Guidelines

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"I'm not here for committing a crime — I'm here for failing to comply with a guideline."

Treatment of Community-Acquired Pneumonia

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- SWAB/ NVALT guideline 2011, replaced SWAB guideline 2005

- Empirical treatment must cover the most likely causative pathogen.
- Clinical presentation and additional tests cannot reliably distinguish causative pathogens.
- Therefore, the “severity of illness” should be used for choosing optimal treatment.

- Severity of illness:
  - Mild
  - Moderate-severe
  - Severe

- Based on AMBU65 or PSI or ‘Pragmatism’ (2005)
- Based on any of AMBU65 or PSI or ‘Pragmatism’, but always use the same for categorization (2011)

Pneumonia Severity Index

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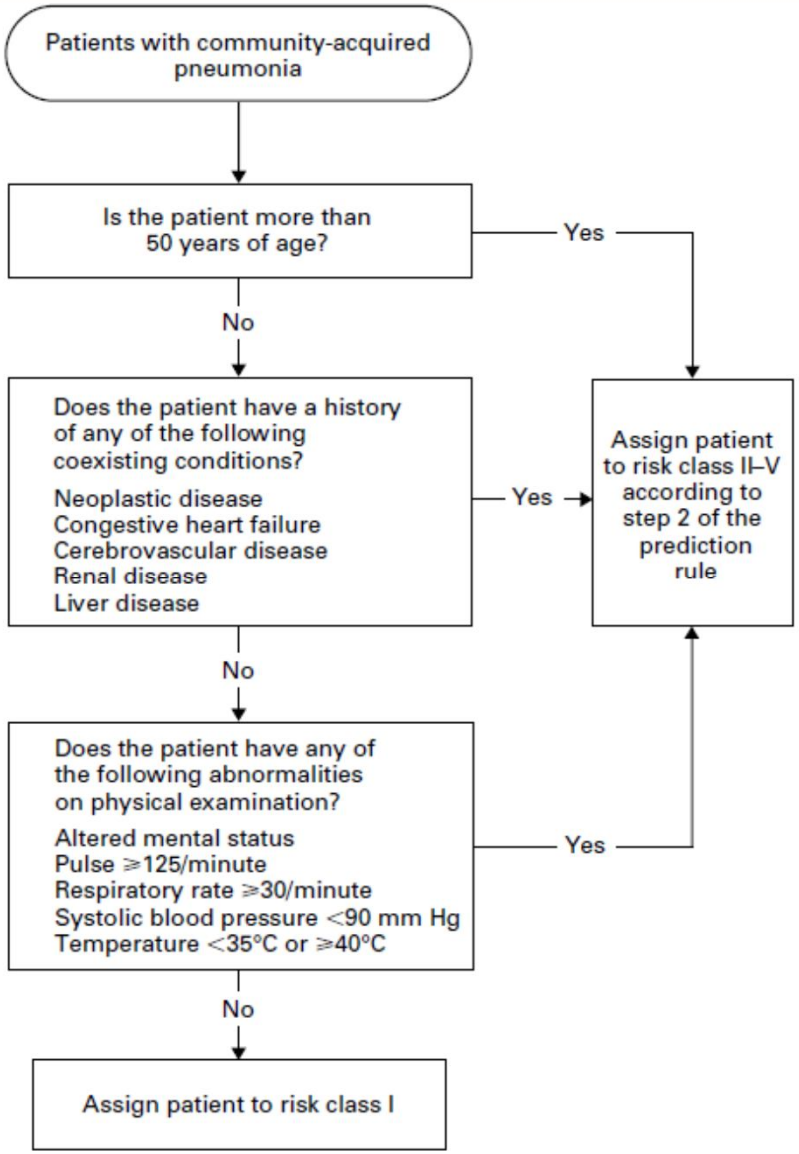

TABLE 2. POINT SCORING SYSTEM FOR STEP 2 OF THE PREDICTION RULE FOR ASSIGNMENT TO RISK CLASSES II, III, IV, AND V.

CHARACTERISTIC	POINTS ASSIGNED*
Demographic factor	
Age	
Men	Age (yr)
Women	Age (yr) − 10
Nursing home resident	+10
Coexisting illnesses†	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10
Physical-examination findings	
Altered mental status‡	+20
Respiratory rate ≥30/min	+20
Systolic blood pressure <90 mm Hg	+20
Temperature <35°C or ≥40°C	+15
Pulse ≥125/min	+10
Laboratory and radiographic findings	
Arterial pH <7.35	+30
Blood urea nitrogen ≥30 mg/dl (11 mmol/liter)	+20
Sodium <130 mmol/liter	+20
Glucose ≥250 mg/dl (14 mmol/liter)	+10
Hematocrit <30%	+10
Partial pressure of arterial oxygen <60 mm Hg§	+10
Pleural effusion	+10

Fine et al; N Eng J Med; 1997

Pneumonia Severity Index

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Step 3. Calculation of 30-day mortality		
Risk Class	Total score	Mortality
I	Not applicable	0.1 %
II	≤ 70	0.6 %
III	71 – 90	0.9 %
IV	91 – 130	9.3 %
V	> 130	27.0 %

Mild CAP

Moderate-severe CAP

Severe CAP

AMBU-65 score

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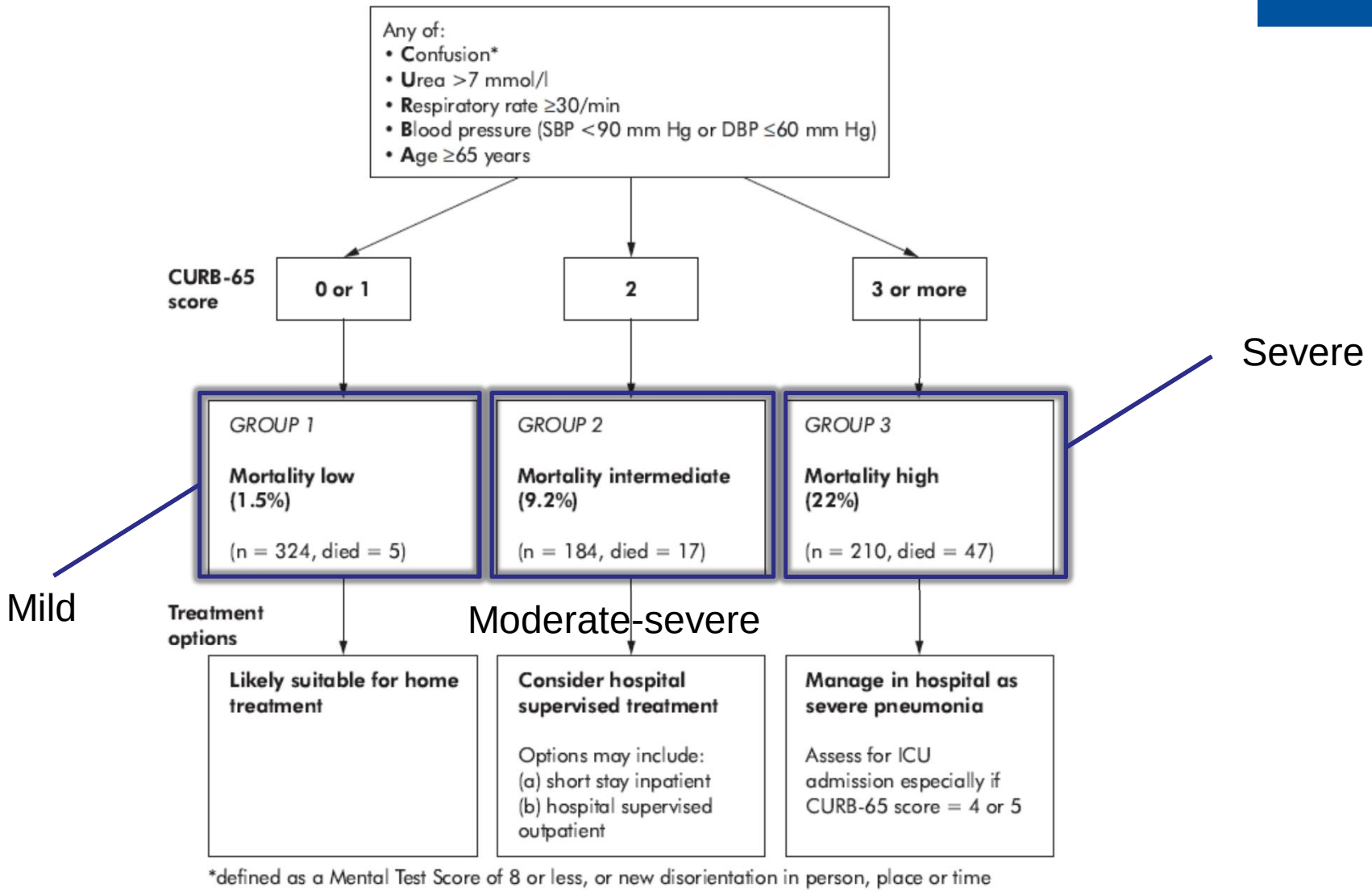

Figure 2 Severity assessment in a hospital setting: the CURB-65 score. One step strategy for stratifying patients with CAP into risk groups according to risk of mortality at 30 days when the results of blood urea are available.

Pragmatic scheme

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- Mild CAP
  - Not hospitalized
- Moderate-severe CAP
  - Hospitalized, on regular ward
- Severe CAP
  - Hospitalized in ICU

Severity	Antibiotic	Route	Dose	Freq.
Mild pneumonia				
1st choice	amoxicillin	oral	500-750 mg	q6h-q8h
2nd choice	doxycycline	oral	100 mg (first dose 200 mg)	q24h
Moderately severe pneumonia				
1st choice	penicillin	IV	1 ME	q6h
	amoxicillin	IV	1000 mg	q6h
Severe pneumonia				
Monotherapy	moxifloxacin *or* levofloxacin	IV / oral IV / oral	400 mg 500 mg	q24h q12h
Combination therapy	penicillin	IV	1 ME	q6h
	ciprofloxacin	IV / oral	400 mg (po 500 mg)	q12h
Combination therapy	cefuroxime *or* ceftriaxone *or* cefotaxime	IV IV IV	750-1500 mg 2000 mg 1000 mg	q8h q24h q6h
	erythromycin	IV	500-1000 mg	q6h

Questions

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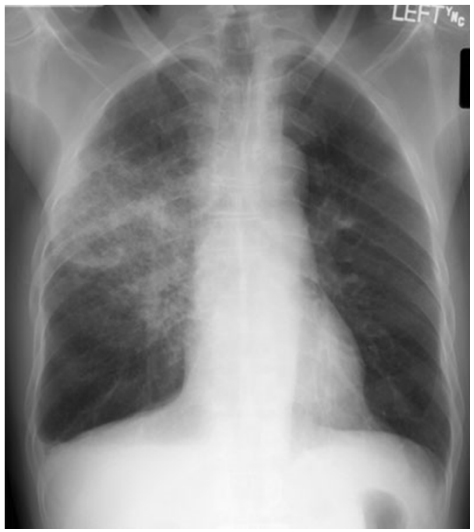
1. To what extent are these recommendations followed?
2. Is there an association between deviation of the recommendation and patient outcome (death in hospital, ICU-admission, duration of hospitalization).



Methods (1)

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- Prospective, observational study Jan 2008 – April 2009.
- 23 NL hospiltals.
- Adults (≥18 yr) with a clinical suspicion of CAP or Lower Respiratory Tract infection diagnosed in Emergency Rooms.

Methods (2)

Definitions

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Definition CAP:

1. New infiltrate on chest X-ray <48 hours of admission

AND

2. ≥ 2 of the following symptoms:

   cough, sputum production, temperature >38^{o}C or <36,1^{o}C, auscultory findings, leucocytosis, CRP >3x upper limit, hypoxemia or dyspneu/ tachypneu.

Antibiotic treatment (1)

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- Antibiotics on admission
- Route of administration (i.v. or oral) irrelevant for analysis.

- Therapy:
  - ‘under treatment’ → antibiotic spectrum narrower than guideline
  - ‘over treatment’→ antibiotic spectrum broader than guideline
  - Correct:

Ernst CAP	Behandeling volgens SWAB richtlijn
Mild	Amoxicilline of Doxycycline
Matig ernstige - Negatieve/geen Legionella - Positieve Legionella	β-Lactam monotherapy Macrolide of Quinolone monotherapie
Erstig	Moxifloxacine monotherapie OF Penicilline & Ciprofloxacine OF Penicilline & Macrolide OF Cephalosporine & Macrolide

Results – patients

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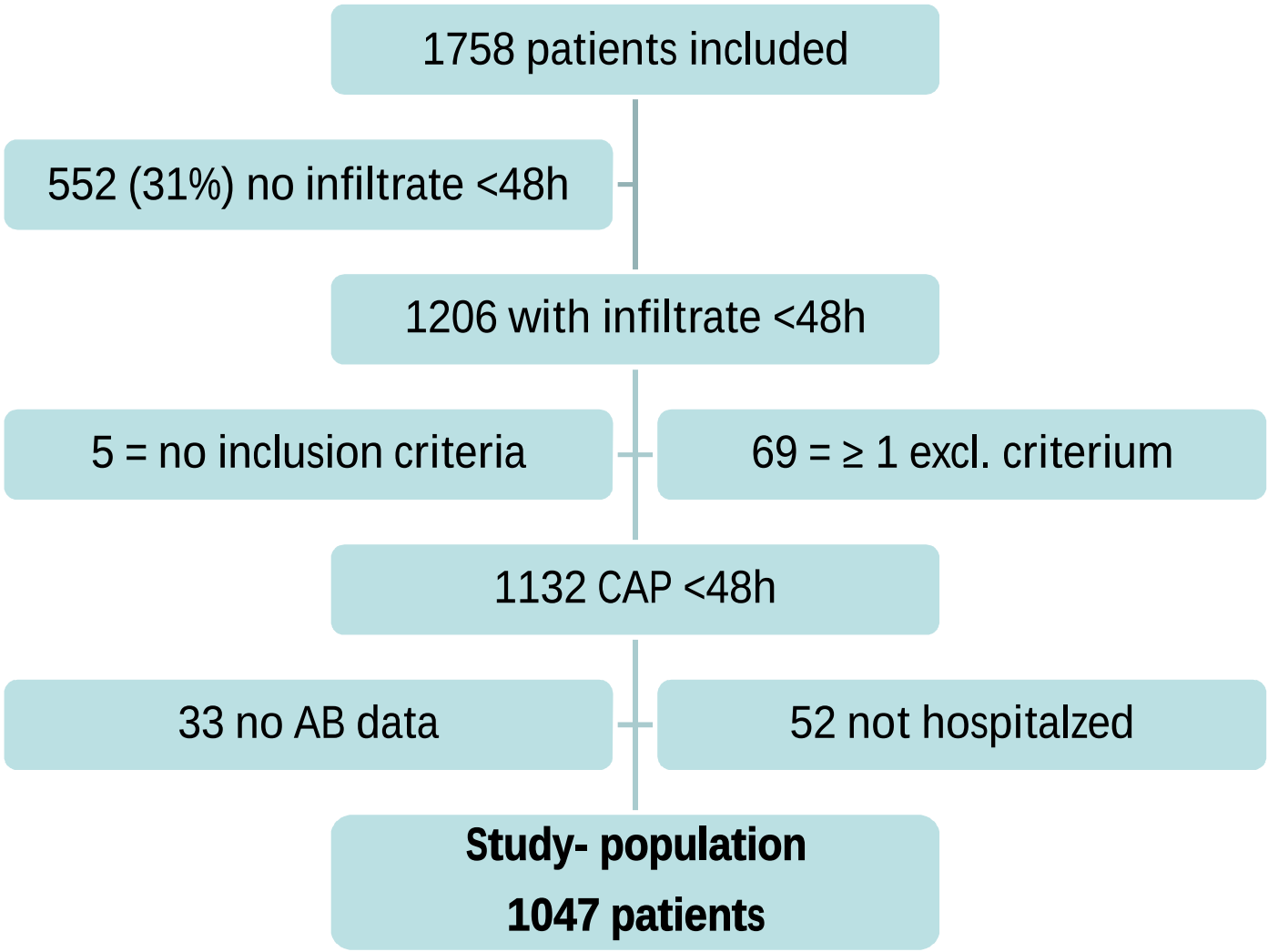

Empiric therapy

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	β-Lactam	Macrolide	Quinolone	Tetracycline	Other
β-Lactam	659 (62.9%)				
Macrolide	27 (2.6%)	14 (1.3%)			
Quinolone	254 (24.3%)	3 (0.3%)	42 (4.0%)		
Tetracycline	1 (0.1%)	-	-	14 (1.3%)	
Other	18 (1.7%)	-	2 (0.2%)	-	10 (1.0%)

n=1044

Not included:

- 3 pts → combination of 3 AB (β-lactam + OR macrolide + aminoglycoside, OR quinolone + aminoglycoside, OR quinolone + tetracycline).

Therapy adherent to guideline per risk category

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Severity of CAP		Antibiotic treatment according to guideline						
		Under treatment	% of class	Compliant treatment	% of class	Over treatment	% of class	
PSI	Mild	0	0,0	39	13,0	261	87,0	300
	Moderate -Severe	9	1,5	389	63,1	218	35,4	616
	Severe	83	63,4	23	17,6	25	19,0	131
		92	8,9	451	43,1	504	48,1	1047
CURB	Mild	0	0,0	51	10,6	430	89,4	481
	Moderate -Severe	9	2,6	230	67,6	101	29,7	340
	Severe	135	59,7	38	16,8	53	23,5	226
		144	13,8	319	30,5	584	55,7	1047
Pragmatic	Mild	-	-	-	-	-	-	-
	Moderate -Severe	20	2,0	648	63,9	346	34,1	1014
	Severe	11	33,3	11	33,3	11	33,3	33
		31	3,0	659	62,9	357	34,1	1047

Comparisons of scoring systems

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			CURB65			
			Mild	*Moderate-Severe*	*Severe*	Total
Pragmatic *Moderate-Severe*	**PSI**	*Mild*	259	33	4	296
		Moderate	206	261	130	597
		Severe	10	35	76	121
Pragmatic *Severe*	**PSI**	*Mild*	2	2	0	4
		Moderate	4	9	6	19
		Severe	0	0	10	10

Guideline adherence and hospital mortality

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- ‘under treatment’ was compared to ‘correct treatment or over treatment’ for associations with hospital mortality using logistic regression, adjusted for PSI score

		PSI	CURB65	Pragmatic
Clinical outcome				
Hospital mortality **(n=1036, 69 died)**				
	N with under treatment	89	143	31
	Crude OR	3.70 (2.01 – 6.79)	2.58 (1.47 – 4.53)	2.14 (0.73 – 6.31)
	Adjusted OR	0.77 (0.37 – 1.61)	1.06 (0.57 – 1.98)	1.90 (0.59 – 6.06)

Guideline adherence and combined endpoint

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		PSI	CURB65	Pragmatic
ICU admission (n=1013, 67 ICU)				
	N with under treatment	88	140	21
	Crude OR	2.50 (1.28 – 4.87)	1.72 (0.93 – 3.19)	2.42 (0.69 – 8.42)
	Adjusted OR	1.06 (0.49 – 2.29)	1.02 (0.52 – 1.97)	2.71 (0.76 – 9.72)
Combined endpoint (n=1035, 112 endpoints)				
	N with under treatment	89	143	31
	Crude OR	3.60 (2.15 – 6.04)	2.21 (1.38 – 3.55)	2.50 (1.05 – 5.94)
	Adjusted OR	1.09 (0.59 – 2.02)	1.07 (0.64 – 1.81)	2.38 (0.94 – 6.03)

Guideline deviation was not associated with prolonged duration of hospital stay.

Conclusion

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- Classification of disease severity on 3 different scoring systems causes large variation in composition of patient groups.
- The proportion of patients with guideline adherent treatment varied from 30.5% (AMBU65) to 62.9% (pragmatic).

- There are no significant associations between ‘under treatment’ (vs correct/ over treatment) and one of the outcome parameters, even after adjustment for disease severity.
- Deviation from the pragmatic treatment scheme tended to be associated with poor outcome.

SWAB sepsis guideline recommendations

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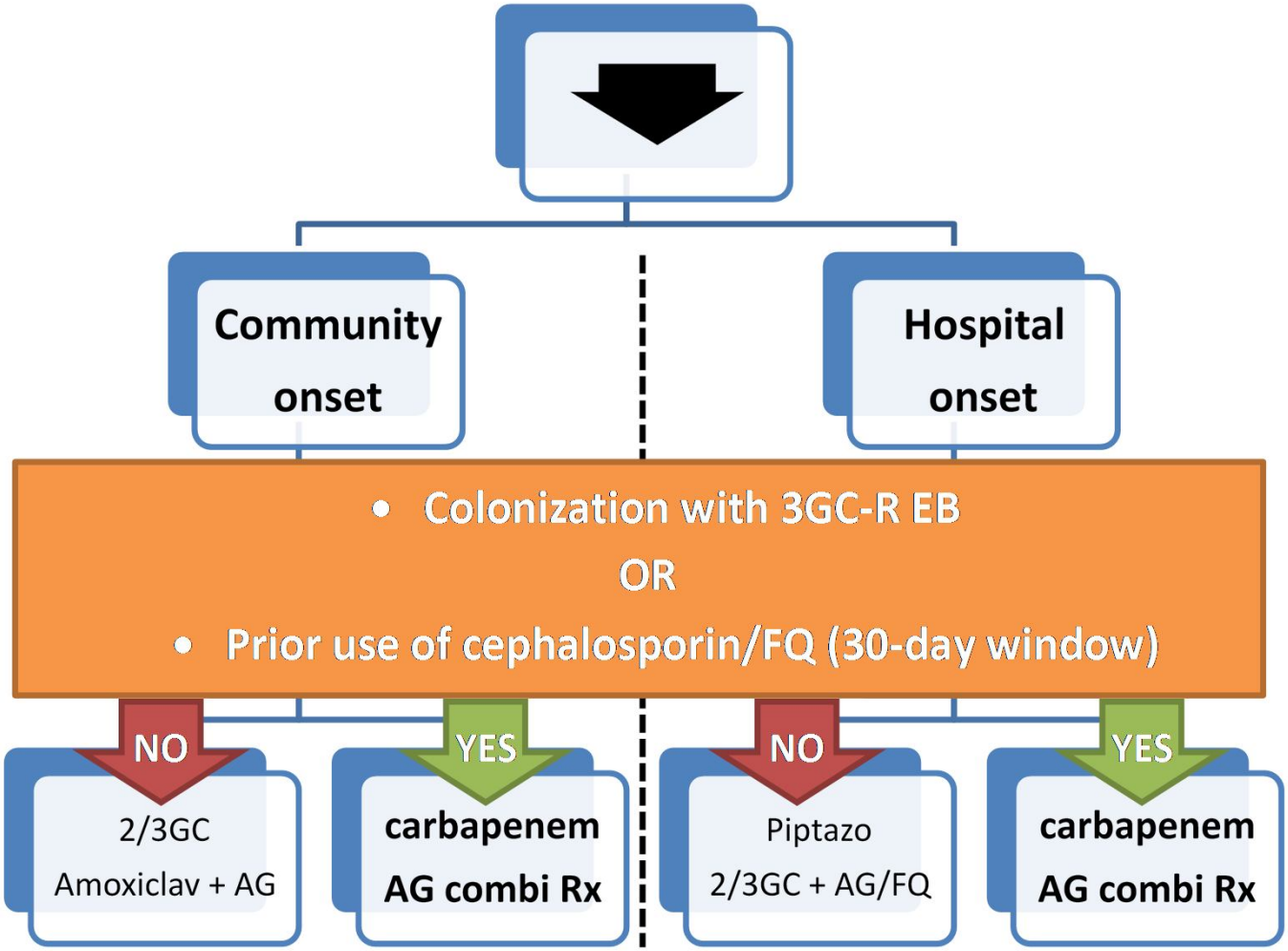

Questions

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1. How well do these criteria predict the presence of ESBL-producing Enterobacteriaceae as a cause of infection in patients with sepsis?

2. To what extent are these recommendations adhered to?

3. Does guideline adherence improve the quality of empirical antibiotic therapy?

Evaluation of SWAB sepsis guideline

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- Retrospective cohort study
- 1/1/2008 – 1/1/2010
- Two hospitals
  - UMC Utrecht
  - Tergooi Hilversum/Blaricum
- Inclusion of sepsis cases:
  - Blood culture + start β-lactam / FQ / AG
  - ≥ 18 years

n = 9422

Guideline adherence for ESBL risk

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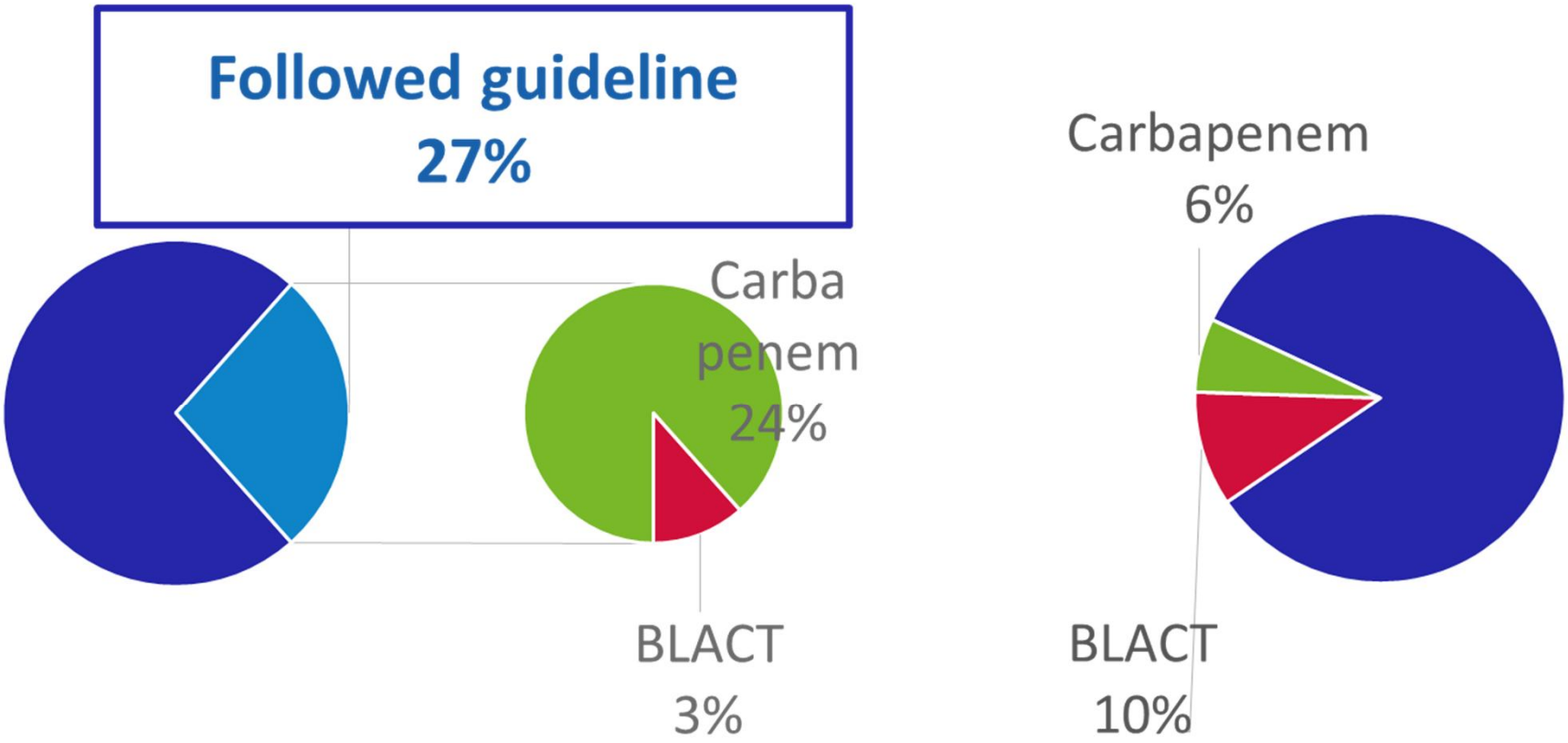
Patients at risk of ESBL: 19%

Not at risk 81%



Culture results

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- Of 9,422 episodes:
  - 773 (8.2%) were Enterobacteriaceae BSIs
  - 64 (0.7%) were caused by 3GC-R EB.

Resistant Enterobacteriaceae in sepsis

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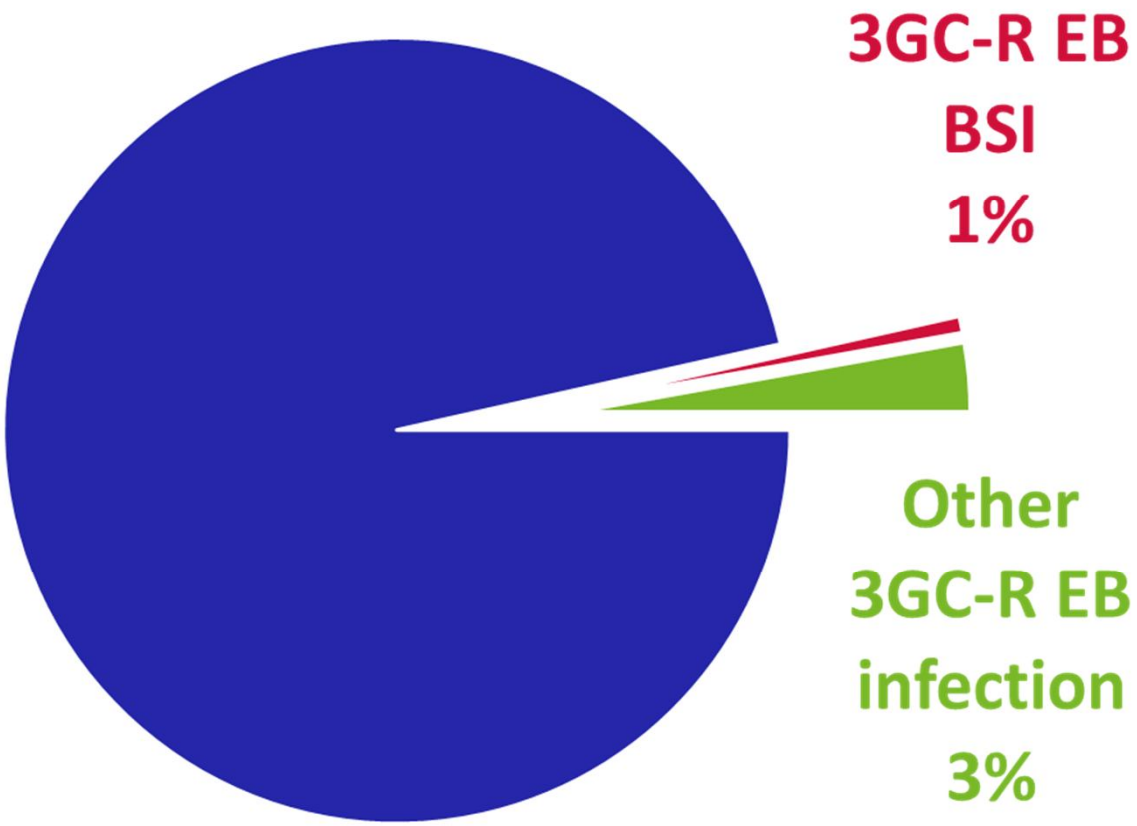

Guideline performance

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	Sensitivity for 3GC-R EB BSI	Prevalence in entire cohort	Positive predictive value
Prior colonization with 3GC-R EB (90 days)	42%	4%	7.4%
Prior 2/3GC or FQ use (30 days)	31%	17%	1.3%
Any of both (at risk of ESBL)	50%	19%	1.8%

Analysis of 762 Enterobacteriaceae BSIs

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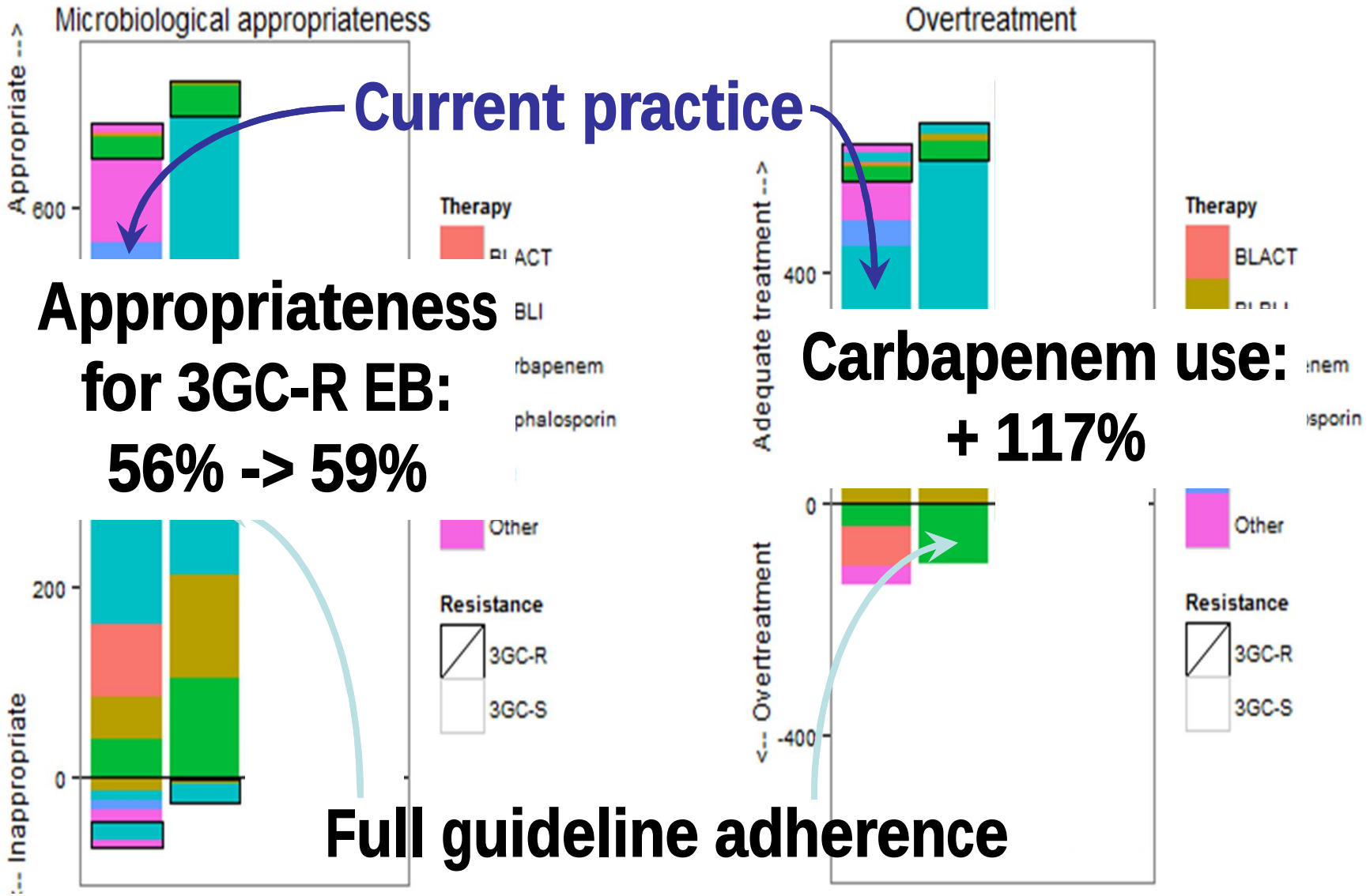

Current practice

Appropriateness for 3GC-R EB: 56% -> 59%

Carbapenem use: + 117%

Full guideline adherence

Conclusions

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In patients receiving empirical treatment for sepsis, prior colonization with 3GC-R Enterobacteriaceae and prior antibiotic use have low positive predictive value for infections caused by 3GC-R Enterobacteriaceae.

Strict guideline adherence would unnecessarily stimulate broad-spectrum antibiotic use.

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Appropriateness of Empirical Treatment and Outcome in Bacteremia Caused by Extended-Spectrum-β-Lactamase-Producing Bacteria

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Antimicrobial Agents and Chemotherapy p. 3092–3099 July 2013 Volume 57 Number 7

Retrospectively, information was collected from 232 consecutive patients with ESBL bacteremia (due to *E. coli*, *K. pneumoniae* and *E.cloacae*) between 2008 and 2010.

Appropriate therapywithin 24 h after bacteremia onset was prescribed to 37% of all patients and to 54% of known ESBL carriers.

The day 30 mortality rate was 20%.

Associated with day 30 mortality in a multivariable analysis were:

- Charlson comorbidity index of>3
- age of>75 years
- intensive care unit (ICU) stay at bacteremia onset
- a non-UTI bacteremia source
- presentation with severe sepsis

- but not inappropriate therapy within<24 h (adjusted OR 1.53; 95% CI 0.68 to 3.45)

Conclusion

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If guideline adherence is considered a quality indicator of antibiotic stewardship, A-teams may lead to more (=broader) antibiotic use, without necessarily improving patient outcome and with the potential of increasing antibiotic resistance.

Vragen

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