

70^o 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

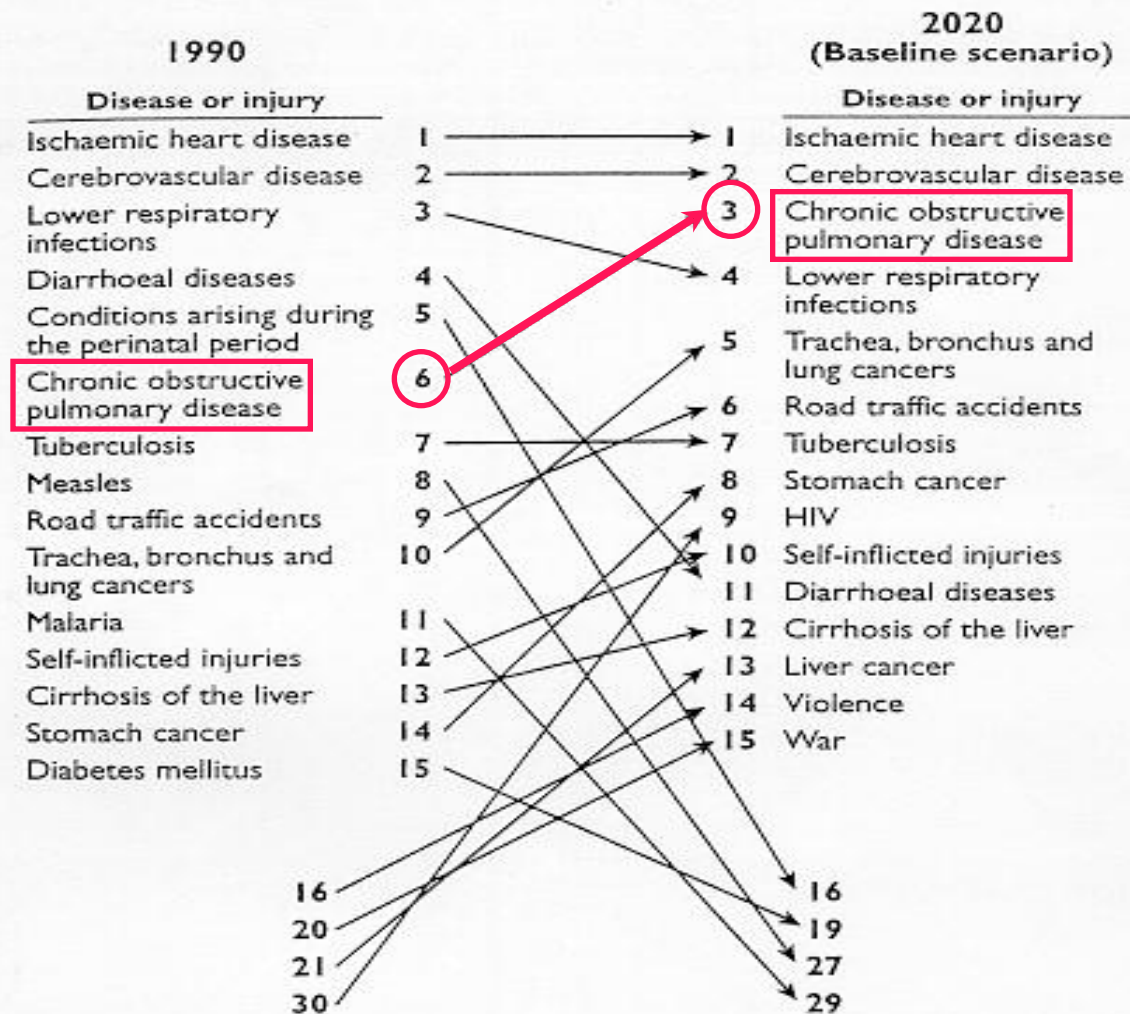
CASA DI CURA CLINIC CENTER S.P.A. - NAPOLI

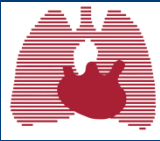
Disclosures:

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

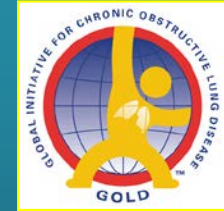


Change in rank order of deaths for the 15 leading causes, world, 1990–2020

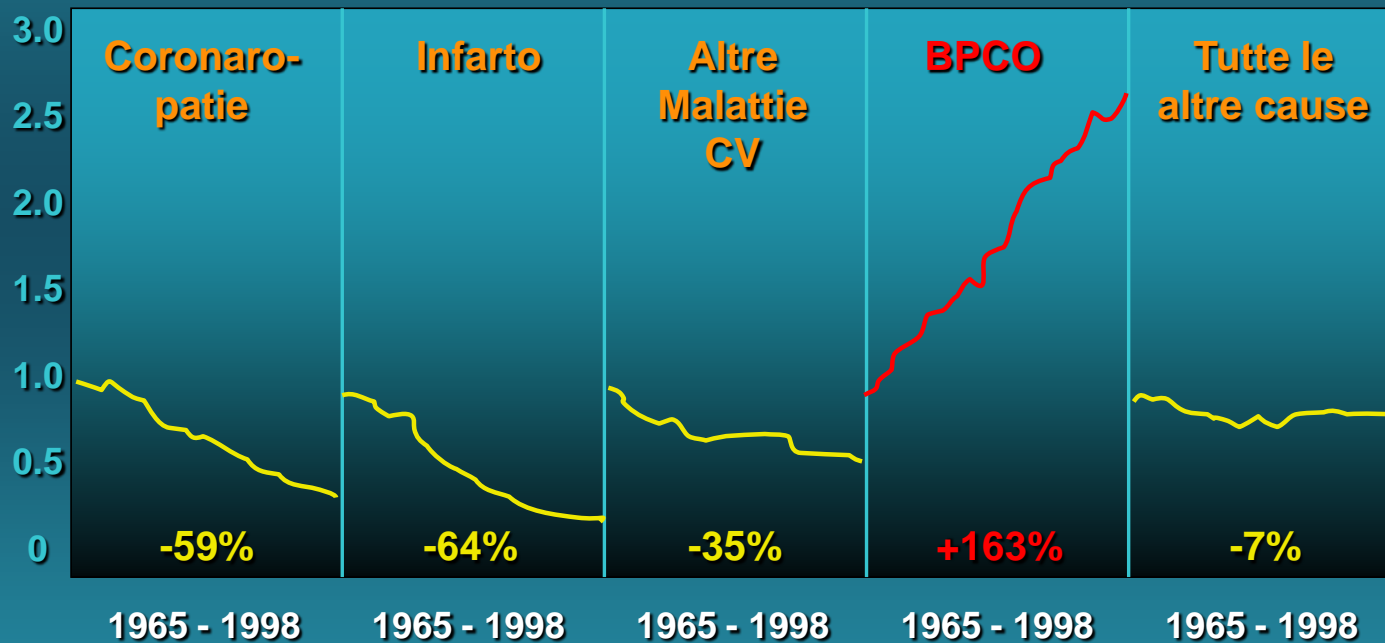




VARIAZIONE PERCENTUALE DELLE MORTI PER ETA' IN U.S.A.



Proporzione della frequenza del 1965





ERS

EUROPEAN
RESPIRATORY
SOCIETY



EUROPEAN LUNG
white book

RESPIRATORY HEALTH AND DISEASE IN EUROPE



europaan respiratory society every breath counts



ERS

EUROPEAN
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SOCIETY



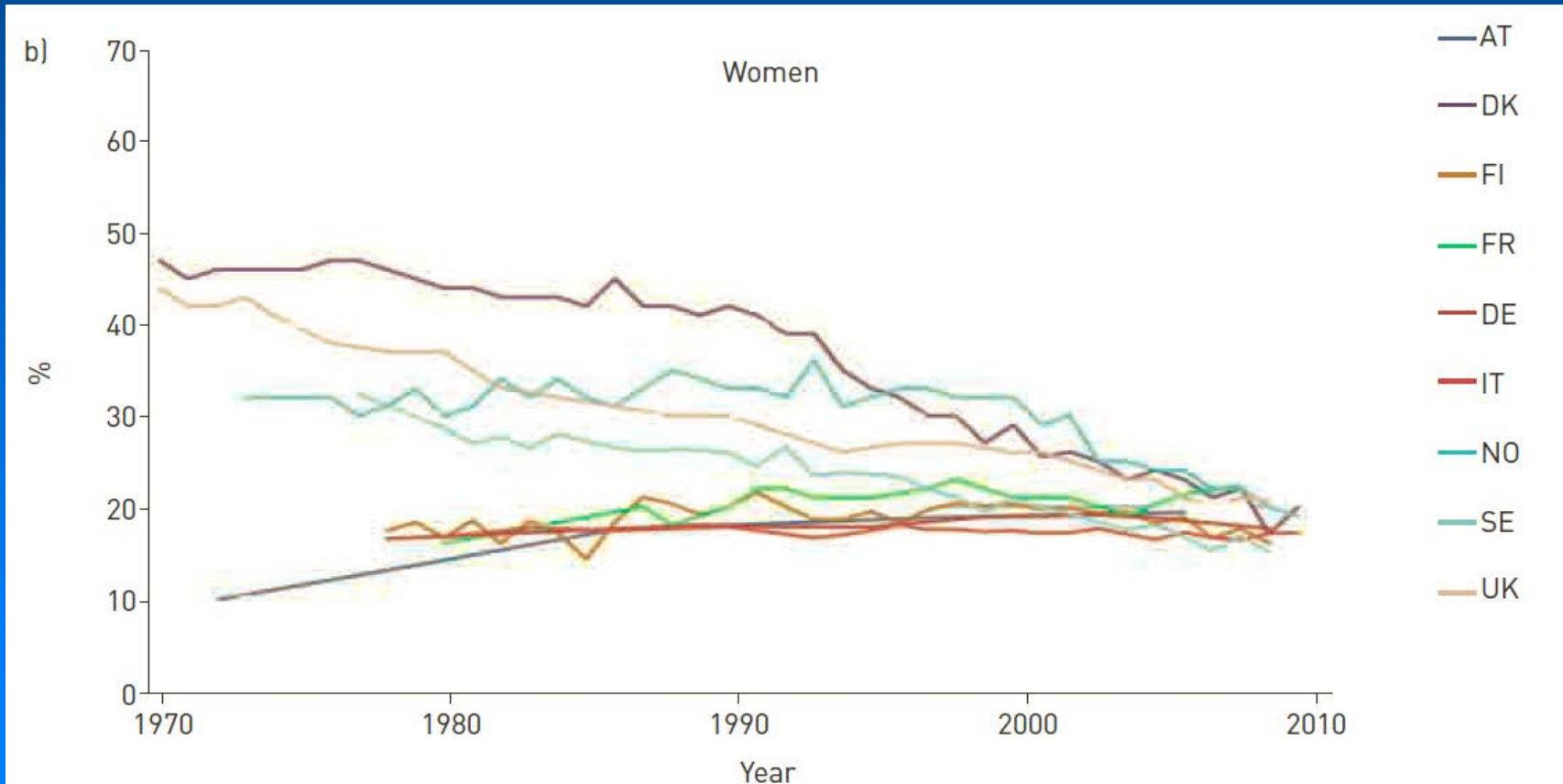
“

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

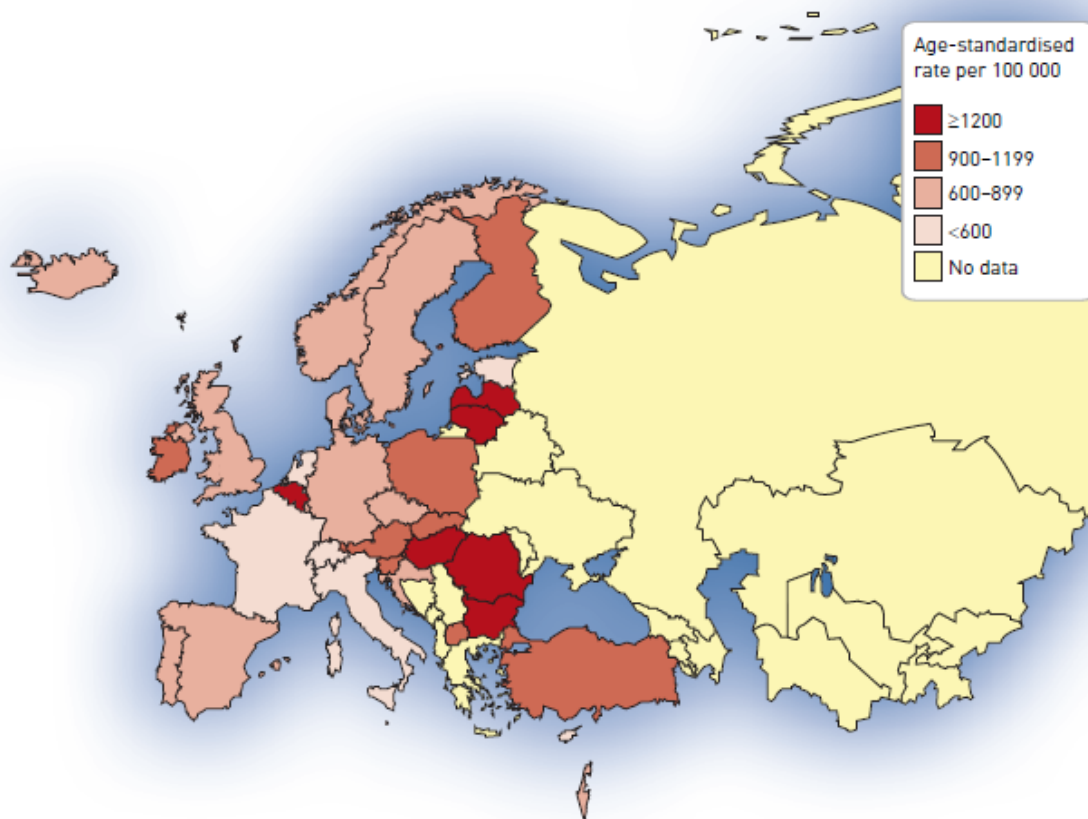


Figure 6 – Age-standardised admission rates for all respiratory conditions. The figure shows International Short Hospital Mortality Tabulation (HMT) categories only (as these are covered by both data sources, giving a wider comparable set of countries). Combined rates are shown for asthma, COPD, bronchiectasis, 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).



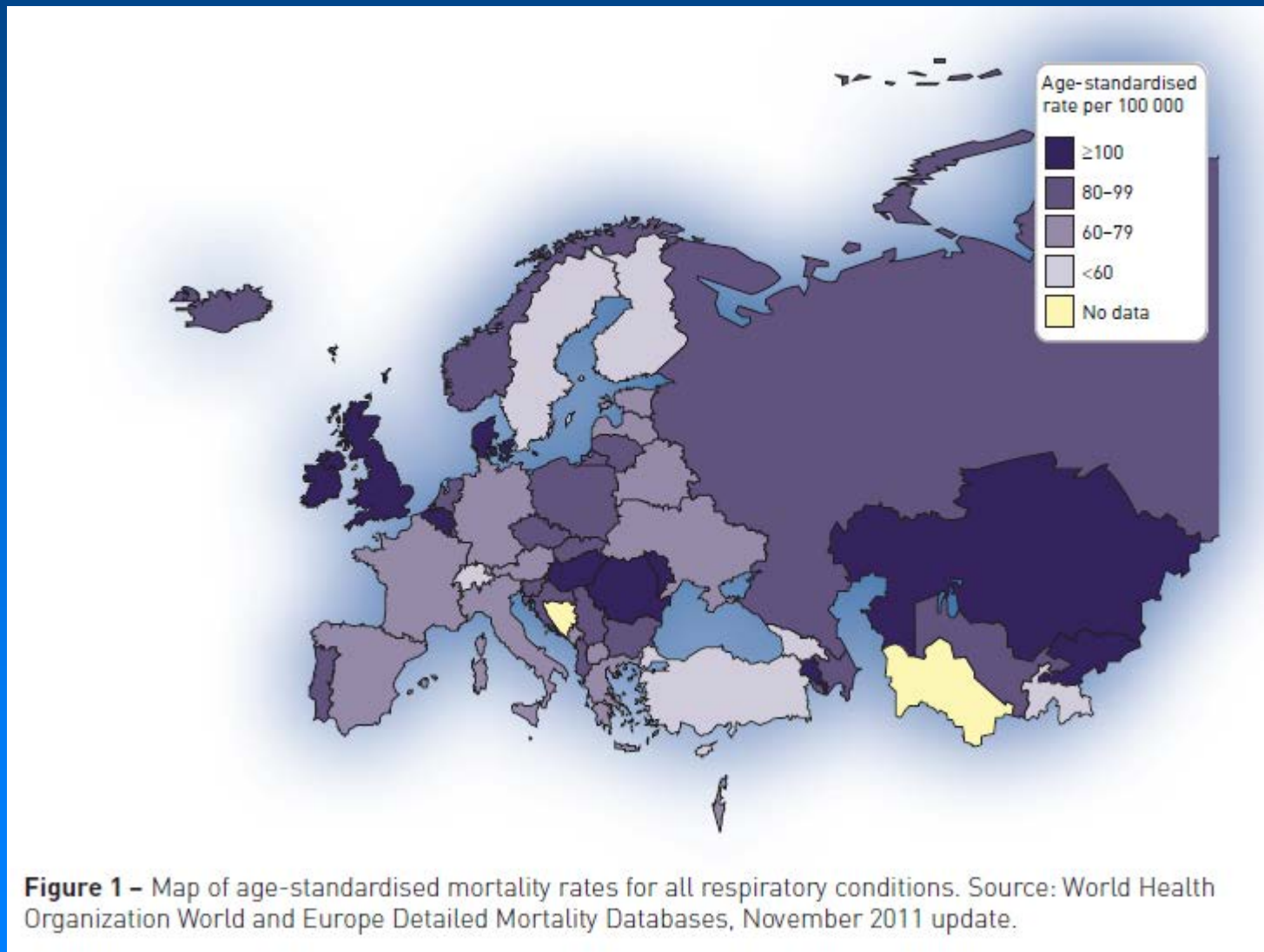
MORTALITA'



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%)
Lower respiratory infections	3.5 million (6.1%)	0.23 million (2.3%)
COPD	3.3 million (5.8%)	0.25 million (2.5%)
Diarrhoeal diseases	2.5 million (4.3%)	0.03 million (0.3%)
HIV/AIDS	1.8 million (3.1%)	0.08 million (0.8%)
Trachea/bronchus/lung cancer	1.4 million (2.4%)	0.38 million (3.9%)
Tuberculosis	1.3 million (2.4%)	0.08 million (0.8%)
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'

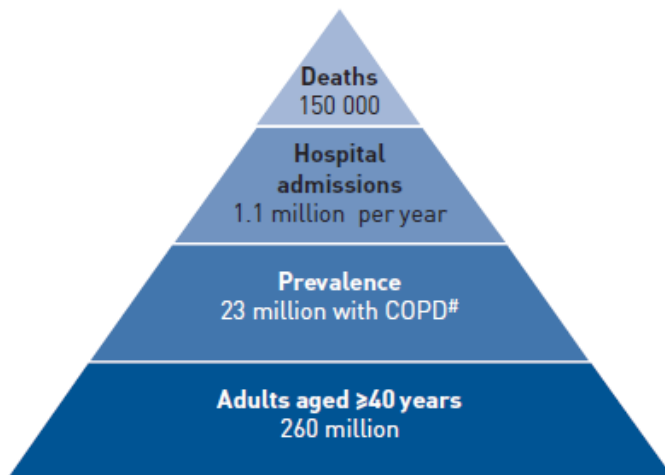




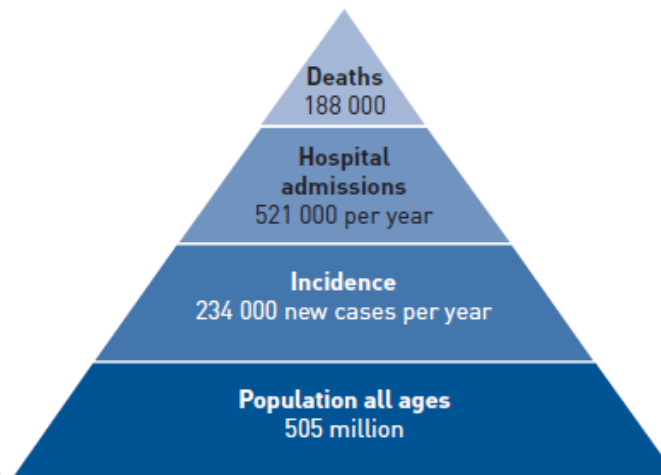
BPCO - TUMORI - TBC



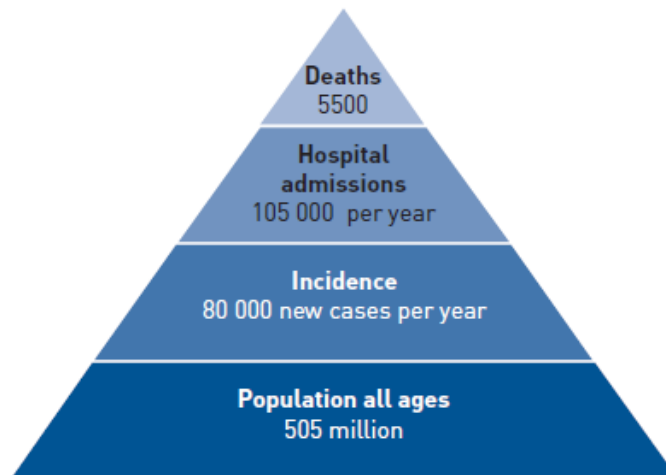
c) COPD in older adults



d) Lung cancer



e) Tuberculosis





PROSPETTIVE



Percentage of deaths worldwide	2008	2015	2030
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
Percentage of deaths in WHO European region	2008	2015	2030
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

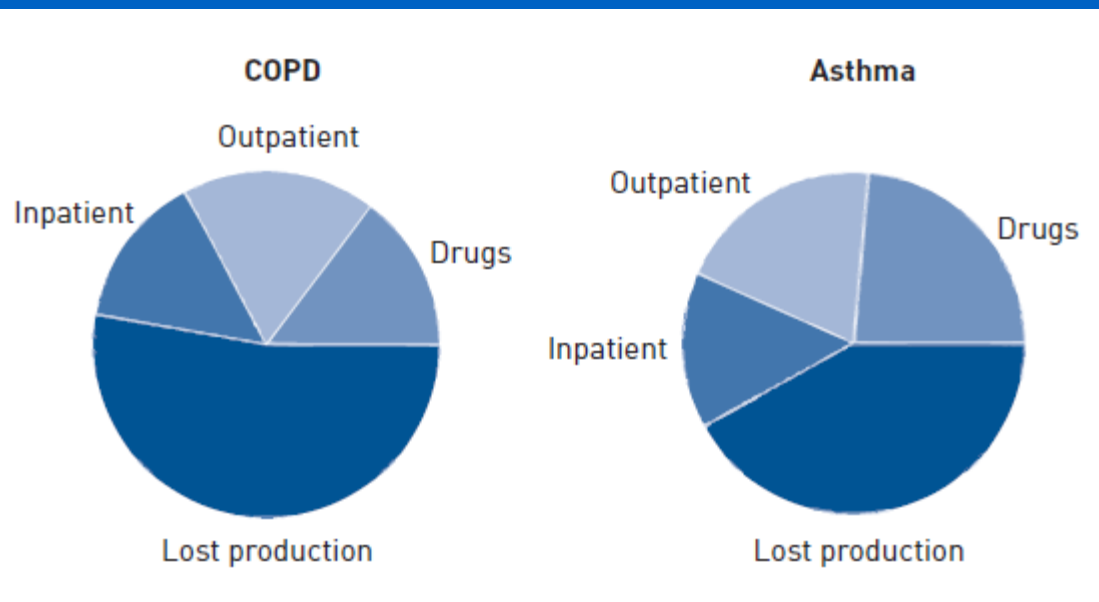
Percentage of DALYs worldwide	2008	2015	2030
Lower respiratory infections	5.4	4.6	3.2
COPD	2.3	2.7	3.8
Trachea/bronchus/lung cancer	0.9	1.0	1.4
Tuberculosis	2.0	1.6	1.1
Percentage of DALYs in WHO European region	2008	2015	2030
Lower respiratory infections	1.5	1.3	1.0
COPD	2.0	2.0	2.2
Trachea/bronchus/lung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



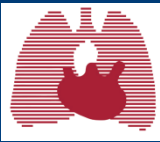


COSTI



	Direct costs [#] € bn	Indirect costs [¶] € 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 [#]	#	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

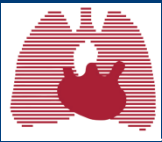
Disease	DALYs lost per year (thousands)	Annual monetised value € bn
Lung cancer	1873	103.0
COPD	1691	93.0
TB	103	5.6
Pneumonia/ALRI	790	43.5
Asthma	697	38.3
Total	5154	283.4



BRONCOPATIA CRONICA OSTRUTTIVA

AMERICAN COLLEGE OF
CHEST
PHYSICIANS





**ASMA
BRONCHIALE**

FIBROSI

TUMORI

**INSUFFICIENZA
RESPIRATORIA**

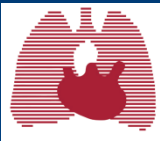
OSAS

**RIABILITAZIONE
RESPIRATORIA**



B.P.C.O.

TRAPIANTO



**ASMA
BRONCHIALE**

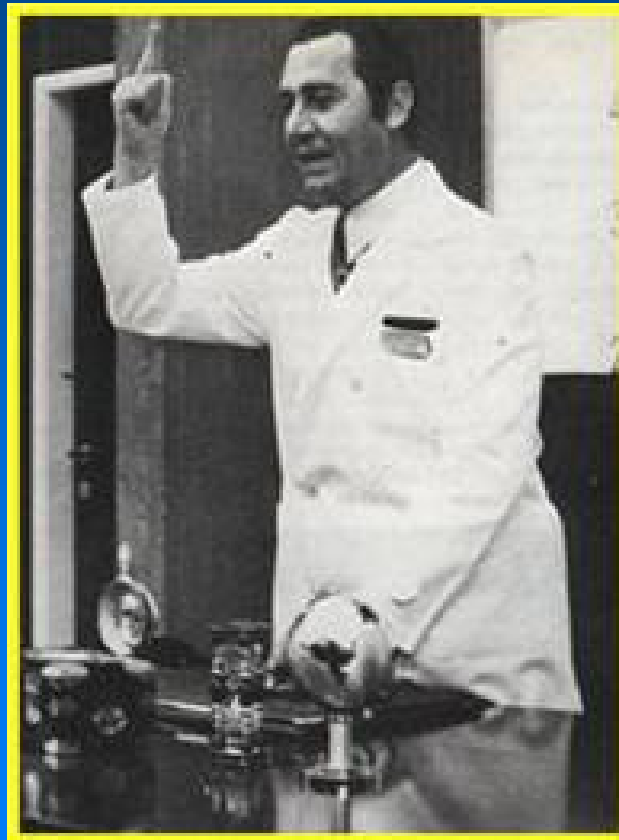
FIBROSI

TUMORI

**INSUFFICIENZA
RESPIRATORIA**

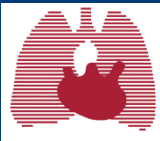
OSAS

**RIABILITAZIONE
RESPIRATORIA**



B.P.C.O.

TRAPIANTO



FISIOPATOLOGIA DELLA BPCO

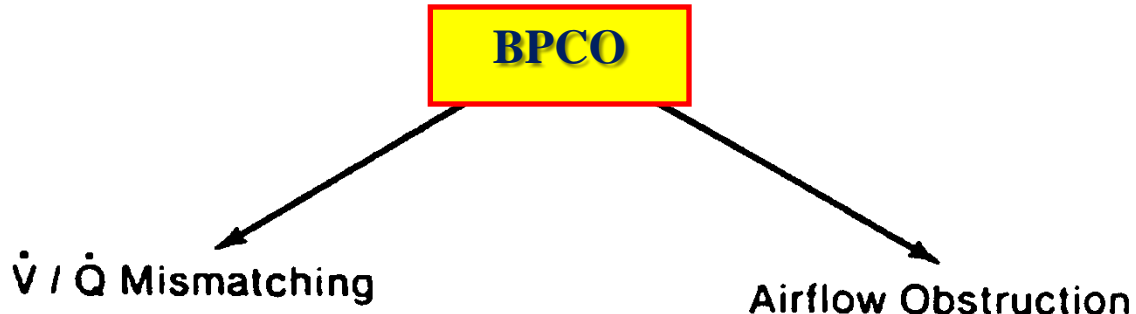


BPCO

LIMITAZIONE ESERCIZIO FISICO - DISPNEA



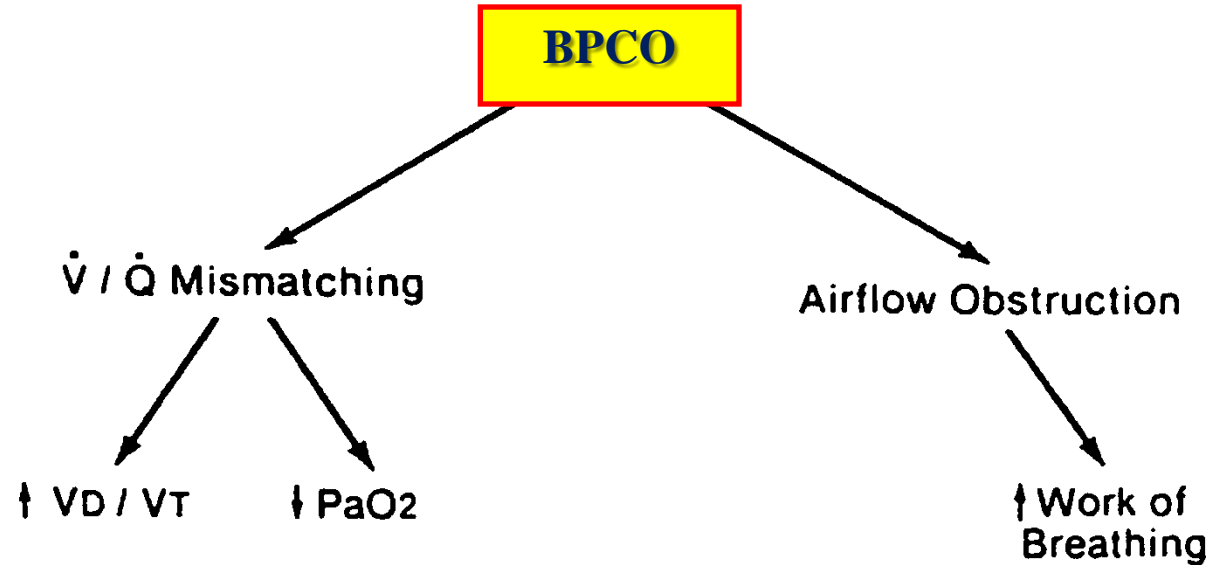
FISIOPATOLOGIA DELLA BPCO



LIMITAZIONE ESERCIZIO FISICO - DISPNEA



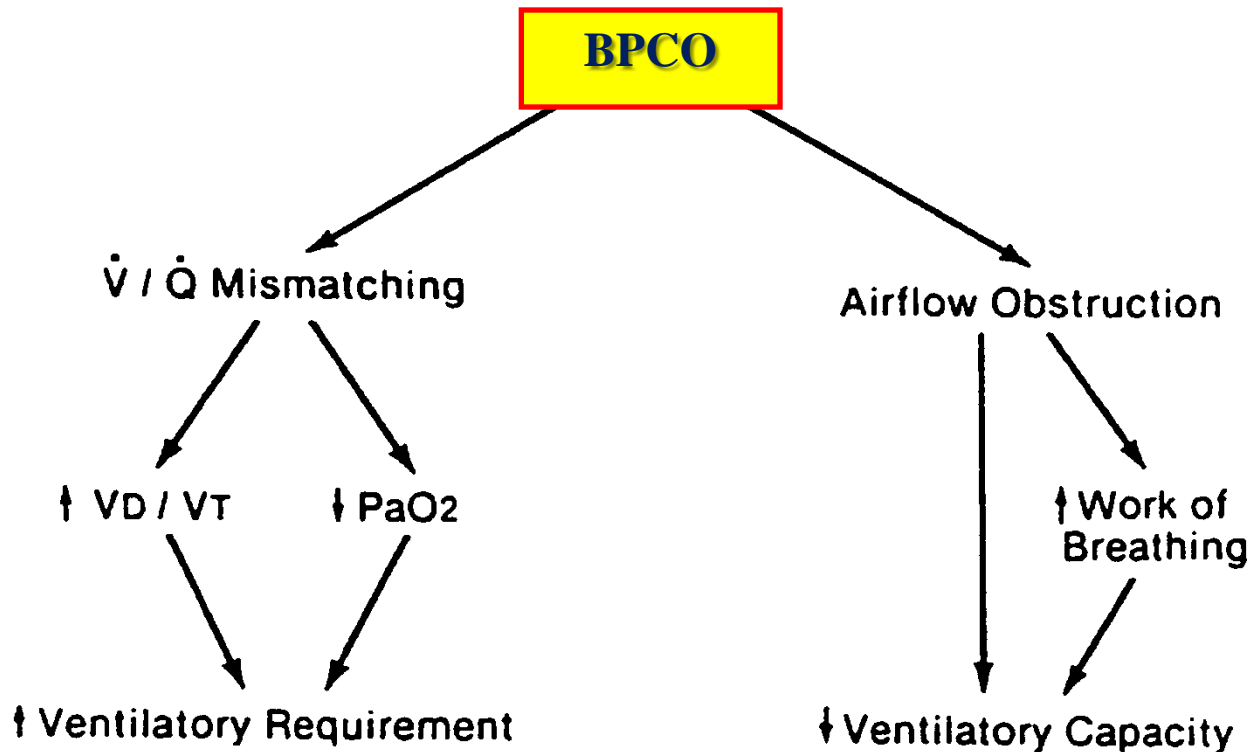
FISIOPATOLOGIA DELLA BPCO



LIMITAZIONE ESERCIZIO FISICO - DISPNEA



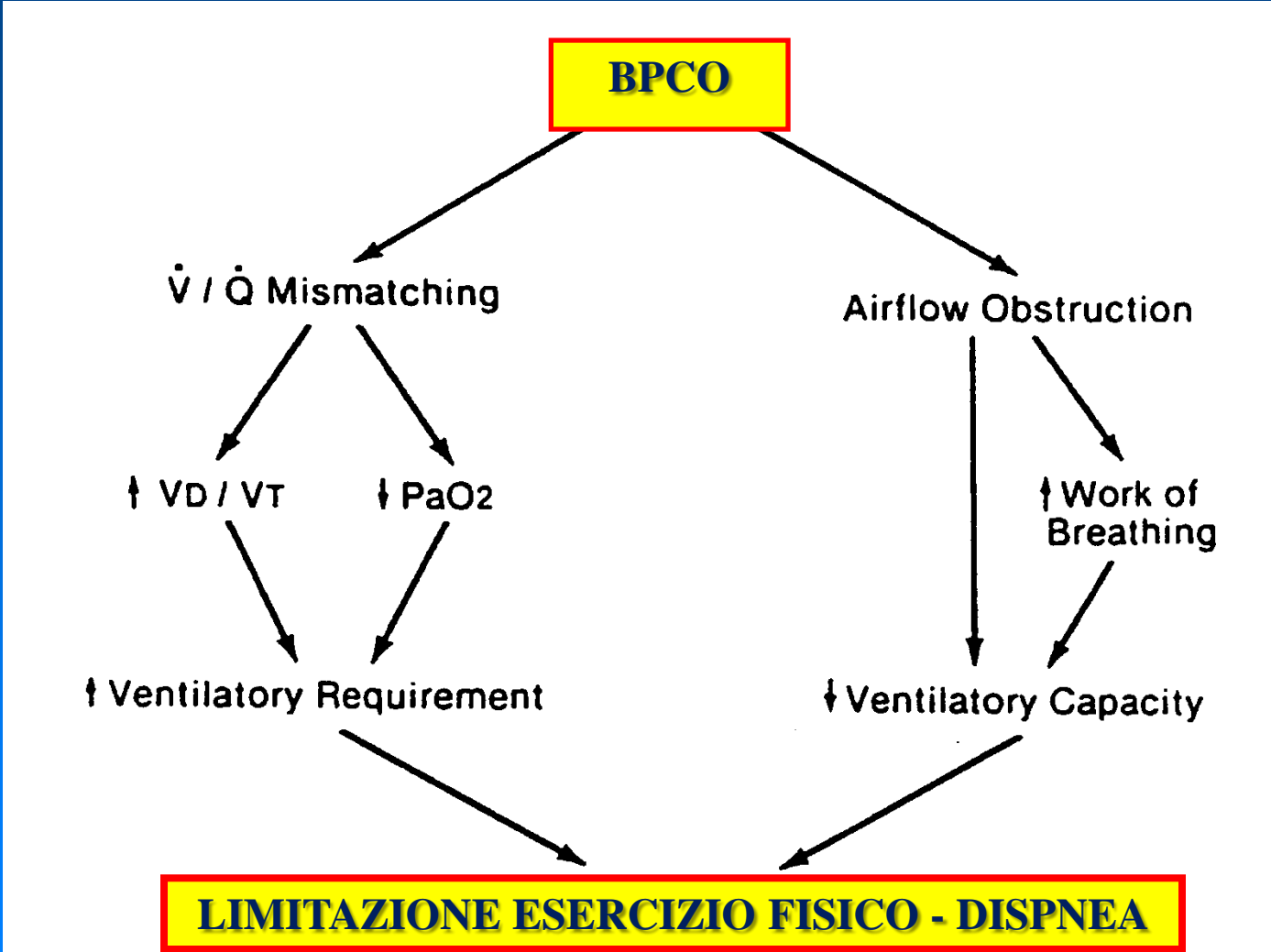
FISIOPATOLOGIA DELLA BPCO



LIMITAZIONE ESERCIZIO FISICO - DISPNEA



FISIOPATOLOGIA DELLA BPCO



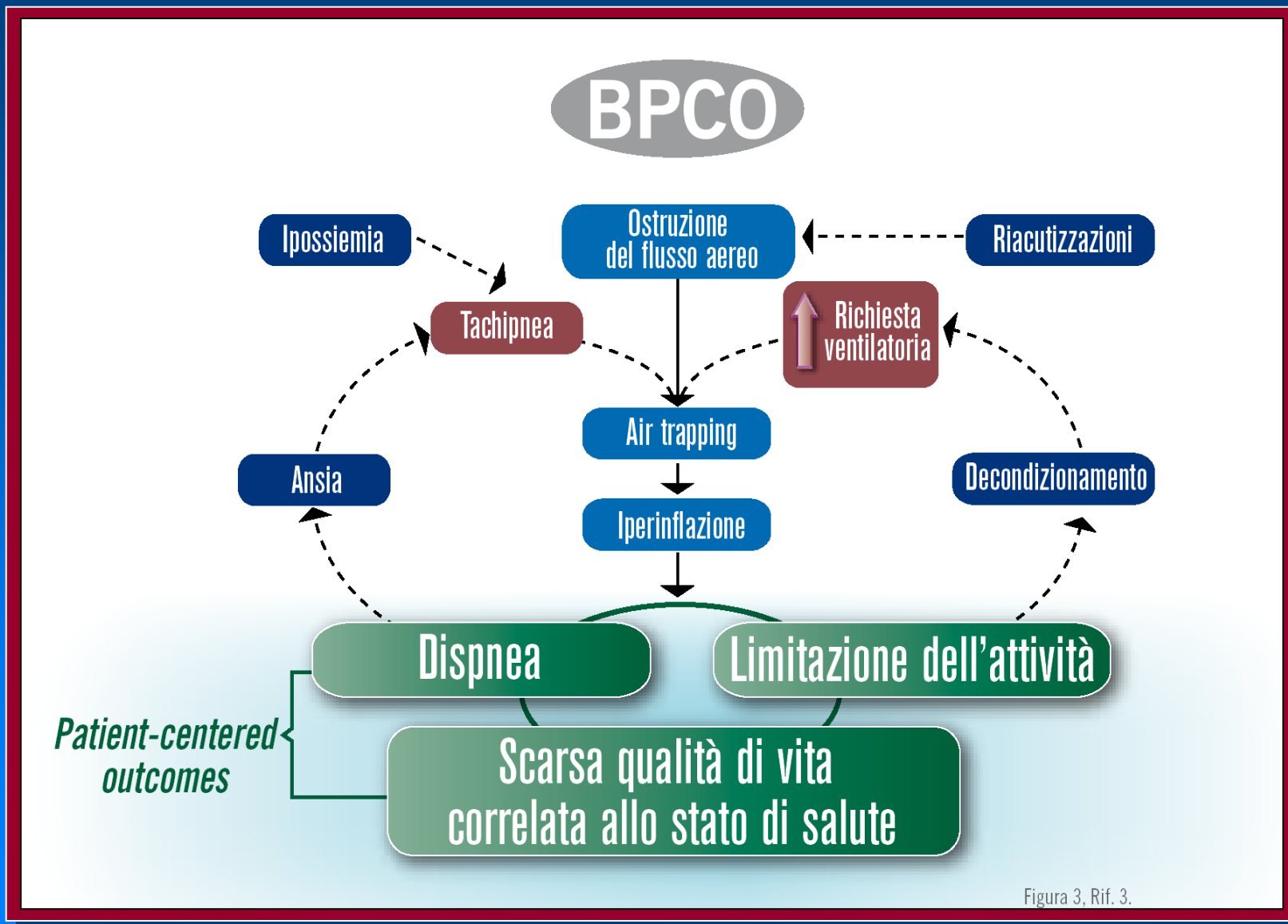
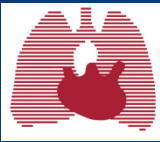


Figura 3, Rif. 3.

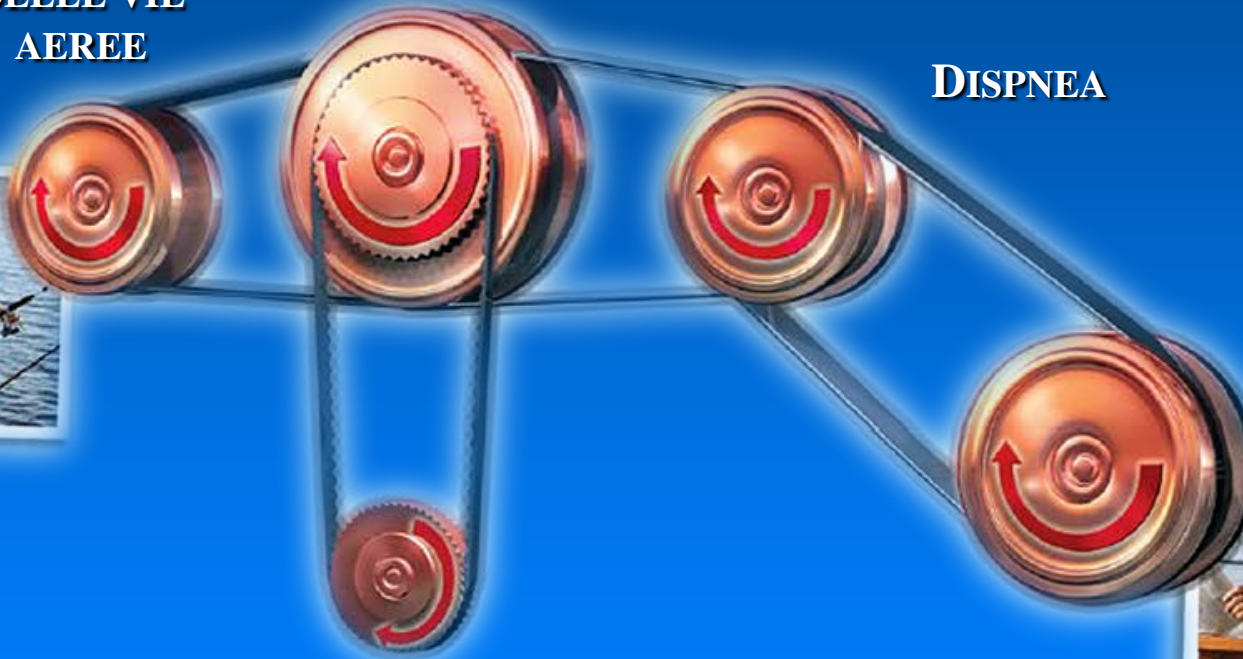


MODIFICAZIONI DEL DECORSO CLINICO

**OSTRUZIONE
DELLE VIE
AEREE**

**AIR
TRAPPING**

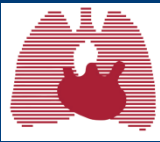
DISPNEA



RIACUTIZZAZIONI



**INATTIVITÀ
DISABILITÀ**

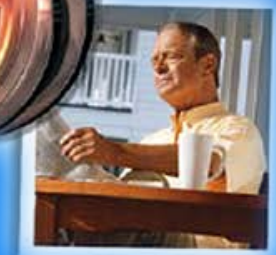
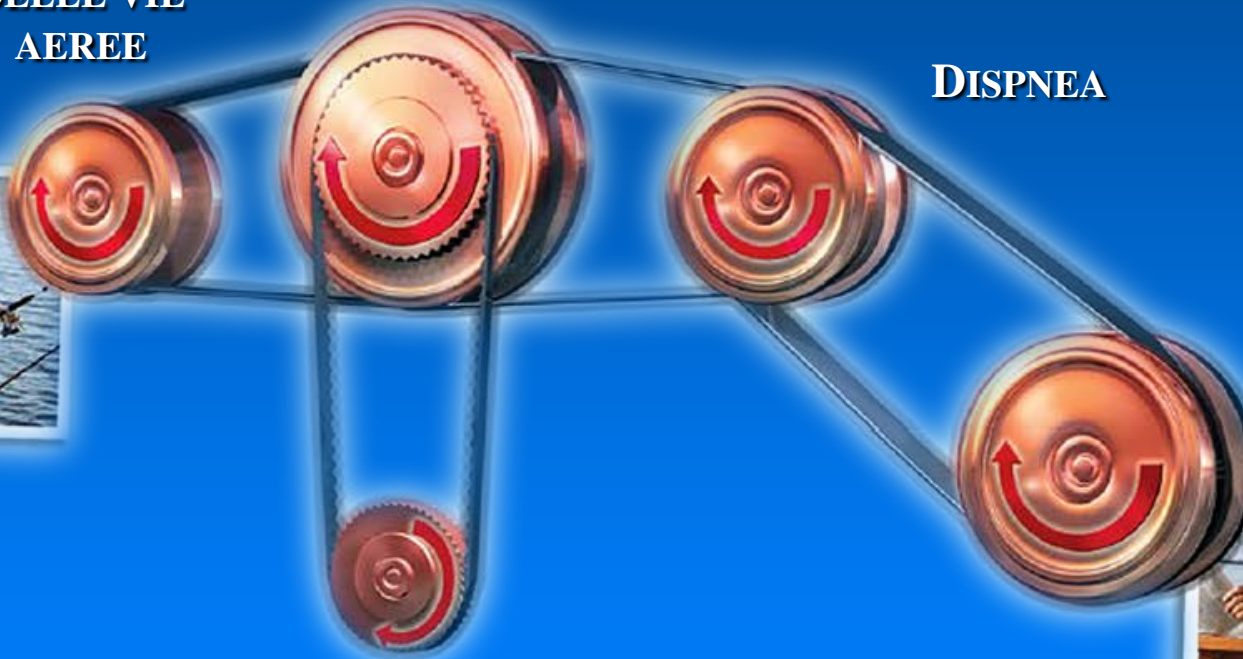


MODIFICAZIONI DEL DECORSO CLINICO

**OSTRUZIONE
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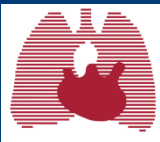
**AIR
TRAPPING**

DISPNEA



RIACUTIZZAZIONI

**INATTIVITÀ
DISABILITÀ**



GIU 2010

REVIEW

Prevention of exacerbations of COPD with pharmacotherapy

M. Miravittles



REVIEW

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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 ⁻¹ for 5 days every 2 months	1 yr	25 (46 [#])
CALVERLEY [40]	Fluticasone	500 µg every 12 h	3 yrs	18
KARDOS [60]	Fluticasone	500 µg every 12 h	1 yr	35 [†]
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 ⁻¹	1 yr	27
BARR [46]	Tiotropium	18 µg·day ⁻¹	4 yrs	14 [†]
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 ⁻¹	1 yr	25%
DECRAMER [68]	NAC	600 mg·day ⁻¹	3 yrs	1 (21 [‡])



REVIEW

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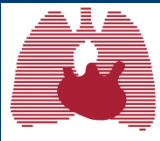
TABLE 1 Strategies aimed at preventing exacerbations

Proven efficacy

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

Questioned efficacy

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



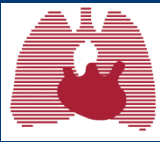
REVIEW

Prevention of exacerbations of COPD with pharmacotherapy

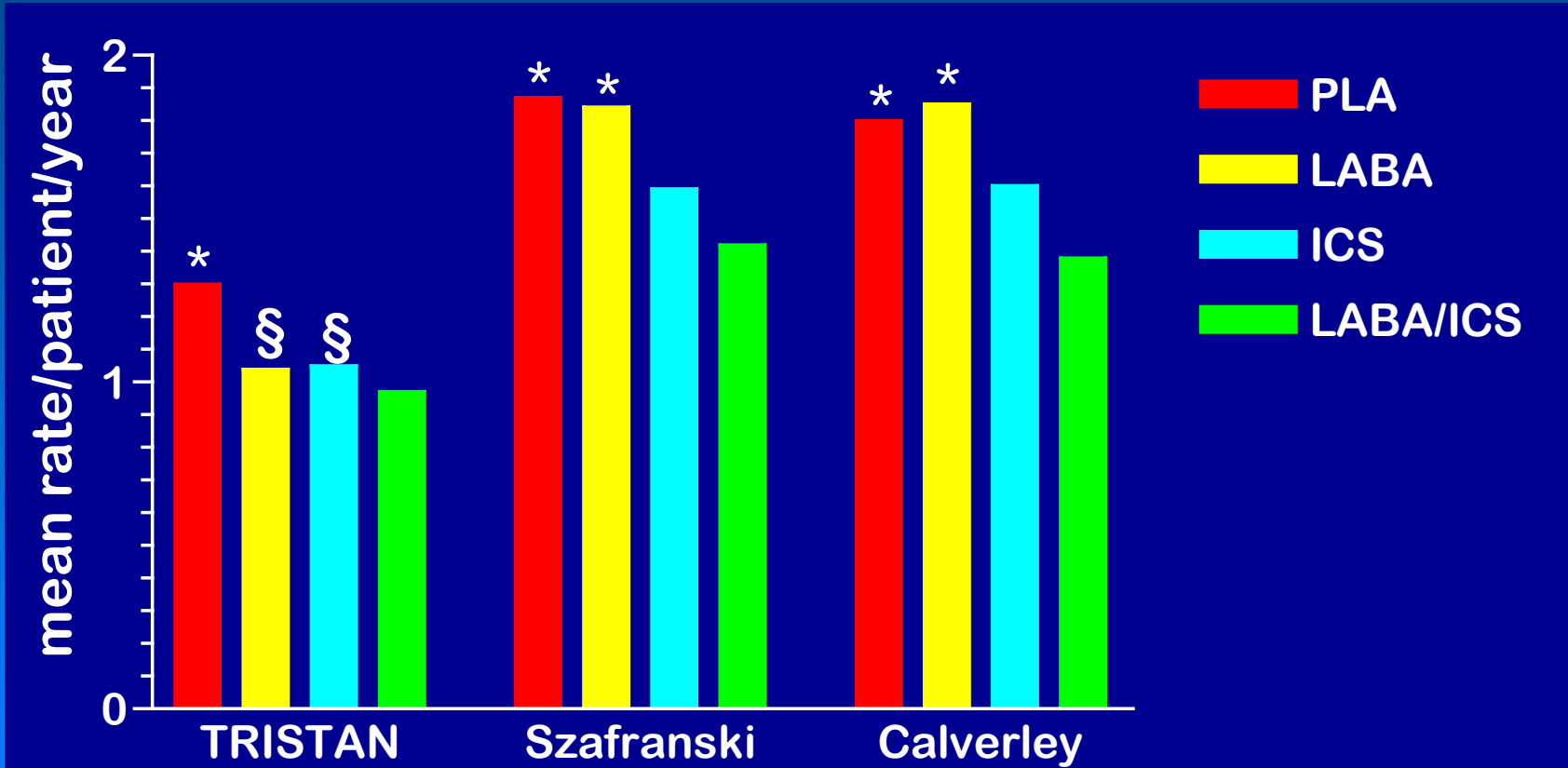
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BRONCODILATATORI STERIODI



Riacutizzazioni gravi e terapia con ICS/LABA



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



CHEST™

The NEW ENGLAND
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ESTABLISHED IN 1812

FEBRUARY 22, 2007

VOL. 356 NO. 8

Salmeterol and Fluticasone Propionate and Survival
in Chronic Obstructive Pulmonary Disease

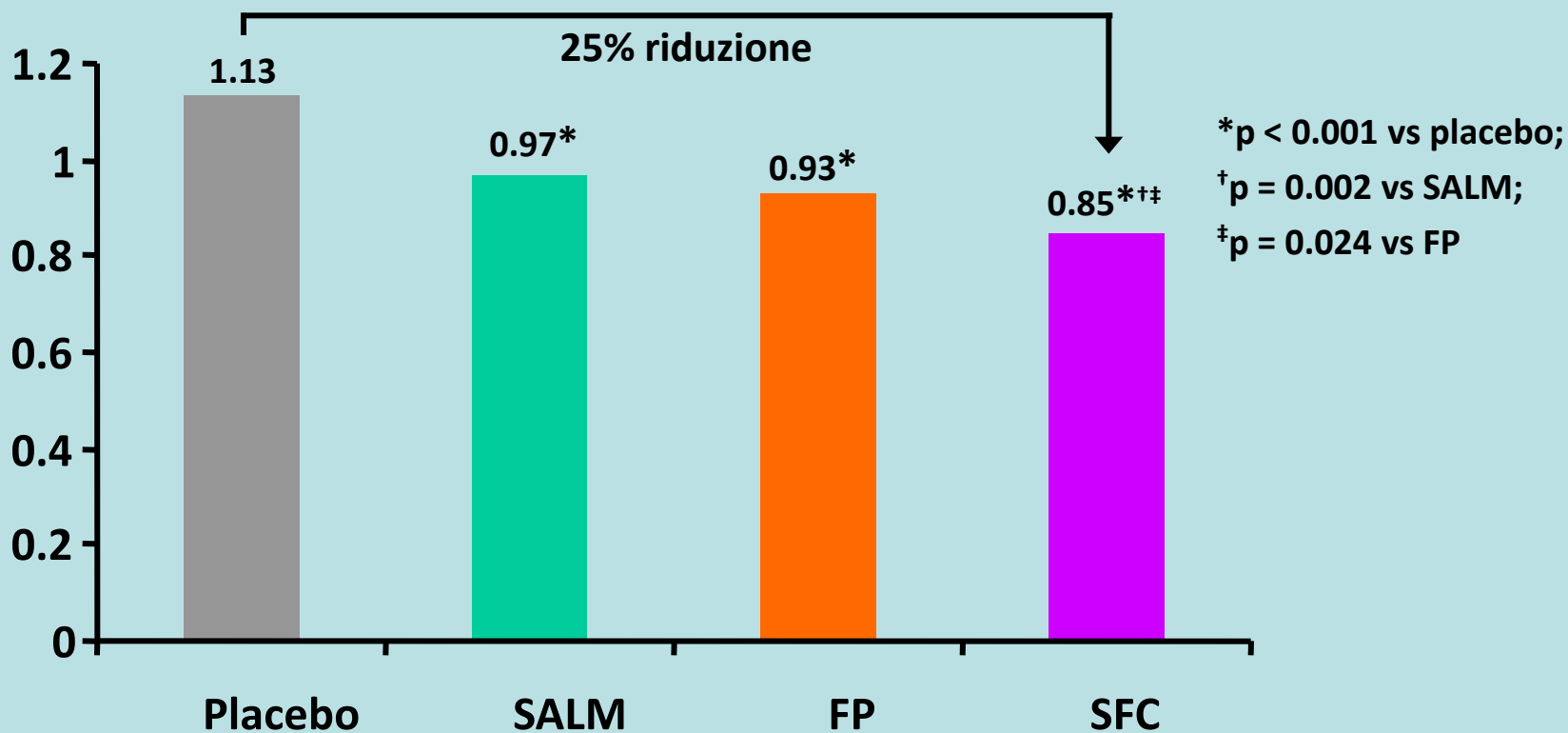
Peter M.A. Calverley, M.D., Julie A. Anderson, M.A., Bartolome Celli, M.D., Gary T. Ferguson, M.D., Christine Jenkins, M.D.,
Paul W. Jones, M.D., Julie C. Yates, B.S., and Jørgen Vestbo, M.D., for the TORCH investigators*



Riacutizzazioni moderate e gravi

Studio TORCH

Numero medio di riacutizzazioni/anno





The NEW ENGLAND
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OCTOBER 9, 2008

VOL. 359 NO. 15

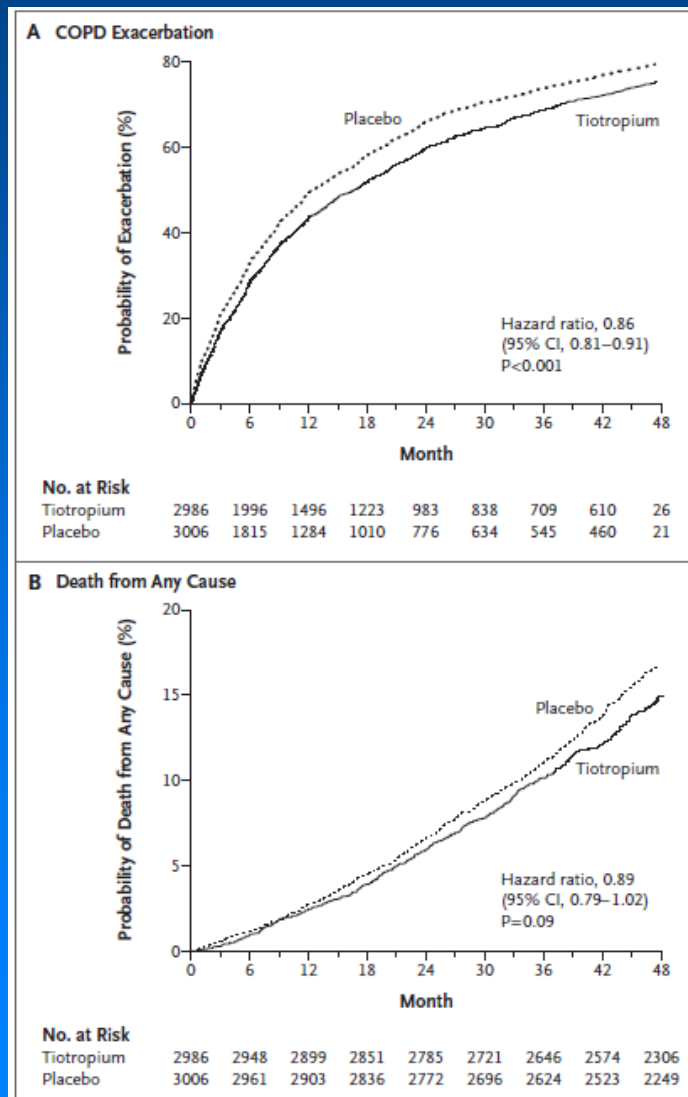
A 4-Year Trial of Tiotropium in Chronic Obstructive
Pulmonary Disease

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





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MARCH 24, 2011

VOL. 364 NO. 12

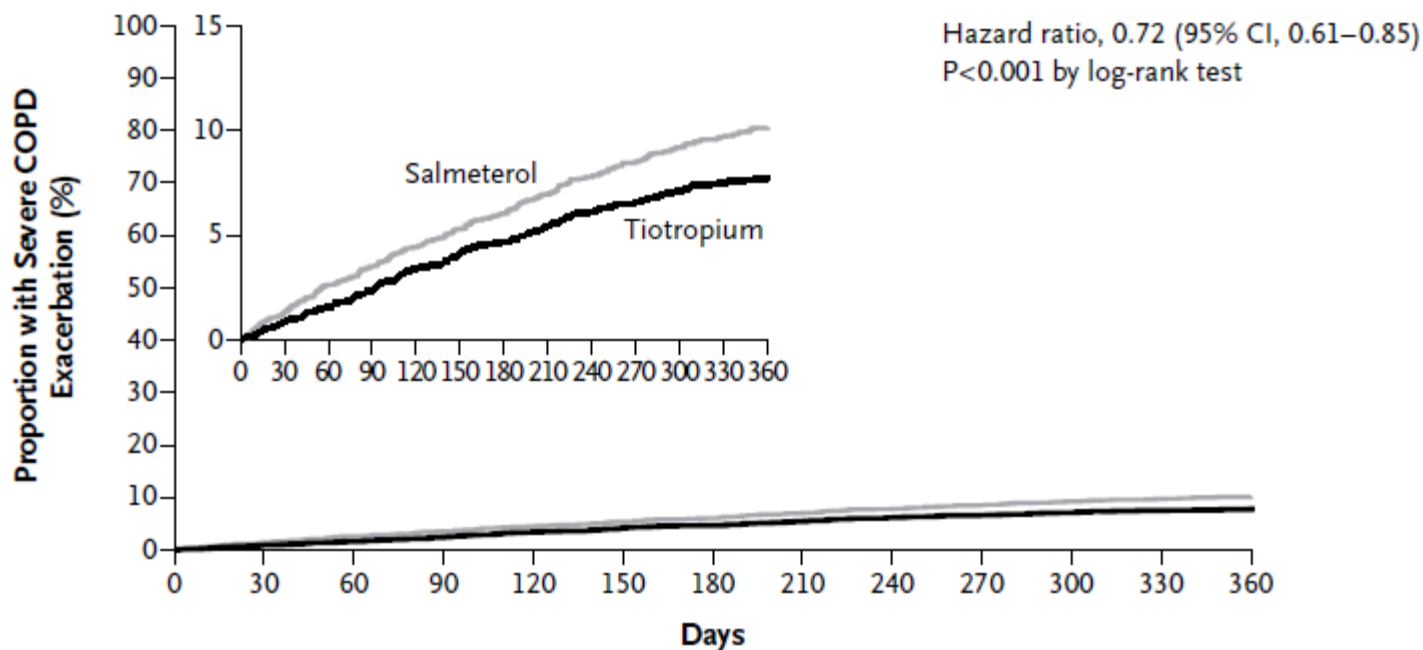
Tiotropium versus Salmeterol for the Prevention
of Exacerbations of COPD

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*



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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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TABLE 1 Strategies aimed at preventing exacerbations

Proven efficacy

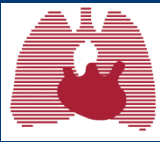
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MUCOLITICI



APR 2008

ORIGINAL PAPER

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

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



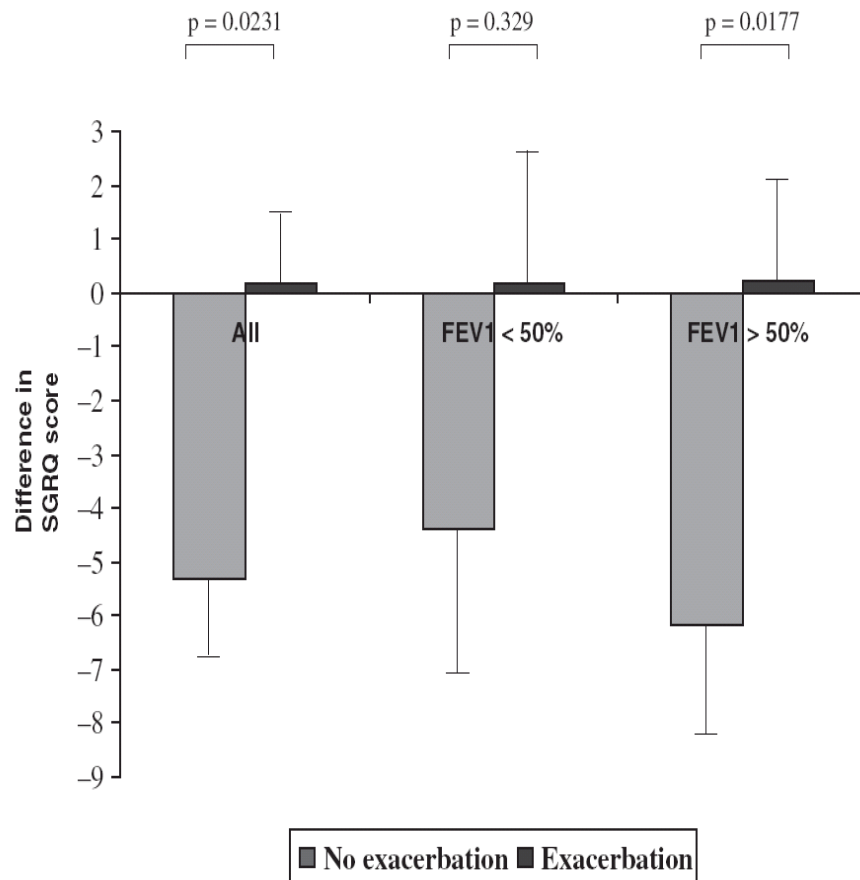
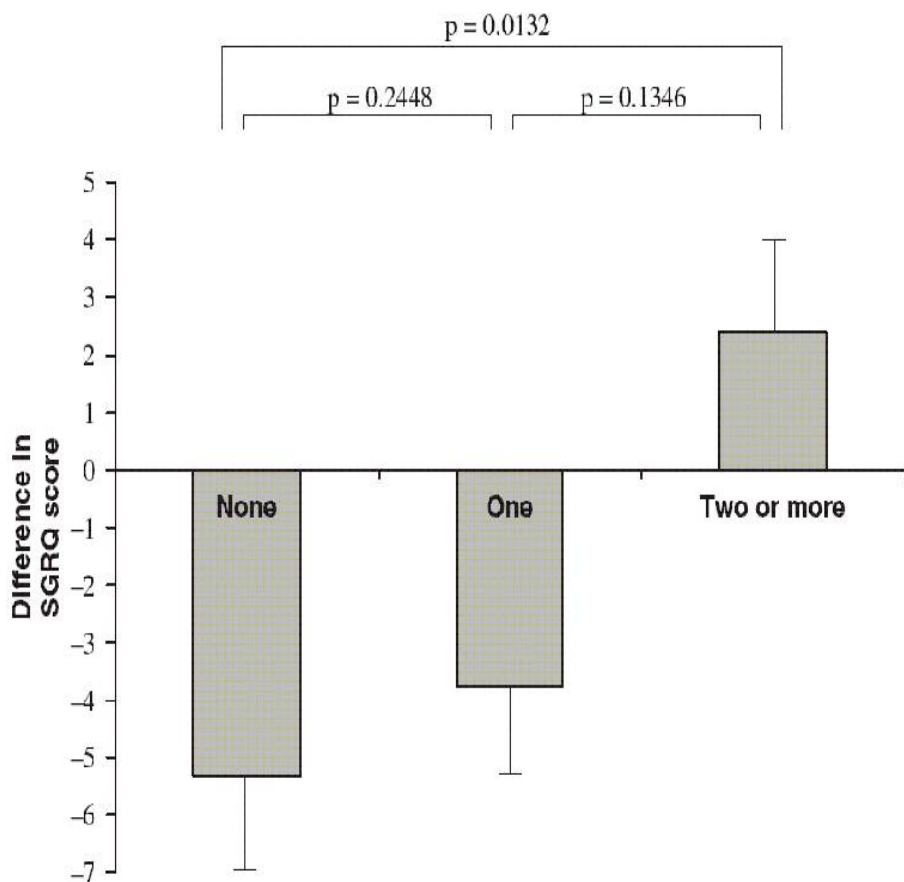
ORIGINAL PAPER

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APR 2008



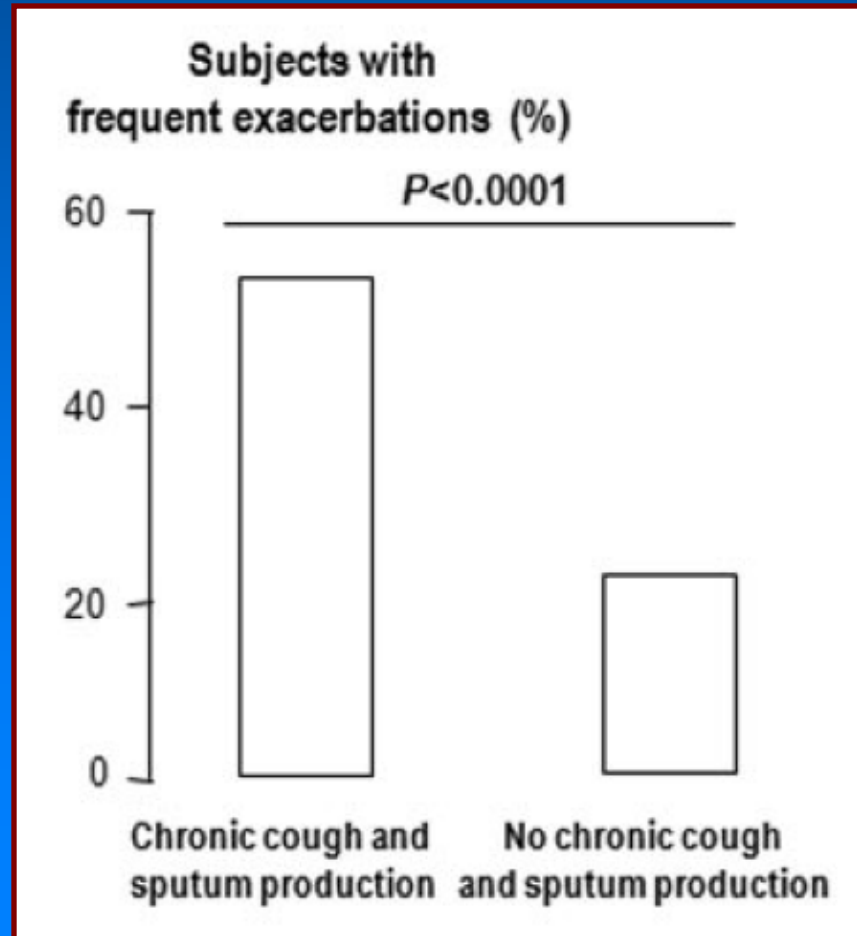


Cough and Sputum Production Are Associated With Frequent Exacerbations and Hospitalizations in COPD Subjects*



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†





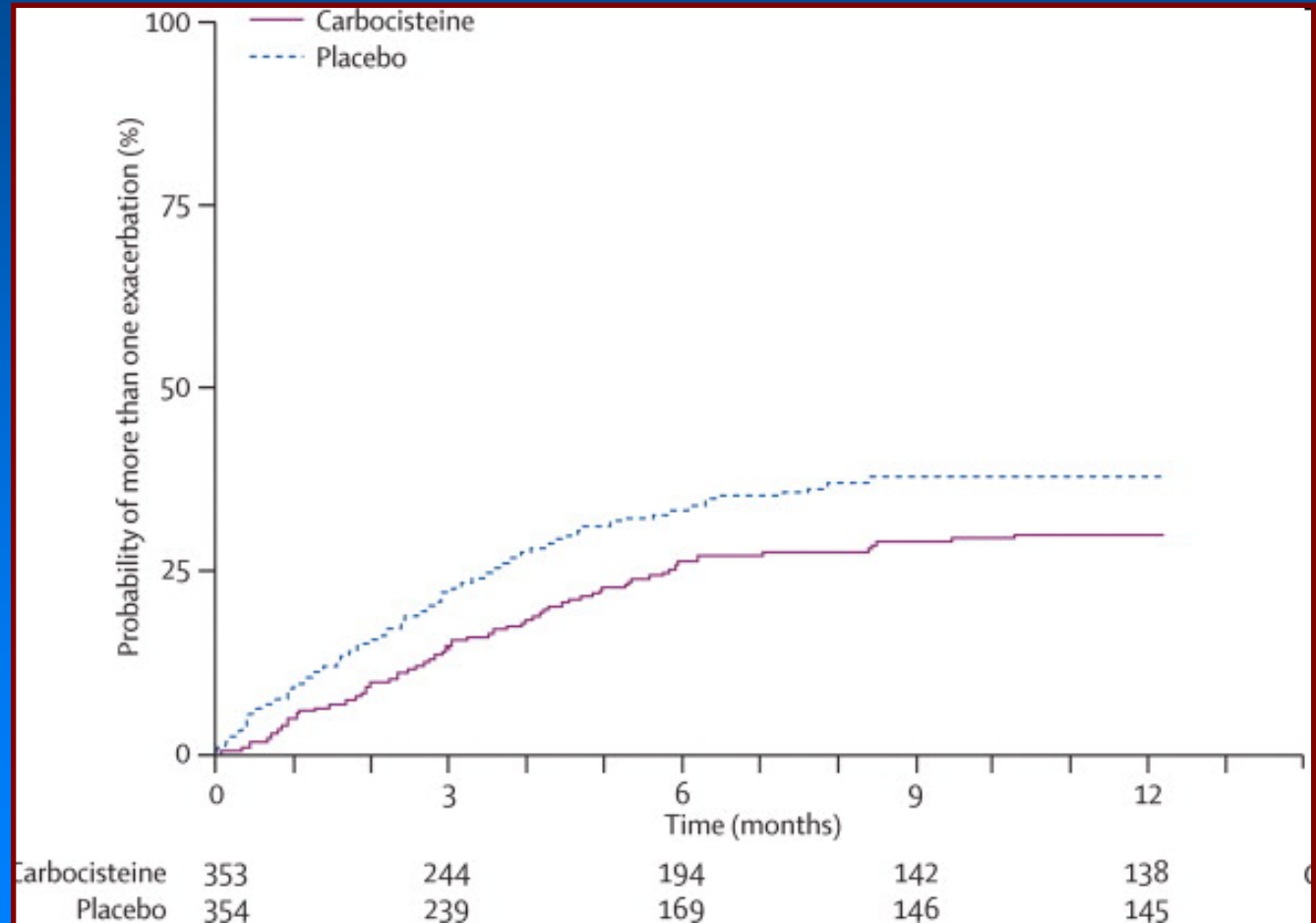
GIU 2008

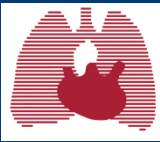
Effect of carbocisteine on acute exacerbation of chronic obstructive pulmonary disease (PEACE Study): a randomised placebo-controlled study

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





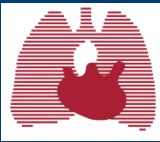
REVIEW

Prevention of exacerbations of COPD with pharmacotherapy

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ANTIBIOTICI



GEN 2010

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

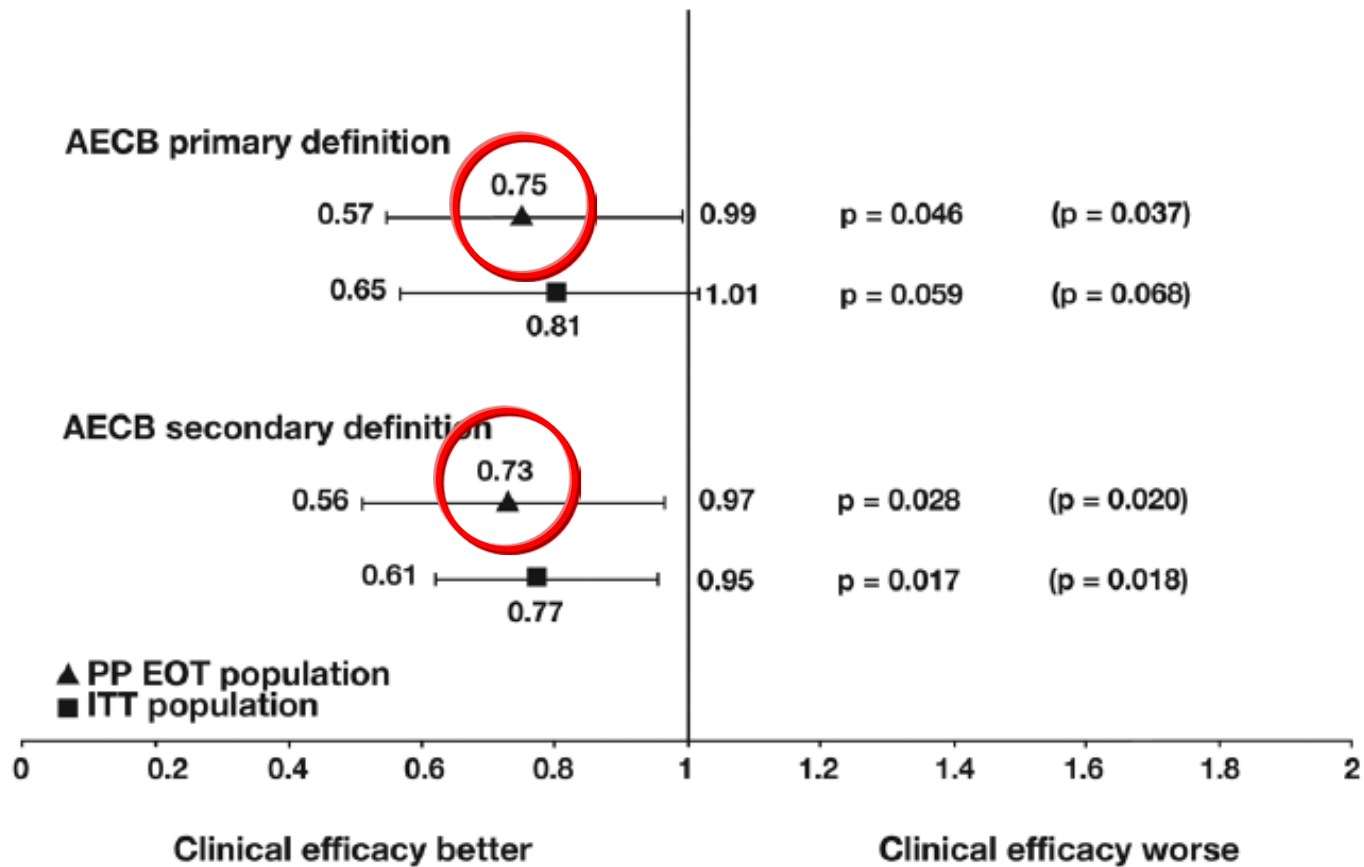
Sanjay Sethi^{1*}, Paul W Jones², Marlize Schmitt Theron³, Marc Miravittles⁴, Ethan Rubinstein⁵, Jadwiga A Wedzicha⁶, Robert Wilson⁷, the PULSE Study group



GEN 2010

(A) PP EOT and ITT population

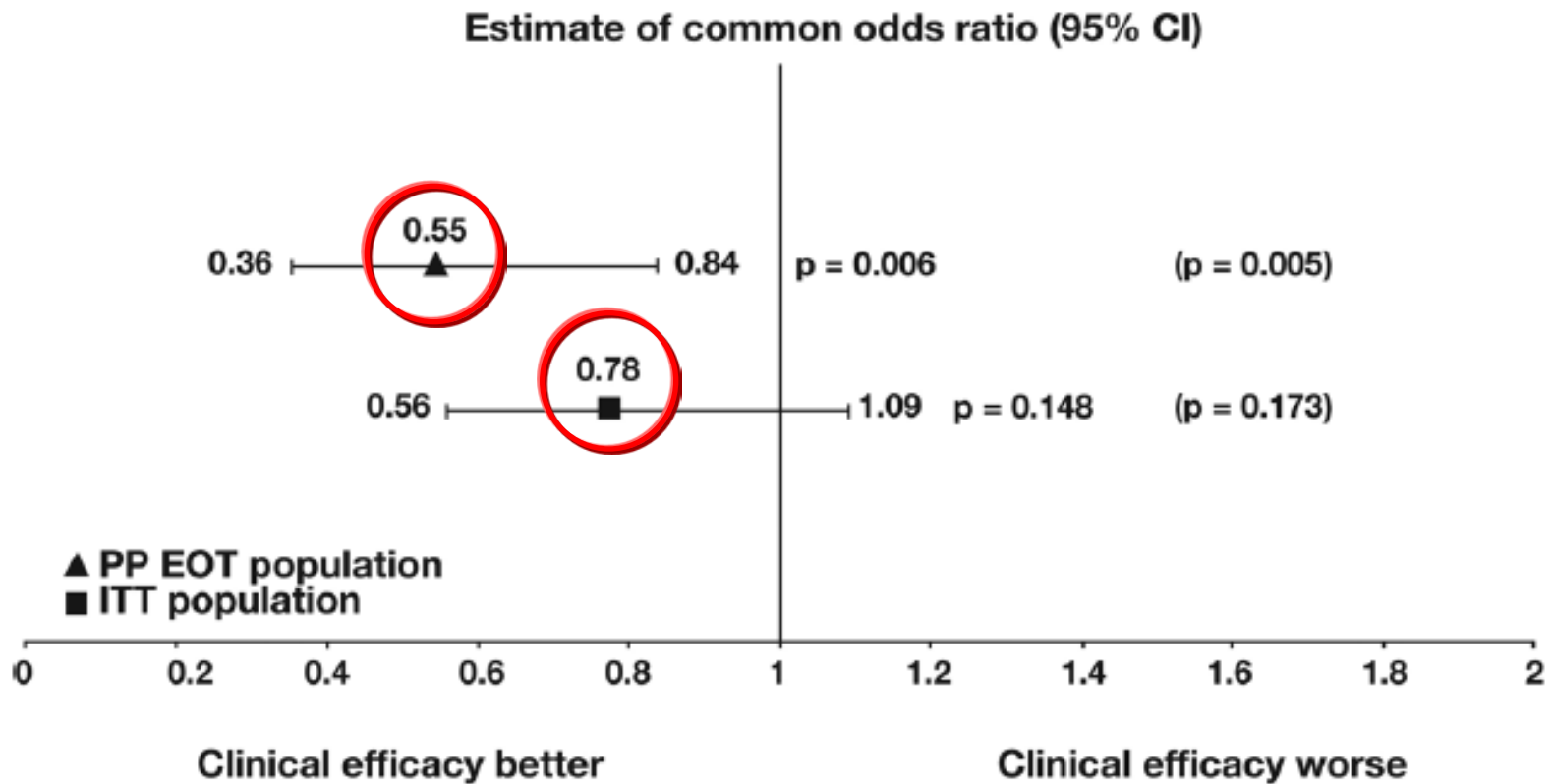
Estimate of common odds ratio (95% CI)





GEN 2010

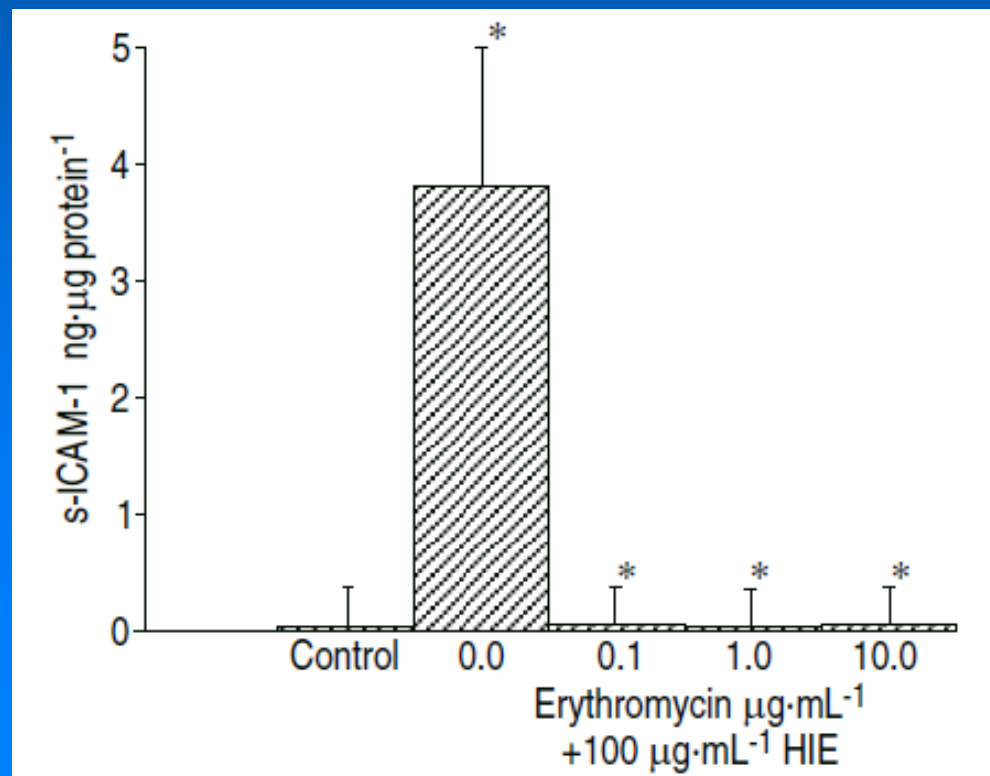
(B) Mucopurulent/purulent sputum subgroup





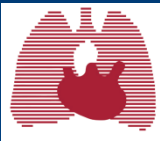
Effect of erythromycin on *Haemophilus influenzae* endotoxin-induced release of IL-6, IL-8 and sICAM-1 by cultured human bronchial epithelial cells

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



1995



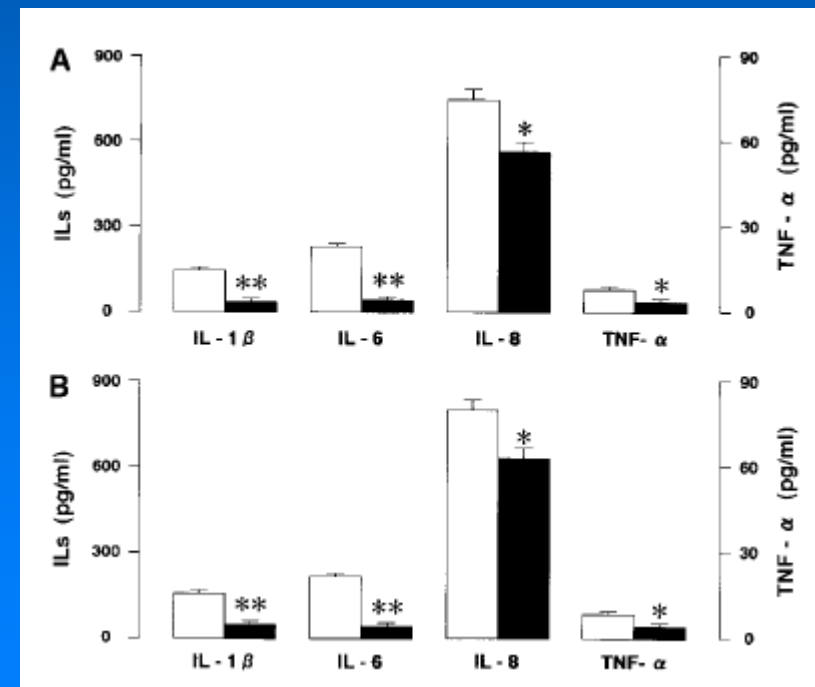
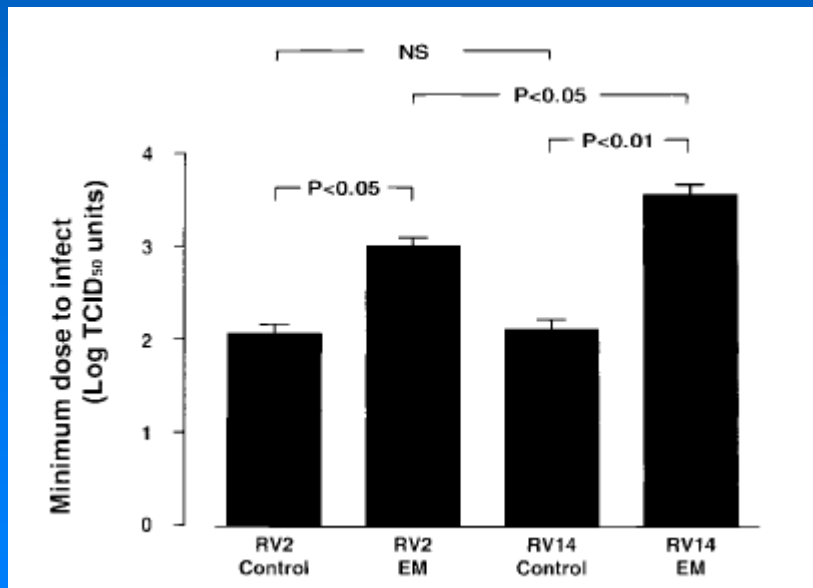


Erythromycin Inhibits Rhinovirus Infection in Cultured Human Tracheal Epithelial Cells

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



2002

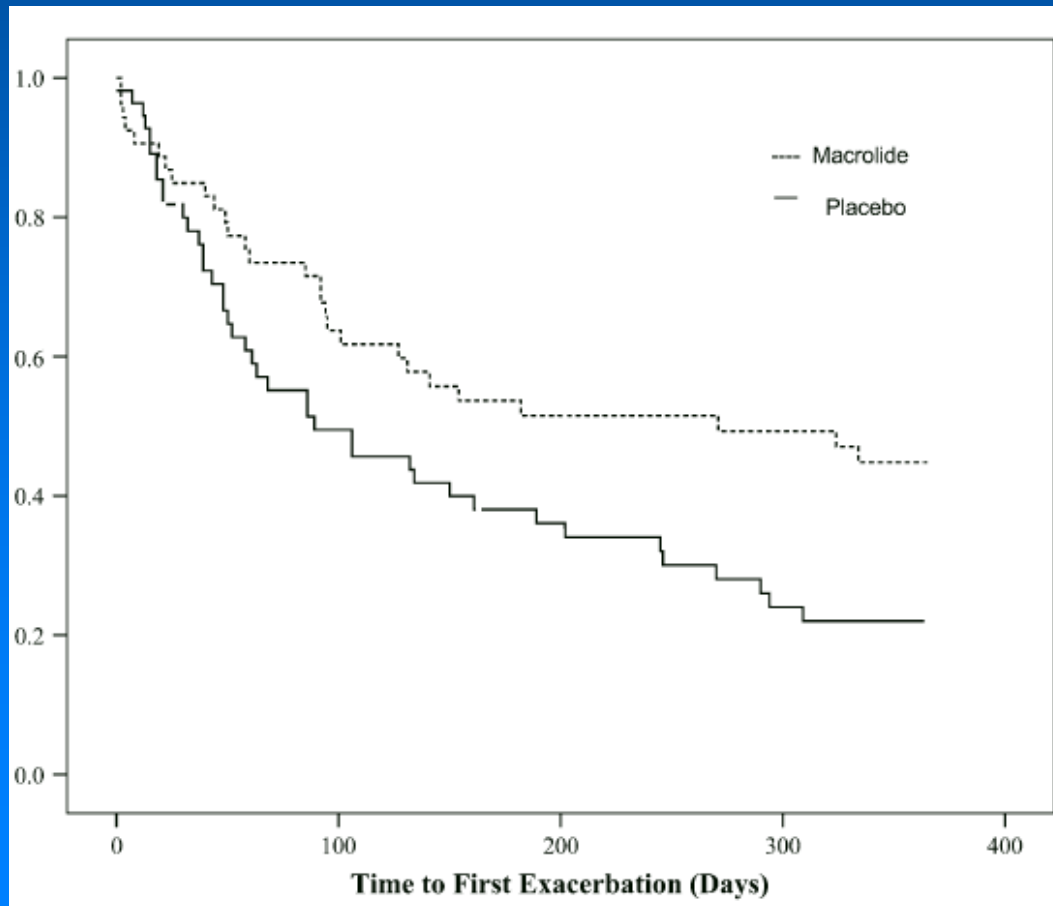


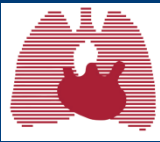


Long-term Erythromycin Therapy Is Associated with Decreased Chronic Obstructive Pulmonary Disease Exacerbations

Terence A. R. Seemungal^{1,2*}, Tom M. A. Wilkinson^{2*}, John R. Hurst², Wayomi R. Perera², Ray J. Sapsford², and Jadwiga A. Wedzicha²

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 N¹](#), [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^{1,2}](#), [Greg Hodge^{1,2}](#), [Hubertus Jersmann^{1,2}](#), [Geoffrey Matthews¹](#), [Jessica Ahern¹](#), [Mark Holmes^{1,2}](#), and [Paul N. Reynolds^{1,2}](#)



Azithromycin Maintains Airway Epithelial Integrity during *Pseudomonas aeruginosa* Infection

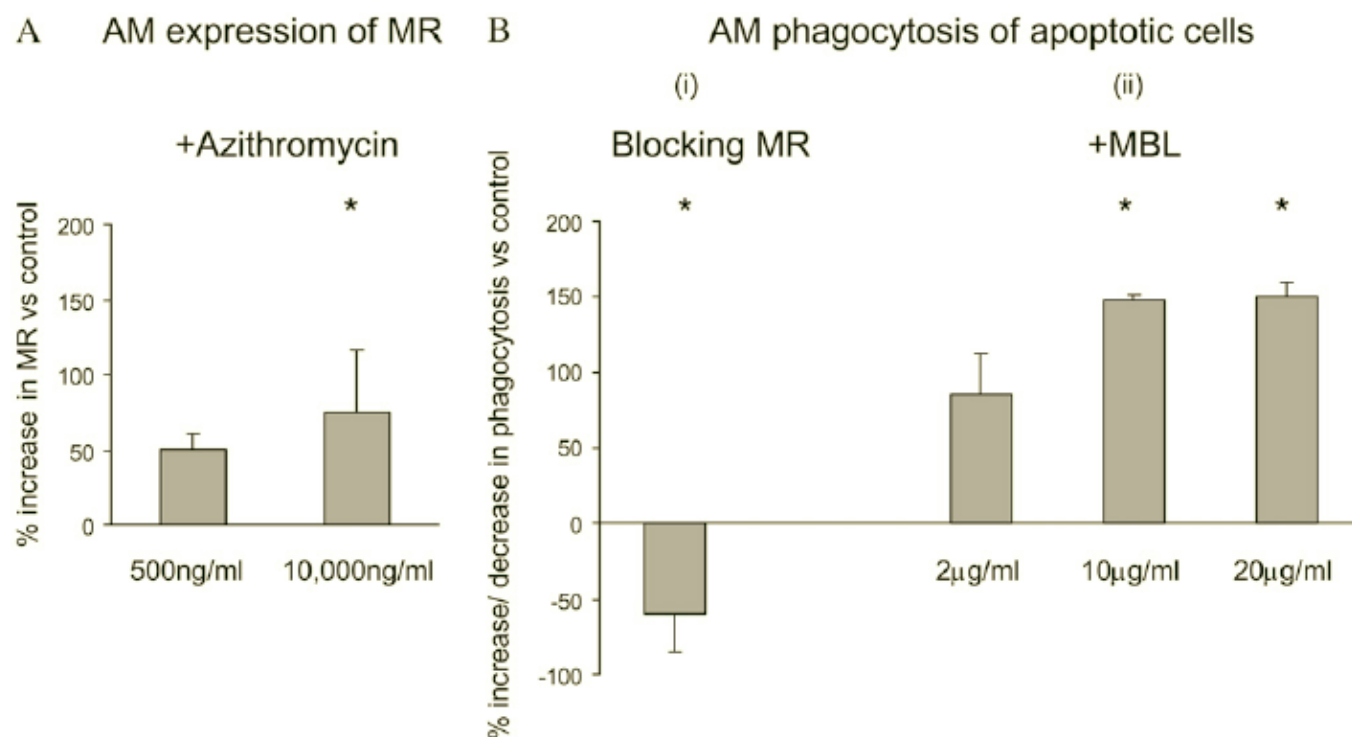
[Skarphedinn Halldorsson^{1,2}](#), [Thorarinn Gudjonsson^{2,3,4}](#), [Magnus Gottfredsson^{5,6}](#), [Pradeep K. Singh⁷](#), [Gudmundur Hrafn Gudmundsson^{1,2}](#), and [Olafur Baldursson^{2,8,9}](#)



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Sandra Hodge^{1,2}, Greg Hodge^{1,2}, Hubertus Jersmann^{1,2}, Geoffrey Matthews¹, Jessica Ahern¹, Mark Holmes^{1,2}, and Paul N. Reynolds^{1,2}

LUG 2008



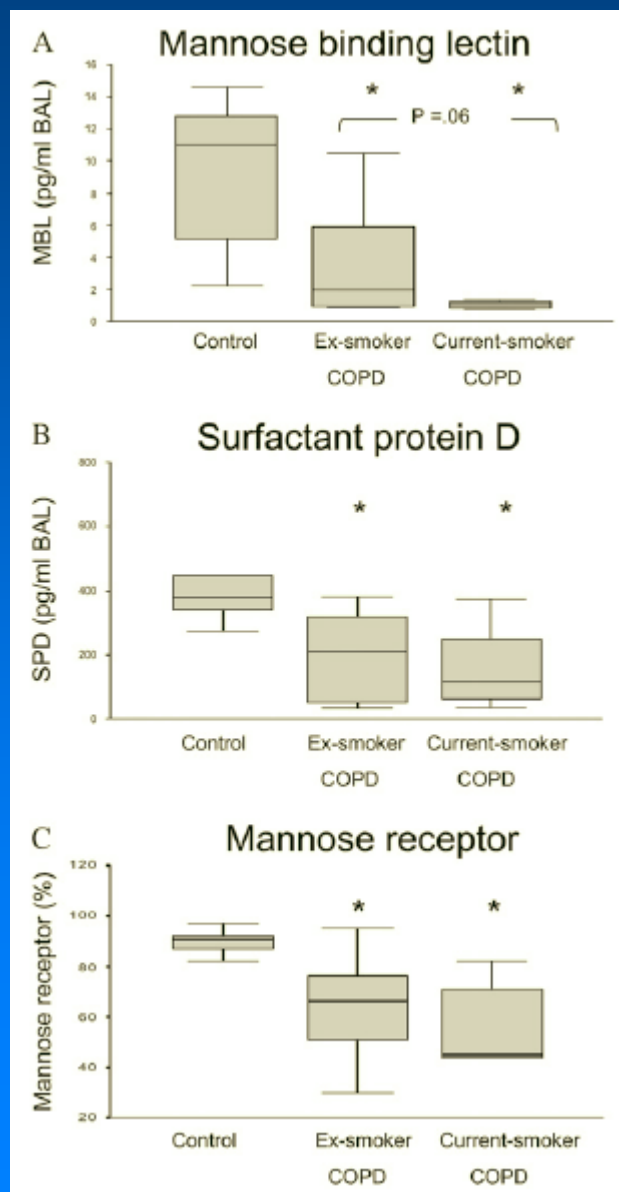


Azithromycin Improves Macrophage Phagocytic Function and Expression of Mannose Receptor in Chronic Obstructive Pulmonary Disease

Sandra Hodge^{1,2}, Greg Hodge^{1,2}, Hubertus Jersmann^{1,2}, Geoffrey Matthews¹, Jessica Ahern¹, Mark Holmes^{1,2}, and Paul N. Reynolds^{1,2}



LUG 2008

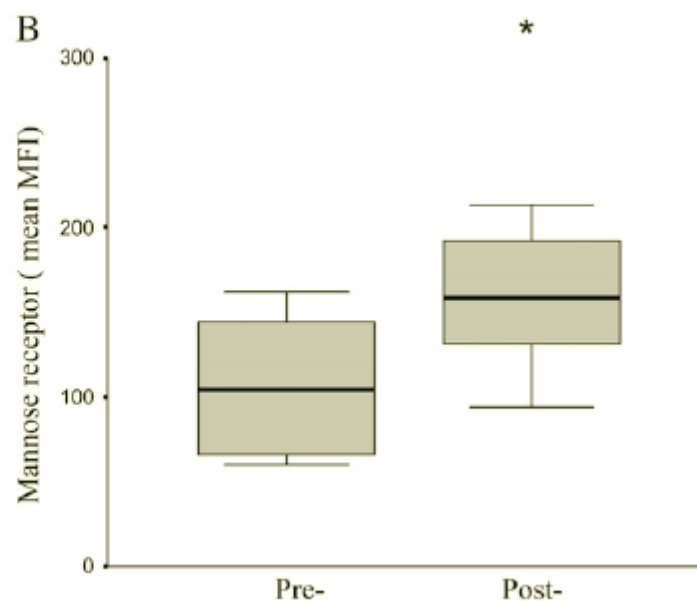
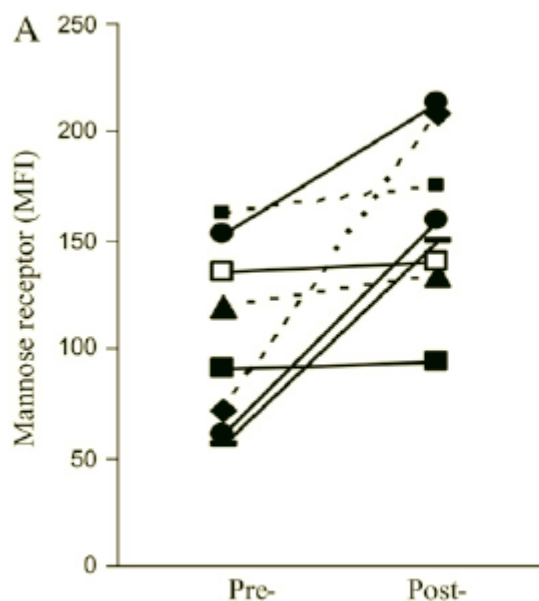




Azithromycin Improves Macrophage Phagocytic Function and Expression of Mannose Receptor in Chronic Obstructive Pulmonary Disease

Sandra Hodge^{1,2}, Greg Hodge^{1,2}, Hubertus Jersmann^{1,2}, Geoffrey Matthews¹, Jessica Ahern¹, Mark Holmes^{1,2}, and Paul N. Reynolds^{1,2}

LUG 2008

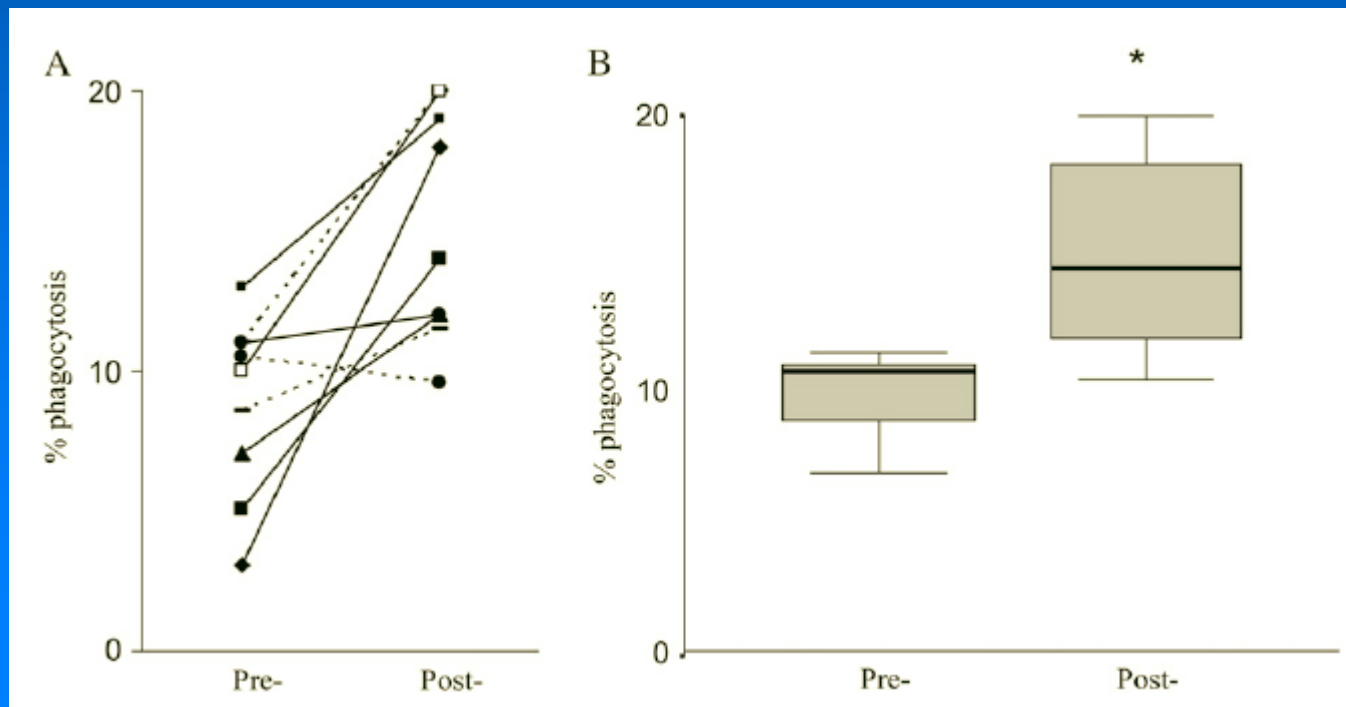




Azithromycin Improves Macrophage Phagocytic Function and Expression of Mannose Receptor in Chronic Obstructive Pulmonary Disease

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LUG 2008

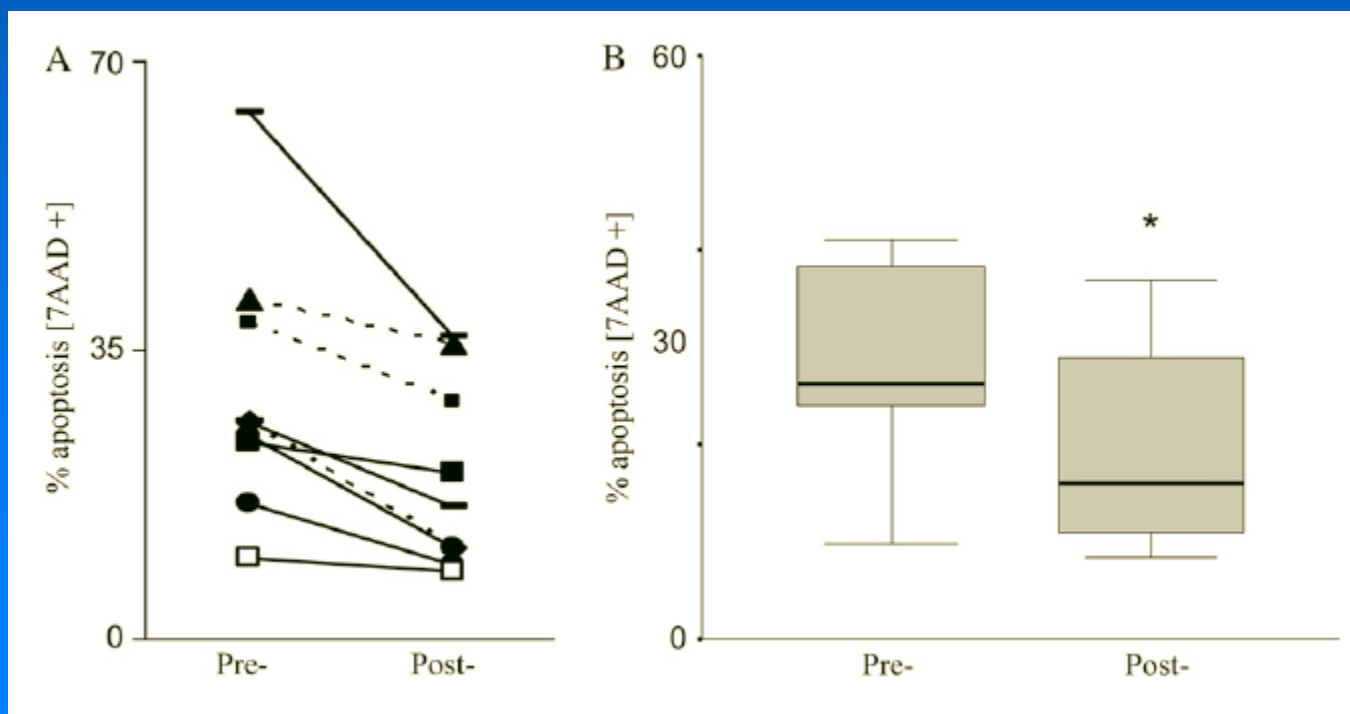




Azithromycin Improves Macrophage Phagocytic Function and Expression of Mannose Receptor in Chronic Obstructive Pulmonary Disease

Sandra Hodge^{1,2}, Greg Hodge^{1,2}, Hubertus Jersmann^{1,2}, Geoffrey Matthews¹, Jessica Ahern¹, Mark Holmes^{1,2}, and Paul N. Reynolds^{1,2}

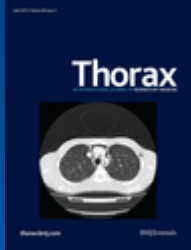
LUG 2008



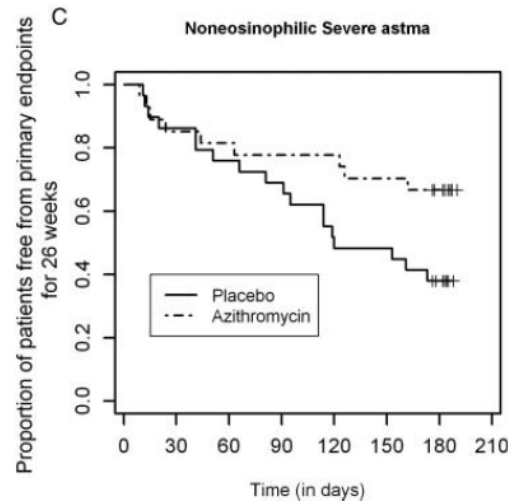
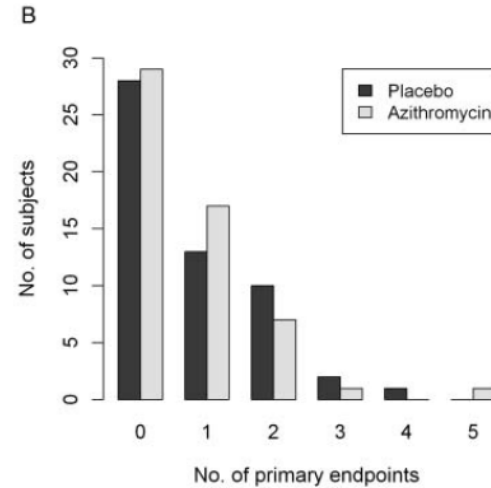
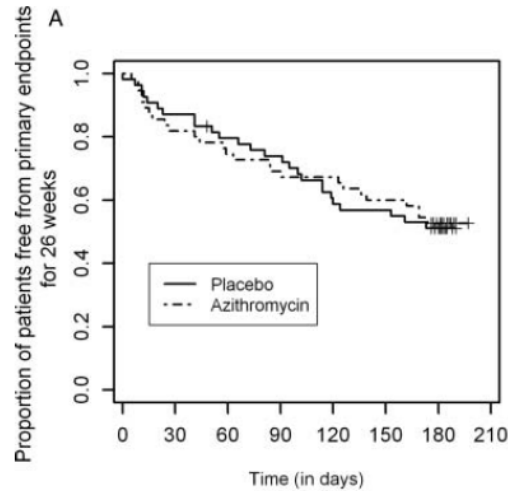


Azithromycin for prevention of exacerbations in severe asthma (AZISAST): a multicentre randomised double-blind placebo-controlled trial

Guy G Brusselle,¹ Christine VanderStichele,¹ Paul Jordens,² René Deman,³ Hans Slabbynck,⁴ Veerle Ringoet,⁵ Geert Verleden,⁶ Ingel K Demedts,⁷ Katia Verhamme,⁸ Anja Delporte,¹ Bénédicte Demeyere,¹ Geert Claeys,⁹ Jerina Boelens,⁹ Elizaveta Padalko,⁹ Johny Verschakelen,¹⁰ Georges Van Maele,¹¹ Ellen Deschepper,¹¹ Guy F P Joos¹



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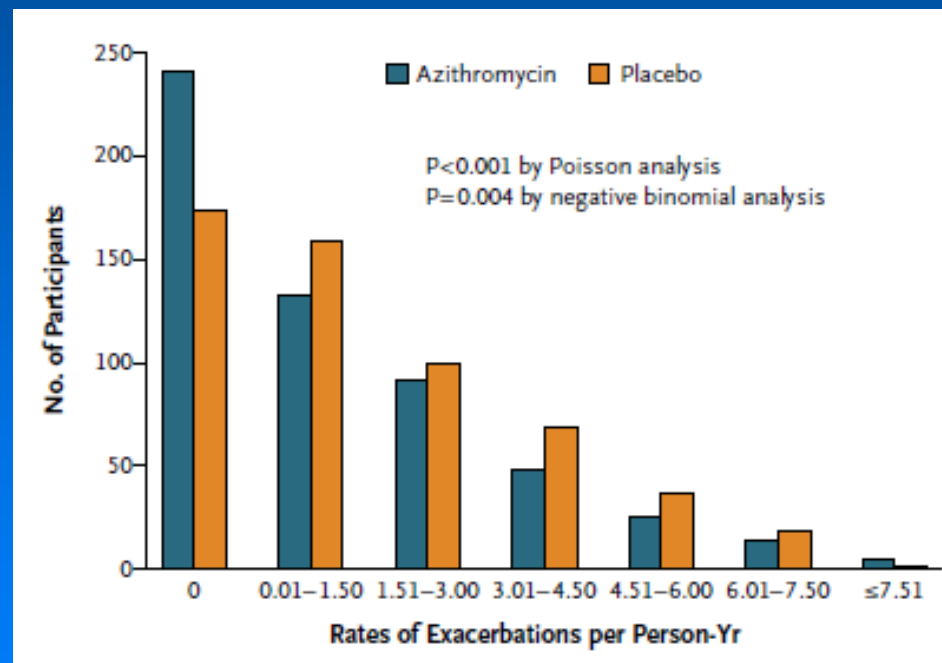
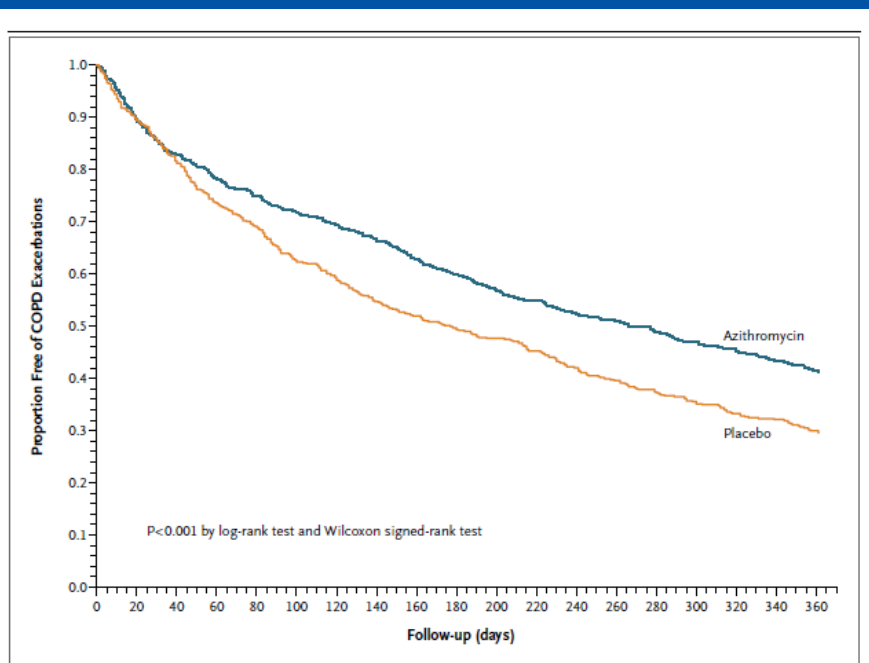
ESTABLISHED IN 1812

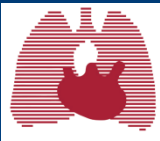
AUGUST 25, 2011

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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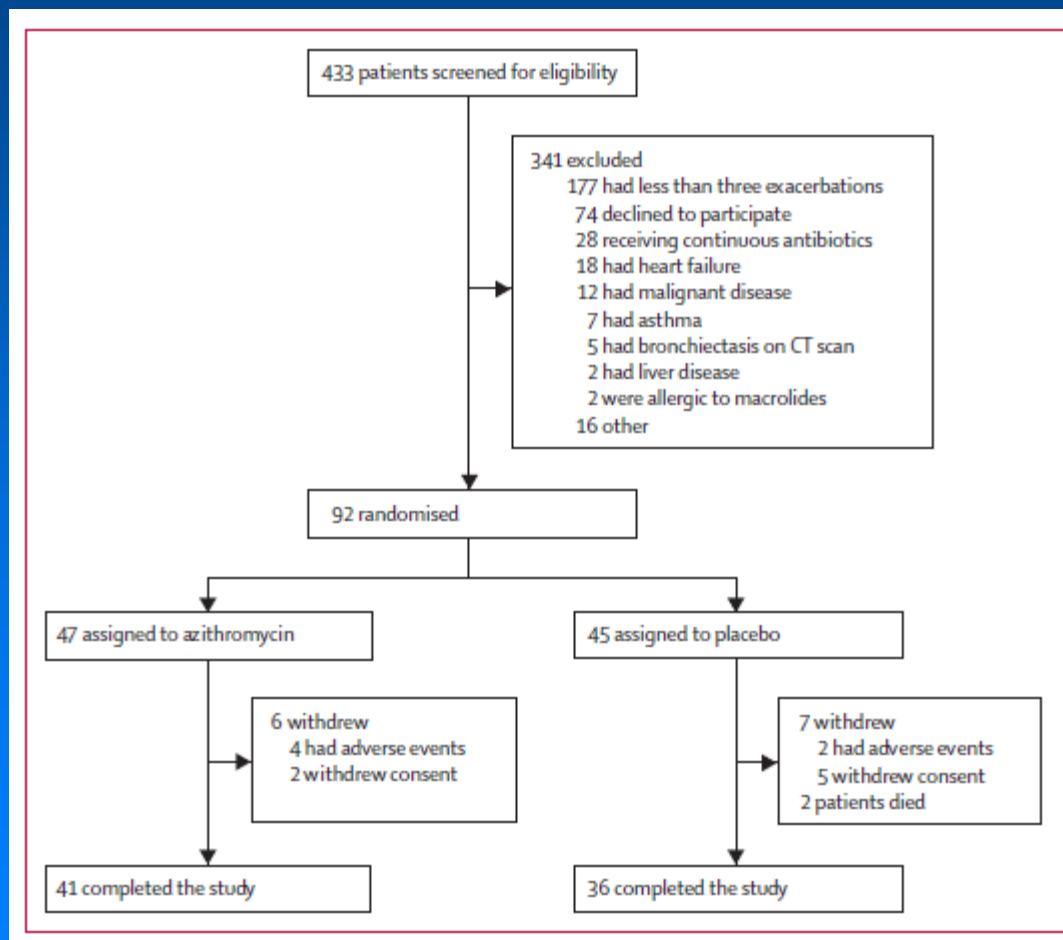
THE LANCET Respiratory Medicine

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**

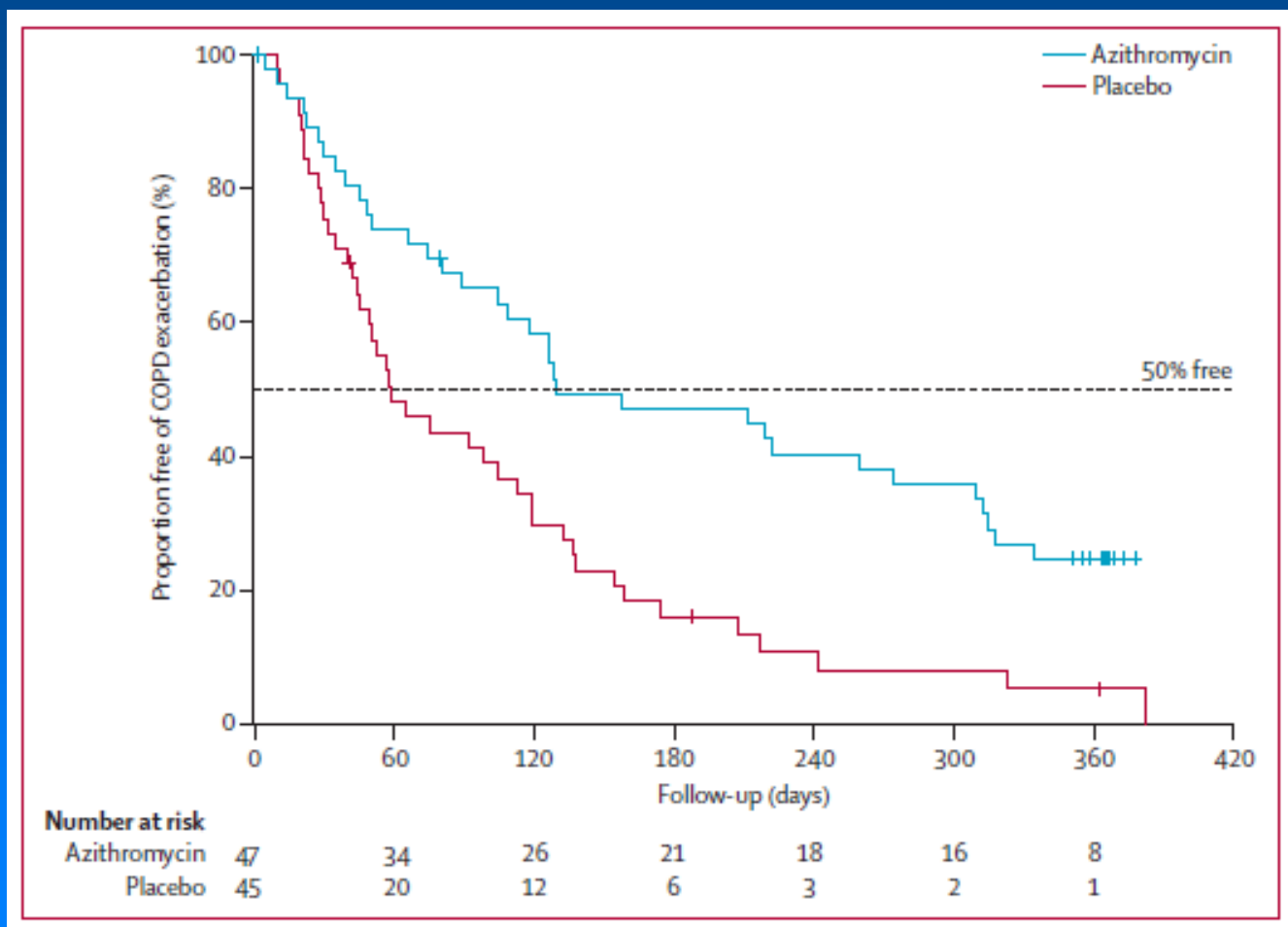


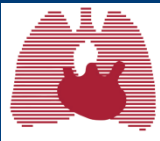
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Epidemiologia, fattori di rischio e gestione del paziente

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U.F. PNEUMOLOGIA E
RIABILITAZIONE RESPIRATORIA
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