

# Top Ten Publications in SARI: Where do We Stand in 2012

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## First influenza season after the 2009 pandemic influenza: characteristics of intensive care unit admissions in adults and children in Vall d'Hebron Hospital

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Clin Microbiol Infect 2011

- **Observational prospective study**
  - Comparing September 2009-January 2010 with September 2010-January 2011
  - Patients admitted to the ICU

# Main Differences

## n=53 (38 adults, 15 children)

|                                                 | 2009-2010 | 2010-2011 | p     |
|-------------------------------------------------|-----------|-----------|-------|
| Mean age, children                              | 7         | 0.8       | 0.05  |
| Pneumonia                                       | 56.5%     | 83.3%     | <0.05 |
| Resp. symptoms w/o opacities                    | 39.1%     | 6.7%      | <0.05 |
| Acute exacerb. COPD or bronchitis/bronchiolitis | 21.7%     | 3.3%      | <0.05 |
| SOFA >5                                         | 9.1%      | 43.8%     | <0.05 |
| APACHE II >10                                   | 36.4%     | 75%       | <0.05 |
| Pao <sub>2</sub> /Fio <sub>2</sub> <100 mHg     | 35%       | 68.8%     | <0.05 |

# Outcomes and Risk Factors

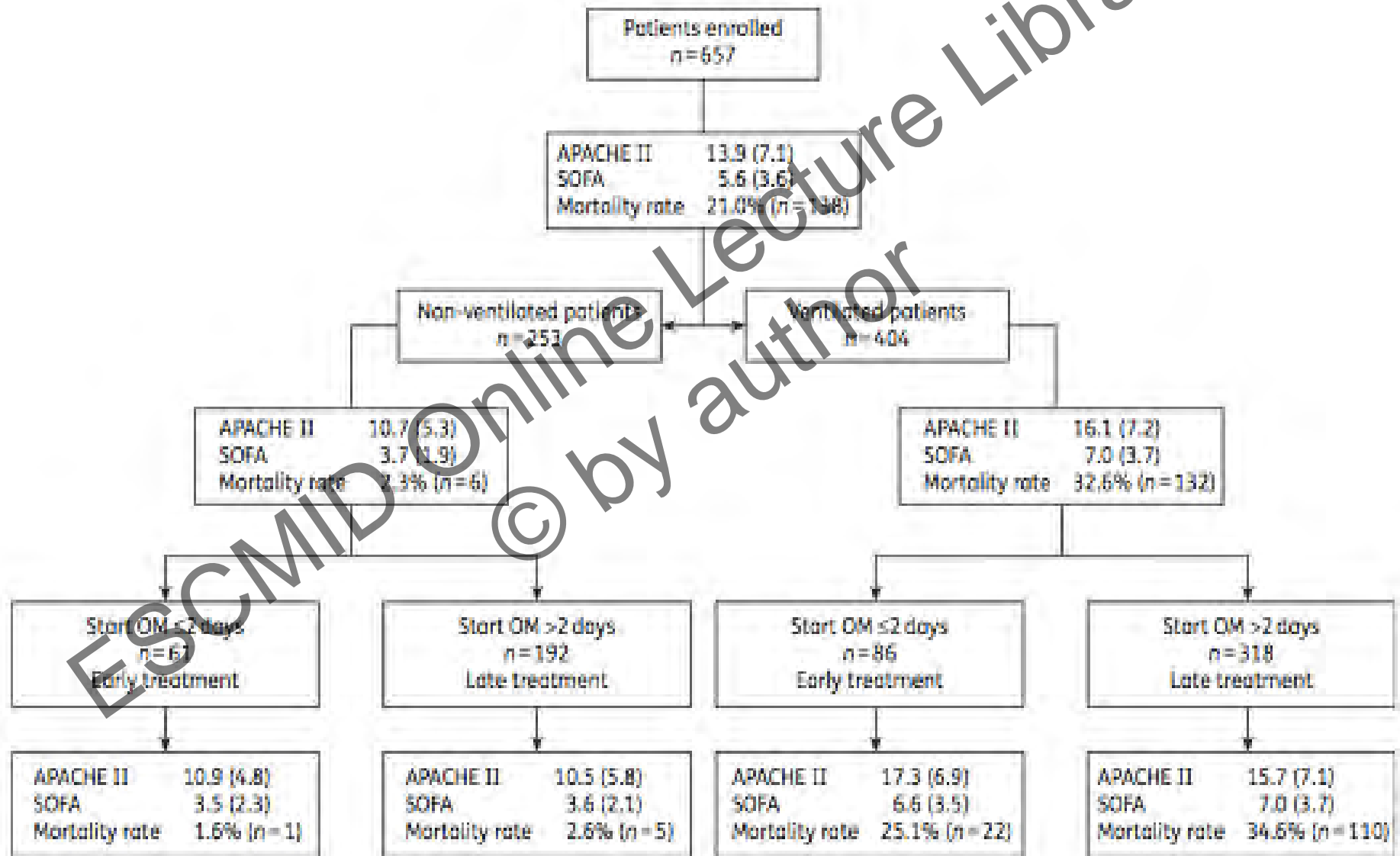
- **No difference**
  - ICU mortality
  - Hospital stay
  - Days of mechanical ventilation
- **Obesity frequency increased**
  - 13.3% vs 21.7%
- **Pregnancy**
  - 41.7% ICU admitted women
- **Vaccination**
  - 0% vs 4.3%
- **Treatment**
  - Less steroids and more azithromycin in 2010-2011

## **Impact of early oseltamivir treatment on outcome in critically ill patients with 2009 pandemic influenza A**

Alejandro Rodríguez<sup>1\*</sup>, Emili Díaz<sup>1</sup>, Ignacio Martín-Loeches<sup>1</sup>, Alberto Sandiumenge<sup>1</sup>, Laura Canadell<sup>2</sup>, Juan J. Díaz<sup>3</sup>, Juan C. Figueira<sup>4</sup>, Asunción Marques<sup>5</sup>, Francisco Álvarez-Lerma<sup>6</sup>, Jordi Vallés<sup>7</sup>, Bárbara Baladín<sup>8</sup>, Fernando García-López<sup>9</sup>, Borja Suberviola<sup>10</sup>, Rafael Zaragoza<sup>11</sup>, Sandra Trefler<sup>12</sup>, Juan Bonastre<sup>13</sup>, José Blanquer<sup>14</sup> and Jordi Rello<sup>12</sup> on behalf of the H1N1 SEMICYUC Working Group†

- **148 ICUs in Spain, April-December 2009**
- **657 patients with H1N1 2009 infection**
- **Early treatment with oseltamivir ( $\leq 2$  days) vs late treatment groups compared**

# Characteristics of Patients Enrolled in the Study



# Mechanically Ventilated (MV) Patients with Effective Therapy

- 385 MV patients with >4 doses of oseltamivir
- Median duration of tx 10 days
  - 79 (20.5%) early therapy (ET)
  - 306 late therapy (LT)
- Mortality higher in LT (34.3% vs 21.5%, OR:1.9, 95% CI 1.06-3.41)
  - ICU stay, hospital stay, MV days significantly longer in LT
- In multivariate model ET independently associated with reduced ICU mortality



# Severe 2009 A/H1N1v influenza in pregnant women in Spain\*

Enrique Maraví-Poma, MD, PhD, HonProf, FCCS, ERC, FCCM; Ignacio Martín-Loeches, MD, PhD; Eva Regidor, MD; Clara Laplaza, MD; Koldo Cambra, MSc, PhD; Sara Aldunate, MD; Jose Eugenio Guerrero, MD; Ana Loza-Vazquez, MD; Elena Arnau, MD; Jordi Almirall, MD; Leonardo Lorente, MD, PhD; Angel Arenzana, MD; Monica Magret, MD; Roberto Reig Valero, MD; Enrique Marquez, MD; Nagore Gonzalez, MD, PhD; Jesús Francisco Bermejo-Martin, MD, PhD; Jordi Rello, MD, PhD; Grupo Español de Trabajo de Gripe Grave A (SEMICYUC)

**Crit Care Med 2011;39:945**

- **148 Spanish ICU, April 2009-February 2010**
- **234 women in reproductive age**
  - **50 (21.4%) pregnant**
  - **7 deaths (14%) in pregnant vs 22 (12%) in non-pregnant**
  - **Viral pneumonia more frequent in pregnant woman (OR:4.9)**
  - **Lowest rate in those with antiviral tx within 48h symptom onset (63.6% vs 82.6%, p=0.03)**
    - » **Only 14% pregnant women received early tx**



## **Community-acquired respiratory coinfection in critically ill patients with pandemic 2009 influenza A(H1N1) virus.**

Martín-Loeches I, Sanchez-Corral A, Diaz E, Granada RM, Zaragoza R, Villavicencio C, Albaya A, Cerdá E, Catalán RM, Luque P, Paredes A, Navarrete I, Rello J, Rodríguez A; H1N1 SEMICYUC Working Group.

- **645 ICU patients with SARI**
- **Co-infection in 113 (17.5%)**
  - **55% *S. pneumoniae***
  - **Older (47.5 ± 15.7 vs 43.8 ± 14.2, p<0.05)**
  - **Higher APACHE II and SOFA scores**
  - **More patients with**
    - » **Vasopressors (64% vs 39%)**
    - » **MV (69% vs 59%)**
    - » **3 days longer ICU stay**
  - **Increased ICU mortality (26% vs 16%, not significant with Cox RA)**

## **Early corticosteroids in severe influenza A/H1N1 pneumonia and acute respiratory distress syndrome.**

Brun-Buisson C, Richard JC, Mercat A, Thiébaud AC, Brochard L; REVA-SRLF A/H1N1v 2009 Registry Group.

### **Collaborators (122)**

Université Paris Est-Créteil and INSERM U955, Créteil, France. christian.brun-buisson@hmn.aphp.fr

- **208 patients with H1N1 2009 and ARDS**
  - 83 (40%) received steroids (median eq. 270 mg hydrocortisone/d, median 11 d)
  - Steroid tx associated with higher mortality
    - » Crude analysis; 33.7% vs 16.8%, p=0.004
    - » MV analysis: HR, 2.82, p=0.002
  - Steroid tx  $\leq 3$  d of MV caused higher mortality
  - More acquired pneumonia
  - A trend to a longer MV

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

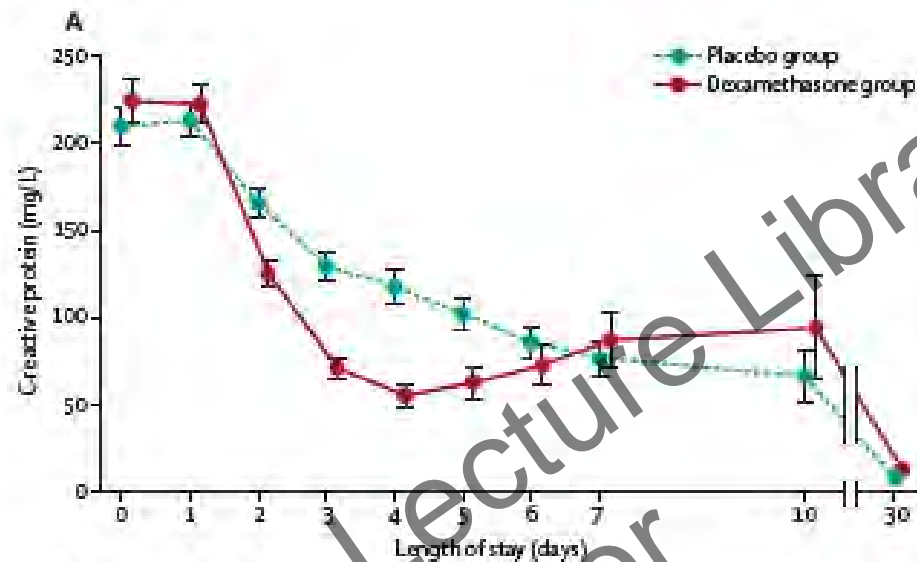
Sabine C A Meijvis, Hans Hardeman, Hilde H F Remmelts, Rik Heijlbergen, Ger T Rijkers, Hellen van Velzen-Blad, G Paul Voorn, Ewoudt M W van de Garde, Henrik Endeman, Jan C Grutters, Willem Jan W Bos, Douwe H Biesma

**Lancet 2011;377:2023**

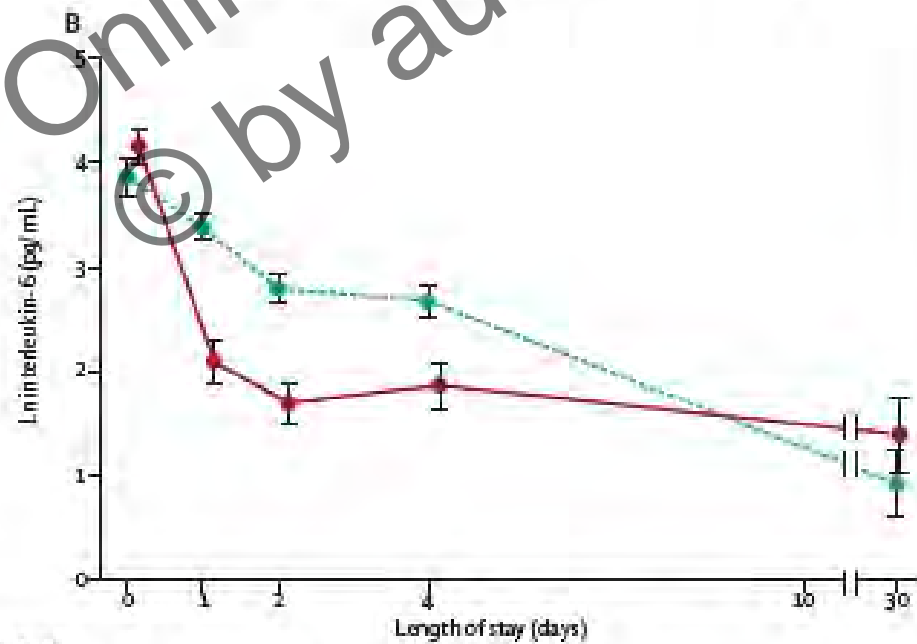
- **Double blind, placebo controlled trial, 2007-2010 in Netherlands**
- **>18, adults with CAP**
  - Patients with immunosuppression or requiring immediate transfer to ICU excluded
- **5 mg, iv, od dexamethasone for 4 d vs placebo**
- **304 patients**
  - 153 placebo, 151 dexa group
- **143 (47%) had a PSI class 4-5**
  - 64 placebo, 79 dexa group

# Results

- Median length of stay 6.5 days in dexta vs 7.5 days ( $p=0.048$ )
- No difference
  - In hospital mortality (5% in each arm)
  - ICU admission (5% vs 7%,  $p=0.47$ )
  - Readmission in 30 d (5% in each arm)
- Hyperglycemia
- 44% in dexta vs 23% in placebo ( $p<0.0001$ )



| Number at risk      |  | 0   | 1   | 2   | 3   | 4   | 5  | 6  | 7  | 10 | 30  |
|---------------------|--|-----|-----|-----|-----|-----|----|----|----|----|-----|
| Placebo group       |  | 153 | 141 | 135 | 131 | 104 | 84 | 75 | 53 | 39 | 112 |
| Decamethasone group |  | 151 | 130 | 125 | 121 | 91  | 70 | 49 | 33 | 23 | 115 |



| Number at risk      |  | 0   | 1   | 2   | 4  | 10 | 30 |
|---------------------|--|-----|-----|-----|----|----|----|
| Placebo group       |  | 146 | 127 | 118 | 88 | 45 | 45 |
| Decamethasone group |  | 133 | 93  | 80  | 75 | 36 | 36 |



# Conclusions

- **Faster decline in CRP and IL-6 in dexamethasone group is in accordance with reduced inflammatory response**
- **Benefits with dexamethasone must be weighed against potential side effects**

## Marked Reduction in 30-Day Mortality Among Elderly Patients with Community-acquired Pneumonia

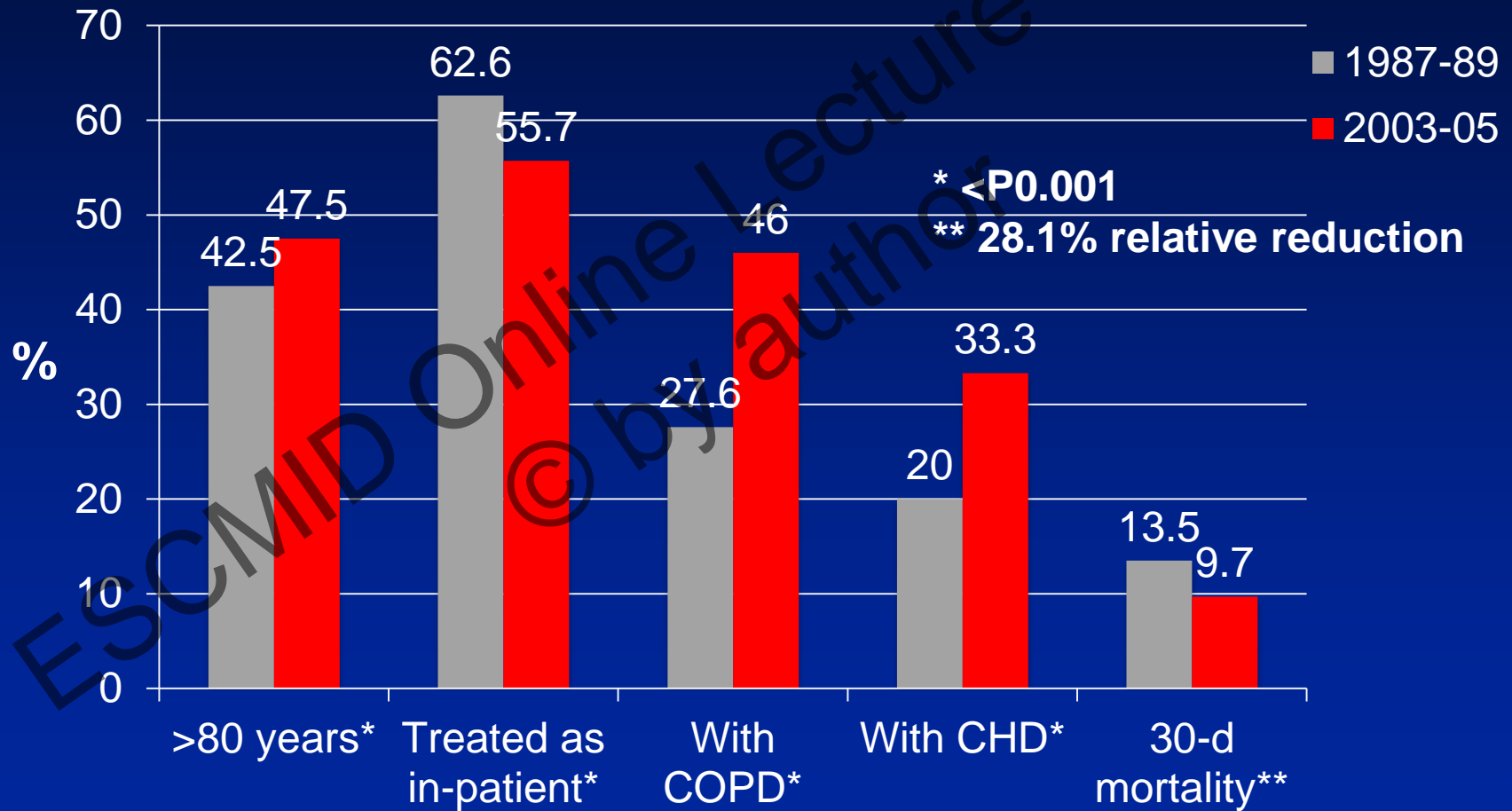
Gregory W. Ruhnke, MD, MS, MPH,<sup>a</sup> Marcelo Coca-Perraillon, MA,<sup>b</sup> Barrett T. Kitch, MD, MPH,<sup>c,d</sup> David M. Cutler, PhD<sup>b,e</sup>

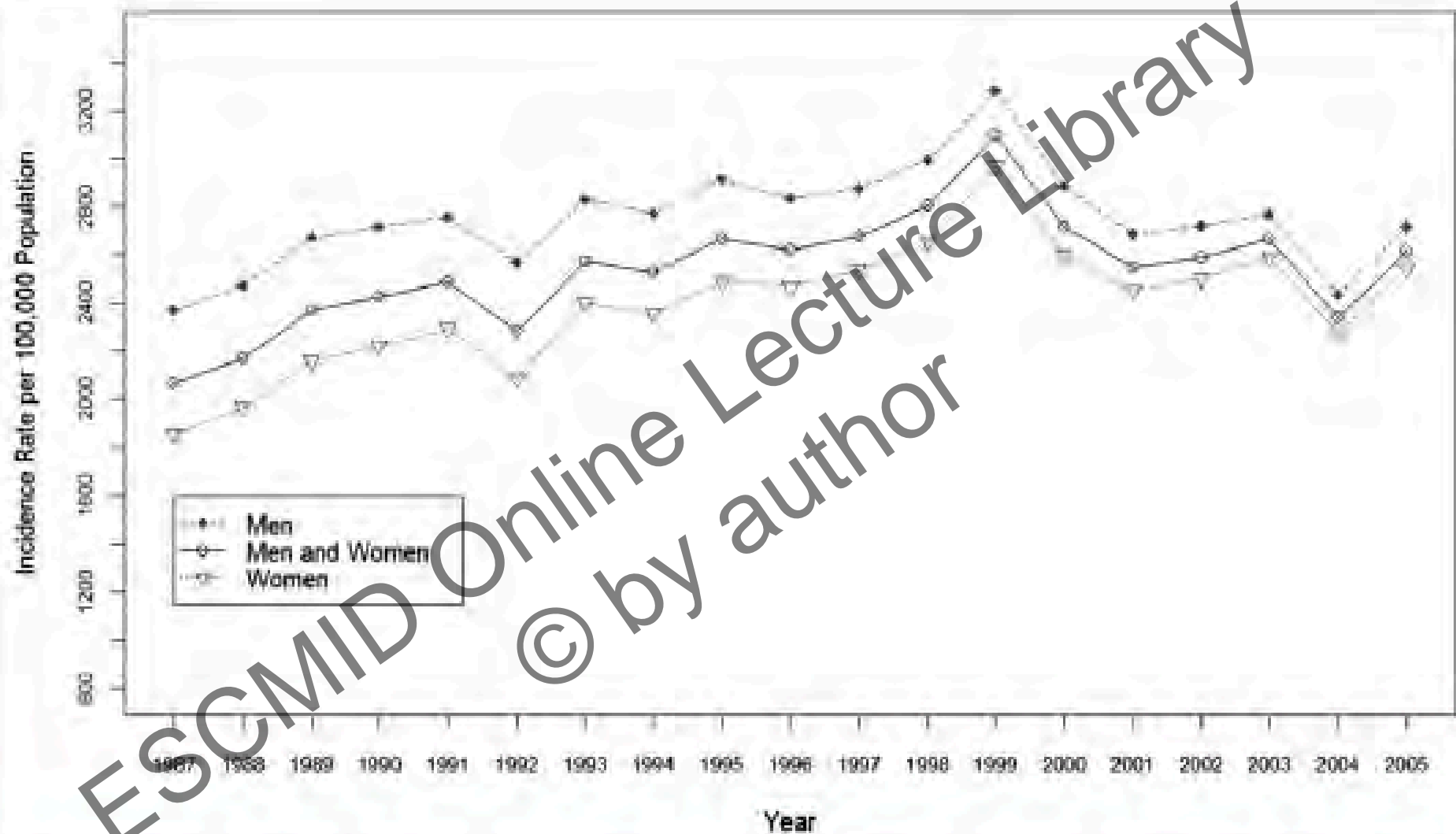
<sup>a</sup>Section of Hospital Medicine, University of Chicago, Ill; <sup>b</sup>National Bureau of Economic Research, Cambridge, Mass; <sup>c</sup>Mongan Institute for Health Policy, Massachusetts General Hospital, Boston; <sup>d</sup>North Shore Medical Center, Salem, Mass; <sup>e</sup>Harvard University, Cambridge, Mass.

Am J Med 2011;124:171

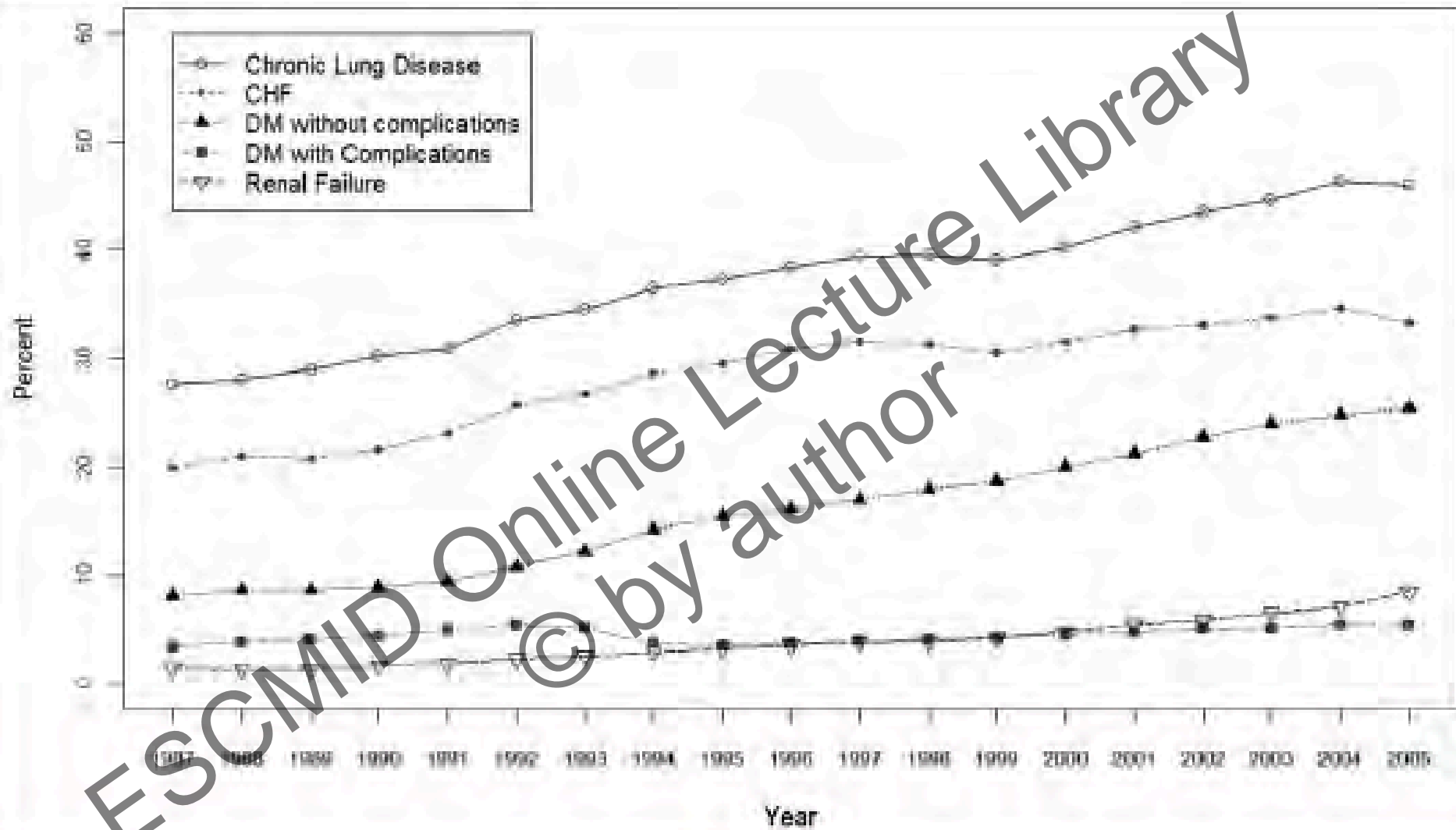
- Medicare claims to identify pneumonia
  - 2.654.955 cases between 1987-2005
  - A random sample of 20% aged >65 years
  - Incidence, co-morbidities, 30-day mortality

# Results



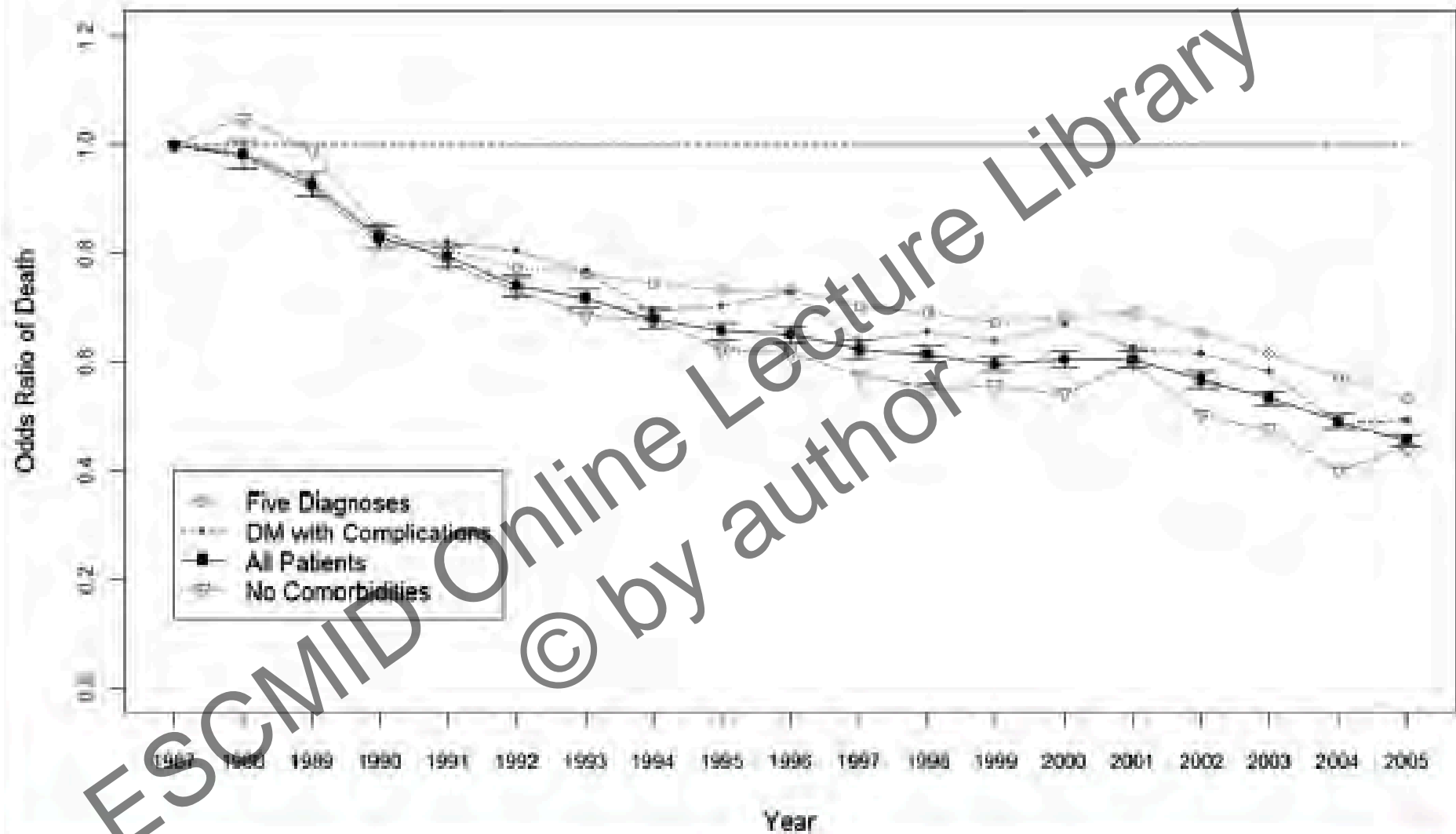


**Figure 1** Standardized incidence of community-acquired pneumonia among elderly adults. Trends for men and women are standardized for age. Trends for the combined sample are standardized to the sex and age distribution of the elderly Medicare population in the year 2000.



**Figure 2** Trends in the frequency of selected comorbid conditions among inpatients and outpatients diagnosed with community-acquired pneumonia. CHF = congestive heart failure; DM = diabetes mellitus.





**Figure 4** Multivariate-adjusted mortality trends. This figure shows the odds ratio of death 30 days after a diagnosis of community-acquired pneumonia in each year relative to reference year 1987. DM = diabetes mellitus.

# Conclusions

- Incidence of CAP increased as has
  - Proportion of  $\geq 80$  years
  - Frequency of comorbidities
- 30-d mortality markedly reduced in elderly after adjustment of comorbidities
- Vaccination and guideline – concordant antibiotics may be responsible for such decrease

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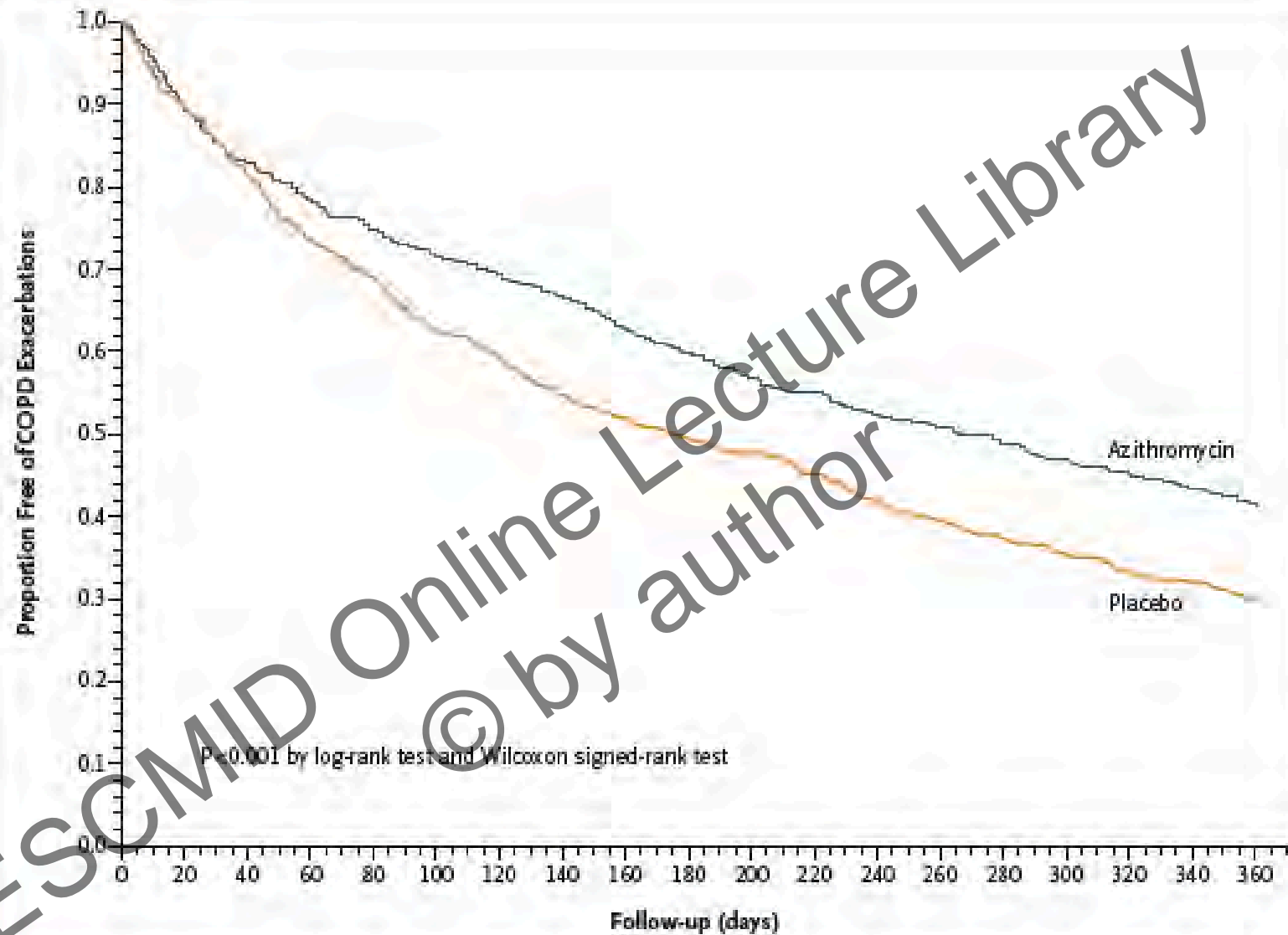
## Azithromycin for Prevention of Exacerbations of COPD

Richard K. Albert, M.D., John Connett, Ph.D., William S. Bailey, M.D., Richard Casaburi, M.D., Ph.D., J. Allen D. Cooper, Jr., M.D., Gerard J. Criner, M.D., Jeffrey L. Curtis, M.D., Mark T. Dransfield, M.D., MeiLan K. Han, M.D., Stephen C. Lazarus, M.D., Barry Make, M.D., Nathaniel Marchetti, M.D., Fernando J. Martinez, M.D., Nancy E. Madinger, M.D., Charlene McEvoy, M.D., M.P.H., Dennis E. Niewoehner, M.D., Janos Porsasz, M.D., Ph.D., Connie S. Price, M.D., John Reilly, M.D., Paul D. Scanlon, M.D., Frank C. Scuba, M.D., Steven M. Scharf, M.D., Ph.D., George R. Washko, M.D., Prescott G. Woodruff, M.D., M.P.H., and Nicholas R. Anthonisen, M.D., for the COPD Clinical Research Network

- **Prospective, placebo controlled, randomized trial in patients with COPD**
  - **To determine whether azithromycin (AZ) will decrease the frequency of acute attacks**

# Results

- In addition to usual treatment
  - 259 mg AZ / d for one year in 570 patients
  - Placebo in 572 patients
- One year follow-up 89% in AZ group and 90% in placebo
- Median time to exacerbation
  - 266 days in AZ
  - 174 days in placebo ( $p < 0.001$ )
- The frequency of exacerbation
  - 1.48 per year vs 1.83 ( $P = 0.001$ )
- Hearing decrements more frequent in AZ group
  - 25% vs 20% ( $p < 0.04$ )
- More R bacterial colonization in AZ group



**Figure 2.** Proportion of Participants Free from Acute Exacerbations of Chronic Obstructive Pulmonary Disease (COPD) for 1 Year, According to Study Group.

The analyses were based on the participants who were randomly assigned to the group minus those who did not return for any follow-up assessment — 558 participants in the azithromycin group, of whom 317 (57%) had an acute exacerbation, and 559 in the placebo group, of whom 380 (68%) had an acute exacerbation.



# Understanding the potential role of statins in pneumonia and sepsis\*

Sachin Yende, MD, MS; Eric B. Milbrandt, MD, MPH; John A. Kellum, MD; Lan Kong, PhD;  
Russell L. Delude, PhD; Lisa A. Weissfeld, PhD; Derek C. Angus, MD, MPH

Crit Care Med 2011;39:1871

- **28 US emergency department**
- **1895 patients hospitalized for CAP**
- **Comparisons**
  - **Prior statin use before admission vs no prior use**
  - **Prior statin users who continue to use in hospital vs no prior use or no in-hospital use**

# Results

- No difference in severe sepsis risk in both cohorts
- 90-d mortality was lower in continued statin users
  - After adjustment with patient characteristics and propensity for statin use, no mortality difference
- No difference in coagulation, inflammatory or lymphocyte surface markers

## **Recombinant tissue factor pathway inhibitor in severe community-acquired pneumonia: a randomized trial.**

Wunderink RG, Laterre PF, Francois B, Perrotin D, Artigas A, Vidal LO, Lobo SM, Jhan JS, Hwang SC, Dugemier T, LaRosa S, Wittebole X, Dhainaut JE, Doig C, Mendelson MH, Zwingelstein C, Su G, Opal S; CAPTIVATE Trial Group.

- **Tifacogin shown to provide mortality benefit in sCAP subgroup of a previous sepsis trial**
- **Multicenter, randomized, placebo-controlled, double-blind, 3-arm study**
  - 2005-2008, in 188 centers in 5 continents
  - Continuous infusion of tifacogin 0.025 or 0.075 mg/kg/h or placebo over 96 h

# Results

- 2138 randomized patients (946, 238, 918 patients)
  - Higher dose tificogin discontinued during the 1<sup>st</sup> interim analysis
- 28 d mortality was similar in both low-dose tificogin and placebo groups (18% vs 17.9%)
- Adverse and serious adverse events was similar

**THANK YOU...**

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