ΛΙΑΠΙΚΟΥ ΑΔΑΜΑΝΤΙΑ
ΕΠΙΜ.Α,ΠΝΕΥΜΟΝΟΛΟΓΙΑΣ
ΝΝΘΑ ΣΩΤΗΡΙΑ ο

ΟΞΥ ΕΜΠΥΡΕΤΟ
ΚΑΙ
ΠΥΚΝΩΣΗ/ΠΥΚΝΩΣΕΙΣ
ΣΕ ΑΚΤΙΝΟΓΡΑΦΙΑ ΘΩΡΑΚΟΣ

7ο ΕΚΠΑΙΔΕΥΤΙΚΟ ΣΥΜΠΟΣΙΟ
Α' ΚΛΙΝΙΚΗΣ ΕΝΤΑΤΙΚΗΣ ΘΕΡΑΠΕΙΑΣ
ΙΑΤΡΙΚΗΣ ΣΧΟΛΗΣ ΕΚΠΑ

ΠΕΡΙΣΤΑΤΙΚΟ 1

Γυναίκα 44 ετών, καπνίστρια, νοσηλεύτρια σε οίκο ευγηρίας, παρουσιάζεται στα επείγοντα, τον Ιανουάριο, με συμπτώματα:

i.Βήχα από 4 ημέρου που αυξήθηκε τις τελευταίες 2 μέρες και έγινε παραγωγικός.

ii.Πυρετό ως 38^{O} C ,αίσθημα κακουχίας, από 2ημέρου

Είναι HIV-αρνητική

ΚΛΙΝΙΚΗ ΕΞΕΤΑΣΗ

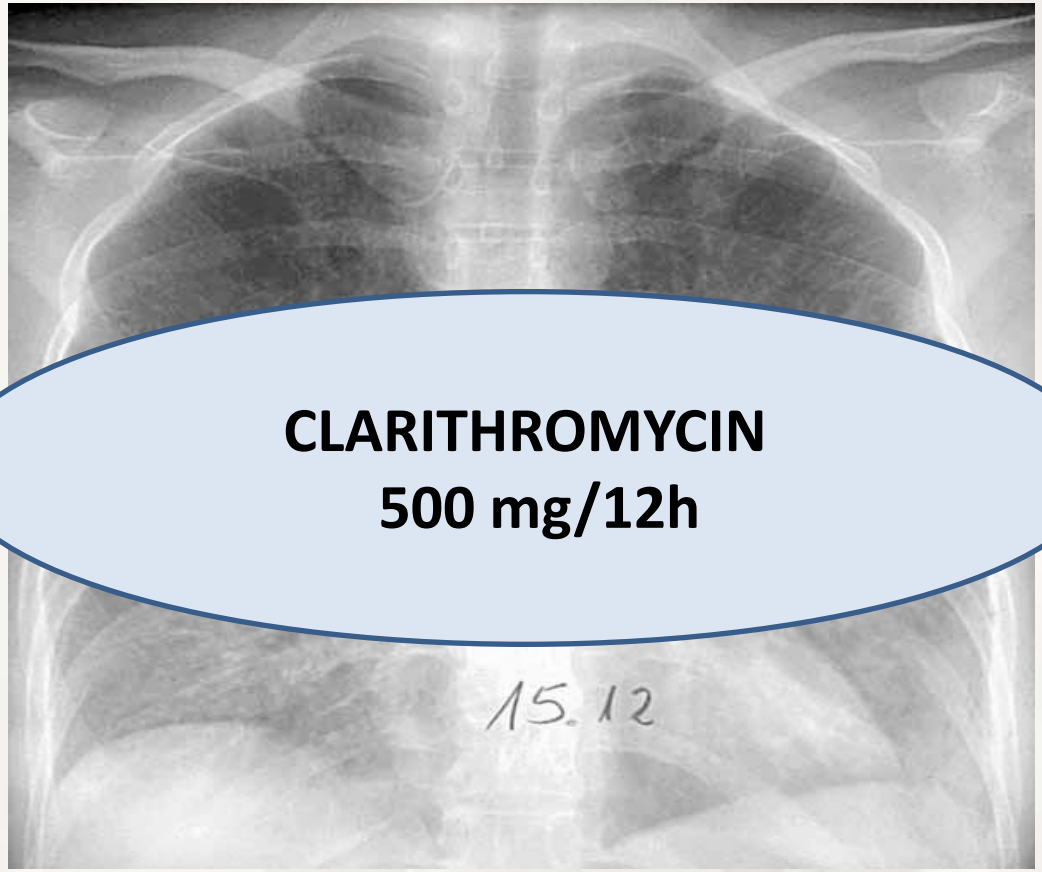
ΑΚΡΟΑΣΗ ΘΩΡΑΚΟΣ

Ήπιοι ΜΡ αμφω –

Ζωτικά σημεία: ΑΠ=125/80mmHg , HR=84/min,

RR-20/min

SO2: 98% σε 21% O2



CLARITHROMYCIN
500 mg/12h

ΠΕΡΙΣΤΑΤΙΚΟ 1
3η μέρα-Επιδείνωση

Φυσική εξέταση: Δύσπνοια, Ταχύπνοια

Θερμοκρασία: 39.0ο C,

HR :110/min, & RR: 30 /min

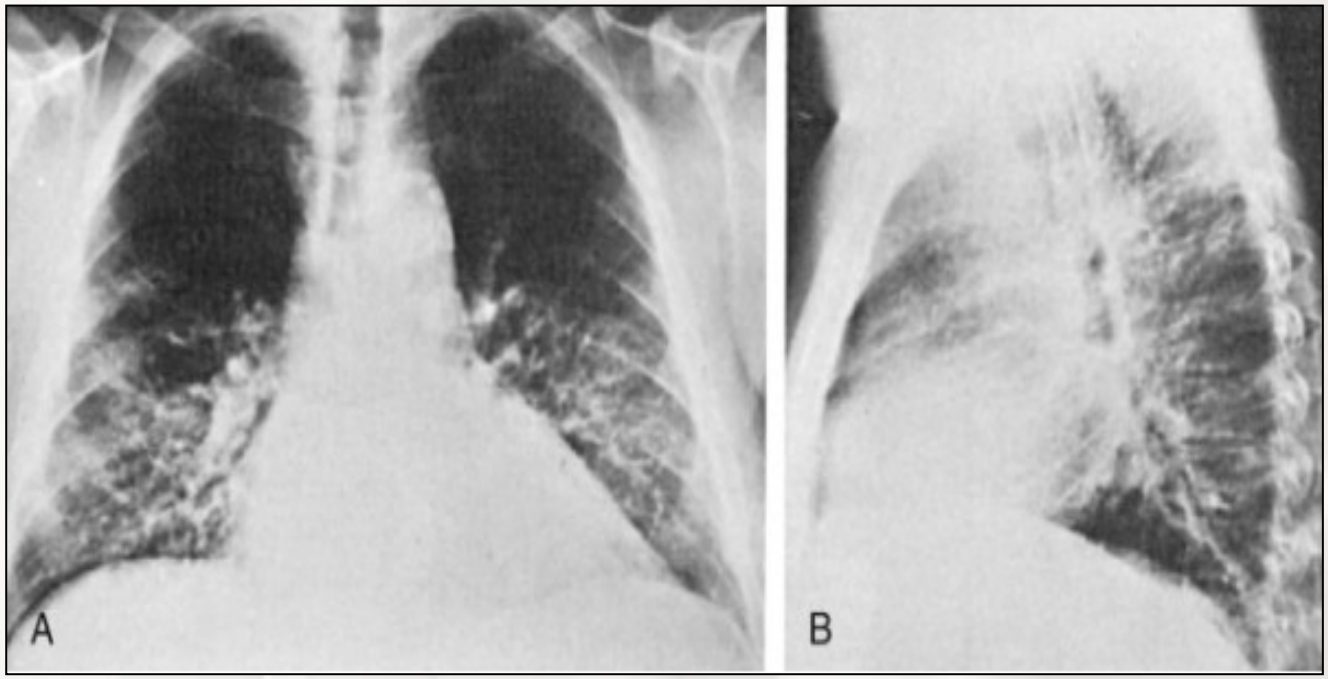
ΑΠ=125/60mmHg

Ακρόαση: Διάχυτοι ΜΜΡ στις βάσεις των πνευμόνων

ΔΙΑΓΝΩΣΗ

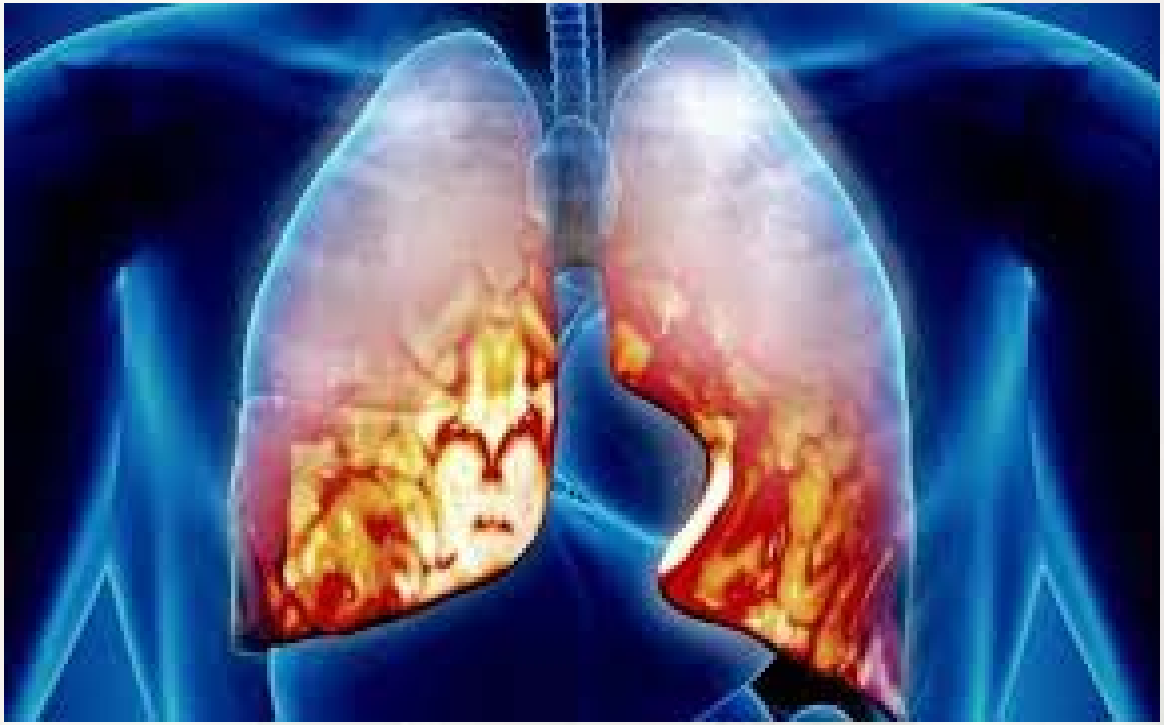
ΕΡΓΑΣΤΗΡΙΟ

- Hct=38
- WBC=5200
- PLT=200000
- CRP=23 ⬆
- BUN=28



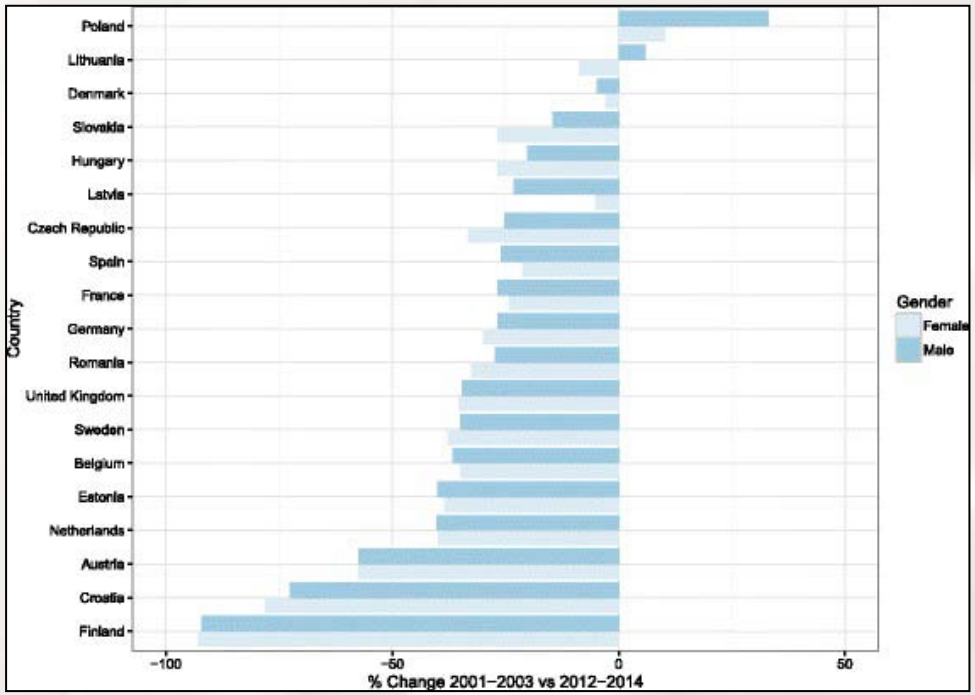
SO2 89%, PO2=60/PCO2=35,/PH=7,46
HCO3=31,2

ΠΝΕΥΜΟΝΙΑ ΤΗΣ ΚΟΙΝΟΤΗΤΑΣ



Η ΠΝΕΥΜΟΝΙΑ ΕΊΝΑΙ ΚΟΙΝΗ ΚΑΙ ΣΟΒΑΡΗ

- **3,370,000 ετήσιες περιπτώσεις** στην Ευρώπη το 2018
- **1 εκατομμύριο νοσηλείες** στην Ευρώπη
- **~20% των ασθενών με πνευμονία νοσηλεύονται**
- **4th αιτία θανάτου παγκοσμίως με 2.4 εκατομμύρια θανάτους αποδιδόμενους σε** LRTI το 2016



Marshall DC et al. *Respir Res.* 2018;19:81.

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Community-Acquired Pneumonia Requiring Hospitalization among U.S. Adults

Table 2. Estimated Annual Incidence Rates of Hospitalization for Community-Acquired Pneumonia, According to Year of Study, Study Site, Age Group, and Pathogen Detected.*

Variable	Incidence of Pneumonia-Related Hospitalization (95% CI) *no. of cases per 10,000 adults per yr*
Year of study†	
Yr 1 and 2	24.8 (23.5–26.1)
Yr 1	29.2 (27.2–31.2)
Yr 2	20.6 (19.1–22.3)
Study site	
Chicago	26.7 (25.0–28.4)
Nashville	21.9 (20.0–23.8)
Age group	
18–49 yr	6.7 (6.1–7.3)
50–64 yr	26.3 (24.1–28.7)
65–79 yr	63.0 (56.4–70.3)
≥80 yr	164.3 (141.9–189.3)

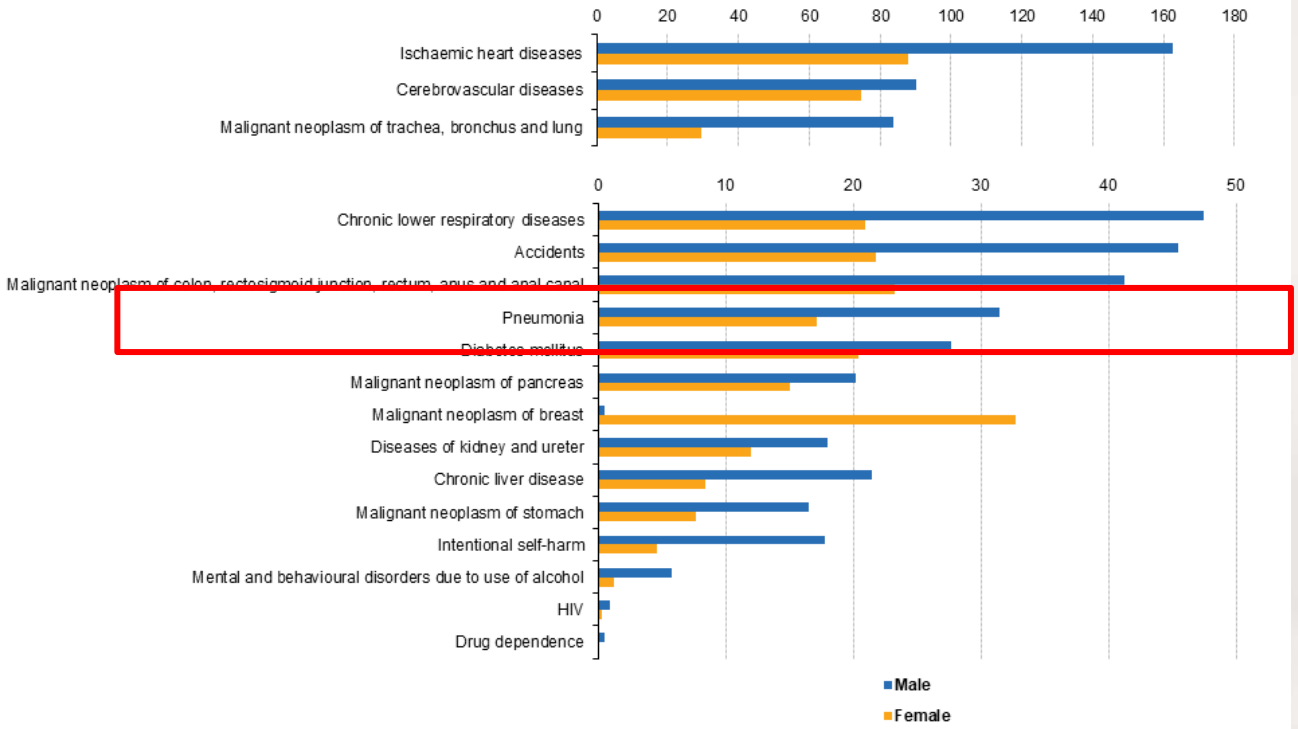
24,8/10000 ενήλικοι 2259 pts με RX CAP

Jain S et al,NEJM 2015

DOI: 10.1056/NEJMoa1500245

ΑΙΤΙΕΣ ΘΑΝΑΤΟΥ-EUROSTAT

Causes of death — standardised death rate, EU-27, 2016
(per 100 000 inhabitants)



Note: the figure is ranked on the average of male and female. Note the difference in the scales employed in the two parts of the figure.
Source: Eurostat (online data code: hlth_cd_asdr2)

eurostat

ΠΝΕΥΜΟΝΙΑ ΚΟΙΝΟΤΗΤΑΣ

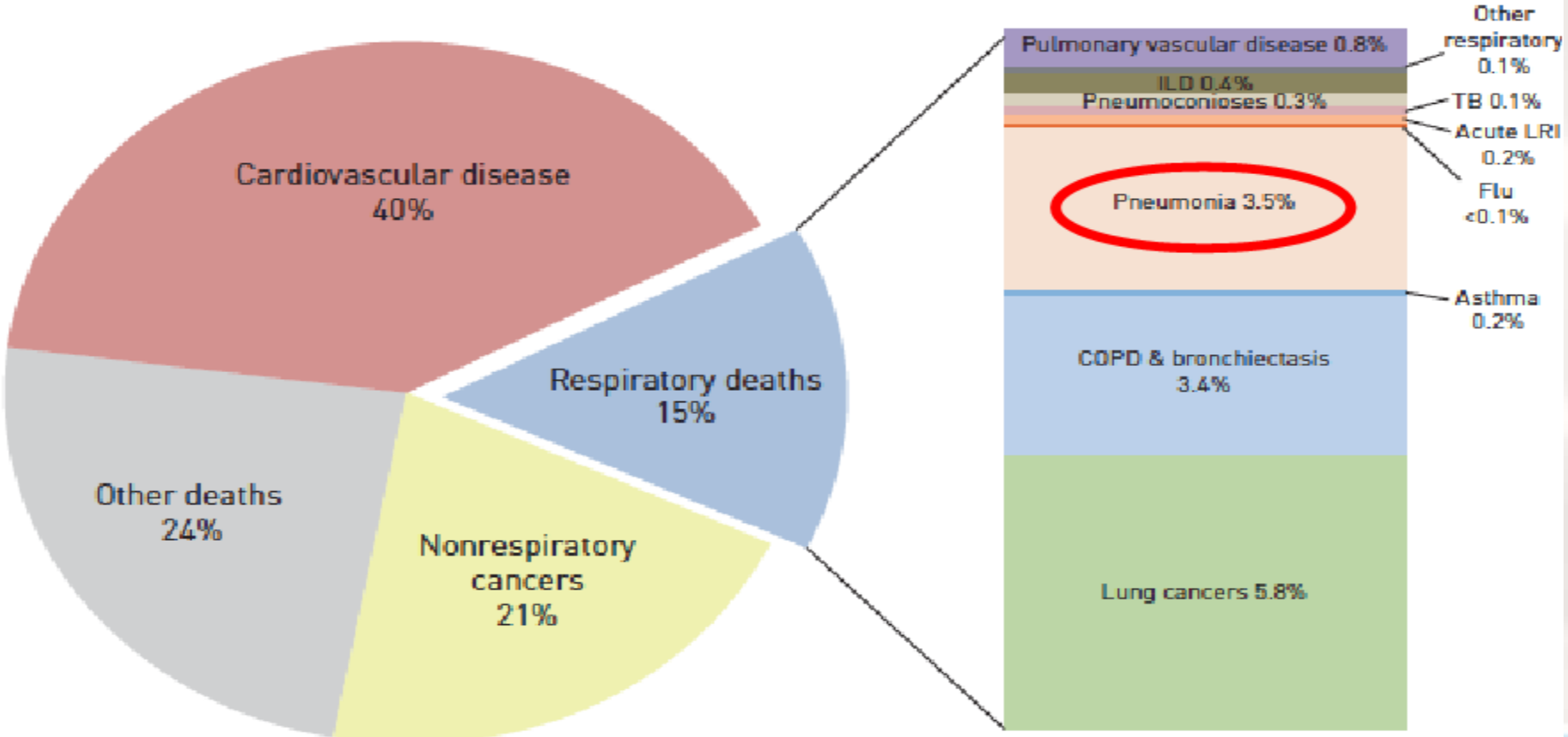


Figure 3 – Percentage of deaths in selected European Union countries, by respiratory condition. ILD: interstitial lung disease; TB: tuberculosis; LRI: lower respiratory infections; COPD: chronic obstructive pulmonary disease. The countries represented are those for which full ICD-10 coding of diagnoses was available for both hospital admissions and deaths (Austria, Croatia, Cyprus, Czech Republic, Denmark, Finland, Latvia, Lithuania, Luxembourg, Malta, Poland, Slovenia, Slovakia, UK). Source: World Health Organization World and Europe Detailed Mortality Databases.

Diagnosis and Treatment of Adults with Community-acquired Pneumonia

An Official Clinical Practice Guideline of the American Thoracic Society and Infectious Diseases Society of America

Joshua P. Metlay*, Grant W. Waterer*, Ann C. Long, Antonio Anzueto, Jan Brozek, Kristina Crothers, Laura A. Cooley, Nathan C. Dean, Michael J. Fine, Scott A. Flanders, Marie R. Griffin, Mark L. Metersky, Daniel M. Musher, Marcos I. Restrepo, and Cynthia G. Whitney; on behalf of the American Thoracic Society and Infectious Diseases Society of America

THIS OFFICIAL CLINICAL PRACTICE GUIDELINE WAS APPROVED BY THE AMERICAN THORACIC SOCIETY MAY 2019 AND THE INFECTIOUS DISEASES SOCIETY OF AMERICA AUGUST 2019

Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, Oct 1, 2019

International Perspective on the New 2019 American Thoracic Society/Infectious Diseases Society of America Community-Acquired Pneumonia Guideline

A Critical Appraisal by a Global Expert Panel

Mathias W. Pletz, MD; Francesco Blasi, MD, PhD; James D. Chalmers, MD, PhD; Charles S. Dela Cruz, MD, PhD; Charles Feldman, MB BCh, DSc; Carlos M. Luna, MD, PhD; Julio A. Ramirez, MD; Yuichiro Shindo, MD, PhD; Daiana Stolz, MD, MPH; Antoni Torres, MD, PhD; Brandon Webb, MD; Tobias Welte, MD; Richard Wunderink, MD; and Stefano Aliberti, MD

Chest. 2020 Aug 25

ΕΡΩΤΗΣΗ 1.ΝΟΣΗΛΕΙΑ?

a. CURB II στη κλινική

b. CURB III στη ΜΑΦ

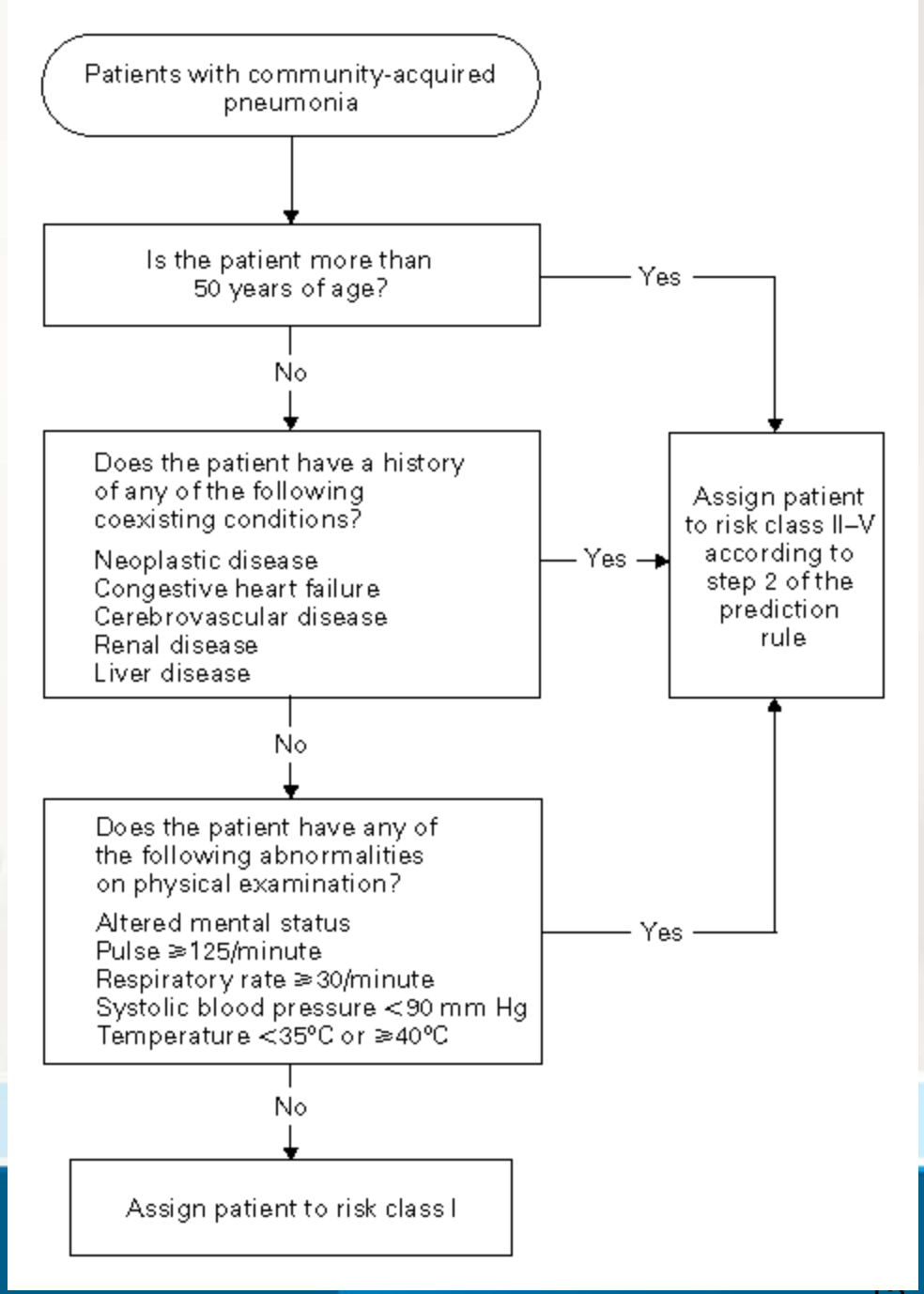
c. SO2 <90% - στη κλινική

d. Στο σπίτι με οξυγονοθεραπεία

PSI

- Pneumonia
- Severity
- Index

Fine MJ, N Engl J Med. **1997 Jan 23;336(4):243-50**



Pneumonia Severity Index

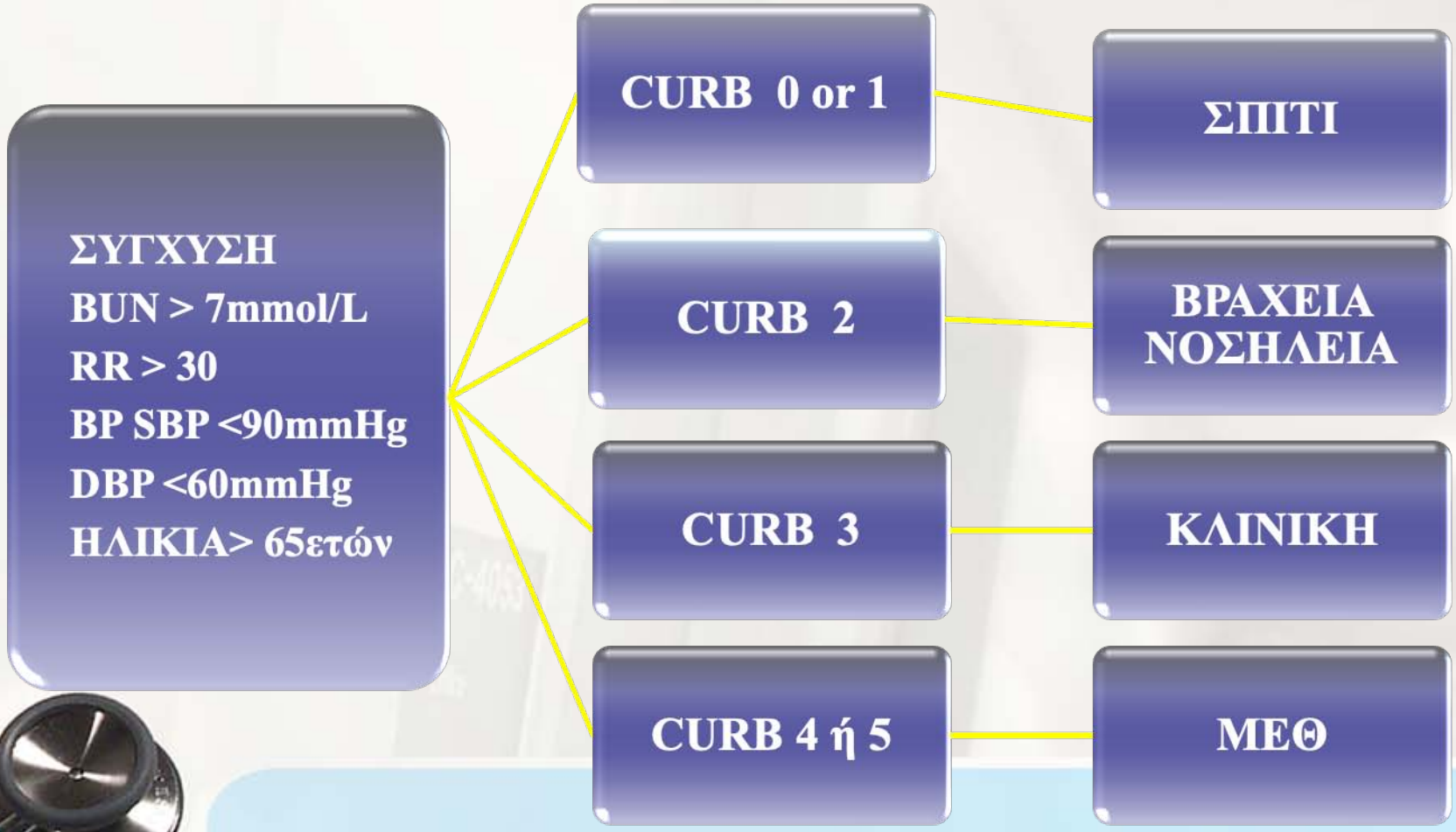
Characteristic	No. of Points Assigned
Demographic factors	
Age	
Men	Age (in yr)
Women	Age (in yr) − 10
Nursing home resident	+10
Coexisting illnesses	
Neoplastic disease	+30
Liver disease	+20
Congestive heart failure	+10
Cerebrovascular disease	+10
Renal disease	+10
Findings on physical examination	
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 beats/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 or oxygen saturation <90%	+10
Pleural effusion	+10

Stratification of Risk Score

Risk	Risk Class	Score	Mortality
Low	I	Based on algorithm	0.1%
Low	II	≤70	0.6%
Low	III	71–90	0.9%
Moderate	IV	91–130	9.3%
High	V	>130	27.0%

Fine MJ, N Engl J Med. 1997 Jan

CURB 65 Rule – CAP



ERJ 2001;17:200-5, Thorax 2003; 58: 377-382

Question 6: Should a Clinical Prediction Rule for Prognosis plus Clinical Judgment versus Clinical Judgment Alone Be Used to Determine Inpatient versus Outpatient Treatment Location for Adults with CAP?

In addition to clinical judgement, we recommend that clinicians use **a validated clinical prediction rule** for prognosis, preferentially the **Pneumonia Severity Index (PSI)** (*strong recommendation, moderate quality of evidence*) over the CURB-65 (tool based on confusion, urea level, respiratory rate, blood pressure, and age >65) (*conditional recommendation, low quality of evidence*), to determine the need for hospitalization in adults diagnosed with CAP.

Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, Oct 1, 2019

Τι μικροβιολογικές εξετάσεις θα κάνετε?

QUESTION 1: IN ADULTS WITH CAP, SHOULD GRAM STAIN AND CULTURE OF LOWER RESPIRATORY SECRETIONS BE OBTAINED AT THE TIME OF DIAGNOSIS?

Recommendation:

- ❑ We recommend not obtaining sputum Gram stain and culture routinely in adults with CAP managed in the outpatient setting (*strong recommendation, very low quality of evidence).*

- ❑ We recommend obtaining pre-treatment Gram stain and culture of respiratory secretions in adults with CAP managed in the hospital setting who:

a) are classified as severe CAP ,or
b) are being empirically treated for MRSA or *P. aeruginosa* (*strong recommendation, very low quality of evidence)*

Question 2: In Adults with CAP, Should Blood Cultures Be Obtained at the Time of Diagnosis?

- We recommend not obtaining blood cultures in adults with CAP managed in the outpatient setting (*strong recommendation, very low quality of evidence).*
- We suggest not routinely obtaining blood cultures in adults with CAP managed in the hospital setting (*conditional recommendation, very low quality of evidence).*
- We recommend obtaining pretreatment blood cultures **in adults with CAP managed in the hospital setting** who:

- 1. are classified as severe CAP *(strong recommendation, very low quality of evidence); or*
- a. are being empirically treated for MRSA or *P. aeruginosa* (*strong recommendation, very low quality of evidence*); or
- b. were previously infected with MRSA or P. aeruginosa, especially those with prior respiratory tract infection (*conditional recommendation, very low quality of evidence);* or
- c. were hospitalized and received parenteral antibiotics, whether during the hospitalization event or not, in the last 90 days (*conditional recommendation, very low quality of evidence*).

Risk factors for MRSA or *Ps aeruginosa*

- prior respiratory isolation of MRSA or *P. aeruginosa*
- or recent hospitalization AND receipt of parenteral antibiotics (in the last 90 d)

Question 3: In Adults with CAP, Should Legionella and Pneumococcal Urinary Antigen Testing Be Performed at the Time of Diagnosis?

- We suggest **not routinely testing urine for pneumococcal antigen** in adults with CAP, except in adults with severe CAP (conditional recommendation, low quality of evidence).
- We suggest **not routinely testing urine for Legionella antigen** in adults with CAP (*conditional recommendation, low quality of evidence), except:*

  A. in cases where indicated by epidemiological factors, such as association with a Legionella outbreak or recent travel (*conditional recommendation, low quality of evidence*); or B. severe CAP

Am J Respir Crit Care Med Vol 200, Oct 1, 2019

Question 4: In Adults with CAP, Should a Respiratory Sample Be Tested for Influenza Virus at the Time of Diagnosis?

When influenza viruses are circulating in the community, we recommend testing for influenza with a rapid influenza molecular assay (i.e., influenza nucleic acid amplification test), which is preferred over a rapid influenza diagnostic test (i.e., antigen test) (*strong recommendation, moderate quality of evidence).*

Διάγνωση: Σοβαρή CAP

a. Πτύελα: Gram χρώση και καλ/γεια.
b. Καλ/γειες αίματος.
c. Αντιγόνα ούρων για *Legionella pn.* & *Streptococcus pneumoniae*.
d. PCR για influenza
e. ± άλλες
    a. FOB+BAL
    b. Θωρακοκέντηση

IDSA /ATS Consensus Guidelines on the Management of CAP in Adults. CID2007; 44:S27–72

ΕΡΩΤΗΣΗ 2. ΠΟΙΟ ΤΟ ΠΙΘΑΝΟΤΕΡΟ ΠΑΘΟΓΟΝΟ?

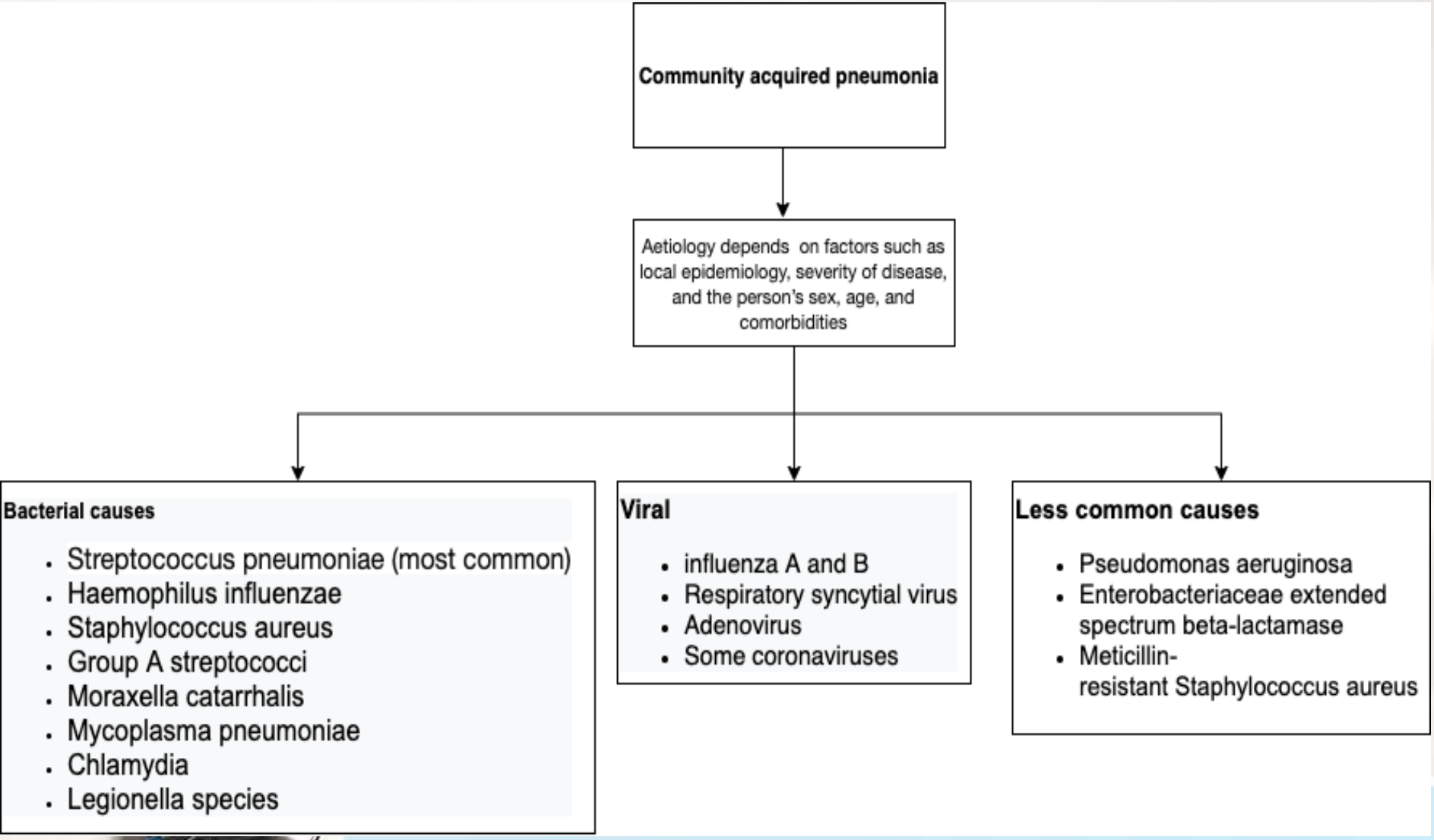
a. *Streptococcus pneumoniae*

b. *H. Influenzae*

c. *Pseudomonas aeruginosa*

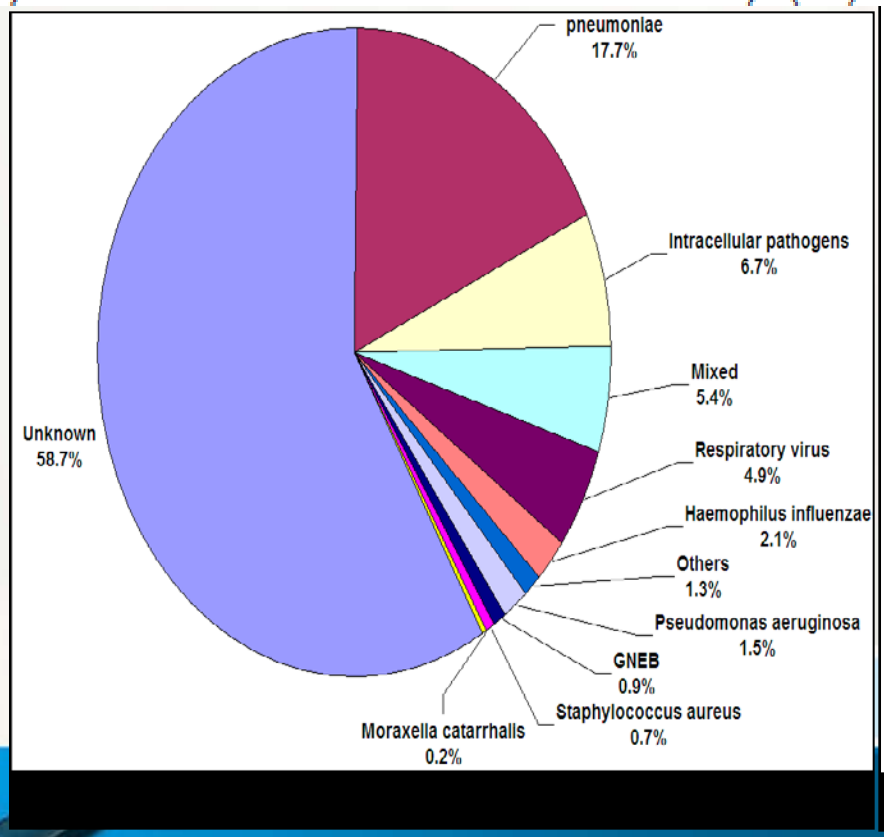
d. Staph aureus

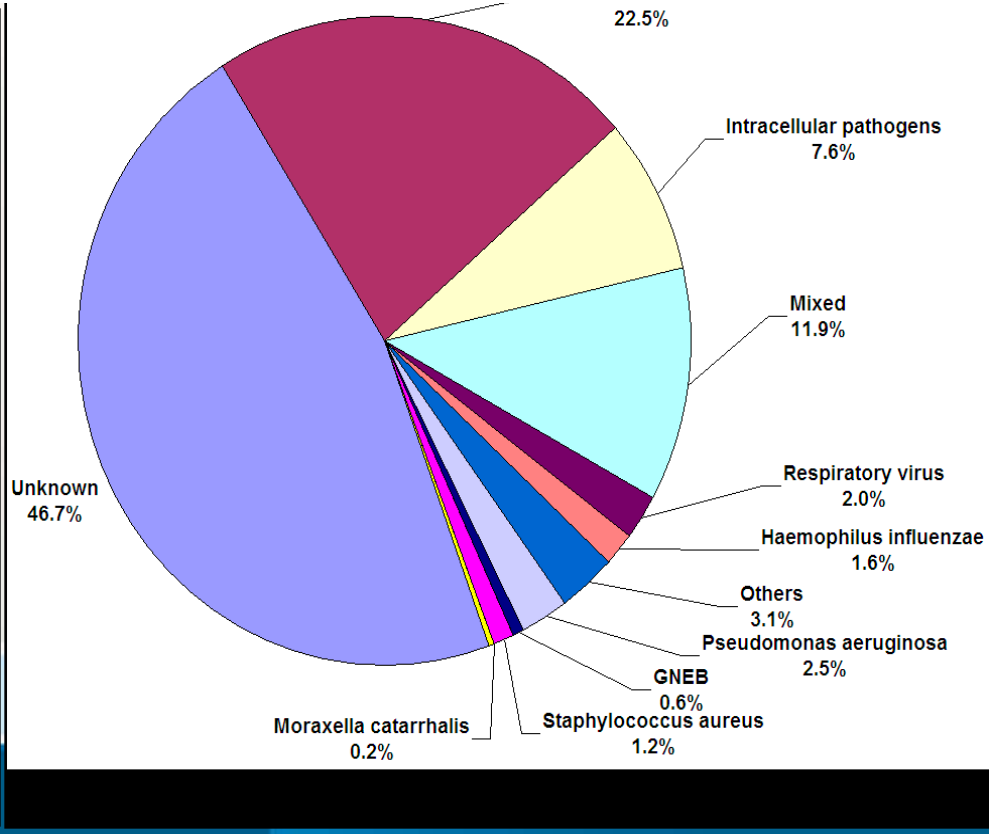
e. A + d


Community acquired pneumonia
Aetiology depends on factors such as local epidemiology, severity of disease, and the person's sex, age, and comorbidities
Bacterial causes
Streptococcus pneumoniae (most common)
Haemophilus influenzae
Staphylococcus aureus
Group A streptococci
Moraxella catarrhalis
Mycoplasma pneumoniae
Chlamydia
Legionella species
Viral
influenza A and B
Respiratory syncytial virus
Adenovirus
Some coronaviruses
Less common causes
Pseudomonas aeruginosa
Enterobacteriaceae extended spectrum beta-lactamase
Meticillin-resistant Staphylococcus aureus

ΑΙΤΙΟΛΟΓΙΑ ΠΝΕΥΜΟΝΙΑΣ

(B) Patients Admitted to Ward; (C) Patients Admitted to Intensive Care Unit.





Catia Cilloniz, Int. J. Mol. Sci.2016

Comprehensive Molecular Testing for Respiratory Pathogens in Community-Acquired Pneumonia

Naomi J. Gadsby,[1] Clark D. Russell,[1,2] Martin P. McHugh,[1] Harriet Mark,[1] Andrew Conway Morris,[3] Ian F. Laurenson,[1] Adam T. Hill,[4] and Kate E. Templeton[1]

[1]Medical Microbiology, Department of Laboratory Medicine, Royal Infirmary of Edinburgh, [2]College of Medicine and Veterinary Medicine, University of Edinburgh, [3]Department of Anaesthesia, University of Cambridge, and [4]Respiratory Medicine, Royal Infirmary of Edinburgh, United Kingdom

Fast multiplex real-time polymerase
assays for 26 respiratory bacteria an

***S. pneumoniae* in 36%, *H. influenzae* in 40%, *Moraxella* in 14%, *S. aureus* in 10%, *Klebsiella* in 4%, *Pseudomonas* in 3%, *Mycoplasma or Legionella* in <2% each**

- Of these, **78%** had a bacterial pathogen detecte but only 32% were culture-positive ($p < .0001$)
- Viruses were present in 30% of cases; 82% of these were co-detections with bacteria
- Molecular testing had the potential to **enable de-escalation** in number and/or spectrum of antimicrobials in 77% of patients.

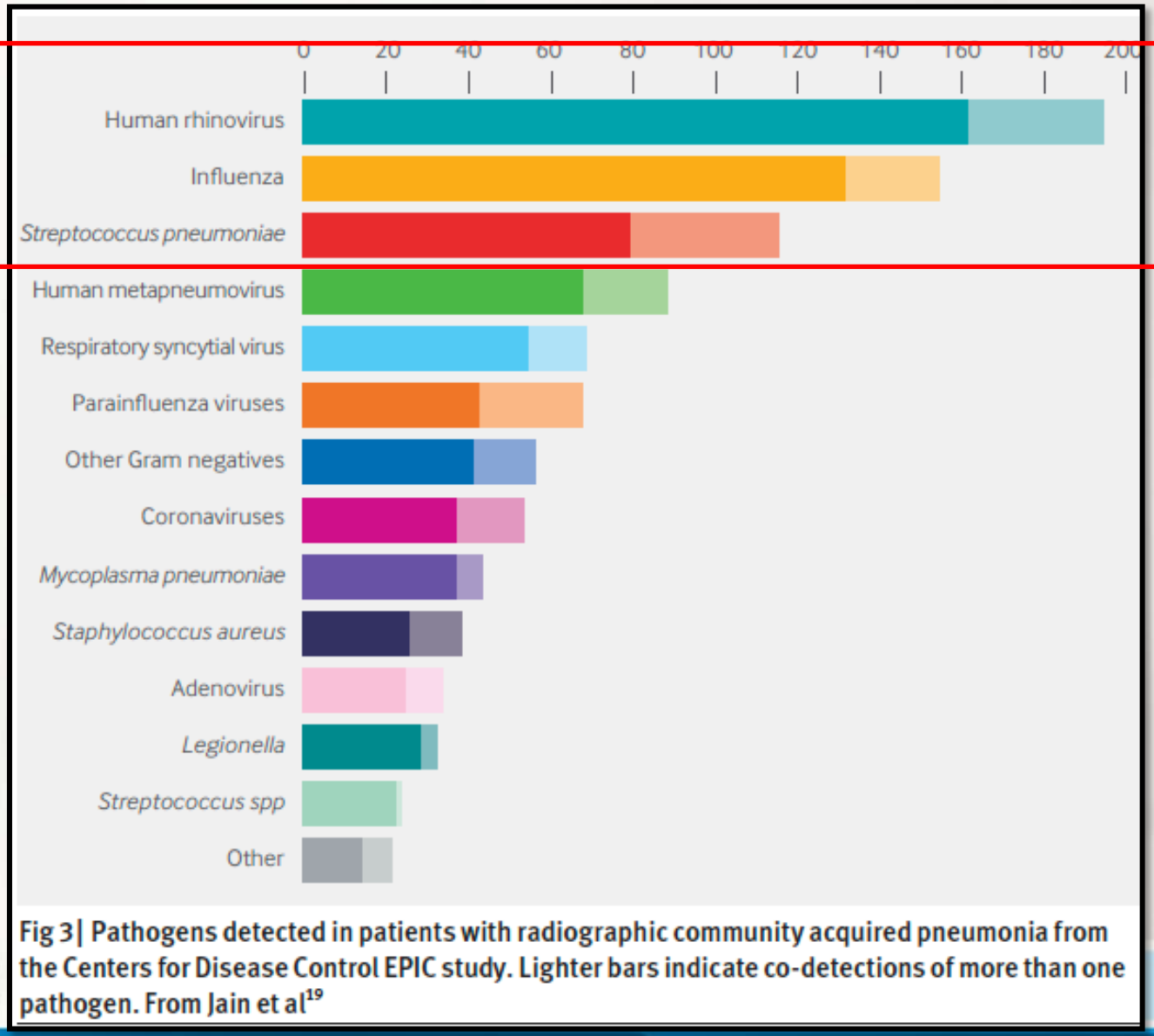


Fig 3| Pathogens detected in patients with radiographic community acquired pneumonia from the Centers for Disease Control EPIC study. Lighter bars indicate co-detections of more than one pathogen. From Jain et al[19]

Jain S et al,NEJM 2015

Review article

Systematic review of respiratory viral pathogens identified in adults with community-acquired pneumonia in Europe

Y. Alimi[a], W.S. Lim[b], L. Lansbury[a], J. Leonardi-Bee[a], J.S. Nguyen-Van-Tam[a,*]

[a] Health Protection and Influenza Research Group, Division of Epidemiology and Public Health, University of Nottingham School of Medicine, Nottingham, UK
[b] University Hospitals NHS Trust, Nottingham, UK

Journal of Clinical Virology 95 (2017) 26–35

Studies included in quantitative synthesis (meta-analysis) (n = 20 articles; 21 studies)*

Proportion of virus in:

Studies: 6% to 45%

Meta-analysis: 22%

Mixed : 10%

16 studies with PCR t
29% virus

Table 2
Summary of individual pathogen-specific *meta*-analyses for respiratory viruses most commonly identified in European adult patients with CAP.

Virus type	Pooled%	95% CI	No. of studies (and patients) included in pathogen-specific *meta*-analysis	I^2(%)
Influenza (A or B)	9	7–12	17 (6487)	93.45
Rhinovirus	5	4–7	12 (3324)	88.22
Coronavirus	4	2–7	7 (1343)	80.37
Parainfluenza	3	2–5	14 (5600)	88.35
Human metapneumovirus (hMPV)	2	1–2	10 (1779)	7.49
Respiratory syncytial virus (RSV)	2.	1–3	17 (5968)	82.42
Adenovirus	1	0 – 1	13 (3166)	32.88

Enterovirus, poliovirus, cytomegalovirus, coxsackie virus, varicella-zoster virus, human bocavirus and herpes simplex virus were detected in < 1% of adult patients with CAP.

Evolving Understanding of the Causes of Pneumonia in Adults, With Special Attention to the Role of Pneumococcus

Daniel M. Musher,[1,2] Michael S. Abers,[3,4] and John G. Bartlett[5]

Table 3. Etiology of Community-Acquired Pneumonia, Studies Since 2010

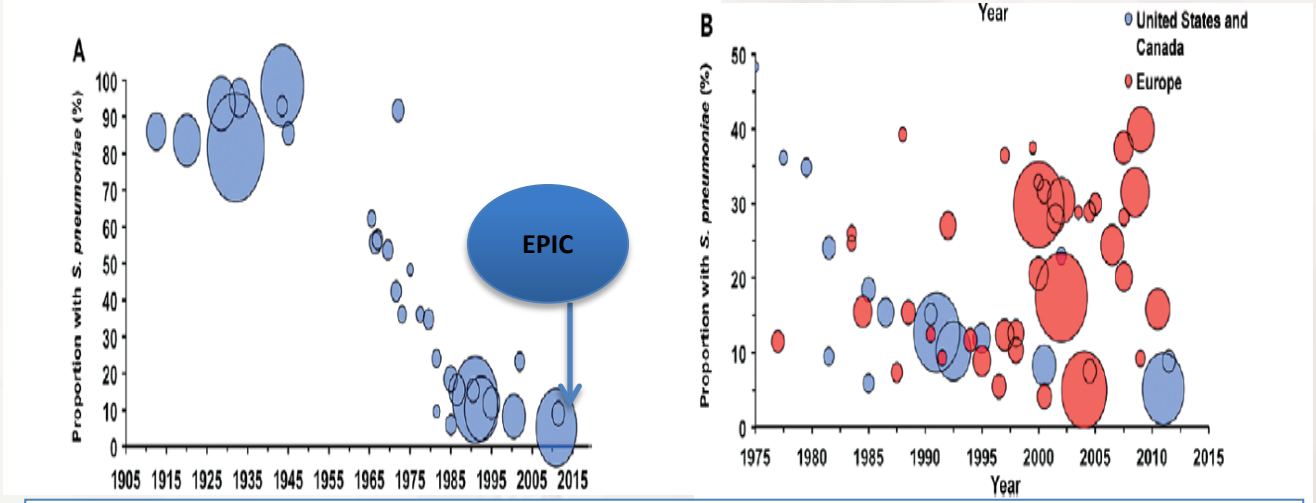
Pathogen	Percentage of Patients		
	Houston [33]	Centers for Disease Control and Prevention [34]	Netherlands [136]
Bacteria	29	15	30
Streptococcus pneumoniae	9	5	16
Haemophilus	6	<1	7
Staphylococcus aureus	5	2	3
Pseudomonas	3	<1	2
Legionella	1	1	1
Mycoplasma, Chlamydia	–	<3	1
Other	6	3	3
Nocardia	1	0	0
Mycobacteria	2	1	<1
Fungi (*Pneumocystis*)	3	1	2
Viruses	20	27	3
Rhinovirus	13	9	–
Coronavirus	3	2	–
Human metapneumovirus	2	4	–
Influenza	1	6	3
Parainfluenza	2	3	–
Respiratory syncytial virus	2	3	–
No pathogen	55	62	66

Musher D, CID 2017

Evolving Understanding of the Causes of Pneumonia in Adults, With Special Attention to the Role of Pneumococcus

Daniel M. Musher,[1,2] Michael S. Abers,[3,4] and John G. Bartlett[5]

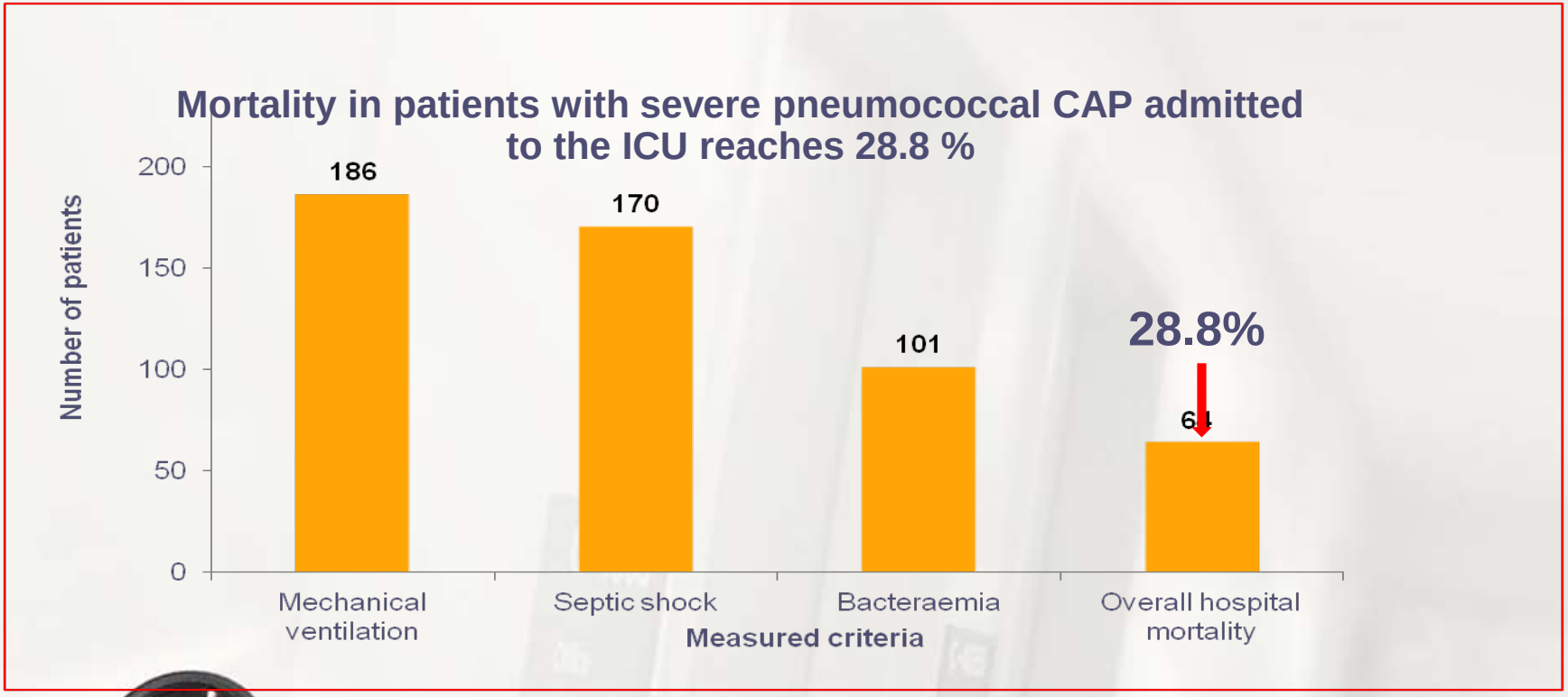
The area of each circle is proportional to the number of patients in each study



We identified 31 studies(21 120 patients) from the United States and Canada published between 1917 and 2015 and 37 studies (21 166 patients) from Europe. We included studies that applied validated pneumococcal tests to ≥50% of patients

CID 2017;65(10):1736-1744

ΚΙΝΔΥΝΟΣ ΘΝΗΤΟΤΗΤΑΣ ΣΟΒΑΡΗΣ ΠΝΕΥΜΟΝΙΟΚΟΚΚΙΚΗΣ ΠΝΕΥΜΟΝΙΑΣ ΣΤΗ ΜΕΘ[1]



Prospective analysis of 222 patients ICU admitted in France, to determine risk factors of mortality in these patients for severe *S. pneumoniae* CAP, in 2001-2008.[1]

1. Mongardon N, et al. Critical Care. 2012, 16:R155.

MDRs IN CAP

- Methicillin-resistant *S. aureus* (MRSA)
- *Pseudomonas aeruginosa* resistant to antipseudomonal penicillins, cephalosporins, carbapenems, and quinolones
- *Acinetobacter baumanii*
- Vancomycin-resistant *Enterococcus*
- *Enterobacteriaceae* producing extended-spectrum B-lactamases (ESBL)

PCR INFLUENZA A(+)

Influenza

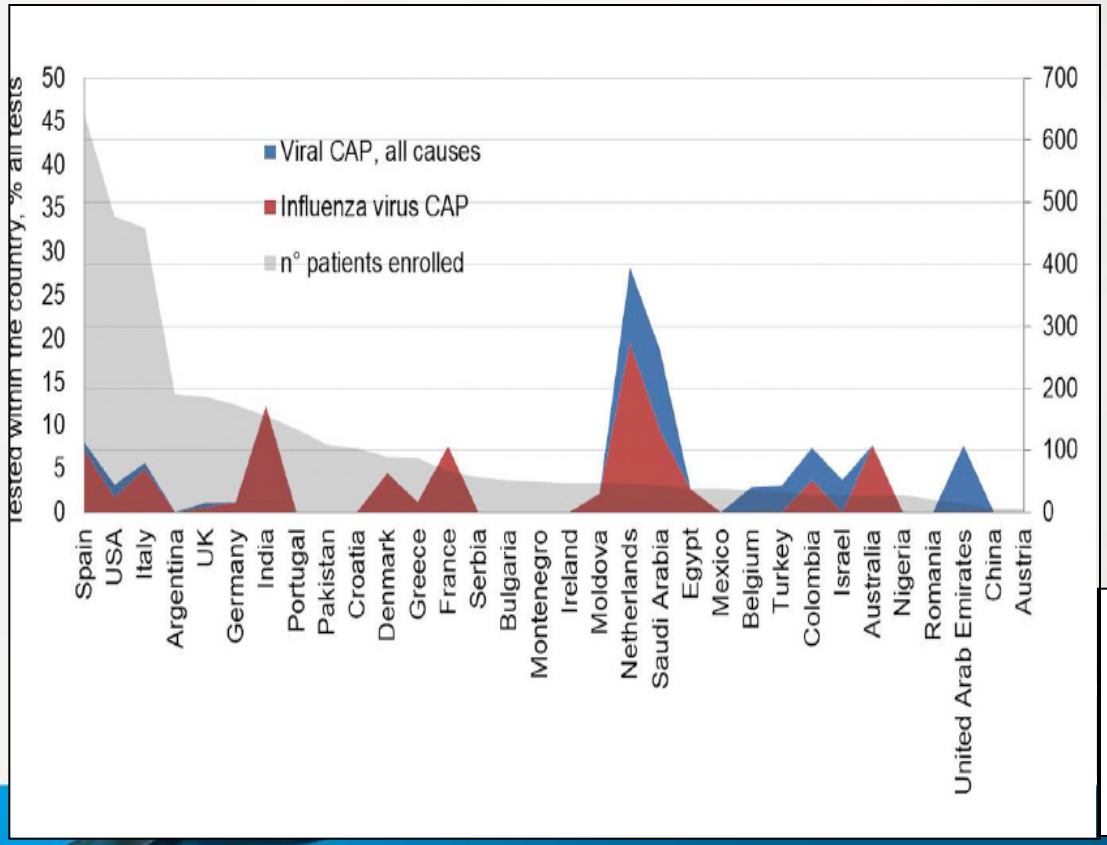
- Influenza pandemics occur when new viruses are introduced into the population
- Historic pandemics of 1918 (H1N1- 50 million deaths worldwide), 1957 (H1N1 and H2N2), 1968 (H3N2)
- Avian influenza H5N1 – 1997 outbreak, 58% with PNA
- Novel H1N1 **influenza A virus** emerged in Mexico and USA in Spring 2009
  - High risk populations: infants, young kids, healthy adults 20-40s, pregnant/postpartum women, immunocompromised, obesity, DM, COPD, asthma
  - Elderly less susceptible to H1N1 due to prior exposure
  - Mortality in hospitalized pts 7% -17%

Murray and Nadel's Textbook of Respiratory Medicine 5th Edition

An international perspective on hospitalized patients with viral community-acquired pneumonia

Eur J Intern Med. 2019 Feb;

GLIMP Study Group



- 553 (14.9%) patients with CAP underwent nasal swab.
- Viral CAP was diagnosed in 157 (28.4%) patients.
- *Influenza virus* was isolated in 80.9% of cases.
- Prevalence of empirical treatment with oseltamivir was 5.1%

Fig. 3. Prevalence of influenza virus CAP (red area) in relation to all cause viral CAP (blue area). The ratio between swabs positive for influenza compared to all positive swabs by each country is reported in the left sided vertical axis. Absolute patients enrolled in the study (grey area) are reported in the right sided vertical axis. Only countries that have performed at least one viral swab are shown. (For in-

ΠΕΡΙΣΤΑΤΙΚΟ 1
ΘΕΡΑΠΕΙΑ

- Η πρώτη αντβ δόση πρέπει να δίνεται στα επείγοντα

- Σε ασθενείς με CAP & **septic shock,** θα πρέπει να χορηγηθεί εντός μίας ώρας

ΕΡΩΤΗΣΗ 3 :ΠΟΙΑ Η ΑΝΤΒ. ΘΕΡΑΠΕΙΑ?

a. Μοξιφλοξασίνη

b. Κεφτριαξόνη + Μακρολίδη

c. Λεβοφλοξασίνη+ Οσελταμιβίρη

d. Μοξιφλοξασίνη+ Οσελταμιβίρη+ Λινεζολίδη

Table 4. Initial Treatment Strategies for Inpatients with Community-acquired Pneumonia by Level of Severity and Risk for Drug Resistance

	Standard Regimen	Prior Respiratory Isolation of MRSA	Prior Respiratory Isolation of *Pseudomonas aeruginosa*	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for MRSA	Recent Hospitalization and Parenteral Antibiotics and Locally Validated Risk Factors for *P. aeruginosa*
Nonsevere inpatient pneumonia*	β-Lactam + macrolide† or respiratory fluroquinolone‡	Add MRSA coverage§ and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for *P. aeruginosa*‖ and obtain cultures to allow deescalation or confirmation of need for continued therapy	Obtain cultures but withhold MRSA coverage unless culture results are positive. If rapid nasal PCR is available, withhold additional empiric therapy against MRSA if rapid testing is negative or add coverage if PCR is positive and obtain cultures	Obtain cultures but initiate coverage for *P. aeruginosa* only if culture results are positive
Severe inpatient pneumonia*	β-Lactam + macrolide† or β-lactam + fluroquinolone‡	Add MRSA coverage§ and obtain cultures/nasal PCR to allow deescalation or confirmation of need for continued therapy	Add coverage for *P. aeruginosa*‖ and obtain cultures to allow deescalation or confirmation of need for continued therapy	Add MRSA coverage§ and obtain nasal PCR and cultures to allow deescalation or confirmation of need for continued therapy	Add coverage for *P. aeruginosa*‖ and obtain cultures to allow deescalation or confirmation of need for continued therapy

Question 9: In the Inpatient Setting, Which Antibiotic Regimens Are Recommended for Empiric Treatment of CAP in Adults without Risk Factors for MRSA and P. aeruginosa?

- A.**Combination therapy** with a β-lactam (ampicillin/sulbactam 1.5–3 g /6 h, cefotaxime 1–2 g /8 h, ceftriaxone 1–2 g daily, or ceftaroline 600 mg every 12 h) **and** a macrolide (azithromycin 500 mg daily or clarithromycin 500 mg twice daily) (*strong recommendation, high quality of evidence), or*
- B. **Monotherapy** with a respiratory fluoroquinolone (levofloxacin 750 mg daily, moxifloxacin 400 mg daily) (*strong recommendation, high quality of evidence*).
- C. **For contraindications to both macrolides and fluoroquinolones**: combination therapy with a β-lactam + docycycline 100mg twice daily

Question 13: In Adults with CAP Who test Positive for Influenza, Should the Treatment Regimen Include Antiviral Therapy?

We recommend that antiinfluenza treatment, such as **oseltamivir**, be prescribed for adults with CAP who test positive for influenza in the inpatient setting, independent of duration of illness before diagnosis (*strong recommendation, moderate quality of evidence*).

Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, Oct 1, 2019

Question 14: In Adults with CAP Who Test Positive for Influenza, Should the Treatment Regimen Include Antibacterial Therapy?

Standard antibacterial treatment be initially prescribed for adults with clinical and radiographic evidence of CAP who test positive for influenza in the inpatient and outpatient settings (*strong recommendation, low quality of evidence)*

Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, Oct 1, 2019

Clinical Practice Guidelines by the Infectious Diseases Society of America: 2018 Update on Diagnosis, Treatment, Chemoprophylaxis, and Institutional Outbreak Management of Seasonal Influenza[a]

Timothy M. Uyeki,[1] Henry H. Bernstein,[2] John S. Bradley,[3,4] Janet A. Englund,[5] Thomas M. File Jr,[6] Alicia M. Fry,[1] Stefan Gravenstein,[7] Frederick G. Hayden,[8] Scott A. Harper,[9] Jon Mark Hirshon,[10] Michael G. Ison,[11] B. Lynn Johnston,[12] Shandra L. Knight,[13] Allison McGeer,[14] Laura E. Riley,[15] Cameron R. Wolfe,[16] Paul E. Alexander,[17,18] and Andrew T. Pavia[19]

Hospitalized Patients.

3. During influenza activity:
   - Clinicians should test for influenza on admission in all patients requiring hospitalization with acute respiratory illness, including pneumonia, with or without fever *(A-II)*.
   - Clinicians should test for influenza on admission in all patients with acute worsening of chronic cardiopulmonary disease (eg, COPD, asthma, coronary artery disease, or congestive heart failure), as influenza can be associated with exacerbation of underlying conditions *(A-III)*.
   - Clinicians should test for influenza on admission in all patients who are immunocompromised or at high risk of complications and present with acute onset of respiratory symptoms with or without fever, as the manifestations of influenza in such patients are frequently less characteristic than in immunocompetent individuals *(A-III)*.
   - Clinicians should test for influenza in all patients who, while hospitalized, develop acute onset of respiratory symptoms with or without fever, or respiratory distress, without a clear alternative diagnosis *(A-III)*.

For Patients Who Are Recommended to Receive Antiviral Treatment for Suspected or Confirmed Influenza, Which Antiviral Should Be Prescribed, at What Dosing, and for What Duration?

Recommendations

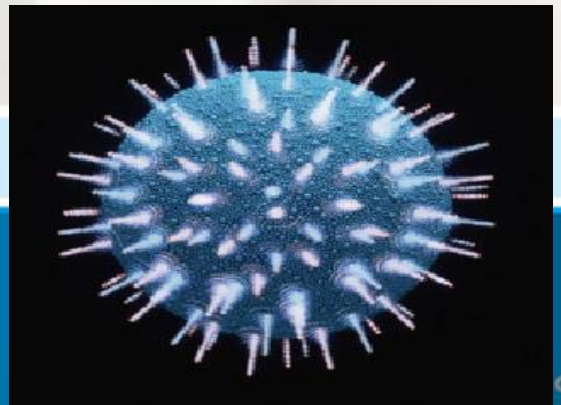
20. Clinicians should start antiviral treatment as soon as possible with a single NAI (either oral oseltamivir, inhaled zanamivir, or intravenous peramivir) and not use a combination of NAIs *(A-1)*.
21. Clinicians should not routinely use higher doses of FDA-approved NAI drugs for the treatment of seasonal influenza *(A-II)*.
22. Clinicians should treat uncomplicated influenza in otherwise healthy ambulatory patients for 5 days with oral oseltamivir or inhaled zanamivir, or a single dose of intravenous peramivir *(A-1)*.
23. Clinicians can consider longer duration of antiviral treatment for patients with a documented or suspected immunocompromising condition or patients requiring hospitalization for severe lower respiratory tract disease (especially pneumonia or acute respiratory distress syndrome [ARDS]), as influenza viral replication is often protracted *(C-III)*.

ΑΝΤΙΙΚΑ ΦΑΡΜΑΚΑ

Table 4. Administration characteristics of influenza antivirals and associated adverse effects.

Antiviral	Activity	Route of administration	Dosage (5 days)	Adverse effects
Amantidine	Influenza virus A	Oral	100 mg/day[a]	CNS and gastrointestinal events
Rimantadine	Influenza virus A	Oral	100 mg/day	Mild CNS and gastrointestinal events
Zanamivir	Influenza viruses A and B	Inhaled	2 Inhalations twice/day	Bronchospasm
Oseltamivir	Influenza viruses A and B	Oral	75 mg twice/day[a]	Mild gastrointestinal events

[a] Dosage adjustment required with renal dysfunction.



Neuraminidase inhibitors for preventing and treating influenza in adults and children (Review)

Jefferson T, Jones MA, Doshi P, Del Mar CB, Hama R, Thompson MJ, Spencer EA, Onakpoya IJ, Mahtani KR, Nunan D, Howick J, Heneghan CJ

APRIL 2014

Cochrane Library

Cochrane Database of Systematic Reviews

- For the treatment of adults, oseltamivir reduced the time to first alleviation of symptoms by 16.8 hours (95% confidence interval (CI) 8.4 to 25.1 hours, $p < 0.0001$). This represents a reduction in the time to first alleviation of symptoms from 7 to 6.3 days.
- Treatment of adults with oseltamivir had **no significant effect on hospitalisations**: risk difference (RD) 0.15% (95% CI -0.78 to 0.91).
- In prophylaxis trials, oseltamivir and zanamivir reduced the risk of symptomatic influenza in individuals (oseltamivir: RD 3.05% (95% CI 1.83 to 3.88)
- Oseltamivir significantly reduced self reported, investigator-mediated, unverified pneumonia (RD 1.00%, 95% CI 0.22 to 1.49); number needed to treat to benefit (NNTB) = 100 (95% CI 67 to 451) in the treated population.
- The use of oseltamivir increases the **risk of adverse effects**, such as nausea, vomiting, psychiatric effects and renal events in adults and vomiting in children.

Safety and effectiveness of neuraminidase inhibitors in situations of pandemic and/or novel/variant influenza: a systematic review of the literature, 2009–15

C. Boikos[1], C. Caya[1], M. K. Doll[1], H. Kraicer-Melamed[1], M. Dolph[1], G. Delisle, N. Winters[1], G. Gore[2] and C. Quach[1,3,4]*

J Antimicrob Chemother 2017; **72**: 1556–1573

- **Results:** Overall, 165 studies were included (95% observational), which were generally of low methodological quality due to lack of adjustment for confounding variables. In studies reporting adjusted estimates in general populations, NI treatment appeared likely to be effective against mortality (primarily if administered within 48 h of symptom onset) and potentially effective in reducing pneumonia. NIs appeared effective in reducing secondary transmission when indicated for prophylaxis.
- Limited, low-quality data suggest NIs are likely safe in general populations and may be safe in pregnant women and children.
- Data are scarce regarding safety of NIs in adults and high-risk individuals.

7Η ΜΕΡΑ -ΕΠΙΔΕΙΝΩΣΗ

- Δύσπνοια, εμπύρετο ως 38 C και πυώδη πτύελα
- Ταχύπνοια, Υπόταση, Σύγχυση

  RR:36, HR:110, BP: 90/50 mmHg

  WBC: 25000(μ/L), PLT:500000(μ/L), CRP: 30mg/dL
- Αέρια αίματος σε 40%MV: 62/30/7,49(PO2/FiO2=209)

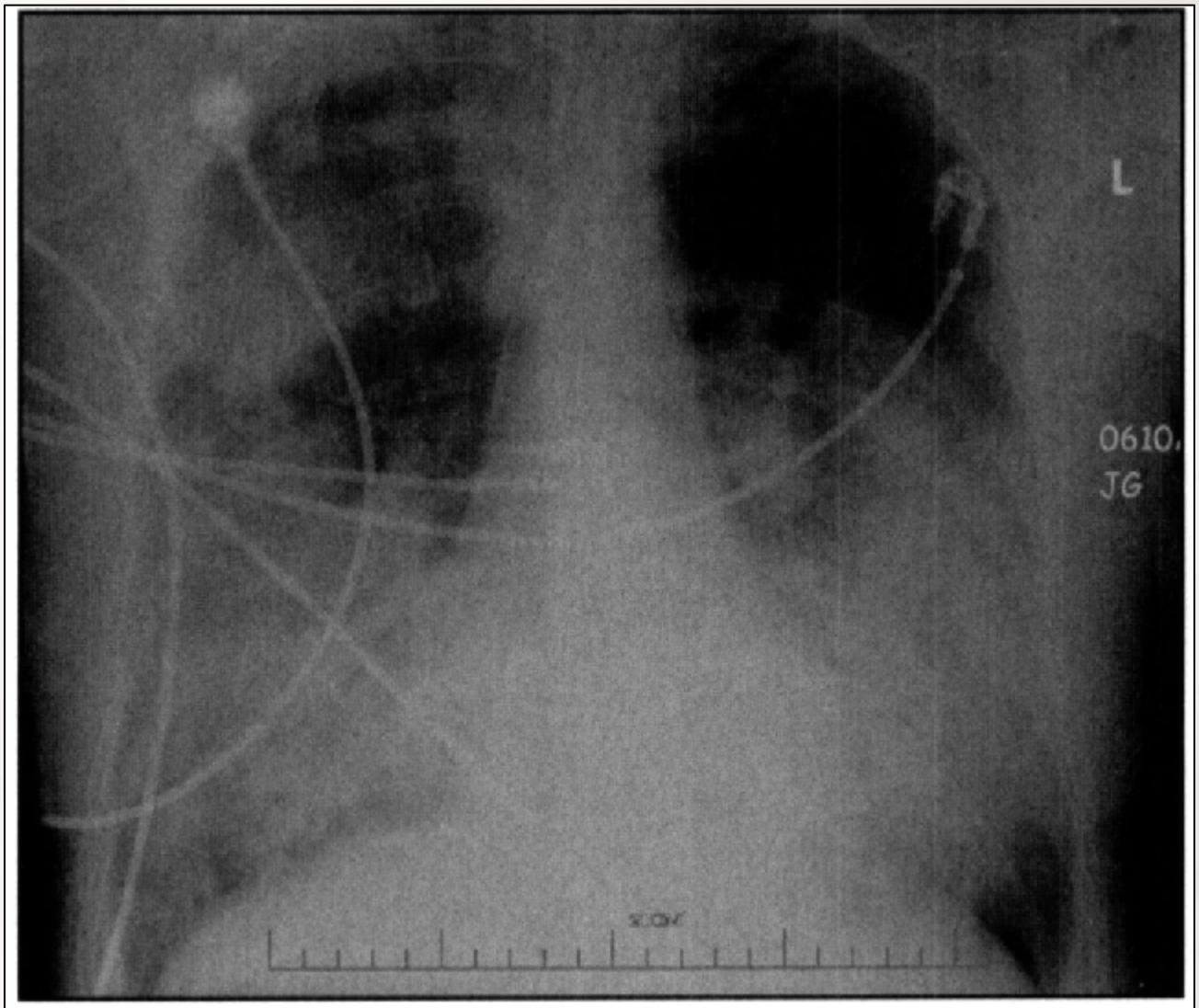


Figure 2. Bilateral multilobe pneumonia (Case 1).

ΕΙΣΑΓΩΓΗ ΜΕΘ

INTUBATED

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

Lionel A. Mandell,[1,a] Richard G. Wunderink,[2,a] Antonio Anzueto,[3,4] John G. Bartlett,[7] G. Douglas Campbell,[8] Nathan C. Dean,[9,10] Scott F. Dowell,[11] Thomas M. File, Jr.[12,13] Daniel M. Musher,[5,6] Michael S. Niederman,[14,15] Antonio Torres,[16] and Cynthia G. Whitney[11]

ICU ADMISSION

Δευτερεύοντα κριτήρια

- Αναπνευστική συχνότητα >30 αναπν./ λεπτό
- PaO2 / FiO2 < 250
- Πολυλοβώδη διηθήματα
- Σύγχυση /Αποπροσανατολισμός
- Ουραιμία (U >20 mg/dL)
- Λευκοπενία (WBC < 4000 cells/mm3)
- Θρομβοκυτοπενία (PLT< 100000 cells/mm3)
- Υποθερμία (Θ < 36 ºC)
- Υπόταση που απαιτεί επείγουσα χορήγηση υγρών

3 of minors

Πρωτεύοντα κριτήρια

- Μηχανική αναπνοή
- Σηπτικό σοκ που απαιτεί αγγειοσυσπαστικά

1 of majors

ΠΟΙΕΣ ΟΙ ΕΠΟΜΕΝΕΣ ΕΝΕΡΓΕΙΕΣ?

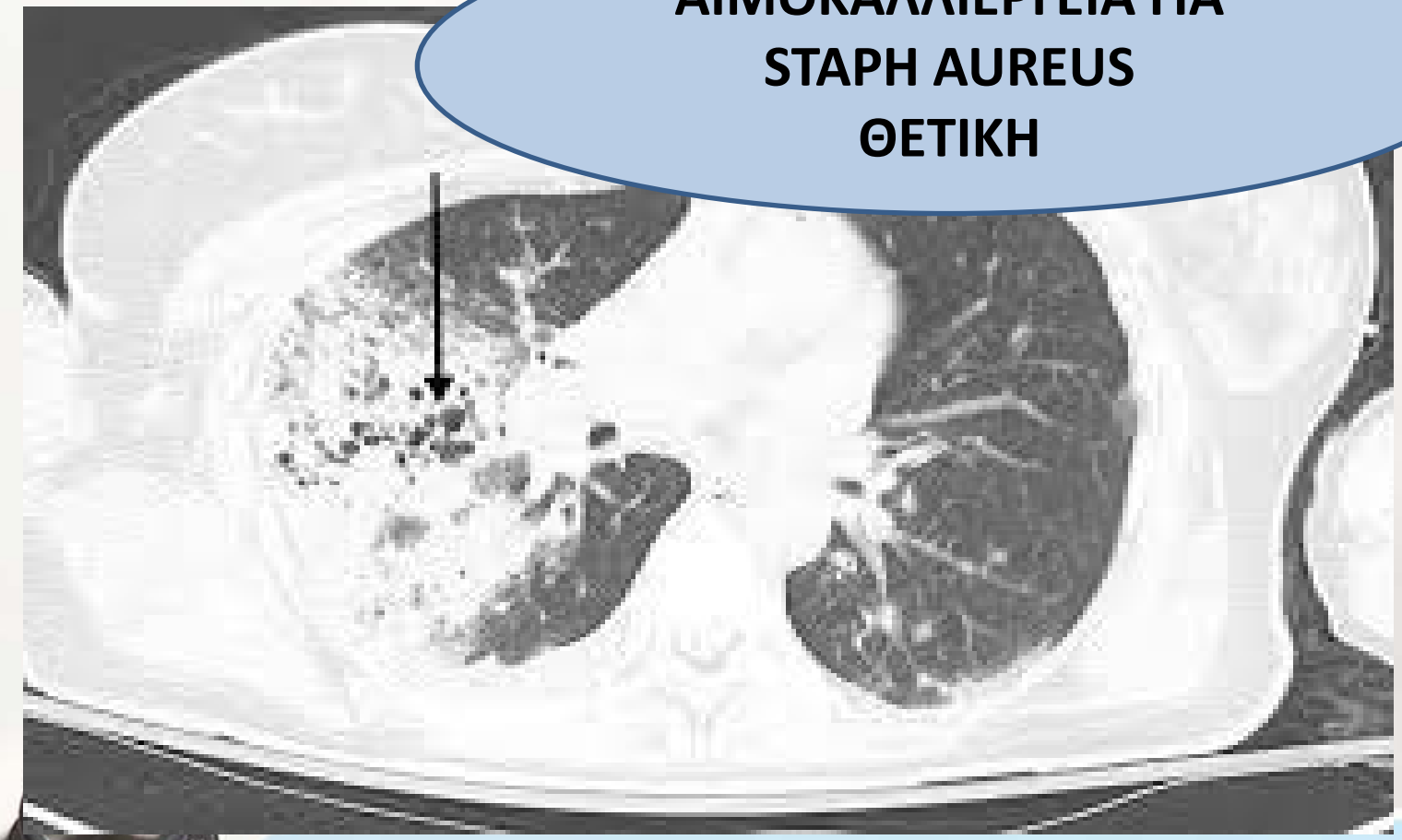
a. Λήψη αιμοκαλλιεργειών και καλ/γειών βρογχικών εκκρίσεων και αναβάθμιση της αντιβίωσης

b. Αναμονή αποτελεσμάτων και διενέργεια αξονικής τομογραφίας θώρακος

c. Αναβάθμιση εμπειρικά της αντιβίωσης

d. Βρογχοσκόπηση και λήψη BAL

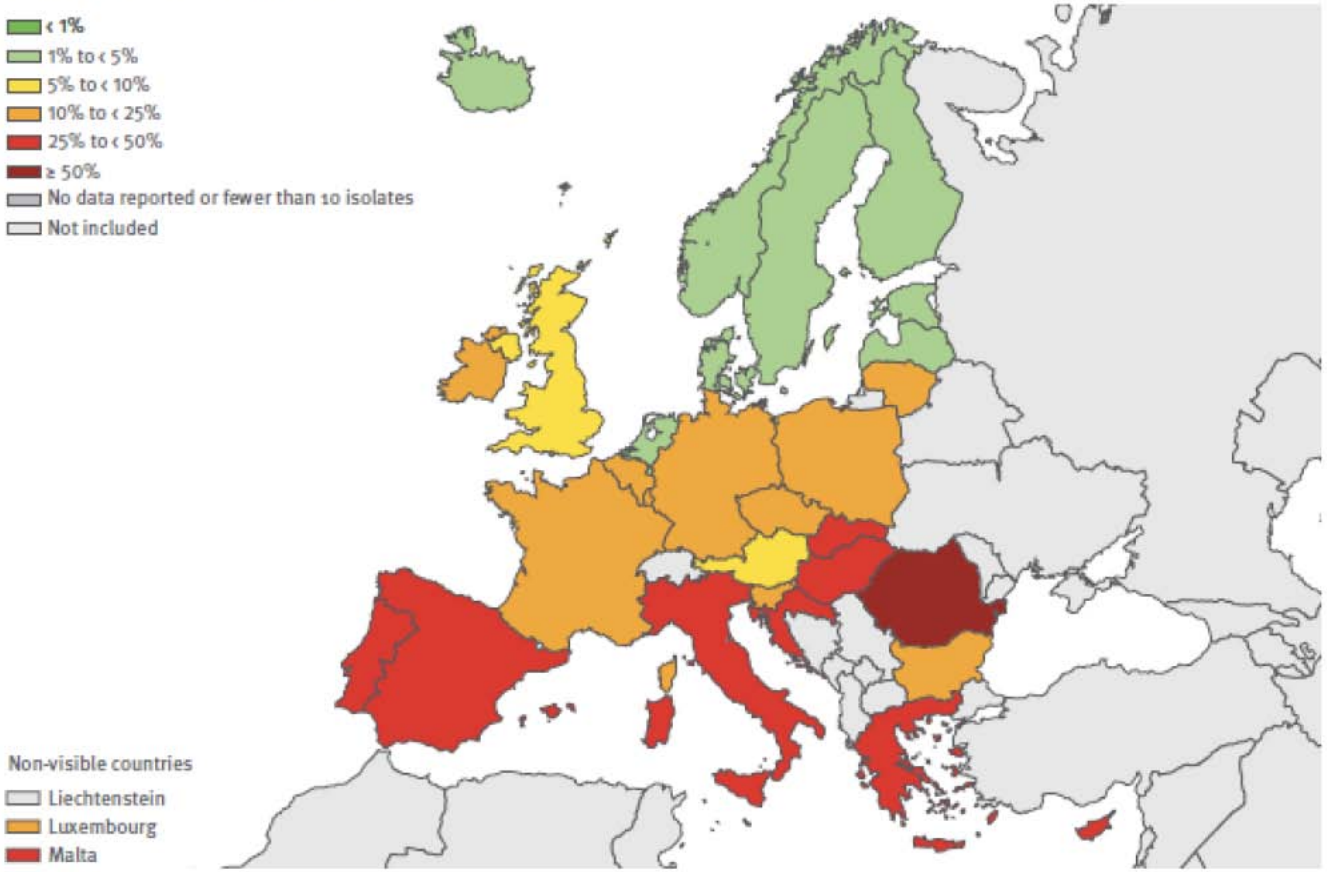
ΑΙΜΟΚΑΛΛΙΕΡΓΕΙΑ ΓΙΑ
STAPH AUREUS
ΘΕΤΙΚΗ



Προσθήκη ΛΙΝΕΖΟΛΙΔΗ 600mg/12h και μετά από 4 μέρες απυρεξία και την επόμενη αποσωλήνωση

MRSA. EARS, 2016

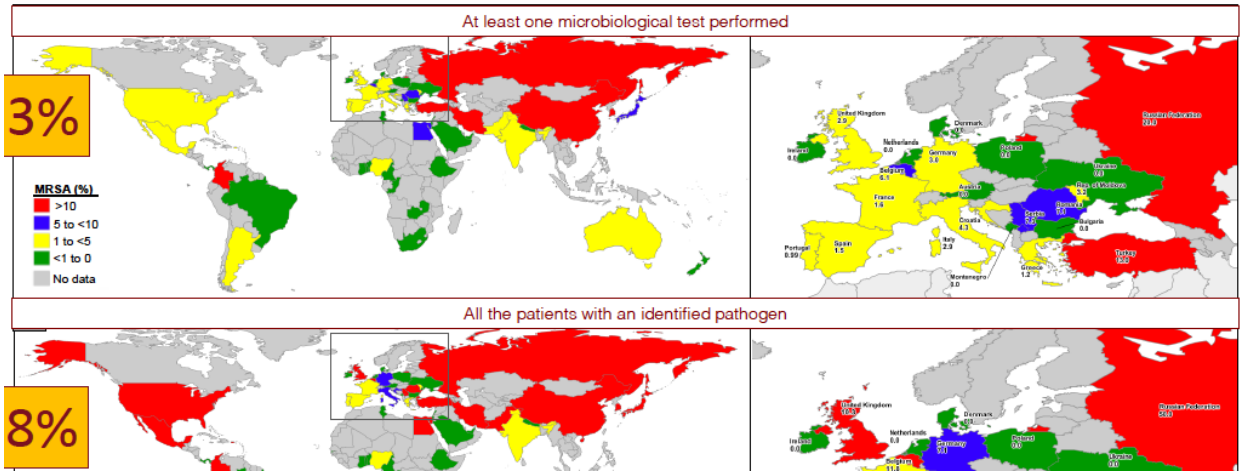
Figure 3.25. *Staphylococcus aureus*. Percentage (%) of invasive isolates with resistance to meticillin (MRSA), by country, EU/EEA countries, 2016



Global initiative for meticillin-resistant *Staphylococcus aureus* pneumonia (GLIMP): an international, observational cohort study

Lancet Infect Dis 2016

Stefano Aliberti, Luis F Reyes*, Paola Faverio, Giovanni Sotgiu, Simone Dore, Alejandro H Rodriguez, Nilam J Soni, Marcos I Restrepo, on behalf of the GLIMP investigators†*



ΕΠΙΠΤΩΣΗ MRSA

Global initiative for MRSA(GLIMP): an international, observational cohort study

Stefano Aliberti , Luis F Reyes , Paola Faverio , Giovanni Sotgiu , Simone Dore , Alejandro H Rodriguez , Nilam J Soni , Marcos I Restrepo , **GLIMP investigators**

- **METHODS**: International, multicentre study of community-dwelling, adult patients admitted to hospital with pneumonia who had microbiological tests taken within 24 h of presentation. We recruited investigators from 222 hospitals in 54 countries to gather point-prevalence data for all patients admitted with these characteristics during 4 days randomly selected during the months of March, April, May, and June in 2015.
- **RESULTS**: 3702 patients hospitalized with pneumonia were enrolled, with 3193 patients. 1173 (37%) had at least one pathogen isolated .
- The overall prevalence of confirmed MRSA pneumonia was 3·0% (n=95), with differing prevalence between continents and countries.
- Three risk factors were independently associated with MRSA pneumonia: previous MRSA infection or colonisation (OR 6·21, 95% CI 3·25-11·85), recurrent skin infections (2·87, 1·10-7·45), and severe pneumonia disease (2·39, 1·55-3·68).

LancetInfectDis.2016

Increased incidence of co-infection in critically ill patients with influenza

Ignacio Martin-Loeches[1,2*], Marcus J Schultz[3], Jean-Louis Vincent[4], Francisco Alvarez-Lerma[5], Lieuwe D. Bos[3], Jordi Solé-Violán[6], Antoni Torres[7] and Alejandro Rodriguez[8,9]

Intensive Care Med 2016

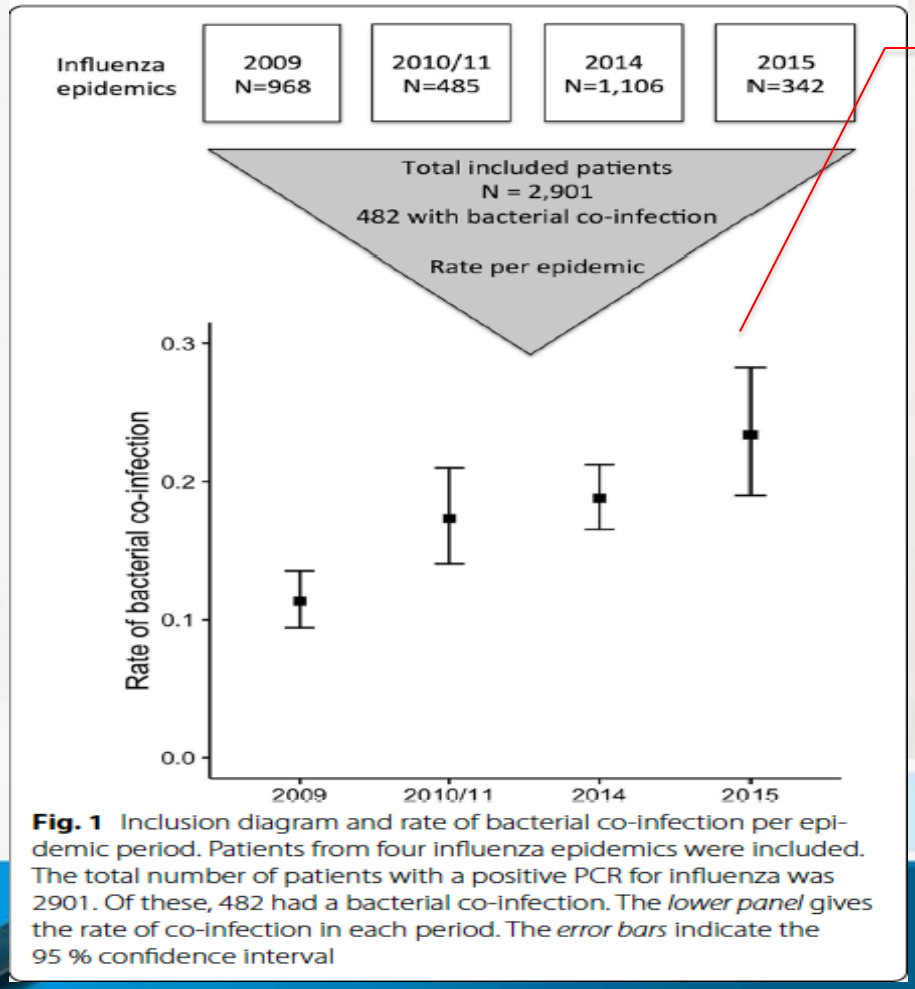


Fig. 1 Inclusion diagram and rate of bacterial co-infection per epidemic period. Patients from four influenza epidemics were included. The total number of patients with a positive PCR for influenza was 2901. Of these, 482 had a bacterial co-infection. The *lower panel* gives the rate of co-infection in each period. The *error bars* indicate the 95 % confidence interval

Staphylococcus aureus, Streptococcus pneum, and H. influenzae

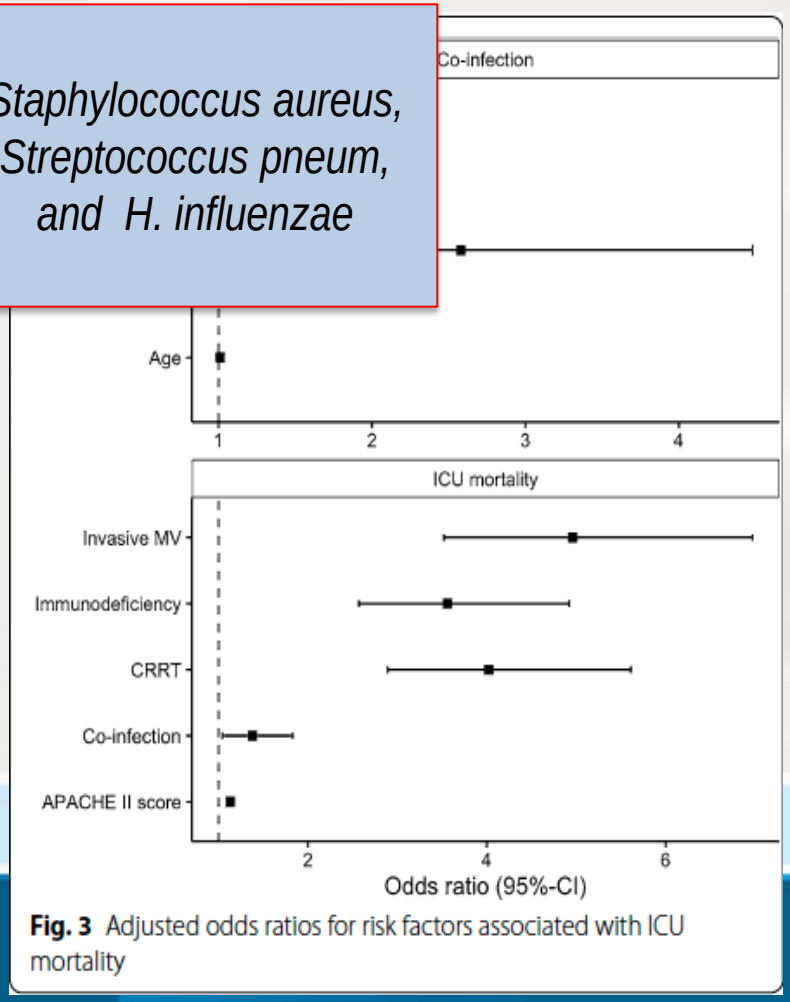


Fig. 3 Adjusted odds ratios for risk factors associated with ICU mortality

Community-Acquired Pneumonia Due to Pandemic A(H1N1)2009 Influenzavirus and Methicillin Resistant *Staphylococcus aureus* Co-Infection

Ronan J. Murray[1]*, James O. Robinson[2], Jodi N. White[3], Frank Hughes[3], Geoffrey W. Coombs[2], Julie C. Pearson[2], Hui-Leen Tan[2], Glenys Chidlow[1], Simon Williams[1], Keryn J. Christiansen[2], David W. Smith[1]

1 Division of Microbiology and Infectious Diseases, PathWest Laboratory Medicine WA, Queen Elizabeth II Medical Centre, Perth, Western Australia, Australia,

Methodology/Principal Findings: Patients with community–acquired pneumonia (CAP) caused by co-infection with pandemic A(H1N1)2009 influenzavirus and cMRSA were prospectively identified at two tertiary hospitals in one Australian city during July to September 2009, the period of intense influenza activity in our region. Detailed characterization of the cMRSA isolates was performed. 252 patients with pandemic A(H1N1)2009 influenzavirus infection were admitted at the two sites during the period of study. Three cases of CAP due to pandemic A(H1N1)2009/cMRSA co-infection were identified. The clinical features of these patients were typical of those with *S. aureus* co-infection or sequential infection following influenza. The 3 patients received appropriate empiric therapy for influenza, but inappropriate empiric therapy for cMRSA infection; all 3 survived. In addition, 2 fatal cases of CAP caused by pandemic A(H1N1)2009/cMRSA co-infection were identified on post–mortem examination. The cMRSA infections were caused by three different cMRSA clones, only one of which contained genes for Panton-Valentine Leukocidin (PVL).

PLoS ONE January 2010 | Volume 5 |

REVIEW

Polymicrobial community-acquired pneumonia: An emerging entity

CATIA CILLÓNIZ,[1] ROK CIVLJAK,[2] ANTONELLO NICOLINI[3] AND ANTONI TORRES[1]

- Colonization by *S. aureus* was associated with enhanced risk of decease in adults and children infected with influenza virus; in particular MRSA co-infection was associated with severe disease and death in adults .
- When a viral respiratory infection occurs, it damages the respiratory epithelium, thus increasing the adhesion of bacteria to the mucosa. In fact, it generates the expression of molecules, such as glycoproteins, on the infected host cell membrane used by bacteria as specific receptors, thereby contributing to bacterial adherence and the establishment of bacterial infection.
- Influenza virus reduces human nasal and tracheal epithelial ciliary function: the ciliary beat frequency is reduced and ciliary motion becomes uncoordinated resulting in decreased mechanical clearance of bacteria.

REVIEW

Polymicrobial community-acquired pneumonia: An emerging entity

CATIA CILLÓNIZ,[1] ROK CIVLJAK,[2] ANTONELLO NICOLINI[3] AND ANTONI TORRES[1]

- Moreover, several species of *S. aureus* secreted proteases that cleave influenza haemagglutinin, a step required for the normal cycle of viral replication and for the spread of the virus inside the host.

Respiratory viruses / Host interaction

<u>Induce alteration in epithelial cells</u>
- reduced ciliary function
- decreased epithelial barrier function
- upregulation of surface receptors for bacterial adhesion

<u>Virus-mediated compromised innate immune cells (lung macrophages, neutrophils)</u>
- suppressed phagocytosis
- impaired microbial killing
- depressed leukocyte migration

<u>Dysfunctional inflammatory response: acute lung injury</u>
- neutrophil influx
- cytokine storm

Question 12: In the Inpatient Setting, Should Adults with CAP Be Treated with Corticosteroids?

- ***Recommendation:*** We recommend **not** routinely using corticosteroids in adults with nonsevere CAP (*strong recommendation, high quality of evidence*).
- We suggest not routinely using corticosteroids in adults with severe CAP (*conditional recommendation, moderate quality of evidence)*.
- We suggest **not routinely using corticosteroids in adults with severe influenza** pneumonia (*conditional recommendation, low quality of evidence).*
- We endorse the Surviving Sepsis Campaign recommendations on the use of corticosteroids in patients with CAP and **refractory septic shock**

Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, Oct 1, 2019

QUESTION 16: In adults with CAP who are improving, should follow up chest imaging be obtained?

Σε ασθενείς με CAP ασυμπτωματικούς την 5η-7η μέρα, δεν προτείνουμε follow-up ακτινογραφία θώρακος (*conditional recommendation, low quality of evidence*).

Am J Respir Crit Care Med Vol 200, Iss 7, pp e45–e67, 2019

ΕΥΧΑΡΙΣΤΩ