Severe Community Acquired Pneumonia

Clinical case

- 67 yr old male
- Admitted from 6S after 2 days worsening dyspnea despite NIV
  - RR 38; P/F ratio 28; O2 Sat 89%
  - Temp 39; CVS W.N.L.; CRP and PCT high; Creat 129
  - CXR LLL infiltrates
- PMH
  - COPD
  - DM II
  - Steroids - inhaled recently oral
  - Recently started on neuroleptics
- Hospitalized 6/52 ago for infective exacerbation of COPD
  - Rx Augmentin

What are your main considerations?

Outline of lectures

- Definition
- The “known knowns”
- Pathology
- Guidelines
- Treatment
- Ealing Hospital and CAP
- Conclusion

Outline of lectures

- **Definition**
- The “known knowns”
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Definition

- Symptoms of an acute lower respiratory tract illness developing outside of or within the first 48 hours of hospital
  - New focal chest signs
  - At least one systemic feature
  - No other explanation for the illness

- Severe CAP
  - Best defined as needing ITU admission

What CAP is Not

- Health Care–Associated Pneumonia (HCAP)
  - Risk of MultiDrug-Resistant (MDR) pathogens, Pseudomonas and increased mortality
    - Hospitalisation for 2 days or more < 90 days
    - Residence in a nursing home or extended care facility
    - Indwelling intravascular device
    - Chronic dialysis; home wound care; or a family member with an MDR pathogen

Controversial

- Hospital-acquired pneumonia (HAP)
  - A respiratory infection develops ≥ than 48 h after hospital admission
  - HAP with mechanical ventilation = ventilator-associated pneumonia (VAP)

Current Infectious Disease Reports 2009, 11:349–356 AJRCCM 2005;171:388-416 Lancet Infect Dis 2011; 11: 248–52

Outline of lectures

- Definition
- **The “known knowns”**
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- Conclusion

“Known knowns”

CAP - A deadly disease

- 1st cause of death from infection
- 1st cause of severe sepsis
- 6th commonest cause of death worldwide
- ITU mortality - **25-40%**

Mortality has changed little since introduction of penicillin !!!

JAMA 1999; 281: 61–66.

Effects of treatment

1938

“outcomes compared in 200 patients with lobar pneumonia treated +/- sulphonamide.

Striking is the fact that **three-quarters survived without antibiotics!”**

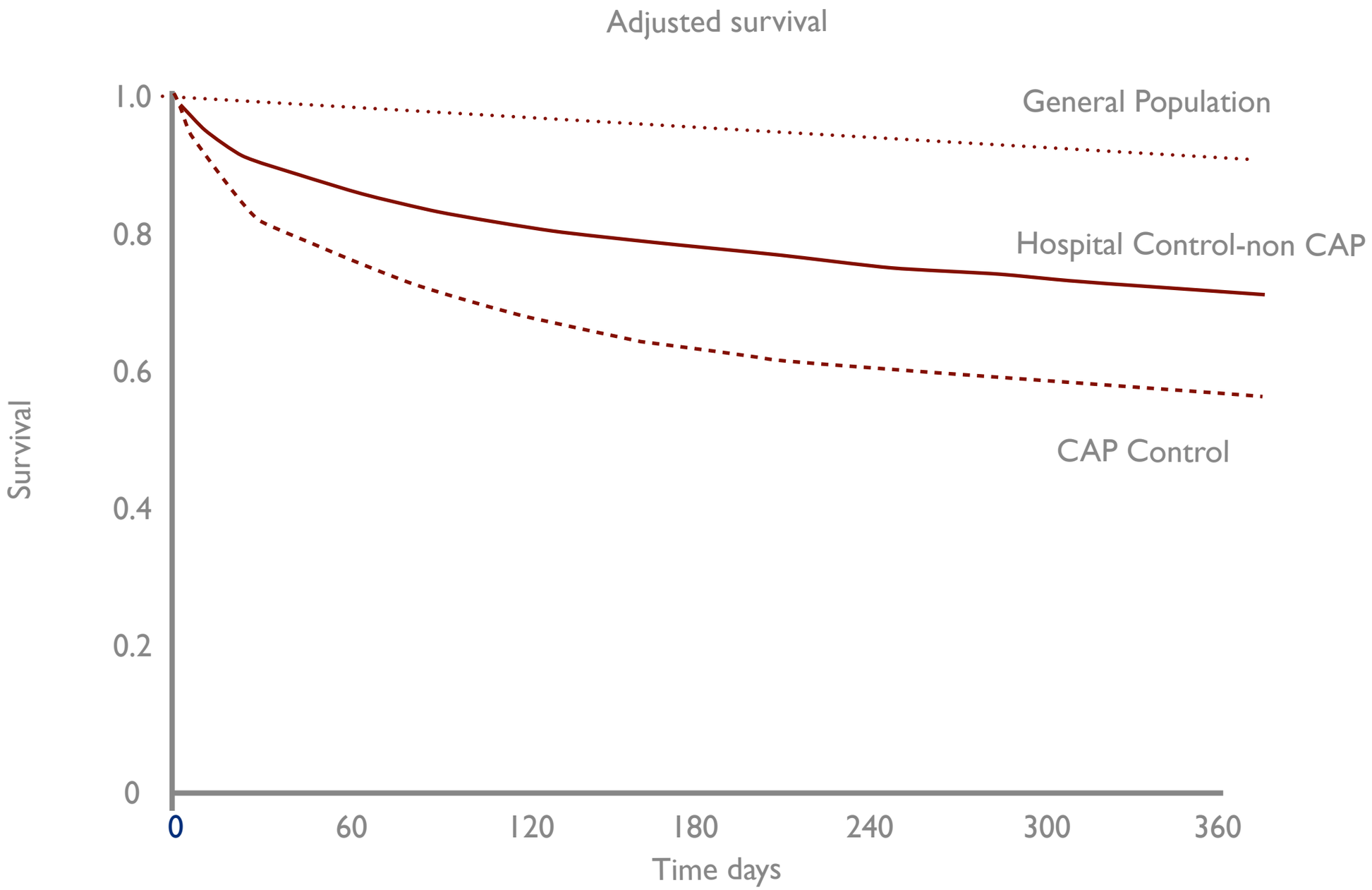
Lancet 1938; ii: 14–9

2012

“Although antibiotherapy was adequate in 92.3% of cases, **hospital mortality reached 28.8%**.”

Mongardon et al. Critical Care 2012, 16:R155

CAP-Long term mortality

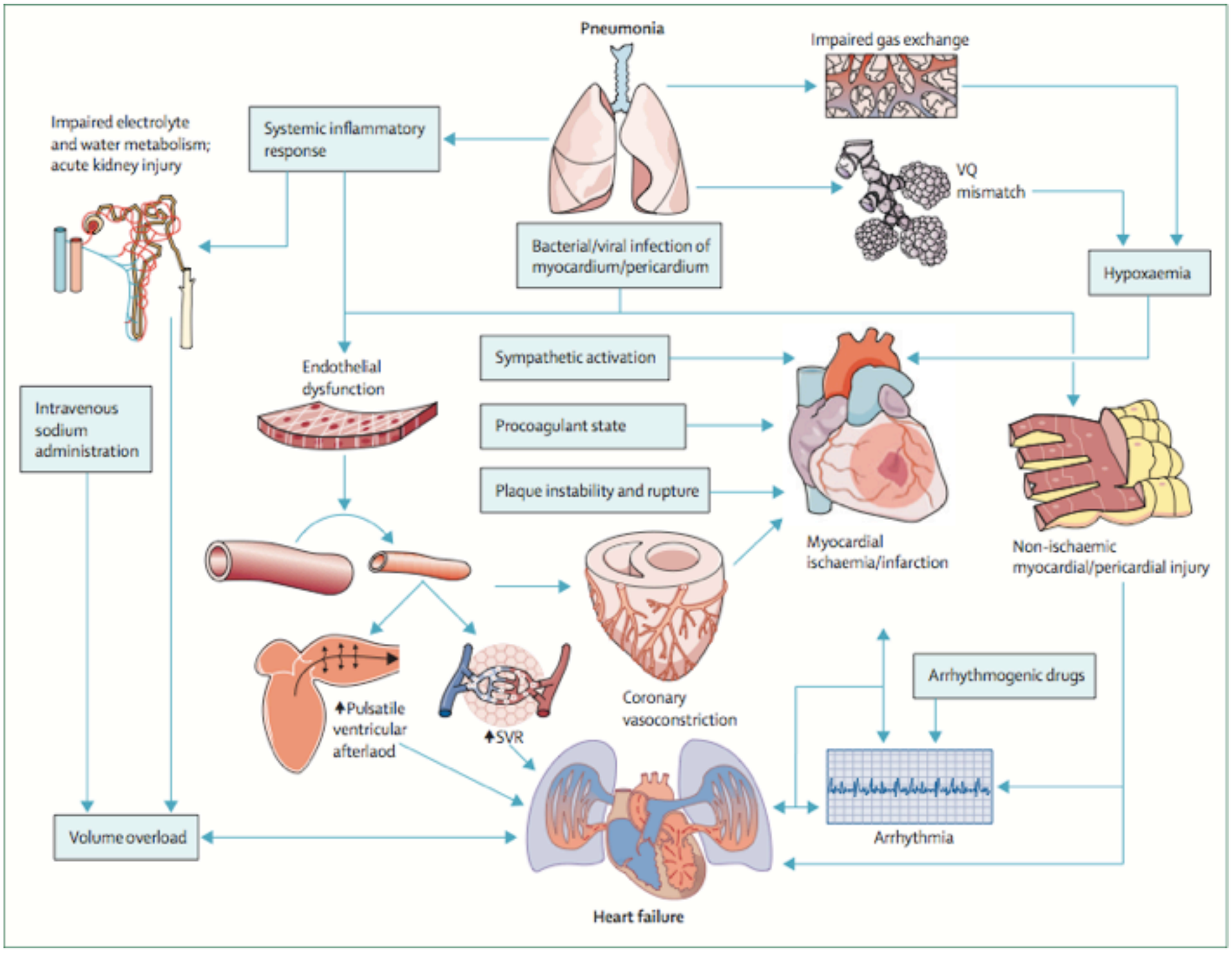


1 in 3 survivors of CAP will be dead in the following year

Arch Intern Med. 2003;163:317-323

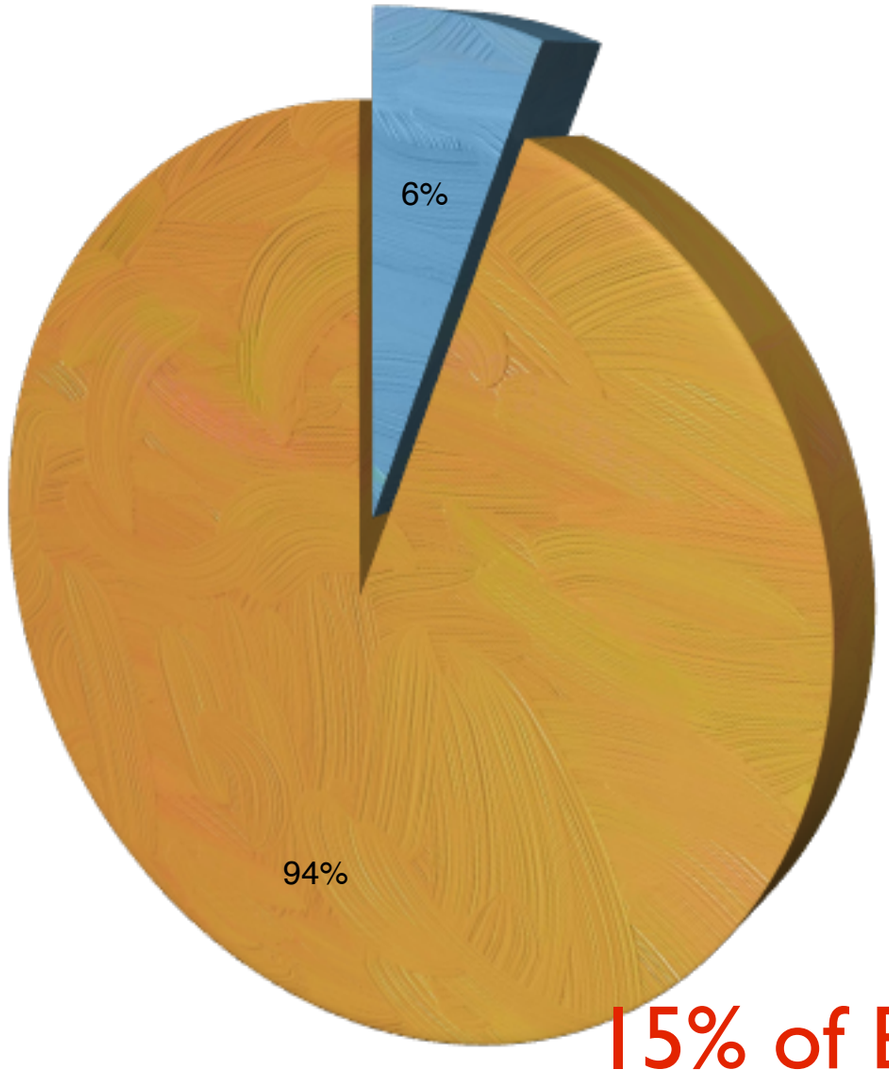
CAP-Long term mortality-New

Acute pneumonia and the cardiovascular system



Lancet published online January 16, 2013

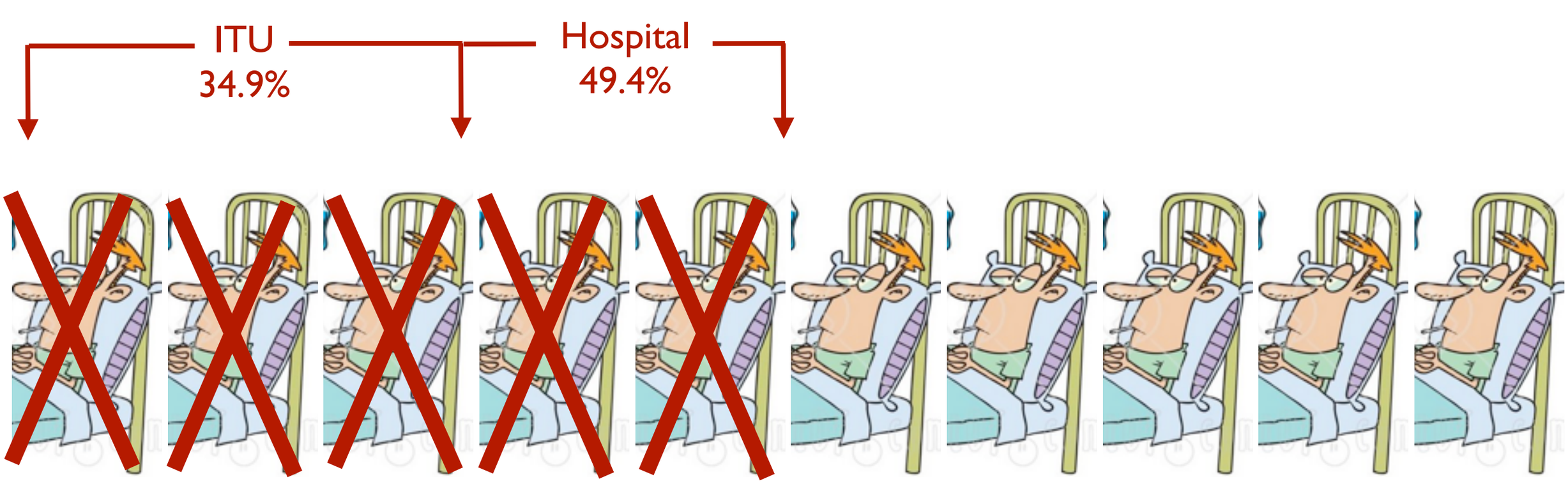
301,871 <u>total</u> admissions in the UK's ICNARC Case Mix Database



<u>15%</u> of Ealing ITU admissions due to CAP

Critical Care 2006, 10:S1

17,869 CAP cases in the UK ICNARC Case Mix Database



Critical Care 2006, 10:S1

Outline of lectures

- Definition
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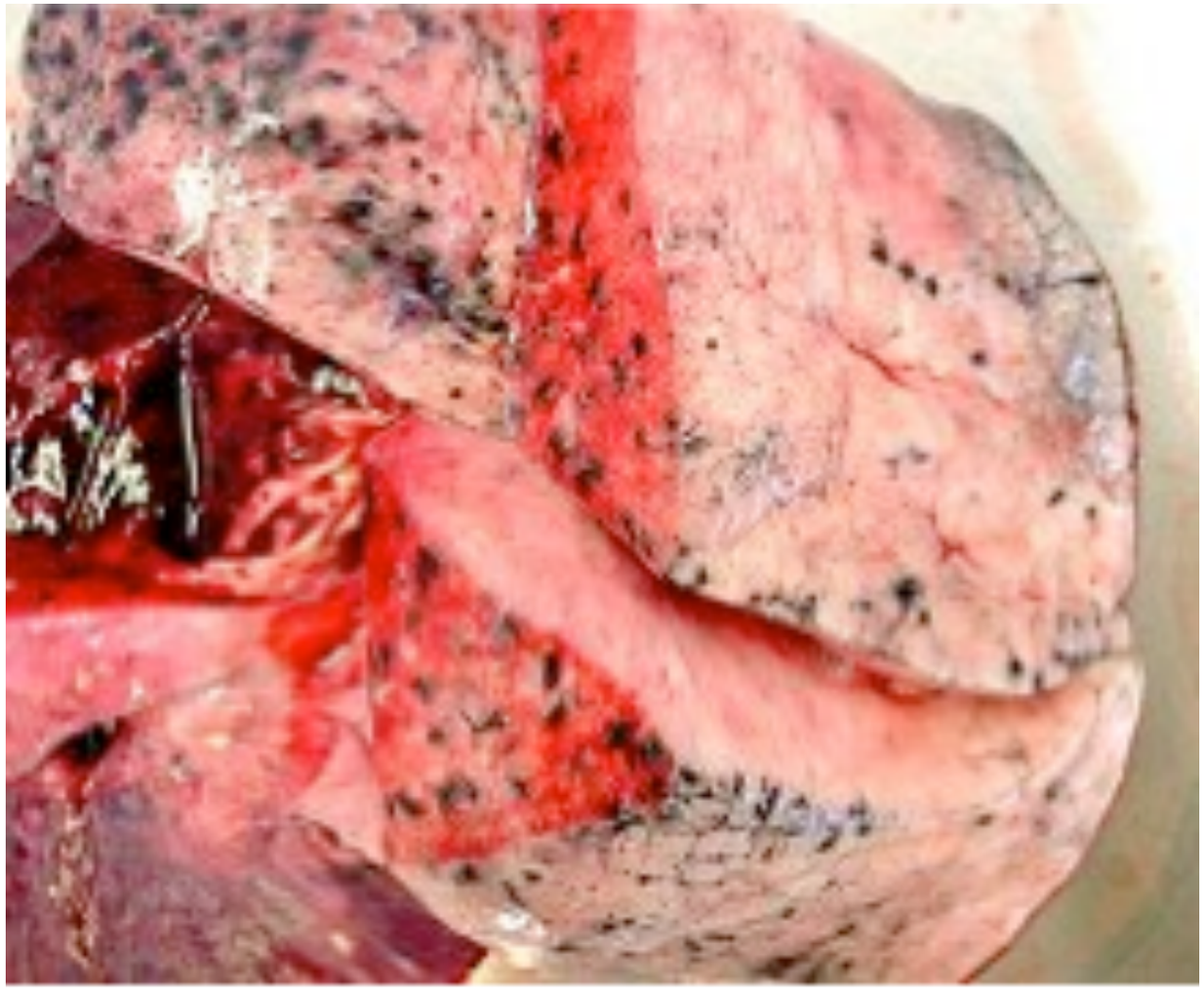
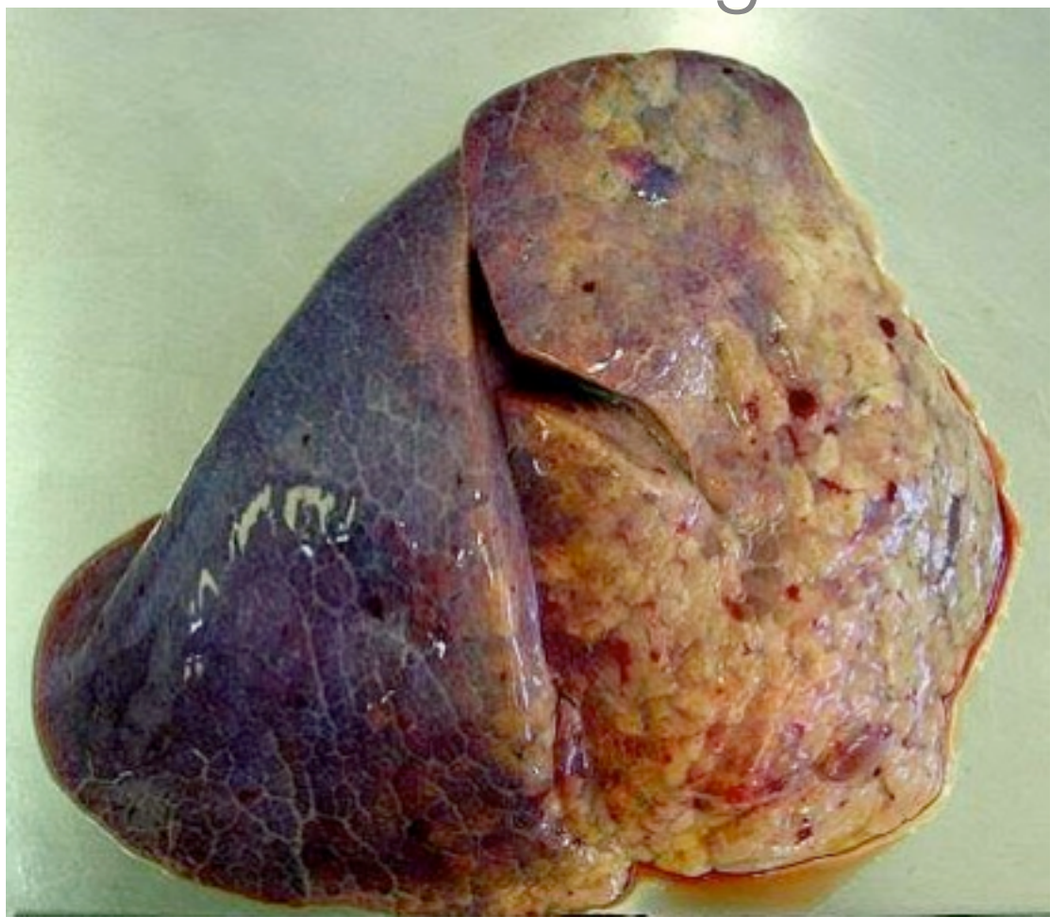
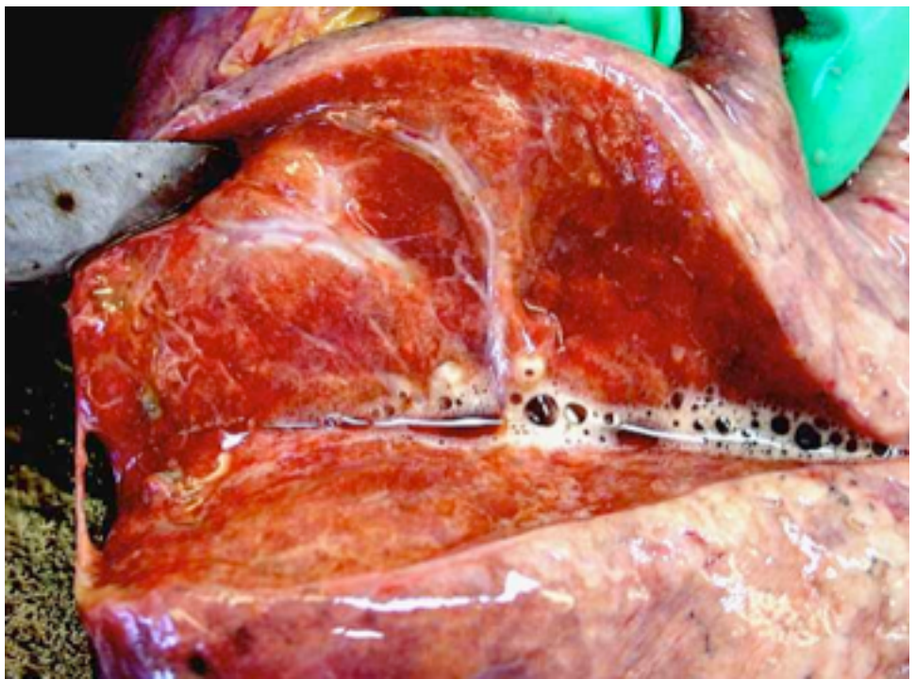
Pathology

Normal lung



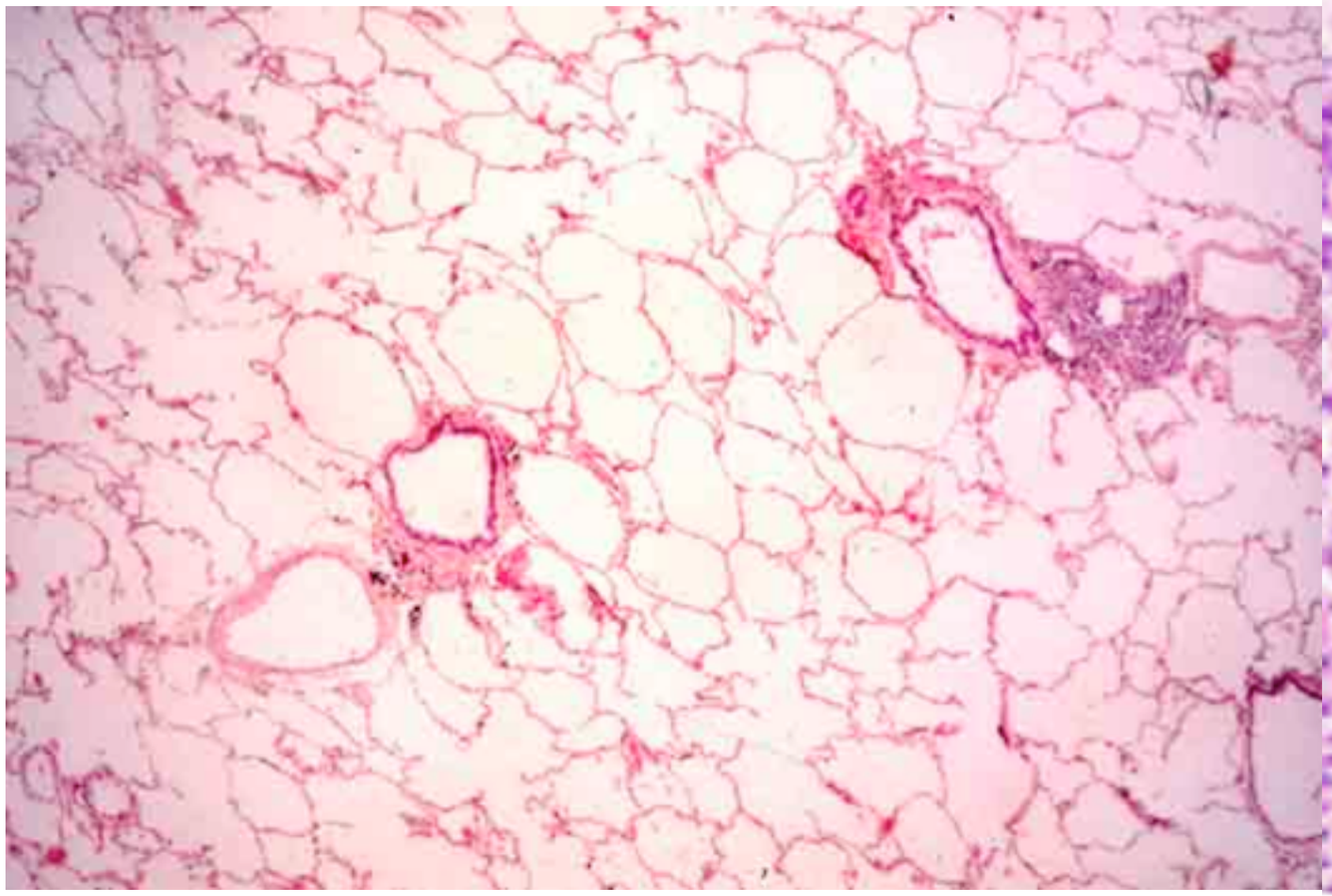
CAP lung



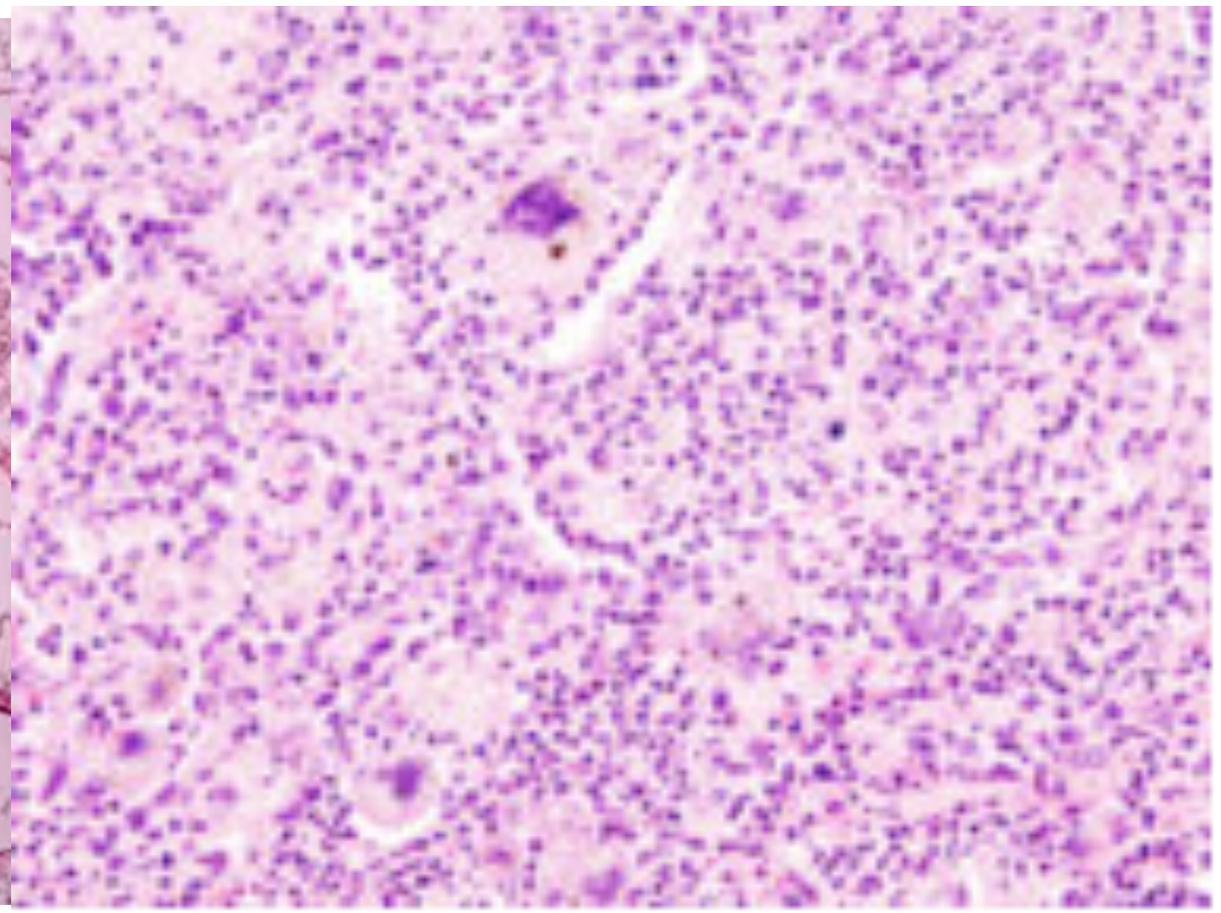


Pathology

Normal lung



Infected lung



A Progressive disease

Local Infection → LRTI, mild pneumonia

Pulmonary spread → Acute respiratory failure

Systemic spread → Sepsis → Severe sepsis → Septic shock → Multiple organ failure

Illness progression in first 72 hrs = increased risk for death

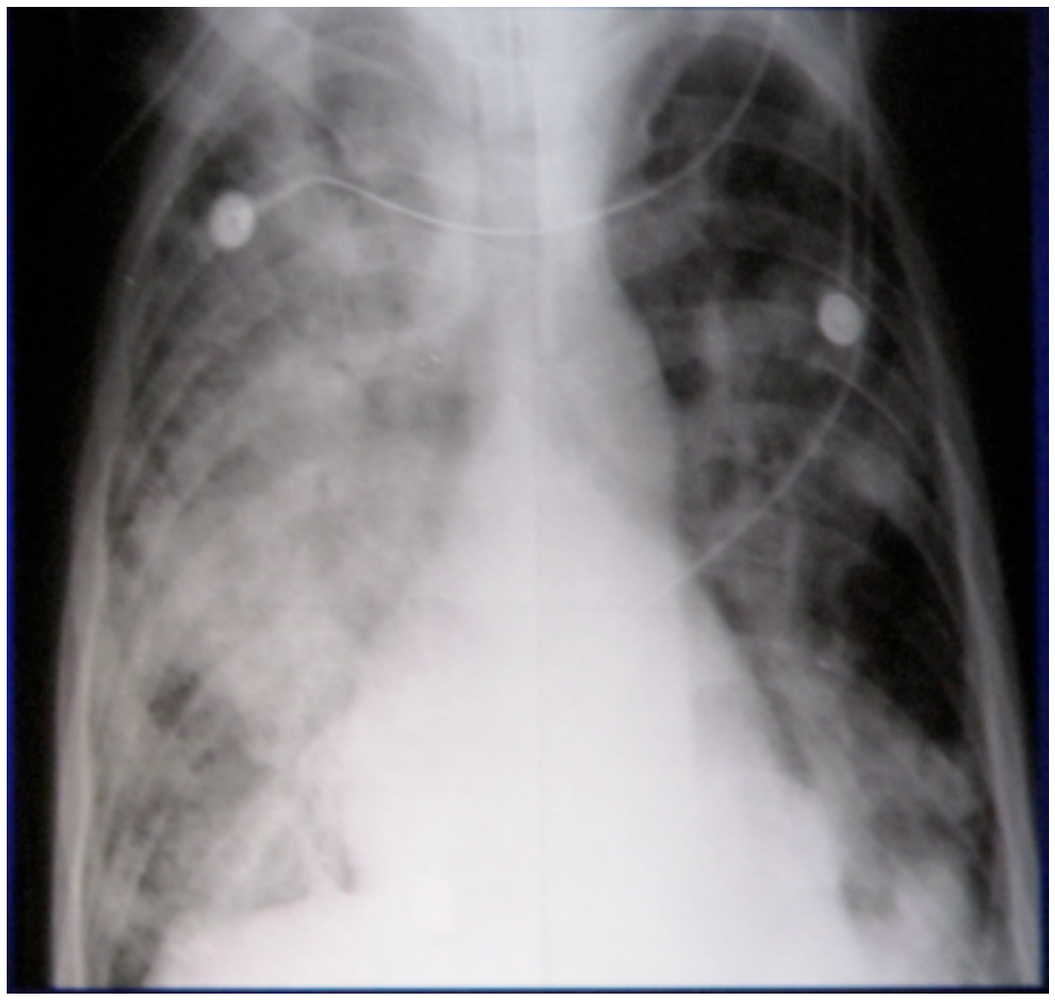
Critical Care 2008, 12(Suppl 6):S2

Why do patients with severe CAP die?

- MOF strongest association with Risk of Death:
  - Shock - X 13
  - Acute Renal Failure - X 4.8
  - APACHE score > 24 - X 2.22
- Beware the first **72** hours
- Mortality of severe CAP has unchanged in 40 years
- Uncertain why immunocompetent patients die despite adequate antibiotics
- We should be seeking adjuvant therapies

Intensive Care Med (2009) 35:430–438

Compare with cause of death in ARDS



Severe CAP is a systemic disease

16% from irreversible respiratory failure

74% ** from sepsis and multiple organ failure

Am Rev Respir Dis. 1985 Sep;132(3):485-9.

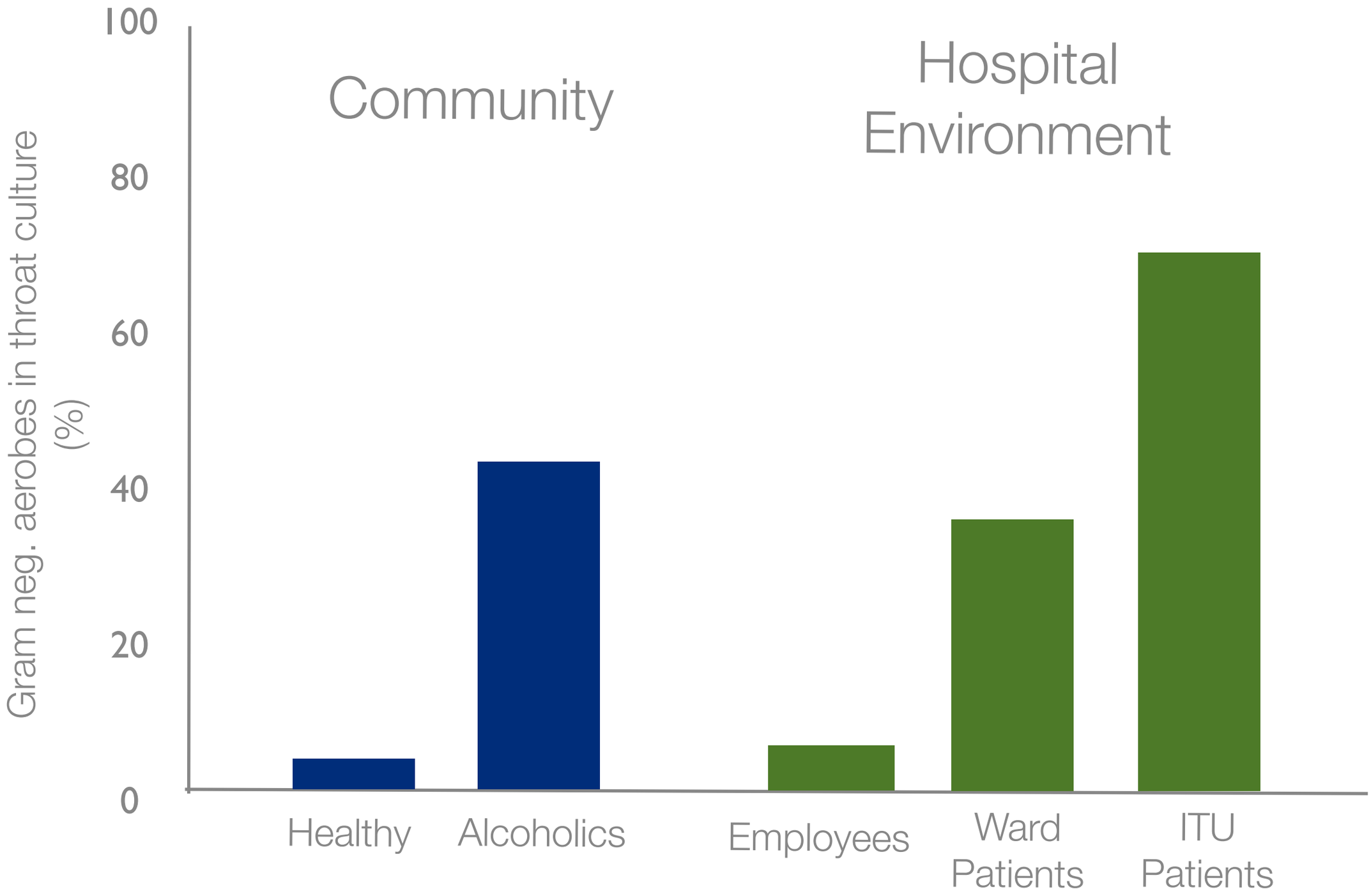
Aspiration

Example

"Current use of antipsychotics associated with ~ 60% increase in the risk of pneumonia"

J Am Geriatr Soc. 2008;56(4):661-666.

Pathogenesis of CAP- Change in mouth flora



NEJM 1969;281:1137

Common aetiologies of severe CAP

None 25 - 50%
S. pneumoniae
S. aureus
Legionella species
Gram-negative bacilli
H. Influenzae

File TM Lancet 2003;362:1991-2001

Common etiologies of ITU CAP in UK

Table 2 Studies of community acquired pneumonia (CAP) conducted in the UK

		Where managed		
		Community	Hospital	Intensive care unit
		1 study* (n = 236)	5 studies† (n = 1137)	4 studies‡ (n = 185)
1	*Streptococcus pneumoniae*	36.0 (29.9 to 42.1)	39 (36.1 to 41.8)	21.6 (15.9 to 28.3)
	Haemophilus influenzae	10.2 (6.3 to 14.0)	5.2 (4.0 to 6.6)	3.8 (1.5 to 7.6)
2	*Legionella* spp	0.4 (0.01 to 2.3)	3.6 (2.6 to 4.9)	17.8 (12.6 to 24.1)
3	*Staphylococcus aureus*	0.8 (0.1 to 3.0)	1.9 (1.2 to 2.9)	8.7 (5.0 to 13.7)
	Moraxella catarrhalis	?	1.9 (0.6 to 4.3)	?
*	Gram-negative enteric bacilli	1.3 (0.3 to 3.7)	1.0 (0.5 to 1.7)	1.6 (0.3 to 4.7)
	Mycoplasma pneumoniae	1.3 (0.3 to 3.7)	10.8 (9.0 to 12.6)	2.7 (0.9 to 6.2)
	Chlamydophila pneumoniae	? (?)	13.1 (9.1 to 17.2)	? (?)
	Chlamydophila psittaci	1.3 (0.3 to 3.7)	2.6 (1.7 to 3.6)	2.2 (0.6 to 5.4)
	Coxiella burnetii	0 (0 to 1.6)	1.2 (0.7 to 2.1)	0 (0 to 2.0)
	All viruses	13.1 (8.8 to 17.4)	12.8 (10.8 to 14.7)	9.7 (5.9 to 14.9)
	Influenza A and B	8.1 (4.9 to 12.3)	10.7 (8.9 to 12.5)	5.4 (2.6 to 9.7)
	Mixed	11.0 (7.0 to 15.0)	14.2 (12.2 to 16.3)	6.0 (3.0 to 10.4)
	Other	1.7 (0.5 to 4.3)	2 (1.3 to 3)	4.9 (2.3 to 9.0)
	None	45.3 (39.0 to 51.7)	30.8 (28.1 to 33.5)	32.4 (25.7 to 39.7)

The references for the ITU aetiologies are either irrelevant or old

BTS Guidelines Thorax 2009;64(Suppl III):iii1–iii55

Common etiologies of ITU CAP

New slide?

Table 1 Frequency of isolation of causative organisms of community-acquired pneumonia in Europe by country* [2 5 10–53 55]

	Percentage means of frequency of isolation in each country												
Pathogen	**Denmark**	**Estonia**	**Finland**	**France**	**Ireland**	**Italy**	**Slovenia**	**Spain**	**Switzerland**	**Netherlands**	**Turkey**	**UK**	**Germany**
Streptococcus pneumoniae	26.1	25.8	68.3	37.2	37	11.9	17.7	33.7	48.9	44.5	25.5	42.1	40
Haemophilus influenzae	10.7	2.4	6.6	10.3	18	5.1	2.9	5.3	14.6	12.3	44.9	12.3	8
Legionella spp.	4.3	0	0	2.0	0	4.9	2.9	12.9	8.6	6.7	0	9.1	3.1
Staphylococcus spp.	1.6	4.3	0	11.7	0	6.5	0	3.2	9.1	1.0	1.0	2.6	5
Moraxella catarrhalis	1.1	12.0	4.4	3.3	10	1.0	2.9	2.7	5.5	1.0	12.2	0.8	0
Gram-negative bacilli	2.7	41.6	0	16.8	0	24.3	1.5	7.9	4.7	9.4	4.1	2.6	7
Mycoplasma pneumoniae	9.5	6.2	16.34	0.7	1.3	7.0	32.4	8.4	9.7	14.0	0	5.3	5.6
Chlamydophila spp.	1.6	5.3	20.2	1	0	2.4	26.5	7.2	3.2	7.6	0	5.9	1.3
Coxiella burnetii	0	0	0	0.2	0	0.4	0	6.2	0	0.7	0	0.3	0
Viruses	6.3	0	15.9	1.7	0	11.6	0	5.9	0	16.5	0	18.6	9
No pathogen identified	59.8	52.4	39.8	35.6	39.4	67.3	39.8	56.8	67.1	35.3	40.6	38.4	NR

Table 2 Aetiology of community-acquired pneumonia in Europe by treatment setting[2 5 10–53 55]

	Percentage means		
Pathogen	**Outpatient**	**Hospital**	**Intensive care unit**
S pneumoniae	38	27	28
M pneumoniae	8	5	2
H influenzae	13	6	7
Chlamydophila pneumoniae	21	11	4
Staphylococcus aureus	1.5	3	9
Enterobacteriaceae	0	4	9
Pseudomonas aeruginosa	1	3	4
Legionella spp.	0	5	12
C burnetii	1	4	7
Respiratory viruses	17	12	3
Unclear	50	41	45

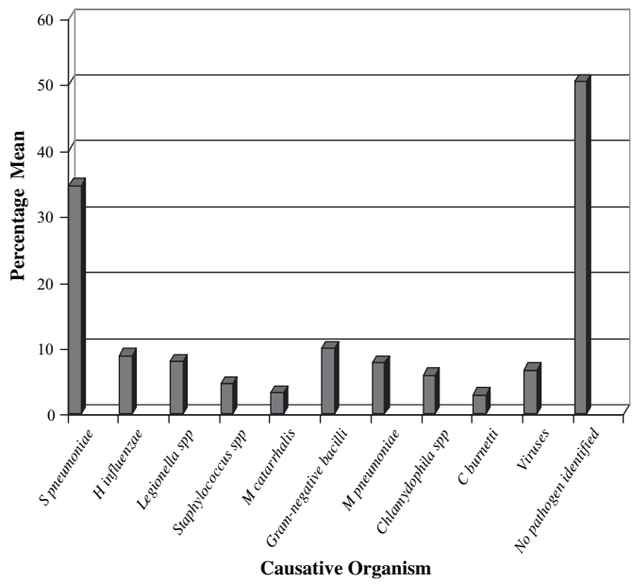


Figure 2 Frequency of causative organisms of community-acquired pneumonia (CAP) in Europe. Data are presented as percentage means of frequency of isolation of the respective pathogens from the studies included.

Thorax 2012;67:71e79. doi:10.1136/thx.2009.129502

Pneumococcal CAP in ITU

New slide?

Introduction: Community-acquired pneumonia (CAP) account for a high proportion of ICU admissions, with Streptococcus pneumoniae being the main pathogen responsible for these infections. However, **little** is **known** on the clinical features and outcomes of **ICU** patients with pneumococcal pneumonia. The aims of this study were to provide epidemiological data and to determine risk factors of mortality in patients admitted to ICU for severe S. pneumoniae CAP.

Methods: We performed a retrospective review of two prospectively-acquired multicentre ICU databases (2001-2008). Patients admitted for management of severe pneumococcal CAP were enrolled if they met the 2001 American Thoracic Society criteria for severe pneumonia, had life-threatening organ failure and had a positive microbiological sample for S. pneumoniae. Patients with bronchitis, aspiration pneumonia or with non-pulmonary pneumococcal infections were excluded.

Results: **Two hundred and twenty two** patients were included, with a median SAPS II score reaching 47 [36-64]. Acute respiratory failure (n = 154) and septic shock (n = 54) were their most frequent causes of ICU admission. **Septic shock** occurred in 170 patients (**77%**) and mechanical ventilation was required in 186 patients (84%); **renal replacement therapy** was initiated in 70 patients (**32%**). **Bacteraemia** was diagnosed in **101** patients. The prevalence of S. pneumoniae strains with **decreased susceptibility to penicillin** was **39.7%**. Although **antibiotherapy** was **adequate** in **92.3**% of cases, **hospital mortality** reached **28.8%**. In multivariate analysis, independent **risk factors** for **mortality** were **age** (OR 1.05 (95% CI: 1.02-1.08)), **male** sex (OR 2.83 (95% CI: 1.16-6.91)) and **renal replacement therapy** (OR 3.78 (95% CI: 1.71-8.36)). **Co-morbidities**, **macrolide** administration, concomitant **bacteremia** or **penicillin susceptibility** did **not** influence outcome.

Conclusions: In ICU, **mortality** of pneumococcal CAP remains **high despite adequate antimicrobial** treatment. Baseline demographic data and renal replacement therapy have a major impact on adverse outcome.

Mongardon et al. Critical Care 2012, 16:R155

Outline of lectures

- Definition
- The “known knowns”
- Pathology
- **Guidelines**
- Treatment
- Ealing Hospital and CAP
- Conclusion

So many guideline....so little evidence!

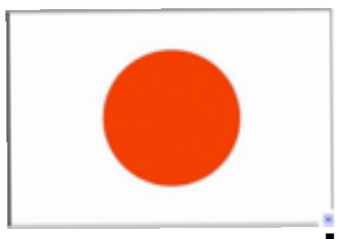
"..... more **eminence** based then **evidence** based"

Infectious Diseases Society of America/American Thoracic Society Consensus Guidelines on the Management of Community-Acquired Pneumonia in Adults

THE BRITISH THORACIC SOCIETY
GUIDELINES FOR THE MANAGEMENT OF COMMUNITY ACQUIRED PNEUMONIA IN ADULTS
UPDATE 2009

ERS TASK FORCE IN COLLABORATION WITH ESCMID
Guidelines for the management of adult lower respiratory tract infections

Canadian Guidelines for the Initial Management of Community-Acquired Pneumonia: An Evidence-Based Update by the Canadian Infectious Diseases Society and the Canadian Thoracic Society



Japanese guidelines for the management of community-acquired pneumonia

Guidelines - International comparison

			
Best Level Evidence	21%	15%	9.6%

US guidelines “mainly based on European studies”

UK guidelines scope “not aimed at patients with known predisposing conditions such as cancer or immunosuppression admitted with pneumonia “

ITU patients are routinely **excluded** from CAP trials

Current Opinion in Infectious Diseases 2007, 20:170–176

Last word on guidelines

"it is important to recognise that these are simply guidelines ..... it remains the **responsibility of the physician** .....to make the best **judgement** for an individual patient"

British Thoracic Society CAP guidleines - 2009

What they agree on

- Score, score, score.....!!!
- Diagnostic approach
- Time is of the essence
  - Antibiotic administration
  - ITU admission
- Don’t miss target with antibiotic therapy
  - Risk factors for MDRs
- “Protect” our antibiotics
  - De-escalate

Severity of illness scores

Severity of CAP - Scores

Almost all major decisions depend on initial severity assessment

- Determine:
  - Entry to ITU
  - Antibiotic treatment

Severity scores for CAP

- CURB-65
- Pneumonia Severity Index (PSI)
- CAP PIRO (for ITU mortality)

Current Infectious Disease Reports 2009, 11:343–348

Severity scores for CAP

	Mechanical ventilation	Shock	Age	Gender	Co-morbid disease	Confusion	HR	BP	RR	T	PO2/FiO2	Arterial PH	Multilobar infiltrate	Hematocrit	Na	glycemia	Urea	albumin	Leucocytes	Thrombocytes
PSI			■	■	■	■	■	■	■	■	■	■	■	■	■	■	■			
CURB-65			■			■		■	■								■			
CRB-65			■			■		■	■											
CURB						■		■	■								■			
CORB						■		■	■		■									
ATS 1993	■	■						■	■		■		■				■			
ATS 2001	■	■						■			■		■							
ATS/IDSA 2007	■	■				■		■	■	■	■		■				■		■	■
SMART-COP						■	■	■	■		■	■	■					■		
SCAP			■			■		■	■		■	■	■				■			
REA-ICU			■	■	■		■		■		■	■	■		■		■		■	

Figure 2 Components of the main severity scores. Criteria used in the score appear as shaded areas. BP, blood pressure; HR, heart rate; RR, respiratory rate; T, temperature.

CURB-65

1 point given for each of:

Confusion
Urea (>7mmol/L)
Respiratory rate (>=30)
BP (SBP <90 or DBP <60)
Age (>=**65**)

Risk class	Mortality (%)	Recommended site of care
0	0.7	Outpatient
1	2.1	Outpatient
2	9.2	Short hospital stay/supervised outpatient
3	14.5	Hospital, assess for ITU
4	40	Hospital, assess for ITU
5	57	Hospital, assess for ITU

Lim WS Thorax 2003;58:377-382

Marti et al. Critical Care 2012, 16:R141
http://ccforum.com/content/16/4/R141

CRITICAL CARE

RESEARCH Open Access

Prediction of severe community-acquired pneumonia: a systematic review and meta-analysis

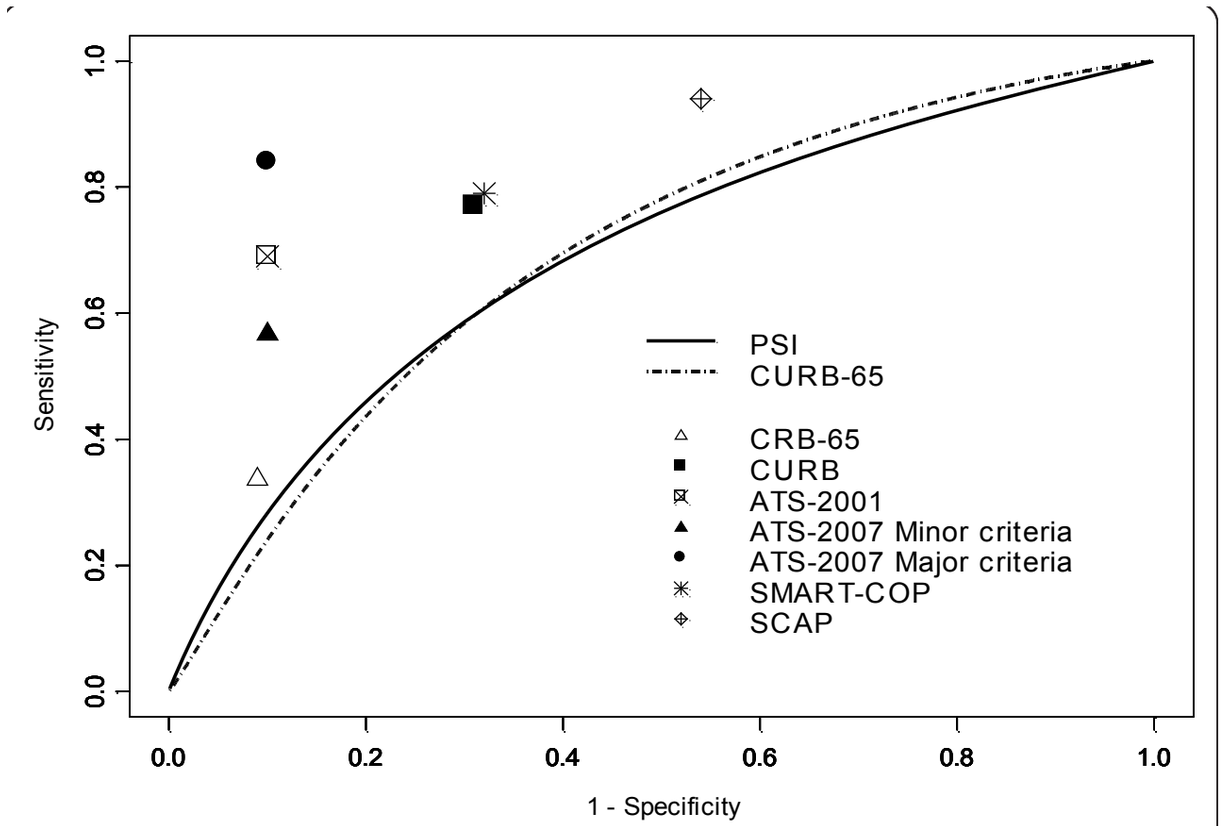
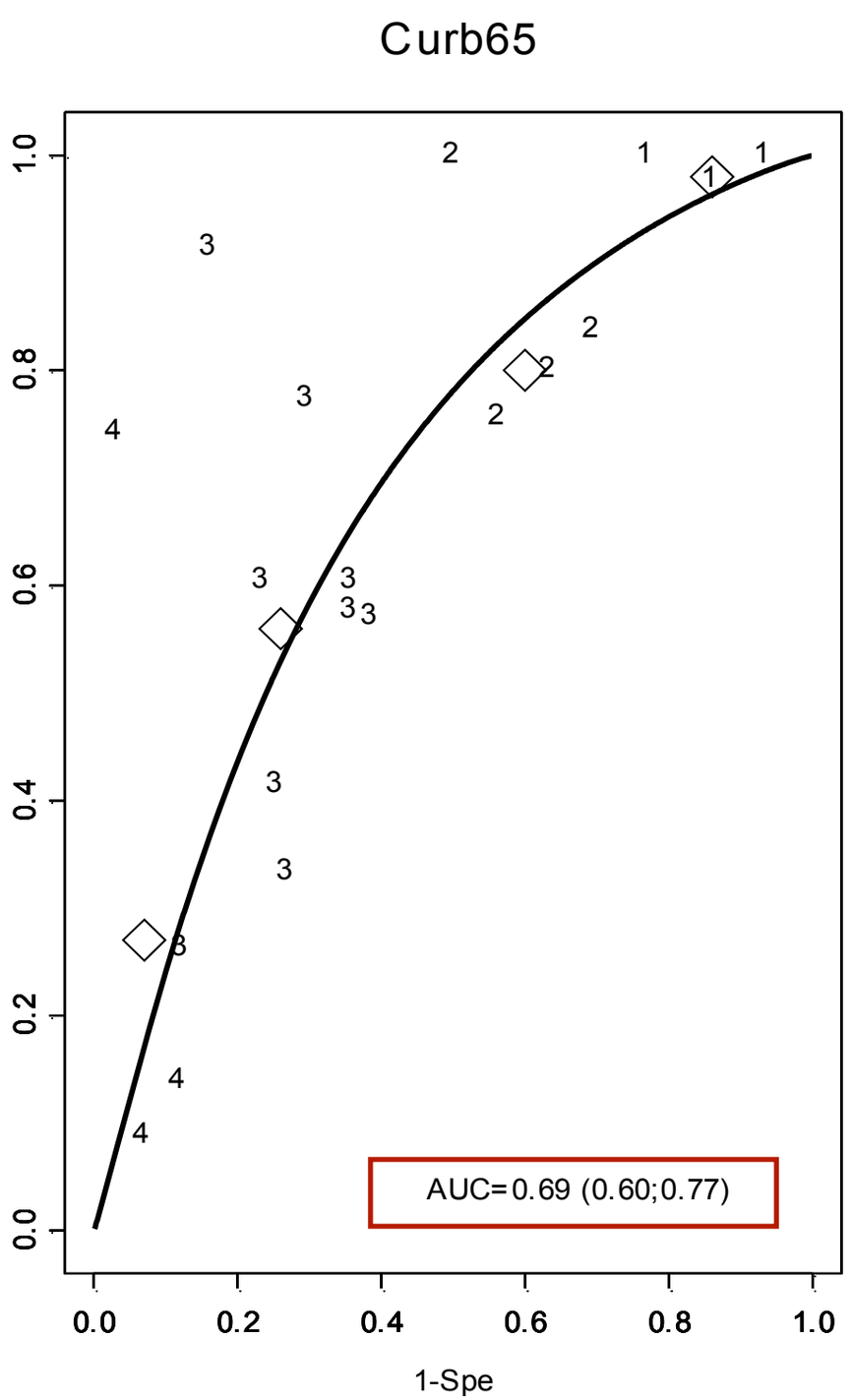


Figure 4 Pooled discriminative performance of the principal scores for severe CAP compared with Pneumonia Severity Index (PSI) and CURB-65 ROC curve.



"New severity scores for predicting the need for ITU such as ATS/IDSA minor criteria, SCAP score and SMART-COP have better discriminative performances compared with PSI and CURB-65"

Severity assessment tools to guide ICU admission in CAP

Meta-analysis of 6 studies using CURB-65

- Mortality prediction - moderate
- ITU admission - poor

Severity scores are better for predicting hospital mortality then need for ITU

Intensive Care Med (2011) 37:1409–1420

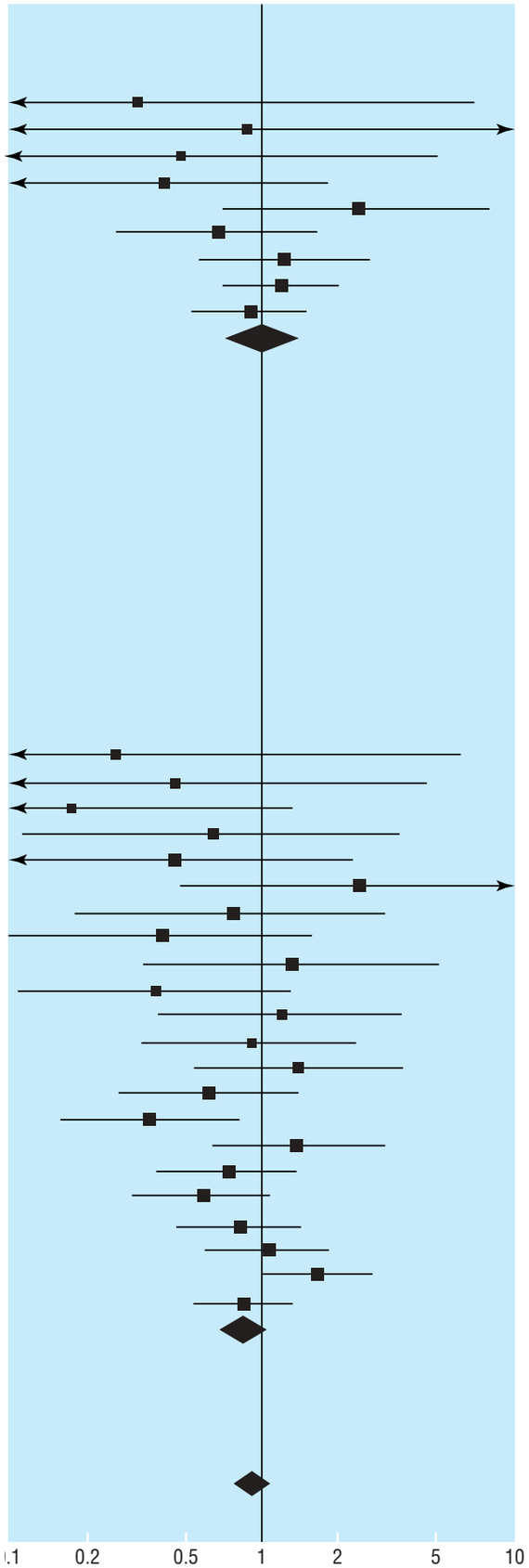
Intensive Care Med (2011) 37:214–223

CURB-65 not great for the sickest

Score	Sensitivity	Specificity	PPV	NPV	AUC %
PSI IV+V	77	53	18	95	0.68
CURB-65 >3	50	71	19	93	0.64

Intensive Care Med (2011) 37:214–223

Mono v combination antibiotics for severe infection

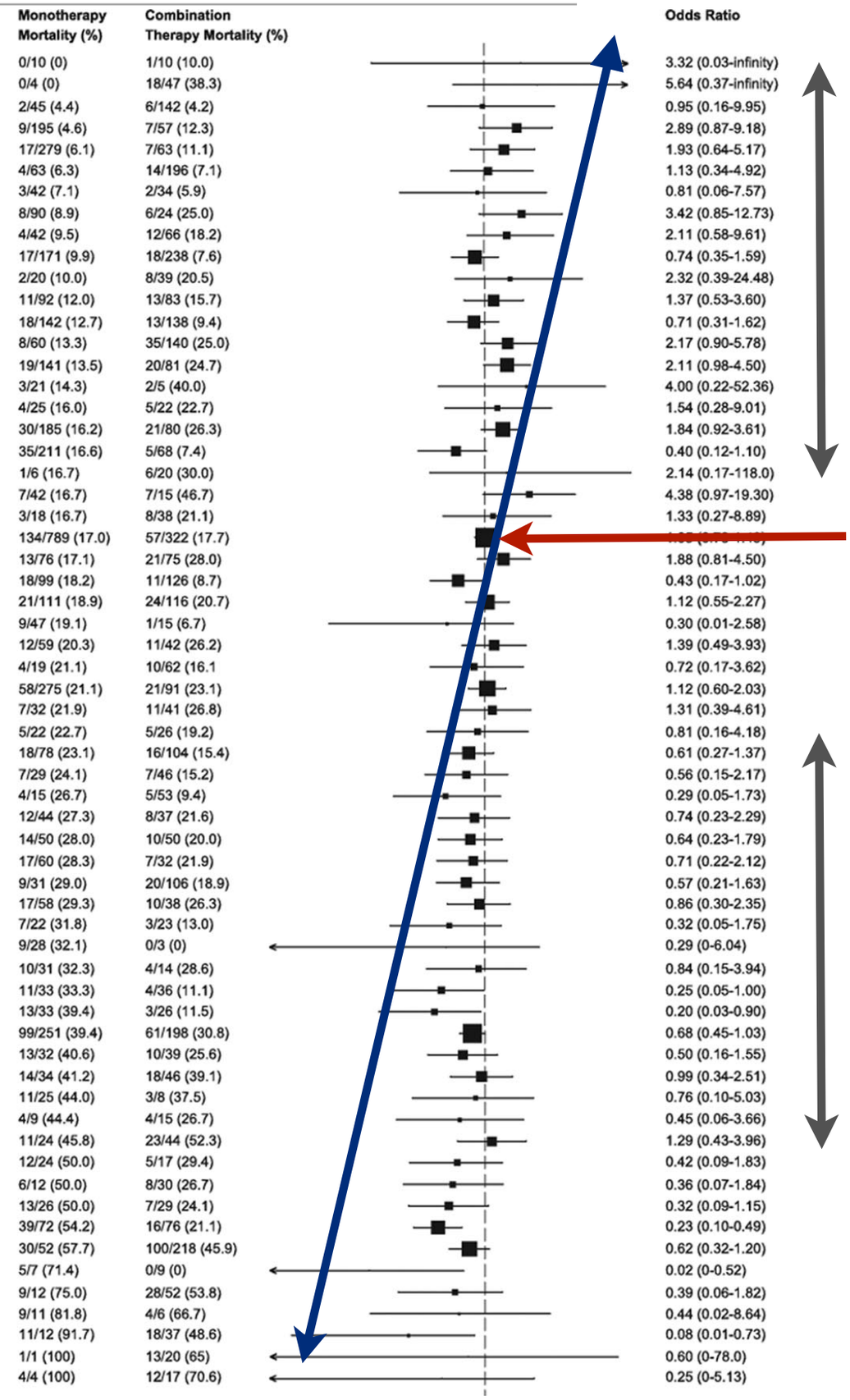


No Mortality Difference ???

BMJ 2004; 328: 668 – 679

This is why we stratify for Risk of Death

Increasing Mortality



Monotherapy Mortality (%)	Combination Therapy Mortality (%)	Odds Ratio
0/10 (0)	1/10 (10.0)	3.32 (0.03-infinity)
0/4 (0)	18/47 (38.3)	5.64 (0.37-infinity)
2/45 (4.4)	6/142 (4.2)	0.95 (0.16-9.95)
9/195 (4.6)	7/57 (12.3)	2.89 (0.87-9.18)
17/279 (6.1)	7/63 (11.1)	1.93 (0.64-5.17)
4/63 (6.3)	14/196 (7.1)	1.13 (0.34-4.92)
3/42 (7.1)	2/34 (5.9)	0.81 (0.06-7.57)
8/90 (8.9)	6/24 (25.0)	3.42 (0.85-12.73)
4/42 (9.5)	12/66 (18.2)	2.11 (0.58-9.61)
17/171 (9.9)	18/238 (7.6)	0.74 (0.35-1.59)
2/20 (10.0)	8/39 (20.5)	2.32 (0.39-24.48)
11/92 (12.0)	13/83 (15.7)	1.37 (0.53-3.60)
18/142 (12.7)	13/138 (9.4)	0.71 (0.31-1.62)
8/60 (13.3)	35/140 (25.0)	2.17 (0.90-5.78)
19/141 (13.5)	20/81 (24.7)	2.11 (0.98-4.50)
3/21 (14.3)	2/5 (40.0)	4.00 (0.22-52.36)
4/25 (16.0)	5/22 (22.7)	1.54 (0.28-9.01)
30/185 (16.2)	21/80 (26.3)	1.84 (0.92-3.61)
35/211 (16.6)	5/68 (7.4)	0.40 (0.12-1.10)
1/6 (16.7)	6/20 (30.0)	2.14 (0.17-118.0)
7/42 (16.7)	7/15 (46.7)	4.38 (0.97-19.30)
3/18 (16.7)	8/38 (21.1)	1.33 (0.27-8.89)
134/789 (17.0)	57/322 (17.7)	[illegible]
13/76 (17.1)	21/75 (28.0)	1.88 (0.81-4.50)
18/99 (18.2)	11/126 (8.7)	0.43 (0.17-1.02)
21/111 (18.9)	24/116 (20.7)	1.12 (0.55-2.27)
9/47 (19.1)	1/15 (6.7)	0.30 (0.01-2.58)
12/59 (20.3)	11/42 (26.2)	1.39 (0.49-3.93)
4/19 (21.1)	10/62 (16.1	0.72 (0.17-3.62)
58/275 (21.1)	21/91 (23.1)	1.12 (0.60-2.03)
7/32 (21.9)	11/41 (26.8)	1.31 (0.39-4.61)
5/22 (22.7)	5/26 (19.2)	0.81 (0.16-4.18)
18/78 (23.1)	16/104 (15.4)	0.61 (0.27-1.37)
7/29 (24.1)	7/46 (15.2)	0.56 (0.15-2.17)
4/15 (26.7)	5/53 (9.4)	0.29 (0.05-1.73)
12/44 (27.3)	8/37 (21.6)	0.74 (0.23-2.29)
14/50 (28.0)	10/50 (20.0)	0.64 (0.23-1.79)
17/60 (28.3)	7/32 (21.9)	0.71 (0.22-2.12)
9/31 (29.0)	20/106 (18.9)	0.57 (0.21-1.63)
17/58 (29.3)	10/38 (26.3)	0.86 (0.30-2.35)
7/22 (31.8)	3/23 (13.0)	0.32 (0.05-1.75)
9/28 (32.1)	0/3 (0)	0.29 (0-6.04)
10/31 (32.3)	4/14 (28.6)	0.84 (0.15-3.94)
11/33 (33.3)	4/36 (11.1)	0.25 (0.05-1.00)
13/33 (39.4)	3/26 (11.5)	0.20 (0.03-0.90)
99/251 (39.4)	61/198 (30.8)	0.68 (0.45-1.03)
13/32 (40.6)	10/39 (25.6)	0.50 (0.16-1.55)
14/34 (41.2)	18/46 (39.1)	0.99 (0.34-2.51)
11/25 (44.0)	3/8 (37.5)	0.76 (0.10-5.03)
4/9 (44.4)	4/15 (26.7)	0.45 (0.06-3.66)
11/24 (45.8)	23/44 (52.3)	1.29 (0.43-3.96)
12/24 (50.0)	5/17 (29.4)	0.42 (0.09-1.83)
6/12 (50.0)	8/30 (26.7)	0.36 (0.07-1.84)
13/26 (50.0)	7/29 (24.1)	0.32 (0.09-1.15)
39/72 (54.2)	16/76 (21.1)	0.23 (0.10-0.49)
30/52 (57.7)	100/218 (45.9)	0.62 (0.32-1.20)
5/7 (71.4)	0/9 (0)	0.02 (0-0.52)
9/12 (75.0)	28/52 (53.8)	0.39 (0.06-1.82)
9/11 (81.8)	4/6 (66.7)	0.44 (0.02-8.64)
11/12 (91.7)	18/37 (48.6)	0.08 (0.01-0.73)
1/1 (100)	13/20 (65)	0.60 (0-78.0)
4/4 (100)	12/17 (70.6)	0.25 (0-5.13)

<15% mortality favors Mono-therapy

15-25% mortality No difference

>25% mortality favors Combination therapy

EALING ITUs
R.o.D. = 47%

Crit Care Med 2010 Vol. 38, No. 8

Last word on severity scores for sCAP

"In our experience, physicians ...must make decisions or recommendations for individual patients, always consider physiologic data when they assess patients and make **clinical judgments** about prognosis, but they consider other non quantifiable things, too."

Use a score as a drunkard uses a lamppost.... more for support than illumination

Crit Care Med 2011 Vol. 39, No. 3

Diagnosis

Diagnosis

For all severe cases of CAP

- Blood cultures (before antibiotics)
- Sputum cultures (before antibiotics)
- Urinary antigens
  - Pneumococcus
    - Legionella
- Pleural tap
- Atypical screen, TB, etc

Microbiological diagnosis not found -->25-60%

Blood cultures

- Best sign of severity of illness

--> **3 X increased mortality**

- Pathogen targeted therapy
- Greater certainty than sputum or serology
- Only positive in 14% (low diagnostic yield)

Chalasani NP et al Chest 1995;108:932-936 Rello J, et al Chest 2009 Fine MJ et al JAMA 1996;275:134

Sputum cultures

- Need good quality - ex. at time of ETT ***
  - Ask for Legionella
- Failure to detect Staph.aureus or Gram neg. is strong evidence against
- Many of the commonly seen pathogens unaffected by a single dose of antibiotic (unlike Strep. pneumonia)

Chalasani NP et al Chest 1995;108:932-936 IDSA/ATS Guidelines for CAP in Adults • CID 2007:44 (Suppl 2) • S27

Urinary antigens

Pneumococcal

- Detects pneumococcal pneumonia **after** antibiotics
- 44% of Strep. pneumonia diagnosed on urinary antigens
- Sensitivity 50-80%
- Specificity 90%
- Still positive after 3 days

Legionella

- Sensitivity 70-90%
- Specificity 90%
- Positivity from day 1 - lasts weeks
- Is insufficient to rule out

Legionnaires' disease bacteria IS found at the Playboy Mansion, a month after mystery illness hits 200 party guests

By PAUL THOMPSON and DAILY MAIL REPORTER

Arch Intern Med. 2011 Jan 24;171(2):166-72.

Quantitative bacterial load in blood

- Compare viral load in management (HIV, Hep C)
- Recent assay detects pneumococcal DNA (PCR)
    - 2 X as sensitive as blood cultures
    - Specificity 100%
    - Results in < 3hrs
- Load - strong predictor of risk of shock/death
- Bacterial load challenges paradigm of host response as cause of mortality
- Same seen in meningococcaemia
- Therefore a significant new diagnostic and prognostic tool

Chest 2009;136:832–840.

Am J Respir Crit Care Med Vol 183. pp 157–164, 2011

Pleural tap

- Tap all pleural parapneumonic effusions
- If pH <7.2 or pus --> drain

"Never let the Sun set on a parapneumonic effusion"

Outline of lectures

- Definition
- The “known knowns”
- Pathology
- Guidelines
- **Treatment**
- Ealing Hospital and CAP
- Conclusion

Principles of treatment

Did they say “modern medicine”???

Sir William Osler (1849-1919)
"Father of modern medicine."

“Pneumonia is one of the diseases in which a **timely venesection** may save life.... to be of service it should be done early.... in a full blooded, healthy man with a high fever and bounding pulse the abstraction of from twenty to thirty ounces of blood (1.5 to 2 pints) is in every way beneficial.”

'The Principles and Practice of Medicine'-**1923**

Principles of treatment

In 1938 outcomes compared in 200 patients with lobar pneumonia treated +/- sulphonamide.

sulphonamide treated group - mortality from 27% -> 8%.

Striking is the fact that **three-quarters survived without antibiotics!**

Lancet 1938; ii: 14–9

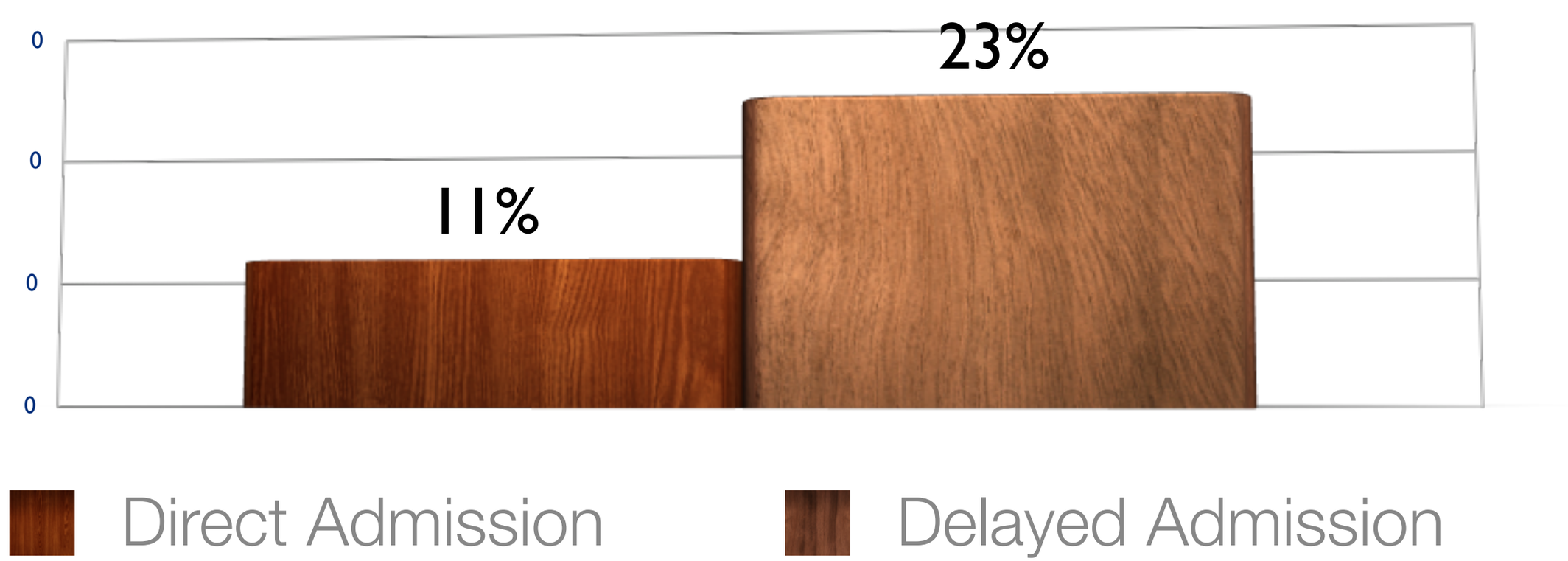
Principles of treatment

- **Early admission to ITU**
- Early antibiotics
- Appropriate antibiotics
- Antibiotic stewardship
- Optimise pharmacokinetics/dynamics
- Adjunctive therapies

Cost of delayed admission to ITU

...45% of patients with CAP who ultimately require ICU ...initially admitted to non-ICU setting...

Mortality



Crit Care Med 2009; 37:2867–2874 Chest 2010;137;552-557

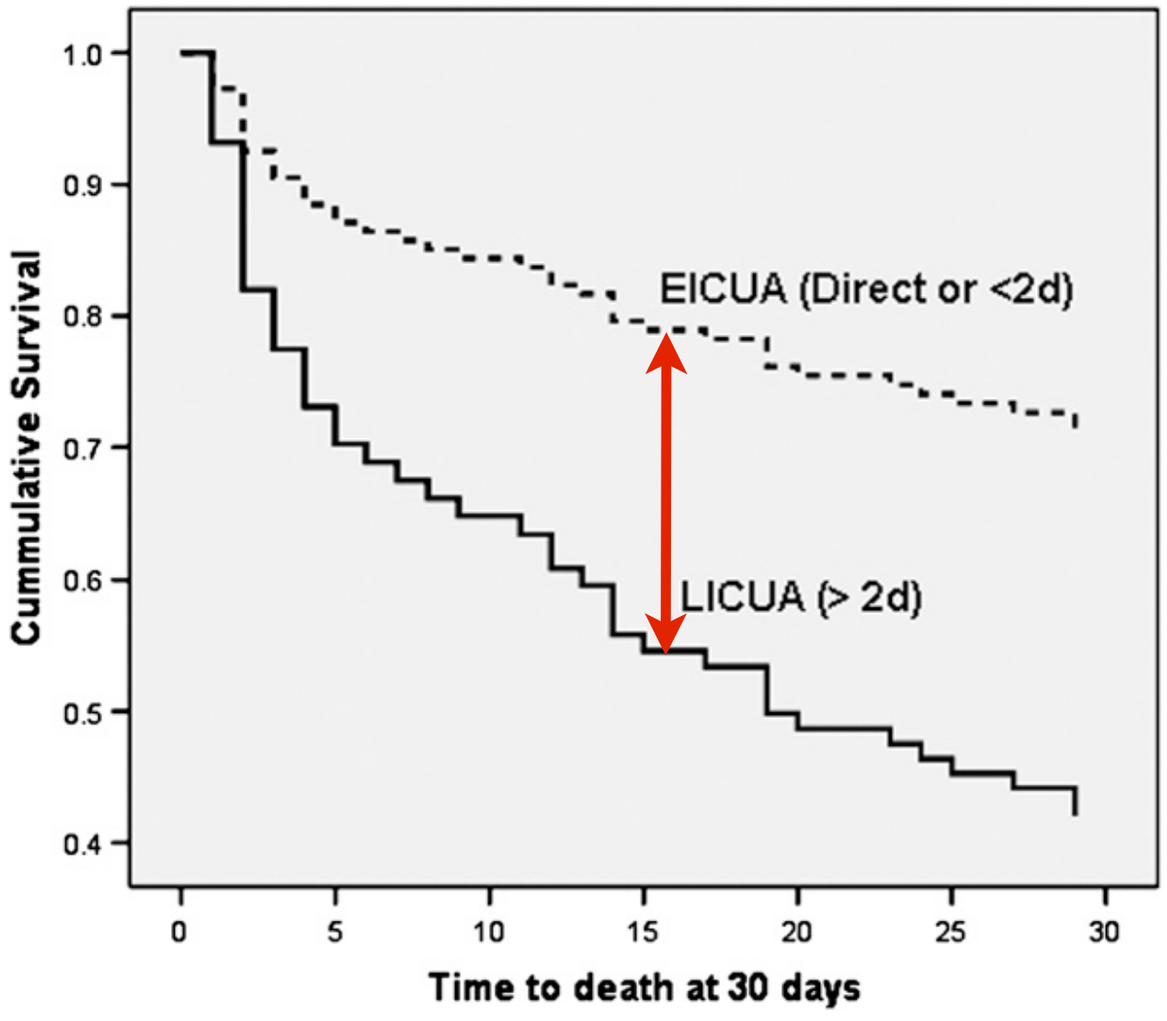
Cost of delayed admission to ITU

CHEST Original Research

CRITICAL CARE MEDICINE

Late Admission to the ICU in Patients With Community-Acquired Pneumonia Is Associated With Higher Mortality

Marcos I. Restrepo, MD, MSc, FCCP; Eric M. Mortensen, MD, MSc; Jordi Rello, MD, PhD; Jennifer Brody, MD; and Antonio Anzueto, MD

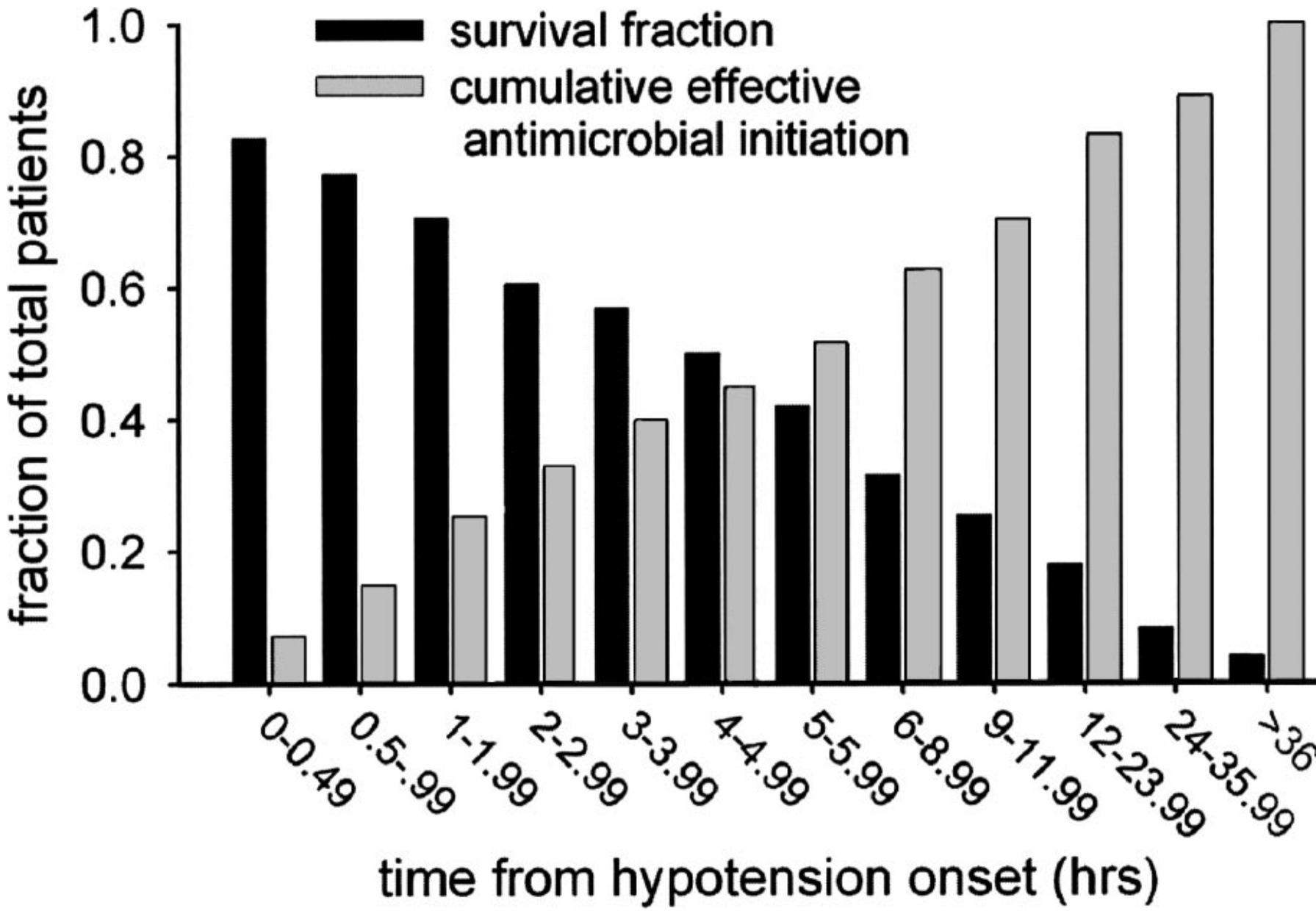


Chest 2010;137;552-557

Principles of treatment

- Early admission to ITU
- **Early antibiotics**
- Appropriate antibiotics
- Antibiotic stewardship
- Optimise pharmacokinetics/dynamics
- Adjunctive therapies

Cost of delayed antibiotic treatment



8% more die with each hours delay!

Crit Care Med 2006; 34:1589–1596

TABLE 5. Recommendations: Initial Resuscitation and Infection Issues

C. Diagnosis

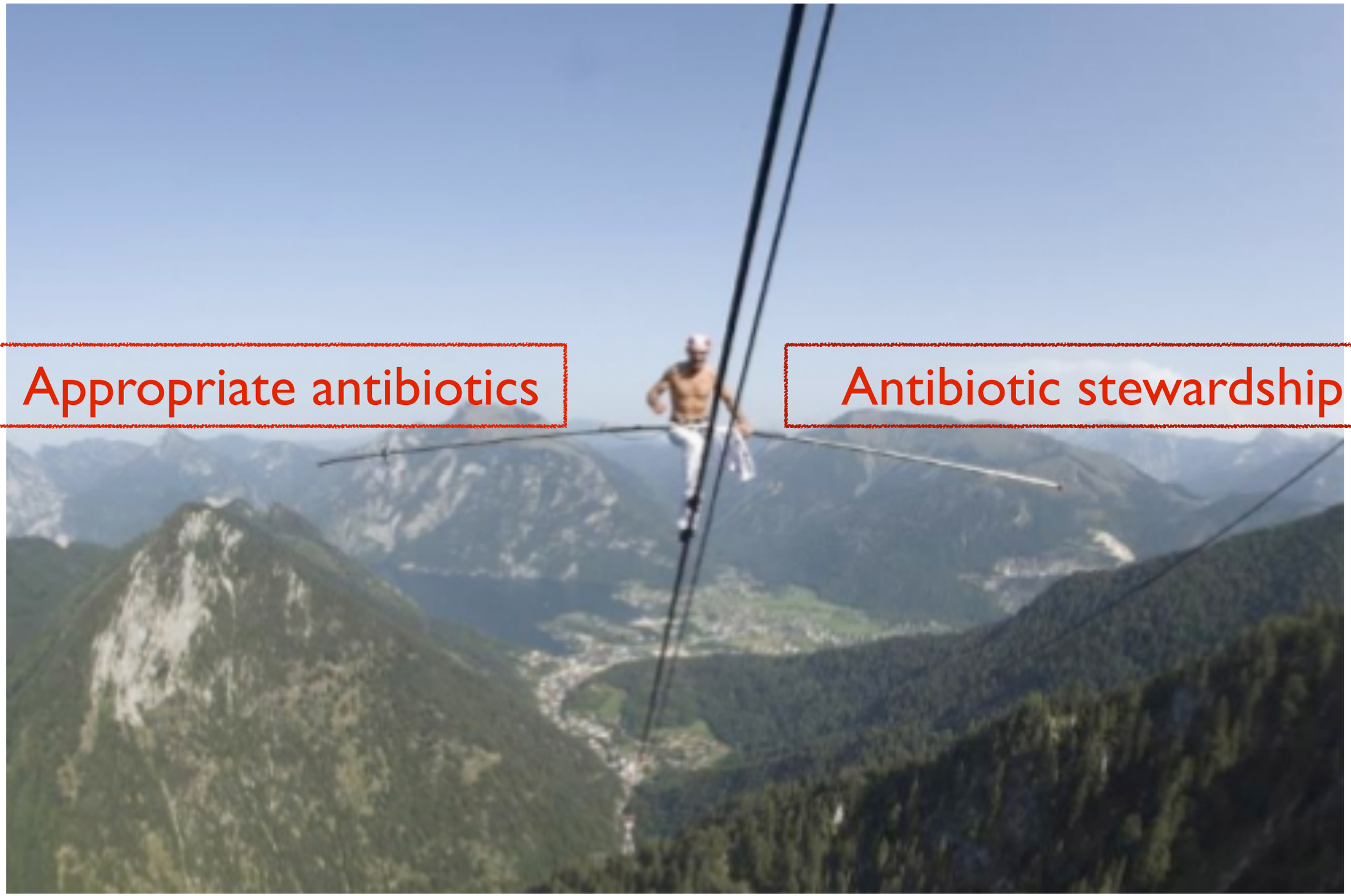
1. Cultures as clinically appropriate before antimicrobial therapy if no significant delay (> 45 mins) in the start of antimicrobial(s) (grade 1C). At least 2 sets of blood cultures (both aerobic and anaerobic bottles) be obtained before antimicrobial therapy with at least 1 drawn percutaneously and 1 drawn through each vascular access device, unless the device was recently (<48 hrs) inserted (grade 1C).

D. Antimicrobial Therapy

1. Administration of effective intravenous antimicrobials within the first hour of recognition of septic shock (grade 1B) and severe sepsis without septic shock (grade 1C) as the goal of therapy.

2a. Initial empiric anti-infective therapy of one or more drugs that have activity against all likely pathogens (bacterial and/or fungal or viral) and that penetrate in adequate concentrations into tissues presumed to be the source of sepsis (grade 1B).

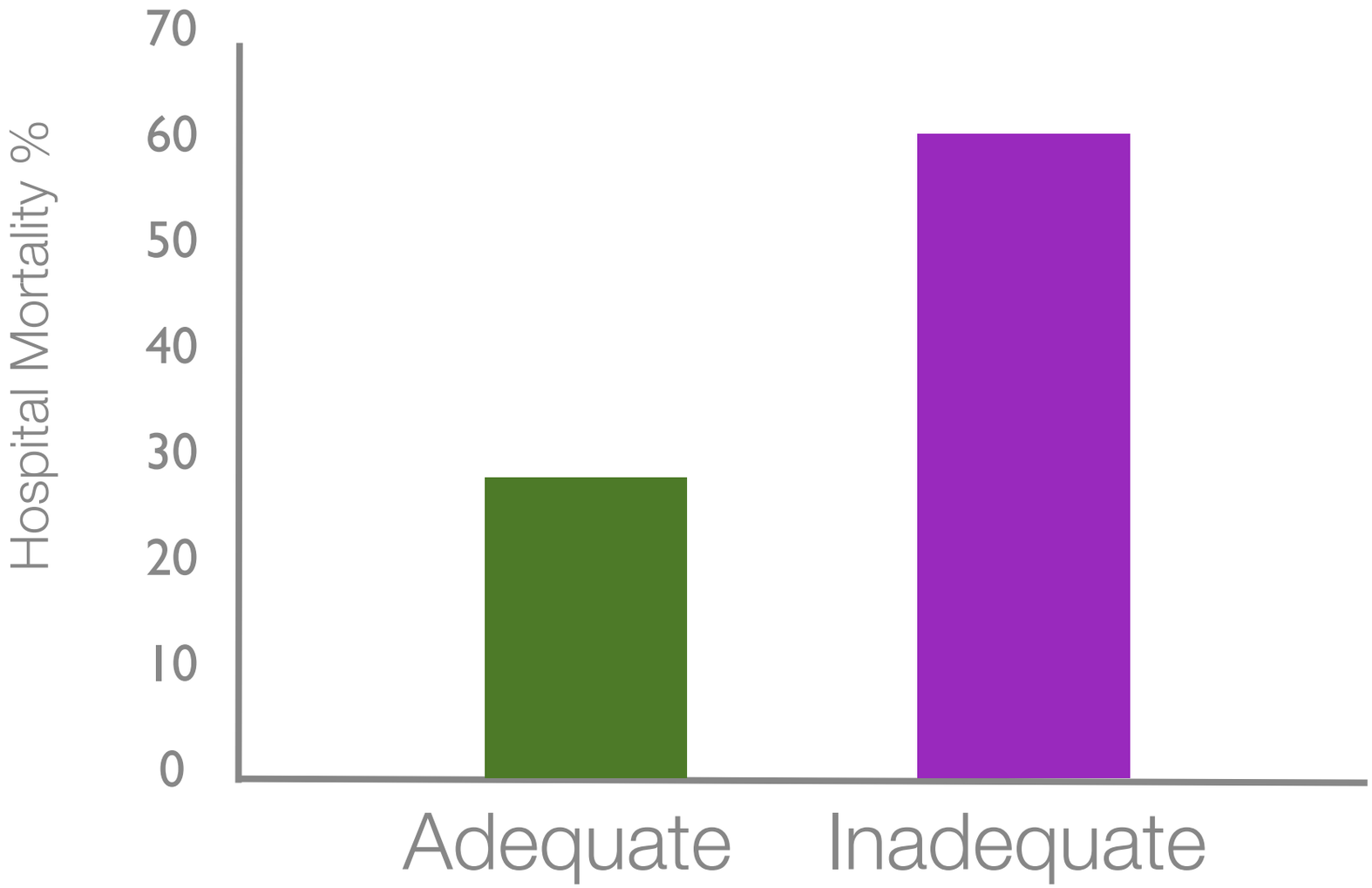
Delicate balancing act



Principles of treatment

- Early admission to ITU
- Early antibiotics
- **Appropriate antibiotics**
- Antibiotic stewardship
- Optimise pharmacokinetics/dynamics
- Adjunctive therapies

Inadequate antimicrobial therapy -get it right first time or people die!



CHEST / 118 / 1 / JULY, 2000 CHEST 1999; 115:462–474 CHEST / 136 / 5 / NOVEMBER, 2009

Importance of getting it right first time

Variable	Relative Odds Ratio
Underlying Diseases	3.09
Shock	2.85
Bacteraemia	2.63
Ineffective initial antibiotic	4.71

Leroy et al. Intensive Care Medicine (1995) 21:24-31

Appropriate antibiotics

Empirical “best guess” based on:

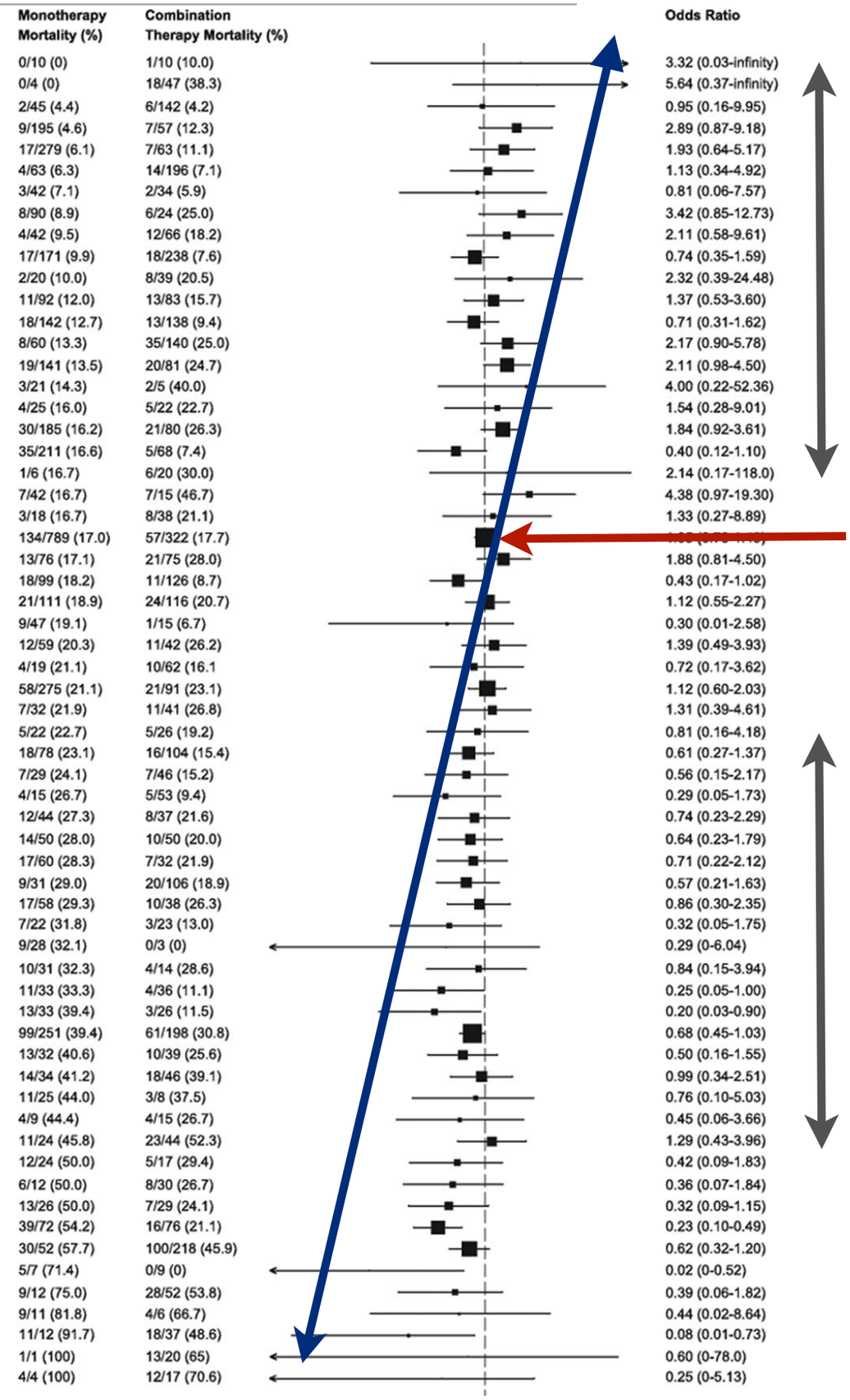
- Severity of illness (scores)
- Past antibiotics
  - (<90 days) - most important factor
- Past hospitalization
  - (<90 days)
- Co-morbidities
- Local resistance patterns
- Other
  - past flu
  - travel

Severity of illness

- Determines aetiology
  - ITU differs from general ward
    - Legionella and Staph. aureus more frequent in ITU
    - Gram negative may be more frequent in severely ill

This is why we stratify for Risk of Death

Increasing Mortality



Monotherapy Mortality (%)	Combination Therapy Mortality (%)	Odds Ratio
0/10 (0)	1/10 (10.0)	3.32 (0.03-infinity)
0/4 (0)	18/47 (38.3)	5.64 (0.37-infinity)
2/45 (4.4)	6/142 (4.2)	0.95 (0.16-9.95)
9/195 (4.6)	7/57 (12.3)	2.89 (0.87-9.18)
17/279 (6.1)	7/63 (11.1)	1.93 (0.64-5.17)
4/63 (6.3)	14/196 (7.1)	1.13 (0.34-4.92)
3/42 (7.1)	2/34 (5.9)	0.81 (0.06-7.57)
8/90 (8.9)	6/24 (25.0)	3.42 (0.85-12.73)
4/42 (9.5)	12/66 (18.2)	2.11 (0.58-9.61)
17/171 (9.9)	18/238 (7.6)	0.74 (0.35-1.59)
2/20 (10.0)	8/39 (20.5)	2.32 (0.39-24.48)
11/92 (12.0)	13/83 (15.7)	1.37 (0.53-3.60)
18/142 (12.7)	13/138 (9.4)	0.71 (0.31-1.62)
8/60 (13.3)	35/140 (25.0)	2.17 (0.90-5.78)
19/141 (13.5)	20/81 (24.7)	2.11 (0.98-4.50)
3/21 (14.3)	2/5 (40.0)	4.00 (0.22-52.36)
4/25 (16.0)	5/22 (22.7)	1.54 (0.28-9.01)
30/185 (16.2)	21/80 (26.3)	1.84 (0.92-3.61)
35/211 (16.6)	5/68 (7.4)	0.40 (0.12-1.10)
1/6 (16.7)	6/20 (30.0)	2.14 (0.17-118.0)
7/42 (16.7)	7/15 (46.7)	4.38 (0.97-19.30)
3/18 (16.7)	8/38 (21.1)	1.33 (0.27-8.89)
134/789 (17.0)	57/322 (17.7)	[illegible]
13/76 (17.1)	21/75 (28.0)	1.88 (0.81-4.50)
18/99 (18.2)	11/126 (8.7)	0.43 (0.17-1.02)
21/111 (18.9)	24/116 (20.7)	1.12 (0.55-2.27)
9/47 (19.1)	1/15 (6.7)	0.30 (0.01-2.58)
12/59 (20.3)	11/42 (26.2)	1.39 (0.49-3.93)
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13/26 (50.0)	7/29 (24.1)	0.32 (0.09-1.15)
39/72 (54.2)	16/76 (21.1)	0.23 (0.10-0.49)
30/52 (57.7)	100/218 (45.9)	0.62 (0.32-1.20)
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9/12 (75.0)	28/52 (53.8)	0.39 (0.06-1.82)
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<15% mortality favors Mono-therapy

15-25% mortality No difference

>25% mortality favors Combination therapy

EALING ITUs
R.o.D. = 47%

Crit Care Med 2010 Vol. 38, No. 8

Impact of previous antibiotic therapy

Recent antibiotic exposure (<90 days) associated:

- Most important factor in antibiotic resistance
- Greater administration of inappropriate antibiotics
- Increased hospital mortality

"Clinicians caring for patients with severe sepsis or septic shock should consider recent antibiotic exposure when formulating empiric antimicrobial regimens"

Crit Care Med 2011; 39:1859 –1865

Recent hospitalization

Risk of MDR Pathogens

HAP, VAP

HCAP

CAP

Morbidity and Mortality

Craven D Curr Opin Infect Dis 2006;19:153-160

Co-morbidities

UK guidelines -

- COPD
  - "There are no relevant UK studies and no new data"
- Diabetes
  - "No new data were found"
- Alcoholic patients
  - "There are no UK studies"
- Steroids
  - "There are no UK studies and no new data"
- Aspiration pneumonia
  - "There are no UK studies"

"since 2001 only one additional study of adults admitted to hospital with CAP has been published"

Thorax 2009;64(Suppl III):iii1–iii55. doi:10.1136/thx.2009.121434

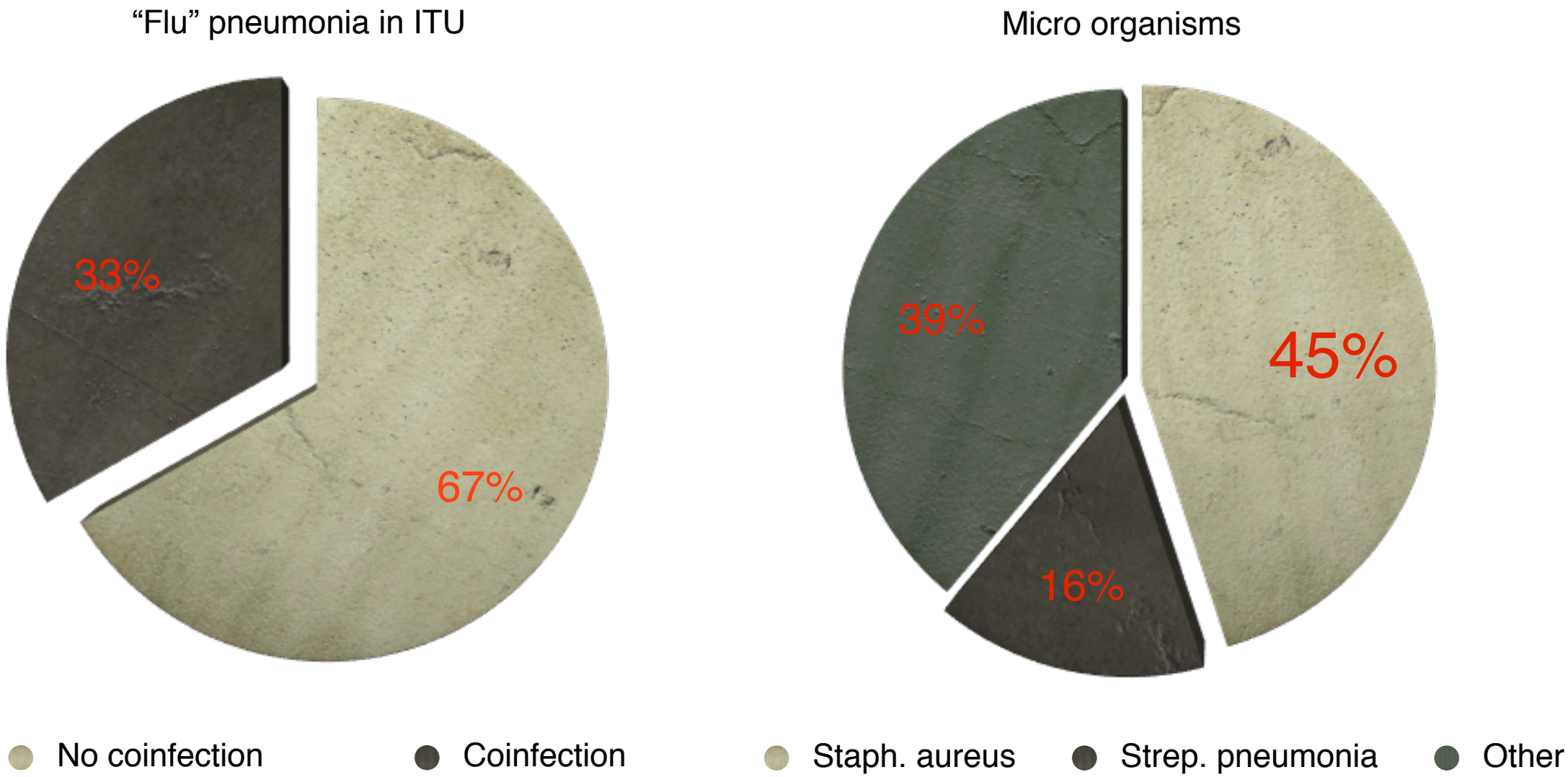
Co-morbidities

- MDRs more frequent
- COPD
  - Strep. pneumonia
  - H. influenza
  - Pseudomonas, Staph. aureus
  - Gram neg.
- Diabetes
  - Bacteraemic pneumococci
- Alcoholic
  - Bacteraemic pneumococci
  - Gram neg.
  - Anaerobes (? kissable?)
  - TB
- Ch Renal Failure (dialysis)
  - MRSA
- Steroids
  - Gram neg., ? legionella

Other considerations

- Recent history of “flu”
  - 3% of “flu” get CAP
  - 67% of post-flu CAP in ITU have staph. aureus
- If v. sick, cavitating lesions, bilateral
  - Think PVL-MRSA
- Recent history of travel (< 2 weeks)
  - Consider Legionella

Bacterial co-infection in influenza



Bacterial co-infection in influenza

- Micro-organisms - colonise nasopharynx
  - **Staph. aureus** - 45% (62% are MRSA)
  - Strep. pneumonia - 16%
  - If HAP risk factors
    - Pseudomonas
    - Resistant Gram negatives
- Diagnosis
  - Virus antigen tests - **false negatives in 70%**
  - In severe “flu” CAP, cannot diagnose co-infection on clinical grounds
- Treatment
  - **Early** (4-8 hrs of hospitalisation)
    - Antivirals and antibiotics
  - **On target**
    - Beta-lactams and macrolide
    - If severe (pleural effusion, leucopenia, haemoptysis, cavitating) - think **MRSA**
      - add Vancomycin or Linezolid

JAMA, January 16, 2013—Vol 309, No. 3

Principles of treatment

- Early admission to ITU
- Early antibiotics
- Appropriate antibiotics
- **Antibiotic stewardship**
- Optimise pharmacokinetics/dynamics
- Adjunctive therapies

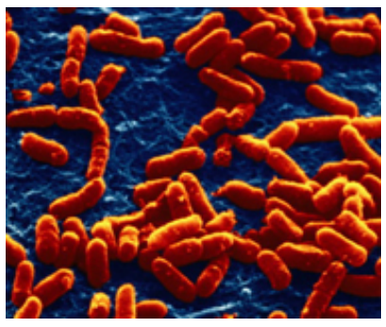
But by being too aggressive you may prepare tomorrows problems

NHS choices
Your health, your choices

The rise of drug-resistant E. coli

Behind the Headlines
Brought to you by the NHS Knowledge Service

Tuesday February 19 2008



guardian.co.uk

The reason why this deadly E coli makes doctors shudder

It is past time for health authorities to curb the antibiotic misuse that created the resistance of this aberrant E Coli strain

Antibiotic exposure and resistance development in *Pseudomonas aeruginosa* and *Enterobacter* species in intensive care units

Crit Care Med 2011; 39:000 – 000

The NEW ENGLAND JOURNAL of MEDICINE

NDM-1 — A Cause for Worldwide Concern

Robert C. Moellering, Jr., M.D.

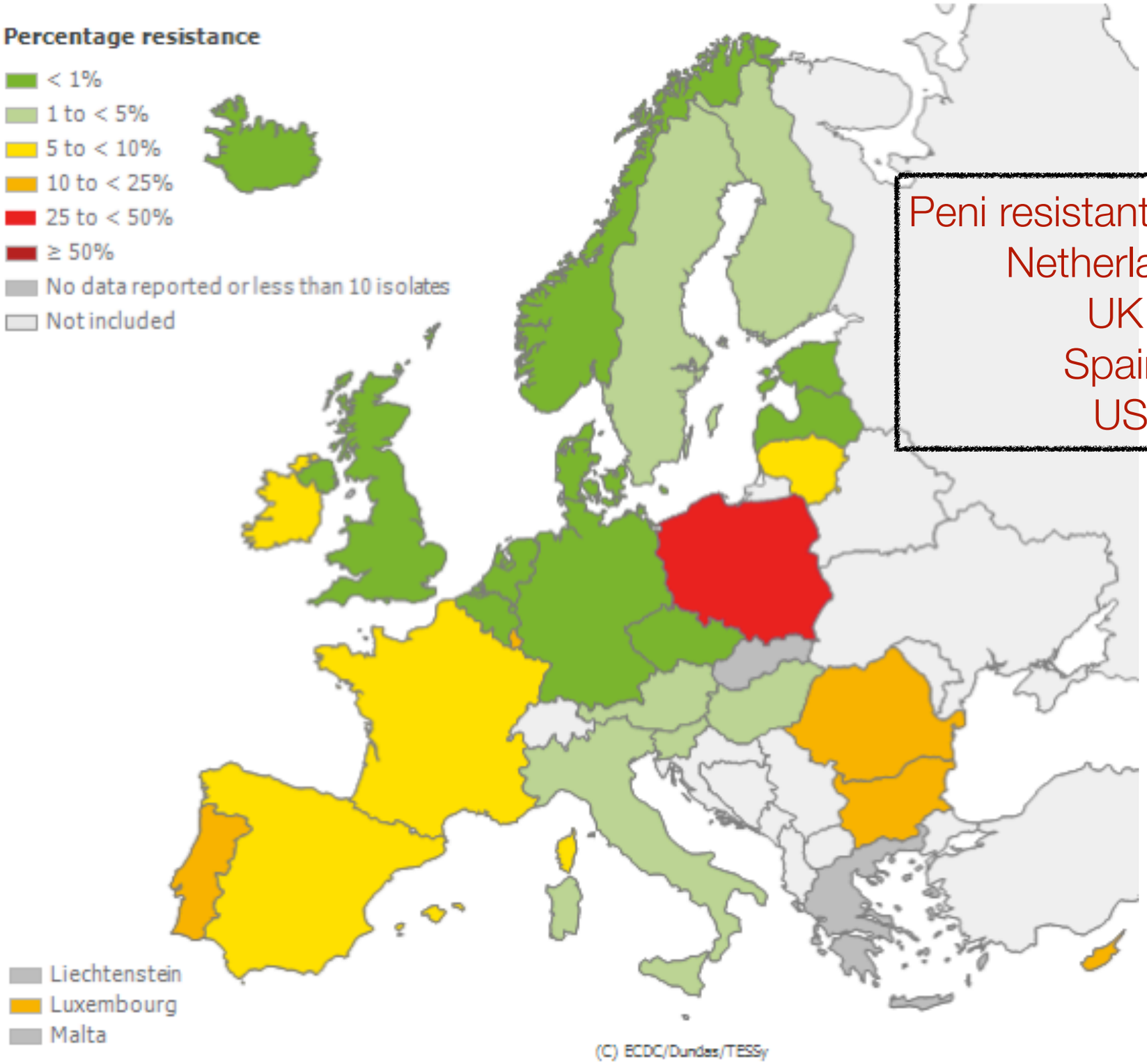
n engl j med 363;25 nejm.org december 16, 2010

"if you reproduced every 20 minutes, you would get smart quickly, too"

Avoid poor antibiotic stewardship

- De-escalate
  - Good microbiological diagnosis is essential !!
- Short courses
  - PCT guided?

Local ecology - Pneumoccocal resistance to penicillin



Peni resistant St.Pneumonia:
Netherlands 0.5%
UK 1.5%
Spain 9.2%
US 16%

http://ecdc.europa.eu/en/activities/surveillance/EARS-Net/database/Pages/graph_reports.aspx

Principles of treatment

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- Early antibiotics
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- **Optimise pharmacokinetics/ dynamics**
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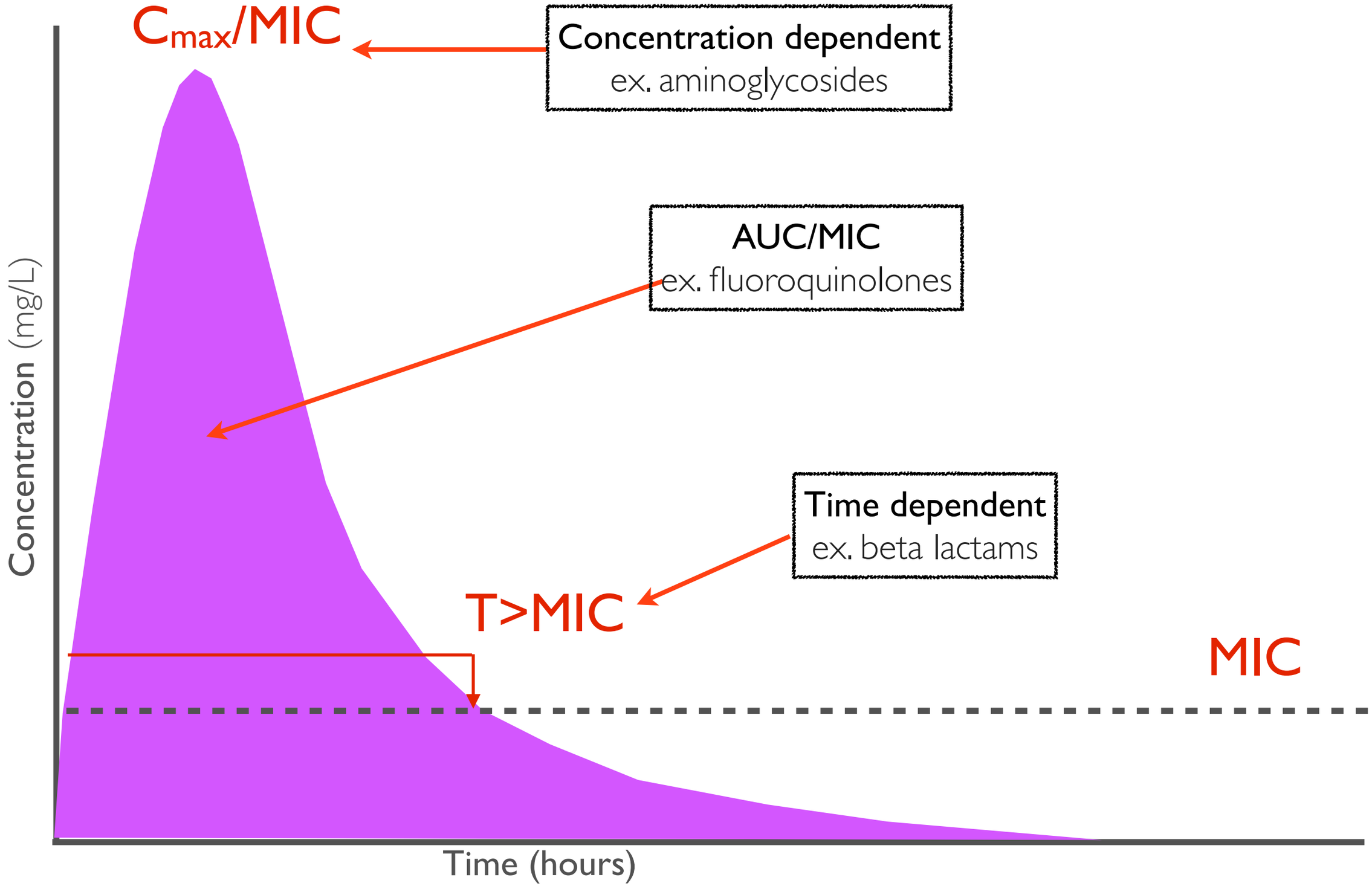
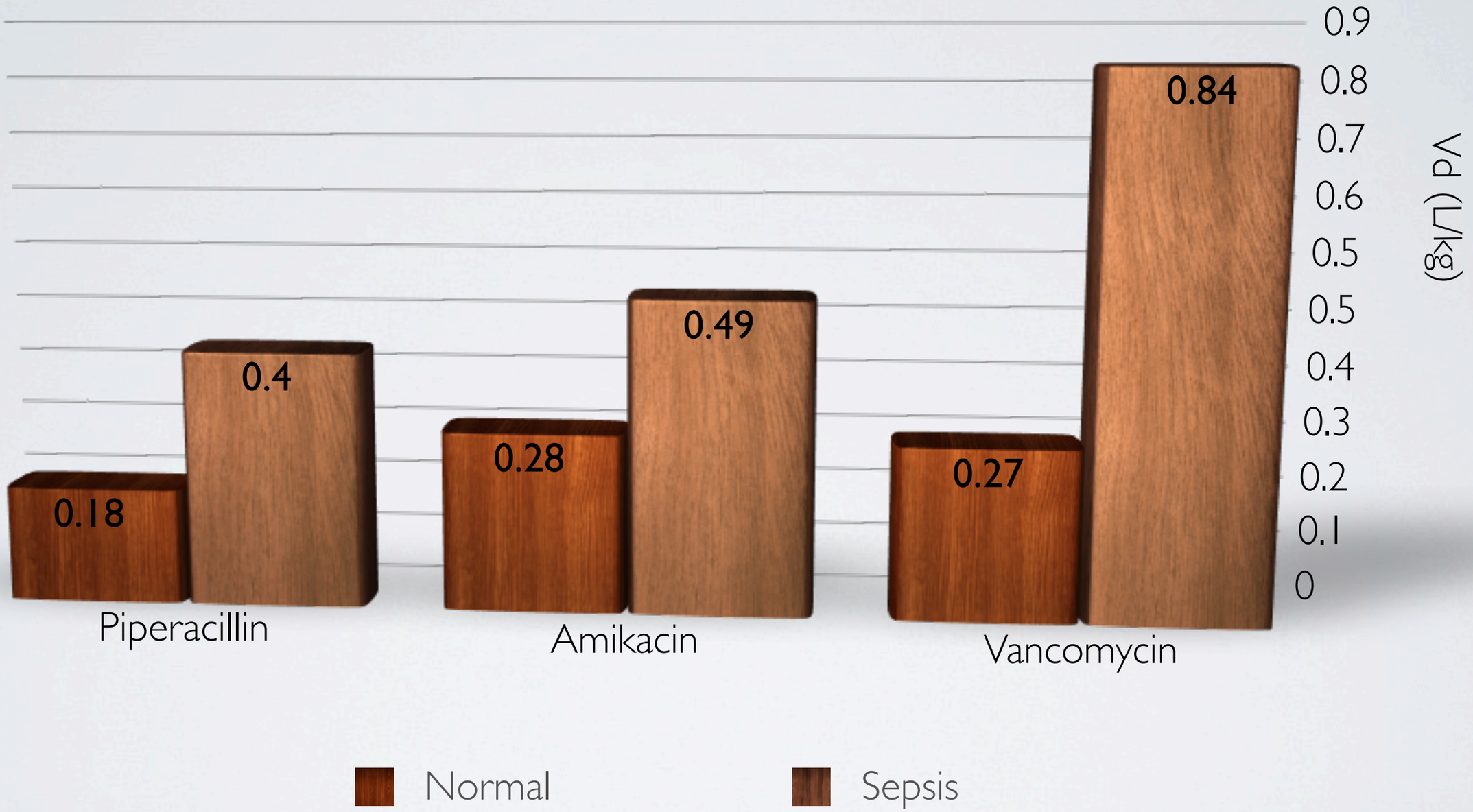
Why correct dosing matters

Pharmacokinetic/dynamic parameters of antibiotics



Increased Vd in Sepsis



Roberts, Int J Antimicrob Agents 2009
Galvez, Int J Antimicrob Agents 2011

LOW EXPOSURE TO ANTIBIOTICS ENABLES DEVELOPMENT OF RESISTANCE

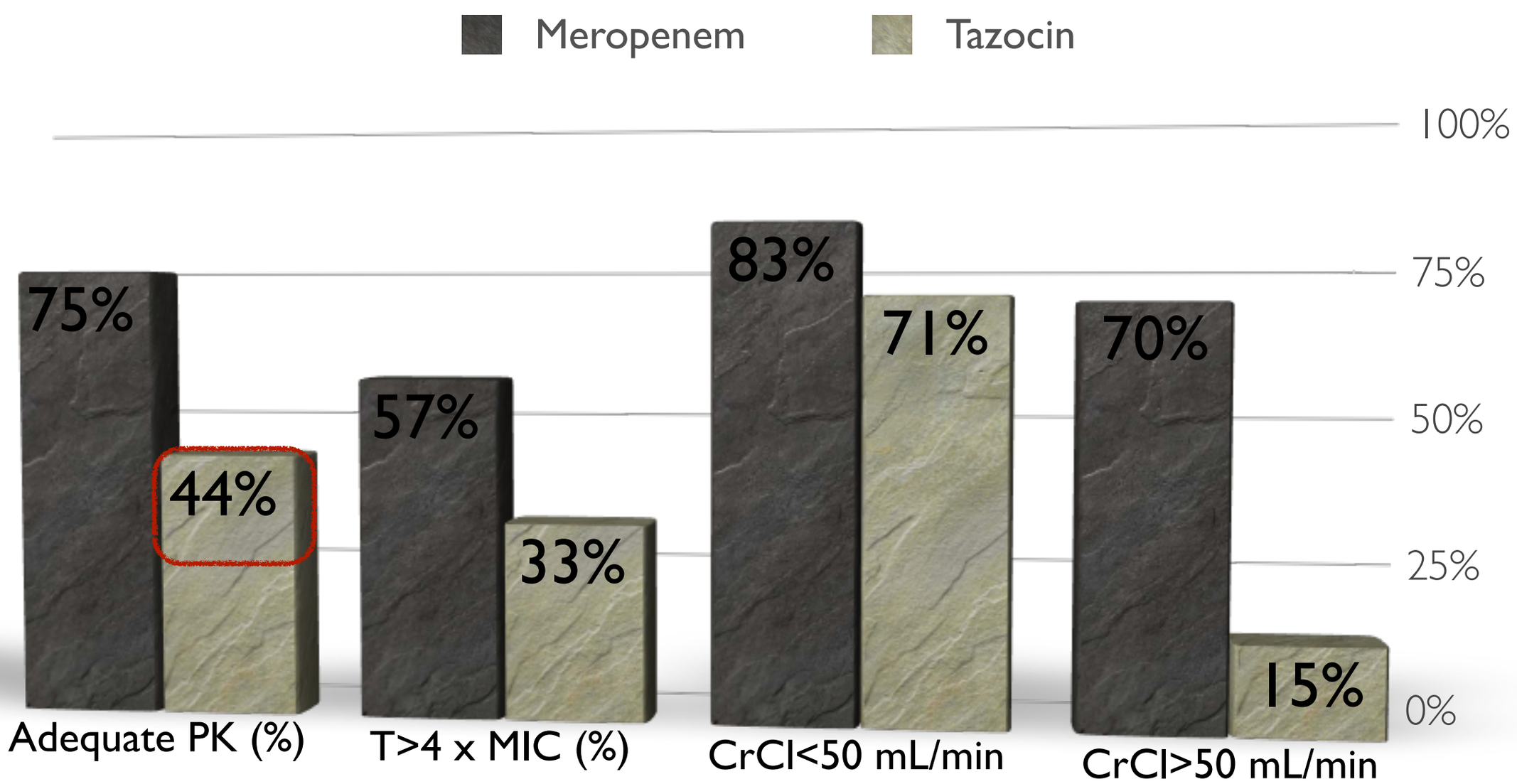
Antibiotic resistance—What's dosing got to do with it?

Jason A. Roberts, B Pharm (Hons); Peter Kruger, MBBS, FJFICM; David L. Paterson, MBBS, FRACP, PhD; Jeffrey Lipman, MBBCh, FJFICM, MD

Objective: This review seeks to identify original research articles that link antibiotic dosing and the development of antibiotic resistance for different antibiotic classes. Using this data, we tributing to the increasing rate of antibiotic resistance. Fluoroquinolones have widely been researched and publications on other antibiotic classes are emerging. Developing dosing regi-

Crit Care Med 2008; 36: 2433-2440

INSUFFICIENT ANTIBIOTIC CONCENTRATIONS IN THE EARLY PHASE OF SEPSIS



Adequate = % of time the serum drug concentration > 4 X MIC of Pseudomonas

Taccone et al Critical Care 2010

Principles of treatment

- Early admission to ITU
- Early antibiotics
- Appropriate antibiotics
- Antibiotic stewardship
- Optimise pharmacokinetics/dynamics
- **Adjunctive therapies**

Adjunctive therapies

- Consider that despite appropriate antibiotics, mortality has changed little

- Look for adjunctive therapies
  - Macrolides
  - Steroids
  - NIV

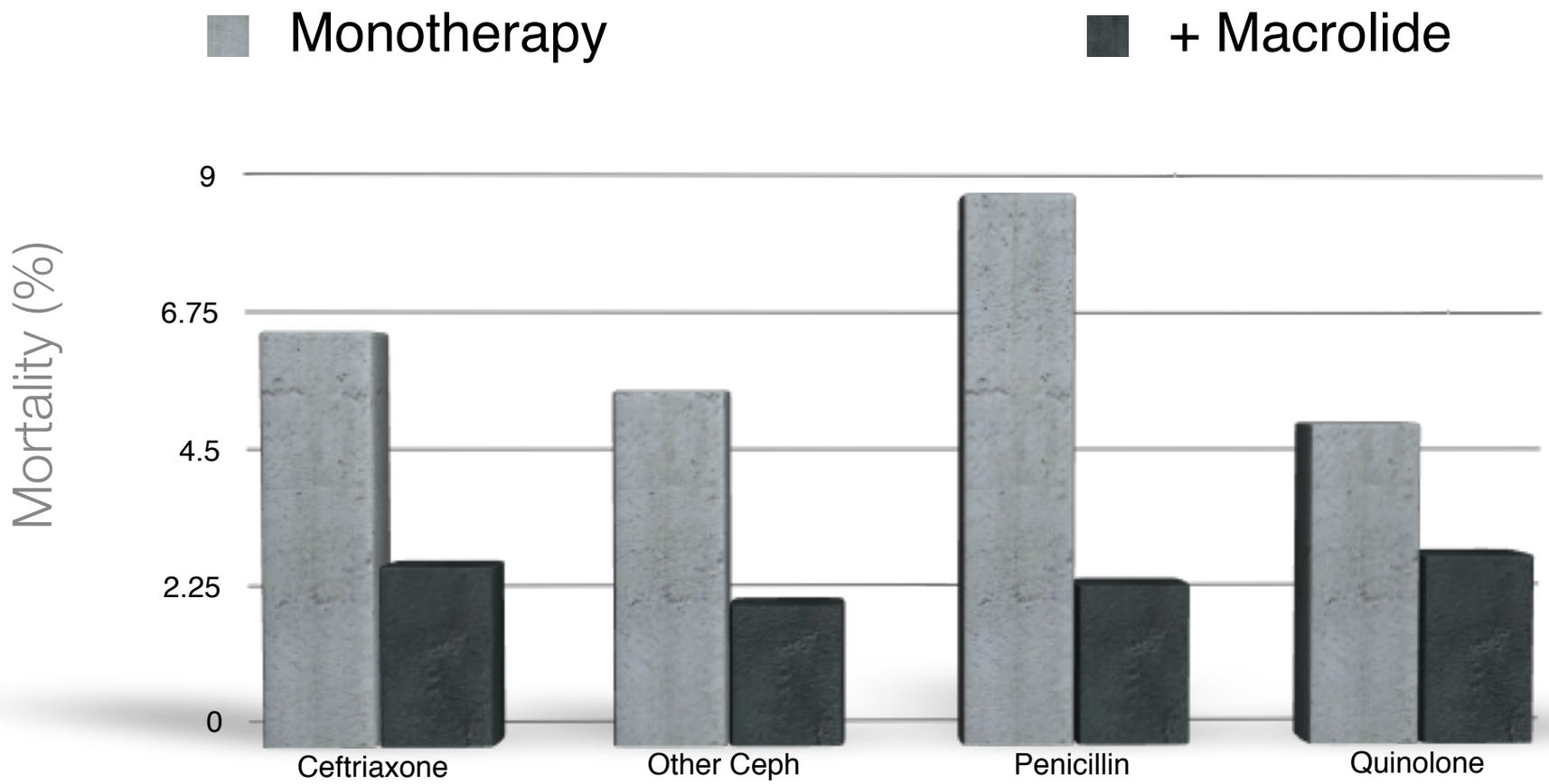
Macrolides

Why a macrolide?

At sub-mimimum inhibitory concentration

- Immunomodulation
  - inhibits pro-imflammatory cytokines
  - inhibits Quorum Sensing
- Inhibits pneumolysin
- Panbronchioloitis (Japan)
  - survival rates at 10 yrs with low dose macrolides 15%-->90%

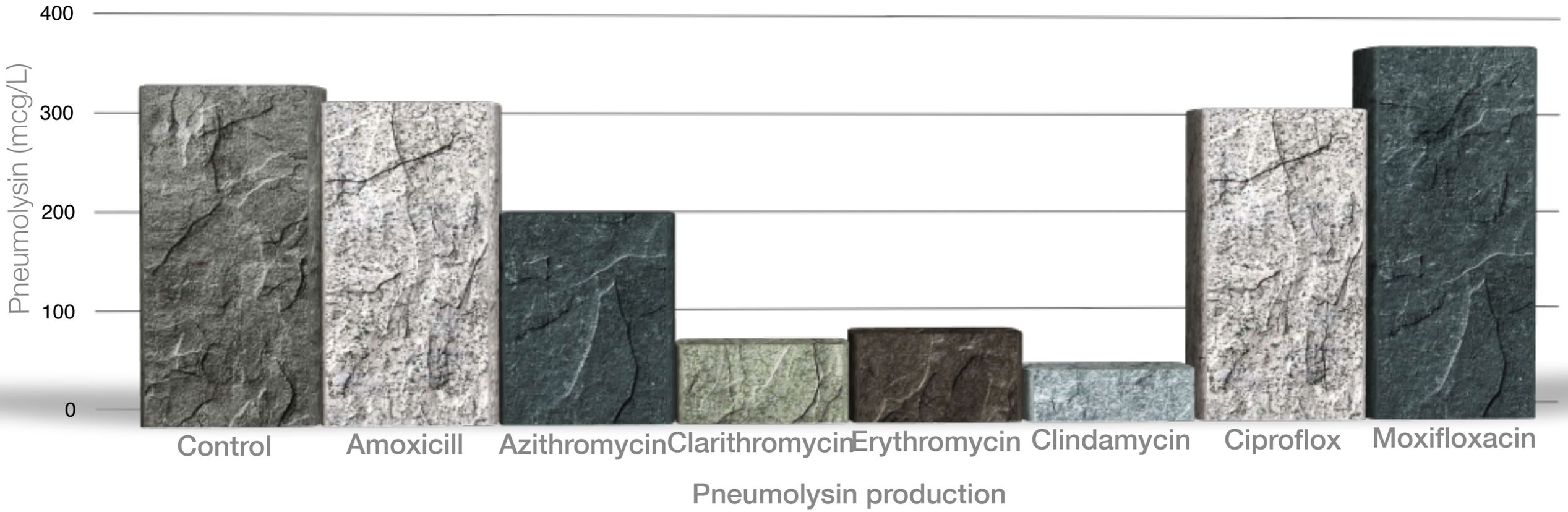
Macrolide combination therapy - does it work?



"...macrolides should be obligatory in all cases of severe community-acquired pneumonia. With odds ratios for **death ranging from two to six times greater in non-macrolide-treated patients**"

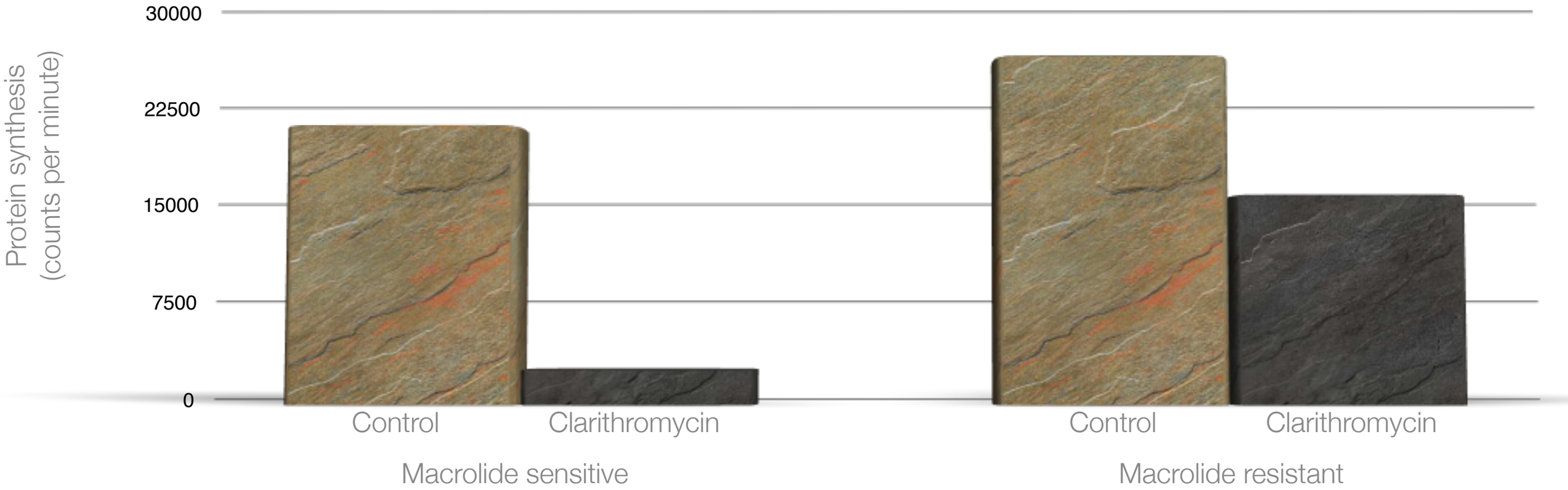
Brown, Chest 2003 Intensive Care Med (2010) 36:562–564

Pneumolysin inhibition



Journal of Antimicrobial Chemotherapy (2007) 60, 1155–1158

Pneumolysin inhibition-even in resistant organisms



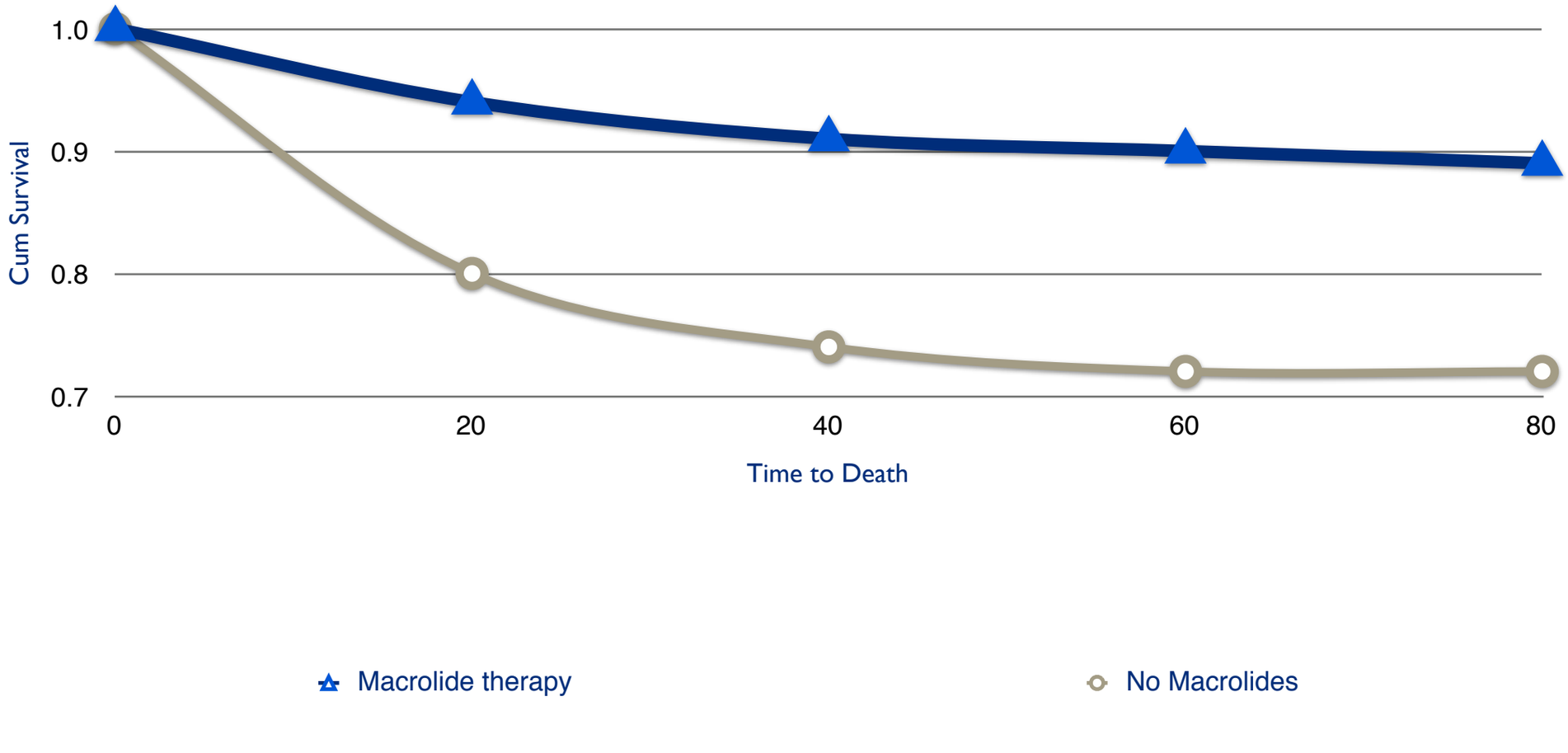
Journal of Antimicrobial Chemotherapy (2007) 60, 1155–1158

Macrolides-Quorum Sensing

- Quorum Sensing = bacterial cell to cell communication
- Major factor in:
    - virulence
    - biofilm formation
- Seen in:
    - Staph. aureus, Strep. pneumonia. E.coli and Pseudomonas
- In 30-50% of severe sepsis/septic shock

Critical Care 2010, 14:181.

Why a macrolide?



Restrepo et al, Eur Respir J, 2008

Steroids

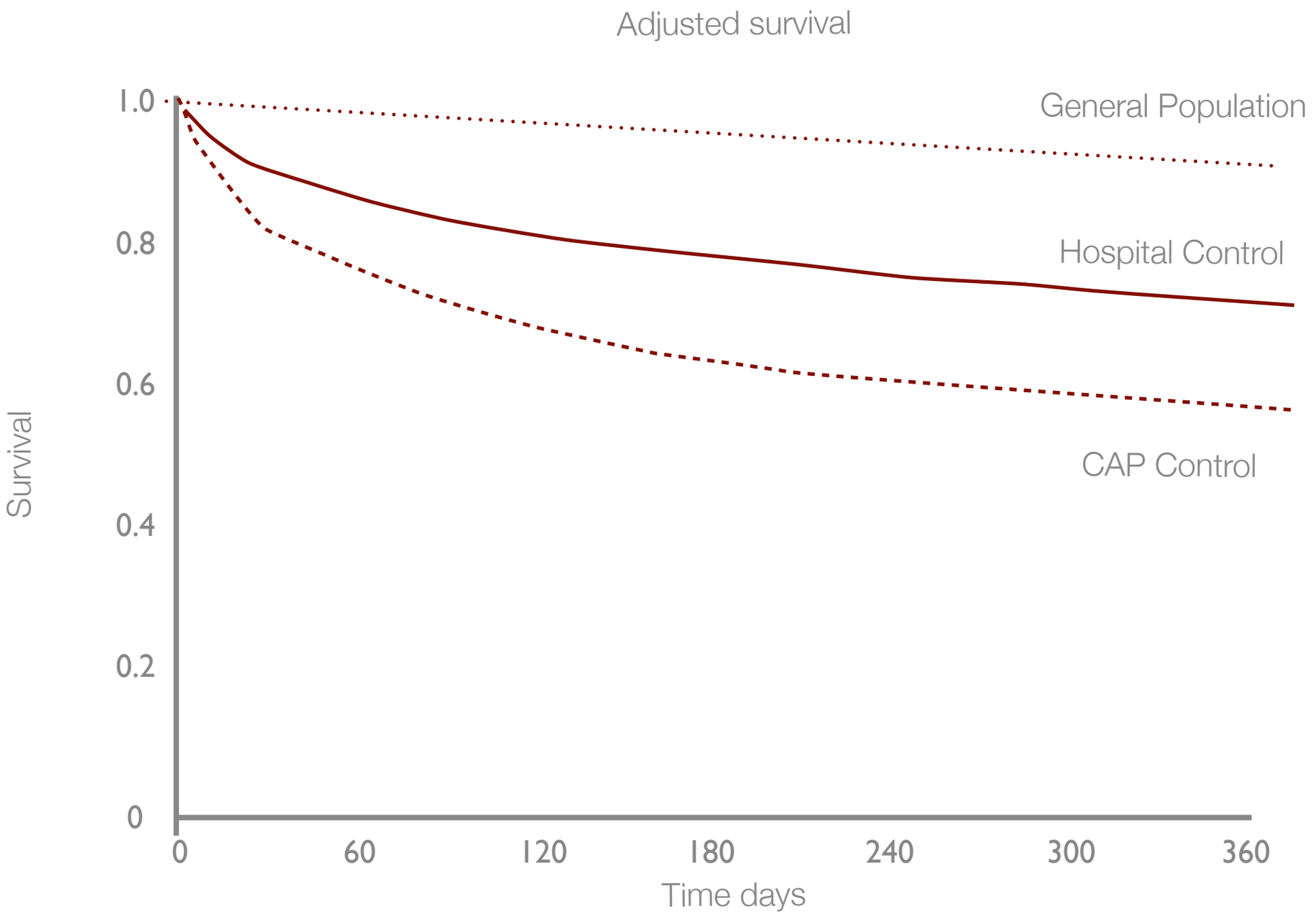
Steroids for CAP?

"Available studies do not support the recommendation of corticosteroids as a standard of care for patients with severe CAP"

But.....

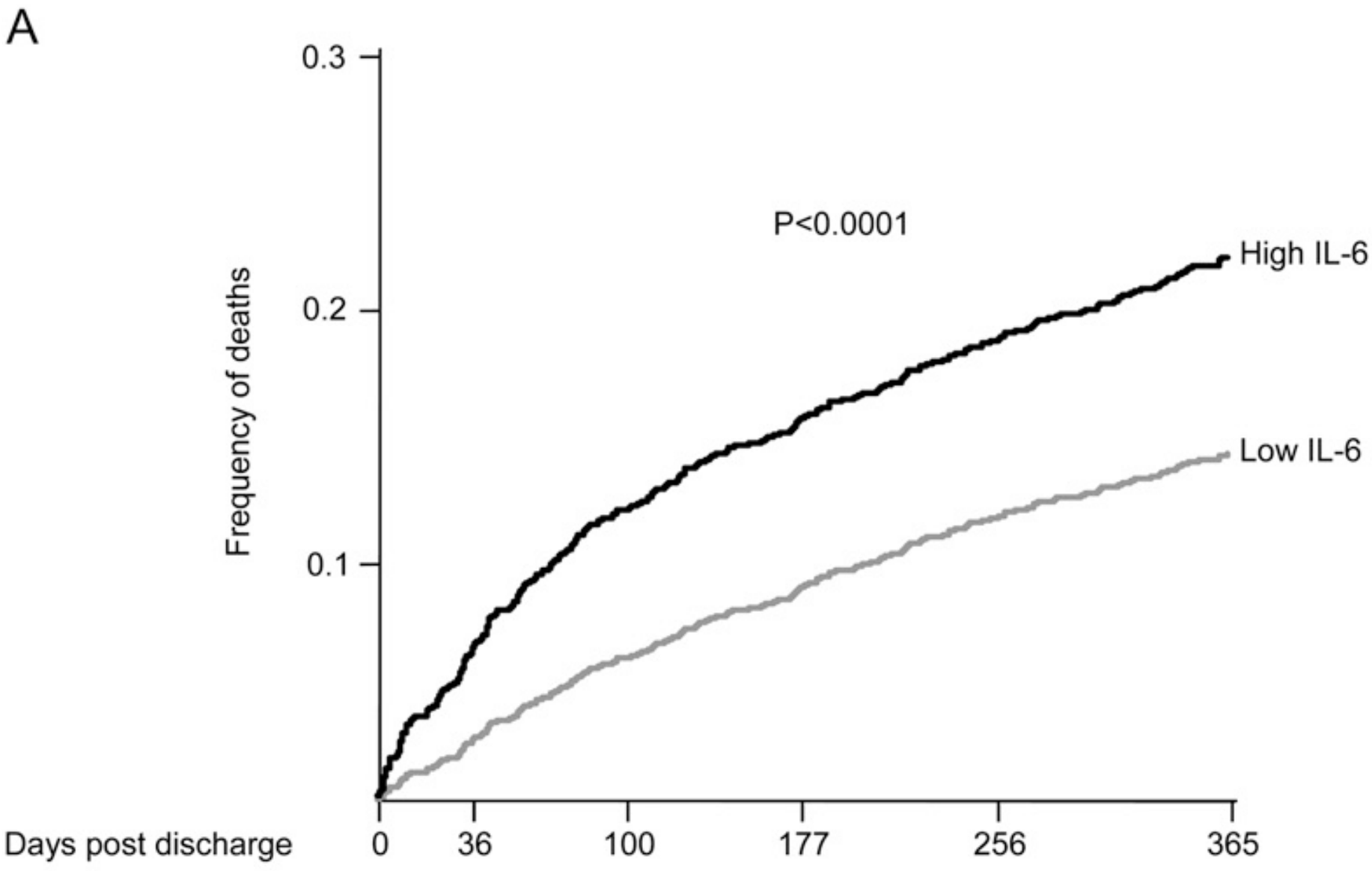
Critical Care 2008, 12:R76

...but long term outcomes?



Critical Care 2008, 12:R76

Persistent inflammation, defined as elevated circulating levels of IL-6 and IL-10 at hospital discharge after community-acquired pneumonia, is associated with all-cause and cause-specific mortality over one year, despite resolution of clinical signs of an acute infection.



Am J Respir Crit Care Med Vol 177. pp 1242–1247, 2008

Dexamethasone and length of hospital stay in patients with community-acquired pneumonia: a randomised, double-blind, placebo-controlled trial

"laboratory models ... characterised systemic inflammation as short-lasting. The fundamental idea that treatment should be continued until disease resolution was omitted from the design of glucocorticoid trials in sepsis.

increased concentrations of tumour necrosis factor (TNF) α and interleukin 6 **persisted for weeks after clinical resolution of pneumonia**, ...and predicted subsequent 90-day and 1-year mortality (mostly cardiovascular).....adds excess mortality for years.

So watch this space!

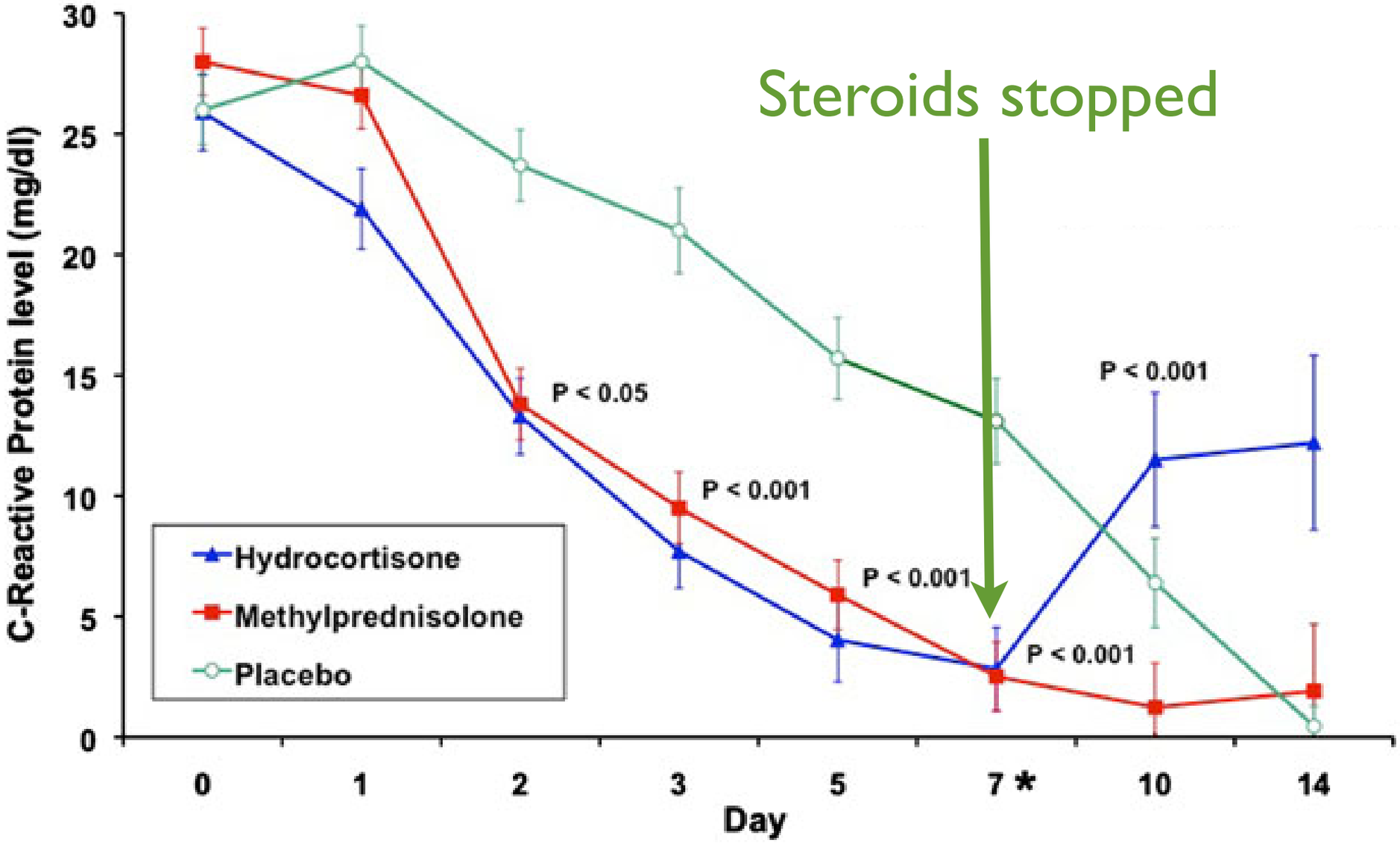
patients with community- acquired pneumonia discharged from hospital—irrespective of initial severity—still have **long-lasting, subclinical, low-grade systemic inflammation.**

longitudinal measurements have shown that persistent elevation of circulating concentrations of inflammatory cytokines over time is the **central pathogenetic process contributing to morbidity and mortality** in community-acquired pneumonia, sepsis, and acute respiratory distress syndrome

We strongly urge future trials to extend the duration of anti-inflammatory treatment to achieve biological resolution and prevent rebound inflammation

Lancet Vol 377 June11,2011

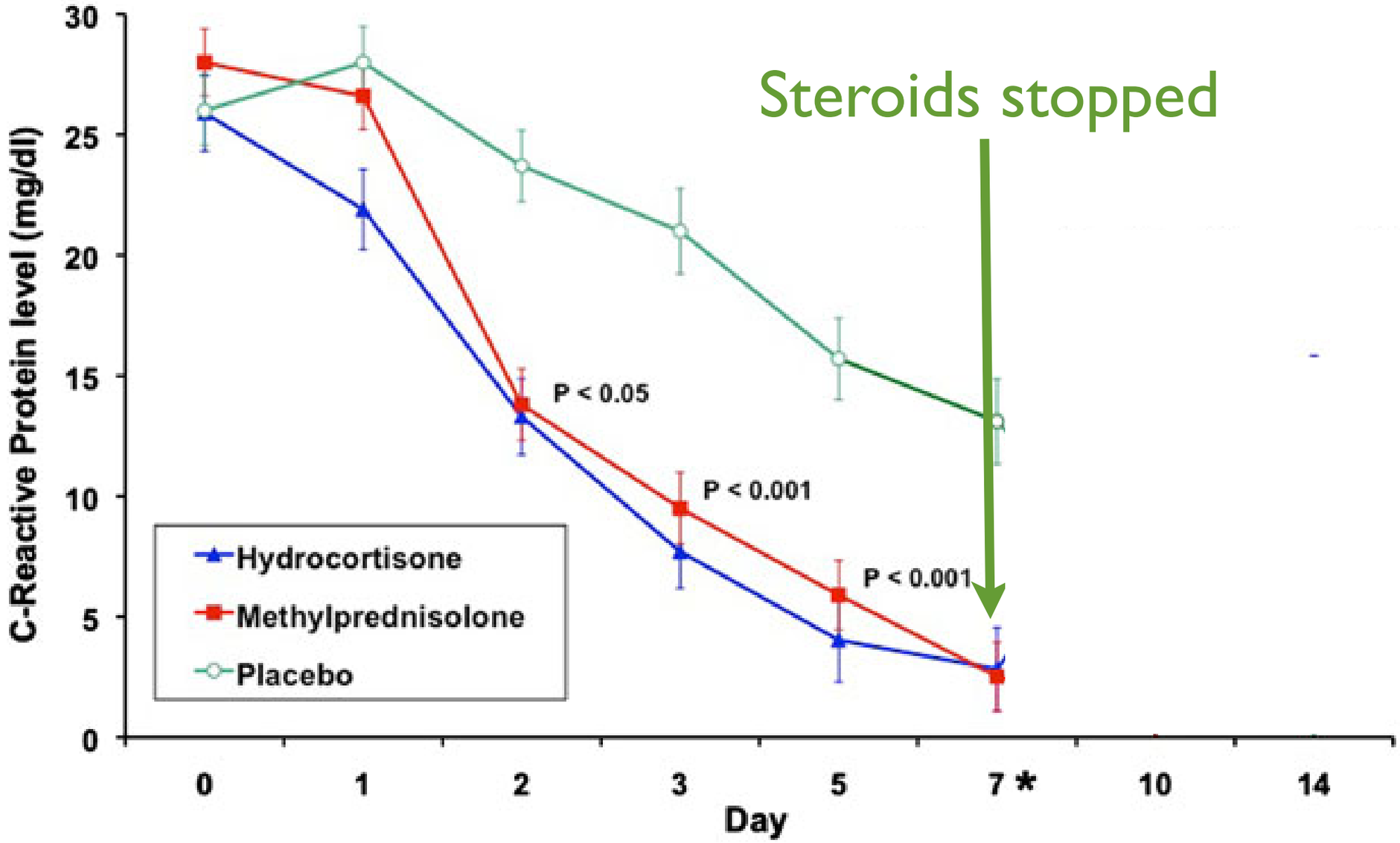
Steroid treatment in severe CAP: duration of treatment affects inflammation



Intensive Care Med (2011) 37:1553–1554

Lancet Vol 377 June11,2011

Steroid treatment in severe CAP: duration of treatment affects inflammation



Intensive Care Med (2011) 37:1553–1554

Lancet Vol 377 June11,2011

THE AMERICAN JOURNAL of MEDICINE®

Plasma Interleukin-10 Levels and Adverse Outcomes in Acute Coronary Syndrome

"plasma IL-10 levels were shown to be significantly and independently related to risk for cardiac-related death or nonfatal myocardial infarction over a 5-year follow-up period"

The American Journal of Medicine Volume 124, Issue 8 , Pages 724-730, August 2011

APC for CAP?

"There was no evidence suggesting a survival benefit by the administration of activated protein C"

Jury is still out...await outcome of recent trial.

Journal of Antimicrobial Chemotherapy (2008) 62, 661–668

APC for CAP?

- PROWESS trial - (APACHE >25 only) the absolute decrease in mortality was 6.1%
- Subsequent trial - survival benefit **not** observed
- In the first 3 trials, the rate of serious bleeding was approximately 1 patient in 20.
- In a postlicensure survey, the rate of **serious bleeding was more than 3-fold** higher than in the original trials.
- Fatal events associated with the agent increased significantly and the **risk of death was approximately 1 in 150**
- After initial enthusiasm for the use of activated protein C, evidence suggests that the **risks of this agent may potentially outweigh its benefits.**
- The treatment effect has thus been **inconsistent** and activated protein C is now being **reassessed in 2 new prospective trials.**

JAMA, July 13, 2011—Vol 306, No. 2

Non invasive ventilation

Non invasive ventilation

"In patients with severe CAP who received NIV, over 50% will improve but later require intubation. Therefore **very close observation is required and only in an HDU or ITU**"

BTS GUIDELINES FOR THE MANAGEMENT OF COMMUNITY ACQUIRED PNEUMONIA IN ADULTS

"... demonstrated no benefit between patients with and without NIV in terms of in-hospital mortality and length of hospital stay."

Journal of Antimicrobial Chemotherapy (2008) 62, 661–668

ICU mortality rate was 39% in COPD patients initially intubated and 50% in those who did not respond to noninvasive ventilation

Eur Respir J 2006, 27:1210- 1216.

Tissue Factor Inhibitor

Am J Respir Crit Care Med. 2011 Jun 1;183(11):1561-1568. Epub 2011 Feb 4.

Recombinant Tissue Factor Pathway Inhibitor in Severe Community-acquired Pneumonia: A Randomized Trial.

2,138 randomized patients studied.

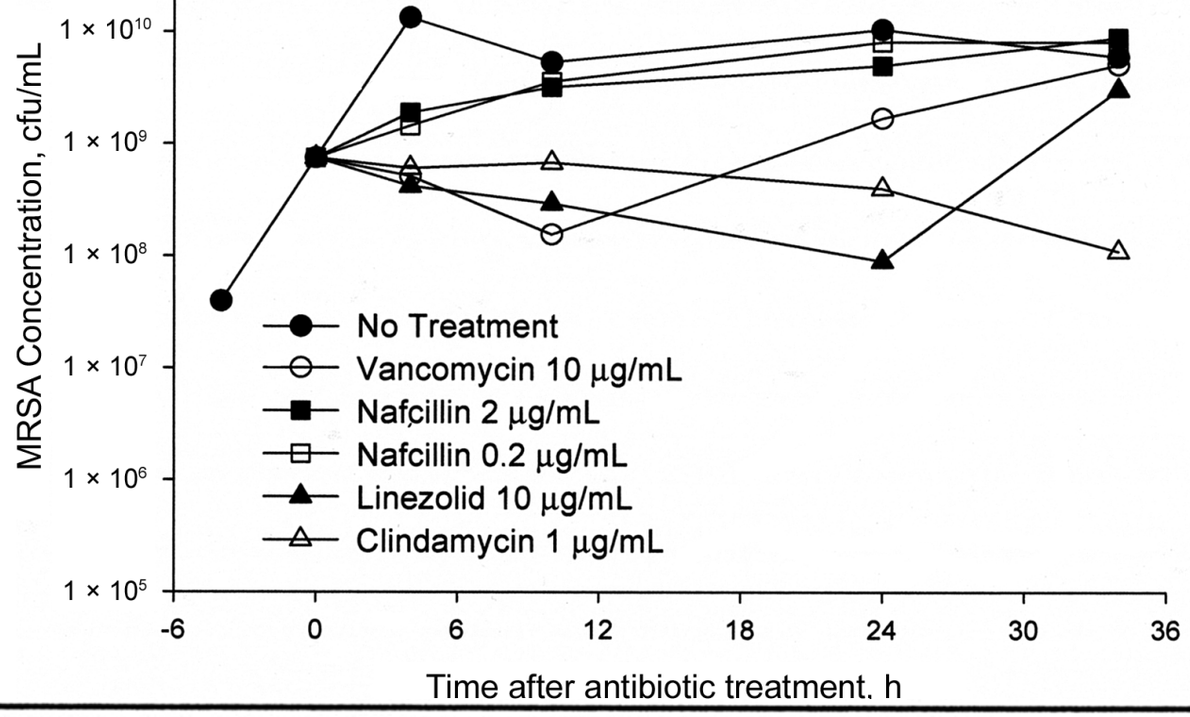
Tifacogin (recombinant human tissue factor pathway inhibitor) showed **no mortality benefit** in patients with sCAP despite evidence of biologic activity.

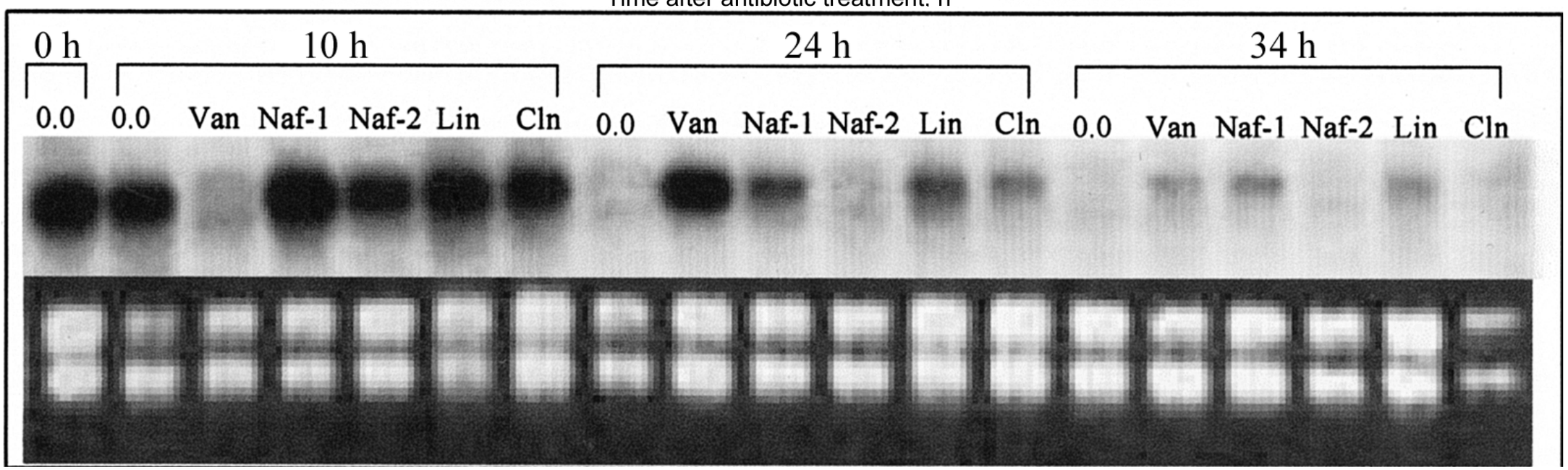
CA-MRSA pneumonia

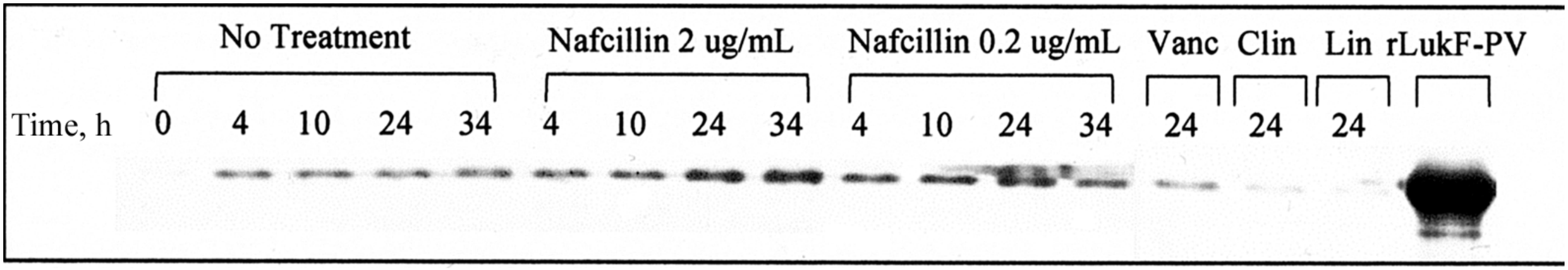
- Epidemiologically, genotypically and phenotypically **distinct** from hospital acquired MRSA
- May represent healthcare associated CAP
- Suspect if:
  - unresponsive CAP
  - **post 'flu'**
  - haemoptysis
  - cavitation
  - very ill
- Most contain the gene for Panton-Valentine leucocidin
  - a toxin associated with **necrotizing pneumonia** and **shock**
  - abscess formation and empyema
  - Therefore look out for cavitary lesions
- Suspect if patient v. toxic or drop in leucocytes
- Rx
  - Linezolid (or Vanc), Clindamycin, Rifampicin
  - IgG

CA-MRSA CAP?

Recently, increasing numbers of cases of methicillin-resistant Staphylococcus aureus (MRSA) pneumonia have been reported, particularly in association with influenza virus infection.49,50 Mortality rates appear somewhat higher than for non-MRSA severe CAP (as opposed to severe sepsis) at 26% – 33%, the clinical course is more rapid and the recovery period is prolonged, with some patients requiring months of critical care support despite single-organ failure.51 Community-acquired MRSA has greater susceptibility to antibiotics (with the exception of b-lactams), and is characterized by the presence of a type IV staphylococcal cassette chromosome mec element (SCCmecIV) and the expression of genes governing production of Panton–Valentine leucocidin (implicated as a causative agent in cavitation).52,53 Case reports have described a disease process characterized by high fever, severe necrotizing pneumonia with haemoptysis, leu- copenia, respiratory failure and shock. In patients presenting with particularly severe CAP, especially in the presence of hae- moptysis, shock and an influenza-like prodromal illness, MRSA should be considered. The recent Infectious Diseases Society of America/American Thoracic Society guidelines recommend either vancomycin or linezolid for CAP due to community-acquired MRSA. Linezolid may be preferred due to its superior lung penetration.


MRSA Concentration, cfu/mL
1 × 10^10
1 × 10^9
1 × 10^8
1 × 10^7
1 × 10^6
1 × 10^5
-6
0
6
12
18
24
30
36
Time after antibiotic treatment, h
No Treatment
Vancomycin 10 μg/mL
Nafcillin 2 μg/mL
Nafcillin 0.2 μg/mL
Linezolid 10 μg/mL
Clindamycin 1 μg/mL


0 h
10 h
24 h
34 h
0.0
0.0 Van Naf-1 Naf-2 Lin Cln
0.0 Van Naf-1 Naf-2 Lin Cln
0.0 Van Naf-1 Naf-2 Lin Cln


No Treatment
Nafcillin 2 ug/mL
Nafcillin 0.2 ug/mL
Vanc
Clin
Lin
rLukF-PV
Time, h
0 4 10 24 34
4 10 24 34
4 10 24 34
24
24
24

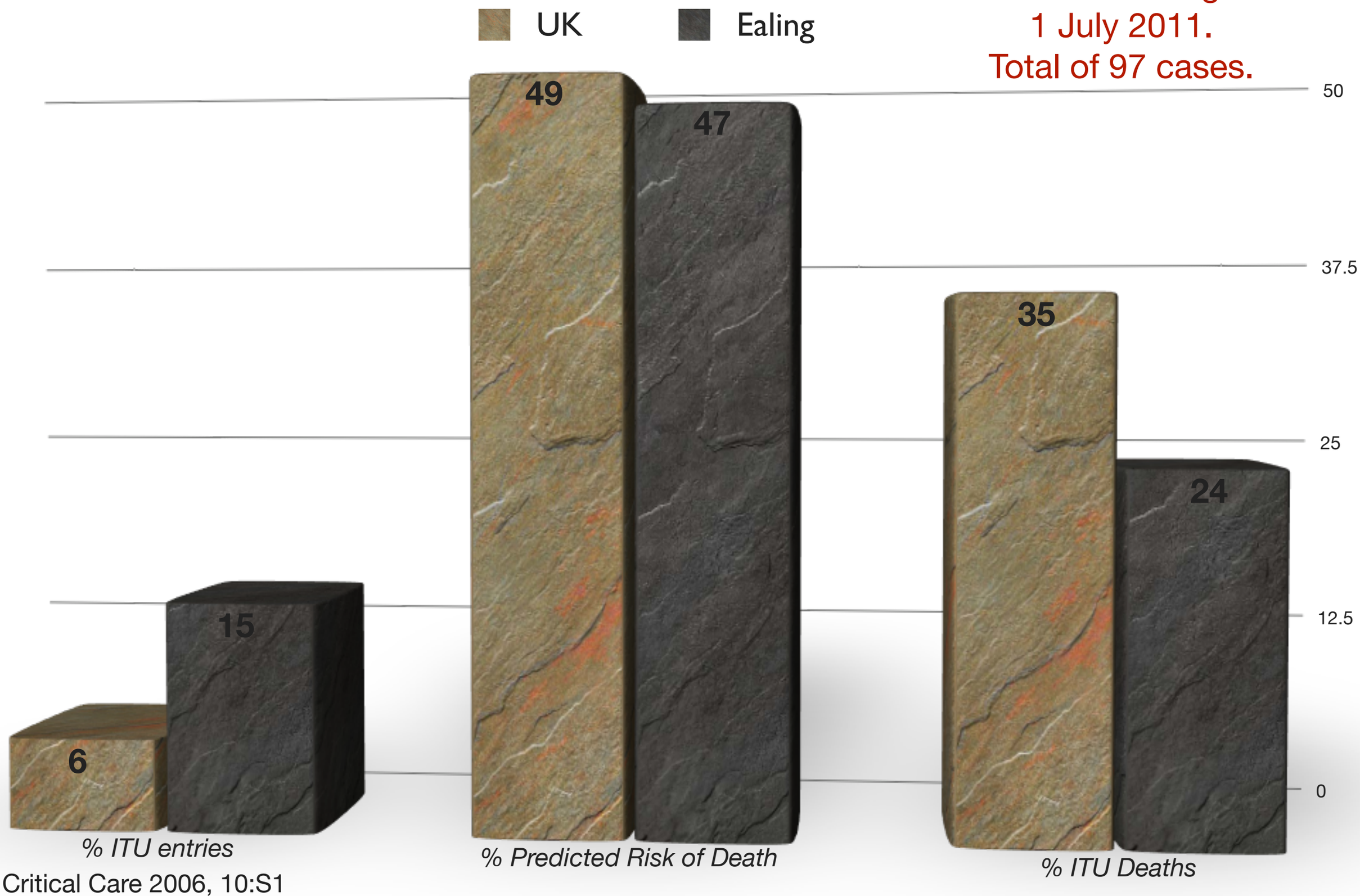
Failure to respond

- May take up to 72 hours for temperature to normalize
- Exclude:
  - Wrong antibiotic
  - Wrong diagnosis
  - Wrong dosage
  - Viral, fungal or opportunistic pathogen
  - Unusual pathogen
  - Superadded complication
  - Complicated pleural effusion/empyema
  - Other infection
    - Endocarditis
    - Purulent pericarditis
    - Septic arthritis
    - Meningitis
    - Etc

What about Ealing?

Severe Community Acquired Pneumonia
UK's ICNARC Case Mix Database vs Ealing ITU

Admissions from 3 August 2009 - 1 July 2011.
Total of 97 cases.



Critical Care 2006, 10:S1

Some future audits ?

- CURB-65 score done on entry
- Were the appropriate cultures/diagnostic tests performed prior to antibiotics (ex. urinary antigens)
- Delay before ITU entry when admission was appropriate for ITU
- Delay until appropriate antibiotic therapy
- Appropriateness of antibiotics
- Were patients stratified (ex. COPD, Hemodialysis, etc)

Clinical case

- 67 yr old male
- Admitted from 6S after 2 days worsening dyspnea despite NIV
  - RR 38; P/F ratio 28; O2 Sat 89%
  - Temp 39; CVS W.N.L.; CRP and PCT high; Creat 129
  - CXR LLL infiltrates
- PMH
  - COPD
  - DM II
  - Steroids - inhaled recently oral
  - Recently started on neuroleptics
- Hospitalized 6/52 ago for infective exacerbation of COPD
  - Rx Augmentin

What are your main considerations?

Recap

- CAP still a “Killer”
- Severity scoring is the main starting point
- Get cultures off early
    - Blood
    - Sputum
    - Urinary antigens
- If ETT, get good aspirate to micro
- Antibiotics on time and on target
- Get dosing right...for ITU patient
- Know your local microbiologic ecology

???

Download :

http://www.jvsmedicscorner.com

Marik - CAP

Marik - CAP

Health care associated pneumonia (HCAP)

- Distinguish patients from an acute or chronic health care facility from pneumonia developed in community

- HCAP includes:
  - Hospital acquired pneumonia
  - Ventilator acquired pneumonia
- Distinction important:
  - High risk of:
    - Multi drug resistant (MDR) micro-organsims and MRSA
      - Pseudomonas
      - ESBL producing -Klebsiella
      - Acinetobacter
      - Enterobacter
      - Enterococcus
    - Strongly consider **de-escalation therapy**
      - Ex. Meropenem or Tazocin
        PLUS
      - Aminoglycoside or levofloxacin
        PLUS
      - Vancomycin or Linezolid

Marik - CAP

Complicated pleural effusion/empyema

"Never let the sun set on a pleural effusion complicating pneumonia..."

- Distinguish between a benign para-pneumonic effusion and an early empyema

- Drain if:
  - pH <7.2 (most sensitive indicator)
  - Glucose < 2.22 mmol/L
  - WBCs > 10,000/mL

Marik - CAP

- 6th leading cause of death in US
- About 20-35% of hospitalised CAP need ITU
  - 1 in 3 will die!
- 1 in 5 will be in septic shock
  - 60 will die
- Risk of death
  - Severity at presentation
  - Co-morbidities

Marik - CAP

Co-morbidities

- COPD
- Asthma
- Diabetes
- Renal insufficiency
- CHF
- CAD
- Malignancy
- Alcoholism
- >70 yrs old
- Chronic liver disease

Co-morbidities increase risk of death
and
alter the aetiological organisms

Marik - CAP

Aetiology

- Depends on **severity** and presence of **co-morbidities**
- In **severe** CAP - 60% have isolated a pathogen
  - Strep. pneumonia (15-46%)
  - Legionella (0-23%)
  - Staph aureus (0-22%)
  - H. Influenza (0-14%)
  - Gram negatives (4-25%)
  - Polymicrobial (17%)
  - “Atypicals” (2-33%)
    - Chlamydia pneumoniae
    - Mycoplasma pneumoniae
    - Legionella

Marik - CAP

Associated with co-morbidities (some examples)

- Strep. pneumonia
  - COPD
  - Seizures
  - CHF
- Gram negatives
  - Residence in long term facility
  - Cardiopulmonary disease
  - Recent antibiotics
  - Multiple medical co-morbidities
- Pseudomonas aeruginosa
  - Broad spectrum antibiotics for >7 days in past month
  - Structural lung disease
  - Steroids
  - Malnutrition
  - Undiagnosed HIV
  - Neutropenia
- Legionella
  - AIDS
  - Haematological malignancy
  - End stage renal disease

Marik - CAP

Diagnostic tests for severe CAP

- Blood cultures
- Urinary antigens for Legionella and Strep. pneumonia
- Expectorated sputum
- Intubated require fresh endotracheal aspirate
- Screening for HIV
- Nasopharyngeal swab for influenza during outbreak (PCR)

Marik - CAP

Non-infectious diseases masquerading as CAP

- Pulmonary embolism
- Pulmonary malignancy
- Tuberculosis
- Radiation pneumonitis
- Drug induced pneumonitis (amiodarone, etc)
- Eosinophilic pneumonia

Initial antibiotic treatment

Marik - CAP

- 1st Choice
  - Beta lactam (ex. taz, augmentin, etc)
  - *PLUS*
  - Clarithromycin or respiratory fluoroquinolone(levofloxacin)
- **Penicillin allergy**
  - Respiratory fluoroquinolone
  - **PLUS**
  - Aztreonam
- **Risk of Pseudomonas infection**
  - Anti-pneumococcal, anti-pseudomonal beta-lactam
    - Tazocillin
    - Meropenem
      - **PLUS**
      - Levofloxacin OR Tazocin
        - *OR*
      - Aminoglycoside and Macrolide
        - *OR*
      - Aminoglycoside and levofloxacin (anti-pneumoccoal fluoroquinolone)
  - **Penicillin allergy**
    - Aztreonam
      - **PLUS**
      - Aminoglycoside and levofloxacin (anti-pneumoccoal fluoroquinolone)
- **Risk of Community acquired MRSA**
  - Add Vancomycin or linezolid

Initial Antibiotic Selection- inpatient

Non-ICU

β-lactam (IV or IM) + macrolide (IV or Oral)

or

β-lactam (IV or IM) + doxycycline (IV or Oral)

or

Quinolone monotherapy (IV or Oral)

ICU

β-lactam (IV) + macrolide (IV)

or

β-lactam (IV) + quinolone (IV)

If documented β-lactam allergy:
Quinolone (IV) + Clindamycin (IV)

or

Quinolone (IV) + Vancomycin (IV)

Pseudomonal Risk*

*In addition to the antibiotics listed under ICU, if the patient had a secondary ICD-9 code of bronchiectasis, or a positive response to the bronchiectasis question, or malnutrition [as reflected by a serum albumin below 3], these antibiotics would also be considered acceptable:

Antipseudomonal β-lactam (IV) + Antipseudomonal quinolone (IV)

Or

Antipseudomonal β-lactam (IV) + Aminoglycoside (IV) + either a [Macrolide (IV) or Antipneumococcal quinolone (IV)]

If documented β-lactam allergy:Aztreonam (IV) + Aminoglycoside (IV) + Antipneumococcal quinolone (IV)

Adapted from IDSA: ***Update of Practice Guidelines for the Management of Community Acquired Pneumonia in Adults. CID 2003;37:1405-1432***

Initial Antibiotic Selection

30-day mortality - Community-dwelling Patients (14,150 patients)

Initial Antibiotics	30-day mortality N/D (%)	Adjusted Odds Ratio† aOR (95% CI)	P Value
3rd generation cephalosporin*	277/3072 (9.0)	Reference	Ref
Macrolide monotherapy‡	19/431 (4.4)	0.63 (.39-1.04)	0.069
2nd generation cephalosporin	73/844 (8.6)	1.13 (.85-1.51)	0.406
Quinolone monotherapy‡	121/1716 (7.1)	**0.78 (.62-.98)**	**0.037**
At least 1 aminoglycoside	80/445 (18.0)	**1.51 (1.11-2.04)**	**0.008**
Cephalosporin + macrolide‡	231/3618 (6.4)	**0.74 (.61-.89)**	**0.002**
Cephalosporin + quinolone‡	63/723 (8.7)	0.90 (.67-1.22)	0.506
ß-lactam/ß-lactamase inhibitor + macrolide‡	17/158 (10.8)	1.12 (.65-1.94)	0.689

***monotherapy with cefotaxime or ceftriaxone.**

†Results adjusted for age, gender, neoplastic disease, cardiovascular disease, altered mental status, respiratory rate ≥ 30/min, systolic BP < 90 mmHg, temperature < 35C or ≥ 40C, pulse ≥ 125/min, blood pH < 7.35, BUN > 10.7 mmol/L, sodium < 130 mEq/L, hematocrit < 30%, pO2 < 60 mmHg, pleural effusion, admission to ICU in the first 24 hours after arrival, antibiotics administered within the first 4 hours after arrival, and US census region.

‡These antibiotic combinations include patients receiving either oral or parenteral macrolides or quinolones.

Bratzler DW. Houck PM, et al. [abstract] American Thoracic Society, 2003.

Organisms Causing CAP in Hospitalized Patients Requiring ICU Admission

- Overall up to 10% of admitted patients with CAP are brought to the ICU
  - 30% caused by *Streptococcus pneumoniae*
  - 50-60% have an unknown etiology
  - Other reported organisms
    - *Legionella*
    - *H.influenza*
    - *S.aureus*
    - *P.aeruginosa* (underlying bronchiectasis)
    - Enterobacteriacae (underlying bronchiectasis)

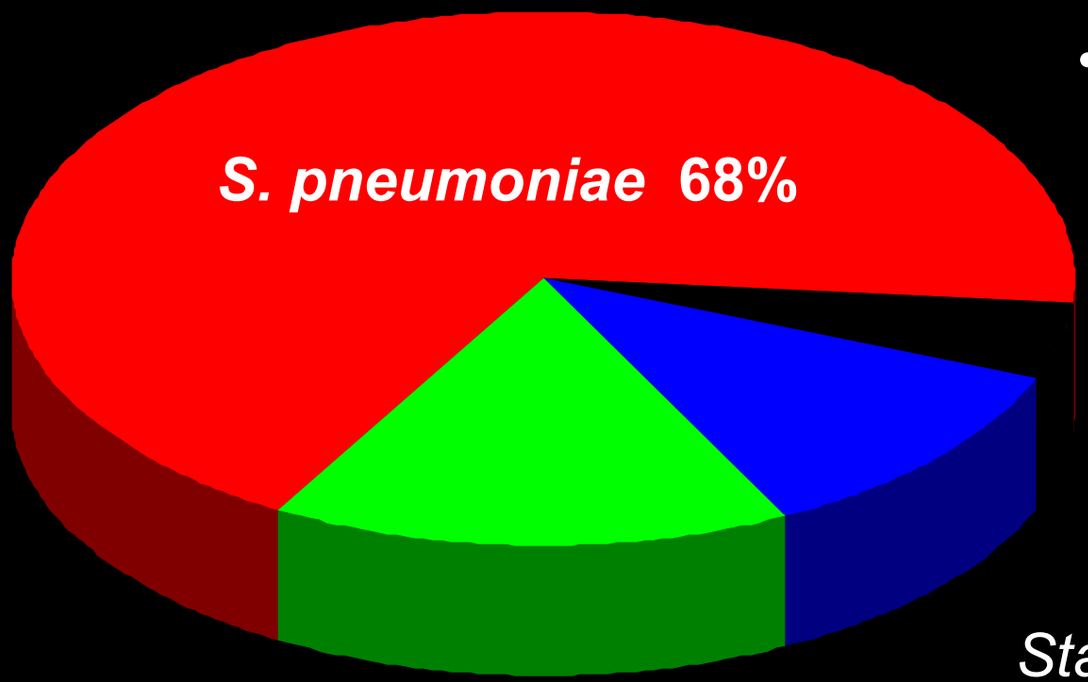
American Thoracic Society 2001. ***Am J Respir Crit Care Med*** Vol.163.1730-1754.

See his carefully

Summary: Current Practice Guidelines

- Antibiotic timing and antibiotic choice represent practice guidelines based on best available current evidence
  - These are retrospective, observational trials and expert (committee) opinion.
    - In some studies the measure of effect, although, statistically significant may be small
  - These guidelines are not based on extensive prospective, randomized controlled trials
    - Antibiotic timing

Pathogens Retrieved by Blood Culture



- Prospective study
- 19 Canadian hospitals
- 760 patients
  - 43 with (+) blood cultures

Campbell SG et al. Chest 2003;123:1142-1150.

Conclusion

- Sixth leading cause of death overall and the number one cause of death from infectious disease in the USA
- Even with modern medical care the case mortality is 12%
- Typical and a typical pathogens must be considered in the choice of antibiotic therapy.
  - PSI should be used for risk stratification
  - Initial antibiotic choice should take into account history, comorbidities and risk stratification.
- Diagnostic tests include sputum gram stain and culture, blood cultures, Legionella urinary antigen test and pneumococcal urinary antigen.
- For patients on parental antibiotics, a switch to oral therapy should be made as soon as possible.