

**70**<sup>o</sup> Congresso  
Nazionale



**Noi, orgogliosamente  
Medici di Famiglia**  
fiducia innovazione  
competenza organizzazione

**6 - 11 ottobre 2014**

Forte Village  
Santa Margherita di Pula

**#orgogliosamentemmg**

# Epidemiologia, fattori di rischio e gestione del paziente

**FRANCESCO DE BLASIO, MD, FCCP**

**U.F. PNEUMOLOGIA E**

**RIABILITAZIONE RESPIRATORIA**

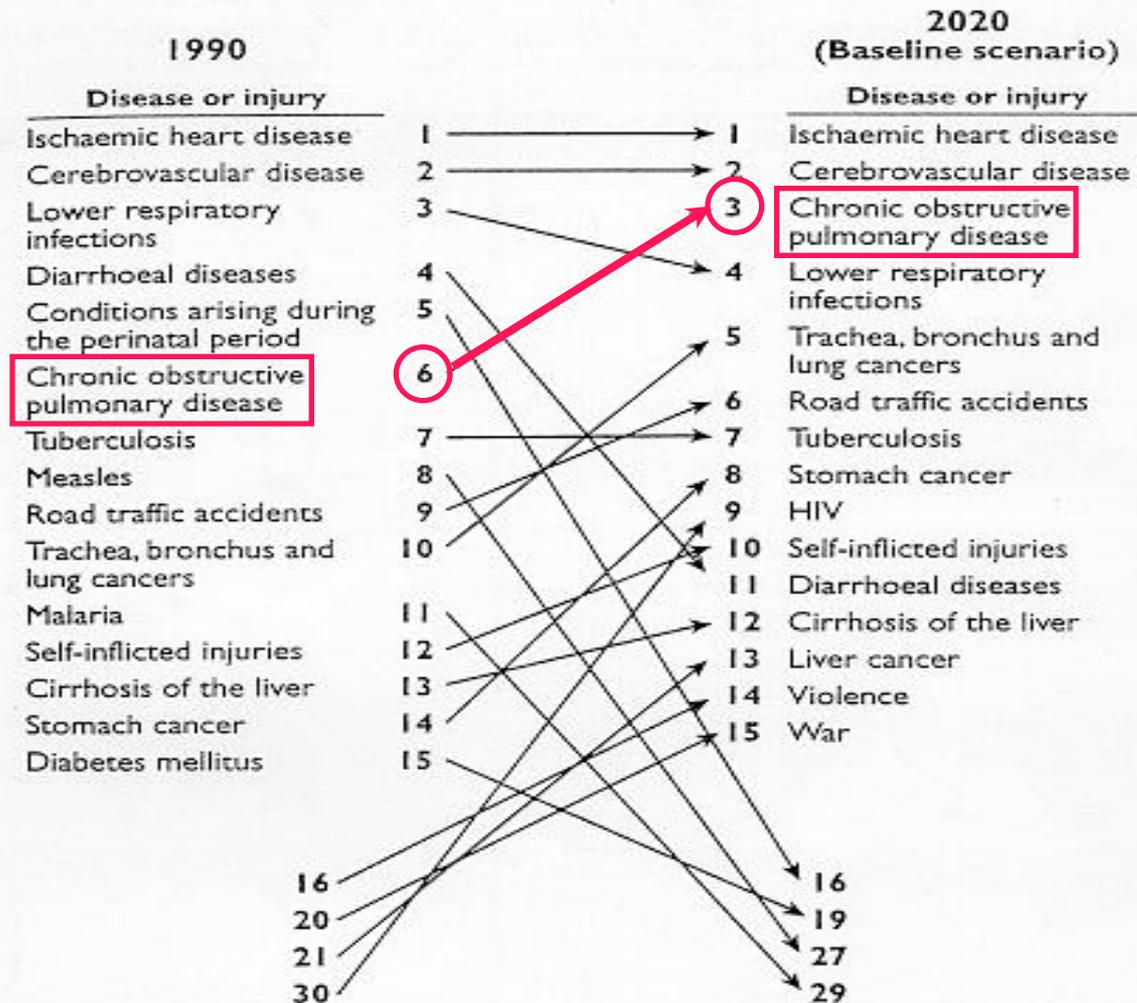
**CASA DI CURA CLINIC CENTER S.P.A. - NAPOLI**

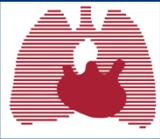
**Disclosures:**

**Il Dr. De Blasio ha ricevuto un grant educativo  
non condizionato da parte di Pfizer**



Change in rank order of deaths for the 15 leading causes, world, 1990–2020

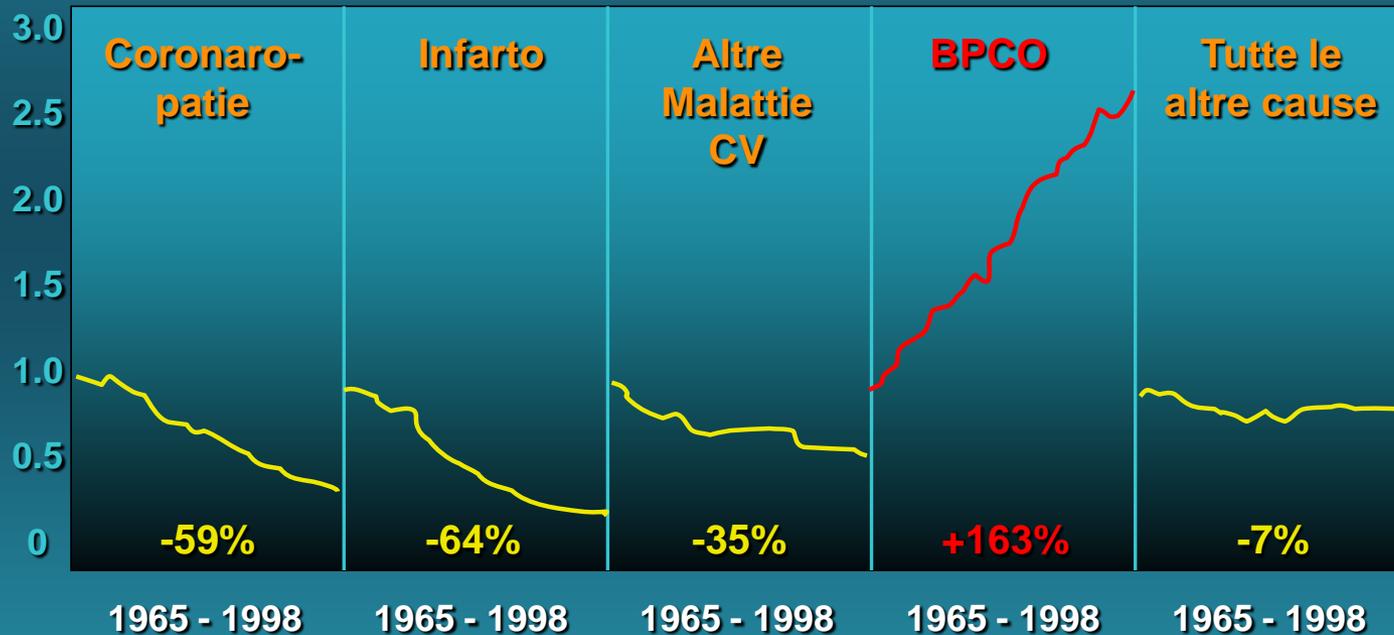




## VARIAZIONE PERCENTUALE DELLE MORTI PER ETA' IN U.S.A.



Proporzione della frequenza del 1965





ERS

EUROPEAN  
RESPIRATORY  
SOCIETY



EUROPEAN LUNG  
*white book*

RESPIRATORY HEALTH AND DISEASE IN EUROPE



european respiratory society every breath counts



ERS

EUROPEAN  
RESPIRATORY  
SOCIETY



“

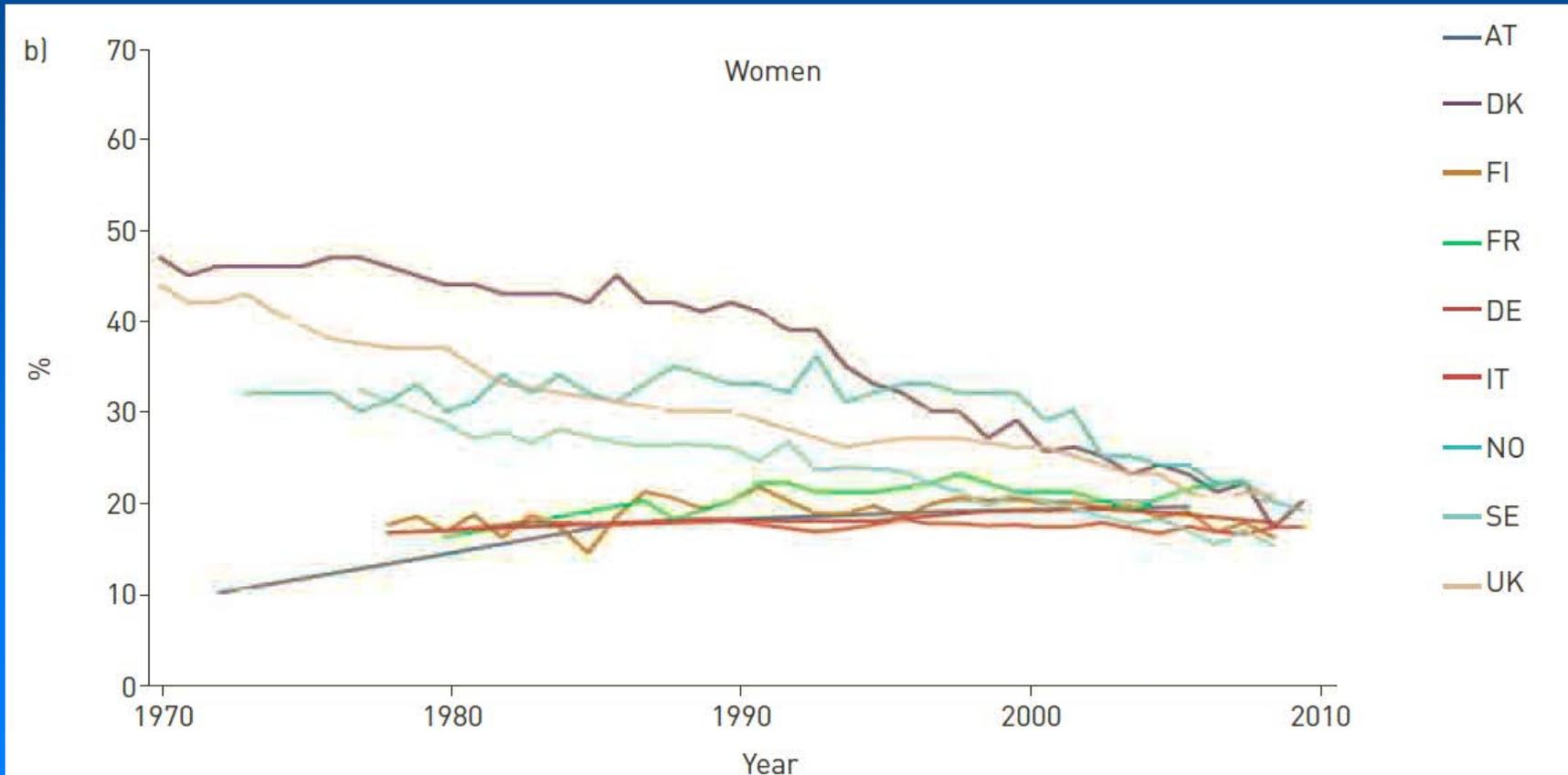
*Each year in EU28 countries, lung diseases cause two-thirds of a million deaths, and at least 6 million hospital admissions, accounting for over 43 million in-patient bed-days*

”



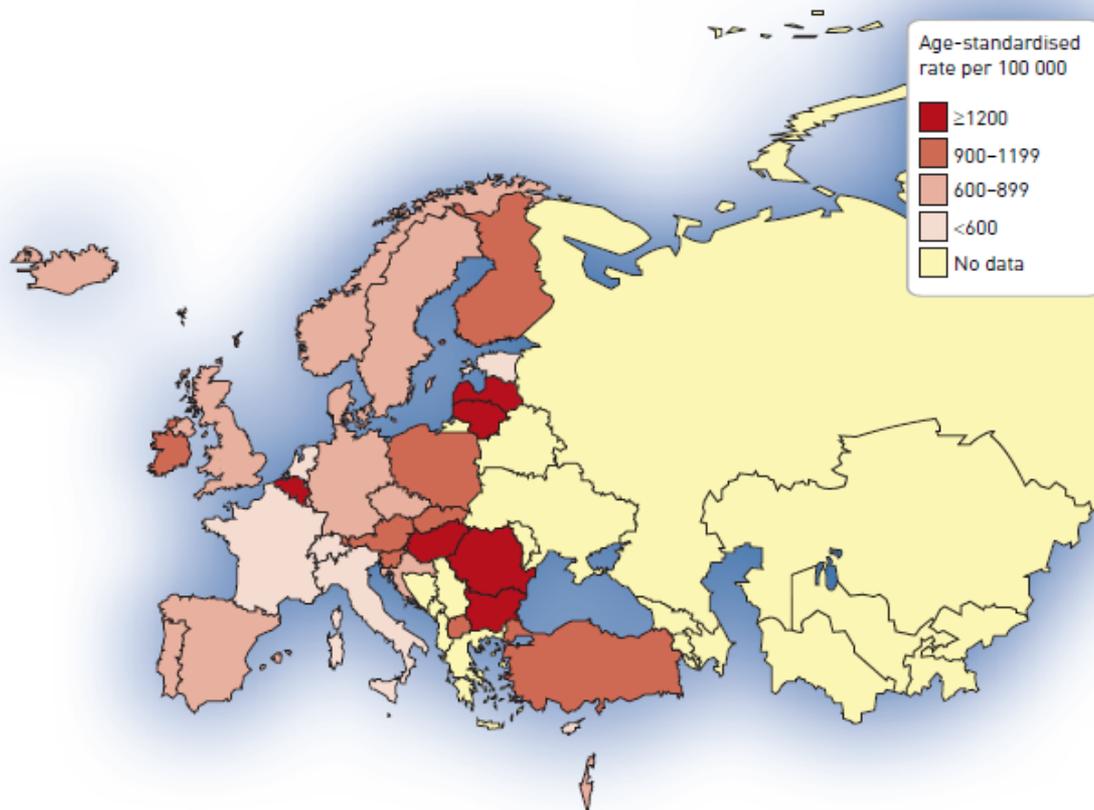


# ABITUDINE AL FUMO





# RICOVERI



**Figure 6** – Age-standardised admission rates for all respiratory conditions. The figure shows International Short Hospital Mortality Tabulation (HMT) categories only (as these are covered by both data sources, giving a wider comparable set of countries). Combined rates are shown for asthma, COPD, bronchiectasis, acute lower respiratory infections, pneumonia, lung cancer, tuberculosis and pulmonary vascular disease. Source: World Health Organization Hospital Morbidity Database (October 2011 update) and Eurostat (March 2012 update).



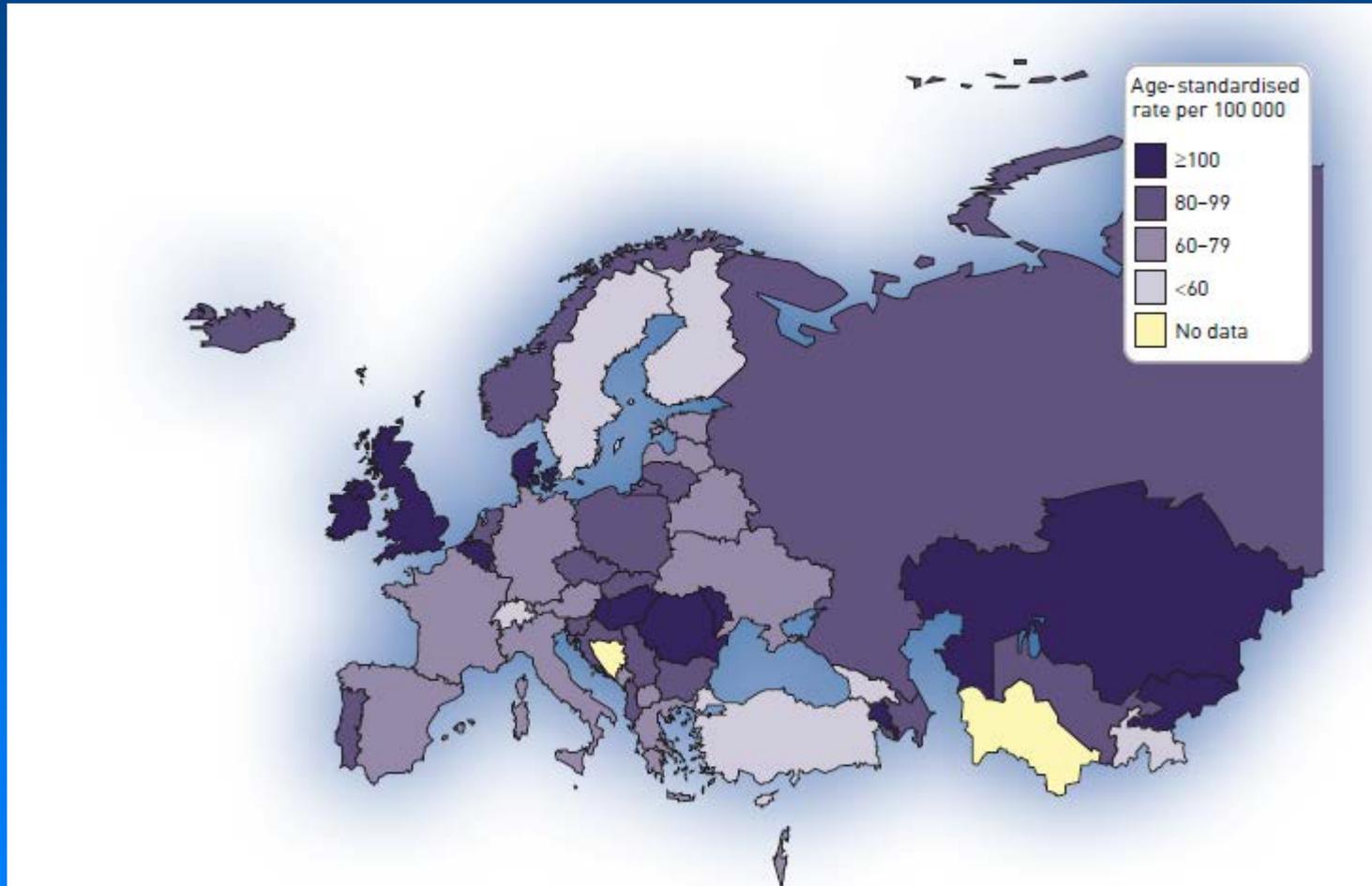
# MORTALITA'



Deaths attributed to	Worldwide	WHO European Region
Ischaemic heart disease	7.3 million (12.8%)	2.40 million (24.7%)
Cerebrovascular disease	6.2 million (10.8%)	1.40 million (14.0%)
<b>Lower respiratory infections</b>	<b>3.5 million (6.1%)</b>	<b>0.23 million (2.3%)</b>
<b>COPD</b>	<b>3.3 million (5.8%)</b>	<b>0.25 million (2.5%)</b>
Diarrhoeal diseases	2.5 million (4.3%)	0.03 million (0.3%)
HIV/AIDS	1.8 million (3.1%)	0.08 million (0.8%)
<b>Trachea/bronchus/lung cancer</b>	<b>1.4 million (2.4%)</b>	<b>0.38 million (3.9%)</b>
<b>Tuberculosis</b>	<b>1.3 million (2.4%)</b>	<b>0.08 million (0.8%)</b>
Diabetes mellitus	1.3 million (2.2%)	0.17 million (1.7%)
Road traffic accidents	1.2 million (2.1%)	0.12 million (1.2%)



# MORTALITA'



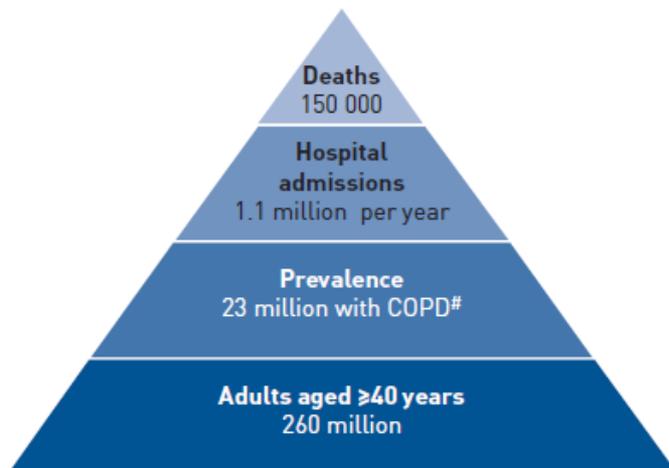
**Figure 1** – Map of age-standardised mortality rates for all respiratory conditions. Source: World Health Organization World and Europe Detailed Mortality Databases, November 2011 update.



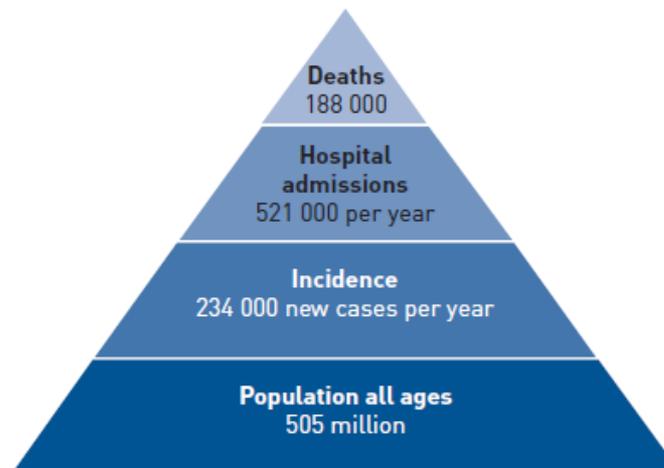
# BPCO - TUMORI - TBC



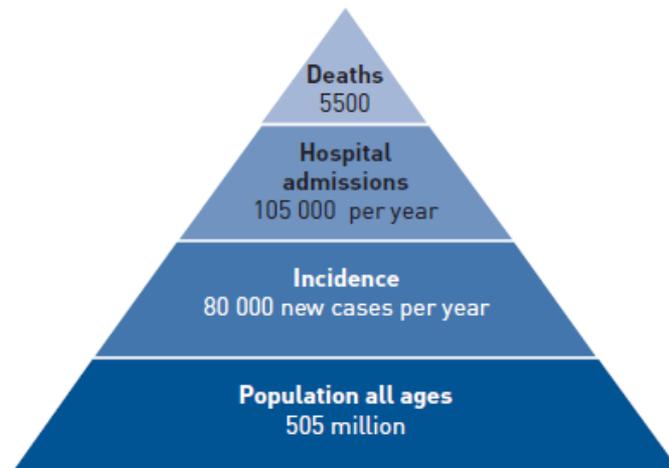
c) COPD in older adults



d) Lung cancer



e) Tuberculosis





# PROSPETTIVE



<b>Percentage of deaths worldwide</b>	<b>2008</b>	<b>2015</b>	<b>2030</b>
Lower respiratory infections	6.1	5.5	4.2
COPD	5.8	6.6	8.6
Trachea/bronchus/lung cancer	2.4	2.8	3.4
Tuberculosis	2.4	1.6	3.4
<b>Percentage of deaths in WHO European region</b>	<b>2008</b>	<b>2015</b>	<b>2030</b>
Lower respiratory infections	2.3	2.2	1.9
COPD	2.5	2.7	3.2
Trachea/bronchus/lung cancer	3.9	3.9	4.1
Tuberculosis	0.8	0.7	0.4

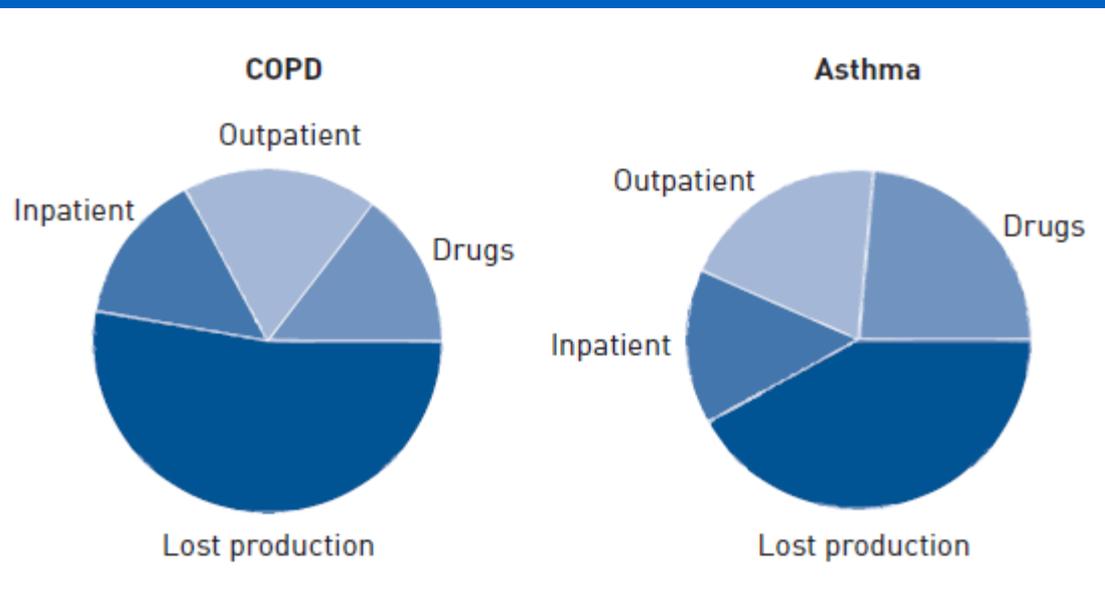
<b>Percentage of DALYs worldwide</b>	<b>2008</b>	<b>2015</b>	<b>2030</b>
Lower respiratory infections	5.4	4.6	3.2
COPD	2.3	2.7	3.8
Trachea/bronchus/lung cancer	0.9	1.0	1.4
Tuberculosis	2.0	1.6	1.1
<b>Percentage of DALYs in WHO European region</b>	<b>2008</b>	<b>2015</b>	<b>2030</b>
Lower respiratory infections	1.5	1.3	1.0
COPD	2.0	2.0	2.2
Trachea/bronchus/lung cancer	2.2	2.2	2.6
Tuberculosis	1.2	1.1	0.6



# COSTI



	Drug cost	Outpatient cost	Inpatient cost	Total direct#	Total indirect¶
COPD	7.1	8.9	7.3	23.3	25.1
Asthma	8.0	6.7	4.8	19.5	14.4





# COSTI



	Direct costs <sup>#</sup> € bn	Indirect costs <sup>¶</sup> € bn	Monetised value of DALYs lost € bn	Total costs € bn
COPD	23.3	25.1	93.0	141.4
Asthma	19.5	14.4	38.3	72.2
Lung cancer	3.35	NA	103.0	106.4
TB	0.54 <sup>#</sup>	#	5.37	5.9
OSAS	5.2	1.9	NA	7.1
Cystic fibrosis	0.6	NA	NA	0.6
Pneumonia/ALRI	2.5	NA	43.5	46.0
Total	55.0	41.4	283.2	379.6

Disease	DALYs lost per year (thousands)	Annual monetised value € bn
Lung cancer	1873	103.0
COPD	1691	93.0
TB	103	5.6
Pneumonia/ALRI	790	43.5
Asthma	697	38.3
Total	5154	283.4



# BRONCOPATIA CRONICA OSTRUTTIVA

AMERICAN COLLEGE OF  
**CHEST**  
PHYSICIANS





**ASMA  
BRONCHIALE**

**FIBROSI**

**TUMORI**

**INSUFFICIENZA  
RESPIRATORIA**

**OSAS**

**RIABILITAZIONE  
RESPIRATORIA**



**B.P.C.O.**

**TRAPIANTO**



**ASMA  
BRONCHIALE**

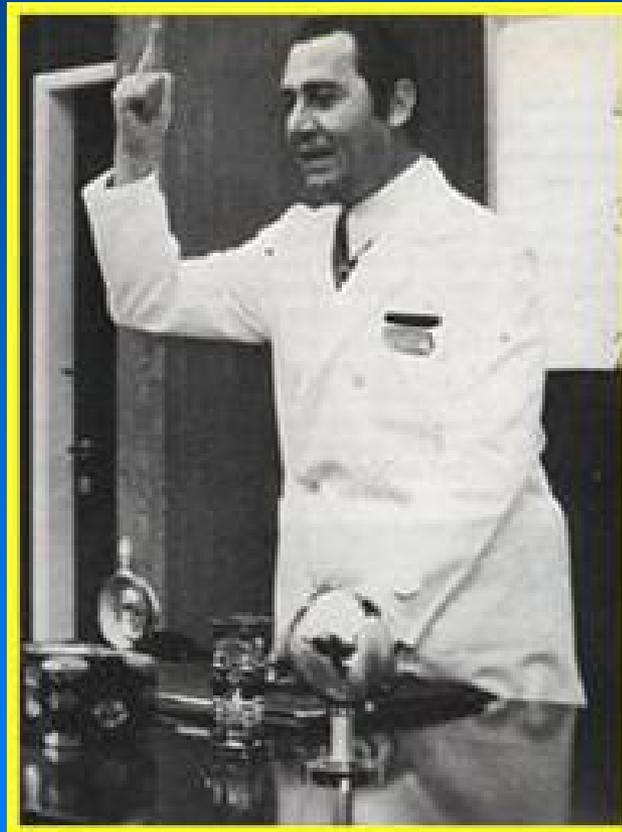
**FIBROSI**

**TUMORI**

**INSUFFICIENZA  
RESPIRATORIA**

**OSAS**

**RIABILITAZIONE  
RESPIRATORIA**



**B.P.C.O.**

**TRAPIANTO**



# FISIOPATOLOGIA DELLA BPCO

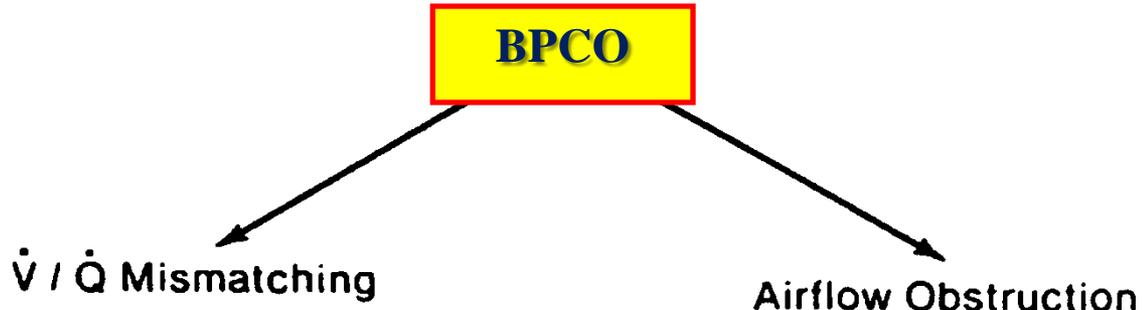


**BPCO**

**LIMITAZIONE ESERCIZIO FISICO - DISPNEA**



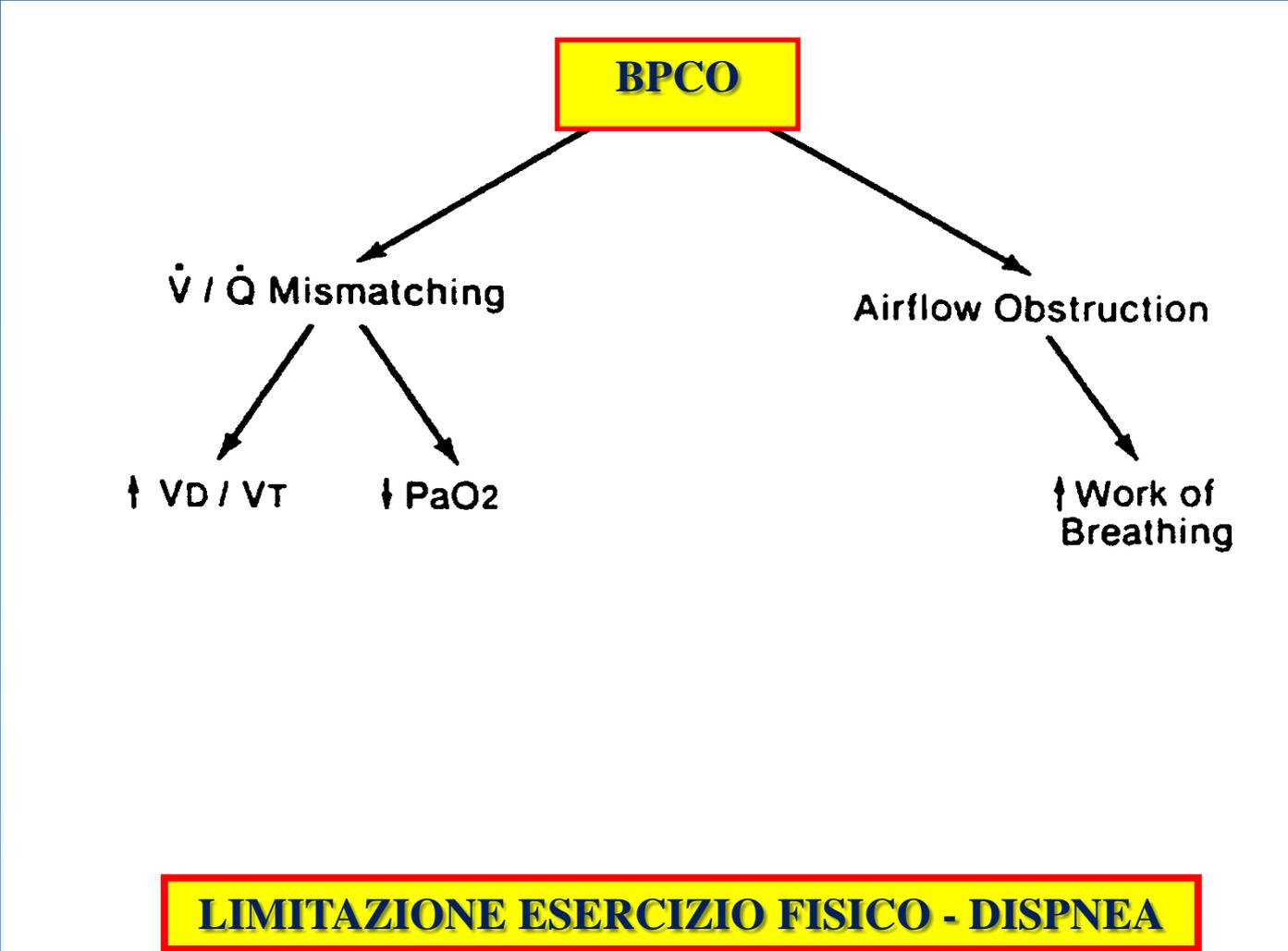
# FISIOPATOLOGIA DELLA BPCO



**LIMITAZIONE ESERCIZIO FISICO - DISPNEA**



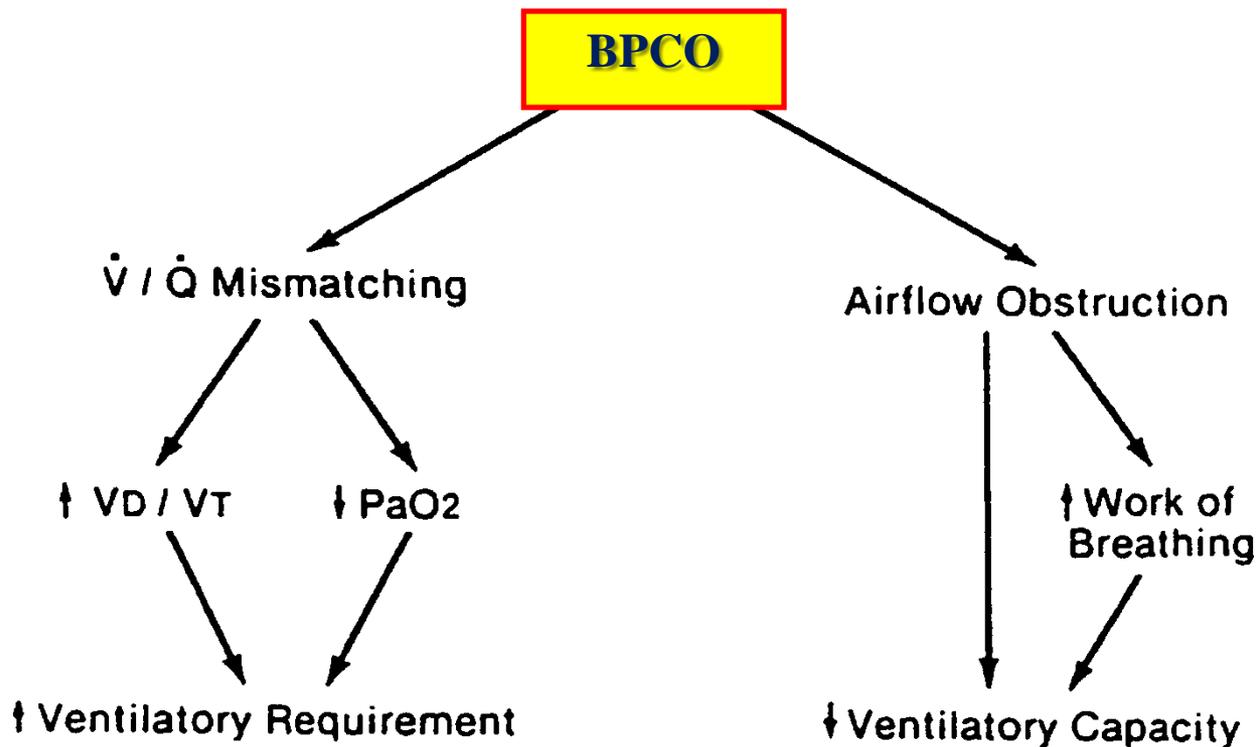
# FISIOPATOLOGIA DELLA BPCO



**LIMITAZIONE ESERCIZIO FISICO - DISPNEA**



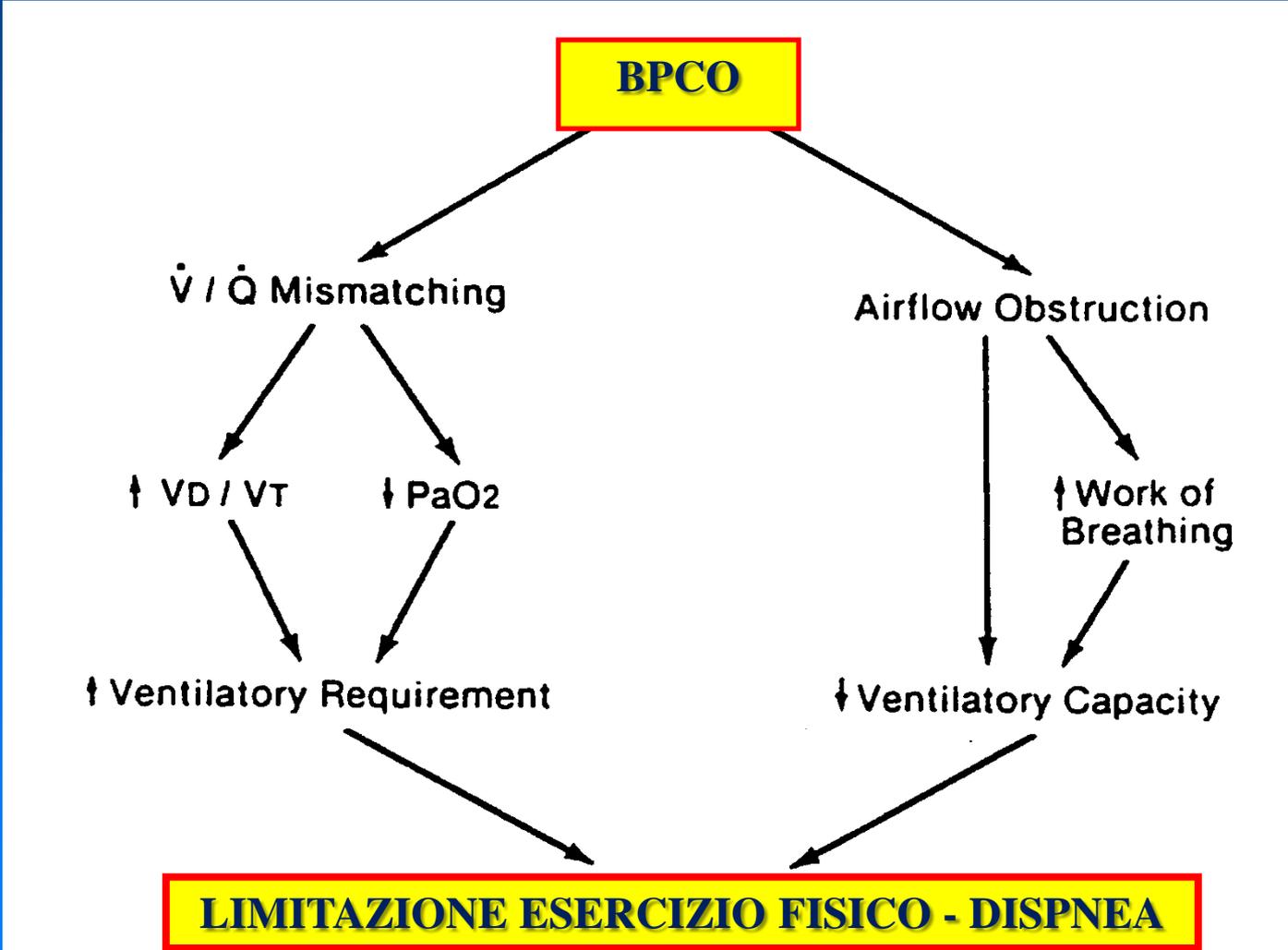
# FISIOPATOLOGIA DELLA BPCO



**LIMITAZIONE ESERCIZIO FISICO - DISPNEA**



# FISIOPATOLOGIA DELLA BPCO



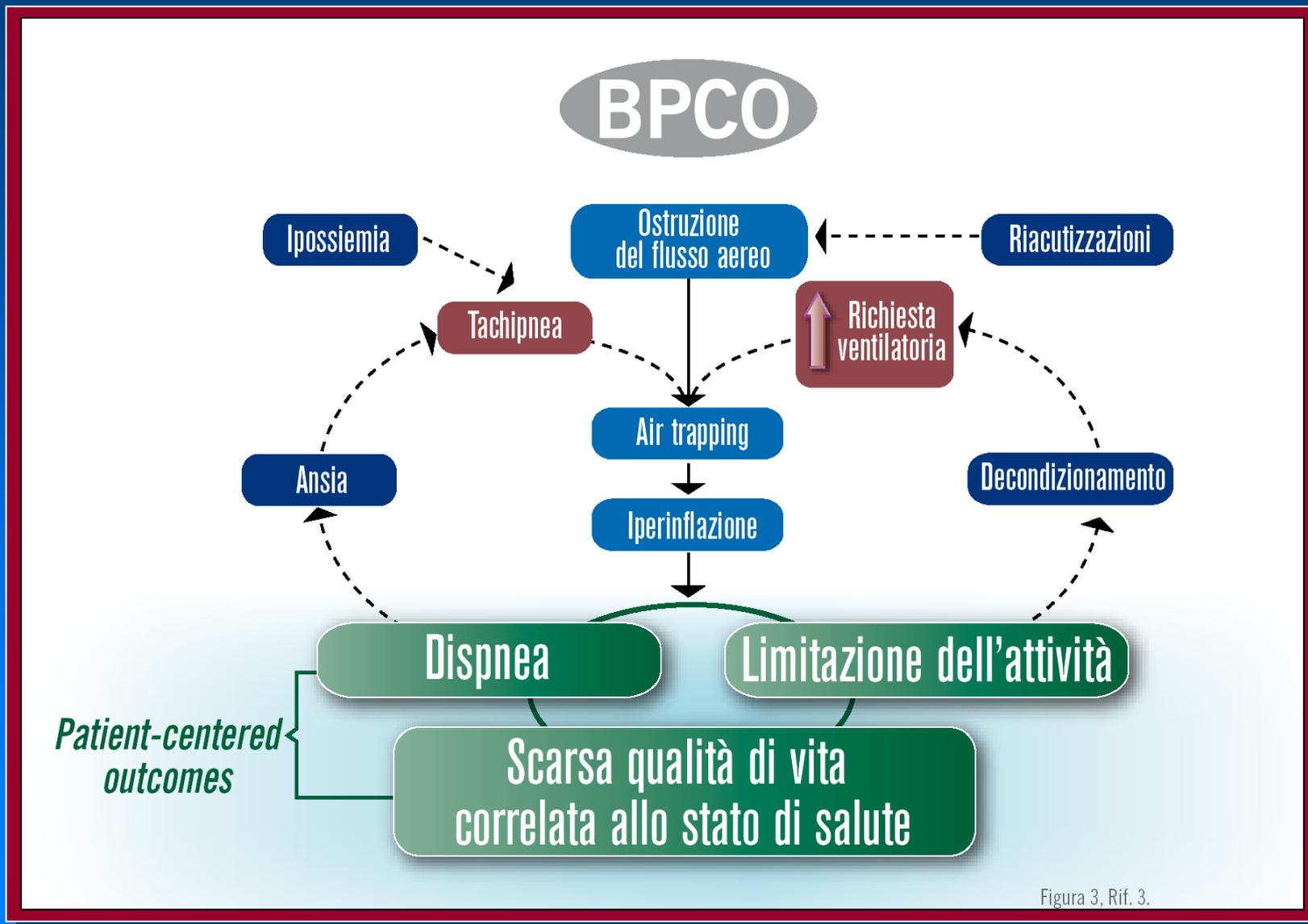


Figura 3, Rif. 3.



# MODIFICAZIONI DEL DECORSO CLINICO

**OSTRUZIONE  
DELLE VIE  
AEREE**

**AIR  
TRAPPING**

**DISPNEA**



**RIACUTIZZAZIONI**



**INATTIVITÀ  
DISABILITÀ**



# MODIFICAZIONI DEL DECORSO CLINICO

**OSTRUZIONE  
DELLE VIE  
AEREE**

**AIR  
TRAPPING**

**DISPNEA**



**RIACUTIZZAZIONI**



**INATTIVITÀ  
DISABILITÀ**



**GIU 2010**

## **REVIEW**

# Prevention of exacerbations of COPD with pharmacotherapy

**M. Miravittles**



## REVIEW

# Prevention of exacerbations of COPD with pharmacotherapy

M. Miravittles

GIU 2010

**TABLE 2** Reduction in exacerbations with pharmacotherapy in selected clinical trials

First author [Ref.]	Drug	Dose	Trial duration	Reduction in exacerbations %
SEEMUNGAL [28]	Erythromycin	250 mg every 12 h	1 yr	35
SETHI [32]	Moxifloxacin	400 mg·day <sup>-1</sup> for 5 days every 2 months	1 yr	25 (46 <sup>#</sup> )
CALVERLEY [40]	Fluticasone	500 µg every 12 h	3 yrs	18
KARDOS [60]	Fluticasone	500 µg every 12 h	1 yr	35 <sup>†</sup>
SZAFRANSKI [38]	Budesonide	320 µg every 12 h	1 yr	15
CALVERLEY [40]	Salmeterol	50 µg every 12 h	3 yr	15
STOCKLEY [76]	Salmeterol	50 µg every 12 h	1 yr	30
DUSSER [45]	Tiotropium	18 µg·day <sup>-1</sup>	1 yr	27
BARR [46]	Tiotropium	18 µg·day <sup>-1</sup>	4 yrs	14 <sup>†</sup>
HUBBARD [59]	BFC	320 µg every 12 h	1 yr	25
CALVERLEY [40]	FSC	500/50 µg every 12 h	3 yrs	25
FERGUSON [63]	FSC	250/50 µg every 12 h	1 yr	30.5
ZHENG [69]	Carbocysteine	1500 mg·day <sup>-1</sup>	1 yr	25%
DECRAMER [68]	NAC	600 mg·day <sup>-1</sup>	3 yrs	1 (21 <sup>‡</sup> )



## REVIEW

# Prevention of exacerbations of COPD with pharmacotherapy

M. Miravittles



**GIU 2010**

**TABLE 1** Strategies aimed at preventing exacerbations

### Proven efficacy

- Smoking cessation
- LABAs: salmeterol, formoterol
- Tiotropium
- Combination therapy: LABA/ICS
- Anti-influenza vaccine
- Antipneumococcal vaccine<sup>#</sup>
- Rehabilitation
- Physical exercise
- Self-management plans
- LVRS in selected patients

### Questioned efficacy

- Theophyllines
- Prophylactic antibiotic in selected patients
- Immunomodulators
- Mucolytic agents
- Antioxidants



**REVIEW**

# Prevention of exacerbations of COPD with pharmacotherapy

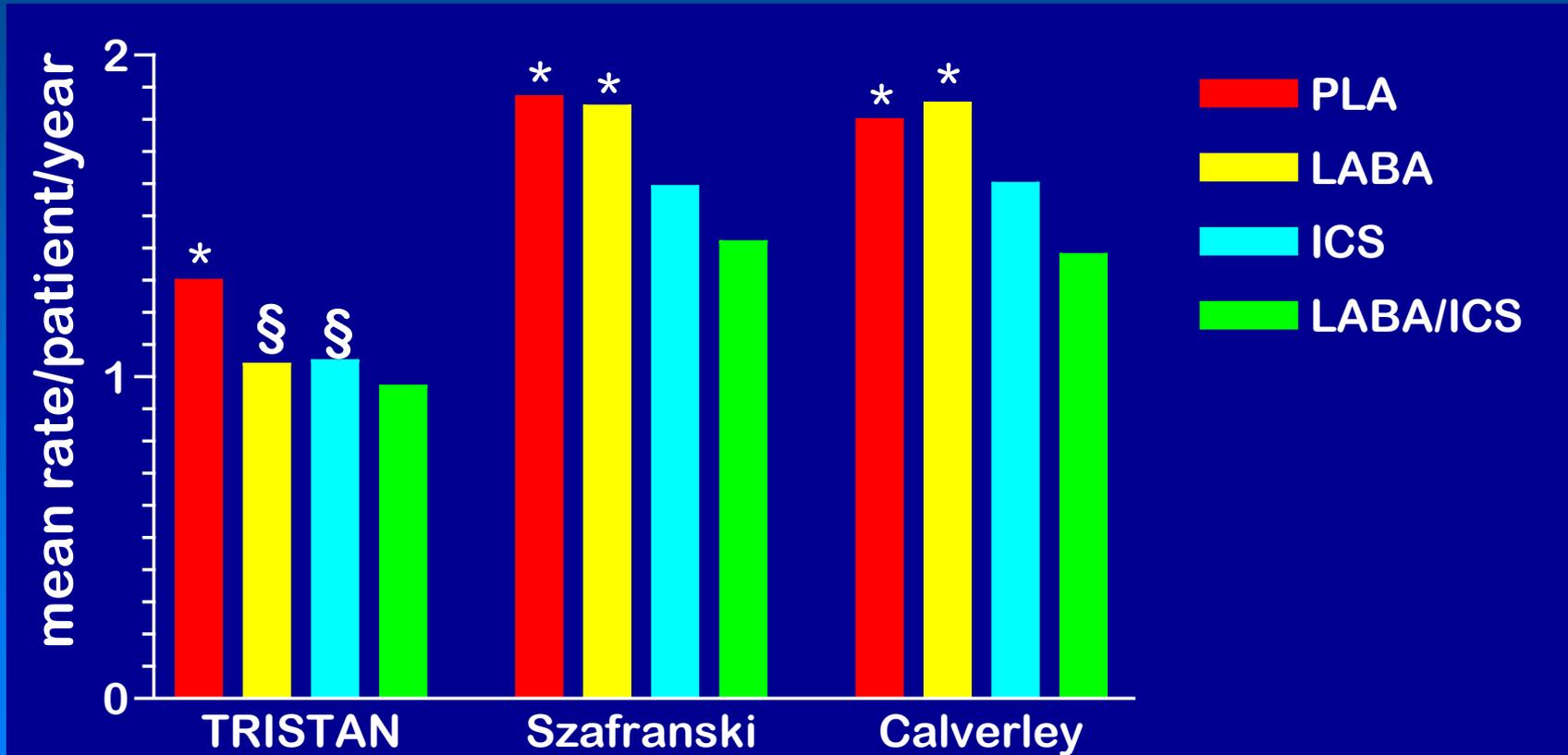
**M. Miravittles**

**GIU 2010**

# **BRONCODILATATORI STERIODI**



# Riacutizzazioni gravi e terapia con ICS/LABA



\*p<0.05 vs combinazione; § p<0.05 vs placebo



CHEST™

*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

FEBRUARY 22, 2007

VOL. 356 NO. 8

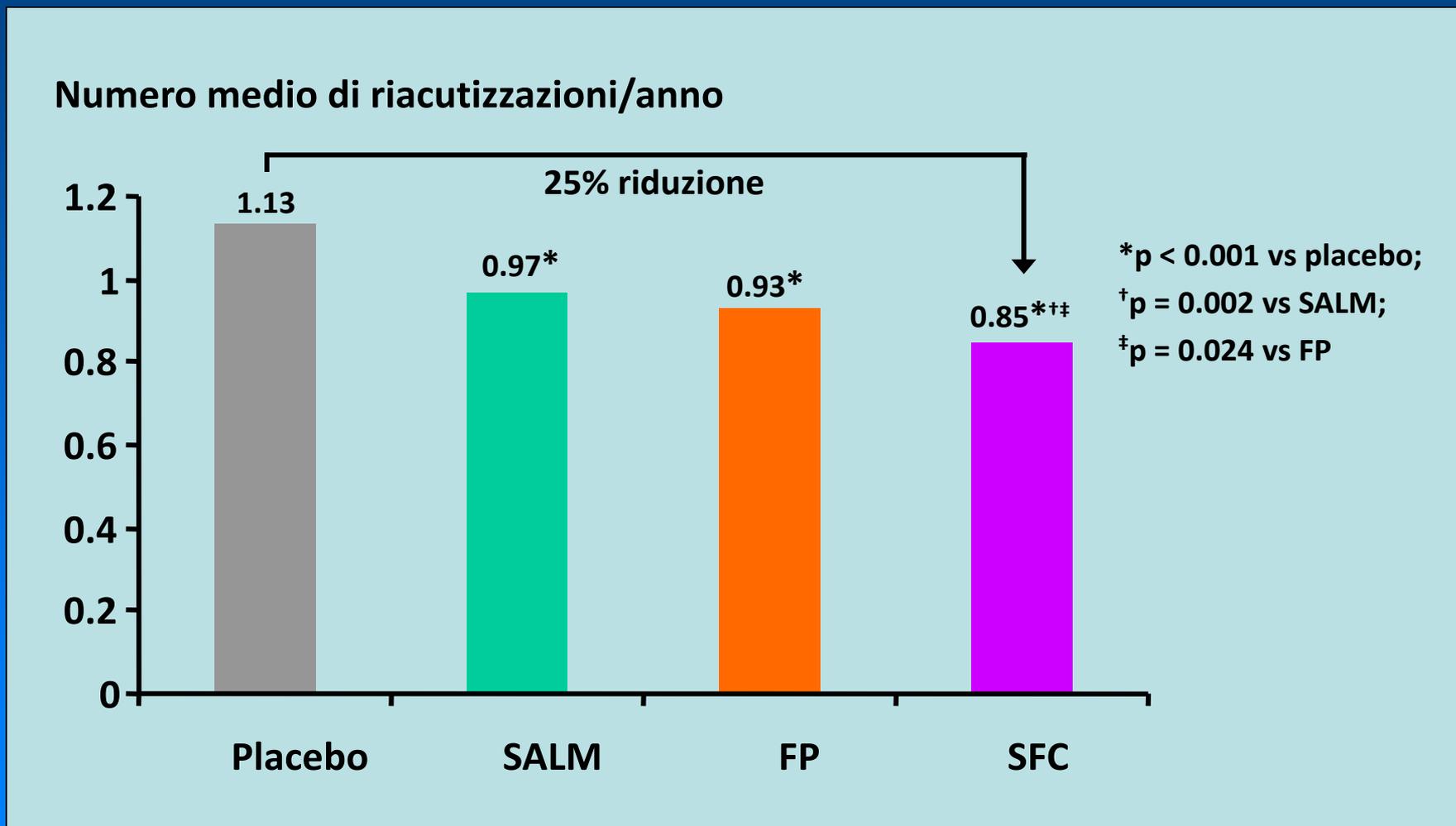
Salmeterol and Fluticasone Propionate and Survival  
in Chronic Obstructive Pulmonary Disease

Peter M.A. Calverley, M.D., Julie A. Anderson, M.A., Bartolome Celli, M.D., Gary T. Ferguson, M.D., Christine Jenkins, M.D.,  
Paul W. Jones, M.D., Julie C. Yates, B.S., and Jørgen Vestbo, M.D., for the TORCH investigators\*



# Riacutizzazioni moderate e gravi

## Studio TORCH





*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

OCTOBER 9, 2008

VOL. 359 NO. 15

A 4-Year Trial of Tiotropium in Chronic Obstructive  
Pulmonary Disease

Donald P. Tashkin, M.D., Bartolome Celli, M.D., Stephen Senn, Ph.D., Deborah Burkhart, B.S.N., Steven Kesten, M.D.,  
Shailendra Menjoge, Ph.D., and Marc Decramer, M.D., Ph.D., for the UPLIFT Study Investigators\*

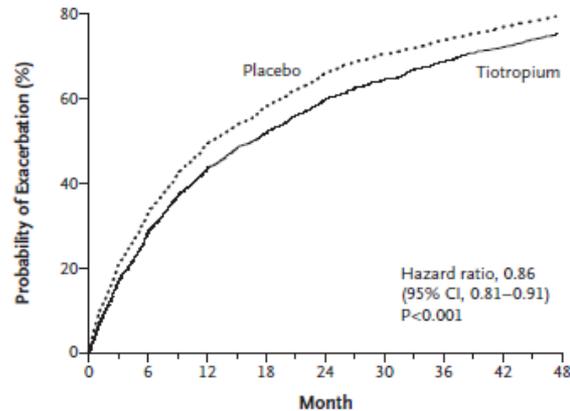


# Riacutizzazioni e Mortalità

## Studio UPLIFT



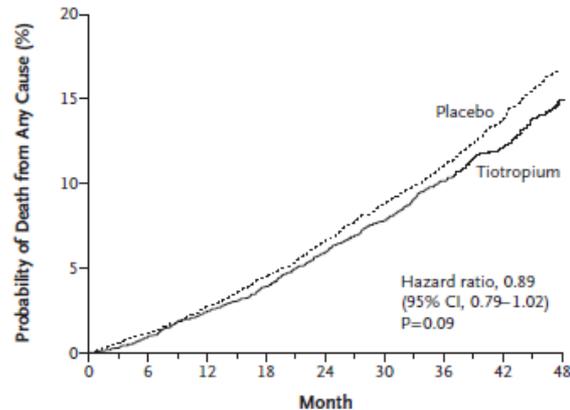
**A COPD Exacerbation**



**No. at Risk**

Tiotropium	2986	1996	1496	1223	983	838	709	610	26
Placebo	3006	1815	1284	1010	776	634	545	460	21

**B Death from Any Cause**



**No. at Risk**

Tiotropium	2986	2948	2899	2851	2785	2721	2646	2574	2306
Placebo	3006	2961	2903	2836	2772	2696	2624	2523	2249



*The* NEW ENGLAND  
JOURNAL *of* MEDICINE

ESTABLISHED IN 1812

MARCH 24, 2011

VOL. 364 NO. 12

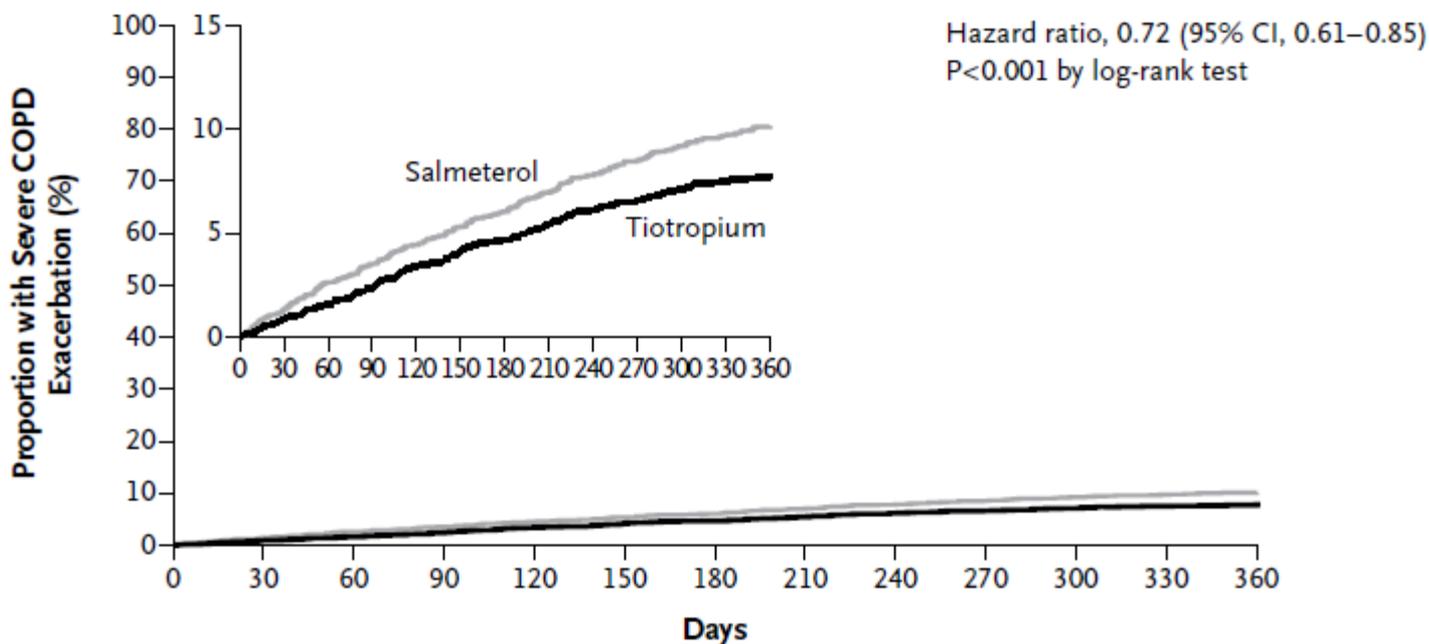
Tiotropium versus Salmeterol for the Prevention  
of Exacerbations of COPD

Claus Vogelmeier, M.D., Bettina Hederer, M.D., Thomas Glaab, M.D., Hendrik Schmidt, Ph.D.,  
Maureen P.M.H. Rutten-van Mölken, Ph.D., Kai M. Beeh, M.D., Klaus F. Rabe, M.D., and Leonardo M. Fabbri, M.D.,  
for the POET-COPD Investigators\*



## Tiotropium versus Salmeterol for the Prevention of Exacerbations of COPD

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for the POET-COPD Investigators\*



### No. at Risk

Tiotropium	3707	3564	3453	3359	3285	3217	3177	3125	3066	3017	2977	2948	2663
Salmeterol	3669	3502	3362	3244	3172	3080	3032	2982	2921	2870	2834	2806	2489



## REVIEW

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GIU 2010



**TABLE 1** Strategies aimed at preventing exacerbations

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LVRS in selected patients

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**REVIEW**

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**M. Miravittles**

**GIU 2010**

**MUCOLITICI**



**APR 2008**

ORIGINAL PAPER

# Exacerbations worsen the quality of life of chronic obstructive pulmonary disease patients in primary healthcare

C. Llor,<sup>1</sup> J. Molina,<sup>2</sup> K. Naberan,<sup>3</sup> J. M. Cots,<sup>4</sup> F. Ros,<sup>5</sup> M. Miravittles,<sup>6</sup> on behalf of the EVOCA study group



ORIGINAL PAPER

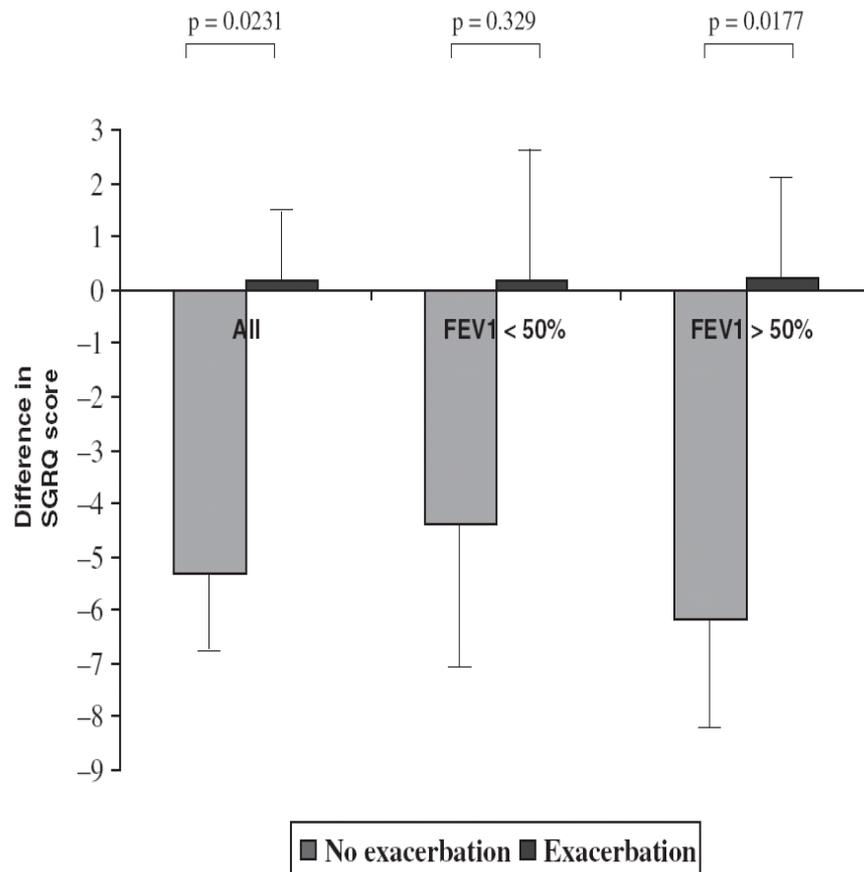
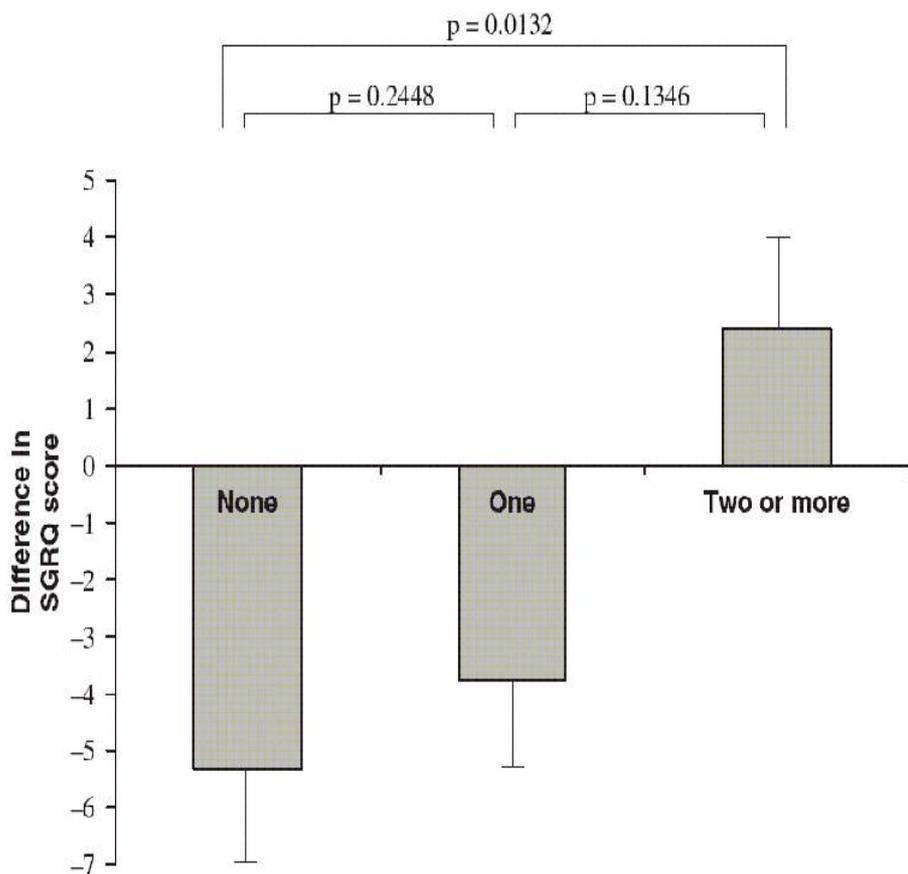
# Exacerbations worsen the quality of life of chronic obstructive pulmonary disease patients in primary healthcare

AMERICAN COLLEGE OF  
**CHEST**  
PHYSICIANS



C. Llor,<sup>1</sup> J. Molina,<sup>2</sup> K. Naberan,<sup>3</sup> J. M. Cots,<sup>4</sup> F. Ros,<sup>5</sup> M. Miravittles,<sup>6</sup> on behalf of the EVOCA study group

APR 2008



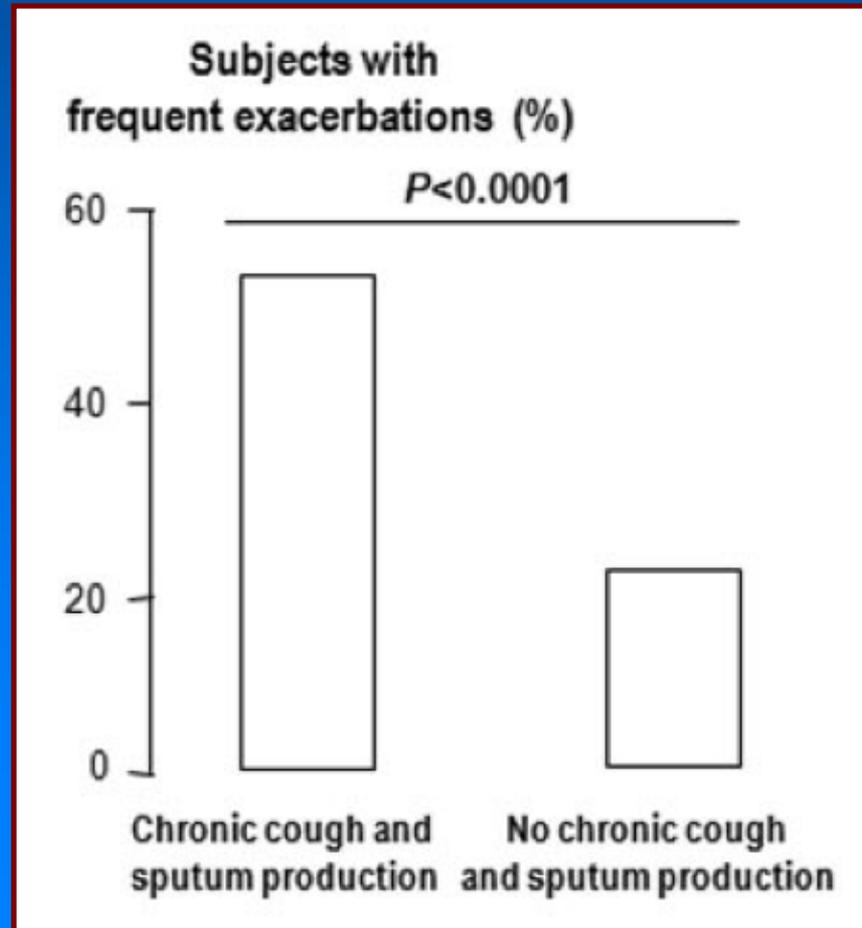


# Cough and Sputum Production Are Associated With Frequent Exacerbations and Hospitalizations in COPD Subjects\*



APR 2009

*Pierre-Régis Burgel, MD, PhD; Pascale Nesme-Meyer, MD; Pascal Chanez, MD, PhD; Denis Caillaud, MD; Philippe Carré, MD; Thierry Perez, MD; and Nicolas Roche, MD, PhD; on behalf of the Initiatives Bronchopneumopathie Chronique Obstructive (BPCO) Scientific Committee†*





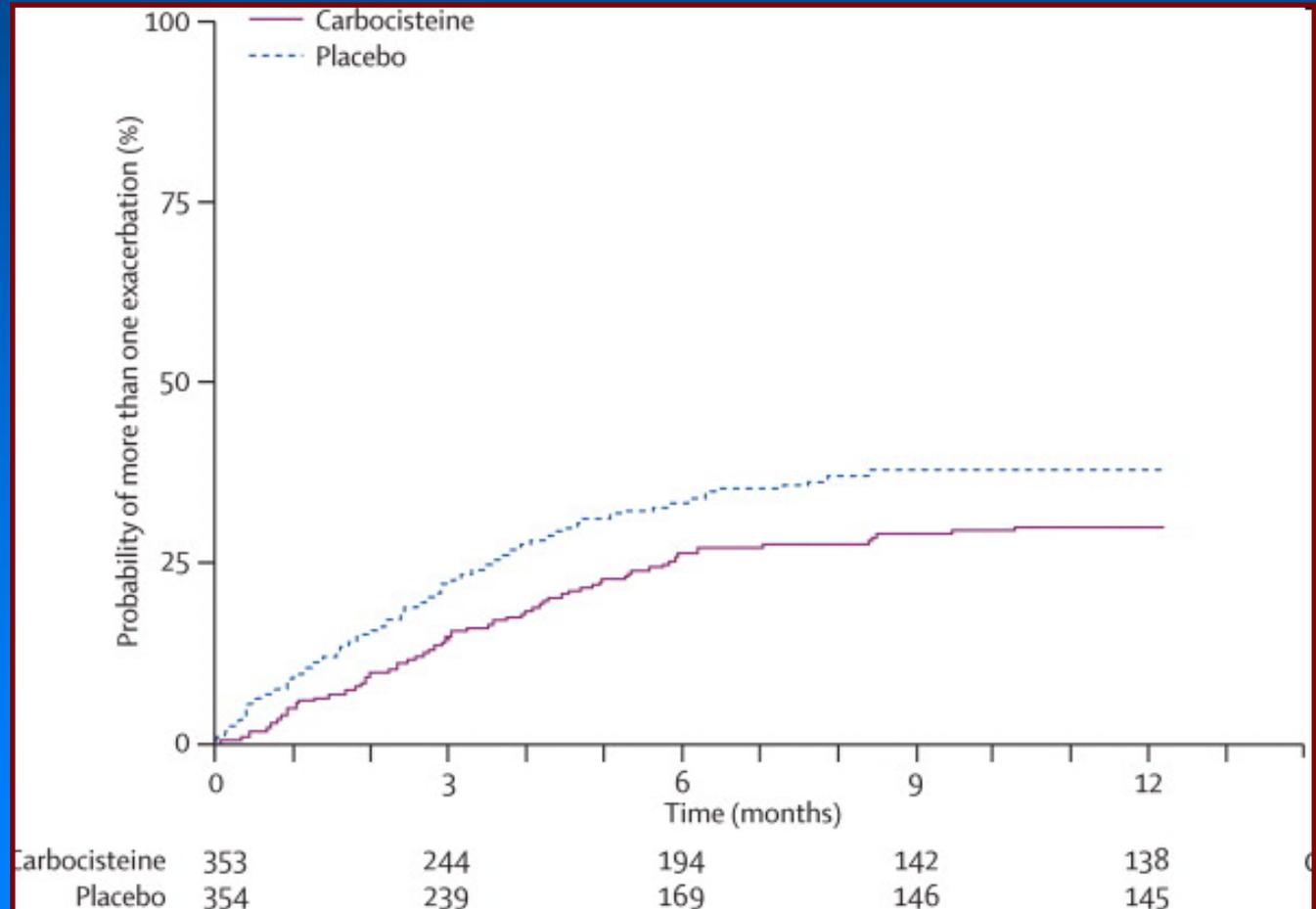
**GIU 2008**

## Effect of carbocisteine on acute exacerbation of chronic obstructive pulmonary disease (PEACE Study): a randomised placebo-controlled study

*Jin-Ping Zheng, Jian Kang, Shao-Guang Huang, Ping Chen, Wan-Zen Yao, Lan Yang, Chun-Xue Bai, Chang-Zheng Wang, Chen Wang, Bao-Yuan Chen, Yi Shi, Chun-Tao Liu, Ping Chen\*, Qiang Li, Zhen-Shan Wang, Yi-Jiang Huang, Zhi-Yang Luo, Fei-Peng Chen, Jian-Zhang Yuan, Ben-Tong Yuan, Hui-Ping Qian, Rong-Chang Zhi, Nan-Shan Zhong*



**GIU 2008**





**REVIEW**

# Prevention of exacerbations of COPD with pharmacotherapy

**M. Miravittles**

**GIU 2010**

**ANTIBIOTICI**



**GEN 2010**

# Pulsed moxifloxacin for the prevention of exacerbations of chronic obstructive pulmonary disease: a randomized controlled trial

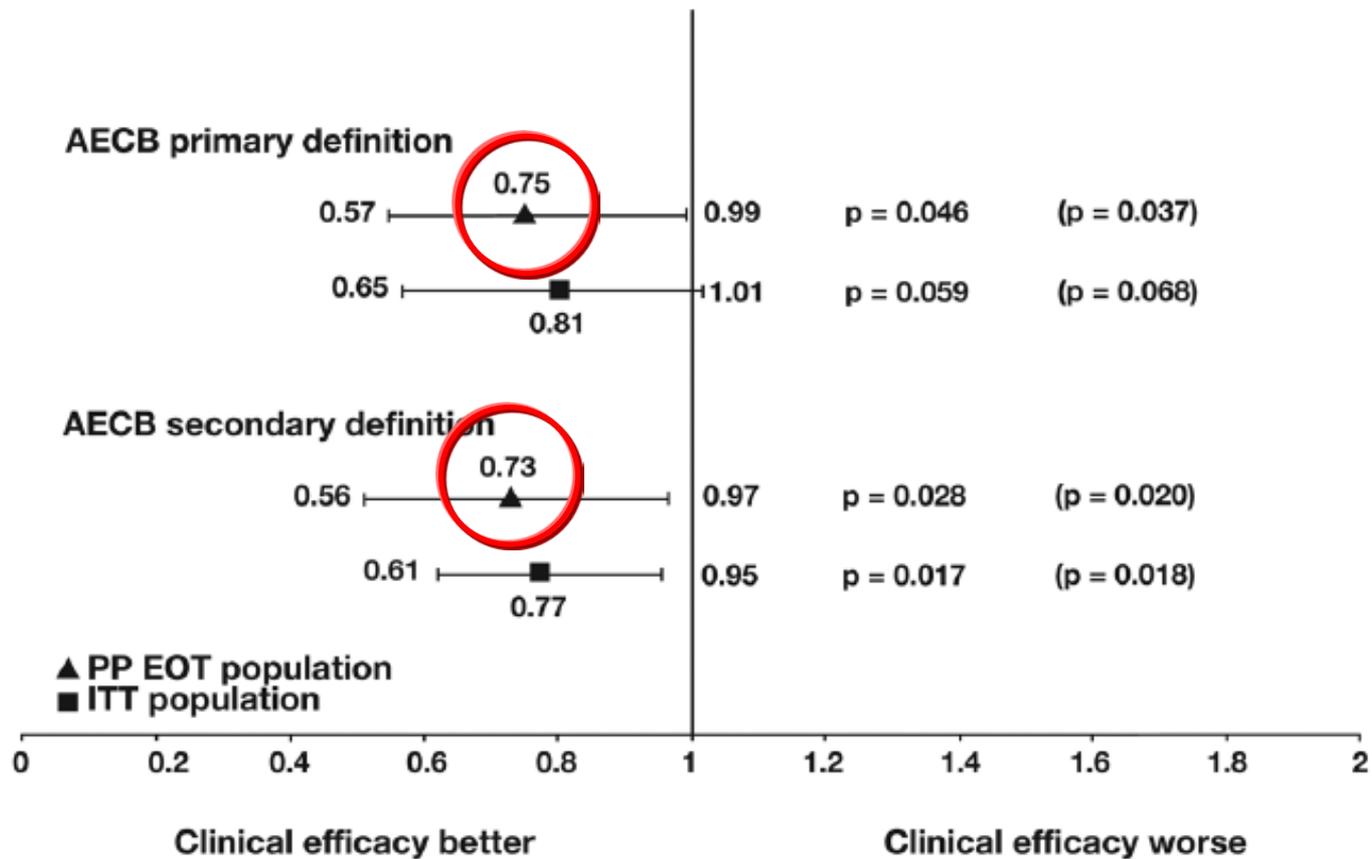
Sanjay Sethi<sup>1\*</sup>, Paul W Jones<sup>2</sup>, Marlize Schmitt Theron<sup>3</sup>, Marc Miravittles<sup>4</sup>, Ethan Rubinstein<sup>5</sup>, Jadwiga A Wedzicha<sup>6</sup>, Robert Wilson<sup>7</sup>, the PULSE Study group



**GEN 2010**

**(A) PP EOT and ITT population**

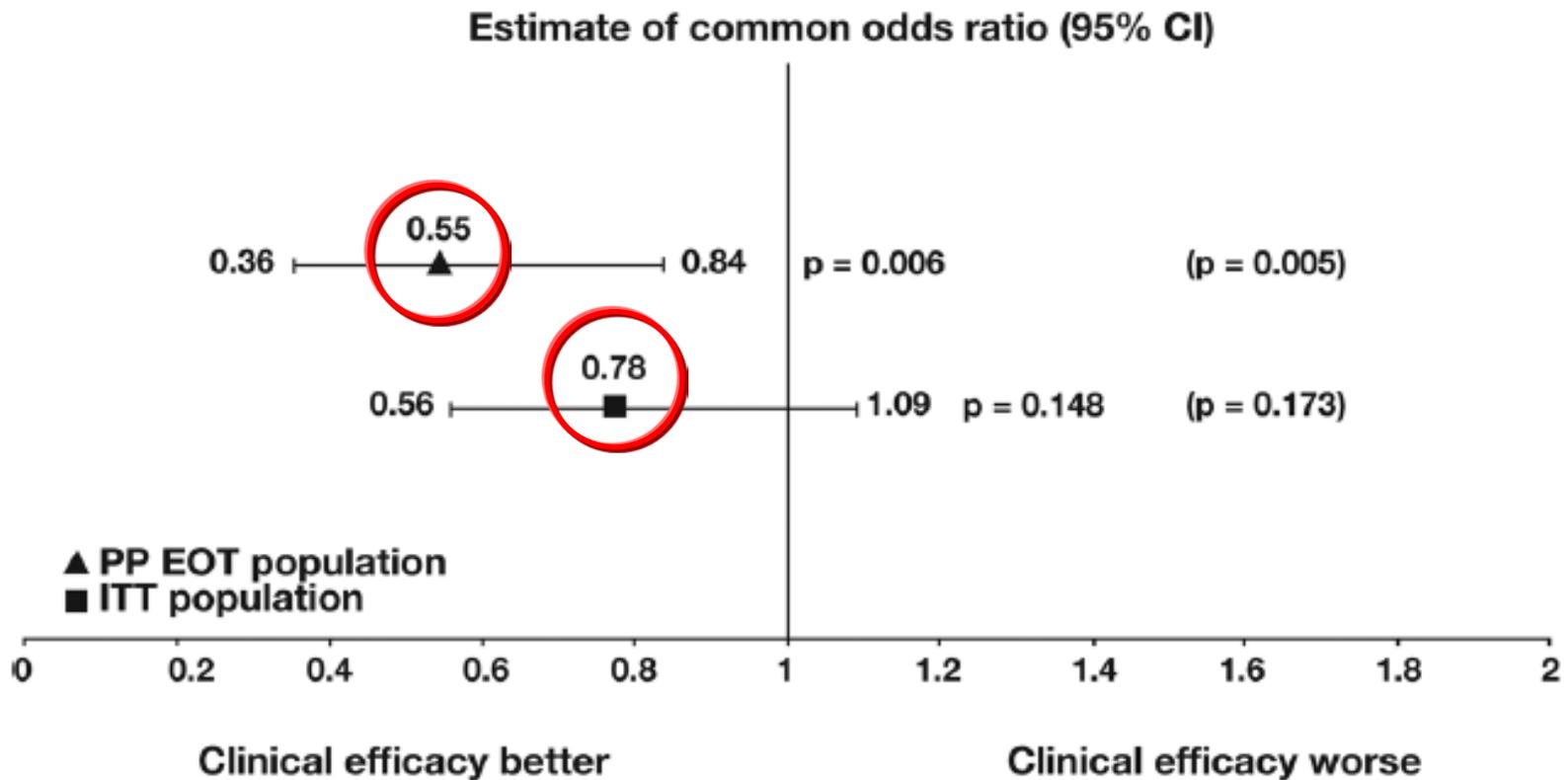
Estimate of common odds ratio (95% CI)





GEN 2010

### (B) Mucopurulent/purulent sputum subgroup

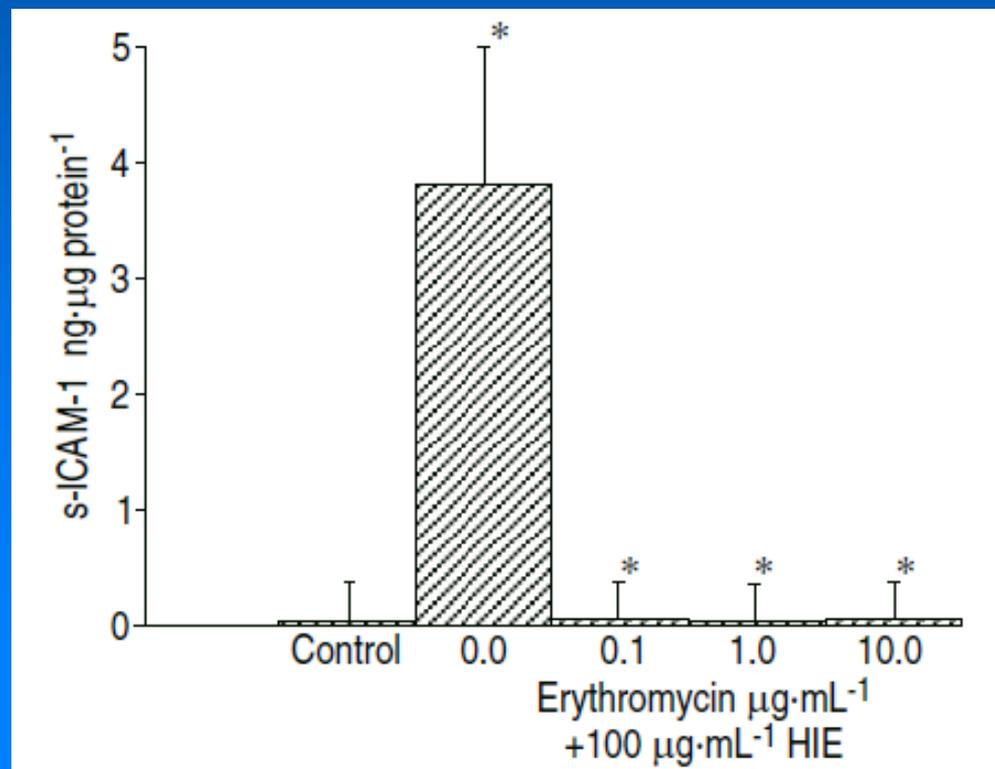




## Effect of erythromycin on *Haemophilus influenzae* endotoxin-induced release of IL-6, IL-8 and sICAM-1 by cultured human bronchial epithelial cells

O.A. Khair, J.L. Devalia, M.M. Abdelaziz, R.J. Sapsford, R.J. Davies

1995



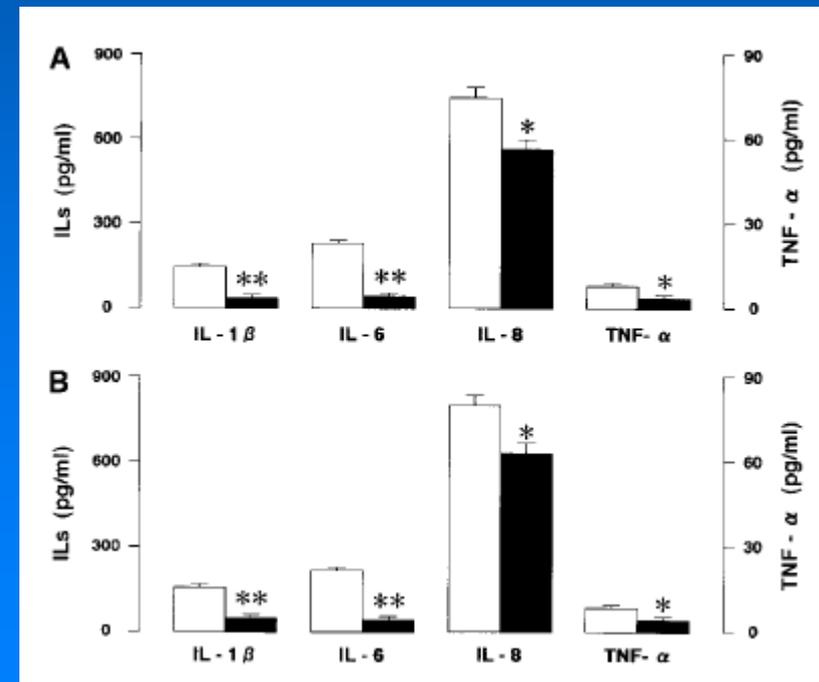
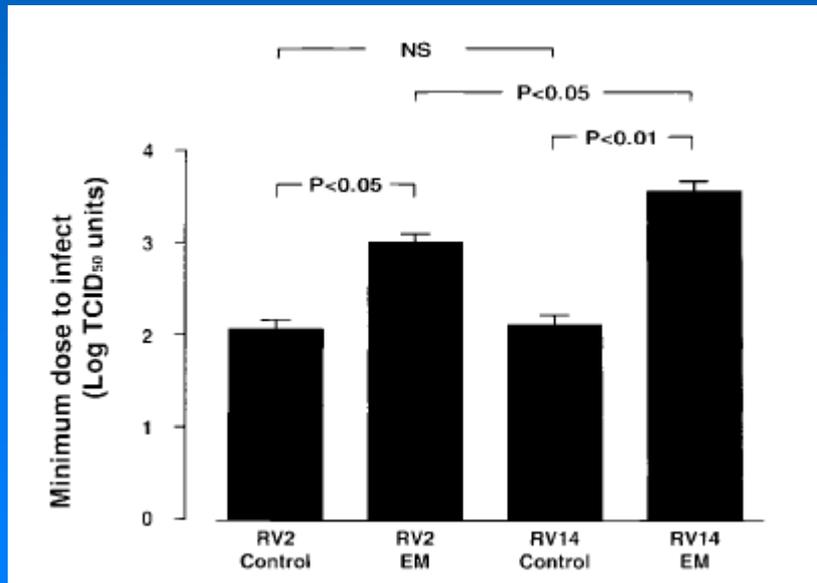


# Erythromycin Inhibits Rhinovirus Infection in Cultured Human Tracheal Epithelial Cells

Tomoko Suzuki, Mutsuo Yamaya, Kiyohisa Sekizawa, Masayoshi Hosoda, Norihiro Yamada, Satoshi Ishizuka, Akiko Yoshino, Hiroyasu Yasuda, Hidenori Takahashi, Hidekazu Nishimura, and Hidetada Sasaki



2002

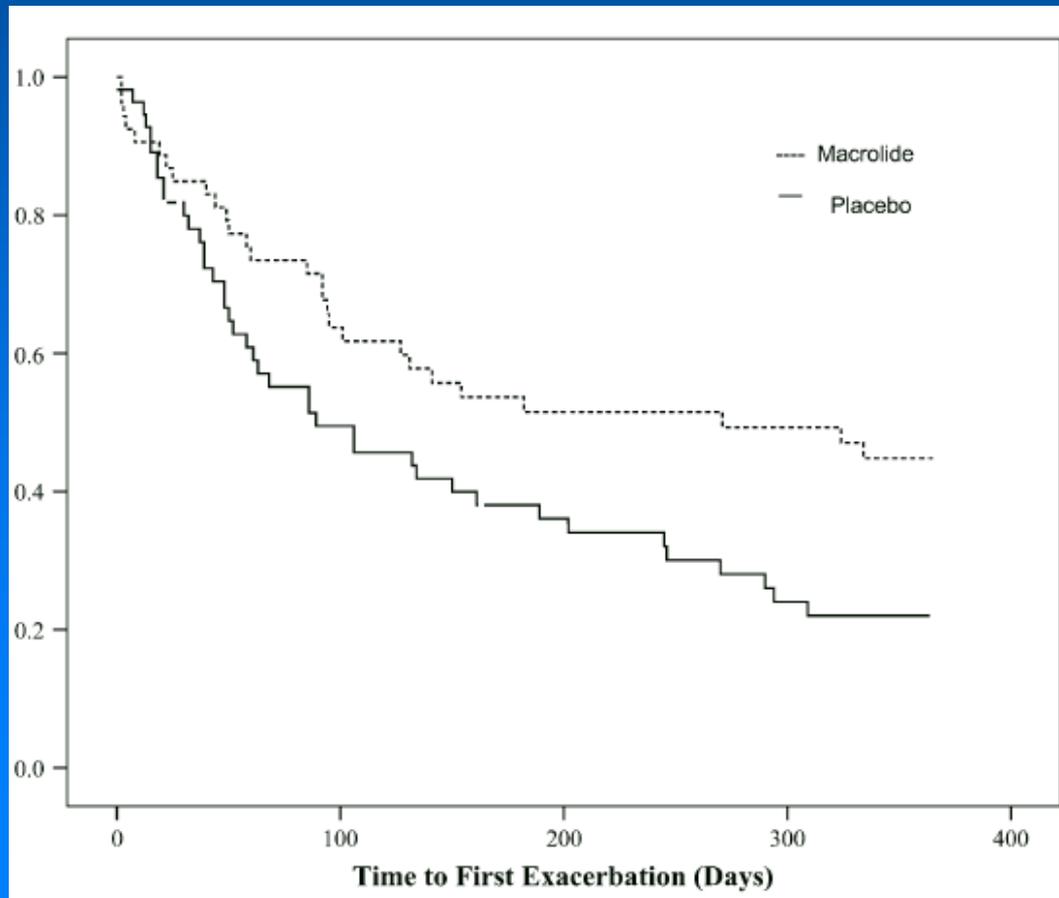




## Long-term Erythromycin Therapy Is Associated with Decreased Chronic Obstructive Pulmonary Disease Exacerbations

Terence A. R. Seemungal<sup>1,2\*</sup>, Tom M. A. Wilkinson<sup>2\*</sup>, John R. Hurst<sup>2</sup>, Wayomi R. Perera<sup>2</sup>, Ray J. Sapsford<sup>2</sup>, and Jadwiga A. Wedzicha<sup>2</sup>

DIC 2008





[Pharmacol Res](#). 2011 May;63(5):389-97. doi: 10.1016/j.phrs.2011.02.001. Epub 2011 Feb 17.

**Macrolide antibiotics broadly and distinctively inhibit cytokine and chemokine production by COPD sputum cells in vitro.**

[Marjanović N<sup>1</sup>](#), [Bosnar M](#), [Michielin F](#), [Willé DR](#), [Anić-Milić T](#), [Culić O](#), [Popović-Grič S](#), [Boqdan M](#), [Parnham MJ](#), [Eraković Haber V](#).



**Azithromycin Improves Macrophage Phagocytic Function and Expression of Mannose Receptor in Chronic Obstructive Pulmonary Disease**

[Sandra Hodge<sup>1,2</sup>](#), [Greg Hodge<sup>1,2</sup>](#), [Hubertus Jersmann<sup>1,2</sup>](#), [Geoffrey Matthews<sup>1</sup>](#), [Jessica Ahern<sup>1</sup>](#), [Mark Holmes<sup>1,2</sup>](#), and [Paul N. Reynolds<sup>1,2</sup>](#)



**Azithromycin Maintains Airway Epithelial Integrity during *Pseudomonas aeruginosa* Infection**

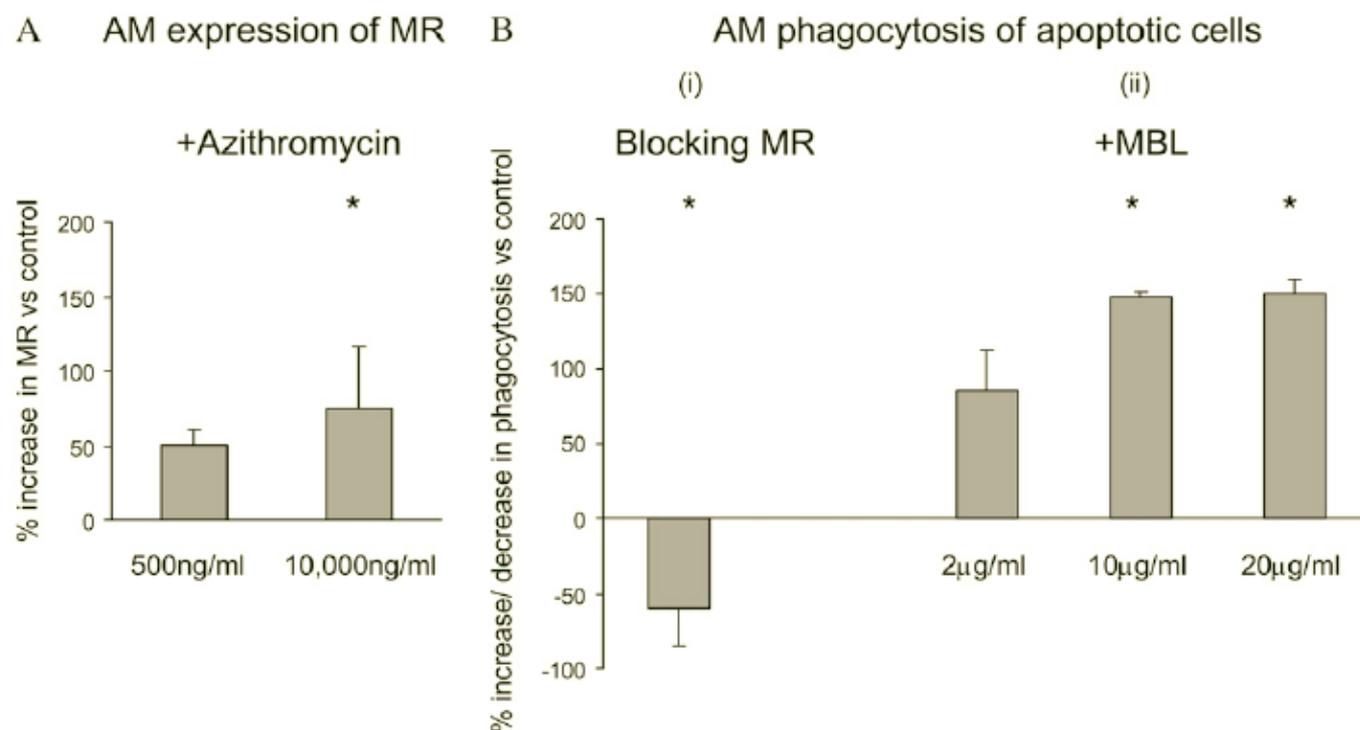
[Skarphedinn Halldorsson<sup>1,2</sup>](#), [Thorarinn Gudjonsson<sup>2,3,4</sup>](#), [Magnus Gottfredsson<sup>5,6</sup>](#), [Pradeep K. Singh<sup>7</sup>](#), [Gudmundur Hrafn Gudmundsson<sup>1,2</sup>](#), and [Olafur Baldursson<sup>2,8,9</sup>](#)



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LUG 2008



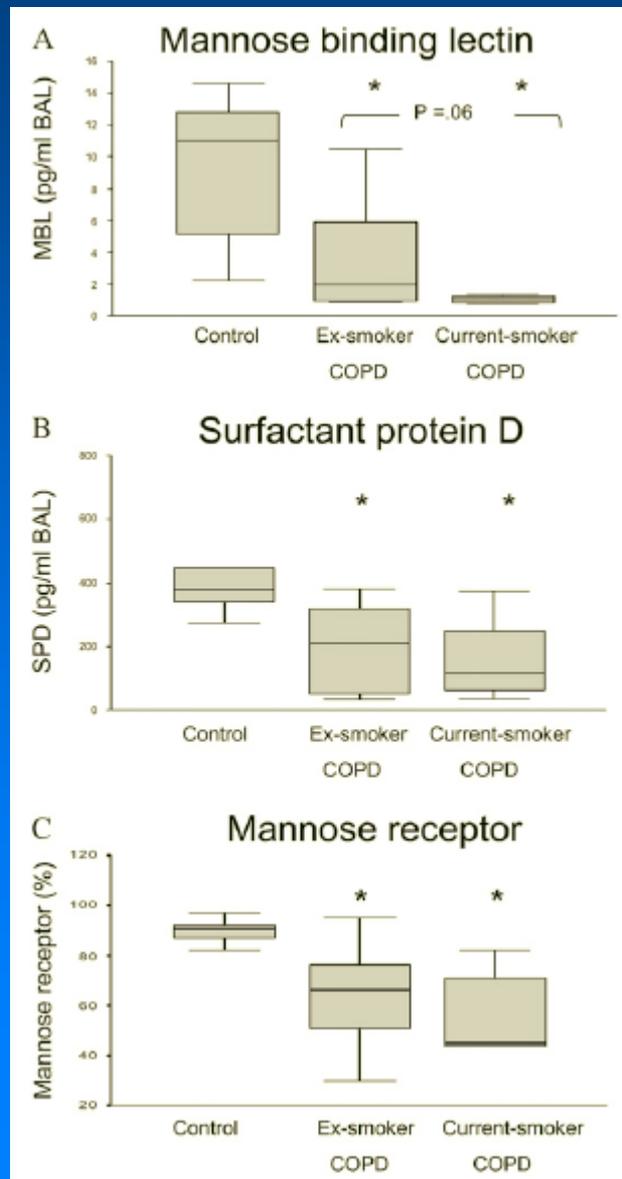


# Azithromycin Improves Macrophage Phagocytic Function and Expression of Mannose Receptor in Chronic Obstructive Pulmonary Disease

Sandra Hodge<sup>1,2</sup>, Greg Hodge<sup>1,2</sup>, Hubertus Jersmann<sup>1,2</sup>, Geoffrey Matthews<sup>1</sup>, Jessica Ahern<sup>1</sup>, Mark Holmes<sup>1,2</sup>, and Paul N. Reynolds<sup>1,2</sup>



LUG 2008

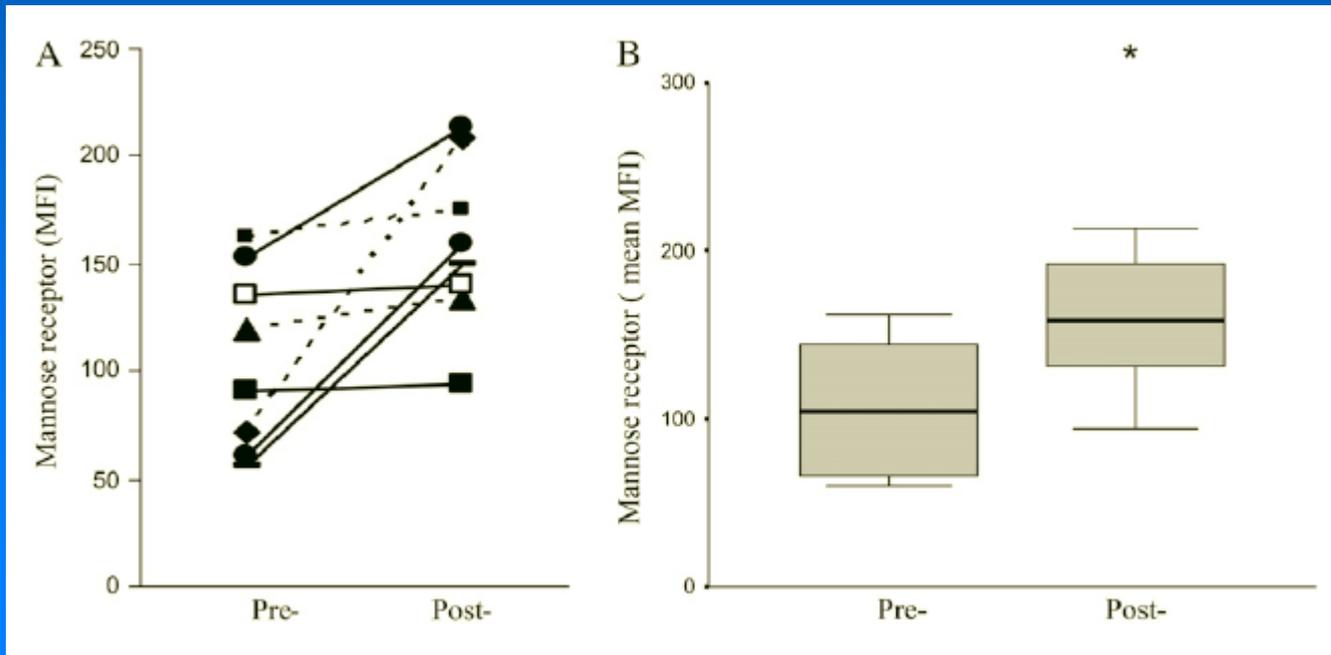




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Sandra Hodge<sup>1,2</sup>, Greg Hodge<sup>1,2</sup>, Hubertus Jersmann<sup>1,2</sup>, Geoffrey Matthews<sup>1</sup>, Jessica Ahern<sup>1</sup>, Mark Holmes<sup>1,2</sup>, and Paul N. Reynolds<sup>1,2</sup>

LUG 2008

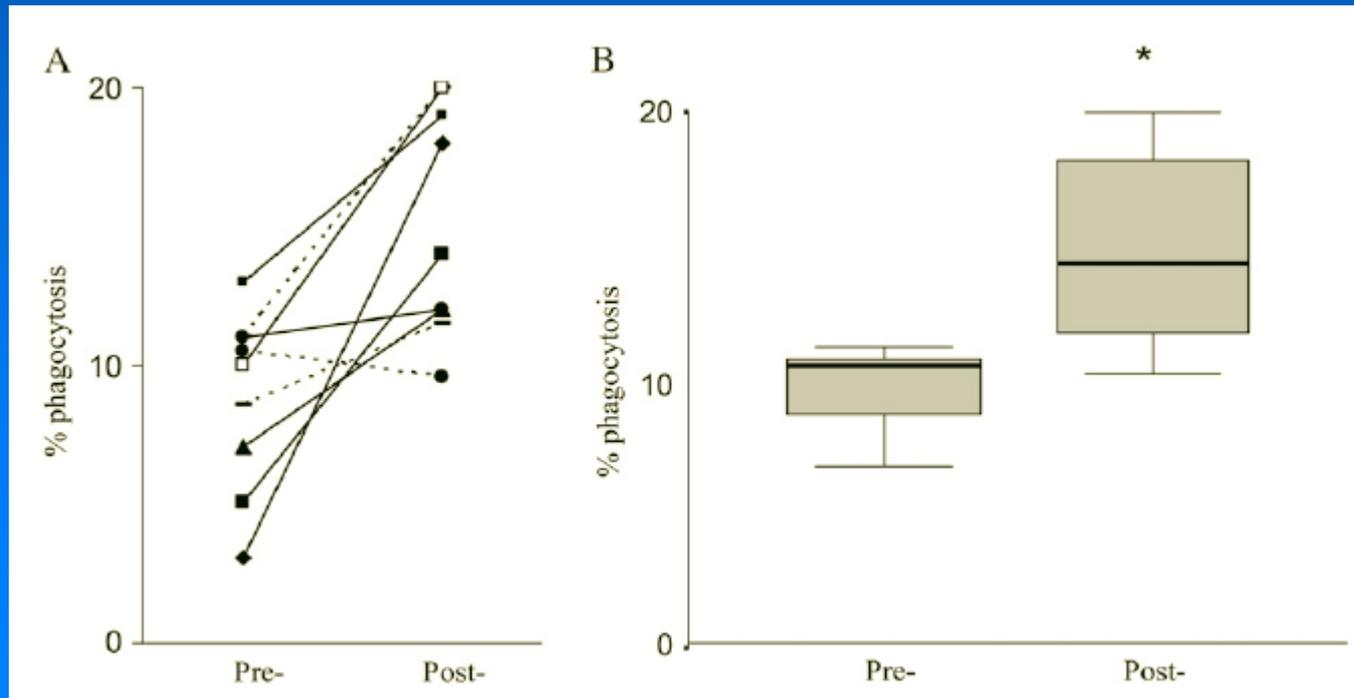




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Sandra Hodge<sup>1,2</sup>, Greg Hodge<sup>1,2</sup>, Hubertus Jersmann<sup>1,2</sup>, Geoffrey Matthews<sup>1</sup>, Jessica Ahern<sup>1</sup>, Mark Holmes<sup>1,2</sup>, and Paul N. Reynolds<sup>1,2</sup>

LUG 2008

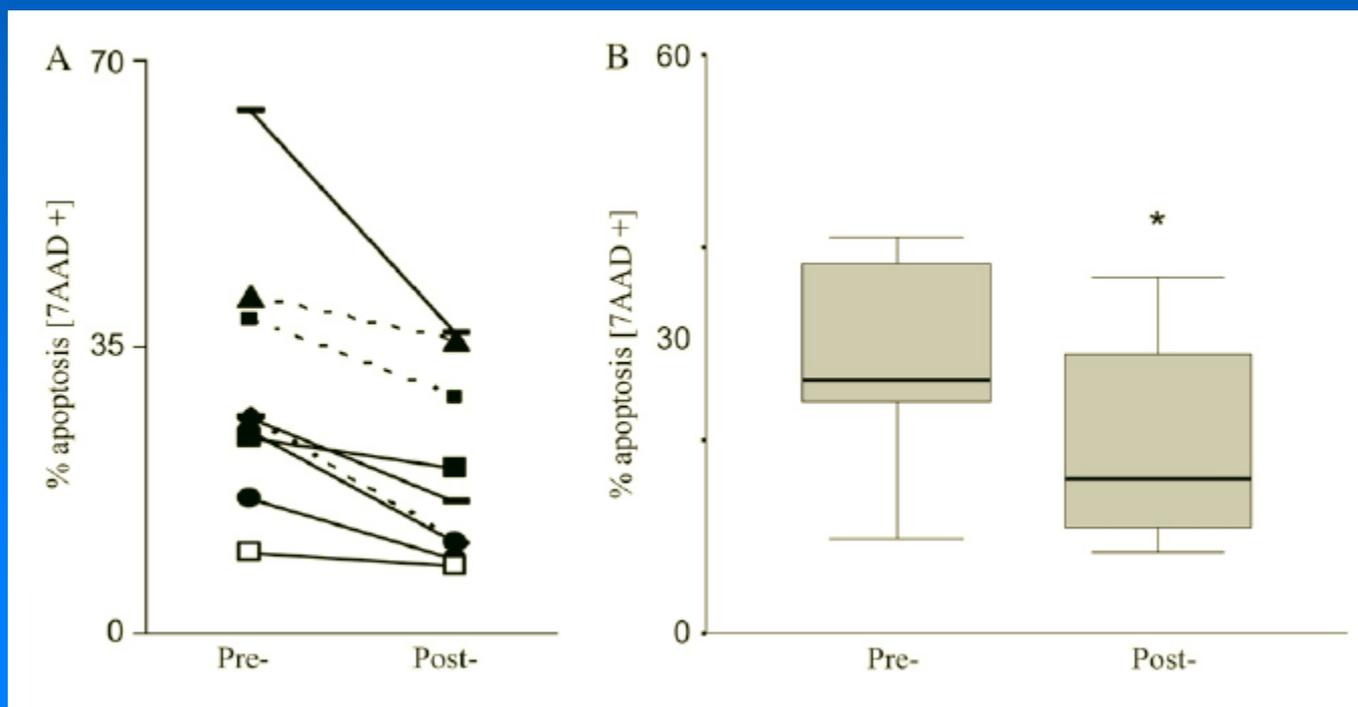




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LUG 2008



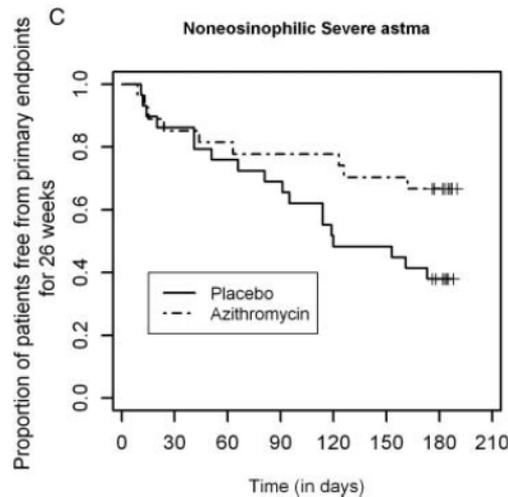
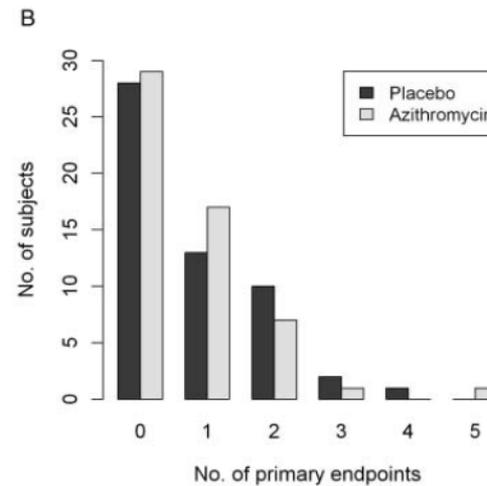
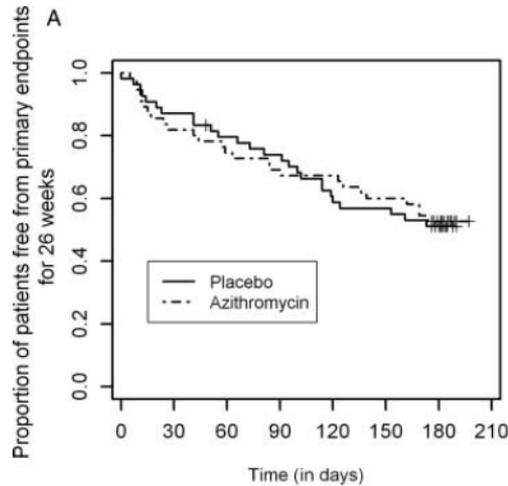


# Azithromycin for prevention of exacerbations in severe asthma (AZISAST): a multicentre randomised double-blind placebo-controlled trial

Guy G Brusselle,<sup>1</sup> Christine VanderStichele,<sup>1</sup> Paul Jordens,<sup>2</sup> René Deman,<sup>3</sup> Hans Slabbynck,<sup>4</sup> Veerle Ringoet,<sup>5</sup> Geert Verleden,<sup>6</sup> Ingel K Demedts,<sup>7</sup> Katia Verhamme,<sup>8</sup> Anja Delporte,<sup>1</sup> Bénédicte Demeyere,<sup>1</sup> Geert Claeys,<sup>9</sup> Jerina Boelens,<sup>9</sup> Elizaveta Padalko,<sup>9</sup> Johny Verschakelen,<sup>10</sup> Georges Van Maele,<sup>11</sup> Ellen Deschepper,<sup>11</sup> Guy F P Joos<sup>1</sup>



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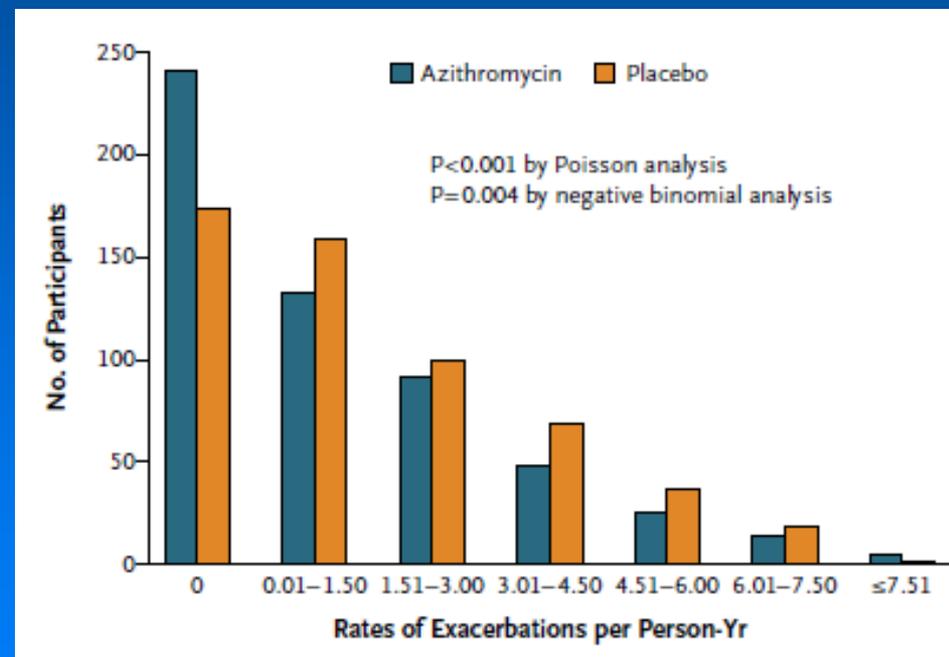
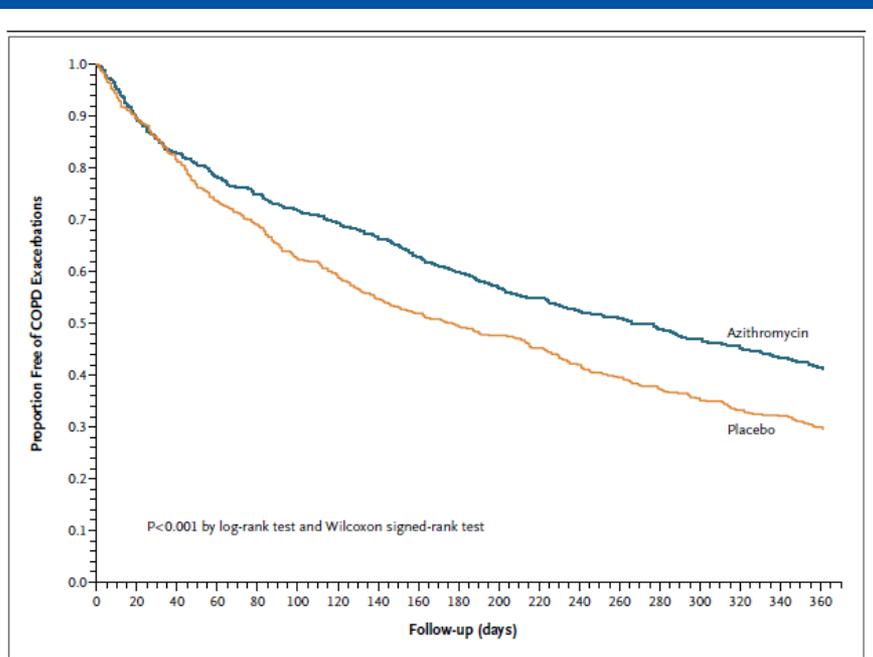
ESTABLISHED IN 1812

AUGUST 25, 2011

VOL. 365 NO. 8

**Azithromycin for Prevention of Exacerbations of COPD**

Richard K. Albert, M.D., John Connett, Ph.D., William C. 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. Sciurba, 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





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# THE LANCET Respiratory Medicine

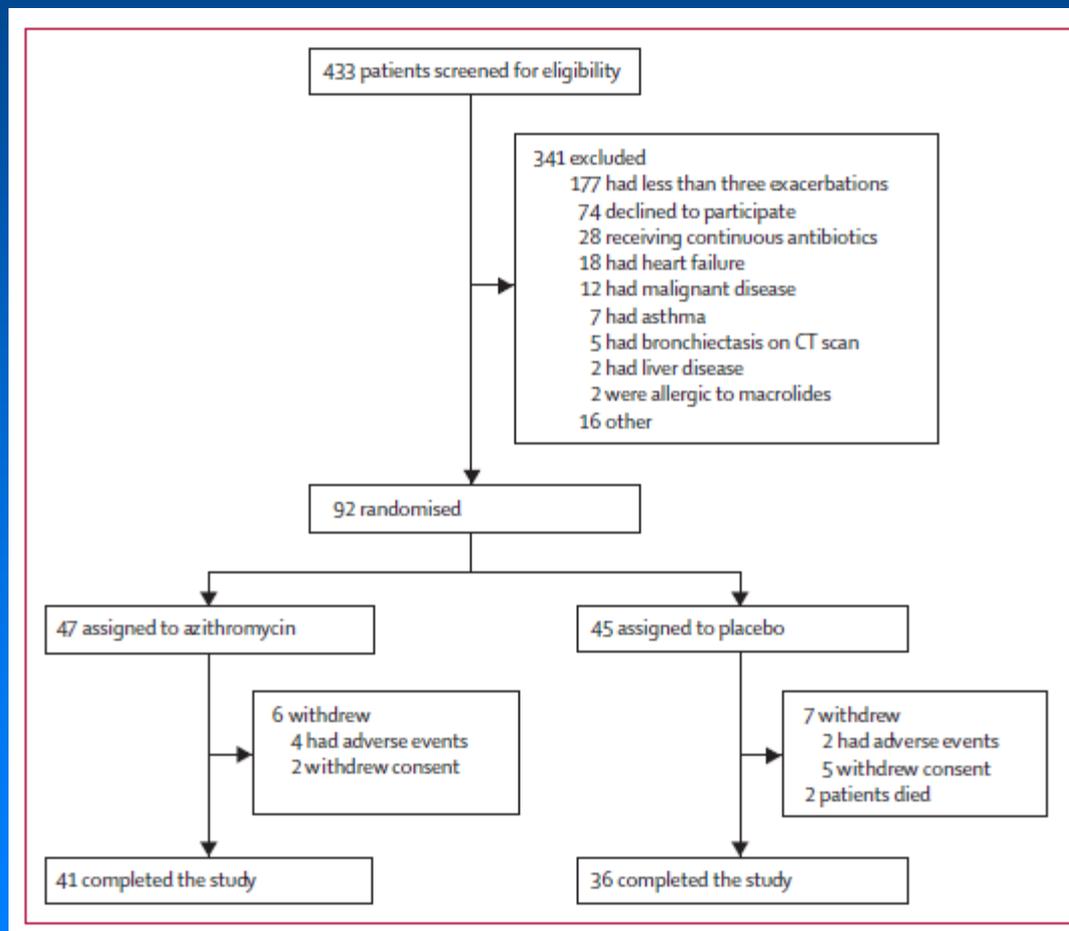
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**Azithromycin maintenance treatment in patients with frequent exacerbations of chronic obstructive pulmonary disease (COLUMBUS): a randomised, double-blind, placebo-controlled trial**

*Sevim Uzun, Remco S Djamin, Jan A J W Kluytmans, Paul G H Mulder, Nils E van't Veer, Anton A M Ermens, Aline J Pelle, Henk C Hoogsteden, Joachim G J V Aerts\*, Menno M van der Eerden\**

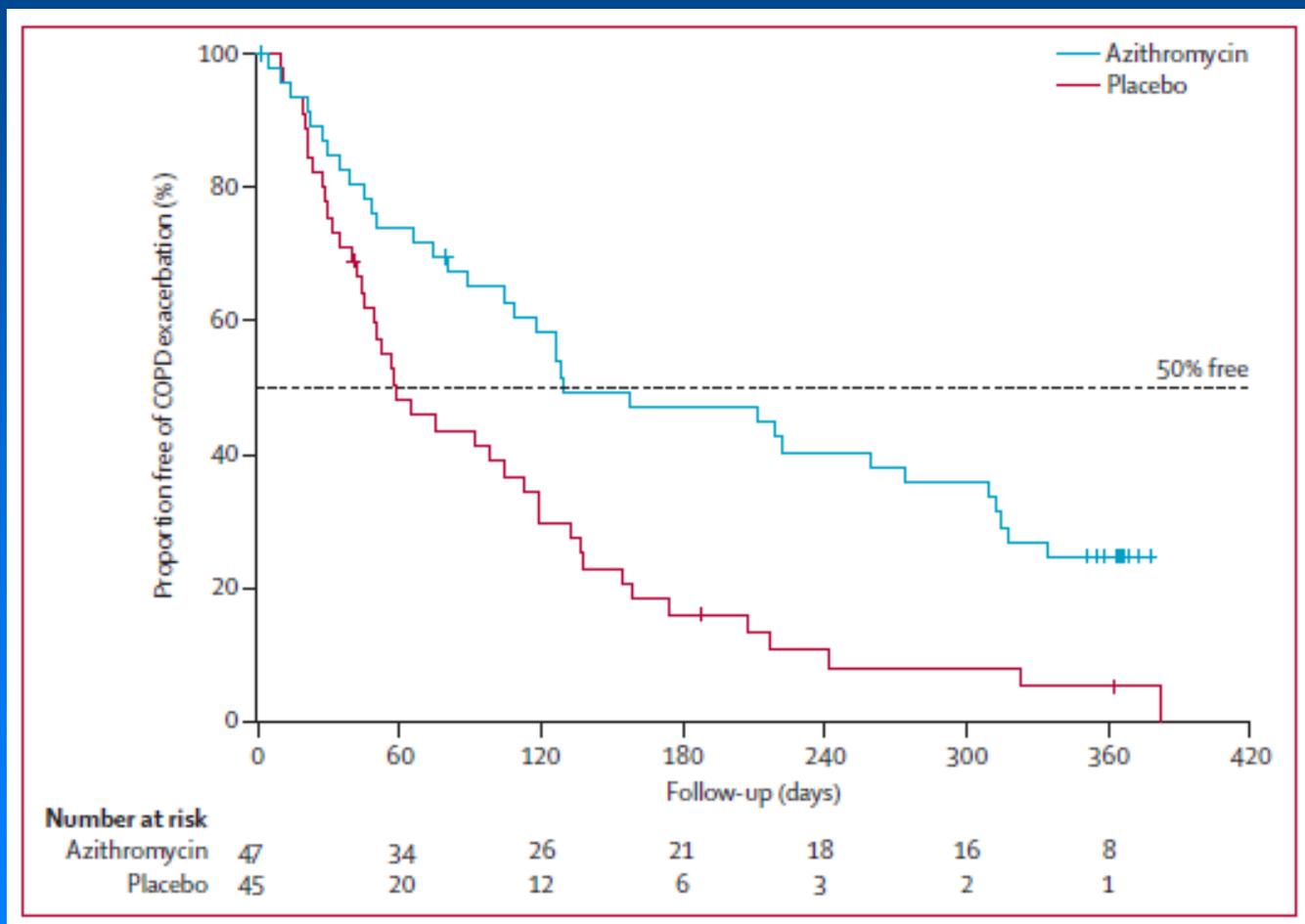


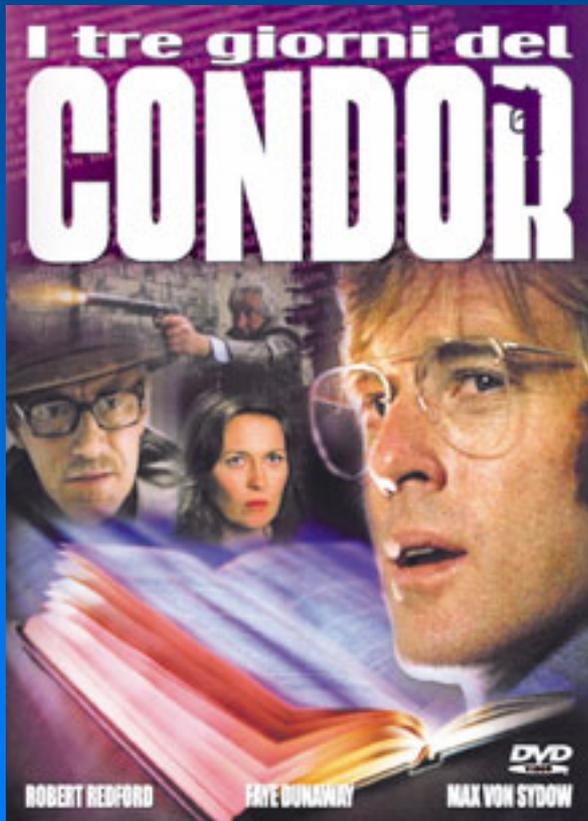
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# Epidemiologia, fattori di rischio e gestione del paziente

**FRANCESCO DE BLASIO, MD, FCCP**  
U.F. PNEUMOLOGIA E  
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