



**CLINICA
MALATTIE
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<http://pneumologia.unimo.it>

Treatment of COPD and its comorbidities

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**Riunione Linee Guida
ARIA, GINA, GOLD
8-10 Marzo 2007
Ferrara**



**Aula Magna
Università
degli Studi di
Ferrara**



University of Modena
& Reggio Emilia, Italy



CHRONIC DISEASE IN THE ELDERLY: Back to the Future of Internal Medicine

Two or more chronic diseases almost invariably develop together in the same patient, particularly in the elderly, often making it difficult to establish a proper diagnosis and assessment of severity

Patient-oriented approach that takes into account the several coexisting components of chronic disease is required

This “change of concept” implies the need for medical specialists to extend their expertise to broader diagnostic and treatment approaches that are traditionally the purview of internal medicine



European Respiratory
Society

European Respiratory Society

ERS Research Seminar

“Complexity of patients with multiple chronic diseases”

Rome, Italy

February 10-11, 2007

www.ersnet.org

www.ersnet.org/learning_resources_player/paper/RS/RS-Rome.htm



European Respiratory
Society

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Saturday, 10 February 2007

08:30-08:45	Introduction	L. Fabbri (Italy) & K. Rabe (The Netherlands)
	Session I: The components of chronic disease: focus on COPD <u>Co-Chairs:</u> W. MacNee (UK) and R. Ferrari (Italy)	
08:45-09:15	Overview of smoking-related disease	D. Mannino (USA)
09:15-09:45	Systemic effects of smoking	W. MacNee (United Kingdom)
10:15-10:45	COPD coronary/peripheral vascular disease	G. Mancini (Canada)
10:45-11:15	COPD and CHF	F. H. Rutten (The Netherlands)
11:15-11:45	COPD and Cancer	S. Spiro (United Kingdom)
11:45-12:15	Sleep disorders in COPD and complex chronic comorbidities	W. McNicholas (Ireland)
12:15-13:00	Discussion	
	Session II : Chronic inflammation: The link between the different components of chronic disease <u>Co-Chairs:</u> P. Barnes (UK) and F. Crea (Italy)	
14:00-14:30	The role of inflammation in diabetes and obesity	M. Porta (Italy)
14:30-15:00	The role of inflammation in myocardial infarction	F. Crea (Italy)
15:00-15:30	The role of inflammation in chronic heart failure	P. Poole-Wilson (United Kingdom)
16:00-16:30	The role of inflammation in cachexia	P. Wagner (USA)
16:30-17:00	The role of inflammation in COPD	R. Djukanovic (UK)
17:00-17:30	Discussion	



Sunday, 11 February 2007

Session II : Chronic inflammation: The link between the different components of chronic disease (part II)

Co-Chairs: J. Drazen (USA) and LM Fabbri (I)

08:30-09:00	Osteoporosis and inflammation	N.A. Hamdy (NL)
09:00-09:30	Hypertension and inflammation	E.L. Schiffrin (Canada)
09:30-10:00	Chronic inflammatory gastrointestinal diseases	F. Pallone (Italy)
10:00-10:30	Mechanisms of exacerbation of respiratory symptoms in patients with metabolic syndrome	B. Müller (Switzerland)

Session III : Treatment of Chronic diseases

Co-Chairs: C. Page (United Kingdom) and K. Rabe (The Netherlands)

11:00-11:30	Treatment strategies for patients with complex chronic comorbidities	J. M. Drazen (USA)
11:30-12:00	Role of anti-inflammatory treatments in complex chronic comorbidities	C. Page (UK)
12:00-12:30	Development of new treatments for complex chronic comorbidities	P. J. Barnes (UK)
12:30-13:00	Discussion	

Session IV : Exacerbation of respiratory symptoms in chronic diseases

Co-Chairs: P. Calverley (UK) and L. Fabbri (I)

14:00-14:30	Mechanisms of exacerbation of respiratory symptoms in patients with COPD	A. Anzueto (USA)
14:30-15:00	Mechanisms of exacerbation of respiratory symptoms in patients with CHF	P. Calverley (UK)
15:00-15:30	Discussion	
15:30	Conclusions	L. Fabbri & K. Rabe

THE NATURAL HISTORY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE:

Mapel DW. Comorbidities of COPD

Comorbid conditions are increased in COPD

Comorbidities increase annual costs

Comorbidities predictors of mortality

Mannino et al, Eur Respir J 2006; 27 (March):635



MECHANISM OF SYMPTOM PRODUCTION

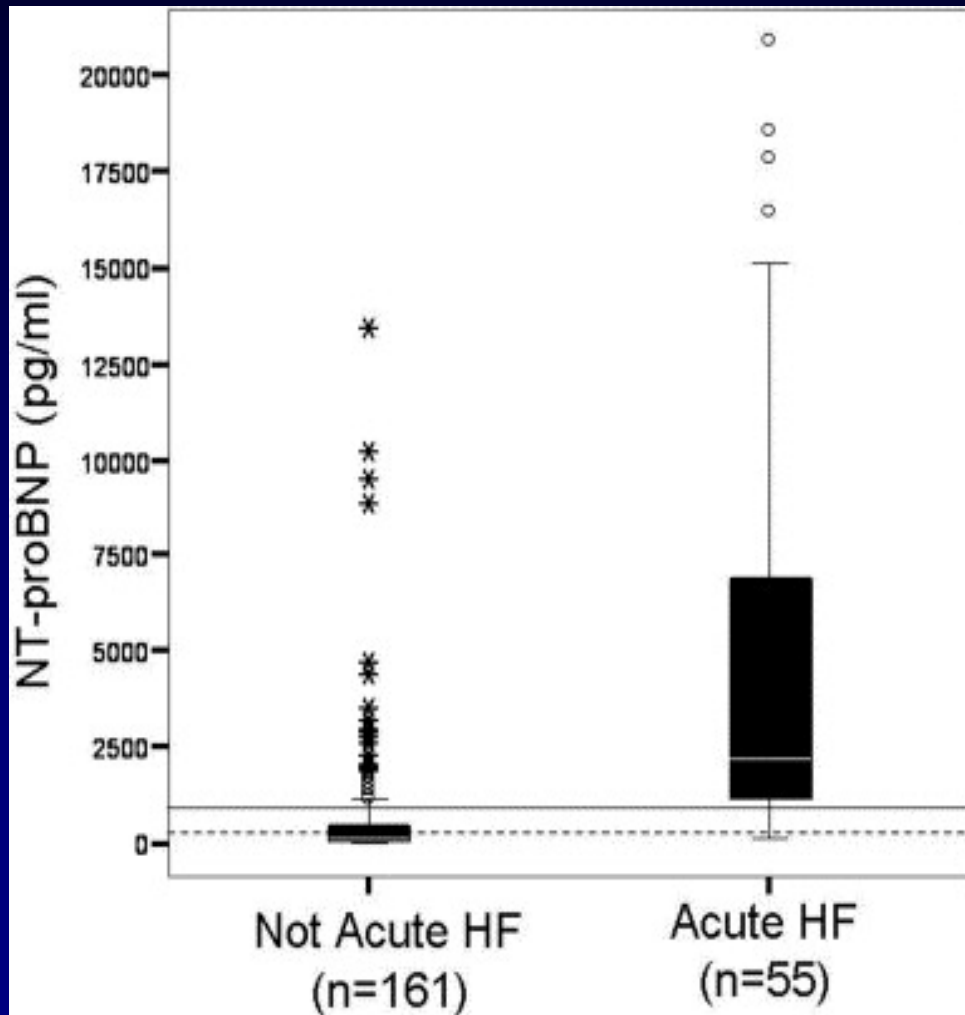
- **Cough:** little direct data; predominantly unproductive. Likely C fibre stimulation secondary to airways oedema plus change in peripheral vs central lung mechanics with loss of cough inhibition. Perhaps direct fluid accumulation but no information on this
- **Sputum production:** only an issue with alveolar flooding
- **Wheeze:** cardiac asthma secondary to airway wall oedema
- **Fatigue:** poorly understood but probably important and related to low cardiac output.
- **Dyspnoea:** altered lung mechanics and increased respiratory drive – low cardiac output + increased J receptor stimulation

Courtesy of PMA Calverley



CHF AND COPD IN THE ED

Courtesy of PMA Calverley



- Secondary analysis of the PRIDE study
- Confined to individuals with diagnosis of airways disease
- Confirms value of BNP testing

PULMONARY EMBOLISM IN PATIENTS WITH UNEXPLAINED EXACERBATION OF COPD

Courtesy of PMA Calverley

25% pulmonary embolism in patients with COPD hospitalized for severe exacerbation of unknown origin

Previous TEP, malignancy, low PaCO₂

Tillie-Leblond et al, Ann Intern Med. 2006;144:390-396.

Therapy at Each Stage of COPD

I: Mild

II: Moderate

III: Severe

IV: Very Severe

- $FEV_1/FVC < 70\%$
- $FEV_1 \geq 80\%$ predicted

- $FEV_1/FVC < 70\%$
- $50\% \leq FEV_1 < 80\%$ predicted

- $FEV_1/FVC < 70\%$
- $30\% \leq FEV_1 < 50\%$ predicted

- $FEV_1/FVC < 70\%$
- $FEV_1 < 30\%$ predicted or $FEV_1 < 50\%$ predicted plus chronic respiratory failure

Active reduction of risk factor(s); influenza vaccination

Add short-acting bronchodilator (when needed)

Add regular treatment with one or more long-acting bronchodilators (when needed); **Add** rehabilitation

Add inhaled glucocorticosteroids if repeated exacerbations

Add long term oxygen if chronic respiratory failure. **Consider** surgical treatments

Courtesy of K.F.Rabe, 2007



Pulmonary rehabilitation in chronic obstructive pulmonary disease

Today the question is no longer "should patients with chronic obstructive lung disease receive pulmonary rehabilitation?" but rather "how should pulmonary rehabilitation be delivered to patients with COPD?"

"which components form the basis of the success of pulmonary rehabilitation programs?"

The review focuses the physiological rationale for exercise training, the potential of the multidisciplinary approach during rehabilitation programs

THE IMPACT OF SMOKING CESSATION ON RESPIRATORY SYMPTOMS, LUNG FUNCTION, AIRWAY HYPERRESPONSIVENESS AND INFLAMMATION

**Smoking cessation reduces symptoms and improves the
accelerated decline in FEV1**

**which strongly indicates that important inflammatory
and/or remodelling processes should be positively affected**

**Data from well-designed studies are lacking regarding the effects
on inflammation and remodelling**

**In COPD, a few histopathological studies suggest
that airway inflammation persists in exsmokers**

Willemse et al, ERJ 2004; 23:464-76

The Effects of a Smoking Cessation Intervention on 14.5-Year Mortality

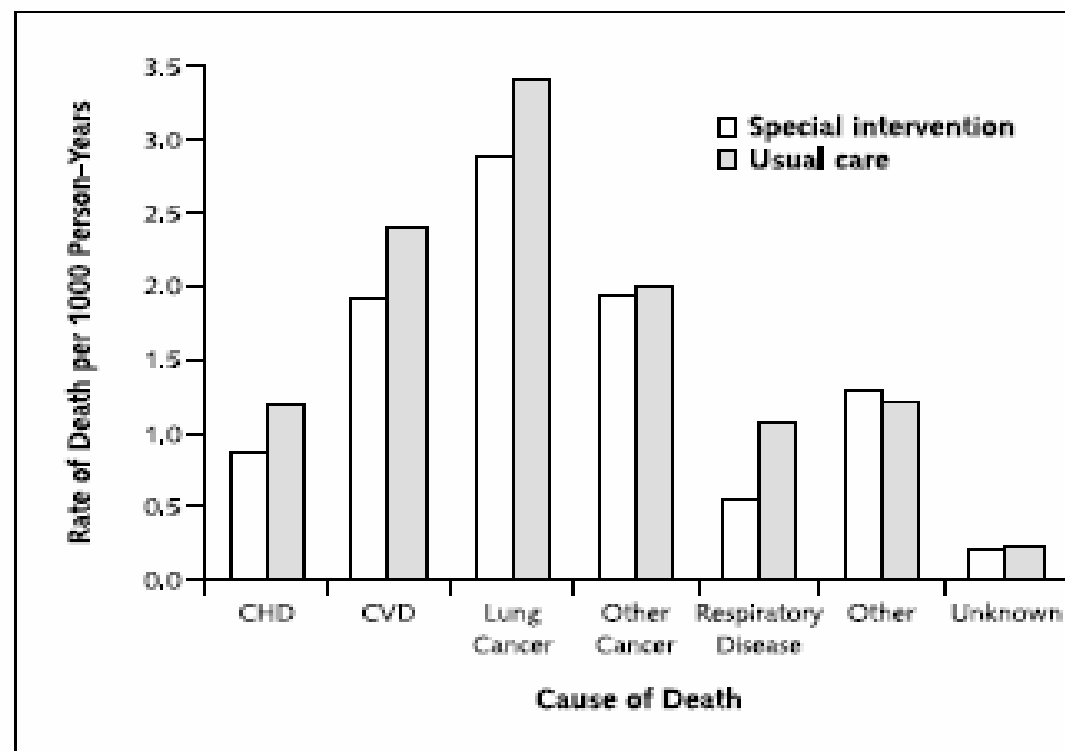
A Randomized Clinical Trial

Nicholas R. Anthonisen, MD; Melissa A. Skeans, MS; Robert A. Wise, MD; Jure Manfreda, MD; Richard E. Kanner, MD; and John E. Connett, PhD, for the Lung Health Study Research Group*

Ann Intern Med. 2005;142:233-239.

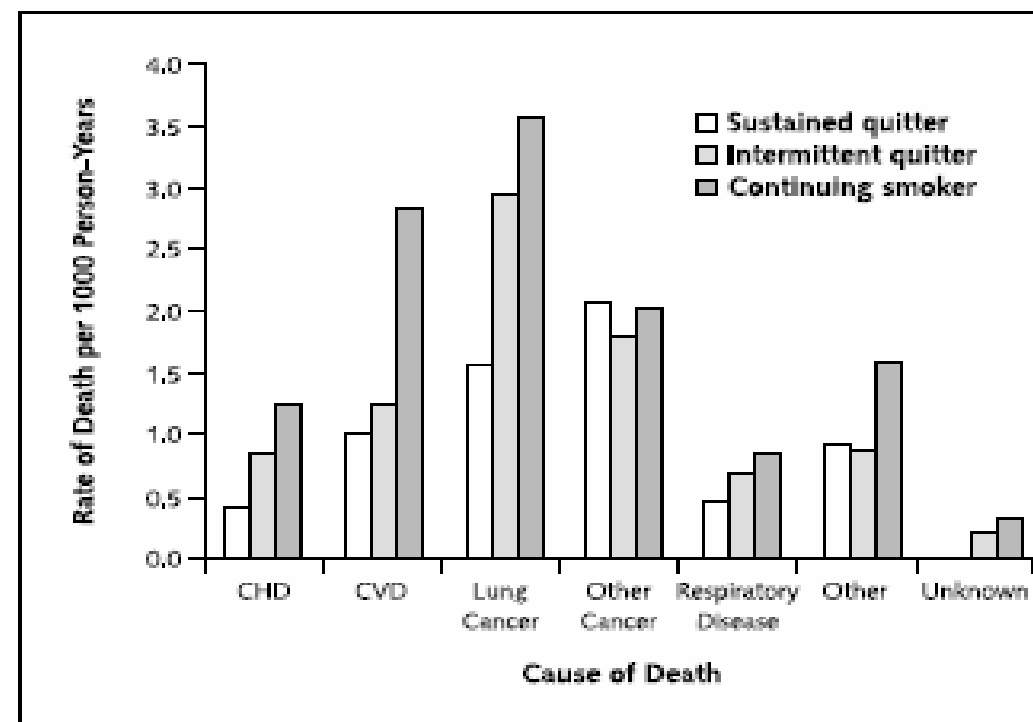
Conclusion: Smoking cessation intervention programs can have a substantial effect on subsequent mortality, even when successful in a minority of participants.

Figure 2. Mortality rates at 14.5 years by cause.



The only significant difference was in respiratory disease other than lung cancer (log-rank test). CHD = coronary heart disease; CVD = cardiovascular disease.

Figure 3. Mortality rates at 14.5 years by cause and smoking status.



Rates were significantly different for coronary heart disease (CHD), cardiovascular disease (CVD), lung cancer, and other causes of death (log-rank test).

The TORCH (TOWards a Revolution in COPD Health) survival study protocol

	Total patients followed up for 3 years
Salmeterol/Fluticasone 50/500bd	1,500
Fluticasone 500bd	1,500
Placebo	1,500
Salmeterol 50 bd	1,500

Duration = 3 years

6,000 patients

Results by May 2006

Therapeutic implications (Rutten FH et al Eur J Heart Fail 2006;8:706-11)

‘drug cocktails’ for CHF treatment can be prescribed without restriction to patients with concomitant COPD

diuretics (high dosages acid-base disturbances)

ACE-inhibitors or Angiotensin II blockers

=> **beta-blockers (cardioselective)** (Salpeter SR et al Ann Intern Med 2002;137:715-25)

aldosterone antagonists

digoxin (may cause pulmonary vasoconstriction)

more caution with ‘pulmonary drug cocktails’ in patients with CHF

Anticholinergics no adverse effects

=> **short-acting / oral beta2-agonist increase mortality**

long-acting beta2-agonist at least less deleterious

REDUCTION OF MORBIDITY AND MORTALITY BY STATINS, ANGIOTENSIN-CONVERTING ENZYME INHIBITORS, AND ANGIOTENSIN RECEPTOR BLOCKERS IN PATIENTS WITH CHRONIC OBSTRUCTIVE PULMONARY DISEASE

These agents may have dual cardiopulmonary protective properties, thereby substantially altering prognosis of patients with COPD. These findings need confirmation in randomized clinical trials

Statin use is associated with reduced mortality in COPD

Treatment with statins was associated with improved survival after chronic obstructive pulmonary disease exacerbation, while inhaled corticosteroids appeared to increase the survival benefit associated with statin use

TREATMENT OPTIONS IN COPD

Barnes and Stockley, Eur Respir J 2005; 25(6):1084-1106

CURRENT OPTIONS

Smoking cessation

Short and long acting beta2-agonists/ anticholinergics

Inhaled corticosteroids, Theophylline

Rehabilitation/Oxygen/Surgery

FUTURE OPTIONS

New antismoking agents

Phosphodiesterase IV inhibitors

Better corticosteroids and bronchodilators/combination

FUTURISTIC OPTIONS

New antismoking agents

Targeted antiinflammatory agents

Antioxidants/mucolytic

Antiprotease/Lung regeneration

Clinical practice guidelines (CPGs) and quality of care for older patients with multiple comorbid diseases: implications for pay for performance

- **This review suggests that adhering to current CPGs in caring for an older person with several comorbidities may have undesirable effects**
- **Basing standards on existing CPGs could lead to inappropriate judgment of the care provided to older individuals with complex comorbidities**
- **Developing measures of the quality of the care needed by older patients with complex comorbidities is critical to improving their care**

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