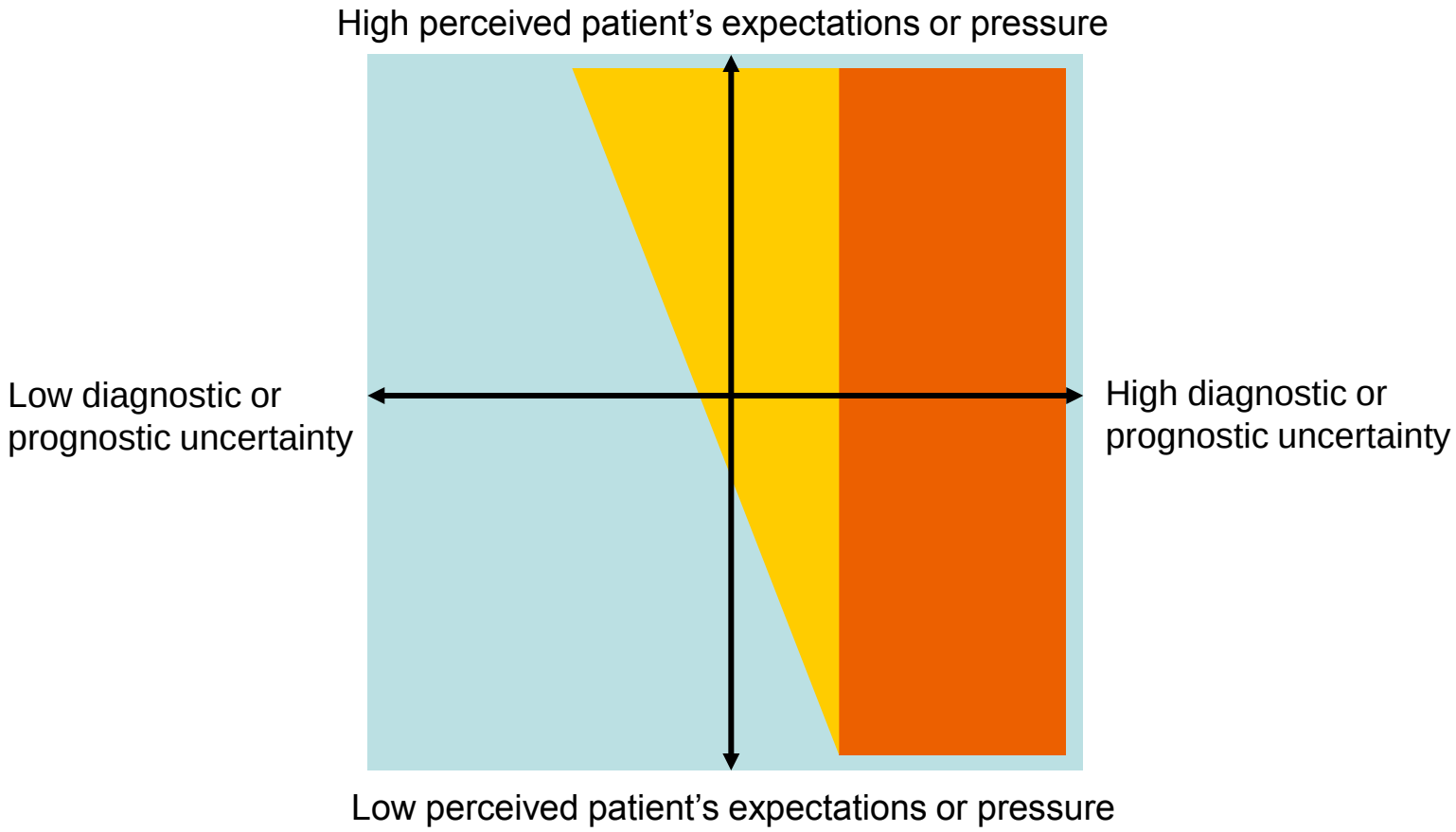
Antibiotic prescribing and use

	Control group (n=129)		CRP assisted group (n=129)	
	Prescribing	AB use	Prescribing	AB use
No antibiotics	37.2%	**43.4%**	43.4%	**56.6%**
Delayed antibiotics	22.5%		17.1%	
Antibiotics	40.3	**56.6%**	39.5%	**43.4%**



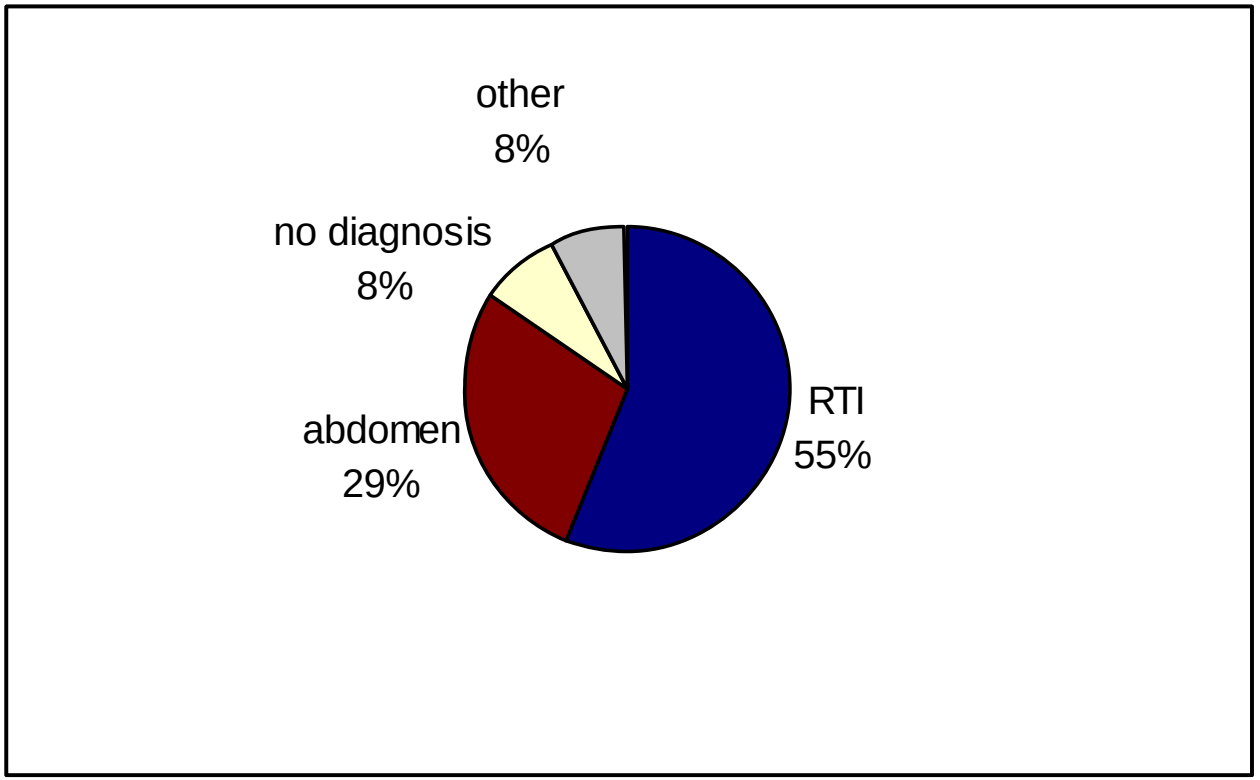


The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults


High perceived patient's expectations or pressure
Low diagnostic or prognostic uncertainty
High diagnostic or prognostic uncertainty
Low perceived patient's expectations or pressure
Communication skills
CRP testing to provide incremental diagnostic information for GP
CRP testing to reassure patients (and provide information for GP)

IMPAC³T

Use of CRP PoC tests during inclusion winter 1



CRP in appendicitis

Meta-analysis (hospital)

Moderately predicts appendicitis

Primary care?

Anderson, Brit J Surg 2004

CRP in COPD

- strong predictor
- best biomarker in exacerbations
- associated with severity, FEV1, pack years
- review: CRP correlated to disease stage

Hurst Am J Respir Crit Care Med 2006,Schneider, BMC Fam Pract 2006, Franciosi Pulm Pharm Therapeutics 2006